



Life Sciences Seminar

Modular integrin nanoclusters are signalling units of cell matrix adhesions.

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Host: Michael Sixt

Cell matrix adhesions attach the cell to the extracellular matrix, sense its force and geometry and convert that information into biochemical signals so that the cell can mount an appropriate response. How do fibroblasts present in connective tissues of various stiffness respond correctly to substrate stiffness and how are these signals converted into biochemical signals? To get insights into these questions, we combine super resolution microscopy and live cell microscopy with nanopatterning of the substrates. Using supported lipid bilayers, we discovered that integrin nanoclusters on integrins are laid out on substrates of all rigidities as a starting point for formation of cell matrix adhesions. They form as a first response to sensing the biochemical ligand and help the cell to sense the substrate rigidity. Using nanopatterned fiber mimetic lines functionalized with RGD, we discovered that assembly of these nanoclusters is sensitive to substrate geometry wherein they assemble only on two dimensional substrates but not on one dimensional substrates. As these nanoclusters bridge the thin fiber mimetic substrates by clustering both ligand bound and unbound (albeit activated) integrins. Further, we discovered that these early nanoclusters serve as differential signalling platforms wherein critical signals required for cell survival and growth including talin cleavage and ligand independent EGFR signalling is activated specifically on rigid substrates. Moreover, we showed that mature adhesions are aggregates of integrin nanoclusters and these clusters serve as signalling platforms to bring about function. Taken together these results indicated that nanoclusters of integrins formed on 2D substrates are key to downstream adhesion signalling needed for survival, motility and growth.

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IST Austria Campus Mondri Seminar Room 1, Central Building



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