Proteins are fundamental to cellular function

Proteins are large, complex molecules that have a range of significant roles in the body and are necessary for the structure, function and regulation of tissues and organs. They maintain the proper balance of proteins by regulating several fundamental processes including protein synthesis and degradation, or the creation and removal of proteins.

Protein homeostasis is critical for cell health

Protein degradation is part of a cell’s protein homeostasis regulatory network that ensures unnecessary proteins are removed from the cellular environment when they are no longer needed or are damaged or faulty in some way. An efficiently functioning proteome, or all the possible proteins in an organism, is fundamental to all cellular processes and critical to the health of the cell and lifespan of the organism.

Protein Degradation in Practice

The Ubiquitin-Proteasome System (UPS) is one of two primary means of protein degradation in cells (the other is lysosomal proteolysis). The UPS tags intracellular proteins for degradation with a small protein called ubiquitin by the E3 ligase enzyme complex. Ubiquitin-tagged proteins are then sent to the proteasome and degraded.

The accumulation of proteins in a cell may lead to detrimental effects

When a cell is unable to degrade abnormal and/or unnecessary proteins, these proteins can accumulate within the cellular environment. The accumulation of proteins within a cell is implicated in the pathogenesis of many diseases, including several malignancies and neurodegenerative disorders.

Targeting a cell’s protein degradation system

Many current approaches to treating cancer focus on inhibiting specific pathways or proteins.

Only up to 10 percent of all human proteins are traditionally considered targetable or “druggable” given their cellular location and/or structural limitations.

Scientists are exploring how to use protein degradation to approach cancer research in a new way – effectively leveraging the body’s natural system to target and remove the pathogenic proteins and maintain homeostasis.

By harnessing the UPS within a cell, the use of targeted protein degradation may be able to target thousands of previously “undruggable” disease-related proteins as proteins that are chemically intractable by direct pharmacology.

Targeted Protein Degradation

A cell’s UPS has the potential to be redirected by introducing synthetic compounds to facilitate and promote the degradation of target proteins that would not otherwise be degraded, potentially resulting in therapeutic effects. Only up to 10 percent of all human proteins are traditionally considered targetable or “druggable” given their cellular location and/or structural limitations.

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