Chapter 1

Introductory Chapter: Molecular Basis of Senescence

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.70214

1. Introduction

In humans, the threshold of normal aging is accepted to involve the age of 60 years. At the same time, the age above the normal aging was divided into three subgroups, including young olds (65–75 years of age), old olds (75–85 years), and eldest olds (above 85 years of age) [1]. Normal aging is defined as weakening of the repair and defense processes of the body. The weakening of the defense in aging organism leads to increase in the level of toxic factors such as reactive oxygen species (ROS), calcium ions, and immuneinflammatory response. The consequence of the change in the level of these molecular factors is the development of age-related diseases, among others, atherosclerosis, tumors and neurodegenerative diseases. Simultaneously, ROS may lead to the damage of macromolecular compounds, such as lipids, proteins, and DNA [2, 3]. ROS may also play an important role in the modulation of transcription factors activation, gene expression, and various life processes of a cell.

2. Genetic factors and normal aging

It seems that the aging process is determined by both changes in the levels of biochemical factors as well as multiple genetic variants. It is believed that normal aging is associated with genes such as *SIRT1, AKT1* and *CDKN1A*, while longevity with e.g. *FOXO3A* and *CETP*. On the other hand, weakness of cognitive function during senescence may be modified by poly-T variants of *TOMM40* and *APOE* alleles via influencing the level of apolipoprotein E [4, 5].

A detailed description of the molecular factors in aging process is provided in the chapter on genetic factors associated with longevity. According to the authors, longevity may be a complex

polygenic trait influenced by many genetic changes. In addition, longevity phenomena are influenced by both epigenetic and environmental factors.

The aging process may be traced based on experimental models using candidate genes enabling early detection of aging before the emergence of typical phenotypes. Such experimental model may be plants because they allow for the examination of complex mechanisms of molecular changes during aging.

In the last years, publications point to the involvement of many molecular factors in the development of normal aging. However, we still did not prevent the pathological changes in the aging organism in the form of cardiologic, neurological, or oncological diseases.

3. Aging and old age diseases

In the aging process, functions of the p53 protein, *genome trader*, are impaired. The p53 protein does not lead to repair cells with damaged DNA or does not direct them to the path of apoptosis. The effect of these functional changes is increased susceptibility to infections, autoimmune diseases and cancers, including malignancies [1, 2]. The pathogenesis of tumors associated with the p53 protein is contained in this book.

In addition, older people often develop neurological diseases including Alzheimer's and Parkinson's diseases, epilepsy, and stroke. Based on the modern knowledge, it is difficult to separate normal and pathological aging, and neurodegeneration of central neurons. More information in the chapter, normal aging and neurodegenerative disorders.

The aging process is not limited to the central nervous system. It also includes other organs such as heart and liver. It is believed that the loss of liver regenerative capacity is disturbed in the elderly. Defective liver cells undergo apoptosis or aging. Aging cells are responsible for fibrosis and hepatocellular carcinoma. Is senescence important in hepatic diseases, available in this book.

Moreover, recently a growing interest focuses on senescent cells in the context of old age diseases, malignancy and insulin resistance, and as a therapeutic goal to prolong health.

4. Summary

Despite current intensive research on the aging process, many questions about the pathomechanism of disorders in the old body remain unanswered. Moreover, the causes of unfavorable changes in the aging organism are not fully understood. It is not known which factors precisely define aging and/or longevity and contributes to the development of senility. Finding unknown paths in the pathogenesis of aging may improve the comfort of life of elderly and protect them from diseases typical for old age.

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