Gene Expression Patterns 5 (2005) 561–568

www.elsevier.com/locate/modgep

Expression pattern of *NOGO* and *NgR* genes during human development

Hassan Al Halabiah[a], Anne-Lise Delezoide[b], Ana Cardona[c], Jean-Marie Moalic[a], Michel Simonneau[a,*]

[a]*Neurogénétique, INSERM E9935, Hôpital Robert Debré, AP-HP, 48 Boulevard Sérurier, 75019, Paris, France*
[b]*Biologie du développement, Hôpital Robert Debré, AP-HP, 48 Boulevard Sérurier, 75019, Paris, France*
[c]*Histotechnology and Pathology Unit, Institut Pasteur, 25 rue du Dr Roux, 75724 Paris Cedex 15, France*

Received 7 September 2004; received in revised form 25 October 2004; accepted 26 October 2004

Abstract

Nogo protein has been identified as the component of central nervous system (CNS) myelin that limits axonal regeneration. We investigated the expression of the genes encoding Nogo and its receptor, NgR, between weeks eight and 23 of human embryonic development, by quantitative radioactive in situ hybridization. At 8 weeks, we detected *NOGO* and *NgR* transcripts in developing neuronal and non-neuronal structures. We focused on two different structures: the brain and the dental germs. During this period of development, *NOGO* and *NgR* transcripts colocalized in the cortical and ventricular zones of the brain, with expression strongest for these two genes in the postmitotic cells of the cortical plate. In developing dental germs, *NgR* was more strongly expressed than *NOGO* at 16 and 21 weeks. *NOGO* and *NgR* were expressed in zones of epithelium–mesenchyme interaction, which induce the differentiation of ameloblasts/odontoblasts. These genes were expressed most strongly in differentiated cells.

Keywords: Nogo; NgR; In situ hybridization; Human brain development; Human tooth development

1. Results and discussion

Nogo proteins belong to the reticulon protein family, the members of which are predominantly located in the endoplasmic reticulum (Brittis and Flanagan, 2001; Oertle and Schwab, 2003). *NOGO* encodes diverse isoforms of the protein, the functions of which are largely unknown, with the exception of the Nogo A—Nogo receptor (NgR) pathway (He and Koprivica, 2004; Woolf and Bloechlinger, 2002). In adults, Nogo A protein is synthesized by oligodendrocytes and interacts with its receptor, NgR, on neurons, resulting in the collapse of central nervous system (CNS) growth cones (Chen et al., 2000; Fournier et al., 2001; GrandPre et al., 2000; Prinjha et al., 2000). NOGO transcripts are produced not only in oligodendrocytes, but also in Schwann cells (Pot et al., 2002) and in various central and peripheral neurons (Hunt et al., 2002, 2003; Josephson et al., 2002). Three proteins—Nogo (Fournier et al., 2001), MAG (myelin-associated glycoprotein; Domeniconi et al., 2002; Liu et al., 2002) and OMgp (oligodendrocyte-myelin glycoprotein; Wang et al., 2002)—interact with NgR. However, the N-terminal region of Nogo A (amino-Nogo) acts in an NgR-independent manner (Liu et al., 2002; Niederost et al., 2002). Nogo B is involved in modulating the behavior of endothelial cells and vascular smooth muscle (Acevedo et al., 2004). A signaling complex consisting of NgR, p75 and LINGO-1 (LRR and Ig domain-containing, Nogo receptor interacting protein) was recently described (Mi et al., 2004; Wong et al., 2002). The patterns of mRNA production for Nogo and NgR have been extensively studied in spinal cord, in both normal and traumatic conditions, in adult rodents (Huber et al., 2002; Lee et al., 2003). In contrast, only a few studies have been done in the spinal cord during human development (Josephson et al., 2001, 2002, 2003; O'Neill et al., 2004). The prenatal expression and function of the Nogo-NgR signaling pathway is largely unknown. We investigated the spatio-temporal patterns of expression of NOGO and NgR by means of radioactive quantitative in situ hybridization at

* Corresponding author. Tel.: +33 1 40 03 1923; fax: +33 1 40 03 1903.
E-mail address: simoneau@infobiogen.fr (M. Simonneau).

1567-133X/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.modgep.2004.10.010

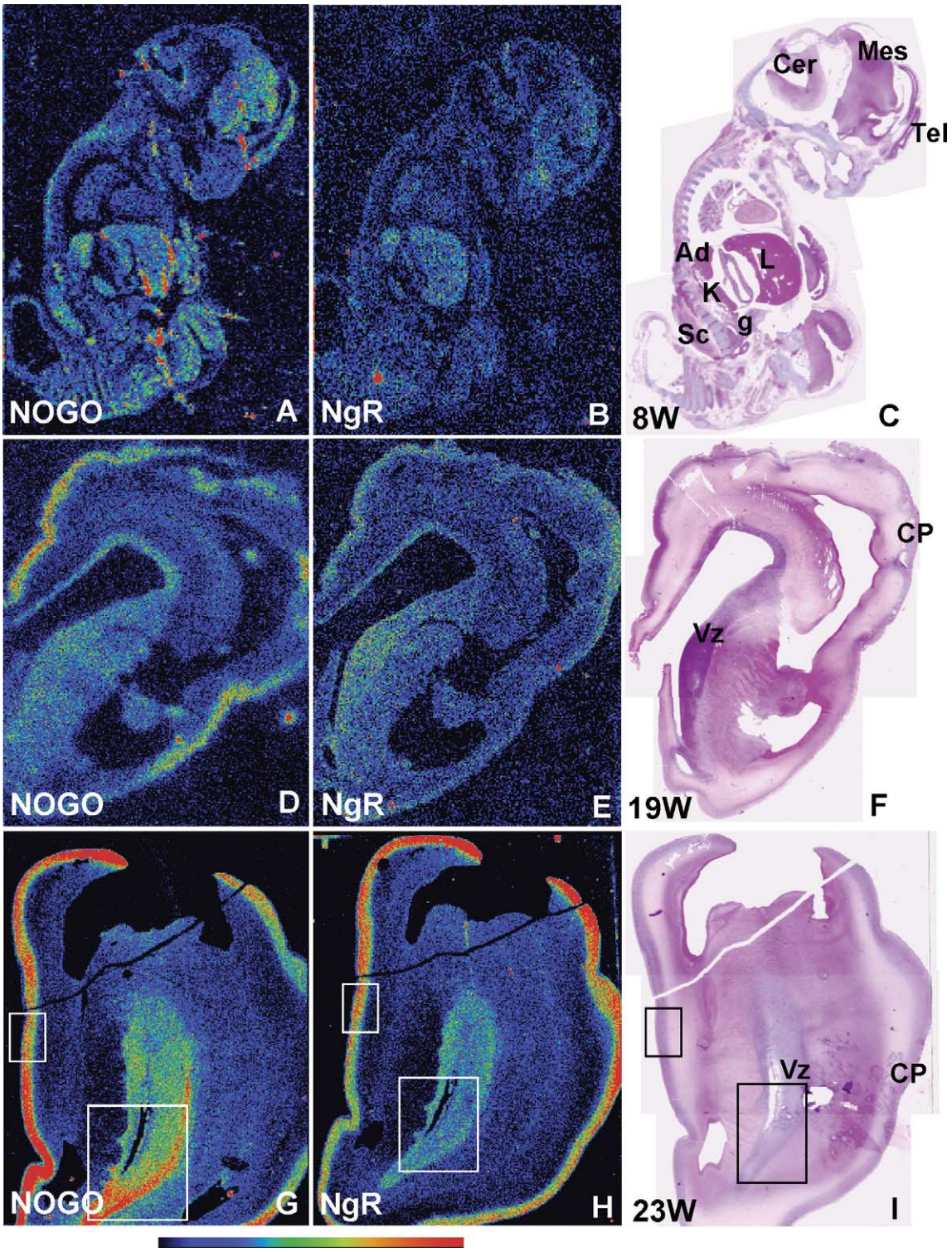

Fig. 1. *NOGO* and *NgR* expression pattern in human embryo. (A–C) Sagittal section of an 8sz W human fetus hybridized with probes for *NOGO* (A), or *NgR* (B) or stained with hematoxylin/eosin/safranin (HES) (C). (A): *NOGO* transcripts are located in the telencephalon (Tel), mesencephalon (Mes), cerebellum (Cer), spinal cord (Sc), adrenal gland (Ad), kidney (K), liver (L) and gut (g). (B): Weak expression of *NgR* in the mesencephalon, adrenal gland and liver. (C): HES staining of a section adjacent to those shown in (A) and (B). (D–F) Coronal section of frontal cerebral lobes at 19 W hybridized with probes for *NOGO* (D), or *NgR* (E) or stained with hematoxylin/eosin/safranin (HES) (F). (D): *NOGO* transcripts in the ventricular zone (Vz) and the cortical plate (CP). (E): Weak *NgR* expression in both Vz and CP. (F): HES staining of a section adjacent to those shown in (D) and (E). (G–I) Coronal section of frontal cerebral lobes at 23 W hybridized with probes for *NOGO* (G), or *NgR* (H) or stained with hematoxylin/eosin/safranin (HES) (I). (G): *NOGO* transcripts in both the germinal proliferative zone (Vz) and the postmitotic cells of cortical plate (CP). (H): *NgR* is expressed in both the Vz and CP. These coronal sections are in a more rostral position than the coronal sections illustrated in (D–F). (I): HES staining of a section adjacent to those shown in (G) and (H).