A Novel Genetic Mechanism of Evading Anti-tumor Immunity In Multiple Human Cancers

Successful treatment of many advanced cancer patients using antibodies against PD-1 and its ligand (PD-L1) is highlighting a critical importance of immune escape in cancer development. Cancer cells are thought to circumvent immune surveillance through PD-1/PD-L1 signaling. However, the genetic basis for PD-L1-PD-L1-mediated immune escape has not been fully understood. In this seminar, I present a unique genetic mechanism of immune escape caused by structural variations (SVs) commonly disrupting the 3’ part of the PD-L1 gene. Widely affecting multiple common cancer types, these SVs invariably lead to a marked elevation of aberrant PD-L1 transcripts that are stabilized by truncation of the 3’-untranslated region (UTR). PD-L1-involving SVs are especially frequent in virally induced cancers. The critical role of the 3’-UTR disruption in cancer immune evasion will be discussed, particularly with regard to viral infection.