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The Interplay between Signaling and Metabolism in Breast Cancer Cell Motility and Metastasis

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The initiation and growth of tumor metastases require tumor cells go through a transition between collective-to-individual cell migration. Understanding the molecular, cellular and physical mechanisms of these different migration modes is limited. We focus on the tumor cell migration induced by Hepatocyte Growth Factor / Scatter Factor (HGF/SF) - Met-signaling, a master regulator of cell motility in normal and malignant processes. Met has been implicated in tumorigenesis and metastasis and several Met targeting agents have been introduced into the clinic, and are currently in all phases of clinical trials. Our analysis demonstrates that Met signaling dramatically alter the morpho-kinetic dynamics of collective migration of tumor cells. It induce a “wave” of increasing velocities that propagates back from the leading edge, increases cells’ orientation and cooperation capabilities. In parallel Met signaling induces amoeboid cell motility that increased cell individuality. The decision making regarding the motility mode is dependent on the extent of activation of unique signal and metabolic cues. We present a combination of molecular imaging, conceptual and modeling framework for the analysis and assessment of the collective mesenchymal to epithelial versus amoeboid motility. Combined together our analysis can contribute to the understanding of metastasis and personalizing anti Met targeted therapy.