

Session/Poster#

Presenter

**B30**

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**Transmission of behavioral deficits in rats exposed to folate receptor alpha antibody in utero.**

**Objectives:** 1. Investigate the behavioral deficits in rats exposed to folate receptor alpha autoantibodies (FRAb) during fetal development. 2. Investigate the heritability of this autism spectrum disorder (ASD)-like phenotype by determining whether it is transmitted to a subsequent generation.

**Background:** Folate deficiency is known to lead to disruptions in neurodevelopment including neural tube defects and developmental anomalies such as ASD. Folate receptor alpha is the main transporter of folate from the mother to the fetus and into the brain. A major subset of the ASD population and their family members have autoantibodies against folate receptor alpha that may cause neuroinflammation and block folate transport in the developing fetus.

**Methods:** Our laboratory has produced rat-specific FRAb that when injected intraperitoneally into a dam at gestation day 8, will produce a litter with ASD-like behavioral deficits. This phenotype can be prevented when the dam is given D, L-folinic acid, dexamethasone, or a combination of both at the time of FRAb exposure. We tested both the litter directly exposed to FRAb and the offspring of those with an affected phenotype using a battery of social and learning tests.

**Results:** We observed deficits in social communication, social interaction, learning and memory in both the first and second generations which suggests transmission of the behavioral phenotype associated with FRAb exposure.

**Conclusion:** The intergenerational transmission of this phenotype to animals not directly exposed to FRAb suggests that it may be mediated by epigenomic changes. We hypothesize that treatment of the directly exposed generation with folinic acid prior to mating may prevent transmission of behavioral deficits to a subsequent generation by altering the epigenome. This may be a strategy to decrease the risk of ASD in families with a history of the disorder.