

Effects of Increased Dosage EGCG Treatment on Cognitive Deficits in the Ts65Dn Down Syndrome Mouse Model

Hardeep Dhillon¹, Irushi Abeysekera¹, Megan Stringer², Charles Goodlett², Randall Roper¹

¹Department of Biology, IUPUI School of Science; ²Department of Psychology, IUPUI School of Science

Abstract

Down syndrome (DS), caused by trisomy of human chromosome 21 (Hsa21), is the leading genetic cause of cognitive impairment and results in a constellation of phenotypes. Although symptomatic and therapeutic treatments exist for some DS phenotypes, treatments generally do not address the genetic etiology. The Ts65Dn mouse model, which contains a triplication of approximately half the gene orthologs of Hsa21, exhibits hippocampal learning and memory deficits as well as cerebellar motor and spatial deficits similar to those present in individuals with DS. DYRK1A, one of the genes overexpressed in DS, has been identified as a potential cause of cognitive impairment; therefore normalization of DYRK1A activity may be a valid form of treatment. We have shown that Epigallocatechin-3-gallate (EGCG), a major polyphenol of green tea, can rescue skeletal deficits found in the Ts65Dn mouse model at a low dosage. When this same low dosage was used to rescue behavioral deficits, however, it was ineffective. We hypothesize that high dose EGCG treatment lasting throughout the behavioral testing period will rescue the cognitive deficits observed in Ts65Dn mice. Trisomic mice and euploid littermates were given EGCG or water (control) for 7 weeks while being tested sequentially on novel object recognition (NOR) and Morris water maze (MWM). Our current data set shows that Ts65Dn mice exhibit deficits in learning and memory; further data will be collected in order to identify the effect of EGCG. Data showing pure EGCG as being ineffective will suggest the importance adding a supplemental compound, while data showing pure EGCG as an effective form of treatment will strongly support use of EGCG in translational studies in individuals with Down syndrome.

Mentors: Randall Roper, Department of Biology, IUPUI School of Science; Charles Goodlett, Department of Psychology, IUPUI School of Science