Misfolded membrane proteins cleared from cells by 'reubiquitinase'

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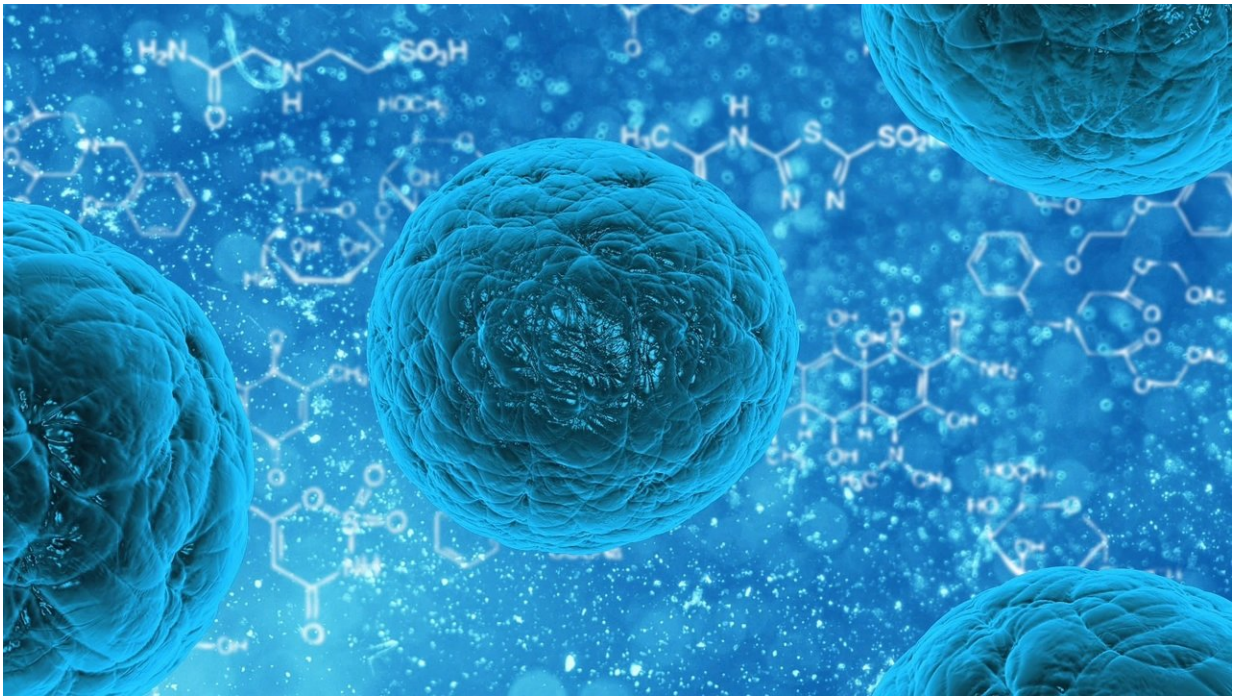

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Chinese researchers recently discovered a protein quality control mechanism called 'reubiquitination.' The mechanism, according to the researchers, could promote the elimination of misfolded membrane proteins, minimize their dwell time in cells, and thereby reduce their probability to form toxic aggregates in the human body.

Discovered by a research team from the Shanghai Institute of Organic Chemistry of the Chinese Academy of Sciences, the 'reubiquitinase' RNF126 adds a small protein called ubiquitin to unfolded membrane protein intermediates in cytosol, and targets them to the degradation machinery—the proteasome—for destruction.

Misfolded proteins in cells and organisms are normally cleared by a protein quality control mechanism called the ubiquitin-proteasome system. If not, they tend to form pathological aggregates that are believed to damage cells (e.g., neurons), and ultimately cause various diseases of aging, such as neurodegeneration.

The results show that RNF126-mediated reubiquitination is important for normal cell physiology. Without reubiquitination, targeting of misfolded proteins to the proteasome could be delayed, and this increases the risk of protein aggregation and cellular stress, which could gradually lead to various diseases.

In addition, the function of RNF126 as a reubiquitinase might be required for rapid proliferation of certain cancer cells, making it a potential therapeutic target.

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