

## CURRICULUM VITAE

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## **Nectins and necls: Roles in cell migration, adhesion, and proliferation**

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When migrating cells contact other cells, they stop migration and proliferation. This phenomenon is known for a long time as contact inhibition of cell movement and proliferation. Transformation of cells causes disruption of cell-cell adhesion, increase of cell motility, and loss of the contact inhibition of cell movement and proliferation, eventually leading transformed cells to uncontrolled cell proliferation, invasion into surrounding tissues, and finally metastasis to other organs. Cell-cell adhesion is mainly mediated by cell-cell adherens junctions (AJs). Cadherins are key  $\text{Ca}^{2+}$ -dependent cell-cell adhesion molecules at AJs. Cadherins are associated with the actin cytoskeleton through  $\alpha$ - and  $\beta$ -catenins.  $\beta$ -Catenin is a cadherin- and  $\alpha$ -catenin-binding protein, whereas  $\alpha$ -catenin is a  $\beta$ -catenin- and actin filament-binding protein. We have recently found novel  $\text{Ca}^{2+}$ -independent Ig-like cell-cell adhesion molecules, named nectins, at AJs. Nectins constitute a family consisting of four members, nectin-1, -2, -3, and -4. Nectins are associated with the actin cytoskeleton through afadin, a nectin- and actin filament-binding protein. Nectins are furthermore associated with cadherins through afadin and catenins and involved in formation of AJs in cooperation with cadherins. In addition, nectins induce activation of Cdc42 and Rac small G proteins, which regulate cell-cell adhesion through reorganization of the actin cytoskeleton, gene expression through activation of a mitogen-activated protein kinase cascade, and cell polarization through cell polarity proteins. On the other hand, five nectin-like molecules (necls), which have domain structures similar to those of nectins but do not bind afadin, have recently emerged and appear to play different roles from those of nectins, but in cooperation with nectins. We have recently found that one of them, named necl-5, plays roles in cell migration and proliferation in cooperation with nectin-3 and integrins. Furthermore, necl-5 is up-regulated in transformed cells. Accumulating evidence suggests that nectins and necl-5 are cooperatively involved in contact inhibition of cell movement and proliferation. In this symposium, we describe the roles of nectins and necls in cell migration, adhesion, and proliferation.