E3 ubiquitin ligase

A ubiquitin ligase (also called an E3 ubiquitin ligase) is a protein that recruits an E2 ubiquitin-conjugating enzyme that has been loaded with ubiquitin, recognizes a protein substrate, and assists or directly catalyzes the transfer of ubiquitin from the E2 to the protein substrate. The ubiquitin is attached to a lysine on the target protein by an isopeptide bond.

E3 ligases interact with both the target protein and the E2 enzyme, and so impart substrate specificity to the E2. Commonly, E3s polyubiquitinate their substrate with Lys48-linked chains of ubiquitin, targeting the substrate for destruction by the proteasome. However, many other types of linkages are possible and alter a protein's activity, interactions, or localization. Ubiquitination by E3 ligases regulates diverse areas such as cell trafficking, DNA repair, and signaling and is of profound importance in cell biology. E3 ligases are also key players in cell cycle control, mediating the degradation of cyclins, as well as cyclin dependent kinase inhibitor proteins.

The human genome encodes over 600 putative E3 ligases, allowing for tremendous diversity in substrates.

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Last update: **2024/06/07 02:51**