

## **E-CADHERIN EXTRA-CELLULAR DOMAIN INTERACTION EXAMINED BY ATOMIC FORCE MICROSCOPY**

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In tissue formed from cell monolayers, such as intestinal epithelia, cell adhesion is mainly achieved by trans-membrane proteins called cadherins, whose binding is  $[Ca^{++}]$  dependent. E-cadherin mediated adhesion initiates epithelial cell development into extended tissues, but the mechanisms for this adhesion are not well characterized.

During cell adhesion, membrane contacts initially coalesce individual cell surface E-cadherins into aggregates along contacting membranes. These aggregates later coalesce into larger plaques. We studied the effects on the binding interaction of the isolated extra-cellular domain of this high concentration of E-cadherins using atomic force microscopy (AFM) as a probe of trans-interaction forces in recombinant E-cadherin. Specially modified AFM cantilevers measured adhesion strength from single-bond level through to higher concentrations found in plaques, with pico-Newton force resolution. We characterized the dependence of extra-cellular homophilic E-cadherin trans-binding on surface protein density.

Studies indicate that cell-cell communication and adhesion respond to local variations of free  $[Ca^{++}]$  in the intercellular regions. Our novel AFM force spectroscopy method revealed elementary and multiple  $[Ca^{++}]$  dependent molecular recognition, with forces ranging from 15 to 200 pN.