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CHARACTERIZING THE MOLECULAR FUNCTION OF THE MUTAGEN SENSITIVITY GENE, *MUS109*

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DNA repair pathways are essential in repairing damage that otherwise could cause genomic instability and cancer. Because mutations in DNA repair genes are linked to numerous human diseases, elucidating the molecular functions of DNA repair pathways will improve our understanding of disease mechanisms. *Drosophila melanogaster* has orthologs to most human DNA repair genes, so we can study mutants with reduced DNA repair function to investigate mechanism. Our work investigates the function of *mus109*, which is thought to be involved in DNA repair because allelic mutants are sensitive to various DNA damaging reagents. There are three available *mus109* mutant alleles: the lethal mutant loss of function allele $mus109^{lS}$, and the hypomorphic alleles $mus109^{D1}$ and $mus109^{D2}$. Our collaborators at Winthrop University used complementation crosses of these mutant alleles to map the location of *mus109* on the X chromosome and confirmed mutant sensitivity to the DNA alkylating reagent methyl methansulfonate (MMS). We performed a protein sequence alignment comparing *mus109* mutant alleles and found that mutations in each allele result in a loss of nuclease and/or helicase domains. To elucidate *mus109* involvement in various DNA repair pathways, we tested larval sensitivity of different allele combinations to DNA damaging reagents. We have preliminary data suggesting that different mutant alleles have different responses to bleomycin, a chemotherapeutic that causes double strand breaks. Hypomorph $mus109^{D1}/mus109^{D2}$ larvae are not sensitive to bleomycin whereas $mus109^{lS}/mus109^{D2}$ larvae are mildly sensitive. We also have preliminary data suggesting $mus109^{D1}/mus109^{D2}$ larvae are not sensitive to the single-strand break-inducer, camptothecin. These data indicate that *mus109* is involved in DNA repair pathways that resolve double-strand breaks and that *mus109* alleles have variable sensitivities to different mutagens, which could be explained by the variation in protein output for each allele. We plan to continue to assess *mus109* mutant larval sensitivity to reagents such as the replication fork staller, hydroxyurea, to further characterize the function of the gene in DNA repair.