

P008 An RNAi screen to identify regulators of F-actin associated with adherens junctions

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Precise regulation of cell tension and contractility is necessary for formation of epithelia. Cell-cell junctions are known to transduce forces between epithelial cells and are essential for polarisation and morphogenesis of tissue. In order to polarise appropriately, reorganisation of the cytoskeleton and increased contraction are required. These processes act together to change a flat cell into a cuboidal cell shape.

Adherens junctions are essential for regulation of cell morphology and tension in epithelial cells. These junctions contain Ca^{2+} -dependant classical cadherins, which connect cells and act as signalling scaffolds regulating junction dynamics. Adhesive cadherin receptors trigger actin remodelling in two distinct ways: Firstly di-novo polymerisation of actin at cell-cell contacts which stabilises clustered cadherins. Secondly, compaction of pre-existing peripheral thin bundles of actin facilitates increase in cell height and formation of cuboidal morphology. Understanding the molecular mechanisms through which cell-cell adhesion can affect actin dynamics and actomyosin contraction will provide insights into the regulation of epithelial polarisation and homeostasis. We intend to determine the molecular mechanism of cadherin induced contractility and actin remodeling in epithelial cells. This will be done by carrying out a RNAi screen of cytoskeletal proteins, Rho GTPases, key organisers of structural effectors in the cytoskeleton and signalling proteins. Through this we expect to identify proteins that uniquely regulate actin dynamics and cadherin function during epithelial polarisation.