

To make and keep: diverse modes of cadherin-cooperativity determine contact formation and adhesive recognition

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Classical cadherin adhesion molecules are key determinants of tissue patterning in metazoan organisms. These adhesion receptors support a wide range of biological activities, ranging from dynamic cell-upon-cell rearrangements during morphogenesis, cell-cell recognition and intercellular cohesion. It has long been appreciated that cadherins function in intimate cooperation with the actin cytoskeleton. Increasingly we are also coming to appreciate that diverse modes of cadherin-actin cooperativity accompany the many biological functions of cadherins. In our recent work, we have begun to characterize two patterns of cadherin-actin interaction. The first involves functional cooperation between E-cadherin and the Arp2/3 actin nucleator complex that is regulated by the GTPase, Rac, to support efficient assembly of cell-cell contacts. We postulate that this plays a central role in regulating local membrane protrusiveness during contact formation and remodelling. The second pattern links large cadherin clusters to prominent actin cables, and requires myosin 2 in a Rho kinase-dependent pathway. We propose that coupling of cadherins to actin cables provides a mechanism for the long-distance mechanical integration of cells to one another. Notably, both cadherin-Arp2/3 and cadherin-bundle interactions can co-exist even within individual contacts, suggesting that the strict spatio-temporal regulation of different modes of cadherin-actin cooperativity is critical for the assembly and remodelling of cell-cell contacts.