EMBRYONIC BONE DEVELOPMENT AND NFAT EXPRESSION IN THE TS65DN MOUSE MODEL FOR DOWN SYNDROME

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Down syndrome (DS) is a common genetic disorder that occurs in approximately 1 out of every 750 live births. DS phenotypes include cognitive deficits, altered craniofacial features, muscle hypotonia, heart defects, and abnormal bone structure. The Ts65Dn mouse model is the most common organismal model used to study DS phenotypes. This model exhibits a number of phenotypic traits comparable to those of humans with DS, including bone anomalies. Past studies have shown that Ts65Dn mice exhibit weaker trabecular bone due to less trabeculae. They have also been shown to have less bone mineral density and bone mineral content at 6 weeks of age when compared to their euploid counterparts, with the severity of these defects lessening by 16 weeks. No studies of bone development have yet decisively identified the origin of these defects. We hypothesized that abnormal endochondral ossification is responsible for the presence of these deficiencies in bone mineral content and bone mineral density. Aberrant expression of *Nfat* has been implicated as the molecular cause of many DS-related phenotypes, and activity of Nfat can be determined based upon its localization. Specifically, Nfat has been shown to control many aspects of bone development, which makes it of special interest to this research. To test our hypothesis of a bone deficit present during embryonic development of Ts65Dn embryos, we are comparing cartilaginous template characteristics, progression of the mineralization front, osteoclast activity, percent bone volume, and Nfat localization in euploid and trisomic mouse femurs at embryonic day 17.5. Our preliminary data show lower percent bone volumes in trisomic femurs, suggesting that endochondral ossification in Ts65Dn mice lags behind that of their euploid counterparts. These results indicate that DS bone phenotypes do indeed originate during embryonic development and create a foundation for future work on their treatment.

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