

Investigating Transgenerational Phenotypes and Altered Behavior in *C. elegans* Mutants With Inappropriately Inherited Histone Methylation

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The proper formation of a zygote requires extensive epigenetic reprogramming to enable appropriate inheritance of histone methylation. In *C. elegans*, this reprogramming is mediated by the H3K4me2 demethylase SPR-5 and the H3K9 methyltransferase MET-2. Double-mutants lacking both SPR-5 and MET-2 suffer from severe chemotaxis defects, developmental delay, and sterility after a single generation. These phenotypes are associated with synergistic increases in both H3K4me2 and ectopic germline gene expression in somatic tissues. However, what is not yet known and what my project sought to answer was whether transgenerational accumulation of H3K4 methylation in single-mutants (*spr-5* or *met-2*) can lead to a similar chemotaxis defect as observed in the double-mutants (*spr-5;met-2*). After conducting chemotaxis assays on *C. elegans* single- and double-mutants for 30 generations, I observed that there was not a severe chemotaxis defect in the single-mutants. However, brood counts of each generation revealed that sterility of *spr-5* and *met-2* single-mutants increased steadily, suggesting that transgenerational accumulation of methylation is occurring and leading to ectopic germline gene expression causing sterility. Thus, failure to observe a severe chemotaxis defect suggests that the genes ectopically expressed in the double-mutants but not in the single-mutants may be causing majority of the chemotaxis defect in the double-mutants. RNAseq analysis of L4 worms from generations F7, F13, and F22 of single- and double-mutants has allowed me to narrow down these genes to 460. Gene ontology analysis indicates that this gene set is enriched in meiotic genes, suggesting that ectopic expression of meiosis genes in neurons of double-mutants is responsible for their severe behavioral defect.

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