Analysis of rat *MIER family member 3* targeted mutation (*Mier3^{tm}*) mammary gland ultrastructure using transmission electron microscopy.

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MIER family member 3 (MIER3) is a human and rat genetic-association nominated breast-cancer susceptibility gene. Rat *Mier3* is differentially expressed between cancer susceptible and resistant mammary glands. Human/rat *MIER3/Mier3* encode nuclear proteins predicted to be co-repressors of transcription. Gene editing (CRISPR/Cas9) was used to target *Mier3* in Spraque Dawley rats. Founders with premature stop codon mutations (tm), were used to establish SD-*Mier3^{tm}* strains. Homozygous *Mier3$^{tm/tm}$* females were fertile, lactated normally, and less susceptible to developing chemically induced mammary carcinomas. Histological analysis of hematoxylin and eosin (H&E) stained mammary glands revealed *Mier3$^{tm/tm}$* females had less eosin staining than females with non-mutated references alleles (*Mier3$^{+/+}$)*. This difference was visually apparent and significantly different in epithelial ductal structures and adipocyte rich stroma. Eosin is a negatively charged molecule that broadly stains positively charged molecules like collagen and type II cytokeratin, which are abundant, positively charged, proteins in mammary gland tissue. We used transmission electron microscopy (TEM) to gain insight into the ultrastructural morphology of *Mier3$^{tm/tm}$* mammary glands. A preliminary observational analysis of TEM images suggested that collagen fibrils were less organized and not as densely packed in *Mier3$^{tm/tm}$* mammary glands compared to *Mier3$^{+/+}$* reference glands.

This work was supported by NIH P20GM103436 and UofL Dept. of Biochemistry & Molecular Genetics.