Supplementary information

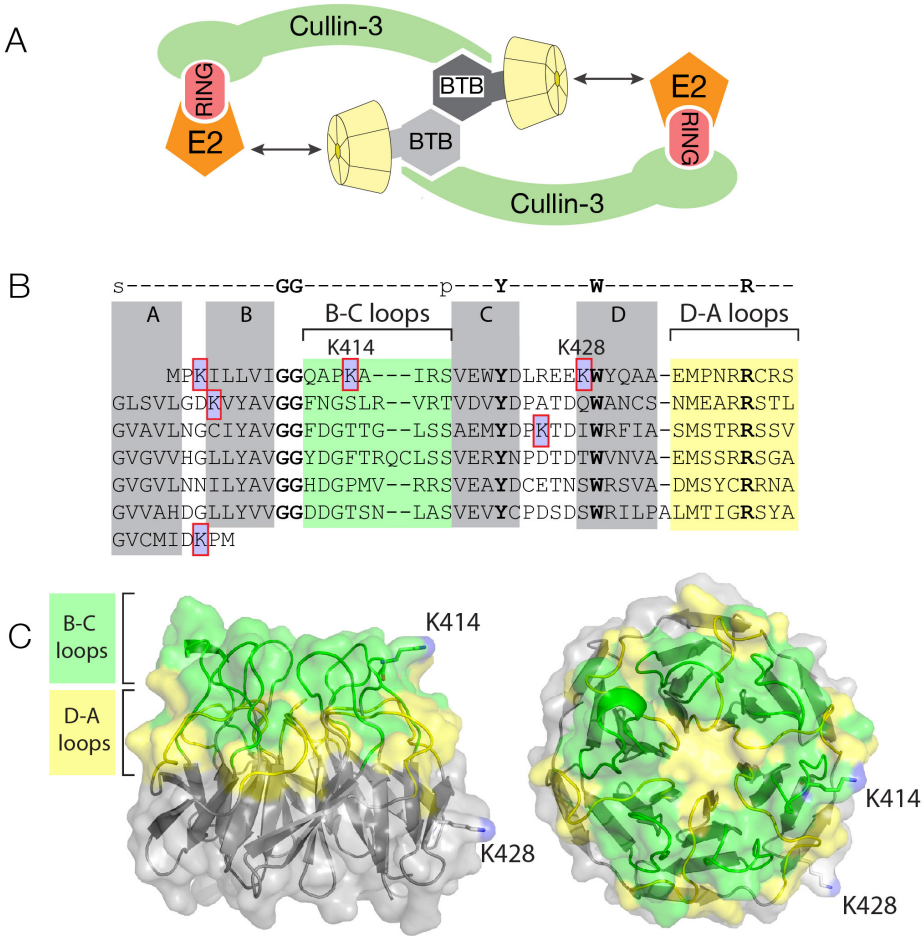

Figure S1. Lysine residue positions in Kelch KREP domain. (A) 2D cartoon of hypothetical CRL3^{Kelch} structure based on structural modeling in (Stogios et al., 2005). The "top", substrate binding surface of each KREP domain is oriented toward the E2 ubiquitin conjugating enzyme. SRS autoubiquitylation can be inhibited when excess substrate is present (Deshaies, 1999), consistent with SRS autoubiquitylation occurring across the cleft between the SRS substrate binding domain and the E2 enzyme (double arrow). (B) Sequence of Kelch KREP domain. The six lysine residues are indicated. The four β-strands that make up each blade of the β-propeller structure are highlighted in gray and labeled A - D. Sequence loops between the B-C and D-A strands are highlighted in in green and yellow, respectively, and correspond to the green and yellow structural elements in C. (C) Homology model of Drosophila Kelch created using the Phyre2 homology modeling server (http://www.sbg.bio.ic.ac.uk/~phyre2/; Kelley and Sternberg, 2009) based on the structure of the human Kelch ortholog KLHL2/Mayven (PDB: 2XN4; Canning et al., 2013). Two lysine residues, K414 and K428, are surface-exposed, and K414 is located in a B-C loop extending from the 'top' surface of the Kelch β-propeller, presumably oriented toward the E2 enzyme in the assembled CRL.