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Oncostatin M induces migratory and morphological changes in mammary epithelial cells

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Abstract

Cells in vivo are continuously exposed to a range of small messenger proteins (microenvironmental ligands). Microenvironmental ligands bind to cell-surface receptors and trigger protein cascades that impact many aspects of cell behavior. Aberrations in the ligand signaling network ¬¬can drive the progression of many different pathologies, including cancer. Our prior research has characterized the molecular and phenotypic changes that occur in MCF10A cells, a mammary epithelial cell line, treated with a panel of six microenvironmental ligands that target different canonical path¬¬ways. Cells exposed to the perturbagens were assayed for gross phenotypic, proteomic, RNA expression, and epigenetic changes.

The cytokine Oncostatin M (OSM) induced unique and distinctive changes in cell phenotype. OSM treated cells formed compact multicellular clusters that migrated collectively around the dish with enduring cell-to-cell adhesions. This response was in stark contrast to the single cell migration and transitory cell adhesions that characterized cell behavior in the other ligands assessed. Collective cell migration plays an important role in development, the immune response, and cancer metastasis. Elucidating the molecular mechanism that drives OSM-induced collective migration can improve our understanding of these fundamental processes.

Systematic analysis of the molecular data implicated G-protein-coupled-receptor signaling (GPCRS) in OSM-induced collective migration. Additional experimental results support the involvement of protease activated GPCRs. However, delineating the precise mechanism underlying the phenotype requires further investigation. Comparative network analysis has been developed to unbiasedly nominate genes putatively involved in the emergence of the phenotype. Focused siRNA screens will be used to clarify the molecular mechanism linking OSM signaling to collective cell migration.