Cullin Ring Ligases (CRL)

The cullin-RING ubiquitin ligases (CRLs) are a superfamily of multi-component RING-E3 complexes that comprise a cullin scaffold protein and a catalytic RING subunit, Rbx1 or Rbx2. To date, seven closely related cullin proteins, Cul1, Cul2, Cul3, Cul4A, Cul4B, Cul5 and Cul7 have been identified. The cullin proteins exist in complex with Rbx1 or Rbx2 and form different subfamilies of CRLs, CRL1–CRL5 (Figure 1). The largest of these families the Skp1-Cullin1 (Cul1)-F-Box Protein (FBP) (SCF) ligases, comprise an adaptor protein Skp1 which forms a bridge between Cul1 and an FBP. The FBP is responsible for binding the substrate and is referred to as the specificity factor while Rbx1 recruits ubiquitin-loaded E2 conjugating enzyme which - as part of the CRL complex - enables ubiquitylation of the substrate (Bennet *et al.*, 2010; Zimmerman *et al.*, 2010; Lydeard *et al.*, 2013).

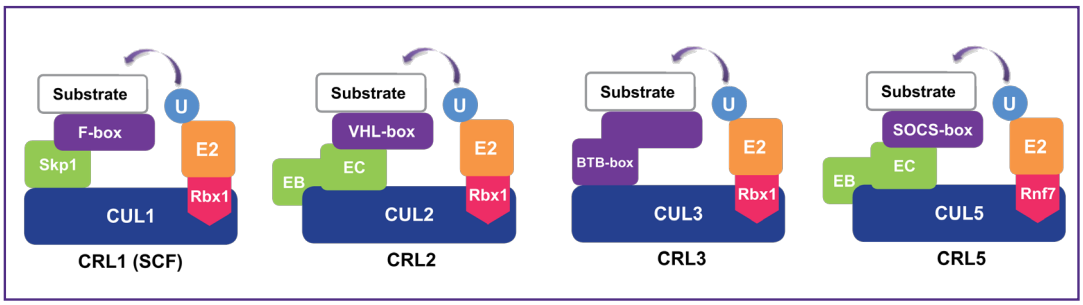

Figure 1: Cullin scaffold proteins (CUL1, CUL2, CUL3 and CUL5): Dark blue box; Rbx1 and Rnf7 (Rbx2): Red arrow; Ubiquitin (U)-charged E2 enzymes (E2): orange box with light blue circle; Skp1, Elongin C (EC) and Elongin B (EB) adaptor proteins (green box); F-box, BTB-box, VHL-box, and SOCS-box protein substrate receptors (purple box). (Modified from Zimmerman *et al.*, 2010; Sarikas *et al.*, 2011).

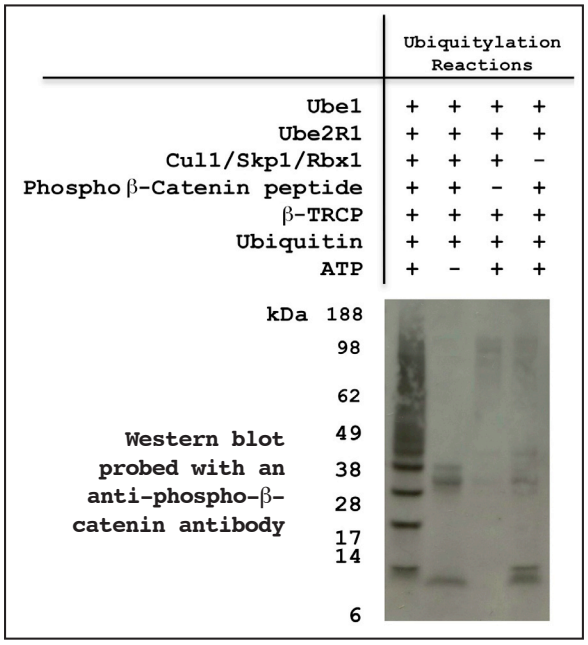

Figure 2: Cul1/Rbx1/Skp1 catalysed phospho β-Catenin Ubiquitylation: The activity of Cul1/Skp1/Rbx1 was validated through its ability to catalyse the generation of polyubiquitin chains in the presence of the E1 activating enzyme His-Ube1, the E2 conjugating enzyme His-Ube2R1, ubiquitin, the F-box protein Beta-Transducin Repeat Containing Protein (βTrCP), and the substrate phospho-β-Catenin. Incubation of a reaction for 60 minutes at 30˚C containing His-Ube1, His-Ube2R1, ubiquitin, Cul1/Skp1/Rbx1, β-TrCP, phospho-β-Catenin and ATP was compared alongside three control reactions with either ATP, phospho-β-Catenin, or Cul1/Skp1/Rbx1 excluded from the reaction. Analysis of these reactions by Western blotting using an anti-phospho-β-Catenin antibody identified ubiquitylated phospho-β-Catenin substrate only in the presence of both ATP and Cul1/Skp1/Rbx1.

The cullin proteins have been associated with a number of human diseases such as Alzheimer's Disease, Rheumatoid Arthritis, Leukaemia as well as gastric, renal and bladder cancers. For more information on these associations visit the new **Therapeutic Areas and the Ubiquitin System** section on the Ubiquigent website.

Ubiquigent now offers a number of purified Cullin heterodimers, a heterotrimer and two antibodies as part of a growing portfolio of E3 ubiquitin ligases to help facilitate your research.

CRL Research Products

Description	Cat. #	Size	Price
Cul1/Rbx1 [untagged]	63-1000-025	25 µg	£245 €295
Cul1/Rbx1/Skp1 [untagged]	63-1001-025	25 µg	£295 €355
Cul2/Rbx1 [untagged]	63-1004-025	25 µg	£245 €295
Cul3/Rbx1 [untagged]	63-1003-025	25 µg	£245 €295
Cullin3 (human; residues 554 - 768), pAb	68-0004-100	100 µg	£215 €259
Cul5/Rnf7 [untagged]	63-1002-025	25 µg	£245 €295
Cullin5 (human; residues 577 – 689), pAb	68-0005-100	100 µg	£215 €259

References:

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Sarikas A, Hartmann T, Pan ZQ (2011) The cullin protein family. *Genome Biol.* **12** 220.

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