Induction of embryonic stem cell differentiation by physical cues

Mouse embryonic stem cells (mESCs) are pluripotent stem cells capable of differentiating into many cell types based on the growth factors and physical cues provided by the microenvironment. These biophysical cues of the substrate are found to regulate cellular processes ranging from cell division to cell differentiation. Subtle changes in bio-chemical or physical parameters of the micro-environment are found to trigger lineage specific differentiation. neurological diseases like Parkinson's disease and Alzheimer disease. Our innovation lies in targeting generation of dopaminergic neurons (DNs) from mESCs mechanically (i.e., by combining substrate stiffness and substrate topography) without using chemical morphogens. We propose that combination of substrate stiffness and topography can be used as an attractive strategy to trigger differentiation of mouse ESCs into functional DNs.

Differentiation is long term process regulating



mESCs cultured on flat PDMS substrates or on grooved substrates for 2 weeks. mESCs were stained for β -tunulin III

For applications of stem cells for regenerative medicine, a critical need is to come up with scalable systems that can be used for long term maintenance of stem cells in their undifferentiated state and/or to induce directed differentiation. Usage of soluble factors in regulating stem cell state is expensive, and does not induce uniform differentiation with high specificity and yield.

In our lab, we are working on multiple strategies for inducing mESC differentiation using physical cues. In one such approach, we are combining stiffness and topography as two tunable physical cues for inducing mESC differentiation into dpominergic neurons (DNs), that are damaged in many transcriptional networks. mESCs have tendency to randomly differentiate into neuroectoderm. Our initial studies have indicated that the absence of LIF triggers differentiation and culturing of single mESCs on 5 µm parallel microgrooves crosslinked with fibronectin can trigger differentiation of single mESCs into dopaminergic neurons.