The Journal of Neuroscience, July 26, 2006, 26(30):7907-7918; doi:10.1523/JNEUROSCI.1299-06.2006

Development/Plasticity/Repair

Origin of Oligodendrocytes in the Subventricular Zone of the Adult Brain

Bénédicte Menn,[1] Jose Manuel Garcia-Verdugo,[2] Cynthia Yaschine,[1] Oscar Gonzalez-Perez,[1] David Rowitch,[3] and Arturo Alvarez-Buylla[1]

[1]Department of Neurosurgery and Developmental and Stem Cell Biology Program, University of California at San Francisco, San Francisco, California 94143, [2]University of Valencia, 46010 Valencia, Spain, and [3]Department of Pediatric Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02115

Correspondence should be addressed to Arturo Alvarez-Buylla, Department of Neurosurgery and Developmental and Stem Cell Biology Program, University of California at San Francisco, Box 0525, San Francisco, CA 94143. abuylla@stemcell.ucsf.edu

Glial fibrillary acidic protein (GFAP)-positive astrocytes (type B cells) in the subventricular zone (SVZ) generate large numbers of new neurons in the adult brain. SVZ stem cells can also generate oligodendrocytes *in vitro*, but it is not known whether these adult primary progenitors generate oligodendrocytes *in vivo*. Myelin repair and oligodendrocyte formation in the adult brain is instead associated with glial-restricted progenitors cells, known as oligodendrocyte progenitor cells (OPCs). Here we show that type B cells also generate a small number of nonmyelinating NG2-positive OPCs and mature myelinating oligodendrocytes. Some type B cells and a small subpopulation of actively dividing type C (transit-amplifying) cells expressed oligodendrocyte lineage transcription factor 2 (Olig2), suggesting that oligodendrocyte differentiation in the SVZ begins early in the lineage. Olig2-positive, polysialylated neural cell adhesion molecule-positive, PDGF receptor α-positive, and β-tubulin-negative cells originating in the SVZ migrated into corpus callosum, striatum, and fimbria fornix to differentiate into the NG2-positive nonmyelinating and mature myelinating oligodendrocytes. Furthermore, primary clonal cultures of type B cells gave rise to oligodendrocytes alone or oligodendrocytes and neurons. Importantly, the number of oligodendrocytes derived from type B cells *in vivo* increased fourfold after a demyelinating lesion in corpus callosum, indicating that SVZ astrocytes participate in myelin repair in the adult brain. Our work identifies SVZ type B cells as progenitors of oligodendrocytes in normal and injured adult brain.

Key words: **adult oligodendrogenesis; CNS stem cells; oligodendrocyte progenitors; SVZ astrocyte; myelin repair; Olig2**

Received Oct. 24, 2005; revised June 19, 2006; accepted June 21, 2006.

Correspondence should be addressed to Arturo Alvarez-Buylla, Department of Neurosurgery and Developmental and Stem Cell Biology Program, University of California at San Francisco, Box 0525, San Francisco, CA 94143. abuylla@stemcell.ucsf.edu