KHDC3 in Grandparents Regulates Gene Expression in the Livers of Wild-Type Females

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It has become increasingly apparent that a person's environment has the potential to alter gene expression via the transgenerational inheritance of non-DNA factors. These factors likely accumulate in an individual's germ cells and alter gene expression, leading to the non-Mendelian inheritance of phenotypes or diseases such as diabetes, obesity, and cardiovascular disease. As oocytes are particularly susceptible to accumulating epigenetic markings, pregnant women are at a particular risk of passing on such conditions to future generations of offspring. However, the molecular driver behind this process is currently unknown, and has not been significantly studied via the maternal germline. This project explores the effect that a potential epigenetic regulator— the KHDC3 gene— has on the gene expression of wild-type F2 mice. It examines both WT mice with WT grandparents, and WT* mice whose grandparents are KHDC3-deficient. Liver RNA was isolated and purified, cDNA was produced, and qPCR was used to compare liver metabolic gene expression between cohorts. Ultimately, WT* mice with deficient grandparents exhibited upregulation in the genes CYP17A1, CAPN3, THEM7, and 2610507I01Rik compared to the WT control group ($p<0.05$). Other metabolic genes, germ cell small RNAs, and phenotypic changes will ultimately be studied to gain a deeper understanding of the epigenetic changes mediated by KHDC3. This study provides novel data supporting KHDC3 as a regulator of the non-Mendelian inheritance of diseases such as Metabolic Syndrome via the maternal germline, which holds both preventative and therapeutic implications for addressing generational disease.

Awards Won:

Third Award of $1,000