Parkin

Parkin is an E3 ubiquitin ligase that plays a prominent role in mitochondrial quality control, mitochondrial-dependent cell death pathways, and other diverse functions. Understanding the numerous roles of parkin has introduced many new possibilities for therapeutic modalities in treating both autosomal recessive Parkinson's disease and sporadic Parkinson's disease. Patel et al. reviewed parkin biology with an emphasis on mitochondrial-related functions and propose a novel, potentially disease-modifying therapeutic approaches for treating this debilitating condition [1].

Parkin is a 465-residue E3 ubiquitin ligase that plays a critical role in ubiquitination- the process whereby molecules are covalently labeled with ubiquitin (Ub) and directed towards degradation in proteasomes or lysosomes. Ubiquitination involves the sequential action of three enzymes. First, an E1 ubiquitin-activating enzyme binds to inactive Ub in eukaryotic cells via a thioester bond and mobilizes it in an ATP-dependent process. Ub is then transferred to an E2 ubiquitin-conjugating enzyme before being conjugated to the target protein via an E3 ubiquitin ligase.

There exists a multitude of E3 ligases, which differ in structure and substrate specificity to allow selective targeting of proteins to intracellular degradation.

In particular, parkin recognises proteins on the outer membrane of mitochondria upon cellular insult and mediates the clearance of damaged mitochondria via autophagy and proteasomal mechanisms.

Parkin also enhances cell survival by suppressing both mitochondria-dependent and -independent apoptosis.

see PARKIN mutation.

1)
Patel J, Panicker N, Dawson VL, Dawson TM. Cell Biology of Parkin: Clues to the Development of New Therapeutics for Parkinson's Disease. CNS Drugs. 2022 Nov 15. doi: 10.1007/s40263-022-00973-7. Epub ahead of print. PMID: 36378485.