Abstract for an Invited Paper
for the MAR09 Meeting of
The American Physical Society

Single-molecule Force Spectroscopy of Intercellular Adhesion in Cancer

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The progression of several human cancers correlates with the loss of a-catenin from E-cadherin-rich intercellular junctions and loss of adhesion. However, the potential role of a-catenin in directly modulating the adhesive function of individual E-cadherin molecules in human cancer is unknown. Here we use single-molecule force spectroscopy to probe the tensile strength, lifetime, and interaction energy between live human parental breast cancer cells lacking a-catenin and these cells where a-catenin is re-expressed. We find that the tensile strength and lifetime of single E-cadherin bonds between parental cells are significantly lower over a wide range of loading rates. Statistical analysis of the force-displacement spectra reveals that single cadherin bonds between cancer cells feature an exceedingly low energy barrier against tensile forces and low molecular rigidity. These results suggest that the loss of a-catenin drastically reduces the adhesive force between individual cadherin pairs on adjoining cells, explain the global loss of cell adhesion in human breast cancer cells and show that the forced expression of a-catenin in cancer cells can restore both higher intercellular avidity and intermolecular E-cadherin affinity.