

**Cover illustration**

In the ubiquitin system, proteins are either targeted to the proteasome for degradation or sent to different locations in the cell. (Artwork by N. Spencer.)

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THE UBIQUITIN SYSTEM

The destruction of proteins is as important as their synthesis for the maintenance of protein homeostasis in cells. In eukaryotes, the ubiquitin–proteasome system is responsible for most of this protein degradation: the small protein ubiquitin acts as a death warrant, tagging and targeting other proteins to the large proteolytic chamber of the proteasome.

The discovery in the 1970s that certain proteins are ubiquitylated before degradation was awarded the 2004 Nobel Prize in Chemistry. It is now known that ubiquitin-mediated destruction plays a crucial part in cell-cycle regulation, DNA repair, cell growth and immune function, as well as in hormone-mediated signalling in plants. More recently, ubiquitin has been shown to have numerous non-proteolytic functions, including involvement in vesicular trafficking pathways, regulation of histone modification and viral budding.

Given the central role of the ubiquitin system in diverse cellular processes, it is not surprising that its dysfunction contributes to cancer and to neurodegenerative and immunological disorders. An understanding of the ubiquitin system is therefore important in devising treatments for such diseases.

With topics as diverse as the origin of the ubiquitin system and cancer therapy targeting the ubiquitin pathway, this Insight provides both an introduction and an update to the most topical themes in ubiquitin research.

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