Transcriptional activity of different endogenous retrovirus families in a mouse model of autism

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Human Endogenous Retroviruses (HERVs) have been implicated in many neurological and neuropsychiatric disorders. In a previous study, we demonstrated that specific HERV families show a distinctive expression profile in peripheral blood mononuclear cells (PBMCs) from Autistic Spectrum Disorders (ASD) patients compared to healthy controls. In particular, in autistic patients the transcriptional activity of HERV-H correlates negatively with age and positively with the severity of the clinical signs of the disease. These findings suggest that HERVs could play a role in the etiopathogenesis of ASD. In order to deeply understand the potential role of retroelements in the ASD, a mouse model of autism was selected.

CD-1 outbred mice, prenatally exposed to valproic acid (VPA), an inhibitor of the histone deacetylases, were used. Indeed, VPA an antiepileptic drug, when administered during pregnancy represents an important ASD risk factor for humans, whereas in rodents triggers some behavioural impairment resembling those found in ASD.

In this mouse model, we found a different transcriptional profile of several retroelements (ETnI, ETnIIα, ETnIIβ, ETnIIγ, MusD and IAP) both in embryos and in samples (blood and brain) from offspring of VPA-treated and untreated mice, supporting our hypothesis that ERV deregulation could be involved in the ASD-like behavioural phenotype. No differences were detected in the transcriptional activity of retroelements in treated and untreated mothers. The results confirm the susceptibility of the fetus to treatment with VPA, as predicted in humans, and that the VPA effects take place during fetus development. The data obtained are consistent with those observed in our previous work on humans, demonstrating that the animal model chosen is eligible for studying the possible involvement of retroelements in the onset and progression of ASD. Furthermore, our data support the hypothesis of early epigenetic changes contributing to the mechanism of VPA-induced neurobehavioral alterations and candidate ERV as effectors downstream of the VPA-induced

epigenetic alteration. Modification in inflammation pattern in offspring of VPA-treated and untreated mice will be discussed.