

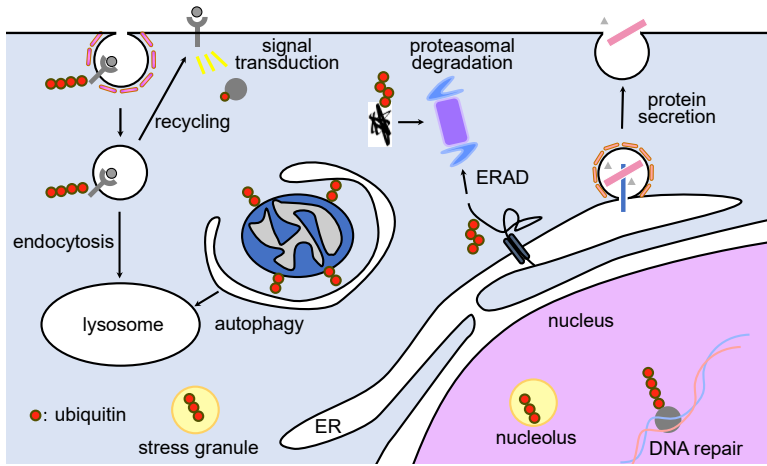


Regulation of cell function by ubiquitin system

Cell Biology Center

<https://komada-lab.jimdo.com/>

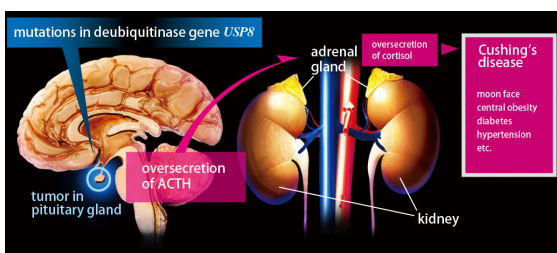
- Discovery of novel cellular events regulated by ubiquitin system
- Functional analysis and engineering of ubiquitin-related enzymes
- Manipulation of ubiquitin system for the development of industrial application and therapeutic approach



Ubiquitin, a small protein, can be covalently attached to various proteins. This reaction, called as ubiquitination, is catalyzed by ubiquitin ligases and antagonized by deubiquitinating enzymes. Ubiquitin can form some linkage types of poly-ubiquitin chains. Structurally different chains are recognized by different decoder proteins. It enables ubiquitination to display many functions including the induction of degradation, translocation, and protein-complex formation of target proteins. Through these mechanisms, ubiquitination regulates many cellular events.

We aim to discover novel cellular events regulated by protein ubiquitination, and to identify the responsible ubiquitin-related enzymes and decoder proteins. Furthermore, using chemo-technology and protein engineering, we are trying to manipulate ubiquitin system for the development of industrial application and therapeutic approach.

Our finding:
ubiquitin system regulates various cellular events.

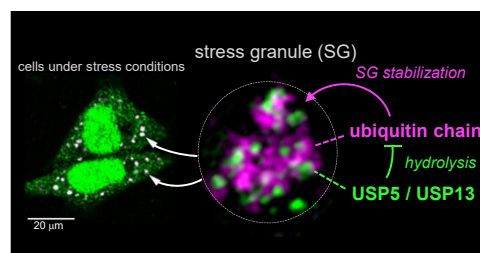


Ubiquitin system and tumorigenesis

Deubiquitinating enzyme USP8 deubiquitinates growth factor receptors and promotes their recycling to the plasma membrane, thereby potentiating growth factor signaling.

Hyperactive mutant form of USP8 induces excess growth factor signaling and tumorigenesis. When it expresses in the pituitary, it causes Cushing's disease.

→ We showed that many ubiquitin-related proteins can be therapeutic targets for tumors.

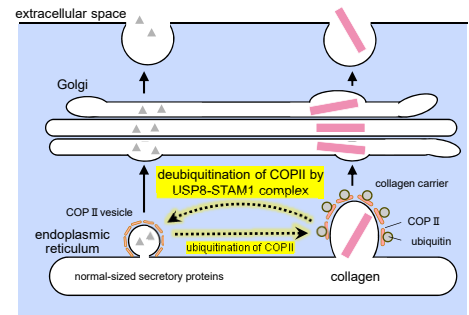


Ubiquitin system and stress granule

Stress granules are cytoplasmic compartment containing RNA-protein complexes. Excess formation of stress granules contributes to the onset of neurodegenerative diseases.

Two deubiquitinating enzyme (USP5 and USP13) promote stress granule disassembly.

→ We showed that the activators of these deubiquitinating enzymes may be therapeutic targets for neurodegenerative diseases.



Ubiquitin system and collagen production

Collagen is transported by atypical large carriers coated by COP II proteins in mammalian cells, and then secreted to the extracellular space.

The formation of the large carriers are regulated by the ubiquitination of a COP II protein.

→ We showed that high collagen-producing cells may be developed by manipulating the ubiquitin-related enzymes targeting the COP II protein.