Circulating tumor cell clusters

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Abstract

The metastatic spread of cancer occurs through the generation and hematogenous dissemination of circulating tumor cells (CTCs). Among these, CTC clusters have recently emerged as key players in the metastatic process. With a combination of microfluidic technologies and single cell-resolution molecular analysis applied to cancer patients and mouse models, we gained fundamental insights into the biology, vulnerabilities, and clinical implications of CTC clusters. For instance, we found that their physical features enable molecular changes that promote stemness and metastasis, allowing us to define new treatment concepts aimed at suppressing their metastatic potential. Further, we investigated CTC heterogeneity at the single cell level, revealing fundamental interactions that occur between CTCs and immune cells and that accelerate metastasis formation, as well as microenvironment signals that impact on CTC generation. More recently, we also gained important insights into CTC generation dynamics and timing of CTC intravasation. Together, our findings support a model whereby upon defined microenvironmental cues and in a time-dependent fashion, CTCs form multicellular aggregates to expand their metastatic ability, providing a new rationale for targeting these interactions in cancer.