



The Role of the Proteolytic System of the Host Cell in Physiology and In the Early Stages of Viral Infection

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Abstract

Understanding the regulatory function of proteolytic enzymes is of fundamental importance in the biological control of physiological processes. Dysfunction of proteinases and their regulation leads to viral, oncological, cardiovascular and other diseases. Proteolytic activation is most common among viruses of different taxonomic groups and concerns mainly glycoproteins, which perform the functions of adsorption and fusion.

Keywords: Infectious process; Proteinases; Regulation

Introduction

Over the past 10 years, the concept of the role of proteolytic enzymes in the body has changed significantly. It became apparent that proteolysis is a special form of biological control [1,2]. Analysis of extensive material has shown that limited proteolysis serves as a triggering mechanism for many biological processes and provides a rapid physiological response of the body to changing conditions or an external signal [3-6]. Understanding the regulatory function of proteolytic enzymes is of fundamental importance. This is important both for deciphering the most complex biological processes, such as cell division and transformation, morphogenesis, metamorphosis, metabolic adaptive restructuring, etc., and for elucidating the molecular basis of pathology [7-8]. It is already clear that the dysfunction of proteolytic enzymes and their regulation underlies many pathological conditions [9]. These include disorders of the cardiovascular system, acute and chronic inflammatory processes, oncological and endocrine diseases, nervous and muscular dystrophies, viral diseases, psychological and nervous disorders [10-13]. It is obvious that clarification of the specific functions of individual proteinases is a necessary condition for understanding

the pathogenesis of these diseases, their diagnosis and rational therapy.

However, the regulatory role of proteolytic enzymes is diverse and not yet fully understood. The participation of proteolytic enzymes in regulation is associated with two types of proteolysis: complete degradation of protein molecules and limited proteolysis reactions, i.e. specific hydrolysis of certain peptide bonds. By causing complete degradation of protein molecules, proteinases determine the rate of protein breakdown in the body and are involved in regulation [14,15]. Proteinases are involved in the fate of protein and its transformation at the earliest stages of biosynthesis and accompany the protein. Proteinases are involved in protein processing by removing the initiator amino acid or signal peptide from the synthesized precursor protein, which determines the start of translation and transport of the polypeptide chain. This often occurs during the growth of the half-peptide chain or immediately after its completion. They activate inactive precursors, a kind of reserve form of physiologically active peptide proteins. In many cases, this is the beginning of many physiological processes [16]. Proteinases cause modification and inactivation of active proteins. This (especially in the case of key metabolic enzymes) can lead to a restructuring of metabolism, to

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"switching on" or p2 for virology (continued): "switching" of physiological processes, as well as the implementation of the degradation of protein molecules. Restricted proteolysis is the easiest way to obtain a diverse set of products with different physiological properties. Therefore, with the help of specific proteinases, the information encoded in the same biosynthetic precursor can be used to the fullest extent. Indeed, with the formation of several active products from one precursor, a rapid generalized response of the organism to an external signal can be achieved. This is the case, for example, with painful stress. In response to a nerve impulse, ACTH-releasing factor enters the pituitary gland from the pain receptor from the hypothalamus. It causes rapid release from POMK ACTH, Beta-LPG and Beta-endorphin. Each of them acts on its own target tissues, causing cascades of biochemical reactions that determine the complex response of the body to pain [17].

To understand the role of proteinases in the bio control of physiological processes, it is necessary to know the mechanisms of regulation of their activity. They are carried out mainly in 3 ways:

- Many proteolytic enzymes are synthesized as inactive precursors. For the formation of enzymes, activation of zymogens is required [18,19].
- A powerful system of proteinase inhibitors is present in blood plasma, cells and tissues, specifically blocking the activity of individual enzymes or groups of enzymes. Proteinase activity can appear only after inactivation or removal of the corresponding inhibitor. Imbalance in the proteinase-inhibitor system is often the cause of the pathological process [18].
- In many cases, proteinases and their substrates are spatially separated. They can be localized both in different subcellular fractions of the same cell, and in different types of cells and tissues; in some cases, they can be found in different parts of the body [17].

Coordinated Functioning of all mechanisms of regulation of proteinase activity, namely: spatial association of proteolytic enzyme and substrate due to transport of any component, formation of enzymes from an inactive precursor and removal of an inhibitor makes it possible to carry out strict temporal and spatial control of physiological processes and their rapid implementation. Proteolytic activation is widespread among viruses of various taxonomic groups. In picorn and toraviruses, cleavage of the precursor protein is the main mechanism leading to the formation of functional proteins. Most other viruses have proteolytic activation and mainly concerns viral glycoproteins that perform adsorption and fusion functions. As a result of limited proteolysis, the protein molecule is cleaved into two subunits, such as the hem agglutinin of the influenza virus, or a

small fragment is cleaved from it, such as in both glycoproteins of paramyxoviruses, HN and F [20].

Proteolytic activation is a highly specific process carried out by certain proteinases of cellular or viral origin [21]. Thus, the proteolytic activation of influenza viruses and paramyxoviruses is carried out by trypsin-like proteinases of the cell, which hydrolyze the peptide bond between arginine and lysine, chymotrypsin and hemolysis cleave the precursor protein with a shift by 3 and 1 amino acid, respectively, and at the same time proteolytic activation does not occur, and the vision fusion the cell does not occur [22]. The fusion proteins of influenza viruses and paramyxoviruses are activated by many proteinases. Both these and other proteinases are found in the chorionallantoic fluid of a chick embryo, but upon fractionation it can be separated [23]. For maximum cleavage of influenza virus hem agglutinin and Sendai virus F-protein in vitro, it took about 4 hours of incubation at t-37 C. Proteolytic activation is an important event in the infectious cycle of viruses. If it is violated, the assembly of viral particles will occur, however, the forming virions will not be infectious, since they do not contain active fusion proteins that ensure the penetration of the virus into healthy cells. Therefore, proteolytic activation determines the infectious activity of the virus and its ability to generalize infection. Apparently, the properties of the virus to infect certain tissues of the body are determined by the presence in organs and tissues of enzymes necessary for the proteolytic activation of viral progeny. The importance of proteolytic activation in the infectious process, its versatility for proteolysis inhibitors is a prerequisite for its use as a target for the treatment of viral infection. This approach to the therapy of viral diseases opens up prospects for the creation of drugs with a wide antiviral spectrum of action, since for certain viruses it is possible to select specific inhibitors of proteolysis that effectively block proteolytic processing. Now proteolytic enzymes are of interest in almost all areas of medicine. This is due to the fact that a number of diseases are currently known, in the pathogenesis of which proteinases are involved. If we analyze what kind of malfunctions and regulation of proteinases lead to pathology, the following reasons can be distinguished:

- Disruption of proteinase formation or the appearance of a defective enzyme, which occurs, for example, in some hereditary diseases, in particular hemophilia [24].
- The appearance of a foreign proteinase, this is observed in viral and some bacterial infections [25].
- Violation of regulation of proteolytic activity, in particular, imbalance in the proteinase-inhibitor balance [26,27]. This may be due to a defect in the inhibitor and is observed for example, with emphysema of the lungs and some forms of muscular dystrophy.

- In many cases, pathological processes are associated with the release of intracellular enzymes. This occurs in acute and chronic inflammations of various origins [28]. The processes of tumor invasion and metastasis are also associated with the release of proteinases. There is evidence of a correlation between the metastatic potential of some tumors and the activity of certain proteinases [29]. In many cases, the functions of certain proteinases have not yet been established, and the elucidation of their specific role in the development of a particular pathology should contribute not only to understanding the molecular basis of various diseases, but also to outline the ways of their scientifically grounded diagnosis and rational therapy.

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