Over the past twenty years, there has been a significant increase in the rate of Autism Spectrum Disorders (ASD) diagnoses. In addition, ASD have an extreme sex bias as four males are diagnosed for every female. Recently, mouse genetic knockout models have been used to study the molecular changes in the brain associated with ASD. Over the past summer in the Reyes Lab, I examined the impact of 16p11.2 hemideletion (del/+) in male and female mice. This particular hemideletion is of interest to the Reyes Lab firstly because it is the most common copy number variation associated with neurological disorders, with approximately fifteen percent of those with the 16p11.2 hemideletion being diagnosed with ASD. Secondly, it can be accurately studied in mouse knockout models, as the seventh mouse chromosome is analogous with respect to the 27 genes of interest located at the 16p11.2 locus. Of these 27 genes, the Reyes Lab has taken particular interest in the expression of the MAPK3 gene because it an important signaling kinase in the striatum that is activated by dopamine and adenosine signaling in the striatum. For my summer project, I examined the activation of MAPK3 (ERK1), and a related kinase, MAPK1 (ERK2), in the striatum. Striatal function is implicated in the core deficits of autism, including social motivation and repetitive behaviors, and 16p11 del/+ males show specific deficits in striatally-mediated operant learning, suggesting that molecular sex differences in this region may explain the behavioral phenotype. The ERK 1 and ERK 2 proteins, while related, have slightly different function. ERK1 activity has previously been shown to inhibit synaptic plasticity and learning in the striatum while ERK 2 has been shown to be beneficial to striatal function. As expected, both male and female hemideleted (del+) mice have the expected 50% decrease in expression of ERK1. However, through western blot analysis, we found increased activation of ERK1 in male del/+ after consuming sucrose, suggesting that this over-activation may contribute to male deficits in reward learning. In addition, we found that female del/+ have increased protein levels of ERK2. These data suggest that sex differences in the development or function of the ERK signaling pathway in the striatum are triggered by the loss of the genes in the 16p11.2 region. However, it is not clear how ERK1 is being over-activated, or ERK2 expression is being increased, and the Reyes lab is currently investigating whether other genes in the 16p11.2 region may play a role in signaling and protein synthesis pathways.