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The Role of Atp-Ases in the Transport Processes of Biological Membranes

[1] Abdurashidov A., [2] Muidinova N., [3] Makhkamova M., [4] Tuychieva D.
[1] 1st year master's degree in biophysics and biochemistry
[2] Lecturer of the Department of Genetics and Biotechnology
[3] 2nd year student of the biological direction
[4] Candidate of Biological Sciences, Professor of the Department of Genetics and Biotechnology

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Annotation: ATPases are enzymes that catalyze the hydrolysis of adenosine triphosphate (ATP) and play a key role in the transport of ions and molecules across biological membranes. The article discusses the main classes of ATPases, including P-, V-, F-type and ABC transporters, their molecular mechanisms of work and physiological role. The pathophysiological aspects of ATPase dysfunction associated with diseases such as neurodegenerative disorders, hypertension, cancer, and cystic fibrosis are discussed. Modern methods for studying the structure and function of these enzymes, as well as promising therapeutic strategies, including targeted regulation of ATPase activity and inhibition of specific transport systems, are presented.

Keywords: ATPases, membrane transport, P-type ATPases, V-type ATPases, F-type ATPases, ABC transporters, ion gradient, cellular homeostasis, neurodegenerative diseases, pharmacological inhibitors.

Introduction. ATPases are enzymes that catalyze the hydrolysis of adenosine triphosphate (ATP) with the release of energy necessary for the active transport of ions and molecules across biological membranes. They are key elements in maintaining cell homeostasis, affecting osmotic balance, nerve impulse transmission, and intracellular signaling [1]. Dysfunction of these enzymes is associated with the development of various pathological conditions, including neurodegenerative diseases, arterial hypertension and oncological processes [2].

Historical review of ATPase research. The study of ATPase began in the middle of the 20th century. In 1957, Jens Skou discovered Na+/K+-ATPase, for which he received the Nobel Prize [1]. In the following decades, other ATPases were identified, including Ca2+-ATPase and H+-ATPase.

Classification of ATPase. ATPases are divided into several main classes depending on their structure and mechanism of action:

1. P-type ATPases - Phosphorylated enzymes that transport cations across the membrane. Example: Na+/K+-ATPase, which maintains the electrochemical gradient of sodium and potassium [3].

2. V-type ATPases – Vacuolar proton pumps that transport protons across the membrane by adjusting the pH of the organelles. They play an important role in lysosomes, endosomes, and osteoclasts [4].

3. F-type ATPases (ATP synthases) – Use a proton gradient to synthesize ATP, participating in mitochondrial oxidative phosphorylation [5].

4. ABC transporters – Transport a variety of molecules, including lipids, drugs, and xenobiotics, using ATP energy [6].

Mechanisms of ATPase operation.

P-type ATPases, such as Na+/K+-ATPase, operate on a post-Albers cycle that includes conformational changes, phosphorylation, and dephosphorylation of the catalytic site [7]. This process provides active transport of Na+ and K+ against their concentration gradient. Ca2+-ATPases of the plasma membrane (PMCA) and sarcoplasmic reticulum (SERCA) regulate calcium levels in the cytoplasm by controlling muscle contraction and cell signaling [8]. Vacuolar V-ATPases create a proton gradient necessary for protein degradation in lysosomes and bone reabsorption by osteoclasts [9]. F-type ATP synthase works by the mechanism of rotational catalysis, synthesizing ATP from ADP and phosphate due to the energy of the proton gradient [10].

Detailed mechanisms of operation of P-type ATPase. ATPases. P-types work by phosphorylation of the aspartate residue in the catalytic center. This leads to conformational changes that allow for ion transport. Na+/K+-ATPase goes through the E1-E2 cycle, in which three Na+ ions are excreted from the cell, and two K+ ions are transferred inside [3]. Ca2+-ATPases (SERCA and PMCA) ensure the removal of calcium from the cytosol, preventing its toxic accumulation [4].

V-type and F-type ATPases: differences and role. V-type ATPases transport protons, creating a pH gradient in endosomes, lysosomes, and osteoclasts. They work by the mechanism of rotational catalysis, in which the hydrolysis of ATP causes the rotation of subunits and the transport of H+ [5]. F-type ATPases, on the other hand, use a proton gradient to synthesize ATP in mitochondria. This process is critical for the production of cellular energy [6].

ABC transporters carry organic molecules, including drugs, lipids, and peptides. For example, the protein CFTR (associated with cystic fibrosis) regulates the transport of chlorides in the respiratory system [7]. P-glycoprotein plays a key role in multidrug resistance in tumors [8].

ATPases are also involved in the regulation of many physiological processes, for example:

- Nerve transmission: Na+/K+-ATPase maintains the membrane potential of neurons, which is necessary for the generation of an action potential [11].- Acid-base balance: V-ATPases regulate the pH of endosomes, lysosomes, and other organelles, ensuring their normal functioning [12].- Cell proliferation: ABC transporters are involved in the export of growth factors and drug resistance of cancer cells [13].- Muscle contraction: Ca2+-ATPases of the sarcoplasmic reticulum regulate the return of calcium, which determines the frequency and strength of contractions [14].

ATPase dysfunction leads to a number of diseases. how:

- Wilson's disease (mutation in the ATP7B gene), a disorder of copper transport, leading to its accumulation in the liver and brain [15].
- Cystic fibrosis (CFTR, ABC transporter defect). impaired ion transport in epithelial cells [16].
- Neurodegenerative diseases, decreased Na+/K+-ATPase activity is associated with Alzheimer's and Parkinson's disease [17].
- Cancer, hyperactivity of V-ATPase contributes to the survival of tumor cells in an acidic environment [18].

Clinical aspects and therapeutic approaches for ATPase deficiency:

1. Hypertension - Inhibition of Na+/K+-ATPase may lower blood pressure.

2. Neurodegeneration – a decrease in Na+/K+-ATPase activity is associated with Alzheimer's disease [9].

3. Osteoporosis – suppression of V-ATPase inhibits the activity of osteoclasts, preventing bone destruction [10].

Future research consists of the following, current research is aimed at studying the exact mechanisms of ATPase and developing drugs that selectively affect their activity. Of particular interest is the use of V-ATPase inhibitors in cancer therapy, as well as gene therapy for ABC transporter mutations [11].

Conclusion. ATPases play a key role in the transport of ions and molecules across biological membranes, maintaining cell homeostasis. Disruption of their function leads to many diseases, including neurological, cardiological and oncological pathologies. The study of the molecular mechanisms of these enzymes is a promising area for the development of new therapeutic strategies.

Based on this, it should be noted that in order to improve the study of this process, it is necessary to focus on several areas:

1. Deep structural analysis: the use of cryo-electron microscopy and X-ray diffraction analysis for a detailed study of conformational changes in ATPase. Modeling the interaction of ATPase with various ligands and inhibitors.

2. Genetic and molecular research, development of genetic models (CRISPR/Cas9) to study ATPase mutations and their impact on cellular processes. Analysis of ATPase expression in various tissues and conditions, including pathological conditions.

3. In vitro and in vivo functional studies, development of new methods for recording ATPase activity (for example, optical ion sensors). Creation of transgenic animals to study disorders associated with ATPase dysfunction.

4. Pharmacological research, search for new ATPase inhibitors and activators for therapeutic purposes. Testing of drugs that affect the work of ATPases in models of neurodegeneration, cancer and cardiovascular diseases.

5. Data integration and artificial intelligence, the use of AI to analyze big data about the structure

and functions of ATPase. Computer simulation of ATPase dynamics and prediction of mutation effects.

The development of these areas will allow not only a deeper understanding of the mechanisms of ATPase, but also the creation of new strategies for the treatment of related diseases.

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