NIH Award from the National Institute on Alcohol and Alcoholism

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- Project: Prenatal Alcohol: Hormone-Regulated Genes and Behavior
- Start Date: July 1, 2009
- Total Award Amount: $41,723

How the results of this project will benefit society:
Children exposed to alcohol prenatally frequently exhibit behavioral problems including attention deficit/hyperactivity (ADHD) disorder and learning deficit; the prevalence of which is close to 60 percent among youth diagnosed with fetal alcohol spectrum disorder. A large percentage of children born to mothers with mild hypothyroxinemia or with resistance to thyroid hormones are also diagnosed with ADHD. Thus, there seems to be a close and enigmatic relationship between prenatal alcohol exposure, thyroid function, and cognitive impairment. Our long-term goal is to understand the interaction between alcohol and the maternal-fetal thyroid function, as a potential mechanism by which prenatal ethanol induces behavioral deficits in the offspring. We anticipate that thyroxine (T4) treatment protocols successful in the fetal alcohol exposed animal model can potentially be implemented in clinical trials.

The problem the project is trying to solve:
The goal of this project is to elucidate the role of perinatal thyroid hormonal milieu in the cognitive function of the fetal alcohol exposed rat. During the previous funding period, we have shown that alcohol consuming pregnant dams have suppressed thyroid function. We have also shown that their adult offspring exhibit thyroid function abnormalities, despair-like behavior and cognitive impairments. The suppressed maternal thyroid function seems to cause these behavioral abnormalities, since prenatal thyroxine (T4) administration reversed the behavioral deficits in the fetal alcohol exposed (FAE) offspring.

How this project will work:
We hypothesize that the decreased thyroid hormone milieu of the alcohol consuming pregnant dam affects, via the placenta, the expression of thyroid hormone-regulated genes in the fetal brain, and thereby impact the cognitive and emotional behavior of the adult FAE offspring. Based on this hypothesis, we will investigate:

- The effects of administering different doses of T4 to alcohol consuming dams on (a) the expression of uterine and placental genes that restrict or modulate thyroid hormone exposure of the fetus; and (b) on the expression of genes regulated by thyroid hormones in specific regions of the fetal brain
- Determine a dose of T4 that reverses the behavioral consequences of FAE but does not alter the adult thyroid function adversely
- Develop perinatal thyroid hormone treatment paradigms subsequent to the alcohol exposure, aimed at finding one that reverses the FAE behavioral deficits and normalizes the thyroid function of the adult FAE offspring.

This award is funded under the American Recovery and Reinvestment Act of 2009, NIH Award number: 3R01AA013452-06S1.