Supervisor: A/Prof Yen Choo (yen.choo@ntu.edu.sg)

Field	Details
Title	**Direct Cell Reprogramming for Biomedical Applications**
Remarks	**Funding support will be provided for a suitable candidate**
Project Description	The manufacture of advanced stem cell-based products and therapies through directed differentiation faces significant challenges in achieving efficient, reliable, and scalable production of specialized cell types especially in a cGMP setting. Cell differentiation approaches involve stepwise culture of (pluripotent) stem cells to direct their development into target cell types. However, current manufacturing methods are generally not fit for purpose - being often hampered by complex, lengthy and costly protocols, low cell yield, purity and/or quality, and inconsistent outcomes - limiting industrial applications. Direct (or forward) cell programming offers a promising alternative by enabling the direct conversion of one cell type into another by activating gene regulatory networks that determine cell identity. This approach has the potential greatly to streamline the manufacturing process, reduce the time and resources required, and improve the consistency and functionality of cellular products. As the advanced therapy field develops, establishing robust, scalable manufacturing technology platforms (such as by direct cell programming) will become key to the success of the regenerative medicine and cell therapy industry. Programming of cells using lineage control networks has the potential to transform how we make cell therapies and immunotherapies, develop regenerative medicines, and create cellular models for research. However, identifying specific combinations of master regulatory genes known as transcription factors (TFs) that lead to highly efficient conversion of a scalable starting cell (e.g. iPSC, fibroblast) into desired cell types for biomedical applications (e.g. T cell, b cell) remains a significant challenge and a longstanding, critical bottleneck in the field. In this programme we will use an innovative combinatorial screening technology to rapidly assess the effectiveness of thousands of combinations of TFs in programming various human cell types into specific lineages that enable high value biomedical applications. Cell types we may derive in this project have diverse applications, including in: 1) developing advanced cellular/tissue models for biomedical R&D, 2) cGMP manufacturing of cell and gene therapies, including allogeneic immunotherapies, and 3) in vivo reprogramming for regenerative medicine and autologous immunotherapies.