

## **Effects of Epigallocatechin-3-gallate Treatment on Cognitive Deficits in a Down Syndrome Mouse Model**

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Down syndrome (DS) is caused by three copies of human chromosome 21 (Hsa21) and results in a constellation of phenotypes that include intellectual disability (ID) and skeletal abnormalities. Ts65Dn mice, the most extensively studied model of DS, have three copies of approximately half the genes on Hsa21 and display many DS related phenotypes including skeletal and ID deficits. *DYRK1A* is found in three copies both in humans with DS and in Ts65Dn mice; *DYRK1A* has increased expression in humans with DS and is involved in a number of critical pathways including CNS development and osteoclastogenesis. Epigallocatechin-3-gallate (EGCG), the main polyphenolic compound found in green tea, inhibits Dyrk1a activity, and we have shown previously that a three-week treatment with EGCG during adolescence normalizes some skeletal abnormalities in Ts65Dn mice. The current study tested the hypothesis that a similar 3-week treatment with EGCG will also rescue cognitive deficits observed in Ts65Dn mice. Trisomic mice and euploid littermates were given EGCG or water (control) for three weeks during adolescence. Following termination of the treatment, the mice were tested sequentially (over 5 weeks) on locomotor activity (two daily 30-min sessions in an activity chamber), novel object recognition (NOR) memory, acquisition of delayed non-matching to place (DNMP) spatial working memory in a t-maze, or spatial learning and memory in the Morris water maze (MWM). Results to date indicate that Ts65Dn mice exhibit deficits in the learning and memory tasks compared to controls, but the 3-week EGCG treatment did not significantly improve their performance. We hypothesize that for EGCG to be effective for improving cognitive deficits of the Ts65Dn mice, it needs to be present in the brain during the behavioral testing period; our ongoing studies are testing this with continuous EGCG treatment throughout the behavioral testing process

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