# Ubiquitin-Proteasome System

Protein degradation via proteasomes is a very sophisticated process. The system is called **ubiquitin-proteasome system**(UPS) also known as ubiquitin-proteasome pathway(UPP). The entire function is based around protein named **ubiquitin** of size about 76 aminoacids, 8,5kDa. This protein was first discovered in 1975 without its purpose being explained. Name "ubiquitin" refers to its presence in every eukaryotic cell("ubiquitous" means being everywhere). Ubiquitin takes part in ubiquitination of protein which means it binds to a protein. This is a complex and important reaction to similar extent as other post-translation modification of proteins called phosphorylation[1].

## Processes of ubiquitination

1. Ubiquitin in cell is first bonded to **ubiquitin-activating enzyme E1** while using energy from ATP.
2. Then, ubiquitin is transported to ubiquitin-transporting(ubiquiting-conjugating) **enzyme E2**.
3. Afterwads, ubiquitin is transported by **ubiquitin-ligase E3** to a **protein and marks it for degradation**(PDG). Ubiquitin-ligase E3 is protein- specific.

In other words, E1 and E2 enzymes have mainly ubiquitin-transporting function and E3 enzymes on the other hand definitely bind ubiquitin to PDG(recognized only by these enzymes). Ubiquitins are bonded to PDG in chain-like structure. E3 enzymes distinguish different PDGs because there are not many types of E1 enzymes(according to [2] there are at least 2 E1 enzymes - Uba6 and Ube1) and not many types of E2 enzymes while there are hundreds of types of E3 enzymes, specializing in PDG preferences.

### Ubiquitin-ligases

We recognize 2 families of ubiquitin-ligases, being different by presence of active domain: they either contain **HECT domain**(homologous to E6-Associated Protein C-Terminus), or **RING domain**(really interesting new gene)[3][4]. Besides the regular E1-E2-E3 cascade, there are other known enzymes, E4, which can support growing of polyubiquitin chain[5].

### Ubiquitin bonds

The key question is the way of linkage between individual ubiquitins in the chain. Not every polyubiquitin chain is a "death sentence". The most common bond of two ubiquitins in polyubiquitin chain is via **lysine 48**(so called K48 chains) or **lysine 63**(so called K63 chains), though there are chains of ubiquitins linked via lysine 6, 11, 27, 29, or 33. Unusually are these branched[6]. Science today is not sure of the meaning of this many signals. Mainly the K48 chains are the "death sentence" while K63 play other roles in cell signalling. Not long ago, it was shown that proteins marked with K63 chains can be recognized by proteazomes and degraded by them[7]. There is also a possibility of K63 chains being reformed into K48 chain[8] while staying on the protein.

## Deubiquitination

Besides ubiquitination of preoteins, there is opposite process taking place in eukaryotic cell called deubiquitination. Enzymes responsible for this process are called **deubiquitinases**(DUB for short). We can ditinquish them into 5 groups:

1. ubiquitin C-terminal hydrolases,
2. ubiquitin specific proteases,
3. proteases of domain of Machado-Joseph disease,
4. proteases of ovarian tumors,
5. proteases with JAMM domain[9].

Today, there are 75 known DUBs that interact with hundreds of proteins and that play large amount of different roles[10]. Worth noting that one of JAMM domain deubiquitinases, in human cells called **Poh1**, is part of eukaryotic proteasome and play key role in its function.

# Links

## Related Articles

- Degradation of proteins
- Proteasome
- Proteasome inhibitors
- Translation

## Source


- CVEK, Boris. Od ubikvitinu k antabusu. *Britské listy : deník o všem, o čem se v České republice příliš nemluví* [online]. 2011, roč. -, s. -, dostupné také z <https://blisty.cz//legacy.blisty.cz/art/56680.html>. ISSN 1213-

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