Brief Communications

Dorsal Radial Glia Generate Olfactory Bulb Interneurons in the Postnatal Murine Brain

Rachel E. Ventura[1] **and James E. Goldman**[1,2]

[1]Center for Neurobiology and Behavior and [2]Department of Pathology, Columbia University, New York, New York 10032

During embryogenesis, dorsal radial glia generate pyramidal cell neurons but not interneurons, and are thought to degenerate or transform into astrocytes in the postnatal brain. Ventral radial glia, in contrast, retract their processes to form GFAP+ subventricular zone (SVZ) astrocytes that continue to generate interneurons into adulthood. We sought to fate map dorsal radial glia by codelivering an adenovirus expressing Cre recombinase and a lentivirus expressing dsRedExpress to the dorsal cortical surface of ROSA26R-YFP mice. Whereas the adenovirus is retrogradely transported to the cell body, the VSV-G (vesicular stomatitis virus G) pseudotyped lentivirus is not and allows us to control for viral diffusion from the site of infection. We found that dorsal radial glia give rise to gray and white matter astrocytes and oligodendrocytes. In addition, the dorsal radial glia fate map to astrocytes lining the dorsal aspect of the SVZ that persist at least 8 weeks postnatally. Finally, we found that dorsal radial glial-derived cells generate granule cell and periglomerular interneurons in the olfactory bulb and continue to form interneuronal precursors into adulthood.

Key words: **radial glia; subventricular zone; olfactory bulb; interneuron; dorsal; development; postnatal**

Introduction

The developing rodent telencephalon is thought to be spatially specialized such that the ventral but not dorsal primordium generates GABAergic interneuronal precursors. The vast majority, if not all, of the interneurons of the dorsal neocortex derive from precursors that have migrated tangentially from the ventrally situated caudal, medial, and lateral ganglionic eminences (Anderson et al., 1997; Wonders and Anderson, 2006). Olfactory bulb interneurons as well are thought to derive from ventral sources, based on homotopic, homochronic transplant studies and fate mapping of ventral radial glia (Wichterle et al., 1999, 2001; Merkle et al., 2004).

Unlike other neurons in the brain, interneurons of the olfactory bulb continue to be born throughout life. In the early postnatal (Luskin, 1993) and adult (Lois and Alvarez-Buylla, 1994) rodent, the interneuronal precursors of the olfactory bulb are generated in the subventricular zone (SVZ) of the striatal wall of the lateral ventricle from GFAP+ astroglial-like cells (Doetsch et al., 1999). In addition to the striatal SVZ, however, a more dorsal expansion of the SVZ persists postnatally in the dorsolateral corner of the lateral ventricle, just underneath the corpus callosum (Smart, 1961). Whereas ventral radial glia give rise to the interneuron-generating astrocytes in the SVZ along the lateral wall of the lateral ventricle (Merkle et al., 2004), dorsal radial glia are believed to senesce postnatally or retract their processes and become white and gray matter astrocytes (Schmechel and Rakic, 1979). However, previous analyses of the fates of dorsal radial glia were limited by inferences from static images or use of dyes that become diluted as cells divide (Voigt, 1989; Chanas-Sacre et al., 2000). We sought to more fully assess the fates of dorsal radial glia and determine whether they, like their ventral counterparts, give rise to SVZ astrocytes and generate olfactory bulb interneurons.

Work by others reveals that dorsal progenitors are competent to generate interneurons *in vitro* (Gotz and Bolz, 1994; He et al., 2001; Gulacsi and Lillien, 2003). *In vivo* fate mapping of the dorsal Emx1 lineage found some olfactory bulb cells, although these were not further described in terms of GABAergic expression (Gorski et al., 2002; Willaime-Morawek et al., 2006). In addition, Willaime-Morawek et al. (2006) found that Emx1-derived stem cells migrate from dorsal to ventral regions and generate striatal interneurons, further bolstering the idea of an expanded capability of dorsal cells.

However, the ability of cells of dorsal origin to upregulate ventral markers *in vivo* (Letinic et al., 2002; Willaime-Morawek et al., 2006) and *in vitro* (Hack et al., 2004) points toward difficulties in relying solely on genetic means for fate mapping. We thus used an anatomical fate-mapping strategy to label early postnatal dorsal radial glia and found that these cells retract to form astrocytes in the early postnatal and adult SVZ and generate periglomerular and granule cell interneurons in the olfactory bulb. These findings expand our understanding of the capacity of dorsal radial glia to generate diverse cell types and could inform the development of future cell replacement strategies.

Materials and Methods

Lentiviral vectors and virus preparation. The lentiviral vector F-CMV::Red was made by inserting a *Pac*I site upstream of the cytomegalovirus (CMV) promoter in the pSIREN-ZsGreen vector (Clontech, Mountain View, CA), replacing the ZsGreen with dsRedExpress (Clontech), and

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Correspondence should be addressed to James E. Goldman, P&S 15-420, 630 West 168th Street, New York, NY 10032. E-mail: jeg5@columbia.edu.

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then subcloning the *Pac*I, *Eco*RV CMV::dsRed cassette from pSIREN-dsRed into the *Pac*I, *Hpa*I site on the FUW lentivirus (Lois et al., 2002). To generate virus, the lentiviral vector was cotransfected with the vesicular stomatitis virus G (VSV-G) viral envelope and gag-pol Δ8.9 into gp293 cells (Clontech) using Calcium Phosphate Transfection kit (Clontech). Growth medium was added to cells after 12 h, and supernatant was harvested 48 h after transfection. Viral stocks were concentrated and titered to 1×10^7 cfu/ml using 3T3 cells. Ad5-CMV-Cre-GFP (Adeno-Cre) was purchased from Baylor Vector Development Laboratory (Houston, TX), titered using 3T3 cells, and used at 1×10^{10} cfu/ml, except where noted.

Viral injections. Mouse pups at postnatal day 1–2 (P1/2) were deeply anesthetized by immersion in ice and positioned in a stereotaxic apparatus. To target the subpial cortical surface overlying the dorsolateral SVZ at the level of septal nuclei, a 10 μl Hamilton (Reno, NV) syringe with a 33 gauge needle or a 10 μl Nanofil syringe (World Precision Instruments, Stevenage, UK) with a 35 gauge needle was placed under the skull at −1.5 mm caudal, 1.2 mm lateral from bregma. The needle was then advanced between the skull and the surface of the brain in the rostrocaudal plane to 1 mm rostral, 1.2 mm lateral from bregma, and 0.2 μl of a 1:1 (v/v) mixture of adenovirus and lentivirus was ejected (see Fig. 1). For the dorsolateral SVZ injections, 0.15 μl of lentivirus was ejected at a flow rate of 0.1 μl/min, using the following stereotaxic coordinates: 0.7 rostral, 1.2 lateral, 1.3 depth from bregma. All animal procedures were performed in accordance with Columbia University Institutional Animal Care and Use Committee guidelines.

Animals, histology, immunohistochemistry. R26R-YFP mice (Srinivas et al., 2001) (a gift from Tom Jessell, Columbia University, New York, NY; available from The Jackson Laboratory, Bar Harbor, ME; stock no. 06148) were anesthetized by intraperitoneal injection of ketamine (75 mg/kg; Aveco, Fort Dodge, IA) and xylazine (5 mg/kg; Mobay, Shawnee, KS) and were transcardially perfused with 4% paraformaldehyde in PBS, pH 7.4. Mouse brains were postfixed for 2 h and then cryoprotected with 30% sucrose/PBS. Serial coronal or parasagittal sections were cut (10 μm) using a cryostat, air-dried, and stored at −80°C until use. Immunofluorescence was performed using the following antibodies: sheep anti-green fluorescent protein (GFP) (1:200; Biogenesis, Kingston, NH), mouse anti-GFP (1:200; Invitrogen, Eugene, OR), mouse anti-Zebrin II (1:100; provided by R. Hawkes, University of Calgary, Calgary, Alberta, Canada), mouse anti-CC1 (1:50; Oncogene Sciences, Uniondale, NY), rabbit anti-NG2 (1:400; provided by W. Stallcup, The Burnham Institute, La Jolla, CA), rabbit anti-GFAP (1:1000; DakoCytomation, High Wycombe, UK), mouse anti-neuronal-specific nuclear protein (NeuN) (1:250; Chemicon, Temecula, CA), mouse anti-RC2 (Developmental Studies Hybridoma Bank, University of Iowa, Iowa City, IA), rabbit anti-tyrosine hydroxylase (TH) (1:500; Chemicon), and mouse anti-GAD67 (1:1600; Chemicon). Antigen retrieval was performed before immunolabeling with antibodies to Zebrin II and GFAP as described previously (Marshall and Goldman, 2002). Secondary detection was performed by incubating slides with the appropriate isotype-specific Alexa 488, Alexa 568, or Alexa 647 antibodies at a 1:2000 dilution (Invitrogen). Stained sections were examined and photographed using a Zeiss (Oberkochen, Germany) Axiophot 200 fluorescent microscope equipped with an Axiocam (Zeiss) and OpenLab imaging software (Improvision, Lexington, MA) or a Zeiss LSM510 Meta confocal microscope.

Results

Pial delivery of an adenovirus initially labels radial glia and transforming astrocytes

We sought to specifically label dorsal radial glia on postnatal day 1/2, by relying on the defining property of radial glia that they extend processes from the ventricle to the subpial cortical surface. We codelivered an adenovirus expressing a Cre recombinase, GFP fusion protein, and a VSV-G pseudotyped lentivirus expressing dsRedExpress to the subpia of R26R-YFP mice (Fig. 1). Whereas the adenovirus can be retrogradely transported from radial glial endfeet to the cell body (Merkle et al., 2004), the VSV-G pseudotyped lentivirus is not retrogradely transported

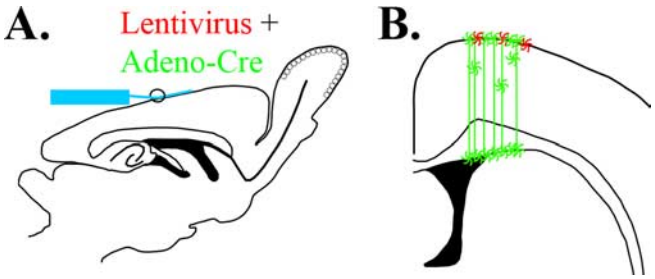

Figure 1. Strategy for labeling dorsal radial glia and progeny. ***A***, The injection needle containing a lentivirus encoding dsRedExpress and an adenovirus encoding Cre recombinase (Adeno-Cre) is inserted between the skull and brain of R26R-YFP mice and then advanced rostrally. The fluid is ejected on the subpial cortical surface overlying the SVZ at the level of the septal nuclei. ***B***, The adenovirus is retrogradely transported to the cell bodies of infected radial glia, where Cre and subsequently YFP is expressed, allowing long-term fate mapping. In this schematic, the radial glia and transforming astrocytes seen after initial labeling are shown in green. The lentivirus, in contrast, is not retrogradely transported, and infected cells (red) mark the site of injection.

(Mazarakis et al., 2001) and thus provides a readout of viral diffusion. Because the adenovirus remains extrachromosomal and is lost by cells as they divide, it was important to perform these experiments in mice with a floxed reporter for long-term fate mapping. This method allowed us to label a cohort of radial glia whose subpial endfeet lie at the point of viral delivery, to delineate the processes and somas of these cells, and then to follow their progeny.

We analyzed the mice at 4 d, 3 weeks, and 8 weeks after delivery of the virus. With each brain analyzed and at each time point, we took care to assure that the injection needle had disrupted the pial layer but had not entered into the parenchyma of the cortex by tracking the localization of lentiviral infected cells, making sure they were limited to subpial and layer I astrocytes (Fig. 2*A*). In addition, we assured that the virus infected a well circumscribed area on the cortical surface of maximum diameter of 1 mm (Fig. 2*B*).

In contrast to the superficial labeling of cells with the lentivirus 4 d after injection, we observed yellow fluorescent protein-positive (YFP+) (adenoviral labeled) astrocytes throughout the cortex and subcortical white matter (Fig. 2*B*) and a collection of YFP+ cell bodies located at the dorsal aspect of the dorsolateral SVZ (Fig. 2*C*). At 4 d, many of the cells labeled were Zebrin II+ (Fig. 2*D*), consistent with the notion that these are early SVZ astroglial cells (Staugaitis et al., 2001), and nearly all of the cells were Pax6+, consistent with their dorsal origin (data not shown). In addition, many of the cells still had processes that coursed through the cortex, some of which were RC2+, further confirming that they are radial glia (Fig. 2*B*, inset). Thus, the YFP+ cells, which must have had pial-attached processes at the time of adenoviral labeling, appeared after 4 d mostly as an astrocytic population, some having retained the radial processes and others having become cortical or white matter astrocytes.

Dorsal radial glia generate white and gray matter astrocytes and oligodendrocytes in the postnatal brain

We next determined the fates of dorsal radial glia at later time points in development. The transforming astrocytes we observed at 4 d after infection remained at 3 and 8 weeks as both white and gray matter astrocytes, localized in a radial manner underneath the site of viral infection (Fig. 2*A*). In addition, consistent with the recent report that cortical oligodendrocytes have both pallial and subpallial origins (Kessaris et al., 2006), we found YFP+ cells

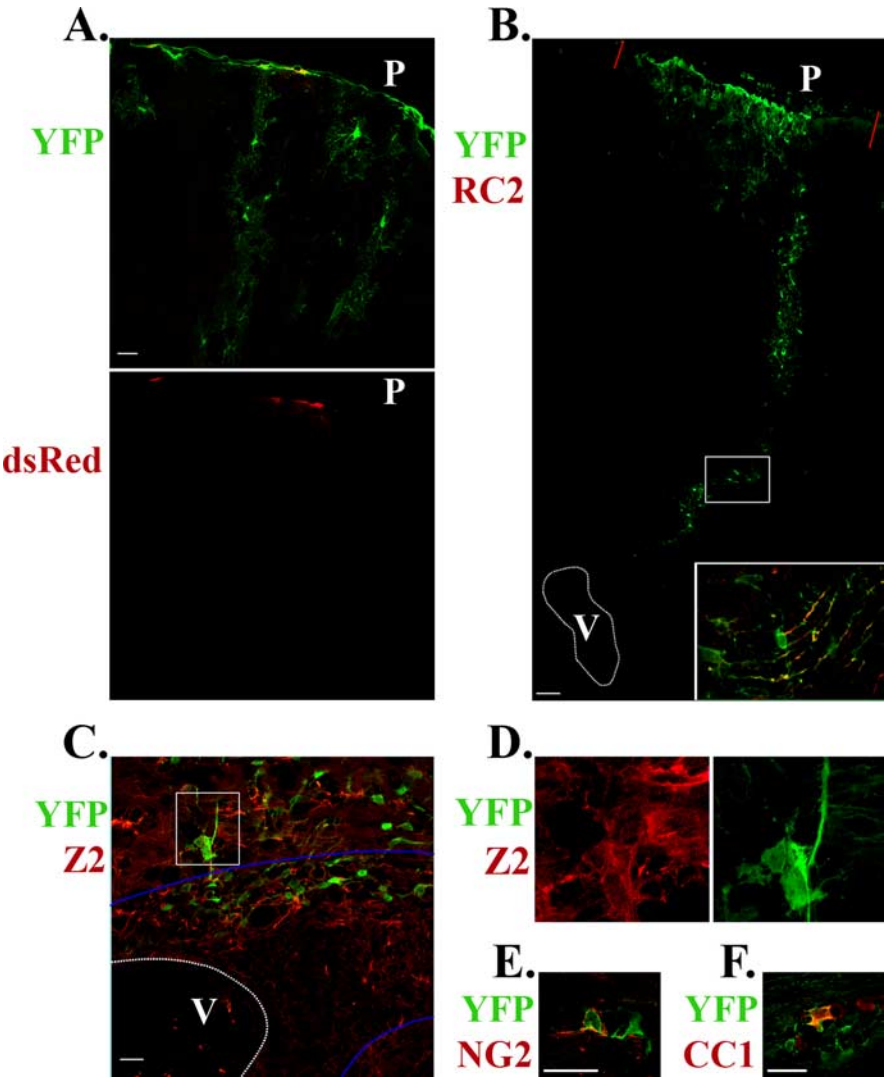

Figure 2. Adenoviral and lentiviral codelivery to the dorsal subpia can be used mark dorsal radial glia and descendents. ***A***, Brains are selected for analysis when they meet the criteria that the cortical surface is not damaged and the dsRedExpress containing lentivirus only infects cells in the outer cortical layer. Three weeks after codelivery of the lentivirus and a Cre-containing adenovirus to R26R-YFP mice at P1/2, the lentivirus remains confined to subpial astrocytes (red). In contrast, the adenovirus has been retrogradely transported to cells throughout the cortex that had pial attachments at the time of viral delivery, and these cells can be traced long term by examining YFP fluorescence. In the cortex, YFP+ astrocytes can be observed. ***B***, Four days after infection, astrocytes and RC2+ radial glial processes (inset) can be seen in the radial strip from the subpial surface to the subventricular zone. Brains are only considered for analysis when the area on the cortical surface that was in contact with the adenovirus (demarcated by red lines) is <1 mm in diameter. ***C***, Dorsolateral subventricular zone (borders outlined in blue) at 4 d after infection reveals YFP+ cells along the dorsal border. ***D***, Expanded view of boxed region in ***C*** reveals colocalization of YFP with the radial glial and astrocytic marker Zebrin II (ZII). ***E***, ***F***, Three weeks after labeling dorsal radial glia with the adenovirus, NG2+ oligodendrocyte precursors (***E***) and CC1+ oligodendrocytes (***F***) are observed in the subcortical white matter. Dorsal is up in ***A–D***. The dotted line demarcates ventricle. V, Ventricle; P, pial surface. Scale bar, 20 μm (in all images).

in both the cortex and subcortical white matter that were positive for the oligodendrocyte precursor marker NG2 (Fig. 2*E*) or the oligodendrocyte marker CC1 (Fig. 2*F*). Thus, at least some of the dorsal radial glia generate oligodendrocyte precursors and oligodendrocytes in the postnatal brain.

Dorsal radial glia retract processes to become SVZ astrocytes that form the dorsal edge of the dorsolateral SVZ

We next sought to determine the contribution of radial glial-derived cells to the dorsolateral SVZ at later postnatal stages. At both 3 and 8 weeks after infection with the adenovirus, we found YFP+ cells residing along the dorsal aspect of the SVZ (Fig. 3*A*), and many had become multiprocessed GFAP+ cells (Fig. 3*B*). Our observation of YFP+, GFAP+ cells within the SVZ at 3 and 8 weeks after infection suggests that at least some of these cells are a stable or a self-renewing population.

We next considered whether the progeny of the dorsal radial glial cells we infected with an adenovirus subsequently migrated to more ventral positions in the SVZ, as was reported for cells of the Emx1 lineage (Willaime-Morawek et al., 2006). We examined the distribution of cells within the SVZ at 3 weeks after infection. Nearly all of the labeled cells in the SVZ were located in the dorsolateral aspect of the lateral ventricle, with <1% located more ventrally along the striatal wall (three hemispheres analyzed; 1 of 301 cells were ventral) (Fig. 3*A*). Many of the YFP+ cells within the dorsolateral SVZ appeared to have a migratory morphology, although presumably these were migrating in the rostrocaudal rather than dorsoventral axis.

Dorsal radial glia give rise to olfactory bulb interneurons in the postnatal brain

To determine whether the dorsal radial glial-derived cells in the SVZ generate interneurons, we looked for YFP+ cells in the rostral migratory stream (RMS) and olfactory bulb. Three weeks after infection, we found YFP+, GAD67+, NeuN+ granule cell interneurons (Fig. 4*A*) and YFP+, TH+ periglomerular interneurons (Fig. 4*B*) in the olfactory bulb. In every brain we analyzed in which the adenovirus succeeded in infecting cells on the subpial surface overlying the SVZ, we found YFP+ cells in the olfactory bulb (8 of 12 hemispheres). To further assure that our results were not attributable to adenoviral diffusion from the subpial surface to the SVZ, we repeated our experiments using low-titer adenovirus (1×10^7 cfu/ml) so that the ratio of lentiviral to adenoviral infectious particles was 1:1. Again, in every brain we analyzed in which the adenovirus succeeded in infecting cells on the subpial surface overlying the SVZ, we found YFP+ cells in the olfactory bulb (two of eight hemispheres).

Qualitatively, the numbers of olfactory bulb cells generated from the radial glial infection seemed comparable with those generated from our typical lentiviral injections into the dorsolateral SVZ (Fig. 4*C*) (our unpublished observations). Presumably, the dorsolateral SVZ contains cycling and slowly dividing cells of both ventral and dorsal origins, all of which should be labeled by a lentivirus. To gain a better quantitative sense of the contribution of dorsal radial glia to postnatal olfactory bulb neuronogenesis, we counted every 12th section through the olfactory bulb 3 weeks after labeling the radial glia. To contextualize our findings, we injected the dsRedExpress lentivirus directly into the dorsolateral SVZ of postnatal day 1/2 pups and adjusted the lentiviral

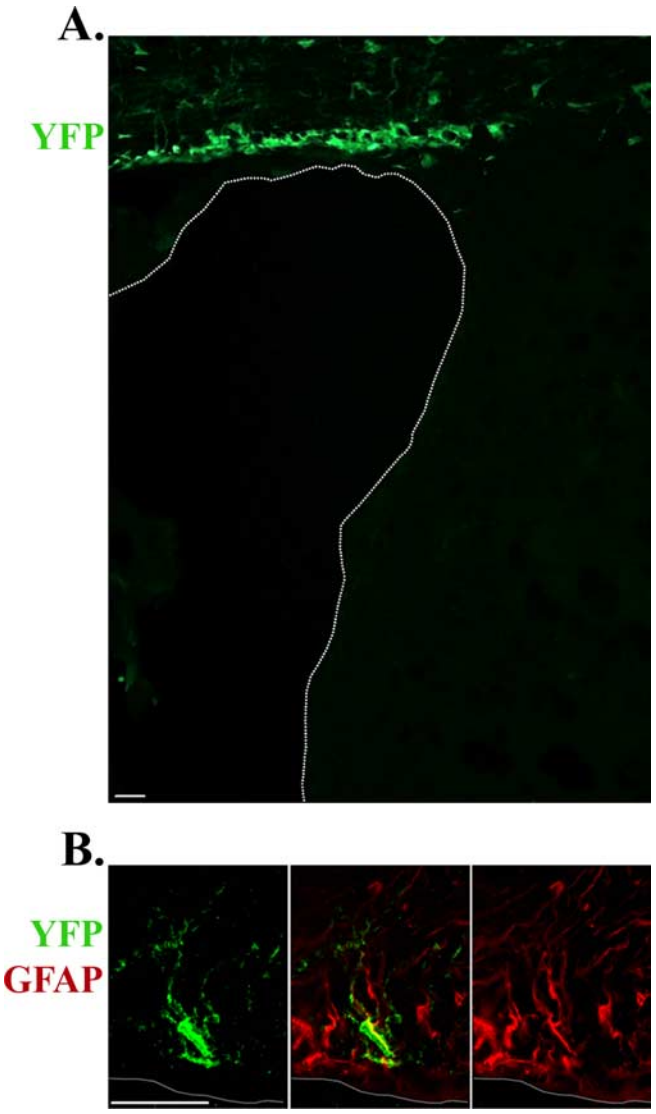

Figure 3. Descendents of dorsal radial glial reside in the dorsal aspect of the SVZ in the postnatal brain and include GFAP+ astrocytes. ***A***, Three weeks after dorsal radial glia were infected with the adenovirus, YFP+ progeny can be observed along the dorsal wall of the lateral ventricle and along the dorsal edge of the dorsolateral SVZ. We rarely if ever observed YFP+ cells ventral to the dorsolateral expansion of the SVZ. ***B***, Eight weeks after infection with the adenovirus, some YFP+ cells remain in the dorsolateral aspect of the SVZ, and many of these are GFAP+. The dotted line demarcates ventricle. V, Ventricle. Scale bar, 20 μm (in all images).

volume so that we infected similar numbers of SVZ cells as we did with our adenoviral radial glial labeling (Fig. 4*D*). When we then looked 3 weeks after infection at the olfactory bulb, we indeed found that the numbers of olfactory bulb cells generated from the lentiviral SVZ labeling was within the range of variability of those generated from adenoviral labeling of dorsal radial glia (Fig. 4*D*).

All of the cells generated from our injections had the morphology of interneurons. We could detect the neuronal marker NeuN in 95.6% of the cells and the GABA-synthesizing enzyme GAD67 in 77.0% of the cells (two hemispheres; 354 cells). Of the total cells that had migrated to the olfactory bulb 3 weeks after the adenoviral infection, 6.2 ± 0.9% were periglomerular (four hemispheres; 1712 cells) and 24.7 ± 6.5% of the periglomerular cells were TH+ (two hemispheres; 49 cells). For the lentiviral injection directly into the SVZ, 4.8 ± 0.8% of the cells were periglomerular (four hemispheres; 1113 cells) and 17.7 ± 3.2% of the periglomerular cells were TH+ (two hemispheres; 23 cells). We found no significant difference in the percentage of TH+ periglomerular cells generated from our dorsal adenoviral versus our SVZ lentiviral infections.

Next, we investigated whether dorsal radial glial-derived cells in the adult SVZ continue to generate interneurons. Eight weeks after infection with the adenovirus, we found YFP+, TuJ1+ cells with a migratory morphology in the RMS (Fig. 4*E*). Presumably, these would have been recently generated from the YFP+ cells in the SVZ.

Discussion

In the rodent, whereas radial glia from ventral sources generate glutamatergic and GABAergic neurons and retract to form SVZ astrocytes that persist into adulthood, radial glia from dorsal sources were previously understood to form only glutamatergic neurons and eventually to degenerate or become parenchymal astrocytes. We sought to fate map the dorsal radial glia in rodents to determine whether their *in vivo* capacity to generate multiple neuronal types was as limited as previously understood. We found that dorsal radial glia, like their ventral counterparts, retract their processes to become GFAP+ cells in the early postnatal and adult SVZ and that they generate olfactory bulb interneurons and oligodendrocytes (glial derivations from dorsal radial glia are the subject of a study in preparation).

To quantitatively understand the contribution of dorsal radial glia to postnatal olfactory bulb interneuron generation, we compared the numbers of olfactory bulb cells generated from our radial glial labeling with those generated from labeling the dorsolateral SVZ directly with a lentivirus. We show that the generation of olfactory bulb interneurons from dorsal radial glia is a robust phenomenon, and is comparable with the generation of interneurons from the dorsolateral SVZ as a whole. Furthermore, although there was no significant difference between the percentage of TH+ periglomerular cells formed from our dorsal adenoviral infections and our SVZ lentiviral infections, there was a trend toward an increased formation of TH+ periglomerular cells from the dorsal infection. This would be consistent with the high Pax6 immunoreactivity found in our dorsal adenoviral-infected cells and reports that Pax6 drives formation of TH+ periglomerular cells (Hack et al., 2005; Kohwi et al., 2005). A more complete understanding of whether dorsal and ventral radial glia use the same molecular programs to generate interneurons postnatally and whether there are subtle differences in the subtypes of olfactory bulb interneurons generated by them awaits additional study.

During embryogenesis, dorsoventral gradients of diffusible factors create regional differences in the cell types generated. Whether diffusible factors important for the postnatal neurogenic niche, such as sonic hedgehog, are present in different levels along the dorsoventral axis is unclear. Willaime-Morawek et al. (2006) document dorsal Emx1 derived cells migrating to more ventral regions of the SVZ, presumably where they are exposed to the ventral environment and gain competence to generate striatal interneurons. In contrast to their findings, we report that the astrocytic progeny of dorsal radial glia that come to reside at the SVZ border remain in register with their radial glial precursors, apparently not mixing with ventral cells or migrating extensively in a dorsoventral direction. This suggests that in the postnatal brain, diffusible factors important for interneuronal generation are indeed present at the dorsal border of the dorsolateral SVZ. Why we see different results from those of Willaime-Morawek et al. may be because the migratory Emx1-derived cells they ob-

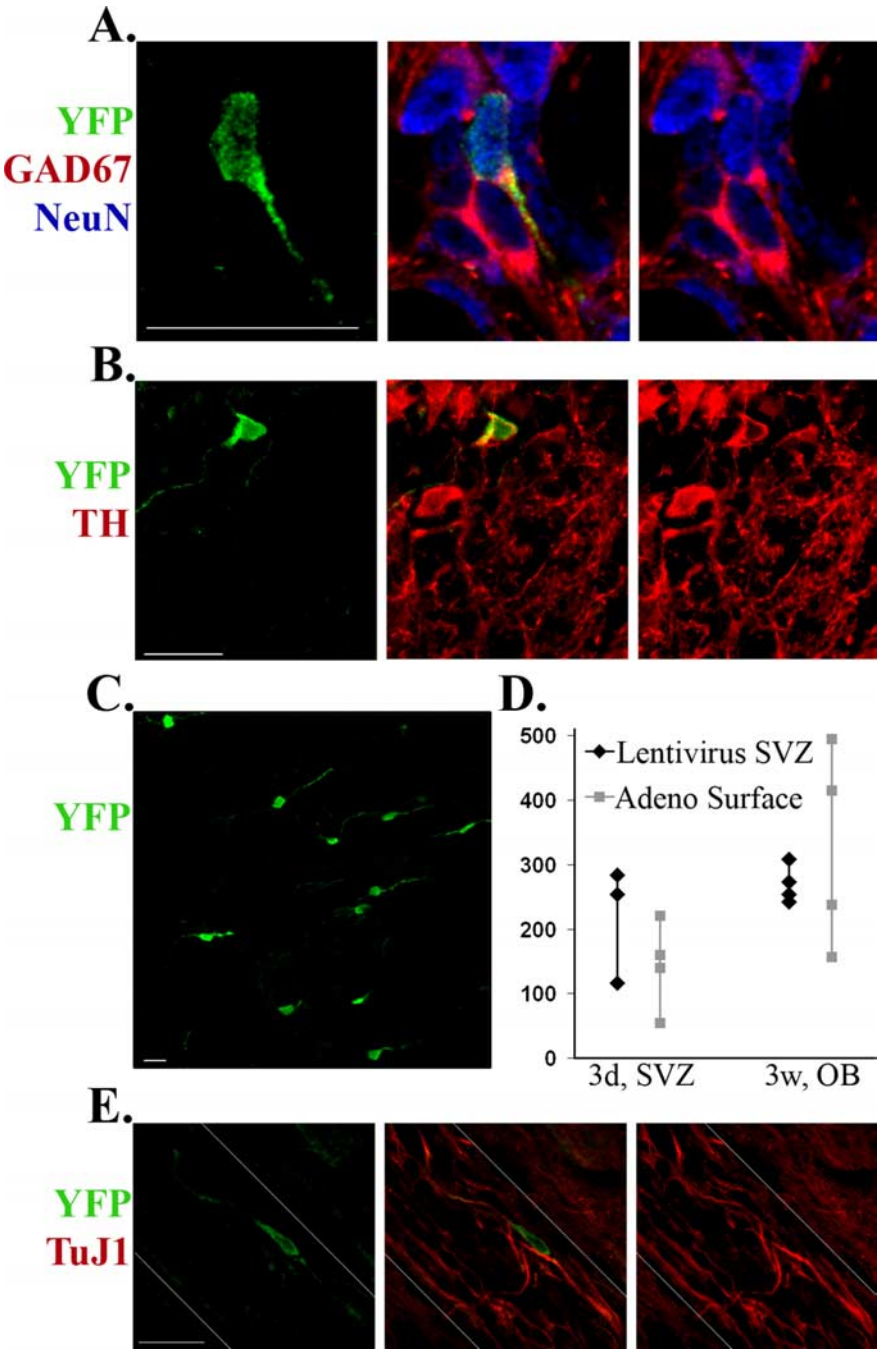

Figure 4. Dorsal radial glia generate olfactory bulb interneurons. ***A***, At 3 weeks after infection with the adenovirus, cells positive for YFP, the GABA-producing enzyme GAD67, and the neuronal marker NeuN can be observed in the granule cell layer of the olfactory bulb. ***B***, At 3 weeks after infection, cells positive for YFP and the dopamine-synthesizing enzyme TH can be found around the glomeruli of the olfactory bulb. ***C***, Lower-magnification view of radial glial descendents in the olfactory bulb granule cell layer 3 weeks after infection. ***D***, A dsRedExpress lentivirus was injected into the dorsolateral SVZ (black diamonds) or a Cre adenovirus was injected into the subpial surface to label radial glia (gray squares). Labeled SVZ cells were counted at 3 d after infection or labeled olfactory bulb cells were counted at 3 weeks after infection. Cell numbers represent totals from every 12th section through the SVZ or olfactory bulb, and each point graphed is a separate hemisphere counted. The numbers of olfactory bulb cells generated from the infection of dorsal radial glial is comparable with that generated from the SVZ infection. Adeno, Adenovirus; OB, olfactory bulb. ***E***, At 8 weeks after infection, YFP+ cells continue to be found in the rostral migratory stream (demarcated by dotted line). Presumably, these cells are migratory interneuronal precursors that were newly generated from YFP+ cells in the SVZ. The processes of the YFP+ cell shown here colocalize with the neuronal marker TuJ1. Scale bar, 20 μm (in all images).

served were generated from radial glia that had retracted their pial processes before postnatal day 1/2, which is the earliest time point that we label radial glia in this study.

In contrast to the thin subventricular region along the lateral wall of the lateral ventricle, the dorsolateral SVZ is much more expanded and contains some radial glial-derived astrocytic cells that are relatively far from the ventricle. The ventricle, and its ependymal lining, may provide important signals for the generation of interneurons in the postnatal brain. It is unclear from our experiments whether it is only the radial glial-derived cells in close proximity to the ventricle that are able to generate interneurons.

Because dorsal radial glial-derived cells generate olfactory bulb interneurons, it is conceivable that they are competent to generate neocortical interneurons *in vivo* under normal or diseased states, as occurs in humans (Letinic et al., 2002). When we placed an adenovirus driving Cre recombinase under the dorsal pial surface overlying the rostral-most SVZ at P1/2 and looked 6 weeks later, we found GABA+, NeuN+ cells in the border between white matter and cortical layer VI. These cells had the morphology of neurons, not glia, although we could not detect GAD67 in them (our unpublished observations). These results and others (Xu et al., 2003) support the notion that dorsal proliferative zones may generate limited numbers of interneurons. Why dorsal radial glia do not generate neocortical interneurons as robustly as ventral cells is open for additional study. Perhaps the dorsal radial glial-derived cells only become able to generate interneurons later in development, after most neocortical interneurons have already formed. Or perhaps dorsal radial glial-derived cells only become competent to generate limited subtypes of interneurons, not the full array found in the neocortex.

In this study, we report a way to label specific populations of dorsal radial glial-derived cells without invading the parenchyma. This technique provides a novel way to study dorsal radial glia and their derivatives and provides an alternative to transplant studies and genetic fate mapping, which either involves altering cells by removing them from the brain or relying on markers for cells of ventral and dorsal origin that may be less applicable as the animal ages. We also report that derivatives of dorsal radial glia generate olfactory bulb interneurons and remain in the SVZ for at least 8 weeks of postnatal age, perhaps longer, suggesting a previously unappreciated diversity in the population of SVZ cells capable of generating interneurons.

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