Behavioral and Metabolic Characterization of a Mouse Model of Autism Spectrum Disorder and a Possible Therapeutic Effect of Palmitoylethanolamide

1)Cristiano C. 2)Coretti L. 3)Lama A. 4)Russo R. 5)Mattace raso G. 6)Lembo F. 7)Chiariotti L. 8)Meli R. 9)Calignano A.

Dept of Pharmacy, University of Federico II

Alterations of microbiota-gut-brain axis have been invoked in the pathogenesis of autism spectrum disorders (Parracho HM et al., 2005). Mouse models could represent an excellent tool to understand how gut dysbiosis and related alterations may contribute to autistic phenotype (Crawley JN, 2012). One of the earliest and most studied animal model showing autistic-like phenotype is BTBR T + tf/J (BTBR) inbred mouse strain (McFarlane HG et al., 2008).

Moreover, the role of PPAR-alpha receptor in the central nervous system and the similar behavioral phenotype between BTBR and PPAR-alpha null mice recently reported (D'Agostino et al., 2015) suggest a possible role of this receptor in ASD worthy of further investigation.

In this study, we firstly characterized gut microbiota profile, behavioral phenotype, intestinal integrity and immunological features of BTBR compared to C57 control mice. Then we started preliminary experiments to evaluate possible positive effect of the endogenous PPAR-alpha agonist, Palmitoylethanolamide, on BTBR mice.

Behavioral results confirmed social deficit and repetitive behavior in BTBR compared to control mice. We identified Bacteroides, Parabacteroides, Sutterella, Dehalobacterium and Oscillospira genera as key drivers of gut microbiota profiles associated with selected pathological traits in BTBR mice. We also found that BTBR mice present an increased gut permeability and altered cytokines pattern in colon tissue compared to control mice. In addition, preliminary behavioral data showed a possible therapeutic application of Palmitoylethanolamide to improve repetitive behavior in BTBR mice.

Taken together, and our preliminary findings indicate that future investigation could be useful to find treatments that can improve pathological traits in ASD and to understand the possible role of this endogenous compound and its mechanism of action on ASD symptoms.

Crawley JN (2012). Dialogues Clin Neurosci. 14(3):293-305.

D'Agostino G (2015). Dialogues Clin Neurosci. 14(3):293-305.

McFarlane HG (2008). Genes Brain Behav. 7(2):152-63.

Parracho HM (2005). J Med Microbiol. 54(Pt 10):987-91.