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Mechanisms of Cell Adhesion and Migration on Simple and Complex Surfaces

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Coordinated motion is a hallmark of animal behavior at diverse length scales, ranging over about 9 orders of magnitude for individuals and about 3 orders of magnitude more for populations. My laboratory is studying selected biophysical and biochemical aspects of cell adhesion and migration with a view towards novel materials applications in biotechnology and medicine. The cells of this talk are normal human dermal fibroblasts, skin cells. The materials are non-woven electrospun fibers made of synthetic polypeptides. We have characterized physical properties of these materials. We have analyzed cell interactions with fibers by microscopy. Specific protein constituents of focal adhesions (FAs) have been stained with fluorescent antibodies, and cell migration in real time has been monitored by phase-contrast microscopy and confocal laser-scanning microscopy. Analysis of samples stained for specific focal adhesion proteins showed that the surface density of FAs on fibers, 6 x $10^{-3}\mu m^2$, was about 2-fold higher than on glass, essentially a planar substrate. Further analysis showed that the average angle between the major axis of focal adhesions and the fiber trajectory was 22 deg., roughly half of the expected value for random orientation. The alignment data have been interpreted in terms of beam statistical mechanics, yielding a flexural rigidity of 8.3 x 10^{-26} N-m^2. This stiffness is about 10^3-fold smaller than for microtubules and 25% greater than for actin filaments. Modeling based on this result is consistent with the experimental result that FA alignment increases as fiber diameter decreases. We have also utilized near-UV circular dichroism spectroscopy and intrinsic fluorescence emission spectroscopy to obtain Langmuir isotherms for cytoplasmic tails of integrin β subunits associating with intracellular focal adhesion constituents in vitro. Dissociation constants obtained by fitting a single-site model to the experimental data range from 8.3 μM to 50 nM at ambient temperature. Taken together, the results suggest that the coupling between FAs and stress fibers is tight and highly specific, and there is a quantifiable thermal limit to the energy cost a cell will pay to form an adhesion site. The results further suggest a limit to the benefits that can be derived from cellular interaction with disorganized nanostructured materials.