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Chapter

Introductory Chapter: Cardiomyocyte - Fundamental Unit of Heart Life and Disease

Angelos Tsipis

1. Introduction

In the field of cardiology, some of the most dramatic advances in recent years have come from understanding the molecular and cellular basis of cardiovascular disease. The knowledge of the pathological basis of disease in some cases allows the development of new strategies for prevention and treatment. This book was planned not only to convey the new facts of cardiovascular diseases but also to boost the excitement and challenges of research in the dynamic area of modern molecular and cellular biology of cardiology.

2. Cardiomyocyte: structure and function

Cells are the fundamental unit of life, and the large number of them reflects the diversity of their function. The myocardium is composed principally of specialized muscle cells called cardiomyocytes. The major components of cardiac myocytes, cell membrane (sarcolemma) and T-tubules, necessary in excitation-contraction coupling, thereby facilitate a fast and synchronous contraction across the entire cell volume, sarcoplasmic reticulum, nucleus, and contractile elements. Cardiomyocytes contain many more mitochondria than skeletal muscle cells reflecting the dependence of cardiac muscle cell on aerobic metabolism. The functional intracellular contractile unit of cardiac muscle is the sarcomere that contains the contractile proteins myosin and actin. Sarcomeres also contain the regulatory proteins troponin and tropomyosin. Functional integration of myocytes is mediated by intercalated disks, which join individual cells and within which specialized intercellular junctions permit mechanical and electrical coupling. Intercalated disk contains various junctional complexes including the zonula adherens, desmosomes, and gap junctions. One of the most important types of adhesive interactions required for the formation and maintenance of tissues is that mediated by the cadherin family. The expression and distribution of many of these junctional components are often perturbed in cardiovascular disease [1–4]. One of the components of intercalated disks is gap junctions which facilitate synchronous myocyte contraction by providing electrical coupling. Deregulation of gap junction in cardiovascular disease may contribute to electromechanical dysfunction and arrhythmias. In addition, the cardiac conduction system consists of specialized myocardial fibers that conduct electrical impulses more readily than surrounding myocardial fibers and regulate the rate and the rhythm of the heart.

3. Cardiomyocyte: the basis of life and cardiac disease

The etiology of heart failure involves the interaction of multiple parameters, such as genetic predisposition, environment factors, and chance. Research advances and clinical investigations recognized familial transmission for many cardiomyopathies and confirmed the hypothesis that cardiomyopathies are characterized as *genetic disorders*. Numerous theories regarding the cause of idiopathic dilatative cardiomyopathy have been proposed such as viral myocarditis, autoimmune response against myocardial epitopes, and genetic factors that appear to be more important than previously believed. Nowadays, studies based on a more careful evaluation of disease inheritance and on prospective systematic family screening revealed a high frequency of genetic transmission of the disease in different populations. However, the true frequency is probably still underestimated due to the absence of early markers of the disease and reduced penetrance. Mutations in several known genes including those encoding dystrophin, δ-sarcoglycan, troponin T, β-myosin heavy chain, actin, lamin A/C, and desmin have been identified as a cause of a phenotype [3, 5, 6].

Cells are poised between survival and apoptosis, and their fate rests on a balance of powerful intracellular and extracellular forces, whose signals constantly act upon and counteract each other. In many circumstances, apoptosis is a self-protective programmed mechanism that leads to the suicide of a cell when its survival is deemed detrimental to the organism. In other instances, apoptosis is a pathological process that contributes to many disorders. Although increasing experiment data suggest that necrosis and apoptosis occur in heart failure, the relation between the two conditions and the relevant pathophysiological mechanism are less clear. Significant progress has been made in demonstrating the role of apoptosis in various heart diseases and in elucidating the molecular mechanisms of cardiac apoptosis. The progressive loss of cardiac myocytes is one of the most important pathogenic components of the heart failure. Even though the rate of apoptosis in heart failure is relatively low in absolute numbers, it is significantly higher than that in the normal heart, which has essentially negligible baseline apoptosis. Recently, animal models of heart failure incorporating transgenic technology have confirmed that myocyte apoptosis itself is sufficient to induce heart failure. The elevated presence of p53, Bax, and Bak-positive cells in dilated cardiomyopathy is associated with progressive loss of myocytes in heart failure. On the other hand, increased expression of the antiapoptotic protein bcl-2 in the human myocardium with dilated cardiomyopathy may be a compensation for the loss of myocytes and a possible compensatory antiapoptotic mechanism in the diseased group. Furthermore, the elevated expression of proapoptotic proteins is associated with the progressive loss of myocytes by apoptosis and may play a role in the evolution of the chronic heart failure in patients with old myocardial infarction and chronic ischemic disease. Immunohistochemistry of proapoptotic Bax and antiapoptotic bcl-2 protein demonstrated higher levels of both of these proteins in the diseased group of patients with acute myocardial infarction than normal hearts. A 1.3- and twofold increase in Bax and bcl-2 positive samples was observed in diseased group with acute myocardial infarction compared with the control group. The increased expression of antiapoptotic proteins in acute myocardial infarction represents a possible compensatory mechanism of salvaged myocytes. The prevalence of the apoptotic mechanism or this compensatory antiapoptotic may influence the evolution of heart failure in heart diseases. Thus, the pharmacological manipulation of apoptosis represents an active frontier of drug development [7].

Cell and molecular biology is a rapidly growing field of research and transfers knowledge, from basic cardiology science and preclinical studies, to the clinical cardiology. At the present time, cell priming, bio-nanotechnology, and tissue

engineering are coming up as valuable techniques for cell- and tissue-based therapy application in clinical cardiology. The integration of multilevel biological data and the connection with the clinical practice reveal the potential of personalized medicine and future implications for prognosis, diagnosis, and management of cardiovascular diseases.

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