

P008 CHIP mediated degradation and DNA damage dependent stabilization regulates base excision repair proteins
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Base excision repair (BER) is the major pathway for processing of simple lesions in DNA, including single strand breaks, base damage and base loss. The scaffold protein XRCC1, DNA polymerase β and DNA ligase III α play pivotal roles in BER. Although all these enzymes are essential for development, their cellular levels must be tightly regulated since increased amounts of BER enzymes lead to elevated mutagenesis, genetic instability and are frequently found in cancer cells. Here we report that BER enzyme levels are linked to and controlled by the level of DNA lesions. We demonstrate that stability of BER enzymes increases after formation of a repair complex on damaged DNA and that the proteins not involved in a repair complex are ubiquitinated by the E3 ubiquitin ligase CHIP and subsequently rapidly degraded. These data identify a novel mechanism controlling cellular levels of BER enzymes and correspondingly the efficiency and capacity of BER.