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Epiphyseal cartilage alterations in a mouse model of diastrophic dysplasia

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Diastrophic dysplasia (DTD) is a recessive disease characterized by synthesis and secretion of undersulfated proteoglycans (PGs) and consequent alterations in the architecture and mechanical properties of the extracellular matrix. We have generated a mouse model for this disease (dtd mouse), whose phenotype recapitulates essential aspects of DTD in man. Thus, this animal model is a powerful tool to study the role of PG sulfation in skeletal development.
In dtd mice long bones are shorter compared to wild-type. Since longitudinal bone growth depends on several well regulated events in the growth plate, we decided to analyze this tissue in mice at postnatal day 21, when the growth rate is maximal, combining histology and immunohistochemistry. In mutant animals, the cartilage matrix stains less intensely than normal with cationic dyes such as toluidine blue as a consequence of PG undersulfation. The architecture of the growth plate is preserved in dtd mice, but the relative extension of the different zones forming the growth plate is altered, probably as a consequence of both reduced chondrocyte proliferation and altered chondrocyte differentiation. In fact, apoptosis assays revealed a significant reduction in the number of terminally differentiated cells, and proliferation assays revealed a significantly reduced proliferation rate in the growth plate of mutant animals.
For the future, we plan to analyze the distribution of several signalling factors in the growth plate of wild-type and dtd mice by *in situ* hybridization, in order to better elucidate how PG undersulfation can affect chondrocyte proliferation and differentiation.

This work will be presented at the XXIst meeting of the Federation of the European Connective Tissue Society (FECTS), that will be held in Marseille, 9-13 July 2008.