Transmissible Cancer in Tasmanian Devil (Sacrophilus harrisii) and Canine Animal Populations Explained through Immune System Downregulation in Immunocompetent Hosts by Ravinder Singh Chale

Transmissible cancer has been shown to occur in the Tasmanian Devil as well as canine animal populations, known as Devil Facial Tumor Disease (DFTD) and Canine Transmissible Venereal Tumor (CTVT), respectively. Both malignancies show remarkable ability to be transmitted as allografts into hosts. How DFTD, as well as CTVT, avoid detection by immunocompetent hosts is of particular interest as these malignancies are rarely seen in nature. Both transmissible cancers show the ability to downregulate the host immune system enabling proliferation. DFTD is characterized by epigenetic modifications of ?2m, TAP1, TAP2, and MHC DNA promoter regions; crucial proteins required in detection and surveillance of foreign material. Downregulation in DFTD may be achieved by altering the activity of histone deacetylases. DFTD has caused widespread destruction of devil populations placing the species on the brink of extinction. CTVT consists of a proliferative phase during which the tumor evades immune detection, allowing it to proliferate; as well as a regressive phase where hosts show the ability to mount an effective immune response. Alteration of TGF-? signaling in CTVT likely impedes the antigen processing capabilities of canine hosts in addition to hindering the ability of natural killer cells to detect immune system downregulation. Immunosuppressive cytokines such as CXCL7 may contribute to a favorable microenvironment enabling the proliferation of CTVT. When viewed from an evolutionary paradigm both DFTD as well as CTVT may conform to a model of host-parasite co-evolution first put forth by J.B.S. Haldane. Furthermore, certain genetic characteristics such as genetically active transposons in CTVT and chromosome rearrangements in DFTD have been shown to play important roles in promoting survival of both transmissible cancers. Understanding the mode of transmission for these transmissible cancers may shed light on mechanisms for human malignancies, in addition to serving as a paradigm for treatment in the future.