Cancer, Stem cells & Developmental biology

The Master's & The PhD Programme

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Mechanisms of cell sensing of the nanoscale topography and mechanics of the ECM

The mechanical properties and nanotopography of the extracellular matrix have an important impact on cell phenotype. Such physical cues been shown to regulate cell adhesion and spreading, cell motility, proliferation and differentiation in a wide range of cells, stem cells as well as cancer cells. However, mechanisms underlying mechanical and nanotopography sensing remain unclear. We are interested in developing nanoscale engineered extra-cellular matrices to study such mechanisms. In particular, we show that focal adhesions, typically regarded as essential mechanosensors, are not primary sensors of the nanotopography and that the dynamics of the microscale acto-myosin network acts instead as a global sensor of nanoscale topography and geometry. In contrast, our results demonstrate that mechanosensing occurs primarily at the nanoscale: we show that cells can directly sense the nanoscale mechanics of their environment. Indeed, we made the surprising observation that adherent cells can spread and proliferate at the surface of low viscosity liquids. Although this does not seem to agree at first glance with the general vue that bulk mechanical properties of materials are essential to sustain focal adhesion maturation, cytoskeletal assembly and cell spreading, we discovered that cell adhesion to liquid substrates is mediated by the assembly of a protein nanosheet, at the interface between the two liquids (an oil and the tissue culture medium). The strength of these nanosheets, depending on parameters regulating its assembly, can sustain shear forces generated by cells during their spreading. We show that cell spreading at such liquid interfaces is mediated by integrin ligation, focal adhesion formation and acto-myosin contractility. In addition, we show that this behaviour depends on the interfacial mechanical properties of the protein layer assembled. Finally, we show that keratinocyte differentiation is not initiated by spreading at the surface of liquids, despite the absence of bulk mechanical properties. Our results suggest that nanoscale mechanical properties of biomaterials may dominate over bulk physical properties. This concept has important implications for the design of biomaterials in the field of regenerative medicine.

See:

http://biointerfaces.qmul.ac.uk/

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