

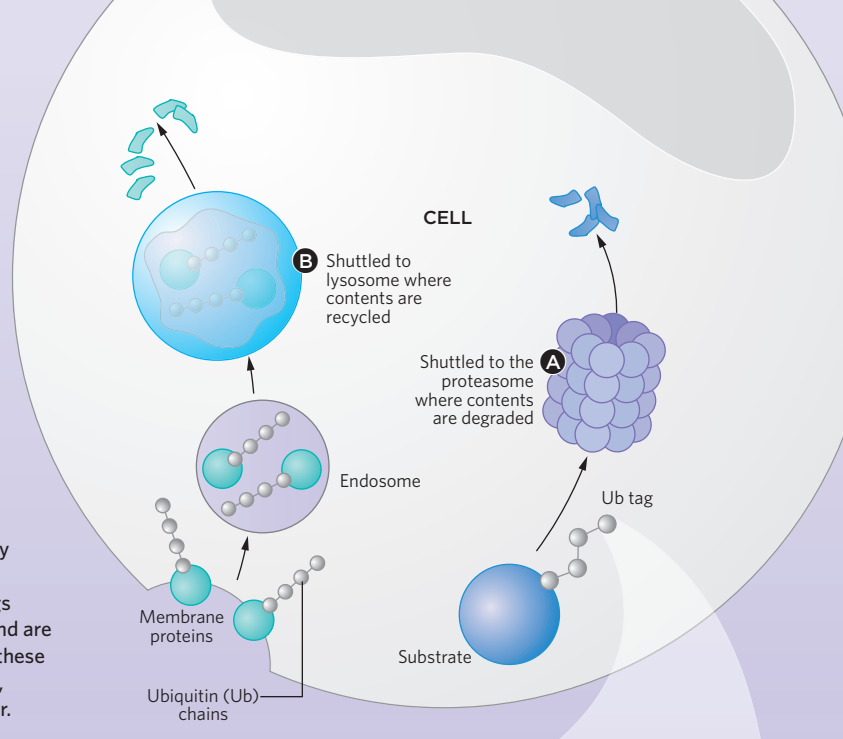
UBIQUITIN BASICS

Despite its discovery as a protein that seems to show up everywhere, at least in eukaryotic cells, researchers are only beginning to scratch the surface of all of the cellular functions that involve ubiquitin.

Ubiquitin can bind to proteins as a monomer, or in long chains that bend or branch. Not much is known, however, about the receptors that decode these various shapes and relay their messages.

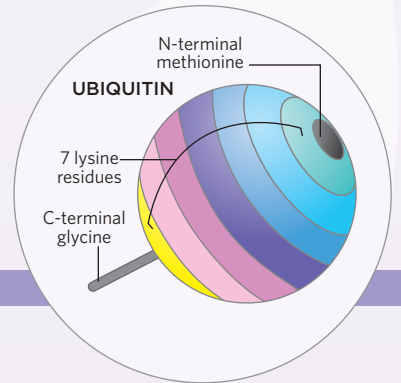
LITTLE MESSENGERS

Ubiquitin (Ub) is best known for tagging proteins for degradation. A four-monomer-long ubiquitin chain connected via the lysine-48 of each Ub is used to mark proteins destined for proteasomal degradation **(A)**. Accessory proteins called E1, E2, and E3 help choose which protein should be tagged and recruit ligases to link the Ub monomers into a chain. Ubiquitin also tags membrane proteins, which then pinch inward into endosomal vesicles and are trafficked to the lysosome for digestion **(B)**. In addition to degradation via these two pathways, however, ubiquitin appears to also play a role in DNA repair, apoptosis, and the transport of proteins from one part of the cell to another.



DIFFERENT LINKS FOR DIFFERENT KINKS

Ubiquitin owes much of its diversity of function to the simplicity and flexibility of its linkages. Not only can it form long chains or polymers, those polymers can take on many shapes: branching, buckling, and even including other ubiquitin-like molecules. The C-terminus of each ubiquitin molecule can bind to one of the seven exposed lysine residues (Lys) on the neighboring Ub, as well as to its N-terminus. How the molecules link up determines the shape of the chain and the message it conveys to the receptors. (Artistic representation of ubiquitin molecule at right depicts how lysine binding affects chain shape. The C-terminus of Ub will bind one of the lysine residues, which in real life sit in specific positions on the molecule, rather than encircle it.)

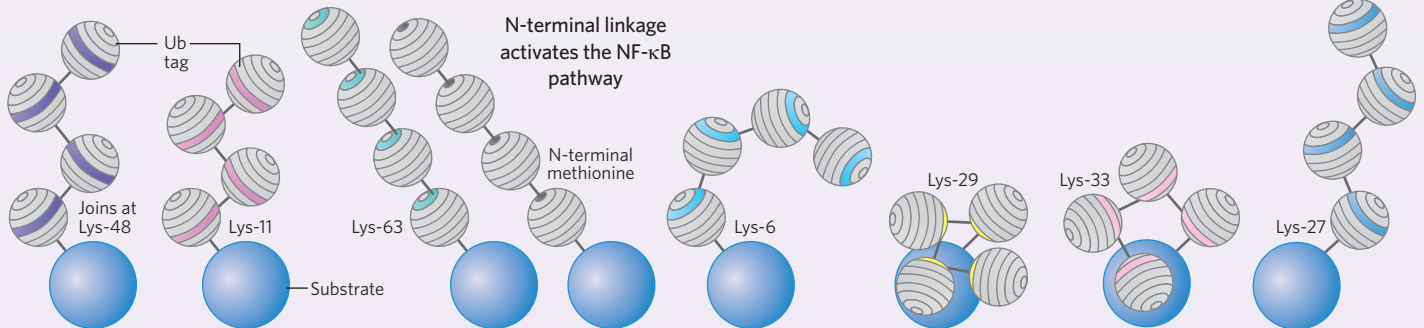


HOMOGENEOUS POLYUBIQUITIN

Linkage via Lys-48 and Lys-11 targets tagged proteins to the proteasome

Lys-63-linked chains are involved in NF- κ B activation, DNA repair, and targeting proteins to the lysosome

Lys-6, Lys-29, Lys-33 and Lys-27 linkages: function unknown



MONOUBIQUITINATION

Proteins tagged with one or many single ubiquitin molecules are involved in protein interactions and localization

HETEROGENOUS

Unknown

BRANCHED/FORKED

Unknown

MIXED CHAIN

Mixed chains traffic proteins regulating apoptosis or transcription

