EGCG from different sources: differential stability and effects on treating bone phenotypes related to Down syndrome

Jared R. Thomas¹, Irushi S. Abeysekera², Joshua D. Blazek², and Randall J. Roper²

¹ Ivy Tech Community College- Central Indiana, Bridges to the Baccalaureate Program

²Department of Biology, Indiana University-Purdue University Indianapolis

Down Syndrome (DS) is a genetic disorder caused by trisomy of human chromosome 21 (Hsa21). DS phenotypes include cognitive impairment, craniofacial abnormalities, low muscle tone, and skeletal deficiencies. The Ts65Dn mouse model exhibits similar phenotypes as found in humans with DS, including deficits in skeletal bone. Over-expression of DYRK1A, a serine-threonine kinase encoded on Hsa21, has been linked to deficiencies in DS bone homeostasis. Epigallocatechin-3-gallate (EGCG), an aromatic polyphenol found in green tea (GT), is a known inhibitor of Dyrk1a activity. Normalization of Dyrk1a activity by EGCG may have the potential to regulate bone homeostasis, by increasing bone mineral density (BMD) and bone strength. We hypothesized that EGCG obtained from different vendors would differ in stability as well as success in ameliorating skeletal deficiencies. EGCG from different sources was subjected to degradation analysis because of its low bioavailability due to strong antioxidative characteristics. We also hypothesized that phosphoric acid would stabilize EGCG and prevent breakdown in an aqueous solution. We performed High Performance Liquid Chromatography-Mass Spectrometry (HPLC-MS) on EGCG from different sources to determine the amount of EGCG degradation in solution. Our analyses showed differential stability in EGCG from different sources or with phosphoric acid. We chose EGCG from three sources to test the hypothesis that these compounds would have differing effects treating bone phenotypes associated with DS. Three-week-old Ts65Dn and control male mice were treated with EGCG for three weeks. At six weeks of age, mice were sacrificed and femurs were extracted. BMD, bone strength, as well as architecture of the femur were assessed. Our results indicate that EGCG from different sources has diverse effects on the correction of bone phenotypes associated with DS. Our work is important to understand how EGCG from different sources may affect DS phenotypes as the EGCG is translated to human use.

Mentor: Randall J. Roper, Department of Biology, Indiana University-Purdue University Indianapolis