Overexpression of interferon alpha or beta receptors in the brain of adult Ts1Cje mouse model of Down syndrome

ABSTRACT

Introduction: Down syndrome (DS) is a generic disorder with trisomy of human chromosome 21 (HSA21) and all DS patients exhibited intellectual disability. Ts1Cje mouse model of DS has partial triplication of mouse chromosome 16 (MMU16) which is homologous to HSA21. The JAK (Janus kinase) and STAT (signal transducer and activator of transcription) signalling pathway is involved in neurogenesis and gliogenesis regulation. Cytokines especially the interferons (IFN) family is the major activator of JAK-STAT signalling pathway. Furthermore, interferon receptor genes (Ifnar), Ifnar2 and Ifngr2 are located at the triplicated region in MMU16 and also in HSA21.

Method: Gene expression of Ifnar1, Ifnar2, Ifngr2 and associated genes in JAK-STAT signalling pathway (Jak1, Jak2, Stat1, Stat3 and Stat6) in the cerebral cortex and cerebellum between Ts1Cje and wild type control at four time-points; post natal day (P)1, P15, P30 and P84 was investigated by using qRT-PCR techniques. Western blotting was used to confirm the overexpression of Ifnar1, Ifnar2 and Stat1 in the cerebral cortex and cerebellum of Ts1Cje aged P84.

Results: Ifnar1, Ifnar2, Ifngr2 and Stat1 were significantly overexpression in the cerebral cortex and cerebellum of Ts1Cje at various time points as compared to control littermates. Protein expression analysis confirmed the overexpression of Ifnar1 and Stat1 in the cerebellum of Ts1Cje mouse at P84 as compared to wild type. The findings suggest that overexpression of interferon receptors will increase sensitivity towards interferon levels in Ts1Cje mouse brain. Consequently, the over-stimulated JAK-STAT signalling pathway may contribute to the defective neurogenesis the Down syndrome mouse brain.