The role of JAK-STAT signalling in the developing brain of Ts1Cje mouse model for Down syndrome

ABSTRACT

Introduction: The JAK-STAT signalling pathway is essential for proper regulation of the gliogenesis process during brain development. Both Down syndrome (DS) individuals and DS mouse model showed reduced number of neuron but increase number of astrocyte in the brain; suggesting that dysregulation of JAK-STAT signalling pathway may have occurred and led to neurogenic-to-gliogenic shift in the DS brain. Such a shift in the DS brain may contribute to the intellectual disability seen in the DS individual and learning and memory impairment in the mouse model. Therefore, understanding the role JAK-STAT signalling in the DS brain at early stage may implicate the underlying mechanism(s) causing the shift and provide novel therapeutics targets for cognition therapy among DS individuals.

Method: In this study, the whole brain of Ts1Cje and disomic mice was collected at embryonic day (E) 10.5, E14 and postnatal day (P) 1.5. Here, we focus on Jak1, Jak2, Stat1, Stat3 and Stat6, which have been shown to express highly or stably during early brain development.

Results: Both RT-qPCR and western blot analysis revealed the expression of Jak1 as significantly reduced in Ts1Cje at E14. In addition, phosphorylated Jak2 and Stat6 expression levels were decreased in Ts1Cje at E14 as compared to disomic mice. Our findings suggest that JAK1 is important for astrocytic differentiation while JAK2 is essential for neural stem cells proliferation and STAT6 is crucial in mediating immune signalling. Thus, further investigation on the function of Jak1, Jak2 and Stat6 may provide insight into neurogenic-to-gliogenic shift occur in the DS brain.