Mammalian Synthetic Biology – Foundations and Applications to Programmable Organoids

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Mammalian synthetic biology has recently emerged as a field that is revolutionizing how we design and engineer biological systems for diagnostic and medical applications. In this talk, we will describe our integrated computational / experimental approach to engineering complex behavior in mammalian cells with applications to Programmable Organoids derived from iPS cells. In our research, we apply design principles from electrical engineering and other established fields. These principles include abstraction, standardization, modularity, and computer aided design. But, we also spend considerable effort towards understanding what makes synthetic biology different from all other existing engineering disciplines by discovering new design and construction rules that are effective for this unique discipline. We will present Programmable Organoids, a new platform for drug discovery that enables rapid and effective drug screening. Based on programmed differentiation into synthetic mammalian tissues having multiple cell type architectures that are similar to human organs, Programmable Organoids mimic the response of a target organ to both positive and negative effects of drug candidates. Factors that can be non-destructively measured include cell state, viability, and function. Because they are synthetic, Programmable Organoids can host a large array of live-cell biosensors, built-in to one or more cell types, providing a rapid and real-time spatial readout of pathway-specific biomarkers including miRNAs, mRNAs, proteins, and other metabolites. Organoids programmed with both general and disease specific sensors then provide detailed information that can be used to identify candidates for further analysis. We envision a programmable common platform that can be shared among multiple drug candidates.