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Internal Seminar

Differential Adhesion Hypothesis Revised: Is there Experimental and Proteomic Evidence?

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We analysed the mechanical properties of three epithelial/mesenchymal cell lines (MCF-10A, MDA-MB-231, MDA-MB-436) associated with properties from benign to metastatic tumours, to quantify the role of cell cohesion in cell sorting and compartmentalization. The analysis included quantitative mass spectroscopy SILAC, of the underlying proteome of the cell lines. We developed a unique set of methods to measure cell – cell adhesiveness, cell stiffness and cell shapes, and compare the results to predictions from cell sorting in mixtures of cell populations. We find that the final sorted state is extremely robust among all three cell lines independent of epithelial or mesenchymal state, suggesting that cell sorting may play an important role in organization and boundary formation in tumours. Furthermore, SILAC mass spectroscopy of these cell lines reveals significant differences in the proteome, especially parts and pathways of it associated with related cellular function and structures, i.e. adhesion, metabolism, cytoskeleton. SILAC analysis was able to intertwine tumour-associated proteins of cells with their found mechanical properties. We find that surface densities of adhesive molecules fail to correlate with measured cell – cell adhesion, but do correlate with cell shapes, cell stiffness and the rate at which cells sort, in accordance with an extended version of the differential adhesion hypothesis (DAH). SILAC mass spectroscopy reassembles and supports the experimental findings on a proteomic level and bridges the gap from observable macro- and mesoscopic quantities, given above, down to molecular details of cells. Surprisingly, the DAH does not correctly predict the final sorted state. This suggests that these tissues are not behaving as immiscible fluids, cells can be kinetically trapped and that dynamical effects such as directional motility, friction and jamming may play an important role in tissue compartmentalization across the epithelial − mesenchymal transition.

Wednesday, Oct 5th 2016

11:30 AM (Tea/Coffee at 11:15 AM)

Seminar Hall, TCIS