Proceedings of the 5th International Conference on Nanotechnology: Fundamentals and Applications
Prague, Czech Republic, August 11-13, 2014
Paper No. 144

Material-driven Protein Assembly to Engineer the Cellular Microenvironment

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Extended Abstract

Fibronectin (FN) is a ubiquitous glycoprotein and an essential component of the extracellular matrix (ECM). Most cells assemble rich FN matrices via an integrin-dependent process that incorporates FN molecules into growing matrix fibrils FN fibrils that form linear and interconnected networks. The assembly of FN matrix is the initial step that triggers the organisation of other ECM proteins and direct cell adhesion, migration and signalling. The functional properties of the FN matrix are diverse, as they possess binding sites for multiple ECM components, including collagens, heparin, growth factors and other FN molecules. FN in solution has a compact conformation that is maintained by intramolecular interactions between $III_{2\text{-}3}$ and $III_{12\text{-}14}$ modules. However, integrin binding of FN molecules induces the formatio of integrin clusters, which groups together cytoplasmic proteins and promotes the formation of focal complexes. These complexes activate the polymerization of the actin cytoskeleton and intracellular signaling pathways. Receptor clustering by dimeric FN helps to organize FN into short fibrils. After that, cell contractility contributes to FN fibril formation. through a progressive extension of the FN molecule and the exposure of binding sites that mediate lateral interactions between FN molecules. Initial thin fibrils grow in length and thickness as the matrix matures and FN fibrils are converted in an insoluble form. Proper integration of extracellular signals with active intracellular pathways plays a crucial role in the initiation, progression and regulation of FN matrix assembly (Singh et al. 2010).

Significant effort has been devoted to engineer materials that recapitulate the characteristics of the ECM, such as materials presenting cell-adhesive motifs or protease-degradable cross-links). Here we show material-based approaches to reconstitute the network structure and bioactivity of FN fibrillar matrices. We demonstrated that adsorption of individual FN molecules onto particular surface chemistries induced the exposure of self-assembly sites, driving FN fibril assembly, a process that we named material-driven FN fibrillogenesis (Salmeron-Sanchez et al. 2011). We identified poly(ethyl acrylate) (PEA) as a simple and robust surface chemistry able to trigger this process for this purpose. We investigated the organization of FN molecules at the material (PEA) interface and studied its analogy with the physiological cell-induced FN fibrillogenesis. The resulting FN matrix assembled at the material interface consists of a protein network with enhanced biological activity: it supports cell adhesion, matrix remodeling, and trigger cell differentiation. Moreover, it provides a robust platform to engineer advanced microenvironments in combination with growth factors to tune stem cell differentiation and promote tissue repair.

References

Salmerón-Sánchez M., Rico P., Moratal D., Lee T.T., Schwarzbauer J.E., García A.J. (2011). Role of material-driven fibronectin fibrillogenesis in cell differentiation. Biomaterials, 32, 2099-2015

Singh P., Carraher C., Schwarzbauer J.(2010). Assembly of fibronectin extracellular matrix. Annu. Rev. Cell Dev. Biol, 26, 397-419