Oral Session 1

Research Study

Title: "**Intracellular galectin-3 as a novel prognostic indicator of melanoma metastasis**"

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Introduction and Objective. Melanoma is a life-threatening skin cancer that is known for its aggressive behavior and poor outcomes in the patients who develop distant metastasis. Despite recent advances in melanoma management, a reliable biomarker for predicting, detecting, and monitoring the metastatic risk of primary tumors is still lacking. Galectin-3 (Gal-3), a β-galactoside-binding protein, is widely expressed by many human epithelial and immune cells. High serum Gal-3 levels have been reported to be positively correlated with late-stage disease in melanoma patients, where it is theorized to bind surface glycosylated proteins to promote melanoma cell invasion and metastasis. However, Gal-3 levels within the melanoma cell and its relationship to melanoma progression is still poorly understood.

Methods. A secondary data analysis was conducted using The Cancer Genome Atlas (TCGA) database to compare the Gal-3 expression profiles of 103 primary tumors versus 368 metastatic tumors obtained from patients with melanoma. The functional significance of intrinsic Gal-3 on melanoma cell behavior was investigated through a series of experimental in-vitro studies performed on SKMEL2 melanoma cell line after Gal-3 silencing using small interfering RNA. The invasion and migration capacity of Gal-3 silenced cells were evaluated using the transwell assay with and without Matrigel, respectively. CCK-8 assay was used to detect the changes in cell proliferation capacity. Additionally, expression levels of proteins involved in the Wnt/β-catenin signaling pathway, a key metastasis-regulating pathway, were assessed using western blotting. For normally distributed data involving two groups, unpaired two-tailed Student's t-test was used. For non-normally distributed data, analysis was performed using a Mann–Whitney test; normality was assessed using a Shapiro–Wilk test.

Results. TCGA data analysis has shown a significantly higher expression of Gal-3 in primary melanoma samples compared to metastatic melanomas (P < 0.001), suggesting that intracellular Gal-3 potentially negatively regulates primary melanoma progression to metastatic disease. Melanoma cell migration and invasion were remarkably enhanced in Gal-3 silenced cells compared to mock control cells (P < 0.01, P < 0.01 respectively), with no significant change in proliferation rate. Proteins involved in the Wnt/β-catenin pathway, namely β-catenin, Cyclin D1 and C-myc, were upregulated in Gal-3 depleted cells compared to its control (P < 0.001, P < 0.001, P < 0.05 respectively).

Conclusions-Implications. These findings illuminate the apparent opposing roles of Gal-3 in melanoma progression, with intracellular Gal-3 serving as a metastasis-suppressive molecule. Importantly, this study reveals the potential of analyzing melanoma cell-intrinsic levels of Gal-3 to better predict the metastatic potential and clinical outcome in primary melanoma patients.