Dominique Joseph

Waynesville, MO

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Senior

Biological Sciences; German

Faculty Mentor: Dr. Charlotte Phillips, Biochemistry

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Characterizing Bone Microarchitecture and Histology in the G610C Osteogenesis Imperfecta Murine Model

Dominique Joseph, Catherine Omosule, Victoria Gremminger, Youngjae Jeong, Ferris Pfeiffer, and Charlotte Phillips

Osteogenesis imperfecta (OI), known as brittle bone disease, is an incurable connective tissue disorder varying in severity. OI is primarily due to mutations in type I collagen genes and is clinically manifested in type I collagen-containing tissues, primarily bone. Anti-resorptive drugs, bisphosphonates, are currently the standard care for OI. Although bisphosphonates have been shown to increase bone mass, they inhibit osteoclast activity particularly in children. Thus, suitable therapeutic options for managing OI are still needed.

Previous studies in the moderately severe osteogenesis imperfecta murine model (*oim*), demonstrated sex differences in bone microarchitecture, biomechanical properties, and biochemical composition. In this study we sought to further characterize and compare growth rates, body tissue composition, and bone histological, microarchitectural and biomechanical properties of male and female heterozygous *G610C* OI mice. In this study, male and female Wt and *+/G610C* mice were weighed twice weekly. At 16 weeks (the age of peak bone mass) mice were sacrificed and their hindlimb muscles and bones harvested for analyses.

We found that although *+/G610C* male and female mice have similar muscle and body weights as Wt counterparts, femoral bone microarchitecture is compromised as evidenced by decreased bone mineral density, volume, trabecular number, and increased trabecular spacing. Bone biomechanical strength is also decreased in both *+/G610C* sexes. While only female *+/G610C* mice displayed decreases in femoral maximal load, yield load, and stiffness relative to their Wt counterparts, both *+/G610C* sexes present with greater than 34% reductions in femoral ductility and work to fracture. Overall data suggests that though there are genotypic bone microarchitecture differences, sex differences may be less prevalent in the *G610C* mouse model than in the *oim* model. Histological analyses of osteoblasts and osteoclasts number and function are currently underway to define their cellular contribution to compromised G610C bone.