Interrogating the roles of KMT2C and KMT2D in cartilage and skeletal development

Dimitrios V. Bikas, Gabrielle A. Quickstad, Karl B. Shpargel

Genetics and Molecular Biology Program, Department of Genetics, University of North Carolina at Chapel Hill

Mutations in KMT2D, a histone 3 lysine 4 (H3K4) methyltransferase, have been implicated in Kabuki syndrome, a craniofacial development disorder. Patients often present with facial dysmorphology, in addition to skeletal abnormalities concerning spinal curvature, shortened peripheral bone length, and joint problems. Although the craniofacial irregularities have been explored in depth, the roles of KMT2D and its functional homolog KMT2C have yet to be thoroughly studied in the context of broader cartilage and skeletal morphology. Previously, our lab has observed that a chondrocyte-specific knockout of KMT2C and KMT2D leads to alterations in chondrocyte differentiation in shortened long bones when compared to wildtype samples. These observations implicate KMT2C/D more broadly in skeletal development. *Kmt2c&d* double knockout (DKO) mice display gross morphological changes in tibial growth plate thickening, lack of columnar chondrocyte organization, and overproliferation of articular cartilage as compared to wildtype samples. Altered expression of chondrocyte markers indicates altered chondrocyte differentiation in DKO long bone growth plates. This investigation will develop a stronger understanding of the cellular mechanisms associated with KMT2C and KMT2D, in the context of cartilage and skeletal development.