The crystal structure of the UBR box of UBR4 reveals type-2 N-degron binding mechanism

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The N-end rule pathway is a proteolytic system that degrades short-lived proteins with destabilizing N-terminal amino acids (N-degrons) by N-recognins. N-degrons are classifed into type-1 with positive amino acids (Arg, Lys, and His) and type-2 with bulky hydrophobic amino acids (Phe, Tyr, Trp, Leu, and Ile). UBR proteins (UBR1–UBR7) is a subfamily of E3 ligases and is one of the well-known N-recognins, which recognize substrates and mediate degradation through the ubiquitin-proteasome system (UPS). These UBR proteins share the UBR boxes that is a domain of ~70 amino acids coordinating three zinc ions and this domains recognize N-degrons. One of them, UBR4, is implicated in various biological processes, such as yolk sac vascular development, neurogenesis, neuronal survival, cell adhesion, cell migration and myofiber size determination. We have determined the crystal structure of UBR box of UBR4 to understand the feature of substrate binding mechanism. This structure is different from the UBR boxes of UBR1 and UBR2, which has been extensive structural studies, in zinc coordination residues and substrate-binding pocket. We also identified that the UBR box of UBR4 exhibits binding affinity for type-2 N-degrons unlike another UBR boxes.

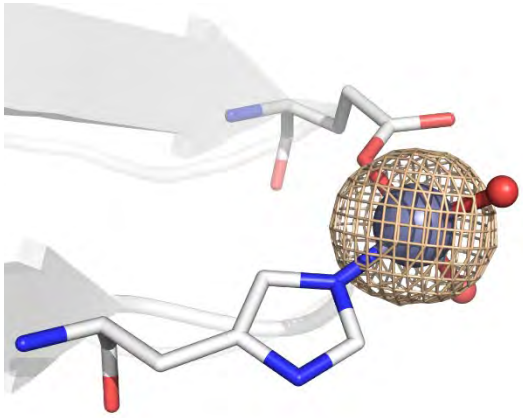

Figure 1. This is a figure caption (Heading 6 style, Times New Roman 9 pt).

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