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Microbial dysbiosis and probiotic treatment in a genetic model of autism spectrum disorders

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Gut microbiome may influence brain development and behavior, mainly through the modulation of physiological metabolism and the immune system. Recent studies have determined that the microbiome has direct effects on behavior, and may be dysregulated in neurodevelopmental conditions. Considering that neurodevelopmental conditions such as autism have a strong genetic etiology, it is necessary to understand if genes associated with neurodevelopmental disorders, such as *Shank3*, can influence the gut microbiome, and if probiotics can be a therapeutic tool. Using 16S high-throughput sequencing, we have determined the gut microbiome community of the *Shank3* KO mouse model, and its relative controls. In this study, we have identified dysregulation of several genera and species of bacteria in both the gut and colon of *Shank3* KO mice, in addition to a sex-dependent dysregulation of the immune system. *L. reuteri*, a species with decreased relative abundance in the *Shank3*KO mice, positively correlated with the expression of GABA receptor subunits in the brain. Treatment of *Shank3* KO mice with *L. reuteri* induced an attenuation of unsocial behavior and a decrease in repetitive behaviors, in males and just decrease in repetitive behaviors in females, without affecting anxiety. *L. reuteri* treatment also induced an increase in GABA receptor expression in multiple brain regions, and affected serum immune system markers. This study has confirmed that genetic differences associated with autism can induce changes in the microbiota profile. In addition, this study identifies bacterial species that are sensitive to an autism-related mutation, and further suggests a therapeutic potential for probiotic treatment.

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