# POST-TANSLATIONAL MODIFICATIONS OF PROTEINS AND THEIR ROLE IN THE PATHOGENESIS OF DISEASES

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**Abstract:** The article examines the molecular mechanisms of post-translational modifications (PTMs) of proteins, which represent biochemical alterations occurring after the process of translation. PTMs play a crucial role in regulating protein structure, functional activity and intracellular localization. The paper discusses the principal types of PTMs-such as phosphorylation, acetylation, ubiquitination and others-and highlights their involvement in the development of oncological, neurodegenerative and metabolic diseases.

## PROTEINLARNING POST-TRANSLATSION MODIFIKATSIYALARI VA ULARNING KASALLIKLAR PATOGENEZIDAGI ROLI

**Annotatsiya:** Ushbu maqolada proteinlarning post-translatsion modifikatsiyalari (PTM) — translatsiyadan so‘ng yuz beradigan biokimyoviy o‘zgarishlarning molekulyar mexanizmlari tahlil qilinadi. PTMlar oqsillarning strukturasi, faolligi va hujayra ichidagi lokalizatsiyasini boshqarishda hal qiluvchi rol o‘ynaydi. Maqolada asosiy PTM turlari (fosforillanish, atsetillanish, ubiquitinatsiya va boshqalar) hamda ularning onkologik, neyrodegenerativ va metabolik kasalliklar rivojlanishidagi o‘rni yoritilgan.
**Kalit so‘zlar:** PTM, fosforillanish, ubiquitinatsiya, atsetillanish, glikozillanish, oksidativ stress, signal transduktsiya, proteasoma, epigenetika, patogenez.

## ПОСТТРАНСЛЯЦИОННЫЕ МОДИФИКАЦИИ БЕЛКОВ И ИХ РОЛЬ В ПАТОГЕНЕЗЕ ЗАБОЛЕВАНИЙ

**Аннотация:** В статье рассматриваются молекулярные механизмы посттрансляционных модификаций (ПТМ) белков, представляющих собой биохимические изменения, происходящие после завершения процесса трансляции. Посттрансляционные модификации играют ключевую роль в регуляции структуры, функциональной активности и внутриклеточной локализации белков. В работе рассматриваются основные типы ПТМ, включая фосфорилирование, ацетилирование, убиквитинирование и другие виды модификаций, а также освещается их участие в развитии онкологических, нейродегенеративных и метаболических заболеваний.
**Ключевые слова:** посттрансляционные модификации (ПТМ), фосфорилирование, убиквитинирование, ацетилирование, гликозилирование, окислительный стресс, передача сигнала, протеасома, эпигенетика, патогенез.

## 1. INTRODUCTION

Proteins are the principal functional molecules of cells, and their biological activity is determined not only by their amino acid sequence. Post-translational modifications (PTMs) represent key regulatory mechanisms that control protein conformation, enzymatic activity, and degradation. To date, more than 400 types of PTMs have been identified, and these modifications play essential roles in regulating cellular signaling, gene expression, and apoptosis [7]. Dysregulation of these mechanisms can lead to severe pathological conditions.

## 2. METHODS

In this study, the international scientific literature published in recent years on the topic was reviewed, with particular emphasis on data from leading scientific journals, including *Nature*, *Cell*, and *Science*, as well as fundamental biochemistry textbooks such as *Lehninger* and *Alberts* [1, 2]. The role of PTMs in the pathogenesis of various diseases was investigated using a comparative analysis approach.

## 3. RESULTS AND DISCUSSION

Proteins perform a wide range of functions in the human body, including structural, enzymatic, transport, and protective functions. According to the World Health Organization (WHO), protein-energy malnutrition can lead to severe conditions such as kwashiorkor and marasmus in children, while in adults it may contribute to sarcopenia and impaired immune function.

**Phosphorylation:** Phosphorylation is regulated by protein kinases and phosphatases. It plays a central role in controlling intracellular signaling pathways, including the mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt) pathways, and consequently acts as an important mediator in the regulation of other PTMs. In neoplastic diseases, constitutive activation of tyrosine kinases can promote uncontrolled cellular proliferation [5]. In type 2 diabetes mellitus, aberrant phosphorylation of insulin receptors and downstream signaling proteins contributes to the development of insulin resistance.

**Acetylation:** Acetylation occurs predominantly at lysine residues and plays an important role in the regulation of gene expression. Epigenetic dysregulation may result in the suppression of tumor suppressor genes, thereby contributing to tumor development and progression [6, 8].

**Ubiquitination:** Ubiquitination targets proteins for proteasomal degradation. This process is mediated by a cascade of E1, E2, and E3 enzymes and interacts with phosphorylation-dependent signaling pathways to regulate protein stability. In neurodegenerative diseases such as Alzheimer's and Parkinson's diseases, impairment of this system contributes to the accumulation of misfolded and damaged proteins [4, 9].

**Glycosylation:** Glycosylation plays an important role in regulating membrane receptors and immune responses. In diabetes mellitus, an increase in glycated hemoglobin (HbA1c) reflects chronic non-enzymatic glycation and represents a clinically relevant consequence of abnormal protein glycation [10].

### 3.3. The Proteasome System and Epigenetics

The 26S proteasome complex plays a central role in maintaining protein homeostasis. In oncology, pharmacological inhibition of the proteasome, for example with bortezomib, represents an important therapeutic strategy. In addition, epigenetic alterations mediated by histone modifications contribute to the establishment and maintenance of long-term pathological cellular responses [3].

## 4. CONCLUSION

Post-translational modifications are essential regulatory mechanisms that finely control cellular processes. Their complex interplay and dysregulation constitute an important molecular basis of numerous complex diseases. The application of modern proteomic approaches to the study of these processes provides substantial opportunities for the identification of novel diagnostic biomarkers and the development of targeted therapeutic strategies.

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