

RMB CVRC Seminar

The Robert M. Berne Cardiovascular Research Center Presents

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Affiliations:

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Cell-specific LRP1 signaling in acute myocardial infarction

Improving the treatment of acute myocardial infarction (AMI) to prevent heart failure (HF) and death remains an urgent unmet medical need. The AHA estimates that every 42 seconds an American will have an AMI, and despite the improvement in treatment and prognosis, a significant number of patients develop continue to develop HF or die. Low-density lipoprotein receptor related protein-1 (LRP1) is a membrane receptor known as scavenger for the serine protease inhibitor (SERPIN)-enzyme complex (SEC), linked to anti-inflammatory and cytoprotective signaling. We and others have described the protective activities of LRP1 in ischemia-reperfusion injury during AMI. We showed that non-selective LRP1 agonists, and more recently, that a targeted small peptide selectively engaging LRP1, SP16, reduced infarct size in experimental animal models. LRP1's role in ischemia-reperfusion injury and infarct healing is, however, complex as LRP1 is involved not only in the cell survival pathway but also in the wound healing and repair process regulating fibroblast proliferation. We identified distinct LRP1 cell-specific functions in cardiomyocytes and fibroblasts in myocardial ischemia-reperfusion and infarct healing that can be leveraged for therapeutic purposes. Using computational models of cell-specific LRP1 signaling networks, cellular in vitro studies and preclinical animal models, we identified a protective signaling of LRP1 in cardiac myocytes and a proliferative, profibrotic effects in cardiac fibroblasts following experimental AMI.

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Refreshments served