Abstract View

Neuroscience Meeting 2001

GENES THAT ARE DIFFERENTIALLY EXPRESSED IN RADIAL GLIAL CELLS

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The C6-R cell line, generated in our lab from C6 glioma, has been shown to have unique properties that mimic authentic radial glia and integrate into CNS tissue after transplantation into brain and spinal cord (Exp. Neurol. 168:310-22, 2001). In order to analyze genes that control radial phenotype we applied cDNA microarray (genechip) techniques to search for genes that are selectively expressed in radial glia. Total RNAs were isolated from C6-R and C6 cells, and gene expression profiles were examined using Affymetrix RN-U34 Neuro genechips. From duplicate experiments, we found 79 genes that were changed by at least 2-fold, 43 genes were upregulated and 36 genes were downregulated in C6-R by comparison to C6. One of the most dramatic changes was seen with FGFR-1 mRNA, which is upregulated in C6-R by 13.7 fold. When C6-R cells were treated with bFGF (10 ng/ml) in serum-free medium, they retracted their processes and formed neurosphere-like aggregates within 4 days. In control treatment with PDGF, C6-R cells maintained their radial morphology even though they have upregulated levels of PDGFR mRNA. This result suggests that bFGF appears to have specific effects on C6-R cells and may regulate their radial morphology. In parallel studies on C6-R cells, we are screening for genes that are selectively expressed in primary radial glia using genechips. Cultures enriched in radial glia are derived from rat E14 cortex after treatment with bFGF and LIF. We reason that genes that are identified in both systems are prime candidates for inducing or maintaining radial glial phenotype. The gene profile comparison analysis will be discussed.

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Neuroscience Meeting 2002

Abstract

Microtubules are important for Radial Glial Morphology: Involvement of MAPs and MARKs

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Radial glia are a polarized cell type, that in most neural regions appear only transiently during development. They have long been recognized as glia or glial progenitors that support neuronal migration. Recently, several groups have provided evidence that radial glia also give rise to neurons and appear to be the major dividing precursor cells in the embryonic cortical ventricular zone (Noctor SC et al., 2002). The morphology of radial glia is striking in that they extend their long radial fibers from the ventricular zone all the way to pial surface, providing guides to support radial neuronal migration. We reasoned that the unique morphology of radial glia may be due to the composition and organization of their cytoskeleton. In this present study, we have used C6R, a radial glial like cell line and isolated perinatal Bergmann glia to ask what are the critical cytoskeletal elements in radial glial cells and how they are organized to maintain the radial morphology. Drug treatments with nocadazole and cytochalasin D, real-time RT-PCR and in situ hybridization have been applied in this investigation. Our results showed that 1) microtubules, not actin, are critical to the polarized morphology of radial glial cells; 2) certain microtubule-associated-proteins (MAPs) (e.g. MAP-4 or MAP-7) are present in radial glia and may be responsible for organizing the microtubule filament into the radial pattern; and 3) Microtubule-affinity-regulating kinases (MARKs) may be involved in regulating the phosphorylation state of MAPs and thereby their functions in radial glia.

Key words: radial glia; Bergmann glia; real time RT-PCR; in situ hybridization; microtubule-associated-proteins (MAPs); microtubule-affinity-regulating kinases (MARKs).

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Abstract View

A LINEAGE STUDY ON RADIAL GLIA: RELATIONSHIP WITH NEURONAL-RESTRICTED PRECURSORS (NRPS) AND GLIAL-RESTRICTED PRECURSORS (GRPS)

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Radial glia are among the first cells that develop in neuroepithelia and are characterized by their unique ability to span this tissue in the embryonic central nervous system. Radial glia have long been thought of as glia or glial progenitors that support neuronal migration during neurogenesis. Recent evidence indicate strongly that radial glia can give rise to neurons and appear to be the major dividing precursors in the embryonic cortical ventricular zone (Noctor SC et al., 2002). Neuronal-restricted precursors (NRPs) and glial-restricted precursors (GRPs) are also derived from neuroepithelial cells during development and are thought to be the major precursors that give rise to all the cell types in the mature CNS (Mayer-Proschel M et al., 1997). The relationship between radial glia and these restricted precursors is not clear. In the present study, we took advantage of an immortalized radial glial-like cell line, L2.3 and primary cell culture to investigate potential relationships and to clarify the lineage sequence among these cells in vitro. Using immunohistochemistry with cell type specific markers (BLBP for radial glia, 5A5 for NRPs and A2B5 for GRPs) and clonal analysis, we found that 1) A2B5 and 5A5 co-localize extensively with BLBP-positive radial glia in developing embryonic forebrain suggesting they are GRPs and NRPs, respectively, and this co-localization appears to be temporally and spatially regulated; 2) radial glia appear earlier and seem to become or give rise to restricted precursors during development. This study indicates there is close relationship between radial glia and restricted precursors, and also suggests potential methods to isolate radial glia by using cell surface markers of restricted precursors in certain regions and stages of development.

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