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Calpains; Insights Into the Pathogenesis of Heart Failure

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Abstract : Heart failure (HF) prevalence, as a global cardiovascular problem, is increasing gradually. A variety of molecular mechanisms contribute to HF. Proteins involved in cardiac contractility regulation, such as ion channels and calcium handling proteins, are altered. Additionally, epigenetic modifications and gene expression can lead to altered cardiac function. Moreover, inflammation and oxidative stress contribute to HF. The progression of HF can be attributed to mitochondrial dysfunction that impairs energy production and increases apoptosis. Molecular mechanisms such as these contribute to the development of cardiomyocyte defects and HF and can be therapeutically targeted. The heart's contractile function is controlled by cardiomyocytes. Calpain, and its related molecules, including Bax, VEGF, and AMPK, are among the proteins involved in regulating cardiomyocyte function. Apoptosis is facilitated by Bax. Cardiomyocyte apoptosis is regulated by this protein. Furthermore, cardiomyocyte survival, contractility, wound healing, and proliferation are all regulated by VEGF, which is produced by cardiomyocytes during inflammation and cytokine stress. Cardiomyocyte proliferation and survival are also influenced by AMPK, an enzyme that plays an active role in energy metabolism. They all play key roles in apoptosis, angiogenesis, hypertrophy, and metabolism during myocardial inflammation. The role of calpains has been linked to several molecular pathways. The calpain pathway plays an important role in signal transduction and apoptosis, as well as autophagy, endocytosis, and exocytosis. Cell death and survival are regulated by these calcium-dependent cysteine proteases that cleave proteins. As a result, protein fragments can be used for various cellular functions. By cleaving adhesion and motility proteins, calcium proteins also contribute to cell migration. HF may be brought about by calpain-mediated pathways. Many physiological processes are mediated by the calpain molecular pathways. Signal transduction, cell death, and cell migration are all regulated by these molecular pathways. Calpain is activated by calcium binding to calmodulin. In the presence of calcium, calmodulin activates calpain. Calpains are stimulated by calcium, which increases matrix metalloproteinases (MMPs). In order to develop novel treatments for these diseases, we must understand how this pathway works. A variety of myocardial remodeling processes involve calpains, including remodeling of the extracellular matrix and hypertrophy of cardiomyocytes. Calpains also play a role in maintaining cardiac homeostasis through apoptosis and autophagy. The development of HF may be in part due to calpain-mediated pathways promoting cardiomyocyte death. Numerous studies have suggested the importance of the Ca2+ - dependent protease calpain in cardiac physiology and pathology. Therefore, it is important to consider this pathway to develop and test therapeutic options in humans that targets calpain in HF. Apoptosis, autophagy, endocytosis, exocytosis, signal transduction, and disease progression all involve calpain molecular pathways. Therefore, it is conceivable that calpain inhibitors might have therapeutic potential as they have been investigated in preclinical models of several conditions in which the enzyme has been implicated that might be treated with them. Ca 2+ - dependent proteases and calpains contribute to adverse ventricular remodeling and HF in multiple experimental models. In this manuscript, we will discuss the calpain molecular pathway's important roles in HF development.

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