Translation of Novel Biologics for Myocardial Restoration

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Abstract:

We discovered the mitochondria-rich extracellular vesicles (MEVs) generated from induced pluripotent stem cell (iPSC) derived cardiomyocytes (iCMs). The MEVs transfer their mitochondrial payload efficiently into the injured cardiomyocytes, which harbor damaged mitochondria, to restore the intracellular bioenergetics and function of the ischemic myocardium. Furthermore, these MEVs contain non-mitochondrial proteomic cargo that augment PGC-1α mediated mitochondrial biogenesis, enabling sustained improvement of intracellular bioenergetics. This novel therapeutic approach will transform and advance the future of heart failure therapy and other mitochondria related disorders, which afflict human health. Pharmacologic therapies have improved survival in heart failure (HF) patients over the past three decades. Despite these pioneering efforts, HF is still the leading diagnosis of hospital admission, highlighting a need for innovative treatment strategies. HF represents bioenergetic imbalance. This disruption of the balance between energy supply and demand underlies the pathogenesis of HF. Cardiac tissue samples from all forms of cardiomyopathy patients exhibit abnormal mitochondrial structure and function, resulting in diminished ATP production despite increased metabolic energy demands in the failing heart. The current HF pharmacologic regimen, including β blockers, ivabradine, and renin–angiotensin-aldosterone antagonism, attempts to correct this imbalance by reducing cardiac workload, namely, energy demand. These therapeutics are essentially non-curative because they do not target the primary energy source of the failing heart. Therefore, it is essential to develop an innovative therapy that targets the intracellular bioenergetic supply directly. This lecture will discuss our translational effort of novel biologics from stem cell derived extracellular vesicles as the main effector of myocardial restoration.