Development and Application of New Micro and Nanotechnologies to Study Cell Navigation

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Cell navigation underlies many critical biological processes such as development, nerve repair or cancer. Due to the significance of this process, its role in the treatment of health disorders is currently under heavy scrutiny. Despite the potential impact of understanding cell navigation, studies of its underlying molecular mechanism have been limited in large part due to the constraints of available methods to produce complex substrate-bound protein patterns.

In this talk, I will discuss how we developed a range of novel surface patterning methods to study cell navigation at the cellular, molecular and biophysical levels. Specifically, a novel haptotaxis assay was developed relying on 1) novel geometrical designs to create digital nanodot gradients of record dynamic range, 2) a low-cost lift-off nanocontact printing method to pattern protein down to 100 nm dots, and 3) the optimization of the reference surface, or the non-patterned surface, to ensure that cells respond to the patterned ligand via appropriate biochemical transduction pathways. This assay was applied to planar surfaces to study cell navigation but also to arrays of high aspect ratio PDMS pillars to study cell mechanotransduction during cell choice. Applications for all the developed methods will be discussed with a focus on the study of axonal navigation.

To study how cells integrate multiple sensing mechanisms, the molecules in the haptotaxis assay were covalently grafted to the surface to withstand high flow rates. This assay was then integrated into a microfluidic device to simultaneously present cells with substrate-bound and soluble protein cues. This tool for the first time enables the study of the relationship between haptotaxis (migration driven by immobilized cues) and chemotaxis (migration driven by soluble cues).