

Extended Treatment with a High Dosage of EGCG to Rescue Appendicular Bone Abnormalities in a Down Syndrome Mouse Model

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Individuals with Down syndrome (DS) show significant abnormalities in cognitive abilities, muscle tone, and bone homeostasis. DS is caused by a triplication of the 21<sup>st</sup> human chromosome (Hsa21). Previous research conducted by our lab using mouse models indicates that three copies of *Dyrk1a* causes the appendicular skeletal deficits associated with DS. Ts65Dn mouse model carries 50% of the genes homologous to Hsa21, and exhibit excellent phenotypic model for the skeletal deficits seen in individuals with DS, such as low bone mineral density, altered bone structure, and decreased cortical bone. Epigallocatechin-3-gallate (EGCG) is a green tea polyphenol that inhibits Dyrk1a activity. In a previous study, we showed that a three-week, low dose (10mg/kg/day) treatment of EGCG rescued bone mineral density, and trabecular bone to that of euploid levels, but not cortical bone. We hypothesize that increasing the concentration and duration of the treatment will be sufficient enough to more fully restore bone abnormalities by rescuing femoral bone mineral density, bone volume, and improving overall bone strength. This project explores the effects of using a prolonged seven-week, high dosage (100mg/kg/day) treatment on specific bone phenotypes. Dual Energy X-ray absorptiometry (DXA), MicroCT, and mechanical testing will be used as our means of analysis of the treated and untreated bones.

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