

AN EXPRESSION SURVEY OF GENES CRITICAL FOR TOOTH DEVELOPMENT IN HUMAN EMBRYONIC TOOTH GERM

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INTRODUCTION: The recent development of new molecular technology allows fast proliferation of studies on molecular mechanisms underlying tooth morphogenesis in mice. The tooth phenotype seen in mouse mutants is often found in humans carrying mutations in the counterpart gene. It indicates that human and mouse tooth development does not only share many similarities in morphological processes but may also utilize similar molecular mechanisms. Understanding the molecular mechanisms underlying the human odontogenesis is a prerequisite to the realization of human tooth regeneration in the future. Here we report the expression of several regulatory genes in the human embryonic tooth germ and a comparison of the expression patterns between the mouse and human.

METHODS: Human embryos of eighth to fourteenth week gestation were collected and fixed in 4% PFA at 4°C overnight and then processed for paraffin sectioning at 10 μm. To obtain human tooth germ at late differentiation stage, premolar tooth germs were dissected out from 14-week old human embryos and grafted under the kidney capsule of adult male nude mice. All the probes except *BMP4* that were used for examining human gene expression in this study were amplified from exon of each gene using human genomic DNA. Section in situ hybridization was performed as described previously [1Zhang et al., 1999].

RESULTS: In the developing human tooth germ, *BMP4* expression was detected in the dental papilla mesenchyme as well as the dental epithelium at the cap stage in both incisor and premolar. The expression in the inner enamel epithelium became significant in both incisor and premolar at the bell stage, while the expression in the dental papilla was maintained at a relatively lower level. *BMP4* expression was also detected in the odontoblasts and ameloblasts of the grafted teeth. *MSX1* expression was restrictedly detected in the dental papilla mesenchyme of tooth germ at the cap stages of both incisor and premolar. *MSX1* transcripts were also detected in the odontoblasts and ameloblasts of the tooth graft after long term culture. *PITX2* expression was detected only in the dental epithelium of tooth germs at the late bud

stage, the cap stage and the bell stage. The expression of *PITX2* was found in ameloblasts of the graft. *FGF8* transcripts were strongly detected in the dental epithelium but also slightly in the dental mesenchyme. In addition, *FGF8* expression in the dental epithelium appears to be restricted to the central portion where the enamel knot will form. *PAX9* was found to be expressed in both dental mesenchyme and dental epithelium of incisor and premolar at the cap stage. *SHOX2* expression was indeed mainly localized in the dental epithelium.

DISCUSSION & CONCLUSIONS: Our results show that these genes exhibit basically similar expression patterns in the human tooth germ as compared to that in the mouse. However, slightly different expression patterns were also observed for some of the genes. Our results indicate that the human and mouse teeth do not only share considerable homology in odontogenesis[2] but also utilize similar underlying molecular networks.

REFERENCES: ¹ Y.D. Zhang, X. Zhao, Y.P. Hu, St. Amand, et al (1999). *Msx1* is required for the induction of *Patched* by *Sonic hedgehog* in the mammalian tooth germ. *Dev. Dyn.* **215**, 45-53. ² Y.D. Zhang, Z. Chen., Y. Song, et al (2005). Making a tooth: growth factors, transcription factors, and stem cells. *Cell Res.* **15**, 301-316.

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