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Ultra-high content analysis of circulating and solid tumor cells

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Abstract

Metastatic spread of cancer is responsible for the vast majority of cancer-related deaths highlighting the need to better understand the cellular mechanisms underlying this phase of cancer, and to monitor disease progression. Our team combines the discovery of a novel circulating tumor cell population, that co-expresses cancer cell and immune cell epitopes (called a hybrid cell), cutting-edge multiplex cyclic immunofluorescence (cyCIF) for interrogation of large panels of proteins on the same tissue section or blood smear, and powerful software (QITissue) that allows for the visualization and analysis of many biomarkers at once. This combination creates a platform that supports non-invasive, real-time monitoring of disease evolution. We set out to determine if disseminated or peripheral blood hybrid cells (called circulating hybrid cells, CHCs) harbored identical expression profiles as tissue-bound hybrid cells. To do this we generated and validated an array of cancer, immune, structural, signaling and phenotypic-specific cyCIF ab-oligos then probed patient matched tumors and peripheral blood specimen for discrete and aligned phenotypes. We identified eight computationally defined subpopulations of hybrids enriched in circulation and one EMT population conserved across tissue and blood hybrids. These finding lays the foundation for further developing detection and phenotypic analyses of CHCs as a potential non-invasive (i.e., liquid biopsy, blood-based biopsy) readout for tumor burden as well as subpopulations of CHCs associated with increased risk for metastatic disease.