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Title: Mechanisms of Metastatic Awakening

Abstract

The physical dissemination of aggressive primary tumor cells via hematogenous routes can occur with relatively high efficiency. Indeed, even the subsequent extravasation can occur reasonably efficiently. However, the subsequent step, involving the outgrowth of micrometastatic colonies, is usually highly inefficient and often results in the formation of micrometastases or single disseminated tumor cells (DTCs) that enter into a dormant but nonetheless viable state for extended periods of time, undergoing low rates of attrition inflicted by still-unclear biological processes. This issue is particularly acute in the case of clinical breast cancers in which such cells may persist for months if not years and, with great delay, erupt to form aggressive metastatic colonies. In principle, the awakening of such cells might be driven entirely by cell-autonomous processes that occur in the absence of external stimuli. Our work indicates, however, that such awakening is often triggered by cell-non-autonomous mechanisms, notably the inflammation of the tissue microenvironment in which the DTCs are embedded. Some of the details of these processes will be described.