Gene expression pattern

Expression of Deltex1 during mouse embryogenesis: comparison with Notch1, 2 and 3 expression

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Abstract

The Notch signalling pathway defines a phylogenetically conserved cell–cell communication process that enables cell-fate specification in multicellular organisms. Deltex is a component of the Notch signalling network that physically interacts with the ankyrin repeats of Notch. Here, we report on the expression pattern of the Deltex1 gene during mouse embryonic development and, furthermore, we compare its expression with that of the Notch1, 2 and 3 genes. Complementary and combinatorial expression patterns between Deltex1 and the three Notch genes were observed throughout embryogenesis since Deltex1 expression was related either to cytodifferentiation (i.e. neuronal tissues) or to cell proliferation events (i.e. eye, vascular structures, hematopoiesis). © 2001 Elsevier Science Ireland Ltd. All rights reserved.

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Notch signalling in vertebrates controls the commitment of cells to differentiate and, furthermore, the choices between alternative differentiation pathways (Artavanis-Tsakonas et al., 1999). Notch signalling has been shown to be essential for normal development of many tissues and organs, such as the neural tube, eyes, and vascular tissues. Moreover, it has been shown that aberrant Notch signalling is linked with cancers and genetic diseases. Notch signalling is activated upon binding of the Notch receptors to their membrane-bound ligands Delta and Jagged (Artavanis-Tsakonas et al., 1999; Lendahl, 1998).

The cytoplasmic proteins Deltex are thought to be positive regulators of the Notch signalling. Three Deltex proteins have been reported recently in mammals (Matsuno et al., 1998, Kishi et al., 2001). It has been shown that Deltex binds to the ankyrin repeats of the Notch intracellular domain (Matsuno et al., 1995), but the exact in vivo function of Deltex is as yet largely unknown. In situ hybridization and Northern blot analysis on human and mouse embryonic tissues gave conflicting and inconclusive results (Matsuno et al., 1998; Kishi et al., 2001). Overlapping expression patterns have been observed between the three Deltex and the Notch1 genes in the nervous system of the mouse embryos (Kishi et al., 2001), suggesting a role for Deltex in regulation of neurogenesis. However, from the in situ hybridization results previously presented, a possible function of Deltex in neuronal cell proliferation or differentiation is not evident.

Here, we present a detailed investigation on Deltex1 expression during mouse embryogenesis using a new digoxigenin-labelled probe. Deltex1 expression was compared to Notch1, 2 and 3, Delta1 and Islet1 gene expression to clearly demonstrate the complementarity of these genes in specific proliferation and cytodifferentiation areas.

1. Results and discussion

1.1. Nervous system

At embryonic day 10.5 (E10.5), the Deltex1 gene was found to be expressed in many cells in the neuroepithelium (data not shown), which is in agreement with recently presented results (Kishi et al., 2001). Notch1, 2 and 3 were also expressed in scattered cells in the neuroepithelium, while Notch2 expression was restricted to cells in the basal plate (data not shown). The expression pattern of Deltex1 seems to be dynamic, since at E12.5, Deltex1 expression in the cortex was restricted to areas containing post-mitotic...
differentiating neurons while Notch receptors were expressed in the proliferative ventricular zone (Fig. 1). In the spinal cord, Deltex1 was strongly expressed in the mantle region, in post-mitotic neurons that have migrated from the proliferative ventricular zone (Fig. 1II). Some of the Deltex1-positive cells were also expressing Islet1, which indicates their differentiation into motoneurons. However, rare positive cells were observed in the ventricular zone that could represent newly generated post-mitotic neurons (red arrowheads in Fig. 1II.D). In contrast, Notch1, 2 and 3 were expressed in the ventricular zone, with Notch2 expression restricted to the ventral region. No expression of Deltex1 was observed in the peripheral ganglia (Fig. 1III.A).

At E14.5, as differentiation proceeded in the spinal cord, Deltex1 was strongly expressed throughout this tissue, while Notch1 expression was restricted to cells around the central canal (Fig. 3). Sympathetic ganglia were Deltex1-positive at this developmental stage, while dorsal root ganglia (DRGs) remained negative.

1.2. Olfactory epithelium

Deltex1 expression appeared at E12.5, in a few cells of the olfactory epithelium. Transcripts for all three Notch genes were detected in this tissue but in different cellular compartments (Fig. 2 and Lindsell et al., 1996). A population of strongly labelled cells was observed between the olfactory epithelium and the forebrain (Fig. 2A,B). This expression is correlated with the migration of luteinizing hormone-releasing hormone (LHRH) neurons from the olfactory placode to the forebrain (Yoshida et al., 1999).

At E14.5 and E16.5, many more olfactory epithelial cells...
expressed Deltex1 (Fig. 3 and data not shown), while Notch1 expression was observed in proliferating cells of the basal epithelium (Fig. 3).

1.3. Developing eye

In the developing eye, Deltex1 was expressed across all layers of the retina between E12.5 and E16.5, while, as previously described (Lindsell et al., 1996), Notch1 was prominently expressed in the proliferating zone of the retina (Fig. 3 and data not shown).

1.4. Thymus, cardiovascular system

In agreement with previously reported results (Felli et al., 1999; Kishi et al., 2001), we found that Deltex1 and Notch1 were both strongly expressed in the developing thymus (Fig. 3).

Deltex1 mRNA was detected in endothelial cells of the blood vessels (Fig. 4) and in the aorta (Fig. 4 I.C), while only Notch3 transcripts were observed in the forming blood vessels (Fig. 4 I.B). It is now well established that appropriate regulated Notch signalling is required during vascular development (Gridley, 2001). Deltex1 was also expressed in heart tissues (Fig. 4 I.C), whereas Notch1 mRNA was absent (Fig. 4 I.D).

1.5. Palatal rugae

From E12.5–E14.5, Deltex1 transcripts were found at sites of the oral cavity where palatal rugae are formed under the control of epithelial–mesenchymal interactions. Deltex1 expression in the mesenchymal components of the rugae was correlated with Notch3 and Delta1 expression (Fig. 4II.).

In summary, Deltex1 expression is widespread in the developing nervous system. Expression is found in regions
containing post-mitotic differentiating neurons and in general seems to coincide with the down-regulation of Notch expression. In contrast, in non-neuronal tissues that express Deltex1, such as thymus and palatal rugae, we see apparent co-expression of Deltex1 and Notch genes.

2. Experimental procedures

Swiss mice were used at embryonic stages (E10.5–E16.5). In situ hybridization on cryosections, using digoxigenin-labelled antisense riboprobes for mouse Notch1, Notch2, Notch3, Delta1, and rat Islet1 was carried out using the method previously described (Mitsiadis et al., 1998). A plasmid containing a 3.8 kb transcript of the mouse Deltex1 gene was isolated from a Stratagene mouse brain cDNA library. The sequence is identical to the sequence entered into the Genbank database under the accession number AB015422 and called MDTX1 by Kishi et al. (2001).

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References


