

The Effect of 200mg/kg EGCG Oral Gavage Treatment on the Cerebellar-Dependent Behavior in a Down Syndrome Mouse Model

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Trisomy 21 (Ts21) causes deficits in motor and cognitive ability that are hallmark phenotypes in Down syndrome (DS). The Ts65Dn mouse model of DS has about 50% of the orthologous genes that are triplicated from human chromosome 21, including the *Dual specificity tyrosine-phosphorylation-regulated kinase 1A (Dyrk1A)* gene. Three copies of *Dyrk1A* have been implicated in the motor and cognitive deficits and altered cerebellar structure and function may contribute these impairments in Ts65Dn mice. Epigallocatechin 3-gallate (EGCG) is a catechin found in green tea and an inhibitor of Dyrk1A activity. We hypothesize that a 200mg/kg EGCG treatment given by oral gavage will inhibit Dyrk1A activity in the cerebellum of Ts65Dn mice and rescue deficits in motor coordination while performing the balance beam task. Evidence of improvement in this task would be observed as a reduction of paw slips as the animal traverses across beams of varying widths. In previous studies, EGCG treatment was placed in the animal's water to be consumed but EGCG rapidly degrades in solution and it is difficult to control treatment doses via treatment in drinking water, due to each animal's consumption behavior. This study utilized a daily oral gavage treatment of EGCG to control the dose and limits loss due to degradation. Results to date indicate that the Ts65Dn mice show deficits on the balance beam task relative to the euploid mice, particularly at the narrowest beam width used. The EGCG treatment does not appear to improve the performance of the Ts65Dn mice, though the lack of observed effects of EGCG may be due to the relatively low numbers of Ts65Dn-EGCG treated mice that have completed testing so far. One notable trend is that we will continue to test additional mice to gain sufficient power to determine conclusively whether EGCG improves motor coordination performance in Ts65Dn mice.