

Integrative Modeling of the ASCC2:K63Ub2 Complex to Better Understand DNA Alkylation Damage Repair

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The ALKBH3-ASCC complex plays a vital role in repairing alkylation damage in DNA. ASCC2, a subunit of the ASCC complex, localizes the ALKBH3-ASCC complex by binding to K63-linked polyubiquitin chains assembled at alkylation damage sites. ASCC2 has been shown to bind K63-linked polyubiquitin chains with enhanced affinity compared to monoubiquitin or other types of polyubiquitin chains. The purpose of this study is to determine the structural basis for ASCC2's enhanced affinity for K63-linked polyubiquitin chains. To study this, models of the ASCC2:K63Ub2 complex will be generated using NMR, ITC, and SAXS experimental data to visualize the interaction interfaces and elucidate the basis for this specificity. A better understanding of the alkylation damage repair pathway will prove useful to studies working toward treating alkylation damage diseases, as well as utilizing alkylation damage as a type of chemotherapy.