

Examining the role of Hoxb8 microglia in brain function Michael Adkins (Naveen Nagarajan) Department of Human Genetics

Abstract:

Hoxb8 mutant mice display compulsive grooming and hair removal behavior, similar to humans with obsessive-compulsive disorder (OCD) spectrum disorder trichotillomania. Previous research has shown that approximately 40% of microglia cells express this Hoxb8 gene. In order to learn about the function of this unique Hoxb8-microglia population and its links to OCD trichotillomania, we investigated the role of Hoxb8 function in early brain development. We used a well-established model of whisker-to-barrel pathway that is amenable to experience dependent modifications. Using sensory deprivation methodology we manipulated the amount of synaptic information in contra versus ipsilateral brain hemispheres. Trimming a mouse's whiskers alters barrel formation within the barrel field. Without the development of barrels we hypothesized that Hoxb8-microglia will not receive the signal that is needed to invade the barrel field essential for brain function. If Hoxb8-microglia show altered migration to the barrel field under trimmed conditions, then it will evidential that altered synaptic information affects Hoxb8 microglia proliferation. Support for Hoxb8-microglia neuronal maintenance is paramount to understanding the role of Hoxb8 microglia in early brain development and its involvement in mediating and modulating OCD like behaviors. Previously Hoxb8 mutant mice have been shown to exhibit corticostriatal circuit defects, but more evidence is needed to prove that defective Hoxb8 microglia neuronal maintenance is the causal factor for the observed behavioral defects. Therefore, this research seeks to understand the function of Hoxb8 microglia by studying their proliferation properties in response to whisker trimming. Currently we are acquiring data and establishing the methods essential to conduct this research. Although we have preliminary data that support our hypothesis, the sample size, the number of subjects needed for the experiments still need to be increased before we achieve conclusive answers to our hypothesis. Thus, the results will be made available once the experiments reaches higher sample size and solid conclusions.