Regulation of cell polarity orientation during the epithelial-mesenchymal transition process

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Organization of cells into epithelium depends on cell interactions with both the extracellular matrix (ECM) and adjacent cells. The role of cell-cell adhesion in the regulation of epithelial topology is well described. ECM is better known to promote cell migration and provide a structural scaffold for cell anchoring but its contribution to multicellular morphogenesis is less understood. We developed a minimal model system to investigate how ECM affects the spatial organization of intercellular junctions. In this minimal system the mechanism of cell positioning can be distinguished from the mechanism of cell polarity orientation. Fibronectin micropatterns were used to constrain the location of cell-ECM adhesion (1). We found that ECM affects the degree of stability of intercellular junction positioning and polarity.

EMT is a normal developmental process of cellular plasticity defined by loss of epithelial cell morphology, dissociation of cell-cell contacts, reduction in proteins mediating cell-cell contacts, remodelling of the actin cytoskeleton and acquisition of a fibroblastic cell shape. Moreover, EMT is strongly associated with the conversion of early stage tumors into invasive malignancies (2). Using our minimal model system and different EMT state cells induced either by TGFβ1, or by genetic modifications, we explored the regulation of polarity orientation (3). We found that the capability to orient cell polarity in relation with external adhesive cues is maintained in TGFβ1 treated cells. In contrast, additional perturbations, such as the inhibition of the kinase activity of Src or depletion of CK2β, can lead to complete epithelium architecture deconstruction with mispositioned and mispolarised cells.

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