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Commentary

Involvement of Protein Post-Translational Modifications in Diseases and Biological Processes

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DESCRIPTION

Posttranslational Modifications (PTMs) are chemical changes that occur on some proteins after they are synthesized by ribosomes. These changes can affect the structure, function, interactions and regulation of proteins in various ways. PTMs are important for many biological processes, such as cell signaling, gene expression, protein degradation, enzyme activity and cellular response to stress.

There are more than 400 different types of PTMs that have been identified so far. They can be classified into two main categories: covalent and non-covalent modifications. Covalent modifications involve the formation or breaking of chemical bonds between the amino acid side chains or the termini of proteins and other molecules, such as phosphate, sugar, lipid, metal ion or another protein. Non-covalent modifications involve the binding or dissociation of molecules to proteins without changing their covalent structure, such as allosteric regulation, protein folding or protein-protein interactions.

Some of the most common and well-studied covalent PTMs

- Phosphorylation is the addition of a phosphate group to serine, threonine or tyrosine residues by kinases or the removal of a phosphate group by phosphatases. Phosphorylation can alter the charge, conformation and binding affinity of proteins, and is involved in many signalling pathways and cellular functions.
- Glycosylation is the attachment of carbohydrate chains to asparagine, serine or threonine residues by glycosyltransferases or the removal of carbohydrate chains by glycosides. Glycosylation can affect the folding, stability, localization and recognition of proteins by other molecules, such as receptors, antibodies or lectins. Glycosylation is also important for cell-cell communication and immune response.
- Ubiquitination is the covalent linkage of one or more ubiquitin molecules to lysine residues by ubiquitin ligases or the removal of ubiquitin molecules by deubiquitinating enzymes. Ubiquitination can mark proteins for degradation by proteasomes or lysosomes, or regulate their activity, localization and interactions with other proteins. Ubiquitination is involved in many cellular processes, such as cell cycle control, DNA repair, transcription regulation and signal transduction.
- Acetylation is the transfer of an acetyl group from acetyl-CoA to lysine residues by acetyltransferases or the removal of an acetyl group by deacetylases. Acetylation can neutralize the positive charge of lysine residues and affect their interaction with DNA or other proteins. Acetylation is mainly associated with histone proteins that wrap around DNA and regulate gene expression by altering chromatin structure and accessibility. Acetylation can also modulate the function of non-histone proteins involved in metabolism, cytoskeleton dynamics and nuclear transport.

Some examples of non-covalent PTMs

- Allosteric regulation is the binding of a molecule to a site on a protein that is different from its active site and affects its activity or conformation. Allosteric regulation can be positive (activating) or negative (inhibiting) depending on the type of molecule and protein involved. Allosteric regulation is a common mechanism for controlling enzyme activity and feedback loops in metabolic pathways.
- Protein folding is the process by which a polypeptide chain adopts a specific three-dimensional structure that determines its function. Protein folding is assisted by molecular chaperones that prevent misfolding and aggregation of proteins under normal or stressful conditions. Protein folding can also be influenced by other PTMs, such as phosphorylation or glycosylation that can stabilize or destabilize certain conformations. Protein folding is essential for proper protein function and quality control in cells.
- Protein-protein interactions are the physical association between two or more proteins that mediates their function or

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regulation. Protein-protein interactions can be transient or stable depending on the strength and specificity of their binding sites. Protein-protein interactions can form complexes that perform specific tasks in cells, such as transcription factors that bind to DNA and regulate gene expression; signal transducers that relay signals from receptors to effectors; or structural components that maintain cell shape and integrity.

PTMs are chemical modifications to proteins that occur after they have been translated and have a broad variety of impacts on the function and structure of the target proteins. These mechanisms occur on almost all proteins, and many domains within proteins have numerous amino acids changed by various modifications. These changes, which play key roles in a variety of cellular processes, frequently have a powerful impact on the function of a modified protein. There is compelling proof that disruptions in PTMs can result in a variety of illnesses. As a result, learning more about a target protein's possible PTMs can help us better comprehend the molecular processes in which it participates.