

Poster Presentation

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KCTD proteins as Cullin3 E3 Ligase adapters

A. Ji¹, G. Privé²

¹University of Toronto, Department of Biochemistry, Toronto, Canada, ²University Health Network, Princess Margaret Cancer Center, Toronto, Canada

Cullin3 (Cul3) is an ubiquitin E3 ligase responsible for catalyzing the transfer of an ubiquitin moiety from an E2 enzyme to a target substrate protein. The C-terminal region of Cul3 binds RBX1/E2-ubiquitin, while, the N-terminal region interacts with various BTB domain proteins which serve as substrate adaptors. Previously, our group determined the crystal structures of the homodimeric BTB proteins SPOP and KLHL3 in complex with the N-terminal domain of Cul3, revealing the determinants responsible for the BTB/Cul3 interaction [1, 2]. A second class of BTB-domain containing proteins, the KCTD proteins, are also Cul3 substrate adaptors but these do not share many of the previously determined features for Cul3 binding. Furthermore, KCTD proteins form homotetramers and homopentamers via BTB oligomerization rather than the previously described homodimers. Despite these differences, many KCTD proteins interact with Cul3 with dissociation constants of approximately 50 nM. While the target substrates for many of the KCTD/Cul3 E3 ligase complexes are unknown, recent studies have implicated the GABA β 2 receptor as an interactor of KCTD 8, 12, 12b and 16. Here, we report the pentameric crystal structure of the KCTD9 BTB domain and our progress on the structural characterization of Cul3/KCTD/substrate complexes.

[1] W. Errington, M. Khan, S. Bueler, et al., *Structure*, 2012, 20, 1141-53, [2] A. Ji, G. Prive, *PLoS One*, 2013, 8, e60445

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