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ORAL PRESENTATION

Ursolic acid improves social behavior and regulates Th1, Th17, and T regulatory cell-related transcription factor signaling in the BTBR T+ Itpr3tf/J mouse model of autism

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Autism spectrum disorder (ASD) is a complex neurodevelopmental syndrome characterized by unusual social interaction, limited communication, and repetitive patterns of behavior or interests. The BTBR T+ Itpr3tf/J (BTBR) inbred mice are often used as a model for ASD since they display several genetic features linked with autism. Ursolic acid, a natural compound found in various plants, has shown potential as a therapy for multiple inflammatory conditions and related experimental models, including Parkinson's disease, arthritis, diabetes, and myasthenia gravis. The current study is to investigate the probable effects of ursolic acid on self-grooming, marble burying, open field, and three-chambered sociability tests, and evaluate the overall social behaviors in BTBR mice. In addition, we will study the impact of Ursolic acid on the expression of Th1, Th17, and Treg to variety of inflammatory modulators in CD4+ T cells in the spleen of BTBR and C57BL/6 mice using flow cytometry. We also want to investigate the effect of Ursolic acid on mRNA expression levels of some genetic bases in the brain by running the qRT-PCR. We expect that treatment with Ursolic acid will improve behavioral issues in BTBR mice.

Background: Autism spectrum disorder (ASD) is a complex neurodevelopmental syndrome characterized by unusual social interaction, limited communication, and repetitive patterns of behavior or interests. The BTBR T+ Itpr3tf/J (BTBR) inbred mice are often used as a model for ASD since they display several genetic features linked with autism. Ursolic acid, a natural compound found in various plants, has shown potential as a therapy for multiple inflammatory conditions and related experimental models, including Parkinson's disease, Arthritis, Diabetes, and Myasthenia gravis.

Methods: Self-grooming, marble burying, open field, and three-chambered sociability tests are conducted to evaluate overall social behaviors in BTBR mice. The expressions of Th1, Th17, and Treg on variety of inflammatory modulators was tested in CD4+ T cells in the spleen of BTBR and C57BL/6 mice using flow cytometry technique. We investigated the effect of Ursolic acid on mRNA expression levels on some genetic bases in brain by running qRT-PCR.

Results: We found that treatment with Ursolic acid reduced repeated behaviors and enhanced social interaction in BTBR mice. Also, it inhibited Th1-related cytokines (IFN- γ and TNF- α) by decreasing their expression in CD4+ T cells and brain tissue, and it inhibited the transcription factor signaling associated with Th1 by reducing STAT1-, STAT4-, and T-bet-expressing CD4+ T cells. In addition, Th17 expression was significantly suppressed by reducing IL-17A-, STAT3-, and ROR γ t-expressing CD4+ T cells in the spleen and brain cells. Beside Ursolic acid enhanced Treg cells by increasing IL-10, TGF- β 1, and Foxp3 in CD4+ T cells.

Conclusion: Our results suggested that the protective properties of Ursolic acid regulate Th1/Th17/Treg signaling pathways. This study indicated that Ursolic acid could treat and prevent autism-like behaviors and aberrant molecular changes. Ursolic acid could be a viable therapeutic target and effective anti-inflammatory treatment for ASD and other neuroimmunological diseases.

Biography

Thamer H. Albekairi has completed his PhD at the age of 33 years from Texas Tech University Health Sciences Center. He is an assistant professor at King Saud University. He has published more than 40 papers.