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The majority of cancer-related deaths result from the metastatic spread of tumor cells, which travel from the primary lesion to distant organs via the bloodstream. Gaining insights into the mechanisms of blood-borne tumor cell dissemination, particularly through the detection and molecular profiling of circulating tumor cells (CTCs) in patients' blood, has revolutionized cancer research.

However, the bloodstream presents a hostile environment for CTCs. Although primary tumors are thought to release thousands of cells into circulation daily, only a small fraction of these cells survive long enough to be detected as CTCs in a blood sample. Within the immunological synapse, numerous inhibitory receptors have been identified, with programmed cell death protein-1 (PD-1) and its ligand, PD-L1, being key players in counteracting immune escape strategies utilized by tumor cells.

In my talk, I will introduce the concept of Liquid Biopsy and explore: (i) the role of PD-L1-expressing CTCs and extracellular vesicles as crucial biomarkers in liquid biopsy for breast and non-small cell lung cancers, and (ii) metastasis-competent CTCs from colon and breast cancers as a means to identify novel immune checkpoint inhibitors. Notably, these aggressive and selectively enriched CTC clones can seed secondary tumors in distant organs. Interestingly, despite enduring continuous immune attacks, they do not express PD-L1.