HETEROTYPIC CELL-CELL INTERACTION OF HUMAN STEM CELLS FOR NERUAL DIFFERENTIATION OF HYBRID SPHEROIDS

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Organoids, the condensed 3-D tissues emerged at the early stage of organogenesis, are a promising approach to regenerate functional and vascularized organ mimics [1]. While incorporation of heterotypic cell types such as human mesenchymal stem cells (hMSCs) and human induced pluripotent stem cells (hiPSCs) derived neural progenitors aid neural organ development, the interactions of secreted factors during neurogenesis have not been well understood. The objective of this study is to investigate the impact of the composition and structure of 3-D hybrid spheroids of hiPSCs and hMSCs on dorsal cortical differentiation and the secretion of extracellular matrices and trophic factors in vitro. The hybrid spheroids were formed at different hiPSC:hMSC ratios (100:0, 75:25, 50:50, 25:75, 0:100) using direct mixing or pre-hiPSC aggregation method, which generated dynamic spheroid structure. The cellular organization, proliferation, neural marker expression, the secretion of extracellular matrix proteins and the cytokines were characterized. The incorporation of MSCs upregulated Nestin and β-tubulin III expression (the dorsal cortical identity was shown by Pax6 and TBR1 expression), matrix remodeling proteins and the secretion of transforming growth factor-β1 and prostaglandin E2. This study indicates that the appropriate composition and structure of hiPSC-MSC spheroids promote neural differentiation and trophic factor and matrix secretion due to the heterotypic cell-cell interactions.

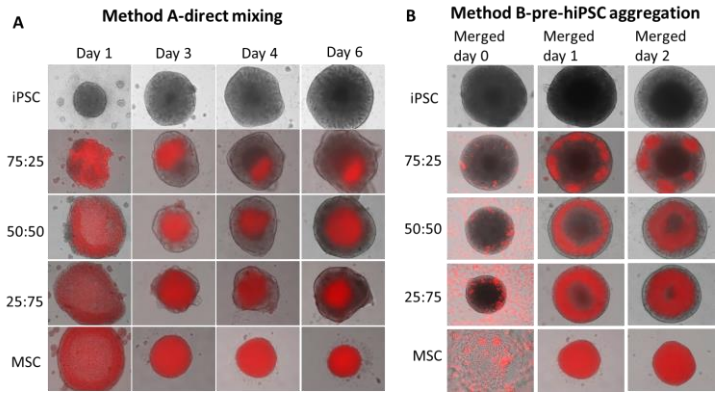

Figure 1 – Aggregate spatial cell distribution of hiPSC-hMSC spheroids formed by method A and method B

1. Takebe, T., et al., Vascularized and complex organ buds from diverse tissues via mesenchymal cell-driven condensation. Cell stem cell, 2015. 16(5): p. 556-65.