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APOPTOSIS OF CARDIOMIOCYTES: TYPICAL AND SPECIFIC MECHANISMS

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Apoptosis is an evolutionarily developed defensive-adaptive typical pathological process. At the beginning of the century, after more than twenty years of research on apoptosis, the prevailing idea was that highly differentiated cells, such as myocardial cells, are not eliminated by apoptosis. The first researchers of this process, using light and fluorescence microscopy, were unable to obtain a complete picture of the apoptotic degradation of myocardial cells.

Electron microscopy, laser scanning, flow cytometry, single-photon emission computed tomography, magnetic resonance imaging, magnetic resonance spectroscopy, and positron emission tomography were used to determine apoptotic cells in the myocardium. Up-to-date research methods clearly indicate the existence of genetically programmed death of myocardiocytes – cells that are at the terminal stage of differentiation.

Today, knowledge about apoptosis includes the following most important parts. Apoptosis plays an important role in the morphogenesis of the organism, being a “tool” for maintaining the balance between the processes of cell proliferation and death. Apoptosis is an energy-dependent process. There are two main apoptosis pathways: receptor-mediated and mitochondrial. Subcellular molecular mechanism of apoptosis consists of stages: induction, transduction, translocation, implementation of the apoptogenic genetic program. It is known that some proteins are apoptosis inducers (proteins of the Bs1-2 family – Bad, Bax, J3ik, Bid, Bak), others are its inhibitors (Bcl-2, Bcl-X). The apoptotic zone remains very clean – "apoptotic cell death bodies" are rapidly engulfed by phagocytes without damaging of surrounding cells with inflammation.

To obtain the data about apoptosis, heart tissues was taken from patients who died from cardiovascular diseases. The studied diseases include chronic heart failure, arterial hypertension, myocardial infarction, macro-focal post-infarction cardiosclerosis, cardiomyopathies, etc. It is the evidence that apoptosis is a certain part of the mechanism of these diseases development. In addition, apoptotic degradation of myocardial cells of various mammalians (guinea pigs, dogs, rats, rabbits) was studied in corresponding experiments.

For cardiomyocytes there have been revealed specific features of apoptosis. The first, two pathways of apoptosis development – “receptor-dependent” with the participation of cell death receptors and “mitochondrial” – are not alternative to each other; they identify more and more intersections of these paths, ensuring the achievement of the only end goal of the process. The second, in addition to these options, there are at least three other ways to include apoptotic death of cardiomyocytes: calcium- dependent, oxidative and angiotensin.

As apoptosis is a part of pathogenesis of the certain heart diseases, potentially it is possible to inhibit it at different stages of it’s development. To date, pharmacological agents have appeared that can effectively inhibit cardiomyocyte apoptosis induced by various stimuli. These means are still mainly used in experimental conditions. At the same time, some experience of their use in clinical practice has been accumulated. Based on modern concepts of the mechanisms of apoptosis development, the basis of pathogenetic therapy for myocardial damage caused by the activation of apoptosis is the blockade (inhibition) of this process at different stages of its development: induction, transduction, translocation, implementation of the apoptogenic genetic program.