The power of circulating tumor cells in immuno-oncology

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Cancer-related deaths are mainly caused by metastatic spread of tumor cells from the primary lesion to distant sites via the blood circulation. Understanding the mechanisms of blood-borne tumor cell dissemination by the detection and molecular characterization of circulating tumor cells (CTCs) in the blood of patients with cancer has opened a new era in cancer research.

However, blood is known to be a hostile environment for CTCs. Although the primary tumor presumably sheds thousands of cells into the bloodstream every day, only a very small percentage of these cells survive in the bloodstream and become detectable as CTCs in a blood sample. Within the immunological synapse, a multitude of inhibitory receptors have been identified. Programmed cell death protein-1 (PD-1) and its ligand, PD-L1, have been one of the most prominent examples to antagonize immune escape mechanisms employed by tumor cells.

In my talk, I will discuss about *(i)* $CTC^{PD\text{-}L1(+)}$ plus extracellular vesicles expressing PD-L1 as important biomarkers in *liquid biopsy* in breast and non-small cell lung cancers as well as *(ii)* metastasis-competent CTCs from colon and breast cancers to discover new targetable immune checkpoint inhibitors. Indeed, these more aggressive and selected clones of CTCs have the capacity to initiate secondary tumors in distant organs; interestingly, they are not expressing PD-L1 but survived the constant immune attacks.