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DISCOVERY OF NOVEL BACTERIAL DNA GYRASE INHIBITORS

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by

Eddy E. Alfonso Maqueira

2023

To: Dean Michael R. Heithaus
College of Arts, Sciences and Education

This dissertation, written by Eddy E. Alfonso Maqueira, and entitled Discovery of Novel Bacterial DNA Gyrase Inhibitors, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

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DEDICATION

I dedicate this dissertation to Monica and my parents for their constant love and support.

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ABSTRACT OF THE DISSERTATION

DISCOVERY OF NOVEL BACTERIAL DNA GYRASE INHIBITORS

by

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Bacterial DNA gyrase is a type IIA DNA topoisomerase. Due to its essential role in DNA replication and transcription, this enzyme is a validated target for discovering and developing new antibiotics. DNA gyrase is the target of fluoroquinolones (FQs), one of the most effective and prescribed antibiotics in the world. However, the emergence of resistant bacterial strains to FQs and other antibiotics in the last decades has stimulated the search for non-FQ gyrase inhibitors with antimicrobial activities. Based on a supercoiling-dependent fluorescence quenching (SDFQ) method, a high-throughput screening (HTS) assay to identify inhibitors targeting bacterial DNA gyrase has been established. After screening the National Institutes of Health's Molecular Libraries Small Molecule Repository library containing 370,620 compounds using this SDFQ HTS method, 2891 new gyrase inhibitors were discovered. Subsequently, 235 compounds were acquired to analyze their inhibition activities against bacterial DNA gyrase using gel- and SDFQ-based DNA gyrase inhibition assays, in which 155 new bacterial DNA gyrase inhibitors with a wide structural diversity were identified. Several of them have potent antibacterial

activities. These newly discovered gyrase inhibitors include several DNA gyrase poisons that stabilize the gyrase-DNA cleavage complexes and provide new chemical scaffolds for the design and synthesis of bacterial DNA gyrase inhibitors that may be used to combat multidrug-resistant bacterial pathogens.

In a second effort to discover novel bacterial DNA gyrase inhibitors, a pool of naturally occurred polyphenols was screened. It was discovered that digallic acid and several food additives based on gallic acid, such as dodecyl gallate, are potent DNA gyrase inhibitors. Interestingly, the IC_{50} of these gallate derivatives against DNA gyrase is correlated with the length of the hydrocarbon chain connected to gallic acid. These new bacterial DNA gyrase inhibitors are ATP-competitive inhibitors of DNA gyrase. It was found that digallic acid and gallate derivatives also potently inhibit *E. coli* DNA topoisomerase IV. Furthermore, it was demonstrated that several gallate derivatives have strong antimicrobial activities against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA). This study provides a solid foundation for the design and synthesis of gallate-based DNA gyrase inhibitors that may be used to combat antibacterial resistance.

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SUPPLEMENTARY INFORMATION

ACRONYMS

°C	Degree Celsius
µL	Microliter
µM	Micromolar
ADPN	Adenosine 5′- (β, γ-imido) triphosphate
ATCC	American type culture collection
ATP	Adenosine triphosphate
bp	Base pair
BSA	Bovine serum albumin
CFX	Ciprofloxacin
CPD	Compound
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
DSB	Double strand breaks
DTT	Dithiothreitol
EDTA	Ethylenediaminetetraacetic acid
FDB	Fragment-based design
FQs	Fluoroquinolones
gyr	Bacterial DNA gyrase
gyrA	Subunit A of bacterial DNA gyrase
gyrB	Subunit B of bacterial DNA gyrase
HCL	Hydrochloric acid

HTS	High throughput screening
IC_{50}	Half maximal inhibitory concentration
IPYs	Imidazopyrazinones
Kac	Potassium acetate
KCl	Potassium chloride
kDa	Kilodalton
kDNA	Kinetoplast DNA
K_i	Inhibitor constant
K_M	Michaelis constant
M	Molar
MDs	Molecular dynamics
mg	Milligram
$MgCl_2$	Magnesium chloride
MHIIB	Müller-Hinton II broth
MIC	Minimum inhibitory concentration
mL	Milliliter
MLSM	Molecular libraries small molecule repository
mM	Millimolar
MoA	Mechanism of action
MRSA	Methicillin-resistant Staphylococcus aureus
MW	Molecular weight
NADH	Nicotinamide adenine dinucleotide $(NAD)^{+}$ hydrogen)

NBTIs	Novel bacterial type II topoisomerase inhibitors
ng	Nanogram
nm	Nanometer
nM	Nanomolar
NMR	Nuclear magnetic resonance
PAINS	Pan-assay interference compounds
QRDR	Quinolone resistance-determining region
QZs	Quinazolinediones
Rx	Relaxed
SAR	Structure activity relationship
Sc	Supercoiled
SD8	Symocyclinone SD8
SDFQ	Supercoiling-dependent fluorescence quenching
SDS	Sodium dodecyl sulfate
SGD	Structure-guided design
TAE	Tris-acetate-EDTA buffer
UV	Ultraviolet
Vmax	Maximum velocity
VMD	Visual molecular dynamics
WT	Wild type

I. BACTERIAL DNA GYRASE: STRUCTURE, FUNCTION, AND INHIBITORS

Abstract

Bacterial DNA gyrase, a type II topoisomerase that plays an essential role in important cellular processes such as DNA replication and transcription, is a validated target for antibacterial chemo-therapy. For example, fluoroquinolones, one of the most effective and prescribed antibiotics in the market, target bacterial DNA gyrase. Unfortunately, resistance to fluoroquinolones has emerged. Severe side effects are associated with the use of these antibiotics for certain patients. This leads to the search for novel compounds targeting bacterial DNA gyrase with potential to be developed into new antibiotics. In this chapter, I will briefly discuss bacterial DNA gyrase: biochemistry, structure, and more importantly as a target for discovering new antibiotics. I will also review different bacterial DNA gyrase inhibitors identified/discovered/synthesized in the last few decades from natural and synthetic sources. Additionally, I will discuss several novel high throughput screening (HTS) methods that can accelerate the discovery of new bacterial DNA gyrase inhibitors. The discovery of new inhibitors for bacterial DNA gyrase represents a promising scientific approach to address the issue of antibacterial resistance.

Antimicrobial resistance

Since their discovery, antibiotics have been one of the pillars of modern medicine. Antimicrobial therapy has allowed the treatment of deadly infections and facilitated complex medical procedures. However, the emergence of resistant bacterial strains threatens the clinical efficacy of antibiotics [1, 2], presenting a severe medical challenge for health systems worldwide [3]. According to the CDC, antibiotic-resistant pathogens cause over 2.8 million infections and 35,000 deaths annually in the US [4]. By 2050, diseases caused by antibiotic-resistant bacteria will be one of the leading causes of death globally, killing more than 10 million people annually [5].

Several factors have contributed to the rise of antimicrobial-resistant pathogens in the last two decades. Firstly, bacteria's extraordinary genetic adaptability allows them to respond to various environmental stresses, including the presence of antibiotic molecules [6]. Mechanisms such as target region mutations, reduced drug uptake, increased efflux mechanisms, chemical modification or degradation of drug molecules, and changes in metabolic pathways are used by bacteria to evade the action of antimicrobials. Additionally, bacteria can acquire resistance genes through genetic information transfer processes like transformation, conjugation, and transduction, resulting in the development of antimicrobial-resistant strains [6, 7].

Apart from natural factors responsible for the rise of resistant bacterial strains, the misuse of antibiotics has been a significant contributor to this problem. Self-medication and abusive prescription of antibiotics have played critical roles in accelerating this issue, particularly in developing countries [8, 9]. Global antibiotic consumption has risen by 65% from 2000 to 2015, and estimates indicate that worldwide antibiotic consumption will increase by 200% by 2030 compared to 2015 [10]. This trend emphasizes the importance of discovering new antimicrobial molecules that can help combat resistant pathogens.

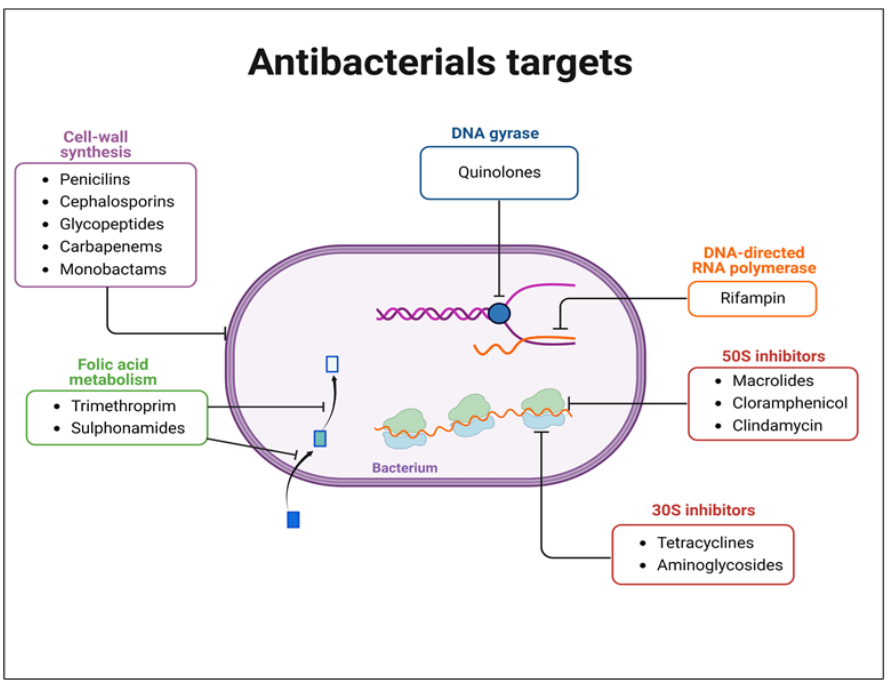


Figure 1. Types of antibiotics and their targets in bacteria: cell-wall synthesis, protein synthesis, DNA gyrase, DNA-directed RNA polymerase, and folic acid metabolic enzymes.

In addition to the factors mentioned above, a significant contributing factor to the rise of antibiotic-resistant pathogens is the lack of development of major new types of antibiotics in the last 30 years [11]. This is partly due to the low investment in antibiotic development, which comprises less than 5% of the annual budget in the pharmaceutical industry. Additionally, the high production costs of novel antibiotics, which can reach nearly 1 billion dollars, and the long development time (approximately ten years) further discourage the development of new antibiotics. The World Health Organization (WHO) has expressed concern about this issue, noting that just 1 out of 5 new antibiotics represents an innovative treatment that could help combat antimicrobial resistance [12, 13].

Our current antibiotics target key bacterial processes such as cell wall and membrane synthesis, DNA and RNA synthesis, and metabolism and protein synthesis (Figure 1). A recurring strategy to obtain new antibiotics has been introducing chemical modifications into existing drugs to improve their capabilities. For example, between 1981 and 2005, over 70% of the new antibacterials filed were derivatives of known antibiotics like penicillins, cephalosporins, quinolones, and macrolides [11]. This approach has provided new variants of the original compounds with improved pharmacological properties, as seen in the case of fluoroquinolones [14]. However, this strategy represents a short-term solution since the limited number of initial scaffolds constrains our ability to produce new antibiotics through chemical modification.

Topoisomerases as drug targets

Among the molecular targets for antimicrobial therapy, DNA topoisomerases have been one of the most exploited targets in recent decades. These enzymes are crucial in controlling the topology of DNA in cells, facilitating processes such as replication, chromosome segregation, DNA repair, and transcription (Figure 2) [15-17]. Due to their essential role in critical biological processes and their ability to introduce nicks on one or both DNA strands, topoisomerases have become important drug targets [18-20]. Topoisomerases are classified according to the strands they cleave as part of their catalytic cycle. Type I introduces nicks on one strand of DNA, while type II introduces double-strand breaks (DSB) in DNA. In both cases, the cleaved DNA remains attached to the enzyme through a phosphodiester bond formed between a well-conserved tyrosine and one or both ends of the broken strand [21].

Bacterial DNA gyrase, a type II topoisomerase, has a unique capability of introducing transient double-stranded breaks on DNA at the expense of ATP consumption [22]. This enzyme is found only in bacteria and generates negative supercoiled DNA, which is essential in removing the positive (+) supercoils that accumulate ahead of the replication fork due to the movement of this complex during DNA replication [23, 24]. Additionally, the positive supercoils that arise due to the topological tensions generated during transcription by the transcription bubble are also removed by the activity of bacterial DNA gyrase [25, 26].

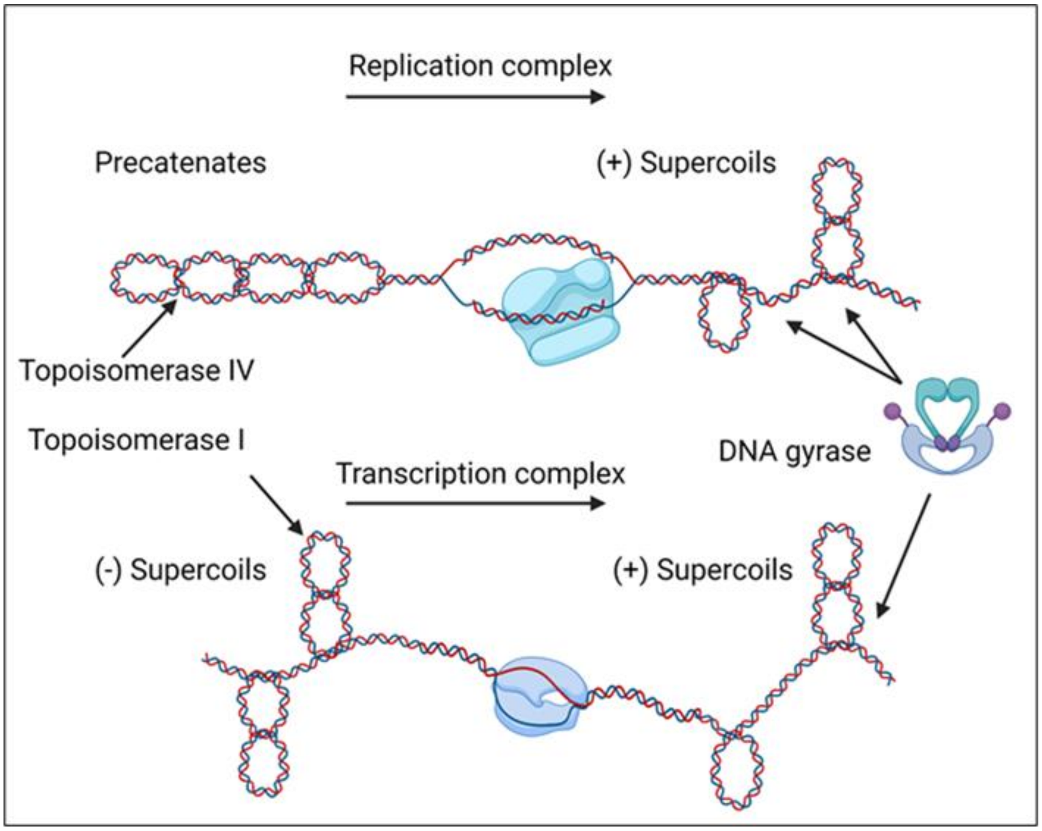


Figure 2. Reactions catalyzed by bacterial DNA gyrase and topoisomerase IV. Positive supercoils formed during DNA replication and transcription in the cell are resolved by the activity of bacterial DNA gyrase. This enzyme relaxes positive supercoils by introducing negative supercoils. Topoisomerase IV removes the catenates formed behind the replication fork, allowing the separation of daughter chromosomes. Topoisomerase IV can also remove DNA knots and positive supercoils from DNA.

The inhibition, downregulation, or mutations in the enzyme can decrease the efficiency of DNA replication and gene expression processes, eventually leading to cell death. The crucial role of bacterial DNA gyrase in coordinating these events in the cell is also reflected in morphological and physiological changes associated with a growth rate reduction in bacteria cells when the enzyme's activity is compromised [27, 28].

Deregulation of the enzymatic activity can cause an imbalance in the equilibrium between DNA cleavage and the re-ligation processes, accumulating double-strand breaks. The increment of unsolved DSB on DNA can be interpreted by cellular DNA repair systems as permanent DNA damage, activating processes such as the SOS response and non-homologous end joining (NHEJ), eventually leading to cell death [29-31]. All these factors validate the potential of bacterial DNA gyrase as a target for antimicrobial therapy [32, 33].

Topoisomerases I, III, and IV (Figure 2) are other topoisomerases found in bacteria cells [34-36]. Topoisomerase IV processes the catenates behind the replication fork generated by the topological tensions during DNA replication. This enzyme unknots the DNA and relaxes positive (+) supercoils but has a higher decatenating activity than bacterial DNA gyrase [37, 38]. The primary function of topoisomerase I is to relax the negative supercoiled DNA formed behind the transcription bubble [39, 40]. Although this enzyme represents a validated drug target, no inhibitors for topoisomerase I have been developed [41, 42]. Topoisomerase III act as a decatenase *in vivo*, unlinking replicating daughter chromosome [43]. The coordinated action of the DNA supercoiling activity of DNA gyrase and the DNA relaxing activity of topoisomerase I and topoisomerase IV maintains the topology of DNA in bacteria cells [44].

Bacterial DNA gyrase: Structure and catalytic cycle

DNA gyrase is a type II topoisomerase consisting of an A_2B_2 heterotetramer [45, 46]. The molecular weights of *E. coli* gyrase subunit A (gyrA) and B (gyrB) are

97 and 90 kDa, respectively [47, 48]. Three structurally well-defined gates are found in the enzyme: the N-gate, the DNA-gate, and the C-gate. The N-gate is located on the gyrB subunit and works as a clamp that traps DNA after ATP binding [47, 49]. The ATPase domain of the enzyme is part of the GHKL family, a protein domain present in other ATPases such as histidine kinase, HSP90, and other types II topoisomerases [50]. The DNA-gate, located on the gyrB-gyrA interface, is formed by the TOPRIM domain of gyrB and a Winged Helix Domain (WHD) domain of gyrA [51-53]. The TOPRIM (topoisomerase-primase) domain is conserved in bacterial primases like DnaG and bacterial type IA and type II topoisomerases. This domain contains two conserved aspartates (DxD) that are responsible for binding Mg^{2+} or other divalent cations necessary for the enzyme's activity. The Winged Helix Domain hosts a conserved catalytic tyrosine essential for DNA cleavage. This tyrosine performs a nucleophilic attack over a phosphate in the backbone of DNA and remains attached to the newly generated DNA break [52, 54, 55]. The C-gate is located in the gyrA subunit of the enzyme, securing the stability of the dimer. The trapping, cleavage, re-ligation, and release of the DNA require an elegantly coordinated opening and closing of N-, DNA-, and C-gates.

The DNA- and C-gates regulate the strand passage mechanism proposed in the late 1970s for DNA gyrase [46, 56-58]. Significant conformational changes occur on the enzyme in each cycle catalyzed by the hydrolysis of two ATP molecules. A DNA duplex (G-segment) binds to the DNA gate, initiating the negative supercoiling process Figure 3). The C-terminal domain (CTD) of gyrA contributes to the bending and wrapping of the DNA around the enzyme, positioning another segment of the same DNA molecule (T-segment) between the open clamps of gyrB [59]. Cooperative ATP binding promotes the dimerization of gyrB subunits, which close the N-gate and trap the T-segment [60-62]. The dimerization of the gyrB subunits is essential to secure the T-segment and promote the enzyme's ATP hydrolysis, ensuring the energy needed to perform the catalysis [63, 64]. The intrinsic ATPase activity of gyrB is stimulated by the presence of gyrA and DNA [65]. The energy provided by the hydrolysis of one molecule of ATP facilitates the conformational changes required for introducing a double-strand break on the G-segment [66-68]. The T-segment is transported through the gap (strand passage), and the G-segment break is then resealed. The T-segment is released from the enzyme through the C-gate. The hydrolysis of the second molecule of ATP opens the N-gate and resets the enzyme to the initial conformation, completing the catalytic cycle. The movement of the T-segment across the enzyme is ensured by transient protein-DNA interactions that stabilize the DNA binding in each step [69]. For instance, a cluster of basic residues at the C-gate of DNA gyrase of *S. pneumoniae* coordinates the exit of the DNA through this gate. Mutations on these residues affect the DNA supercoiling kinetics but not the enzyme's DNA cleavage or ATPase activity [70].

Bacterial DNA gyrase inhibitors

Bacterial DNA gyrase inhibitors are classified into two different inhibitors according to their effect on the enzyme: catalytic and poison inhibitors. Catalytic inhibitors are compounds that reversibly block the binding of ATP or DNA to the enzyme, limiting the energy disposition or blocking the interaction with DNA (Figure 4). Usually, these inhibitors bind to gyrB, and sometimes are called gyrB inhibitors. Poison inhibitors stabilize the cleavage complex formed by the enzyme and the DNA during the strand passage step of the cycle, interrupting the rejoining of the G-segment (Figure 4). This process converts the enzyme into a DNA-cutting molecular machine, causing the accumulation of DSB or nicked DNA [71, 72]. Since poison inhibitors typically target gyrA, they are also called gyrA inhibitors.

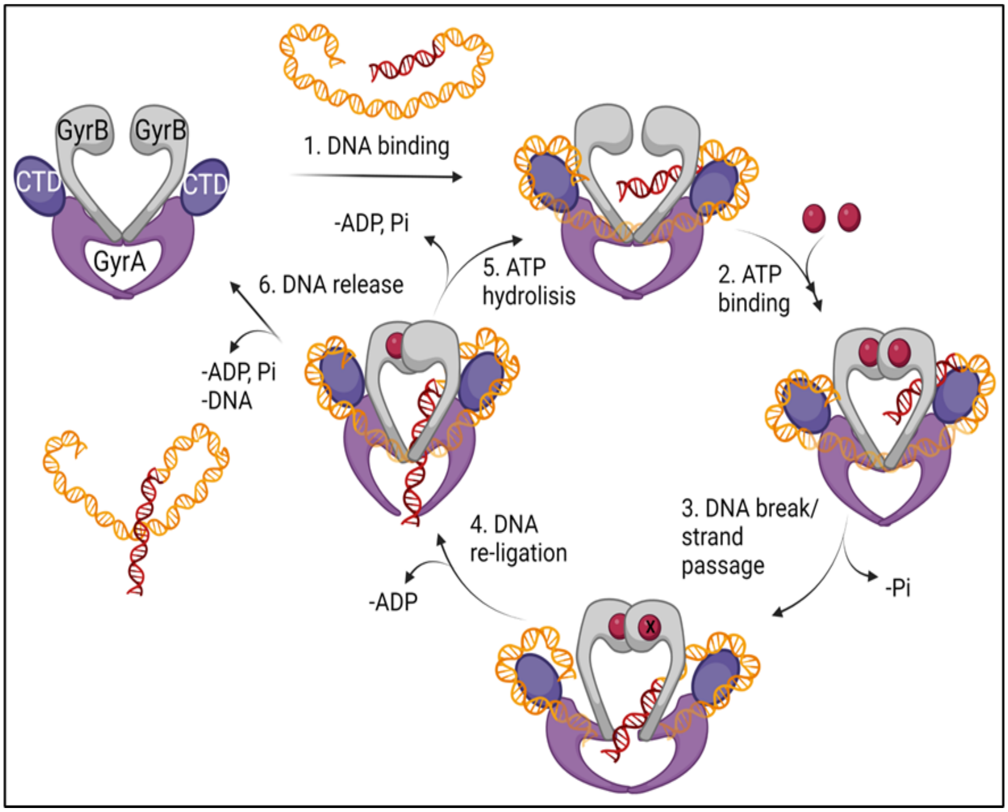


Figure 3. Bacterial DNA gyrase catalytic cycle. After the DNA (double-stranded) and ATP binding (1 and 2), a double-strand break is introduced (3) and a segment of DNA is translocated through the enzyme (strand passage). The DNA covalently bounded to the enzyme is then re-ligated (4) and the second molecule of ATP is hydrolyzed, returning the enzyme to the initial conformation (5) while the supercoiled DNA is released (6).

So far, five binding sites in bacterial DNA gyrase have been discovered/identified for different gyrase inhibitors: the ATP binding sites in gyrB, the surface of the DNA-gate located at the interface of gyrA and gyrB, the quinolone binding site, the binding site for new bacterial topoisomerase inhibitors (NBTIs), and a hinge pocket between the TOPRIM in gyrB and the WHD in gyrA. The first two binding sites are usually associated with catalytic inhibitors that competitively limit the enzyme's access to essential substrates. For example, aminocoumarins, cyclothialidine, and other natural and synthetic inhibitors bind to the ATP binding site on gyrB [73-77]. Simocyclinones bind to the surface of the DNA-gate, blocking the DNA binding to the enzyme [78, 79]. They are catalytical inhibitors. The other three binding sites are typically used by gyrase poison inhibitors (Figure 5). Examples are quinolones, NBTIs, and thiophenes [80-82].

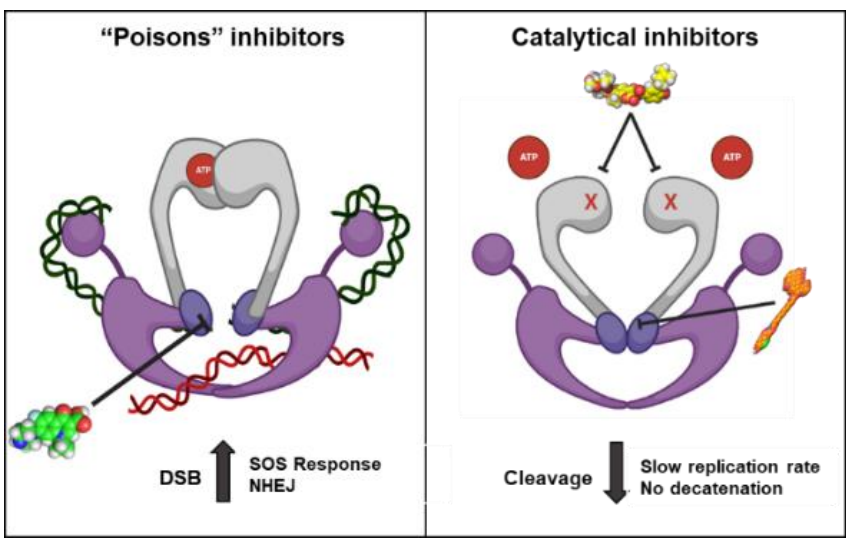


Figure 4. Two types of bacterial DNA gyrase inhibitors: poisons and catalytical inhibitors. Gyrase poisons (left) block the re-ligation of DNA, generate double-strand breaks (DSB), and activate DNA repair pathways such as SOS response and NHEJ. Catalytic inhibitors (right) inhibit the activity of gyrase (ATP or DNA binding inhibition) without damaging DNA.

In the following sections, I will discuss certain detailed information on the origin, chemical structures, mechanism of action, and antibacterial activity of some well-characterized bacterial gyrase inhibitors.

DNA gyrase poison inhibitors

Quinolones

Nalidixic acid was the first quinolone-based gyrase poison inhibitor discovered in 1962 during the synthesis of chloroquine [83]. Based on its antibacterial activity, this compound was used to treat urinary infections caused by Gram-negative bacteria [83-86]. Evidence that nalidixic acid and other quinolones inhibit bacterial DNA gyrase was reported in 1976 [72]. While the therapeutic use of nalidixic acid was limited due to its weak inhibitory activity against bacterial DNA gyrase, the introduction of a fluorine group to the 6-position of quinolones (Figure 7 a) dramatically changes their anti-gyrase and anti-bacterial activities and marks the starting point of turning fluoroquinolones to one of the most used antibiotics in the world.

Structural modifications in each generation of fluoroquinolones have been guided by structure-activity relationship studies and microbiological and pharmacological characterizations (Figure 7c). Common features of fluoroquinolones include a nitrogen group at position N-1, a carboxylic acid at C-3, a ketone group at position C-4, and a fluorine atom at C-6 position (Figure 7a). These modifications are essential for their antibacterial activity. For example, the fluorine atom at position C-6 was selected from a group of potential substituents, including NO_2, CH_3, $COCH_3$, Cl, and Br [87]. In addition, a notable decrease in the binding with bacterial DNA gyrase and cell penetration has been observed for derivatives without the fluorine atom, highlighting the importance of this chemical substitution [88]. Substitutions such as piperidines and pyrrolidine derivatives in C-7 and methoxy groups in C-8 have also expanded the clinical spectrum of fluoroquinolones [89-91].

The carboxylic acid at position C-3 and the keto group at C-4 are essential for the binding of these drugs to bacterial DNA gyrase. Early structure-activity relationship studies demonstrated their importance [92]. The binding mechanism of fluoroquinolones to DNA gyrase is based on the formation of a water-metal ion (Mg^{2+}) bridge through two conserved residues, Serine and Aspartic (positions 83 and 87 in *E. coli* gyrase, respectively), located near the DNA cleavage site (Figure 7b). These two residues form hydrogen bonds to two of four water molecules that coordinate an Mg^{2+} ion with the two oxygens of the keto (C-4) and carboxylic acid (C-3) group of fluoroquinolones [93, 94].

The role of magnesium in the drug binding was observed in the crystal structure of gyrase-drug-DNA complexes [94]. The antibacterial activity of fluoroquinolones is lost when the carboxylic acid at position C-3 is changed further demonstrating the importance of the carboxylic acid at position C-3 [92]. Additionally, mutations of these two residues, Ser83 and Asp87, are the main source of resistance to fluoroquinolones [94-96].

The bactericidal effect of fluoroquinolones is based on their dual inhibitory activity over bacterial DNA gyrase and topoisomerase IV, essential enzymes that control DNA topology in bacterial cells. The binding mechanism of fluoroquinolones to topoisomerase IV is similar to that of DNA gyrase, as both involve the formation of a water-metal ion bridge through conserved Serine and Glutamic residues (positions 80 and 84 in *E. coli* topoisomerase IV, respectively).

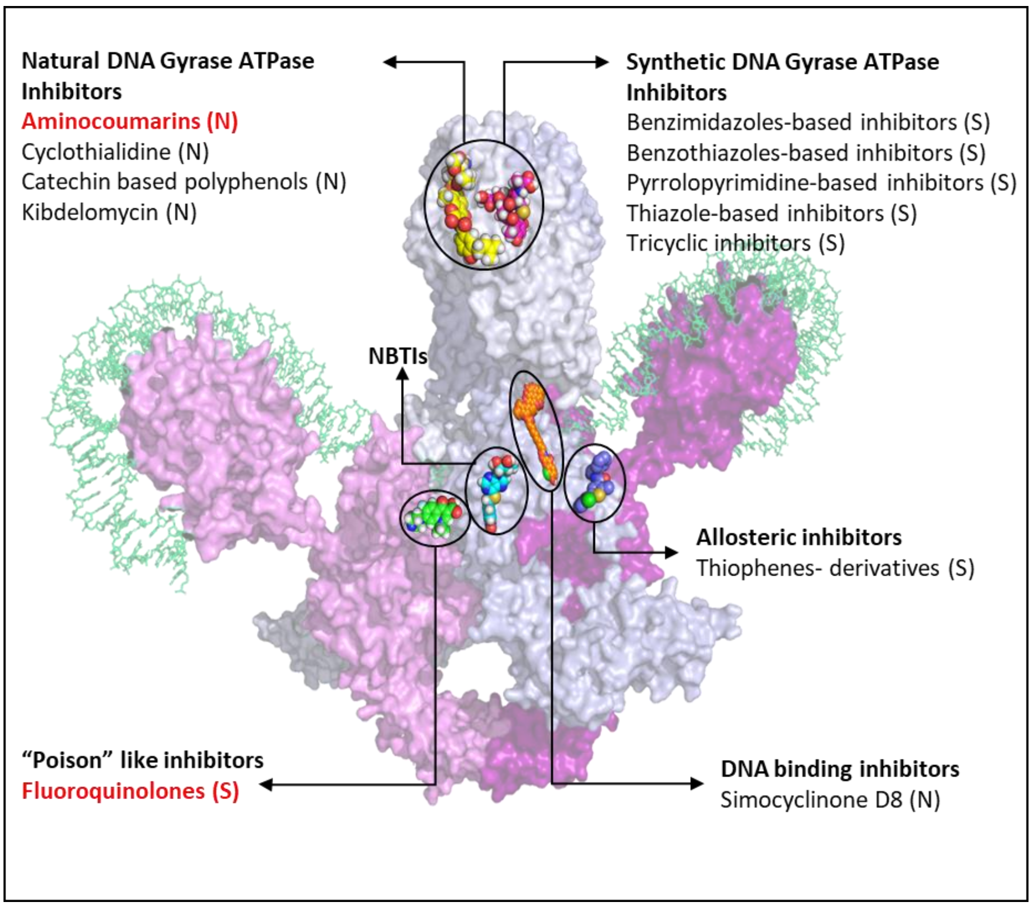


Figure 5. Target sites of *E. coli* DNA gyrase. The structure of *E. coli* DNA gyrase was retrieved from PDB (6RKW). gyrB and gyrA are colored in gray and violet, respectively. DNA is highlighted in green. Gyrase inhibitors in space-filling model and their binding sites on the enzyme are shown. (N) represents inhibitors obtained from natural sources, while (S) indicates synthetic inhibitors.

Point mutations at Ser83 and Asp87 of gyrA and Ser80 and Glu84 of parC, are the primary cause of resistance to fluoroquinolones. These residues are located at the N-terminal domain of gyrA/parC, in an area called the quinolone-resistance-determining region (QRDR) since it accounts for over 90% of mutations that confer resistance to these drugs.

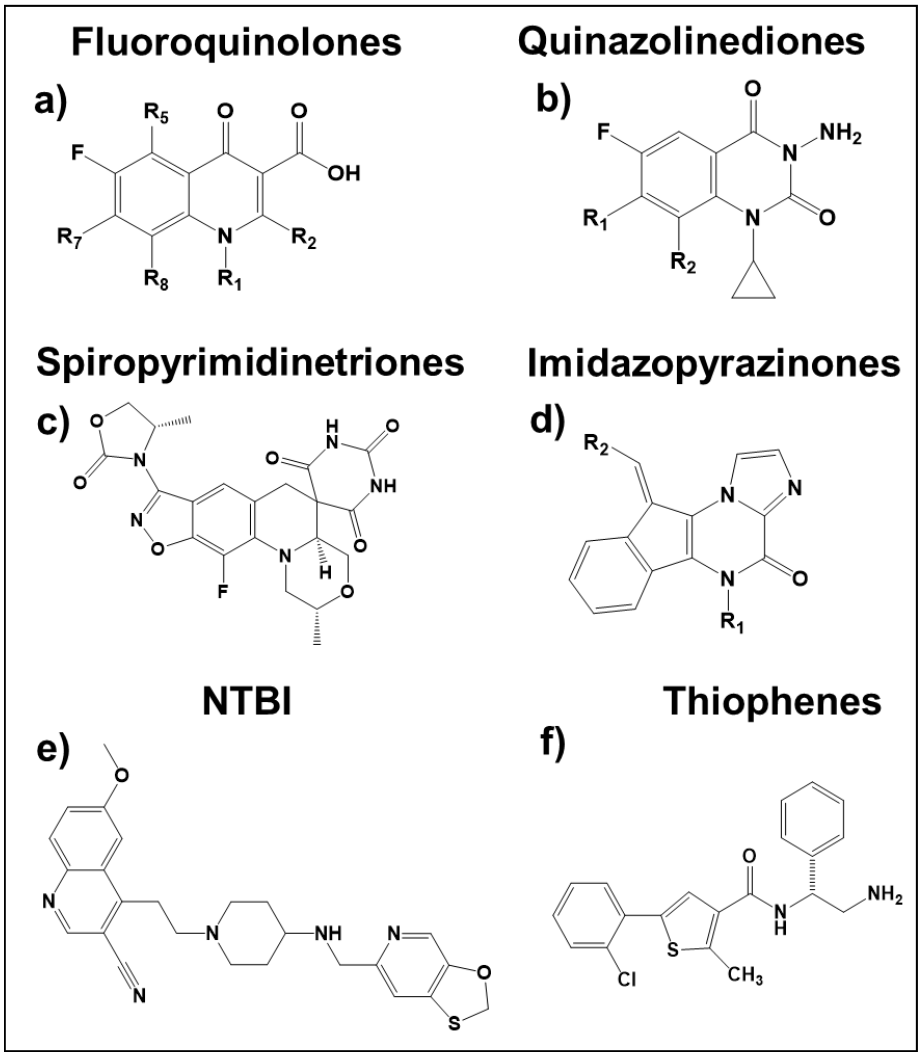


Figure 6. Chemical structure of various gyrase subunit A inhibitors. Compounds **a-d** bind to the DNA cleavage site of the enzyme, blocking the rejoining of the transient DNA gap created during the strand passage step. Compound **e** (NBTIs) binds the two-fold symmetry axis of bacterial DNA gyrase. Compound **f** allosterically inhibits bacterial DNA gyrase, binding to a hinge pocket between the gyrB and gyrA subunits.

Although these mutations usually appear combined, a single change at the conserved Serine can notably reduce the bactericidal activity of fluoroquinolones [97-99]. In addition, mutations that also increase the resistance to fluoroquinolones may occur at Asp426 and Lys447of gyrB [100, 101].

Resistance to fluoroquinolones is not only due to gyrA mutations destabilizing the drug-enzyme interaction. Plasmid-encoded resistance mechanisms against fluoroquinolones are also globally distributed, including Qnr proteins, aminoglycoside acetyltransferase AAC(6')-Ib-cr, and efflux pump proteins like Qep [102-108]. Plasmids carrying Qnr genes, a protein that can protect DNA gyrase and topoisomerase IV from fluoroquinolones by binding to these enzymes, can be transferred horizontally between cells [105-107]. Efflux pumps such as OqxAB, QepA1, and QepA2 that reduce intracellular drug concentrations and lead to resistance have also been identified in different continents [102, 108].

Although fluoroquinolones have been extensively used since the 1980s to treat several bacterial infections, bacterial resistance to these drugs has been a worldwide phenomenon in the last thirty years. Furthermore, the clinical use of fluoroquinolones has been undermined by the severe side effects caused by these drugs such as tendon and joint lesions, headaches, dizziness, phototoxicity, and cardiovascular disorders. These adverse reactions have caused the FDA to withdraw some fluroquinolones from the market [109-111]. Therefore, there is an urgent need for novel antibacterial drugs, structurally different from fluoroquinolones, that target bacterial DNA gyrase.

Since bacterial DNA gyrase is a validated target for antibacterial therapy, efforts to identify novel drugs that overcome bacterial resistance to fluoroquinolones and have antibacterial activity are ongoing. Quinazolinediones, imidazopyrazinones, and spiropyrimidinetriones are three gyrase poison inhibitors structurally different from fluoroquinolones. Below is a brief discussion of these three new gyrase poison inhibitors and their anti-gyrase and anti-bacterial activities.

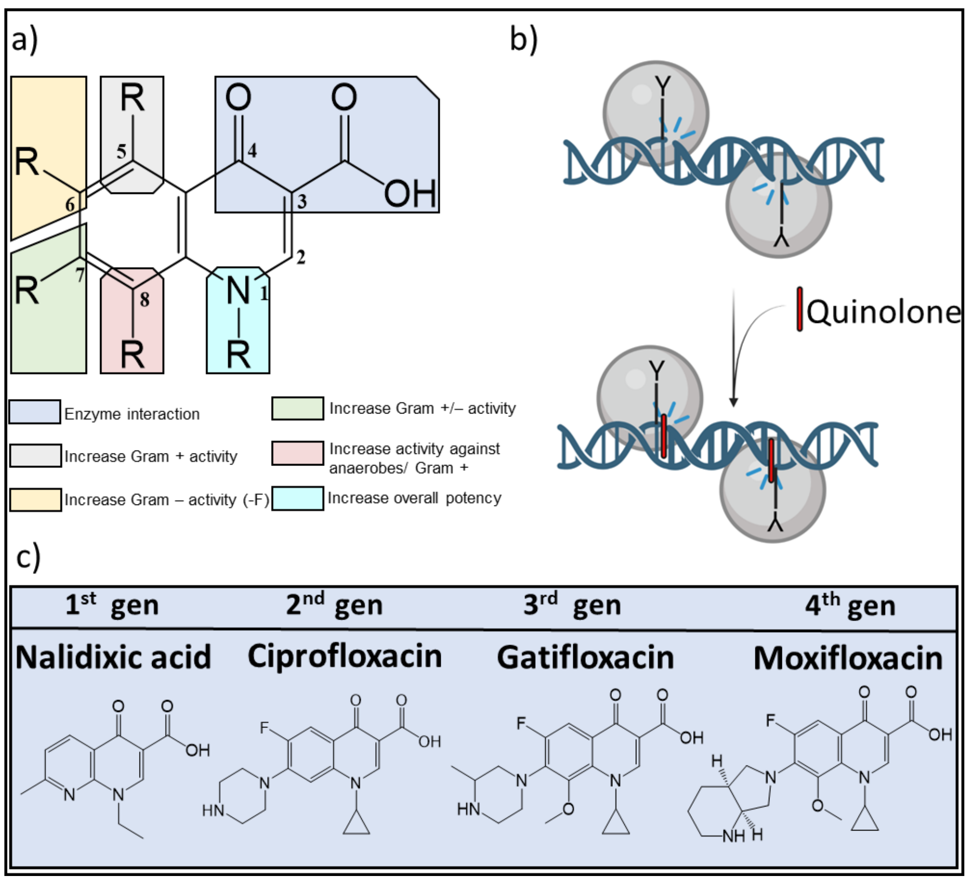


Figure 7. a) Core structure and structure-activity relationships (SARs) of fluoroquinolones (FQs). **b)** Bacterial DNA gyrase (gray) cleavage complex stabilized by FQs (red). Y indicates the position of the active site tyrosine. **c)** Quinolone examples of different generations.

Quinazolinediones

The first gyrase poison I would like to discuss is quinazolinediones (QZs). The chemical structure of QZs is similar to that of fluoroquinolones (Figure 6 b), with the main difference being an amino group at position 3 and a carbonyl group at C-2. Consequently, it can occupy the fluoroquinolones binding sites of bacterial DNA gyrase [93]. Due to QZs not having an acidic group at position C-3, these compounds establish other interactions with the enzyme. Although the carbonyl substitution at C-2 can form a hydrogen bond with the conserved Arg 121 (*E. coli* gyrA), QZs rely more on substitutions in positions C-7 that establish interactions with acidic residues in gyrA clustered around this group. Crystallographic and biochemical studies have shown the binding mode used by QZs, including their capacity to associate with the enzyme without using the water-metal ion bridge. This binding mechanism helps these drugs overcome resistance to fluoroquinolones related to mutations in the conserved serine and acidic residue [93, 112].

Like fluoroquinolones, quinazolinediones are also gyrase-poisons since they stabilize the cleavage complex formation in bacterial DNA gyrase. The DNA breakage caused by QZs differs in reversibility, metal ion interaction, and involvement of the gyrB (parE) TOPRIM domain, from that caused by fluoroquinolones [113]. The accumulation of double-strand breaks of DNA induced by QZs explains the antibacterial activity of these drugs. Quinazolinediones are very effective against Gram-positive bacteria and *E. coli* efflux pump knock-out strains, with MICs comparable to those obtained for ciprofloxacin. However, their activity against wild-type *E. coli* is poor, indicating these compounds are substrate for efflux pumps [114]. It is essential to mention that some QZs derivatives that can overcome fluoroquinolone resistance in bacterial gyrase due to chemical modifications at position C-7 can also interact and inhibit human topoisomerase IIα. In addition, some quinazolinediones have cytotoxic effects against human cells lines [115]. These unwanted effects represent a serious challenge for the development of quinazolinediones-based drugs. Efforts to find C-7 derivatives uniquely targeting bacterial enzymes can significantly benefit from SAR analysis and crystallographic studies [93, 112].

Spiropyrimidinetriones

Spiropyrimidinetriones (Figure 6 c) are bacterial DNA gyrase poison inhibitors that stabilize the formation of complexes between DNA and the enzyme, leading to the accumulation of double-strand breaks [116]. These compounds have a dual inhibitory activity against bacterial DNA gyrase and DNA topoisomerase IV similar to fluoroquinolones, with their anti-gyrase IC_{50} comparable to ciprofloxacin [117]. However, their activity against topoisomerase IV is less potent [118]. Spiropyrimidinetriones can partially overcome resistance to fluoroquinolones caused by gyrase mutations. Protein crystallization data of AZD0914, a spiropyrimidinetrione, with *S. aureus* gyrase show that this compound binds to the fluoroquinolone binding site of gyrase. While both molecules share the same binding site, spiropyrimidinetriones are more susceptible to mutations at the gyrB subunit, suggesting a different binding mechanism for these drugs [118, 119].

So far, AZD0914 has been tested for its anti-bacterial activities [117]. It shows a potent antibacterial against both Gram-positive and -negative bacteria, including *Neisseria gonorrhoeae*. Due to its potent anti-bacterial activities, low toxicity against human cells, and other properties, orally administered AZD0914 has been developed to treat bacterial infections [117, 120, 121]. Another significant feature of these gyrase poison inhibitors is their high level of specificity. AZD0914 has a weak inhibitory activity over human topoisomerases IIα (IC_{50} >400 µM) and IIβ (IC_{50} = 79 µM), improving the inhibitory values of ciprofloxacin against these enzymes (110 and 111 µM, respectively). Based on these results, orally administrated AZD0914, commercially named Zoliflodacin, has advanced to phase III clinical trials [122].

Imidazopyrazinones

Imidazopyrazinones (IPY) (Figure 6 d) are the third bacterial DNA gyrase poison inhibitors that also bind to the fluoroquinolone-binding pocket. Interestingly, these poison inhibitors can stabilize the DNA cleavage complex with the enzyme without forming a water-metal ion bridge. IPYs are obtained from the hybridization of quinazolinediones and tetracyclic imidazopyrazinones [123]. These compounds exhibit an inhibitory activity similar to ciprofloxacin against bacterial DNA gyrase [124]. In addition, IPYs also showed antibacterial activity against Gram-positive and Gram-negative strains [123]. Crystallographic studies in *S. aureus* gyrase show that IPYs bind to DNA gyrase with an orientation similar to fluoroquinolones. Interactions of IPYs through hydrogen bonds with Ser84 and Arg122 have been observed in *S. aureus* gyrase. Although IPYs do not form a water-metal ion bridge with the enzyme, Mg^{2+} is required to stabilize the complex with DNA gyrase. Their significant antibacterial activity and their resistance to mutations at the QRDR such as Asp87A in *E. coli*, make them promising compounds for further development. No cytotoxicity or specificity studies have been reported for imidazopyrazinones [123, 124].

Novel bacterial topoisomerase inhibitors (NBTIs)

NBTIs (Figure 6e and 8a) were discovered in the 1990s as part of the efforts to develop novel drugs with antibacterial activity that overcome fluoroquinolone resistance [80]. Structural studies show that NBTIs have a unique binding site within the enzyme interacting with the central DNA base pair and the gyrA α3 helices, making them effective against fluoroquinolone-resistant mutations in DNA gyrase [80, 125].

Structually, NBTIs can be divided into three parts: a left-hand side (LHS) moiety that intercalates with the DNA, a right-hand side (RHS) moiety that interacts with the gyrA subunit of bacterial DNA gyrase, and a linker connecting these two chemical moieties (Figure 8 a). Optimization efforts using tricyclic or bicyclic substitutions, such as quinolines and naphthyridines in the LHS [126-129], and different structures for the linker region [130-133] have improved the pharmacological properties of NBTIs. An interaction between the linker and Asp82 (*E. coli* gyrA) has proven to be crucial for the antibacterial activity of NBTIs.

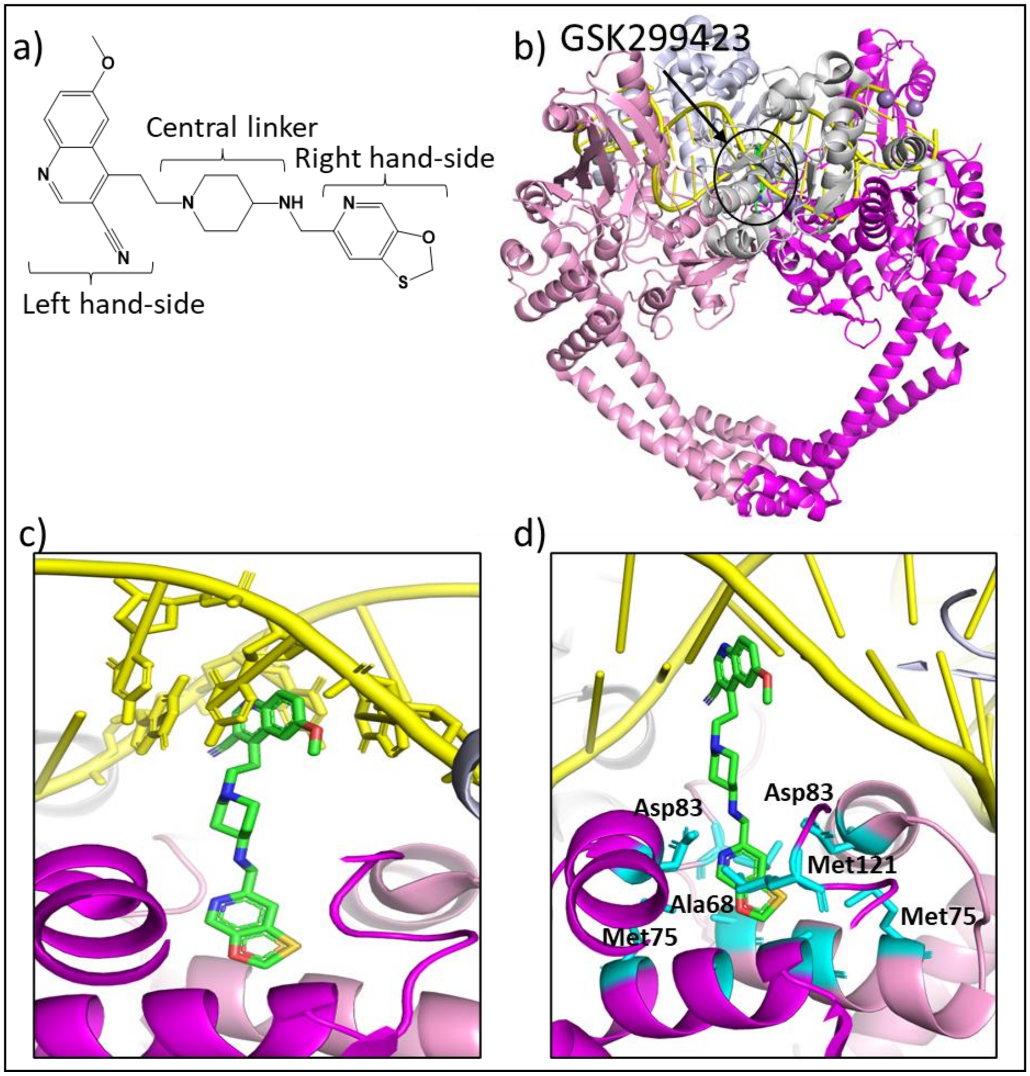


Figure 8. Chemical structure of NBTIs (example: GSK299423) and their interaction with bacterial DNA gyrase. (A) GSK299423 contains a left-side moiety for DNA binding, a right-side moiety for gyrase interaction, and a central linker. (B) Cartoon representations of GSK299423 (green) binding to *S. aureus* DNA gyrase (PDB code 2XCS). (C) The bicyclic group of the left-side moiety of GSK299423 intercalates into DNA base pairs. (D) The right-side moiety of GSK299423 interacts with hydrophobic residues (Met 75, Met121, Asp83, Ala68) in *S. aureus* gyrA. DNA gyrase A subunits are represented in pink and violet, the gyrase B subunits are gray, and the DNA is yellow.

Substituents such as pyridoxazinone/pyridothiazinone and pyridodioxane/oxathiinopyridazine are the most frequently used RHS moieties. Interactions of RHS with conserved amino acid residues Ala67, Gly71, Ile 74, and Met120 in *E. coli* gyrA (Figure 8d) are crucial for the proper binding of NBTIs to bacterial DNA gyrase [125, 134].

NBTIs' mechanism of action favors the accumulation of nicked DNA rather than promoting DSB formation. This difference with fluoroquinolones is due to their distinctive binding mode. Dual inhibitory activity against bacterial DNA gyrase and topoisomerase IV has been observed for NBTIs as well. In Gram-negative bacteria, DNA topoisomerase IV seems to be the primary target, while bacterial DNA gyrase is the main target in Gram-positive strains [135].

Based on their potent antibacterial activity, several NBTIs has been taken into clinical trials [125]. For instance, Gepotidacin (GSK 299423), a NBTI, is at clinical trials to treat acute skin bacterial infections, uncomplicated urinary tract infections (uUTI) and uncomplicated urogenital gonorrhea [136-138]. However, the cardiotoxicity effects associated with NBTIs constitute the main challenge for the clinical use of these compounds. Continuous optimization efforts are required to fully exploit the antibacterial activity of these drugs while minimizing cardiotoxic effects [139].

Thiophenes

Thiophenes (Figure 6 f) are a novel class of bacterial DNA gyrase poison inhibitors that induce the accumulation of DNA single- and double-stranded breaks. Their unique mechanism of action is based on the binding to a newly identified pocket located on the interfaces of the TOPRIM (gyrB) and WHD (gyrA) domains [82] (Figure 6f). This region is conserved among DNA gyrases from Gram-negative and -positive bacteria but absent in human type II topoisomerases [82]. Interestingly, this pocket is only observed in the DNA-bound enzyme, indicating that thiophenes bind to an intermediate of DNA gyrase upon the enzyme binding to DNA. One unique feature of thiophenes is that they do not directly interact with the gyrase DNA cleavage sites. These gyrase poison inhibitors bind to a so-called "hinge pocket" of gyrase and disrupt the movement of TOPRIM and WHD of DNA gyrase. Because of their distant binding site from the DNA cleavage site of DNA gyrase, thiophenes are classified as allosteric inhibitors [82].

The potent antibacterial activity against Gram-negative bacteria, including clinically relevant strains resistant to fluoroquinolones, and their specific binding site highlight the potential of thiophenes as antibacterial drugs although they are cytotoxic to human cells [82].

DNA gyrase catalytic inhibitors

DNA gyrase catalytic inhibitors mainly target the ATP binding site of gyrase subunit B (gyrB) since the ATP binding site plays a crucial role in the energy requirement for bacterial DNA gyrase’s supercoiling activity. Crystal structures of the 43-kDa amino-terminal domain of gyrB in complex with a nonhydrolyzable ATP analog reveal details how ATP binds to DNA gyrase and demonstrate the importance of the interaction between gyrase residue Asp73 and the amino group of the adenine of ATP [49]. So far, tremendous efforts have been devoted to identify and synthesize inhibitors targeting the ATP binding site of gyrB [140-144]. Here I will briefly review the current status of DNA gyrase catalytic inhibitors according to their original sources: either naturally-occurring (Figure 9) or synthetic nature (Figure 10). Nevertheless, detailed information can be found in these excellent review articles [145, 146]

Naturally occurring DNA gyrase catalytic inhibitors

Aminocoumarins

Aminocoumarins, such as novobiocin, clorobiocin, and coumermycin A1 (Figure 9), are natural bacterial DNA gyrase inhibitors identified from *Streptomyces* species [147-149]. The structure of aminocoumarins consists of a 3-amino-4,7-dihydroxycoumarin ring flanked by an L-noviose sugar moiety and an aromatic acid group. A chlorine atom replaces a methyl group at position 8 of the coumarin ring in clorobiocin, while coumermycin A1 is formed by two L-noviose sugar and two aminocoumarin moieties [150]. Novobiocin was initially studied as an inhibitor of DNA synthesis in bacteria, but the inhibition over bacterial DNA gyrase was discovered shortly after the discovery of DNA gyrase [151, 152].

These compounds are ATP-competitive inhibitors of bacterial DNA gyrase, with a K_i in the nano molar range, 4 orders of magnitude less than the K_M for gyrase ATPase [48, 151, 153, 154]. Aminocoumarins bind to the entrance of the ATP binding site in gyrB, at a 24-kDa sub-domain containing the GHKL domain residues according to the crystal structure obtained by Gilbert and Maxwell [155]. The interaction of aminocoumarins with the enzyme dissociates the energy source needed for the catalytic cycle.

Bacterial resistance to aminocoumarins mainly comes from the mutations in residues Arg136 and Asp73 of gyrB, indicating the importance of these two amino acid residues for interactions with aminocoumarins [155-158]. Although aminocoumarins are potent bacterial DNA gyrase inhibitors *in vitro*, only novobiocin has been used therapeutically. Nevertheless, novobiocin has been withdrawn from clinical use due to its toxicity and high affinity for serum proteins [146]. In addition, the poor inhibitory effect over Gram-negative bacteria has limited their broad use as effective antibiotics [150, 159, 160]. However, recent efforts have been made to obtain aminocoumarin-based antibiotics with improved inhibitory activities and enhanced antibacterial activity against Gram-negative bacteria [149, 161].

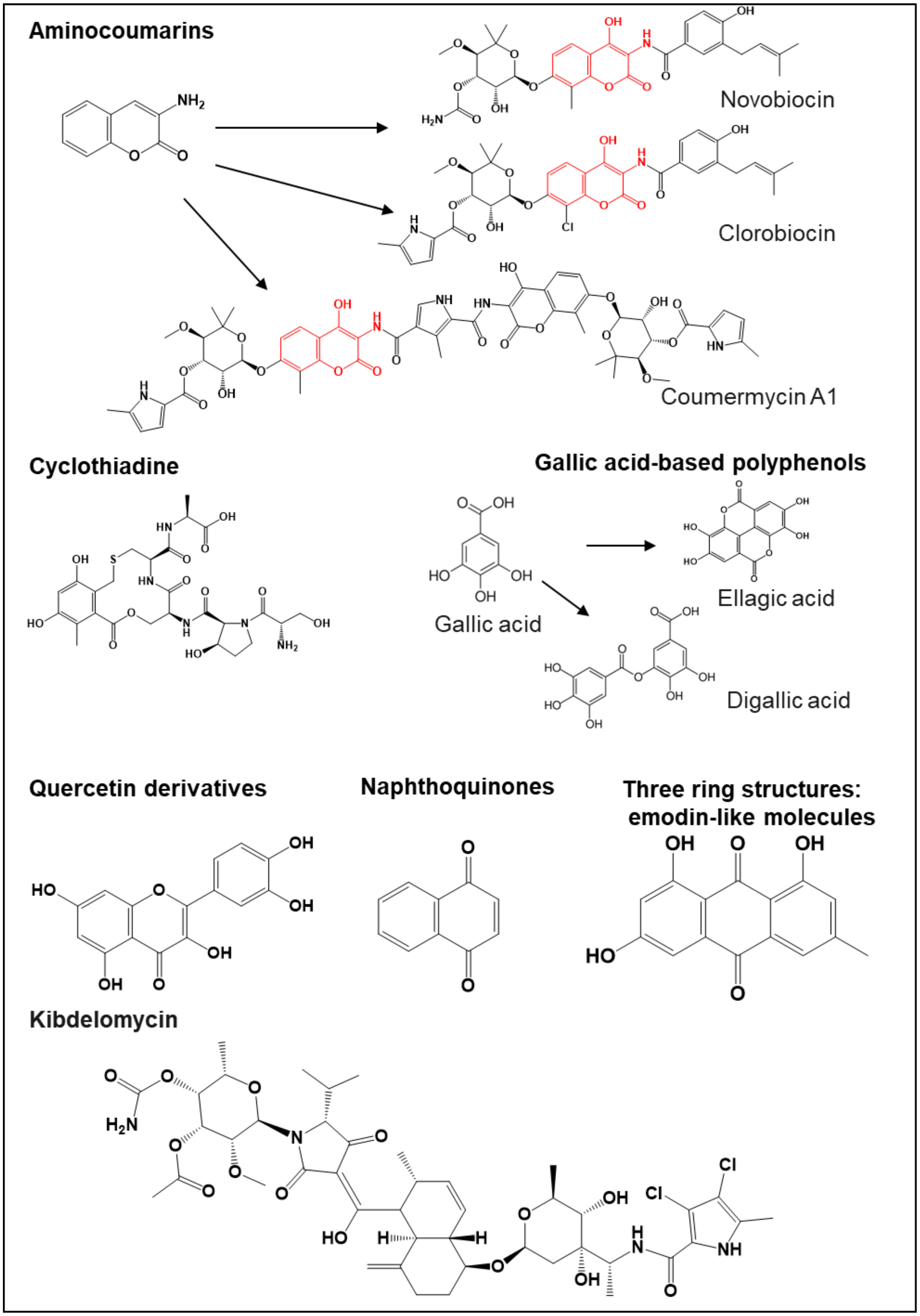


Figure 9. Chemical structure of gyrase subunit B inhibitors from natural sources. The aminocoumarin ring in novobiocin, clorobiocin, and coumermycin A1 is highlighted in red.

Cyclothialidine

Cyclothialidine (Figure 9) is a DNA gyrase inhibitor produced and isolated from Streptomyces spp. It was discovered in the early 1990s as part of a screening campaign conducted by Roche and was the first non-coumarin ATPase gyrase inhibitor identified [162]. These cyclic peptides are two-fold more potent than novobiocin and coumermycin A1 and highly selective, as they do not inhibit other topoisomerases, including human topoisomerase I and IIα. Comprehensive studies of their mechanism of action showed that cyclothialidine acts as a competitive inhibitor of the ATP binding with gyrB. Mutant enzymes resistant to novobiocin were inhibited by cyclothialidine, indicating that it binds to a binding site different from the one used by novobiocin [73, 163, 164].

In contrast with the high selectivity and potency against bacterial DNA gyrase *in vitro*, the activity of cyclothialidine *in vivo* has been limited. Initial studies only showed antibacterial activity against *Eubacterium* spp. strains, known for their high susceptibility to antibiotics [162]. This reduced activity against bacterial cells is associated with the poor permeabilization ability of this molecule to bacterial cell membrane. Derivatization efforts have been conducted to enhance cyclothialidine *in vivo* activities. Derivatives obtained from ligand-based optimization with enhanced antibacterial properties have been obtained [165, 166]. This strategy improved minimum inhibitory concentrations (MICs) of certain derivatives, especially against Gram-positive bacteria, including drug-resistant strains [146, 166].

Gallic acid-based polyphenols

Gallic acid-based polyphenols (Figure 9) are secondary metabolites produced by certain plants, including *Camellia sinensis*, the source of green tea. The abundance of these polyphenols in green tea has been associated with certain health benefits [167]. Among these polyphenols, ellagic acid, (-)-Epigallocatechin gallate (EGCG), (-)-Epigallocatechin (EGC), and (-)-Epicatechin gallate (ECG) are known bacterial DNA gyrase inhibitors. These natural compounds specifically bind to the 24-kDa sub-domain at the N-terminal of gyrB, competing with ATP for the binding site. Molecular docking analysis and NMR spectroscopy show that the galloyl moiety of these compounds tightly binds with the residues located in the interior of the ATP binding pocket of the enzyme [168].

Other derivatives of gallic acid, including food preservatives such as octyl and dodecyl gallate, have been synthesized and studied for their antibacterial activity. Although these synthetic gallates have anti-bacterial activity against Gram-positive bacteria, their mechanism of action has not yet been fully understood [169, 170]. A recent study showed that the antibacterial activity of these gallates may stem from their anti-gyrase activity [171].

Quercetin derivatives

Quercetin (Figure 9) is a plant polyphenol with potent antibacterial activity [172]. It inhibits the ATPase activity of bacterial DNA gyrase by competing with ATP for the same binding site with a K_D of 15 µM in the 24 kDa fragment of *E. coli* gyrB [173]. Recently, it was reported that quercetin exhibits dual inhibitory activity against bacterial DNA gyrase and topoisomerase IV [174], which may be the mechanism for its antibacterial activity. Quercetin has a more potent anti-bacterial activity against Gram-positive bacteria than against Gram-negative strains, likely due to its cell membrane permeability. However, through derivatization efforts, quercetin analogues with improved antibacterial activity compared to antibiotics like vancomycin have been obtained. [174].

Naphthoquinones

Naphthoquinones (Figure 9) and their derivatives are natural bacterial DNA gyrase inhibitors with a naphthalene ring and two carbonyl groups in positions 1, 2 or 1, 4. Several derivatives have antibacterial activities [175]. For instance, diosporyn, a naphthoquinone derivative, has anti-bacterial activity against *E. coli*, *S. aureus*, and *Mtb* DNA gyrases with MICs in the range of 15 µM. Diospyrin and other naphthoquinones inhibit DNA gyrase by binding to the N-terminal of gyrB without competing with ATP. Surface plasmon resonance results indicate that diospyrin binds to the 43-kDa fragment of gyrB of *E. coli* with a $K_D = 10^{-4}$ M. These results indicate diosporyn binds to the N-terminal domain of gyrB, but does not overlay the ATP-binding site of the enzyme [142]. The anti-gyrase and antibacterial activities of these natural compounds and their unique mechanism of action, point to further studies to develop novel drug candidates based on their structure.

Emodin derivatives

Emodin (Figure 9) is a natural anthraquinone found in plants including some fruits with known antibacterial activity frequently used in Chinese traditional medicine [176]. Haloemodins, obtained through derivatization of this polyphenol, exhibit dual inhibitory activity against bacterial DNA gyrase and topoisomerase IV. Emodin also inhibits human DNA topoisomerase II [177]. The dual inhibitory activity over bacterial topoisomerases could explain the potent antibacterial activity shown by emodin and some derivatives. Similar to other natural compounds, the antibacterial activity of emodin and derivatives is more potent against Gram-positive bacteria. These compounds effectively inhibit bacterial strains resistant to vancomycin and methicillin such as *E. faecium* and *S. aureus*. Studies on rabbit models have shown the *in vivo* antibacterial activity of haloemodins against *S. aureus* infections. The control of bacterial infections after treatment with haloemodins indicates the potential use of these compounds as antibacterial drugs [178].

Kibdelomycin

Kibdelomycin (Figure 9), obtained from *Kibdelosporangium sp.*, represents the first of a new class of natural gyrB inhibitors. With a potent and selective inhibitory activity against bacterial DNA gyrase, this compound has a broad antibacterial spectrum against Gram-positive bacteria [179]. Co-crystallization studies in the presence of novobiocin with the 24-kDa fragment of gyrase B and the 43-kDa fragment of *S. aureus* topoisomerase IV showed a novel binding mechanism for this compound. In both structures, a clamp-like mechanism for kibdelomycin binding to gyrase was observed. The pyrrolamide group of kibdelomycin interacts with the interior of the ATP binding pocket, and the sugar group binds to residues on the protein surface. The binding of kibdelomycin to gyrase also affects the dimerization of gyrB and parC. This new mechanism of action might explain the absence of cross-resistance to novobiocin-resistant strains [74]. The bactericidal activity of kibdelomycin and its novel mechanism of action confirms the importance of natural compounds as a source of antibacterial drugs.

Natural compounds represent an inexhaustible source of potentially biologically active molecules, with derivatives accounting for 37% of all drugs approved and 55% of antibacterial drugs from 1981 to 2019 [180]. Due to the importance of natural compounds as a source of antibacterial drugs and the variety of polyphenols with anti-gyrase activity (Figure 9), a screening study was conducted using a small library containing polyphenols [171]. The *in vitro* inhibition of bacterial DNA gyrase and the antibacterial activity of some of these compounds were analyzed. The results of this study are detailed in Chapter III of this dissertation.

Synthetic DNA gyrase catalytic inhibitors

Several pharmaceutical companies have been pursuing the development of compounds into antibiotics targeting the ATPase site of bacterial DNA gyrase due to the importance of ATP in the enzyme's catalytic cycle [181]. Despite a large number of compounds with anti-gyrB ATPase and anti-bacterial activities have been synthesized by different pharmaceutical companies, such as AstraZeneca, in the past 30 years (Figure 10), so far, no gyrB inhibitors have been successfully developed into antibiotics [146]. Strategies of synthesizing new gyrase inhibitors targeting the gyrB ATPase site include fragment-based screening, virtual and enzyme-based high throughput screening, and scaffold hopping focusing on disrupting the interaction between Asp73 and ATP at gyrB [146]. Here I will briefly discuss a few examples of synthetic gyrB inhibitors including pyrrolamides, benzimidazoles, benzothiazoles, and triazolopyridines obtained through these methods. For further information about additional synthetic gyrB inhibitors, please refer to several excellent review articles published previously [145, 146, 182].

Pyrrolamides

The first gyrB inhibitor in this group was discovered/identified in 2012 by Zeneca (now AstraZeneca) through a fragment-based screening of compounds binding to the 24 kDa N-terminal fragment of *S. aureus* gyrB using NMR [140]. This group of compounds showed potent antibacterial activity against Gram-positive bacteria and dual inhibitory activity against bacterial gyrase and topoisomerase IV, similar to aminocoumarins. An analog (AZD5099) with improved antibacterial activity was obtained through optimization efforts following structure-guided drug design. AZD5099 exhibited high anti-bacterial activity against *S. pneumoniae* in mouse lung infection models. However, this drug was discontinued when taken into clinical trials, as AZD5099 showed a high variability between participants and indications of causing mitochondrial changes [140, 146].

Benzimidazoles and benzothiazoles

Another synthetic gyrB inhibitor, a substituted 2-aminobenzimidazol was discovered/identified by Vertex Pharmaceuticals from a virtual and enzyme-based high throughput screening in the early 2000s. Through derivatization efforts from the initial hit, benzimidazoles with dual inhibitory activity against DNA gyrase and topoisomerase IV were obtained. These compounds showed an *in vitro* inhibitory activity more potent that the one of novobiocin for both enzymes and broad-spectrum activity against Gram-positive strains with MIC values in the range of 0.03 to 0.12 μg/mL [141, 143]. However, a 16-fold decrease in antibacterial activity in the presence of serum and poor aqueous solubility caused Vertex to stop the clinical development of benzimidazoles [146].

Benzothiazoles, constitute an example of scaffold-hop as they were obtained by Prolysis in 2008 from the initial Vertex benzimidazole series [146]. Benzothiazoles improved the MIC activity of benzimidazoles, with values between 0.03 to 0.06 μL/mL for Gram-positive bacteria, including respiratory tract pathogens. These compounds also showed MIC values lower to those of novobiocin for Gram-positive bacteria, including resistant strains of *S. aureus*, *E. faecium*, and *S. pneumoniae*. Similar to benzimidazoles, benzothiazoles have a low aqueous solubility that affects its bioavailability. In addition, the antibacterial activity of these compounds is reduced (~16-fold) in the presence of serum proteins [146].

Triazolopyridine-based inhibitors

Pfizer and Prolysis independently developed triazolopyridines based on the scaffold of benzimidazoles from Vertex in another example of scaffold-hop (Figure 10). Pfizer obtained derivatives of triazolopyridine with a potent antibacterial activity against Gram positive strains and *N. gonorrheae* (MIC of 0.06 μg/mL) [146, 183]. The *in vitro* inhibitory activity of these derivatives against type II bacterial topoisomerases was similar to the one of novobiocin. However, Pfizer did not pursue further development of triazolopyridine-based inhibitors based on the reduced pharmacokinetic activities of these compounds due to its low aqueous solubility [146].

In the case of Prolysis, triazolopyridine-based inhibitors also showed antibacterial activity against a panel of Gram-positive bacteria including *S. aureus*, *S. aureus* MRSA, S. *pneumoniae*, and *E. faecalis*. Although dual inhibitory activity over bacterial DNA gyrase and topoisomerase IV was observed, no further reports regarding these compounds have been disclosed by Prolysis [146].

Despite numerous efforts and millions of dollars invested, searching for a synthetic gyrase B inhibitor has been largely unsuccessful. The ATP binding site of type II bacterial topoisomerases remains elusive for the biopharmaceutical industry. Future antimicrobials will require new strategies to combat bacterial infections.

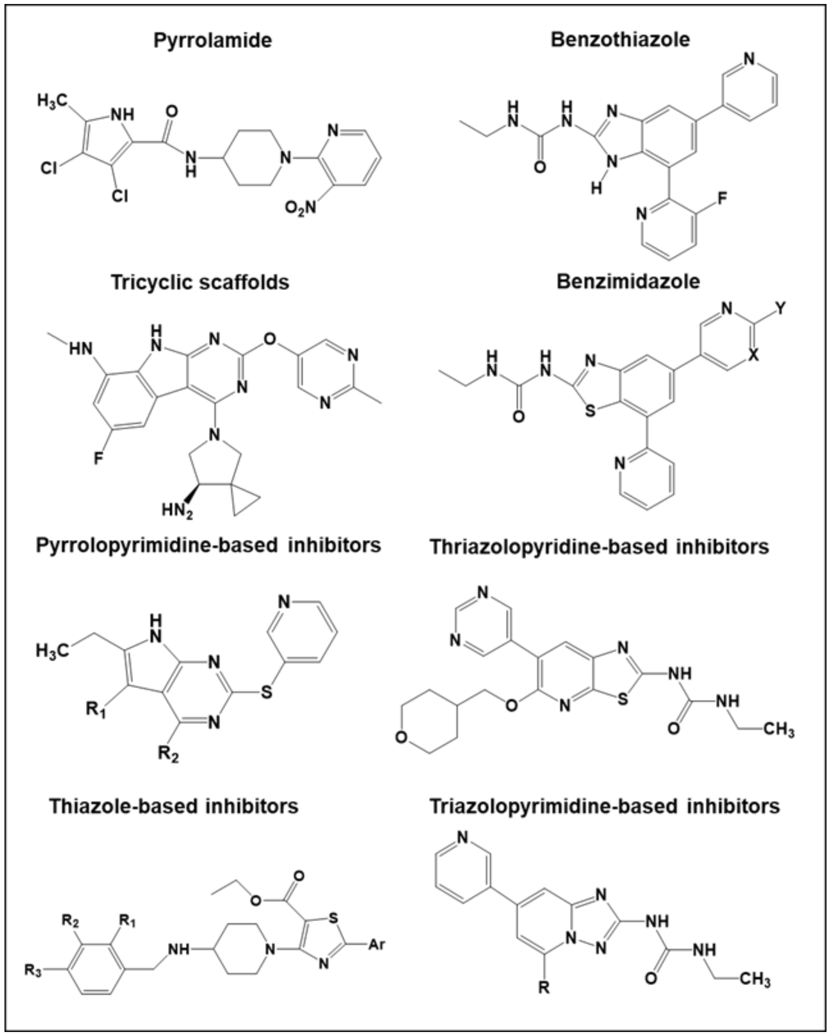


Figure 10. Chemical structure of certain synthetic gyrase subunit B inhibitors.

High throughput screening (HTS) methods to discover new bacterial DNA gyrase inhibitors

One of the major challenges in discovering and developing new anti-gyrase drugs is the lack of efficient methods to screen molecular libraries that can contain millions of chemically diverse molecules with potential and-gyrase and antibacterial activity [184]. Therefore, there is a need for fast, cost-effective, and reliable high throughput screening (HTS) methods to identify biologically active compounds in these libraries [185].

Although gel-based assays are considered the gold standard to validate bacterial DNA gyrase inhibitors, they are time-consuming and labor-intensive, making it difficult to screen a large number of samples [186]. The emergence of antimicrobial resistance and the robustness of bacterial DNA gyrase as a target for antibacterial therapy have prompted efforts to develop screening methodologies that accelerate the discovery of novel inhibitors for bacterial DNA gyrase. Only a limited number of screening methods have been developed, but unfortunately, most methods cannot be automated for high-throughput screening (HTS) processes [186-188].

Recently, two fluorescence-based HTS assays have been developed in our laboratory (Figure 11). The first HTS assay (Figure 11a) relies on the ability of bacterial DNA gyrase to supercoil relaxed fluorescence-labeled DNA circular plasmids in the absence of inhibitors, leading to the quenching of the fluorophore [189, 190]. This supercoiling-dependent fluorescence quenching (SDFQ) method uses the fluorescence intensity of the fluorophore as a topological state reporter of the plasmid. Therefore, this assay can be used to identify bacterial DNA gyrase inhibitors [189, 190]. Chapter II of this dissertation focuses on the development of a miniature, automatic SDFQ-based HTS assay and the use of this HTS assay to screen the National Institutes of Health's Molecular Libraries Small Molecule Repository (MLSMR) library containing 370,620 compounds.

The second method is based on the selective degradation by T5 exonuclease of an “AT” repeat-based hairpin present in a supercoiled plasmid, such as pAB1 (Figure 11) [191]. Since T5 exonuclease does not digest relaxed pAB1, this method can differentiate supercoiled and relaxed pAB1 and therefore can be used to identify inhibitors targeting different DNA topoisomerases [191]. The discrimination property of T5 exonuclease between supercoiled and relaxed pAB1 stems from the flap endonuclease (FEN) activity of T5 exonuclease that specifically recognizes and nicks the AT hairpin of supercoiled pAB1. The nicked pAB1 can be subsequently degraded by the 5’-3’ exonuclease activities of T5 exonuclease [191]. In contrast, the AT repeat of the relaxed pAB1 adopts a double-stranded form and does not form a hairpin. As a result, T5 exonuclease cannot digest it [191].

The readout of this method is based on the fluorescence intensity of a DNA intercalating dye such as ethidium homodimer 1 or ethidium bromide. Since the sc pAB1 is completely degraded by T5 exonuclease, a weak signal is obtained after the staining of these DNA samples with a fluorescence DNA intercalating dye. In contrast, a stronger fluorescence signal is obtained in DNA samples in the presence of a bacterial DNA gyrase inhibitors where the plasmid remains in the relaxed form. An HTS assay was developed and used to screen a 50-compound library containing known bacterial gyrase inhibitors, achieving a Z' over 0.5 [191].

This HTS assay can also be used to identify inhibitors targeting other DNA topoisomerases or to discover new DNA intercalators [191].

Virtual screening methods have been recently used to discover bacterial DNA gyrase inhibitors [192, 193]. These methods have become more feasible with the expansion of small molecule libraries and the growing number of protein structures solved by x-ray crystallization or NMR, coupled with advances in machine learning. Virtual screening methods combine structure-based and ligand-based analysis to identify potential drug candidates. Docking analysis, optimization of lead compounds, and evaluation of pharmacological properties of ligands are some advantages of virtual screening methods [194, 195].

Virtual screening methods have led to the discovery of novel bacterial DNA gyrase inhibitors with potent *in vitro* and antibacterial activity [196, 197]. However, neither of these molecules has advanced to clinical trial stages, and false-positive hits, which are also frequent in HTS, are often obtained. Nonetheless, these computer-based methods will play a crucial role in the future of drug discovery. Therefore, virtual screening is expected to play a crucial role in the future of drug discovery. Combining virtual screening with HTS could lead to more efficient drug discovery strategies that leverage the benefits of both methods.

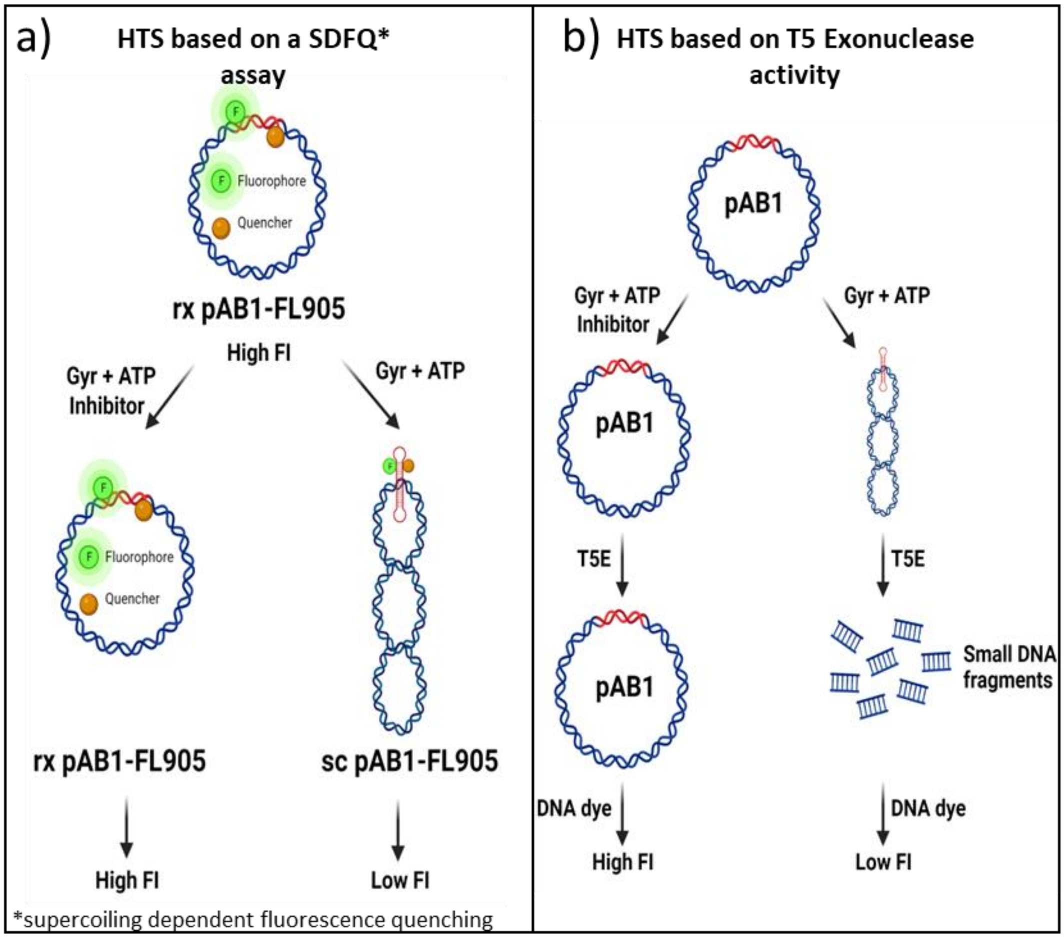


Figure 11. High Throughput Screening (HTS) assays to identify/discover bacterial DNA gyrase inhibitors. (**a**) HTS assays based on supercoiling dependent fluorescence quenching (SDFQ) using fluorescence-labeled DNA molecules. The readout is based on the fluorescence intensity of the fluorophore in the synthetic DNA oligomer inserted into a gapped DNA. (**b**) HTS assays based on T5 Exonuclease activity to digest supercoiled plasmid pAB1 containing an "AT" hairpin structure.

II. NOVEL AND STRUCTURALLY DIVERSIFIED BACTERIAL DNA GYRASE INHIBITORS DISCOVERED THROUGH A FLUORESCENCE-BASED HIGH-THROUGHPUT SCREENING ASSAY

Abstract

Bacterial DNA gyrase, a type IIA DNA topoisomerase that plays an essential role in bacterial DNA replication and transcription, is a clinically validated target for discovering and developing new antibiotics. In this article, based on a supercoiling dependent fluorescence quenching (SDFQ) method, we developed a high-throughput screening (HTS) assay to identify inhibitors targeting bacterial DNA gyrase and screened the National Institutes of Health's Molecular Libraries Small Molecule Repository library containing 370,620 compounds in which 2891 potential gyrase inhibitors have been identified. According to these screening results, we acquired 235 compounds to analyze their inhibition activities against bacterial DNA gyrase using gel- and SDFQ-based DNA gyrase inhibition assays and discovered 155 new bacterial DNA gyrase inhibitors with a wide structural diversity. Several of them have potent antibacterial activities. These newly discovered gyrase inhibitors include several DNA gyrase poisons that stabilize the gyrase-DNA cleavage complexes and provide new chemical scaffolds for the design and synthesis of bacterial DNA gyrase inhibitors that may be used to combat multidrug-resistant bacterial pathogens. Additionally, this HTS assay can be applied to screen inhibitors against other DNA topoisomerases.

Introduction

Antibiotic resistance is a serious threat to modern human society [198-200]. It can affect anyone anywhere in the world as the World Health Organization warned (https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance). The United States Centers for Disease Control and Prevention estimated that antibiotic-resistant bacteria infect more than 2.8 million people annually in the United States and, as a result, more than 35,000 Americans die (https://www.cdc.gov/drugresistance/national-estimates.html). Antibiotic resistance is especially high risk to patients who receive cancer chemotherapy or undergo complex surgeries including organ and bone marrow transplantation due to the fact that these patients are much more vulnerable to bacterial infections [200]. The emergence of multiple drug-resistant bacteria, so-called "superbugs" that are resistant to almost all antibiotics, makes the situation much worse [198]. Without new antibiotics, it is difficult or impossible to treat certain infections by these "superbugs" [199]. A pandemic caused by "superbugs" is likely to occur in the future due to the fact that there is no treatment when these diseases emerge [201]. Bacterial DNA gyrase, a type II topoisomerase that can introduce (−) supercoils to DNA substrates, is an important and clinically validated target for discovering and developing new antibiotics.[21, 181, 202-204] This enzyme has two different subunits, gyrA and gyrB, which form an active A_2B_2 complex.6 Because DNA gyrase only exists in bacteria and is an essential enzyme to bacteria [22, 205, 206], it is possible to identify inhibitors targeting DNA gyrase without affecting human topoisomerases [202, 207]. Additionally, DNA gyrase can form covalent enzyme-DNA complex intermediates [45, 208, 209], a property that makes gyrase an excellent bactericidal target. Indeed, fluoroquinolones (FQs) are among the most successful antibiotics targeted to DNA gyrase [210, 211]. The mechanism of action (MoA) of FQs is to stabilize the enzyme-DNA cleavage complex, which is ultimately responsible for cell death [80, 212]. This gyrase poisoning mechanism makes FQs among the most effective and prescribed antibiotics [213, 214]. Unfortunately, bacterial resistance to FQs has emerged [215-219] and makes the development of new, more effective antibiotics an urgent issue, especially for Gram-negative bacterial infections [220]. Furthermore, since FQs have been explored extensively, the limit and potential of what FQs can provide likely have been reached [213]. Therefore, it is necessary to develop new types of compounds targeting DNA gyrase. Novel bacterial topoisomerase inhibitors (NTBIs) including gepotidacin and zoliflodacin are examples of this effort [125, 221]. They are bacterial gyrase poisons [221] and currently under phase 3 clinical trials for the treatment of gonorrhea [122, 222]. Nevertheless, more gyrase inhibitors/poisons with novel chemical scaffolds are needed. To achieve this, one may screen chemical compound libraries to yield synthetic entities/scaffolds for further development. One challenge is to develop rapid and efficient high-throughput screening (HTS) assays to identify inhibitors from thousands of compounds in small molecule libraries.

Recently, we pioneered a new method to produce fluorescently labeled, relaxed (Rx) or supercoiled (Sc) DNA molecules to study DNA topoisomerases by supercoiling dependent fluorescence quenching (SDFQ) or fluorescence resonance energy transfer [189, 190]. This assay stems from a property of alternating (AT)n sequences in the closed circular plasmids that undergo rapid cruciform formation−deformation depending on the supercoiling status of the plasmids [223, 224]. The distance between a pair of fluorophore-quencher inserted in the (AT)n sequence is dramatically changed when the plasmids adopt the Sc or Rx form, triggering corresponding changes in the fluorescence intensity [189]. These DNA molecules are excellent tools to examine relaxation/supercoiling kinetics of various DNA topoisomerases [190] and can be configured into HTS assays to identify topoisomerase inhibitors [189]. In this article, we have established an SDFQ-based HTS assay to identify inhibitors targeting bacterial DNA gyrase. After screening the National Institutes of Health’s Molecular Libraries Small Molecule Repository (MLSMR) library containing 370,620 compounds, we identified 155 new bacterial DNA gyrase inhibitors. Several are DNA gyrase poisons, specific DNA gyrase inhibitors that stabilize the gyrase-DNA cleavage-complexes and convert gyrase to a DNA damaging machine.

Materials and methods

Materials

Proteins and Plasmids. *E. coli* DNA gyrase was purified according to the purification procedures published previously [225]. His-tagged human DNA topoisomerase IIα C-terminal deletion mutant (hTopo2α-ΔCTD) that lacks the 310 aa residues in the C-terminus was purified using a Ni-NTA column from yeast strain RegΔ1 carrying plasmid YEpWobb-hTopo2α-ΔCTD. Plasmid YEpWobb-hTopo2α-ΔCTD is a gift from Dr. Nei-Li Chan at National Taiwan University. *E. coli* DNA topoisomerase I was purified as described previously [226]. *E. coli* DNA topoisomerase IV is a gift from Keir Neuman at NIDDK. Pyruvate kinase/lactic dehydrogenase enzymes from rabbit muscle were purchased from Sigma-Aldrich, Inc. Plasmid pAB1 was described previously [189]. Fluorescently labeled plasmids pAB1_FL905 and pAB1_FL924 were synthesized as described previously [189].

Chemicals.

LOPAC compound library, phosphoenol pyruvate, and NADH were purchased from Sigma-Aldrich, Inc. The MLSMR compound library was a compound collection at the Sanford Burnham Prebys Medical Discovery Institute. Vendors and sources of other chemical compounds are shown in Table S4. The identities of these chemical compounds were confirmed using mass spectrometry.

SDFQ HTS Assay.

Using pAB1_FL905, the assay was performed in 2 μL of 1 × DNA gyrase buffer (20 mM Tris-Acetate pH 7.9, 50mMKAc, 10mM $MgCl_2$, 2mMDTT, 1mM ATP, 0.1 mg/mL BSA). The following is the procedure: (1) Using the BioRAPTR, dispensed 1 μL of *E. coli* DNA gyrase (350 ng/ μL) with a final concentration in assay 175 ng/μL. (2) Using the BioRAPTR, dispensed 1 μL of DNA Rx pAB1_FL905 (6.425 ng/μL); final concentration in assay is 3.2125 ng/μL in assay. (3) Spun plate at 800 rpm for 30 s. (4) Incubated the plate at 37 °C for 2 h in the dark and read the plate on the Envision measuring fluorescence (excitation@484 nm, emission@ Em520). Z′-factor was calculated using the following equation:

$$Z' = 1 - \frac{3(\sigma_p\ +\ \sigma_n)}{\left|\mu_p -\ \mu_n\right|}$$

where σ_p, σ_n, μ_p, and μ_n represent the sample standard deviations and means for positive (p) and negative (n) controls, respectively. The robust Z′-factor (RZ’) was calculated using the medians rather than the means.

SDFQ HTS Assay.

Using pAB1_FL924, the assay was performed in 2 μL of 1 × DNA gyrase buffer. The following is the procedure: (1) Using the BioRAPTR, dispensed 1 μL of *E. coli* DNA gyrase (350 ng/μL) with a final concentration in assay 175 ng/μL. (2) Using the BioRAPTR, dispensed 1 μL of DNA Rx pAB1_FL924 (6.425 ng/μL); final concentration in assay is 3.2125 ng/μL in assay. (3) Spun plate at 800 rpm for 30 s. (4) Incubated the plate at 37 °C for 2 h in the dark and read the plate on the Envision measuring fluorescence (excitation at 531 nm, emission at Em595).

SDFQ-based DNA Gyrase Inhibition Assays.

The assays were performed in 30 μL of 1 × gyrase buffer containing 400 ng of of Rx pAB1_FL905 at 37 °C. 100 ng of DNA gyrase (8.9 nM) was used to supercoil the Rx pAB1_FL905 in the presence of different concentrations of a gyrase inhibitor. The fluorescence intensity at λ_{em} = 521 nm was monitored with

λ_{ex} = 494 nm in a microplate reader. The IC_{50} values were estimated by nonlinear fitting of the following equation:

$$F = F_{min} \frac{F_{max} - F_{min}}{1 + 10^{(\log(IC_{50}) - x)P}}$$

where *F* is the fluorescence intensity at the x concentration of an inhibitor, F_{max} and F_{min} are the maximum and minimum fluorescence of the DNA sample, respectively, and *P* is a slope parameter. Novobiocin was used as a positive control.

Agarose Gel-Based DNA Gyrase Inhibition Assays.

The assays were performed in 30 μL of 1 × gyrase buffer containing 400 ng of of Rx pAB1 at 37 °C. 100 ng of DNA gyrase was used to supercoil the Rx pAB1 in the presence of different concentrations of a gyrase inhibitor. After 15 min of incubation with the inhibitor at 37 °C, all reactions were stopped with 1 μL of stop solution (3% SDS and 250 mM EDTA). Samples were analyzed by electrophoresis in 1% w/v agarose gels followed by ethidium bromide staining and photographed under UV light. Novobiocin was used as a positive control.

DNA Gyrase-Mediated DNA Cleavage Assay.

250 ng of plasmid pBR322 and 20 nM of *E. coli* DNA gyrase were mixed and incubated in 1 × gyrase buffer at 37 °C for 15 min in the presence of an inhibitor or compound. After the incubation, 0.2% SDS and 0.1 mg/mL proteinase K were added to the reaction mixtures to trap the gyrase-inhibitor-DNA complex and digest the gyrase, respectively, by incubating for an additional 30 min at 37 °C. DNA samples were analyzed in 1% agarose gel containing 0.5 μg/mL ethidium bromide

in 1 × TAE buffer and photographed under UV light. Ciprofloxacin was used as a positive control.

Minimum Inhibitory Concentrations Assays.

Antibacterial MICs were obtained from three independent experiments using broth microdilution methods in 96-well plates according to Clinical and Laboratory Standards Institute guidelines. Cells were grown from a singles colony in MHIIB medium for 18 h at 37 °C in agitation. The cultures were then diluted to OD_{600} of 0.1 using MHIIB medium. 50 μL of the diluted cultures were added to 50 μL of serially diluted compounds in MHIIB in a 96-well plate and incubated at 37 °C for another 18−20 h. After OD_{600} was measured to monitor the inhibition, and 0.02% resazurin was added to each well and incubated for 4 h at 37 °C. After the incubation, fluorescence with a wavelength of 494 and 521 nm for excitation and emission, respectively, was measured using a plate reader and used to calculate the MIC values. Bacterial strains *S. aureus* (ATCC 14775), MRSA (ATCC BAA44), *B. subtilis* (ATCC 6633), *E. coli* (ATCC 25922), and *E. coli* BAS3023 that carries an imp4213 mutation [227] were used to determine the MICs. Ciprofloxacin and novobiocin were used as positive controls.

***E. coli* DNA Gyrase ATPase Assays.**

The assays were performed in 60 μL of 1 × gyrase ATPase buffer containing 50 nM of *E. coli* DNA gyrase or gyrB, 200 ng of Rx pAB1, 0.8mM of Phosphoenol pyruvate, 1.2 units of pyruvate kinase, 1.7 units of lactate dehydrogenase, and 0.4 mM of NADH at 37 °C. After the reaction mixtures were incubated 37 °C for 5 min, 2 mM of ATP was added to initiate the reaction. Absorbance at 340 nm was used to monitor the ATPase activities at 37 °C in a spectrophotometer.

Molecular Dynamics Simulation.

In order to get an accurate binding model of all selected compounds with *E. coli* DNA gyrase, we first performed molecular dynamics (MD) simulations to generate multiple conformations of the *E. coli* DNA gyrase subunit A and subunit B, respectively. Considering the different possible binding models of drugs on gyrA subunit, we constructed two gyrA subunits with short DNA segments that were nicked on both strands but at different positions to mimic the DNA double-strand break from FQ binding and NBTIs binding. Using the Charmm-Gui web interface [228], the three subunits were solvated in a cubic water box with TIP3 water, and the system was neutralized by adding 0.15 M of $MgCl_2$. The final systems contained ∼31,000 (gyrB), ∼218,000 (gyrA-FQ), and ∼222,000 (gyrA-NBTI) atoms respectively. NAMD 2.14 [229] was used to perform all-atom molecular dynamics with CHARMM36m [230] force field. The particle mesh Ewald method [231] was used for calculating the long-range ionic interactions. The systems were minimized for 100,000 steps, followed by a 250 ps equilibration at 310 K with 1 fs time step. 200 ns (gyrB) and 100 ns (gyrA) production simulation with 2 fs time step were performed at a constant pressure of 1 atm and T = 310 K. The Nose−Hoover Langevin piston method [232] was used for pressure coupling, with a piston period of 50 fs and a decay of 25 fs, and the Langevin temperature coupling with a friction coefficient of 1 ps^{-1} was used for maintaining the temperature. From the simulation trajectory, 1000 protein pdb frames for gyrB and 500 protein pdb frames for both gyrA systems were extracted using Visual Molecular Dynamics [233] for further in silico docking studies. After docking, another 100 ns MD simulation was performed for each protein−drug complex with the same input settings as described above.

***In Silico* Docking Studies.**

Chloro-IB-MECA and compound 48 were docked to 1000 MD-generated gyrB conformations. Compounds 40 and 154 were, respectively, docked to 500 MD-generated gyrA conformations (NBTI nicking model) and 500 MD-generated gyrA conformations (FQ nicking model). The protein pdb files and compounds structure were first converted to pdbqt format for docking. AutoDock Vina 1.1.2 [234] was used to perform molecular docking. Using custom scripts, compounds were screened against the protein conformations, and the resulting scores of the complexes were sorted and ranked according to their binding affinities.

Results

Establish Miniaturized, Automated SDFQ HTS Assays and Screen the LOPAC Library.

Based on the SDFQ assays using the fluorescently labeled Rx plasmid pAB1_FL905 (Figure 1a), we have established a miniaturized, automated primary HTS assay in a 1536-well format to identify bacterial DNA gyrase inhibitors. After a series of experiments, 2 μL of volume, 120 min of incubation time, 175 ng/μL of *E. coli* DNA gyrase, and 3.21 ng/μL of Rx pAB1_FL905 were optimal and chosen for the assay (Figure 1b, c). The fluorescence intensity was measured at the excitation wavelength of 484 nm and emission wavelength of 520 nm. The assay tolerated up to 4% DMSO without any significant change in signal. We used a known bacterial DNA gyrase inhibitor, novobiocin as the positive control. Results in Figure 1d clearly demonstrate that novobiocin is a potent gyrase inhibitor with an IC_{50} of 26 nM. Similar conditions were also obtained for a secondary SDFQ HTS assay in which Rx pAB1_FL924 (Figure 1a) was used as the DNA substrate (Figure 1e,f). The excitation wavelength of 531 nm and emission wavelength of 595 nm were used for the secondary HTS assay.

To validate HTS readiness, we screened the Sigma LOPAC1280 library of 1280 pharmacologically active compounds using the primary HTS assay. Figure 2a and Table 1 show the results. The following are screening statistics: Z′ = 0.70 and 41 hits/compounds of more than 40% inhibition activities with a hit rate of ∼3.2%. The hits include three known gyrase inhibitors (lomefloxacin, ofloxacin, and trovafloxacin) and several known DNA topoisomerase II inhibitors such as suramin [235], aurintricarboxylic acid [236],38 and emodin[177].

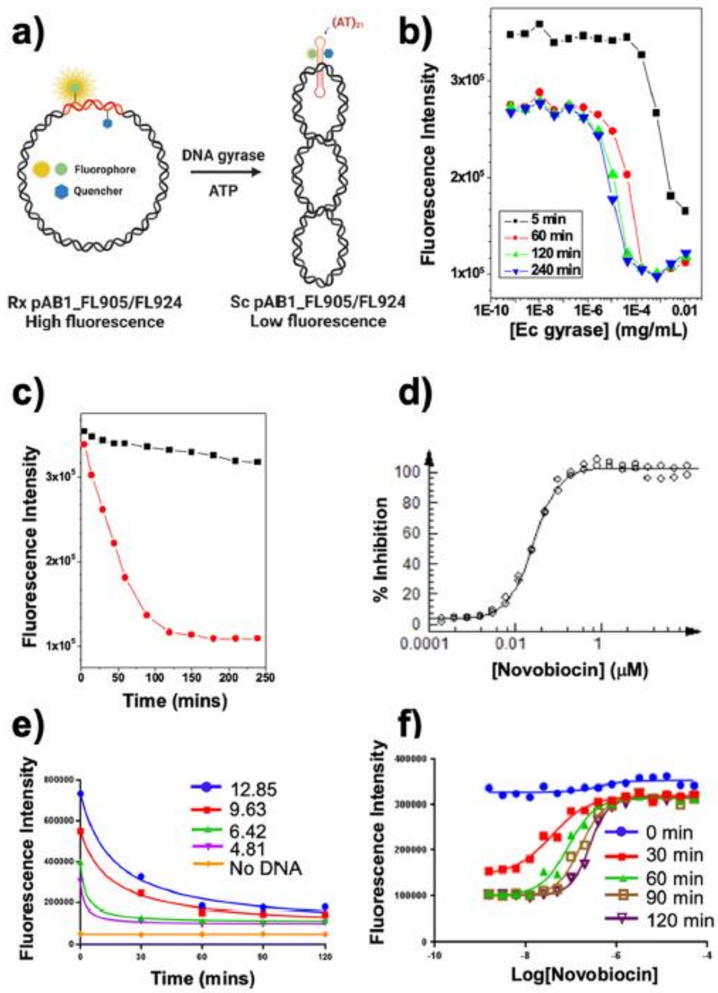


Figure 1. SDFQ assays to determine the optimal conditions for the HTS assays. All assays were performed as described for the HTS format in the Materials and Methods section. (**a**) SDFQ assay catalyzed by DNA gyrase. Plasmid pAB1_FL905 contains fluorescein and dabcyl as the fluorophore and quencher, respectively. Fluorescence was measured using λ_{ex} = 484 nm and λ_{em} = 520 nm. Plasmid pAB1_FL924 carries TAMRA and BHQ2 as the fluorophore and quencher, respectively. Fluorescence was measured using λ_{ex} = 531 nm and λ_{em} = 595 nm. (**b**) Different amounts of *E. coli* DNA gyrase were used in the SDFQ assays. (**c**) Time courses in the presence (red dots) or absence (black dots) of *E. coli* DNA gyrase (175 ng/mL). 6.42 ng/mL of Rx pAB1_FL905 was used in these assays. (**d**) Novobiocin potently inhibited *E. coli* DNA gyrase. The IC_{50} was determined to be 26 nM as described in the Materials and Methods section. The slope was determined to be 1.462. Assays used 3.21 ng/λL of pAB1_FL905 and 175 ng/λL of *E. coli* DNA gyrase. Fluorescence was measured using λ_{ex} = 484 nm and λ_{em} = 520 nm. The fluorescence signals of positive and negative controls are 812,515 ±15,320 and 338,057 ± 26,067, respectively. (**e**) SDFQ assays with different concentrations of pAB1_FL924 in ng/λL. (**f**) Novobiocin potently inhibited *E. coli* DNA gyrase activities. Fluorescence was measured using λ_{ex} = 531 nm and λ_{em} = 595 nm. The x-axis is the logarithm of novobiocin concentrations in molar (M). Different curves represent the incubation time in min.

Although the Sigma LOPAC1280 library carries two additional DNA gyrase inhibitors, nalidixic acid and oxolinic acid, their IC_{50} values against *E. coli* DNA gyrase are more than 30 μM [237], and it is not surprising that they are not included on the hit list since 5 μM of compounds was used. We also noticed that some compounds per se have very strong fluorescence, which results in more than 100% inhibition (Figure 2a and Table S1). They are false positives and should be excluded from the hit list.

Unexpectedly, two new *E. coli* DNA gyrase inhibitors were discovered from the pilot screen: chloro-IB-MECA (Figure 2b) and metergoline (Figure S1a). Their inhibition against *E. coli* DNA gyrase were confirmed by using agarose gel-based DNA gyrase assays (Figures 2c and S1b). Metergoline is a dopamine agonist and serotonin antagonist [238, 239] and inhibits gyrase activities at 100 and 200 μM for agarose gel-based assays (Figure S1b). Chloro-IB-MECA is an adenosine analogue and an antagonist of adenosine A3 receptors [240]. It potently inhibits *E. coli* DNA gyrase activities with an IC_{50} of 2.4 μM (Figure 2c,d). The LOPAC library also contains two similar adenosine analogues: IB-MECA and AB-MECA (Figure S1c). IB-MECA also inhibits *E. coli* DNA gyrase with an IC_{50} of 50.7 μM (Figure 2c,d). AB-MECA does not inhibit *E. coli* gyrase activities at all (Figure 2c). The ATPase assays of *E. coli* DNA gyrase show that chloro-IB-MECA and IB-MECA are ATP competitive inhibitors of *E. coli* DNA gyrase (Figure 2e). Interestingly, chloro-IBMECA did not strongly inhibit *E. coli* DNA topoisomerase I, *E. coli* DNA topoisomerase IV, human DNA topoisomerase I, and human DNA topoisomerase IIα (Figure S1d, e). It did not cause gyrase-mediated DNA double-stranded breaks as well (Figure S1f). The experimental results from the pilot screen demonstrate that our SDFQ-based assays are HTS-ready for an HTS campaign to identify new bacterial DNA gyrase inhibitors.

Screen the MLSMR Compound Library.

We screened the MLSMR compound library containing 370,620 compounds according to the workflow in Figure S2. The SDFQ primary assays were performed using a compound concentration of 5 μM. The screening results are summarized in Figure 3a and Table 1. Specifically, 2891 compounds have more than 40% inhibition activities against *E. coli* DNA gyrase with a hit rate of 0.78 (Table 1). We retested these 2891 compounds using the primary and secondary assays and found that 929 compounds have more than 32% inhibition activities against *E. coli* DNA gyrase in both assays with an assumption of up to a 20% variation (Table S2). We also analyzed the fluorescence results and found that some compounds have very high fluorescence at the wavelengths used for the signal detection which gives much more than 100% inhibition activities (Figure 3a and Table S2). These highly fluorescent compounds are false positives and were excluded from the potential DNA gyrase inhibitors.

We decided to conduct a more detailed analysis for the top 218 hits with gyrase inhibition activities between 50 and 120% in both primary and secondary assays (Table S3). Among these 218 compounds include 25 known gyrase inhibitors, such as novobiocin and ciprofloxacin, and 82 DNA intercalators or potential DNA intercalators, such as 9-aminoacridine [241], echinomycin [242], and several anthracyclines [243].

Table 1. SDFQ HTS Screen Statistics

	Pilot Screen	**HTS**
No. of compounds	1280	370,620
Tested concentration	5 µM	5 µM
Z' value	0.7	0.81
RZ' value	0.68	0.83
S/B[a]	2.5	2.7
No. of compounds with inhibition > 40%	41	2.891
Hit rate	3.20%	0.78%

S/B[a] represents signal versus background ratio.

When DNA intercalators bind to (−) Sc plasmid pAB1_FL905, they significantly unwind the plasmid DNA molecule and temporarily convert it into the relaxed or (+) supercoiled DNA molecule [244]. As a result, the AT hairpin structure is converted into the double-stranded form [224], and the fluorescence intensity of pAB1_FL905 is greatly enhanced. Figure S3 shows two examples in which ethacridine and echinomycin, DNA intercalators, significantly increase the fluorescence intensity of (−) Sc pAB1_FL905 upon binding to (−) Sc pAB1_FL905. Please note that ethacridine and echinomycin does not have fluorescence per se under this experimental condition. Interestingly, both intercalators also inhibited *E. coli* DNA gyrase activities at higher concentrations (Figure S3c, d), likely through DNA binding and blocking gyrase accessing to the plasmid DNA molecules. Due to this reason, we consider DNA intercalators as “false” positives. Detecting 25 known gyrase inhibitors among the 218 top hits demonstrates the success of the SDFQ HTS campaign.

Novel DNA Gyrase Inhibitors.

We purchased/obtained 235 compounds (Table S4) for further analyses based on the screening results and following selection criteria: (1) Compounds have similar inhibition activities against *E. coli* DNA gyrase in both primary and secondary assays; (2) compounds with more than 150% inhibition activities against DNA gyrase are excluded; 3) known DNA gyrase and topoisomerase II inhibitors are also excluded; (4) DNA intercalators or potential DNA intercalators are generally not selected; and (5) we did not specifically exclude pan-assay interference compounds (PAINS).

After we confirmed the identities of these compounds using mass spectrometry, agarose gel-based assays were used to determine their inhibition activities against *E. coli* DNA gyrase (Figure S4). Our results showed that 155 compounds are *E. coli* DNA gyrase inhibitors with an IC_{50} value of <200 μM (Figure S4). Among these 155 new gyrase inhibitors, 77 have an IC_{50} of <50 μM (Figure S4). Agarose gel-based and SDFQ-based titration experiments were used to determine the IC_{50} values of these 77 new DNA gyrase inhibitors and showed that 45 have an IC_{50} of <25 μM and 33 have an IC_{50} of <15 μM (Figure 3b, Figure S5, and Table S4).

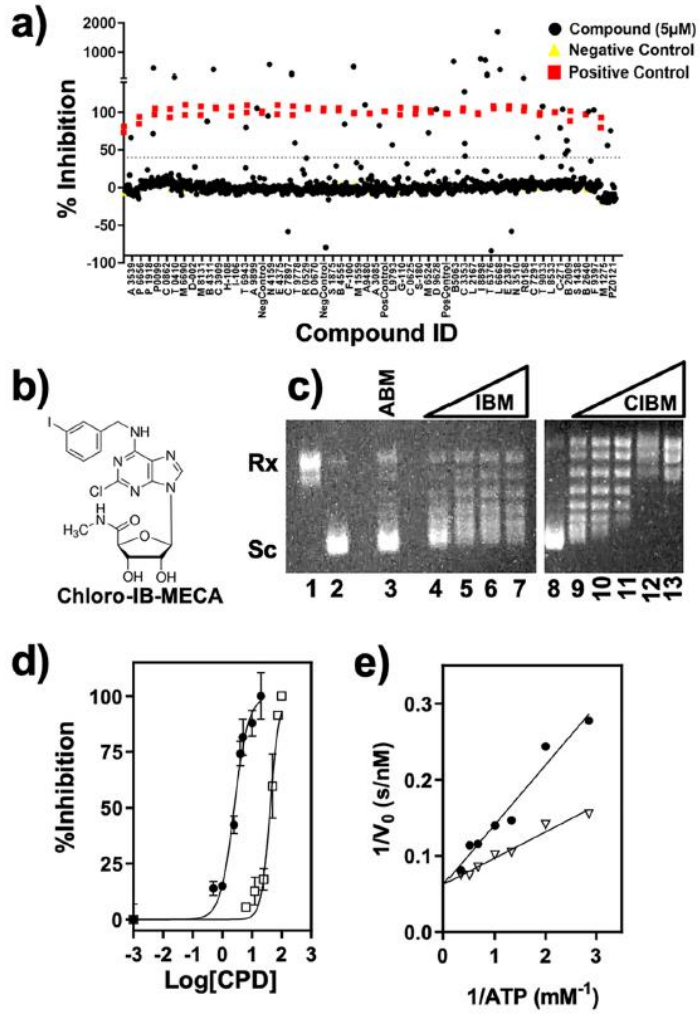


Figure 2. (**a**) The pilot screening of the LOPAC library at 5 μM for *E. coli* DNA gyrase inhibitors. DMSO and novobiocin were used as negative (yellow triangles) and positive (red squares) controls, respectively. Black dots are the screened compound results. The x-axis represents the catalog numbers of certain compounds from the LOPAC compound library (Sigma-Aldrich). (**b**) The chemical structure of chloro-IB-MECA (CIBM), a new gyrase inhibitor. (**c**) Gel-base DNA gyrase assays to confirm that CIBM and IB-MECA (IBM) inhibit *E. coli* DNA gyrase activities. Lanes 1 and 2 contain relaxed (Rx) and supercoiled (Sc) pAB1. Lanes 3−13 are DNA samples from DNA gyrase assays. Lane 3 contains 200 μM of AB-MECA (ABM). Lanes 4−7 contain 25, 50, 75, and 100 μM of IBM, respectively. Lanes 8−13 contain 0, 5, 10, 20, 50, and 100 μM of CIBM, respectively. (**d**) SDFQ-based gyrase assays in the presence of CIBM (solid circles) and IBM (open squares). The IC_{50} values against *E. coli* DNA gyrase are 2.4 ± 0.9 and 50.7 ± 4.7 μM, respectively. The standard deviations are calculated according to three independent experiments. The x-axis log[CPD] represents the logarithm of compound concentrations in μM. (**e**) Inhibition of *E. coli* DNA gyrase ATPase activities by CIBM in the presence of Rx pAB1. Closed circles and open down triangles represent the ATP hydrolysis in the absence and presence of 500 nM of CIBM, respectively. V_{max} are 16.3 and 16.6 nM/s for the ATPase activities of gyrase in the absence and presence of 500 nM of CIBM, respectively. K_M are 0.59 and 1.35 mM in the absence and presence of 500 nM of CIBM, respectively. The dissociation of the gyrase-CIBM complex K_i is calculated to be 388 nM.

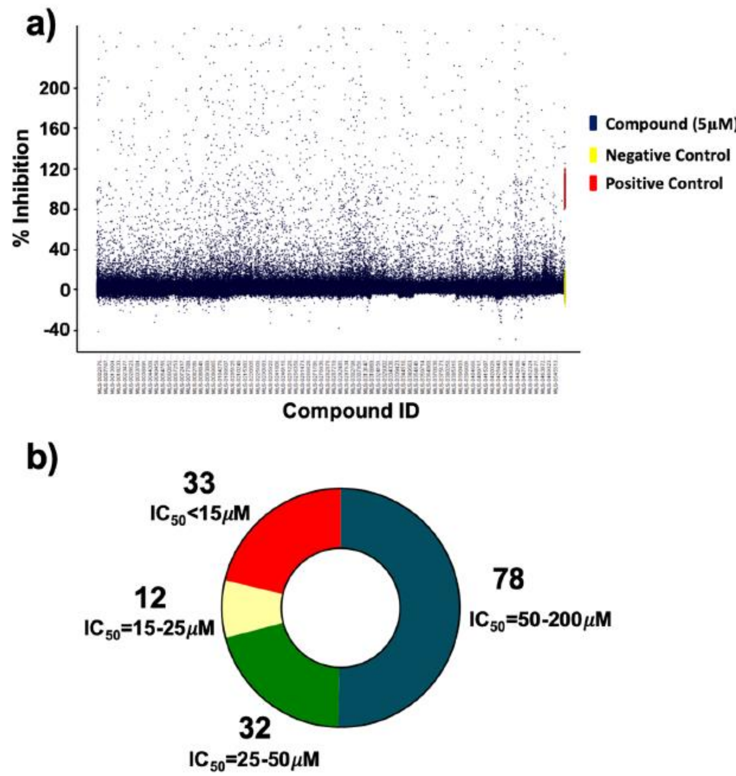


Figure 3. (**a**) The screening of the MLSMR compound library for *E. coli* DNA gyrase inhibitors. DMSO and novobiocin were used as negative and positive controls, respectively. The data are trimmed with 531 compounds >250% activities not shown. (**b**) 155 new gyrase inhibitors have an IC_{50} < 200 μM against *E. coli* DNA gyrase, and 33 compounds have an IC_{50} < 15 μM.

According to their chemical structures, these 155 new gyrase inhibitors can be divided into 10 groups: (1) psoralen derivatives, (2) quinazoline derivatives, (3) dihydroxynaphthalene-2-carboxylate and quinolinedione derivatives, (4) isatinphenylhydrazone derivatives, (5) amino-benzothiazole derivatives, (6) thiazolo[3,2-a]benzimidazole derivatives, (7) pyridothieno-pyrimidine derivatives, (8) compounds containing a rhodamine moiety, (9) fluorone derivatives, and (10) other compounds. We conducted a more detailed study for several new gyrase inhibitors and determined their MoA. For instance, compound 154, N-(6-chloro-4-phenylquinazolin-2-yl)-guanidine, is a quinazoline derivative (Figure 4a) and strongly inhibits *E. coli* DNA gyrase activities with an IC_{50} of approximately 7 μM (Figure 4b, c). Intriguingly, compound 154 also causes the gyrase-mediated DNA double-stranded breaks and single-stranded nicks (Figure 4d). A likely MoA of this gyrase inhibitor is to stabilize the enzyme-DNA cleavage complex, which leads to the DNA breaks and nicks. In other words, compound 154 is a bacterial DNA gyrase poison. Although the induced DNA breaks and nicks are generally proportional to the added inhibitor, high concentrations of compound 154 inhibit the formation of the double-stranded DNA breaks (compare lanes 4 to 6 of Figure 4d). Since human DNA topoisomerase IIα is a type IIA topoisomerase [203, 245] we also determined whether compound 154 inhibits human DNA topoisomerase IIα and found that it inhibits human DNA topoisomerase IIα with an estimated IC_{50} of ~50 μM (Figure 4e). As expected, compound 154 also causes the human topoisomerase IIα-mediated DNA nicks and double-stranded breaks (Figure 4f). Apparently, compound 154 is a human DNA topoisomerase IIα poison as well.

Compound 40, 1-[(4-carbamoylphenyl) carbamoyl] ethyl 1,4-dihydroxy-naphthalene-2-carboxylate (Figure 5a), also inhibits *E. coli* DNA gyrase activities with an IC_{50} of 50 μM (Figure 5b, c). Similar to compound 154, it causes gyrase-mediated DNA double-stranded breaks and single-stranded nicks and is a bacterial DNA gyrase poison (Figure 5d).

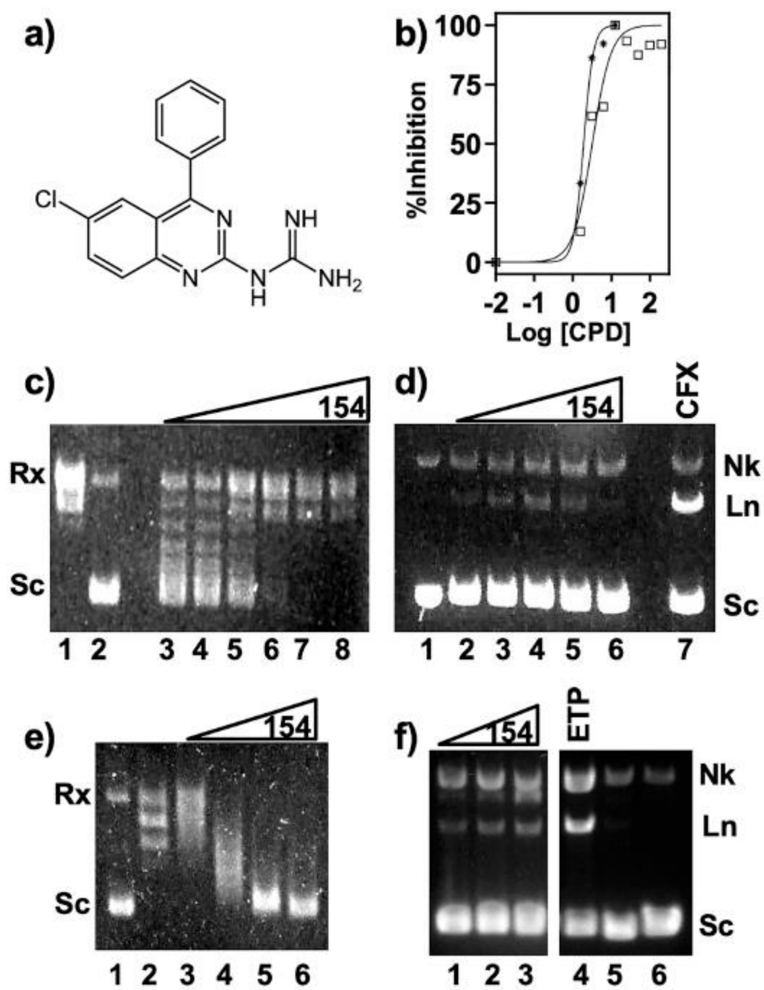


Figure 4. Compound 154 is a bacterial DNA gyrase poison. (**a**) Chemical structure of compound 154. (**b**) SDFQ-based gyrase assays in the presence of compound 154 (open squares) and novobiocin (stars). The IC_{50} values against *E. coli* DNA gyrase are 3.1 ± 0.7 μM. The standard deviations are calculated according to three independent experiments. (**c**) Agarose gel-based gyrase inhibition assays for compound 154. Lanes 3−8 correspond to 1.56, 3.12, 6.25, 12.5, 25, and 50 μM of the compound, respectively. Lanes 1 and 2 are relaxed and supercoiled plasmid pAB1, respectively. (**d**) Gyrase-mediated DNA cleavage assays were performed as described in the Materials and Methods section using plasmid pBR322. Lane 1 does not contain a gyrase inhibitor. Lanes 2−5 contain 5, 25, 50, 100, and 200 μM of compound 154, respectively. Lane 7 contains 50 μM of ciprofloxacin (CFX). (**e**) Agarose gel-based inhibition assays against human DNA topoisomerase IIα for compound 154. Lanes 3−6 correspond to 0, 25,50, and 100 μM of the compound, respectively. Lanes 1 and 2 are supercoiled and relaxed plasmid pAB1, respectively. (**f**) Human DNA topoisomerase IIα-mediated DNA cleavage assays were performed as described in the Materials and Methods section using plasmid pBR322. Lanes 1−3 contain 50, 100, and 200 μM of compound 154, respectively. Lane 4 contains 100 μM of etoposide (ETP). Lanes 5 and 6 contain DNA samples from the assay mixtures in the absence of ETP and human DNA topoisomerase IIα, respectively. Symbols Rx, Sc, Nk, and Ln represent relaxed, supercoiled, nicked, and linear DNA, respectively.

We noticed that compound 40 causes many more DNA nicks than double stranded DNA breaks (compare lanes 1 to 4 of Figure 5d). Compound 40 does not inhibit human DNA topoisomerase IIα (Figure 5e). It does not cause the human topoisomerase IIα-mediated DNA nicks and double-stranded breaks (Figure 5f).

Among these new DNA gyrase inhibitors are 12 psoralen derivatives. A preliminary structure−activity relationship has been determined. Figures 6 and S6 show our results. All psoralen derivatives except compounds 118 and 122 inhibited *E. coli* DNA gyrase activities. The 9-methyl group enhances the anti- DNA gyrase potency. A bulky hydrophobic group at the third position and a carboxyl group at the sixth position are required for the anti-DNA gyrase activities. Our ATPase assays showed that all psoralen derivatives are ATP competitive inhibitors of DNA gyrase (Figure S7). A further analysis of compound 48 shows that it inhibited the ATPase activities of *E. coli* DNA gyrase with a K_i (the dissociation constant for the inhibitor) value of 150 nM (Figure S7). These psoralen derivatives did not greatly inhibit *E. coli* DNA topoisomerase I and human DNA topoisomerase IIα with IC_{50} > 100 μM (Figure S7). They did not cause gyrase-mediated DNA cleavage and are not DNA poisons (data not shown).

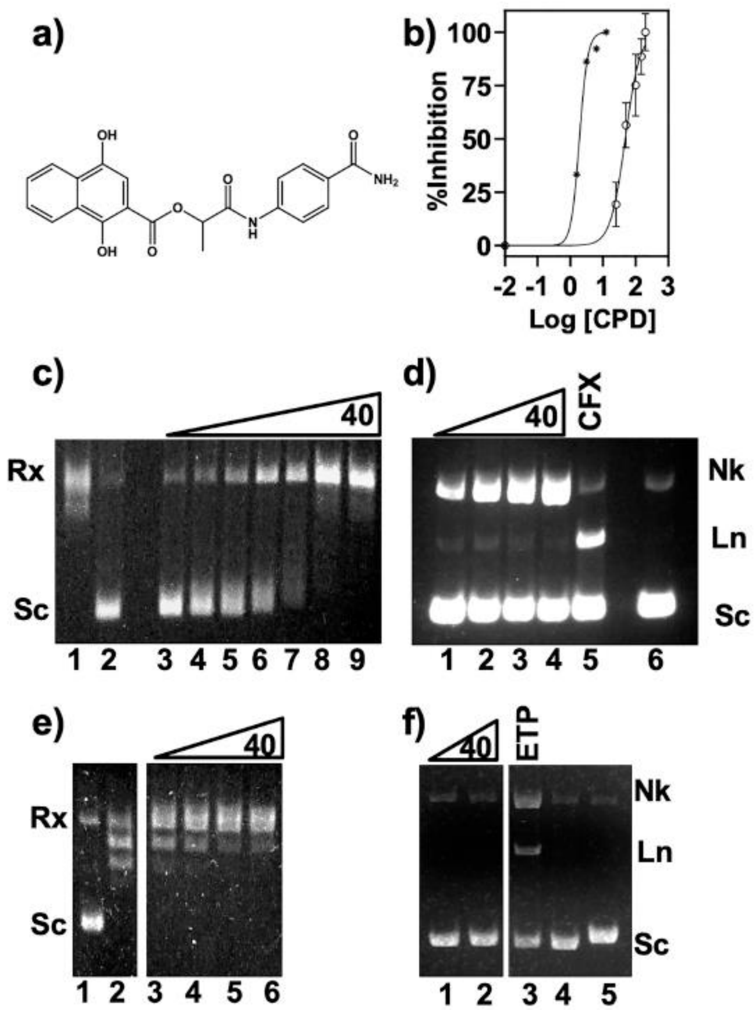


Figure 5. Compound 40 is a bacterial DNA gyrase poison. (**a**) Chemical structure of compound 40. (**b**) SDFQ-based gyrase assays in the presence of compound 40 (open circles) and novobiocin (solid stars). The IC_{50} values against *E. coli* DNA gyrase are 47.6 ± 3.7 μM. The standard deviations are calculated according to three independent experiments. (**c**) Agarose gel-based gyrase inhibition assays for compound 40. Lanes 3−9 correspond to 6.25, 12.5, 25, 50, 100, 150, and 200 μM of compound 40, respectively. Lanes 1 and 2 are relaxed and supercoiled plasmid pAB1, respectively. (**d**) Gyrase-mediated DNA cleavage assays were performed as described in the Materials and Methods section using plasmid pBR322. Lanes 6 and 1−4 contain 0, 25, 50, 100, and 200 μM of compound 40, respectively. Lane 5 contains 50 μM of ciprofloxacin (CFX). (**e**) Agarose gel-based inhibition assays against human DNA topoisomerase IIα for compound 40. Lanes 3−6 correspond to 12.5, 25, 50, and 100 μM of compound 40, respectively. Lanes 1 and 2 are relaxed and supercoiled plasmid pAB1, respectively. (**f**) Human DNA topoisomerase IIα-mediated DNA cleavage assays were performed as described in the Materials and Methods section using plasmid pBR322. Lanes 1 and 2 contain 100 and 200 μM of compound 40, respectively. Lane 3 contains 100 μM of etoposide (ETP). Lanes 4 and 5 contain DNA samples from the assay mixtures in the absence of etoposide and human DNA topoisomerase IIα, respectively. Symbols Rx, Sc, Nk, and Ln represent relaxed, supercoiled, nicked, and linear DNA, respectively.

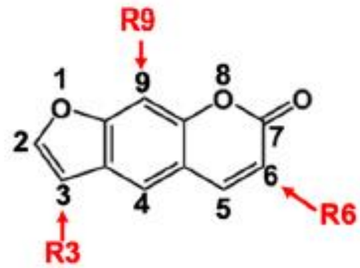
Antibacterial Activities

We carried out antibacterial studies for compounds 40 and 154 and the 12 psoralen derivatives. Both Gram-positive and -negative strains are included. Table 2 shows our results. Compound 154 showed significant antibacterial activities against all bacterial strains including the wild-type *Escherichia coli* strain ATCC 25922, *Staphylococcus aureus* ATCC 14775, and methicillin-resistant *Staphylococcus aureus* (MRSA) ATCC 33591. Compound 40 showed anti-*Bacillus subtilis* activities with a minimal inhibitory concentration (MIC) value of 100 μM. Certain psoralen derivatives showed potent antibacterial activities against *Staphylococcus aureus* ATCC 14775 and MRSA ATCC 33591. For instance, the MIC values of compounds 119 and 120 against *Staphylococcus aureus* ATCC 14775 and MRSA ATCC 33591 are 0.39 and 0.78 μM, respectively. Intriguingly, the antibacterial activities of these psoralen derivatives are correlated with the anti-DNA gyrase activities. As shown above, the 9-methyl group enhances the anti-gyrase potency and is also required for the antibacterial activities against *S. aureus* and MRSA. Likewise, a bulky hydrophobic group at the third position and a carboxyl group at the sixth position are required for the anti-gyrase and antibacterial activities as well. Although compound 125 potently inhibited *E. coli* DNA gyrase, it did not inhibit the growth of *S. aureus* and MRSA (Table 2). Possibly, the amine in the bulky hydrophobic group at the third position prevented the entry of the compound to bacterial cells. Further studies are needed to confirm this hypothesis.

Discussion

We have established a miniaturized, automated HTS assay based on the SDFQ assay [189, 190] to identify *E. coli* DNA gyrase inhibitors. This HTS assay demonstrated excellent statistics for two screens: a pilot screen of the LOPAC library and a full HTS campaign of the MLSMR library with Z′ values at 0.7 and 0.81, respectively (Table 1). After the pilot screen, we discovered two new gyrase inhibitors: chloro-IB-MECA (Figure 2b) and metergoline (Figure S1a). Since chloro-IB-MECA is an adenosine analogue and a potent gyrase inhibitor (Figure 2c, d), this result suggests that adenosine analogues have potential to be developed into antibiotics targeting bacterial DNA gyrase. More importantly, after the HTS campaign of screening the MLSMR compound library, we discovered 155 new gyrase inhibitors that provide novel and diverse chemical structures and scaffolds for further development.

This new HTS assay has several advantages. First, it can be automated for HTS studies, an advantage over existing screening assays [186-188, 246]. Our successful HTS campaign of screening the MLSMR library attests the power and potential of this assay. This HTS assay not only can be used to screen and identify bacterial DNA gyrase inhibitors but also can be applied to screen and identify inhibitors of other DNA topoisomerases, such as bacterial DNA topoisomerase I, human DNA topoisomerase 1, and human DNA topoisomerase IIα. Second, unlike previous HTS efforts mainly targeted the gyrB ATPase domain of bacterial gyrase [146], this HTS assay, employed relaxed DNA as the substrate, would identify inhibitors that affect all possible steps of the catalytic cycle of *E. coli* DNA gyrase, including DNA binding, DNA cleavage, strand passage, and DNA relegation.



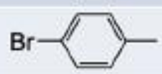
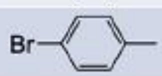
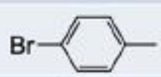
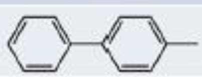
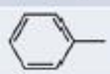
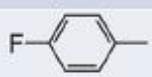
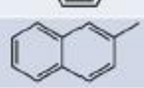
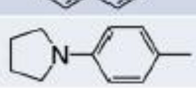
CPD#	R3	R6	R9	IC_{50} (µM)
25		$(CH_2)_2COOH$	H	11.5
46		$(CH_2)_2COOH$	H	11.4
48		$(CH_2)_2COOH$	CH_3	4.2
117		CH_2COOH	CH_3	15.7
118		CH_3	CH_3	>200
119		$(CH_2)_2COOH$	CH_3	7.7
120		$(CH_2)_2COOH$	CH_3	7.9
121		$(CH_2)_2COOH$	CH_3	28
122	CH_3	$(CH_2)_2COOH$	CH_3	>200
123		$(CH_2)_2COOH$	CH_3	28.1
124		$(CH_2)_2COOH$	CH_3	5.5
125		$(CH_2)_2COOH$	CH_3	4.9

Figure 6. Psoralen derivatives are potent gyrase inhibitors with antibacterial activities. The IC_{50} against *E. coli* were determined using the SDFQ- and confirmed with gel-based gyrase inhibition assays.

Table 2. Minimal Inhibitory Concentrations (MIC) against various bacterial strains by Microbroth Dilution

Cmpd No.	MIC (μM)				
	E. coli **ATCC 25922**	***E. coli*** **imp BAS3023**	***S. aureus*** **ATCC 14775**	**MRSA ATCC 33591**	***B. subtilis*** **ATCC 6633**
40	>200	>200	>200	>200	100
154	50	25	12.5-25	12.5-25	50
25	>200	>200	>200	>200	25
46	>200	>200	>200	>200	6.25
48	>200	>200	3.125	3.125	>200
117	>200	>200	0.78	0.78	>200
118	>200	>200	200	200	>200
119	>200	>200	0.39	0.78	>200
120	>200	>200	0.39	0.78	>200
121	>200	100	3.125	3.125	50
122	>200	>200	200	200	>200
123	>200	>200	1.56	1.56	6.25
124	>200	>200	1.56	1.56	25-50
125	>200	>200	>200	>200	>200

For example, ethacridine and echinomycin are two DNA intercalators and bind to DNA with high affinity [242, 247]. They also potently inhibited *E. coli* DNA gyrase activities (Figure S3c,d), although DNA intercalation/unwinding of pAB1_FL905 by these two intercalators interferes with the fluorescence signal detection (Figure S3a,b). In fact, many DNA intercalators are among the hits of this HTS campaign (Table S3). It is likely that DNA binding by DNA intercalators is the inhibition MoA. As discussed above, we identified more than 10 different groups of *E. coli* DNA gyrase inhibitors. While chloro-IB-MECA and psoralen derivatives are competitive inhibitors of *E. coli* DNA gyrase (Figures 2e and S7), compounds 40 and 154 stabilize the gyrase-DNA cleavage complex and cause DNA double-stranded breaks and single-stranded nicks (Figures 4 and 5). Additionally, this HTS assay is a cost-effective assay and only uses 6.42 ng in 2 μL per assay/well in 1536 well plates. Approximately 2.5 mg of Rx pAB1_FL905 was used to screen 370,620 compounds in the MLSMR library for the primary assay. It is feasible to conduct more screens in the future for bacterial DNA gyrase and other DNA topoisomerases.

A major difficulty of this HTS assay is the fluorescence interference caused by certain compounds that have very strong fluorescence per se. This interference results in over 100% inhibition. We are considering these fluorescent compounds as false positives. However, some compounds with high fluorescence may be gyrase inhibitors and will be missed here. An orthogonal screening assay using a different mechanism, such as the T5 exonuclease-based HTS assays [191], may be used to identify these gyrase inhibitors. Nevertheless, as stated above, the HTS assay is an excellent assay to identify inhibitors targeting the catalytic cycle of DNA topoisomerases including DNA gyrase. It cannot differentiate catalytic inhibitors and poisons, although DNA topoisomerase poisons also inhibit the catalytic activities of DNA topoisomerases. Gel-based DNA cleavage assays are required to identify DNA topoisomerase poisons. Indeed, 8 DNA gyrase poisons have been identified in this study (Table S4).

The most exciting result of this HTS campaign is the discovery of 155 new DNA gyrase inhibitors (Table S4). Some of them showed potent antibacterial activities (Table 2), and eight are gyrase poisons (Table S4). For instance, compound 154, a quinazoline derivative, is a new DNA gyrase poison with significant antibacterial activities (Figure 4 and Table 2). Structurally, this new gyrase poison is different from quinolones [211] and quinolone-like gyrase poisons, quinazolinediones [248, 249]. It does not carry a quinone moiety and a carboxy group that can interact with the quinolone-resistance-determining region of DNA gyrase [250, 251], suggesting that compound 154 may overcome quinolone-resistant mutations [250]. In other words, compound 154 provides a promising new scaffold for the development of novel antibiotics to treat FQ-resistant bacterial infections [250]. Compound 154 is a small-size molecule with a molecular weight of 297.75 Da and should have great potential for derivatization and bacterial cell penetration [146]. According to its chemical structure, it is likely that compound 154 binds to bacterial DNA gyrase through gyrase-mediated DNA intercalation [250]. Indeed, our molecular modeling results show that compound 154 nicely intercalates into DNA base pairs near the gyrase cleavage sites in the gyrase-DNA-drug complex although compound 154 does not directly interact with DNA gyrase (Figure 7a, b). Interestingly, compound 154 is also a human DNA topoisomerase IIα poison with a higher IC_{50} value. This is not very surprising since bacterial DNA gyrase and human DNA topoisomerase IIα belong to type 2A topoisomerases [203, 245].

Previous results showed that certain FQs and quinazoline derivatives are human DNA topoisomerase IIα poisons too [252, 253]. The scaffold of compound 154 may be developed into specific bacterial gyrase or human topoisomerase IIα inhibitors/poisons depending on design and derivatization.

Compound 40, a 1,4-dihydroxy-2-naphthoic acid derivative, is another new *E. coli* DNA gyrase poison discovered in this study (Figure 5). Although it does not strongly inhibit *E. coli* DNA gyrase activities (Figure 5b, c), compound 40 induces the formation of gyrase-mediated DNA nicks and double-stranded breaks (Figure 5d). Noticeably, it induces much more single stranded DNA nicks than the double-stranded breaks (Figure 5d).

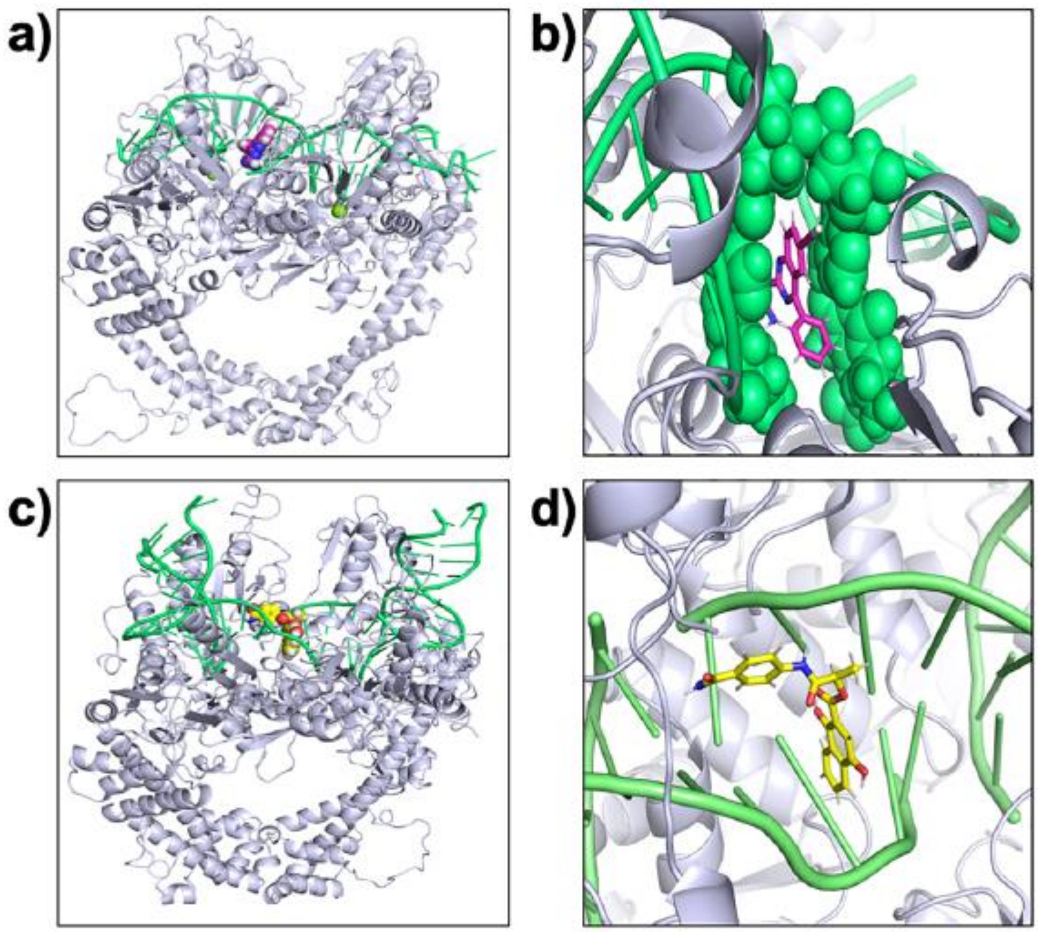


Figure 7. Molecular models of compounds 154 (**a** and **b**) and 40 (**c** and **d**) binding to gyrase-DNA complexes. Molecular models were constructed as described in the Materials and Methods section. (**a**) Compound 154 is shown in space fill model. (**b**) Compound 154 (stick model) intercalates between DNA base pairs (space fill models). (**c**) Compound 40 is shown in space fill model. (**d**) Compound 40 (stick model) intercalates between DNA base pairs (green).

Compound 40 carries a fused six-member aromatic ring system with a delocalized conjugated π system that may intercalate into DNA base pairs, connecting to a benzamide group through a flexible linear linker (Figure 5a). This structure feature is similar to that of NBTIs [125], although the linker is shorter. We therefore performed a molecular modeling studies based on a cryoEM structure of *E. coli* DNA gyrase nucleoprotein complex with gepotidacin, an NTBI [254]. Our molecular modeling results show that the fused six-member aromatic ring system intercalates into DNA base pairs of the nicking site (Figure 7c,d), and the benzamide group lies on the floor of the major groove (Figure 7c,d), unlike the binding of gepotidacin to the gyrase nucleoprotein complex likely due to the short linker of compound 40. In contrast to compound 154, compound 40 does not inhibit human DNA topoisomerase IIα and cause topoisomerase IIα-mediated DNA nicks and double stranded breaks as well (Figure 5c,d). In other words, compound 40 is a specific gyrase poison. Among the 155 new gyrase inhibitors, compounds 81, 205, and 234 have similar chemical structures and also cause gyrase-mediated DNA nicking (Table S4).

Many of these newly discovered gyrase inhibitors are catalytic inhibitors of *E. coli* DNA gyrase including chloro-IB-MECA and psoralen derivatives. Chloro-IB-MECA is the first adenosine analogue gyrase inhibitor discovered so far. As expected, chloro-IB-MECA is an ATP competitive inhibitor of *E. coli* DNA gyrase. Nevertheless, chloro-IB-MECA does not strongly inhibit other DNA topoisomerases. Some minor modifications significantly affect the IC_{50} values against *E. coli* DNA gyrase, suggesting specific interactions exist between chloro-

IB-MECA and *E. coli* DNA gyrase. These results suggest that adenosine analogues should be explored as specific gyrase inhibitors in the future although previous campaigns to identify antibiotics targeting the ATPase domain of bacterial DNA gyrase have not been successful [146]. Psoralen derivatives are another type of ATP competitive inhibitor of *E. coli* DNA gyrase. Similar to chloro-IBMECA, certain modifications are critical for their anti-gyrase activities. Figure S8 shows our molecular modeling results of these two new gyrase inhibitors binding to the ATP binding pocket of gyrB. Both compounds form a hydrogen bond with residue Asp73 of gyrB [49, 146].

MIC results showed that compound 154 has potent antibacterial activities against *E. coli*, *S. aureus*, MRSA, and *B. subtilis* (Table 2) and has potential to be developed into broad spectrum antibiotics. Our preliminary MTT cell viability results, however, show that compound 154 is cytotoxic toward human A549 cells (data not shown). Future medicinal chemistry modifications should focus on synthesizing and selecting derivatives with less cytotoxicity. Since compound 154 is also a human DNA topoisomerase IIα poison (Figure 4f), this compound and derivatives can be developed into anticancer drugs. Further studies are required. We also noticed that compound 40 and 12 psoralen derivatives do not have strong antibacterial activities against *Escherichia coli* strains ATCC 25922 and BAS3023 (Table 2). It is possible that these compounds cannot cross the *E. coli* cell envelope and inhibit DNA gyrase *in vivo*. Additionally, the lack of antibacterial activity of compound 40 may stem from the fact that it is an ester and might be hydrolyzed in cell-based assays. More studies are needed to confirm this possibility.

Nevertheless, certain psoralen derivatives have potent antibacterial activities against *S. aureus*, MRSA, and *B. subtilis* (Table 2). More importantly, their antibacterial activities correlate with their anti-DNA gyrase activities. As stated above, a bulky hydrophobic group at the third position and a carboxyl group at the sixth position are required for their anti-gyrase activities. Interestingly, these two groups are also required for their antibacterial activities, indicating that the DNA gyrase is the cellular target of these psoralen derivatives.

Conclusions

In summary, we have developed an HTS assay based on the SDFQ assay and screened the LOPAC and MLSMR libraries. After the screen, we identified 155 new bacterial DNA gyrase inhibitors including catalytic inhibitors and gyrase poisons. Not only can this HTS assay be applied to screen inhibitors against other DNA topoisomerases, but also the new gyrase inhibitors provide a wealth of chemical structures/scaffolds to develop new generations of antibiotics targeting bacterial DNA gyrase that combat multidrug-resistant bacterial pathogens.

III. POTENT INHIBITION OF BACTERIAL DNA GYRASE BY DIGALLIC ACID AND OTHER GALLATE DERIVATIVES.

Abstract

Bacterial DNA gyrase, an essential enzyme, is a validated target for discovering and developing new antibiotics. Here we screened a pool of polyphenols and discovered that digallic acid is a potent DNA gyrase inhibitor. We also found that several food additives based on gallate, such as dodecyl gallate, potently inhibit bacterial DNA gyrase. Interestingly, the IC_{50} of these gallate derivatives against DNA gyrase is correlated with the length of hydrocarbon chain connecting to the gallate. These new bacterial DNA gyrase inhibitors are ATP competitive inhibitors of DNA gyrase. Our results also show that digallic acid and certain gallate derivatives potently inhibit *E. coli* DNA topoisomerase IV. Several gallate derivatives have strong antimicrobial activities against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA). This study provides a solid foundation for the design and synthesis of gallate-based DNA gyrase inhibitors that may be used to combat antibacterial resistance.

Introduction

Prokaryotic DNA gyrase is a type IIA DNA topoisomerase essential to bacterial survival [203, 245]. Due to its importance, bacterial DNA gyrase is a validated and highly valuable target for discovering new antibiotics to treat bacterial infection [22, 181, 202]. Fluoroquinolones (FQs), which target bacterial DNA gyrase, are among the most prescribed and successful antibiotics [210, 211, 255]. The mechanism of antibacterial activities of FQs is to stabilize the gyrase-DNA cleavage-complex [81, 212, 221], which is ultimately responsible for cell death [251]. Since certain bacteria have another type IIA DNA topoisomerase, topoisomerase IV [34], FQs also target topoisomerase IV and stabilize DNA□topoisomerase IV complexes which leads to generate DNA double breaks during DNA replication [256, 257]. This gyrase and topoisomerase IV dual poisoning mechanism makes FQs among the most effective antibiotics [251]. Unfortunately, FQ resistance has emerged [215, 217-219, 250]. New and more effective antibiotics are needed to treat FQ resistant bacterial infections [150, 251, 258]. Additionally, FQs have been explored extensively [213, 251]. It is likely that the limits and potential of FQs have been reached [213, 251]. Another concern for the use of FQs is that these compounds can cause serious side effects including tendonitis and tendon rupture, peripheral neuropathy, hyperglycemia, and aortic dissections and aortic aneurysm [259-263]. As a result, US Food and Drug Administration (FDA) issued several warnings for the use of FQs and added black box warnings on all FQs [111]. Therefore, there is a need to develop and identify new types of compounds targeting bacterial DNA gyrases for treating bacterial infections.

Natural products, such as polyphenols, are rich sources to identify antibiotics or antibacterial agents [111, 264-266]. For instance, ellagic acid, found in a large variety of foods including pecan, walnuts, cranberries, strawberries, and pomegranates [267], is a potent bacterial DNA gyrase inhibitor [268] and has antibacterial activities [269, 270]. Antibiotic novobiocin, produced by *Streptomyces niveus* [271], is also a polyphenol [272] and has strong antibacterial activities especially against Gram-positive bacteria [146]. It potently inhibits bacterial DNA gyrase [146]. Mechanistically, novobiocin is a competitive inhibitor of the ATPase of bacterial DNA gyrase with the inhibition dissociation constant K_i of ~10 nM [154, 190]. Structural studies showed that novobiocin competes with ATP for the ATP-binding site of gyrB [63]. However, due to its toxicity, novobiocin has been withdrawn from clinical use [146]. Other polyphenols, such as epigallocatechin gallate (EGCG) [168], haloemodin [178], and quercetin [173] also have anti-bacterial DNA gyrase activity. Nevertheless, chemically, these polyphenols are not easy to be modified or derivatized, which is required for improving their potency. This prompted us to identify polyphenol- based gyrase inhibitors that can be easily modified/derivatized.

Herein we report the discovery of a new potent bacterial DNA gyrase inhibitor digallic acid after we screened a pool of naturally occurring polyphenols. We also find that several food additives based on gallic acid or gallate potently inhibit bacterial DNA gyrase. These gallate derivative inhibit bacterial DNA topoisomerase IV as well. Two derivatives octyl gallate and dodecyl gallate have strong anti-bacterial activities against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA). These simple gallate-based gyrase inhibitors can be easily modified/derivatized and should have potential to be developed into anti-bacterial agents.

Materials and methods

Materials

Human topoisomerase I, IIα, and kinetoplast DNA (kDNA) were purchased from TopoGen, Inc. (Buena Vista, CO). *E. coli* DNA gyrase and topoisomerase I were purified as described previously [190, 226]. *E. coli* DNA topoisomerase IV was kindly provided by Keir C. Neuman at the National Heart, Lung, and Blood Institute. Ethidium bromide, buffer-saturated phenol, and ethanol were purchased from Fisher Scientific, Inc. Gallic acid, ellagic acid, butyl gallate, octyl gallate, and dodecyl gallate were bought from Fisher Scientific, Inc. Digallic acid was purchased from Santa Cruz Biotechnology, Inc. Phenyl gallate (NSC333571) and biphenyl gallate (NSC406820) were obtained through NCI Developmental Therapeutics Program. Vendors of other polyphenols analyzed in this study are provided in Table S1. Plasmid pAB1 and fluorescently labeled plasmid pAB1_FL905 were described previously [189].

Gel- and supercoiling dependent fluorescence quenching (SDFQ)-based gyrase DNA supercoiling and inhibition assays

DNA supercoiling assays were carried out in 30 μL of 1×gyrase buffer (35 mM Tris-HCl, 24 mM KCl, 4 mM $MgCl_2$, 2 mM DTT, 0.1 mg/mL BSA, 6.5% glycerol, and 1.75 mM ATP, pH 7.5) containing 8.9 nM of *E. coli* DNA gyrase and 400 ng of relaxed plasmid pAB1 or pAB1_FL905. The reaction mixtures were incubated at 37 °C for 30 minutes. For gel-based assays, the reactions were stopped by the addition of 1 μL of stop solution (2% SDS and 200 mM EDTA). DNA samples were analyzed by using 1% agarose gels in 1×TAE buffer followed by ethidium bromide staining and photographed under UV light. For SDFQ-based assays, DNA samples were transferred to a 384-well plate. Fluorescence measurements were performed in a Biotek Synergy H1 Hybrid Plate Reader using a wavelength of 494 nm and 521 nm for excitation and emission, respectively. For DNA gyrase inhibition assays, each compound was mixed with *E. coli* DNA gyrase and incubated on ice for 5 min. Then, relaxed pAB1 was added to initiate the supercoiling reaction.

DNA relaxation assays by different DNA topoisomerases

DNA relaxation assays by *E. coli* DNA topoisomerase I, human DNA topoisomerase I, and human DNA topoisomerase IIα was described previously [190]. DNA relaxation assays by *E. coli* DNA topoisomerase IV was performed in 20 μL of 1×topoisomerase IV buffer (35 Mm Tris-HCl, 24 mM KCl, 4 mM $MgCl_2$, 2 mM DTT, 0.1 mg/mL BSA, 6.5% glycerol, 100 mM potassium glutamate, and 1.75 mM ATP, pH 7.5) containing 2 nM of DNA topoisomerase IV and 200 ng of supercoiled plasmid pAB1. The reaction mixtures were incubated at 37 °C for 30 minutes and stopped by the addition of 1 μL of stop solution (2% SDS and 200 mM EDTA). DNA samples were analyzed by using 1% agarose gels in 1×TAE buffer followed by ethidium bromide staining and photographed under UV light.

DNA decatenation assays by *E. coli* DNA topoisomerase IV

DNA decatenation assays by *E. coli* DNA topoisomerase IV was performed in 30 μL of 1×topoisomerase IV buffer (35 mM Tris-HCl, 24 mM KCl, 4 mM $MgCl_2$, 2 mM DTT, 0.1 mg/mL BSA, 6.5% glycerol, 100 mM potassium glutamate, and 1.75 mM ATP, pH 7.5) containing 1 nM of DNA topoisomerase IV and 200 ng of kDNA. The reaction mixtures were incubated at 37°C for 30 minutes and stopped by the addition of 1 μL of stop solution (2% SDS and 200 mM EDTA). DNA samples were analyzed by using 1% agarose gels in 1×TAE buffer followed by ethidium bromide staining and photographed under UV light.

***E. coli* DNA gyrase cleavage assays**

250 ng of plasmid pBR322 and 20 nM of *E. coli* DNA gyrase were mixed and incubated in 1×gyrase buffer at 37°C for 15 minutes in the presence of an inhibitor or compound. After the incubation, 0.2% SDS and 0.1 mg/ml proteinase K were added to the reaction mixtures to trap the gyrase-inhibitor-DNA complex and digest the gyrase, respectively, and incubated for an additional 30 min at 37°C. DNA samples were analyzed in 1% agarose gel containing 0.5 μg/mL ethidium bromide in 1×TAE buffer and photographed under UV light.

E. coli DNA gyrase and topoisomerase IV ATPase linked assay

A linked assay that couples the ATP hydrolysis with the conversion of NADH to NAD^+ was used to determine the ATPase activity of *E. coli* DNA gyrase. Briefly, the assays were conducted in 60 μL of 1×ATPase buffer (10 mM Tris·HCl (pH 7.5), 0.2 mM EDTA, 1 mM magnesium chloride, 1 mM DTT, and 2% (w/v) glycerol) containing 50 nM of *E. coli* DNA gyrase or gyrB, 200 ng of relaxed pAB1, 0.8 mM of phosphoenol pyruvate, 1.2 units of pyruvate kinase, 1.7 units of lactate dehydrogenase, and 0.4 mM of NADH at 37°C. After the reaction mixtures were incubated at 37°C for 5 minutes, 2 mM of ATP was added to initiate the reaction. Absorbance at 340 nm was used to measure the ATPase activities at 37°C.

Minimum inhibitory concentrations assays

Antibacterial minimum inhibitory concentrations (MICs) were obtained from three independent experiments using broth microdilution methods in 96-well plates according to Clinical and Laboratory Standards Institute guidelines [273]. Cells were growth from a singles colony in Müller-Hinton II broth (MHIIB) (Becton Dickinson) medium for 18 h at 37°C in agitation. The cultures were then diluted to OD600 of 0.1 using MHIIB medium. 50 μL of the diluted cultures were added to 50 μL of serially diluted compounds in MHIIB in a 96-well plate and incubated at 37°C for another 18–20 h. After OD_{600} was measured to monitor the inhibition, 0.02% resazurin was added to each well and incubated for 4 hours at 37°C. After the incubation, fluorescence with a wavelength of 528 nm and 590 nm for excitation and emission, respectively, was measured using a plate reader and used to calculate the MIC values. Bacterial strains *S. aureus* ATCC 14775, MRSA ATCC BAA44, *B. subtilis* ATCC 6633, *E. coli* ATCC 25922, and *E. coli* BAS3023 that carries an *imp4213* mutation [227, 274] conferring permeability to small molecules were used to determine the MICs.

Molecular dynamics simulation and docking

To perform docking against a flexible receptor, conformations of the *E. coli* DNA gyrase subunit B were generated using molecular dynamics (MD) simulations. Charmm-Gui web interface [228], was used to prepare the simulation system. Specifically, gyrase subunit B was solvated in a cubic water box with TIP3 water and the system was neutralized by adding 0.15 M of $MgCl_2$ resulting in a system containing ~31,000 atoms. The particle mesh Ewald (PME) method [231] was used for calculating the long-range ionic interactions. The systems were minimized for 100,000 steps, followed by a 250 ps equilibration at 310 K with 1 fs time step. 200-ns production simulation with 2-fs time step were performed at a constant pressure of 1 atm. and T=310 K. The Nose-Hoover Langevin-piston method [232] was used for pressure coupling, with a piston period of 50 fs and a decay of 25 fs, and the Langevin temperature coupling with a friction coefficient of 1 ps^{-1} was used for maintaining the temperature. From the simulation trajectory, 1,000 protein pdb frames of gyrase subunit B conformations were extracted using Visual Molecular Dynamics (VMD) [233] for molecular docking.

Digallic acid, dodecyl gallate, and biphenyl gallate were docked to 1,000 MD-generated gyrase subunit B conformations. The protein pdb files and the small molecule structures were first converted to pdbqt format for docking. AutoDock Vina 1.1.269 was used to perform molecular docking. The compounds were screened against the protein conformations and the resulting scores of the complexes were sorted and ranked according to their binding affinities using custom scripts. Another 100-ns molecular dynamics simulation was performed for each top-ranked protein-drug complex with the same input settings described above.

Results and discussion

Since several naturally occurring polyphenols, such as ellagic acid and EGCG, are potent bacterial DNA gyrase inhibitors [168, 268], we decided to examine the inhibition activities of a group of polyphenols collected in our laboratory against *E. coli* DNA gyrase (Figure S1). As expected, ellagic acid, EGCG, and 3,5-dicaffeoylquinic acid strongly inhibit *E. coli* DNA gyrase (Figures 1, S1, and S2). We found that tannic acid also potently inhibits *E. coli* DNA gyrase with an IC_{50} of 1 μM (Figure 1e). Since tannic acid is composed of several digallic acids covalently attached to a glucose (Figure 1a), we reasoned that digallic acid, found in *Pistacia lentiscus* and other plants and fruits [275],] should also strongly inhibit *E. coli* DNA gyrase. Indeed, our results showed that digallic acid potently inhibit *E. coli* DNA gyrase with an estimated IC_{50} of 2 μM (Figure 1f). In contrast, gallic acid does not inhibit *E. coli* DNA gyrase up to 500 μM (Figure 1g, Figure S1, and Table 1).

Table 1. IC_{50} values [μM] of gallate derivatives against *E. coli* DNA gyrase and topoisomerase IV.

Compound	DNA gyrase		Topoisomerase IV	
	Gel-based	SDFQ	Gel-based	SDFQ
Gallic Acid	>500	N/A[a]	>500	N/A[a]
Digallic Acid	2	1.9	8	7.3
Butyl Gallate	>100	>100	>100	>100
Octyl Gallate	50	25.96	50	41.2
Dodecyl Gallate	15	13.77	50	36.9
Phenyl Gallate	>100	>100	>100	>100
Biphenyl Gallate	20	18.8	25	23.6
Novobiocin	0.5	0.45	10	4.3

[a] Not available.

Next, we obtained several compounds with a gallic acid or gallate attached to a hydrophobic moiety through an ester bond (Figure 2a-e) and tested their inhibition activities against *E. coli* DNA gyrase. Our results are shown in Figure 2f and g. All these gallate derivatives inhibit *E. coli* DNA gyrase (Figure 2 and Table 1). Interestingly, a long hydrophobic chain or group significantly increase the inhibition activities of these gallate derivatives against *E. coli* DNA gyrase. For example, the IC_{50} value of dodecyl gallate is much lower than that of butyl gallate (Figure 2 and Table 1). Likewise, the IC_{50} value of biphenyl gallate is also lower than that of phenyl gallate (Figure 2 and Table 1).

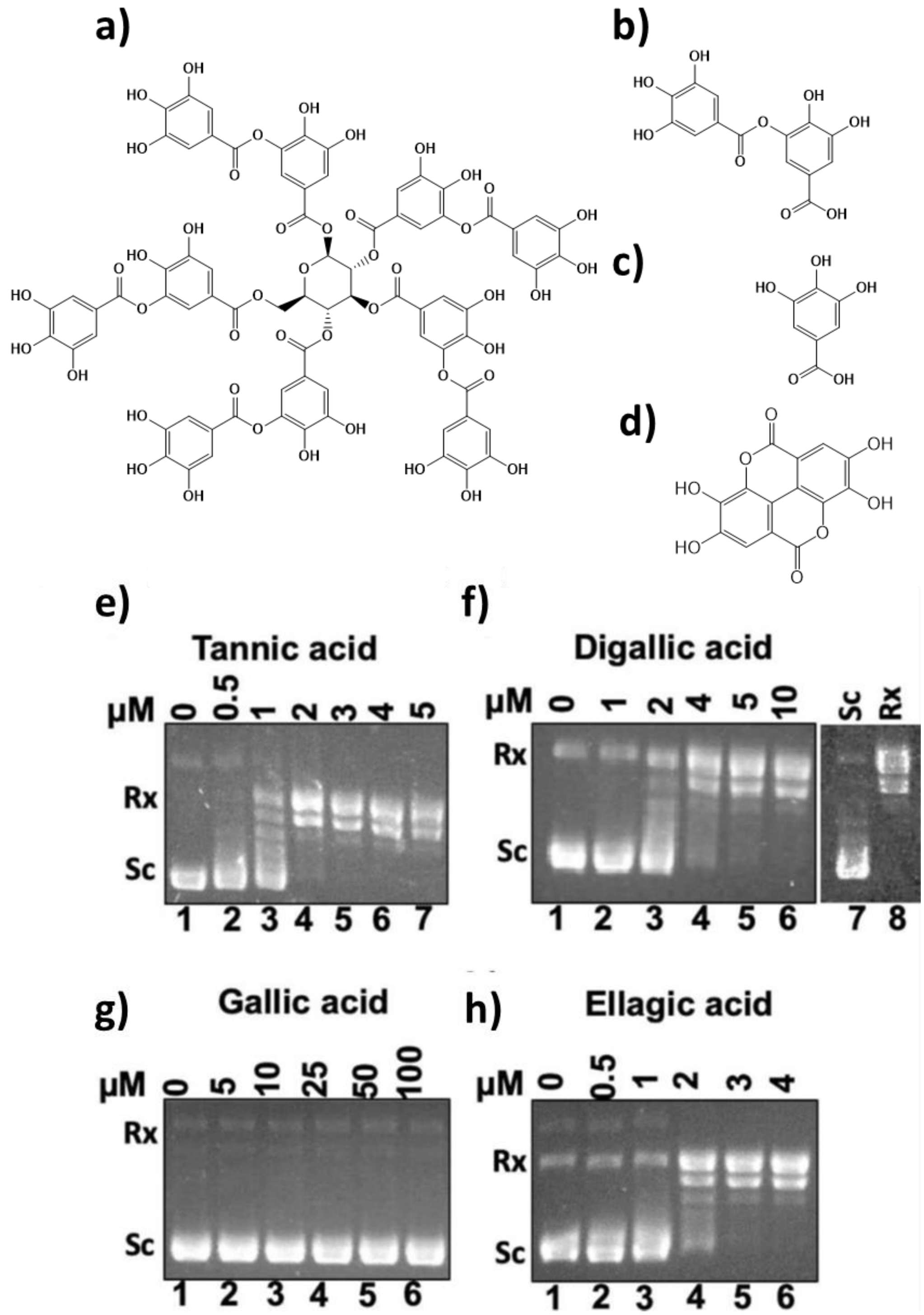


Figure 1. (**a–d**) Chemical structure of (**a**) tannic acid, (**b**) digallic acid, (**c**) gallic acid and (**d**) egallic acid. (**e–h**) Inhibition of *E. coli* DNA gyrase supercoiling activities by tannic acid, digallic acid, gallic acid, and ellagic acid. Novobiocin was used as a positive control (Figure S3). Symbols: Rx, relaxed plasmid pAB1; Sc, supercoiled pAB1.

The inhibition of *E. coli* DNA gyrase by these gallate derivatives was also confirmed using a supercoiling-dependent fluorescence quenching (SDFQ) assay (Figure 3a). As shown in Fig. 3a and our previous publications [189, 190], supercoiling of the fluorescently-labeled plasmid pAB1_FL905 greatly decreases the fluorescence intensity of the plasmid.

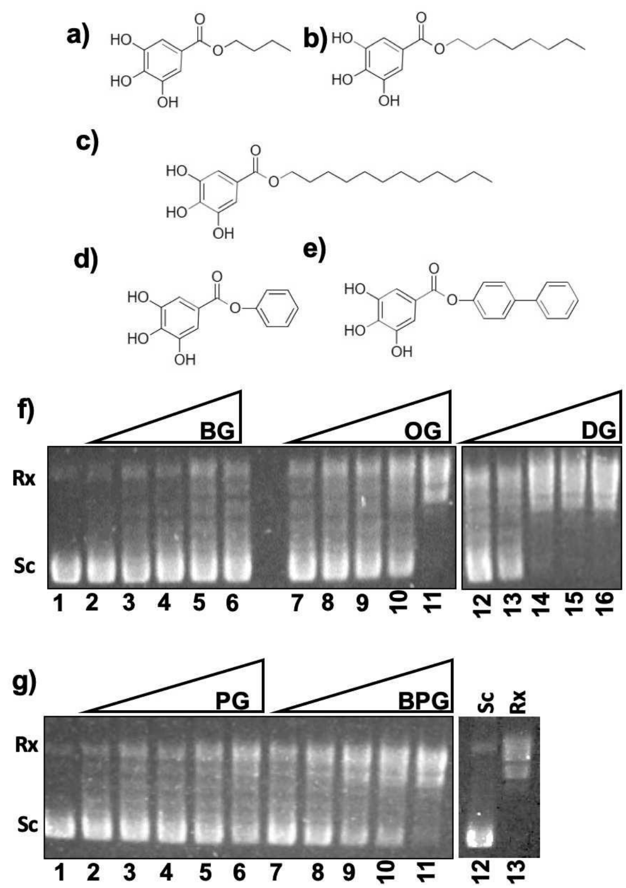


Figure 2. (**a–e**) Chemical structure of gallate derivatives. (**a**) butyl gallate (BG), (**b**) octyl gallate (OG), (**c**) dodecyl gallate (DG), (**d**) phenyl gallate (PG), and (**e**) biphenyl gallate (BPG). (**f** and **g**) Inhibition of E. coli DNA gyrase by gallate derivatives. Symbols: Rx, relaxed plasmid pAB1; Sc, supercoiled pAB1. (**f**) Lanes 1–6 contain 0, 5, 10, 20, 50 and 100 μM of butyl gallate, respectively. Lanes 7–11 indicate 5, 10, 20, 50 and 100 μM of octyl gallate, respectively. Lanes 12–16 indicate 5, 10, 20, 50 and 100 μM of dodecyl gallate, respectively. (**g**) Lanes 1–6 contain 0, 5, 10, 20, 50 and 100 μM of phenyl gallate, respectively. Lanes 7–11 indicate 5, 10, 20, 50 and 100 μM of biphenyl gallate, respectively. Lanes 12 and 13 represent supercoiled and relaxed plasmid pAB1, respectively.

In the presence of a gyrase inhibitor, the fluorescence intensity of pAB1_FL905 should not change. The SDFQ assay is an excellent assay to quantitatively analyze the inhibition of DNA gyrase by inhibitors Indeed, the IC_{50} values obtained through the SDFQ assays are almost identical to those obtained by gel-based gyrase inhibition assays (Table 1).

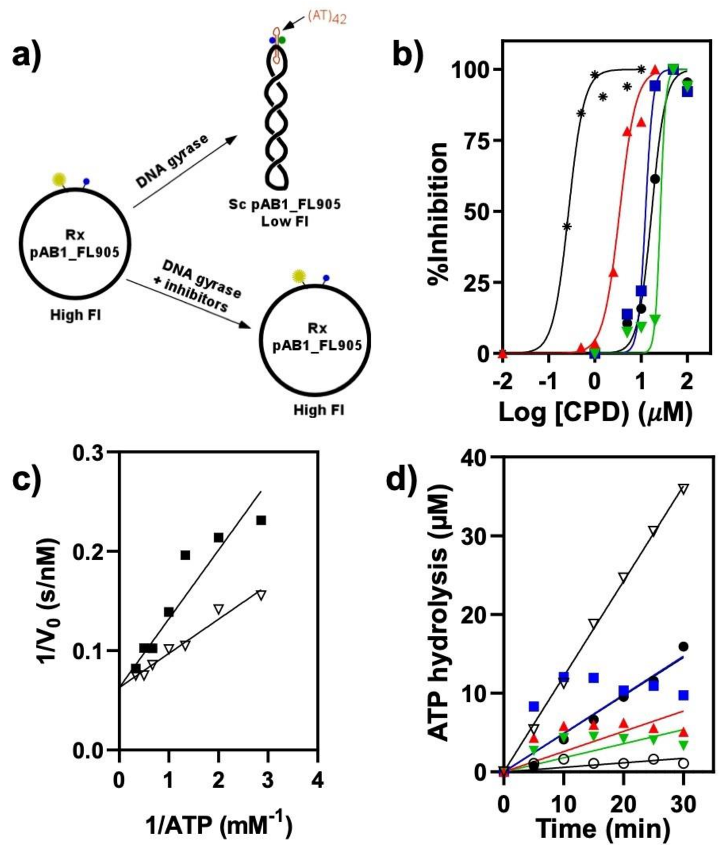


Figure 3. (**a** and **b**) SDFQ-based DNA gyrase supercoiling assays. (**a**) An experimental strategy to study DNA gyrase inhibitors. The IC_{50} values can be determined by a titration experiment. (**b**) Titration experiments to determine the IC_{50} of digallic acid (red up triangles), octyl gallate (green down triangles), dodecyl gallate (blue squares), biphenyl gallate (black circles), and novobiocin (stars). (**c** and **d**) Digallic acid and other gallate derivatives are competitive inhibitors of the ATPase activities of *E. coli* DNA gyrase. The ATPase assays were performed as described in Material and Methods. (c) Lineweaver- Burk plot or double-reciprocal plot of *E. coli* DNA gyrase in the absence (open triangles) or presence (closed squares) of 500 nM digallic acid. (d) ATP hydrolysis activities of *E. coli* DNA gyrase in presence of different gallate derivatives (100 μM). Symbol: DNA gyrase only, open down triangles; digallic acid, red up triangles; octyl gallate, green down triangles; dodecyl gallate, blue squares; biphenyl gallate, black circles; and novobiocin (open circles).

Previous studies showed that ellagic acid (a condensed dimer of gallic acid) and epigallocatechin gallate (a gallate derivative) are competitive inhibitors of bacterial DNA gyrase's ATPase [168]. In this study, we also conducted the ATPase kinetic studies in the absence or presence of digallic acid or other gallate derivatives. Our results are shown in Figure 3c and d. As expected, digallic acid and other gallate derivatives greatly inhibit the ATPase activities of *E. coli* DNA gyrase (Figure 3c and d). Fitting of these kinetic results to the Michaelis- Menten equation yielded the following kinetic parameters: K_M of 0.59± 0.22 mM and Vmax of 16.3±2.5 nM/s in the absence of an inhibitor and K_M of 1.44±0.73 mM and Vmax of 17.8±5.0 nM/s in the presence of 500 nM of digallic acid. These results demonstrate that digallic acid is a competitive inhibitor of bacterial DNA gyrase's ATPase (Figure 3c): the intercept on the 1/V0 axis of the Lineweaver- Burk or double-reciprocal plot is the same in the presence or absence of digallic acid showing that digallic acid competes with ATP for its binding sites of *E. coli* gyrase. The K_i was calculated to be 347 nM.

We also tested the inhibition activities of digallic acid and other gallate derivatives against *E. coli* DNA topoisomerase IV. Our results are shown in Figure 4 and Figure S3b for relaxation and also in Figure S4 for decatenation. Novobiocin is a known topoisomerase IV inhibitor with an IC_{50} of ~10 μM, which is consistent with previously published results [153]. Digallic acid potently inhibits *E. coli* topoisomerase IV with an estimated IC_{50} ~8 μM for relaxation (Figure 4a and d) and ~4 μM for decatenation (Figure S4a and c).

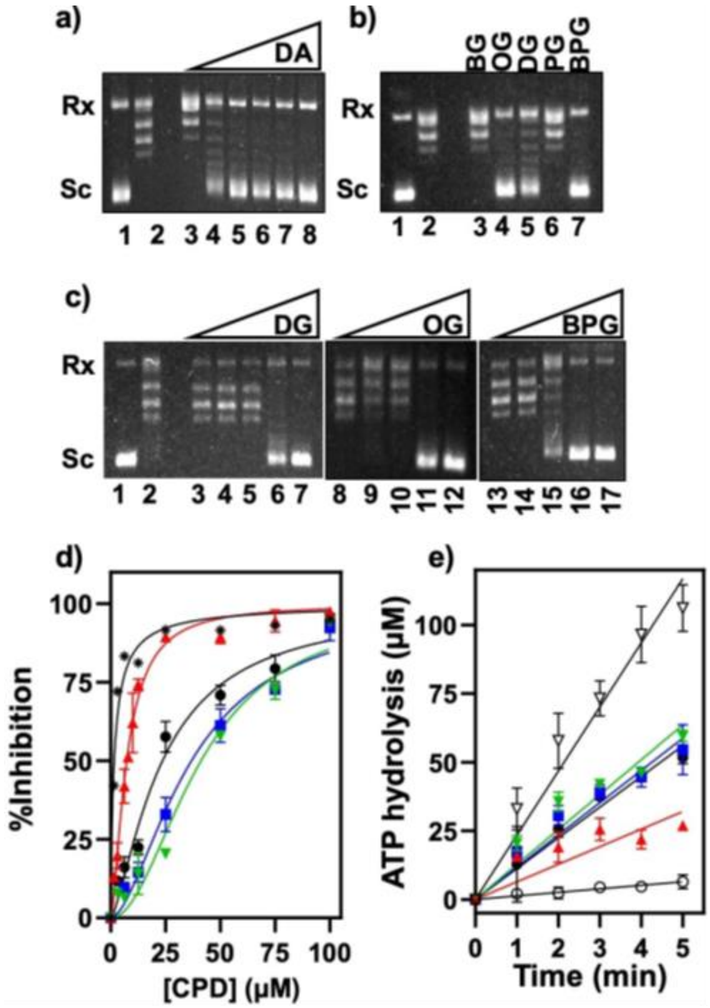


Figure 4. Inhibition of *E. coli* DNA topoisomerase IV by digallic acid and other gallate derivatives. Relaxation assays by *E. coli* DNA topoisomerase IV were performed as described under Material and Methods. The ATPase assays were performed as described in Material and Methods as well. (**a**) Digallic acid potently inhibits *E. coli* DNA topoisomerase IV. Lanes 2–8 contain 0, 6.25, 8, 10, 12.5, 25, and 50 μM of digallic acid, respectively. Lane 1 is supercoiled plasmid pAB1. IC_{50} of digallic acid against *E. coli* DNA topoisomerase IV was estimated to be ~8 μM. (**b**) Inhibition of gallate derivatives against *E. coli* DNA topoisomerase IV at 100 μM. (**c**) Titration experiments to determine IC_{50} of dodecyl gallate, octyl gallate, and biphenyl gallate against *E. coli* DNA topoisomerase IV. Symbols: Digallic acid, DA; butyl gallate, BG; octyl gallate, OG; dodecyl gallate, DG; phenyl gallate, PG; and biphenyl gallate, BPG; Ln, linear DNA, Nk, nicked DNA, Rx, relaxed DNA, Sc, supercoiled DNA. (**d**) SDFQ-based DNA relaxation assays to determined IC_{50} of digallic acid (red up triangles), octyl gallate (green down triangles), dodecyl gallate (blue squares), biphenyl gallate (black circles), and novobiocin (stars). The supercoiled, fluorescently-labeled plasmid pAB1_FL905 was used. Fluorescence measurements were performed in a Biotek Synergy H1 Hybrid Plate Reader using a wavelength of 494 nm and 521 nm for excitation and emission, respectively. (**e**) ATP hydrolysis activities of *E. coli* DNA topoisomerase IV in presence of different gallate derivatives (100 μM). Symbol: DNA gyrase only, open down triangles; digallic acid, red up triangles; octyl gallate, green down triangles; dodecyl gallate, blue squares; biphenyl gallate, black circles; and novobiocin (open circles).

Octyl gallate, dodecyl gallate, and biphenyl gallate also strongly inhibit *E. coli* DNA topoisomerase IV (Figure 4b, c and d; Figure S4b and c; Table 1). As expected, gallic acid does not inhibit *E. coli* DNA topoisomerase IV up to 500 μM (Figure S3c and Table 1). Interestingly, digallic acid and these gallate derivatives also inhibit the ATPase activities of bacterial DNA topoisomerase IV (Figure 4e). In contrast, at 100 μM, digallic acid and other gallate derivatives do not inhibit *E. coli* DNA topoisomerase I (Figure 5a), human DNA topoisomerase I (Figure 5b), and IIα (Figure 5c).

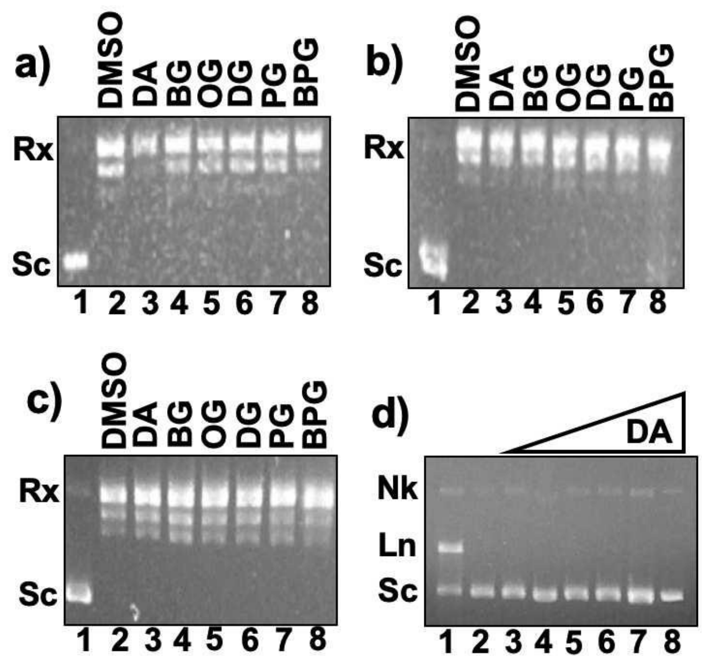


Figure 5. Digallic acid and gallate derivatives did not strongly inhibit *E. coli* DNA topoisomerase I (**a**), human DNA topoisomerase I (**b**), and human DNA topoisomerase IIα (**c**). 100 μM of compounds were used. (**d**) DNA gyrase mediated DNA cleavage assays were performed as described under Material and Methods. Lanes 2–6 contain 0, 6.25, 12.5, 50, 100, 150, and 200 μM of digallic acid, respectively. Lane 1 contains 10 μM of ciprofloxacin. Symbols: Digallic acid, DA; butyl gallate, BG; octyl gallate, OG; dodecyl gallate, DG; phenyl gallate, PG; and biphenyl gallate, BPG; Ln, linear DNA, Nk, nicked DNA, Rx, relaxed DNA, Sc, supercoiled DNA.

These results suggest that these gallic acid derivatives only target bacterial DNA gyrase and topoisomerase IV. Additionally, our DNA cleavage assays showed that digallic acid and other gallate derivatives are not bacterial DNA gyrase poisons, specific DNA gyrase inhibitors that stabilize and stimulate gyrase-mediated double-stranded breaks and single-stranded nicks [80] (Figure 5d).

Figure 6 shows molecular models for digallic acid, dodecyl gallate, and biphenyl gallate binding to *E. coli* DNA gyrase B subunit. These models were generated by molecular docking with the crystal structure of gyrase B subunit (PDB ID: 1EI1), followed by 100 ns molecular dynamics simulations as described in Material and Methods. Our method is validated by docking ADPNP to *E. coli* DNA gyrase subunit B followed by molecular dynamic simulation (Figure S5), which resulted in a similar complex to the experimentally obtained ADPNP-*E. coli* DNA gyrase complex (PDB ID: 1EI1). Similar to novobiocin, digallic acid, dodecyl gallate, and biphenyl gallate also bind to the ATP binding site of the gyrase B subunit [63, 73]. Digallic acid, dodecyl gallate or biphenyl gallate form a hydrogen bond with Asp73 (Figure 6). Previous studies have shown that hydrophobic interactions significantly contribute to the binding of novobiocin to the protein [63, 73]. We also find that the hydrophobic groups of gallate derivatives are in contact with the hydrophobic amino acids, which may greatly enhance the inhibition against *E. coli* DNA gyrase. Several gallate derivative, such as butyl gallate, octyl gallate, and dodecyl gallate, are widely used as food additives and were shown to have antibacterial activities [169].

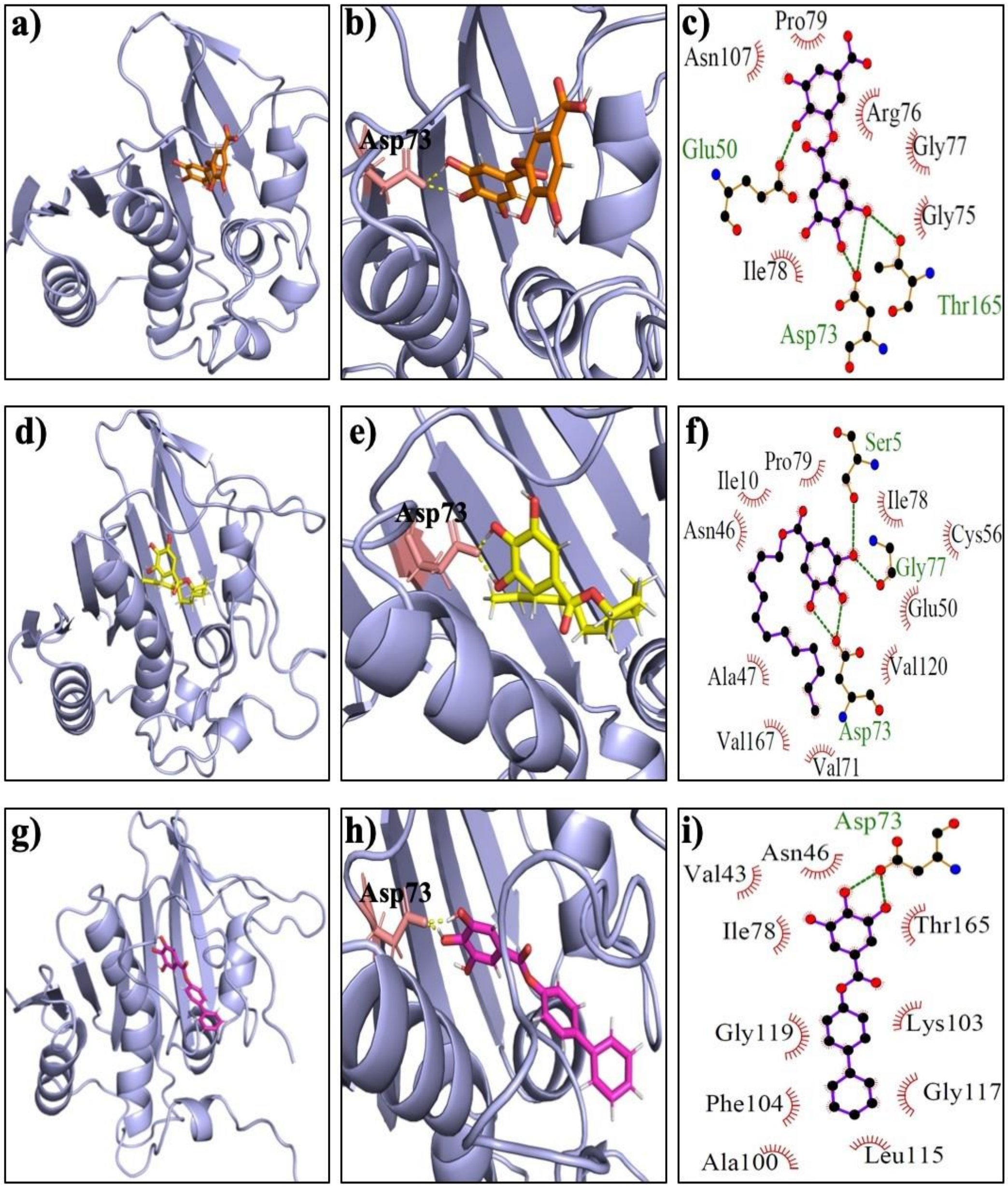


Figure 6. Molecular models of digallic acid (**a–c**), dodecyl gallate (**d–f**), and biphenyl gallate (**g–i**) binding to the ATP binding pocket of *E. coli* DNA Gyrase B. Molecular models were constructed as described in Materials and Methods. A hydrogen bond is formed between all gallate derivatives (digallic acid, dodecyl gallate, and biphenyl gallate) and residue Asp73. **c**, **f**, and **i** shows schematic 2-D representations of *E. coli* DNA gyrase-ligand complexes. Hydrogens bonds are highlighted as green dashed lines. Hydrophobic contacts are shown as an arc with spokes radiating towards the ligand atoms.

In this study, we also tested the antibacterial activities of digallic acids and these gallate derivatives and determined their MIC against several bacterial strains. Our results are summarized in Table 2. Consistent with previously published results [169], octyl and dodecyl gallate showed antibacterial activities against *B. subtilis*, *S. aureus*, and MRSA. Digallic acid also showed some antibacterial activities against these two gram-positive bacteria. Interestingly, the antibacterial activities of these gallate derivatives are coincided with their inhibition against bacterial DNA gyrase, suggesting that DNA gyrase is a potential target for these compounds for their antibacterial activities. Biphenyl gallate showed some antibacterial activities against *E. coli*. Nevertheless, these gallate derivatives do not have strong antibacterial activities against Gram-negative *E. coli* strains ATCC 25922 and BAS3023. A likely scenario is that these compounds could not enter *E. coli* cells by crossing bacterial cell wall and membrane to inhibit DNA gyrase *in vivo*. Another possibility is that these gallate derivatives are ester and may be hydrolyzed in the MIC assays. Additional studies are needed to confirm these possibilities.

One advantage of these new gallate-based gyrase inhibitors is that they can be easily modified/derivatized to enhance their potency. For instance, new functional groups can be attached to the gallate through an ester or amide bond. Using a combined effort of biochemistry, molecular modeling, medicinal chemistry, and antibacterial testing, new antibacterial agents targeting bacterial DNA gyrase can be developed/ synthesized.

Table 2. Antibacterial activity of gallate derivatives.

Bacterial strains	MIC (μM)							
	Digallic acid	**Butyl gallate**	**Octyl gallate**	**Dodecyl gallate**	**Phenyl gallate**	**Biphenyl gallate**	**CFX**	**NOV**
E. coli ATCC 25922	200	>200	200	200	200	50	1.25	<6.25
E. coli imp BAS3023	200	>200	100	200	200	50	40	<6.25
S. aureus ATCC 14755	>200	>200	12.5-25	25.5	>200	50-100	0.4	<6.25
MRSA ATCC 33591	>200	>200	>200	>200	>200	>200	0.0125	157.5
B. subtilis ATCC 6633	>200	>200	50	200	>200	200	0.0019	6.25

CFX and NOV represent ciprofloxacin and novobiocin, respectively.

Conclusions

In summary, we found that digallic acid and several gallate derivatives are potent bacterial DNA gyrase inhibitors. Our results show that a long hydrophobic chain or group attached to the gallate moiety significantly increases the gyrase inhibition activities of these gallate derivatives although gallic acid per se does not inhibit *E. coli* DNA gyrase. These new gyrase inhibitors are competitive inhibitors of bacterial DNA gyrase's ATPase and do not cause gyrase-mediated single-stranded nicks and double-stranded breaks. They also inhibit *E. coli* DNA topoisomerase IV and do not inhibit *E. coli* DNA topoisomerase I, human DNA topoisomerase I, and human DNA topoisomerase IIα.

IV. TARGETING BACTERIAL DNA GYRASE AND TOPOISOMERASE IV *IN VITRO* AND *IN VIVO* BY A NEWLY IDENTIFIED QUINAZOLINE GYRASE INHIBITOR

Abstract

Fluoroquinolones are highly effective antibiotics, targeting bacterial DNA gyrase and topoisomerase IV. However, the emergence of resistant bacterial strains and adverse side effects associated with their use have significantly compromised their efficacy and clinical use. Consequently, there is an urgent need for new antibiotics targeting bacterial DNA gyrase and topoisomerase IV that can overcome fluoroquinolone resistance. Through a screening campaign of the National Institutes of Health's Molecular Libraries Small Molecule Repository library, a novel bacterial DNA gyrase inhibitor, CPD154 (N-(6-chloro-4-phenylquinazolin-2-yl) guanidine, a quinazoline derivative) was discovered. This quinazoline compound demonstrated potent dual poisoning inhibitory activity against *E. coli* DNA gyrase and topoisomerase IV. The *in vivo* inhibitory activity of CPD154 against DNA gyrase was also analyzed. CPD154 interacts with bacterial enzymes through a mechanism of action similar to fluoroquinolones. This compound also exhibited a potent bactericidal effect against *E. coli*. Our results indicate that CPD154 has a great potential as a scaffold for derivatization efforts to develop new drugs with anti-gyrase and antibacterial activity.

Introduction

Fluoroquinolones have been a highly effective broad-spectrum antibiotic since their discovery, as they target bacterial DNA gyrase and topoisomerase IV through a dual inhibitory mechanism [276, 277]. By stabilizing the DNA-cleavage complex on these enzymes, fluoroquinolones obstruct the DNA re-ligation step, leading to cell death [278-280]. However, the rise of resistance to fluoroquinolones has become a global medical problem [281-283], primarily based on mutations on the enzyme binding site [1, 284, 285]. Fluoroquinolones interact with their target enzymes through a water-metal ion bridge, which depends on highly conserved residues in gyrA/parC subunits that stabilize a Mg^{2+} ion through hydrogen bonds [93, 94, 96]. Mutations in these residues are frequently observed in clinical isolates resistant to fluoroquinolones [286, 287], limiting their use in antibacterial therapy. Moreover, serious side effects associated with the use of fluoroquinolones have led to FDA warnings (https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-increased-risk-ruptures-or-tears-aorta-blood-vessel-fluoroquinolone-antibiotics), and restricted their consumption [111, 288]. The current scenario highlights the need for the development of novel antibacterial drugs that target bacterial DNA gyrase and topoisomerase IV while overcoming fluoroquinolone resistance.

As part of our efforts to contribute to the decline of antibacterial resistance, a novel quinazoline (compound 154) was discovered through high-throughput screening (HTS) of the National Institutes of Health's Molecular Libraries Small

Molecule Repository library. Compound 154 demonstrated potent *in vitro* inhibitory activity against *E. coli* DNA gyrase and antibacterial activity against various Gram-positive and -negative strains. Additionally, this drug is a bacterial DNA gyrase-poison inhibitor that stabilizes DNA-cleavage complex formation. To elucidate the inhibitory mechanism of compound 154 against bacterial DNA gyrase and assess its potential inhibitory activity against other bacterial topoisomerases, we conducted biochemical studies. Here, we present the dual inhibitory activity of compound 154 and its ability to overcome some of the most common fluoroquinolone-resistant mutations. Furthermore, we evaluated the *in vivo* gyrase inhibition activity of this drug, as well as its potent antibacterial activity against *E. coli*. Our findings suggest that compound 154 could serve as a scaffold for the development of novel drugs with anti-gyrase and broad-spectrum antibacterial activity.

Materials and methods

Materials

E. coli DNA gyrase was purified as described previously [190, 226]. *E. coli* DNA topoisomerase IV was kindly provided by Keir C. Neuman at the National Heart, Lung, and Blood Institute. Ethidium bromide, buffer-saturated phenol, and ethanol were purchased from Fisher Scientific, Inc. Compound 154 was bought from Molport, Inc. IPTG was obtained from Anatrace (Maumee, OH). The luciferase assay system was obtained from Promega Corporation. Plasmid pAB1 and fluorescently labeled plasmid pAB1_FL905 were described previously [189].

Gel- and supercoiling dependent fluorescence quenching (SDFQ)-based gyrase DNA supercoiling and inhibition assays

DNA supercoiling assays by *E. coli* DNA gyrase in the absence or presence of a potential gyrase inhibitor were carried out in 30 μL of 1×gyrase buffer (35 mM Tris-HCl, 24 mM KCl, 4 mM $MgCl_2$, 2 mM DTT, 0.1 mg/mL BSA, 6.5% glycerol, and 1.75 mM ATP, pH 7.5) containing 8.9 nM of *E. coli* DNA gyrase and 400 ng of relaxed plasmid pAB1 or pAB1_FL905. For bacterial DNA gyrase inhibition assays, each compound was mixed with *E. coli* DNA gyrase and incubated on ice for 5 min. Then, relaxed pAB1 was added to initiate the supercoiling reaction. The reaction mixtures were incubated at 37°C for 30 minutes. Two assays, SDFQ-based gyrase assay and agarose-gel based gyrase assay, were used to analyze our results. For SDFQ-based assays, DNA samples were transferred to a 384-well plate. Fluorescence measurements were performed in a Biotek Synergy H1 Hybrid Plate Reader using a wavelength of 494 nm and 521 nm for excitation and emission, respectively. For gel-based assays, the reactions were stopped by the addition of 1 μL of stop solution (2% SDS and 200 mM EDTA). DNA samples were then analyzed by using 1% agarose gels in 1×TAE buffer followed by ethidium bromide staining and photographed under UV light.

Gel and supercoiling dependent fluorescence quenching (SDFQ)-based Topoisomerase IV (WT and mutants) relaxation and inhibition assays

DNA relaxation assays by *E. coli* DNA topoisomerase IV in the absence or presence of a potential gyrase inhibitor were performed in 20 μL (gel-based assay) or 30 μL (SDFQ-based assay) of 1×topoisomerase IV buffer (40 mM Tris-HCl (pH 8), 100 mM potassium glutamate, 10 mM magnesium acetate, 10 mM DTT, 0.05 mg/mL BSA, and 1 mM ATP) containing 2 nM of DNA topoisomerase IV and 200 ng of supercoiled plasmid pAB1 or pAB1_FL905. The reaction mixtures were incubated at 37 °C for 30 minutes. For topoisomerase IV inhibition assays, each compound was mixed with *E. coli* topoisomerase IV and incubated on ice for 5 min. Then, supercoiled pAB1 was added to initiate the supercoiling reaction. Two assays, SDFQ-based gyrase assay and agarose-gel based gyrase assay, were used to analyze our results. For SDFQ-based assays, DNA samples were transferred to a 384-well plate. Fluorescence measurements were performed in a Biotek Synergy H1 Hybrid Plate Reader using a wavelength of 494 nm and 521 nm for excitation and emission, respectively. For gel-based assays, the reactions were stopped by the addition of 1 μL of stop solution (2% SDS and 200 mM EDTA). DNA samples were analyzed by using 1% agarose gels in 1×TAE buffer followed by ethidium bromide staining and photographed under UV light.

E. coli **DNA gyrase and topoisomerase IV cleavage assays**

Plasmid pBR322 (250 ng) was mixed with 20 nM of *E. coli* DNA gyrase or 10 nM of *E. coli* DNA topoisomerase IV in 20 μL of 1×gyrase buffer or 1×topoisomerase IV buffer and incubated at 37°C for 15 minutes in the presence of an inhibitor or compound. After the incubation, 0.2% SDS and 0.1 mg/ml proteinase K were added to the reaction mixtures to trap the gyrase-inhibitor-DNA complex and digest the gyrase, respectively. After incubating for an additional 30 min at 37°C, DNA samples were analyzed in 1% agarose gel containing 0.5 μg/mL ethidium bromide in 1×TAE buffer and photographed under UV light. In the reactions where the effect of $MgCl_2$ concentration was analyzed, 1×gyrase buffer or 1×topoisomerase IV buffer in the presence of different concentrations of Mg^{2+} was used.

Antibacterial minimum inhibitory concentration (MIC) assays

Antibacterial MICs were obtained from three independent experiments using broth microdilution methods in 96-well plates according to Clinical and Laboratory Standards Institute guidelines [273]. Briefly, cells from a single colony were grown in Müller-Hinton II broth (MHIIB) medium (Becton Dickinson) for approximately 18 hours at 37°C in agitation. The cultures were then diluted to an OD_{600} of 0.1 using MHIIB medium. 50 μL of the diluted cultures were added to 50 μL of serially diluted compounds in MHIIB in a 96-well plate and incubated at 37°C for another 18–20 hours. After OD_{600} was measured to monitor the cell growth, 0.02% resazurin was added to each well and incubated for 4 hours at 37°C. After the incubation, fluorescence intensity with a wavelength of 528 nm and 590 nm for excitation and emission, respectively, was measured using a plate reader and used to calculate the MIC values. Bacterial strains *S. aureus* ATCC 14775, MRSA ATCC BAA44, *B. subtilis* ATCC 6633, M. smegmatis MC 2115, *E. coli* ATCC 25922, and *E. coli* BAS3023 that carries an *imp4213* mutation [227, 274] conferring permeability to small molecules were used to determine the MICs.

Antibacterial time-kill assays

Time-kill assays were performed using the microdilution method in 96-well plates according to the Clinical and Laboratory Standards Institute guidelines [289]. Results were obtained from three independent experiments. Cells were grown from a single colony in Müller-Hinton II broth (MHIIB) (Becton Dickinson) medium for 18 h at 37°C in agitation. The cultures were then diluted to OD600 of 0.00001 using MHIIB medium. 100 μL of the diluted cultures (~1 x 10^5 CFU/mL) were added to 100 μL of serially diluted compound 154 in MHIIB in a 96-well plate and incubated at 37°C for another 18-20h. Aliquots (10 μL) corresponding to MIC, 2×MIC, and 4×MIC were removed from the plates after time intervals (0, 4, 8, and 24h) and diluted in 90 μL of sterile PBS. 100 μL of cells dilutions were plated in LB plates and incubated at 37°C for 24h. A growth control consisting of cells without compound 154 was streaked in each trial. The number of viable cells was determined by counting colonies after the incubation time. After 24h of incubation, 10 μL of cells obtained from the three drug concentrations tested were inoculated in 5 mL of LB and incubated for 18 h at 37°C in agitation. Cell growth was checked by measuring OD600. Ciprofloxacin was used as control. Bactericidal activity was defined as a reduction (higher or equal to) ≥ 3 log10 in CFU/mL from the initial inoculum at the time specified, while bacteriostatic activity was considered a reduction (not greater than) <3 log10 CFU/mL.

For the drop plate assay, 10 μL of cells incubated for the time specified (4, 8, and 24h) in the presence of the three drug concentrations tested were directly inoculated in LB plates and incubated at 37°C for 24h. The presence of viable cells was observed after the incubation time.

Luciferase assay

Luciferase assays were performed as described previously [290]. Briefly, *E. coli* strains FL1181 and FL1182 were grown overnight in LB. The overnight culture was then diluted (1:100) in fresh LB and grown until OD600 reached ~0.2. Then, 500 µM of IPTG and different concentrations of a DNA gyrase inhibitor (ciprofloxacin and compound 154) were added. Cells were incubated in agitation at 37°C until OD600 reached ~0.5. After 10 µL of a solution containing 1M K_2HPO_4(pH 7.8) and 20 mM EDTA was added to 50 µL of cells, the samples were quickly frozen in liquid nitrogen for 3 min and then thawed in a water bath at room temperature for 10 min to yield 60 µL of cell lysate. 300 µL of freshly prepared lysis mix containing 1×cell culture lysis reagent, 1.25 mg/ml lysozyme, and 2.5 mg/ml BSA were added to the cell lysate and incubated at room temperature for another 10 min. Finally, 100 µL of luciferase assay reagent (Promega) were added to 20 µL of the cell lysate and analyzed by a Promega GloMax 20/20 single-tube luminometer.

Expression of β-galactosidase

The expression level of β-galactosidase was measured by using Miller's assay [291]. Briefly, bacterial cells were grown as described under the Luciferase assay to an OD600 of ~0.5 and incubated on ice for 20 minutes. After 100 µL of bacterial cell culture was mixed with 900 µL of Z buffer (60 mM Na_2HPO_4,40 mM

NaH_2PO_4,10 mM KCl, 1 mM $MgSO_4$, and 50 mM β-mercaptoethanol), the cells were lysed by adding ~60 µL of chloroform and 30 µL of 0.1% SDS. The cells lysates were then equilibrated to 30 °C for 5 min. After 200 µL of 4 mg/mL ortho-Nitrophenyl--galactoside (ONPG) were added to the cell lysates, samples were incubated for an additional 15 min at 30 °C. 500 µL of 1 M Na_2CO_3 were used to stop the reactions. After cell debris was removed by centrifugation at 13,000 rpm for 1 min, OD420 and OD550 were measured in a Cary 50 spectrophotometer. β-Galactosidase activities (E) were calculated using the following equation,

$$E = 1000 \times \frac{A420 - 1.75 \times A550}{t \times v \times A600}$$

where t and v represent reaction time and cell culture volume, respectively.

Results and Discussion

Dual inhibitory activity of CPD154 against *E. coli* type II DNA topoisomerases, gyrase and topoisomerase IV

Previous studies showed that CPD154 is an *E. coli* DNA gyrase poison [292]. Here, we confirm that CPD154 can poison *E. coli* DNA gyrase even at 0.78 µM, a concentration much lower than its IC_{50} against this enzyme (Figure 1a). We also did another experiment in which increasing concentrations of *E. coli* DNA gyrase were titrated into the gyrase-mediated DNA cleavage mixtures in the presence of 25 µM of CPD154, which resulted in the generation of increasing amounts of linearized and nicked DNA molecules (Figure 1b). In contrast to fluoroquinolones which strongly induce the cleavage of double-stranded DNA, compound 154 caused the accumulation of single- and double-stranded DNA breaks. The linearized DNA molecules generated by CPD154 are comparable to those of ciprofloxacin (compare lanes 5-7 with lane 8).

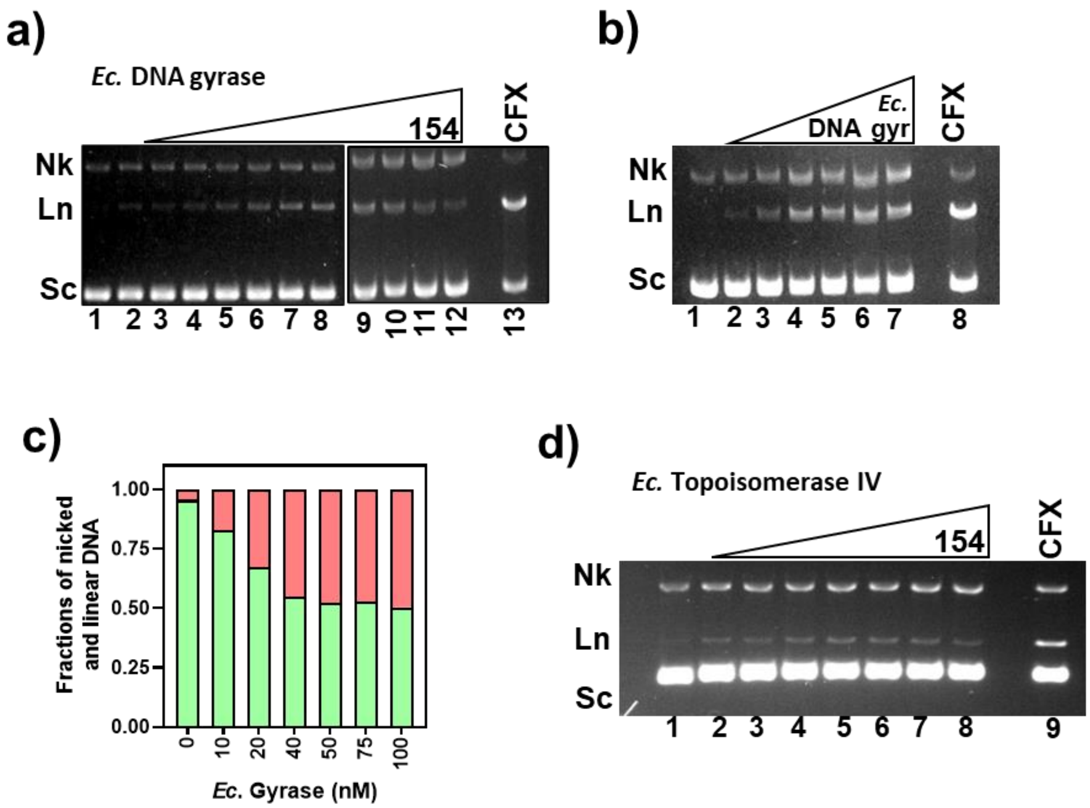


Figure 1. Cleavage complex formation induced by CPD154. (a) *E. coli* DNA gyrase (20 nM) cleavage reactions in presence of CPD154. Lanes 1−12 correspond to 0, 0.78, 1.56, 3.12, 6.25, 8, 10, 12.5, 25, 50, 75, and 100 μM of the compound, respectively. Lane 13 correspond to 50 μM of ciprofloxacin. (b) *E. coli* DNA gyrase cleavage activity in presence of 25 μM of CPD154. Lanes 1−7 correspond to 0, 10, 20, 40, 50, 75, and 100 nM of DNA gyrase, respectively. Lane 8 correspond to 50 μM of ciprofloxacin and 20 nM of *E. coli* DNA gyrase. (c) Graphical analysis of data in B. Nicked (green) and linear (red) DNA are represented as fractions of the DNA processed by the enzyme. (d) *E. coli* topoisomerase IV (10 nM) cleavage reactions in presence of CPD154. Lanes 1−8 correspond to 0, 1.56, 3.125, 6.25, 12.5, 25, 50, and 100 μM. Lane 9 correspond to 50 μM of ciprofloxacin. (Symbols Nk, Ln, and Sc represent nicked, linear, and supercoiled DNA, respectively.

Since bacterial DNA gyrase poisons, such as FQs, also act as a poison for bacterial DNA topoisomerase IV, we evaluate the effect of CPD154 over topoisomerase IV (Figure 1d). As expected, CPD154 is also a poison to bacterial topoisomerase IV. This effect was observed at 1.56 μM of CPD154, a concentration much lower than the IC_{50} against topoisomerase IV.

In this study, we also determined the IC_{50} of CPD154 against *E. coli* DNA gyrase and topoisomerase IV to be 3.1 ± 0.7 μM and 9.1 ± 2 μM, respectively (Figure 2 and Table 1).

Table 1. IC_{50} values [μM] of compound 154 and ciprofloxacin against *E. coli* DNA gyrase and topoisomerase IV.

Compound	*Ec.* DNA gyrase		*Ec.* Topoisomerase IV	
	Gel-based	SDFQ	Gel-based	SDFQ
CPD154	12.5	3.1	20-50	9.1

Effects of Mg^{2+} over the *E. coli* DNA gyrase cleavage complex formation induced by ciprofloxacin and CPD154

We investigated the impact of Mg^{2+} concentration on the inhibitory activity of ciprofloxacin and CPD154, as Mg^{2+} is required for the interaction between fluoroquinolones and bacterial DNA gyrase and topoisomerase IV [293] (Figure 3). We confirmed that Mg^{2+} is required for the formation of gyrase (or topoIV)-DNA-FQ covalent complexes (Fig. 3a and c). As expected, Mg^{2+} is required for the formation of gyrase (or topoIV)-DNA-CPD154 covalent complexes (Figure 4b and d). Interestingly, a slightly higher concentration of Mg^{2+} is required for CPD154 to induce gyrase-mediated, single- and double-strand DNA breaks (Figure 3c and f). For example, the minimum Mg^{2+} concentration to induce gyrase-mediated DNA nicks or double-strand breaks for ciprofloxacin and CPD154 are 0.4 and 0.8 mM, respectively. Likewise, the minimum Mg^{2+} concentration to induce topoisomerase IV-induced DNA nicks or double-strand breaks for ciprofloxacin and CPD154 are 1 and 3 mM, respectively.

The proposed mechanism for the binding of fluoroquinolones to bacterial DNA gyrase involves a water-metal ion bridge (Figure 3a). A Mg^{2+} atom facilitates the interaction between two conserved residues on the enzyme and the keto groups at C3/C4 positions of the drug (Figure 3a) [93, 94, 294]. While Mg^{2+} is the ion that stabilize this interaction *in vivo*, other divalent cations can also stabilize the drug-enzyme cleavage complexes [294, 295].

Our findings indicate that ciprofloxacin required about half the concentration of Mg^{2+} compared to CPD154 to stabilize DNA cleavage complexes with wild-type *E. coli* DNA gyrase. A recent study comparing a structurally more complex quinazolinedione with ciprofloxacin using wild-type *E. coli* enzyme showed a similar requirement of Mg^{2+} for both drugs [290]. The difference with our results may be due to the structure of CPD154. The guanidine moiety at position C2 of CPD154 appears to form hydrogen bonds with the Mg^{2+} of the water-metal ion bridge. Molecular modeling suggests that the orientation and distance between the amino groups of the guanidine and the Serine and Aspartic acid residues could facilitate this interaction (Figure 4).

Magnesium concentration also plays a crucial role in the ATPase activity of DNA gyrase, and topoisomerase IV since this divalent ion is required for ATP binding. As mentioned before, fluoroquinolones need Mg^{2+} to bind to bacterial topoisomerases type II, DNA gyrase, and topoisomerase IV, via a water-metal ion bridge. Our results indicate that CPD154 also requires Mg^{2+} to stabilize a cleavage complex with bacterial DNA gyrase and topoisomerase IV. An ATPase assay titrating [Mg^{2+}] should be performed to determine the effect of this divalent ion on the ATP hydrolysis activity of bacterial DNA gyrase and topoisomerase IV. Since ciprofloxacin and CPD154 do not inhibit the ATPase activity of these enzymes, we expect an increase of the ATPase activity dependent on the magnesium concentration in the presence of these drugs.

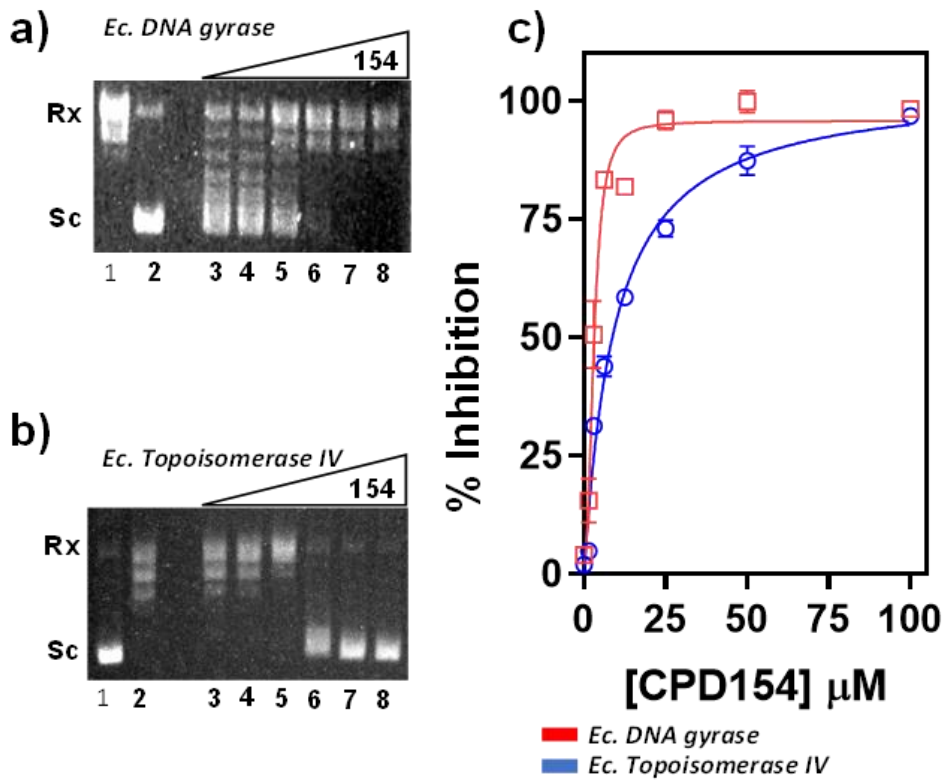


Figure 2. Dual inhibitory activity of CPD154 over bacterial DNA gyrase and topoisomerase IV (a) Agarose gel-based *E. coli* gyrase inhibition assays for compound 154. Lanes 3−8 correspond to 1.56, 3.12, 6.25, 12.5, 25, and 50 μM of the compound, respectively. Lanes 1 and 2 are relaxed and supercoiled plasmid pAB1, respectively. (b) Agarose gel-based *E. coli* topoisomerase IV inhibition assays for compound 154. Lanes 3-8 correspond to 1.56, 3.12, 6.25, 12.5, 25, and 50 μM of the compound, respectively. Lanes 1 and 2 are supercoiled and relaxed plasmid pAB1, respectively. (c) SDFQ-based assays in the presence of compound 154 and DNA gyrase (red squares) and topoisomerase IV (blue circles). The IC_{50} values against *E. coli* DNA gyrase and topoisomerase IV are 3.1 ± 0.7 μM and 9.1 ± 2 μM, respectively. The standard deviations were calculated from three independent experiments. Symbols Rx and Sc represent relaxed and supercoiled DNA, respectively.

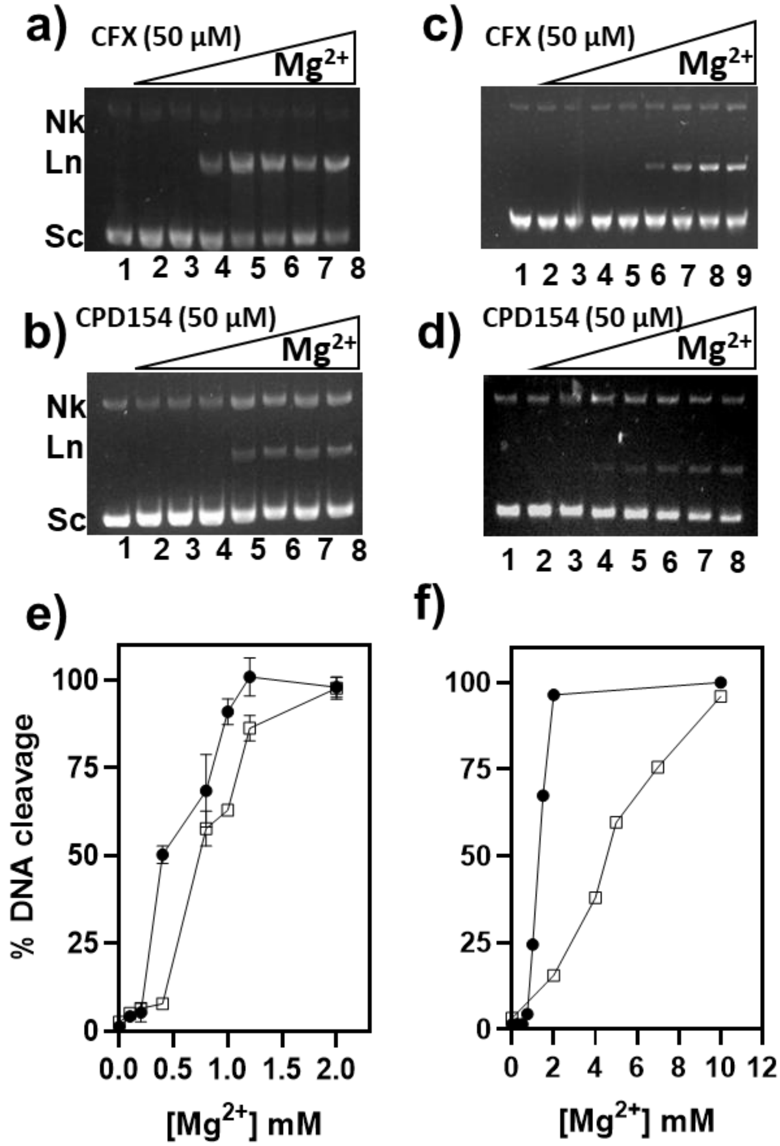


Figure 3. Effects of Mg^{2+} over DNA cleavage complexes formation induced by ciprofloxacin and CPD154 in *E. coli* DNA gyrase and topoisomerase IV. (a) DNA gyrase cleavage reactions in presence of ciprofloxacin (50 µM) and increasing concentrations of Mg^{2+}. Lanes 1-8 represents 0, 0.2, 0.4, 0.8, 1, 1.2, 1.4, and 2 mM of Mg^{2+}. (b) DNA gyrase cleavage reactions in presence of CPD154 (50 µM) and increasing concentrations of Mg^{2+}. Lanes 1-8 represents 0, 0.2, 0.4, 0.8, 1, 1.2, 1.4, and 2 mM of Mg^{2+}. (c) Topoisomerase IV cleavage reactions in presence of ciprofloxacin (50 µM) and increasing concentrations of Mg^{2+}. Lanes 1-9 represents 0, 0.25, 0.35, 0.5, 0.75, 1, 1.5, 2, and 10 mM of Mg^{2+}. (d) Topoisomerase IV cleavage reactions in presence of CPD154 (50 µM) and increasing concentrations of Mg^{2+}. Lanes 1-8 represents 0, 1, 2, 3, 4, 5, 7, and 10 mM of Mg^{2+} (e) Graphical representation of data in A and B. Ciprofloxacin and CPD154 are represented by black dots and empty squares, respectively. (f) Graphical analysis of data in C and D. Ciprofloxacin and CPD154 are represented by black dots and empty squares, respectively.

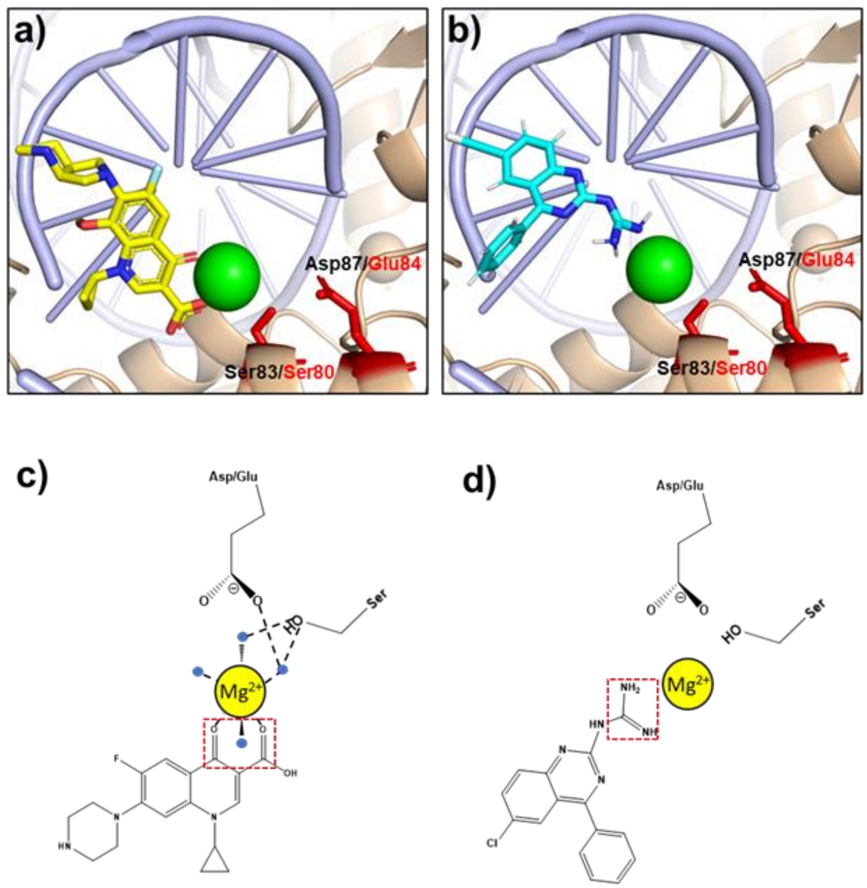


Figure 4. Molecular model of the interaction of moxifloxacin (a) and CPD154 (b) at the cleavage site of *E coli* gyrase A. The magnesium atom and the residues involved in the water-metal ion are highlighted in green and red, respectively. The residues corresponding to DNA gyrase are indicated in black, while the residues corresponding to topoisomerase IV are represented in red. Modified from Wohlkonig *et al*. (c and d) Diagram of the water-metal ion bridge interaction between ciprofloxacin and magnesium (c) and interaction of compound 154 with magnesium (d). *E. coli* DNA gyrase/topoisomerase IV residues involved in this interaction are also depicted here. Mg^{2+} ion are represented as yellow spheres. Water molecules are highlighted in blue. Hydrogen bonds are represented as dashed lines. Chemical groups involved in the interaction with magnesium in both molecules are highlighted in a red box

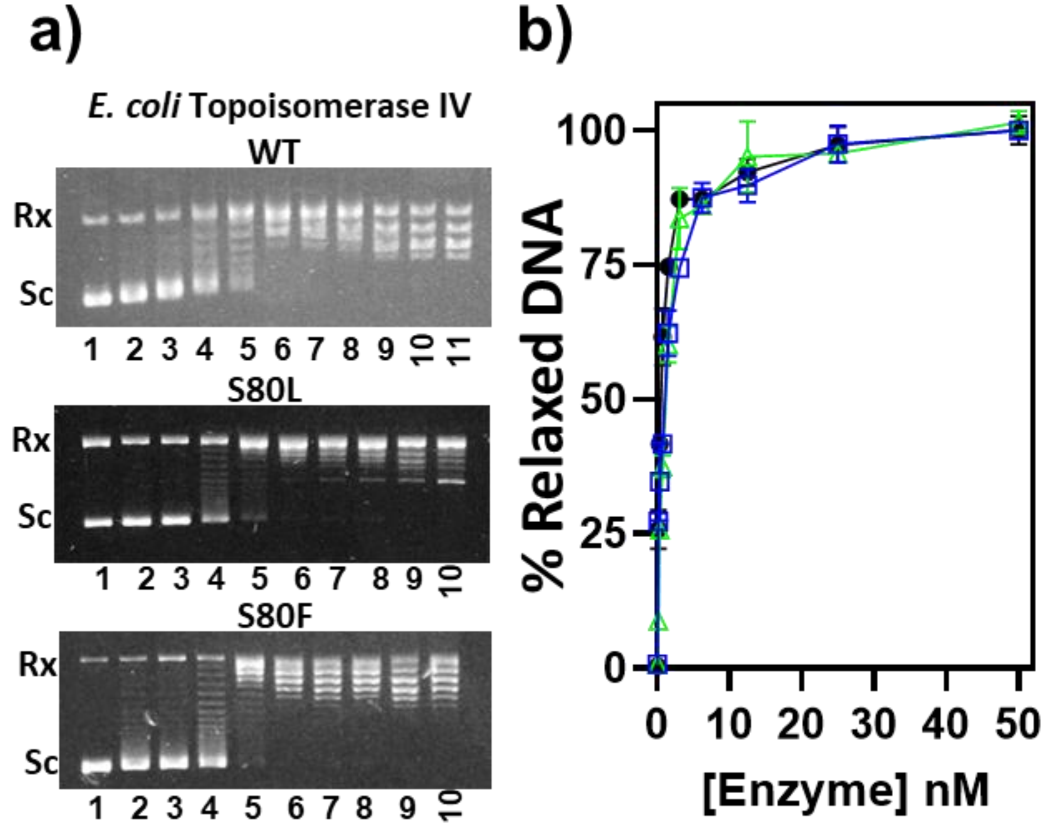


Figure 5. Effects of mutations on the FQs binding site over the relaxation activity of *E.coli* topoisomerase IV (a) DNA relaxation activity of wild-type and mutants of *E. coli* topoisomerase IV. For wild-type (WT) Topoisomerase IV, lanes 1-11 represent 0, 0.062, 0.125, 0.25, 0.5, 1.56, 3.1, 6.25, 12.5, 25, and 50 nM of the enzyme(upper gel). For both mutants (S80L/S80L), lanes 1-10 represent 0, 0.19, 0.39, 0.78, 1.56, 3.1, 6.25, 12.5, 25, and 50 nM of topoisomerase IV. (middle and bottom gel). (b) Graphical representation of data in A. *E. coli* topoisomerase IV WT and mutants S80L and S80F are represented by black dots, empty blue squares, and empty green triangles, respectively. Symbols Rx and Sc represent relaxed and supercoiled DNA, respectively.

Effects of mutations on the FQs binding site of *E. coli* topoisomerase IV for the stabilization of the cleavage complex induced by ciprofloxacin and CPD154

We conducted additional experiments to assess the importance of the residues involved in the water-metal ion bridge for the interaction between CPD154 and topoisomerase IV. Two *E. coli* topoisomerase IV enzymes carrying mutations at position 80 of parC were used. The first one, S80L, has been identified in clinical isolates of quinolone-resistant *E. coli* [257, 296]. The second mutant, S80F, is similar to a common mutation in Gram-positive bacteria *B. anthracis*'s DNA gyrase, which also confers resistance to fluoroquinolones [297].

The enzymatic activity of wild-type, parC(S80L), and parC(S80F) *E. coli* topoisomerase IV was first evaluated. These mutations did not affect the DNA relaxation activity of the enzyme (Figure 5a, b). In the absence of any drug, similar concentrations of WT and S80 mutant enzymes were able to completely relax 200 ng of supercoiled DNA (Figure 5). Therefore, these mutations do not interfere with the enzyme's catalytic activity. Consequently, resistance to fluoroquinolones is more likely due to limited interaction with the drug rather than a decreased enzymatic activity.

Since the DNA relaxing activity of these enzymes was practically equal, the WT and S80 mutants of *E. coli* topoisomerase IV were treated with increasing concentrations of ciprofloxacin and compound 154 to evaluate changes in enzymatic activity in the presence of these drugs. Both drugs completely inhibited *E. coli* topoisomerase IV WT and mutants at concentrations higher than 50 µM, with parC mutants requiring higher concentrations of ciprofloxacin to be inhibited compared to the wild-type enzyme. The band quantification analysis of Figure 6a indicates an IC_{50} for ciprofloxacin of ~4.5, ~15.62, and ~8.4 µM for *E. coli* topoisomerase IV WT, S80L, and S80F, respectively. For CPD154 (Figure 6b), image analysis indicates an IC_{50} of ~9.1, ~11.11, and ~21.53 μM for *E. coli* topoisomerase IV WT, S80L, and S80F, respectively.

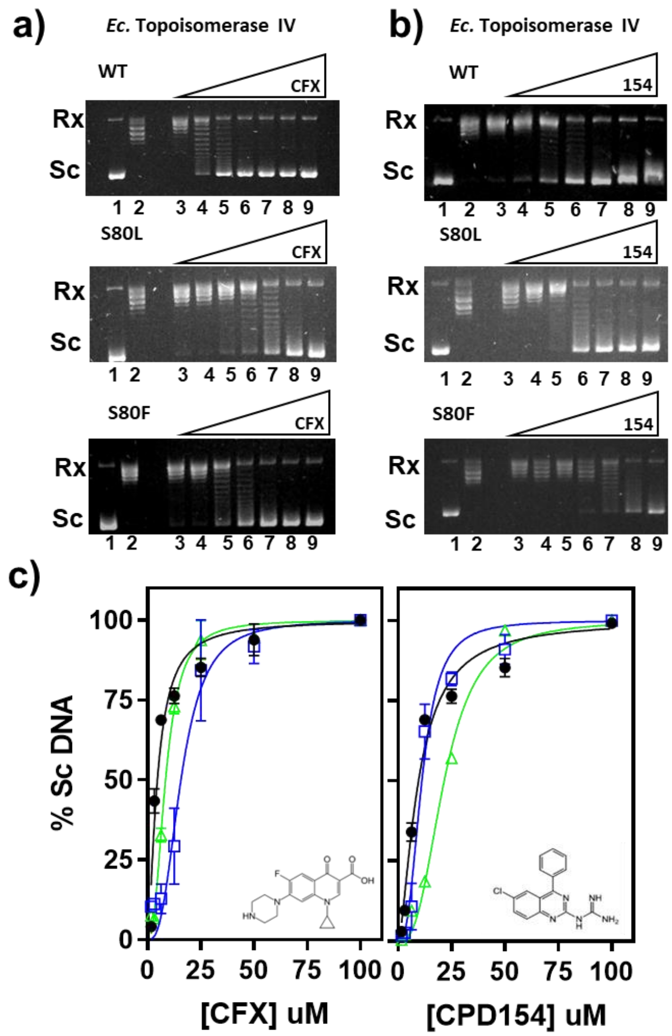


Figure 6. Inhibition of wild-type and mutants of *E. coli* topoisomerase IV by ciprofloxacin and CPD154. (a) DNA relaxation activity of wild-type (WT) and mutants (S80L and S80F) of *E. coli* topoisomerase IV in presence of ciprofloxacin (50 µM). Lanes 3-9 represents 1.56, 3.1, 6.25, 12.5, 25, 50, and 100 µM of ciprofloxacin, respectively. (b) DNA relaxation activity of wild-type (WT) and mutants (S80L and S80F) of *E. coli* topoisomerase IV in presence of CPD154(50 µM). Lanes 3-9 represents 1.56, 3.1, 6.25, 12.5, 25, 50, and 100 µM of CPD154, respectively. In all cases, lanes 1 and 2 are relaxed and supercoiled plasmid pAB1, respectively. (c) Graphical analysis of the DNA relaxation activity of *E. coli* topoisomerase IV showed in *A* and B*.* *E. coli* topoisomerase IV WT, S80L, and S80F are represented by black dots, empty blue squares, and empty green triangles. Drug structures are shown in corresponding panels. Symbols Rx and Sc represent relaxed and supercoiled DNA, respectively.

The IC_{50} of ciprofloxacin was notably affected when the Serine at position 80 was changed by a Leucine or Phenylalanine residue. Nevertheless, CPD154 is less susceptible to a Leucine in position 80 of parC with a ratio of IC_{50} (mutant/WT) of just 1.2, while for ciprofloxacin, the IC_{50} increased ~3.5 times. The IC_{50} value obtained for CPD154 with the S80F mutant was ~2.3 higher than that obtained with the wild-type enzyme. A two-times increase in IC_{50} value was observed for this mutant with ciprofloxacin, compared to the *E. coli* topoisomerase IV WT. Overall, CPD154 overcame, to some extent, the resistance to fluoroquinolone associated with the S80L mutation, representing a potential scaffold to develop novel compounds to treat bacterial drug resistance.

***In vivo* inhibition activity of bacterial DNA gyrase and antibacterial effect of CPD154**

We investigated the inhibition of gyrase by CPD154 *in vivo* using a two divergent coupled promoters system. This system employs two promoters that initiate transcription in opposite directions. Firefly luciferase, under the control of PgyrA, is coupled to a divergent IPTG-inducible promoter. Since PgyrA is a supercoiling-sensitive promoter and is stimulated by DNA relaxation, the activity of PgyrA is reduced in the presence of IPTG. However, if ciprofloxacin inhibits gyrase by stalling the movement of the transcription bubble, an increase in firefly luciferase activity is expected. We used β-galactosidase activity as a control, as LacZ is under the control of the IPTG-inducible promoter.

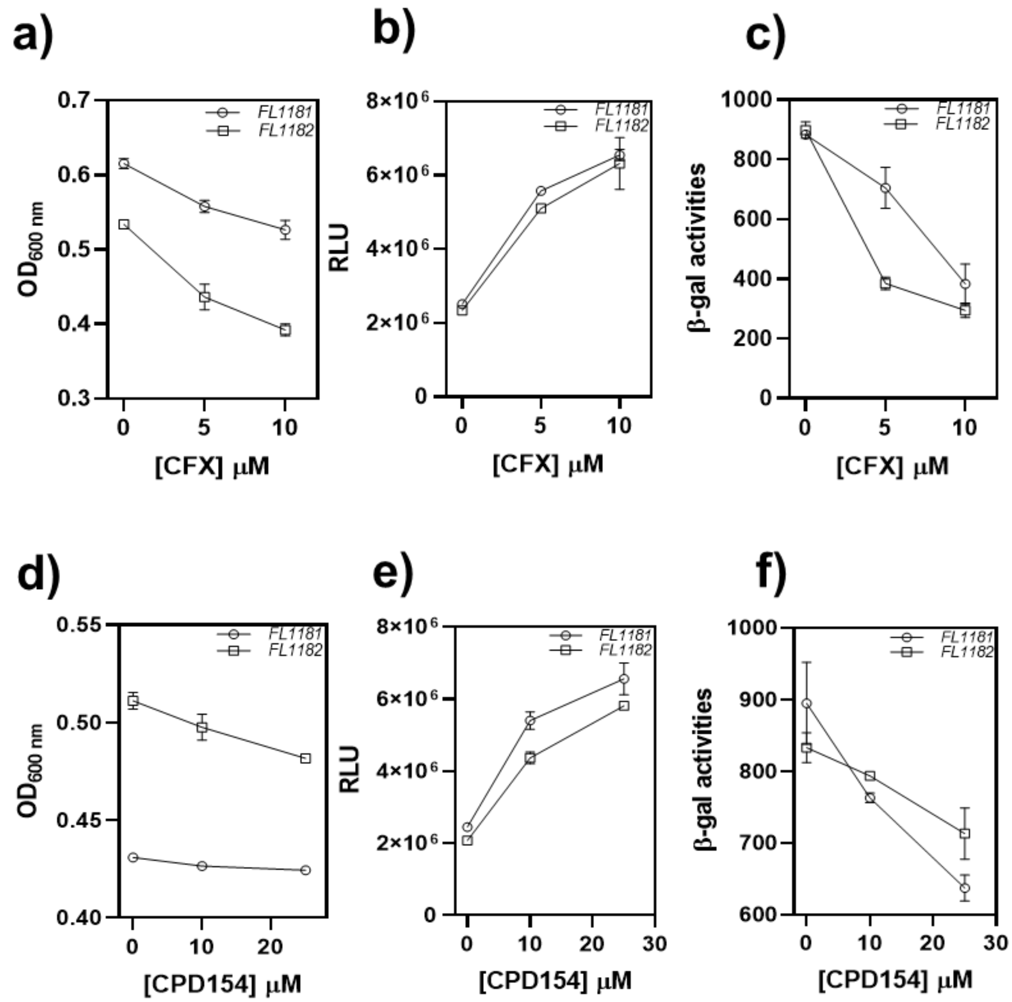


Figure 7. Bacterial growth is affected by the presence of DNA gyrase inhibitors (a and d). DNA gyrase inhibitors significantly enhanced the expression of firefly luciferase for FL1181 (b and e) and notably reduced the expression of β-galactosidase (c and f).

For both strains tested, CPD154 showed results similar to those of ciprofloxacin (Figure 7). As expected, CPD154 affected the growth of both bacterial strains used in our assays. In addition, in the presence of CPD154, β-galactosidase activity decreased notably, indicating a termination of transcription of the IPTG-inducible promoter. Since CPD154 is a bacterial gyrase DNA poison and stabilizes cleavage complexes with the enzyme and DNA, the (−) supercoils behind the RNA polymerase are not formed. In contrast, firefly luciferase expression increased substantially when the cells were treated with CPD154. Our results indicate that CPD154 inhibits bacterial DNA gyrase *in vivo*.

The bactericidal activity of CPD154 was evaluated against *E. coli* using a time-kill assay. Time-kill assays are commonly used to investigate the pharmacodynamics of new antimicrobial agents. CPD154 exhibited rapid bactericidal activity against *E. coli* at concentrations of 200, 100, and 50 µM (Figure 8a). A ≥ 3log10 reduction in viable cells compared to the initial inoculum was observed after 4 h of exposure with 200 and 100 µM of CPD154. However, this effect was not observed until after 24 h of incubation with 50 µM of CPD154. Regardless of the concentration, regrowth was not observed after 24 h of incubation with the drug.

The presence of viable cells was also analyzed using a drop plate assay for *E. coli* (ATCC 25922) with serial dilutions of CPD154. No viable cells were observed after 24 h of incubation with any of the three-drug concentrations tested (Figure 8b).

Compound 154's potent antibacterial activity may be attributed to the presence of a guanidine moiety. This group carries a positive charge at physiological pH, which may facilitate interaction and passage through the negatively charged bacterial membrane. Other natural and synthetic compounds containing guanidine groups have also demonstrated potent broad antibacterial effects, including activity against mycobacteria [298, 299]. Recent efforts to molecularly hybridize pyrrolic-based DNA gyrase inhibitors have resulted in compounds with improved antibacterial activity against Gram-negative strains, which can be attributed to the incorporation of a guanidine group [300].

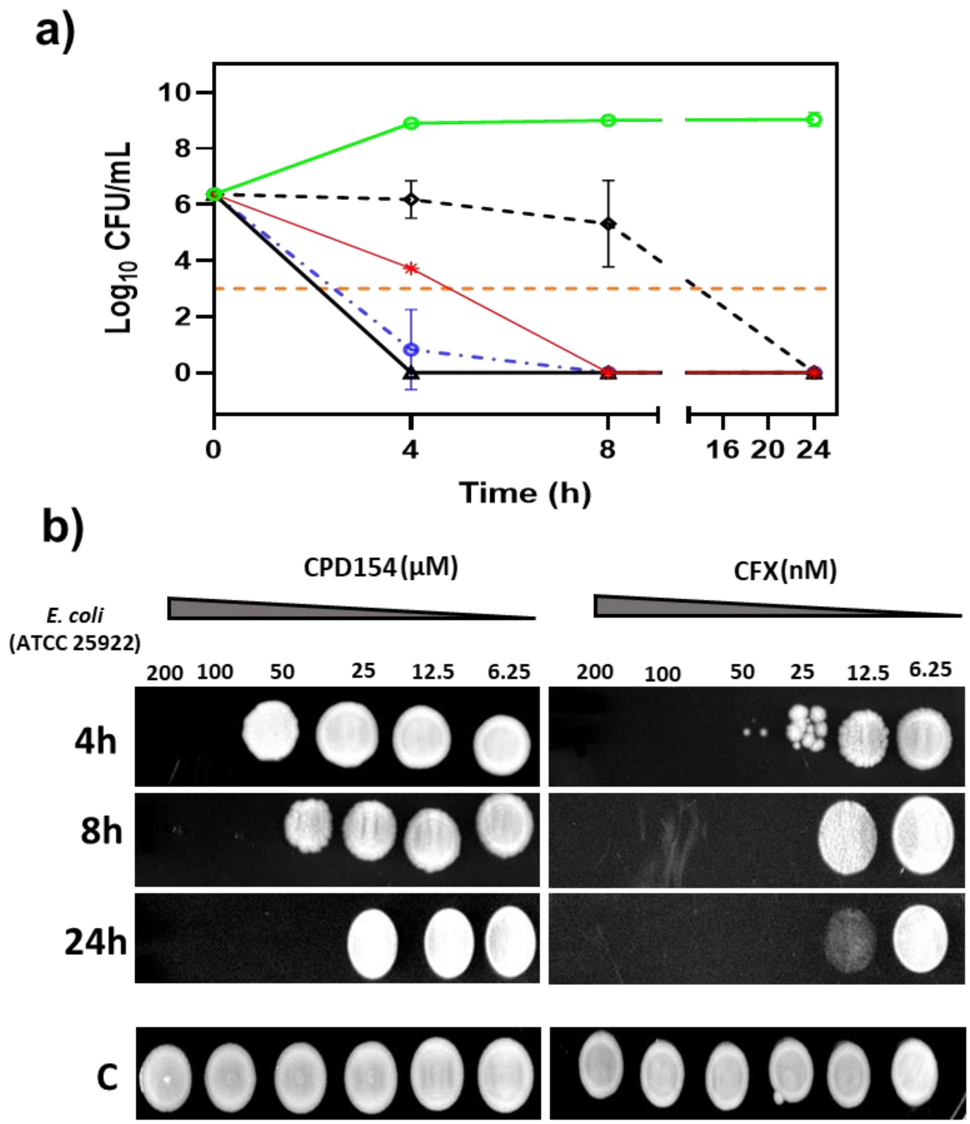


Figure 8. Bactericidal activity of CPD154. (A) Time-kill curves of CPD154 and ciprofloxacin against *E. coli* (ATCC 25922). The bactericidal level is indicated by the orange dashed line, growth control (green circle), 4xMIC (black triangles), 2xMIC (blue circles), MIC (black diamonds), and ciprofloxacin (200nM) (red stars). Samples were taken at 0, 4, 8 and 24 h to determine viable bacterial numbers. (B) Drop plate assay for *E. coli* (ATCC 25922) in presence of serial dilutions of compound 154 (left) and ciprofloxacin (right).

Conclusions

In summary, compound 154 has been shown to possess dual inhibitory activity against *E. coli* DNA gyrase and topoisomerase IV. The binding mechanism of CPD154 to stabilize the DNA-cleavage complexes with these enzymes has been elucidated through different approaches. CPD154's capacity to overcome fluoroquinolone resistance caused by mutations in the binding site and its strong antibacterial activity indicates its potential as a foundation in studies to generate broad-spectrum antibiotics.

Future directions

Although our results showed that CPD154 targets bacterial DNA gyrase and topoisomerase IV *in vitro* and *in vivo*, additional studies are needed to fully support the on-target mechanism of action for this compound. Three experiments can be used to demonstrate that CPD154 is targeting DNA gyrase and topoisomerase IV in vivo. The first experiment is to treat *E. coli* cells carrying plasmid pBR322 using CPD154, which should result in the production of positively supercoiled plasmid DNA [301]. DNA poisons, such as CPD154, should also result in the generation of linearized plasmid DNA. The second experiment is an induced mutation study of *E. coli* cells by CPD154 [302-304]. Specifically, *E. coli* strain MG1655 will grow in LB plates or liquid in the presence of an increasing sublethal concentrations of CPD154 (a sub-MIC concertation of CPD154 will be used at a starting point). These growth conditions should induce mutations to the *E. coli* genomic DNA. We will purify *E. coli* genomic DNA and sequence the genomic DNA of *E. coli* mutants by whole genome DNA sequencing. Mutations on DNA gyrase and/or topoisomerase IV will indicate the on-target mechanism for CPD154. The third *in vivo* experiment is the induction of *E. coli* SOS response by CPD154. We will use a method developed in Tse-Dinh's lab to study how the covalent topoisomerase-DNA complexes induce the SOS response in *E. coli* cells [305] . Specifically, plasmid pDinlux will be transformed to *E. coli* strains MG1655 or BAS3023 (BAS3023 carrying the Imp4213 mutation [306]) is more permeable to small molecule compounds). Since pDinlux contains the luxCADBE gene under the control of an SOS induction promoter, the dinD1 promoter, small molecules causing DNA damages will induce the SOS response and the expression of luciferase [306]. We expect that CPD154 will induce the expression of luciferase for *E. coli* strains MG1655 containing pDinlux, indicating that it targets DNA gyrase *in vivo*.

A few *in vitro* experiments can be performed to further demonstrate that CPD154 is a DNA gyrase poison inhibitor. Analogs of CPD154 may be purchased/synthesized for structure-activity relationship (SAR) studies. These analogs will be evaluated according to their anti-gyrase and anti-bacterial activities. After SAR studies, more potent and specific derivatives of CPD154 may be obtained. *E. coli* DNA gyrase-CPD154-DNA co-crystal structure may be solved using X-ray crystallography or cryo-electron microscopy. This structural information will demonstrate how CPD154 stabilizes gyrase-DNA covalent complex and provide insight into drug design. Additionally, biochemical assays can be used to study how CPD154 and analogs interact with gyrase mutants carrying FQ mutations.

SUPPLEMENTARY INFORMATION

Chapter II

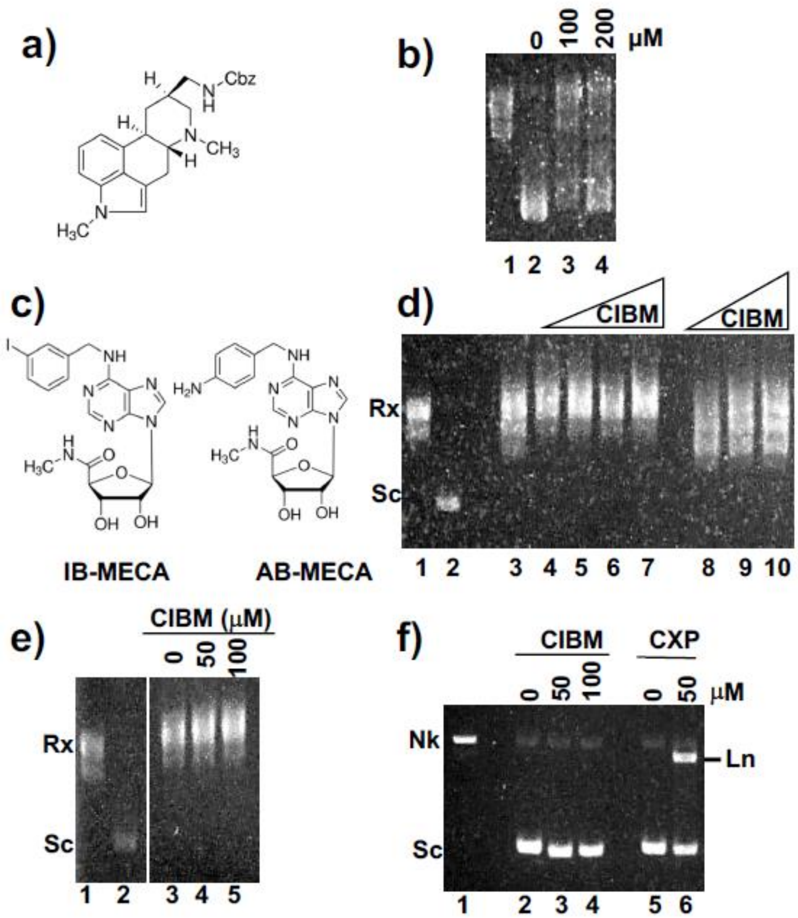


Fig. S1. a) Chemical structure of metergoline. **b**) Agarose gel-based gyrase assays to confirm that metergoline inhibited *E. coli* DNA gyrase activities. **c**) Chemical structures of IB-MECA and AB-MECA. **d**) Chloro-IB-MECA did not inhibit *E. coli* DNA topoisomerase IV (lanes 4-7) and human DNA topoisomerase 2α (lanes 8-10). Lanes 1 to 5 are DNA samples from the relaxation assays with *E. coli* topoisomerase IV in presence of 0, 50, 100, 150, 200 µM of chloro-IB-MECA, respectively. Lanes 6 to 8 are DNA samples from the relaxation assays with human topoisomerase 2α in presence of 0, 50 and 100 µM of chloro-IB-MECA, respectively. **e**) Chloro-IB-MECA did not inhibit *E. coli* DNA topoisomerase I.**f**) Chloro-IB-MECA is not a *E. coli* DNA gyrase poison. Gyrase-mediated DNA cleavage assays were performed as described in Materials and Methods using plasmid pBR322. Symbols Rx, Sc, Nk, and Ln represent relaxed, supercoiled, nicked, and linear DNA, respectively.

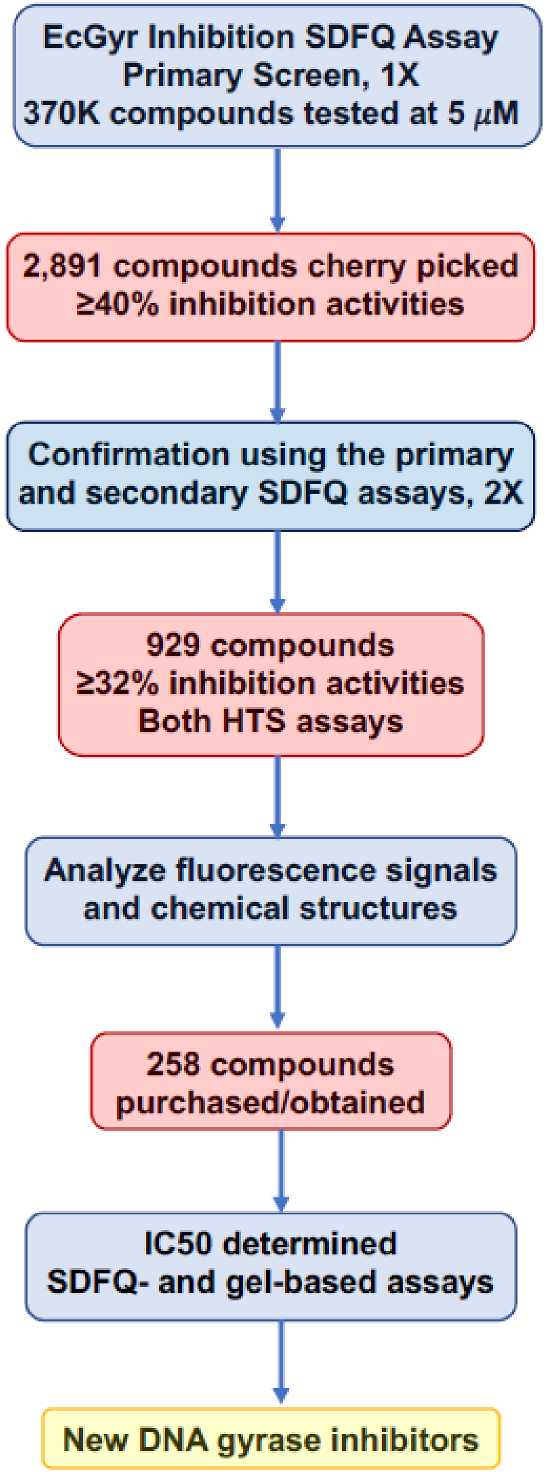


Fig. S2. The workflow of the HTS assay screening the MLSMR library S4

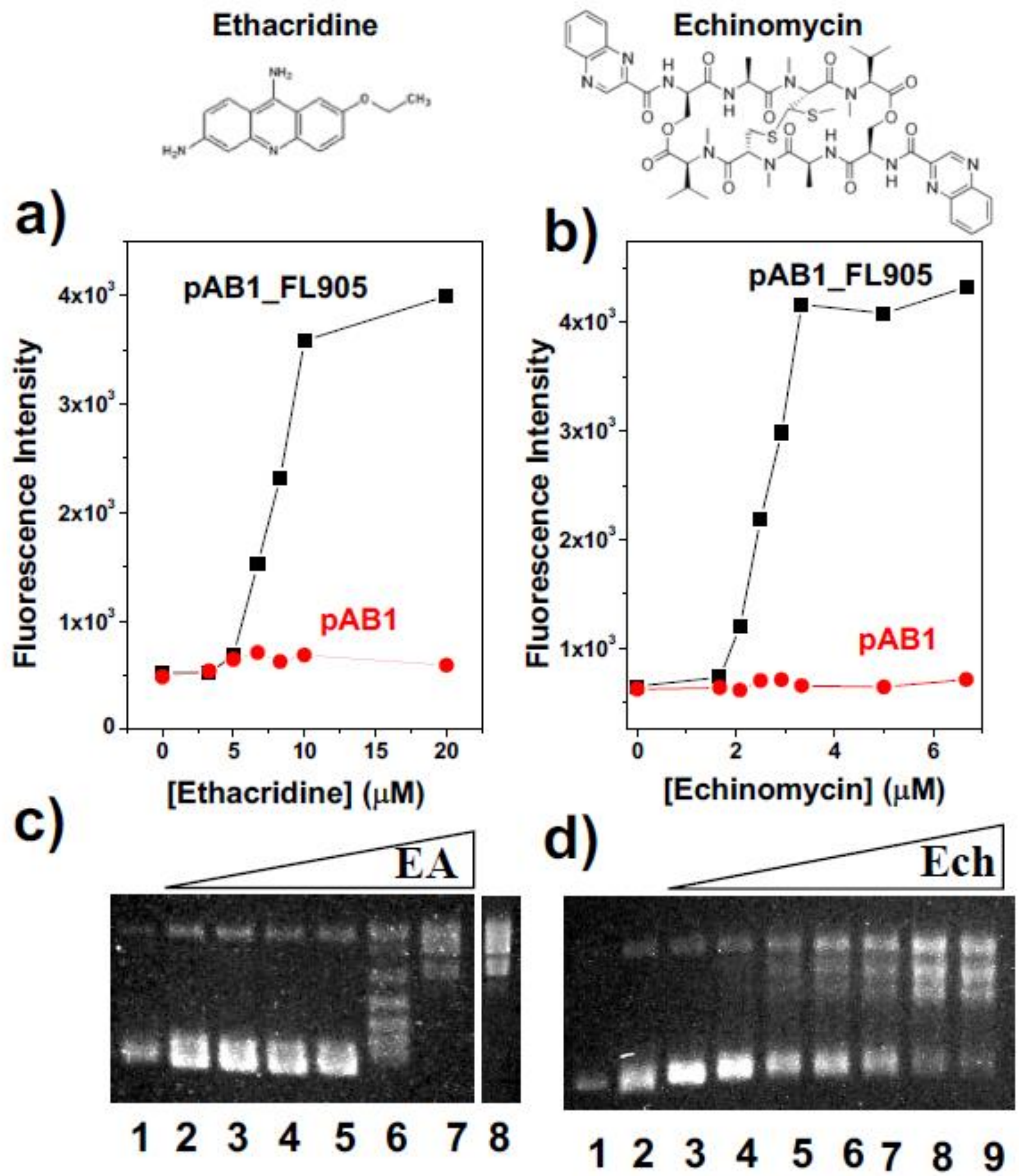
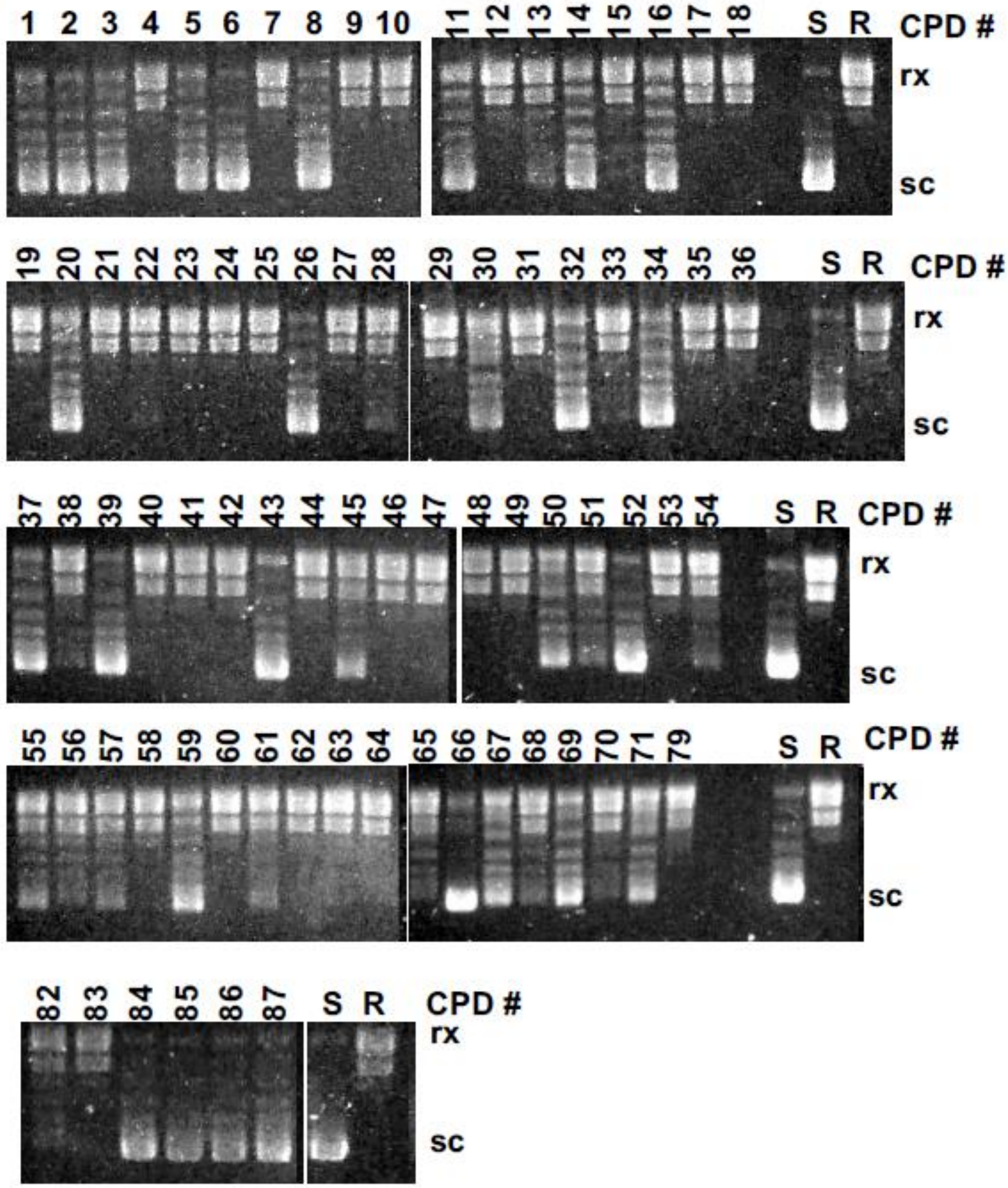


Fig. S3. The fluorescence intensity was significantly increased after ethacridine (**a**) and echinomycin (**b**) intercalated and unwound the sc pAB1_FL905 (black squares). Ethacridine and echinomycin do not have fluorescence in the presence plasmid pAB1. Ethacridine (EA, c) and echinomycin (Ech, d) inhibited *E. coli* DNA gyrase activities. **c**) Lane 1 represent supercoiled pAB1. Lanes 2-7 contain 0, 3.12, 6.25, 12.5, 25, and 50 μM of ethacridine. Lane 8 is relaxed pAB1. d) Lane 1 represent supercoiled pAB1. Lanes 2-9 contain 0, 12.5, 25, 50, 75,, 100, 150, and 200 μM of echinomycin.

a)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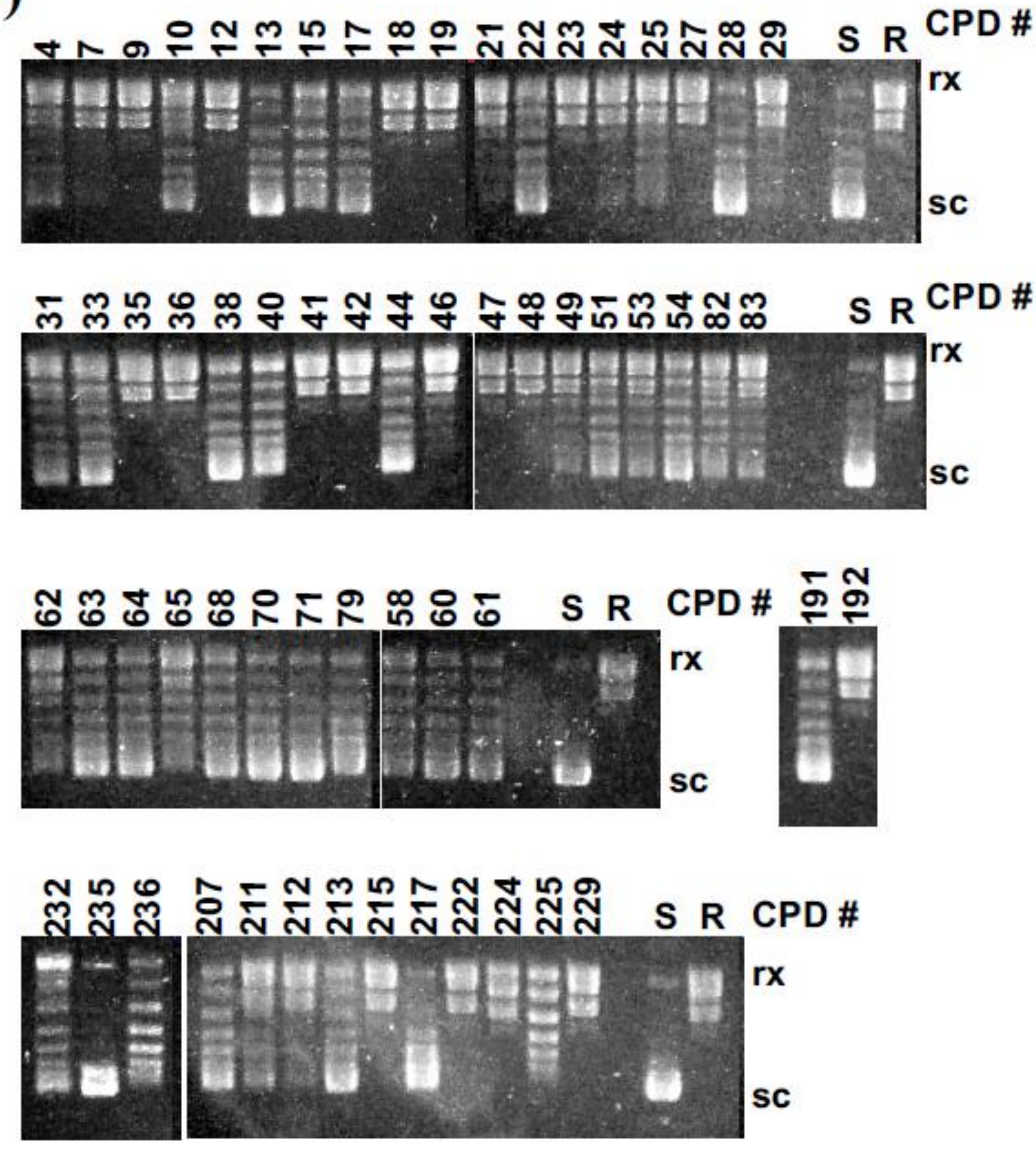
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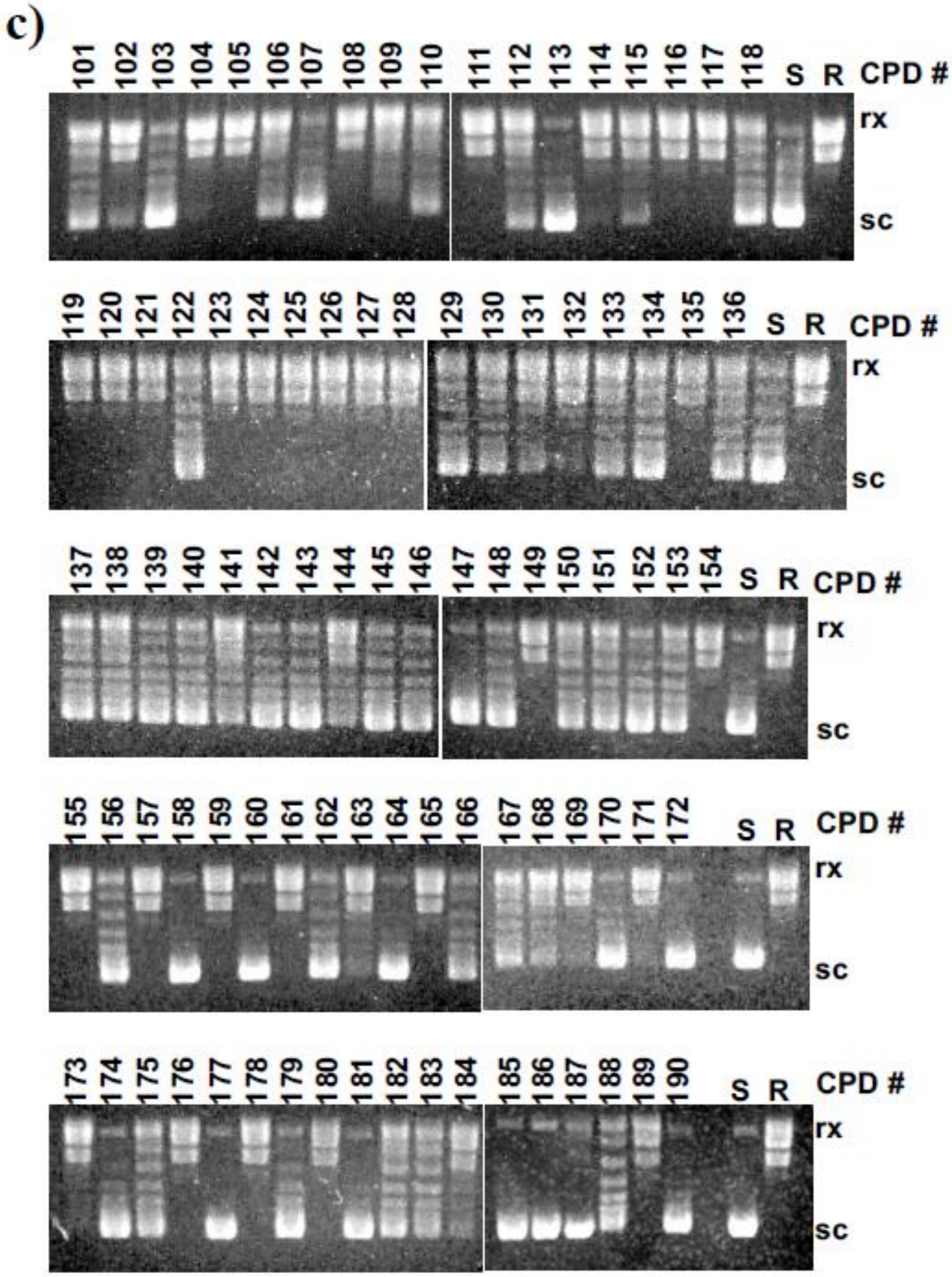
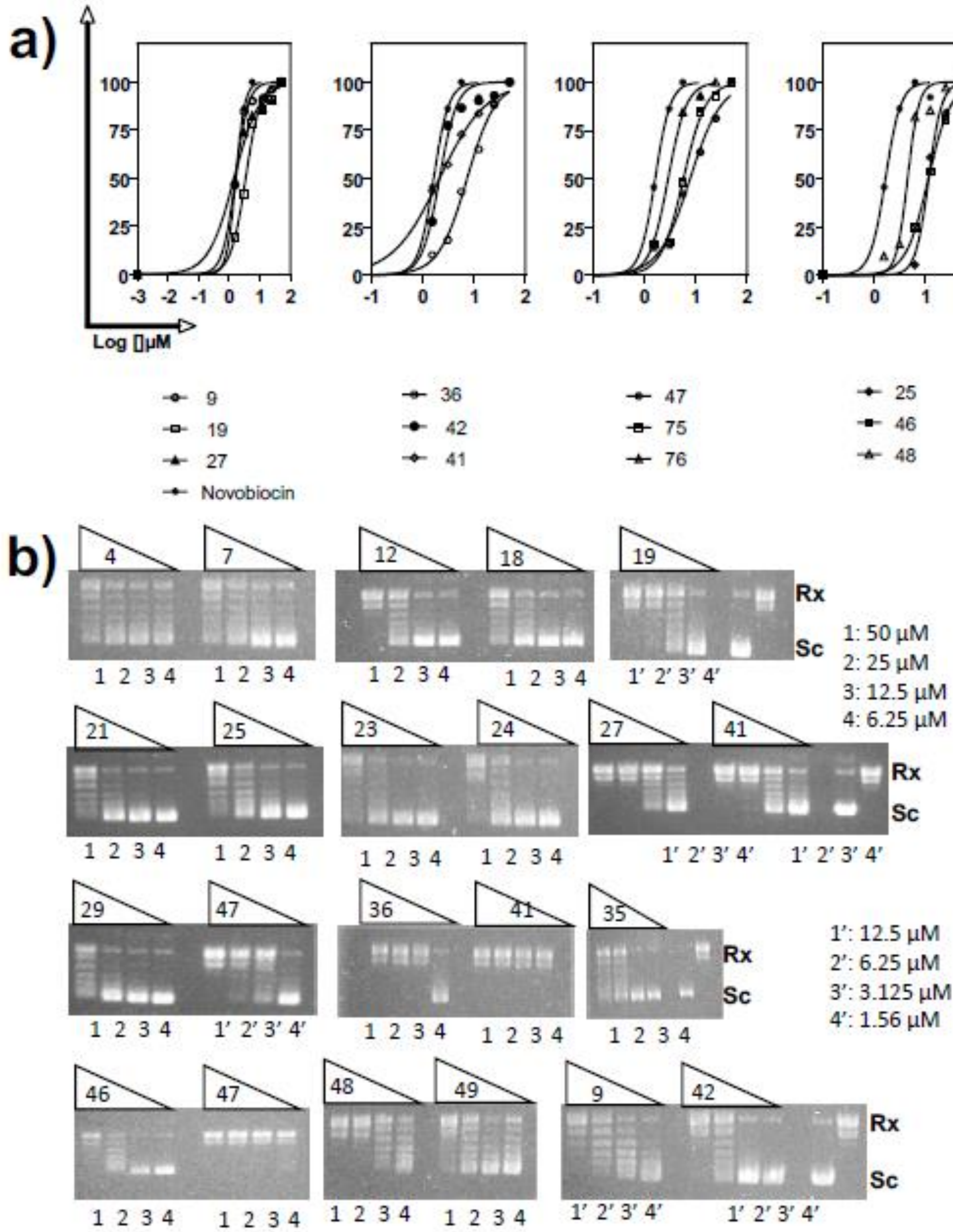


Fig. S4. Agarose gel-based gyrase assays to identify inhibitors against *E. coli* DNA gyrase. **a**) 200 µM of compounds were used. S and R represented supercoiled and relaxed pAB1 samples. **b** and **c**) 50 µM of compounds were used. S and R represented supercoiled and relaxed pAB1 samples. Symbols: rx, relaxed; sc, supercoiled. Compound numbers (CPD #) are indicated.


a)
100
75
50
25
0
-3 -2 -1 0 1 2
-1 0 1 2
Log []μM
9
19
27
Novobiocin
36
42
41
47
75
76
25
46
48
b)
4
7
12
18
19
21
25
23
24
27
41
29
47
36
35
46
48
49
9
42
Rx
Sc
1 2 3 4
1' 2' 3' 4'
1: 50 μM
2: 25 μM
3: 12.5 μM
4: 6.25 μM
1': 12.5 μM
2': 6.25 μM
3': 3.125 μM
4': 1.56 μM

c)

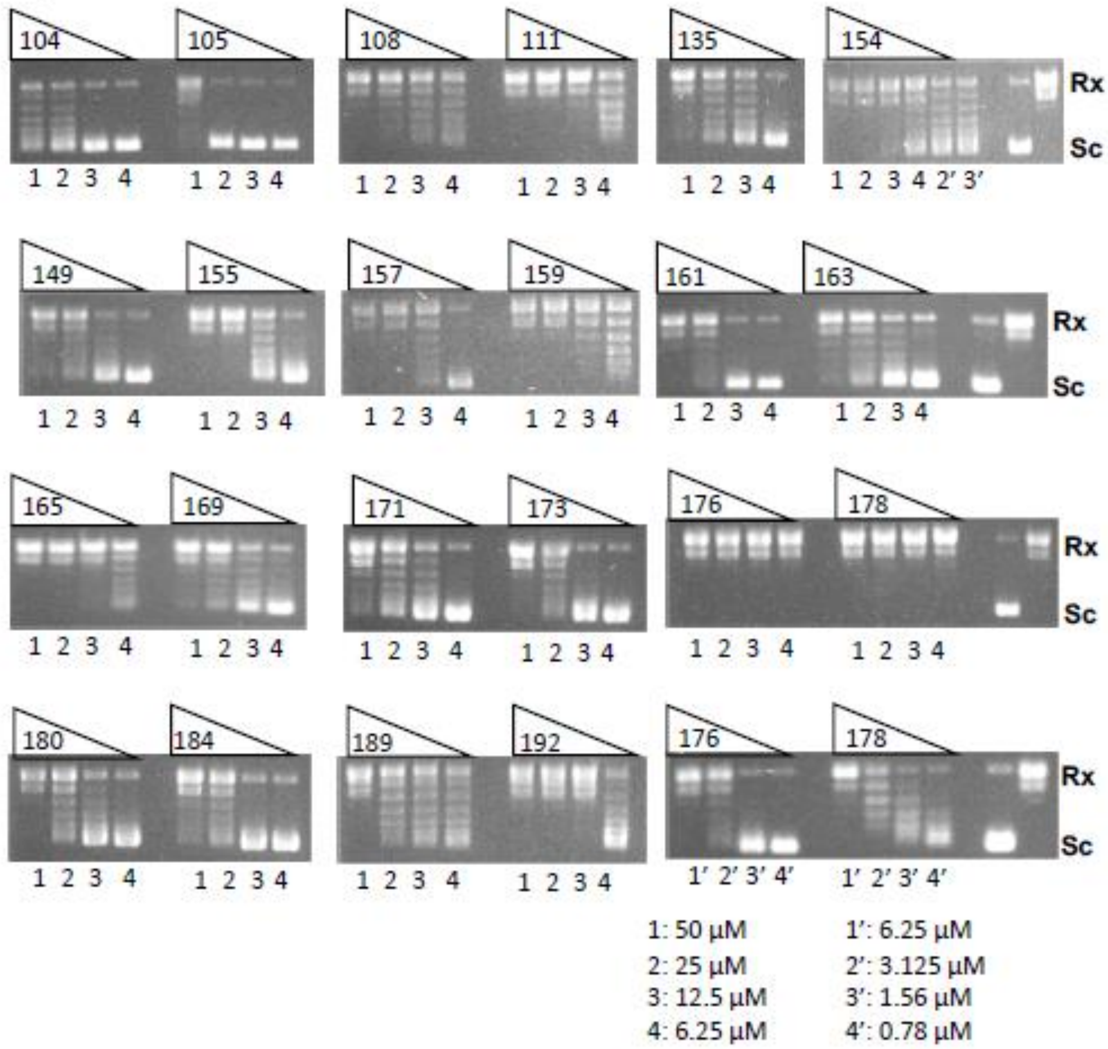


Fig. S5. a) SDFQ-based gyrase titration assays to determine the IC_{50} of the new gyrase inhibitors against *E. coli* DNA gyrase. Below of the plots are symbols for different compounds. **b** and **c**) Agarose gel-based gyrase titration assays to determine IC_{50} values against *E. coli* DNA gyrase. Compound numbers are indicated above the gels. Lanes 1 to 4 contain 50, 25, 12.5, and 6.25 µM of compounds, respectively. Lanes 1’ to 4’ contain 12.5, 6.25, 3.125, and 1.56 µM of compounds, respectively.

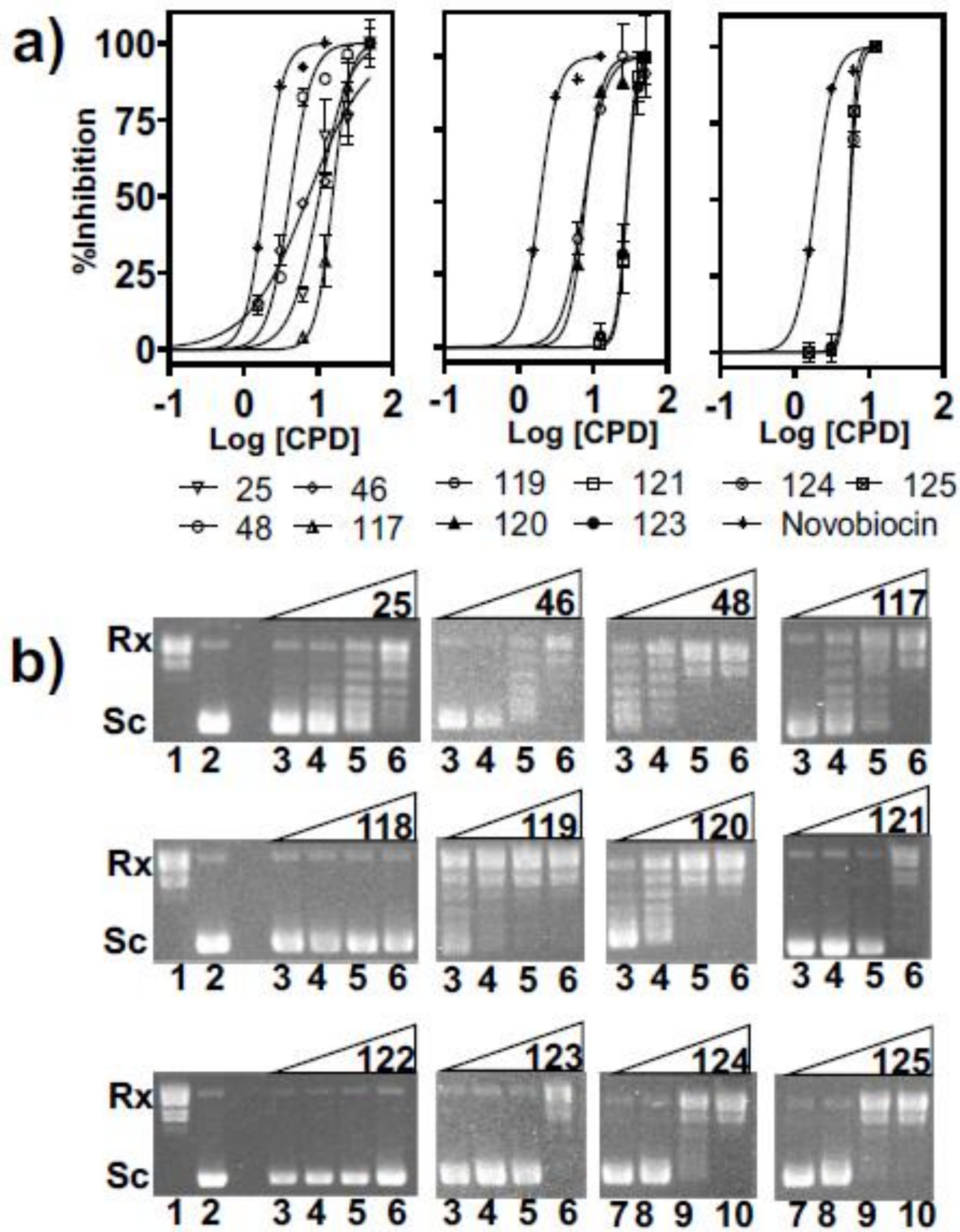


Figure S6. *E. coli* gyrase inhibition assays with psoralen derivatives. **a**) SDFQ-based gyrase titration assays to determine the IC_{50} against *E. coli* DNA gyrase. **b**) Agarose gel-based gyrase inhibition assays for psoralen derivatives. Compound # are placed above the gels. Lanes 3-6 correspond to 6.25, 12.5, 25 and 50 μM of the compounds, respectively. Lanes 7-10 correspond to 1.56, 3.13, 6.25 and 12.5 μM of the compounds respectively. Lanes 1 and 2 are relaxed (Rx) and supercoiled (Sc) pAB1, respectively.

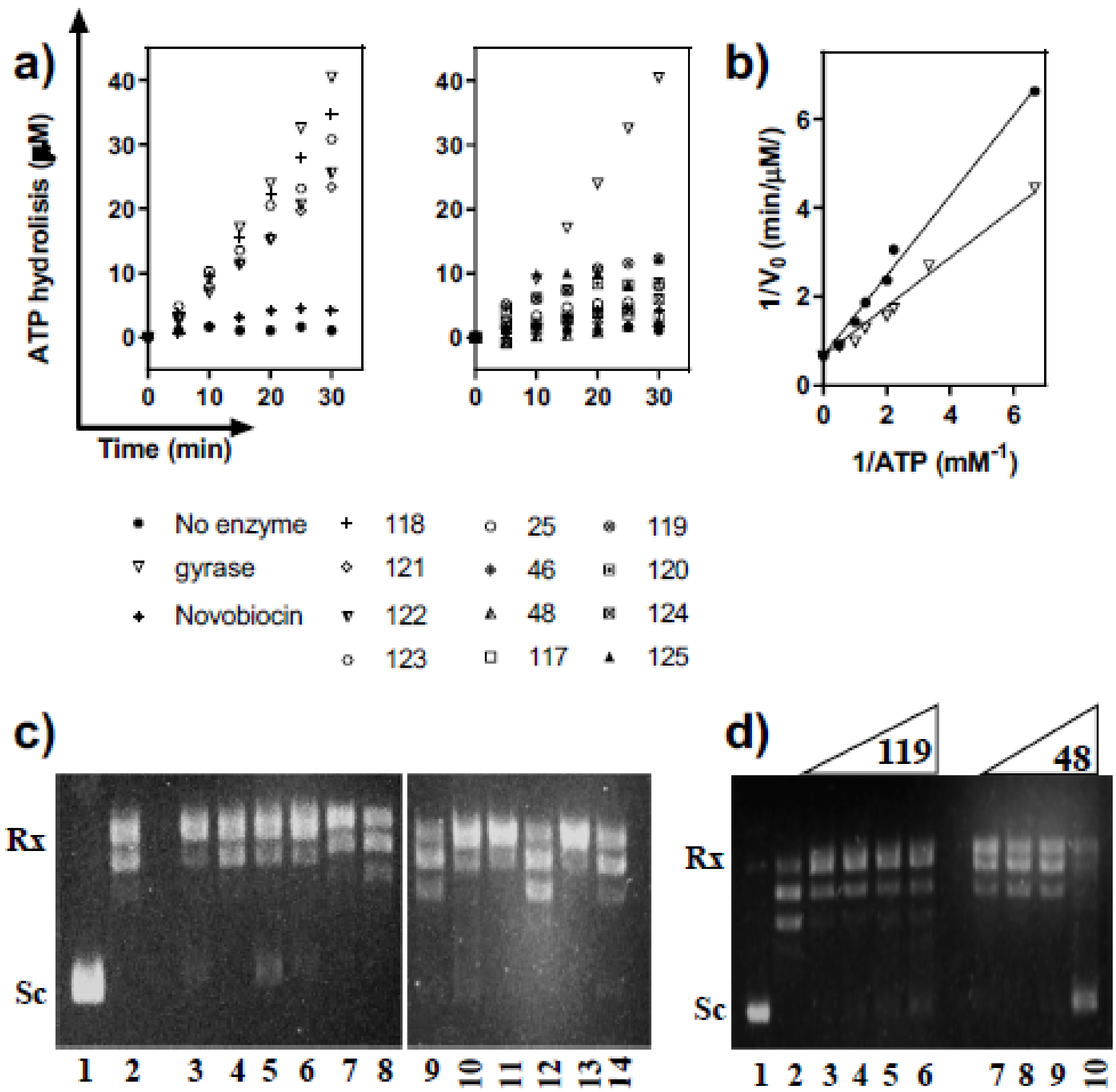


Figure S7. a) Inhibition of ATPase activities of *E. coli* DNA gyrase by psoralen derivatives. The ATPase assays were performed as described in Methods. **b**) Compound 48 is an ATP competitive inhibitor of *E. coli* DNA gyrase. Lineweaver−Burk plot of *E. coli* DNA gyrase in the absence (open triangles) or presence (closed circles) of 500 nM of compound 48. **c**) Psoralen derivatives are not potent inhibitors against *E. coli* DNA topoisomerase I. Lanes 3-14 contain 50 μM of compounds 25, 46, 48, 117, 118, 119, 120, 121, 122, 123, 124, and 125, respectively. Lanes 1 and 2 are supercoiled and relaxed pAB1. **d**) Compounds 48 and 119 are not potent inhibitors against human DNA topoisomerase 2α. lanes 3-6 contain 25, 50, 100, and 200 μM of compound 119, respectively. Lanes 7-10 contains 50, 100, and 200 μM of compound 48, respectively. Lanes 1 and 2 are supercoiled and relaxed pAB1.

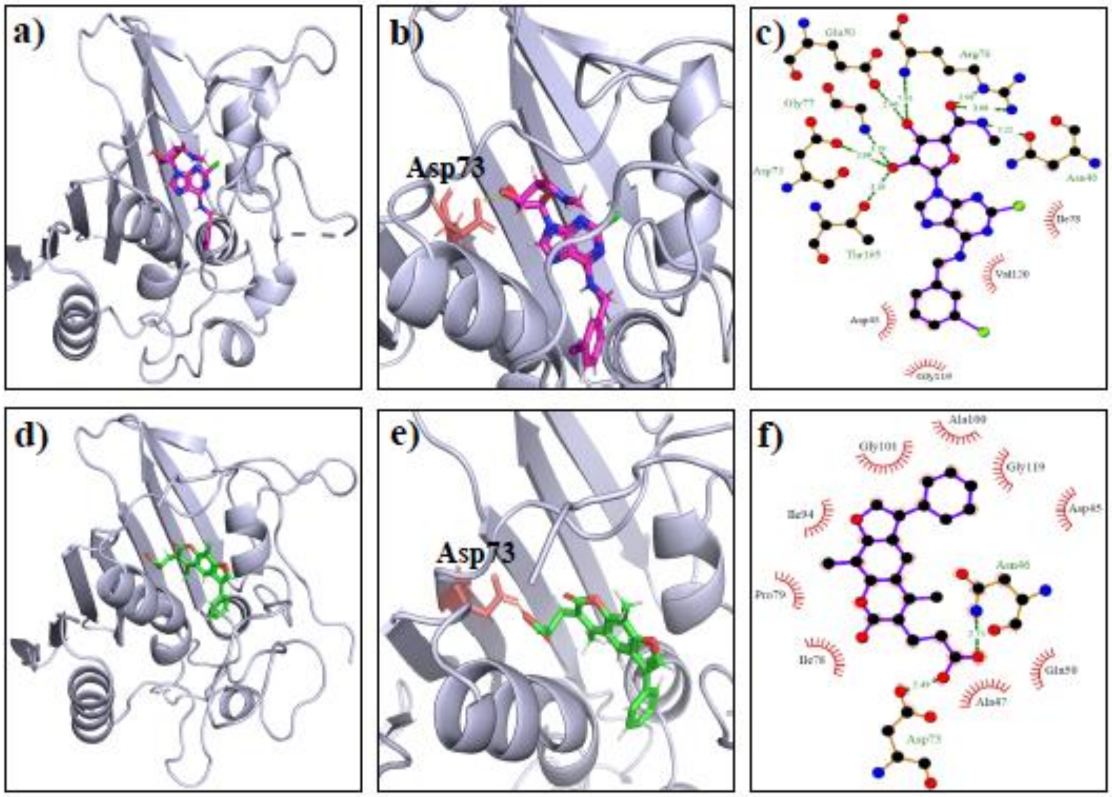


Figure S8. Molecular modeling analysis of Cl-IB-MECA (**a**-**c**) and compound 48 (**d**-**f**) binding to the ATP binding pocket of *E. coli* DNA Gyrase B. Molecular models were constructed as described in Methods. A hydrogen bond is formed between the inhibitors (Cl-IB-MECA (b) and compound 48 (**e**)) and residue Asp73. **c** and **f** show schematic 2-D representations of *E. coli* DNA gyrase-ligand complexes. Hydrogens bonds and distances are highlighted as green dashed lines. Hydrophobic contacts are shown as an arc with spokes radiating towards the ligand atoms.

Table S1. *E. coli* DNA gyrase inhibitors identified by screening the LOPAC Library			
Sigma Cat No.	**Name**	**Pubchem CID**	**Inhibition Activities (%)**
A0966	4-Amino-1,8-naphthalimide	1720	1704.9
T7697	I-OMe-Tyrphostin AG 538	5353685	776.8
T2067	Tyrphostin AG 879	135419190	731
S3442	SB 216763	176158	683.9
T2705	Topotecan hydrochloride hydrate	5515	582.6
I1656	Idarubicin hydrochloride	636362	512
Q3251	Quinacrine dihydrochloride	6239	459.4
S9692	SU 6656	5312137	412.7
D9766	Dipyridamole	3108	411.9
G6416	GW5074	5924208	277.5
M4008	Morin hydrate	16219651	249.6
S-154	Sepiapterin	135398579	182.9
S8442	SU 5416	5329098	151.3
E3380	Ellipticine	3213	127.4
L2906	Lomefloxacin hydrochloride	68624	109.8
S2671	Suramin sodium salt	8514	107.8
PZ0015	Trovafloxacin mesylate	62960	105.4
A9605	AC-93253 iodide	16078948	104
A1895	Aurintricarboxylic acid	2259	104
D3943	DAPH	1697	102.9
E7881	Emodin	3220	101.1
O8757	Ofloxacin	4583	95
R-115	Reactive Blue 2	656725	87.9
PZ0012	Sunitinib malate	6456015	84.3
D2926	Diphenyleneiodonium chloride	2733504	82.5
M6760	Myricetin	5281672	79.8
S5567	SP600125	8515	79.1
L2037	β-Lapachone	103178327	75.4
B9685	BAY 61-3606 hydrochloride hydrate	71563345	72.8
N8652	NF 023 hydrate	6093160	71.6
N1786	NSC 95397	262093	66.5
C-277	Chloro-IB-MECA	3035850	66.3
A-242	Alloxazine	5372720	62.6
T7540	Tyrphostin 47	667601	59.1
C3353	CGP-74514A hydrochloride	11957495	58.5
P0547	Pentamidine isethionate salt	8813	56.7
PZ0115	CP-31398 dihydrochloride hydrate	56972205	56
D5439	2,3-Dimethoxy-1,4-naphthoquinone	3136	49
A8981	AS-252424	11630874	44.7
J4829	JFD00244	2817242	41.6
T7822	Tyrphostin AG 538	5328760	40.4

Table S2. *E. coli* DNA gyrase inhibitors identified by screening the MLSMR Library

		Primary Screen	Hit Reconfirmation using Primary assay				Hit Reconfirmation using pAB1_FL924			
CPD ID	PUBCHEM_SID	% Act	% Act 1	% Act 2	Avg % Act	Std Dev	% Act 1	% Act 2	Avg % Act	Std Dev
MLS-0210866	87338067	305.57	389.6	383	386.32	4.662	5498.3	5549.3	5523.8	36.094
MLS-0412321	57260390	156.45	150.9	152.2	151.55	0.927	5377.3	5368.9	5373.1	5.9438
MLS-0074372	99454010	107.09	87.9	93.4	90.66	3.856	5370.8	5350.2	5360.5	14.579
MLS-0412321	99355593	177.71	161.6	168	164.79	4.582	5370.2	5341.8	5356	20.069
MLS-0254967	24810829	204.87	115	119	116.96	2.816	5280.6	5296.1	5288.4	10.928
MLS-0285976	24804590	1797.9	1453.9	1452.8	1453.30	0.784	5264.9	5250.4	5257.6	10.263
MLS-0401009	57266590	255.3	185.8	178.8	182.29	4.951	4908.2	4904	4906.1	2.9424
MLS-0421276	57264490	1763.2	1440.6	1461.9	1451.30	15.089	4882.2	4921.7	4902	27.896
MLS-0320069	49670904	982.11	595.2	643.4	619.31	34.030	4488.7	4307.8	4398.2	127.96
MLS-0444439	92763441	68.6	53.8	57.8	55.83	2.837	4327.6	4369.4	4348.5	29.608
MLS-0323146	49668469	500.45	291.2	279.2	285.23	8.473	3521.9	4180.5	3851.2	465.7
MLS-0318041	99495581	453.65	337.7	348.2	342.98	7.434	3812.9	3824.1	3818.5	7.9004
MLS-0084965	14724300	1485.7	1271.8	1300.8	1286.30	20.475	3697.6	3880.8	3789.2	129.54
MLS-0439352	92764854	58.18	49.9	52.7	51.30	2.041	3177.3	3255.9	3216.6	55.537
MLS-0258570	24833935	401.33	349.5	326.6	338.01	16.201	3154.8	3182.2	3168.5	19.385
MLS-0274625	24781172	724.51	540	512.1	526.06	19.762	3164.7	3149.5	3157.1	10.752
MLS-0284347	24805365	106.06	64.5	64.2	64.38	0.199	2848.3	2758.2	2803.3	63.709
MLS-0465090	121286207	1714.5	1439.5	1441.4	1440.40	1.339	2641.4	2645.4	2643.4	2.8742
MLS-0448386	99360623	1709.8	1428.4	1433.8	1431.10	3.808	1955.5	2829.2	2392.4	617.81
MLS-0224603	22405246	1803.7	1399.6	1463.5	1431.50	45.202	2057.1	2243.7	2150.4	131.95
MLS-0327205	49667711	1606	1457	1456.9	1456.90	0.110	2059.3	2194.7	2127	95.763
MLS-0092584	17408695	229.26	64.4	67.3	65.88	2.057	1865.9	2353.9	2109.9	345.04
MLS-0213957	17507787	346.59	105.7	142.7	124.22	26.187	2036.1	2030.6	2033.4	3.8788
MLS-0208789	17511470	86.5	71.1	70.8	70.97	0.203	1775.8	1843.8	1809.8	48.075
MLS-0209141	17512321	744.47	623.4	649.3	636.36	18.280	1729.8	1853	1791.4	87.123
MLS-0236301	24832577	1630.1	1448.8	1455.8	1452.30	4.946	1849.6	1725	1787.3	88.083
MLS-0204777	22401237	899.66	364.8	404.6	384.68	28.106	1592.4	1846	1719.2	179.29
MLS-0445255	92764853	86.43	70	75.1	72.59	3.603	1767.3	1659.8	1713.5	76.039
MLS-0095667	17403527	834.72	468.3	473	470.61	3.324	1695.4	1657.6	1676.5	26.719
MLS-0218122	87337068	121.92	120.6	114.9	117.73	4.026	1590.4	1553.7	1572.1	25.961
MLS-0293465	26663572	1575.6	923.5	1172.2	1047.80	175.830	1498.3	1612	1555.1	80.41
MLS-0326162	49665286	376.02	231.6	347.8	289.74	82.152	1311.8	1453.6	1382.7	100.27
MLS-0445052	92764134	631.41	496	498.7	497.35	1.847	1294.2	1309.5	1301.9	10.812
MLS-0003115	855879	54.26	53.2	55	54.09	1.297	1160.1	1194.8	1177.4	24.539
MLS-0281566	24804996	1529.9	1089.2	1141.2	1115.20	36.715	1148.3	1177	1162.6	20.309
MLS-0296314	26664251	94.2	90.3	93.7	91.98	2.426	1036.7	1056.9	1046.8	14.305
MLS-0252729	24781294	1688.2	1445.3	1446.9	1446.10	1.124	1033.1	1042.9	1038	6.8999
MLS-0279197	87349492	200.64	112.1	102.4	107.24	6.838	1004.5	1008.1	1006.3	2.5251
MLS-0444916	92764864	103.66	120.6	132	126.27	8.054	1008.8	991.7	1000.2	12.051
MLS-0251839	24809038	600.23	548.3	566.9	557.59	13.215	1002.1	939.3	970.69	44.456
MLS-0311001	24815104	470.33	330.2	371.2	350.71	29.029	972.9	967.7	970.31	3.704
MLS-0252936	85305352	1039.4	664.9	660.5	662.67	3.109	955.6	976.7	966.18	14.931
MLS-0270698	24791835	47.31	52.2	51.6	51.86	0.426	933.8	959.8	946.82	18.39
MLS-0272957	24788180	1432.4	824.6	829.2	826.89	3.288	738.4	1095.9	917.15	252.75
MLS-0252955	87349591	1059.9	574.5	673	623.72	69.673	880.1	921.6	900.88	29.354
MLS-0252217	24821031	1744.2	493.9	649	571.47	109.710	871	903	886.99	22.605
MLS-0101953	24807803	1393.4	889.1	570.7	729.93	225.150	964.2	759.3	861.73	144.87
MLS-0305051	26663544	92.55	65.2	67.5	66.32	1.606	847.8	866.8	857.27	13.46
MLS-0327351	49667132	1295.3	1127.6	1131.2	1129.40	2.509	832.1	865.3	848.7	23.505
MLS-0447002	99494336	57.58	66.6	53.8	60.18	9.018	831.5	852.4	841.97	14.789
MLS-0271845	24816522	95.05	67.2	70.5	68.83	2.360	886.8	762.4	824.57	87.994
MLS-0267502	24812344	167.45	136.4	151.9	144.17	10.996	814.2	825.1	819.61	7.7164
MLS-0210564	17513131	1016.7	847.7	865.3	856.51	12.471	839.1	778	808.56	43.241
MLS-0211624	17510327	1832.1	395.6	339.7	367.67	39.507	669.8	930.8	800.28	184.59

MLS-0207445	17512316	356.3	276.8	282.8	279.84	4.235	768.7	784.7	776.67	11.293
MLS-0300459	26667370	672.87	566.9	590.7	578.77	16.841	712.5	743.2	727.87	21.679
MLS-0282204	24797341	1803.4	1468.5	1467.4	1467.90	0.800	681.9	670.6	676.24	7.9474
MLS-0074707	14742165	2042.2	1405.2	1480.9	1443.10	53.543	739.7	570.2	654.94	119.86
MLS-0297492	26664070	103.51	72.2	70.4	71.31	1.321	640.1	640.2	640.16	0.095164
MLS-0305393	26662708	161.66	139.5	143.4	141.41	2.751	595.6	653	624.31	40.6
MLS-0259491	24817295	1775.1	272.8	361.9	317.34	62.957	546.5	698.8	622.67	107.73
MLS-0294556	26663191	83.03	83.4	72.5	77.95	7.718	580.9	561.6	571.27	13.678
MLS-0320961	49679995	1572.5	1451.3	1457.5	1454.40	4.388	549.8	565.9	557.83	11.366
MLS-0273048	24783794	88.25	62.9	69.5	66.18	4.634	508.6	549.9	529.23	29.183
MLS-0073998	14742829	302.18	349.6	353.7	351.67	2.868	501.5	546.4	523.96	31.762
MLS-0395170	47194303	61.08	55.6	59.7	57.64	2.901	506.9	503.3	505.11	2.5516
MLS-0345533	47204454	119.42	115.7	119.5	117.61	2.661	455.5	459.8	457.62	3.054
MLS-0220227	22402609	158.22	118.5	123.9	121.19	3.770	427.6	472.9	450.28	32.021
MLS-0069429	14746919	59.63	55.3	73.4	64.34	12.798	516.5	373.3	444.92	101.28
MLS-0350564	49642972	1696.1	1452.2	1448.6	1450.40	2.541	437	433.8	435.41	2.2993
MLS-0338697	49674898	254.81	222.1	226.7	224.36	3.246	430.3	434.2	432.23	2.74
MLS-0215634	17511646	61.03	95.6	101.7	98.62	4.305	386.4	475.1	430.74	62.756
MLS-0207843	87337067	69.83	78.4	79.6	79.02	0.835	475.4	366	420.73	77.352
MLS-0101953	17387304	1823.7	755.3	633.5	694.40	86.189	330.8	500.3	415.54	119.86
MLS-0261638	24821366	782.23	308.7	319.8	314.28	7.839	394.1	416.2	405.14	15.681
MLS-0444567	92764857	59.91	64.1	64	64.01	0.074	394.2	411	402.57	11.875
MLS-0276758	24797499	46.01	56.1	62.4	59.22	4.444	387.4	409	398.24	15.27
MLS-0233708	17431874	113.36	110.6	197.9	154.22	61.758	395.5	393.4	394.45	1.4782
MLS-0224042	22415777	737.34	735.8	674.9	705.34	43.057	436.4	344.2	390.29	65.141
MLS-0245662	24802733	278.97	181.1	183.6	182.34	1.810	376.5	386.4	381.44	6.9657
MLS-0218294	17503970	1829.2	1458.7	1469.3	1464.00	7.511	751.7	4.7	378.23	528.23
MLS-0073937	87346612	1214.3	532.8	482.4	507.58	35.598	422.6	315.2	368.91	75.966
MLS-0343101	47199367	972.5	646.7	742.5	694.58	67.750	277.1	453.6	365.37	124.84
MLS-0442463	89855845	225.27	126.5	123.5	124.99	2.117	456.7	273.6	365.13	129.43
MLS-0444535	92764434	71.67	53.7	57	55.40	2.340	332	394.5	363.24	44.168
MLS-0216733	17506296	1823.6	1469.1	1461.9	1465.50	5.118	584.8	134.9	359.86	318.1
MLS-0253189	24809826	201.44	124.1	130.4	127.29	4.447	345.2	366.9	356.08	15.346
MLS-0312443	26661007	53.01	49.2	53.3	51.26	2.865	350	352.5	351.23	1.7774
MLS-0348610	49643995	328.24	221.9	254.4	238.16	22.957	290	402.1	346.08	79.254
MLS-0253694	24822843	954.83	707.1	732.1	719.60	17.670	329.9	348.3	339.12	12.984
MLS-0035667	7973721	1833.1	1447.2	1456.1	1451.60	6.295	332.5	345.7	339.06	9.3137
MLS-0439672	93576975	1528.3	1164.5	1195.5	1180.00	21.963	337.4	327.5	332.46	7.0488
MLS-0079276	14733010	110.17	113.1	89	101.06	17.011	340.7	312.8	326.75	19.733
MLS-0439485	92764865	79.83	87.3	93.7	90.51	4.572	318.8	309.8	314.31	6.3953
MLS-0084237	14721422	1021.4	888.8	906.1	897.48	12.236	324.4	300.7	312.6	16.757
MLS-0374449	49827544	172.27	171.4	191.7	181.57	14.383	287.4	328.8	308.08	29.265
MLS-0318708	49671788	1493.4	1411.8	1400	1405.90	8.366	301.5	303.7	302.6	1.5519
MLS-0462482	99495574	251.82	215.5	213.5	214.51	1.382	293.4	306.7	300.07	9.4276
MLS-0450900	99359808	1815.3	1129.8	1444.4	1287.10	222.440	294.3	305.2	299.77	7.6906
MLS-0101305	17401648	105.13	75.9	83.6	79.75	5.412	303.5	290.1	296.79	9.4837
MLS-0258164	87337059	78.76	71.4	73.7	72.54	1.634	310.1	282.5	296.32	19.504
MLS-0074669	87336634	1494.2	1104.4	1444.8	1274.60	240.680	194.9	394	294.44	140.79
MLS-0039739	857272	271.91	315.5	307.5	311.47	5.655	311.4	261.8	286.6	35.015
MLS-0229334	22405789	178.39	99	108	103.50	6.364	254.9	314.7	284.8	42.337
MLS-0034143	7974300	824.31	844.6	860.2	852.43	11.011	273.1	286.6	279.86	9.513
MLS-0075328	14744491	424.1	370.2	243.8	307.04	89.375	231	327.1	279.02	67.938
MLS-0093159	17401852	132.46	128.5	130	129.27	1.059	275.3	277.2	276.23	1.3509
MLS-0214231	17506321	556.27	591.4	614.2	602.83	16.130	271	272.3	271.69	0.91094
MLS-0218459	22409459	239.9	496.9	513.6	505.25	11.873	275.2	254.8	265.03	14.423
MLS-0096086	17387063	1489.1	578.6	533.2	555.88	32.118	168.4	356.8	262.62	133.22
MLS-0439514	87336247	217.97	186.4	193.5	189.95	4.980	254	269.9	261.95	11.282
MLS-0348832	47204251	174.01	113.5	116.4	114.94	2.023	252.3	266	259.16	9.7082

MLS-0203436	22415218	51.62	48.2	54	51.10	4.114	270.4	235.2	252.8	24.892
MLS-0109411	17401691	128.21	73.8	76.5	75.14	1.934	218.6	281.4	249.99	44.385
MLS-0047308	87335230	127.1	102.6	107.5	105.07	3.497	250.5	246.7	248.61	2.6561
MLS-0074403	87336709	689.36	616.9	614.5	615.70	1.677	254.2	242.9	248.56	7.9347
MLS-0251644	24824436	419.18	267	304.2	285.61	26.311	234.2	254.2	244.19	14.191
MLS-0388603	49674689	103.77	102.4	104.1	103.27	1.244	232.3	247.5	239.91	10.772
MLS-0061944	7971429	1569	1440.4	1441.4	1440.90	0.666	238.5	238.9	238.67	0.31223
MLS-0224465	22417017	337.81	78	183.1	130.53	74.334	296	181	238.49	81.292
MLS-0225601	87349119	905.33	630.6	682.9	656.74	37.015	238.7	236.8	237.79	1.3549
MLS-0391412	17504794	361.14	305.6	381.1	343.36	53.403	242.9	227.8	235.38	10.694
MLS-0218775	22405113	1804.2	1471.2	1467.4	1469.30	2.738	226.4	243.1	234.75	11.789
MLS-0439948	92764282	94.72	97.5	112.5	105.01	10.581	219.7	244.7	232.21	17.678
MLS-0349681	49641105	141.11	157.2	151.1	154.15	4.357	224	236	230	8.499
MLS-0074403	14744575	1023.5	697.4	655.6	676.51	29.537	228.9	231.1	229.99	1.5163
MLS-0219547	22413210	180.21	158	175	166.52	12.023	220.2	237	228.62	11.877
MLS-0330712	49649053	110.19	116.1	115.2	115.63	0.647	230.6	217.9	224.24	9.0286
MLS-0238379	24808986	195.98	133.7	29.5	81.58	73.705	200.2	226.8	213.51	18.805
MLS-0215158	17513591	580.85	430.6	457	443.81	18.695	198.3	228.3	213.27	21.221
MLS-0018935	857242	51.9	43.4	61.4	52.38	12.757	215.8	210.6	213.2	3.6557
MLS-0349750	47196452	388.92	52.4	175.9	114.16	87.356	314.2	111.7	212.97	143.16
MLS-0360734	49821045	45.02	42.7	63	52.87	14.353	411.3	6.3	208.83	286.39
MLS-0327168	49667162	828.8	802.1	817.5	809.77	10.911	202	213.9	207.94	8.3858
MLS-0030243	7976421	150.13	93.5	88.9	91.19	3.260	237.9	175.8	206.9	43.91
MLS-0223542	17511643	655.02	511.5	498.6	505.03	9.139	191.5	208	199.76	11.687
MLS-0222432	17505722	486.97	407	402.4	404.71	3.285	201.5	196.7	199.09	3.3922
MLS-0207270	22401361	77.59	77.6	75.2	76.41	1.639	194.4	198.2	196.26	2.6801
MLS-0449619	99358245	452.91	356.9	369.3	363.08	8.767	190.3	199.6	194.95	6.5208
MLS-0094174	17387624	180.68	168.4	176.5	172.42	5.744	236.5	145.6	191.03	64.262
MLS-0267122	24785466	1726.5	1447.2	1348	1397.60	70.151	227.7	154.2	190.95	51.919
MLS-0552883	125001396	310.19	307.9	306.2	307.02	1.177	192.9	187.2	190.06	4.0177
MLS-0270739	89853715	367.98	256.8	288.4	272.60	22.307	175	203.3	189.16	19.996
MLS-0008281	85273042	234.87	280.8	302	291.43	14.985	198.7	178.9	188.76	14.002
MLS-0440121	92763436	108.13	107.4	103.3	105.35	2.930	188.6	185	186.82	2.5745
MLS-0095530	14740286	595.56	185.1	272	228.53	61.413	180.6	186.2	183.38	3.9589
MLS-0219963	22401347	201.24	168	174.2	171.07	4.382	173	193.3	183.13	14.378
MLS-0225756	17512364	1799	1116	1282.2	1199.10	117.580	244.4	118.7	181.57	88.911
MLS-0439302	93577073	93.86	71.5	71	71.21	0.360	179.5	182.1	180.81	1.8275
MLS-0228006	89851176	240.5	324.9	378.4	351.66	37.866	163.6	197.6	180.58	24.053
MLS-0208408	22402596	103.38	35.6	118.7	77.11	58.771	354.7	5.8	180.29	246.7
MLS-0036133	7975757	71.6	63.8	70.8	67.30	4.928	179.4	180.9	180.17	1.037
MLS-0425023	56436619	54.71	55	62.9	58.95	5.571	175.5	183.3	179.41	5.5615
MLS-0058368	862594	58.23	53.4	55.1	54.24	1.222	175.1	180.4	177.74	3.7538
MLS-0412425	56463116	110.9	114.9	118.7	116.78	2.709	175.4	178.6	176.98	2.2764
MLS-0221748	24822874	1805.9	1454.5	1449.4	1452.00	3.597	177.2	176.6	176.92	0.38616
MLS-0205721	17432496	308.35	294.2	301.6	297.88	5.226	53.3	300.2	176.79	174.58
MLS-0450221	99357617	387.03	309.5	304.7	307.10	3.348	182.4	169.8	176.09	8.9526
MLS-0031288	7973727	292.72	273.7	270.7	272.18	2.119	160.5	180.9	170.7	14.377
MLS-0295479	26665336	112.79	108.4	108.6	108.50	0.138	171	169.6	170.27	0.99021
MLS-0036658	7977444	1352.1	1185.5	1183.1	1184.30	1.702	169.3	170.3	169.84	0.69687
MLS-0439077	26659913	105.23	79	72.9	75.99	4.314	158.2	180.6	169.39	15.812
MLS-0098725	87345881	223.22	587.5	536.3	561.88	36.172	217.8	120.6	169.23	68.723
MLS-0304329	26660217	74.59	59.5	56.5	58.01	2.115	170.1	167	168.54	2.2401
MLS-0442193	89853211	587.19	448.3	478.6	463.44	21.392	162.8	171	166.89	5.7647
MLS-0460143	103162522	1686.6	1444.4	1437	1440.70	5.238	166.2	164.1	165.18	1.4882
MLS-0342817	47198419	835.44	400.9	490.4	445.64	63.322	135.9	188.2	162.09	36.987
MLS-0099777	17414983	239.14	159.1	159.1	159.08	0.025	162.2	157.5	159.82	3.2946
MLS-0097208	17407086	113.94	82.9	91.5	87.19	6.100	155.9	161.4	158.67	3.9054
MLS-0256826	24824701	295.4	325.9	350.8	338.37	17.629	168.5	142.7	155.61	18.237

MLS-0322619	49665326	1597.4	1449.2	1453.7	1451.40	3.154	153.9	156.8	155.35	2.0422
MLS-0101290	17401563	483.53	73.9	80.5	77.20	4.680	105.6	205	155.29	70.324
MLS-0462930	99355650	99.41	178.8	190.8	184.81	8.499	155.4	152.9	154.14	1.7731
MLS-0343290	49644674	479.55	404.8	376.5	390.65	20.064	231.5	76.5	154.03	109.57
MLS-0098473	17413739	277.4	244.8	258.8	251.80	9.836	149.7	156.9	153.26	5.084
MLS-0205478	22401236	414.75	359.3	387.2	373.25	19.682	291.4	14.4	152.89	195.87
MLS-0099521	17412157	77.7	58.3	62.6	60.45	3.016	146.3	154.4	150.34	5.6819
MLS-0548816	144097107	57.52	67.2	54.2	60.69	9.206	143.3	155.1	149.22	8.3029
MLS-0549947	144097106	66.09	140.2	126.5	133.36	9.689	145.4	151.2	148.29	4.0703
MLS-0085016	14724311	170.16	99.4	97.8	98.59	1.078	153.9	139.5	146.67	10.161
MLS-0256051	24840465	151.98	163.1	159.7	161.43	2.426	144.1	148.1	146.11	2.7753
MLS-0071818	14735144	1862.4	1461.2	1459.5	1460.40	1.234	143.3	146.8	145.08	2.4539
MLS-0215612	85274191	878.4	581.9	578.2	580.08	2.618	139.6	147.3	143.43	5.4772
MLS-0458463	103074411	1674.5	1445.7	1441.4	1443.50	3.011	143.3	143.1	143.17	0.14156
MLS-0294740	87346235	133.1	98.2	95.9	97.04	1.676	140.9	140.4	140.64	0.33434
MLS-0332225	49676750	57.01	70.6	67.8	69.22	2.011	134.4	136.3	135.31	1.3337
MLS-0074591	56323093	252.2	182.2	181.5	181.88	0.501	105.5	163.6	134.54	41.115
MLS-0221748	22415142	1589.5	1445.8	1452.2	1449.00	4.547	133.3	133.1	133.17	0.12329
MLS-0106091	26664480	182.75	159.2	171.2	165.17	8.462	134.9	129.1	132	4.0488
MLS-0412256	57264268	291.09	351.9	356.1	354.01	2.997	133.9	129.9	131.92	2.8383
MLS-0367346	49824745	121.32	109	98.4	103.69	7.536	10.9	251.9	131.44	170.41
MLS-0450933	99356002	270.27	187.8	186.2	186.98	1.101	127.8	132.6	130.18	3.4102
MLS-0076531	14741147	68.32	43.7	57.6	50.64	9.786	236.9	22.8	129.87	151.38
MLS-0443963	93576781	1429.2	1440.6	1446.9	1443.80	4.453	119.7	137.4	128.51	12.507
MLS-0210087	17509917	77.36	178	181	179.51	2.167	127.6	129.2	128.44	1.1283
MLS-0058879	50086678	137.79	168.5	168.3	168.44	0.128	149.9	106.7	128.3	30.493
MLS-0312651	26665560	496.74	373	390.2	381.61	12.140	131.5	124	127.71	5.3084
MLS-0235272	22405508	78.42	79.6	80.3	79.95	0.466	116.9	137.8	127.38	14.777
MLS-0304847	26659237	203.21	160.3	152.4	156.38	5.582	131.9	121.5	126.7	7.3886
MLS-0442814	89854989	166.3	149.6	155.4	152.53	4.114	124.2	127	125.62	2.0232
MLS-0295828	26671439	187.34	251.3	222.6	236.95	20.304	139.4	111.4	125.4	19.839
MLS-0104919	89852597	687.64	159	195.4	177.16	25.728	114.4	135.8	125.09	15.151
MLS-0007848	3712249	92.41	74	74	74.01	0.004	123.4	126.6	125	2.2539
MLS-0552770	143471981	112.77	112.7	118.9	115.77	4.373	132.9	114.9	123.89	12.693
MLS-0335094	49724846	121.72	107.8	138.7	123.25	21.904	124.7	121.7	123.22	2.117
MLS-0221640	17511606	1080.5	765.8	757.4	761.61	5.971	135.6	110.3	122.97	17.918
MLS-0224028	17504516	126.48	98.8	99.2	99.00	0.293	122.1	123.8	122.97	1.2152
MLS-0217615	17511204	1209.5	968.2	964.8	966.52	2.396	114.9	130.7	122.79	11.224
MLS-0229763	22409656	123.66	148.2	132.2	140.17	11.288	164.7	80.2	122.45	59.786
MLS-0358930	49716952	858.85	788.2	819.4	803.83	22.074	118.2	126.5	122.38	5.87
MLS-0312151	87348736	130.42	138.7	137.8	138.25	0.618	117.5	125.7	121.61	5.8016
MLS-0225437	22402678	44	61.6	64.1	62.84	1.809	137.4	104.6	120.97	23.218
MLS-0226083	17514053	58.81	67.6	59.3	63.42	5.861	117.1	124.3	120.69	5.0412
MLS-0210474	17513072	48.88	51.9	56.5	54.20	3.253	117.2	122.6	119.9	3.7795
MLS-0309195	26726160	344.27	268.7	258.5	263.60	7.156	108	127.9	117.97	14.103
MLS-0409546	56318532	78.5	66	83.4	74.69	12.333	117.4	117.1	117.22	0.20671
MLS-0088478	87335964	199.48	109.2	113.9	111.55	3.390	119.5	113.8	116.67	4.0097
MLS-0094617	17402075	649.42	336.6	347	341.80	7.391	120.8	111.3	116.06	6.6782
MLS-0295773	26671507	81.14	85.3	87.6	86.49	1.620	116.7	114.7	115.71	1.4121
MLS-0552746	143471984	1326.5	1106.3	1207.8	1157.00	71.789	118.5	112.7	115.6	4.0985
MLS-0069417	14733849	795.75	498.3	535.1	516.70	26.007	45.1	185.5	115.3	99.297
MLS-0202656	17513756	53.34	53.8	60.3	57.02	4.609	110.6	119.8	115.2	6.4462
MLS-0439004	57264815	60.43	48.3	51.9	50.14	2.528	117.4	111.3	114.37	4.2957
MLS-0444843	92763982	105.95	99.6	104.8	102.20	3.649	107.4	120.7	114.08	9.417
MLS-0329963	49669717	150.29	113.7	120.4	117.05	4.757	133.8	93.4	113.59	28.606
MLS-0203053	22401238	111.47	88.4	96.6	92.48	5.806	108.6	117.4	112.99	6.252
MLS-0273125	24780573	96.8	101	95.7	98.34	3.799	111.5	112.8	112.14	0.91378
MLS-0552225	125001398	111	113.7	114.7	114.21	0.672	108.6	115.3	111.95	4.759

MLS-0425911	85146466	1723.9	1175.8	1202.6	1189.20	18.987	109.7	112.9	111.29	2.2594
MLS-0214165	17508313	594.24	692.5	748.5	720.50	39.623	103.3	118.2	110.71	10.546
MLS-0256832	24810463	110.49	86.4	70	78.18	11.640	126.1	93.8	109.98	22.831
MLS-0222535	17513560	62.31	134	124.1	129.07	7.019	96.5	123.1	109.79	18.814
MLS-0444611	92764840	98.15	95.4	95.2	95.30	0.101	109.2	109.8	109.54	0.43425
MLS-0294576	26662576	249.3	185.3	188.4	186.85	2.228	107.8	111.1	109.46	2.2987
MLS-0234496	17431609	104.78	106.3	111.4	108.85	3.672	102	116.9	109.45	10.569
MLS-0552778	143471982	574.45	510.4	544.4	527.41	23.993	107.2	109.9	108.52	1.9233
MLS-0319994	49670411	99.15	93.3	95.4	94.32	1.484	106	107.5	106.73	1.0485
MLS-0284334	87349413	712.02	482.2	476.7	479.46	3.828	104.7	108.3	106.51	2.565
MLS-0552288	125001399	262.97	197.6	205.8	201.67	5.783	103.7	109	106.37	3.768
MLS-0421950	57257545	133	81	96.4	88.73	10.871	99.2	112.5	105.86	9.3514
MLS-0283161	24782122	91.68	90.1	98.9	94.49	6.262	104.8	106.8	105.76	1.4174
MLS-0285192	24807880	103.26	94.3	97.2	95.73	2.055	102.2	109.1	105.64	4.9032
MLS-0462644	103162706	99.38	101.1	95.9	98.52	3.640	107.8	103.3	105.55	3.2321
MLS-0450768	99356320	95.85	85.4	90.9	88.16	3.922	107.6	103.4	105.49	2.9594
MLS-0301037	26667397	107.81	95.5	94.6	95.06	0.640	106	104.5	105.25	1.0034
MLS-0052467	4241848	149.23	119.2	138.7	128.98	13.785	101	108.7	104.84	5.4022
MLS-0294661	26670798	68.18	52.9	55.5	54.21	1.895	95.8	113.7	104.79	12.676
MLS-0440003	92763358	85.34	83.1	84.9	84.00	1.208	100.9	107.8	104.34	4.8958
MLS-0320071	49671128	103.15	95.2	99.5	97.37	3.056	106.6	101.6	104.11	3.5971
MLS-0440040	92764839	97.63	94.9	93.4	94.14	1.031	111.1	96.9	103.98	10.086
MLS-0301037	51087949	100.15	101.6	98.8	100.22	1.955	103.8	104.1	103.92	0.23396
MLS-0462642	49681601	91.11	91.9	102	96.97	7.130	104.9	102.8	103.84	1.4378
MLS-0095640	14740282	535.06	165.7	171.8	168.75	4.247	112.7	94	103.35	13.273
MLS-0057548	24841017	1215.7	454.2	446.8	450.50	5.247	102.5	104.1	103.28	1.1518
MLS-0320679	49649045	101.47	98.8	101.2	99.99	1.673	98.9	107	102.96	5.7828
MLS-0069765	14738357	78.33	74.9	71.9	73.42	2.096	95.8	109.6	102.71	9.7077
MLS-0307751	26732568	87.43	88.5	88.5	88.50	0.054	104.1	100.9	102.52	2.285
MLS-0010472	4242820	101.2	92.5	94	93.23	1.071	97	107.5	102.25	7.3625
MLS-0449103	99356259	93.24	98.8	98.9	98.87	0.046	101.5	103	102.24	1.0209
MLS-0440199	92763927	152.49	143.5	140.7	142.10	1.990	101.2	103	102.14	1.2758
MLS-0295447	26658614	102.08	99.5	101.1	100.28	1.096	94.4	109.7	102.06	10.825
MLS-0440002	92764852	197.09	182.3	186.6	184.46	2.996	101.3	102.8	102.03	1.0978
MLS-0439871	92764757	84.62	87.2	90	88.62	1.964	103.8	99.2	101.52	3.2239
MLS-0543368	124753430	1739.7	1433.4	1440.8	1437.10	5.239	104.1	98.2	101.15	4.1332
MLS-0449663	99360565	200.3	192.6	202.4	197.48	6.937	97	104.4	100.73	5.2254
MLS-0552813	125001395	233.07	234.6	246.3	240.42	8.262	99.6	101.4	100.49	1.3288
MLS-0088378	14742465	105.69	88.7	100.8	94.79	8.542	97.7	103.3	100.48	3.928
MLS-0301399	26664947	94.39	103.4	100.7	102.05	1.951	101.2	98.8	100	1.6767
MLS-0303501	26661126	98.21	93.8	95.1	94.46	0.957	102.1	97.6	99.838	3.2193
MLS-0214497	22405109	1844	1478.3	1471.9	1475.10	4.552	96.1	102.6	99.353	4.6203
MLS-0354964	49672752	98.28	98.9	93.9	96.41	3.523	94.9	103.7	99.33	6.2463
MLS-0218286	22405114	1764.3	1449.1	1455.6	1452.40	4.601	94.2	104	99.107	6.9007
MLS-0221642	22412151	99.06	95.5	94.6	95.05	0.660	102.2	95.9	99.066	4.4083
MLS-0341049	87337510	419.81	355.4	357.4	356.40	1.384	97.2	100.9	99.046	2.5857
MLS-0366178	49676452	147.33	144.5	149.8	147.12	3.749	95.8	102.3	99.018	4.5994
MLS-0552813	143471985	155.53	171.9	167.9	169.90	2.795	96	101	98.458	3.5322
MLS-0269613	24785386	618.09	491	480.6	485.79	7.386	101.6	95.3	98.439	4.4224
MLS-0295203	26671247	95.86	95.6	96.6	96.09	0.758	102.9	93.9	98.408	6.416
MLS-0318538	49665172	284.9	239.9	249.6	244.73	6.840	94	102.8	98.397	6.191
MLS-0552861	125001394	86.75	92	92.2	92.12	0.149	98	98.4	98.194	0.23536
MLS-0099513	17403417	61.44	43.9	57.4	50.66	9.534	104.8	91.6	98.19	9.3791
MLS-0300411	26730337	77.76	62	63.4	62.69	1.023	95.2	101.2	98.165	4.2596
MLS-0543940	134216142	129.07	107.5	111	109.21	2.484	98.7	97.2	97.927	1.0674
MLS-0412233	56463011	220.2	149	171.4	160.20	15.880	100.8	94.9	97.825	4.2044
MLS-0445106	92764838	104.05	101	104.8	102.91	2.638	99	96.3	97.682	1.9203
MLS-0003163	855596	94.86	94.6	92.2	93.36	1.690	99.4	95.8	97.578	2.5491

MLS-0264261	24823240	222.17	171.5	177.7	174.60	4.362	96.4	98.4	97.379	1.3908
MLS-0306197	26663489	101.04	89.3	91.6	90.43	1.626	100	93.9	96.991	4.3077
MLS-0214165	17506129	500.85	546.2	589.2	567.70	30.340	98.3	95.3	96.805	2.1208
MLS-0230925	22414089	68.46	61.5	63.2	62.33	1.183	99.2	94.3	96.721	3.465
MLS-0306712	26662413	566.72	501.9	521.3	511.60	13.761	93.9	99.1	96.483	3.6318
MLS-0324653	49669871	98.1	89.9	91.7	90.83	1.270	96.7	95.7	96.236	0.72236
MLS-0002959	855829	363.93	349.8	344.1	346.96	4.061	92.5	99	95.764	4.5779
MLS-0420799	57267192	64.46	54.1	52	53.04	1.522	95.5	95.7	95.597	0.09764
MLS-0293174	26666366	82.69	55.4	57.1	56.23	1.205	95.1	95.6	95.39	0.3547
MLS-0412451	56463184	89.02	87.4	96.2	91.82	6.255	91.8	96.9	94.345	3.643
MLS-0371495	49677218	90.35	90.2	89.1	89.62	0.786	94.2	93.9	94.053	0.14819
MLS-0542613	92764750	63.11	65.4	69.9	67.61	3.166	91	97.1	94.025	4.3078
MLS-0025260	7978420	341.25	198.4	151.6	174.97	33.077	104.5	83.5	93.997	14.902
MLS-0412292	57260400	90.57	98.8	95.8	97.28	2.114	97.1	90.9	93.983	4.3703
MLS-0101627	17411890	634.46	712.1	725	718.52	9.111	92.5	95.4	93.946	2.081
MLS-0440083	92764842	83.1	81	79.6	80.32	0.946	89.2	98.6	93.923	6.6581
MLS-0341433	49642423	95.99	94.7	95.3	94.99	0.437	94.8	92.7	93.754	1.4214
MLS-0291827	49681682	93.16	101.2	95.1	98.14	4.284	91.1	96.2	93.653	3.6282
MLS-0357036	49672722	58.06	60.8	64.8	62.82	2.843	90.2	96.9	93.549	4.7684
MLS-0342526	47201137	114.26	66.9	73.4	70.14	4.560	74.7	111.9	93.306	26.339
MLS-0318020	49681620	97.5	97.1	92.9	95.00	2.935	90.9	95.5	93.214	3.2591
MLS-0207270	17511114	65.09	46.1	58.5	52.32	8.774	81.7	104.7	93.207	16.236
MLS-0444236	93576680	84.78	89.6	94.7	92.13	3.617	93.2	92.9	93.058	0.24579
MLS-0059977	7968423	89.39	94.4	90.3	92.34	2.891	92.7	93.4	93.044	0.43947
MLS-0386652	49829219	88.14	91.7	91.9	91.81	0.170	90	94.9	92.446	3.4232
MLS-0330949	49647788	89.62	88.3	92.5	90.42	2.947	94.5	90.4	92.434	2.9033
MLS-0462599	99495765	59.03	81.5	71.9	76.73	6.821	91.1	92.8	91.98	1.1938
MLS-0205154	17433320	1398	1020.1	1086.3	1053.20	46.790	89.9	93.9	91.868	2.8459
MLS-0319286	49679494	60.84	49.7	57.8	53.76	5.712	82.9	100.4	91.65	12.439
MLS-0369996	49722299	480.09	487.2	485.7	486.43	1.051	89.6	93.4	91.48	2.6972
MLS-0231986	22400426	60.23	54.9	55.5	55.21	0.435	95.7	86.5	91.127	6.5256
MLS-0280912	24807290	90.37	73.1	74	73.54	0.630	93.6	88	90.821	3.95
MLS-0330872	49665521	99.73	86.3	86.5	86.39	0.119	91	90.2	90.589	0.59362
MLS-0354856	49676095	113.3	97	97.4	97.19	0.249	89.2	91.5	90.351	1.6819
MLS-0081053	87349603	88.15	80.1	81.8	80.93	1.205	90.8	88.3	89.521	1.7744
MLS-0079775	14731941	106.65	100.9	100	100.47	0.647	87.1	90.2	88.659	2.1385
MLS-0211719	17514537	77.85	55.2	59.5	57.34	3.010	81.8	94.4	88.083	8.9382
MLS-0305500	26660734	88.64	92.2	91	91.64	0.847	91.9	84.2	88.025	5.4346
MLS-0543575	121283145	681.88	531.9	520.2	526.04	8.310	88.3	87.2	87.783	0.78556
MLS-0266629	24793940	60.98	61.6	63	62.27	0.994	172.7	2.4	87.575	120.45
MLS-0445078	92764797	170.09	131.2	129.4	130.33	1.266	88.8	86.1	87.442	1.9376
MLS-0073782	14742355	104.7	91.6	89.4	90.49	1.591	98.8	75.7	87.221	16.338
MLS-0444729	92764809	89.43	88.2	84.5	86.31	2.631	84.7	89.2	86.924	3.2053
MLS-0276331	24790995	103.44	94.2	97.8	96.02	2.547	85	88.4	86.699	2.4206
MLS-0107942	17386130	1766.3	1479	1435.3	1457.10	30.863	92.2	81.1	86.652	7.8147
MLS-0079906	87344560	108.38	93.9	102.2	98.08	5.867	83.6	89	86.277	3.826
MLS-0291827	11533038	87.91	83.6	92.4	88.03	6.237	85.5	87	86.215	1.0691
MLS-0036423	7974131	183.71	175.1	169.8	172.43	3.726	83.5	88.7	86.108	3.6427
MLS-0215122	17513225	86.09	59.2	61.4	60.29	1.608	95	77.2	86.064	12.598
MLS-0239698	24784880	90.67	87.7	90	88.86	1.636	84.8	87.2	85.992	1.7388
MLS-0310007	89851969	302.21	115.7	170.3	142.98	38.643	83.7	88.1	85.889	3.1233
MLS-0280282	24790272	98.84	75.2	73.2	74.23	1.432	81	90.6	85.802	6.769
MLS-0079914	14733092	101.18	96.3	93.2	94.75	2.237	80.3	91.1	85.665	7.6525
MLS-0203306	87348329	404.73	407.1	420.6	413.84	9.589	83.5	87	85.236	2.4729
MLS-0545966	136947366	80.77	89.9	81.2	85.57	6.191	88	81.9	84.915	4.3352
MLS-0328253	49665385	305.75	281.9	293.6	287.76	8.240	86.7	82.9	84.794	2.6657
MLS-0542250	136948559	1437.5	1443.4	1441.4	1442.40	1.450	85	84.3	84.622	0.52067
MLS-0306134	26661656	313.69	308.1	328.8	318.48	14.648	86.4	82.6	84.546	2.6899

MLS-0291891	24788424	69.75	74.6	75.5	75.02	0.665	88.7	79.5	84.082	6.5129
MLS-0343709	49640990	72.23	73.6	73.2	73.39	0.264	72.3	95.6	83.953	16.476
MLS-0202369	22406124	1811.4	1468.7	1465.9	1467.30	1.940	81.3	86.3	83.827	3.548
MLS-0262586	24835021	90.77	83.7	87.8	85.71	2.896	82.8	84.4	83.615	1.1449
MLS-0039503	862420	84.32	91.7	80.1	85.90	8.165	90	77	83.506	9.1842
MLS-0443963	93576780	1429.2	1435.4	1440.8	1438.10	3.783	79.5	87.5	83.47	5.6826
MLS-0022806	843122	270.93	291.3	240.9	266.06	35.638	92.1	74.3	83.203	12.528
MLS-0066598	56320848	58.91	57.2	59.3	58.24	1.434	78.4	87.7	83.023	6.5481
MLS-0202334	22406442	75.22	98.4	95.3	96.84	2.146	83.8	82.1	82.959	1.2298
MLS-0203040	17516591	678.76	725.5	680.7	703.14	31.678	86.3	79.6	82.93	4.7654
MLS-0550087	144097111	86.53	101.5	114	107.74	8.808	84.4	81.4	82.909	2.0692
MLS-0029349	4255295	272.09	350.4	358.3	354.34	5.644	67.1	98.2	82.649	21.968
MLS-0260501	24817344	98.35	85.6	106.6	96.12	14.819	81	82.8	81.911	1.2245
MLS-0300493	26666944	71.32	49.6	56.7	53.17	4.996	82.3	81.4	81.889	0.63723
MLS-0445109	92763868	98.59	95	91.6	93.27	2.383	83.4	80.2	81.769	2.2698
MLS-0342020	47195345	94.16	62.5	58.3	60.40	2.998	81.3	81.6	81.425	0.19139
MLS-0321870	49665355	944.57	955.5	815.6	885.55	98.866	82.5	80.2	81.397	1.6262
MLS-0264360	24823801	147.08	80.9	100.2	90.53	13.610	75.4	87.2	81.282	8.3107
MLS-0329230	49647370	187.09	309.9	285.9	297.90	16.912	105.8	56.4	81.12	34.928
MLS-0227079	17513201	66.23	53.4	49.2	51.28	3.004	78.5	83.6	81.059	3.6611
MLS-0207900	87348072	94.74	88.2	84.2	86.20	2.860	74.3	87.3	80.792	9.1689
MLS-0292429	26665058	81.53	91.1	87.7	89.39	2.394	78.5	82.9	80.68	3.1046
MLS-0412241	56463287	79.29	80	82.1	81.05	1.487	75	86.1	80.538	7.83
MLS-0099145	17387421	163.4	66.5	59.6	63.06	4.835	84.2	76	80.1	5.8181
MLS-0383735	49816280	84.3	90.5	86.5	88.51	2.828	79.5	80.5	80.017	0.73921
MLS-0270906	24791788	132.27	90.5	93.2	91.83	1.897	80.1	79.7	79.939	0.29492
MLS-0312829	26664961	91.38	95.5	99.1	97.31	2.561	75.9	83.6	79.731	5.4082
MLS-0088999	14742342	93.07	88.8	80	84.41	6.249	79.2	80	79.606	0.60203
MLS-0263622	24837393	151.56	180.1	191.3	185.67	7.950	74.9	83.7	79.287	6.2699
MLS-0202776	99495726	168.84	131.2	135	133.09	2.681	82.8	75.2	79.034	5.3801
MLS-0222739	17505450	115.35	71.3	99.1	85.21	19.625	71.5	86.5	78.984	10.601
MLS-0305265	26663972	85.83	86.2	93	89.58	4.850	75.7	82	78.833	4.44
MLS-0387266	49826455	106.23	77.8	96.7	87.25	13.360	76.2	81.3	78.747	3.5441
MLS-0445248	92764796	810.05	692.4	679.8	686.12	8.932	74.6	80.5	77.535	4.1277
MLS-0058115	85303865	1146.9	1398.4	1417.9	1408.10	13.774	73.1	81.7	77.427	6.0855
MLS-0099608	17403180	148.65	127.2	131.2	129.19	2.795	74.3	80.4	77.356	4.3425
MLS-0104183	89851437	124.73	81.9	76.4	79.16	3.850	84.7	69.4	77.067	10.835
MLS-0441774	89854664	87.41	87.4	86.6	87.00	0.590	75.7	77.6	76.641	1.3117
MLS-0444798	92764758	140.04	114.4	115.6	114.99	0.861	76.4	76.7	76.583	0.22711
MLS-0444943	92764843	76.43	78.9	76.4	77.61	1.758	78.5	74.7	76.579	2.6876
MLS-0350590	47204346	812.34	653.9	657.1	655.52	2.277	77	76.1	76.573	0.6649
MLS-0204754	87346654	74.31	71.1	68.6	69.82	1.775	74.9	77.5	76.172	1.8294
MLS-0221113	22412732	425.02	108.3	337.8	223.03	162.280	37.8	113.9	75.813	53.827
MLS-0207587	87347052	84.14	59.4	66	62.67	4.683	76.2	75.3	75.735	0.58808
MLS-0315447	26657808	83.46	74.5	79.1	76.82	3.230	70	81.3	75.662	7.946
MLS-0084359	14726526	89.4	72.2	74.5	73.34	1.604	75.2	75.7	75.445	0.41152
MLS-0090529	14742237	58.02	63.4	48.5	55.95	10.549	78.7	72	75.378	4.7318
MLS-0441379	89854852	127.04	92	92	91.99	0.041	74.3	76.5	75.359	1.5596
MLS-0252272	24809205	90.77	64.3	65.6	64.93	0.916	76.5	74.1	75.301	1.7027
MLS-0286318	24797546	103.15	80.2	85.3	82.76	3.628	74.4	75.9	75.155	1.1071
MLS-0209266	17512008	441.92	371.7	364.8	368.23	4.873	74.3	75.9	75.058	1.126
MLS-0261792	24830097	88.82	81.4	88.7	85.07	5.129	75.3	74.6	74.935	0.48387
MLS-0295683	26658182	192.23	147.1	91.1	119.11	39.562	70.9	78.2	74.554	5.1535
MLS-0295415	26665872	49.44	57.6	63.6	60.60	4.289	76.7	71.9	74.264	3.382
MLS-0309234	26726318	201.93	202.4	213.1	207.71	7.561	74.6	73.9	74.224	0.51488
MLS-0242321	24831303	398.61	443.2	464.8	453.97	15.255	75.8	72.6	74.188	2.2494
MLS-0279818	24806066	88.72	78.3	78.9	78.61	0.478	75.8	72.5	74.153	2.2676
MLS-0205065	17433115	100.13	87.3	91.2	89.26	2.806	69.7	78.3	74.043	6.0759

MLS-0440664	89853596	110.39	99.6	101.2	100.42	1.167	74.7	72.6	73.673	1.4969
MLS-0367149	49736177	583.07	588.8	591.3	590.05	1.793	72.1	75.2	73.671	2.1783
MLS-0214738	17431439	98.1	114.7	128.6	121.66	9.789	141.9	4.7	73.34	97.004
MLS-0445041	92764824	102.7	99.1	96.3	97.72	1.987	72.3	74.1	73.2	1.278
MLS-0444248	93576592	78.31	76.9	76.4	76.68	0.376	77.5	68.4	72.963	6.4695
MLS-0202297	22406207	541.12	335.9	366.7	351.32	21.780	82.1	63.6	72.877	13.075
MLS-0452622	99356417	106.32	93.6	96.8	95.19	2.275	77.9	67.7	72.824	7.2468
MLS-0100483	17406808	152.69	112.9	123.2	118.08	7.253	51.4	93.8	72.596	29.995
MLS-0089847	87345622	1148	782.4	792	787.22	6.800	64.3	80.9	72.576	11.764
MLS-0301691	26666219	87.64	77.4	77.7	77.54	0.180	65.8	78.8	72.297	9.1858
MLS-0441671	89854666	80.49	84	82.3	83.17	1.232	72.7	70.7	71.674	1.4005
MLS-0293727	26662208	86.44	79.5	87.9	83.74	5.934	65.4	77.8	71.588	8.761
MLS-0313767	26727902	87.18	81.9	82.5	82.22	0.462	69.2	73.4	71.307	2.9842
MLS-0213955	17432419	60.26	60.1	60.6	60.36	0.329	61.6	81	71.307	13.682
MLS-0264345	14745181	100.25	67.6	66.3	66.98	0.929	70.4	72	71.163	1.13
MLS-0442396	89854667	79.2	83.2	85.1	84.18	1.317	71.7	70.4	71.034	0.89847
MLS-0258899	24823256	63.98	59.8	54.7	57.24	3.568	66.5	75.4	70.968	6.2758
MLS-0441313	89855383	196.03	166.4	178.5	172.47	8.592	72.1	69.7	70.939	1.6927
MLS-0096954	17407909	91.62	70.1	71.2	70.62	0.804	69.8	70.9	70.315	0.78126
MLS-0220743	17505825	84.63	60.4	64.5	62.42	2.875	70.5	70	70.256	0.40713
MLS-0214943	17513238	71.17	60.3	50.4	55.34	7.015	74.3	65.5	69.897	6.2684
MLS-0245804	24782999	79.79	71.8	71.8	71.80	0.035	65.8	73.5	69.646	5.4555
MLS-0235837	11533045	103.27	103.2	105	104.12	1.297	71.6	67.3	69.432	3.0845
MLS-0207106	22401657	242	218.5	236.3	227.39	12.545	66.1	72.1	69.126	4.2607
MLS-0450017	99360563	183.04	82.7	82.5	82.62	0.119	69.2	68.6	68.926	0.44467
MLS-0412755	56463046	77.42	81.1	81.2	81.15	0.079	66.5	70.8	68.657	3.0719
MLS-0303405	26663027	90.48	57.5	63.1	60.32	3.974	64.3	72.9	68.596	6.0839
MLS-0234537	17431926	242.85	187.6	201.8	194.66	10.031	71.3	65.3	68.327	4.2425
MLS-0202306	17512759	90.13	79.9	79.3	79.59	0.433	68.7	67.1	67.87	1.1136
MLS-0324260	49669868	94.03	83.2	90.9	87.05	5.441	69.3	66.3	67.812	2.0746
MLS-0033005	89853417	106.29	77.7	79.8	78.77	1.520	66.2	69.4	67.791	2.2886
MLS-0449817	99356264	72.92	79.5	81.8	80.64	1.677	69.3	65.8	67.557	2.5123
MLS-0312440	26660706	183.5	173.6	178	175.79	3.154	66.6	68.1	67.356	1.0353
MLS-0078056	14730431	46.59	191.1	133.5	162.30	40.757	82.5	51.8	67.122	21.711
MLS-0206423	17433772	83.2	80.8	85.4	83.08	3.288	68.2	65.7	66.957	1.7438
MLS-0287161	24806227	1753.3	1234.3	1265.3	1249.80	21.885	71.4	62	66.725	6.6263
MLS-0318401	49665039	1075.5	904.8	917.2	911.02	8.800	67.1	66.1	66.596	0.73014
MLS-0048849	46500766	130.61	100.1	101	100.53	0.676	66.8	66.4	66.581	0.26195
MLS-0445159	92764458	73.68	55.9	63.6	59.75	5.434	66.4	66.6	66.481	0.1394
MLS-0220156	22401517	210.9	168	152.1	160.06	11.274	56.7	76.1	66.411	13.708
MLS-0105761	50085435	49.38	54.1	56.6	55.35	1.770	59.6	72.8	66.205	9.3013
MLS-0107750	17386314	389.33	353	360.6	356.78	5.405	60.2	71.5	65.838	8.0336
MLS-0307088	26728771	279.77	343.4	372	357.69	20.178	63.2	68.5	65.818	3.7473
MLS-0265435	24836071	96.98	53.2	66.9	60.06	9.701	52.7	78.2	65.433	18
MLS-0211292	17504796	345.35	242.3	337.7	290.01	67.464	94.7	35.8	65.249	41.702
MLS-0251683	24809151	82.14	64	68.2	66.11	2.920	64.1	66.4	65.247	1.6181
MLS-0303419	26661852	58.31	51.8	53	52.42	0.856	63.3	66.9	65.074	2.5464
MLS-0205857	17432537	749.12	469	517.5	493.25	34.245	59	70.7	64.844	8.2415
MLS-0250326	24824835	124.84	107.5	104.9	106.20	1.871	60.6	69	64.811	5.9109
MLS-0080733	14735407	84.88	80.7	81.6	81.16	0.643	62.4	67.1	64.741	3.3692
MLS-0277099	24807574	78.65	56.4	58.4	57.40	1.396	63.5	65.9	64.662	1.6967
MLS-0271525	24834980	93.59	73.8	79.4	76.61	3.908	61.6	67.4	64.497	4.0744
MLS-0241470	24787080	917.05	686.7	887.4	787.07	141.940	81.9	46.5	64.229	25.043
MLS-0322825	49671668	68.36	80.1	65	72.53	10.654	61.6	66.5	64.062	3.4653
MLS-0401568	56322863	71.27	76.9	77.7	77.32	0.580	59.1	68.9	63.981	6.9665
MLS-0219273	17505785	173.17	103.2	112.4	107.81	6.494	98.7	29.2	63.922	49.113
MLS-0229773	22416685	651.91	747.5	735	741.26	8.815	76.6	51	63.781	18.101
MLS-0297152	26664430	54.75	54.4	51.5	52.96	2.034	79.4	47.5	63.426	22.525

MLS-0292937	26671422	1037.8	710.4	737	723.73	18.829	58.3	67.8	63.056	6.7648
MLS-0225972	17511958	104.57	84.4	84.8	84.58	0.273	63.3	62.5	62.901	0.62799
MLS-0220700	17504946	80.41	65.6	63	64.29	1.785	55.6	69.9	62.772	10.145
MLS-0229546	22414608	113.11	88.9	85.2	87.10	2.611	59	66.2	62.633	5.1007
MLS-0363994	49677386	80.43	79.8	82.3	81.07	1.739	61.8	62.4	62.133	0.44327
MLS-0240917	24813619	81.06	73	73.5	73.25	0.392	66.9	57.2	62.052	6.8024
MLS-0220270	89853821	1049.2	632.4	637.4	634.93	3.551	85.2	38.4	61.764	33.105
MLS-0203125	22403203	114.76	90.9	95	92.95	2.924	57.5	65.9	61.719	5.9375
MLS-0215070	17507231	73.55	69.7	70.7	70.17	0.680	61	62.3	61.638	0.96239
MLS-0301400	26664781	56.97	48.9	51.7	50.32	1.980	59.3	63.9	61.561	3.2679
MLS-0292978	26671511	358.56	350.9	424	387.44	51.661	72.9	49.7	61.323	16.394
MLS-0222687	87335192	90.19	71.2	64.2	67.71	4.934	62.6	60	61.296	1.774
MLS-0227519	22410385	56.58	50.9	57.2	54.04	4.459	59.1	63.5	61.279	3.1218
MLS-0068144	14730721	64.07	49.9	51	50.42	0.777	61.5	61	61.244	0.29412
MLS-0244070	24814573	925.43	676.1	749.2	712.62	51.703	66.6	55.8	61.232	7.6454
MLS-0367356	49824705	74.91	76.4	76.8	76.62	0.295	57.9	64.3	61.12	4.5303
MLS-0245817	24783175	87.13	76.6	74.7	75.63	1.352	58.6	63.6	61.07	3.5617
MLS-0263575	24837296	78.22	71.3	72.2	71.77	0.632	63.5	58.5	60.991	3.5158
MLS-0548062	144095703	139.41	89.1	87.6	88.38	1.033	58.8	63.1	60.922	3.0128
MLS-0319397	49674405	586.14	269.7	394.1	331.89	88.007	38.6	83.2	60.913	31.571
MLS-0214591	17431653	333.25	47.1	113.5	80.30	46.931	79.9	41.7	60.798	27.016
MLS-0313524	24832741	85.77	76.2	77	76.60	0.593	55.5	66.1	60.787	7.4606
MLS-0248811	24823466	912.07	424.8	298.3	361.57	89.423	69.3	52.3	60.769	12.002
MLS-0266887	89852743	144.22	101.5	119.3	110.41	12.535	59.6	61.4	60.508	1.2838
MLS-0307495	26731542	65.54	56.5	57.2	56.81	0.488	56	64.7	60.361	6.1981
MLS-0328825	49648765	77.73	76.4	76.5	76.44	0.095	60.4	60.3	60.35	0.027651
MLS-0025352	7974859	199.5	194.4	215.2	204.81	14.647	63.4	57.3	60.344	4.2952
MLS-0000659	99455957	47.79	49.1	53.1	51.12	2.849	71.1	49.5	60.308	15.269
MLS-0086803	14720875	69.36	68.8	53.9	61.35	10.472	67.3	53	60.133	10.066
MLS-0264916	87349386	1038.7	806.7	784.7	795.74	15.573	55.6	64	59.792	5.9394
MLS-0349131	49641306	74.84	76.1	68.1	72.06	5.642	62.5	57	59.76	3.9255
MLS-0073945	14744004	104.33	81	80.5	80.77	0.384	58.4	61.1	59.723	1.8835
MLS-0339544	47199811	84.35	43.9	58.7	51.29	10.444	55.5	63.6	59.529	5.756
MLS-0240015	24814114	100.1	54.3	60.1	57.18	4.124	57.9	60.6	59.281	1.8828
MLS-0106578	56320881	138.83	140.5	155	147.79	10.256	56.8	61.1	58.982	3.0227
MLS-0217633	17511183	94.96	74.1	69.5	71.81	3.275	58.1	59.1	58.593	0.66968
MLS-0439963	92764426	349.73	309.5	311.7	310.60	1.501	64.3	51.9	58.104	8.7836
MLS-0318172	46501219	54.23	62	66.3	64.14	3.078	56.7	58.9	57.807	1.5994
MLS-0092106	17411010	186.82	116.1	119.8	117.95	2.659	63.2	51.7	57.483	8.1417
MLS-0369079	50086472	60.65	372.9	281.4	327.17	64.691	53.3	61.6	57.427	5.8454
MLS-0291547	24824134	86.81	77.3	83.9	80.58	4.701	54	60.8	57.405	4.8206
MLS-0343331	49644238	126.72	100.3	105.2	102.76	3.504	59.3	55.2	57.265	2.9162
MLS-0552634	125001391	78.74	80.4	85.3	82.81	3.460	60.7	53.8	57.245	4.8884
MLS-0093095	17410551	626.4	528	531.2	529.60	2.291	57.9	56.4	57.186	1.0624
MLS-0303476	26662341	76.75	56.9	59.8	58.39	2.060	60.2	54.2	57.176	4.2342
MLS-0211675	17504890	255.08	69.6	90.5	80.04	14.761	57.2	56.8	57.01	0.29448
MLS-0440860	87336674	70.79	63.9	63.6	63.74	0.178	58	55.8	56.887	1.5717
MLS-0075126	14743867	75.57	65.5	69.1	67.31	2.504	52.6	60.4	56.542	5.5189
MLS-0450642	99360993	412.55	356.7	340.6	348.66	11.353	117.3	-4.3	56.508	85.97
MLS-0347855	47200698	70	68	70.2	69.15	1.553	55.2	57.2	56.189	1.4408
MLS-0293193	26669939	53.56	55.7	54.5	55.08	0.831	56.5	55.8	56.115	0.48302
MLS-0035998	7975145	299.92	585.2	576.4	580.80	6.202	35.5	76.6	56.034	29.107
MLS-0037357	87348069	308.54	200.8	198.4	199.61	1.731	53.4	58.5	55.953	3.6381
MLS-0006255	99456920	82	76	78.8	77.38	1.994	55.7	56.2	55.933	0.39146
MLS-0043862	847157	88.2	88	92.5	90.27	3.163	55.4	56.4	55.909	0.66052
MLS-0015989	848842	60.02	55.9	56.8	56.35	0.651	56.1	55.5	55.814	0.44745
MLS-0018995	103051229	253.71	258.6	266.1	262.37	5.261	56.1	55.1	55.615	0.6977
MLS-0294843	26664270	424.81	297.8	224.8	261.31	51.598	68	43.1	55.547	17.559

MLS-0338627	49674298	41.27	67.7	79	73.31	7.984	44.4	66.5	55.413	15.612
MLS-0324443	49648272	89.23	75	76	75.48	0.700	52.7	58	55.358	3.7907
MLS-0211078	17504207	75.51	72.1	77.2	74.62	3.636	51.4	59.2	55.312	5.5446
MLS-0231954	22400427	244.38	258.6	270.8	264.70	8.681	51.6	59	55.298	5.2443
MLS-0092253	17408241	267.26	301.4	305.3	303.35	2.691	56.8	53.7	55.233	2.1716
MLS-0312736	87347432	82.08	119	225	171.99	74.983	70.2	40.2	55.214	21.194
MLS-0316661	47193949	95.7	53.5	54.7	54.07	0.838	54.1	56.2	55.127	1.5065
MLS-0543795	134216141	90.54	113.3	118.4	115.84	3.628	55.2	54.4	54.801	0.53326
MLS-0439563	92763749	52.64	56.6	57.8	57.21	0.866	50.7	58.9	54.784	5.8359
MLS-0457738	103162647	748.88	570.9	589.4	580.14	13.134	55.2	54.2	54.723	0.70175
MLS-0312678	26664933	269.06	246.8	247.1	246.99	0.228	51.5	57.6	54.596	4.3087
MLS-0245816	24783001	76.34	63.2	65.5	64.33	1.608	50.3	58.4	54.378	5.73
MLS-0296809	26671289	241.58	196.6	185	190.79	8.185	54.3	54.3	54.286	0.039083
MLS-0322644	49670065	137.13	67.7	88.5	78.08	14.669	59.9	48.6	54.26	8.0367
MLS-0458584	103059960	80.79	60.6	60.8	60.69	0.133	51.5	56.7	54.117	3.7133
MLS-0268678	24827574	78.96	63.3	62.4	62.86	0.666	54.8	53.4	54.102	0.92185
MLS-0345191	47198778	1397.7	404.9	434.4	419.67	20.860	91.8	16.3	54.082	53.371
MLS-0259105	24823236	1777	1214.1	1058.6	1136.40	110.010	49.2	58.8	53.975	6.8056
MLS-0238619	26671284	112.4	93.5	97.8	95.68	3.034	54.7	53.3	53.969	0.97411
MLS-0552873	125001388	124.01	129.6	133.5	131.56	2.701	53.8	53.9	53.852	0.1255
MLS-0012490	859184	89.7	105.3	97.7	101.49	5.346	44.3	63.4	53.842	13.489
MLS-0226546	22416870	74.85	61.3	68.5	64.89	5.089	58.8	48.8	53.802	7.1279
MLS-0449241	99357601	96.58	92.9	77.2	85.04	11.154	53.3	53.9	53.6	0.44424
MLS-0292485	26658052	89.08	60.9	70.8	65.88	6.976	47.9	59.3	53.6	8.1
MLS-0222733	17504835	103.59	62.6	63.4	63.01	0.593	52.3	54.6	53.442	1.5975
MLS-0289709	24791387	53.17	82.8	88.1	85.47	3.715	52.5	54.3	53.388	1.3198
MLS-0261429	24820791	190.16	187.7	185.5	186.60	1.500	52.5	54.2	53.323	1.2245
MLS-0391934	56323090	743.47	607.7	609.2	608.44	1.092	53.7	52.6	53.133	0.80248
MLS-0074305	14726672	144.92	102.8	103.2	103.01	0.284	55.8	50.5	53.124	3.7601
MLS-0075221	14744185	182.06	107.8	98.3	103.04	6.701	49.5	56.6	53.047	5.0565
MLS-0092123	17411136	69.34	51.4	49.3	50.35	1.525	60.3	45.6	52.93	10.377
MLS-0245623	24814463	64.84	58.7	52.3	55.49	4.490	51.6	54.2	52.908	1.8883
MLS-0253436	24817276	186.47	99.5	108.8	104.15	6.619	63.4	42.4	52.907	14.905
MLS-0209102	17512265	43.7	71.2	68.4	69.78	1.951	-2.7	108.3	52.777	78.522
MLS-0304998	26663490	83.28	69.6	69.7	69.68	0.072	52.7	52.6	52.677	0.092186
MLS-0291625	24825143	771.77	774.8	776.7	775.74	1.368	50.1	54.6	52.393	3.1857
MLS-0290028	24796327	69.78	162.5	158.9	160.71	2.594	65.7	38.4	52.04	19.287
MLS-0046423	4256562	119.99	102	108.3	105.16	4.439	50.4	53.4	51.908	2.0881
MLS-0294743	26670801	218.16	143.1	140.4	141.74	1.866	54.6	49.2	51.904	3.8229
MLS-0000058	46500841	190.05	160.5	161.8	161.12	0.931	52.8	50.8	51.808	1.3875
MLS-0351996	47202958	61.87	64.6	68.1	66.31	2.481	54.3	49.2	51.779	3.6058
MLS-0313324	24832689	75.05	69.2	75.3	72.22	4.303	51	52.4	51.709	1.0043
MLS-0233570	17510584	441.15	293.4	208.6	251.02	59.938	55.1	48	51.546	5.0501
MLS-0035369	7974716	67.66	61.6	64.1	62.88	1.748	51.6	51.4	51.504	0.13119
MLS-0440217	89854747	276.19	243.9	259.4	251.65	10.943	47.3	55.3	51.309	5.5993
MLS-0318365	49665155	975.38	821.1	820.2	820.66	0.609	48.9	53.3	51.054	3.1093
MLS-0313279	24779871	112.2	100.7	105.2	102.97	3.180	47.8	53.7	50.737	4.2053
MLS-0073097	14723140	152.51	212.3	135.2	173.75	54.461	80.7	20.6	50.667	42.491
MLS-0259782	24836778	121.89	97.8	91.9	94.87	4.163	51.5	49.8	50.648	1.2328
MLS-0299121	26663988	69.07	79.2	77.5	78.36	1.200	51.1	50	50.539	0.79229
MLS-0355583	49716177	58.66	69.3	64.5	66.87	3.415	52.8	48	50.401	3.3522
MLS-0346031	49641429	76.34	58	65.5	61.76	5.315	43	57.4	50.215	10.182
MLS-0444628	93577189	51.54	56.6	59.3	57.94	1.938	47.6	52.8	50.195	3.6651
MLS-0238619	24803540	399.83	206.5	244.8	225.64	27.040	48.3	51.4	49.876	2.1887
MLS-0440173	92764363	1741.3	1442.7	1436.2	1439.40	4.571	49.5	50	49.719	0.37215
MLS-0285604	24788058	1919.8	1444.3	1447	1445.70	1.911	46.4	53	49.709	4.6373
MLS-0202917	17516576	240.39	123.9	112.2	118.08	8.262	48.6	50.5	49.591	1.356
MLS-0543944	134216126	246.78	213.1	238.7	225.89	18.070	49.4	49.1	49.252	0.18238

MLS-0233030	22402458	1548.9	1367.6	1377.2	1372.40	6.796	46.6	51.8	49.208	3.6628
MLS-0104559	14730779	139.57	125	138.2	131.62	9.332	48.6	49.7	49.168	0.79696
MLS-0088590	14743285	113.45	85.8	86.1	85.93	0.232	50.5	47.8	49.164	1.8716
MLS-0091948	49679608	76.04	106.9	100.8	103.85	4.295	23.1	74.8	48.96	36.551
MLS-0297811	26671331	54.73	47.4	52.7	50.02	3.756	50.2	47.7	48.957	1.7422
MLS-0210201	22401267	91.26	97.3	112.6	104.97	10.855	47	50.9	48.942	2.7213
MLS-0250761	49681542	60.23	66.3	65.9	66.13	0.287	50.2	47.2	48.708	2.0857
MLS-0391382	17431860	59.94	53.2	62.2	57.72	6.372	46.9	50.3	48.579	2.4185
MLS-0272713	89856098	332.98	95.3	98.1	96.73	1.989	33.2	63.8	48.479	21.599
MLS-0343470	49644305	74.2	59.5	56.6	58.02	2.038	48.5	48.3	48.405	0.16288
MLS-0543936	134216127	367.48	338	336.6	337.30	1.039	50	46.8	48.368	2.2746
MLS-0458236	99494408	256.03	200.9	204.3	202.59	2.387	47.2	49.4	48.335	1.5442
MLS-0076158	14743474	96.8	95.6	96.2	95.92	0.391	52.6	43.9	48.252	6.1114
MLS-0018970	856072	154.9	124.1	127.5	125.82	2.386	51.6	44.7	48.182	4.8743
MLS-0363308	49820585	242.7	205.6	208.5	207.03	2.051	45.5	50.7	48.084	3.7146
MLS-0324604	49680884	89.94	73.5	66.9	70.20	4.703	46	50.1	48.081	2.8916
MLS-0542805	99355605	150.86	98.8	101.6	100.22	1.958	49.6	46.4	48.026	2.2629
MLS-0224064	22402141	74.57	66.2	67.8	67.02	1.121	44.2	51.3	47.756	5.0678
MLS-0444435	92763346	56.82	57	57.3	57.15	0.267	47.9	47	47.418	0.62645
MLS-0317746	17413265	66.03	77.5	82.9	80.19	3.863	51.5	43.3	47.399	5.7892
MLS-0225473	22401032	126.14	89.8	107.7	98.74	12.700	51.5	43	47.213	6.0178
MLS-0219888	22400937	92.43	84.3	91.9	88.07	5.383	43.4	50.8	47.08	5.2146
MLS-0258970	26725982	258.85	208.5	210.2	209.38	1.233	45.4	48.6	47.039	2.2609
MLS-0229200	17514698	443.51	86.4	36.2	61.31	35.466	52.9	40.9	46.921	8.5182
MLS-0244143	24781295	85.6	63.5	66.3	64.91	2.000	43.5	50.3	46.876	4.7955
MLS-0016420	865172	64.06	53.7	54	53.85	0.259	48.3	45.3	46.828	2.1295
MLS-0233645	17510826	125.57	292.1	220.5	256.32	50.616	59.9	33.7	46.786	18.559
MLS-0019666	842312	52.57	77	81.2	79.14	2.956	42.8	50.6	46.69	5.4663
MLS-0426375	85147439	60.98	56.6	59.1	57.84	1.770	42.6	50.5	46.528	5.5699
MLS-0323723	49669138	51.93	51.2	52.2	51.67	0.725	45	48	46.486	2.1649
MLS-0010980	4248599	89.55	77.5	74.7	76.12	1.977	48.3	44.7	46.457	2.5431
MLS-0035374	93576886	100.59	92.7	85.9	89.29	4.793	47.3	45.5	46.431	1.285
MLS-0393684	26660076	106.44	82.8	84.9	83.88	1.478	46.9	45.9	46.371	0.7018
MLS-0102061	17403305	82.12	83.8	84.1	83.98	0.244	44.8	47.9	46.339	2.2246
MLS-0462076	103162591	68.27	86	90.5	88.28	3.162	48.3	44.2	46.27	2.8708
MLS-0258970	24822971	210.22	184.9	189.3	187.10	3.131	48.3	44.1	46.221	2.9325
MLS-0551686	144095705	140.49	207.5	211.2	209.33	2.638	44.6	47.6	46.096	2.1604
MLS-0202618	17504456	1477.6	1465.8	1465.6	1465.70	0.115	53	39	45.979	9.8882
MLS-0097327	17406955	197.83	137.2	135.1	136.12	1.480	46.2	45.3	45.754	0.64573
MLS-0292430	26665164	570.06	130.3	197.5	163.91	47.521	32.4	59.1	45.747	18.885
MLS-0296639	26671199	1356.3	1136.9	1134.1	1135.50	1.985	46.5	44.9	45.696	1.1067
MLS-0236695	24782581	62.45	51.3	62.8	57.03	8.146	45.2	46	45.591	0.55906
MLS-0002774	56422610	106.11	95.8	95	95.44	0.561	46.5	44.7	45.576	1.2759
MLS-0312240	103060754	360.75	285.5	309.6	297.56	17.085	45.2	45.4	45.28	0.12999
MLS-0442857	89852978	121.22	95.1	86.6	90.83	6.005	43.8	46.7	45.239	2.0349
MLS-0292517	26670183	89.08	81.8	73.6	77.70	5.858	44.7	45.6	45.141	0.66781
MLS-0439131	87349767	106.82	77.7	79.8	78.77	1.500	44	46.1	45.048	1.4911
MLS-0109003	17401632	80.56	61	61.1	61.09	0.084	43.5	46.2	44.815	1.9197
MLS-0231322	22404661	56.28	51.1	52.2	51.64	0.775	43	46.3	44.669	2.319
MLS-0074305	14741956	99.26	98.9	105.2	102.04	4.435	44.4	44.9	44.636	0.36264
MLS-0316180	47194052	95.06	50.1	52.1	51.07	1.398	44	45.2	44.595	0.82387
MLS-0044139	4245397	842.27	909.3	912.5	910.90	2.319	46.2	42.9	44.584	2.3187
MLS-0344955	49645066	105.28	77.1	71.4	74.26	4.010	45.1	43.9	44.471	0.84635
MLS-0223623	17511829	151.74	194.6	189	191.79	3.962	49.6	39.1	44.386	7.4255
MLS-0323277	49647004	90.55	82.3	83.5	82.89	0.884	40.4	48.3	44.367	5.5702
MLS-0552531	143471986	140.68	129.7	138.9	134.31	6.521	46.3	41.8	44.059	3.223
MLS-0241405	24803594	54.57	61.2	63.2	62.19	1.399	45.8	42.2	43.968	2.5672
MLS-0305656	26660918	63.14	52.3	53.2	52.73	0.671	42.3	44.8	43.57	1.8004

MLS-0436018	87334148	61.15	64.3	63.8	64.01	0.342	43.1	43.7	43.398	0.37085
MLS-0237894	24783267	363.6	250.5	259.9	255.21	6.685	40.7	45.9	43.323	3.6692
MLS-0543903	134216135	91.89	68.4	80.2	74.28	8.337	39.1	47.1	43.141	5.6488
MLS-0238111	24782671	76.42	58.3	56.4	57.36	1.332	41.5	44.8	43.138	2.3331
MLS-0372024	49734441	129.96	114.3	122	118.18	5.435	42.4	43.8	43.103	1.0295
MLS-0351704	47204543	816.62	841.6	832.5	837.05	6.376	44.9	41.3	43.09	2.5313
MLS-0225308	17513148	94.05	62.6	59.4	61.00	2.314	34.6	51.3	42.976	11.816
MLS-0013899	85304455	1083.6	760.8	774.4	767.61	9.571	45.3	40.7	42.957	3.2437
MLS-0248116	24825193	131.27	89.4	97.2	93.30	5.479	45.9	39.9	42.912	4.2579
MLS-0009786	24840976	104.38	50.2	56.8	53.49	4.625	43	42.6	42.829	0.26211
MLS-0014684	863744	118.17	70.8	75.4	73.09	3.239	26.7	58.8	42.777	22.709
MLS-0244993	24814611	61.82	58	60.7	59.35	1.935	40.3	45.3	42.771	3.528
MLS-0293072	26671414	146.04	104.9	108.8	106.85	2.730	41.5	43.8	42.628	1.6657
MLS-0217182	17516645	65.08	55	57.8	56.41	1.979	40.8	44.1	42.422	2.3399
MLS-0318563	49679511	60.74	51.4	55.4	53.40	2.895	38.9	45.8	42.387	4.8699
MLS-0222748	22413230	202.68	200.4	192.2	196.26	5.808	41.7	43	42.357	0.94952
MLS-0442690	89854665	63.9	67.1	63.9	65.48	2.236	40.9	43.7	42.286	2.0175
MLS-0221872	17511563	599.61	556.1	570.3	563.24	10.039	44.6	39.7	42.117	3.4721
MLS-0351587	47203747	112.61	97.1	99.5	98.31	1.661	38	45.6	41.792	5.3883
MLS-0543955	134216130	292.41	260	260.5	260.23	0.333	35.7	47.7	41.685	8.5261
MLS-0206511	22407015	69.4	61.5	62.1	61.79	0.389	40.3	42.8	41.569	1.746
MLS-0000718	857091	74.52	73.6	73.2	73.41	0.258	41.9	41.1	41.48	0.52557
MLS-0224991	87336016	1410.2	798.2	840.3	819.23	29.783	38.2	44.5	41.353	4.4691
MLS-0056527	7973792	66.55	61.7	69.7	65.71	5.700	43.1	39.3	41.194	2.6628
MLS-0109411	26670256	103.08	56.8	66	61.38	6.535	45.9	36.4	41.17	6.7015
MLS-0323252	49647116	83.77	68.8	79.6	74.19	7.599	41.3	40.9	41.099	0.23416
MLS-0401043	57261644	54.08	58.3	59.3	58.78	0.741	38.1	43.9	40.975	4.1017
MLS-0265009	24804731	1206.2	64.6	409.7	237.17	244.030	33	49	40.971	11.329
MLS-0358356	49674369	504.02	475.6	490.2	482.92	10.358	39	42.9	40.926	2.7629
MLS-0046074	7973417	92.87	83.2	88.6	85.93	3.801	39.9	41.8	40.888	1.3461
MLS-0258990	24822937	171.43	150.6	144.9	147.76	4.023	40.8	40.9	40.849	0.13552
MLS-0456016	103159731	129.62	107.9	107.8	107.85	0.042	41.9	39.6	40.743	1.6789
MLS-0450173	99357757	257.72	247.2	243.9	245.54	2.313	40.5	40.9	40.703	0.30658
MLS-0449334	99356301	67.5	86	110.4	98.19	17.203	39.3	42.1	40.688	1.9277
MLS-0234410	17431571	63.77	59.4	61.7	60.55	1.561	43.9	36.9	40.415	4.9525
MLS-0291499	24824064	68.81	70.4	80	75.18	6.816	39.5	41.2	40.322	1.2229
MLS-0013318	87347551	785.6	391.4	389.2	390.27	1.575	40.8	39.6	40.223	0.84225
MLS-0327521	49665497	260.65	165.7	60.3	113.03	74.531	40.5	39.8	40.137	0.50116
MLS-0231882	22404448	88.39	86.6	71.8	79.21	10.411	41	39.2	40.08	1.2533
MLS-0281188	24805312	544.33	392.2	406.5	399.37	10.149	52.2	27.8	40.004	17.227
MLS-0099513	17415420	42.51	49.1	50.8	49.95	1.136	62.2	75.5	68.841	9.3976
MLS-0003242	855680	51.52	49.4	50.4	49.88	0.721	1097.3	1109.4	1103.4	8.5744
MLS-0093723	17409843	52.45	49.6	50.1	49.82	0.357	37.5	48.1	42.779	7.4836
MLS-0101158	14735724	66.6	41.6	57.9	49.74	11.534	183.4	463.4	323.42	197.99
MLS-0365973	49822071	42.15	48.4	51.1	49.74	1.892	42.9	42.2	42.573	0.50548
MLS-0046376	863309	98.32	57.1	42.3	49.72	10.500	44.1	41.2	42.647	1.9907
MLS-0211794	17509800	115.82	51.6	47.8	49.70	2.734	102.8	108.1	105.44	3.7138
MLS-0327819	49668975	69.93	47.1	52.2	49.64	3.646	63.6	59.7	61.669	2.7171
MLS-0245879	24781479	54.8	48.4	50.8	49.62	1.685	4071.8	4162.5	4117.2	64.111
MLS-0057194	862208	53	45.8	53.1	49.41	5.152	52.3	48.9	50.59	2.4365
MLS-0233908	14730199	93.72	48.3	49.7	49.04	0.976	59.3	47	53.188	8.6823
MLS-0210773	17505640	66.45	47.2	50.8	48.99	2.532	73.1	79.7	76.432	4.6802
MLS-0439189	87336264	50.48	50.7	46.6	48.61	2.893	1067.3	1040.1	1053.7	19.249
MLS-0548812	144097109	51.94	47	50.1	48.55	2.126	56.5	60.4	58.468	2.794
MLS-0304480	26658633	55.51	48.2	48.9	48.55	0.482	377	378.1	377.54	0.73961
MLS-0021956	857094	66.83	46.1	49.7	47.91	2.532	71.8	81	76.43	6.4819
MLS-0031409	3713891	40.96	43.3	51.6	47.44	5.832	5495.3	5494.3	5494.8	0.70193
MLS-0233189	87347057	87.03	49	45.6	47.33	2.379	49	52.5	50.764	2.4423

MLS-0019259	7974463	42.54	45.4	49.2	47.30	2.738	44.7	55.4	50.02	7.5519
MLS-0071130	14736039	51.33	45.1	49.2	47.17	2.869	228.1	135.5	181.8	65.505
MLS-0458234	103060340	45.85	46.4	47.5	46.91	0.779	165.2	151.1	158.13	9.9913
MLS-0220651	17505829	60.61	43.8	50	46.90	4.374	62.3	74.1	68.155	8.3479
MLS-0262373	24830685	124.18	59.4	34.1	46.74	17.934	77.5	45.1	61.252	22.913
MLS-0218480	26671549	40.13	45.2	48.2	46.72	2.083	52.1	48.2	50.14	2.7015
MLS-0442286	89851485	44.15	47.5	45.4	46.48	1.477	39.2	49.5	44.334	7.3237
MLS-0211137	17510195	55.31	44.4	48.6	46.46	2.959	63.4	70.6	66.999	5.0678
MLS-0045331	863226	43.07	47.7	45	46.35	1.951	116.7	101.2	108.95	10.982
MLS-0222568	17513574	74.58	40.8	51.9	46.32	7.835	62	56.7	59.388	3.7551
MLS-0040419	860781	110.28	50.1	42.2	46.17	5.585	53.3	56.9	55.069	2.546
MLS-0034411	85304588	49.13	46.8	45.4	46.11	1.007	48.5	44.7	46.604	2.6383
MLS-0370396	49825111	49.11	47.8	43.7	45.77	2.886	170.8	175.7	173.24	3.4485
MLS-0344061	49644536	57.86	31	60	45.52	20.530	39.7	203.2	121.48	115.62
MLS-0218122	22404926	162.39	46	44.6	45.30	1.005	1258.4	1252.1	1255.2	4.4487
MLS-0301604	26666086	43.19	43	47.4	45.23	3.112	69.2	62.9	66.075	4.4338
MLS-0211391	17504485	43.07	43.7	46.3	45.00	1.782	540.3	538.2	539.26	1.4676
MLS-0400094	57261334	49.58	45.5	44.5	44.97	0.686	4921	4939.3	4930.2	12.935
MLS-0339847	47203861	75.47	42.6	47.2	44.89	3.238	49.2	56.6	52.882	5.2146
MLS-0289636	24783824	51.13	40.4	49	44.67	6.096	42.3	58.7	50.482	11.571
MLS-0351225	49643486	54.09	43.1	46.1	44.62	2.161	53.7	61.7	57.713	5.6536
MLS-0440137	92763382	72.06	44.4	44.7	44.55	0.249	48.5	45.4	46.982	2.1831
MLS-0247756	24781660	60.24	44.4	43.6	44.01	0.570	49.2	44.5	46.848	3.294
MLS-0058809	85273204	68.93	41.7	46.2	43.96	3.178	33.3	49.2	41.276	11.213
MLS-0449616	99356018	44.26	41	46.8	43.89	4.114	94.5	109.9	102.19	10.897
MLS-0027012	852615	84.42	45.3	42.1	43.73	2.264	25.7	60.6	43.129	24.716
MLS-0232476	22412207	46.7	41.2	46.1	43.65	3.478	115.8	146.2	131.01	21.438
MLS-0549951	144089967	41.46	40.9	45.9	43.43	3.526	85.5	86.7	86.097	0.81249
MLS-0284620	24802242	44.94	41.8	44.8	43.34	2.120	45.5	47.3	46.36	1.2586
MLS-0073238	14743124	227.25	41.4	44.9	43.14	2.516	370	384.7	377.34	10.412
MLS-0229252	87337276	92.97	64	22.2	43.09	29.600	648.7	762.9	705.79	80.729
MLS-0320890	49648785	71.72	41.2	44.7	42.97	2.460	57.8	61.3	59.538	2.4518
MLS-0375050	49819048	60.28	41.9	43.7	42.81	1.243	285.7	329.7	307.72	31.101
MLS-0263118	24833410	43.48	42.5	42.7	42.57	0.114	49.2	47	48.113	1.5701
MLS-0346976	47198077	55.02	43.4	41.6	42.48	1.295	104.1	96.1	100.1	5.5996
MLS-0036133	22405523	46.01	40	44.7	42.38	3.339	235.8	240.8	238.3	3.4989
MLS-0041686	3713317	43.34	40.5	43.8	42.14	2.353	55.3	49.1	52.201	4.4482
MLS-0323786	49668562	48.91	41.6	42.6	42.08	0.693	188.9	194.5	191.71	3.995
MLS-0302777	26659756	63.65	40.7	43.4	42.01	1.893	184.9	182.4	183.63	1.7515
MLS-0205958	17512724	44.38	39.7	44	41.84	3.023	1063.4	1128.8	1096.1	46.207
MLS-0211766	17513109	51.18	39	44.4	41.70	3.821	66	77.5	71.735	8.1639
MLS-0398511	56315830	56.2	40.7	42.5	41.61	1.309	45.9	43.7	44.797	1.5929
MLS-0354480	49731854	62.32	41.3	41.9	41.60	0.365	54.9	51.9	53.42	2.1222
MLS-0448344	99358564	46.62	40.3	42.5	41.41	1.585	55.6	52.7	54.166	2.0293
MLS-0282083	24807086	45.9	42.1	40.3	41.19	1.243	41.1	45.2	43.165	2.8518
MLS-0308354	26725855	49.97	37.3	44.9	41.08	5.329	47.7	53	50.332	3.7252
MLS-0258900	24817138	41.83	39.5	42.3	40.89	1.982	344	350.6	347.3	4.7091
MLS-0550821	144089769	48.52	38.3	43.1	40.68	3.434	47.4	50.2	48.785	1.9824
MLS-0322951	49668694	43.26	36	44.6	40.32	6.054	4382	4724.6	4553.3	242.24
MLS-0324089	49646131	48.22	41.1	39.4	40.27	1.212	396.7	395.8	396.27	0.6636
MLS-0296819	24825251	42.84	40.8	39.7	40.26	0.792	62.9	64.8	63.877	1.325
MLS-0229252	22405609	98.85	13.4	67.1	40.25	37.962	693.4	737.7	715.52	31.345
MLS-0107054	17387127	333.92	119.1	128.2	123.65	6.408	39.8	39.9	39.867	0.1091
MLS-0303159	26724326	91.62	109.3	117.2	113.27	5.601	40.6	39.1	39.863	1.11
MLS-0057191	87346853	106	139	142.8	140.90	2.728	42.2	37.4	39.808	3.3402
MLS-0221132	22416907	66.7	67.6	70.5	69.03	2.063	37.4	42.1	39.76	3.3014
MLS-0265054	24833424	68.22	51.3	48.1	49.71	2.271	39.9	39.3	39.602	0.44691
MLS-0338090	49715541	119.26	122.6	132.1	127.35	6.783	40.6	38.5	39.552	1.4871

MLS-0272665	24788901	174.31	125	143.2	134.06	12.852	39.2	39.9	39.53	0.50851
MLS-0445040	93577541	131.67	115.2	115.1	115.14	0.067	39.7	39.1	39.367	0.41216
MLS-0388619	50085422	210.76	174.6	185.3	179.98	7.560	39.5	39.2	39.356	0.20019
MLS-0083834	14727580	58.21	40.3	39.9	40.10	0.327	38.5	40.1	39.304	1.1309
MLS-0096726	56323573	41.53	49.4	47.8	48.61	1.083	35.4	42.9	39.158	5.3552
MLS-0267154	24787811	354.26	324.2	325.7	324.95	1.033	42.9	35.3	39.08	5.3765
MLS-0543981	134216131	312.57	269.9	269.4	269.63	0.345	38.1	40	39.033	1.3735
MLS-0058577	56423578	155.54	175	181.6	178.28	4.670	39.5	38.3	38.914	0.87777
MLS-0328228	49665687	1536.3	1316.2	1287.4	1301.80	20.412	42.6	35.2	38.906	5.2285
MLS-0000194	24840760	87.12	61.5	66.6	64.02	3.620	36.7	41.1	38.902	3.1397
MLS-0092306	17411771	537.18	622.1	674.2	648.14	36.827	40.3	37.2	38.766	2.1825
MLS-0100711	17403649	73.97	89.9	100.1	95.02	7.236	34.7	42.3	38.534	5.366
MLS-0322128	49667306	1600.5	1452.4	1452.4	1452.40	0.000	35.7	41.2	38.47	3.8615
MLS-0374120	49819136	45.49	36.8	46.7	41.76	7.005	35	41.7	38.356	4.7571
MLS-0056660	87339902	298.06	618.8	625.5	622.14	4.741	34.4	42.3	38.333	5.6292
MLS-0019640	852576	167.13	113.1	110.5	111.81	1.806	43.7	32.7	38.226	7.7892
MLS-0057733	56320513	117.86	71.1	70.1	70.62	0.688	37.3	39	38.146	1.2162
MLS-0229056	17514297	182.88	141.6	199.3	170.43	40.768	45.7	30.4	38.048	10.79
MLS-0215249	17516217	67.73	60.7	58.8	59.75	1.401	37.6	38.3	37.967	0.51446
MLS-0213013	17509349	61.35	68.8	71.9	70.34	2.175	34.5	41.1	37.834	4.6532
MLS-0080710	14731349	75.92	51.6	57.5	54.58	4.183	36.1	39.4	37.765	2.3287
MLS-0110034	14739565	55.1	47	49.7	48.34	1.873	39.5	36	37.738	2.4946
MLS-0238165	24782656	71.55	44.6	51.3	47.96	4.678	34.1	41	37.559	4.8633
MLS-0303294	26660138	156.64	165.8	168.4	167.06	1.849	34.3	40.9	37.558	4.6632
MLS-0458342	103050711	52.4	57.4	62.8	60.11	3.811	38.7	36.3	37.541	1.7014
MLS-0269103	24788198	1353.9	636.6	674.5	655.57	26.769	27.4	47.3	37.375	14.101
MLS-0203906	17432058	54.86	52.8	51.4	52.10	0.929	37.9	36.6	37.276	0.91272
MLS-0095209	17413454	72.88	87.9	98.2	93.06	7.293	34.9	39.6	37.21	3.3243
MLS-0069480	89850519	49.03	42.9	55.4	49.12	8.859	37.3	36.9	37.132	0.26488
MLS-0222693	17504421	79.48	41.4	58.1	49.72	11.800	39.4	34.8	37.119	3.2899
MLS-0298819	26665303	87.78	53.4	53.5	53.44	0.099	38.5	35.6	37.025	2.072
MLS-0312903	26664782	48.2	44	49.9	46.92	4.183	33.5	40.5	37.022	4.9839
MLS-0034413	7978402	239.6	226.8	213	219.93	9.735	36.5	37.5	37.016	0.70898
MLS-0225866	17505308	51.99	52.6	53.7	53.16	0.773	36.1	37.9	37.008	1.3057
MLS-0354539	49675230	75.75	81.5	83.4	82.42	1.323	40.9	33	36.911	5.5957
MLS-0456538	103073481	117.18	107.6	107.6	107.61	0.006	38.9	34.8	36.844	2.8622
MLS-0299310	26659839	1640.5	1440.5	1451.4	1445.90	7.768	34.7	39	36.813	3.0329
MLS-0207484	17512463	60.82	42.2	49.9	46.04	5.394	32.8	40.7	36.776	5.5654
MLS-0220299	22402862	300.03	189.8	216.4	203.10	18.803	32.7	40.7	36.711	5.6479
MLS-0225921	17505275	65.37	66.1	69.4	67.74	2.302	33.4	39.9	36.657	4.5711
MLS-0014300	87348963	152.49	105.2	109.2	107.18	2.817	31.2	41.8	36.471	7.493
MLS-0313295	24779870	59.22	57.6	58.8	58.17	0.873	35.8	37.2	36.46	0.97751
MLS-0461911	103060755	43.56	39.1	43.9	41.50	3.399	39.8	33	36.4	4.8749
MLS-0205623	17516320	159.85	150.2	106.3	128.24	31.015	19.9	52.8	36.352	23.258
MLS-0422750	57256334	70.91	61.1	65.8	63.44	3.284	35.6	37	36.326	1.0079
MLS-0317869	56463344	109.9	99.4	103.6	101.50	3.038	36.5	36.1	36.294	0.33394
MLS-0251789	24826346	1149	1071.2	1132.9	1102.10	43.644	31	41.5	36.246	7.4483
MLS-0065143	24801003	45.58	45.1	49.5	47.31	3.122	38.5	34	36.228	3.1623
MLS-0237109	24809562	371.07	338.4	329	333.70	6.678	0.5	71.8	36.166	50.432
MLS-0202333	87335239	1227	1007.5	1143.7	1075.60	96.310	29.5	42.7	36.113	9.3396
MLS-0004440	87337925	48.85	42.7	46.2	44.48	2.503	29.8	42.3	36.068	8.8128
MLS-0441592	89854169	54.8	60.3	65.6	62.98	3.742	33.8	38.2	36.03	3.1258
MLS-0213457	17511701	89.91	71.3	71.4	71.36	0.113	37.4	34.5	35.98	2.0365
MLS-0259221	24817349	324.62	303.1	308.8	305.94	4.026	34.2	37.6	35.899	2.4563
MLS-0308347	26725796	55.96	83.8	77.2	80.49	4.669	39.5	32.3	35.897	5.074
MLS-0210183	17509419	52.76	47.9	49.8	48.84	1.347	36.9	34.5	35.696	1.6622
MLS-0344893	49644908	170.9	310.8	306.2	308.53	3.265	31.8	39.4	35.583	5.336
MLS-0308522	26725774	59.41	58.9	62.9	60.90	2.897	38.4	32.8	35.56	3.9644

MLS-0096139	17416154	45.68	49.9	51.3	50.57	0.993	36.5	34.5	35.469	1.4083
MLS-0306067	26660672	99.74	60.4	62.3	61.36	1.375	34.3	36.6	35.421	1.5986
MLS-0088581	14743452	103.08	93.7	94.2	93.95	0.378	35.3	35.5	35.393	0.10378
MLS-0252898	24811960	336.87	86.6	90.7	88.64	2.953	21.8	48.8	35.327	19.099
MLS-0097027	17406912	240.13	225.1	239.4	232.22	10.084	33	37.6	35.31	3.2513
MLS-0087449	87346570	84.19	52.4	59	55.70	4.665	33.3	37.3	35.29	2.8008
MLS-0225864	17504042	44.55	42.5	43.3	42.89	0.521	35.6	34.5	35.074	0.79608
MLS-0551814	144095687	51.1	41.6	47.9	44.72	4.427	37.3	32.8	35.071	3.1674
MLS-0003297	85148703	186.48	226.8	231.6	229.17	3.426	38.3	31.8	35.062	4.5488
MLS-0313578	24779811	65.21	64.4	60.8	62.62	2.567	36	34	34.973	1.3887
MLS-0544865	134215512	43.31	43.5	44.1	43.80	0.405	33.5	36.4	34.939	2.0488
MLS-0358933	49828437	45.89	52.3	53.7	52.99	0.966	35.3	34.5	34.906	0.53356
MLS-0022853	861123	81.58	46.9	53.2	50.06	4.454	31.7	38.1	34.868	4.5137
MLS-0075760	14729494	132.6	79	80.4	79.70	0.971	34.1	35.6	34.855	1.0781
MLS-0046007	4241422	55.88	48	49.8	48.91	1.308	36.1	33.5	34.834	1.8295
MLS-0082745	14726646	68.68	55	53.4	54.18	1.141	34.6	34.8	34.695	0.18842
MLS-0424695	85149011	130.19	265.2	250.2	257.71	10.626	34.1	35.2	34.677	0.75076
MLS-0225888	17504012	45.14	41.7	48.4	45.02	4.760	33.8	35.4	34.6	1.1456
MLS-0096932	17406951	428.19	385.1	459.1	422.12	52.304	29.5	39.7	34.579	7.1846
MLS-0088549	14742449	93.45	73.3	73.1	73.21	0.096	35.8	33.4	34.568	1.6916
MLS-0323599	49668319	106.57	114.6	118.2	116.40	2.507	33.9	35	34.435	0.81827
MLS-0303496	26660183	170.39	96.1	118.1	107.11	15.596	33	35.8	34.386	1.999
MLS-0098080	17407112	185.3	105	121.4	113.20	11.625	40.8	27.9	34.361	9.1729
MLS-0298001	26664034	41.48	47.7	54.6	51.18	4.899	34.7	33.9	34.272	0.55736
MLS-0229763	89851169	173.84	159.9	155.7	157.77	2.976	39.4	29.1	34.266	7.3102
MLS-0322631	49665230	168.74	134.5	141.2	137.89	4.737	25.7	42.5	34.091	11.924
MLS-0105217	17385795	57.84	50.5	41.7	46.12	6.259	31.9	36.3	34.082	3.0774
MLS-0001366	858874	529.61	648.2	687.9	668.06	28.097	30.2	37.9	34.066	5.4362
MLS-0077546	14738085	63.03	47.1	48.6	47.82	1.090	34.5	33.6	34.066	0.66219
MLS-0439994	92763311	102.54	60.7	77.8	69.21	12.097	34.9	33.1	34.035	1.2563
MLS-0245261	24802470	1563	1332	1448.3	1390.20	82.214	36.2	31.8	33.991	3.122
MLS-0291858	26671124	58.58	43.2	38.3	40.72	3.472	32.7	35.3	33.968	1.8236
MLS-0311998	24779201	1787	1449.4	1446.9	1448.10	1.799	31.8	36.1	33.936	2.9958
MLS-0099847	17416013	40.52	40.1	43	41.59	2.051	34.7	33.1	33.908	1.0914
MLS-0093257	17401490	48.94	15.6	93.7	54.66	55.268	36.1	31.7	33.884	3.1426
MLS-0068188	14746176	88.57	64	68.7	66.38	3.298	33.8	33.3	33.572	0.33573
MLS-0030435	85273047	167.46	161.9	200.3	181.07	27.183	34.2	32.7	33.454	1.0342
MLS-0310072	26725737	69.92	53.4	58.4	55.89	3.525	35.8	30.8	33.336	3.5222
MLS-0018902	859717	148.42	108.4	111.2	109.79	2.014	32.3	34.3	33.322	1.4363
MLS-0086881	14727573	101.87	96.9	105.5	101.20	6.086	35.1	31.6	33.306	2.475
MLS-0075760	14734769	96.52	48.8	50.6	49.69	1.227	32.3	34.2	33.246	1.2864
MLS-0039499	87347889	182.84	119.7	124.7	122.23	3.540	34.8	31.6	33.219	2.2949
MLS-0365799	49822669	48.96	50.6	52.1	51.34	1.028	32.7	33.6	33.163	0.68434
MLS-0350724	47201880	379.51	319.5	278.5	298.99	29.027	32.7	33.5	33.098	0.6096
MLS-0245799	24783174	69.26	56.8	57.4	57.09	0.423	30.3	35.8	33.086	3.8892
MLS-0085596	14722270	510.73	249.6	273.2	261.40	16.714	29.7	36.2	32.95	4.6036
MLS-0354546	49724812	44.52	45.5	49.3	47.39	2.711	29.7	36.2	32.911	4.6107
MLS-0001062	858000	57.52	44.6	44.1	44.33	0.309	31.1	34.4	32.754	2.35
MLS-0271474	24827207	98.53	66.7	61.6	64.12	3.597	33.2	32.1	32.686	0.79101
MLS-0425163	49714628	851.67	1141.5	1269.2	1205.40	90.317	24.2	41.2	32.68	12.048
MLS-0014152	864292	58.53	56.6	56.2	56.40	0.292	34.4	30.8	32.577	2.5318
MLS-0294376	26727372	73.5	50.1	57.2	53.64	5.015	31.4	33.7	32.556	1.6615
MLS-0062765	87341104	83.35	73.7	77	75.38	2.311	30.2	34.7	32.455	3.1961
MLS-0295487	26665295	166.81	132	130.6	131.31	1.002	26.3	38.5	32.401	8.5625
MLS-0545262	134215496	40.42	37.7	42.8	40.29	3.623	29.9	34.8	32.37	3.5023
MLS-0219606	22410442	83.78	61.2	71.7	66.49	7.426	32.2	32.1	32.17	0.10866
MLS-0279004	24808456	136.87	186.2	190.3	188.22	2.917	35.8	28.4	32.137	5.2293
MLS-0364644	49821574	91.64	53.2	59.1	56.15	4.188	32.3	31.9	32.117	0.32403

MLS-0223204	87346653	59.74	43.2	36.6	39.90	4.640	36.3	39	37.636	1.931
MLS-0319135	49649382	64.21	30.5	49.1	39.83	13.167	692.1	634.4	663.27	40.782
MLS-0101137	17416169	47.55	42.3	37.2	39.79	3.600	193.3	30	111.65	115.43
MLS-0231619	22404228	42.04	42	37.3	39.62	3.302	278.4	231.1	254.73	33.479
MLS-0259246	24823138	40.63	38.2	41	39.59	1.924	77.1	75.8	76.448	0.91209
MLS-0338293	49716595	56.67	37.8	41.1	39.46	2.333	54.3	51.4	52.832	2.0388
MLS-0348684	49642589	64.48	37.7	41	39.38	2.357	43.6	41.7	42.654	1.4037
MLS-0397658	56323698	51.5	40.2	38.4	39.31	1.306	33.4	34	33.724	0.45407
MLS-0204483	17516895	52.43	37.1	41.3	39.23	2.953	216	221.9	218.92	4.1573
MLS-0010679	863262	55.72	37.7	40.7	39.18	2.146	73.2	60.8	66.996	8.7831
MLS-0245856	24814503	75.12	39	39.2	39.13	0.161	47.3	47.3	47.306	0.051828
MLS-0307948	26725703	46.8	38.6	39.6	39.12	0.709	121.8	112.3	117.05	6.6585
MLS-0217653	17433296	62.48	37.6	40.5	39.04	2.032	128.5	125.4	126.98	2.1829
MLS-0229802	22413803	51.78	36.6	41.5	39.03	3.500	29.9	36.5	33.194	4.6572
MLS-0210418	17513073	40.07	39.6	37.7	38.66	1.338	86	84.2	85.103	1.24
MLS-0415796	57268442	57.38	37.5	39.7	38.57	1.568	55.1	57.8	56.426	1.904
MLS-0096618	17416250	54.95	36.8	40.3	38.50	2.478	49.5	53.1	51.3	2.6105
MLS-0336916	49728303	102.29	25.5	51.5	38.47	18.396	48.6	22.6	35.641	18.39
MLS-0044743	852342	93.21	40.6	36.3	38.47	3.017	31.9	32.8	32.372	0.67138
MLS-0355512	49735817	60.83	38.9	38	38.43	0.640	56.7	57.8	57.245	0.79494
MLS-0406854	56436624	46.57	36.8	39.9	38.33	2.214	30.7	42.2	36.457	8.1101
MLS-0306124	26662906	52.68	38.4	37.9	38.12	0.362	60.4	62.4	61.404	1.3624
MLS-0445021	92764810	52.58	38.6	37.5	38.06	0.772	85.6	76.8	81.221	6.255
MLS-0297810	26664055	66.4	47	28.8	37.90	12.834	51.8	39.9	45.871	8.41
MLS-0470390	125306190	42.07	37.9	37.5	37.70	0.242	52.3	48.6	50.427	2.619
MLS-0273941	24791901	40.53	40.1	35.3	37.66	3.404	43.6	49	46.319	3.7898
MLS-0314686	26725289	43.54	36	39.2	37.63	2.275	39	50.1	44.539	7.8949
MLS-0452310	99356440	46.31	35.8	39.2	37.52	2.406	60.8	71	65.892	7.1747
MLS-0412796	56463571	41.52	36.2	38.8	37.51	1.849	135.9	23.7	79.763	79.332
MLS-0306955	26729665	54.19	35.2	39	37.13	2.676	33.4	31.3	32.373	1.4631
MLS-0400257	56318475	67.04	37.2	36.9	37.07	0.184	35.2	35.2	35.201	0.050547
MLS-0439773	92764404	63.54	39.6	34.4	37.03	3.701	36.2	43.8	40.008	5.3231
MLS-0307077	26729947	44.73	34.6	38.9	36.75	3.083	63	59.3	61.144	2.5799
MLS-0210792	17505765	53.81	35.3	37.7	36.53	1.718	39.9	48.1	43.978	5.7961
MLS-0444560	92764245	53.8	38.6	34.3	36.46	3.054	36.2	37.2	36.671	0.72043
MLS-0210791	17510191	49.71	34.5	37.6	36.06	2.216	35.6	33.9	34.786	1.2019
MLS-0448553	99454607	62	36.3	35.6	35.94	0.457	47.8	50.2	49.004	1.7549
MLS-0394884	47194703	43.79	36.3	35.4	35.85	0.596	49.5	54.3	51.913	3.365
MLS-0103150	17402081	42.93	35.2	35.5	35.33	0.249	55.9	59.2	57.532	2.3272
MLS-0307958	26725881	49.92	35.3	35.2	35.25	0.048	60.9	55.6	58.243	3.7605
MLS-0111625	49667548	40.18	36.2	34	35.09	1.522	33.2	34.9	34.054	1.1591
MLS-0328720	49649742	40.95	31.9	37.5	34.74	3.967	222.3	229.5	225.91	5.0958
MLS-0035576	7972143	48.6	22.1	47	34.54	17.604	86.6	96.8	91.72	7.2427
MLS-0461682	103051061	44.78	34.1	34.9	34.51	0.555	32.3	35.2	33.739	2.061
MLS-0213021	22405888	50.56	29.7	39.2	34.46	6.708	44.9	56.9	50.881	8.4598
MLS-0056697	4241708	43.83	30.8	38	34.39	5.074	57	60.7	58.815	2.6237
MLS-0222585	22401760	114.42	26.1	42.3	34.23	11.459	287.8	210.7	249.3	54.516
MLS-0214846	17508253	40.53	30.7	37.7	34.20	4.963	41.9	47.4	44.639	3.9312
MLS-0299322	26669538	44.97	33.3	34.9	34.07	1.153	37.1	39.4	38.27	1.6188
MLS-0253745	24828685	41.63	34.3	33.7	34.01	0.391	249.3	232	240.64	12.199
MLS-0092692	17401215	43.6	31.6	36.3	33.95	3.334	61.7	64.7	63.227	2.1439
MLS-0093042	17410548	41.1	31.7	35.9	33.81	3.023	91.2	89.4	90.294	1.2726
MLS-0343956	47197639	179.18	34.4	33.2	33.80	0.917	45.8	37.1	41.436	6.1185
MLS-0387428	49716563	56.94	30.6	36.7	33.64	4.364	30.2	35.3	32.743	3.5574
MLS-0550212	144089961	46.3	32.8	34.5	33.63	1.234	43.2	45	44.093	1.2945
MLS-0246817	24810134	63.82	34.5	32.8	33.63	1.238	96.2	108.7	102.41	8.8443
MLS-0096560	17406914	40.47	32.7	34.3	33.49	1.100	48	41.8	44.864	4.4014
MLS-0207843	22404927	41.64	34.1	32.7	33.39	0.933	413.4	550.8	482.12	97.167

MLS-0070765	14729514	48.67	32	34.5	33.28	1.780	51.9	44.5	48.213	5.1947
MLS-0214415	17432852	41.36	22.4	43.8	33.08	15.140	24.3	40.2	32.23	11.259
MLS-0104764	17386668	72.81	34.8	29.9	32.33	3.464	41.1	37.4	39.238	2.5944
MLS-0384307	49823883	63.55	31.4	32.9	32.17	1.089	55.7	57.3	56.496	1.1138
MLS-0440437	87337274	74.87	31	33.2	32.09	1.526	1329.4	1261.5	1295.4	47.997
MLS-0291590	24819835	95.11	121.2	130.9	126.03	6.850	28.2	35.4	31.826	5.1042
MLS-0001840	861557	249.82	239.9	252.7	246.31	9.046	27.5	36.1	31.805	6.0646
MLS-0260973	24831279	77.36	79	79.7	79.37	0.522	34.7	28.9	31.802	4.1063
MLS-0256526	24789736	60.61	57.6	61	59.32	2.405	29.7	33.9	31.786	2.9287
MLS-0287130	24803754	75.54	45.1	68.3	56.71	16.374	37.1	26.4	31.756	7.5163
MLS-0074056	87346876	290.69	334	332.3	333.15	1.141	30.5	33	31.739	1.8144
MLS-0039992	858850	51.9	51.8	56.6	54.22	3.403	32.1	31.1	31.6	0.66887
MLS-0283956	24803229	72.63	56.6	51.7	54.15	3.449	34.5	28.5	31.524	4.2329
MLS-0240392	24822771	60.74	46	50.2	48.08	2.969	31.9	31.1	31.495	0.51191
MLS-0367241	49819998	41.38	41.2	39.5	40.38	1.196	30.5	32.4	31.441	1.3557
MLS-0051055	4244304	66.48	62.9	65.5	64.19	1.817	29.8	33	31.396	2.2092
MLS-0043436	85301582	141.34	120.3	129.5	124.86	6.506	32.4	30.4	31.366	1.4121
MLS-0078441	14729838	49.37	39	33.8	36.39	3.658	31.2	31.2	31.162	0.0050145
MLS-0107555	89852400	103.92	181.2	182.8	182.00	1.147	29.1	33	31.054	2.8205
MLS-0208072	17513975	75.87	47.7	49.3	48.51	1.137	28.9	33.2	31.046	3.0553
MLS-0466569	121285352	44.08	36.4	33.4	34.95	2.119	25.3	36.7	31.039	8.0567
MLS-0309917	26731589	113.07	74.9	73.5	74.21	0.979	29.8	32.1	30.966	1.6201
MLS-0321500	49648331	97.22	80.1	82	81.05	1.296	26.3	35.4	30.847	6.4001
MLS-0229076	22402674	41.33	48.3	53	50.67	3.327	30.2	31.4	30.783	0.81958
MLS-0018986	857662	60.19	47.2	48.3	47.75	0.832	28.7	32.9	30.778	2.9429
MLS-0389135	49677944	46.45	44.4	49.2	46.76	3.408	27.9	33.5	30.718	3.9838
MLS-0210065	22401831	281.03	168.4	138.7	153.53	20.997	35.2	26.2	30.707	6.3469
MLS-0273194	24786601	152.15	127	123.8	125.43	2.238	18.8	42.3	30.553	16.652
MLS-0005606	3716071	209.41	156.9	164.1	160.48	5.089	33.7	27.4	30.543	4.4576
MLS-0016237	863985	239.2	439	366.5	402.73	51.261	55.3	5.8	30.527	34.99
MLS-0092464	17406933	54.82	43	52	47.53	6.381	27.6	33.4	30.477	4.0704
MLS-0330984	49669940	390.49	338.4	342.3	340.35	2.815	28.4	32.5	30.448	2.9296
MLS-0323450	49665517	821.44	220.3	281.7	251.00	43.458	26.1	34.7	30.398	6.0571
MLS-0392099	22407648	45.26	29.9	35.6	32.77	4.079	31.8	29	30.37	1.975
MLS-0203055	22401257	111.81	134.8	133.6	134.20	0.786	29.4	31.2	30.315	1.3119
MLS-0322574	49667041	631.68	565	566.7	565.86	1.217	32.8	27.8	30.305	3.5993
MLS-0266560	24792326	56.58	40	39	39.53	0.690	31.8	28.8	30.299	2.1411
MLS-0090380	87348861	93.79	37.3	35.6	36.49	1.188	29.2	31.3	30.211	1.4806
MLS-0303330	26661819	59.54	42.5	41.5	41.99	0.664	26.3	34.1	30.178	5.4838
MLS-0067825	7965274	78.53	61.3	57.3	59.31	2.844	31.6	28.7	30.115	2.0308
MLS-0209318	17505307	56.08	38.4	42.3	40.39	2.770	19.7	40.5	30.096	14.698
MLS-0305674	26659910	80.31	68.2	67.7	67.96	0.344	29	31.2	30.074	1.5739
MLS-0215449	17513829	53.16	48.2	49.5	48.83	0.950	32.3	27.7	30.029	3.2429
MLS-0233923	14719378	52.49	52.6	40.6	46.60	8.516	33	26.9	29.985	4.2917
MLS-0089529	14737260	53.48	44.1	44.4	44.28	0.207	29.4	30.5	29.927	0.74366
MLS-0236677	87348071	85.8	87	63.8	75.43	16.402	29.3	30.5	29.921	0.84624
MLS-0259298	24823565	65.93	41	48.3	44.67	5.190	28	31.8	29.902	2.636
MLS-0311982	24791506	1136.2	847.7	881	864.37	23.546	28.5	31.2	29.884	1.9087
MLS-0000966	856223	202.19	152.1	155.7	153.90	2.527	31.3	28.5	29.876	1.9632
MLS-0271681	24791266	45.84	140.3	114	127.14	18.598	25.9	33.7	29.768	5.54
MLS-0093873	17413956	42.81	30.9	58.7	44.79	19.660	31.5	28	29.754	2.4579
MLS-0040244	857581	59.1	54.7	58.8	56.76	2.876	27.6	31.8	29.722	2.987
MLS-0204657	22400576	68.36	56.2	60.4	58.26	2.985	27.8	31.5	29.645	2.594
MLS-0229055	22400377	242.16	209.9	208.5	209.21	0.948	29.4	29.8	29.621	0.30335
MLS-0231004	22412359	56.1	56.8	58.2	57.50	0.944	26.5	32.6	29.597	4.3161
MLS-0223583	17513328	43.83	34.9	35.2	35.04	0.255	32.1	27	29.557	3.5529
MLS-0312095	87348995	45.13	43.7	44.7	44.18	0.670	30.8	28.1	29.469	1.8921
MLS-0002827	855964	55.76	62.8	61.4	62.08	1.024	30.3	28.6	29.445	1.1933

MLS-0307075	26670813	114.33	146	142	143.99	2.882	25.5	33.3	29.422	5.5103
MLS-0340805	49645276	45.3	45.9	49.7	47.81	2.652	26	32.8	29.405	4.8392
MLS-0311096	24791634	54.68	62.2	69.3	65.72	5.039	35.1	23.7	29.397	8.0528
MLS-0241354	24783818	40.37	43.4	47.6	45.48	2.996	29.3	29.4	29.38	0.093461
MLS-0456275	103159551	99.76	87.6	91	89.33	2.391	29.7	28.9	29.317	0.5772
MLS-0246890	24779618	43.08	41.3	46	43.65	3.297	32	26.5	29.233	3.93
MLS-0439940	92764283	236.08	188.8	208.9	198.87	14.207	26.9	31.5	29.215	3.293
MLS-0299842	26670281	77.49	72.5	71.6	72.05	0.608	30.4	28	29.167	1.6772
MLS-0412316	56463114	53.42	45.7	50.6	48.16	3.469	26.4	31.9	29.118	3.8718
MLS-0295457	26665310	76.77	79.4	79.5	79.44	0.057	31.8	26.2	29.033	3.9751
MLS-0253538	24817100	93.44	73.1	81	77.07	5.628	30.3	27.7	29.01	1.7842
MLS-0078039	87346581	143.33	63.2	59	61.08	2.933	32.7	25.2	28.951	5.2954
MLS-0450172	99357871	52.67	48.8	47.9	48.36	0.594	27.2	30.7	28.943	2.4852
MLS-0305289	26659038	43.02	35	40.2	37.57	3.676	28	29.9	28.913	1.359
MLS-0016701	87338532	754.95	584	588.6	586.27	3.269	29.7	28	28.835	1.2279
MLS-0078175	14730430	123.1	72.9	80.4	76.65	5.323	30.8	26.9	28.834	2.7586
MLS-0450556	99358093	50.91	41.9	44.8	43.35	2.034	31.2	26.3	28.74	3.4204
MLS-0090852	47193986	70.9	57.5	58.9	58.20	0.949	26.3	31.1	28.684	3.4321
MLS-0210336	17513132	454.26	611.4	667.1	639.29	39.388	28.6	28.8	28.667	0.12196
MLS-0079320	14737910	109.44	91.1	103.7	97.39	8.899	29.3	28	28.644	0.90659
MLS-0043021	85273043	193.73	129	130.8	129.89	1.261	30.6	26.6	28.636	2.8242
MLS-0324484	49664937	68.27	45.3	44.5	44.88	0.543	30.2	27	28.61	2.2379
MLS-0053260	844253	54.03	57.5	53.2	55.33	3.039	30.2	27	28.58	2.2853
MLS-0047030	24839820	48.08	27.7	36.7	32.20	6.418	24.8	32.3	28.533	5.3215
MLS-0308007	87346202	401.86	324.9	337.1	330.98	8.598	26.7	30.3	28.511	2.5438
MLS-0223068	17513483	82.18	55.7	39.8	47.75	11.236	28.4	28.6	28.508	0.15034
MLS-0331532	47203201	1573	1443.3	1443.3	1443.30	0.004	26	30.8	28.428	3.4213
MLS-0284039	24788072	50.68	85.8	83.2	84.48	1.836	26.4	30.5	28.417	2.9062
MLS-0096236	17414093	75.68	56.4	56.1	56.22	0.188	31	25.8	28.402	3.7212
MLS-0019411	50086104	62.28	44.4	50.2	47.29	4.127	28.6	28.2	28.367	0.2632
MLS-0320656	49647603	47.04	47	53.3	50.13	4.432	31.6	25	28.307	4.6811
MLS-0326660	49667452	51.85	43.7	48.1	45.91	3.120	24.4	32.1	28.277	5.413
MLS-0456481	103074696	43.94	60	57.6	58.81	1.733	30.7	25.8	28.267	3.441
MLS-0452897	99356437	142.41	119.5	123.1	121.33	2.563	25.8	30.6	28.196	3.3481
MLS-0348506	47204381	226.43	99.7	60.5	80.08	27.679	27.2	29	28.091	1.2793
MLS-0089580	14737481	650.58	380.6	392	386.28	8.025	28.7	27.4	28.014	0.89991
MLS-0331429	47203027	62.24	54.9	58.4	56.65	2.449	33.3	22.6	27.948	7.5183
MLS-0094859	17409250	1011.2	1456.4	676.3	1066.30	551.650	8.3	47.5	27.943	27.717
MLS-0440520	87336050	330.91	281.2	267.2	274.18	9.913	26	29.9	27.932	2.7948
MLS-0229982	22402919	45.19	31.3	39.3	35.31	5.627	28.2	27.6	27.928	0.44882
MLS-0093805	17413246	186.2	65.9	79.4	72.67	9.499	30.8	25.1	27.916	4.0337
MLS-0367580	50085766	90.95	65.7	67.5	66.62	1.240	22.8	33.1	27.908	7.2776
MLS-0330788	49649158	336.57	342.8	296.1	319.48	33.045	21.8	34	27.9	8.6208
MLS-0000797	87347332	45.52	34.5	32.5	33.51	1.425	25.4	30.3	27.884	3.471
MLS-0309072	24823831	316.97	237.8	236.6	237.23	0.831	26.2	29.5	27.838	2.2915
MLS-0232360	22400466	61.3	51.9	50.1	51.00	1.204	27.7	27.9	27.827	0.17119
MLS-0259248	24823043	110.56	91.4	88.2	89.80	2.226	27	28.6	27.79	1.1615
MLS-0035722	7973609	47.09	29.6	34.9	32.27	3.747	28.5	27.1	27.784	1.019
MLS-0324209	49665518	1512	356.4	691	523.70	236.650	32.2	23.3	27.763	6.2481
MLS-0296807	26671025	48.14	39.9	40.9	40.40	0.647	27.2	28.3	27.725	0.77377
MLS-0014251	24841145	59.02	65.5	70.7	68.08	3.631	29.1	26.1	27.602	2.1152
MLS-0353335	49673230	738.16	613	604	608.49	6.375	26.8	28.4	27.601	1.1807
MLS-0215812	17503973	285.25	161.6	188.1	174.82	18.707	29.1	26.1	27.601	2.0769
MLS-0004450	85273130	90.09	86.9	86.2	86.54	0.440	28.8	26.4	27.566	1.6933
MLS-0308525	26726000	58.4	47.8	49.8	48.80	1.386	24.8	30.3	27.565	3.868
MLS-0092340	17409209	62.93	49.7	56.8	53.27	5.062	24.6	30.3	27.407	4.0278
MLS-0098613	17416108	173.18	61.2	50	55.58	7.931	30.2	24.5	27.383	4.0492
MLS-0000487	857576	467.63	239.7	296.3	268.01	40.016	25	29.7	27.346	3.3014

MLS-0364572	49824843	73.77	56.3	64.2	60.25	5.613	27.8	26.6	27.216	0.83339
MLS-0299769	26671050	71.65	57.5	58.3	57.89	0.526	28.9	25.5	27.21	2.3548
MLS-0423486	85148705	569.32	519.2	362.1	440.63	111.050	29.1	25.2	27.178	2.7545
MLS-0216576	87347070	91.14	47.3	41.4	44.35	4.110	28.5	25.8	27.159	1.9381
MLS-0032718	87348937	329.73	239.3	240.2	239.76	0.625	28.1	26.2	27.157	1.3749
MLS-0075183	14743034	554.91	491.9	515	503.44	16.380	24.1	30.2	27.145	4.3312
MLS-0341251	49642517	70.12	63.1	63.4	63.26	0.157	28.6	25.7	27.122	2.0332
MLS-0443960	93576730	52.32	52.7	58.8	55.76	4.310	26.7	27.5	27.105	0.58147
MLS-0309716	24815291	143.68	235.1	189.3	212.23	32.412	13.1	41.1	27.102	19.836
MLS-0026610	4258119	50	54.4	53.4	53.91	0.722	28.9	25.3	27.081	2.5823
MLS-0298978	26671137	74.23	60.2	57.6	58.91	1.882	27.9	26.2	27.046	1.232
MLS-0468275	124753316	504.78	477.3	525.6	501.43	34.128	30.9	23.1	27.012	5.5042
MLS-0455942	103074302	62	59.4	59.4	59.38	0.022	24	29.8	26.907	4.1505
MLS-0292881	26669979	50.91	37.4	57.1	47.28	13.943	26.2	27.4	26.791	0.88999
MLS-0272080	24794011	218.89	170.1	179.2	174.65	6.488	25.7	27.7	26.694	1.4745
MLS-0552777	125001390	1510	1440.8	1438.6	1439.70	1.563	28.3	25	26.65	2.3558
MLS-0012626	859168	51.58	40.2	41.7	40.97	1.032	27.2	25.9	26.556	0.88236
MLS-0057275	860972	45.67	31.5	32.5	32.01	0.713	27.1	26	26.534	0.73576
MLS-0062436	7965908	239.43	228.6	239.6	234.09	7.798	22.1	30.9	26.517	6.2619
MLS-0108926	17401652	397.87	73.9	76.2	75.07	1.637	26.6	26.2	26.434	0.29359
MLS-0019324	87347048	89.71	55.7	64.7	60.21	6.390	24.7	28.2	26.431	2.4399
MLS-0036689	7975642	71.43	43	43.2	43.13	0.136	21.7	31	26.368	6.6196
MLS-0206059	26726094	42.54	34.6	35.6	35.07	0.735	24	28.5	26.252	3.2414
MLS-0012697	859345	155.8	121.6	131.1	126.34	6.691	25.1	27.3	26.17	1.575
MLS-0329272	49647281	54.85	52.4	53	52.70	0.368	26	26.3	26.134	0.18621
MLS-0295178	89853100	81.33	53.1	47.3	50.20	4.116	26.8	25.4	26.078	0.97113
MLS-0452943	99356423	94.02	119.1	121.7	120.41	1.887	29.2	22.7	25.944	4.5393
MLS-0259078	24823305	167.35	183.1	188.2	185.62	3.638	22.6	29.3	25.928	4.7179
MLS-0240215	24813191	62.2	51.9	55.3	53.59	2.419	25.1	26.6	25.86	1.0633
MLS-0070040	14746699	93.74	83.3	88.6	85.97	3.792	26.6	25	25.833	1.1305
MLS-0316137	47193950	101.33	147.8	151.9	149.81	2.889	30.2	21.3	25.754	6.2964
MLS-0450859	99356319	43.31	44.6	45.5	45.08	0.633	25.1	26.2	25.656	0.7226
MLS-0361733	49717069	288.96	261.5	259.6	260.56	1.307	27	24.3	25.631	1.9325
MLS-0000093	24840785	557.22	374.9	485.1	430.03	77.957	28.8	22.5	25.615	4.4456
MLS-0302168	26663375	205.93	144.5	146.9	145.72	1.702	26.7	24.5	25.602	1.5149
MLS-0003135	26663040	41.2	33.7	35.1	34.39	0.978	25.3	25.9	25.573	0.42687
MLS-0340539	49644438	40.46	37.7	42	39.83	3.071	25.3	25.8	25.564	0.3547
MLS-0292876	93576602	118.81	111	110.3	110.68	0.489	25.1	26	25.558	0.59449
MLS-0070295	14729609	64.03	44.3	42.2	43.25	1.524	22.1	28.9	25.528	4.7895
MLS-0449255	103074911	103.79	58	62.6	60.30	3.199	10.8	40.3	25.519	20.851
MLS-0233121	22400855	47.25	35.2	35.6	35.38	0.257	26.8	24.2	25.498	1.8308
MLS-0019900	4261908	83.13	45.6	41.9	43.76	2.605	23.4	27.4	25.389	2.8326
MLS-0387974	49724803	50.13	30.5	35	32.78	3.172	24.2	26.6	25.386	1.7004
MLS-0000045	87346764	180.76	170.6	173.7	172.15	2.246	23.8	26.7	25.244	1.9924
MLS-0036206	7975207	113.59	87.6	91.2	89.40	2.549	25.7	24.6	25.18	0.75076
MLS-0039614	857220	41.65	33.1	35.4	34.29	1.624	25.7	24.6	25.152	0.74157
MLS-0343136	49643845	183.01	161.5	165.1	163.31	2.586	28.7	21.5	25.127	5.1157
MLS-0051478	4251761	43.42	48.5	51.5	50.02	2.164	25.9	24.1	25.034	1.2884
MLS-0207261	17515518	698.49	1314.5	1235	1274.80	56.234	26.4	23.5	24.961	2.076
MLS-0206778	17514206	143.33	112.5	113.6	113.06	0.781	24.7	25.2	24.917	0.365
MLS-0388427	49824538	51.65	31.4	32.7	32.06	0.940	21.9	27.9	24.901	4.2342
MLS-0426150	85148989	47.89	746.1	782.1	764.09	25.464	22.7	26.9	24.81	2.9617
MLS-0228259	22412363	161.84	94.1	89.6	91.86	3.225	14	35.6	24.777	15.247
MLS-0003297	56422380	209.09	334.9	359.1	347.00	17.165	25.2	24.3	24.776	0.61707
MLS-0275426	24801588	459.16	387.7	473.1	430.41	60.406	24.4	25.1	24.739	0.44223
MLS-0251834	24824406	87.62	71.5	75.8	73.65	3.099	24.7	24.7	24.718	0.019966
MLS-0335981	49680518	134.29	114.8	135.9	125.34	14.860	30.8	18.6	24.697	8.5988
MLS-0104657	89852402	97.48	123.4	126.9	125.11	2.478	22.1	27	24.533	3.4502

MLS-0309138	26726319	58.98	46.3	45.3	45.81	0.730	25.8	23.1	24.469	1.9457
MLS-0311850	24830728	155.07	199.4	189.3	194.33	7.117	24.2	24.7	24.459	0.37002
MLS-0274576	24794167	49.89	32.4	35.6	34.01	2.299	20.3	28.5	24.41	5.786
MLS-0222965	17504892	54	35.7	35.6	35.65	0.081	25.9	22.8	24.306	2.1882
MLS-0063227	7971778	46.23	55	52.9	53.95	1.542	23.7	24.9	24.289	0.81379
MLS-0307578	26726211	86.13	646.9	4.7	325.76	454.090	4.7	43.8	24.248	27.66
MLS-0110404	85273407	45.05	34.4	37.9	36.16	2.431	28.5	20	24.246	5.9948
MLS-0105704	16953655	46.15	43.9	44.1	44.00	0.080	26.7	21.8	24.241	3.4852
MLS-0285161	24802044	55.02	37.2	38.8	37.97	1.119	23.3	25.1	24.183	1.2277
MLS-0209081	17512388	262.79	209	215.7	212.34	4.696	23.3	24.9	24.117	1.1513
MLS-0244442	24780522	50.93	45.5	42.5	44.02	2.083	21.5	26.8	24.108	3.746
MLS-0214921	17514406	394.18	792.3	1041	916.62	175.840	26.8	21.4	24.083	3.8216
MLS-0304995	26663492	55.27	47.7	49.1	48.40	0.932	24.5	23.4	23.989	0.78761
MLS-0320737	49646907	40.38	37.8	41.7	39.74	2.776	24	24	23.982	0.0090727
MLS-0432338	85270327	83.51	72.6	72.7	72.67	0.098	24.4	23.4	23.941	0.69687
MLS-0439152	87339675	47.14	57.4	55.9	56.65	1.041	24.8	23	23.895	1.2626
MLS-0462225	103162453	51.92	43.2	37.9	40.57	3.729	24.5	23.2	23.853	0.88457
MLS-0203301	22402303	149.71	198.8	191	194.89	5.554	22.3	25.3	23.833	2.099
MLS-0290355	24787907	69.05	71.4	71.6	71.52	0.107	20	27.5	23.748	5.2597
MLS-0311973	24791517	631.92	481.4	505.1	493.29	16.740	28.8	18.7	23.706	7.1437
MLS-0360685	49821046	61.14	46.8	48.4	47.59	1.097	20.2	27.1	23.646	4.8854
MLS-0320538	49667838	51.53	49.3	52.8	51.03	2.442	21.2	26	23.601	3.4554
MLS-0361800	49820611	44	54.5	55.7	55.07	0.857	26.1	21.1	23.585	3.4904
MLS-0003135	56422124	57.14	58.1	61.3	59.67	2.283	26.8	20.3	23.56	4.5918
MLS-0088562	14742448	93.55	65	73.3	69.14	5.863	24.3	22.7	23.522	1.0971
MLS-0305146	26662455	170.68	107.4	175.8	141.59	48.404	20.3	26.7	23.495	4.4733
MLS-0392300	24830682	165.45	90.2	93.3	91.78	2.169	23.3	23.7	23.49	0.27528
MLS-0345455	47204439	748.66	668.7	682.1	675.39	9.466	26	20.9	23.442	3.5751
MLS-0543982	134216129	144.37	89.7	93.1	91.41	2.454	25.3	21.5	23.4	2.731
MLS-0216163	17433473	691.69	593.2	649.4	621.31	39.705	20.1	26.6	23.342	4.5662
MLS-0355805	49716501	40.52	35.6	38.2	36.89	1.843	23.2	23.5	23.332	0.17757
MLS-0228942	22400374	113.93	133.6	122.3	127.90	7.990	18.3	28.3	23.28	7.0664
MLS-0327739	49665488	602.02	531.8	511.3	521.53	14.486	24.1	22.3	23.19	1.2706
MLS-0428214	85149026	95.89	256.6	338.5	297.56	57.918	25	21.4	23.19	2.536
MLS-0094305	17401322	128.66	85.6	76.5	81.05	6.477	19.3	27	23.152	5.3774
MLS-0246866	24827703	58.97	52.3	56	54.17	2.638	27	19.3	23.108	5.4513
MLS-0079830	56422846	50.82	32.3	50	41.18	12.494	22.6	23.6	23.103	0.72068
MLS-0210641	17515353	152.54	131.1	150.7	140.88	13.820	22.4	23.8	23.092	0.94775
MLS-0464598	121282787	69.34	56.4	65.7	61.07	6.613	21.7	24.4	23.088	1.9072
MLS-0543989	134216093	75.28	39.5	46.1	42.80	4.718	26.4	19.7	23.041	4.7946
MLS-0243746	24832765	246	262.9	265.6	264.27	1.932	22.8	23.2	23.024	0.30354
MLS-0351191	47198536	46.51	45.9	50.5	48.22	3.232	24.2	21.8	22.975	1.6793
MLS-0103875	16953821	184.59	83.8	76.4	80.10	5.204	26.7	19.2	22.969	5.2704
MLS-0000600	56422663	137.73	111.9	110.7	111.32	0.840	24.1	21.3	22.696	2.0116
MLS-0443184	89853969	67.18	34.3	35.5	34.89	0.834	22.8	22.5	22.655	0.21495
MLS-0230858	22414251	63.99	66	49.6	57.81	11.592	18.7	26.5	22.627	5.5002
MLS-0308404	26725773	63.4	50.8	52.8	51.84	1.425	21.8	23.5	22.624	1.192
MLS-0096005	17407661	818.19	759.5	784.9	772.19	17.970	20.2	25	22.57	3.4145
MLS-0303512	26660671	49.09	52	61	56.54	6.354	23.7	21.3	22.452	1.6975
MLS-0067832	865351	40.22	64.1	71.4	67.76	5.192	18.9	25.9	22.398	4.9453
MLS-0231650	22405003	97.86	71.6	75.8	73.66	2.988	19.3	25.4	22.364	4.3392
MLS-0271833	24831892	200.51	171.4	173.5	172.46	1.497	20.7	24	22.344	2.3348
MLS-0096633	14736519	40.21	36	39.2	37.59	2.294	20.9	23.7	22.339	1.9694
MLS-0229034	17514336	380.7	446.9	440.7	443.79	4.348	19.7	25	22.337	3.7014
MLS-0316024	47194040	90.11	64.2	59.1	61.67	3.590	22.7	21.9	22.321	0.53476
MLS-0308768	24809641	219.12	221.3	226.4	223.85	3.631	20.6	24	22.316	2.379
MLS-0014992	858898	52.94	42.2	42.5	42.36	0.163	21.8	22.8	22.291	0.68726
MLS-0040885	89856082	49.58	49	41	45.00	5.664	23.4	21.2	22.289	1.5128

MLS-0012403	859427	83.27	58.6	62.1	60.37	2.459	20	24.6	22.287	3.2642
MLS-0272348	24818936	43.05	39.4	40.1	39.75	0.444	21.5	23	22.259	1.1011
MLS-0012685	859141	66.82	64.9	62.7	63.77	1.572	22.9	21.5	22.204	1.006
MLS-0019037	856584	134.22	97.7	94.9	96.29	2.033	22.2	22.1	22.168	0.1128
MLS-0077397	14730631	628.98	338.8	263.3	301.03	53.421	28.7	15.6	22.167	9.2498
MLS-0265223	24820809	58.98	54.4	55.9	55.13	1.100	22.7	21.5	22.113	0.88574
MLS-0226942	17511534	55.17	55.3	58.1	56.71	2.007	20.4	23.8	22.1	2.3559
MLS-0349957	47199273	1055.2	943.6	942.5	943.04	0.749	17.5	26.7	22.087	6.4537
MLS-0328880	49648705	41.49	40.8	40.6	40.67	0.152	18.9	25.3	22.076	4.5506
MLS-0087402	56320746	40.53	42.9	42.6	42.72	0.241	21.2	22.9	22.072	1.1731
MLS-0358727	49817407	44.46	29.7	38.9	34.33	6.533	15.8	28.3	22.068	8.807
MLS-0305274	26659297	93.69	65.4	68.8	67.09	2.438	22.3	21.8	22.039	0.39358
MLS-0098703	17387056	834.3	730.4	755.2	742.80	17.594	23.5	20.5	22.029	2.1303
MLS-0350052	49641385	69.5	26.1	71.6	48.85	32.200	20.9	23.1	22.026	1.5709
MLS-0075439	14738596	197.85	122.7	142.8	132.76	14.184	19.8	24.2	22.025	3.0819
MLS-0380049	49827916	67.71	58.3	66	62.18	5.456	23.6	20.4	21.984	2.2384
MLS-0210400	17514894	95.15	58.6	69.8	64.21	7.934	20.2	23.7	21.962	2.4605
MLS-0544001	134216066	56.78	46.1	48.4	47.25	1.668	20.5	23.4	21.947	2.0814
MLS-0426080	85147438	50.13	49	49.9	49.47	0.611	22.5	21.4	21.923	0.74992
MLS-0083305	14722775	439.5	370.9	373.4	372.14	1.806	21.4	22.3	21.873	0.6367
MLS-0079581	14732385	42.72	32.3	32.6	32.46	0.248	19.1	24.6	21.872	3.8509
MLS-0292876	26666677	75.31	73.8	82.4	78.10	6.048	19.5	24.2	21.87	3.352
MLS-0213373	17507150	59.82	38.1	40.4	39.23	1.588	22.7	21	21.852	1.1983
MLS-0059315	7966877	104.64	100.5	110.7	105.59	7.178	20	23.7	21.841	2.5686
MLS-0214552	17431564	448.18	470.6	487.8	479.22	12.175	22.3	21.3	21.815	0.70871
MLS-0389307	49676472	220.04	181.6	174.5	178.06	4.980	17.8	25.5	21.68	5.4673
MLS-0357709	49726989	52.21	63.7	59.5	61.60	3.032	17.5	25.8	21.648	5.8126
MLS-0266862	24791808	1603.3	1260.6	1333.1	1296.80	51.288	22.5	20.7	21.598	1.2112
MLS-0059953	87342167	42.21	40.4	39.9	40.15	0.355	21.5	21.6	21.553	0.073824
MLS-0248905	24823276	149.58	153.1	154.1	153.60	0.694	21.4	21.7	21.536	0.19159
MLS-0087303	14741084	81.45	37	37.5	37.22	0.374	22.5	20.5	21.516	1.3983
MLS-0257913	24829211	49.68	53.3	52.2	52.73	0.795	20.4	22.6	21.493	1.5361
MLS-0218889	22411281	1085.4	837.8	829.8	833.80	5.638	20.7	22.2	21.428	1.0875
MLS-0215202	17510463	955.24	871	875.4	873.21	3.154	22.4	20.4	21.405	1.3695
MLS-0441749	89853732	40.13	33	33.2	33.10	0.193	18.8	24	21.4	3.712
MLS-0266197	24797451	44.04	37.9	37.1	37.50	0.605	28.1	14.7	21.384	9.4445
MLS-0309238	26725899	42.62	42.6	44.1	43.33	1.075	18.6	24.2	21.376	3.9315
MLS-0204684	22400543	365.99	362.3	379	370.65	11.824	15.6	27.1	21.354	8.1537
MLS-0298246	26730489	352.2	326.9	337.3	332.12	7.345	22.2	20.5	21.347	1.246
MLS-0544840	134215511	50.14	41.3	46.1	43.69	3.377	23.4	19.3	21.319	2.8782
MLS-0244167	24805850	80.78	59.6	24.5	42.04	24.829	35.9	6.8	21.314	20.564
MLS-0043527	87347061	95.55	52.4	54.3	53.36	1.302	20.9	21.7	21.31	0.52687
MLS-0087461	14742412	197.69	153	150.8	151.90	1.545	19.6	23	21.306	2.3709
MLS-0441177	89854938	913.37	687.6	344.4	516.02	242.680	18	24.4	21.214	4.5753
MLS-0323064	49668730	87.96	89.2	89.2	89.21	0.017	16.2	26.2	21.211	7.094
MLS-0213637	17433829	850.02	808.3	845.5	826.89	26.332	19.1	23.3	21.2	2.9688
MLS-0078055	14736773	43.12	41.2	44.8	43.03	2.556	23.1	19.3	21.199	2.7532
MLS-0021904	87347566	138.32	108.4	133.2	120.78	17.525	22.5	19.9	21.198	1.8612
MLS-0044145	103073865	83.21	38	35.4	36.67	1.816	18.3	24	21.194	4.0283
MLS-0225998	17516224	56.2	46.1	51.6	48.86	3.867	21.6	20.7	21.119	0.63775
MLS-0213457	17508342	75.64	62.5	63.5	63.02	0.664	19.5	22.7	21.103	2.2233
MLS-0467361	124753153	58.8	50.5	61.2	55.84	7.554	20.5	21.5	21.027	0.70392
MLS-0448107	99357756	47.71	36	38	37.04	1.416	16.9	25.1	21.005	5.7869
MLS-0025214	4256505	61.81	53	53	52.99	0.016	25.9	16.1	20.987	6.9565
MLS-0216465	17509011	981.6	739.1	756	747.51	11.960	19.7	22.3	20.982	1.8339
MLS-0461344	99454208	49.01	49.1	47.5	48.28	1.140	22.4	19.5	20.957	2.1044
MLS-0320393	49665711	461.28	419.8	118	268.87	213.430	20.2	21.6	20.911	0.96732
MLS-0107492	14729353	71.1	36.6	38.2	37.38	1.103	16.6	25.2	20.894	6.1364

MLS-0299091	26658692	54.01	36.8	40.3	38.57	2.432	20.1	21.6	20.861	1.0769
MLS-0460145	99456233	52.09	47.9	49.8	48.82	1.358	23.6	18.1	20.855	3.8436
MLS-0225241	17503835	77.66	65.8	74	69.89	5.747	20.7	20.7	20.718	0.0048782
MLS-0097568	17415952	73.65	35.3	39.7	37.50	3.086	15	26.3	20.649	7.9901
MLS-0030397	85273041	132.74	131.1	131.6	131.34	0.326	23.3	18	20.645	3.7919
MLS-0544010	134216088	56.06	43.7	44.3	44.00	0.407	21.5	19.8	20.643	1.1642
MLS-0316414	49648609	54.36	43.2	42.8	43.02	0.288	19.3	21.9	20.591	1.8905
MLS-0013753	863768	47.62	42.4	45.7	44.01	2.340	21.5	19.7	20.58	1.2467
MLS-0104328	17388061	47.25	33.6	43.2	38.42	6.829	22.6	18.6	20.562	2.8401
MLS-0000616	87346096	85.45	42.2	48.1	45.17	4.160	14	27	20.529	9.2109
MLS-0225765	87346337	1858.5	1469.8	1463.8	1466.80	4.207	19.8	21.2	20.526	0.99388
MLS-0206305	17432625	598.74	536.3	532.3	534.31	2.831	22.3	18.7	20.517	2.5421
MLS-0096536	17414817	141.54	256.3	289.3	272.82	23.345	21.3	19.6	20.476	1.2066
MLS-0239875	24812948	942.91	689.7	719.1	704.39	20.743	19.8	21	20.425	0.87857
MLS-0393753	47196218	558.3	366.5	384.7	375.56	12.862	21.9	18.9	20.42	2.1003
MLS-0292357	26670075	57.5	44.6	37.2	40.94	5.241	13.8	26.9	20.396	9.2648
MLS-0082221	14728440	753.27	393.1	366.8	379.91	18.591	21.2	19.6	20.384	1.0972
MLS-0449563	99355939	127.85	88.6	89.4	88.99	0.562	17.9	22.8	20.354	3.4315
MLS-0223366	22413103	1799.7	1464.6	1472.5	1468.60	5.573	24.7	15.8	20.289	6.2812
MLS-0234292	14730712	65.2	68.1	68.2	68.15	0.020	19.4	21	20.179	1.1305
MLS-0283900	24788148	310.71	250.2	239.8	245.02	7.341	20.9	19.5	20.176	0.97453
MLS-0001619	858693	48.49	39.8	38.5	39.13	0.930	19.7	20.6	20.162	0.64255
MLS-0001054	857798	85.69	83.9	85.9	84.87	1.394	34	6.3	20.156	19.638
MLS-0233226	22407279	60.98	46.9	47.7	47.29	0.585	18.4	21.9	20.131	2.5146
MLS-0221647	17505250	41.56	31.7	34.5	33.12	2.018	21.5	18.7	20.118	2.025
MLS-0349421	47195670	53.66	19.5	53.6	36.58	24.127	21.8	18.3	20.061	2.4436
MLS-0551913	144095816	179.73	165.4	164.3	164.87	0.808	18.2	21.8	20.001	2.5009
MLS-0306812	26729277	43.78	39.3	29.8	34.52	6.704	21.3	18.4	19.851	2.0243
MLS-0388275	49715905	149.17	85.5	102.7	94.11	12.220	16.8	22.8	19.824	4.2647
MLS-0217885	17512691	49.27	96.7	85.7	91.20	7.818	16	23.7	19.819	5.4665
MLS-0439442	87349331	638.83	521.5	527.3	524.44	4.097	18.1	21.5	19.775	2.4092
MLS-0426110	85148993	150.02	81.8	85	83.38	2.259	1	38.5	19.744	26.512
MLS-0283149	24780557	251.32	255.4	244.4	249.92	7.794	18.4	21.1	19.727	1.8709
MLS-0319547	49668157	70.2	44.9	37.3	41.10	5.392	24.5	14.6	19.588	7.0102
MLS-0239693	24782468	59.16	30.2	34.3	32.26	2.904	21.3	17.9	19.571	2.3981
MLS-0251890	24826349	40.43	44.8	50.5	47.67	4.039	20.3	18.7	19.512	1.178
MLS-0059981	87342164	41.05	31.5	32.8	32.14	0.889	19.4	19.6	19.501	0.073388
MLS-0392199	22411413	40.7	35.9	30.9	33.40	3.490	16.4	22.5	19.473	4.3246
MLS-0033908	7972949	58.24	52.8	56.6	54.67	2.707	19.6	19.2	19.422	0.29496
MLS-0262559	24834596	66.1	45.6	45.2	45.43	0.293	27.6	11.2	19.402	11.583
MLS-0102607	17416141	54.88	35.9	40.2	38.04	3.018	18.3	20.5	19.397	1.583
MLS-0071943	14734537	116.86	144.8	153.4	149.14	6.081	15.8	22.9	19.374	4.988
MLS-0204117	17512658	1239.8	882.7	926.7	904.71	31.081	20.3	18.5	19.367	1.2533
MLS-0425850	85149004	46.11	32.9	40.1	36.49	5.110	20	18.7	19.344	0.90158
MLS-0301770	26666960	557.34	590.8	516.2	553.49	52.800	19.3	19.3	19.33	0.014869
MLS-0220299	89853823	223.51	84.1	85.4	84.75	0.879	19.7	18.8	19.259	0.63358
MLS-0463582	121282782	69.2	91.8	97.3	94.52	3.886	22.4	16.1	19.247	4.4867
MLS-0379646	49819194	243.57	208.5	213	210.75	3.160	18.8	19.7	19.228	0.67095
MLS-0294328	26664978	81.85	39.1	42.6	40.85	2.500	20.6	17.8	19.194	2.0012
MLS-0452562	99359483	59.66	49.1	51.1	50.11	1.464	17.9	20.5	19.19	1.8082
MLS-0229292	22413541	48.55	37.4	39.1	38.26	1.183	15.3	23.1	19.19	5.5544
MLS-0291878	26664383	40.09	36.1	38.6	37.33	1.776	21	17.4	19.164	2.5387
MLS-0367171	50086383	41.56	45.3	47.5	46.42	1.524	20	18.3	19.144	1.2525
MLS-0227566	89851585	61.43	50	56.8	53.39	4.786	18.7	19.6	19.114	0.65283
MLS-0308004	26725751	120.63	121.6	126.8	124.22	3.635	17	21	19.014	2.8487
MLS-0456583	99456410	65.76	61.7	65.4	63.59	2.607	19.8	18.2	19.008	1.1194
MLS-0544149	134216128	183.17	143.4	168.5	155.98	17.720	22.7	15.3	19.006	5.188
MLS-0092969	17387979	1174.5	864.6	870.8	867.72	4.374	20.8	17.1	18.978	2.6432

MLS-0445711	87334322	761.59	634.2	729.6	681.89	67.477	21.5	16.4	18.948	3.6464
MLS-0312979	26664885	72.32	44.5	44.8	44.67	0.235	18.9	18.9	18.911	0.021278
MLS-0212927	17507724	510.05	541.7	540.4	541.01	0.908	21.2	16.6	18.909	3.2987
MLS-0052845	4248753	46.31	38.7	46.7	42.69	5.714	17.6	20.1	18.873	1.7505
MLS-0109124	17412701	1514.6	1479.9	1490.7	1485.30	7.631	21.1	16.6	18.859	3.1376
MLS-0099429	17413847	174.86	169.2	162.8	165.97	4.527	23	14.5	18.759	5.9839
MLS-0233918	14731183	1183.8	730.5	789.3	759.92	41.546	18.4	19.1	18.741	0.50603
MLS-0305527	26660080	1090.9	821.2	846.3	833.75	17.727	18.9	18.5	18.713	0.28718
MLS-0289202	24797521	779.67	534	572.8	553.42	27.395	18.1	19.3	18.692	0.80628
MLS-0312734	89853702	81.75	79.5	73.5	76.53	4.265	20.6	16.7	18.659	2.8119
MLS-0357491	49716193	45.19	34.1	35.7	34.92	1.127	19	18.3	18.651	0.43592
MLS-0370932	49721817	78.28	83.8	85.7	84.77	1.361	14.6	22.7	18.638	5.7275
MLS-0211154	17510199	59.74	160.2	134.5	147.32	18.174	16.2	21.1	18.637	3.4646
MLS-0313415	26660711	74.78	49.1	46.9	47.97	1.565	17.8	19.3	18.6	1.0608
MLS-0067822	859507	128.33	123.7	131	127.35	5.192	16.1	21.1	18.592	3.5132
MLS-0261880	24830438	1781.8	1453.2	1450.7	1452.00	1.798	16.5	20.7	18.581	2.9763
MLS-0464228	121282832	107.91	132.7	135	133.82	1.650	22.7	14.5	18.571	5.8264
MLS-0068224	14730728	76.67	64.5	66.3	65.42	1.309	17.6	19.5	18.55	1.3252
MLS-0359683	49824751	42.33	37.8	38.6	38.23	0.591	19.9	17.1	18.521	2.0068
MLS-0543046	121284643	348.47	318.6	332	325.28	9.494	18.4	18.5	18.455	0.05819
MLS-0441836	87335478	44.18	45.7	51.4	48.54	4.010	17.2	19.7	18.42	1.7765
MLS-0328382	49679500	120.64	99.4	108.2	103.82	6.205	17.8	19	18.408	0.79278
MLS-0303738	26660130	50.29	47.7	48.6	48.17	0.608	16.1	20.7	18.399	3.2295
MLS-0019531	50086765	40.32	57.7	56.2	56.96	1.105	21.5	15	18.27	4.5923
MLS-0217975	17510269	582.8	645.1	660.7	652.94	11.032	15.3	21.1	18.234	4.0961
MLS-0211269	17504316	43.56	33	31.5	32.23	1.054	22.9	13.5	18.213	6.6516
MLS-0089268	56320793	56.02	60.8	39.1	49.93	15.361	30.4	5.9	18.147	17.362
MLS-0401644	51085770	63.52	39.8	42.6	41.20	1.988	19.3	16.9	18.143	1.7031
MLS-0033494	7976527	64	47.1	45.7	46.42	1.033	18	18.3	18.138	0.17829
MLS-0348595	49641402	80.22	61.7	61.4	61.55	0.216	18.7	17.5	18.133	0.82475
MLS-0465752	121286402	51.46	35.1	33.6	34.35	1.003	20.5	15.7	18.083	3.4184
MLS-0355158	49733497	62.34	116.1	96.6	106.34	13.815	20	16.1	18.082	2.743
MLS-0015320	845736	485.12	342.2	331.7	336.95	7.474	15.3	20.8	18.061	3.8348
MLS-0466534	121285664	119.89	94.2	93.9	94.03	0.216	17.1	19	18.041	1.3106
MLS-0042163	847299	42.58	36.7	33.2	34.93	2.519	14.1	22	18.041	5.6054
MLS-0081806	14740629	156.86	114.5	121.4	117.97	4.845	16.8	19.3	18.023	1.7835
MLS-0091943	99495584	83.7	86.2	96.3	91.26	7.191	18.9	17.1	17.985	1.2294
MLS-0387456	49668236	47.78	38	36.6	37.28	1.029	19	16.9	17.98	1.4698
MLS-0383083	51085270	587.49	302.6	680.7	491.60	267.360	18.7	17.1	17.938	1.1388
MLS-0299887	26670200	78.65	52.4	50.6	51.50	1.308	12.7	23.1	17.888	7.374
MLS-0409813	56317597	52.18	40.6	45.2	42.87	3.226	19.3	16.5	17.887	1.9571
MLS-0106343	17386092	171.13	147.6	166	156.82	12.972	19	16.8	17.877	1.5638
MLS-0425816	85149012	205.47	354.9	402.4	378.66	33.632	19.9	15.7	17.848	2.9684
MLS-0416708	57260979	49.64	47.8	50.4	49.13	1.856	19	16.7	17.848	1.5787
MLS-0356540	49676883	92.15	87	88.5	87.78	1.087	18.4	17.2	17.831	0.84506
MLS-0411882	56462994	52.12	50.6	58.1	54.36	5.286	15.4	20.3	17.83	3.4315
MLS-0236101	24791574	62.97	62.8	65.3	64.06	1.784	16.4	19.2	17.802	1.9151
MLS-0446787	103076420	51.45	40.8	43.7	42.22	2.028	20.6	15	17.802	3.9326
MLS-0396470	26726123	66.23	49.6	47.1	48.33	1.786	18.2	17.4	17.771	0.53745
MLS-0000015	24840695	56.21	34.9	35.7	35.33	0.575	18.2	17.3	17.751	0.6906
MLS-0240477	24789255	51.37	35	42.7	38.87	5.443	20.7	14.8	17.735	4.1551
MLS-0432330	85269481	49.18	45.2	46.6	45.89	1.041	17.5	18	17.713	0.35384
MLS-0542701	121284598	40.48	35.2	42.5	38.86	5.184	15.1	20.4	17.703	3.7441
MLS-0450031	99361038	682.75	581.3	588.1	584.72	4.813	20.8	14.4	17.622	4.4937
MLS-0326713	49666845	94.82	56	66.1	61.06	7.103	12.9	22.2	17.595	6.5781
MLS-0329509	49668322	60.16	63	62.4	62.68	0.384	16.8	18.3	17.518	1.0654
MLS-0095743	17414219	336.52	246.9	259.4	253.16	8.889	11.1	23.9	17.494	9.0886
MLS-0423434	85148704	171.48	242.4	224.3	233.32	12.774	14.8	20.1	17.461	3.7296

MLS-0070108	14734092	45.42	45.4	44.9	45.14	0.355	19.1	15.9	17.46	2.2544
MLS-0453646	99356436	46.56	44.5	47.3	45.90	2.021	16	18.9	17.438	2.0788
MLS-0095594	14736125	47.82	32.9	34.8	33.81	1.358	19.5	15.3	17.43	2.9642
MLS-0044152	856331	174.21	73.3	73.4	73.33	0.097	12.9	21.8	17.362	6.2409
MLS-0216679	22404423	74.65	76.1	102	89.03	18.319	14.7	20.1	17.361	3.8119
MLS-0091949	49679278	104.31	98.4	97.3	97.85	0.822	20.6	14	17.336	4.6634
MLS-0000079	103073743	84.21	66.9	71	68.94	2.862	20.9	13.7	17.335	5.1099
MLS-0367638	50086492	150.2	165	173.8	169.40	6.249	17.9	16.7	17.29	0.87314
MLS-0358725	49722558	106.01	111.7	114.3	112.96	1.836	17.1	17.4	17.263	0.16633
MLS-0000215	87346574	136.88	101.6	107.8	104.67	4.362	18.1	16.4	17.233	1.1986
MLS-0257435	24826210	339.85	285.7	289.4	287.52	2.635	18.3	16.1	17.211	1.5463
MLS-0092251	17408254	45.37	39.7	45.5	42.59	4.092	19.1	15.3	17.211	2.6743
MLS-0212192	17508621	70.94	67.8	65.6	66.68	1.600	16.8	17.5	17.151	0.44039
MLS-0376786	49724275	73.53	41.1	46.8	43.97	4.005	16.7	17.6	17.133	0.64287
MLS-0232876	22403366	215.31	171.6	170.8	171.23	0.551	14.4	19.8	17.12	3.8021
MLS-0105028	17387053	533.11	532.6	503.8	518.16	20.351	18	16.2	17.106	1.2726
MLS-0440279	89853193	73.65	36.2	64.3	50.25	19.924	14.4	19.7	17.041	3.7815
MLS-0236083	24832067	52.89	36.1	35.8	35.96	0.241	18.3	15.8	17.022	1.7562
MLS-0395644	47194831	739.55	448.9	486.4	467.66	26.545	16.2	17.7	16.979	1.0756
MLS-0081356	14738059	43.03	34.4	34.1	34.27	0.223	16	17.9	16.964	1.3348
MLS-0543926	134216077	122.61	98.7	105.1	101.89	4.579	15.2	18.7	16.962	2.5009
MLS-0109205	17412329	78.99	38.6	43.2	40.87	3.259	17.8	16.2	16.962	1.1188
MLS-0242163	24831370	45.19	32.9	40.2	36.54	5.137	15.9	18.1	16.958	1.5446
MLS-0274890	24829240	723.56	566.5	569.5	568.00	2.152	18.2	15.7	16.925	1.7813
MLS-0392789	87345367	208.79	184.5	185.1	184.79	0.439	17.9	15.9	16.902	1.4622
MLS-0325743	49679782	94.6	49.9	52.7	51.28	1.974	15.8	17.7	16.785	1.3622
MLS-0232520	22413105	117.59	101	107.6	104.32	4.701	17.3	15.9	16.6	0.93078
MLS-0340074	47203362	80.9	66.3	65.4	65.82	0.641	14.7	18.4	16.522	2.6073
MLS-0295876	26671430	44.24	32.3	40.7	36.51	5.955	14.9	18.1	16.503	2.3127
MLS-0326473	49667385	84.73	81.3	86.7	83.99	3.838	17.4	15.6	16.492	1.2278
MLS-0337375	49725269	42.08	39.5	39.7	39.56	0.143	20.4	12.4	16.394	5.6061
MLS-0202933	22401340	86.99	114.2	49.4	81.76	45.819	24.7	8	16.347	11.809
MLS-0030431	847555	93.06	80.9	91.2	86.04	7.260	16.9	15.8	16.305	0.78
MLS-0109152	17412468	1039.1	1150.9	1281.7	1216.30	92.520	18.8	13.8	16.304	3.5399
MLS-0030443	3711903	57.52	17.8	46.5	32.13	20.266	6.7	25.9	16.293	13.599
MLS-0234222	17432381	63.1	51.3	65.6	58.47	10.102	21.1	11.5	16.292	6.7514
MLS-0308375	26725614	333.41	321.4	323.9	322.64	1.819	16.8	15.6	16.219	0.83009
MLS-0311356	24780039	45.31	39.8	42.5	41.16	1.874	15.4	16.7	16.05	0.98728
MLS-0286118	24804831	44.81	43.3	45.5	44.38	1.558	16.1	15.9	16.037	0.13339
MLS-0367527	50085765	84.53	53.3	59.8	56.57	4.619	16.9	15.1	15.984	1.3047
MLS-0357644	49673484	872.76	274.1	382.2	328.14	76.415	16.5	15.4	15.958	0.83166
MLS-0213422	17509358	58.26	66.3	65.9	66.08	0.314	14.7	17.2	15.94	1.7984
MLS-0099881	17409157	43.49	38.1	36.5	37.33	1.160	15.7	16.1	15.896	0.2561
MLS-0442236	89854197	105.43	78.4	92	85.15	9.618	19.1	12.6	15.846	4.6079
MLS-0002602	87346394	88.5	129.8	180.2	155.01	35.624	15.1	16.6	15.829	1.0582
MLS-0403575	51090217	115.18	96.2	98.1	97.13	1.324	11.9	19.7	15.811	5.47
MLS-0004723	863824	244.15	193.1	142.6	167.88	35.681	17.3	14.3	15.791	2.1061
MLS-0355702	49728608	52.07	109.7	113.4	111.56	2.615	17.1	14.4	15.766	1.9282
MLS-0241415	24790934	128.63	149.2	151.7	150.44	1.792	13	18.5	15.755	3.8668
MLS-0321170	49648746	58.15	57.6	56.9	57.24	0.482	14.1	17.3	15.705	2.2332
MLS-0046667	849268	46.77	38.7	39.3	38.99	0.451	20.2	11.2	15.694	6.304
MLS-0251599	24808705	61.94	43.6	44.9	44.21	0.911	16	15.4	15.69	0.46135
MLS-0203364	17512115	161.62	32	33.1	32.52	0.768	17.6	13.7	15.665	2.8021
MLS-0225849	17512049	44.13	36.4	43.2	39.84	4.805	15.6	15.7	15.651	0.11398
MLS-0263548	24837945	56.9	45.8	49.2	47.46	2.423	16.5	14.8	15.631	1.212
MLS-0300052	26670319	49.66	44.8	50.4	47.55	3.959	14.6	16.7	15.628	1.5234
MLS-0312243	87348735	535.85	461.8	617.6	539.74	110.160	16.7	14.5	15.617	1.588
MLS-0267370	24824551	130.11	125	109	117.02	11.327	16.6	14.6	15.606	1.3899

MLS-0028617	843515	139.11	126.6	125.9	126.29	0.492	18	13.1	15.579	3.486
MLS-0002817	855801	53.69	57.3	57.9	57.62	0.439	13.9	17.2	15.552	2.3454
MLS-0286215	24804584	44.41	31.9	36	33.96	2.937	16.4	14.6	15.537	1.2655
MLS-0330105	49666779	169.06	171.6	176.1	173.85	3.188	12.3	18.7	15.522	4.5195
MLS-0357154	49674604	56.7	64.9	66.2	65.53	0.888	14.7	16.3	15.477	1.1505
MLS-0387453	49716149	119.09	46	46.9	46.47	0.639	19.2	11.7	15.452	5.3577
MLS-0209439	22408932	169.25	64.5	64.9	64.67	0.275	14.4	16.5	15.431	1.5066
MLS-0465410	121285672	52.69	46.1	49.2	47.66	2.140	17	13.9	15.43	2.2138
MLS-0461231	99494561	46.26	33.2	35.2	34.22	1.381	11.6	19.3	15.423	5.4512
MLS-0000212	856866	42.8	39.9	45.6	42.74	4.071	17.1	13.6	15.34	2.4449
MLS-0428209	85148994	64.12	392.5	340.1	366.34	37.055	12.1	18.5	15.27	4.5217
MLS-0452921	99356454	88.28	65	69.5	67.22	3.191	14.1	16.4	15.243	1.5733
MLS-0367311	50086382	91.52	233.9	248.1	241.01	10.051	15.1	15.4	15.234	0.2104
MLS-0229446	22413454	55.38	44.9	49.6	47.25	3.333	17.7	12.8	15.234	3.4455
MLS-0263196	24823842	516.64	449.7	447.4	448.56	1.591	14.1	16.3	15.227	1.5242
MLS-0053388	846299	59.83	29.8	39.9	34.85	7.091	13.6	16.8	15.221	2.2514
MLS-0095673	17415568	223.19	54.1	54.7	54.39	0.462	13.2	17.2	15.195	2.8021
MLS-0037325	87347624	64.77	60.2	69	64.57	6.254	17.5	12.8	15.169	3.2963
MLS-0266451	24791066	78.7	58.5	62.2	60.39	2.612	16.7	13.6	15.155	2.2452
MLS-0308999	24824173	45.99	43.4	46.2	44.82	2.024	14.1	16.2	15.148	1.4554
MLS-0377371	51085199	80.02	80.7	77.7	79.20	2.071	13.8	16.5	15.134	1.9381
MLS-0448521	103159245	42.18	38.8	46.7	42.76	5.586	12.6	17.7	15.134	3.5712
MLS-0095137	17412977	946.86	1248.5	1280.9	1264.70	22.946	14.1	16.2	15.118	1.4664
MLS-0330369	49646152	119.94	153.8	172.4	163.10	13.211	22.1	8	15.052	9.9618
MLS-0543953	134216086	78.28	58	53.7	55.84	3.056	14.6	15.5	15.037	0.60448
MLS-0549043	144095826	57.14	59	65.4	62.21	4.572	18	12	15.012	4.2587
MLS-0240792	24788519	40.88	42	43.7	42.81	1.198	16	14	15.004	1.4257
MLS-0232399	22400437	111.2	111.9	121	116.44	6.416	12.4	17.6	14.999	3.7342
MLS-0107485	89850889	141.29	73.6	100.5	87.02	18.999	28.1	1.9	14.995	18.555
MLS-0266034	24787677	84.41	35.1	40.4	37.71	3.744	20.6	9.4	14.989	7.9169
MLS-0240880	24814951	104.87	127.5	142.7	135.12	10.740	14.3	15.7	14.988	0.95219
MLS-0281505	24804732	66.84	47.3	48.2	47.76	0.591	13.9	16.1	14.986	1.5472
MLS-0216618	17505334	74.65	67.2	73.3	70.24	4.362	17.2	12.8	14.985	3.151
MLS-0354585	49674784	66.5	93.8	93.6	93.73	0.120	14.5	15.4	14.973	0.62774
MLS-0057515	4241391	42.43	40.7	45	42.84	3.039	15.4	14.5	14.953	0.65726
MLS-0227165	17513336	731.66	652.3	659.9	656.09	5.325	12.4	17.4	14.905	3.4806
MLS-0255114	24826007	46.92	30.3	34.3	32.28	2.832	11.8	18	14.894	4.427
MLS-0004248	50086219	57.94	46.3	50	48.14	2.593	10.9	18.8	14.879	5.5578
MLS-0215445	17516456	94.82	61.7	58.3	59.99	2.369	14.4	15.3	14.867	0.63553
MLS-0326904	49665222	178.23	131	130.9	130.93	0.030	13.6	16.1	14.858	1.7519
MLS-0347288	49644683	69.32	49.4	54.8	52.06	3.816	15	14.6	14.792	0.3115
MLS-0076007	14731086	47.59	175.2	178.1	176.65	2.007	14.1	15.5	14.79	0.95297
MLS-0316727	47193981	45.77	43	45.1	44.05	1.489	14.5	15.1	14.779	0.39146
MLS-0386298	50085881	47.63	38.2	39.1	38.63	0.600	13.7	15.8	14.766	1.4849
MLS-0449929	99360562	149.72	120	119.9	119.92	0.065	17.5	12	14.752	3.9384
MLS-0000596	87345659	56.62	46.9	48.6	47.78	1.217	12.9	16.6	14.74	2.6074
MLS-0056946	3714332	75.11	59.5	58.3	58.95	0.847	11.8	17.6	14.691	4.1068
MLS-0000043	856036	97.89	90.7	94.4	92.54	2.566	14.6	14.7	14.634	0.091912
MLS-0353177	49673468	43.17	61.9	62.3	62.12	0.301	16	13.2	14.595	1.9817
MLS-0464088	121284656	62.64	50.8	52.4	51.63	1.138	12.4	16.8	14.595	3.1501
MLS-0051155	4246874	94.32	114.6	89.1	101.86	18.021	15.9	13.2	14.558	1.9176
MLS-0223457	17505264	44.51	40.4	46.9	43.62	4.606	15.7	13.4	14.557	1.6063
MLS-0053798	4249341	91.19	66.7	68	67.33	0.904	16.1	13	14.548	2.2314
MLS-0342064	47203113	190.37	168.1	172.3	170.22	2.994	12.7	16.3	14.528	2.5693
MLS-0427141	85198259	360.66	421	346	383.49	53.065	14.9	14.2	14.519	0.48505
MLS-0443875	93576585	56.92	53.2	59.5	56.40	4.448	14	15	14.515	0.74431
MLS-0212149	17508733	315.07	297.5	312.9	305.18	10.871	14.5	14.5	14.51	0.049228
MLS-0388674	49674819	484.59	412.5	472.5	442.52	42.412	4.9	24.1	14.498	13.58

MLS-0264407	24823871	76.52	64.6	70.2	67.39	3.988	14.4	14.6	14.49	0.15676
MLS-0310782	26657691	40.78	38	44	41.01	4.234	12.7	16.2	14.458	2.5126
MLS-0308383	26725827	47.17	44	50.7	47.34	4.690	17.4	11.5	14.448	4.1341
MLS-0368330	50085753	61.69	59.4	65.6	62.54	4.374	9.5	19.3	14.418	6.8931
MLS-0305491	26659545	61.41	63.3	62.2	62.73	0.792	14	14.9	14.415	0.63893
MLS-0311787	26665027	45.55	42.6	42.3	42.44	0.262	20	8.8	14.387	7.9101
MLS-0391098	14743827	105.28	80.1	90.1	85.08	7.043	15.3	13.5	14.38	1.3003
MLS-0380944	51085524	68.51	54.5	53.5	53.97	0.692	14.9	13.9	14.372	0.731
MLS-0203817	17432412	257.51	39.9	39.5	39.69	0.258	14.5	14.2	14.359	0.21199
MLS-0000043	24840756	99.14	82.2	80	81.12	1.512	14.7	13.9	14.342	0.57344
MLS-0019662	844106	43.68	40.1	40.4	40.24	0.170	17.2	11.4	14.312	4.063
MLS-0319505	49647039	525.91	468.9	477.4	473.16	5.969	15.5	13.1	14.306	1.7471
MLS-0316258	49648805	50.06	35	35.7	35.33	0.457	15.6	13	14.278	1.8337
MLS-0211165	17510190	87.3	66.9	78.2	72.57	7.983	14.3	14.3	14.277	0.0070955
MLS-0210424	17506359	59.19	47.8	56.5	52.16	6.117	17.6	10.8	14.204	4.8483
MLS-0002766	860883	42.27	41	43.4	42.22	1.707	10	18.4	14.187	5.918
MLS-0367605	49820584	48.21	56.9	53.1	55.00	2.724	11	17.3	14.165	4.4703
MLS-0464647	121284616	43.51	51.2	50.5	50.82	0.509	16.5	11.8	14.149	3.2734
MLS-0321832	49665245	60.16	52.3	53.7	52.99	1.017	13.6	14.6	14.14	0.71156
MLS-0267533	24824320	112.78	100.6	109.3	104.94	6.108	20.5	7.8	14.119	8.9634
MLS-0110244	17402281	52.79	74.7	76.8	75.73	1.511	10.3	17.8	14.084	5.323
MLS-0107014	17388498	52.56	113.8	111.4	112.58	1.673	21.7	6.5	14.078	10.786
MLS-0222711	22414982	84.69	63.2	64.9	64.08	1.225	15.2	12.9	14.039	1.6804
MLS-0251862	24824512	44.23	44.6	46.1	45.35	1.048	10.6	17.5	14.034	4.8637
MLS-0323288	49665251	86.38	109.4	107	108.20	1.713	12.9	15.1	14.011	1.5333
MLS-0057450	3712264	101	94.6	83.4	89.01	7.859	12.4	15.5	13.99	2.2034
MLS-0014249	103076475	45.87	35.9	33.4	34.65	1.802	13.1	14.9	13.982	1.2872
MLS-0203433	17512842	211.72	293	311.5	302.27	13.049	12.7	15.2	13.963	1.7296
MLS-0543876	134216089	70.98	58.3	62	60.14	2.673	12.7	15.2	13.956	1.7948
MLS-0307783	26726371	271.22	192.1	196.2	194.12	2.914	17.2	10.7	13.946	4.5766
MLS-0295668	26671498	128.61	131.4	135.3	133.36	2.738	16.2	11.7	13.933	3.1386
MLS-0001047	857945	55.12	96.8	100	98.36	2.272	12.8	15.1	13.929	1.6202
MLS-0206086	17515501	558.94	726.6	742.6	734.59	11.345	11.9	15.7	13.804	2.6273
MLS-0302492	24796302	208.48	158.4	164.5	161.45	4.377	14.9	12.7	13.797	1.5897
MLS-0211101	87338342	121.96	99	107.4	103.21	5.993	11.6	15.9	13.761	3.0526
MLS-0213768	17434064	67.52	43.8	50.6	47.20	4.838	13	14.4	13.678	0.95263
MLS-0308365	26725826	353.6	344.6	336.4	340.52	5.788	12.5	14.9	13.661	1.6887
MLS-0081713	14732499	90.4	69.2	64.6	66.86	3.249	16.2	11.1	13.658	3.6422
MLS-0228413	22414109	155.67	146.1	154.7	150.37	6.091	13	14.3	13.632	0.92292
MLS-0543997	134216084	56.31	36.7	42.4	39.53	4.007	14.5	12.8	13.612	1.1864
MLS-0211353	17503737	81.21	46.8	51.5	49.17	3.341	18.2	9	13.606	6.4742
MLS-0233276	14729739	41.33	33.9	38.3	36.08	3.118	16.7	10.4	13.595	4.4571
MLS-0307156	26730095	73.29	58.1	57.6	57.87	0.313	13.6	13.6	13.587	0.050978
MLS-0285757	24802262	78.23	47.4	44.9	46.19	1.778	12.2	14.9	13.564	1.8934
MLS-0093017	17410885	96.77	82.4	89.3	85.84	4.879	13.9	13.2	13.557	0.54229
MLS-0110675	17401923	81.77	118.8	128.4	123.58	6.814	12.5	14.6	13.54	1.5245
MLS-0209342	17516328	199.8	200.3	163	181.63	26.339	4	23.1	13.539	13.477
MLS-0545396	134215499	41.83	35.1	34.3	34.71	0.619	17.3	9.7	13.534	5.37
MLS-0083717	85272030	167.7	129.8	132.8	131.30	2.127	13.6	13.4	13.527	0.13286
MLS-0288298	24798269	338.51	251.4	253.5	252.44	1.479	11.9	15.2	13.517	2.3352
MLS-0064444	4264051	46.72	33.7	41.9	37.81	5.815	14.5	12.5	13.51	1.438
MLS-0239876	24812944	807.16	876.8	942.5	909.68	46.470	10.5	16.4	13.464	4.1582
MLS-0304522	26658938	45.88	45.4	47.8	46.60	1.706	13.7	13.2	13.439	0.39168
MLS-0045339	864200	47.4	75.2	61.9	68.55	9.439	18.7	8.1	13.406	7.5109
MLS-0028447	3715704	40.33	34.8	36.9	35.88	1.509	13.5	13.4	13.403	0.068099
MLS-0287309	24801276	223.65	197.5	196.2	196.87	0.915	14.8	11.8	13.301	2.1398
MLS-0047100	87347063	69.1	36.9	47.3	42.10	7.297	16.5	10	13.262	4.6217
MLS-0288858	24796100	892.38	698.3	735.4	716.86	26.210	12.8	13.7	13.258	0.61646

MLS-0000167	856321	183.24	190.1	197	193.56	4.934	15.9	10.6	13.241	3.7463
MLS-0082183	14728463	753.13	685.1	688.2	686.65	2.255	9.9	16.5	13.236	4.6792
MLS-0079698	14738815	521.06	305.1	292.3	298.67	9.042	10.7	15.7	13.22	3.575
MLS-0001067	857711	226.96	124	179.8	151.93	39.454	12.4	14	13.204	1.0808
MLS-0335170	49680778	97.72	7.3	57.4	32.34	35.477	15.9	10.5	13.191	3.8585
MLS-0304229	26658885	71.34	82.8	80	81.40	2.043	14.6	11.7	13.184	2.0375
MLS-0417080	57260975	53.9	38.3	36.4	37.32	1.361	10.7	15.6	13.126	3.4913
MLS-0410634	51087879	60.35	40.7	30.9	35.78	6.925	12.3	13.8	13.088	1.057
MLS-0243988	24803886	60.04	33.4	41	37.18	5.377	14.1	12.1	13.078	1.389
MLS-0209923	17505965	104.94	93.6	97.6	95.61	2.884	12.9	13.2	13.063	0.19603
MLS-0107932	17386670	71.07	71.1	74.4	72.80	2.331	10.7	15.4	13.033	3.3373
MLS-0311091	24779251	75.01	55.7	147.9	101.80	65.144	12	14	13.007	1.404
MLS-0216031	17505386	95.11	50.7	56.1	53.36	3.831	14.9	11.1	12.995	2.7107
MLS-0271908	24787768	42.94	120.1	104.6	112.36	10.985	16.9	9.1	12.983	5.5192
MLS-0213056	17509765	485.13	386.5	375.4	380.97	7.869	10	15.9	12.973	4.1445
MLS-0111511	14740468	65.12	60.1	60.3	60.18	0.126	14.6	11.3	12.966	2.3237
MLS-0000546	99494546	1522.1	570.5	673.9	622.21	73.072	10.9	15.1	12.963	2.9642
MLS-0448433	99358092	87.62	74.3	79.6	76.92	3.755	12.9	13	12.946	0.083377
MLS-0424659	85149016	311.41	367.6	272	319.76	67.613	10.4	15.4	12.891	3.5073
MLS-0093031	17410872	149.55	125.8	151.6	138.68	18.274	12.1	13.6	12.891	1.056
MLS-0280922	26663501	235.17	209.3	202.7	206.02	4.701	13.4	12.3	12.875	0.78371
MLS-0301432	26670382	76.85	49.9	48.5	49.22	1.015	13.4	12.3	12.87	0.80078
MLS-0043409	3712133	171.9	119.1	139.3	129.21	14.299	11.1	14.7	12.864	2.5497
MLS-0322291	49670329	49.49	117.2	50.2	83.68	47.366	21	4.6	12.829	11.579
MLS-0095880	14742324	86.01	90.5	94.6	92.58	2.907	14.7	10.7	12.731	2.806
MLS-0217340	17431703	352.11	357.3	362.1	359.72	3.358	11	14.5	12.716	2.492
MLS-0202459	22401460	52.94	109.7	100.7	105.19	6.371	19.6	5.8	12.713	9.7299
MLS-0299110	26671120	56.55	67.1	70.6	68.89	2.483	7.6	17.8	12.699	7.2603
MLS-0303793	26659765	122.88	73.5	80.3	76.91	4.854	12.2	13.1	12.683	0.63935
MLS-0308397	26725624	42.87	34.8	37.8	36.33	2.130	12.1	13.2	12.66	0.83264
MLS-0321174	49648895	44.7	37.6	34.7	36.11	2.060	11.8	13.5	12.64	1.1596
MLS-0229053	22400373	352.14	446	436.4	441.17	6.793	15.3	9.8	12.596	3.8864
MLS-0071871	14732770	95.69	67.1	69.1	68.06	1.400	10.7	14.3	12.48	2.5301
MLS-0010445	47193522	103.64	110	114.2	112.14	2.978	12.1	12.9	12.47	0.55148
MLS-0327134	49647548	40.75	27.2	49.5	38.35	15.716	6.8	18.2	12.465	8.0544
MLS-0312447	24822600	83.74	79.2	81.7	80.44	1.818	14	10.9	12.448	2.206
MLS-0420289	57268174	225.23	199.4	268	233.71	48.499	14.3	10.5	12.403	2.6471
MLS-0071786	14729986	60.54	73.1	67.3	70.22	4.091	11.5	13.3	12.376	1.2847
MLS-0271895	24791373	42.98	37.7	27.5	32.57	7.192	14.1	10.6	12.322	2.5018
MLS-0211829	17509276	349.01	98.2	111.7	104.97	9.581	19.7	4.9	12.284	10.476
MLS-0236171	24791636	40.35	31.8	61	46.38	20.673	10.2	14.3	12.25	2.8824
MLS-0225917	17511954	50.15	46.3	47.8	47.02	1.062	15	9.4	12.234	3.9702
MLS-0215280	17513790	41.87	45.5	45.3	45.41	0.192	14.1	10.4	12.227	2.5882
MLS-0299350	26659757	42.58	42	40.6	41.32	1.013	12.8	11.6	12.185	0.8645
MLS-0229284	22413805	40.01	40.1	44.5	42.29	3.066	12.9	11.5	12.182	1.0041
MLS-0027725	87336607	44.78	66.2	53.3	59.73	9.158	10.7	13.6	12.121	2.0242
MLS-0246223	24822207	58.14	53.7	54.9	54.26	0.838	14.2	10	12.084	2.9758
MLS-0289109	24782496	1081.8	769.3	775.7	772.52	4.548	12.3	11.9	12.076	0.30332
MLS-0345525	47204480	243.7	250	256.8	253.41	4.761	11.1	13	12.067	1.341
MLS-0365158	49722557	103.4	96	97	96.48	0.720	7.6	16.5	12.049	6.3315
MLS-0244091	24803502	66.47	50.8	58.2	54.52	5.242	10.4	13.7	12.045	2.3458
MLS-0312802	26666367	164.77	115.1	120.6	117.85	3.845	11.3	12.6	11.985	0.91634
MLS-0374782	49824019	61.09	50.7	52.1	51.41	0.950	11.2	12.6	11.886	1.0274
MLS-0063265	7971573	126.26	114.4	123	118.68	6.088	8.8	14.9	11.864	4.3265
MLS-0548123	144095726	54.37	54.7	59.1	56.87	3.095	9.6	14.2	11.864	3.2625
MLS-0226897	17513335	929.33	683.5	600.6	642.04	58.580	10.1	13.6	11.825	2.48
MLS-0225104	17513873	168.02	106.6	119.8	113.19	9.325	10.6	13	11.769	1.6755
MLS-0071588	14720688	443.56	162.4	137.8	150.10	17.389	11.8	11.7	11.766	0.070606

MLS-0007527	4256664	66.21	24.7	48.3	36.50	16.658	12.2	11.3	11.749	0.6271
MLS-0292639	26669922	167.32	210.1	192.5	201.30	12.493	11.7	11.8	11.739	0.11173
MLS-0033462	7975163	43.77	53	57.1	55.04	2.950	10	13.5	11.725	2.4979
MLS-0066705	56463121	1418.9	1439.5	1452.4	1446.00	9.143	5	18.4	11.704	9.4137
MLS-0219859	22402411	124.72	83.5	79.4	81.47	2.910	11.5	11.9	11.702	0.33307
MLS-0052012	4249165	81.19	41.7	49.2	45.45	5.300	7.2	16.2	11.684	6.3786
MLS-0107611	89853190	132.33	165.8	177.6	171.70	8.388	11.6	11.7	11.651	0.090473
MLS-0372425	49829204	451.45	488.1	488.7	488.38	0.453	10.9	12.4	11.621	1.0822
MLS-0214106	22406745	44.16	39	44	41.50	3.563	11.3	11.9	11.604	0.4843
MLS-0312286	24783488	850.88	775.7	811.5	793.57	25.325	9.9	13.2	11.56	2.3335
MLS-0220644	17504945	105.64	127.5	131.8	129.64	3.013	9.7	13.5	11.56	2.6885
MLS-0275585	24802245	45.45	32.1	36.9	34.48	3.374	9.2	13.9	11.55	3.3763
MLS-0444714	93576990	89.15	79.4	77.5	78.45	1.310	12.7	10.3	11.504	1.7353
MLS-0208537	17517283	61.43	40.4	40.8	40.60	0.216	7.4	15.6	11.467	5.8014
MLS-0218409	22409988	46.43	30.7	34.8	32.74	2.943	9.9	12.9	11.435	2.1354
MLS-0058592	842157	76.22	56.4	62.2	59.26	4.090	14.4	8.4	11.431	4.2296
MLS-0100274	17416239	63.31	42.7	44.2	43.42	1.073	7.4	15.3	11.378	5.6058
MLS-0363254	49820589	59.86	75.6	78.1	76.82	1.766	14.7	7.9	11.315	4.7969
MLS-0071520	87341271	52.39	51.7	58.8	55.28	4.992	11.8	10.8	11.307	0.6718
MLS-0224508	17511926	110.56	101.9	108.4	105.16	4.647	10	12.5	11.298	1.7673
MLS-0218332	17516521	55.09	106	68.3	87.13	26.680	9.6	12.9	11.27	2.3057
MLS-0324173	49671082	84.1	70.5	70.3	70.40	0.141	11.9	10.5	11.224	0.95868
MLS-0099663	17411677	299.92	230.5	236.2	233.36	3.994	10.8	11.6	11.213	0.57278
MLS-0001569	858988	51.71	31.5	33.9	32.70	1.679	11.8	10.6	11.206	0.9091
MLS-0298061	26670987	52.12	46.5	49.4	47.93	2.014	13.6	8.8	11.204	3.4559
MLS-0039636	4255025	64.23	33.1	37.9	35.52	3.368	12.3	10	11.168	1.636
MLS-0412819	56463267	302.77	202	206.4	204.18	3.148	8.5	13.9	11.162	3.8162
MLS-0343806	49641222	45.21	35.2	37.5	36.34	1.585	8.7	13.6	11.151	3.4191
MLS-0313902	26731888	67.92	55.7	28.3	41.98	19.340	11.8	10.4	11.127	1.0002
MLS-0051777	26670601	134.14	122.6	135.8	129.20	9.367	10.4	11.9	11.125	1.0537
MLS-0301025	26667070	1828.2	1437.8	1445.6	1441.70	5.507	13.4	8.8	11.112	3.2741
MLS-0219481	22412761	118.75	55.5	67.4	61.47	8.444	12.2	10.1	11.112	1.4928
MLS-0249557	24823079	200.2	204.8	202.3	203.53	1.737	9.2	13	11.109	2.7103
MLS-0257015	24834758	354.43	328.8	344.3	336.57	10.973	11.3	10.9	11.106	0.23747
MLS-0294451	26662443	650.79	539.1	522	530.59	12.095	10	12.2	11.095	1.5696
MLS-0224656	17515884	740.5	593.9	653.2	623.55	41.979	10.5	11.7	11.085	0.883
MLS-0093749	17410265	128.29	96.8	108.6	102.73	8.353	12.6	9.4	11.024	2.2321
MLS-0047568	4241819	243.81	342.8	243.6	293.19	70.150	16.8	5.2	10.993	8.2483
MLS-0283819	24805731	54.77	47.1	53.4	50.24	4.459	14.1	7.9	10.989	4.3569
MLS-0106984	17386582	40.76	41.8	54.1	47.94	8.682	10.9	11.1	10.982	0.16753
MLS-0053248	863784	53.38	47.1	44	45.58	2.165	10.6	11.3	10.972	0.51638
MLS-0244922	24815089	62.45	49.6	52.9	51.27	2.325	11.2	10.6	10.923	0.44988
MLS-0383869	51088972	195.53	166	176.1	171.06	7.181	13.5	8.4	10.918	3.588
MLS-0446881	103076505	84.89	74.6	77.1	75.83	1.793	13.9	7.9	10.897	4.1914
MLS-0237546	24831695	83.47	55.2	51.1	53.15	2.844	10.8	11	10.882	0.12617
MLS-0036765	7975141	288.1	246.8	262.8	254.80	11.284	8.3	13.5	10.861	3.6698
MLS-0358982	49722555	55.92	43.1	45	44.04	1.349	9.5	12.2	10.841	1.9195
MLS-0238057	24782418	74.93	65.3	68.7	66.98	2.419	9.9	11.7	10.815	1.2677
MLS-0348239	49642129	75.21	75.9	85.8	80.84	6.979	7.6	13.9	10.783	4.4465
MLS-0272899	24786375	145.49	316.4	218.8	267.63	69.004	10.6	10.9	10.773	0.2294
MLS-0304979	26658889	52.2	46.3	50.2	48.26	2.774	8.6	12.9	10.763	3.0493
MLS-0092418	17401872	96.49	46.7	52.2	49.47	3.887	11.9	9.4	10.681	1.7647
MLS-0327171	49667128	395.38	337.4	343.6	340.46	4.389	11.1	10.3	10.676	0.56424
MLS-0292222	26666263	79.95	82.3	86.8	84.52	3.208	11	10.3	10.659	0.45364
MLS-0099419	17403416	326.92	213.2	217.4	215.28	2.984	12	9.3	10.652	1.9727
MLS-0240212	24813276	560.61	416.1	456.3	436.21	28.398	9.1	12.2	10.651	2.2343
MLS-0092735	89851064	663.11	56.8	60.4	58.64	2.555	9.1	12.1	10.606	2.0797
MLS-0295231	26670785	115.33	103.8	99.3	101.53	3.224	9.4	11.8	10.575	1.7238

MLS-0093232	17401488	53.49	62.4	47.7	55.04	10.430	9.9	11.2	10.558	0.9162
MLS-0352981	49725840	95.57	90.8	90.7	90.73	0.055	8.3	12.8	10.552	3.1344
MLS-0015433	4260569	97.35	82.6	87.3	84.95	3.335	16	5.1	10.544	7.7102
MLS-0388511	49815772	52.49	72.5	65.4	68.94	5.018	14.1	6.8	10.483	5.1784
MLS-0083703	85301593	50.3	39.9	39.8	39.87	0.066	10.6	10.3	10.444	0.18048
MLS-0224287	17505716	150.97	159.9	170.4	165.18	7.456	13.9	6.9	10.433	4.9494
MLS-0087390	14745528	99.78	75.7	84.1	79.90	5.928	12	8.8	10.417	2.2527
MLS-0048581	4243300	66.74	48.5	49.8	49.17	0.951	11.1	9.6	10.349	1.0261
MLS-0236120	24791528	131.93	34.6	45.7	40.16	7.905	6.1	14.6	10.329	5.9763
MLS-0071271	14739276	59.59	51	50.7	50.88	0.182	14.7	5.9	10.291	6.2179
MLS-0057809	85303520	96.16	67.6	73.2	70.40	3.969	8.8	11.7	10.264	2.0325
MLS-0226090	17516297	88.71	50.3	45.8	48.06	3.178	10.2	10.3	10.239	0.056324
MLS-0450896	99361063	165.19	95.3	93.5	94.39	1.262	9.3	10.9	10.088	1.1319
MLS-0202997	22402177	180.41	151.4	158	154.74	4.668	9.4	10.8	10.086	0.94731
MLS-0379528	49819918	142.25	116.7	122.4	119.54	4.064	11.8	8.4	10.056	2.3978
MLS-0260169	24836548	259.76	182.2	191.1	186.65	6.334	12.2	7.9	10.019	3.0137
MLS-0103400	17387104	61.23	142.1	145.2	143.65	2.248	10	10	9.9785	0.0035478
MLS-0329217	49647684	89.66	67.6	68.5	68.07	0.658	8.3	11.6	9.9659	2.3399
MLS-0296649	26670887	99.53	92.6	97.5	95.04	3.413	8.7	11.2	9.9386	1.7919
MLS-0207058	17515143	100.7	86.1	90	88.03	2.788	6.6	13.2	9.8979	4.6146
MLS-0450160	99356404	45.44	51.1	44.5	47.81	4.713	13.1	6.7	9.8923	4.5428
MLS-0099694	17411678	126.02	94.9	93.2	94.07	1.192	11.2	8.6	9.8843	1.8136
MLS-0298243	26657558	43	40	39.4	39.69	0.441	8.7	11	9.8776	1.6572
MLS-0027540	87336496	60.45	39.8	44.9	42.36	3.603	9.1	10.6	9.8631	1.091
MLS-0453880	99360413	62.33	72.4	69.3	70.82	2.210	10.2	9.5	9.8519	0.49114
MLS-0073780	14742473	68.82	53.7	51.2	52.43	1.759	10.6	9	9.7998	1.0716
MLS-0364341	49823219	111.85	113.4	119.9	116.64	4.550	10.4	9.1	9.7704	0.91332
MLS-0284615	24807413	56.73	42.9	45.5	44.20	1.793	10.6	8.9	9.7512	1.2107
MLS-0391780	24832745	63.45	58.2	60	59.09	1.270	7.8	11.7	9.7382	2.7974
MLS-0222881	22414848	187.49	252.5	321.1	286.78	48.537	11.8	7.6	9.7095	2.9697
MLS-0224679	22414549	67.72	54	55.2	54.59	0.822	9.5	9.9	9.7038	0.31222
MLS-0338105	49715631	56.7	52.5	57.1	54.79	3.270	9.9	9.5	9.6977	0.22725
MLS-0003385	857880	97.05	66.5	35.9	51.16	21.647	11.8	7.6	9.6946	2.9266
MLS-0468930	124753472	309.8	417.1	435.1	426.10	12.768	6.3	13.1	9.6692	4.795
MLS-0082054	14720549	258.38	65.9	80.6	73.25	10.340	9.2	10.1	9.6589	0.66177
MLS-0343531	49644232	52.92	44	72.8	58.40	20.345	8.4	10.9	9.6491	1.7804
MLS-0059960	87343272	45.59	40.8	38.4	39.61	1.732	10.5	8.8	9.6477	1.176
MLS-0466571	121285684	103.82	69.5	73.5	71.49	2.782	7.6	11.7	9.6462	2.9151
MLS-0543846	134216107	75.53	42.4	50.8	46.62	5.971	8.4	10.9	9.6462	1.7461
MLS-0426202	85147440	88.53	51.8	25.9	38.85	18.280	14	5.2	9.611	6.2492
MLS-0323062	49668802	40.01	65.2	63.1	64.16	1.476	12.5	6.7	9.5889	4.1337
MLS-0348861	49645196	43.46	39.7	45.7	42.74	4.242	7.4	11.7	9.5691	3.0368
MLS-0309121	26726237	210.89	180	179.1	179.56	0.689	8.6	10.5	9.555	1.359
MLS-0311100	24809273	190.25	138.9	142.8	140.84	2.781	9.5	9.6	9.5412	0.018267
MLS-0326890	49668261	49.26	108.3	102.5	105.41	4.063	9.3	9.5	9.4261	0.14732
MLS-0352633	49672972	68.26	66.8	75.3	71.02	6.029	8.7	10	9.3531	0.92714
MLS-0086396	14725704	1845	444.2	1476.5	960.38	729.920	3.4	15.3	9.3463	8.4443
MLS-0208459	17517002	53.7	263	183.9	223.44	55.873	12	6.7	9.3306	3.713
MLS-0428210	85149010	260.42	122.9	171.2	147.05	34.121	7.9	10.6	9.2335	1.9427
MLS-0058592	14728098	65.38	64.8	67.7	66.25	2.072	7.5	11	9.2202	2.4704
MLS-0301730	26727066	296.82	269.1	222.2	245.69	33.170	9.8	8.6	9.1873	0.873
MLS-0225607	17513995	99.17	55.7	52.5	54.10	2.263	10.6	7.7	9.1792	2.0493
MLS-0293185	26664392	1264.2	1178.8	1188.3	1183.50	6.678	10.1	8.3	9.1619	1.2719
MLS-0548376	144097118	56.05	58.3	63.7	60.99	3.817	8.5	9.7	9.1497	0.84853
MLS-0108994	17412480	47.11	66.8	67.8	67.32	0.676	7.5	10.8	9.1443	2.2961
MLS-0343995	49642296	157.83	134.1	145	139.58	7.724	8.2	10	9.0925	1.2456
MLS-0295285	26671203	1015.4	865.8	866.9	866.33	0.737	8.7	9.5	9.0915	0.54886
MLS-0456040	99454729	44.38	33.2	35.3	34.26	1.534	9.8	8.4	9.062	0.99325

MLS-0209881	17505988	102.72	85.1	87.4	86.26	1.578	7.8	10.3	9.0496	1.7793
MLS-0075428	14738594	152.6	94.9	73	83.97	15.505	6.9	11.1	8.9913	2.92
MLS-0015024	7974526	44.13	65.1	61.8	63.45	2.299	7.9	10.1	8.9818	1.5483
MLS-0273324	24826799	48.79	40.9	48.7	44.82	5.540	9.7	8.2	8.9728	1.0591
MLS-0267505	24824585	98.51	141.3	146.1	143.67	3.421	7.5	10.4	8.9236	2.0455
MLS-0098500	17406747	46.71	36	35.8	35.89	0.158	10.9	6.8	8.8669	2.9082
MLS-0440840	89853239	40.21	34.1	36.7	35.45	1.841	9.6	8.1	8.8655	1.0637
MLS-0439089	24801541	46.12	47.4	48	47.71	0.408	5	12.7	8.865	5.4649
MLS-0450826	99360626	107.37	41.4	33.2	37.31	5.781	8	9.8	8.8588	1.278
MLS-0367944	49820318	433.74	392.1	391.6	391.85	0.329	8.9	8.8	8.8444	0.026354
MLS-0202116	87337303	606.82	627.2	621.3	624.23	4.170	5	12.6	8.8315	5.3856
MLS-0292969	26667024	78.97	63.4	62	62.69	0.975	5.5	12.2	8.8221	4.7679
MLS-0222773	22400993	817.89	730.4	753	741.69	15.975	9.6	8	8.8113	1.1593
MLS-0416671	57259756	66.9	60.1	64.7	62.42	3.291	6.5	11.1	8.7974	3.2545
MLS-0086375	14722304	77.26	56.6	28.2	42.39	20.030	11.3	6.2	8.7478	3.6431
MLS-0377055	49823294	105.68	112.7	122.3	117.52	6.777	7.7	9.8	8.736	1.4551
MLS-0452183	99360415	44.33	41.9	44.2	43.02	1.602	8.7	8.7	8.7354	0.010856
MLS-0347763	49646546	149.16	168.9	175	171.94	4.284	8.7	8.7	8.7216	0.017714
MLS-0216924	17512310	388.29	352.8	348.8	350.77	2.807	6.2	11.2	8.7153	3.4894
MLS-0085180	14726141	45.38	58.5	56	57.25	1.763	9	8.4	8.6893	0.42029
MLS-0202116	22406563	734.6	635.1	652.1	643.59	12.076	7.2	10.2	8.6846	2.1403
MLS-0320928	49680120	94.18	55	55	55.01	0.012	6.3	11	8.6731	3.2912
MLS-0205508	17515120	78.46	75.1	72.4	73.77	1.896	7.9	9.4	8.6473	1.0675
MLS-0395523	47195908	140.3	87.8	96.4	92.12	6.080	10.1	7.1	8.6263	2.1286
MLS-0361151	49829205	198.83	187.6	179.8	183.66	5.512	5	12.2	8.6144	5.06
MLS-0308377	26725859	58.86	63.3	66	64.63	1.905	7.9	9.3	8.6046	0.97071
MLS-0228995	22401814	136.41	214.6	268.3	241.46	38.011	6.4	10.8	8.6031	3.1454
MLS-0370009	49820183	252.45	276.9	286.9	281.90	7.111	7.6	9.6	8.5894	1.3808
MLS-0442906	93577494	42.66	35.9	38.9	37.42	2.158	8.5	8.7	8.5754	0.14591
MLS-0253724	24822781	118.71	176.5	180.9	178.70	3.138	5	12.1	8.5562	5.0791
MLS-0102439	17415933	98.46	97.2	99	98.07	1.270	9.7	7.4	8.5475	1.5934
MLS-0316440	49648794	89.5	73.4	76.7	75.05	2.344	9.2	7.8	8.5331	0.96634
MLS-0543965	134216114	54.61	44.4	47.9	46.15	2.436	5.6	11.4	8.5061	4.1124
MLS-0219755	22413297	154.86	110	112.5	111.26	1.737	8	9	8.503	0.67545
MLS-0336985	49727427	60.67	47.3	48.2	47.76	0.619	8	8.9	8.4785	0.65194
MLS-0318578	49668822	53.93	44.1	45.3	44.68	0.880	9.8	7.1	8.4504	1.872
MLS-0283198	24787136	429.83	204.6	204.5	204.52	0.079	9	7.9	8.4475	0.72644
MLS-0279525	24790058	130.2	98.5	106.3	102.39	5.506	9.5	7.4	8.443	1.5306
MLS-0267098	24792791	62	65.1	64.7	64.88	0.265	9.9	6.9	8.4318	2.1122
MLS-0393488	47199268	63.84	35.8	36.1	35.95	0.265	10.5	6.4	8.4273	2.9308
MLS-0383899	51088961	177.21	170.6	132.5	151.53	26.957	8.2	8.6	8.4195	0.29983
MLS-0106435	85147382	48.79	33	42.9	37.99	6.994	7.9	8.9	8.3936	0.70313
MLS-0048938	87349602	72.76	42.1	43.1	42.60	0.679	7.9	8.8	8.3546	0.6154
MLS-0341805	49645110	324.93	298.9	306.6	302.75	5.462	13	3.7	8.3523	6.6265
MLS-0235637	17504732	106.12	80.7	80.6	80.63	0.071	8.2	8.5	8.3464	0.16837
MLS-0210770	17510461	41.58	51.6	48.4	50.03	2.241	6.9	9.7	8.3353	1.9984
MLS-0358127	49675438	269.18	180.7	186	183.36	3.769	11.1	5.5	8.3257	3.9769
MLS-0255935	24813565	46.21	36.3	39.8	38.06	2.455	6.7	9.9	8.324	2.2545
MLS-0085387	14726137	97.37	69.3	68.3	68.81	0.700	4.8	11.8	8.3062	4.9796
MLS-0370028	49730841	48.81	45.9	50.6	48.26	3.276	10.3	6.2	8.2738	2.9167
MLS-0464307	121286501	156.88	141.2	144.4	142.82	2.224	6.6	9.9	8.2699	2.368
MLS-0439279	92763931	64.99	76	85.9	80.95	6.990	6.8	9.7	8.2179	2.0625
MLS-0319442	49647030	71.4	105.4	103.4	104.42	1.395	7	9.4	8.2108	1.745
MLS-0304390	26658982	132.16	108.6	106.9	107.73	1.200	9	7.4	8.2017	1.0892
MLS-0107993	17386634	51.82	38.5	44	41.24	3.855	8.5	7.9	8.1774	0.4533
MLS-0421428	57261282	43.3	46.3	46.4	46.34	0.056	8.7	7.6	8.158	0.82605
MLS-0416701	57265753	65.62	76.4	86.8	81.57	7.372	6.7	9.6	8.1403	1.9943
MLS-0047134	4251763	46.33	41	41.5	41.27	0.313	6.4	9.9	8.1393	2.5204

MLS-0427952	85146995	243.22	130.2	118.5	124.39	8.276	6.2	10	8.1112	2.7319
MLS-0102303	14742141	279.73	291.9	283.8	287.86	5.712	8.8	7.4	8.1003	0.9467
MLS-0092331	17402911	343.87	98	125	111.51	19.079	10.3	5.9	8.0935	3.1112
MLS-0094285	17387645	929.5	588.4	478.1	533.25	77.959	5.2	11	8.0873	4.05
MLS-0391575	26664888	72.52	64.5	71.6	68.05	5.040	6.2	9.8	8.0209	2.5617
MLS-0345395	47204427	329.05	266.1	260.6	263.36	3.834	6.8	9.2	8.0092	1.7087
MLS-0259218	24823253	134.77	121.9	124.7	123.30	1.999	7.4	8.5	7.9897	0.76722
MLS-0220555	22403558	48.31	74.6	73.5	74.09	0.777	10.6	5.4	7.9752	3.7032
MLS-0321041	49667479	57.15	40.9	41.5	41.21	0.432	10.3	5.7	7.972	3.2338
MLS-0037993	865261	40.88	56.4	64.6	60.47	5.790	7	8.9	7.9687	1.3522
MLS-0028652	50086707	61.2	74.3	76.1	75.19	1.263	4.7	11.1	7.915	4.5668
MLS-0551810	144095700	49.76	42	49	45.48	4.980	3.7	12.1	7.9128	5.9119
MLS-0309134	26726384	666.98	344.4	569.8	457.12	159.360	9.7	6.1	7.9057	2.5983
MLS-0075496	14738597	195.98	197	192.1	194.52	3.472	6.1	9.7	7.8972	2.539
MLS-0452796	99356413	77.92	50.5	52.1	51.29	1.095	6.3	9.5	7.8858	2.2842
MLS-0000840	56422689	166.95	520.8	528.8	524.78	5.622	6	9.8	7.8769	2.6997
MLS-0092032	17408311	102.06	56.8	62.4	59.61	3.922	8.2	7.5	7.8671	0.46612
MLS-0216351	17504701	41.43	39.9	41	40.48	0.777	4.9	10.8	7.8645	4.1454
MLS-0451619	99356419	54.2	51.5	47.7	49.58	2.721	4.9	10.8	7.8299	4.1662
MLS-0349923	47199254	89.21	71.4	66.5	68.95	3.444	8.3	7.4	7.8131	0.61997
MLS-0377287	51090401	192.42	123.1	129.8	126.45	4.792	6.8	8.7	7.7777	1.3121
MLS-0544003	134216087	48.67	36.6	32.7	34.67	2.751	6.9	8.7	7.7694	1.2693
MLS-0218238	17514633	341.04	369	404.1	386.55	24.818	5.6	9.9	7.7642	3.002
MLS-0462603	99495592	93.74	64.7	68	66.34	2.309	6.8	8.7	7.7455	1.3892
MLS-0066869	47193671	385.24	384.1	375	379.58	6.434	4.8	10.6	7.7194	4.1402
MLS-0543175	124752975	61.29	52.3	55.4	53.83	2.176	9.1	6.4	7.7169	1.8907
MLS-0016368	865372	45.33	39.5	44.9	42.22	3.850	5.2	10.2	7.6751	3.5369
MLS-0339722	49645303	104.05	84.6	115	99.80	21.442	7.5	7.7	7.602	0.12183
MLS-0110296	17410502	185.53	108.7	180.7	144.69	50.932	0.1	15	7.552	10.593
MLS-0339898	49640946	54.71	51.2	54.7	52.97	2.474	10	5.1	7.5403	3.4399
MLS-0271259	24796037	150.42	85.9	84.6	85.27	0.952	8.2	6.8	7.4754	1.0187
MLS-0236202	24783353	47.98	38	36.1	37.08	1.356	8.3	6.6	7.4535	1.2281
MLS-0017355	858285	48.19	29	43	36.01	9.864	9.5	5.4	7.4182	2.8798
MLS-0370030	49722406	105.56	77.4	93.2	85.30	11.146	11.5	3.4	7.4132	5.7236
MLS-0100045	17401400	45.54	36	37.2	36.61	0.851	9.5	5.3	7.391	2.9284
MLS-0249640	24823085	165.76	130.8	150	140.39	13.597	7.1	7.6	7.3258	0.33985
MLS-0383087	51085272	318.13	268.2	289.2	278.69	14.891	4.3	10.3	7.3191	4.265
MLS-0108319	14727033	1166.6	1133.4	1153.9	1143.70	14.440	8.5	6.2	7.3168	1.6168
MLS-0107641	14731211	210.31	152.1	153.8	152.97	1.217	9.2	5.5	7.3133	2.6028
MLS-0349369	47196109	694.09	549.2	548	548.59	0.807	11	3.6	7.2724	5.2367
MLS-0377373	51089966	44.8	40	45.4	42.70	3.795	7.4	7.2	7.2647	0.12097
MLS-0370000	49735779	50.31	56.2	62.7	59.42	4.586	7	7.5	7.2498	0.4221
MLS-0209178	17516362	51.7	95.3	90.5	92.90	3.436	-1.3	15.8	7.2405	12.038
MLS-0013907	864808	47.84	37	29.7	33.36	5.138	9.7	4.8	7.2394	3.4659
MLS-0284906	26663410	126.77	107.3	100.7	103.98	4.625	8.2	6.2	7.2168	1.3708
MLS-0402234	56316634	41.83	33.4	39.1	36.25	4.029	8.3	6.1	7.2168	1.5316
MLS-0251700	24808872	58.55	47.5	48.8	48.14	0.926	2.6	11.8	7.1945	6.5571
MLS-0271915	89851069	53.06	179.2	199.2	189.21	14.137	6.4	8	7.1841	1.1078
MLS-0041415	85305280	69.62	67.5	51.2	59.32	11.532	9.1	5.3	7.1818	2.6834
MLS-0204497	17515382	178.37	287.3	306.6	296.99	13.636	12.2	2.1	7.1546	7.0857
MLS-0393475	47194273	1598.8	1454.2	1442.9	1448.50	7.974	7	7.2	7.1161	0.10111
MLS-0095875	17414469	108.17	56.1	50.3	53.17	4.108	5.7	8.5	7.0944	1.974
MLS-0001965	56424151	52.09	50.3	54.5	52.42	2.938	5	9.1	7.0341	2.9266
MLS-0261294	24839185	195.69	226.4	243	234.69	11.752	4.2	9.8	7.0281	3.9308
MLS-0109973	17412796	86.92	62.9	55.4	59.17	5.281	9.5	4.5	7.0022	3.5198
MLS-0435115	85271131	82.03	47.3	60.8	54.04	9.583	7.2	6.8	6.9953	0.26663
MLS-0350771	49643452	65.98	39.6	56.4	48.03	11.861	8	6	6.9702	1.3972
MLS-0312080	24840341	123.25	119.5	122.7	121.11	2.285	7.4	6.5	6.9557	0.60494

MLS-0428154	85148995	174.51	71.2	85.6	78.41	10.176	6.2	7.7	6.9552	1.0587
MLS-0217233	22415522	161.97	158.3	151.1	154.70	5.061	6.2	7.6	6.9181	0.95396
MLS-0375584	49826453	62.18	97.5	103.1	100.34	3.964	6	7.8	6.8923	1.2335
MLS-0109303	17412322	114.04	92.3	92	92.16	0.230	5.6	8.2	6.8894	1.8337
MLS-0342770	47202119	438.23	425.3	408.9	417.09	11.564	6.1	7.6	6.8627	1.0282
MLS-0102187	17401788	86.9	46.7	49.4	48.04	1.896	4.2	9.5	6.8131	3.7388
MLS-0076090	99495058	81.98	75	72.3	73.65	1.922	9.2	4.4	6.7945	3.3598
MLS-0279070	24806411	283.65	249.1	288.2	268.65	27.642	8.1	5.5	6.7905	1.7846
MLS-0259566	24817037	274.38	210.9	205.9	208.41	3.578	4.3	9.3	6.7869	3.5158
MLS-0009899	859757	47.51	68.9	54.5	61.73	10.178	9.4	4.2	6.7818	3.6644
MLS-0000877	859409	56.3	48.5	53	50.76	3.190	9.5	3.9	6.7337	3.9823
MLS-0033677	7975837	56.53	49.1	51.3	50.19	1.588	1.9	11.5	6.6988	6.7556
MLS-0295244	26666049	80.73	68.9	70.1	69.53	0.864	7.4	6	6.6727	0.98158
MLS-0373815	49818778	58.09	65.3	68	66.65	1.910	7.6	5.7	6.6696	1.3186
MLS-0267968	24823154	334.94	246.9	255.1	250.98	5.832	7.1	6.2	6.6377	0.65061
MLS-0451839	99361103	63.9	50.4	54.1	52.22	2.609	8.8	4.5	6.6311	3.0702
MLS-0044210	860525	73.94	132.7	146.2	139.47	9.574	4.9	8.2	6.5806	2.3404
MLS-0441764	89854303	261.04	257.1	253.8	255.45	2.396	5.6	7.6	6.566	1.4087
MLS-0364114	49828610	232.42	205.5	211	208.26	3.907	8.4	4.7	6.5633	2.6095
MLS-0093174	17401631	151.37	31.3	35.1	33.21	2.661	7.4	5.7	6.5499	1.1614
MLS-0099763	87347079	41.89	53.6	60.7	57.16	5.010	7.5	5.5	6.5103	1.3829
MLS-0092826	17407033	119	74.2	21.9	48.03	37.007	8.1	4.9	6.4849	2.2193
MLS-0295656	26657768	71.16	66.3	59.3	62.83	4.960	1.8	11.2	6.4784	6.6701
MLS-0263757	24837692	101.03	144.7	157.1	150.93	8.745	8.5	4.5	6.4754	2.8195
MLS-0350201	49640668	53.16	49.4	51.8	50.63	1.675	3.6	9.2	6.4326	3.9436
MLS-0465050	121283267	88.7	142.8	84.4	113.63	41.315	6.3	6.4	6.3867	0.076428
MLS-0347256	47197062	50.42	66.2	90.9	78.56	17.419	9	3.7	6.3654	3.7518
MLS-0223596	17511400	73.9	185.5	151.4	168.43	24.083	4.6	8.1	6.3442	2.4565
MLS-0011991	7966286	145.27	127.6	128.4	128.02	0.536	4.6	8.1	6.3324	2.4748
MLS-0548107	144095701	40.28	32.5	32.2	32.36	0.264	5.3	7.4	6.329	1.5086
MLS-0271915	24791206	187.93	97.3	114	105.65	11.835	6.4	6.2	6.3183	0.14104
MLS-0362531	49824593	44.01	51.2	54.2	52.68	2.133	7.8	4.8	6.3116	2.1282
MLS-0394720	26671218	389.8	315.1	313	314.07	1.444	6	6.6	6.3096	0.43629
MLS-0351157	47198600	151.08	58.8	52.7	55.74	4.358	2.6	10	6.2948	5.2384
MLS-0273854	24794745	239.4	151.6	166.3	158.93	10.376	1.4	11.1	6.2765	6.8417
MLS-0322961	49669704	102.04	76.6	78.2	77.40	1.076	4.6	7.9	6.2755	2.3131
MLS-0302989	26659873	45.46	34.6	38.1	36.34	2.478	11.4	1	6.2377	7.3696
MLS-0013903	865167	57.39	82.4	32.1	57.24	35.526	4.1	8.4	6.225	3.0131
MLS-0442424	87337170	101.29	81.8	91	86.41	6.558	5.2	7.2	6.1906	1.4421
MLS-0043706	850568	67.05	60	63.7	61.85	2.593	6.2	6.2	6.1887	0.015523
MLS-0305082	26664157	50.36	46.8	46.2	46.50	0.422	7.9	4.5	6.1849	2.3926
MLS-0232608	22414645	194.09	220.8	220.5	220.65	0.200	4.3	8	6.1539	2.5945
MLS-0405487	51087744	96.25	58.2	64.2	61.21	4.296	4.8	7.5	6.1469	1.885
MLS-0325704	49678917	188.07	113.2	89.9	101.55	16.461	6.6	5.7	6.1433	0.67008
MLS-0202529	22402247	154.52	157.1	154	155.59	2.199	9.1	3.2	6.1357	4.129
MLS-0304656	26660123	45.59	35.2	40.8	38.02	3.956	6.5	5.8	6.1356	0.51828
MLS-0298858	26665703	1181.7	685	703.2	694.11	12.887	5.5	6.7	6.1274	0.86709
MLS-0445190	92764418	54.31	23.3	46.6	34.95	16.449	4.5	7.7	6.1168	2.2898
MLS-0094912	17408781	736.54	780.8	788.1	784.45	5.163	8.6	3.6	6.1128	3.5821
MLS-0300748	26727041	44.35	36.7	40.9	38.80	2.908	7.2	5	6.1039	1.5095
MLS-0321701	49665460	114.47	95.7	86.7	91.19	6.387	5.5	6.7	6.1036	0.79278
MLS-0442669	89855713	51.38	35.2	36.7	35.96	1.023	3.8	8.3	6.0554	3.1783
MLS-0371507	49676876	55.53	46.5	42.6	44.57	2.785	4.3	7.8	6.0327	2.4803
MLS-0218468	22401173	44.59	36.1	33.9	35.02	1.557	6.1	6	6.0178	0.058542
MLS-0216965	17506421	56.84	76.5	81.7	79.10	3.734	6.5	5.5	6.0149	0.75528
MLS-0543865	134216069	140.55	119.1	118.6	118.88	0.341	5.2	6.8	6.0053	1.1751
MLS-0264005	14744724	147.66	101	145.6	123.31	31.564	4.7	7.2	5.9515	1.8127
MLS-0097445	17406614	135.73	106.1	147.4	126.76	29.170	7.2	4.7	5.9481	1.7234

MLS-0063499	51088625	67.01	63.3	64.9	64.09	1.187	6.1	5.7	5.9402	0.29008
MLS-0044173	87349050	119.31	93.2	95.8	94.49	1.814	8.1	3.7	5.9172	3.0758
MLS-0101476	17413055	51.95	44.5	50.4	47.48	4.153	6.3	5.6	5.913	0.50385
MLS-0217975	17505635	542.84	312.3	340.4	326.35	19.902	4.5	7.3	5.8908	1.9642
MLS-0317941	49681835	237.04	252.4	251.9	252.14	0.362	4.8	6.9	5.8748	1.5064
MLS-0216183	17433641	73.53	71.2	86.1	78.64	10.485	2.9	8.8	5.865	4.1551
MLS-0293797	26666781	111.55	147.3	156	151.65	6.128	5.5	6.2	5.8155	0.49252
MLS-0272748	89851154	40.37	33.1	34.5	33.83	0.986	3.9	7.7	5.8076	2.7089
MLS-0325514	49678912	971	77.8	99.3	88.55	15.263	6.9	4.7	5.8069	1.5778
MLS-0224623	87336491	65.18	3.8	81.6	42.73	55.018	4.4	7.2	5.7821	1.9772
MLS-0044944	87340790	50.79	39.4	43.4	41.40	2.798	8.1	3.5	5.7743	3.2817
MLS-0057876	850954	41.14	30.4	37.1	33.72	4.734	6.8	4.6	5.7079	1.5718
MLS-0069675	14730331	232.83	94.7	82.8	88.74	8.470	8.2	3.2	5.6675	3.5332
MLS-0220143	22401516	57.7	42.7	47.3	44.98	3.227	6	5.3	5.6471	0.46301
MLS-0224510	17517317	40.35	33.8	35	34.41	0.818	4.7	6.5	5.6355	1.2555
MLS-0403673	57267403	94.89	79	84.9	81.94	4.121	5.7	5.5	5.6273	0.14603
MLS-0295088	26670841	258.15	166.2	181.9	174.02	11.092	5.7	5.5	5.5961	0.09346
MLS-0543800	134216070	82.43	44.6	48.5	46.57	2.800	5.3	5.8	5.5957	0.34914
MLS-0284998	24807893	41.99	35.7	32.3	33.98	2.408	8.5	2.7	5.5835	4.1224
MLS-0293074	26729861	54.33	52.4	57.7	55.03	3.735	2.4	8.6	5.5	4.4529
MLS-0045279	7975223	60.23	84	94	89.01	7.105	9.2	1.8	5.4994	5.1881
MLS-0318721	49671604	1163.5	1038	1042.1	1040.00	2.918	4.1	6.8	5.4752	1.9035
MLS-0345579	47204400	46.42	35.7	33.5	34.62	1.563	3	7.9	5.4492	3.5172
MLS-0281040	26667200	62.21	42.2	40.2	41.23	1.399	7	3.8	5.4444	2.2673
MLS-0365229	49815848	76.78	73.4	75.5	74.47	1.492	6.5	4.3	5.3933	1.5527
MLS-0102439	17512114	205.42	191.3	190.6	190.98	0.490	4.5	6.1	5.3222	1.1411
MLS-0102123	17401604	73.21	60.9	64.5	62.71	2.576	5.5	5.1	5.2985	0.34091
MLS-0206670	22407530	42.57	36.8	48.8	42.83	8.472	6.6	3.9	5.2871	1.9257
MLS-0206003	17511369	75.64	70.5	79.9	75.20	6.666	8.6	1.9	5.2827	4.7445
MLS-0236151	24783904	118.36	110.2	85.3	97.74	17.587	5.4	5.1	5.2636	0.18395
MLS-0099136	89853112	124.42	87.4	77.9	82.62	6.732	3.9	6.6	5.2616	1.9151
MLS-0306758	26660419	56.12	54.6	55.8	55.24	0.852	7	3.5	5.2576	2.4474
MLS-0295776	26671512	109.15	77.4	85.5	81.44	5.765	6.5	4	5.2483	1.7035
MLS-0224325	22415800	84.17	89.9	95.7	92.77	4.096	2.7	7.8	5.2237	3.5959
MLS-0214692	87340097	88.5	90.2	87.3	88.76	2.091	5.4	5	5.2197	0.30202
MLS-0097956	17401211	41.44	55.9	75.8	65.85	14.032	4.3	6.1	5.2019	1.3164
MLS-0083778	14721545	95.34	56.8	57	56.86	0.153	2.6	7.8	5.1974	3.6216
MLS-0097347	17401191	660.07	594.9	615.1	604.98	14.280	6.8	3.6	5.1724	2.2506
MLS-0347788	47203428	154.13	135.2	137.4	136.27	1.545	4.3	6	5.1672	1.1846
MLS-0369039	49715936	54.41	42.1	44.6	43.36	1.804	3.8	6.5	5.1642	1.8863
MLS-0268240	24792875	235.49	212.6	220.5	216.55	5.591	4.5	5.8	5.157	0.90656
MLS-0202483	22400511	43.36	48.2	51.7	49.97	2.495	6.4	3.9	5.1466	1.766
MLS-0219020	22405840	67.27	34.8	42.3	38.55	5.256	3.5	6.8	5.1463	2.3412
MLS-0092170	17408229	149.26	156.5	173	164.78	11.660	4.7	5.6	5.1284	0.62835
MLS-0102548	17415839	84.47	71.5	84.1	77.79	8.883	6.2	4	5.1171	1.5817
MLS-0266431	24819482	63.28	52.3	54.9	53.61	1.828	4.1	6.1	5.0918	1.3598
MLS-0424334	93576824	78.7	65.4	67.2	66.34	1.263	6.2	3.9	5.0559	1.5729
MLS-0221693	17504175	86.58	91.3	90.8	91.02	0.374	2.4	7.7	5.0534	3.7338
MLS-0002164	7970166	86.7	48.1	49.9	49.02	1.270	6.3	3.8	5.0509	1.8152
MLS-0251696	24808626	57.93	53.6	54.2	53.90	0.399	2.6	7.5	5.0458	3.4121
MLS-0203409	87349355	137.15	121.8	126	123.94	2.981	3.7	6.4	5.0387	1.9594
MLS-0368853	49829386	56.8	50.2	51.4	50.82	0.829	5.5	4.5	4.9955	0.76729
MLS-0307010	26730070	176.78	147.7	53.4	100.57	66.658	7.1	2.8	4.9812	3.0653
MLS-0203839	22417029	202.6	267.4	273	270.17	3.963	7.5	2.3	4.8904	3.6336
MLS-0077810	14723062	59.76	61.9	66.7	64.29	3.364	7.2	2.6	4.8888	3.3034
MLS-0238371	24808761	280.08	154.5	158.1	156.31	2.483	2.8	7	4.8869	2.9674
MLS-0229063	22402675	200.21	159.8	177.2	168.49	12.326	4.9	4.9	4.8712	0.0088701
MLS-0040725	7972928	44.26	46.3	50	48.15	2.577	5.9	3.8	4.8601	1.4998

MLS-0003894	4249429	75.67	69.6	69.4	69.48	0.161	5.2	4.4	4.8411	0.55437
MLS-0380573	51085211	44.78	49.3	50.9	50.08	1.163	7.7	2	4.8193	4.0348
MLS-0236196	24784415	71.09	98.5	128.6	113.54	21.239	8	1.6	4.8169	4.4852
MLS-0273977	24794777	562.44	475.1	456.5	465.82	13.155	4	5.6	4.8163	1.1521
MLS-0294230	26727811	60.35	54	51.8	52.91	1.603	6.2	3.3	4.7872	2.0375
MLS-0211416	17504445	66.33	43.7	66	54.83	15.732	4.8	4.7	4.7662	0.049228
MLS-0347584	49646746	55.98	37.6	41.7	39.64	2.893	6.7	2.9	4.7606	2.692
MLS-0425832	85149027	90.33	306.8	221.7	264.27	60.221	8.4	1.1	4.7493	5.1492
MLS-0457851	103074324	57.35	56.5	60.6	58.56	2.885	5.8	3.7	4.7418	1.5273
MLS-0306726	26660286	78.94	73.6	74.9	74.26	0.944	5.9	3.5	4.7184	1.7222
MLS-0302645	26660603	169.76	62.4	65	63.68	1.824	7.4	2	4.7067	3.7703
MLS-0245375	24813443	165.08	142	156.7	149.37	10.398	6.9	2.5	4.6977	3.1594
MLS-0214520	22404143	275.87	184.9	107	145.98	55.105	7.3	2.1	4.689	3.6575
MLS-0232724	22405160	60.16	69.6	73	71.29	2.451	0.5	8.8	4.6806	5.8719
MLS-0001850	862505	42.46	62.3	85	73.65	16.085	4.5	4.9	4.679	0.24273
MLS-0095494	17416363	309.3	267.8	258.2	263.03	6.813	3.5	5.8	4.6459	1.583
MLS-0215095	17507093	74.21	67.6	69.2	68.38	1.164	5.9	3.3	4.6376	1.8507
MLS-0339383	47203431	75.9	129.4	145.8	137.63	11.600	3.6	5.7	4.6332	1.4715
MLS-0543857	134216140	59.6	37.1	39.7	38.44	1.834	5.5	3.7	4.6076	1.3062
MLS-0445432	57268333	222.9	185.9	194.1	189.98	5.786	5.8	3.5	4.6048	1.624
MLS-0379715	49827898	42.12	36	42.1	39.05	4.280	5.2	4	4.599	0.85716
MLS-0301197	26664014	45.82	35.3	36.6	35.98	0.920	3.1	6	4.5947	2.047
MLS-0304131	26659078	63.09	55.8	58	56.91	1.536	2.7	6.4	4.5943	2.6232
MLS-0269298	24788199	210.14	230.3	247.9	239.11	12.418	3	6.2	4.5846	2.2308
MLS-0456107	99495189	44.19	35.9	36.7	36.26	0.558	4.2	4.9	4.5648	0.51585
MLS-0264975	24788037	1269.2	973.7	997.6	985.65	16.875	5.2	3.8	4.5432	0.98811
MLS-0205964	17511794	1999.2	1353.2	1437.3	1395.20	59.416	0.5	8.5	4.5141	5.6107
MLS-0306006	26661095	86.97	42.8	45.5	44.18	1.892	6.2	2.7	4.4913	2.4656
MLS-0050074	51089343	74.08	291.2	387.4	339.29	67.999	1	7.9	4.477	4.8885
MLS-0294975	26671072	48.3	41.6	42	41.78	0.304	4.7	4.2	4.4703	0.38998
MLS-0219236	22400656	118.95	158	159.6	158.81	1.137	6.7	2.1	4.4159	3.2127
MLS-0044173	858975	44.73	40.3	42.6	41.47	1.582	3	5.8	4.4087	1.9569
MLS-0366124	49723691	52.84	49.3	48.8	49.03	0.368	4	4.8	4.3806	0.58195
MLS-0209739	17506678	85.52	88.7	91	89.87	1.642	6.8	2	4.3779	3.4207
MLS-0367512	49828915	90.88	141.7	100.1	120.90	29.459	6.6	2.2	4.376	3.0985
MLS-0093342	17407011	372.4	308.1	321.7	314.95	9.621	2.8	5.9	4.3659	2.1729
MLS-0222487	17506113	41.66	126.7	119.7	123.17	4.955	7.9	0.8	4.3645	5.0275
MLS-0344187	47204590	385.44	322.6	321.9	322.27	0.489	3.8	4.9	4.3625	0.80704
MLS-0102121	87346336	56.02	31	34.7	32.83	2.584	3.2	5.4	4.2979	1.527
MLS-0463892	121284614	90.52	86.1	73.1	79.58	9.179	1.7	6.9	4.2959	3.7072
MLS-0206424	17431924	186.26	122.7	138.4	130.55	11.045	4.6	4	4.2763	0.39516
MLS-0249713	24819543	465.94	74.9	69.9	72.40	3.531	6.2	2.3	4.2735	2.721
MLS-0361055	49820324	256.12	266.8	271.6	269.20	3.438	8.1	0.5	4.2703	5.3805
MLS-0406762	51086433	63.72	54.5	53.2	53.88	0.905	4.7	3.8	4.2602	0.67786
MLS-0212031	17513110	141.74	163.6	149.7	156.64	9.844	4.1	4.4	4.2594	0.2559
MLS-0206729	22406739	57.07	65.7	70.8	68.28	3.620	6.1	2.4	4.2418	2.6579
MLS-0237157	24807002	58.52	71.6	66	68.83	3.930	2.8	5.7	4.2411	2.009
MLS-0466050	121285253	46.95	35.2	38.3	36.77	2.214	2.9	5.6	4.2379	1.889
MLS-0050418	4248390	43.21	60.6	63.3	61.97	1.946	2.5	5.9	4.2049	2.363
MLS-0044247	859735	61.91	66.5	75.2	70.86	6.163	3.1	5.3	4.2037	1.6026
MLS-0304552	26660485	166.1	174.6	167.1	170.84	5.341	2.4	6	4.196	2.5502
MLS-0368295	49828594	150.35	71	81.4	76.19	7.308	8.2	0.1	4.1957	5.7219
MLS-0222414	17505427	293	249.5	246.9	248.21	1.826	3.2	5.1	4.1741	1.3159
MLS-0018886	860096	69.9	73.5	81.9	77.71	5.996	7.7	0.7	4.1641	4.9583
MLS-0085396	14718737	380.3	381.4	383.8	382.60	1.634	3.4	4.9	4.1582	1.0177
MLS-0303263	26658395	72.12	61.2	66.6	63.90	3.843	4.4	3.9	4.1534	0.34878
MLS-0299661	26671252	68.14	79.7	86.1	82.90	4.539	5.7	2.5	4.1284	2.2388
MLS-0096255	17408686	72.32	54.3	74.5	64.40	14.347	3.7	4.6	4.1208	0.66037

MLS-0300234	26728221	130.32	100.7	117.3	109.00	11.690	4.7	3.5	4.1029	0.83123
MLS-0110780	22405561	107.32	34.3	33.3	33.84	0.728	3.4	4.7	4.0549	0.97702
MLS-0304470	26658655	117.57	93.2	91.6	92.38	1.144	6.9	1.1	4.0428	4.1033
MLS-0007490	4264332	45.3	37.8	42.3	40.03	3.137	2.4	5.6	3.9621	2.2641
MLS-0449342	99360882	703.11	573.7	572.8	573.28	0.643	6	1.9	3.9489	2.8795
MLS-0236696	24783060	114.73	88	89.2	88.57	0.870	3.9	4	3.9413	0.090486
MLS-0383924	51085510	221.16	195.6	214.1	204.86	13.104	3.1	4.7	3.918	1.1436
MLS-0100365	14734406	70.7	166.1	167.8	166.93	1.202	1.3	6.5	3.9012	3.6189
MLS-0214272	87337062	112.15	99.7	101.3	100.51	1.171	1.3	6.5	3.8875	3.7282
MLS-0428011	85148998	93.28	99.1	141.6	120.38	30.064	3.4	4.3	3.8335	0.67138
MLS-0464934	121286248	680.63	633.4	641.8	637.61	5.981	4.4	3.2	3.8138	0.85678
MLS-0253710	24841359	89.04	53.6	53.4	53.52	0.096	4.4	3.2	3.7959	0.81607
MLS-0013867	865318	40.1	36.9	41	38.96	2.911	2.6	5	3.7901	1.7447
MLS-0074636	14743548	1417.1	1122.3	1200.2	1161.30	55.113	4	3.6	3.7878	0.25401
MLS-0276256	24805134	333.93	253.2	249	251.12	3.000	2.9	4.7	3.7746	1.2872
MLS-0417794	57265477	40.67	32.8	31.9	32.36	0.595	2.7	4.8	3.7497	1.4594
MLS-0423208	85149000	89.61	152.9	62	107.48	64.274	8.8	-1.3	3.7476	7.1366
MLS-0223529	17504648	1457	1465.1	1461.3	1463.20	2.732	3.2	4.2	3.7191	0.73709
MLS-0225234	17512989	872.89	135.8	139.8	137.77	2.803	5.8	1.6	3.7181	2.9736
MLS-0251636	24824459	54.63	38	41.2	39.60	2.285	5.5	1.9	3.7145	2.5336
MLS-0281033	24805089	953.05	778.9	807.8	793.34	20.416	6.3	1.2	3.7073	3.6025
MLS-0032624	89851213	314.1	2	280.8	141.42	197.120	-0.2	7.6	3.7044	5.5231
MLS-0294991	26671204	79.9	65.7	65.9	65.81	0.185	3.3	4.1	3.6992	0.55099
MLS-0205875	17505539	395.47	297.9	303.5	300.69	3.950	4.4	3	3.6965	0.92425
MLS-0424792	85149023	66.07	75.4	119.9	97.65	31.498	4.6	2.8	3.6885	1.2901
MLS-0439402	92764162	159.89	148.4	158.1	153.27	6.850	4.5	2.8	3.6876	1.2029
MLS-0243385	24832495	64.2	55.3	52.3	53.80	2.054	6.9	0.5	3.6839	4.5241
MLS-0003855	856651	194.01	148.2	147	147.59	0.892	2.6	4.7	3.6731	1.5074
MLS-0000221	858507	78.12	142	109.5	125.73	22.995	4.8	2.6	3.6663	1.578
MLS-0418633	57258804	52.82	37.9	33	35.46	3.488	6.5	0.8	3.6596	4.0011
MLS-0275481	24807228	283.87	199.1	199.3	199.19	0.085	4.1	3.2	3.6511	0.64105
MLS-0358737	49828619	41.86	46.2	26.4	36.32	14.022	3.8	3.5	3.6391	0.21602
MLS-0101012	17410629	68.35	43	43.1	43.03	0.040	0.7	6.5	3.63	4.1118
MLS-0040999	4263240	128.29	162.4	182.5	172.46	14.180	3.2	4	3.62	0.58072
MLS-0440743	87335867	42.87	33.5	33.8	33.68	0.199	1	6.2	3.6072	3.7224
MLS-0207320	87347088	306.36	275.1	271.7	273.41	2.373	4.1	3.1	3.6037	0.71758
MLS-0219398	17504959	74.26	49.6	47.4	48.50	1.527	0.5	6.7	3.5939	4.431
MLS-0209973	17508132	61.31	77	146.7	111.86	49.240	5.3	1.8	3.5717	2.4987
MLS-0317251	49645652	51.01	43.4	51.3	47.36	5.595	4.7	2.4	3.557	1.5746
MLS-0410240	51088014	59.09	34.7	41.5	38.11	4.843	4.2	2.9	3.552	0.8715
MLS-0367539	49828253	189.12	188.2	186	187.06	1.566	2.6	4.5	3.5414	1.3462
MLS-0453649	99360418	64.62	63	65.7	64.37	1.888	2.1	4.9	3.5046	1.968
MLS-0305062	26662709	257.64	202.8	201.4	202.08	1.007	3.7	3.3	3.5015	0.26126
MLS-0204783	22400549	269.5	241.4	247.6	244.48	4.410	2	5	3.4986	2.1372
MLS-0276494	24797528	67.42	58.4	61.5	59.95	2.234	2.2	4.8	3.4955	1.8853
MLS-0427505	85146904	266.97	189.6	184.6	187.10	3.490	0.1	6.8	3.4764	4.7093
MLS-0001999	860302	49.23	53	58.9	55.91	4.177	5.4	1.5	3.4486	2.7064
MLS-0043542	3713867	42.73	40.3	46.2	43.23	4.152	4.1	2.7	3.4389	0.98054
MLS-0252925	24840439	170.93	158.8	165.6	162.22	4.820	1.5	5.3	3.4294	2.6853
MLS-0202516	22402085	196.65	204.2	210.1	207.13	4.163	3.1	3.7	3.4155	0.47011
MLS-0318869	49647861	122.15	109.2	114.8	112.04	3.957	1.9	4.8	3.3718	2.0725
MLS-0104862	17387387	50.78	75.3	44.3	59.79	21.913	4.8	1.9	3.3697	2.0835
MLS-0212350	17510324	47.65	63.5	73.9	68.71	7.331	3.6	3.1	3.3369	0.39975
MLS-0444986	92763333	775.78	541.2	524.2	532.70	12.047	5.1	1.6	3.3217	2.4509
MLS-0412403	57264285	104.38	113.2	111.3	112.24	1.315	4.1	2.5	3.3041	1.1086
MLS-0028824	4264751	99.46	123.8	127.6	125.69	2.719	2.7	3.9	3.2898	0.88212
MLS-0323722	49668396	62.44	86.4	92.5	89.42	4.289	3.8	2.7	3.2869	0.78673
MLS-0424710	85149020	41.8	31.9	36.8	34.34	3.487	-0.9	7.4	3.235	5.882

MLS-0412263	56463485	427.71	366	398.6	382.29	23.046	3.4	3	3.2322	0.25925
MLS-0227556	17503971	95.76	93	92.4	92.70	0.378	2.8	3.6	3.2192	0.5455
MLS-0275676	24802949	52.42	58.6	68.3	63.42	6.840	1.2	5.2	3.2136	2.7887
MLS-0248721	24810471	87.95	62.4	71.9	67.17	6.754	4.8	1.6	3.2053	2.235
MLS-0238053	24782426	113.97	154.4	154.9	154.69	0.342	3	3.4	3.1984	0.33985
MLS-0280638	24806160	257.16	202.4	207.9	205.17	3.874	3.2	3.2	3.1777	0.018267
MLS-0216204	17505351	72.76	114.1	125.2	119.65	7.898	4.2	2.1	3.1675	1.503
MLS-0221022	17505864	332.16	276.2	281.2	278.70	3.520	0	6.3	3.1436	4.4221
MLS-0080013	14739330	52.76	41.2	43.7	42.46	1.736	1.9	4.4	3.1436	1.7292
MLS-0396801	16952768	113.86	33.8	41.4	37.59	5.335	3.2	3.1	3.1399	0.066428
MLS-0445075	92763849	70.22	67.3	70.2	68.73	2.026	2.6	3.6	3.0999	0.69741
MLS-0224082	17505484	162.27	206.3	156.5	181.38	35.246	3.1	3.1	3.0981	0.061203
MLS-0341108	49640794	133.44	52.5	36.6	44.55	11.235	4.3	1.9	3.0975	1.7096
MLS-0205158	17431843	117.97	206.6	189	197.79	12.431	4.2	2	3.063	1.5398
MLS-0207845	22405020	120.15	93.9	107.7	100.81	9.787	3.8	2.2	3.0273	1.1318
MLS-0394090	47194740	53.65	40.9	40.7	40.77	0.160	2.6	3.4	2.9758	0.56798
MLS-0255158	24820641	187.11	112.2	133.7	122.93	15.230	5.1	0.9	2.9689	2.9703
MLS-0335795	49735399	41.09	36.9	40.2	38.54	2.300	1.5	4.4	2.9603	2.0046
MLS-0286051	24797187	149.23	92	106.7	99.32	10.404	6.2	-0.3	2.9567	4.5596
MLS-0440977	89855780	47.29	37.6	37.5	37.56	0.100	3.4	2.5	2.9559	0.63705
MLS-0298901	26727331	43.27	48.4	48	48.18	0.311	4.3	1.6	2.9512	1.8696
MLS-0358350	49715480	53.15	51.7	50.1	50.94	1.140	0.6	5.3	2.9493	3.3267
MLS-0102597	17386258	104.22	81.9	81.9	81.93	0.002	2.1	3.7	2.9299	1.1347
MLS-0264082	24823182	61.13	30.4	57.1	43.73	18.848	1.7	4.1	2.9058	1.7129
MLS-0362712	49819063	49.21	41.2	40.6	40.87	0.409	3.2	2.6	2.8983	0.45407
MLS-0389254	49677748	145.99	138.6	152.7	145.63	9.958	2	3.8	2.8945	1.2685
MLS-0242661	24815776	50.6	44.9	42.9	43.90	1.397	4	1.8	2.8821	1.5935
MLS-0224187	17507156	305.25	228	217.6	222.80	7.409	1.3	4.4	2.8736	2.2166
MLS-0214409	17433097	64.15	50.8	56.8	53.80	4.234	3.1	2.7	2.8623	0.28827
MLS-0303577	26661201	50.64	45.7	45.8	45.75	0.036	1.1	4.7	2.8593	2.5383
MLS-0216236	22401288	1592.8	1462.9	1465.8	1464.30	2.043	4	1.6	2.8112	1.7487
MLS-0099339	17385602	55.86	38.8	38.4	38.62	0.294	2.9	2.6	2.7872	0.2068
MLS-0393269	14744279	46.27	39.4	40.4	39.94	0.719	2	3.5	2.7721	1.0219
MLS-0326522	49667064	40.44	37.5	40.6	39.04	2.164	3.1	2.4	2.7599	0.52535
MLS-0373809	49817883	40.21	34.9	38.6	36.75	2.576	4	1.5	2.7236	1.7873
MLS-0259024	24823580	407.56	434.4	488	461.17	37.914	2.5	2.9	2.6787	0.32116
MLS-0314776	26732110	61.38	42	41.5	41.74	0.378	2.8	2.5	2.6755	0.21683
MLS-0374979	51089050	146.38	147	148.1	147.54	0.739	-1.1	6.4	2.6509	5.2445
MLS-0210658	17513005	50.86	34.1	33.9	34.00	0.171	4.2	1.1	2.6475	2.198
MLS-0322666	49669365	50.3	45.5	47.9	46.73	1.697	5	0.3	2.6325	3.3185
MLS-0303917	26658400	367.79	275.7	292	283.85	11.537	2.7	2.5	2.625	0.15506
MLS-0391095	17388419	123.44	102.9	89.7	96.32	9.357	-0.8	6	2.6249	4.7796
MLS-0109123	50086232	323.53	158.3	168.4	163.39	7.137	3.6	1.6	2.62	1.4535
MLS-0234383	17508846	246.98	223.7	215.1	219.39	6.065	2.1	3	2.592	0.63775
MLS-0265153	24833664	117.81	94.1	102.5	98.32	5.922	2.8	2.3	2.588	0.37044
MLS-0297561	26657935	75.82	44.9	51.1	48.00	4.329	0.7	4.4	2.54	2.5956
MLS-0415107	57264417	227.09	158.2	166.4	162.27	5.780	1.2	3.9	2.5375	1.8923
MLS-0296595	26662945	115.84	149.2	142.6	145.86	4.656	1.4	3.6	2.5244	1.5627
MLS-0104737	17386761	45.18	47.9	47.9	47.86	0.011	5.1	-0.1	2.5207	3.697
MLS-0346007	49641657	232.43	201.6	208.4	205.03	4.826	2.2	2.8	2.5195	0.42383
MLS-0419660	57268773	50.75	46.9	49.7	48.29	1.947	1.8	3.2	2.4935	0.98417
MLS-0000556	856954	652.6	404.7	180.2	292.43	158.760	4	1	2.4894	2.1286
MLS-0232854	22404968	40.48	74.2	77.8	76.02	2.555	2.1	2.9	2.4832	0.57344
MLS-0327198	49679634	95.31	71.7	74.5	73.11	1.925	2	3	2.4728	0.69298
MLS-0439410	92764427	113.2	110.2	104.3	107.24	4.135	1.6	3.3	2.4689	1.1694
MLS-0044640	7978362	40.43	42.9	42.8	42.86	0.041	1.3	3.6	2.4647	1.6108
MLS-0338917	49679963	56.16	48.6	52.5	50.57	2.742	3.7	1.1	2.419	1.8577
MLS-0021342	847097	77.71	62.1	39.6	50.87	15.930	2.3	2.6	2.4148	0.22485

MLS-0303328	26661978	64.84	78.3	82.4	80.32	2.885	0.7	4.1	2.4045	2.4593
MLS-0264782	24784228	127.62	111.7	120.7	116.21	6.323	2.3	2.5	2.4027	0.15591
MLS-0294940	26665605	71.25	47.6	83.5	65.51	25.391	2	2.8	2.4018	0.5803
MLS-0369090	49716028	76	43.7	47.8	45.75	2.957	-1.7	6.5	2.3949	5.8398
MLS-0307983	26725923	59.57	34.9	30.5	32.68	3.098	2.1	2.6	2.3868	0.36279
MLS-0311718	24791422	49.93	44.7	46.1	45.36	0.994	1.4	3.3	2.3786	1.3573
MLS-0080507	14731818	376.72	389.7	394	391.87	3.051	1.3	3.4	2.3771	1.4643
MLS-0020135	87347229	48.56	57.2	56.6	56.89	0.423	4	0.7	2.3367	2.3567
MLS-0325926	49648009	86.5	83.6	85.7	84.66	1.480	1.1	3.5	2.3286	1.6668
MLS-0237019	24784284	44.88	36.5	42.3	39.38	4.088	-0.3	4.9	2.3153	3.6772
MLS-0242358	24789266	74.59	69.6	66.4	67.96	2.248	1.6	3	2.2987	0.98515
MLS-0248779	24823422	62.61	91.5	93.7	92.57	1.540	-2.6	7.2	2.2891	6.8884
MLS-0276280	24805157	725.12	551.7	573.4	562.55	15.306	6.3	-1.8	2.2627	5.7023
MLS-0109531	87334421	48.46	48.7	55.1	51.90	4.561	1.3	3.2	2.251	1.3377
MLS-0325121	49680279	149.62	119.3	119.3	119.32	0.004	0.2	4.3	2.243	2.8704
MLS-0416044	56422553	48.36	53.1	48.2	50.64	3.443	-1.1	5.6	2.236	4.6889
MLS-0280922	24807046	312.55	193.7	192.3	192.99	0.967	4.7	-0.3	2.2227	3.5472
MLS-0287607	24797792	54.48	57.4	65.1	61.25	5.418	2.6	1.8	2.217	0.60621
MLS-0053266	850891	64.21	43.6	47.1	45.38	2.468	0.7	3.7	2.1987	2.076
MLS-0312884	87347675	190.29	134.8	160.1	147.49	17.874	2.4	1.9	2.1897	0.36279
MLS-0395674	47194863	69.31	67.8	65.6	66.70	1.503	3.5	0.8	2.1597	1.938
MLS-0354876	49673228	152.19	154.9	166.7	160.79	8.381	3	1.3	2.1269	1.2149
MLS-0104117	17387116	59.8	47.7	44.3	46.01	2.399	4.3	-0.1	2.0855	3.1058
MLS-0031251	4261739	163.64	92.2	92	92.11	0.085	1.4	2.7	2.0421	0.97553
MLS-0094783	17402437	41.48	51	96.4	73.70	32.107	1.3	2.8	2.0297	1.0683
MLS-0375548	49717846	56.14	48.4	52.5	50.46	2.891	0.3	3.8	2.0264	2.4423
MLS-0294738	26671193	98.5	80.5	78.7	79.62	1.269	1.8	2.2	2.0116	0.26296
MLS-0109297	17407608	70.25	65.7	78.9	72.32	9.336	-1	5	1.9955	4.2535
MLS-0298651	26727013	158.82	100.7	120	110.33	13.630	-0.4	4.4	1.9818	3.3994
MLS-0442789	89851533	186.46	163.5	172.6	168.05	6.403	2.6	1.3	1.9641	0.90194
MLS-0369123	49817411	60.76	54.9	52.3	53.60	1.868	3	0.9	1.9562	1.465
MLS-0319331	49679534	376.51	118.1	115.8	116.94	1.687	-0.2	4.2	1.9556	3.1171
MLS-0246840	24779576	66.38	41.7	43.7	42.72	1.382	1.6	2.3	1.9335	0.44818
MLS-0360271	49821582	40.31	47.7	44.6	46.16	2.222	4.2	-0.3	1.9311	3.1707
MLS-0068056	14746404	187.92	96.1	39	67.58	40.405	1.6	2.3	1.9231	0.48797
MLS-0019808	50086145	67.35	47.8	49.5	48.69	1.214	1.9	1.9	1.916	0.03593
MLS-0440252	89852961	64.97	56.7	63.7	60.21	4.939	0.2	3.7	1.9155	2.4696
MLS-0229209	22402074	87.07	70.7	77.7	74.22	4.957	4.6	-0.7	1.9137	3.7657
MLS-0096276	17416360	83.25	44.2	44.6	44.42	0.311	2.2	1.6	1.8879	0.42238
MLS-0076520	14731704	176.24	53.7	50	51.84	2.612	5.4	-1.6	1.8779	4.9261
MLS-0207737	22403518	64.2	42.5	47.7	45.07	3.677	3.8	-0.1	1.871	2.751
MLS-0077905	14738079	103.96	194.5	94	144.26	71.056	4	-0.2	1.8685	2.9621
MLS-0042184	89853649	60.34	58.2	58.9	58.51	0.507	3.1	0.6	1.8548	1.7175
MLS-0238625	24806024	45.8	36.4	36.6	36.52	0.160	2.2	1.5	1.8452	0.46008
MLS-0299770	26670540	392.24	449.8	417.1	433.46	23.112	4.7	-1.1	1.8379	4.0846
MLS-0078794	14738997	56.52	20.6	79.3	49.96	41.500	1.9	1.8	1.8362	0.085228
MLS-0258268	24834514	60.45	34.2	45.3	39.76	7.837	3.3	0.3	1.8344	2.1106
MLS-0077905	14729657	116.84	186.3	116.2	151.24	49.553	-0.1	3.7	1.8249	2.7107
MLS-0216659	17509042	292.03	93.6	99.6	96.59	4.254	-2.2	5.9	1.8205	5.714
MLS-0278476	24803139	303.95	137.2	153.8	145.49	11.782	0.5	3.1	1.7989	1.8611
MLS-0258920	24823124	176.65	141.5	142.7	142.10	0.827	5.5	-1.9	1.7896	5.1879
MLS-0033853	7976922	70.14	57.5	52.7	55.12	3.385	2.6	1	1.7795	1.1263
MLS-0092519	17409264	190.03	46.3	52.1	49.24	4.101	1.6	1.9	1.765	0.20931
MLS-0264975	24787998	1204.1	916.9	921	918.95	2.883	2.7	0.8	1.7565	1.3569
MLS-0208841	17511472	85.03	86.5	62.4	74.47	17.058	2.1	1.3	1.7384	0.56768
MLS-0236830	24833566	49.56	42.2	43.9	43.09	1.197	1.4	2	1.7088	0.43629
MLS-0438889	57258959	423.68	294.7	308.9	301.78	10.068	3.2	0.2	1.7017	2.0815
MLS-0228752	17504238	105.68	102.7	101.7	102.19	0.687	4.8	-1.5	1.6973	4.4549

MLS-0284906	24807861	240.64	164.1	159.1	161.56	3.536	0.2	3.2	1.6971	2.0553
MLS-0215060	22407113	621.5	430.3	694	562.16	186.520	1.4	2	1.6797	0.40314
MLS-0017080	863582	356.43	604.3	352.3	478.27	178.170	1.4	1.9	1.6661	0.39857
MLS-0260556	24830036	146.86	169	82.9	125.92	60.882	2.9	0.4	1.6544	1.8225
MLS-0388609	56322916	76.38	91.4	93.7	92.53	1.605	1.9	1.4	1.6518	0.38822
MLS-0100759	17410799	120.88	53.6	152.1	102.85	69.710	2	1.3	1.6371	0.52056
MLS-0100994	17387597	141.81	45.8	41	43.42	3.395	0.5	2.8	1.6238	1.6005
MLS-0242308	24831641	240.06	102.8	118.5	110.66	11.108	5.5	-2.3	1.6142	5.4683
MLS-0257249	24830045	143.09	104.6	96.9	100.76	5.470	-0.9	4.1	1.5826	3.546
MLS-0206732	22406868	49.4	32.1	33.1	32.60	0.719	1.4	1.7	1.5396	0.22707
MLS-0352255	49645298	89.36	75	80.5	77.76	3.943	3.2	-0.2	1.5178	2.3589
MLS-0369998	49722298	44.91	34.2	34.3	34.29	0.064	-0.2	3.2	1.4723	2.4259
MLS-0111196	14732713	74.59	35.4	60.9	48.16	18.034	1.7	1.2	1.466	0.35479
MLS-0211926	17513027	42.15	109	123.3	116.18	10.131	4.8	-1.9	1.4198	4.7401
MLS-0219388	17505819	86.1	75	83.1	79.05	5.737	1.3	1.5	1.3997	0.1366
MLS-0209106	17512273	52.42	36.5	32.2	34.37	3.088	-0.5	3.3	1.3997	2.6339
MLS-0393836	47195673	40.09	35.8	35.6	35.70	0.191	-1.2	4	1.3928	3.6445
MLS-0054657	4245617	175.32	170.9	171.9	171.43	0.692	2	0.7	1.3813	0.89322
MLS-0232724	26662714	68.08	58.8	61.2	59.98	1.664	-0.6	3.4	1.3794	2.8372
MLS-0016421	862075	334.43	202.1	168.4	185.24	23.847	2.4	0.3	1.373	1.5224
MLS-0011304	26724625	65.51	70.4	80.8	75.62	7.345	2.2	0.5	1.3665	1.1781
MLS-0265009	24830410	839.61	44.9	97.1	71.00	36.892	0.4	2.3	1.3624	1.3886
MLS-0244145	24803514	77.57	78.8	96.9	87.87	12.779	2	0.7	1.3276	0.92336
MLS-0389087	49680172	289.65	234.7	278.9	256.82	31.253	2.5	0.1	1.3069	1.7262
MLS-0341803	49644992	254.09	127.1	127.5	127.31	0.309	-1.6	4.1	1.2929	4.0395
MLS-0263740	24815930	50.56	46.7	48	47.31	0.914	1.6	1	1.2909	0.36766
MLS-0280344	24801154	104.16	98.4	98.8	98.60	0.323	1.2	1.4	1.2786	0.15931
MLS-0384777	49737144	44.88	36.6	34.3	35.48	1.606	1.5	1	1.2758	0.38019
MLS-0098001	17410036	102.03	95	104.1	99.54	6.491	0.7	1.8	1.2244	0.78084
MLS-0215428	22403398	173.92	60.8	63	61.92	1.520	-2.1	4.5	1.1877	4.6159
MLS-0360658	49820435	72.38	144.6	5.8	75.21	98.137	1.6	0.8	1.1836	0.57461
MLS-0300262	26728304	205.58	150.8	170.5	160.66	13.937	1.4	1	1.1762	0.28548
MLS-0076132	56422586	59.43	201.1	189.8	195.43	7.955	2	0.3	1.1294	1.1886
MLS-0075347	85147380	45.15	43.1	43.3	43.22	0.128	1.6	0.6	1.1151	0.66887
MLS-0086400	14725883	59.09	74.6	96.6	85.57	15.552	-2.7	4.9	1.1042	5.3527
MLS-0301412	26665798	61.5	61.9	60.5	61.19	0.982	-1.2	3.4	1.1011	3.3137
MLS-0233552	17432688	76.88	64.6	75.7	70.17	7.876	0	2.2	1.0619	1.5695
MLS-0392908	26657697	130.45	81.2	78.2	79.71	2.097	-1	3.1	1.0371	2.9223
MLS-0281455	24804209	68.27	100	99.1	99.59	0.635	0.5	1.5	1.0353	0.72601
MLS-0257523	24835232	111.97	89.7	90.5	90.11	0.553	-0.4	2.5	1.0263	2.0523
MLS-0206044	17513097	68.47	68	72.3	70.13	3.040	1.7	0.4	1.0253	0.95441
MLS-0226092	17512112	551.78	591.3	464.3	527.80	89.849	0.1	1.9	1.0042	1.2795
MLS-0252985	87349592	666.45	383.9	377.1	380.53	4.818	1.4	0.6	1.0041	0.61301
MLS-0262228	24837805	392.24	141	132.1	136.50	6.287	-1.9	3.9	0.98603	4.1364
MLS-0362444	49815846	65.54	47.7	47.8	47.77	0.051	1.6	0.4	0.98164	0.87573
MLS-0254232	24817456	684.65	512.4	539.6	525.99	19.249	1.1	0.9	0.98041	0.13261
MLS-0252936	87349593	835.48	412.1	465.8	438.97	38.015	4.7	-2.7	0.97492	5.2006
MLS-0327762	49646347	64.48	70.8	70.9	70.85	0.067	1.9	0.1	0.96361	1.2693
MLS-0248400	24820069	43.1	38.2	40.8	39.51	1.870	3.6	-1.7	0.94492	3.7867
MLS-0076111	14743471	126.06	117.1	120.3	118.70	2.295	-2.9	4.8	0.94058	5.3982
MLS-0242793	24815048	250.63	32.2	107.2	69.72	53.044	2.5	-0.6	0.92365	2.2255
MLS-0108183	14729976	297.22	47.6	38.1	42.90	6.714	-2.5	4.3	0.91008	4.7673
MLS-0328376	49735864	105.99	59.5	67.7	63.60	5.791	0.4	1.4	0.90099	0.66576
MLS-0298155	26657478	86.02	84.6	85.2	84.87	0.441	1.2	0.6	0.88811	0.38276
MLS-0373705	49718162	44.91	39.9	44.9	42.37	3.531	2.2	-0.5	0.88632	1.904
MLS-0279502	24780548	107.55	89.4	95.8	92.57	4.555	-0.1	1.8	0.87008	1.3505
MLS-0216290	17511193	94.21	90.3	101.8	96.02	8.143	-0.7	2.3	0.83396	2.1048
MLS-0360744	49820590	62.56	68.4	72.6	70.49	3.006	1.8	-0.2	0.83164	1.4387

MLS-0311316	24833597	110.13	105.9	107.9	106.92	1.379	3.8	-2.2	0.81721	4.2163
MLS-0108788	17412354	251.7	208.3	221.8	215.07	9.568	2.6	-1	0.80403	2.4958
MLS-0102418	17412330	252.01	205.3	220.3	212.81	10.571	0.6	1	0.78985	0.28075
MLS-0389423	49676910	408.21	324	212.2	268.14	79.068	-0.9	2.5	0.77849	2.4014
MLS-0307962	26725655	256.81	52.5	13	32.78	27.943	2	-0.5	0.7313	1.7558
MLS-0356541	49726334	77.07	60.2	62.9	61.57	1.911	0.6	0.9	0.7293	0.21991
MLS-0263126	24833596	53.23	36	36.3	36.15	0.156	5.4	-4	0.71508	6.6114
MLS-0098742	17410457	90.96	60.2	46.5	53.31	9.695	1.1	0.3	0.69797	0.57195
MLS-0305988	24836042	49.52	36.6	35.6	36.11	0.652	0.9	0.4	0.66942	0.37596
MLS-0369813	49715976	77.6	62	62.6	62.31	0.408	-0.1	1.4	0.66728	1.0887
MLS-0223618	22404484	194.25	231.8	233.5	232.67	1.214	3	-1.7	0.66273	3.3564
MLS-0088903	14726747	379.36	312.7	311.7	312.17	0.689	0.4	0.9	0.63564	0.34175
MLS-0324678	49667858	275.6	56.4	25.5	40.93	21.853	-1.2	2.5	0.61169	2.6103
MLS-0222303	17505633	40.14	32.4	35.7	34.06	2.311	-2.4	3.6	0.59468	4.2491
MLS-0283868	24808466	75.65	52.3	50.4	51.31	1.345	2.6	-1.5	0.54236	2.9525
MLS-0233052	22404995	155	79.4	78.2	78.80	0.839	0.3	0.7	0.54012	0.28872
MLS-0294879	26662168	255.66	196.2	172.8	184.48	16.514	-3	4.1	0.53695	4.9916
MLS-0251877	24809110	157.29	124.8	131.3	128.03	4.591	-1.6	2.7	0.52313	3.0553
MLS-0039450	87347860	64.19	48.6	47.5	48.07	0.793	-1.8	2.8	0.5154	3.2901
MLS-0022647	3715767	67.85	68.7	72	70.36	2.297	0.9	0.1	0.49413	0.61289
MLS-0030129	3714729	51.75	33.1	36.6	34.89	2.480	3.7	-2.8	0.44604	4.5614
MLS-0219097	17505608	50.95	56.3	60.7	58.52	3.103	0.4	0.4	0.43224	0.011974
MLS-0281182	24807099	1868.7	460	500.6	480.29	28.753	-0.1	0.9	0.40057	0.64232
MLS-0218177	22403812	92.21	46.9	41.3	44.08	3.977	-0.9	1.7	0.3968	1.829
MLS-0232778	22414237	59.62	31.1	39.7	35.42	6.051	-1.3	2.1	0.37861	2.402
MLS-0447099	103073730	307.36	266.4	274	270.17	5.354	-0.5	1.1	0.34246	1.123
MLS-0306673	26662597	130.64	103	114.3	108.65	7.929	0.7	-0.1	0.34049	0.56161
MLS-0312457	26660961	195.35	195.7	220.6	208.13	17.640	-0.1	0.7	0.33989	0.56501
MLS-0442917	93576953	149.16	133.6	135.9	134.71	1.638	-0.7	1.4	0.33509	1.4912
MLS-0442420	89852452	193.93	168.7	156.5	162.58	8.625	2.2	-1.6	0.3291	2.6989
MLS-0305442	26660177	286.73	237.1	250.5	243.79	9.485	2	-1.3	0.32487	2.3407
MLS-0251634	24826187	57.82	52.9	52	52.42	0.658	1.7	-1.1	0.31286	1.9329
MLS-0416441	57255947	50.25	42.2	46.7	44.44	3.187	-0.2	0.8	0.29275	0.6757
MLS-0299668	26670965	187.71	150.9	157.6	154.22	4.739	-1.3	1.8	0.27501	2.1887
MLS-0369047	49715933	90.93	51.9	57.8	54.86	4.160	0.6	0	0.27259	0.41907
MLS-0251720	24826315	49.41	35.8	37.9	36.88	1.491	1.6	-1.1	0.2651	1.8696
MLS-0425962	85148999	65.15	55.1	58.2	56.67	2.173	-3.2	3.7	0.24835	4.8567
MLS-0074308	14742060	363.73	271.6	275.1	273.33	2.518	1.8	-1.3	0.22353	2.1871
MLS-0202336	22406040	57.46	307.6	169.9	238.77	97.325	-1.8	2.2	0.20922	2.8705
MLS-0108020	17386901	44.31	312.6	397.3	354.95	59.931	1.7	-1.3	0.16415	2.104
MLS-0038703	3717306	59.8	74.6	91.9	83.20	12.236	-3.7	4.1	0.15753	5.5229
MLS-0303905	26658393	773.77	514.1	517.5	515.78	2.373	-1.2	1.4	0.091169	1.8335
MLS-0247498	24826454	320.79	218	229.7	223.85	8.338	-2.3	2.4	0.072845	3.3352
MLS-0254203	24841233	43.76	40.9	34.5	37.73	4.552	-1	1.1	0.067738	1.5039
MLS-0304507	26658422	54.59	42.9	44.3	43.62	0.982	1.8	-1.6	0.060529	2.3977
MLS-0217473	17507342	69.66	31.1	38.2	34.65	5.073	-3.4	3.5	0.046197	4.8536
MLS-0093526	17402866	1344.1	1149.4	1162.2	1155.80	9.103	1.4	-1.3	0.037121	1.9277
MLS-0348772	47203795	219.7	44.7	45	44.84	0.184	1.4	-1.3	0.033996	1.9394
MLS-0110672	17411011	354.89	305.8	312.6	309.22	4.779	1.2	-1.1	0.033967	1.6476
MLS-0304677	26659187	74.26	67.4	64.5	65.94	2.052	3.2	-3.1	0.03049	4.4835
MLS-0350306	49645409	123.56	96.1	101.3	98.67	3.706	-1.2	1.2	0.013833	1.6785
MLS-0307334	26730115	60.56	48.1	51.1	49.59	2.151	0.6	-0.6	-0.0013518	0.91506
MLS-0244176	24830987	105.15	92.2	94.7	93.46	1.729	1	-1.1	-0.047312	1.4975
MLS-0000537	87347338	1486.5	1434.1	1440.2	1437.20	4.285	1.6	-1.8	-0.078092	2.4148
MLS-0295133	26670809	141.06	110.5	115.9	113.18	3.806	0.4	-0.6	-0.095074	0.67886
MLS-0450536	99360630	109.77	109.3	96.6	102.92	8.966	-0.1	-0.1	-0.10309	0.056887
MLS-0293159	26671326	58.76	44.2	49.2	46.68	3.512	-3.4	3.1	-0.18099	4.6169
MLS-0216796	17513055	264.6	90.9	107.3	99.13	11.607	-0.1	-0.2	-0.18743	0.073177

MLS-0208679	17509115	111.9	124	129.4	126.69	3.807	1.5	-1.9	-0.19527	2.3834
MLS-0073405	14745374	54.22	52.5	54.7	53.60	1.603	-0.1	-0.3	-0.19833	0.15416
MLS-0308051	26725775	143.22	47.5	83	65.29	25.100	-0.3	-0.1	-0.20201	0.10026
MLS-0048273	4241213	78.65	243	163	203.03	56.559	-1.4	0.9	-0.2063	1.6193
MLS-0080359	14732908	56.22	61.8	25.8	43.79	25.433	1.2	-1.7	-0.24264	2.03
MLS-0301743	26726894	160.74	119.9	118.5	119.23	0.993	-4	3.5	-0.2681	5.3145
MLS-0247538	24826499	72.47	47.7	57.8	52.76	7.099	3.3	-3.8	-0.2717	5.0145
MLS-0265142	24823336	302.17	262.3	257.5	259.91	3.403	0	-0.5	-0.27471	0.3475
MLS-0225260	17513727	63.27	58.1	55.7	56.88	1.668	-1.9	1.4	-0.27963	2.3341
MLS-0317332	49645657	46.12	43.2	44.5	43.85	0.857	-2	1.4	-0.29995	2.4453
MLS-0035596	7978440	121.9	92.2	89.8	91.00	1.753	3.2	-3.8	-0.31295	4.998
MLS-0043212	92764144	191.83	168	184.6	176.32	11.762	2.1	-2.8	-0.35638	3.4893
MLS-0421970	57266215	136.25	121.9	123.9	122.86	1.401	-2.3	1.5	-0.37842	2.6955
MLS-0241188	24811003	180.83	198.4	230.1	214.27	22.415	0.8	-1.6	-0.37998	1.6999
MLS-0223852	22401533	73.94	39.9	34	36.95	4.118	-1	0.3	-0.38218	0.9136
MLS-0100371	17414392	56.63	95.6	107.5	101.56	8.444	0.2	-1	-0.38296	0.82721
MLS-0014498	863887	46.18	51.3	54.6	52.94	2.341	0.2	-1	-0.4001	0.89322
MLS-0302698	26659214	96.47	91.3	100.4	95.86	6.445	-0.2	-0.6	-0.42701	0.2927
MLS-0438074	85146987	104.4	41.7	46.8	44.21	3.612	-1.4	0.6	-0.43112	1.4284
MLS-0236579	24784615	78.69	34.8	61.9	48.32	19.175	0.7	-1.6	-0.48138	1.6313
MLS-0005707	7977167	49.85	32.7	37	34.83	3.016	-0.3	-0.8	-0.5227	0.3806
MLS-0274628	24781345	310.66	282.5	295.2	288.88	8.966	-1	0	-0.53094	0.68948
MLS-0101160	14738608	54.9	48.5	53	50.72	3.183	-0.6	-0.5	-0.55667	0.11949
MLS-0355718	49714709	103.03	93	89.5	91.25	2.433	-0.6	-0.6	-0.58432	0.035859
MLS-0255797	24840642	51.56	96.4	62.5	79.48	23.991	-2	0.8	-0.58952	1.9559
MLS-0069518	14746141	40.58	34	46.9	40.46	9.130	-0.4	-0.8	-0.60453	0.32253
MLS-0406474	57267626	95.13	123.3	168.5	145.86	31.968	-0.8	-0.5	-0.64045	0.16545
MLS-0075130	14742838	43.38	296	130.1	213.08	117.300	-3.5	2.2	-0.68193	4.0116
MLS-0247175	24822957	43	28.8	44.4	36.59	11.057	-1.4	0	-0.69586	1.0119
MLS-0226562	22415530	110.09	97.2	104	100.62	4.806	-4.4	3	-0.70111	5.2585
MLS-0388060	49825997	139.79	42.1	45.9	44.02	2.717	-2.3	0.9	-0.70172	2.325
MLS-0040242	87347083	59.19	55.3	55.4	55.31	0.074	0.4	-1.8	-0.71265	1.5675
MLS-0300944	26667337	177.94	110.3	136.9	123.62	18.826	-1.8	0.3	-0.74776	1.4413
MLS-0301773	26726836	492.83	485.9	492	488.94	4.307	-5	3.4	-0.8073	5.9436
MLS-0301355	26665390	380.24	289.2	295.3	292.25	4.267	-2.2	0.6	-0.81091	2.02
MLS-0317354	49645495	113.69	97.3	92.6	94.97	3.343	-3	1.3	-0.82639	3.0544
MLS-0418491	57256306	49.99	45.1	56.1	50.62	7.804	-1.3	-0.3	-0.83147	0.69903
MLS-0215023	17509987	158.1	50.7	45.8	48.24	3.494	0.1	-1.8	-0.85195	1.3802
MLS-0094706	17401873	151.95	64.2	55.6	59.93	6.057	-2.2	0.5	-0.88813	1.8942
MLS-0273721	24794776	437.15	328.7	341.2	334.93	8.867	-1.3	-0.6	-0.93257	0.4758
MLS-0332698	49715820	100.02	81.2	72.6	76.88	6.048	-0.4	-1.6	-0.95642	0.85759
MLS-0414118	57268283	60.53	61.7	71.7	66.72	7.108	-0.5	-1.4	-0.97261	0.62904
MLS-0035697	7973771	180.02	184.2	186	185.10	1.326	-3.5	1.5	-1.0007	3.59
MLS-0239914	24810868	317.51	271.4	504.4	387.91	164.760	-0.5	-1.5	-1.0137	0.66272
MLS-0240866	24815830	40.69	36.5	30.2	33.34	4.422	-0.6	-1.5	-1.0649	0.60715
MLS-0302440	26660294	74.05	52.9	58.9	55.92	4.232	-0.1	-2.3	-1.1597	1.5667
MLS-0340346	47202040	43.4	55.3	62.7	58.97	5.212	-2.1	-0.4	-1.2637	1.2205
MLS-0213477	17510671	76.77	65.3	68.8	67.05	2.475	-1.7	-0.9	-1.2995	0.49893
MLS-0314935	26726070	43.51	31.3	40.5	35.88	6.526	-2.9	0.2	-1.3197	2.1779
MLS-0208552	17508221	43.79	32.4	34.6	33.51	1.499	-1.3	-1.3	-1.3258	0.034149
MLS-0464629	121282831	41.05	32.3	35	33.68	1.919	-1.2	-1.4	-1.3326	0.15155
MLS-0204657	24823176	55.87	43.3	42.2	42.76	0.758	-0.9	-1.8	-1.3375	0.67886
MLS-0110565	17411067	84.52	63	38.7	50.85	17.194	-3	0.2	-1.3819	2.2246
MLS-0107139	17387442	95.36	103.3	111.3	107.31	5.708	0	-2.9	-1.4435	2.0371
MLS-0233518	14719363	132.04	118.7	109.9	114.32	6.262	-1.5	-1.5	-1.4773	0.022175
MLS-0042911	861287	279.6	240.5	207.7	224.14	23.198	-4.4	1.5	-1.4866	4.1854
MLS-0302054	26661448	103.67	78.1	77.9	77.99	0.188	-2.7	-0.3	-1.5216	1.6657
MLS-0029600	845557	59.25	36.9	45.5	41.18	6.118	0.5	-3.6	-1.5613	2.8943

MLS-0211861	87349047	54.95	34.4	41.4	37.93	4.973	-1.9	-1.3	-1.6137	0.41733
MLS-0268009	24837832	62.36	46.9	51	48.96	2.868	-2.5	-0.7	-1.6166	1.2273
MLS-0297762	26671425	356.19	250.2	264.4	257.30	10.022	-2.3	-1	-1.6199	0.92185
MLS-0224187	17504068	215.55	347.6	206	276.82	100.140	-0.1	-3.2	-1.6363	2.1878
MLS-0208219	17514186	82.92	77.1	77.5	77.33	0.300	0.9	-4.2	-1.6742	3.642
MLS-0002876	56423120	61.48	58.5	55.5	56.98	2.138	1.9	-5.3	-1.6799	5.0634
MLS-0445208	92763873	72.49	67.5	71.4	69.45	2.778	-2.8	-0.6	-1.6851	1.5629
MLS-0219231	17512796	40.47	36.8	39.7	38.27	2.074	-0.2	-3.2	-1.7021	2.1159
MLS-0216933	22406226	109.33	119.6	125.8	122.69	4.362	0.1	-3.5	-1.715	2.5368
MLS-0371973	49715980	53.47	45.5	49.8	47.65	2.989	-1.9	-1.5	-1.7192	0.25404
MLS-0229301	22414866	45.75	33	31.2	32.11	1.213	-2.4	-1	-1.7281	0.97215
MLS-0202644	17513699	41.52	39.7	45	42.33	3.781	-3.4	-0.1	-1.7288	2.3567
MLS-0272104	24791270	56.96	52.3	49.3	50.82	2.158	-3	-0.5	-1.7313	1.8
MLS-0305288	26663704	46.21	43.4	44.7	44.06	0.897	-3.4	0	-1.7452	2.4034
MLS-0350088	49642965	97.81	55.1	84.9	70.03	21.070	-3.4	-0.1	-1.7535	2.3356
MLS-0301676	26666947	63.53	44.1	50	47.04	4.214	-4.7	1.2	-1.7773	4.1862
MLS-0283373	24789749	49.2	71	69.8	70.41	0.803	-1	-2.6	-1.7893	1.0969
MLS-0441024	89854728	72.81	94.3	96.6	95.48	1.608	-1.2	-2.7	-1.9242	1.0399
MLS-0303387	26660258	50.16	44	45	44.50	0.685	-2.9	-1	-1.9482	1.3666
MLS-0413926	57266140	71.98	76.5	84.8	80.63	5.872	-4.8	0.8	-2.0256	3.944
MLS-0438437	57256211	49.67	35.6	37.3	36.42	1.227	-1.2	-2.9	-2.026	1.1656
MLS-0207311	17511370	140.45	108.5	114.7	111.59	4.407	-3.9	-0.3	-2.0819	2.5474
MLS-0284304	24806606	99.59	94.8	92.5	93.61	1.623	-0.5	-3.8	-2.1152	2.3259
MLS-0247924	24779665	44.51	40.2	38.5	39.36	1.173	-1.3	-2.9	-2.1336	1.1305
MLS-0397821	56319371	65.86	60.5	67.1	63.83	4.676	-6	1.7	-2.1659	5.4125
MLS-0206971	17515082	135.29	93.5	104.7	99.08	7.940	-1	-3.4	-2.2086	1.6613
MLS-0303065	26663131	107.65	111.5	118.5	115.02	4.949	3.8	-8.3	-2.2588	8.5563
MLS-0332222	49675441	48.8	44.9	46.2	45.53	0.885	-3.8	-0.7	-2.2609	2.1442
MLS-0245328	24811139	78.4	44.4	40.6	42.52	2.709	-1.9	-2.7	-2.2867	0.59814
MLS-0250233	24811647	44.75	36.7	36.8	36.78	0.036	-2	-2.6	-2.2957	0.45031
MLS-0219097	24820061	65.17	53.6	52.7	53.10	0.632	-3.2	-1.5	-2.3422	1.1894
MLS-0360272	49821584	44.63	46.1	47.9	47.01	1.300	-1.5	-3.7	-2.6391	1.5687
MLS-0242198	24815187	52.36	43.4	46.2	44.82	1.975	-4.9	-0.4	-2.6639	3.1346
MLS-0021060	851980	72	64.8	61.4	63.09	2.401	-2.3	-3.1	-2.6821	0.5863
MLS-0280043	24785066	50.54	47.4	49.8	48.57	1.728	-4.3	-1.1	-2.698	2.2783
MLS-0232708	22400785	153.28	101.6	109.7	105.66	5.753	-3.4	-2	-2.6997	1.0458
MLS-0204707	22400550	351.29	330.2	334.4	332.29	2.974	-2.9	-2.6	-2.7499	0.18449
MLS-0299722	26671060	74.35	85.1	89.3	87.20	2.913	-3.9	-1.8	-2.8427	1.4943
MLS-0271395	24827342	154.42	149.1	146.1	147.58	2.124	-6.8	0.7	-3.0227	5.3238
MLS-0310727	26671554	61	43.1	45.9	44.52	2.008	-3.8	-2.3	-3.0683	1.0162
MLS-0297470	26664110	84.79	78	86.9	82.46	6.308	-7.3	1	-3.1317	5.8824
MLS-0262144	24830660	79.43	29.6	36.4	32.99	4.855	-1.3	-5.5	-3.4075	3.0029
MLS-0259270	24837054	128.21	99.7	110.3	105.03	7.477	-4.8	-2.1	-3.4306	1.9142
MLS-0110780	17408400	71.88	29.5	35.9	32.69	4.527	-1.8	-5.3	-3.5428	2.5326
MLS-0208366	17514202	82.31	60.8	66.2	63.46	3.824	-5	-2.1	-3.5473	2.0512
MLS-0206109	17516467	107.99	90.9	105	97.93	9.967	-2	-5.3	-3.6574	2.2849
MLS-0360872	49821888	73.79	117.5	115	116.27	1.784	-1.9	-6	-3.9328	2.8946
MLS-0304391	26658943	92.68	102.7	97.5	100.09	3.736	-3.1	-5	-4.0847	1.3423
MLS-0281606	24804135	44.68	41.1	45.3	43.23	2.966	-1.5	-6.9	-4.1978	3.8378
MLS-0395091	26671159	107.12	82.6	82.4	82.49	0.132	-1.4	-7	-4.2333	3.9763
MLS-0419605	57262774	62.73	51.4	57.2	54.26	4.113	-2.8	-5.8	-4.2524	2.1187
MLS-0275595	24805112	198.24	122.8	122.4	122.58	0.260	-4.6	-4	-4.2885	0.4707
MLS-0258467	24834629	68.51	31.9	35.9	33.91	2.795	-4.3	-4.3	-4.3162	0.0050977
MLS-0227852	17507210	102.65	85.2	91.5	88.37	4.446	-5.4	-3.6	-4.4565	1.2657
MLS-0057453	26670455	65.35	65.9	73.3	69.62	5.239	-6.3	-2.8	-4.5655	2.4265
MLS-0107003	16953947	89.81	97.5	96.6	97.05	0.701	-3.1	-6.5	-4.7608	2.4102
MLS-0216643	22406756	65.22	34.1	36.5	35.27	1.679	-3.3	-6.4	-4.8099	2.1931
MLS-0264823	24789849	138.31	158	160.7	159.36	1.858	-6.8	-2.9	-4.8542	2.8136

MLS-0309621	26731702	337.17	265.8	272.9	269.32	4.993	-5.9	-4	-4.9227	1.3411
MLS-0312178	24779393	331.05	273.2	291.1	282.14	12.677	-4.4	-6.7	-5.5274	1.6355
MLS-0444926	92763332	199.81	227	231.9	229.46	3.506	-7.7	-4.9	-6.2824	1.9368
`	89854866	61.85	30.1	33.8	31.98	2.620	39	45.7	42.377	4.7416
MLS-0043736	842430	81.7	29.9	34	31.95	2.846	8.1	6.8	7.445	0.96815
MLS-0233939	14732640	85.73	28.3	35.6	31.94	5.110	25.1	23.6	24.325	1.0858
MLS-0393553	47195386	47.95	29.6	33.9	31.75	3.035	22.6	20.8	21.695	1.2456
MLS-0369986	49717595	52.07	31	32.5	31.72	1.092	19.5	19.5	19.506	0.02333
MLS-0045473	3715155	41.11	33.3	30.1	31.72	2.286	510.4	546.4	528.38	25.412
MLS-0462592	99495757	68.29	31.3	32	31.64	0.448	5.6	10.8	8.2269	3.6786
MLS-0064989	17412184	46.35	32.2	31.1	31.62	0.787	18.2	16.4	17.294	1.2625
MLS-0440995	89854639	41.68	32	31.1	31.57	0.671	19.5	22	20.729	1.757
MLS-0207383	17514565	45.85	39.1	23.9	31.47	10.775	135.5	142.7	139.12	5.1011
MLS-0270225	24792257	49.19	27.8	35.1	31.46	5.146	41.2	34.6	37.877	4.6862
MLS-0084998	14725169	55.56	30.8	32.1	31.45	0.871	17.8	20.7	19.232	2.0852
MLS-0258297	24834394	43.55	30.1	32.8	31.45	1.958	561.5	594.7	578.13	23.498
MLS-0002273	87346613	42.73	31.5	31.3	31.43	0.152	6.2	8.1	7.1624	1.2986
MLS-0272092	24791790	44.96	29.7	33.1	31.42	2.414	20.1	23.3	21.712	2.2282
MLS-0291743	24779433	47.5	31.5	31.2	31.36	0.189	5.5	0.2	2.8456	3.6964
MLS-0218189	17509188	47.81	26.6	36.1	31.35	6.704	8.3	9.2	8.7643	0.67057
MLS-0079796	56422850	43.93	30.2	32.4	31.33	1.548	5.5	11.3	8.4311	4.1052
MLS-0261859	24830311	392.09	19.9	42.7	31.32	16.109	-0.1	6.8	3.3315	4.8748
MLS-0542707	121284526	44.65	29.9	32.7	31.27	1.996	11.8	9	10.411	2.0006
MLS-0020711	863347	40.86	31.1	31.4	31.23	0.177	44.5	38.2	41.342	4.4828
MLS-0427927	85146997	62.1	29.2	33.3	31.22	2.873	0.8	1.9	1.3491	0.75076
MLS-0202055	24807284	43.24	31.4	30.8	31.14	0.417	14.5	19.4	16.949	3.4729
MLS-0294688	26664273	45.57	31.3	30.8	31.03	0.381	133.1	141.7	137.37	6.0683
MLS-0383881	51090245	48.04	30.4	31.7	31.02	0.919	3	-1.5	0.72166	3.1668
MLS-0079090	14729352	69.87	30.8	31.3	31.01	0.353	6.4	3.7	5.0182	1.8863
MLS-0442834	89854589	54.26	29.4	32.6	30.99	2.219	30.5	25	27.76	3.9404
MLS-0211305	17508164	68.41	29.2	32.7	30.91	2.457	27.1	26.6	26.86	0.3681
MLS-0347627	49646431	57.09	27.9	33.8	30.86	4.124	1.6	-2.4	-0.40928	2.8074
MLS-0402721	57256655	43.57	32.2	29.3	30.75	2.064	40	38.9	39.446	0.83512
MLS-0239624	24811156	49.65	26.8	34.6	30.71	5.501	13.3	9.5	11.395	2.7014
MLS-0348597	49645275	40.8	31.5	29.8	30.68	1.182	59.4	61.9	60.674	1.7653
MLS-0018910	859523	41.07	30.1	31.3	30.68	0.825	30.7	36.2	33.464	3.9339
MLS-0214742	17506927	50.19	28.9	32.4	30.68	2.465	-1.4	0	-0.68104	0.97614
MLS-0012726	7978218	49.46	31.7	29.5	30.61	1.583	11.2	15.6	13.393	3.1509
MLS-0465832	121285296	53.93	30.2	30.9	30.58	0.486	19.7	26.6	23.139	4.8767
MLS-0036400	7978092	41.71	31.1	30	30.53	0.767	22.5	17	19.743	3.8365
MLS-0469523	124753368	48.31	30	31	30.48	0.693	26.6	30.1	28.333	2.4644
MLS-0102282	89851591	61.4	27.1	33.8	30.46	4.742	33.7	16.9	25.331	11.873
MLS-0307247	26728967	47.94	32.1	28.4	30.26	2.653	2.6	2.6	2.6115	0.0016992
MLS-0350728	47202228	415.43	22.4	38	30.20	11.072	-4.6	-1	-2.7805	2.536
MLS-0233034	22400391	116.68	33.4	26.8	30.11	4.609	29.8	34.9	32.336	3.579
MLS-0008788	4255611	42.59	24.7	35.3	30.02	7.456	10	9.6	9.8133	0.24259
MLS-0349213	47202381	41.29	28.4	31.3	29.85	2.099	17.3	21.4	19.313	2.9011
MLS-0024156	857663	108.03	31.5	28.1	29.83	2.404	41.7	35.8	38.742	4.1833
MLS-0213903	17432394	577.93	29.3	30.2	29.74	0.617	-4	-4.4	-4.1708	0.26033
MLS-0087604	14744890	57.39	27.8	31.7	29.73	2.726	25.5	20.2	22.854	3.687
MLS-0410567	46500579	55.07	27.8	31.6	29.72	2.725	0	2.8	1.4052	2.0091
MLS-0387491	49716148	78.41	40.3	19	29.64	15.034	18.4	4.8	11.605	9.6337
MLS-0327468	49667969	52.56	30.6	28.5	29.54	1.532	4928.1	4933.8	4931	4.0562
MLS-0247601	24826855	55.45	30.5	28.4	29.47	1.496	14.1	-0.5	6.7908	10.37
MLS-0470025	125305998	48.89	25.3	33.5	29.43	5.825	66	66.9	66.468	0.6301
MLS-0038582	3716608	48.77	26.7	31.9	29.29	3.629	7.6	4.4	5.9691	2.2569
MLS-0256413	26665394	40.59	29.9	28.6	29.25	0.933	8.6	12.8	10.73	2.9836
MLS-0000195	856735	62.57	30.2	28.1	29.17	1.468	7.3	8.4	7.8961	0.77833

MLS-0348609	47202467	55.72	28.4	29.9	29.16	1.056	14	24.8	19.415	7.6759
MLS-0443184	89853954	57.59	29.4	28.7	29.06	0.550	18.3	19.8	19.072	1.0969
MLS-0265365	24824561	53.04	29.7	28.3	29.01	1.028	58.4	60.7	59.539	1.5891
MLS-0309854	26664963	42.58	24.9	33.1	28.98	5.772	6	7.8	6.8972	1.268
MLS-0316322	49648686	54.02	27.5	30.3	28.91	2.031	64.7	5.5	35.089	41.898
MLS-0281040	24790693	42.55	30.2	27.5	28.85	1.942	-2	7.2	2.582	6.4819
MLS-0075091	14743041	58.45	26.1	31.3	28.71	3.639	17.5	22.1	19.804	3.2487
MLS-0294733	26671209	42.96	27.8	29.4	28.63	1.126	17.1	13.8	15.446	2.3943
MLS-0214319	17512840	64.07	27.6	29.6	28.62	1.378	2.4	7.8	5.1024	3.7711
MLS-0077326	14732077	40.19	28.3	28.9	28.60	0.418	37.1	39.9	38.506	1.9991
MLS-0338564	49672700	41.84	29.5	27.5	28.49	1.381	78.3	49.5	63.876	20.361
MLS-0229022	22405568	83.85	28.3	28.7	28.46	0.271	203	1433	818.02	869.72
MLS-0469781	125306005	43.9	26.1	30.7	28.39	3.220	36.4	32.8	34.618	2.5873
MLS-0057356	89852066	42.64	26.9	29.7	28.31	1.964	-0.2	0.2	-0.032598	0.30415
MLS-0228725	22408877	41.34	27.6	28.9	28.24	0.873	51.4	51.8	51.641	0.28916
MLS-0208816	17508392	57.73	28.8	27.6	28.19	0.864	8.3	13.7	11.036	3.8362
MLS-0305209	26662509	46.92	26.4	29.9	28.16	2.501	2.4	4.4	3.418	1.4482
MLS-0312852	26665252	61.81	27.5	28.8	28.16	0.883	24.6	18	21.329	4.6379
MLS-0095943	17387170	44.23	23.8	32.3	28.08	6.028	13.1	15.8	14.462	1.9376
MLS-0265145	24823548	50.84	25.7	30.4	28.05	3.292	13.3	15.7	14.502	1.7418
MLS-0294543	26665016	49.09	33.6	22.4	28.00	7.954	10.9	12.2	11.547	0.97251
MLS-0229022	87337275	94.6	22.4	33.5	27.96	7.858	1540	1524.4	1532.2	11.035
MLS-0449640	99356180	44.95	24.8	31	27.93	4.365	10.3	7.5	8.924	1.9989
MLS-0388425	49729303	44.79	29	26.7	27.88	1.622	18.2	16.9	17.542	0.87192
MLS-0444806	92764518	45.14	24.9	30.8	27.85	4.209	26	31.8	28.902	4.0862
MLS-0277417	24804314	41.16	29.6	26.1	27.82	2.446	25.8	23	24.385	2.0064
MLS-0240411	24823947	47.08	26.5	29.1	27.80	1.831	-1.6	4.5	1.4595	4.3004
MLS-0465488	121286403	43.42	25.5	30	27.75	3.126	37.3	29.5	33.386	5.5476
MLS-0458857	103076100	40.51	26.5	29	27.75	1.784	40.1	45.5	42.795	3.8314
MLS-0018238	846686	45.63	32.9	22.4	27.68	7.406	31.6	22.3	26.947	6.5713
MLS-0283096	24780426	42.34	27.9	27.4	27.65	0.403	11.6	1.5	6.5379	7.1603
MLS-0469951	125305993	41.48	24.5	30.7	27.60	4.350	37	43.2	40.101	4.4424
MLS-0462480	103076488	43.94	31.4	23.4	27.44	5.666	28.2	28	28.118	0.10248
MLS-0394572	47195594	41.67	25.2	29.7	27.42	3.153	14.2	16.7	15.453	1.8
MLS-0010916	860753	65.83	24.6	30	27.34	3.815	22.7	20.5	21.578	1.5625
MLS-0326912	49665274	366.45	25	29.6	27.34	3.250	4.9	3.6	4.233	0.88567
MLS-0074442	14744763	42.72	26.9	27.6	27.23	0.510	5.6	9	7.2932	2.3814
MLS-0461988	103060008	40.69	24.7	29.7	27.21	3.565	5.4	4.6	4.9972	0.57017
MLS-0387031	49824532	62.46	25.1	29.2	27.16	2.859	17.8	41.4	29.618	16.694
MLS-0289548	24798349	45.3	28	26.1	27.05	1.314	285.3	267.3	276.29	12.772
MLS-0223067	17504086	62.16	26.3	27.7	27.03	0.971	26.6	43.3	34.913	11.796
MLS-0038318	862972	52.05	25.5	28.5	27.01	2.176	15.4	24.9	20.17	6.6829
MLS-0352696	49731855	42.09	25	29	26.99	2.809	33.4	32.7	33.056	0.52492
MLS-0048870	4244526	52.62	23.2	30.7	26.95	5.356	17.1	15.7	16.406	0.95798
MLS-0254630	24819845	64.67	25.4	28.5	26.95	2.242	22.2	18.4	20.285	2.6989
MLS-0308210	26725679	41.95	25.9	27.8	26.87	1.311	7.3	4.6	5.99	1.9087
MLS-0306684	26662385	41.96	28.3	25.4	26.85	1.985	15.5	10.9	13.217	3.2601
MLS-0425968	85201108	40.33	25.3	28.3	26.77	2.127	8	125.6	66.795	83.153
MLS-0051005	4245784	62.54	29.7	23.5	26.62	4.423	8.2	10	9.0935	1.3068
MLS-0111559	49643803	47.32	27	26.2	26.59	0.547	51.5	46.6	49.05	3.4429
MLS-0296625	26671143	43.46	24.3	28.8	26.57	3.161	23.6	27.7	25.668	2.9117
MLS-0450072	99361053	45.36	24.7	28.4	26.52	2.635	36.9	36.4	36.625	0.35859
MLS-0316151	47194043	126.22	25.7	27.3	26.51	1.159	22.9	21.8	22.346	0.82763
MLS-0443980	47195130	92.31	26.1	26.7	26.38	0.423	58.2	90.1	74.16	22.574
MLS-0207963	17505959	46.17	26	26.7	26.37	0.491	6.7	1.8	4.2741	3.4948
MLS-0462471	103162541	49.18	27.8	24.9	26.36	2.044	11.6	9	10.263	1.8456
MLS-0268041	24793303	84.82	19	33.7	26.33	10.427	1.5	2.5	1.9668	0.6899
MLS-0004709	47193939	44.09	24.3	28.3	26.31	2.850	4.7	5.7	5.2362	0.71734

MLS-0100237	87346530	45.27	24.3	28.3	26.30	2.834	12.9	14.6	13.763	1.1911
MLS-0203116	87336466	42.5	24.5	27.8	26.16	2.380	18.8	17.9	18.362	0.68873
MLS-0209025	17506008	45.37	24.5	27.8	26.13	2.374	-4	-0.8	-2.3594	2.2507
MLS-0032930	864038	47.11	26.6	25.7	26.13	0.653	-0.5	0.4	-0.045005	0.59325
MLS-0263878	24790123	310.52	23.3	28.9	26.09	3.962	23.9	9.8	16.817	9.9692
MLS-0301369	26667323	65.52	25.2	26.9	26.05	1.185	7.5	14.6	11.046	4.9899
MLS-0084161	14726517	65.11	24.8	27.3	26.04	1.717	19.6	17.9	18.754	1.1815
MLS-0317154	46500250	41.31	24.6	27.4	26.03	1.978	143.5	154.1	148.78	7.4967
MLS-0325176	49672872	45.43	22.5	29.4	25.95	4.909	-0.3	3.7	1.6992	2.7858
MLS-0299261	26669337	48.63	18.6	33.2	25.88	10.287	-1.1	-2.7	-1.9194	1.0888
MLS-0460684	103163250	45.16	25.6	26.2	25.87	0.434	47.7	48.8	48.243	0.74214
MLS-0392900	26657706	45.12	25.3	26.3	25.81	0.741	-2.8	-3.2	-2.993	0.2842
MLS-0108262	14729983	49.77	30.5	21	25.79	6.720	12.3	17.2	14.732	3.4463
MLS-0449933	99360561	53.44	25.3	26	25.63	0.501	35.2	44.7	39.913	6.7214
MLS-0054580	4244959	47.73	22.6	28.3	25.46	4.030	14.2	16	15.095	1.2417
MLS-0009436	103051124	46.33	24.1	26.7	25.42	1.860	17.4	21	19.226	2.5585
MLS-0396194	47194769	46.41	24.9	25.9	25.39	0.714	20.3	19	19.683	0.92143
MLS-0256413	24811791	44.8	24.2	26.3	25.22	1.510	10	4.6	7.3096	3.8191
MLS-0393923	47195958	42.34	24.9	25.5	25.21	0.470	38.6	44.3	41.42	4.0149
MLS-0341725	49645355	151.98	31.2	19	25.10	8.571	16.2	24.4	20.302	5.7383
MLS-0339965	47203369	77.46	24.2	26	25.09	1.322	14.1	11.4	12.766	1.8867
MLS-0231782	22401924	43.42	23.4	26.8	25.08	2.425	0.4	5.9	3.1831	3.8867
MLS-0251421	24802516	43.98	21.4	28.7	25.08	5.157	61.5	56.2	58.838	3.7443
MLS-0208592	17508185	43.8	39.9	10.1	24.98	21.045	0.1	5	2.5506	3.4868
MLS-0255145	24825718	62.96	23.4	26	24.74	1.834	32.4	41.7	37.083	6.5893
MLS-0206846	87345910	50.79	24	25.4	24.73	0.970	44.4	41.6	43.032	1.9873
MLS-0283980	24791537	82.19	20.8	28.4	24.60	5.418	45.5	24.9	35.199	14.551
MLS-0000603	859234	45.34	23.6	25.3	24.45	1.228	6.6	7.1	6.8752	0.38645
MLS-0411823	51089742	60.55	20.1	28.5	24.29	5.970	38	47	42.518	6.3683
MLS-0301490	26664819	88.7	24.5	24.1	24.27	0.285	301.8	318.9	310.33	12.096
MLS-0203761	89852802	58.09	24.3	24.2	24.25	0.058	91.2	96.2	93.711	3.5706
MLS-0444851	93577342	97.49	23	25.1	24.09	1.473	6.9	7.8	7.3692	0.65928
MLS-0283700	24805863	51.25	22.7	25.5	24.07	1.987	13.1	19.6	16.33	4.5676
MLS-0387261	49716560	44.36	10.9	37.2	24.03	18.600	13.1	16	14.553	2.0024
MLS-0314997	26725323	45.83	23.5	23.8	23.67	0.234	82.8	106.8	94.776	16.969
MLS-0030430	843664	142.6	25.1	22.2	23.65	2.012	5	2.1	3.5821	2.0497
MLS-0316680	47194029	55.73	22.6	24.6	23.63	1.404	22.7	34.6	28.651	8.3758
MLS-0469964	125306189	43.49	21.2	25.8	23.51	3.276	62.1	43.9	53.026	12.9
MLS-0042741	859755	49.54	21	25.7	23.35	3.328	15.1	14.5	14.82	0.44452
MLS-0031764	842211	52.15	17.7	29	23.31	7.982	26.8	32.7	29.752	4.2096
MLS-0096379	17414907	43.92	22.6	24	23.27	1.004	33.2	38.9	36.077	4.0166
MLS-0101864	17407180	62.92	23.8	22.7	23.24	0.767	16.8	13	14.9	2.7365
MLS-0330503	49680002	46.15	19.8	26.5	23.15	4.782	13	10	11.527	2.1347
MLS-0214843	17507806	217.16	24.5	21.6	23.04	2.095	-2	-4.5	-3.2306	1.7274
MLS-0247043	24822958	58.49	20.8	25.1	22.95	3.062	267.5	263.2	265.34	3.0408
MLS-0298334	26665638	99.73	23.3	22.4	22.83	0.648	2.6	5.9	4.2966	2.3339
MLS-0203019	22400603	52.47	20.9	24.5	22.72	2.517	41.8	37.3	39.534	3.1479
MLS-0259049	24830376	64.18	18.6	26.9	22.72	5.861	6.1	7.7	6.9049	1.1041
MLS-0448191	99356047	44.61	20.8	23.2	22.00	1.764	23.2	21	22.104	1.4957
MLS-0093455	17408606	58.69	20.2	23.7	21.93	2.510	8.8	3.2	6.0282	3.9631
MLS-0054584	4241254	58.78	21.2	22.6	21.89	0.982	14.5	33.6	24.061	13.46
MLS-0006772	87338738	55.09	21.1	22.4	21.75	0.884	6.1	2.6	4.3479	2.4608
MLS-0253517	24817208	42.63	21.9	21.5	21.72	0.318	18.2	23.3	20.725	3.6139
MLS-0314914	26725319	41.62	21.2	22	21.58	0.533	127.4	109.7	118.53	12.484
MLS-0347210	47202663	42.29	20.7	22.2	21.46	1.071	11.1	16.4	13.749	3.6896
MLS-0424552	85146976	46.07	24.3	18.4	21.36	4.217	1.8	2.9	2.3609	0.75953
MLS-0052307	4251071	60.73	18.5	23.8	21.14	3.772	217.9	209	213.41	6.2786
MLS-0282488	24790280	57.24	15.9	26.3	21.11	7.404	2	1.5	1.7166	0.36577

MLS-0388389	49815773	45.82	16.4	25.6	21.00	6.495	14.2	17.9	16.052	2.6462
MLS-0248679	24810560	148.79	22.1	19.8	20.96	1.618	7	1.5	4.269	3.927
MLS-0040041	24839931	41.65	21.5	20.2	20.89	0.933	8	9.7	8.8586	1.1602
MLS-0274547	24781414	40.85	22.8	18.9	20.87	2.770	29.1	36.6	32.868	5.3047
MLS-0034420	7972581	49.81	25.9	15.6	20.75	7.253	10.9	16.1	13.496	3.6301
MLS-0210304	17507604	52.95	19.4	20.8	20.06	0.988	79.6	82.4	81.015	2.021
MLS-0102266	17401575	52.16	20.3	19.6	19.95	0.434	-3.7	1.6	-1.0199	3.7484
MLS-0348560	49643980	42.03	18.9	20.8	19.86	1.407	13.1	21.6	17.323	6.0122
MLS-0225405	17513886	46.69	19.6	20	19.82	0.260	195	160.9	177.95	24.05
MLS-0267802	24818133	57.16	19.6	19.9	19.75	0.146	2.7	0.4	1.5177	1.6479
MLS-0031621	50086106	40.06	17.7	21.7	19.71	2.776	5.6	10.4	8.0013	3.382
MLS-0307188	47194024	46.12	19.5	19.9	19.68	0.279	14.4	18.7	16.561	3.0035
MLS-0024967	3717110	70.99	19.2	19.8	19.48	0.462	19.3	17.8	18.527	1.0666
MLS-0296976	26670794	46.98	18.4	19.7	19.05	0.892	1.6	4.9	3.2465	2.3178
MLS-0280197	24789007	51.13	19.4	18.7	19.01	0.487	10.7	25.1	17.919	10.208
MLS-0311857	26664308	60.3	17.2	20.7	18.93	2.456	75.9	43.8	59.853	22.732
MLS-0233195	14730197	40.98	20.5	17.3	18.89	2.269	34.9	31.4	33.115	2.4852
MLS-0350282	49642490	40.97	13	24.8	18.89	8.366	-0.6	1.3	0.3789	1.341
MLS-0074728	14744232	43.85	21.2	16.5	18.86	3.308	17	20.7	18.883	2.5999
MLS-0387073	49716564	42.79	17.5	20.2	18.85	1.961	16.9	18.8	17.891	1.3465
MLS-0207546	17514505	43.11	18.9	18.8	18.83	0.084	41.9	48.3	45.132	4.5117
MLS-0216347	17505234	56.62	7.7	29.1	18.44	15.124	8.9	10.2	9.5592	0.90695
MLS-0026313	87336217	53.59	17.6	19.3	18.41	1.190	6.8	9.2	8.0066	1.7058
MLS-0095203	14732315	71.7	18.2	18	18.07	0.135	26.5	25.5	25.959	0.69854
MLS-0027075	3716820	58.23	6.1	29.8	17.96	16.790	3	18.1	10.567	10.631
MLS-0279264	26662323	46	17.8	17	17.41	0.550	17.4	15.7	16.56	1.1466
MLS-0266105	24792009	42.94	15.4	19.2	17.29	2.662	13.5	10.9	12.237	1.8505
MLS-0106754	14733179	41.93	12.1	22.4	17.22	7.290	16.1	20.2	18.147	2.8664
MLS-0265956	24788160	65.6	15.5	18.5	17.03	2.105	26.6	26	26.277	0.39933
MLS-0345909	49643589	52.15	15.7	18.3	17.02	1.848	2.8	0.5	1.6189	1.6309
MLS-0440659	89855708	41.14	16.5	17.5	17.00	0.648	37.8	45	41.413	5.106
MLS-0042549	47193961	51.73	16.6	17.3	16.97	0.502	9.6	10.9	10.252	0.93333
MLS-0352200	47204727	78.45	16.8	16.4	16.61	0.297	3.9	8.1	5.9905	2.9599
MLS-0424422	74373423	73.77	18.9	14	16.43	3.428	12.7	14.8	13.774	1.4485
MLS-0426511	81066048	67.66	16.3	16.3	16.30	0.019	13.8	8.7	11.258	3.6101
MLS-0240750	24815551	46.44	16.8	15.2	16.00	1.110	-0.5	-4.9	-2.7031	3.1572
MLS-0344194	47201220	61.13	14.1	17.9	16.00	2.718	7	9.2	8.1155	1.5126
MLS-0213446	17507910	72.28	13.9	18.1	15.97	2.954	10.5	17.9	14.229	5.2359
MLS-0313513	24779974	62.95	14.5	17.4	15.95	2.067	0.5	2.4	1.464	1.3781
MLS-0215169	17512485	44.86	15.1	16.3	15.70	0.831	1.9	-0.1	0.90232	1.4467
MLS-0002060	858812	43.07	14.1	16.9	15.52	2.007	20.7	20.8	20.757	0.010862
MLS-0315421	26732436	66.68	15.7	15.3	15.50	0.244	5	6.7	5.8462	1.2341
MLS-0001386	87348557	99.58	15	15.9	15.44	0.613	8.6	7.8	8.1913	0.51805
MLS-0426943	85198147	40.92	14.9	15.9	15.40	0.662	9.4	11.5	10.428	1.446
MLS-0464773	121283339	56.11	11.7	18.8	15.25	5.006	11	10.7	10.865	0.25317
MLS-0077253	14732724	52.76	13.2	17.3	15.23	2.921	-0.1	5	2.4713	3.5901
MLS-0097855	17406894	48.28	14.9	15.3	15.10	0.332	145.9	160	152.95	9.9399
MLS-0207234	22401763	48.74	9.4	20.7	15.06	8.045	2.3	1.1	1.6631	0.84797
MLS-0045400	4250128	41.37	10.6	19.1	14.84	6.045	14	7.2	10.575	4.8271
MLS-0316497	49648685	95.18	14.3	14.6	14.45	0.237	2.5	-0.1	1.1845	1.8825
MLS-0057224	87346854	82.51	14.3	14.3	14.32	0.042	7.2	4.8	5.9658	1.6858
MLS-0247361	24826663	45.01	14.9	13.5	14.22	1.011	11.2	12	11.575	0.5905
MLS-0096461	14730036	46.03	13.5	14.9	14.17	0.984	22	20.6	21.28	0.95965
MLS-0031311	7978031	40.69	17.1	11.2	14.17	4.136	18.4	18.7	18.524	0.23396
MLS-0449974	99360649	40.57	11.7	16.6	14.14	3.475	10.9	17.7	14.257	4.8137
MLS-0291618	87345236	65.56	11.3	16.6	13.98	3.718	111.4	102.4	106.88	6.397
MLS-0067333	7967449	58.17	12.4	15.5	13.93	2.154	-0.6	0	-0.31664	0.45547
MLS-0075360	14744867	73.82	17.8	10	13.93	5.481	6.8	4	5.3718	1.9745

MLS-0286705	24801143	78.71	13.3	14.5	13.90	0.912	9.9	13.5	11.71	2.5553
MLS-0261520	24829984	43.03	15.1	12.7	13.89	1.704	-5.2	-2.5	-3.8286	1.9308
MLS-0237486	24815500	75.33	13.2	14.3	13.75	0.823	3	0.5	1.7277	1.7766
MLS-0101756	17406690	50.54	10.5	16.9	13.72	4.565	114	102.7	108.37	7.983
MLS-0078810	14735966	51.02	16.4	11	13.69	3.797	11.2	15	13.117	2.7323
MLS-0202725	22402082	132.13	13.8	13.2	13.49	0.375	-1.3	-1.6	-1.4788	0.23372
MLS-0104657	16953249	132.03	14.6	12.2	13.37	1.698	1.3	2.3	1.8212	0.71065
MLS-0313205	26664679	45.86	12.5	14	13.26	1.060	3	3.3	3.1729	0.19182
MLS-0367528	49821066	41.46	12.8	13.6	13.21	0.552	2.6	0.2	1.4316	1.6944
MLS-0426976	85198192	57.47	10	16.3	13.17	4.417	9.1	6.4	7.736	1.8596
MLS-0466843	124755650	40.6	13	13	12.98	0.011	-0.1	8.5	4.2182	6.1204
MLS-0074109	14742458	54.32	12.4	12.5	12.48	0.066	137.8	134.1	135.95	2.5552
MLS-0228878	17504780	158.69	12.6	12.2	12.38	0.253	34.3	58.1	46.206	16.828
MLS-0263848	24830789	42.18	12	12.6	12.34	0.411	17.1	27	22.048	6.9842
MLS-0286004	24787267	63.43	10.6	14	12.30	2.451	0.6	3.3	1.9413	1.9172
MLS-0387035	49826124	43.55	10.4	13.9	12.12	2.484	6.6	7.1	6.8914	0.34593
MLS-0094519	17409604	41.53	9.9	12.7	11.30	2.046	12.9	21.4	17.137	5.9731
MLS-0241182	26662643	324.3	13.5	8.9	11.17	3.242	13.4	15.6	14.505	1.4944
MLS-0038084	87347058	43.86	11	11	11.01	0.038	9.8	11.2	10.498	1.001
MLS-0342668	47201179	40.79	14	8	10.99	4.245	238.3	366	302.13	90.296
MLS-0078200	14731693	44.16	9.6	12.2	10.90	1.778	3.7	8.5	6.1003	3.3832
MLS-0250633	24822108	46.61	7.6	14.1	10.82	4.603	8.5	7.9	8.2285	0.43374
MLS-0104688	17388187	54.02	9.8	10.9	10.39	0.787	4.8	9.8	7.3257	3.5587
MLS-0444495	92763343	350.52	9.3	10.8	10.05	1.052	16.6	15.9	16.228	0.52579
MLS-0097449	17386002	58.65	9.9	9.5	9.69	0.335	5.8	10	7.9127	2.9834
MLS-0095147	14745880	113.7	8.7	9.3	8.99	0.441	14.3	9.2	11.716	3.5921
MLS-0054704	4241799	49.52	8.4	9.1	8.71	0.477	8.8	4.6	6.6947	3.0081
MLS-0083552	14727982	56.37	5.7	11.5	8.60	4.067	3.9	-4	-0.04855	5.5574
MLS-0234337	17504199	68.6	8.5	8.7	8.58	0.155	13.8	17.3	15.533	2.4508
MLS-0297819	26663670	63.14	13.6	3.4	8.52	7.208	-0.2	-3	-1.5991	2.0395
MLS-0010570	4262781	43.03	8.4	8.3	8.36	0.015	7.3	5.2	6.264	1.4898
MLS-0000794	87347331	50.83	8.2	8.5	8.34	0.209	13.9	12.6	13.272	0.92665
MLS-0444885	92763337	86.11	9.8	6.8	8.27	2.134	4.9	5.7	5.319	0.56726
MLS-0274366	24788137	66.66	6.5	9.9	8.20	2.390	8.4	4.3	6.3525	2.8607
MLS-0247756	24779559	57.54	8	8.2	8.13	0.115	41	31.8	36.418	6.478
MLS-0264364	24822906	43.86	7.3	8.1	7.73	0.586	9.5	13.3	11.395	2.7447
MLS-0106970	16953552	48.71	9	6	7.53	2.100	11.3	8.9	10.111	1.6553
MLS-0351126	49643266	43.74	8.5	6.2	7.32	1.607	6.3	7.6	6.9275	0.90554
MLS-0373218	50086447	75.25	6.7	7.8	7.22	0.801	2	2.6	2.2992	0.41216
MLS-0293599	26661766	40.88	7.9	6.3	7.10	1.134	7.8	7.6	7.7025	0.11881
MLS-0244672	24809503	62.78	7.5	6.6	7.08	0.611	6.7	7.1	6.92	0.24342
MLS-0218875	22411056	43.72	6.9	7	6.95	0.134	2.2	3.8	2.9702	1.1371
MLS-0024741	4257041	116.78	6	7	6.50	0.655	6	3.7	4.8619	1.6085
MLS-0416645	57265589	59.63	6.7	5.9	6.31	0.600	0.9	0.5	0.72991	0.28298
MLS-0282398	24787641	264.05	9.5	3.1	6.28	4.546	1.4	0.6	0.99595	0.60834
MLS-0026642	4255865	141.33	6.3	6.1	6.21	0.083	8.9	7.5	8.1927	1.0023
MLS-0439806	92764029	48.45	7.3	5.1	6.17	1.547	-3.2	0	-1.5625	2.2565
MLS-0070251	14729420	51.29	6.7	5.3	6.01	0.952	3.3	1.7	2.4929	1.1535
MLS-0104366	17388139	46.21	5.5	5.4	5.44	0.079	7.4	9.4	8.3859	1.3641
MLS-0351065	47195101	41.09	5.6	5.2	5.41	0.244	5.4	0	2.7196	3.827
MLS-0262906	24829716	47.31	3.9	6.6	5.24	1.916	3.8	1.3	2.5412	1.7689
MLS-0428110	85201134	47.17	6.4	3.8	5.08	1.836	1.9	3.1	2.5115	0.89239
MLS-0338953	49680307	65.06	4.8	5.2	5.00	0.250	-1.3	5.5	2.1217	4.7856
MLS-0228132	22403527	67.05	2.7	7.2	4.98	3.170	5.9	3.4	4.6417	1.735
MLS-0424410	81066520	43.41	4.2	5.5	4.87	0.927	3.6	-0.4	1.5715	2.8476
MLS-0078536	14731589	1936.3	8.1	1.5	4.78	4.629	-3.1	6.4	1.633	6.6779
MLS-0242541	24811141	81.22	6.2	3	4.60	2.252	16.8	18.2	17.526	0.99152
MLS-0456289	99494946	47.64	4.8	4.4	4.58	0.313	3.6	4.8	4.1991	0.88956

MLS-0258658	24835227	96.24	2.7	6.4	4.52	2.618	1.4	-3.2	-0.90253	3.2499
MLS-0012377	856448	83.43	3.6	5.2	4.38	1.117	1.1	-2.2	-0.54781	2.3229
MLS-0017514	87348833	346.75	2	6.7	4.35	3.359	-2.9	4	0.53549	4.9102
MLS-0089295	14726694	44.67	5.1	3.5	4.28	1.134	6.8	2.6	4.6908	2.9842
MLS-0293669	26666914	356.63	5.1	3.4	4.24	1.234	13.2	6.6	9.9161	4.701
MLS-0218553	22404392	95.66	3.3	4.9	4.11	1.138	0.2	3.2	1.7031	2.113
MLS-0255727	24825321	41.56	3.4	4.6	3.99	0.823	34.4	38.4	36.414	2.7954
MLS-0096929	17407599	52.12	3.5	4.4	3.96	0.656	3.5	1.3	2.3624	1.5713
MLS-0001259	103074680	66	3	4.7	3.89	1.211	3.9	3.5	3.7015	0.22727
MLS-0432244	85270037	80.04	5.5	2.3	3.89	2.314	4	2.8	3.4335	0.85932
MLS-0221868	22403574	42.39	3.9	3.7	3.81	0.156	-6.8	2.3	-2.2428	6.3859
MLS-0101554	17403254	40.31	2	5.2	3.58	2.234	-1.8	3.1	0.61939	3.4831
MLS-0002332	860745	86.58	2.4	4.4	3.39	1.465	1	3.8	2.3851	2.0271
MLS-0449647	99361035	105.17	2	4	2.98	1.406	-0.1	1.7	0.7907	1.2252
MLS-0239913	24814268	47.03	1.6	4.4	2.97	1.982	1.4	2.9	2.1287	1.0463
MLS-0242542	24810956	67.17	2.4	3.4	2.93	0.721	8	8.3	8.1251	0.19584
MLS-0049980	4249399	219.07	2	3.8	2.88	1.283	2.9	0.5	1.7042	1.6507
MLS-0041639	847855	47.31	1.1	4.6	2.88	2.470	-0.2	3.1	1.4511	2.2867
MLS-0278152	24801023	60.54	2.2	3.5	2.83	0.880	2.8	-2.7	0.082457	3.8909
MLS-0545915	136947222	74.18	4.2	1.4	2.79	2.006	-2.2	2.4	0.084529	3.2951
MLS-0335983	49680242	47.45	1.1	4.4	2.73	2.293	-0.6	2.9	1.1854	2.4807
MLS-0251291	24802713	45.91	4.7	0.5	2.60	3.020	-0.2	1	0.39997	0.90231
MLS-0039666	851627	168.27	1.9	3.2	2.57	0.954	0.4	1.3	0.85425	0.5732
MLS-0025941	4260709	132.16	-0.7	5.7	2.54	4.527	2.8	3.4	3.1044	0.4639
MLS-0440755	89853583	46.31	0.3	4.6	2.45	3.057	-1.2	-0.9	-1.024	0.23102
MLS-0026208	87336594	44.8	5.6	-0.7	2.41	4.454	-0.4	0.5	0.045299	0.6109
MLS-0345020	47197534	44.19	0.8	4	2.38	2.291	-3.3	-2.4	-2.8651	0.60269
MLS-0039928	858818	72	-0.1	4.8	2.35	3.414	0.3	1.1	0.68793	0.54604
MLS-0274022	24793502	57.58	0.7	4	2.34	2.349	3.1	-2.9	0.068039	4.2257
MLS-0018941	845505	56.13	-0.8	5.3	2.28	4.325	-1.4	-4.3	-2.8332	2.0572
MLS-0253333	24817177	41.83	0.9	3.6	2.25	1.865	2	3.2	2.6319	0.86663
MLS-0388269	49729254	55.19	2.7	1.8	2.22	0.625	3.4	-1.2	1.1175	3.2541
MLS-0098953	17414749	100.89	3.2	1.1	2.18	1.464	-1.9	-4.7	-3.2902	1.9849
MLS-0012439	865768	46.58	1.6	2.5	2.08	0.619	-0.6	2.2	0.79753	2.0463
MLS-0245276	24803024	78.92	2.1	1.9	2.00	0.071	-1.8	2.2	0.15515	2.8263
MLS-0024719	3711296	396.89	0.5	3.3	1.93	1.966	-2	-0.3	-1.1242	1.1903
MLS-0044229	4263410	137.73	1.6	2.2	1.91	0.432	0	3.3	1.6489	2.3471
MLS-0434270	85269119	65.07	1.8	2	1.86	0.148	2	-0.8	0.61596	1.9882
MLS-0287599	24787525	341.4	3.2	0.5	1.85	1.970	-2.4	-3.7	-3.0644	0.95202
MLS-0058224	4247588	150.29	0.9	2.7	1.82	1.253	0.4	0.1	0.27493	0.18007
MLS-0092873	17387903	81.29	2.4	1.2	1.80	0.841	2.4	-0.5	0.9603	2.0843
MLS-0280288	24789121	42.58	2.4	1.2	1.80	0.875	5.4	-0.1	2.6517	3.9483
MLS-0359718	49822144	368.77	1.4	2.1	1.78	0.513	-5.7	5.5	-0.11295	7.9581
MLS-0057793	3711962	617.08	0.2	3.3	1.75	2.217	-1	-0.1	-0.55194	0.6718
MLS-0291868	24822492	70.51	0.8	2.7	1.73	1.379	4	1.2	2.5709	1.9631
MLS-0411393	56463734	145.88	0.8	2.6	1.70	1.243	1.2	1.2	1.212	0.051388
MLS-0096391	17414988	80.7	-0.3	3.7	1.70	2.775	0.1	0.1	0.087638	0.017965
MLS-0109796	17407417	113.33	0.6	2.8	1.70	1.559	-0.3	0.7	0.16917	0.70982
MLS-0038770	865664	291.72	1.6	1.7	1.65	0.138	3.6	1.1	2.3638	1.748
MLS-0238531	24832247	48.23	1.9	1.3	1.62	0.417	5	-1.1	1.9584	4.3637
MLS-0290407	24788946	115.45	1.2	2	1.60	0.523	-1.2	-0.2	-0.73341	0.72686
MLS-0017850	7973441	75.76	0.1	3.1	1.60	2.098	-4.8	-1.3	-3.0249	2.4511
MLS-0309481	26666372	105.28	0	3.2	1.58	2.235	0.8	1.7	1.2548	0.68045
MLS-0090075	14742150	733.45	1.5	1.6	1.56	0.096	1.6	0.2	0.8962	1.0528
MLS-0050017	4248490	42.42	2.1	1	1.53	0.773	-3.8	-1.9	-2.8533	1.3795
MLS-0035959	7974025	90.19	2.2	0.9	1.53	0.925	6.4	3.8	5.0758	1.87
MLS-0085894	14723489	50.1	1.4	1.6	1.51	0.091	-5.1	-2.3	-3.7132	1.9674
MLS-0096608	17403118	88.55	2.2	0.8	1.50	0.969	-1.2	4.4	1.6117	3.9163

MLS-0109693	17411361	102.22	-0.6	3.6	1.49	2.988	-0.5	0.8	0.15086	0.94043
MLS-0257979	24835064	107	2.1	0.8	1.45	0.980	-0.2	1	0.39967	0.78719
MLS-0426801	85198152	85.89	-0.4	3.2	1.39	2.561	2.8	0	1.4209	1.9536
MLS-0021897	26667463	40.93	-0.3	3.1	1.38	2.407	-1.4	-1.3	-1.3635	0.076455
MLS-0264022	24780682	68.73	1.2	1.5	1.32	0.217	2.7	-0.3	1.1825	2.0854
MLS-0305184	24798786	234.27	0.4	2	1.23	1.140	0.3	3	1.6529	1.975
MLS-0057211	842916	44.13	-1.5	3.9	1.21	3.833	-1.6	1.8	0.081434	2.4415
MLS-0264714	24836342	77.72	-0.1	2.5	1.18	1.820	-4.2	-2.1	-3.1798	1.472
MLS-0441440	89855759	105.7	2.3	0	1.15	1.629	-2.7	1.1	-0.82994	2.6756
MLS-0057780	3714784	98.92	-1.2	3.4	1.10	3.233	0.3	-2.3	-1.0231	1.8671
MLS-0249137	24827686	50.57	0.2	2	1.06	1.267	1.6	-1.7	-0.037699	2.3565
MLS-0038830	865927	43.95	0.1	1.9	1.02	1.244	-1.6	1.5	-0.039983	2.1821
MLS-0031085	4264090	302.24	1.3	0.7	0.99	0.417	3.5	5.5	4.4657	1.405
MLS-0426959	85198182	46.2	0.4	1.5	0.92	0.783	0.1	4.5	2.2903	3.1029
MLS-0093953	17402352	49.65	0.5	1.4	0.91	0.655	2.3	-1.4	0.46193	2.617
MLS-0074138	14742072	51.99	2.4	-0.6	0.89	2.181	2.7	3.1	2.9121	0.25234
MLS-0290091	24797012	823.88	1.2	0.5	0.88	0.484	-2.1	-2.1	-2.081	0.021666
MLS-0078446	14734297	317.22	1	0.6	0.84	0.268	2.5	-0.1	1.2061	1.8119
MLS-0408870	51086200	80.43	1.6	0.1	0.84	1.112	-0.5	2.3	0.86341	1.9977
MLS-0073391	14726333	41.13	-1.5	3.2	0.83	3.318	0.2	-1.4	-0.62462	1.1004
MLS-0307959	26725995	186.3	2.9	-1.3	0.79	3.015	6.8	-4.5	1.1669	7.9929
MLS-0442808	89854016	244.15	1.4	0.1	0.76	0.942	0.1	3.8	1.947	2.6713
MLS-0441445	89855485	107.95	1.5	-0.1	0.74	1.138	-5.7	-1.7	-3.6759	2.8605
MLS-0434363	85268702	102.46	2.9	-1.5	0.72	3.068	1.8	0.9	1.3748	0.64805
MLS-0011156	4247555	48.11	-0.7	2.2	0.71	2.041	1.1	0.5	0.81044	0.36943
MLS-0237093	24809945	164.22	-0.5	1.8	0.63	1.634	-5.3	6.5	0.62827	8.329
MLS-0270542	24818530	176.66	1.5	-0.3	0.62	1.302	0	-1.3	-0.61085	0.90699
MLS-0102590	17416107	77.38	-0.6	1.8	0.61	1.665	2	-0.1	0.9479	1.5078
MLS-0268173	24794948	49.05	-0.4	1.5	0.56	1.293	4.9	-0.2	2.3675	3.6347
MLS-0342322	49643696	50.36	0.6	0.4	0.50	0.081	0	2.2	1.1225	1.5441
MLS-0048845	4251732	437.69	3.3	-2.3	0.49	3.932	-0.5	1.7	0.61998	1.5964
MLS-0003492	4243461	99.49	0.7	0.3	0.46	0.297	6	1.4	3.7074	3.3105
MLS-0270181	24797318	41.01	0.8	0	0.43	0.575	5	-2.1	1.4093	5.0239
MLS-0440125	92764110	40.86	0.3	0.6	0.42	0.188	11.7	10.3	10.962	1.0053
MLS-0040854	4261657	45.23	0	0.8	0.41	0.560	-1.4	-1.5	-1.4388	0.10695
MLS-0310345	26666614	45.81	1	-0.3	0.38	0.936	2.6	-2.8	-0.12061	3.8042
MLS-0368454	49677349	74.22	-1.2	1.9	0.37	2.183	5	3.3	4.1371	1.2486
MLS-0099446	17410910	47.97	-0.8	1.5	0.35	1.606	-1.3	-5.7	-3.4834	3.1173
MLS-0453896	99359191	44.98	-2.4	3.1	0.33	3.930	-0.9	-1.3	-1.0753	0.30007
MLS-0072596	14723596	708.69	-0.5	1.1	0.27	1.150	-3	-1.5	-2.2775	1.0474
MLS-0039022	863264	175.75	0.5	0.1	0.27	0.265	0.9	-0.7	0.066663	1.1481
MLS-0104304	14726829	44.7	-0.6	1.1	0.27	1.165	-1.6	2.3	0.36504	2.7858
MLS-0398165	56317213	621.79	-0.4	0.9	0.26	0.936	1	1.8	1.3693	0.57979
MLS-0439729	89850693	49.61	0.2	0.3	0.25	0.118	0.8	3.5	2.148	1.9152
MLS-0369180	49734971	44.81	1.9	-1.5	0.24	2.401	3.2	1.9	2.532	0.89949
MLS-0450371	99356247	173.39	-0.3	0.8	0.24	0.735	0.8	-2.4	-0.80061	2.3144
MLS-0018513	851303	517.06	0	0.4	0.22	0.264	58.7	93.2	75.922	24.412
MLS-0044740	7977107	206.53	0.3	0.1	0.21	0.104	2.4	-2	0.20226	3.1731
MLS-0318529	49669155	82.95	0.9	-0.5	0.21	0.997	3.4	3.6	3.5157	0.17281
MLS-0444486	93577366	370.65	0.2	0.2	0.19	0.008	0.2	-0.8	-0.30785	0.75001
MLS-0452507	99357191	110.33	-0.8	0.9	0.04	1.194	1.9	1.7	1.8234	0.11595
MLS-0074430	14744811	79.28	-1	1	0.03	1.440	1.4	-0.6	0.37035	1.4363
MLS-0278306	24790358	50.14	-1.6	1.6	0.02	2.230	-0.8	-5	-2.9004	2.924
MLS-0470143	125306951	1015.4	-2.5	2.4	-0.05	3.435	-2.1	-4.1	-3.1025	1.4083
MLS-0238280	24808780	421.89	1.1	-1.3	-0.07	1.725	-1	-1.9	-1.458	0.66144
MLS-0209799	17514976	93.63	-0.6	0.5	-0.08	0.748	2.7	-0.2	1.2241	2.0596
MLS-0249416	24827148	44.52	0.5	-0.8	-0.14	0.940	-3.2	0.2	-1.5153	2.3603
MLS-0362051	49736554	63.04	-0.5	0.1	-0.18	0.410	-4.2	-1.6	-2.8902	1.8184

MLS-0041460	862011	86.05	-0.1	-0.3	-0.22	0.179	-5.4	-6.7	-6.0219	0.89824
MLS-0387121	49729316	50.69	0	-0.5	-0.23	0.317	1.8	0.1	0.9479	1.1393
MLS-0343748	49641169	49.43	-2.4	1.9	-0.24	3.083	0.8	1.6	1.1878	0.55992
MLS-0429433	85268023	95.51	-0.6	0.2	-0.25	0.572	0.7	-4.1	-1.6624	3.4018
MLS-0088950	14730252	47.57	0.7	-1.3	-0.25	1.416	2.7	1	1.8212	1.212
MLS-0455084	103060167	56.87	-1.5	1	-0.26	1.817	-1.4	-2.2	-1.7953	0.5664
MLS-0551674	144095811	50.13	-1.5	0.9	-0.28	1.716	-5.6	-4.3	-4.9452	0.90672
MLS-0237337	24811494	46.58	0.9	-1.5	-0.29	1.724	1.3	2.1	1.685	0.55991
MLS-0013059	861292	55.99	-0.6	0	-0.33	0.444	-3.9	-1.7	-2.8246	1.5337
MLS-0433861	85268712	49.01	-0.3	-0.5	-0.37	0.130	-2.2	0.6	-0.8278	1.9779
MLS-0230223	22408146	197.44	-1.4	0.7	-0.37	1.486	0.4	2.3	1.3191	1.3434
MLS-0010959	7972469	267.99	-1.5	0.7	-0.42	1.576	1.7	3.5	2.604	1.3056
MLS-0008682	848282	82.87	-1.4	0.5	-0.44	1.289	2.7	1.1	1.8826	1.1184
MLS-0445269	93577163	152.5	-1.5	0.6	-0.45	1.490	-0.2	1.8	0.78796	1.389
MLS-0249006	24820494	97.44	-0.6	-0.3	-0.45	0.176	0.7	85.7	43.199	60.094
MLS-0037620	4261028	53.27	-0.6	-0.4	-0.48	0.124	0	-0.2	-0.087841	0.12492
MLS-0456780	103075933	41.14	0	-0.9	-0.48	0.645	-0.4	2.1	0.84325	1.748
MLS-0441780	89854750	336.01	-1.3	0.3	-0.48	1.119	-3	-1.2	-2.109	1.2192
MLS-0029136	846062	651.19	0	-1	-0.50	0.732	-0.7	-4.5	-2.6092	2.6488
MLS-0037307	846887	106.93	-3.4	2.4	-0.51	4.058	0.5	-1.8	-0.66243	1.5876
MLS-0245093	24788917	216.44	-0.2	-0.8	-0.54	0.434	-4	-2.5	-3.245	1.0009
MLS-0253508	24817343	74.76	-0.5	-0.5	-0.54	0.003	1.5	4.6	3.035	2.2311
MLS-0290857	24833114	42.64	-0.7	-0.4	-0.57	0.223	3.7	1.1	2.4262	1.842
MLS-0059885	7965691	50.21	-1.5	0.3	-0.58	1.271	-0.3	-3.6	-1.9461	2.3445
MLS-0340534	49644696	43.25	-2.4	1.2	-0.62	2.526	1.9	-1	0.41281	2.056
MLS-0398314	56322257	1501.4	-0.8	-0.4	-0.63	0.309	-1	694.8	346.88	491.98
MLS-0272041	24795078	42.64	1.9	-3.3	-0.71	3.636	-1	-3	-2.014	1.4537
MLS-0086896	14720597	45.31	-1.5	0	-0.71	1.052	-1.1	-4.2	-2.6444	2.2272
MLS-0439497	92764106	53.83	2	-3.4	-0.72	3.778	0.6	2.1	1.3586	1.0805
MLS-0363059	49730725	144.2	-1.2	-0.4	-0.77	0.542	0.5	3.2	1.8416	1.8992
MLS-0009334	850814	205.59	-0.3	-1.3	-0.77	0.675	-1.2	4.8	1.8155	4.2698
MLS-0101373	17412745	42.56	-2.5	0.9	-0.78	2.435	0.1	-1.3	-0.60128	1.0332
MLS-0086561	14727734	71.13	-2.6	1	-0.78	2.515	-0.4	-0.7	-0.5625	0.17429
MLS-0033624	7974410	41.02	-0.7	-0.9	-0.79	0.141	0.3	-3	-1.3358	2.3146
MLS-0089701	14734209	543.09	-2.7	1	-0.83	2.644	0.4	-0.6	-0.078978	0.70397
MLS-0106729	14730177	93.41	-2	0.4	-0.84	1.698	-1.2	1.9	0.34465	2.2531
MLS-0026629	4264297	82.37	-2.1	0.4	-0.85	1.793	-1.2	-2.5	-1.853	0.87818
MLS-0456549	99454305	46.79	-0.5	-1.4	-0.93	0.627	-1.8	0.7	-0.53514	1.7506
MLS-0244609	24809791	1841.7	-0.6	-1.3	-0.93	0.452	2.2	1.4	1.7689	0.56713
MLS-0441759	89854157	927.24	-0.7	-1.2	-0.93	0.319	1.8	3.6	2.6701	1.2719
MLS-0262015	24831728	45.88	-1.3	-0.5	-0.94	0.551	-2.7	0.8	-0.98934	2.4873
MLS-0448479	103076566	43.33	-0.6	-1.3	-0.95	0.471	-4.6	-1.9	-3.2632	1.9537
MLS-0461984	103076660	176.55	-0.9	-1	-0.96	0.117	2.2	-3	-0.41537	3.6859
MLS-0049960	4252385	45.8	-2.4	0.4	-0.99	1.981	-1.4	-3.7	-2.5611	1.6657
MLS-0364736	49722207	51.1	0.3	-2.3	-1.03	1.859	-0.2	-2.4	-1.2833	1.5644
MLS-0106134	17387208	41.97	0.1	-2.3	-1.11	1.647	-4.2	2	-1.0739	4.3671
MLS-0037395	4255981	47.93	-1.7	-0.5	-1.12	0.853	-3.4	4.7	0.64155	5.7621
MLS-0333743	49730561	71.94	-0.4	-1.9	-1.14	1.105	4.8	8	6.4258	2.2837
MLS-0456195	99454884	86.55	-0.5	-1.8	-1.16	0.978	-5.9	5.6	-0.13952	8.1063
MLS-0456202	103060898	45.73	-1.4	-0.9	-1.16	0.334	-2.9	1.3	-0.77373	2.9547
MLS-0244872	24783537	193.6	-1.4	-0.9	-1.17	0.380	-1.5	0.7	-0.38375	1.5875
MLS-0343913	47200632	48.65	-3.2	0.9	-1.18	2.918	-2	1.6	-0.17343	2.5723
MLS-0389136	49731012	181.12	-2.3	-0.1	-1.24	1.567	8.2	-0.3	3.9219	6.0374
MLS-0231136	22412611	156.64	-1.8	-0.7	-1.25	0.763	-2.6	-1.7	-2.1537	0.68964
MLS-0457315	99494710	51.46	-0.7	-1.9	-1.26	0.861	-1	3.1	1.0669	2.8583
MLS-0543399	121283651	50.8	-2.9	0.3	-1.29	2.213	-5.2	-2	-3.5511	2.2625
MLS-0069395	14731519	119.77	-1.9	-0.8	-1.34	0.733	2.6	1.2	1.9036	1.0428
MLS-0231382	22411646	188.06	-2.6	-0.1	-1.34	1.793	2.3	2.7	2.4891	0.3202

MLS-0406055	57262763	1697.1	-1.5	-1.2	-1.35	0.215	-1.6	-0.9	-1.2112	0.49468
MLS-0450789	99360824	136.49	0	-2.8	-1.36	1.972	-2.1	-1.6	-1.8601	0.37025
MLS-0031808	3717361	70.85	-3.6	0.9	-1.37	3.163	-6.2	-0.3	-3.2444	4.1312
MLS-0086722	14728054	210.18	-1.9	-0.8	-1.37	0.768	-4.3	-4.1	-4.2069	0.099433
MLS-0375256	49821192	153.75	-1.4	-1.4	-1.43	0.016	1	2.7	1.8416	1.2425
MLS-0276659	24796433	44.08	-2.4	-0.5	-1.45	1.333	-4.6	0.3	-2.1327	3.4398
MLS-0259129	24827312	40.18	-1.2	-1.8	-1.48	0.462	-4	-2.8	-3.3886	0.80885
MLS-0401882	56316211	47.06	-1	-2.1	-1.52	0.754	6.5	4.5	5.5063	1.3834
MLS-0303052	26658350	50.49	-1.3	-1.7	-1.54	0.287	-2.4	0.1	-1.1735	1.7528
MLS-0440844	89852476	188.08	-2.7	-0.4	-1.55	1.598	-0.7	-1.5	-1.1241	0.5556
MLS-0469822	125306924	85.07	-0.7	-2.5	-1.60	1.305	-5.5	-1.7	-3.5947	2.7176
MLS-0398028	56318030	149.9	-0.4	-2.9	-1.64	1.737	-2.5	-4.2	-3.3121	1.189
MLS-0442138	87335573	95.83	-2.1	-1.2	-1.66	0.600	-3	-3.8	-3.3658	0.57979
MLS-0032990	852595	79.35	-4.1	0.8	-1.67	3.475	-5.1	-0.7	-2.9023	3.163
MLS-0066557	89855991	58.58	-2.1	-1.3	-1.70	0.514	-2.4	0.5	-0.94475	2.0201
MLS-0103343	17402013	42	-3.6	0.1	-1.72	2.618	0.4	0.1	0.26662	0.17848
MLS-0406844	56321818	162.43	-3	-0.5	-1.73	1.769	4.9	3.4	4.1456	1.0161
MLS-0445094	92763440	86.43	-2.8	-0.7	-1.74	1.503	0.6	-2	-0.68208	1.8487
MLS-0397331	56315007	196.92	-2	-1.5	-1.74	0.318	-2.7	-4.1	-3.4022	1.0295
MLS-0362085	49719705	209	-1.3	-2.2	-1.76	0.673	-4.6	-1.5	-3.031	2.206
MLS-0271336	24818842	602.78	-1.9	-1.7	-1.79	0.091	-1.1	-7.5	-4.3207	4.5052
MLS-0365777	49821597	46.81	-2.6	-1	-1.82	1.133	-1.3	-0.3	-0.78137	0.67311
MLS-0224022	22415790	51.6	-3.1	-0.6	-1.84	1.786	-2.3	-2.9	-2.5818	0.43729
MLS-0390011	49734893	179.17	-3.6	-0.2	-1.87	2.381	-3.6	-1.4	-2.5145	1.559
MLS-0086415	14721240	62.21	-2.5	-1.4	-1.94	0.752	-1.6	-0.5	-1.0719	0.77708
MLS-0422595	57266086	67.4	-0.4	-3.6	-1.98	2.245	-2.3	1.4	-0.43494	2.6078
MLS-0235856	11533066	318.35	-2.8	-1.2	-2.01	1.111	5	3.5	4.2327	1.0904
MLS-0287427	24797207	111.97	-3.9	-0.2	-2.08	2.624	-4	-2.5	-3.2294	1.0204
MLS-0410641	56462947	84.87	-2	-2.2	-2.14	0.134	-0.7	5.9	2.6232	4.6926
MLS-0420266	57269084	133	-1.7	-2.7	-2.20	0.650	1.5	3.7	2.5931	1.5475
MLS-0416713	56424162	98.93	-1.9	-2.6	-2.22	0.496	-5.2	-1.5	-3.3448	2.641
MLS-0316725	46501380	71.33	-1.4	-3.1	-2.25	1.156	3.8	4.1	3.929	0.22811
MLS-0409308	56316358	66.44	-2.3	-2.2	-2.25	0.049	-0.4	-0.5	-0.45724	0.10671
MLS-0041022	862148	353.01	-3.1	-1.4	-2.25	1.158	0	-0.7	-0.3679	0.51095
MLS-0218813	22402159	473.87	-3.2	-1.5	-2.30	1.197	195.7	-0.1	97.794	138.41
MLS-0006443	850333	49.74	-3.3	-1.4	-2.32	1.338	-2.2	-1.1	-1.6036	0.78126
MLS-0406268	56318885	75.68	-4.6	-0.2	-2.40	3.067	-2.1	1.3	-0.37812	2.4185
MLS-0439622	92764507	43.13	-3.2	-1.9	-2.55	0.922	-0.4	0.4	0.02086	0.57633
MLS-0020512	4256365	142.97	-2.2	-2.9	-2.57	0.476	0.5	-4.3	-1.9085	3.3958
MLS-0442102	89852612	58.88	-4.9	-0.2	-2.57	3.329	-2.3	-0.6	-1.4397	1.1756
MLS-0310709	26657567	42.1	-3.8	-1.7	-2.73	1.504	-0.1	-6.7	-3.4175	4.7095
MLS-0467548	124753975	388.52	-3.5	-2	-2.73	1.061	-3.4	-2.8	-3.0822	0.42948
MLS-0228260	22414151	66.12	-4.2	-1.3	-2.75	2.110	-3.1	-2.9	-2.9916	0.10245
MLS-0028410	851206	54.05	-2.5	-3.1	-2.79	0.407	-2.1	-4.3	-3.2099	1.5234
MLS-0226724	22416214	47.73	-2.7	-3.1	-2.90	0.250	1.2	-3.2	-0.99464	3.0632
MLS-0103471	14730090	482.01	-3.1	-2.8	-2.96	0.247	1.7	-5	-1.6769	4.7068
MLS-0220550	22404349	250.88	-4.7	-1.6	-3.12	2.190	5.2	-1.1	2.0705	4.4931
MLS-0405053	56318170	55.57	-3	-3.4	-3.16	0.283	-0.7	-1.5	-1.1067	0.54134
MLS-0543294	121284186	94.41	-3.9	-2.6	-3.25	0.854	5.3	-3.5	0.90746	6.2437
MLS-0007378	864746	56.44	-2.5	-4.1	-3.28	1.111	-1.1	-3.4	-2.2309	1.6334
MLS-0057365	848713	116.07	-5	-1.6	-3.29	2.370	-2.4	-2.1	-2.2317	0.23062
MLS-0551371	144089513	48.25	-2.6	-4.7	-3.63	1.519	-8	-0.7	-4.3587	5.2093
MLS-0445020	92764140	48.15	-16.7	-15.2	-15.96	1.095	-1.3	-3.9	-2.6149	1.7981

The color coding of the cells is as follows: 1) Yellow = compounds with activity between 32% and 40% in both the primary and secondary assay; 2) Green = compounds with activity between 40% and 50% in both the primary and secondary assay; 3) Blue = compounds with activity >50% in both the primary and secondary assay.

Table S3. *E. coli* DNA gyrase inhibitors identified by screening the MLSMR Library with 50-120% inhibition activities.

		Primary Screen	Hit Reconfirmation using Primary assay				Hit Reconfirmation using pAB1_FL924				Known gyrase inhibitors	Potential DNA intercalators
CPD ID	PUBCHEM_CID	% Act	% Act 1	% Act 2	Avg % Act	Std Dev	% Act 1	% Act 2	Avg % Act	Std Dev		
MLS-0210474	17513072	48.88	51.9	56.5	54.20	3.253	117.2	122.6	119.9	3.7795		
MLS-0409546	56318532	78.5	66	83.4	74.69	12.333	117.4	117.1	117.22	0.20671		
MLS-0295773	26671507	81.14	85.3	87.6	86.49	1.620	116.7	114.7	115.71	1.4121		
MLS-0202656	17513756	53.34	53.8	60.3	57.02	4.609	110.6	119.8	115.2	6.4462		
MLS-0439004	57264815	60.43	48.3	51.9	50.14	2.528	117.4	111.3	114.37	4.2957		
MLS-0444843	92763982	105.95	99.6	104.8	102.20	3.649	107.4	120.7	114.08	9.417		Yes
MLS-0203053	22401238	111.47	88.4	96.6	92.48	5.806	108.6	117.4	112.99	6.252		
MLS-0273125	24780573	96.8	101	95.7	98.34	3.799	111.5	112.8	112.14	0.91378		Yes
MLS-0552225	125001398	111	113.7	114.7	114.21	0.672	108.6	115.3	111.95	4.759		
MLS-0256832	24810463	110.49	86.4	70	78.18	11.640	126.1	93.8	109.98	22.831		
MLS-0222535	17513560	62.31	134	124.1	129.07	7.019	96.5	123.1	109.79	18.814		
MLS-0444611	92764840	98.15	95.4	95.2	95.30	0.101	109.2	109.8	109.54	0.43425		Yes
MLS-0234496	17431609	104.78	106.3	111.4	108.85	3.672	102	116.9	109.45	10.569		Yes
MLS-0319994	49670411	99.15	93.3	95.4	94.32	1.484	106	107.5	106.73	1.0485		Yes
MLS-0283161	24782122	91.68	90.1	98.9	94.49	6.262	104.8	106.8	105.76	1.4174		Yes
MLS-0285192	24807880	103.26	94.3	97.2	95.73	2.055	102.2	109.1	105.64	4.9032		Yes
MLS-0462644	103162706	99.38	101.1	95.9	98.52	3.640	107.8	103.3	105.55	3.2321	Yes, novobiocin	
MLS-0450768	99356320	95.85	85.4	90.9	88.16	3.922	107.6	103.4	105.49	2.9594		Yes
MLS-0301037	26667397	107.81	95.5	94.6	95.06	0.640	106	104.5	105.25	1.0034		Yes
MLS-0294661	26670798	68.18	52.9	55.5	54.21	1.895	95.8	113.7	104.79	12.676		
MLS-0440003	92763358	85.34	83.1	84.9	84.00	1.208	100.9	107.8	104.34	4.8958		Yes, echinomycin
MLS-0320071	49671128	103.15	95.2	99.5	97.37	3.056	106.6	101.6	104.11	3.5971		Yes
MLS-0440040	92764839	97.63	94.9	93.4	94.14	1.031	111.1	96.9	103.98	10.086		Yes
MLS-0301037	51087949	100.15	101.6	98.8	100.22	1.955	103.8	104.1	103.92	0.23396		Yes
MLS-0462642	49681601	91.11	91.9	102	96.97	7.130	104.9	102.8	103.84	1.4378	Yes, Tosufloxacin	
MLS-0320679	49649045	101.47	98.8	101.2	99.99	1.673	98.9	107	102.96	5.7828		Yes

MLS-0069765	14738357	78.33	74.9	71.9	73.42	2.096	95.8	109.6	102.71	9.7077		
MLS-0307751	26732568	87.43	88.5	88.5	88.50	0.054	104.1	100.9	102.52	2.285		**Yes**
MLS-0010472	4242820	101.2	92.5	94	93.23	1.071	97	107.5	102.25	7.3625		**Yes**
MLS-0449103	99356259	93.24	98.8	98.9	98.87	0.046	101.5	103	102.24	1.0209		**Yes**
MLS-0295447	26658614	102.08	99.5	101.1	100.28	1.096	94.4	109.7	102.06	10.825	**Yes Clinafloxacin**	
MLS-0439871	92764757	84.62	87.2	90	88.62	1.964	103.8	99.2	101.52	3.2239		**Yes**
MLS-0088378	14742465	105.69	88.7	100.8	94.79	8.542	97.7	103.3	100.48	3.928		
MLS-0301399	26664947	94.39	103.4	100.7	102.05	1.951	101.2	98.8	100	1.6767	**Yes. Chlorobiocin**	
MLS-0303501	26661126	98.21	93.8	95.1	94.46	0.957	102.1	97.6	99.838	3.2193		**yes**
MLS-0354964	49672752	98.28	98.9	93.9	96.41	3.523	94.9	103.7	99.33	6.2463		
MLS-0221642	22412151	99.06	95.5	94.6	95.05	0.660	102.2	95.9	99.066	4.4083		**Yes**
MLS-0295203	26671247	95.86	95.6	96.6	96.09	0.758	102.9	93.9	98.408	6.416		
MLS-0552861	125001394	86.75	92	92.2	92.12	0.149	98	98.4	98.194	0.23536		
MLS-0099513	17403417	61.44	43.9	57.4	50.66	9.534	104.8	91.6	98.19	9.3791		
MLS-0300411	26730337	77.76	62	63.4	62.69	1.023	95.2	101.2	98.165	4.2596		
MLS-0445106	92764838	104.05	101	104.8	102.91	2.638	99	96.3	97.682	1.9203		**Yes**
MLS-0003163	855596	94.86	94.6	92.2	93.36	1.690	99.4	95.8	97.578	2.5491	**Yes, Enrofloxacin**	
MLS-0306197	26663489	101.04	89.3	91.6	90.43	1.626	100	93.9	96.991	4.3077	**Yes, FQ**	
MLS-0230925	22414089	68.46	61.5	63.2	62.33	1.183	99.2	94.3	96.721	3.465		
MLS-0324653	49669871	98.1	89.9	91.7	90.83	1.270	96.7	95.7	96.236	0.72236		**Yes**
MLS-0420799	57267192	64.46	54.1	52	53.04	1.522	95.5	95.7	95.597	0.09764		
MLS-0293174	26666366	82.69	55.4	57.1	56.23	1.205	95.1	95.6	95.39	0.3547		
MLS-0412451	56463184	89.02	87.4	96.2	91.82	6.255	91.8	96.9	94.345	3.643	**Yes, Nadifloxacin**	
MLS-0371495	49677218	90.35	90.2	89.1	89.62	0.786	94.2	93.9	94.053	0.14819		**Yes**
MLS-0542613	92764750	63.11	65.4	69.9	67.61	3.166	91	97.1	94.025	4.3078		
MLS-0412292	57260400	90.57	98.8	95.8	97.28	2.114	97.1	90.9	93.983	4.3703		
MLS-0440083	92764842	83.1	81	79.6	80.32	0.946	89.2	98.6	93.923	6.6581		**Yes**
MLS-0341433	49642423	95.99	94.7	95.3	94.99	0.437	94.8	92.7	93.754	1.4214		**Yes**
MLS-0291827	49681682	93.16	101.2	95.1	98.14	4.284	91.1	96.2	93.653	3.6282	**Yes, Levofloxacin**	
MLS-0357036	49672722	58.06	60.8	64.8	62.82	2.843	90.2	96.9	93.549	4.7684		

MLS-0342526	47201137	114.26	66.9	73.4	70.14	4.560	74.7	111.9	93.306	26.339		
MLS-0318020	49681620	97.5	97.1	92.9	95.00	2.935	90.9	95.5	93.214	3.2591	**Yes, FQ**	
MLS-0207270	17511114	65.09	46.1	58.5	52.32	8.774	81.7	104.7	93.207	16.236		
MLS-0444236	93576680	84.78	89.6	94.7	92.13	3.617	93.2	92.9	93.058	0.24579	**Yes, FQ**	
MLS-0059977	7968423	89.39	94.4	90.3	92.34	2.891	92.7	93.4	93.044	0.43947		
MLS-0386652	49829219	88.14	91.7	91.9	91.81	0.170	90	94.9	92.446	3.4232		**Yes**
MLS-0330949	49647788	89.62	88.3	92.5	90.42	2.947	94.5	90.4	92.434	2.9033	**Yes, FQ**	
MLS-0462599	99495765	59.03	81.5	71.9	76.73	6.821	91.1	92.8	91.98	1.1938		
MLS-0319286	49679494	60.84	49.7	57.8	53.76	5.712	82.9	100.4	91.65	12.439		
MLS-0231986	22400426	60.23	54.9	55.5	55.21	0.435	95.7	86.5	91.127	6.5256		
MLS-0280912	24807290	90.37	73.1	74	73.54	0.630	93.6	88	90.821	3.95		
MLS-0330872	49665521	99.73	86.3	86.5	86.39	0.119	91	90.2	90.589	0.59362		
MLS-0354856	49676095	113.3	97	97.4	97.19	0.249	89.2	91.5	90.351	1.6819		
MLS-0081053	87349603	88.15	80.1	81.8	80.93	1.205	90.8	88.3	89.521	1.7744		**Yes**
MLS-0079775	14731941	106.65	100.9	100	100.47	0.647	87.1	90.2	88.659	2.1385		**Yes**
MLS-0211719	17514537	77.85	55.2	59.5	57.34	3.010	81.8	94.4	88.083	8.9382		
MLS-0305500	26660734	88.64	92.2	91	91.64	0.847	91.9	84.2	88.025	5.4346	**Yes, FQ**	
MLS-0266629	24793940	60.98	61.6	63	62.27	0.994	172.7	2.4	87.575	120.45		
MLS-0073782	14742355	104.7	91.6	89.4	90.49	1.591	98.8	75.7	87.221	16.338		**Yes**
MLS-0444729	92764809	89.43	88.2	84.5	86.31	2.631	84.7	89.2	86.924	3.2053		**Yes**
MLS-0276331	24790995	103.44	94.2	97.8	96.02	2.547	85	88.4	86.699	2.4206		**Yes**
MLS-0079906	87344560	108.38	93.9	102.2	98.08	5.867	83.6	89	86.277	3.826		**Yes**
MLS-0291827	11533038	87.91	83.6	92.4	88.03	6.237	85.5	87	86.215	1.0691	**Yes, FQ**	
MLS-0215122	17513225	86.09	59.2	61.4	60.29	1.608	95	77.2	86.064	12.598		
MLS-0239698	24784880	90.67	87.7	90	88.86	1.636	84.8	87.2	85.992	1.7388		
MLS-0280282	24790272	98.84	75.2	73.2	74.23	1.432	81	90.6	85.802	6.769		
MLS-0079914	14733092	101.18	96.3	93.2	94.75	2.237	80.3	91.1	85.665	7.6525		**Yes**
MLS-0545966	136947366	80.77	89.9	81.2	85.57	6.191	88	81.9	84.915	4.3352		**Yes**
MLS-0291891	24788424	69.75	74.6	75.5	75.02	0.665	88.7	79.5	84.082	6.5129		
MLS-0343709	49640990	72.23	73.6	73.2	73.39	0.264	72.3	95.6	83.953	16.476		**Yes**

MLS-0262586	24835021	90.77	83.7	87.8	85.71	2.896	82.8	84.4	83.615	1.1449		
MLS-0039503	862420	84.32	91.7	80.1	85.90	8.165	90	77	83.506	9.1842		**Yes**
MLS-0066598	56320848	58.91	57.2	59.3	58.24	1.434	78.4	87.7	83.023	6.5481		
MLS-0202334	22406442	75.22	98.4	95.3	96.84	2.146	83.8	82.1	82.959	1.2298		
MLS-0550087	144097111	86.53	101.5	114	107.74	8.808	84.4	81.4	82.909	2.0692		
MLS-0260501	24817344	98.35	85.6	106.6	96.12	14.819	81	82.8	81.911	1.2245		**Yes**
MLS-0300493	26666944	71.32	49.6	56.7	53.17	4.996	82.3	81.4	81.889	0.63723		
MLS-0445109	92763868	98.59	95	91.6	93.27	2.383	83.4	80.2	81.769	2.2698		**Yes**
MLS-0342020	47195345	94.16	62.5	58.3	60.40	2.998	81.3	81.6	81.425	0.19139		
MLS-0227079	17513201	66.23	53.4	49.2	51.28	3.004	78.5	83.6	81.059	3.6611		
MLS-0207900	87348072	94.74	88.2	84.2	86.20	2.860	74.3	87.3	80.792	9.1689		
MLS-0292429	26665058	81.53	91.1	87.7	89.39	2.394	78.5	82.9	80.68	3.1046		**Yes**
MLS-0412241	56463287	79.29	80	82.1	81.05	1.487	75	86.1	80.538	7.83		
MLS-0383735	49816280	84.3	90.5	86.5	88.51	2.828	79.5	80.5	80.017	0.73921		
MLS-0312829	26664961	91.38	95.5	99.1	97.31	2.561	75.9	83.6	79.731	5.4082		**Yes**
MLS-0088999	14742342	93.07	88.8	80	84.41	6.249	79.2	80	79.606	0.60203	**Yes, FQ**	
MLS-0222739	17505450	115.35	71.3	99.1	85.21	19.625	71.5	86.5	78.984	10.601		
MLS-0305265	26663972	85.83	86.2	93	89.58	4.850	75.7	82	78.833	4.44		
MLS-0387266	49826455	106.23	77.8	96.7	87.25	13.360	76.2	81.3	78.747	3.5441		**Yes**
MLS-0441774	89854664	87.41	87.4	86.6	87.00	0.590	75.7	77.6	76.641	1.3117		
MLS-0444943	92764843	76.43	78.9	76.4	77.61	1.758	78.5	74.7	76.579	2.6876		
MLS-0204754	87346654	74.31	71.1	68.6	69.82	1.775	74.9	77.5	76.172	1.8294		**Yes**
MLS-0207587	87347052	84.14	59.4	66	62.67	4.683	76.2	75.3	75.735	0.58808		**Yes**
MLS-0315447	26657808	83.46	74.5	79.1	76.82	3.230	70	81.3	75.662	7.946		
MLS-0084359	14726526	89.4	72.2	74.5	73.34	1.604	75.2	75.7	75.445	0.41152		
MLS-0090529	14742237	58.02	63.4	48.5	55.95	10.549	78.7	72	75.378	4.7318		**Yes**
MLS-0252272	24809205	90.77	64.3	65.6	64.93	0.916	76.5	74.1	75.301	1.7027		
MLS-0286318	24797546	103.15	80.2	85.3	82.76	3.628	74.4	75.9	75.155	1.1071		
MLS-0261792	24830097	88.82	81.4	88.7	85.07	5.129	75.3	74.6	74.935	0.48387		**Yes**
MLS-0295415	26665872	49.44	57.6	63.6	60.60	4.289	76.7	71.9	74.264	3.382		

MLS-0279818	24806066	88.72	78.3	78.9	78.61	0.478	75.8	72.5	74.153	2.2676		
MLS-0205065	17433115	100.13	87.3	91.2	89.26	2.806	69.7	78.3	74.043	6.0759		**Yes**
MLS-0440664	89853596	110.39	99.6	101.2	100.42	1.167	74.7	72.6	73.673	1.4969		
MLS-0214738	17431439	98.1	114.7	128.6	121.66	9.789	141.9	4.7	73.34	97.004		**Yes**
MLS-0445041	92764824	102.7	99.1	96.3	97.72	1.987	72.3	74.1	73.2	1.278		**Yes**
MLS-0444248	93576592	78.31	76.9	76.4	76.68	0.376	77.5	68.4	72.963	6.4695		**Yes**
MLS-0452622	99356417	106.32	93.6	96.8	95.19	2.275	77.9	67.7	72.824	7.2468		
MLS-0301691	26666219	87.64	77.4	77.7	77.54	0.180	65.8	78.8	72.297	9.1858		**Yes**
MLS-0441671	89854666	80.49	84	82.3	83.17	1.232	72.7	70.7	71.674	1.4005		
MLS-0293727	26662208	86.44	79.5	87.9	83.74	5.934	65.4	77.8	71.588	8.761	**Yes, FQ**	
MLS-0313767	26727902	87.18	81.9	82.5	82.22	0.462	69.2	73.4	71.307	2.9842		
MLS-0213955	17432419	60.26	60.1	60.6	60.36	0.329	61.6	81	71.307	13.682		
MLS-0264345	14745181	100.25	67.6	66.3	66.98	0.929	70.4	72	71.163	1.13		**Yes**
MLS-0442396	89854667	79.2	83.2	85.1	84.18	1.317	71.7	70.4	71.034	0.89847		
MLS-0258899	24823256	63.98	59.8	54.7	57.24	3.568	66.5	75.4	70.968	6.2758		
MLS-0096954	17407909	91.62	70.1	71.2	70.62	0.804	69.8	70.9	70.315	0.78126		
MLS-0220743	17505825	84.63	60.4	64.5	62.42	2.875	70.5	70	70.256	0.40713		**Yes**
MLS-0214943	17513238	71.17	60.3	50.4	55.34	7.015	74.3	65.5	69.897	6.2684		
MLS-0245804	24782999	79.79	71.8	71.8	71.80	0.035	65.8	73.5	69.646	5.4555		**Yes**
MLS-0235837	11533045	103.27	103.2	105	104.12	1.297	71.6	67.3	69.432	3.0845		
MLS-0412755	56463046	77.42	81.1	81.2	81.15	0.079	66.5	70.8	68.657	3.0719	**Yes, Novobiocin**	
MLS-0303405	26663027	90.48	57.5	63.1	60.32	3.974	64.3	72.9	68.596	6.0839		**Yes**
MLS-0202306	17512759	90.13	79.9	79.3	79.59	0.433	68.7	67.1	67.87	1.1136	**Yes, FQ**	
MLS-0324260	49669868	94.03	83.2	90.9	87.05	5.441	69.3	66.3	67.812	2.0746		**Yes**
MLS-0033005	89853417	106.29	77.7	79.8	78.77	1.520	66.2	69.4	67.791	2.2886		**Yes**
MLS-0449817	99356264	72.92	79.5	81.8	80.64	1.677	69.3	65.8	67.557	2.5123		**Yes**
MLS-0206423	17433772	83.2	80.8	85.4	83.08	3.288	68.2	65.7	66.957	1.7438	**Yes, FQ**	
MLS-0445159	92764458	73.68	55.9	63.6	59.75	5.434	66.4	66.6	66.481	0.1394		**Yes**
MLS-0105761	50085435	49.38	54.1	56.6	55.35	1.770	59.6	72.8	66.205	9.3013		**Yes**
MLS-0265435	24836071	96.98	53.2	66.9	60.06	9.701	52.7	78.2	65.433	18		

MLS-0251683	24809151	82.14	64	68.2	66.11	2.920	64.1	66.4	65.247	1.6181		
MLS-0303419	26661852	58.31	51.8	53	52.42	0.856	63.3	66.9	65.074	2.5464		Yes
MLS-0080733	14735407	84.88	80.7	81.6	81.16	0.643	62.4	67.1	64.741	3.3692		Yes
MLS-0277099	24807574	78.65	56.4	58.4	57.40	1.396	63.5	65.9	64.662	1.6967		
MLS-0271525	24834980	93.59	73.8	79.4	76.61	3.908	61.6	67.4	64.497	4.0744	Yes, FQ	
MLS-0322825	49671668	68.36	80.1	65	72.53	10.654	61.6	66.5	64.062	3.4653		
MLS-0401568	56322863	71.27	76.9	77.7	77.32	0.580	59.1	68.9	63.981	6.9665		
MLS-0297152	26664430	54.75	54.4	51.5	52.96	2.034	79.4	47.5	63.426	22.525		
MLS-0225972	17511958	104.57	84.4	84.8	84.58	0.273	63.3	62.5	62.901	0.62799		
MLS-0220700	17504946	80.41	65.6	63	64.29	1.785	55.6	69.9	62.772	10.145		
MLS-0229546	22414608	113.11	88.9	85.2	87.10	2.611	59	66.2	62.633	5.1007		Yes
MLS-0363994	49677386	80.43	79.8	82.3	81.07	1.739	61.8	62.4	62.133	0.44327		Yes
MLS-0240917	24813619	81.06	73	73.5	73.25	0.392	66.9	57.2	62.052	6.8024		Yes
MLS-0203125	22403203	114.76	90.9	95	92.95	2.924	57.5	65.9	61.719	5.9375		
MLS-0215070	17507231	73.55	69.7	70.7	70.17	0.680	61	62.3	61.638	0.96239		
MLS-0301400	26664781	56.97	48.9	51.7	50.32	1.980	59.3	63.9	61.561	3.2679		
MLS-0222687	87335192	90.19	71.2	64.2	67.71	4.934	62.6	60	61.296	1.774		Yes
MLS-0227519	22410385	56.58	50.9	57.2	54.04	4.459	59.1	63.5	61.279	3.1218		Yes
MLS-0068144	14730721	64.07	49.9	51	50.42	0.777	61.5	61	61.244	0.29412		Yes
MLS-0367356	49824705	74.91	76.4	76.8	76.62	0.295	57.9	64.3	61.12	4.5303	Yes, FQ	
MLS-0245817	24783175	87.13	76.6	74.7	75.63	1.352	58.6	63.6	61.07	3.5617		Yes
MLS-0263575	24837296	78.22	71.3	72.2	71.77	0.632	63.5	58.5	60.991	3.5158	Yes, FQ	
MLS-0313524	24832741	85.77	76.2	77	76.60	0.593	55.5	66.1	60.787	7.4606		
MLS-0307495	26731542	65.54	56.5	57.2	56.81	0.488	56	64.7	60.361	6.1981		
MLS-0328825	49648765	77.73	76.4	76.5	76.44	0.095	60.4	60.3	60.35	0.027651		
MLS-0000659	99455957	47.79	49.1	53.1	51.12	2.849	71.1	49.5	60.308	15.269		Yes
MLS-0086803	14720875	69.36	68.8	53.9	61.35	10.472	67.3	53	60.133	10.066		
MLS-0349131	49641306	74.84	76.1	68.1	72.06	5.642	62.5	57	59.76	3.9255		
MLS-0073945	14744004	104.33	81	80.5	80.77	0.384	58.4	61.1	59.723	1.8835		
MLS-0339544	47199811	84.35	43.9	58.7	51.29	10.444	55.5	63.6	59.529	5.756		

MLS-0240015	24814114	100.1	54.3	60.1	57.18	4.124	57.9	60.6	59.281	1.8828		
MLS-0217633	17511183	94.96	74.1	69.5	71.81	3.275	58.1	59.1	58.593	0.66968		
MLS-0318172	46501219	54.23	62	66.3	64.14	3.078	56.7	58.9	57.807	1.5994		**Yes**
MLS-0291547	24824134	86.81	77.3	83.9	80.58	4.701	54	60.8	57.405	4.8206		
MLS-0552634	125001391	78.74	80.4	85.3	82.81	3.460	60.7	53.8	57.245	4.8884		
MLS-0303476	26662341	76.75	56.9	59.8	58.39	2.060	60.2	54.2	57.176	4.2342		
MLS-0440860	87336674	70.79	63.9	63.6	63.74	0.178	58	55.8	56.887	1.5717		**Yes**
MLS-0075126	14743867	75.57	65.5	69.1	67.31	2.504	52.6	60.4	56.542	5.5189		**Yes**
MLS-0347855	47200698	70	68	70.2	69.15	1.553	55.2	57.2	56.189	1.4408		**Yes**
MLS-0293193	26669939	53.56	55.7	54.5	55.08	0.831	56.5	55.8	56.115	0.48302		
MLS-0006255	99456920	82	76	78.8	77.38	1.994	55.7	56.2	55.933	0.39146	**Yes, FQ**	
MLS-0043862	847157	88.2	88	92.5	90.27	3.163	55.4	56.4	55.909	0.66052		
MLS-0015989	848842	60.02	55.9	56.8	56.35	0.651	56.1	55.5	55.814	0.44745		
MLS-0338627	49674298	41.27	67.7	79	73.31	7.984	44.4	66.5	55.413	15.612		
MLS-0324443	49648272	89.23	75	76	75.48	0.700	52.7	58	55.358	3.7907		**Yes**
MLS-0211078	17504207	75.51	72.1	77.2	74.62	3.636	51.4	59.2	55.312	5.5446		
MLS-0316661	47193949	95.7	53.5	54.7	54.07	0.838	54.1	56.2	55.127	1.5065		
MLS-0543795	134216141	90.54	113.3	118.4	115.84	3.628	55.2	54.4	54.801	0.53326		
MLS-0439563	92763749	52.64	56.6	57.8	57.21	0.866	50.7	58.9	54.784	5.8359		**Yes**
MLS-0245816	24783001	76.34	63.2	65.5	64.33	1.608	50.3	58.4	54.378	5.73		**Yes**
MLS-0458584	103059960	80.79	60.6	60.8	60.69	0.133	51.5	56.7	54.117	3.7133		
MLS-0268678	24827574	78.96	63.3	62.4	62.86	0.666	54.8	53.4	54.102	0.92185		**Yes**
MLS-0238619	26671284	112.4	93.5	97.8	95.68	3.034	54.7	53.3	53.969	0.97411		
MLS-0012490	859184	89.7	105.3	97.7	101.49	5.346	44.3	63.4	53.842	13.489		
MLS-0226546	22416870	74.85	61.3	68.5	64.89	5.089	58.8	48.8	53.802	7.1279		
MLS-0449241	99357601	96.58	92.9	77.2	85.04	11.154	53.3	53.9	53.6	0.44424		**Yes**
MLS-0292485	26658052	89.08	60.9	70.8	65.88	6.976	47.9	59.3	53.6	8.1		
MLS-0222733	17504835	103.59	62.6	63.4	63.01	0.593	52.3	54.6	53.442	1.5975		
MLS-0289709	24791387	53.17	82.8	88.1	85.47	3.715	52.5	54.3	53.388	1.3198		
MLS-0092123	17411136	69.34	51.4	49.3	50.35	1.525	60.3	45.6	52.93	10.377		

MLS-0245623	24814463	64.84	58.7	52.3	55.49	4.490	51.6	54.2	52.908	1.8883		
MLS-0209102	17512265	43.7	71.2	68.4	69.78	1.951	-2.7	108.3	52.777	78.522		**Yes**
MLS-0304998	26663490	83.28	69.6	69.7	69.68	0.072	52.7	52.6	52.677	0.092186	**Yes, FQ**	
MLS-0046423	4256562	119.99	102	108.3	105.16	4.439	50.4	53.4	51.908	2.0881		
MLS-0351996	47202958	61.87	64.6	68.1	66.31	2.481	54.3	49.2	51.779	3.6058		**Yes**
MLS-0313324	24832689	75.05	69.2	75.3	72.22	4.303	51	52.4	51.709	1.0043		
MLS-0035369	7974716	67.66	61.6	64.1	62.88	1.748	51.6	51.4	51.504	0.13119		**Yes**
MLS-0313279	24779871	112.2	100.7	105.2	102.97	3.180	47.8	53.7	50.737	4.2053		
MLS-0299121	26663988	69.07	79.2	77.5	78.36	1.200	51.1	50	50.539	0.79229		
MLS-0355583	49716177	58.66	69.3	64.5	66.87	3.415	52.8	48	50.401	3.3522	**Yes, FQ**	
MLS-0346031	49641429	76.34	58	65.5	61.76	5.315	43	57.4	50.215	10.182		
MLS-0444628	93577189	51.54	56.6	59.3	57.94	1.938	47.6	52.8	50.195	3.6651		**Yes**

Table S4. 235 compounds purchased/obtained for analyses

CPD ID #	Vendor/origin	PUBCHEM CID	IC_{50} *E. coli* DNA gyrase (µM)	Gyrase Poison
1	Molport	778345	>200	
2	Molport	745625	>200	
3	Molport	1552002	>200	
4	Molport	1652894	25-50	
5	Molport	984068	>200	
6	Molport	759208	>200	
7	Molport	4386631	25-50	
8	Molport	4428545	>200	
9	Molport	5238140	1.69	
10	Molport	4884442	50-200	
11	Molport	3245407	>200	
12	Molport	4539252	25-50	
13	Molport	9115581	50-200	
14	Molport	6602929	>200	
15	Molport	7202928	50-200	
16	Molport	1591623	>200	
17	Molport	1184133	50-200	
18	Molport	1423512	25-50	
19	Molport	2027019	3.55	
20	Molport	665040	>200	
21	Molport	1960206	25-50	
22	Molport	846585	50-200	
23	Molport	1891764	25-50	
24	Molport	135458272	25-50	
25	Molport	1792822	10.62	
26	Molport	24747662	>200	
27	Molport	2030972	1.74	
28	Molport	931313	50-200	
29	Molport	1201959	25-50	
30	Molport	1830951	>200	
31	Molport	1227509	50-200	
32	Molport	44659169	>200	
33	Molport	2019060	50-200	
34	Molport	721180	>200	
35	Molport	136689692	25-50	
36	Molport	1901745	7.4	
37	Molport	664602	>200	
38	Molport	1325392	50-200	
39	Molport	3894821	>200	
40	Molport	24979941	47.62	Yes
41	Molport	3977548	1.48	
42	Molport	1973720	2.18	
43	Molport	913034	>200	

44	Molport	1912931	50-200	
45	Molport	28693	50-200	
46	Molport	1784592	11.23	
47	Molport	1976940	1.87	
48	Molport	1960944	4.28	
49	Molport	1227531	25-50	
50	Molport	1911770	>200	
51	Molport	5751473	50-200	
52	Molport	614439	>200	
53	Molport	5930369	50-200	
54	Molport	786578	50-200	
55	Molport	2896625	50-200	
56	Molport	800465	50-200	
57	Molport	2140739	50-200	
58	Molport	1037842	50-200	
59	Molport	2227134	>200	
60	Molport	135501781	50-200	
61	Molport	5929780	50-200	
62	Molport	5952293	50-200	
63	Molport	5769138	50-200	
64	Molport	1370241	50-200	
65	Molport	2192862	50-200	
66	Molport	1047194	>200	
67	Molport	3453284	50-200	
68	Molport	3509768	50-200	
69	Molport	9551910	50-200	
70	Molport	16248324	50-200	
71	Molport	2428993	50-200	
72	Molport	1329105	12.4	
73	Molport	7192961	7.86	
74	Molport	2229604	50-200	
75	NCI DTP	72721	5.28	
76	TCI	3035850	2.53	
77	Sigma	2733504	>200	
78	Sigma	28693	100-200	
79	TCI	9983292	50-100	
80	ICC	198500	200	
81	NCI DTP	381594	25-50	Yes
82	Chem Scene	10168	50-200	
83	Sigma-Aldrich	3124342	50-200	
84	Alfa Aesar	69845	>200	
85	Alfa Aesar	67502	>200	
86	Combi-Blocks	771620	>200	
87	Maybridge	602011	>200	
101	Molport	1275838	50	

102	Molport	655252	25-50	Yes
103	Molport	5718810	>50	
104	Molport	1184126	25-50	
105	Molport	16194227	25-50	
106	Molport	2869257	200	
107	Molport	135472702	>50	
108	Molport	6409108	15-25	
109	Molport	136273636	2.2	
110	Molport	5171580	50-200	
111	Molport	5049636	3.3	
112	Molport	2522158	50-200	
113	Molport	2359855	>50	
114	MolPort	136579774	27.7	
115	MolPort	135775115	50-200	
116	MolPort	135434997	9.4	
117	MolPort	1280448	15.7	
118	MolPort	1770078	>200	
119	MolPort	1792963	7.7	
120	MolPort	1796169	7.9	
121	MolPort	1792572	28	
122	MolPort	906031	>200	
123	MolPort	1792856	28.2	
124	MolPort	1792978	5.5	
125	MolPort	23605953	4.9	
126	MolPort	135692429	7.8	
127	MolPort	135692433	7.5	
128	MolPort	135692441	2.5	
129	MolPort	2871422	50-200	
130	MolPort	2334042	50-200	
131	MolPort	4049813	50-200	
132	MolPort	135758848	30.9	
133	MolPort	135531071	50-200	
134	MolPort	5014505	50-200	
135	MolPort	16196363	15-25	
136	MolPort	3707522	>200	
137	MolPort	3136927	>200	
138	MolPort	4240945	>200	
139	MolPort	4715263	>200	
140	MolPort	4715440	>200	
141	MolPort	6620816	100	
142	MolPort	3814551	>200	
143	MolPort	3112185	>200	
144	MolPort	3439114	>200	
145	MolPort	4715351	>200	
146	MolPort	4715386	>200	
147	MolPort	1384427	>50	

148	MolPort	655559	50-200	
149	MolPort	135509708	15-25	
150	MolPort	2007309	50-200	
151	MolPort	5762833	50-200	
152	MolPort	666422	50-200	
153	MolPort	3593962	50-200	
154	MolPort	3145916	3.1	Yes
155	MolPort	2276396	15-25	
156	MolPort	136661536	50-200	
157	MolPort	6184643	10	
158	MolPort	663431	>50	
159	MolPort	135926802	6.3	
160	MolPort	1904433	>50	
161	MolPort	1209302	15-25	
162	MolPort	2267112	50-200	
163	MolPort	135403918	15-25	
164	MolPort	750959	>50	
165	MolPort	1839490	50-200	
166	MolPort	698841	50-200	
167	MolPort	629074	50-200	
168	MolPort	2264590	50-200	
169	MolPort	135469884	15-25	
170	MolPort	1507932	>50	
171	MolPort	2291702	15-25	
172	MolPort	692801	>50	
173	MolPort	7514097	15-25	Yes
174	MolPort	3751260	>50	
175	MolPort	12004639	50-200	
176	MolPort	5921430	2	
177	MolPort	644571	>50	
178	MolPort	135851650	1.6	
179	MolPort	4653365	>50	
180	MolPort	7245272	15-25	
181	MolPort	3284301	>50	
182	MolPort	135517119	50-200	
183	MolPort	5756371	50-200	
184	MolPort	1570689	15-25	
185	MolPort	773666	>50	
186	MolPort	6603357	>50	
187	MolPort	3123929	>50	
188	MolPort	774534	50-200	
189	MolPort	1332923	25-50	
190	MolPort	135541115	>50	
191	MolPort	5955891	50-200	
192	MolPort	2262707	8	

201	NCI DTP	135408744	>200	
202	NCI DTP	72313	>200	
203	NCI DTP	227839	>200	
204	NCI DTP	232432	50-200	
205	NCI DTP	237490	50-200	Yes
206	NCI DTP	238958	50-200	
207	NCI DTP	5750779	50-200	
208	NCI DTP	242563	>200	
209	NCI DTP	245287	>200	
210	NCI DTP	65747	>200	
211	NCI DTP	5375071	50-200	
212	NCI DTP	1237173	25-50	
213	NCI DTP	256073	50-200	
214	NCI DTP	11781383	>200	
215	NCI DTP	278675	25-50	
216	NCI DTP	281376	>200	
217	NCI DTP	286440	50-200	
218	NCI DTP	301273	>200	
219	NCI DTP	305108	>200	
220	NCI DTP	42640	>200	
221	NCI DTP	313582	>200	
222	NCI DTP	313614	25-50	
223	NCI DTP	54612176	>200	
224	NCI DTP	319846	25-50	
225	NCI DTP	99927	25-50	
226	NCI DTP	72518	>200	
227	NCI DTP	6144987	50-200	
228	NCI DTP	1373005	50-200	
229	NCI DTP	54601189	25-50	Yes
230	NCI DTP	5953124	>200	
231	NCI DTP	5386914	>200	
233	NCI DTP	385251	>200	
234	NCI DTP	386227	>200	Yes
235	NCI DTP	386523	>200	
236	NCI DTP	5914028	50	
237	NCI DTP	5469860	50-200	
238	NCI DTP	5832532	50-200	
239	NCI DTP	5470321	50-200	
240	NCI DTP	386511	<100	
241	NCI DTP	386521	<100	
242	Fisher Scientific	3220	50-200	
243	Acadechem	7085	12.5-25	
244	Fisher Scientific	2794	>200	
245	Fisher Scientific	11077	100-200	
246	Sigma-Aldrich	7099	<100	

247	Sigma-Aldrich	7019	25-50	
248	Sigma-Aldrich	6438345	25-50	
249	Sigma-Aldrich	62344	50-200	
250				
251	Fisher Scientific	7083	>200	
252	Fisher Scientific	11105	>200	
253	Fisher Scientific	3259	1.6	
254	Sigma-Aldrich	493570	>200	
255	Fisher Scientific	443101	6.25-12.5	
256	Fisher Scientific	6293	25-50	
257	Sigma-Aldrich	2017	25-50	
258	NCI DTP	3197	75-100	

Chapter III

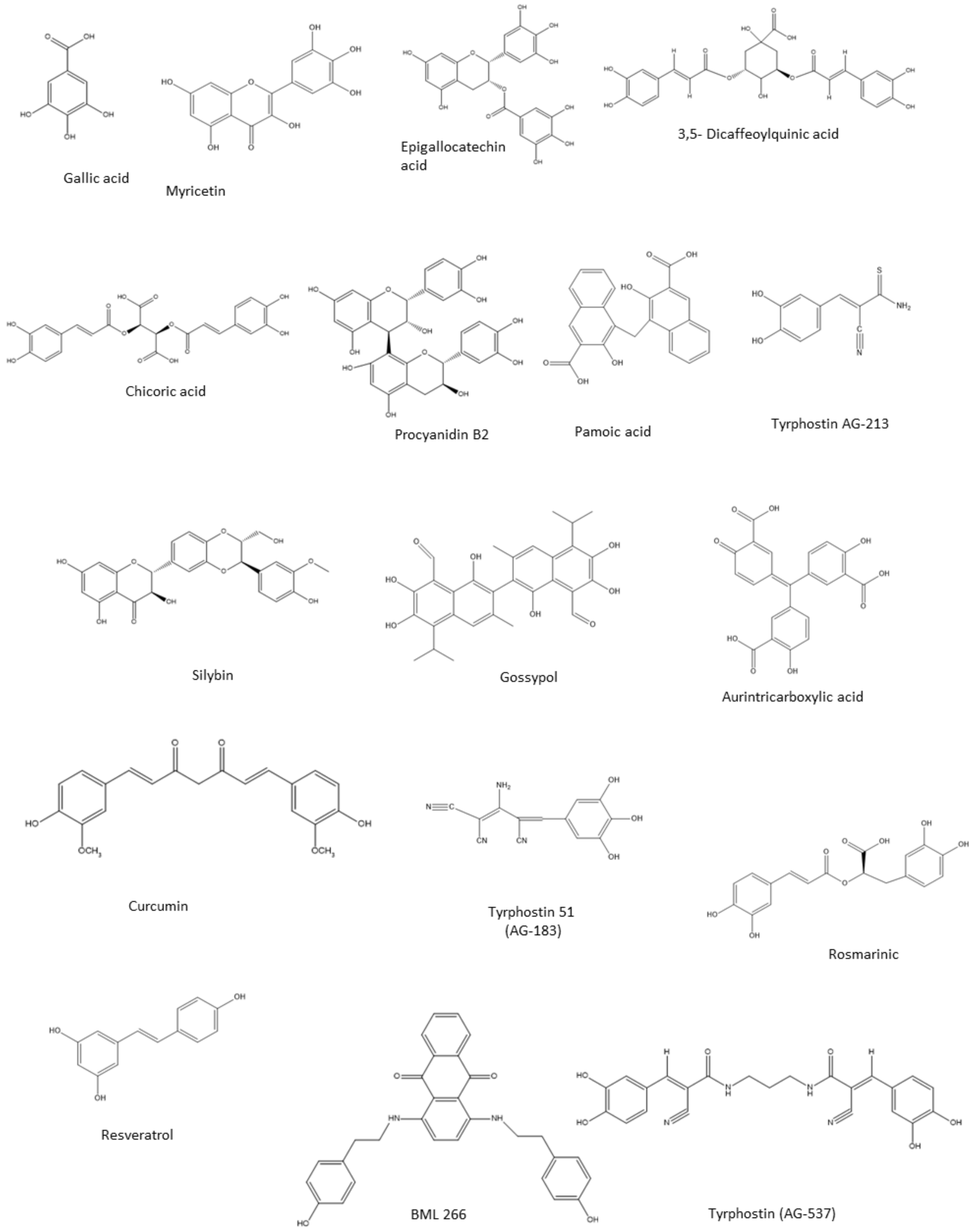


Figure S1. Chemical structures of polyphenols.

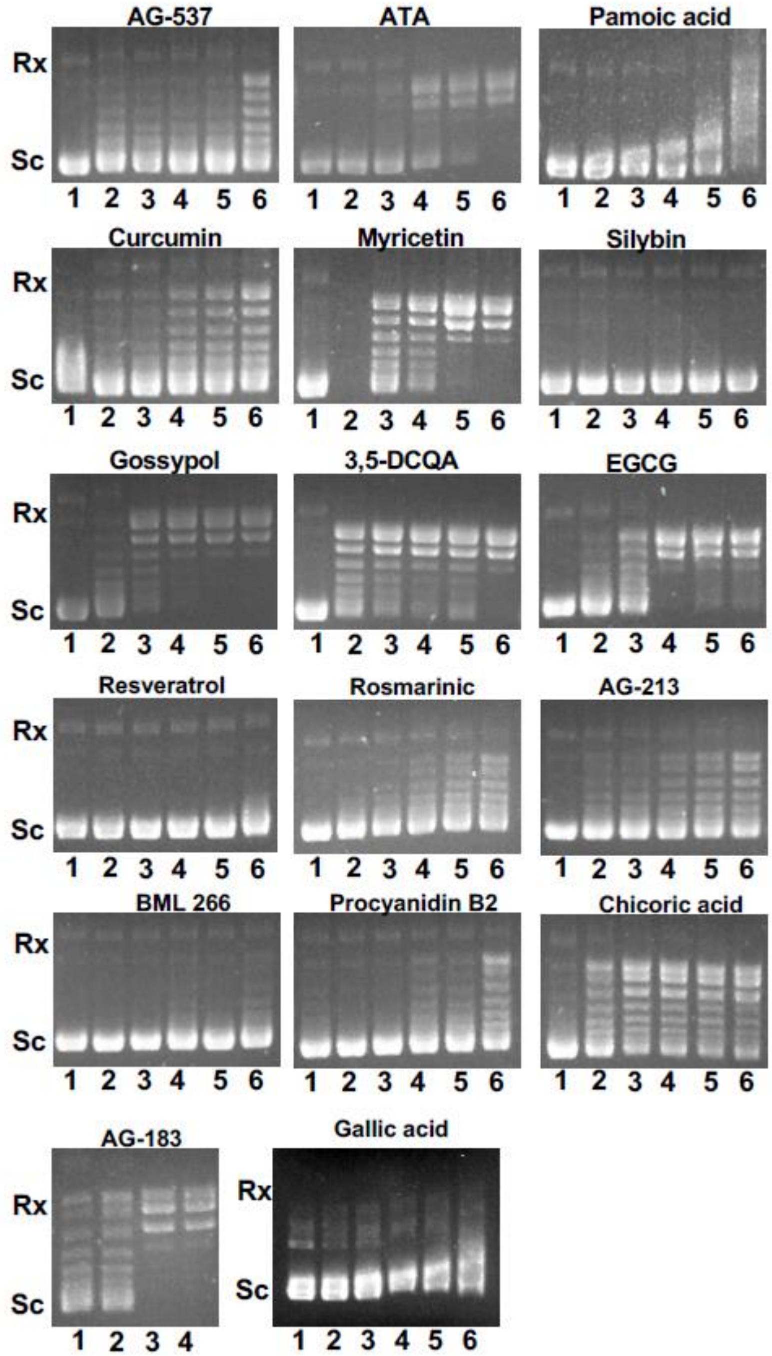


Figure S2. Inhibition of *E. coli* DNA gyrase supercoiling activities by different polyphenols. Lanes 1 to 6 contain 0, 5, 10, 20, 50, 100 μM of compounds, respectively. For AG-183, lanes 1-4 contain 50, 100, 155, and 311 μM of AG-183, respectively. For gallic acid, lanes 1-6 contain 0, 100, 200, 300, 400, and 500 μM of gallic acid, respectively. Symbols: Rx, relaxed plasmid pAB1; Sc, supercoiled pAB1.

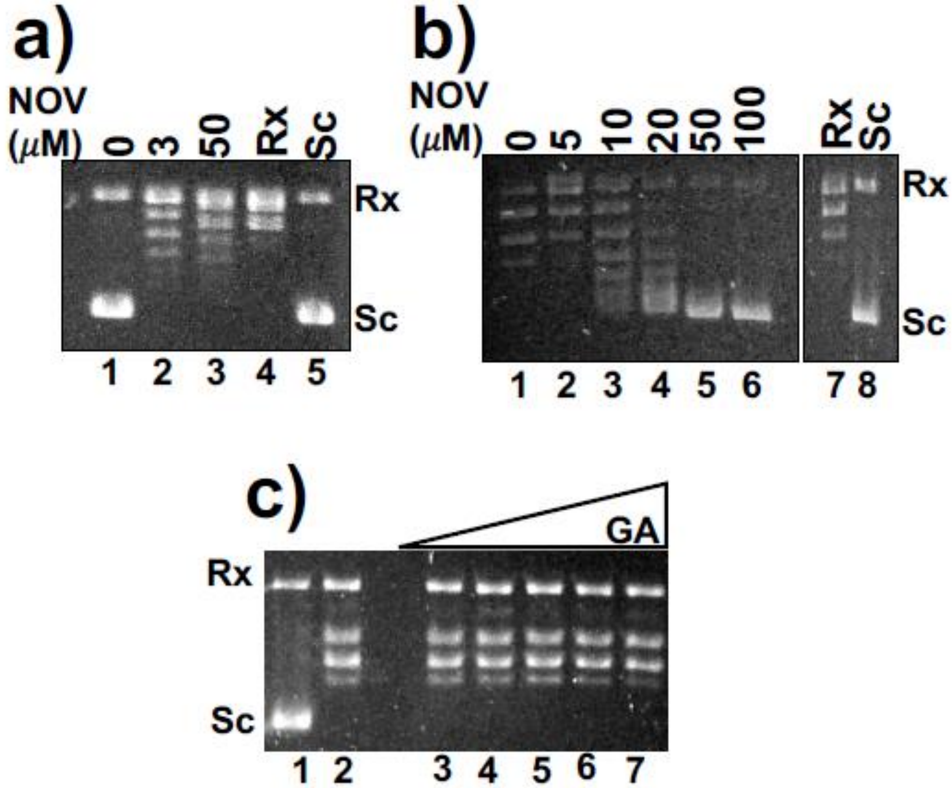


Figure S3. Novobiocin (NOV) potently inhibits *E. coli* DNA gyrase (**a**) and topoisomerase IV (**b**). (**c**) Gallic acid does not inhibit *E.coli* DNA topoisomerase IV. DNA relaxation assays by *E. coli* DNA topoisomerase IV were performed according to Materials and Methods. Lanes 1 is supercoiled (Sc) DNA pAB1. Lanes 2-7 contain 100, 200, 300, 400, and 500 μM of gallic acid, respectively. Rx, relaxed DNA pAB1,

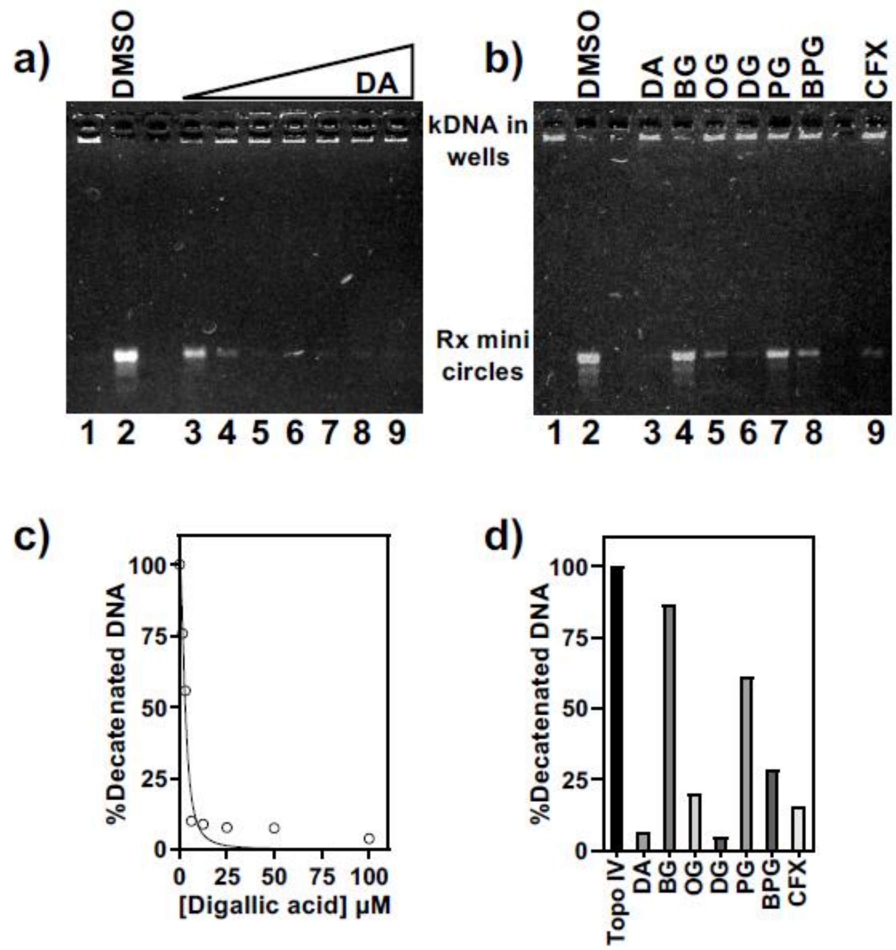


Figure S4. Inhibition of *E. coli* DNA topoisomerase IV-catalyzed decatenation of kinetoplast DNA (kDNA) by digallic acid and other gallate derivatives. *E. coli* DNA topoisomerase IV-catalyzed decatenation reactions were performed as described under Material and Methods. (a) Digallic acid potently inhibits *E. coli* DNA topoisomerase IV. Lanes 2-8 contain 1.56, 3.12,6.25, 12.5, 25, 50, and 100 µM of digallic acid, respectively. Lane 1 is supercoiled plasmid pAB1. IC_{50} of digallic acid against *E. coli* DNA topoisomerase IV was estimated to be ~4 µM. (b) Inhibition of *E. coli* DNA topoisomerase IV by gallic acid derivatives at 100 µM. (c and d) The inhibition of *E.coli* DNA topoisomerase IV-catalyzed decatenation by gallic acid derivatives was quantified by analyzing the agarose gels using Kodak 1D Image Analysis Software. Symbols: Digallic acid, DA; butyl gallate, BG; octyl gallate, OG; dodecyl gallate, DG; phenyl gallate, PG; and biphenyl gallate, BPG; CFX, ciprofloxacin.

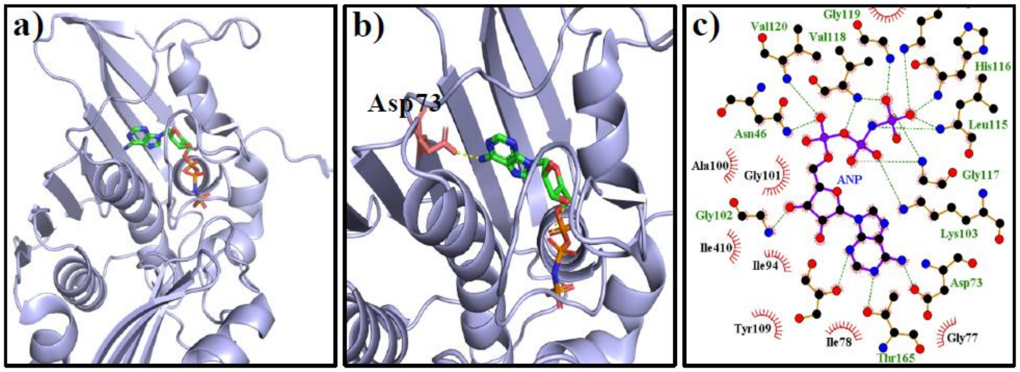


Figure S5. (**a**) and (**b**) Molecular models of ATP analog ADPNP (phosphoaminophosphonic acid-adenylate ester, sticks) binding to the ATP binding pocket of *E. coli* DNA Gyrase subunit B. Molecular models were constructed using the crystal structure of gyrB (PDB ID: 1E11) as described in Materials and Methods. A hydrogen bond is formed between ADPNP and residue Asp73. (**c**) Schematic 2-D representations of *E. coli* DNA gyrase ligand complexes are shown. Hydrogens bonds and distances are highlighted as green dashed lines. Hydrophobic contacts are shown as an arc with spokes radiating towards the ligand atoms.

Table S1. The IC_{50} values of polyphenols against *E. coli* DNA gyrase

Compound	IC_{50} (µM)	Vendors
Tannic acid	1.5	Fisher Scientific, Inc
Ellagic acid	1.75	Fisher Scientific, Inc
Gossypol	12	Santa Cruz Biotechnology, Inc
Epigallocatechin gallate	15	Epigallocatechin gallate
Aurintricarboxylic acid	18	Fisher Scientific, Inc.
Chicoric acid	25	Fisher Scientific, Inc
Myricetin	25	Fisher Scientific, Inc
Procyanidin B2	>50	Santa Cruz Biotechnology, Inc
Tyrphostin 51 AG-183	>100	Fisher Scientific, Inc
Curcumin	>100	Santa Cruz Biotechnology, Inc
Tyrphostin AG-537	>100	Fisher Scientific, Inc
Rosmarinic acid	>100	Santa Cruz Biotechnology, Inc
Tyrphostin AG-213	>100	Fisher Scientific, Inc

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