Human iPSC-Derived Cardiomyocyte Model Reveals the Transcriptomic Bases of SARS-CoV-2 Infection Induced Myocardial Injury

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Multi-organ complications have been the hallmark of severe COVID-19; cardiac injuries have been reported in 20% to 30% of hospitalized COVID-19 patients though the etiology remains poorly understood. This study leveraged genome-wide RNA-sequence data generated using cutting edge induced pluripotent stem cell (iPSC) differentiated cardiomyocyte (CM) and in-vitro modeling of SARS-CoV-2 infection in CMs to understand the molecular mechanisms of COVID-19 myocardial injuries for novel diagnostic and therapeutic development. Raw RNA-sequence data sets, GSE165242 and GSE150392 were aligned to human genome assembly GRCh38 and analyzed for differentially expressed (DE) genes. A total of 2,148 genes were significantly DE between SARS-CoV-2 infected and vehicle treated CMs and showed significant enrichment in cytokine signaling pathways (p-value=4.89E-25) and regulation of heart contraction (p-value=2.51E-19) gene-ontology biological processes. 606 of these DE genes were significantly upregulated during iPSC to CM differentiation. Disease and function annotation analysis of these 606 genes showed significant enrichment and activation of angiogenesis (p-value=4.04E-23; activation Z-score=3.7) and downregulation of heart contraction and related functions (p-value=4.24E-29; activation Z-score=-2.2) in SARS-CoV-2 infected CMs. The upstream regulator analysis identified upregulation of AGT associated proinflammatory genes and significant downregulation of TBX5 and MYOCD transcription factors and their gene networks suggesting remodeling of CM contractility architecture. My study has identified several drug candidates for proinflammatory gene targets and identified TBX5 and MYOCD gene networks as the potential targets for COVID-19 associated cardiac injury drug development.

Awards Won:
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