ELSEVIER

Progress in Neurobiology 83 (2007) 37–52

progress in Neurobiology

www.elsevier.com/locate/pneurobio

Cell fate specification in the mammalian telencephalon

François Guillemot *

National Institute for Medical Research, Mill Hill, London NW74LL, UK

Received 9 October 2006; received in revised form 22 November 2006; accepted 20 February 2007

Abstract

A fundamental feature of neural development in vertebrates is that different cell types are generated in a precise temporal sequence, first neurons, followed by oligodendrocytes and astrocytes. The mechanisms underlying these remarkable changes in progenitor fate during development are not well understood, but are thought to include both changes in the intrinsic properties of neural progenitors and changes in their signaling environment. I discuss the mechanisms that control the specification of neuronal, astroglial and oligodendroglial fates, focusing on the mammalian telencephalon, one of the most extensively used models to study neural specification mechanisms in vertebrates. I first consider the multiple extracellular signals that have been implicated in neural fate specification. Their roles are often complex, with the same signals having different effects at different developmental stages, and different signaling pathways interacting extensively. The selection of a particular cell fate ultimately results from the integration of multiple signals. Signaling pathways regulate cell fates by modulating the expression and activity of numerous transcription factors in neural stem cells. I discuss how transcription factors also act in a combinatorial manner to determine progenitor fates, with individual factors promoting the generation of one or two cell types and repressing alternative fate(s). Finally, I discuss the many levels of regulation involved in preventing premature astrocyte differentiation during neurogenesis, and later on in controlling the transition from neurogenesis to gliogenesis.
© 2007 Elsevier Ltd. All rights reserved.

Keywords: Neurogenesis; Astrocytes; Oligodendrocytes; Signaling pathways; Transcription factors; Cerebral cortex

Contents

Abbreviations: bHLH, basic helix-loop-helix; BLBP, brain lipid binding protein; BMP, bone morphogenetic protein; CBF-1, centromere-binding factor 1; CBP, CREB binding protein; C/EBP, CAAT/enhancer-binding protein; CNS, central nervous system; CNTF, ciliary-derived neurotrophic factor; CSL, CBF1, suppressor of hairless; lag-1; EGF, epidermal growth factor; EGFR, EGF receptor; ERK, extracellular-signal-related kinase; FGF, fibroblast growth factor; GABA, gamma amino-butyric acid; GFAP, glial fibric acidic protein; JAK, janus kinase; LIF, leukaemia inhibitory factor; MEK, mitogen-activated-protein-kinase kinase; OLP, oligodendrocyte progenitor; PCAF, p300/CBP-associated factor; REST/NRSF, RE1-silencing transcription factor/neuron-restrictive silencer factor; SVZ, sub-ventricular zone; PDGF, platelet-derived growth factor; STAT, signal transducer and activator of transcription; VEGF, vascular endothelial growth factor; VZ, ventricular zone

* Tel.: +44 20 8816 2740.
E-mail address: fguille@nimr.mrc.ac.uk.

0301-0082/$ – see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.pneurobio.2007.02.009

1. Introduction

The molecular mechanisms controlling the specification of neural cell fates have been the focus of intense research in recent years. Most of the work in this field has been conducted using as a model the mammalian telencephalon. It is in this system that neural stem cells and the distinct populations of neural progenitors were first discovered, and their cellular properties, such as multipotentiality and symmetric or asymmetric division, were first established (Davis and Temple, 1994; Doetsch et al., 1999; Morshead et al., 1994; Noctor et al., 2004; Reynolds and Weiss, 1992). The cellular lineages linking neural stem cells to neurons, astrocytes and oligodendrocytes have been mostly characterized in the mammalian cortex, through lineage tracing and time lapse microscopy studies in vivo. One of the appealing aspects of the telencephalon as a model system has been the relative ease of pursuing experiments in progenitor cultures (Conti et al., 2005; Davis and Temple, 1994; Gage et al., 1995; Johe et al., 1996; Reynolds and Weiss, 1992), as well as in vivo. Moreover, the telencephalon is the only region of the mammalian nervous system where stem cell populations remain active and produce neurons throughout the life of the organism. Mechanisms involved in cell fate specification in adult progenitors are under intense scrutiny because of the lessons they could teach us on how to treat neurological diseases by cell transplantation or mobilization of endogenous progenitors.

Neural stem cells, particularly abundant at early stages of neural development, are at the origin of most differentiated cells in the mammalian nervous system. Numerous studies, which will be reviewed here, have tracked the intrinsic mechanisms (transcription factors and epigenetic modifications of proteins and DNA) and extrinsic mechanisms (extracellular factors and their intracellular signaling machinery) that instruct these multipotent progenitors to generate neurons, astrocytes or oligodendrocytes. Many of the major signaling pathways that operate during embryonic development have been implicated in the choice between neuronal and glial fates in telencephalic progenitors. Adding to the complexity, there is abundant evidence that these pathways cross-talk extensively, and that the same signal may promote different fates depending on the cellular context, and particularly the level of activity of other signaling pathways. The choice between neuronal and glial fates also involves synergistic and inhibitory interactions between transcription factors, and the regulation of transcription factor expression and activity by signaling pathways.

A fundamental feature of neural development in vertebrates is that different cell types are generated in a precise sequence, first neurons, followed by oligodendrocytes and astrocytes (Bayer and Altman, 1991). Neural stem cells initially divide symmetrically, resulting in a rapid expansion of the progenitor pool. The onset of neurogenesis is marked by a switch to an asymmetric mode of division, whereby stem cells produce another stem cell and a neuron (or a intermediate progenitor committed to neurogenesis). The transition to gliogenesis involves a return to the symmetric division of progenitors. The mechanisms underlying these remarkable changes in progenitor behaviour and fate during development are not understood, but are thought to include both changes in the intrinsic properties of neural progenitors, as well as changes in their signaling environment (Temple, 2001). The specification of neuronal and glial cell types therefore represents a fascinating model in which to investigate the intricacy of interactions between multiple signaling pathways, transcription factors and epigenetic mechanisms in the control of a fate decision.

In the first part of this review, I will discuss the signaling mechanisms regulating the specification of neuronal, astroglial and oligodendroglial fates in the telencephalon. In the second part, I will discuss the transcriptional mechanisms involved in specification of the different neural fates. In the third part, I will discuss some of the mechanisms that are thought to control the transition from neurogenesis to gliogenesis. The regulation of

Download English Version:

https://daneshyari.com/en/article/4353958

Download Persian Version:

https://daneshyari.com/article/4353958

Daneshyari.com