# The Emerging Roles of Large-pore Pannexin 1 Channels in Cardiovascular Diseases

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**Abstract**

Pannexin 1 (PANX1) forms heptameric, large-pore ion channels expressed on the plasma membrane of various vertebrate cells, including neurons, T lymphocytes, vesicular endothelial cells, smooth muscle cells and cardiomyocytes. Activated PANX1 channels can bridge the intracellular compartments and extracellular milieu by permeating both inorganic ions and organic metabolites (e.g., ATP, spermidine or glutamate), thereby coordinating cell-to-cell communications. Our previous work demonstrated that PANX1-mediated ATP release from smooth muscle cells can promote sympathetic vasoconstriction and thus regulate blood pressure. In addition, recent studies also suggest that dysregulated PANX1 channels could contribute to the severity of varying cardiovascular disorders, such as ischemic stroke, myocardial infarction, abdominal aortic aneurysm, and pressure-overload-induced heart failure. In this presentation, I summarize emerging evidence supporting the roles of PANX1 in various cardiovascular diseases and describe the current understanding regarding the activation mechanisms of PANX1 channels. Specifically, I focus on illustrating how α1 adrenergic receptors activate PANX1 in smooth muscles cells and cardiomyocytes through two different non-canonical pathways. Given PANX1's involvement in cardiovascular disorders, I also discuss the potentials and limitations of currently available PANX1 pharmacology as a prospective medical intervention for treating cardiovascular diseases. By reappraising the experimental evidence regarding the pharmacology and regulatory mechanisms of PANX1 channels, we could identify

alternative therapeutic targets and present previously unappreciated strategies for treating cardiovascular diseases.