

## Snapshots and ensembles of BTK and cIAP1 protein degrader ternary complexes

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Heterobifunctional chimeric degraders are a class of ligands that recruit target proteins to E3 ubiquitin ligases to drive compound-dependent protein degradation. Critical to the mechanism of action is the formation of a ternary complex between the target, degrader and E3 ligase to promote ubiquitination and subsequent degradation. However, limited insights into ternary complex structures exist, including a near absence of studies on one of the most widely co-opted E3s, cellular inhibitor of apoptosis 1 (cIAP1). Our results reveal insights from unique ternary complex structures and show that increased ternary complex stability/rigidity need not always correlate with increased degradation efficiency.