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KHDC3 in Grandparents Regulates Gene Expression in Wild-Type Grandchildren

Recently, it has become increasingly apparent that a person's lifestyle— including stress levels, diet, and environmental factors— 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-genetic inheritance of phenotypes and diseases such as cancer, diabetes, or cardiovascular disease. However, the molecular driver behind this process is currently unknown. Here, I explore the effect that a potential epigenetic regulator-- the KHDC3 gene-- has on the gene expression of wild type mice via the maternal germline. I examined both WT mice with WT grandparents, and WT* mice with grandparents who carried a KHDC3-deficiency mutation. Liver RNA was isolated and purified, and cDNA was produced. qPCR was then used to compare gene expression levels between mouse cohorts. Ultimately, WT* mice with deficient grandparents exhibited an upregulation of CYP17A1, CAPN3, THEM7, and 2610507I01Rik compared to the WT control cohort ($p<0.05$). Other genes in the liver, pancreas, oocyte, and pituitary will ultimately be studied to gain a better picture of the epigenetic changes experienced by KHDC3 knockout mice and their descendants. This study provides promising data supporting KHDC3 as a central regulator of epigenetic inheritance, which could ultimately be used to better understand the origins of disease and develop therapeutic solutions by analyzing human epigenetic profiles.