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Project Title:
The role of INO80 chromatin remodeler in DNA damage repair

Project summary:
Genomic DNA, organized as chromatin, is vulnerable to damage that, if unrepaired, can cause genome instability, apoptosis, and diseases. DNA damage response (DDR), including Base Excision Repair (BER) and Nucleotide Excision Repair (NER), are essential for maintaining genome integrity. Chromatin's role in DDR is critical but not fully understood. In October 2023, we submitted a proposal to the National Institute of General Medical Sciences (NIGMS) to study the ATP-dependent chromatin remodeler INO80 in DDR, focusing on its role in BER and NER. The original proposal was based on our findings showing that DNA lesions inhibit INO80's DNA-translocation activity and that INO80 enhances Ape1-mediated AP site cleavage in an ATP-independent manner. Despite the proposal's conceptual novelty and technical innovation, reviewers noted our limited expertise in NER and the reliance on structural methods. To address these concerns, we plan to focus on INO80's role in BER for our resubmission and conduct two functional studies: 1) determining the functional implications of INO80-AP endonuclease interaction *in vivo*, and 2) identifying INO80-associated repair factors in BER. Seed Grant support will help us generate preliminary data for these studies, enhancing our resubmission success.