

INVITED LECTURE T16

Adhesion and mechanosensing at cell-cell junctions

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Cell adhesion is essential for the hierarchical organization of all multicellular organisms. Cell surface adhesion proteins mechanically couple to the extracellular matrix or mediate intercellular junctions. It is also increasingly clear that adhesion proteins trigger intracellular signalling to modulate cell functions. In particular, cadherins are a class of adhesion proteins that mediate cell-cell adhesion in all solid tissues. But they are also signalling proteins that regulate cytoskeletal organization and hence modulate cell shape and cell movements. Cadherins also coordinate with integrins to regulate cell shape, tissue boundaries, and cell migration. While integrins are well known mechanosensors, the mechanisms of mechanotransduction at cadherin-mediated intercellular junctions have not been explored.

In this talk, I describe recent studies of adhesion and mechanotransduction at cadherin junctions. We use micro- and nanomechanical force probes to interrogate both the adhesive properties of cadherin bonds as well as mechanisms of mechanotransduction across cell membranes at cadherin junctions. Direct molecular force measurements quantified differences in cadherin adhesive strengths. Investigations of intracellular signalling responses further reveal relationships between cadherin structure, adhesive strength, and the activation of intracellular signalling pathways. In this context, nanoscale force probes further enabled us to determine whether cadherins, like integrins, are mechanosensors with the capacity to modulate cell mechanics in response to applied force. These studies reveal similarities and important differences between mechanosensing by integrins and cadherins, and emphasize their different roles in regulating cell function and tissue organization.