Characterizing Craniofacial Defects of Cholesterol Synthesis Genes, *Sc5d* and *Dhcr7*

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Objective: Inhibition of *DHCR7* and *SC5D* are associated with developmental disorders, Smith-Lemli-Opitz syndrome and lathosterolosis, respectively, which exhibit craniofacial defects. *DHCR7* and *SC5D* code for significant enzymes in the endogenous cholesterol synthesis pathway. However, it remains unclear how craniofacial bones are affected. In this study, we identified affected craniofacial bones in mice models with *Dhcr7* and *Sc5d* disruptions and characterized defects using high-resolution computed micro-tomography (μCT). We hypothesized that similarities in *Dhcr7* and *Sc5d* phenotypes would be due to cholesterol insufficiency, while differences in phenotypes are attributed to accumulation of intermediate compounds.

Methods: The mice were scanned at 15-μm resolution using a SCANCO vivaCT-40 system. 3D reconstruction μCT imaging analyses was performed using the Dragonfly software [Version 2021.1 for Windows; Object Research Systems (ORS) Inc., Montreal, Canada]. T-test will be performed to determine the significance in differences between the phenotypes.

Results & Conclusion: All measurements were performed using established landmarks in order to identify areas affected in *Dhcr7* and *Sc5d* knockout mice. *Sc5d* knockout mice exhibited the most extreme deviations in phenotypes when compared to wild-type mice than exhibited by *Dhcr7* knockouts. The mandible had the most apparent defect, with *Sc5d* knockouts expressing tooth agenesis. Knockout mice expressed craniofacial bones that were reduced in size and missing anatomical landmarks compared to wild-type craniofacial bones. Further data analysis is still required to determine the statistical significance between the phenotypic differences.

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