Nectin-induced Formation of Cell-Cell Junction Mediated by Small G Proteins

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Nectin is a newly identified cell-cell adhesion molecule with three immunoglobulin-like loops in its extracellular region and localizes at adherens junctions (AJs), one of the specialized cell-cell junctional apparatuses. Nectin as well as cadherin, another cell-cell adhesion molecule at AJs, plays essential roles in the formation of AJs. A series of our studies have revealed that in the process of the formation of cell-cell adhesion between neighboring cells, nectin first *trans*-interacts at primordial cell-cell contact sites and then cadherin is recruited to and clusters at the nectin-based cell-cell adhesion sites, resulting in the establishment of AJs. The *trans*-interaction of nectin induces the activation of Rap1, Rac, and Cdc42 small G proteins through c-Src and reorganizes actin cytoskeleton mediated by these small G proteins. This reorganization of actin cytoskeleton promotes the formation of AJs by increasing the number of cell protrusions such as filopodia and lamellipodia at the cell periphery and enhancing the recruitment of cadherin to the nectin-based cell-cell adhesion sites. Nectin-induced intracellular signaling including the activation of small G proteins requires the activation of integrin, a cell-matrix adhesion molecule, and FAK, a signaling molecule that transduces the integrin-initiated outside-in signals. In addition, nectin physically associates with integrin through their extracellular regions. These results indicate that the cross-talk between a cell-cell adhesion molecule nectin and a cell-matrix adhesion molecule integrin is important for the activation of small G proteins and subsequent formation of cell-cell junctions.