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Cardiac Myocytes Apoptosis, a Potential Target for the Treatment of Myocardial Infarction/Heart Failure

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Cardiovascular diseases are a heterogeneous group of disorders that affect the heart and blood vessels. Myocardial infarction is a disease of worldwide significance and increasing occurrence. It is a death of a segment of heart muscle, which follows interruption of its blood supply. Reduction in death rate and prevention of myocardial infarction are of utmost importance. Apoptosis or programmed cell death is the most common mechanism by which the body eliminates damaged and unwanted cells. Cardiac myocytes undergo apoptosis in various cardiovascular diseases such as ischemia [1,2], ischemia reperfusion [3,4], myocardial infarction and heart failure [5]. Further, the cardiomyocyte loss caused by apoptosis results in progressive myocardial dysfunction in myocardial infarction and heart failure [6]. Apoptosis is mediated by two main signaling pathways such as intrinsic or mitochondrial pathway and extrinsic or death receptor pathway. Intrinsic pathway begins when an injury occurs within the cell. Extrinsic pathway starts outside the cell, when conditions in the extracellular environment determine that a cell must die. Mitochondrial pathway [7] is stimulated by oxidative stress, lack of oxygen and deficiency of nutrient and growth/ survival factor. These stimuli translocate cytochrome-c from the mitochondria to the cytoplasm. Cytochrome- c and cytoplasmic dATP, then binds to and stimulates the oligomerization of Apaf-1 and subsequent recruitment and activation of procaspase-9.This leads to an activation of downstream procaspases-3,-6, and -7. Then proteolysis of specific cellular substrates occur, which leads to apoptosis [8]. In case of death receptor pathway [9], soluble or cell membrane bound ligands bind to cell surface receptors such as Fas and tumour necrosis factor-1 (TNFR-1).When Fas receptor binds to a signaling peptide Fas ligand(FasL), there will be a conformational change in Fas. This facilitates its cytoplasmic tail to recruit Fas-associated death domain protein (FADD) through interaction with the death domains of both molecules. Then, FADD recruits procaspase -8 through homotypic interactions with death effector motif, which in turn causes autoactivation of procaspase- 8. Subsequently, caspase -8 triggers downstream caspases and stimulates apoptosis [8]. In addition, Fas pathway is crucial for the initiation of apoptosis in cardiac myocytes. Thus, mitochondrial apoptotic pathway and Fas mediated death receptor apoptotic pathway are well associated with the pathogenesis of myocardial infarction/heart failure. So, inhibiting cardiac myocyte apoptosis is one of the potential targets for the treatment of myocardial infarction/heart failure.

Bibliography

1. Saraste A., *et al*. "Apoptosis in human myocardial infarction". *Circulation* 95.2 (1997): 320-323.
2. Bialik S., *et al*. "Myocyte apoptosis during acute myocardial infarction in the mouse localizes to hypoxic regions but occurs independently of p53". *Journal of Clinical Investigation* 100.6 (1997): 1363-1372.
3. Buerke M., *et al*. "Cardioprotective effect of insulin like growth factor-1 in myocardial ischemia followed by reperfusion". *Proceedings of National Academy of Science USA* 92.17 (1995): 8031-8035.
4. Fliss H and Gattinger D. "Apoptosis in ischemic and reperfused rat myocardium". *Circulation Research* 79.5 (1996): 949-956.
5. Olivetti G. *et al*. "Apoptosis in the failing human heart". *New England Journal of Medicine* 336.16 (1997): 1131-1141.
6. Krijnen PA., *et al*. "Apoptosis in myocardial ischaemia and infarction". *Journal of Clinical Pathology* 55.11 (2002): 801-811.
7. Hengartner MO. "The biochemistry of apoptosis". *Nature* 407.6805 (2000): 770-776.
8. Lee P., *et al*. "Fas pathway is a critical mediator of cardiomyocyte death and MI during ischemia- reperfusion in vivo". *American Journal of Physiology, Heart and Circulation Physiology* 284.2 (2003): H456-H463.
9. Ashkenazi A and Dixit VM. "Death receptors: signaling and modulation". *Science* 281.5381 (1998): 1305-1308.

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