

BIOCHEMISTRY SEMINAR

Regulation of Cullin 2-RING Ubiquitin Ligases

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Abstract: Ubiquitination, the post-translational addition of ubiquitin to proteins, modulates the stability and function of many key proteins in eukaryotes, impacting processes such as circadian clock, cell cycle, and disease defense. At the core of the ubiquitination process is the E3 ligase, which brings ubiquitin and the target protein together, and enables the transfer of the ubiquitin to its target. My lab investigates the largest family of E3 ligases, known as cullin-RING ligases (CRLs). CRLs are evolutionarily conserved modular protein complexes, featuring a cullin-RING scaffold and an interchangeable substrate receptor module. The substrate specificity of a CRL is determined by which one of the many different substrate receptor modules is recruited to the cullin-RING scaffold. Therefore, properly regulated recruitment of a specific substrate receptor module to the cullin-RING scaffold is critical for CRL function. Using biochemical, biophysical, and cell biological approaches, we study the dynamic assembly and disassembly of CRL complexes. Our research has revealed how CAND1, a cullin-binding protein, collaborates with NEDD8, a ubiquitin-like protein, to establish a functional cellular repertoire of CRLs that precisely target a broad spectrum of cellular proteins for ubiquitination.



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