CALIFORNIA STATE SCIENCE FAIR
2013 PROJECT SUMMARY

Name(s)
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Project Number
S1511

Project Title
Autism and Gut Microbiome: Is There a Link?

Abstract

Objectives/Goals
Autism spectrum disorders (ASD) now affect 1 in 88 children in the U.S and cost $35 billion annually. The hypothesis is that functional interface of genes & environment is metabolism, and that a persistent alteration in metabolism during critical period of neurodevelopment is responsible for ASDs. The gut microbiome contains up to 10^15 bacteria which produce an array of bioactive metabolic products capable of entering systemic circulation & can have profound effects on host metabolism, and immune function in many organs, such as brain. Recent research suggests that gastrointestinal microflora composition may differ between ASD & non-ASD children & an increase prevalence of Clostridia, Bacteriodetes and Sutterella species in ASD. Hypotheses: Significant metabolic changes occur in ASD mice compared with control mice. Stool metabolic profile can be utilized as a screening tool for early detection of ASD.

Methods/Materials
C57BL/6J mice were used. They were exposed in utero to saline, or a simulated viral infection by injection of synthetic ds RNA (Poly I:C) 3mg/kg on E12.5 into pregnant dams (Maternal Immune Activation) to mimic ASD.Stool samples were collected from 4 mth old male controls & ASD (6 mice each).The conc. of 75 polar metabolites were quantified by hydrophilic interaction liquid chromatography&scheduled multiple reaction monitoring on Mass Spectroscopy. Metabolomics is a research field with methods for analysis of low molecular weight compounds in biological systems. Data was analyzed using univariate/multivariate statistical tools implemented by MetaboAnalyst 2.0.

Results
Strong metabolic group differences between ASD &control mice were found:
a) The danger-associated metabolites were increased in autism microbiomes such as nucleotides & deoxynucleosides (GTP,Deoxyadenosine, Inosine, Hypoxanthine, and cAMP), sulfur-containing metabolites (Taurine) & tryptophan, nicotinamide & serotonin precursors.
b)The health-associated metabolites were decreased in the autism microbiome such as vitamin cofactors (Thiamine, Nicotinamide), nucleotide & Krebs cycle precursors (L-Aspartate).

Conclusions/Discussion
An increase in deoxynucleotides & other nucleotides in ASD mice also supports the purinergic theory of autism which is developed by my mentor Dr Naviaux, which teaches that autism is the outcome of ecogenetic factors that lead to persistent increases in neuroinflammation, gut & metabolic abnormalities.

Summary Statement
The study points toward a relationship between gut bacterial metabolic products and ASD mice and opens new avenues of research for advancing knowledge on the consequences of dysbiosis with the potential for identifying novel microbial related drug targets. The stool metabolic profile can also be utilized as a

Help Received
Lab equipment (bacterial cultures, extraction, HILIC and mass spectrometer) were all property of Dr Naviaux's laboratory at UCSD. Dr Kefeng Li taught me how to use HILIC and mass spectrometry. I have taken animal research workshop at UCSD.