DLX HOMEOPROTEINS IMPLICATION IN AMELOBLASTS ORGANIZATION AND FUNCTION.

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INTRODUCTION: Homeobox genes of the *Dlx* family participate in early tooth development through their implication in two major events: tooth initiation and morphogenesis (1). The expression of one member of the family, *Dlx2*, was also reported during amelogenesis, a late stage in tooth development (2). Indeed, using a *Dlx2/LacZ* transgenic mouse model, stage specific expression of *Dlx2* in ameloblasts was observed in mouse continuously growing incisors. A linear inverse relationship between enamel thickness and *Dlx2* expression was also established (2), raising the question of *Dlx* implication in enamel morphological control.

METHODS: In this study, we investigate whether DLX acts as a transcriptional regulator of amelogenin, the major component of enamel organic matrix, using *Dlx2/LacZ* transgenic mice, amelogenin immunohistochemistry, vitamin D receptor mutant mice and amelogenin promoter analysis techniques. We also investigate whether DLX are necessary to ameloblasts organization using *Dlx2* and *Dlx1/Dlx2* mutant mice.

RESULTS: We report, using *Dlx2/LacZ* transgenic mice, that *Dlx2* and amelogenin have complementary expression patterns during both molar and incisor amelogenesis. We also evidence that both amelogenin and *Dlx2* expressions are jointly perturbed in dental cells during rickets using vitamin D receptor KO mice. Sequence analysis of the amelogenin gene promoter revealed five potential response elements for DLX that were shown to be functional for DLX2 in *in vitro* experiments. Moreover, we show that *Dlx2* with *Dlx1* are essential to achieve normal molar ameloblast functional organization (Figure 1) using *Dlx2* and *Dlx1/Dlx2* mutant mice.

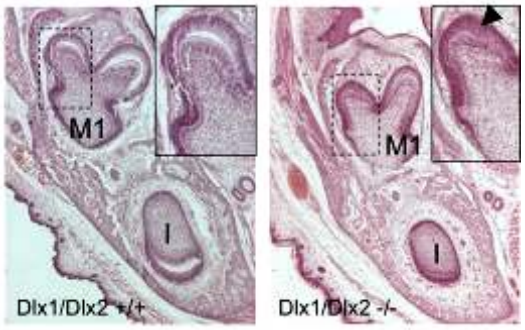

Fig. 1: Dlx1/Dlx2 null mutation impact on mouse molar ameloblasts organization. Ameloblasts of newborn first molar buccal part appear badly organized in double mutant (right) while normal in wild-type mice (left).

DISCUSSION & CONCLUSIONS: This study establishes supplementary functions of *Dlx* family members during tooth development. These functions are a participation in the functional organization of the dental epithelium that remain to be analyzed at molecular level, and the control of enamel morphogenesis via the regulation of amelogenin expression.

REFERENCES: [1]B. Thomas, AS. Tucker, M. Qiu M et al (1997) *Development* **124**:4811-18. [2]F. Lezot, B. Thomas, D. Hotton et al (2000) *J Bone Miner Res* **15**(3):430-41.

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