Autism Spectrum Disorder: Gene and environmental interaction
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Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder that afflicts 1 of every 59 children in the United States. The total economic burden of supporting ASD patients is $126 billion per year [1]. ASD is influenced by a combination of both genetic and environmental factors that often act in combination to confer risk of ASD. Therefore, investigating gene-environments interactions is important to understand the exact causes of ASD[2].

One representative genetic factor for ASD is *Fragile X mental retardation 1* (*Fmr1*), the most common single gene cause of ASD. *Fmr1* provides instructions to make FMRP, a protein that functions as a shuttle to transport mRNA from the nucleus to specific places in the cells where proteins are synthesized[3]. FMRP regulates the production of many genes involved in brain development. For example, previous studies have shown that loss of FMRP leads to a significant increase in the number of neural stem cells in developing brains of rodents and fruit flies[3]. Indeed one of the cellular changes that occurs in individuals with ASD is that they have differences in how much their neural stem cells divide.

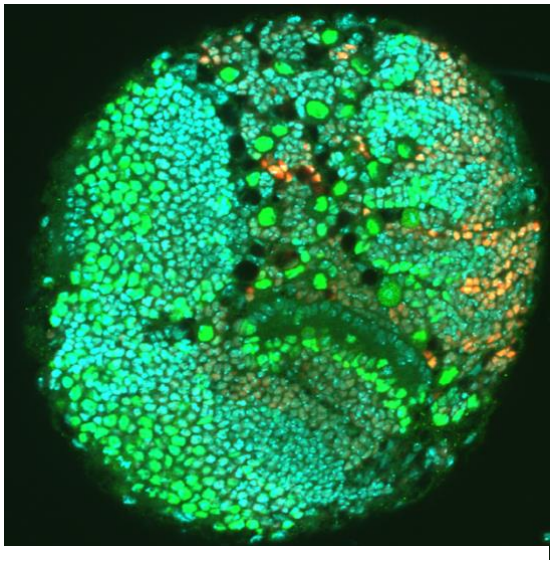

Figure 1. Neuroblasts in fruit fly larval brain (green and red).

Neural stem cells are a group of cells that can divide indefinitely to self-renew and give rise to neurons and glial cells, the main components in the mammalian central nervous system. In fruit flies, neural stem cells are called neuroblasts (Figure 1). In our lab, one of the phenomena we study is how genes and chemicals affect neuroblast proliferation in developing fruit fly brains. Many of the molecular networks that regulate neural stem cell proliferation in humans are the same in fruit flies. That means this research could help us identify gene-environment interactions that affect neural stem cell proliferation in humans with ASD.

One environmental factor that our lab is interested in examining to determine if it interacts with *Fmr1* to further impair neural stem cell proliferation is bisphenol-A (BPA). BPA is one of the most prevalent industrial chemicals worldwide and can be found in a vast array of products, ranging from plastic bags and containers, thermal papers like receipts, to the epoxy resins used to line the inside of metallic food cans and pipes. The chemical structure of BPA mimics that of estrogen, a hormone that plays an important role in the development of embryos, a process called embryogenesis[4]. Therefore, BPA is capable of disrupting the normal activity of estrogen in the body. Studies have also shown that BPA can pass through the placenta in pregnant women and to potentially affect the neurodevelopment of the fetus. In fact, prenatal and early childhood exposure to BPA has been linked to behavioral problems in children *(need reference here).* We have preliminary evidence that supports what other research groups have found—that BPA can indeed affect neurodevelopment. We are currently working to examine how BPA exposure affects fruit flies with mutations in *Fmr1*.

As mentioned above, gene-environment interactions have been shown to play an important role in ASD etiology. However, it is currently unknown whether the impacts of BPA exposure would exacerbate or suppress the overproliferation of neural stem cell due to loss of FMRP in fruit flies. Our lab has been working on this to gain more insights in to the exact causes of ASD, which is the first step to finding ways to potentially decrease the prevalence or severity of ASD.

References

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