Engineering collective behavior in stem cell-driven tissues

Tiam Heydari

UBC/ school of biomedical engineering

Abstract

Through evolution, living systems gain the capability to self-organize via collective complex dynamics. Collective dynamics refers to the population level change which is the result of the complex dynamics of interacting entities. Recently some studies suggest the existence of collective dynamics in stem cell differentiation. In the differentiation process of human pluripotent stem cells (hPSC) in small colonies, cells differentiate more homogenously when the number of cells in the colony is higher. In this work, we hypothesize that collective behavior governs the hPSC differentiation process, and this collective behavior can be dissected in the colonies with a small number of stem cells. We first develop a theoretical tool, based on the concept of entropy to quantify different degrees of collective order in stem cell colonies. Next, we propose a theoretical method to model collective behavior based on the dynamics of individual cells and cell-cell communication. To experimentally validate the theoretical results, we propose to use the micropatterning technology to culture the hPSC cells on very small micropatterns in different BMP4 levels and then follow the culture by quantitative image analysis at the single-cell level from time series of images. Our results can guide the engineering design of synthetic cells with the capability to drive the function and the size of stem-cell driven tissues.

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