

P014 Spatiotemporal regulation of vinculin in cell-cell junction
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Cadherins are important in the control of crucial processes like tumor metastasis, embryonic development and vascular homeostasis. Although the down-regulation of E-cadherin expression (the main epithelial cadherin) is the predominant mechanism resulting in tumor metastasis, alternative mechanisms do exist to (de-) regulate E-cadherin adhesion. We have shown that cytoskeletal contraction, resulting in tension on the E-cadherin complex mediates the HGF-induced down-regulation of cell-cell adhesion without affecting E-cadherin expression, implying that cytoskeletal tension could initiate such an alternative mechanism.

We are currently investigating how tension affects the E-cadherin complex at the molecular level. Preliminary data implicate vinculin as a key player: it strongly localizes in cell-cell junctions when they experience tension and is required for the efficient formation of E-cadherin adhesions (which is tension-dependent as well). To further investigate the role of vinculin in cell-cell junctions we use a FRET-based vinculin biosensor, developed by Chen et al. Loss of FRET indicates the active/open conformation, which depends on simultaneous interactions of the head domain, for instance with members of the E-cadherin complex, and the tail-domain with actin. Live cell imaging of this biosensor in epithelial cells will reveal the spatiotemporal activity of vinculin at cell-cell junctions and thus elucidate its possible role in the cytoskeletal linkage of the E-cadherin complex when it experiences tension.