Abstract Submitted
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Network motifs that stabilize the hybrid epithelial/mesenchymal phenotype[1] MOHIT KUMAR JOLLY, DONGYA JIA, Rice Univ, SATYENDRA TRIPATHI, SAMIR HANASH, SENDURAI MANI, MD Anderson Cancer Center, ESHEL BEN-JACOB, HERBERT LEVINE, Rice Univ — Epithelial to Mesenchymal Transition (EMT) and its reverse – MET – are hallmarks of cancer metastasis. While transitioning between E and M phenotypes, cells can also attain a hybrid epithelial/mesenchymal (E/M) phenotype that enables collective cell migration as a cluster of Circulating Tumor Cells (CTCs). These clusters can form 50-times more tumors than individually migrating CTCs, underlining their importance in metastasis. However, this hybrid E/M phenotype has been hypothesized to be only a transient one that is attained en route EMT. Here, via mathematically modeling, we identify certain 'phenotypic stability factors' that couple with the core three-way decision-making circuit (miR-200/ZEB) and can maintain or stabilize the hybrid E/M phenotype. Further, we show experimentally that this phenotype can be maintained stably at a single-cell level, and knockdown of these factors impairs collective cell migration. We also show that these factors enable the association of hybrid E/M with high stemness or tumor-initiating potential. Finally, based on these factors, we deduce specific network motifs that can maintain the E/M phenotype. Our framework can be used to elucidate the effect of other players in regulating cellular plasticity during metastasis.

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