

Combined Maternal and Offspring Allergic Asthma: A Model of the Double Hit Hypothesis

Student Name: Maddy Berkowitz-Cerasano

Project Advisor: Jared Schwartzer, Ph.D.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that is characterized by social and communication impairments and restricted repetitive behaviors (American Psychiatric Association, 2013). While ASD is based exclusively on behavioral symptomology, many reports note immune dysregulation as a common underlying feature. These immune alterations are thought to begin early in fetal development and population-based studies suggest a link between ASD severity and maternal incidence of allergies and asthma. However, these associative studies are limited in drawing a direct causal link between maternal allergic asthma (MAA) and altered immune and behavioral function in the offspring.

This project examined the effects of MAA and subsequent offspring immune activation on ASD-like behaviors in mice. It was hypothesized that offspring of MAA dams who were later exposed to repeated asthma inductions throughout juvenile development would have more severe ASD-like behaviors. To test this, female C57BL/6J (C57) mice were sensitized to the egg protein ovalbumin (OVA) or phosphate buffered saline (PBS) and later exposed to either aerosolized OVA (i.e. MAA) or PBS- vehicle (i.e. Control), respectively, throughout pregnancy to elicit allergic-asthma episodes. After the final allergic-asthma induction, mice were left undisturbed until birth. Following parturition, offspring of both MAA and Control dams were randomly assigned to undergo either subsequent OVA sensitizations and inductions or PBS-vehicle sensitizations and inductions. The resulting four groups, (Control-PBS, Control-OVA, MAA-PBS, and MAA-OVA) were assessed for ASD-like behavioral deficits following acute asthma inductions using a series of well-validated behavioral tasks. Results indicate that allergic-asthma exposure, either during gestation or in the juvenile period, elicits species atypical behaviors in an anxiety-associated task. These data support the double-hit hypothesis which postulates that multiple environmental insults combine to influence brain and behavior development.