**2017 Atrazine Plos One Summary**

**September 2017**

**Publication**

McBirney M‡, King SE‡, Pappalardo M, Houser E, Unkefer M, Nilsson E, Sadler-Riggleman I, Beck D, Winchester P and Skinner MK (2017) Atrazine induced epigenetic transgenerational inheritance of disease, lean phenotype and sperm epimutation pathology biomarkers. PLoS One. 12(9):e0184306.

‡ These authors are co-first authors on this work.

**Summary**

Ancestral environmental exposures to a variety of environmental toxicants and other factors have been shown to promote the epigenetic transgenerational inheritance of adult onset disease. The current study examined the potential transgenerational actions of the herbicide atrazine. Atrazine is one of the most commonly used herbicides in the agricultural industry, in particular with corn and soy crops. Outbred gestating female rats were transiently exposed to a vehicle control or atrazine. The F1 generation offspring were bred to generate the F2 generation and then the F2 generation bred to generate the F3 generation. The F1, F2 and F3 generation control and atrazine lineage rats were aged and various pathologies investigated. The male sperm were collected to investigate DNA methylation differences between the control and atrazine lineage sperm. The F1 generation offspring (directly exposed as a fetus) did not develop disease, but weighed less compared to controls. The F2 generation (grand-offspring) was found to have increased frequency of testis disease and mammary tumors in males and females, early onset puberty in males, and decreased body weight in females compared to controls. The transgenerational F3 generation rats were found to have increased frequency of testis disease, early onset puberty in females, behavioral alterations (motor hyperactivity) and a lean phenotype in males and females. The frequency of multiple diseases was significantly higher in the transgenerational F3 generation atrazine lineage males and females. The transgenerational transmission of disease requires germline (egg or sperm) epigenetic alterations. The sperm differential DNA methylation regions (DMRs), termed epimutations, induced by atrazine were identified in the F1, F2 and F3 generations. Gene associations with the DMRs were identified. For the transgenerational F3 generation sperm, unique sets of DMRs (epimutations) were found to be associated with the lean phenotype or testis disease. These DMRs provide potential biomarkers for transgenerational disease. The etiology of disease appears to be in part due to environmentally induced epigenetic transgenerational inheritance, and epigenetic biomarkers may facilitate the diagnosis of the ancestral exposure and disease susceptibility. Observations indicate that although atrazine does not promote disease in the directly exposed F1 generation, it does have the capacity to promote the epigenetic transgenerational inheritance of disease.