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Interaction And Structural Properties of the Nat10 Acetyltransferase Studied Using Biophysical Methods and Ai Tools

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NAT10 acetyltransferase plays a crucial role in the regulation of RNA processing, cellular plasticity, and DNA damage response by interacting with key repair proteins. The NAT10 protein forms a symmetrical heart-shaped dimer, but the AlphaFold3 prediction shows that this structure is changed when phosphorylation on serine residues appears on selected amino-terminal tails. We studied how NAT10 contributes to DNA damage responses. When compared to wild-type (wt) counterparts, NAT10-deficient cells were characterized by depletion of DNA repair proteins, including XPC, DDB2, and p53. Also, in p53 double null (dn) cells, NAT10 levels were almost undetectable, and DDB2 expression was significantly reduced. Following UVC irradiation, XPA, and XPC levels decreased in both NAT10 wt and NAT10 dn cells, and DDB2 levels were diminished in NAT10-deficient cells. Despite this downregulation, the DDB2 protein retained its functional role in the DNA damage response. Also, based on AlphaFold3 predictions, we suggest that NAT10 regulates the p53-DDB2 protein complex, and NAT10 depletion potentially alters its functional dynamics. Consistent with this claim, FLIM-FRET analysis revealed that UVC light weakens the p53-DDB2 interaction while simultaneously potentiating the bond between NAT10 and DDB2 proteins. These findings highlight the intricate regulatory role of NAT10 in DNA damage repair.