Three-Dimensional Analyses of Craniofacial and Nasopharyngeal Phenotypes in Ts65Dn Down Syndrome Mice Treated with EGCG, a Dyrk1a Inhibitor.

J. Starbuck[1], E. Harrington[2], K. Kula[1], A. Ghoneima[1] and R. Roper[2]

[1]Department of Orthodontics and Facial Genetics, IU School of Dentistry; [2]Department of Biology, IUPUI

Down syndrome (DS) is caused by having three copies of chromosome 21 (i.e. Trisomy 21). DS is associated with many detrimental phenotypes including intellectual disabilities, heart defects, and abnormal craniofacial development. Additional complications common in individuals with DS arise from this altered craniofacial development such as obstructive sleep apnea, which is associated with restricted oronasal airways and an underdeveloped mandible. Ts65Dn mice are trisomic for about half of the orthologs on human chromosome 21 and display many phenotypes associated with DS including craniofacial abnormalities. Dyrk1a is found in three copies in Ts65Dn mice and individuals with DS. Dyrk1a is thought to play a key role in craniofacial morphogenesis. Epigallocatechin gallate (EGCG) is a green tea polyphenol and inhibitor of Dyrk1a activity. We hypothesize that decreased Dyrk1a activity in Ts65Dn mice will ameliorate craniofacial dysmorphology. To test our hypothesis we compared Ts65Dn mice, Ts65Dn mice treated with EGCG, and Ts65Dn mice without an extra copy of Dyrk1a. Six week old mice were sacrificed and their heads imaged using micro-computed tomography. From the images, we measured nasopharyangeal airway volumes and anatomical landmarks (n = 54) to assess local differences in craniofacial and mandibular morphology between samples. Our preliminary results indicate that EGCG treatment and reduced Dyrk1a copy number increases mean nasopharayngeal airway volume in Ts65Dn mice. Craniofacial morphometric differences were found among all samples. Patterns of variation suggest that both EGCG treatment and reduced Dyrk1a copy number affects craniofacial morphology.

Advisors: Katherine Kula, Department of Orthodontics and Oral Facial Genetics, IU School of Dentistry; Randall Roper, Department of Biology, IUPUI