

Regulation of Cullin-RING Ubiquitin Ligases

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Abstract:

The posttranslational addition of ubiquitin controls the stability and functions of many proteins that play critical roles in eukaryotes, including in hormone signaling, cell division, disease defense, and pattern formation. The final transfer of ubiquitin to a large number of target proteins is mediated by an evolutionarily conserved family of cullin-RING 'E3' ubiquitin ligases (CRLs), which is typified by Skp1–Cul1–F-box (SCF or CRL1) enzymes. The substrate specificity of an SCF complex is determined by which one of the many different F-box substrate receptor proteins is recruited to the Cul1 scaffold. Therefore, tightly regulated recruitment of a specific F-box protein to Cul1 is critical for the proper function of the SCF. Using biochemical, biophysical, and cell biological approaches, I study the dynamic assembly and disassembly of SCF complexes both *in vitro* and *in vivo*, leading to a model of how a key exchange factor collaborates with substrates and other regulators to establish a functional cellular repertoire of SCFs, which is essential for cells to respond to both internal and external signals.