

## Poster Presentation

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### *An UBR-box from a non-N-recognin: Crystal Structure of the UBR domain of UBR6*

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The degradation of many short-lived proteins in eukaryotic cells is carried out by the Ubiquitin Proteasome System. The N-end rule pathway links the half-life of proteins to the identity of its N-terminal residue, also called N-degron. Destabilizing N-degrons, are recognized by E3 ubiquitin ligases termed N-recognins. N-degrons are grouped into type 1, composed of basic residues, and type 2, composed of bulky hydrophobic residues. In mammals, four N-recognins mediate the N-end rule pathway: UBR1, UBR2, UBR4 and UBR5. These proteins share a ~70-residue zinc finger-like motif termed the Ubiquitin Recognin (UBR) box, responsible for their specificity. The mammalian genome encodes at least three more UBR-box proteins: UBR3, UBR6/FBXO11 and UBR7. However, these UBRs cannot recognize any type of N-degrons. Our lab reported the crystal structures of the UBR boxes from the human UBR1 and UBR2, rationalizing the empirical rules for the classification of type 1 N-degrons. Despite the valuable information obtained from those structures there is not a clear explanation for the no recognition of N-degrons by other UBR-box proteins. Here we report the crystal structure of the UBR-box domain from UBR6 also known as FBXO11. UBR6 is a F-box protein of the SKP1-Cullin1-F-box (SCF) ubiquitin ligase complex and does not recognize any type of N-degrons. We crystallized a 77-residue fragment of the UBR-box of UBR6 and determined its structure at 1.7 Å resolution. Unexpectedly, this domain adopts an open conformation compared to UBR1-box, without any N-degron binding pockets. Its zinc-binding residues are conserved as in the N-recognins, but they are arranged in different zinc-binding motifs. Molecules form dimmers stabilized by zinc ions. The crystal had 4 molecules per asymmetric unit and space group P212121. For phasing we used Zn-SAD. With this structure we hope to obtain clues that explain the absence of N-degron recognition in some members of the UBR family.

**Keywords:** Ubiquitin ligase, FBXO11, UBR6