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PROCEEDINGS

A Platform to Examine the Mechanics and Mechanotransduction of Single Cell-Cell Adhesions

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ABSTRACT

Cell-cell adhesions are often subjected to mechanical strains of different rates and magnitudes in normal tissue function and in disease conditions. To date, few strategies exist to directly and quantitatively investigate the effect of mechanical forces exerted by cell-cell adhesions, even less the effect of applied load on the transduction of these forces into biochemical signals. To address this knowledge gap, we designed and fabricated a platform that performs quantitative mechanical characterization of single cell-cell adhesion structures using two photon polymerization of multiple materials [1]. This microsystem provides interrogation and stimulation of cell-cell junctions through defined mechanical tension and allows direct examination of mechanotransduction pathways mediated by cell-cell adhesions. Using this platform, we performed displacement-controlled tensile tests of individual pairs of adherent epithelial cells with a mature cell-cell adhesion. Straining the cytoskeleton-cell adhesion complex system reveals a strain rate-dependent stress relaxation mechanism mediated by cytoskeleton growth. Specifically, under low strain rates, stress relaxation mediated by the cytoskeleton can effectively relax junctional stress buildup and prevent adhesion failure, while high strain rates result in elevated stress levels at cell-cell adhesions and junction rupture. Imaging the cell-cell adhesions when they are subjected to defined strains shows significant clustering of E-cadherin molecules at the adherens junction when strains are over 50% [2]. This E-cadherin clustering is accompanied by the remodeling of the actin cytoskeleton, and thus validating the idea that stress relaxation or buildup are mediated by actin contractility. Collectively, the platform and the biophysical understandings build a foundation for the mechanistic investigation of the adaptive viscoelasticity of cell-cell adhesions.

KEYWORDS

Cell-cell adhesion; cell mechanics; mechanotransduction

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