Cell Proliferation in Gradients of Chemical Cues

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To create complex tissues *ex vivo*, it is essential to understand how multiple cues in the cellular environment interact to control cell growth and patterning. While progress is being made in discovering these interactions, the current models are far from complete. Three environmental cues of interest in fully understanding cell proliferation are cell-cell, cell-substrate, and cell-soluble factor interactions. Previous work has shown that sufficient epidermal growth factor concentrations can act as a switch to override contact inhibition of proliferation caused by cell-cell interactions and that cell-substrate interactions influence this threshold. However, the implications of this quantitative crosstalk among environmental cues for tissue growth and patterning remain to be elucidated. In vivo tissue growth and patterning is driven by gradients of soluble factors. In this work, to investigate the interplay between cell-cell and cell-substratum interactions in tissue growth in a spatial soluble factor gradient, a l-input, m-output gradient generating microfluidic device molded in poly(dimethylsiloxane) (PDMS) using soft lithography is fabricated. Cells can be cultured in the PDMS device and exposed to a gradient of soluble factors. By manipulating the expression of key proteins and observing phenotypic changes, novel connections in signaling pathways can be elucidated.