

Defining the structural basis of ASCC2's specificity for K63-linked polyubiquitin chains using 3D NMR analysis

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DNA damage requires precise repair mechanisms that function in a timely manner to maintain genomic integrity. The ALKBH3-ASCC complex is a DNA alkylation damage repair complex that binds to K63-linked polyubiquitin chains which are assembled at damage sites. ASCC2, a subunit in the complex, selectively binds K63-linked polyubiquitin chains by interacting with two ubiquitins simultaneously. Although the residues on ASCC2 that interact with polyubiquitin chains are known, the specific interactions between ASCC2 and ubiquitin that impart specificity remains unclear. We are using 3D NMR to determine intermolecular distances which will guide our modeling of the ASCC2:K63Ub₂ complex to elucidate how ASCC2's specificity for K63-linked polyubiquitin chains is achieved.