Learning to design and implement synthetic developmental trajectories

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Embryonic development can be thought of as a technological approach to build complex machines, and it relies on naturally evolved genetic circuit of cell-cell communication, information processing and morphogenesis. In the field of synthetic development, we and others are identifying forward-engineering approaches to control self-organization of multicellular systems towards the formation of multicellular structure of user-defined shape, patterns and ultimately function. I will present results from our lab along 3 approaches that we have explored recently. (1) We used synthetic signaling-based circuits for the formation of patterned symmetric, and asymmetric structures in naïve mouse fibroblasts, by using synthetic Notch signaling circuits and genetic control of effectors to control cell-cell adhesion, proliferation and cytoskeletal tension. (2) Used combination of material engineering and cell engineering to spatially control differentiation of mouse embryonic fibroblasts into endothelial precursors and skeletal muscle precursors. To do so, we used a variety of methods for material engineering including microcontact printing, photopatterning, genetic fusion, to pattern the synthetic ligands, alongside engineering of cells with transdifferentiation-inducing synNotch pathways. (3) Screened and identified growth-factors-based protocols that are conducive for the self-organization of mouse embryonic stem cells into contractile and ultimately motile aggregates. To do so, we used cardiogenic mesendoderm induction protocols (Activin/Bmp ligands for mesendoderm induction and VEGF/FGF ligands for cardiogenesis support) inspired by cardiogenic gastruloid protocols. These new cardiogenic mesendoderm induction protocols generate aggregates with high percentage of contractile units (cardiomyocytes), and can autonomously move in a liquid medium. We will discuss how these approaches represent advancements in the field of synthetic development, and to what extent these can be generalized and applied to a larger repertoire of model systems and applications.