Sequential Expression of Notch1, HES5, Jagged2, and Math1 in Molar Tooth Germ of Mouse

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Introduction

Odontogenesis or tooth development is regulated by reciprocal and sequential epithelial-mesenchymal interactions and conserved signaling pathways common to many developmental processes. Previous studies have suggested that the Notch signaling pathway is involved in odontogenesis.

The Notch signaling pathway plays an important role in cell fate decisions through the process of lateral inhibition or inductive signaling. Second class basic helix-loop-helix (bHLH) transcriptional repressors, Hairy and Enhancer of Split (HES) 1, 5, 7 seem to act as Notch effectors by negative regulation of the downstream target genes. The proneural bHLH protein Math1 has been demonstrated to act as positive regulator of differentiation in developmental events. In addition, links between Notch and Math1 pathways were identified in various tissues.

In the present study, we evaluated the expression of Notch1, HES5, Jagged2 and Math1 during embryonic and postnatal stages of molar odontogenesis in wild type mice.

Results

At E13, expression of Notch1 in the tooth bud was restricted to the central cells and absent from the basal cells in contact with the dental mesenchyme (Fig. 1B). Hes5 weak expression was found in the tooth bud, in similar pattern as Notch1 (Fig. 1 C). Jagged2 and Math1 were not expressed either in the dental mesenchyme or dental epithelium during this stage.

At PN1, intense Notch1 expression was present in the stratum intermedium, but absent from the preameloblasts and odontoblasts (Fig. 2 B). Jagged2 and Math1 expression was observed in the odontoblasts at the cuspal areas (Fig.2 C and D).

At PN3, Notch1 positive signals could be detected in the ameloblasts at the tip of the cusps and in the odontoblast layer except for t he cuspal areas (Fig. 3 B). Jagged2 and Math1 showed positive signals in the cuspal ameloblasts and in the entire odontoblast layer (Fig. 3 C and D).

At PN5, Notch1 expression at the ameloblast and odontoblast cells became negative (Fig. 4 B). Jagged2 and Math1 were strongly expressed in the ameloblasts and odontoblasts (Fig. 4 B and C). HES5 appeared negatively expressed during all postnatal stages (Fig. 5 B) In contrast Math1 was the most strongly expressed gene, and its expression remained strong until PN14 (Fig. 5C).

Discussion

The Notch signaling pathway might regulate embryonic odontogenesis mainly through the lateral inhibition mechanism. Jagged2 and Math1 are involved in advanced stages of odontogenesis determining the differentiation of ameloblasts and odontoblasts. Math1 is importantly related to the Notch1 signaling cascade directing the process of odontogenesis toward cell differentiation. Finally, transient expression of Notch1 in differentiating ameloblasts and odontoblasts during postnatal stages suggests that Notch1 signaling may have a specific and brief function in cell differentiation through the inductive signaling process.

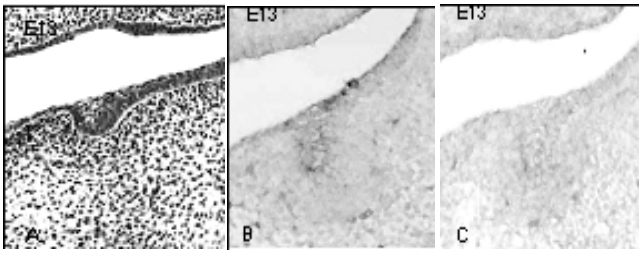

Fig.1

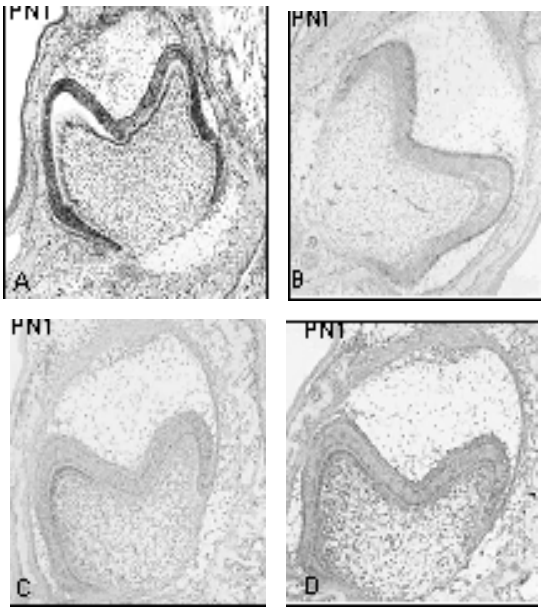

Fig.2

Fig.3

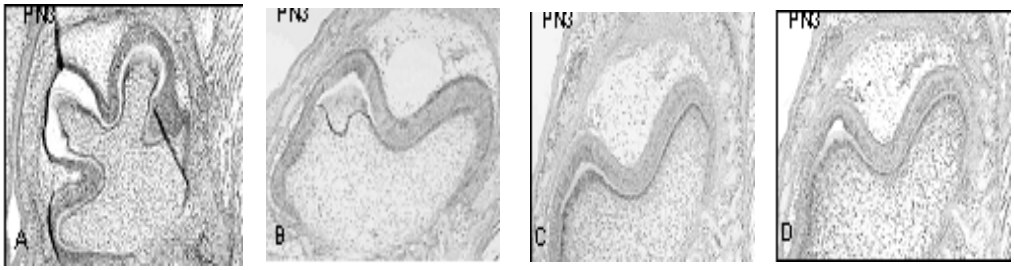

Fig.4

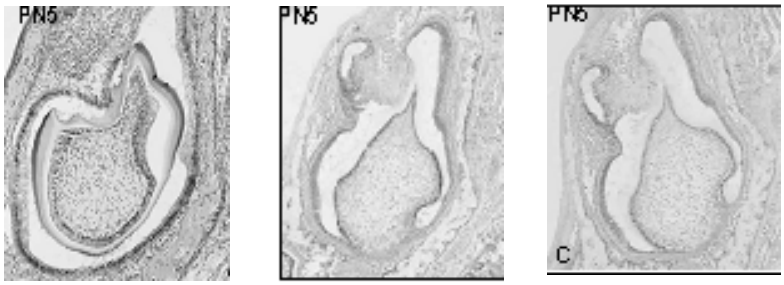

Fig.5