CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

Name(s)
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Project Number
S1712

Project Title
Developing New Drugs to Treat Autism

Abstract

Objectives/Goals
1)Are autism symptoms caused by excess purinergic signaling?
2)Would drugs that block P2X/P2Y signaling of extracellular ATP (such as Suramin) reduce the root cause and will treat ASD symptoms and behaviors in a mouse model?

Methods/Materials
C57BL/6J mice , RNA POLY (I:C) OR Polyinosinicpolycytidylic acid, SURAMIN (P2X/P2Y ANTAGONIST), 0.9% NS, 3CHAMBER CRAWLEY DEVICE, OPEN FIELD TEST SET UP, DIGITAL RECTAL THERMOMETER
1) Total of 80 C57BL/6J mice were used.
2) Mice were exposed in utero to saline (Controls = 40), or a simulated viral infection by injection of RNA (Poly I:C) into pregnant dams (Maternal Immune Activation) to mimic ASD (ASD = 40).
3) 8 weeks after ASD-like behaviors developed, half of control groups (N=20) and half of Poly I: C exposed mice (N=20) were treated with weekly injections of Saline or Suramin.
4) 4 experimental groups of mice (N=20) with equal number of Males & Females were evaluated at 12 weeks of age.
5) Social Approach Experiments: were carried out with classical 3-chamber Crawley social interaction paradigm with automated & hand scoring of the number & duration of social encounters of an experimental mouse with a control mouse placed under an inverted wire cup.
6) Hyperactivity Experiments: Hyperactivity was measured by The Standard Open Field test.
7) Core Body Temperature: was measured using a digital rectal thermometer in mice exposed to saline and Poly (I:C) in utero; & was repeated with anti-purinergic therapy.

Results
Social Behavior was improved by Suramin, Hyperactivity in Male ASD Mice was normalized with Suramin. The MIA Model of autism produced relative hypothermia compared to saline exposed mice, & Suramin restored body temperature in Poly(IC) exposed animals.

Conclusions/Discussion
We hypothesized that drugs that block P2X/P2Y signaling of extracellular ATP will reduce purinergic/neuroinflammatory signaling and thus will treat ASD behaviors in a mouse model, our results support this hypothesis. We believe this research is highly innovative as there are yet no publications that link mitochondrial metabolism to purinergic signaling or purinergic signaling to autism.

Summary Statement
At present there is lack of novel targeted therapy for Autism, the research goal is to develop new treatments.

Help Received
Started Project as a Summer Intern at Dr Naviaux's lab at UCSD