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DNA damage repair response facilitated by the FANCJ helicase and the REV1 polymerase

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Statement of the problem: G-quadruplexes (G4s) are DNA structures formed by guanine-rich nucleic acids. Damaged G4s can interfere with essential cellular processes such as DNA replication and RNA transcription. The human FANCJ helicase facilitates DNA replication through G4-forming regions and participates in interstrand DNA cross-link repair. G4s are also prone to oxidative stress and how such lesions are recognized and processed is not well-understood. REV1 is a translesion DNA polymerase that synthesizes DNA across from damaged templates in human cells. A current model states that REV1 is recruited to a G4 DNA site by the FANCJ helicase, and then participates in the repair process by incorporating cytosine across from a guanine base. In a previous study, we identified an AKKQ amino acid motif within FANCJ that binds to G4 DNA. FANCJ presumably targets a stalled replication fork at a G4-containing DNA site and then recruits REV1 to efficiently replicate DNA across from a G-quadruplex.

Methodology and theoretical orientation: In this work, we aim to test this model by examining the macromolecular interactions between REV1, G4 DNA, and the FANCJ helicase using fluorescence spectroscopy and biolayer interferometry.

Findings: FANCJ binds to REV1 with high affinity, which is consistent with this handoff model. In addition, we show that the FANCJ AKKQ motif also binds to an 8-oxoguanine modified G4, suggesting that FANCJ also recognizes damaged G4 structures.

Conclusion: Based on this evidence, FANCJ can target both G4 and 8-oxoG4 structures, and then bring REV1 to the DNA site in order to bypass the stalled replication fork. We plan to further examine the significance of the FANCJ-REV1 interaction *in vivo* by studying this G4 repair pathway in human cells.

Biography

Mena Jirjees is a Biochemistry student at Oakland University who is also pursuing a minor in Middle Eastern studies. She is currently applying to medical schools, and she is planning on becoming a neonatologist. Additionally, Mena would like to continue with basic science research in the field of cancer mechanisms.

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Kaitlin Lowran recently received her bachelor's degree in Biochemistry from Oakland University. She will begin her doctoral studies in the Biomedical Sciences program at OU starting this fall. She will be working with Dr. Colin Wu for her dissertation work. Kaitlin is interested in DNA repair mechanisms and she recently received a fellowship from the Michigan Space Grant Consortium to study these pathways in microgravity environments.

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