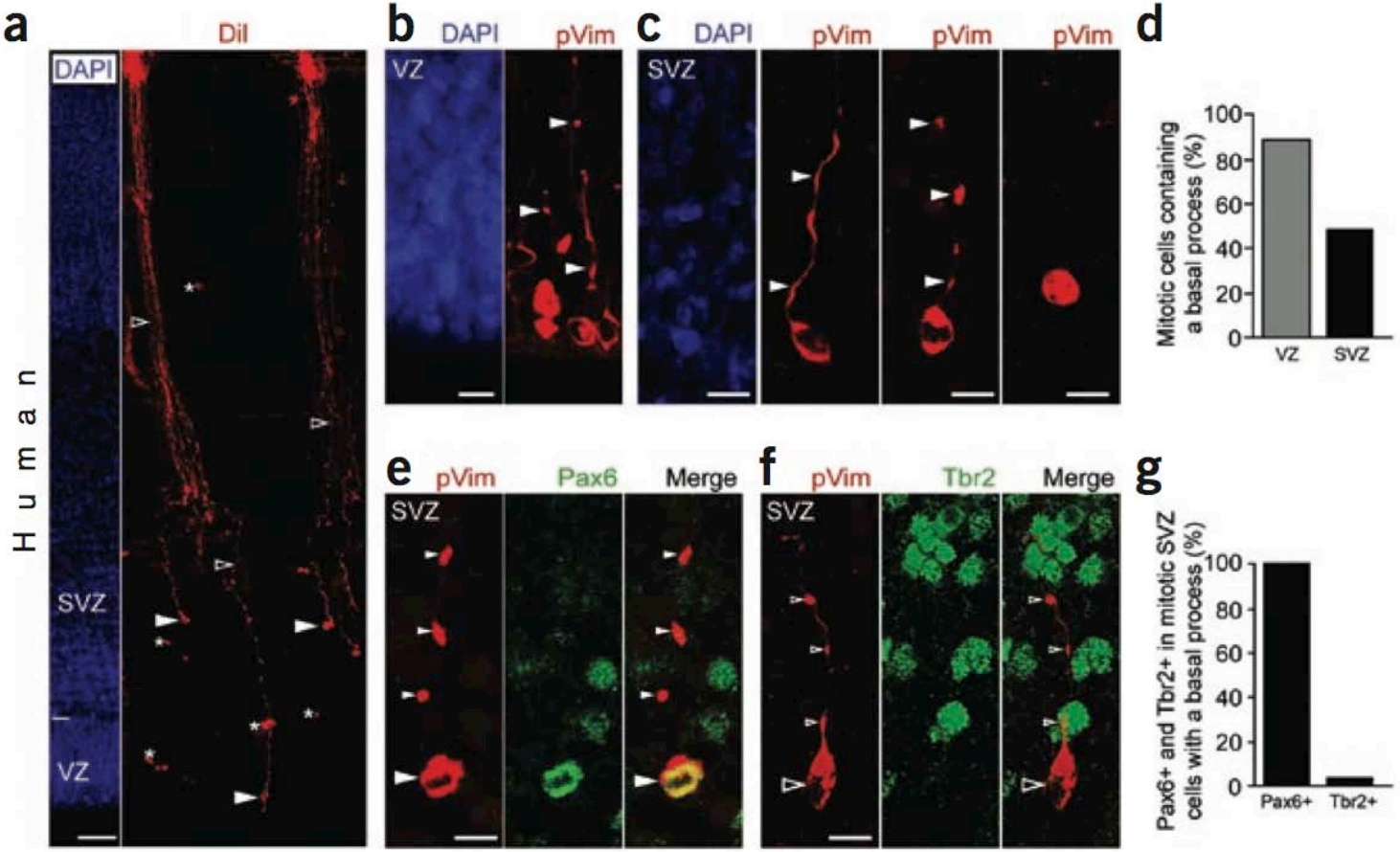
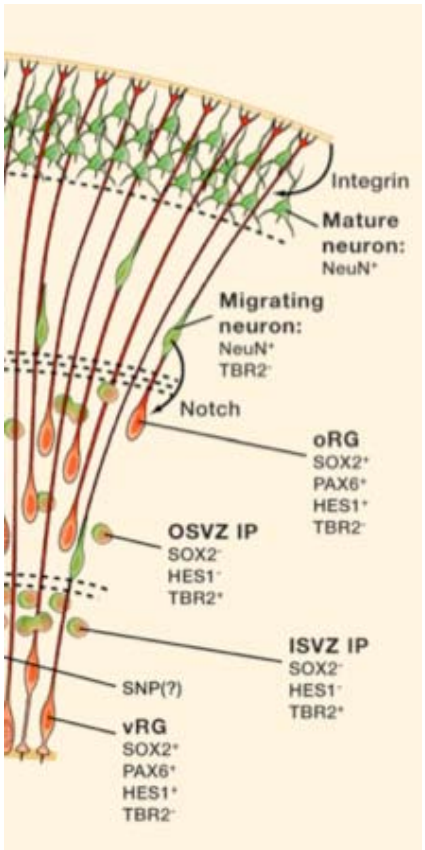
Cours du 24 octobre 2011

OSVZ progenitors of human and ferret neocortex are epithelial-like and expand by integrin signaling

Fietz SA, Kelava I, Vogt J, Wilsch-Bräuninger M, Stenzel D, Fish JL, Corbeil D, Riehn A, Distler W, Nitsch R, Huttner WB

Nature Neuroscience
2010 vol. 13 (6) pp. 690-9





OSVZ progenitors of human and ferret neocortex are epithelial-like and expand by integrin signaling

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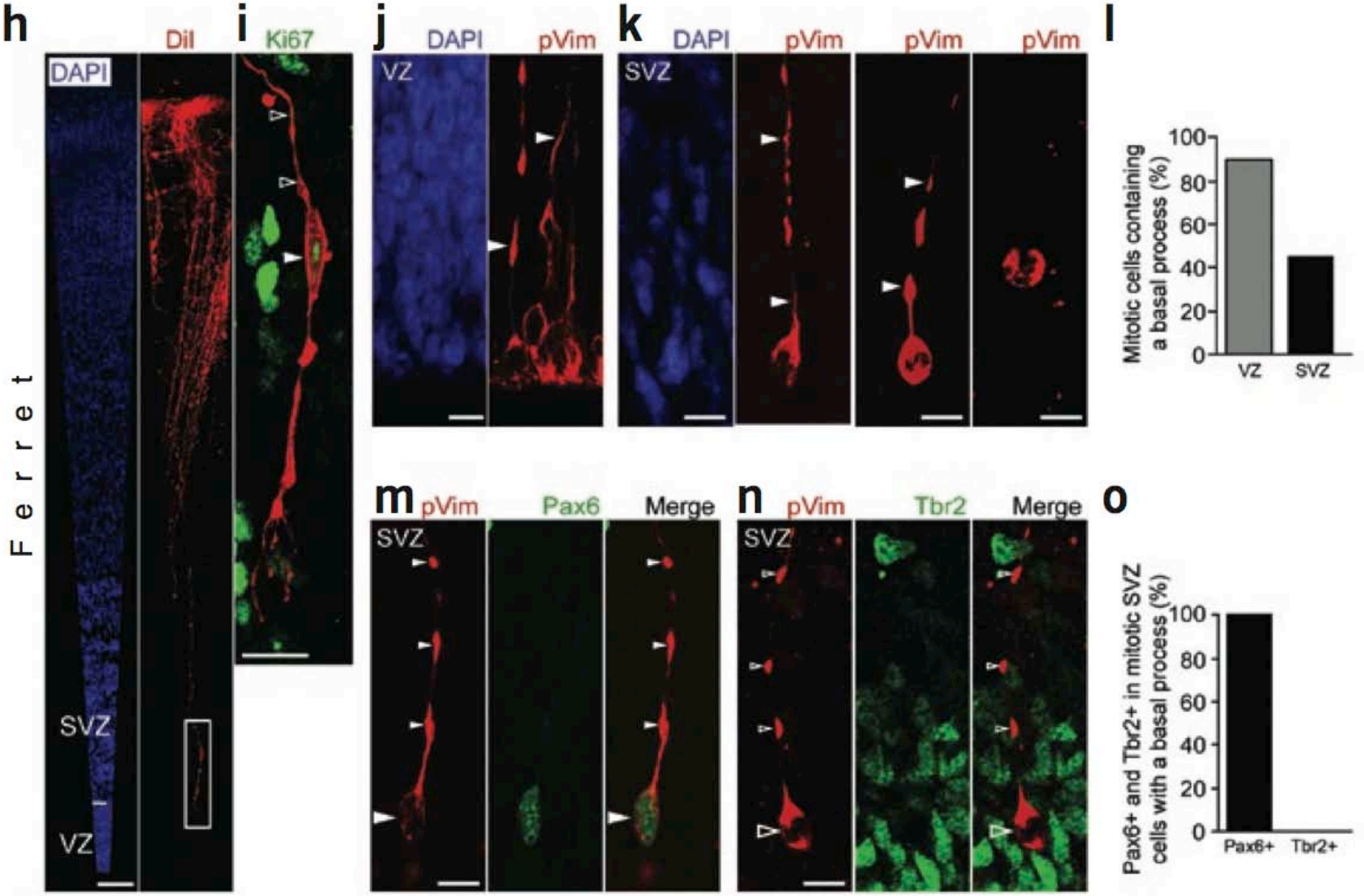
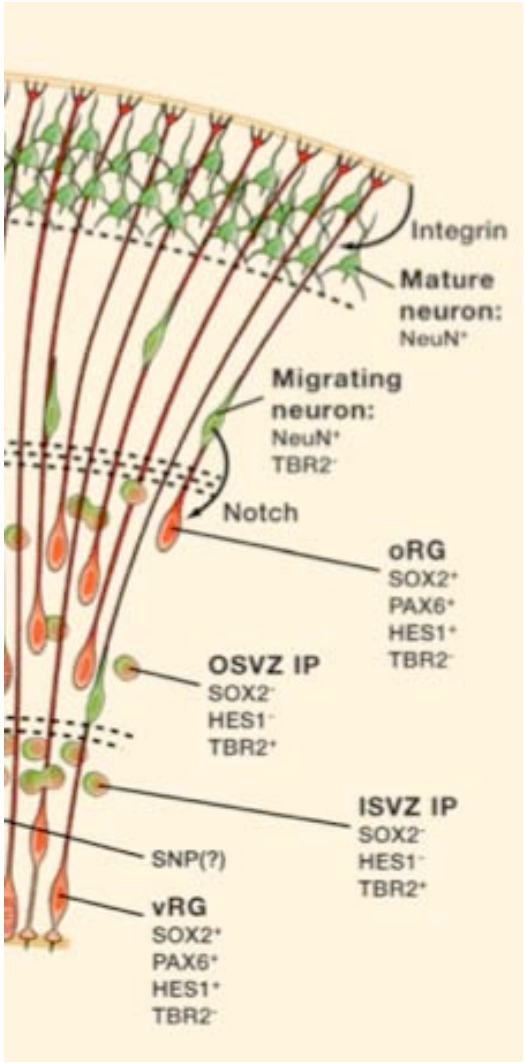


Development and evolution of the human neocortex

Lui JH, Hansen DV, Kriegstein AR

Cell
2011 vol. 146 (1) pp. 18–36



OSVZ progenitors of human and ferret neocortex are epithelial-like and expand by integrin signaling

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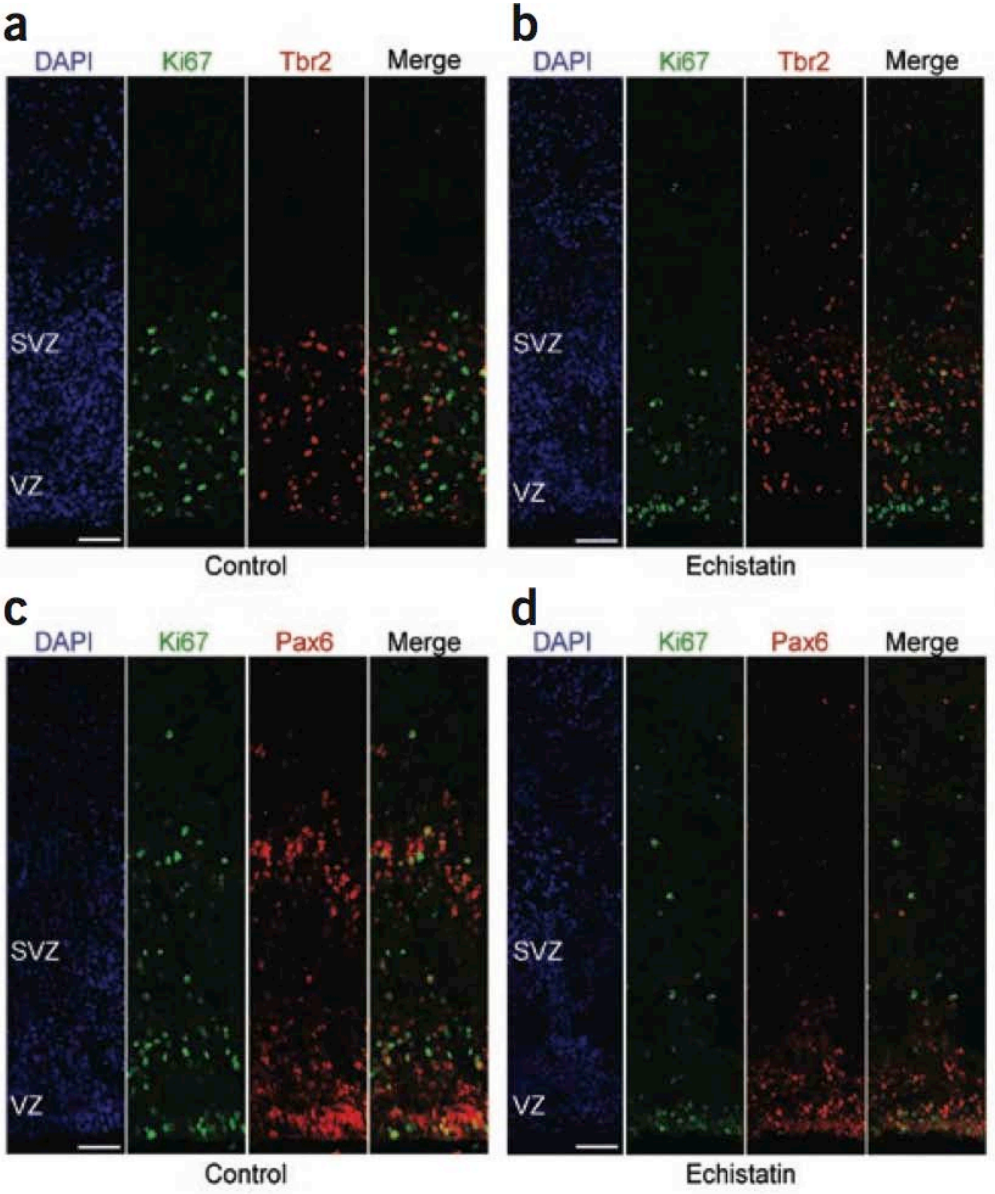
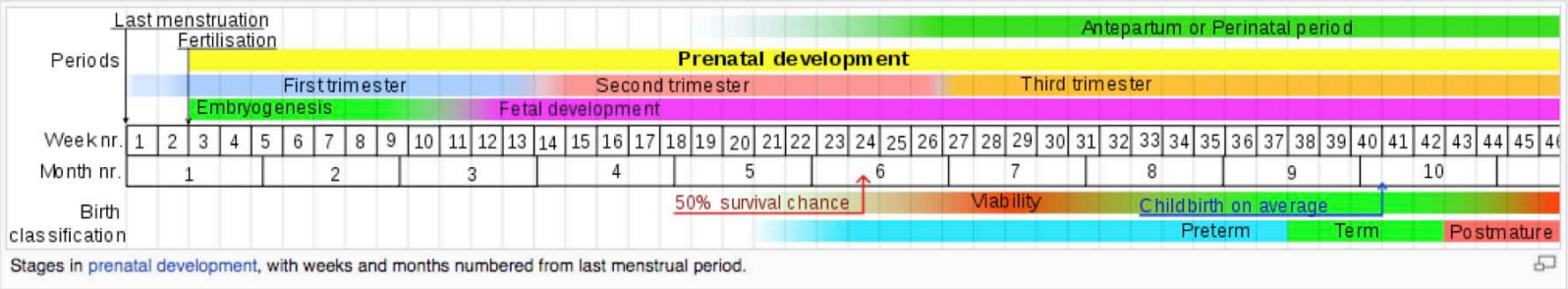
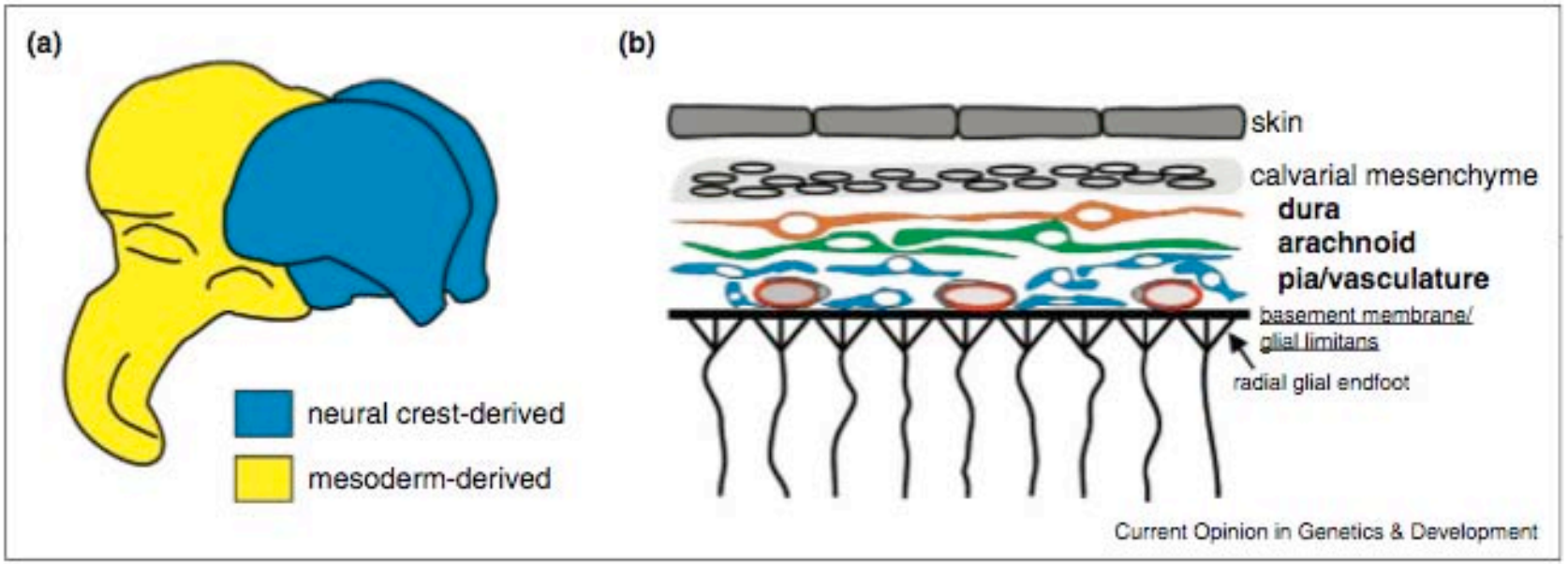


We have got you 'covered': how the meninges control brain development

Siegenthaler JA, Pleasure SJ

Current Opinion in Genetics & Development
2011 vol. 21 (3) pp. 249-55





Origin and structure of the fetal meninges. **(a)** The meninges surrounding the forebrain are neural crest-derived (blue) whereas the meninges covering the rest of the brain and spinal cord originate from the somatic mesoderm. **(b)** The pial meningeal cells and blood vessels are in close contact with the pial basement membrane, the attachment point for radial glial endfeet. The two outer meningeal layers, the arachnoid and dural layers, are single layers of cells beneath the calvarial mesenchyme.

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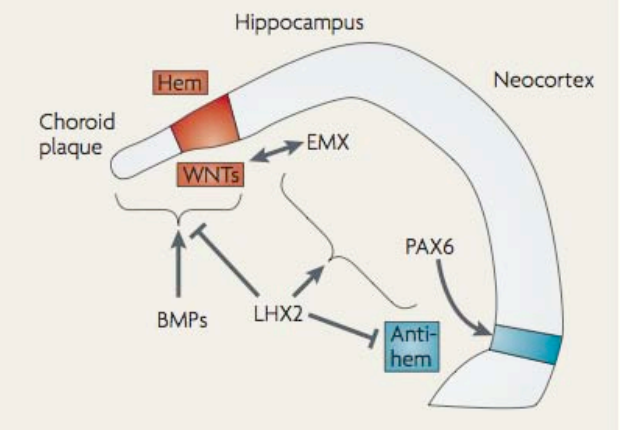
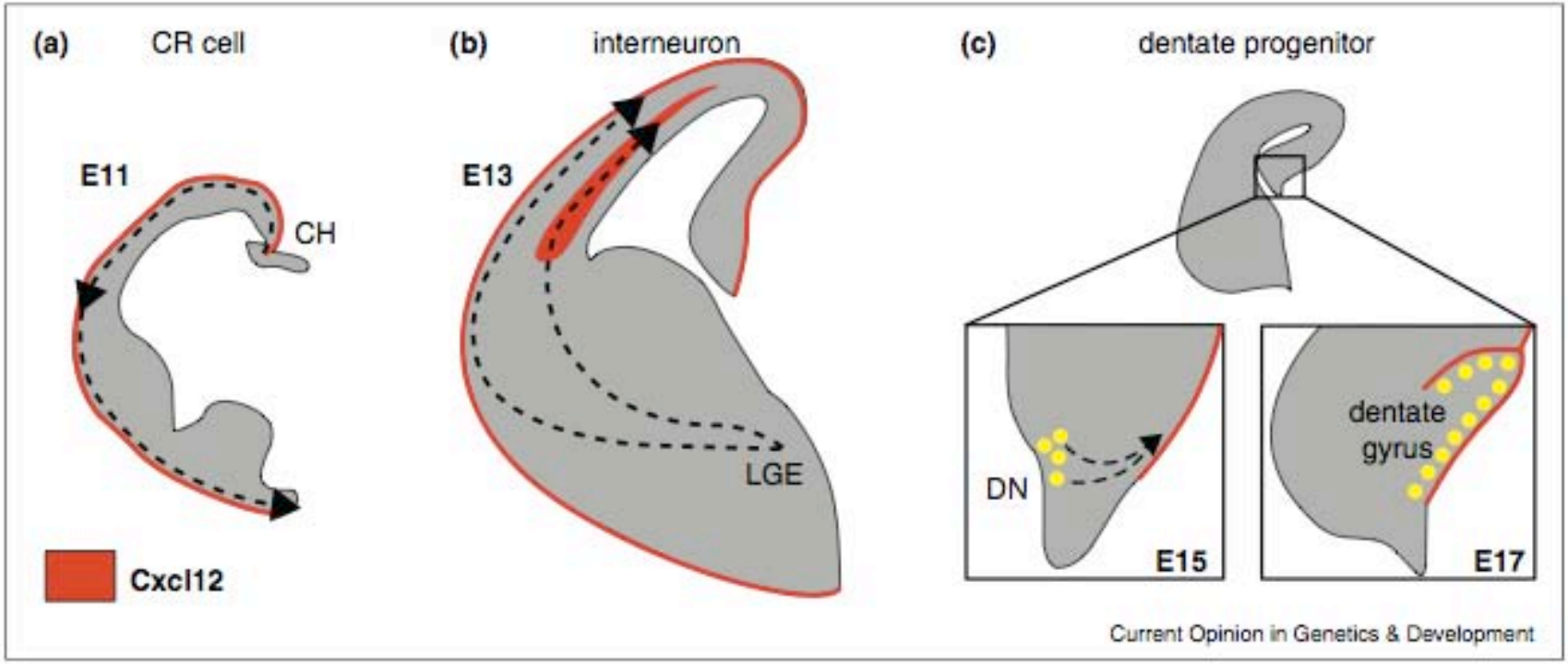


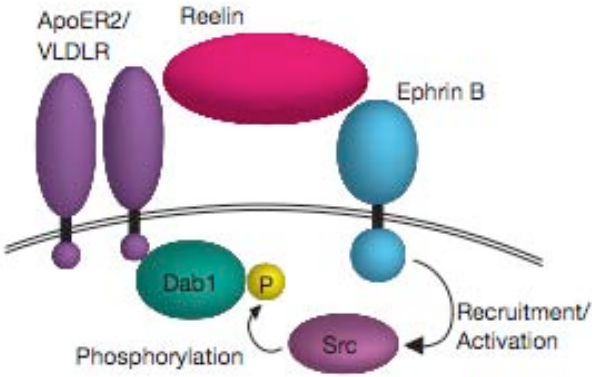


Subpial migratory routes mediated by meningeal-derived Cxcl12. **(a)** Beginning at E11 in the mouse telencephalon, some CR cells originate in the midline cortical hem (CH) then migrate at the periphery, adjacent to the meninges, to cover the entire surface of the forebrain. **(b)** Starting at E13 interneurons migrate from their birthplace in the lateral ganglionic eminence (LGE) to the cortex where they utilize two Cxcl12-lined migratory streams, a subpial route and a deeper path in the SVZ. **(c)** At the beginning of dentate morphogenesis (E15), dentate progenitors migrate away from the neuroepithelium at the dentate notch (DN) toward the Cxcl12-enriched meninges. Two days later, the dentate progenitors are arranged in a subpial neurogenic niche.

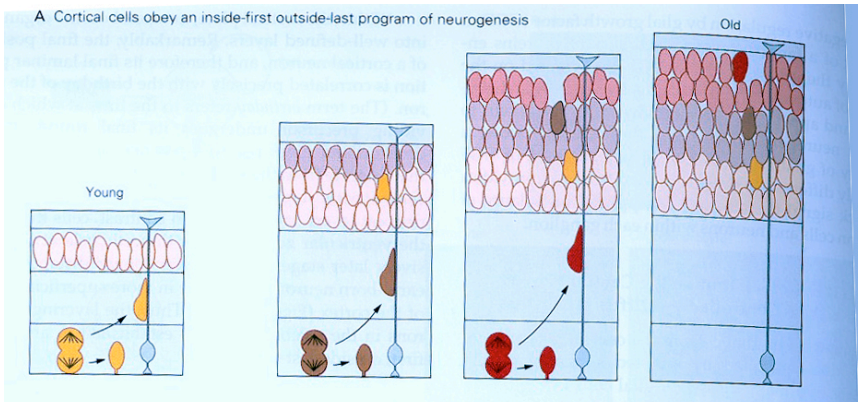
Ephrin Bs are essential components of the Reelin pathway to regulate neuronal migration

Sentürk A, Pfennig S, Weiss A, Burk K, Acker-Palmer A

Nature
2011 vol. 472 (7343) pp. 356-60



Loss of Reelin function in humans results in the severe developmental disorder lissencephaly and it has also been associated with other neurological disorders such as epilepsy, schizophrenia and Alzheimer's disease. The molecular mechanisms by which Reelin activates its receptors and controls cellular functions are largely unknown. Here we show that the neuronal guidance cues ephrin B proteins are essential for Reelin signalling during the development of laminated structures in the brain. We



Autism spectrum disorders: developmental disconnection syndromes

Geschwind DH, Levitt P

Current Opinion in Neurobiology
2007 vol. 17 (1) pp. 103-11

one study [7]. All additional GWA studies discussed further are made on high density SNP arrays. The second pooled DNA GWAS, performed on 660 cases and 1100 controls, identified an intronic SNP of the reelin (*RELN*) gene with a suggestive association (p-value = 2.9×10^{-4}, OR = 1.58) with schizophrenia [8]. This association was female-specific and latter replicated in three independent studies [9–11], thus suggesting that *RELN* is a strong candidate for schizophrenia. Furthermore, *RELN* mutations are also known to cause lissencephaly, a rare brain developmental disorder [12]. The third pooled DNA study was conducted on 574 patients and 605 controls and although no SNP attained a genome-wide significance score, the authors nonetheless emphasized the association of a SNP (p-value = 1.2×10^{-6}) within the coiled-coil domain containing 60 (*CCDC60*) gene [13]; this association was however never validated in subsequent studies.

Mechanisms of synapse and dendrite maintenance and their disruption in psychiatric and neurodegenerative disorders

Lin YC, Koleske AJ

Annu Rev Neurosci
2010 vol. 33 pp. 349-78

Although it is diffusely expressed in neurons, integrin α5, which can pair with β1, localizes to synapses after synaptic stimulation, where it regulates spine stability via Src and Rac activation. This process depends on the activation of GIT1, a signaling adaptor that localizes Rac (Webb et al. 2007). Integrin α5 knockdown in cultured hippocampal neurons leads to an 80% decrease of synapse numbers and a reduced number of spines and dendritic protrusions (Webb et al. 2007). Several integrin ligands, such as laminin and reelin, have also been shown to affect dendritic spine stability (Liu et al. 2001, Seil 1998). Mutations or altered expression of these ligands have been linked to neurological disorders, including schizophrenia and AD, suggesting that altering integrin signaling may be involved in disease pathology (Costa et al. 2001, Huang et al. 1995, Liu et al. 2001, Rodriguez et al. 2000, Zhan et al. 1995).

Cytokines and CNS development

Deverman BE, Patterson PH

Neuron
2009 vol. 64 (1) pp. 61–78

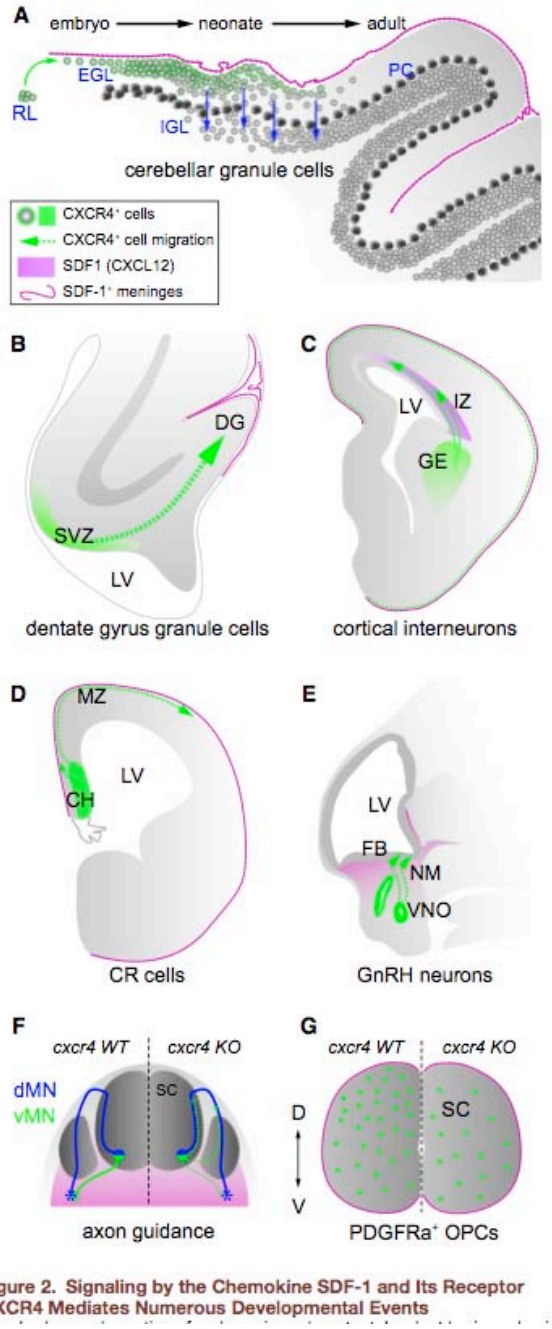
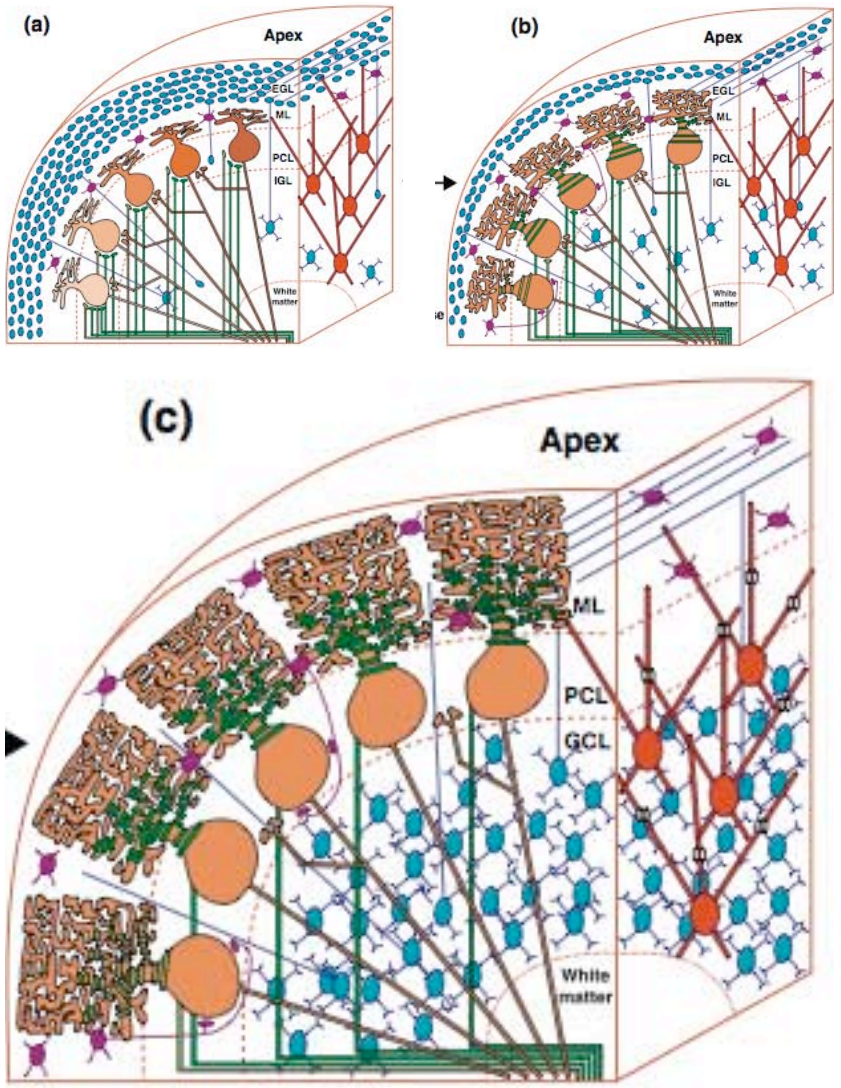


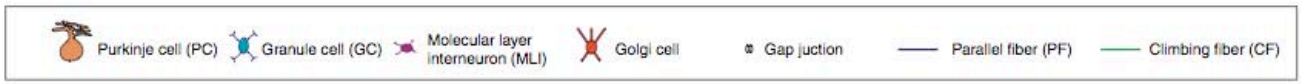
Figure 2. Signaling by the Chemokine SDF-1 and Its Receptor CXCR4 Mediates Numerous Developmental Events

The metamorphosis of the developing cerebellar microcircuit

van Welie I, Smith IT, Watt AJ

rrent Opinion in Neurobiology
11 vol. 21 (2) pp. 245–53





Orienting Fate: Spatial Regulation of Neurogenic Divisions

Neuron 72, October 20, 2011 ©2011 Elsevier Inc. 191

Xiaoqun Wang,[1,2] Jan H. Lui,[1,2] and Arnold R. Kriegstein[1,2,*]
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University of California, San Francisco, 35 Medical Center Way, San Francisco, CA 94143, USA
*Correspondence: kriegsteina@stemcell.ucsf.edu
DOI 10.1016/j.neuron.2011.10.003

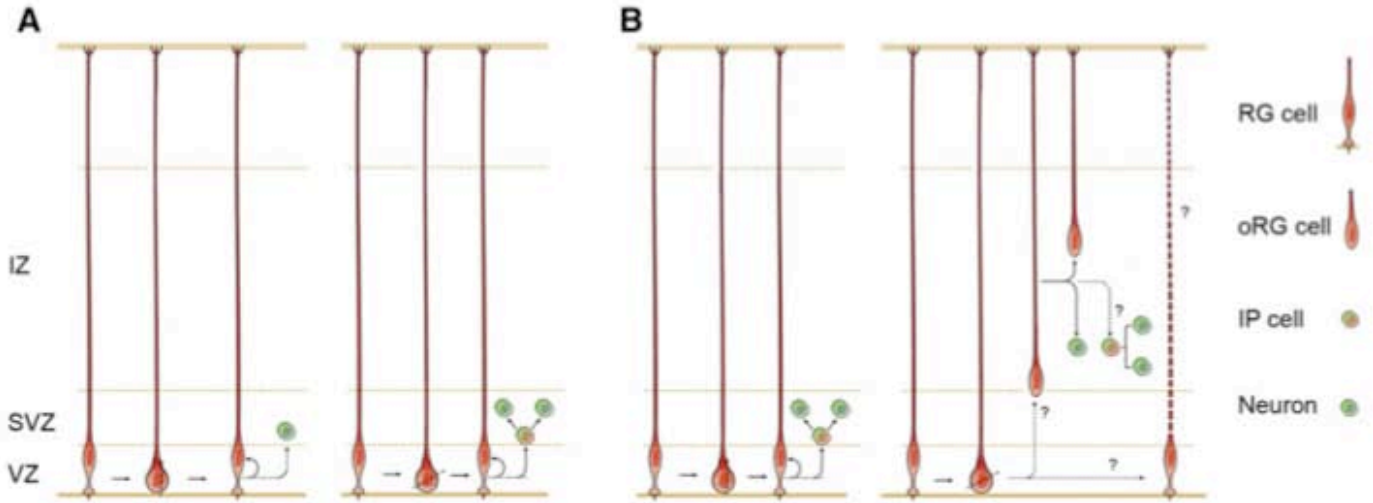
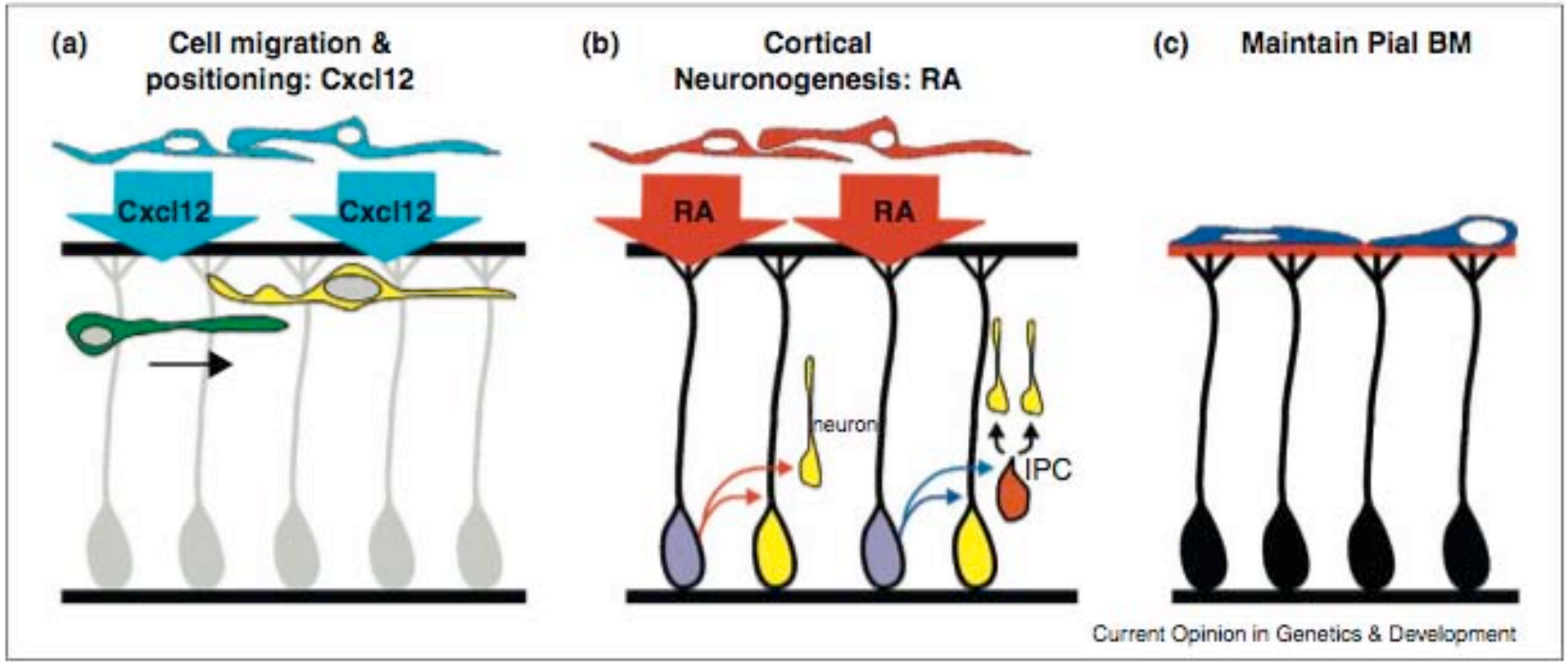


Figure 1. Radial Glial Cell Divisions Mediated by Different Cleavage Plane Orientations
(A) Postiglione et al. propose that radial glial cells (RG) that divide with a vertical cleavage plane generate a neuron and self-renew (left panel). Overexpression of Inscuteable randomizes the cleavage plane angle, which induces a greater proportion of oblique RG cell divisions. The authors observe that the number of IP cells is increased under this mode of division, and suggest that oblique cleavages preferentially produce IP cells (right panel).
(B) An alternative interpretation is that vertical divisions produce IP cells (left panel), and oblique divisions produce oRG cells (right panel; Konno et al., 2008; Shitamukai et al., 2011). The oRG cells may function as nonventricular stem cells that also produce IP cells or neurons (Hansen et al., 2010; Wang et al., 2011).

We have got you 'covered': how the meninges control brain development

Siegenthaler JA, Pleasure SJ

Current Opinion in Genetics & Development
2011 vol. 21 (3) pp. 249–55



Three main functions of the meninges during brain development. **(a)** Through the release of the chemokine Cxcl12, the meninges regulate cell migration and positioning of multiple neuronal populations throughout development. **(b)** During cortical development, RA produced by the meninges induces neural progenitors in the cerebral cortex to produce neurons directly or indirectly through an intermediate progenitor cell (IPC). **(c)** Meningeal fibroblasts in the inner pial layer organize and maintain the BM, a critical attachment point for radial glial endfeet.

Orienting Fate: Spatial Regulation of Neurogenic Divisions

Xiaoqun Wang,[1,2] Jan H. Lui,[1,2] and Arnold R. Kriegstein[1,2,*]
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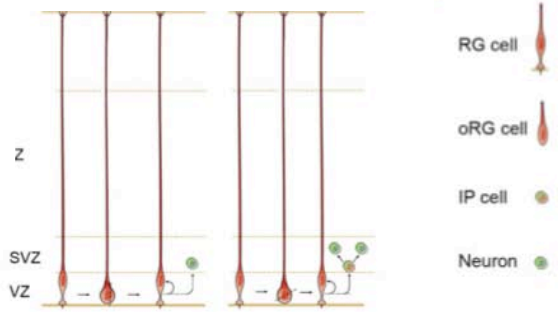
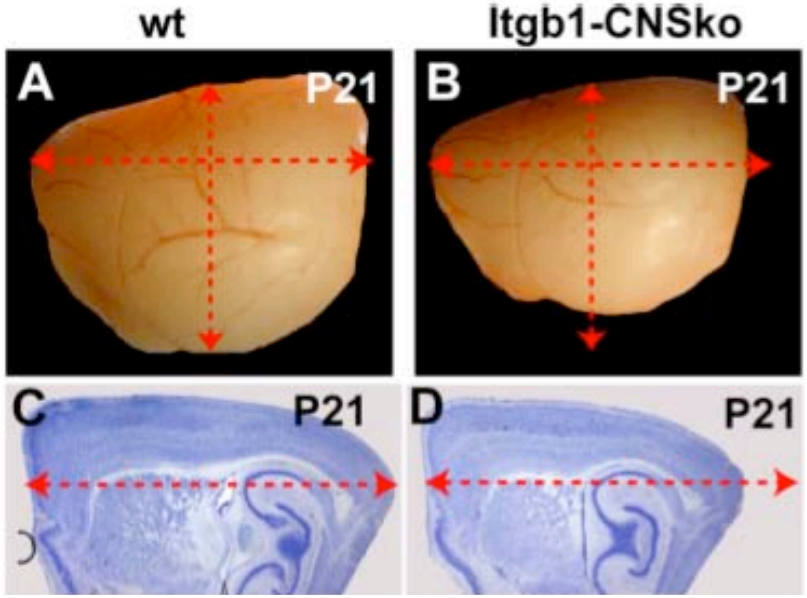
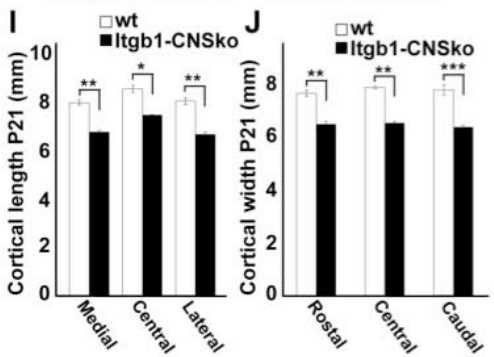
*Correspondence: kriegsteina@stemcell.ucsf.edu
DOI 10.1016/j.neuron.2011.10.003

Neuron 72, October 20, 2011



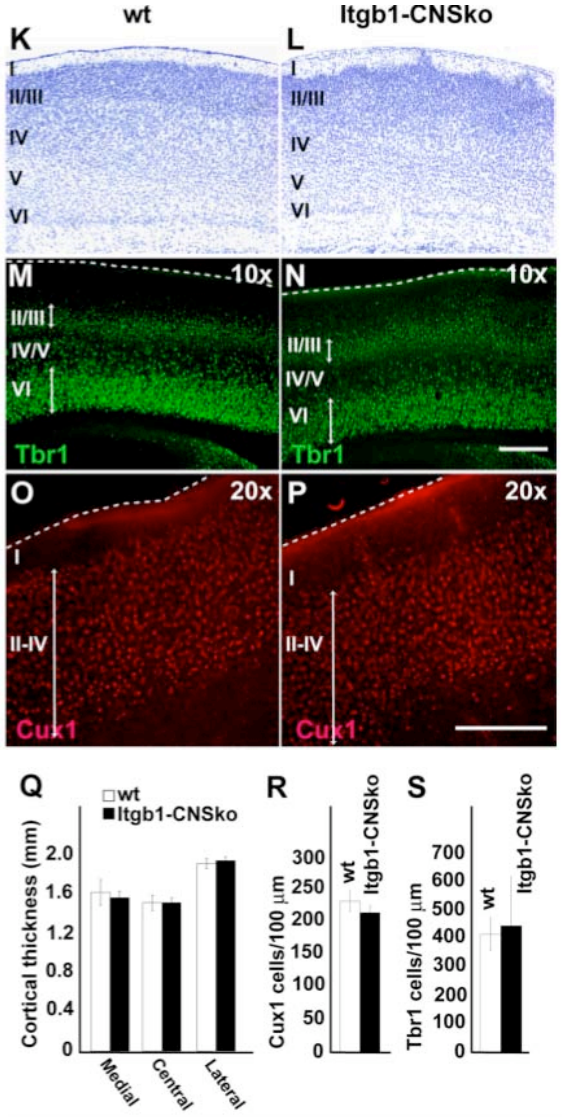




Regulation of radial glial survival by signals from the meninges

Radakovits R, Barros CS, Belvindrah R, Patton B, Müller U

J Neurosci
2009 vol. 29 (24) pp. 7694-705



Regulation of radial glial survival b signals from the meninges

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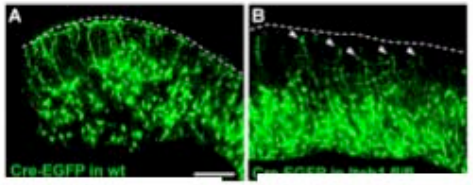

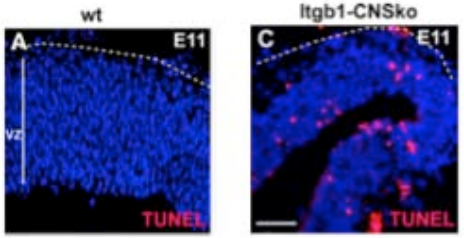

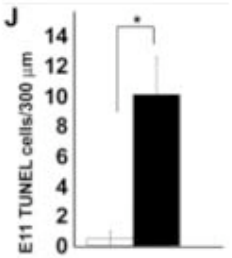

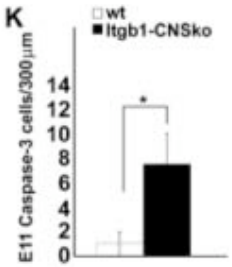

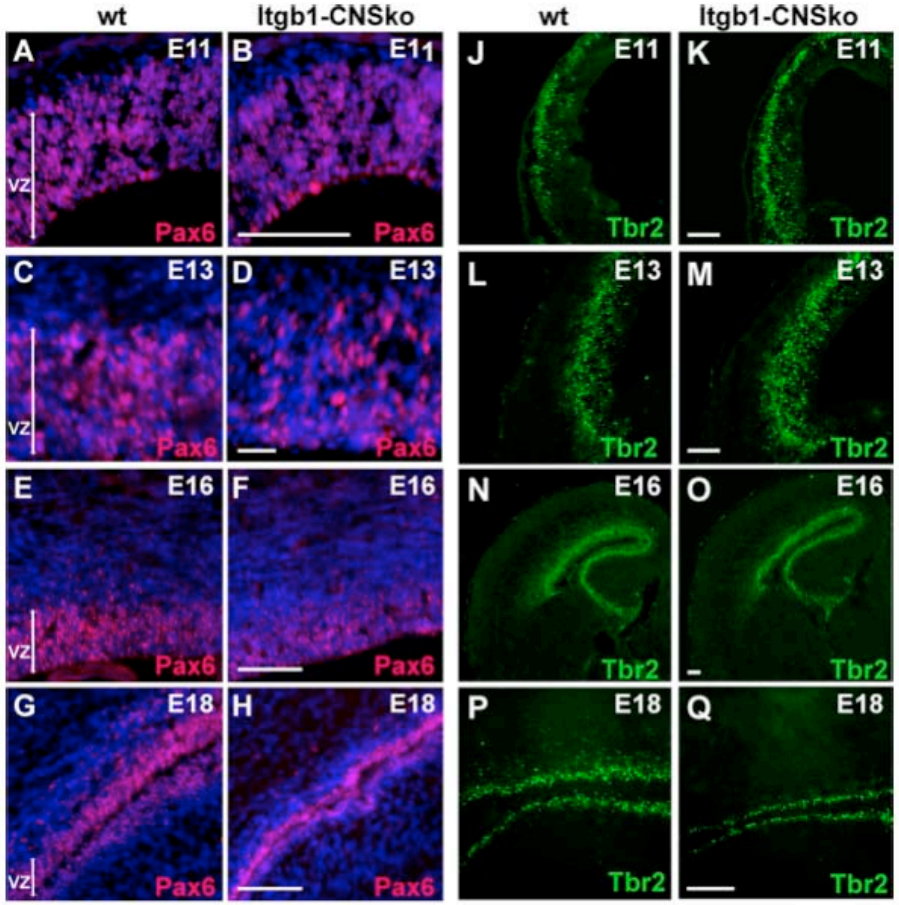

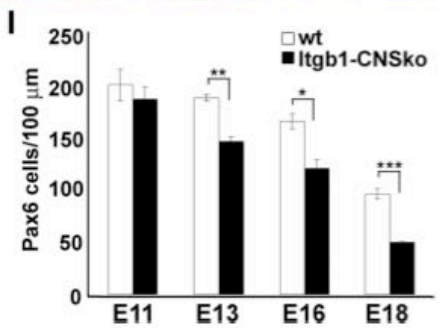

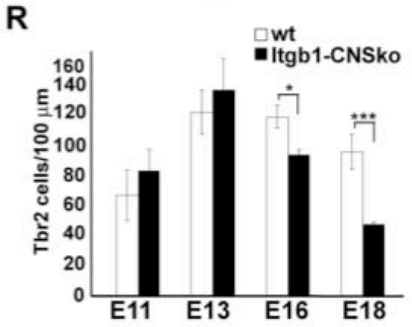

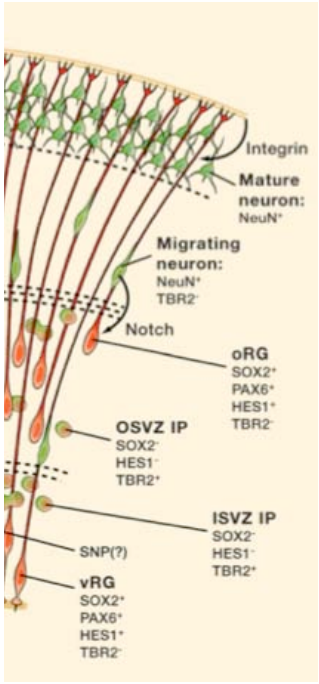

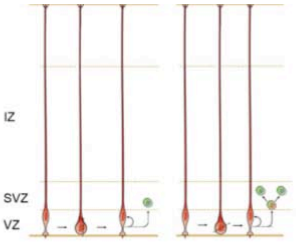

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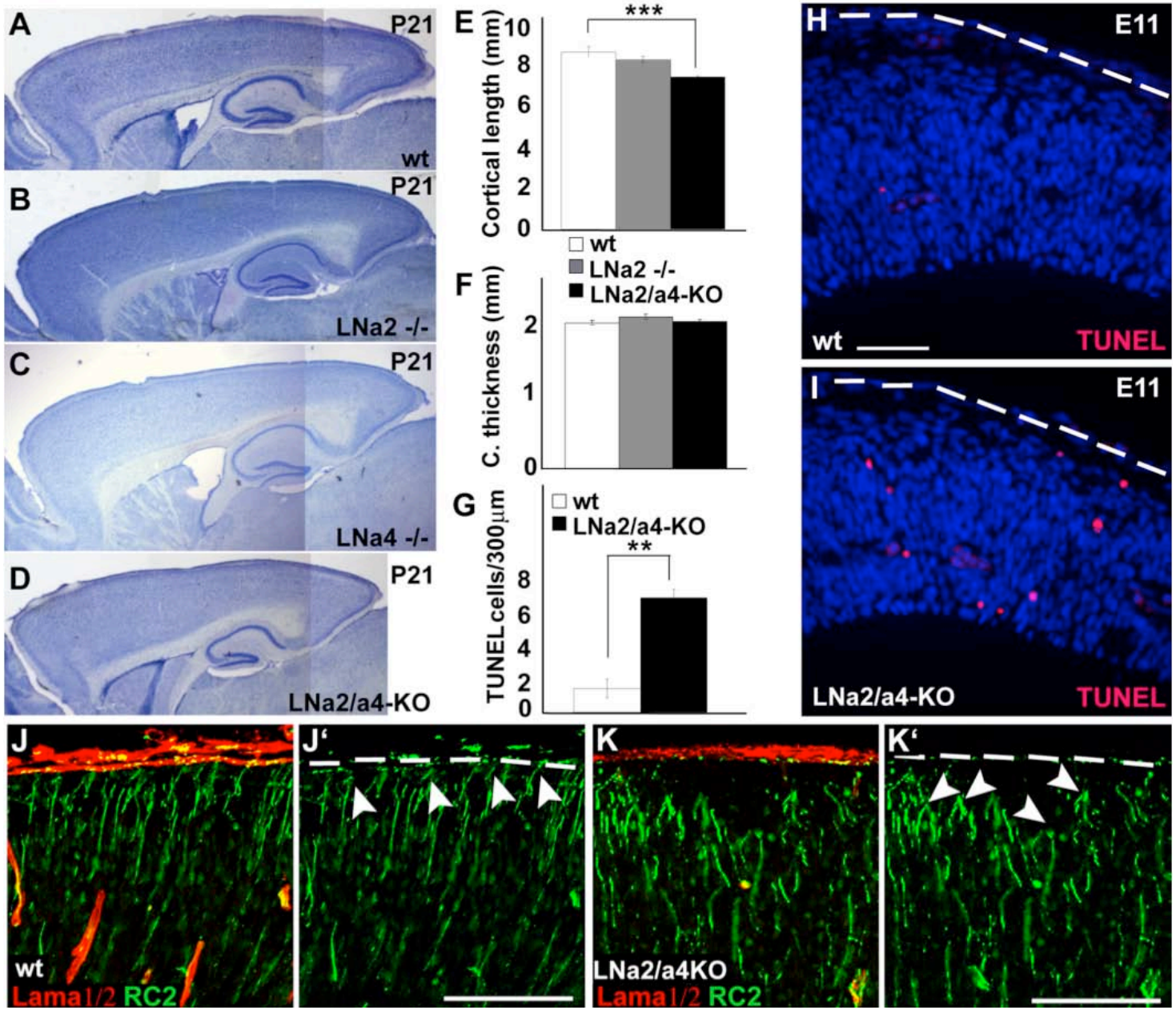
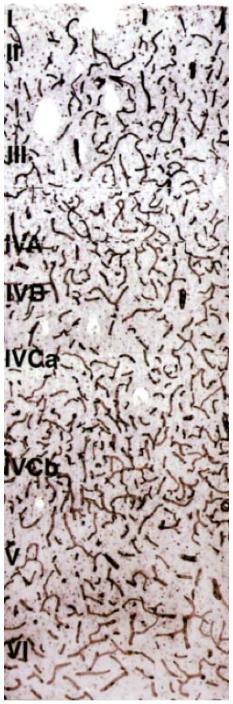
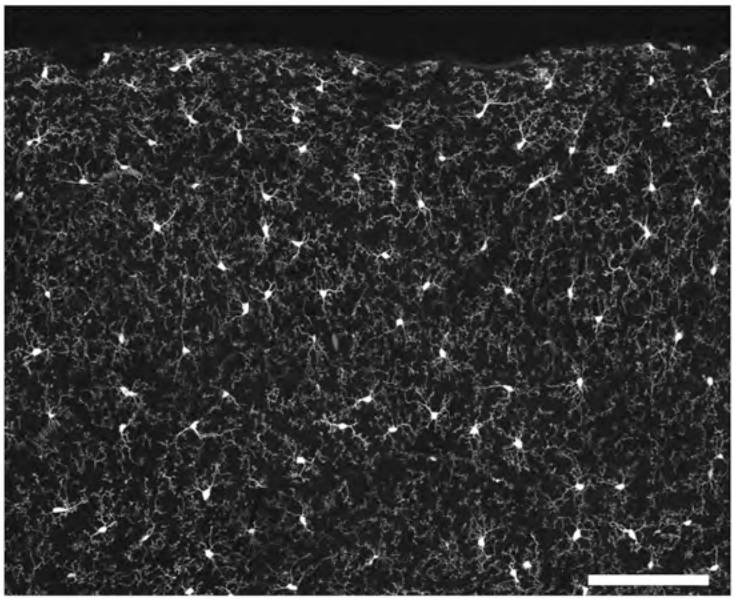


Microglia dynamics and function in the CNS

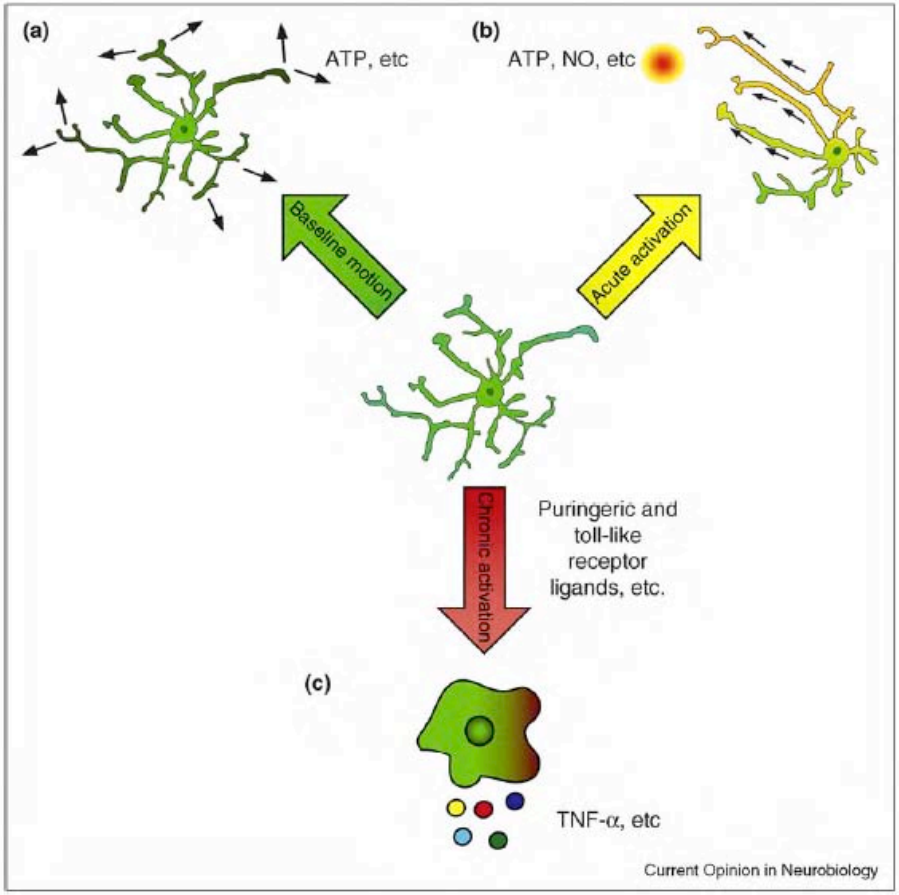
Christopher N Parkhurst and Wen-Biao Gan

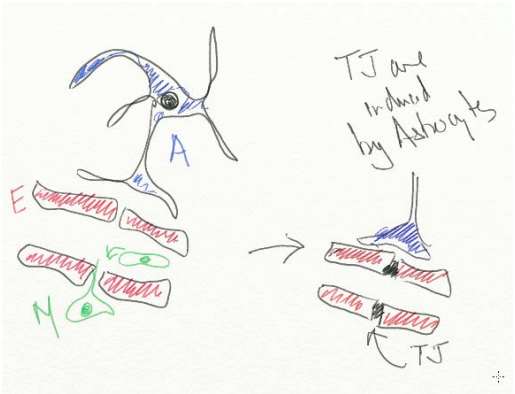
Current Opinion in Neurobiology 2010, **20**:595–600





The multiple activities of microglia. Microglia exist in a highly ramified state within normal brain tissue (center). **(a)** The processes of microglia display constitutive motility which is dependent on ATP signaling. The functional significance of this baseline motility remains unclear. **(b)** Microglial processes are rapidly recruited to sites of CNS tissue damage. The signals responsible for this recruitment include ATP and NO. **(c)** Signaling through many pathways including those utilizing purinergic (P1, P2X, and P2Y) and Toll-like receptors (TLRs) leads to a state of chronic microglial activation. As a result, microglia may release soluble factors that act in a trophic, protective, or inflammatory manner on surrounding CNS cells.

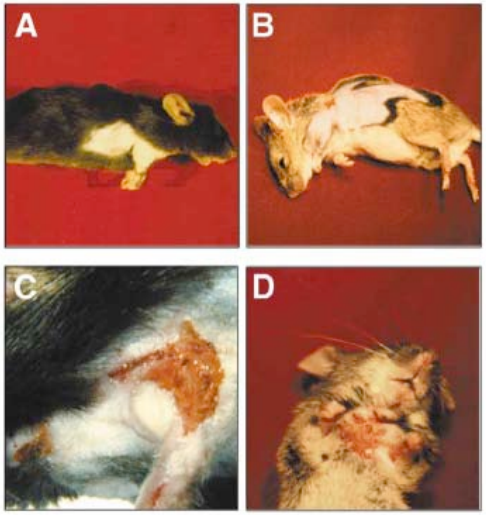




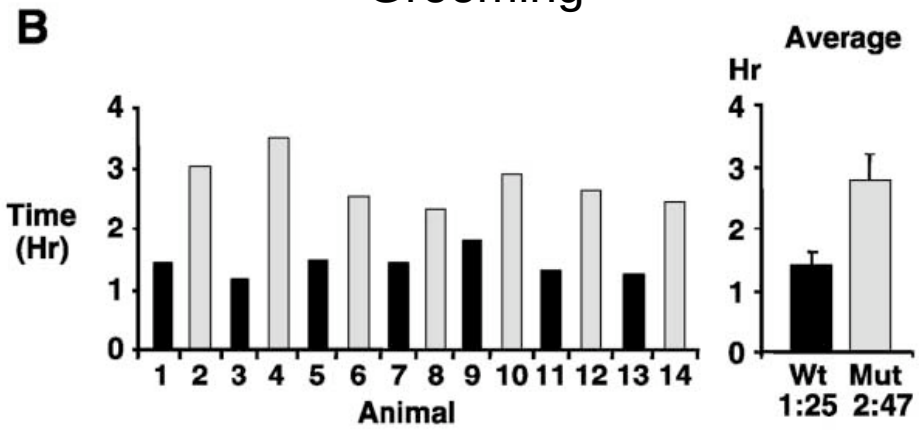
Neuron, Vol. 33, 23–34, January 3, 2002, Copyright ©2002 by Cell Press

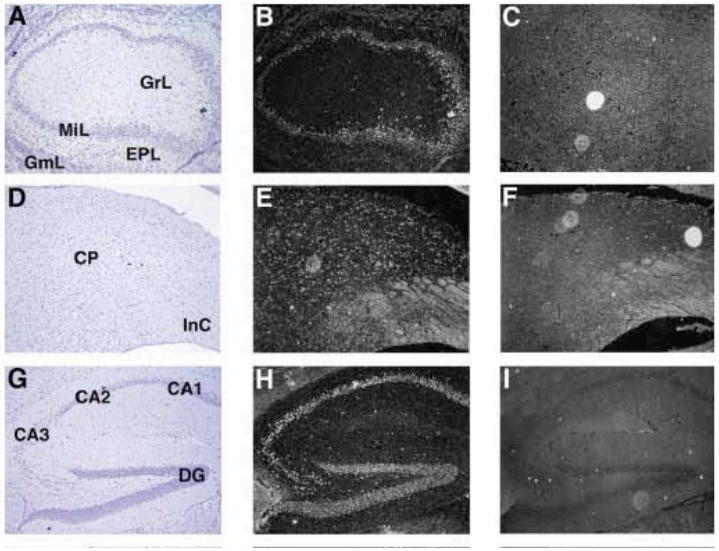
Hoxb8 Is Required for Normal Grooming Behavior in Mice

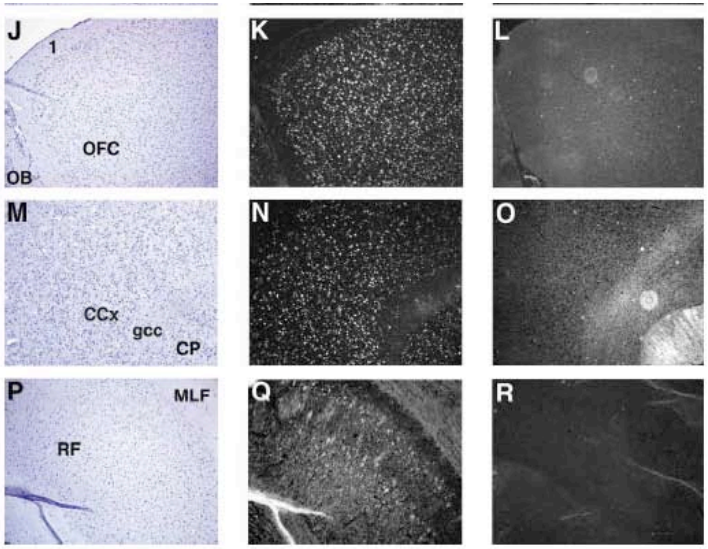
Joy M. Greer and Mario R. Capecchi[1]



Grooming







Hematopoietic Origin of Pathological Grooming in *Hoxb8* Mutant Mice

Shau-Kwaun Chen,[1] Petr Tvrdik,[1] Erik Peden,[1] Scott Cho,[2] Sen Wu,[1] Gerald Spangrude,[2] and Mario R. Capecchi[1,*]

Cell *141*, 775–785, May 28, 2010 ©2010 Elsevier Inc.

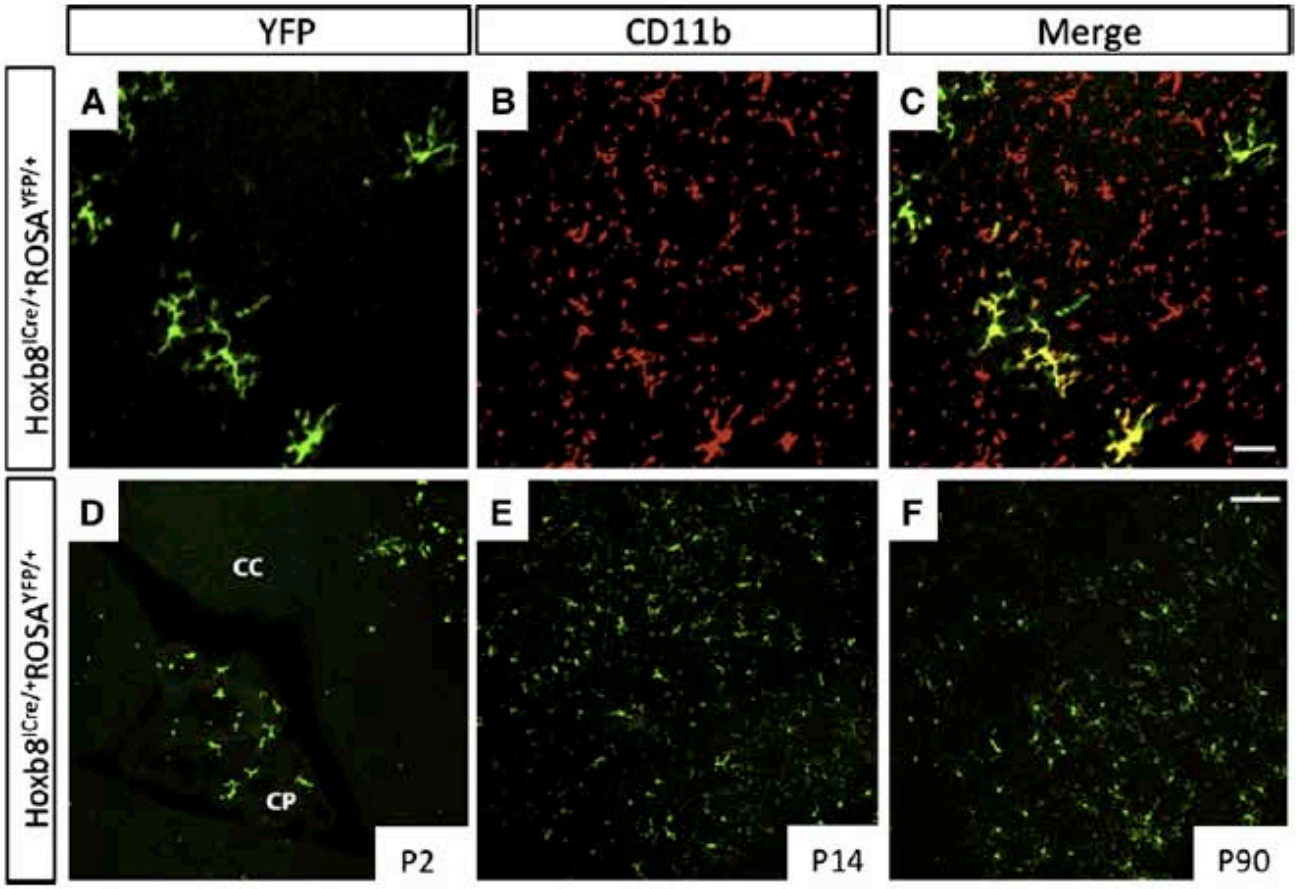


Figure 1. *Hoxb8* Cell Lineage Gives Rise to Brain Microglia

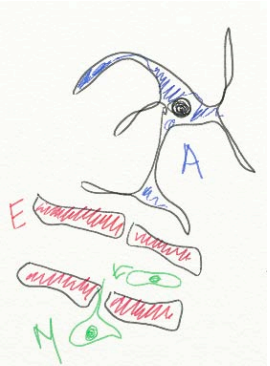
(A–F) Analysis of *Hoxb8* lineage in mice heterozygous for the *Hoxb8-ICre* and *ROSA26*-YFP alleles. To determine if cells of *Hoxb8* lineage in the brain are microglia, the identity of YFP-positive cells was examined by immunohistochemistry. Sagittal sections of the adult cerebral cortex were costained with anti-GFP antibody (A) and anti-CD11b antibody (B).

(C) Colocalization of both signals shows that these cells are microglia.

(D) Cortical microglia originating from the Hoxb8 cell lineage first appear in the brain during the first two postnatal days (P2), in the choroid plexus, and in association with the ventricular lining.

(E) The number of YFP-positive cells markedly increases by P14 throughout the cerebral cortex. This high abundance is maintained in the adult life (F).

CP, choroid plexus; CC, cerebral cortex. See also Figure S1.



Hematopoietic Origin of Pathological Grooming in *Hoxb8* Mutant Mice

Shau-Kwaun Chen,[1] Petr Tvrdik,[1] Erik Peden,[1] Scott Cho,[2] Sen Wu,[1] Gerald Spangrude,[2] and Mario R. Capecchi[1,*]

Cell *141*, 775–785, May 28, 2010 ©2010 Elsevier Inc.

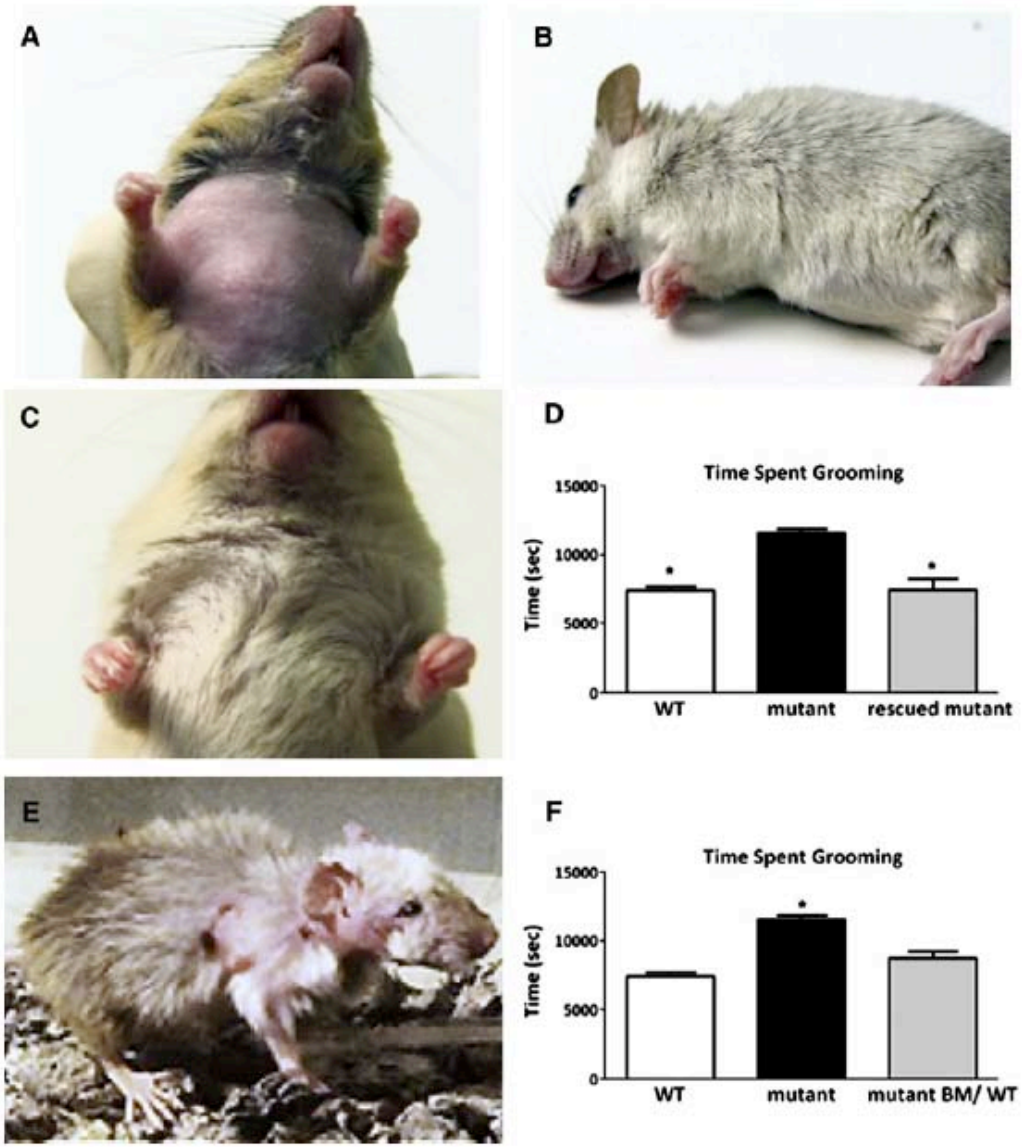


Figure 3. Rescue of Excessive Grooming and Hair Removal Defect in *Hoxb8* Mutant Mice Transplanted with Normal Bone Marrow

(A) *Hoxb8* mutant transplanted with normal bone marrow showing typical hair loss 4 weeks after transplantation.

(B) *Hoxb8* mutant mouse 3 months after transplantation with wild-type bone marrow cells showing complete recovery from hair loss.

(C) A close-up view of the ventral anterior part of the body, which is the primary region of hair removal.

(D) Laboras data collected over a 24 hr period with *Hoxb8* mutant mice transplanted with wild-type bone marrow cells show significant decrease in grooming times relative to *Hoxb8* mutant mice. White bar represents wild-type controls (n = 22) relative to *Hoxb8* mutants (n = 25). Gray bar indicates the grooming time of *Hoxb8* mutant mice rescued by normal bone marrow transplants (n = 6). All values are mean ± standard error of the mean SEM. *$p < 0.05$ versus mutant.

(E) A wild-type mouse, transplanted with *Hoxb8* mutant bone marrow, showing a hair removal and lesion pattern typical of *Hoxb8* mutant mice.

(F) Grooming times of two wild-type mice transplanted with mutant bone marrow that developed hairless patches. These experimental animals (gray column, n = 2) showed elevated grooming times, although not as long as the average observed in a large cohort of *Hoxb8* mutants. Error bars represent SEM. *$p < 0.05$ versus wild type.

See also Figure S3.

Maternal infection and immune involvement in autism

Patterson PH

Trends in Molecular Medicine
2011 vol. 17 (7) pp. 389–94

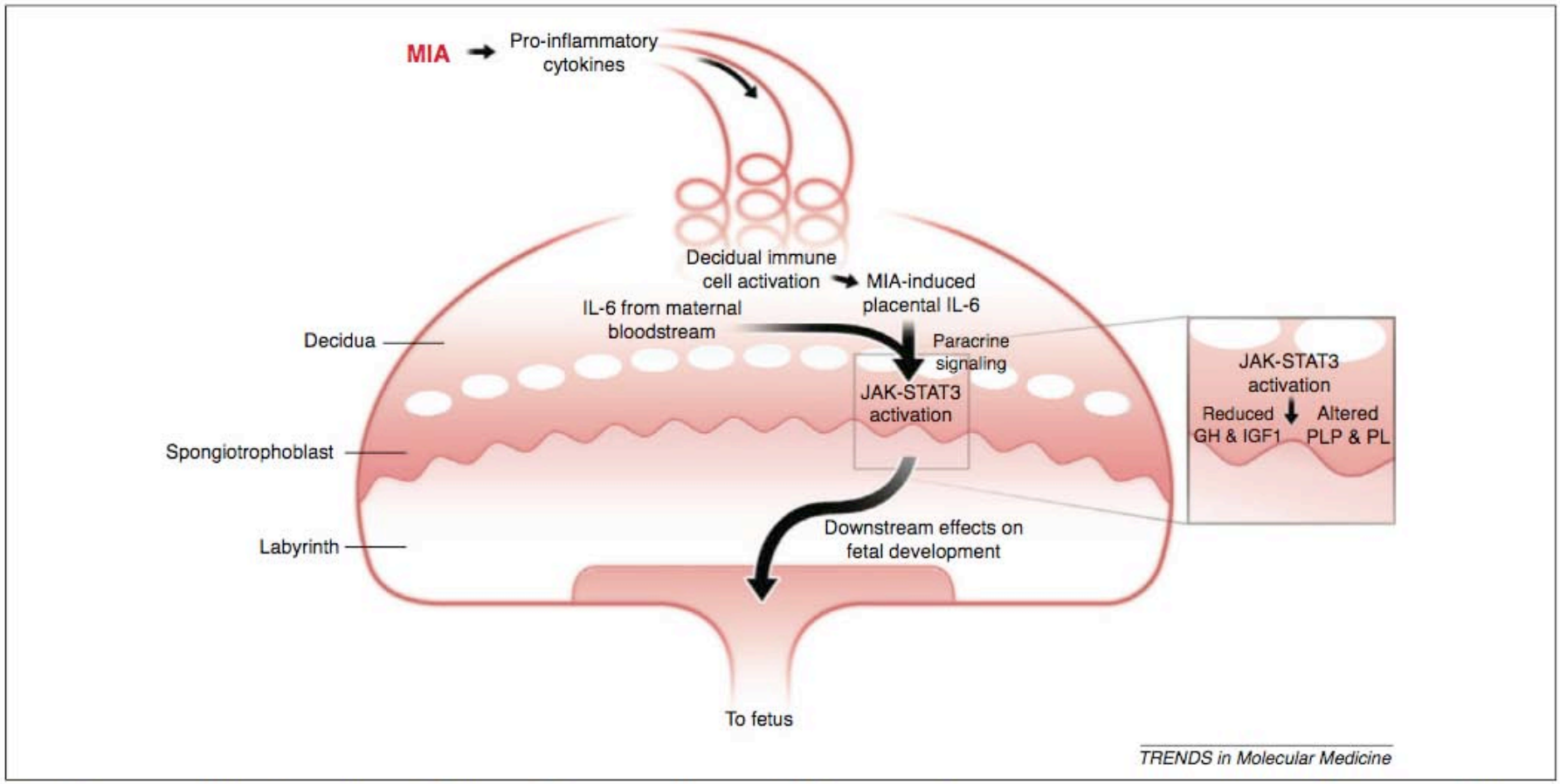


Figure 1. Summary of MIA-induced effects on the placenta. The maternal injection of poly(I:C) activates the maternal immune system, elevating IL-6, which enters the spiral arteries that descend through the decidua and spongiotrophoblast layers, filling the maternal blood spaces of the labyrinth. Resident immune cells in the decidua are activated to express CD69 and further propagate the inflammatory response. IL-6 produced by decidual cells acts on target cells in the spongiotrophoblast layer. The ligation of the IL-6Ra with gp130 causes JAK-STAT3 activation and increases in acute phase proteins, such as SOCS3, and the downregulation of placental growth hormone production. This leads to reduced insulin-like growth factor-binding protein 3 and IGFI. Global changes in STAT3 activation in the spongiotrophoblast layer alter the production of placenta-specific prolactin protein and other prolactin proteins. These various changes in endocrine factors probably lead to acute placental pathophysiology and subsequent effects on fetal development. (Reproduced from [31] with permission.)

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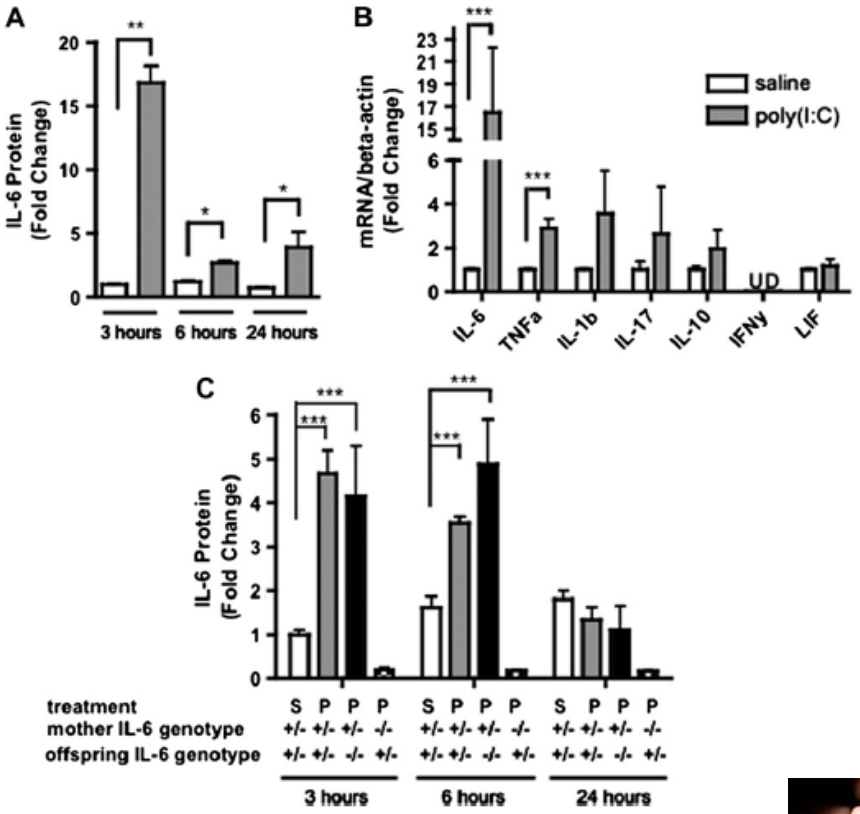

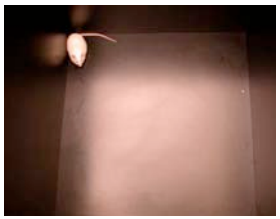

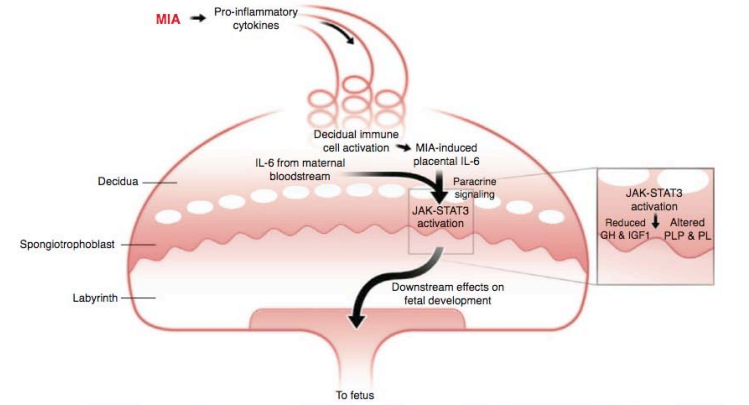

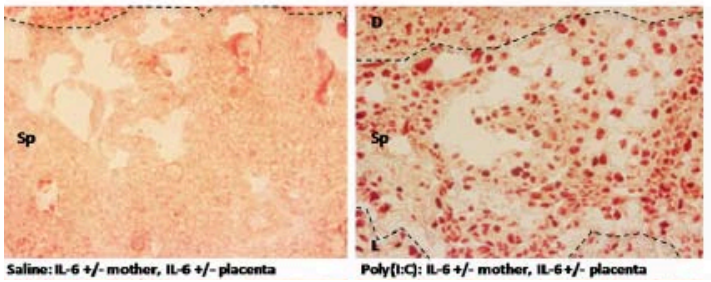

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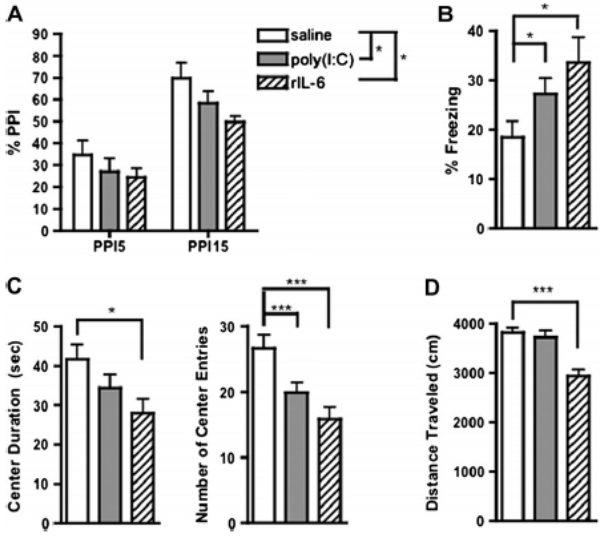

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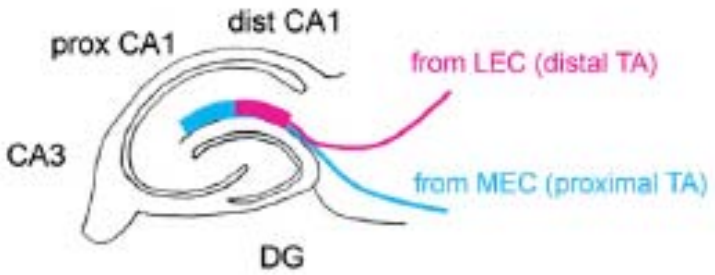

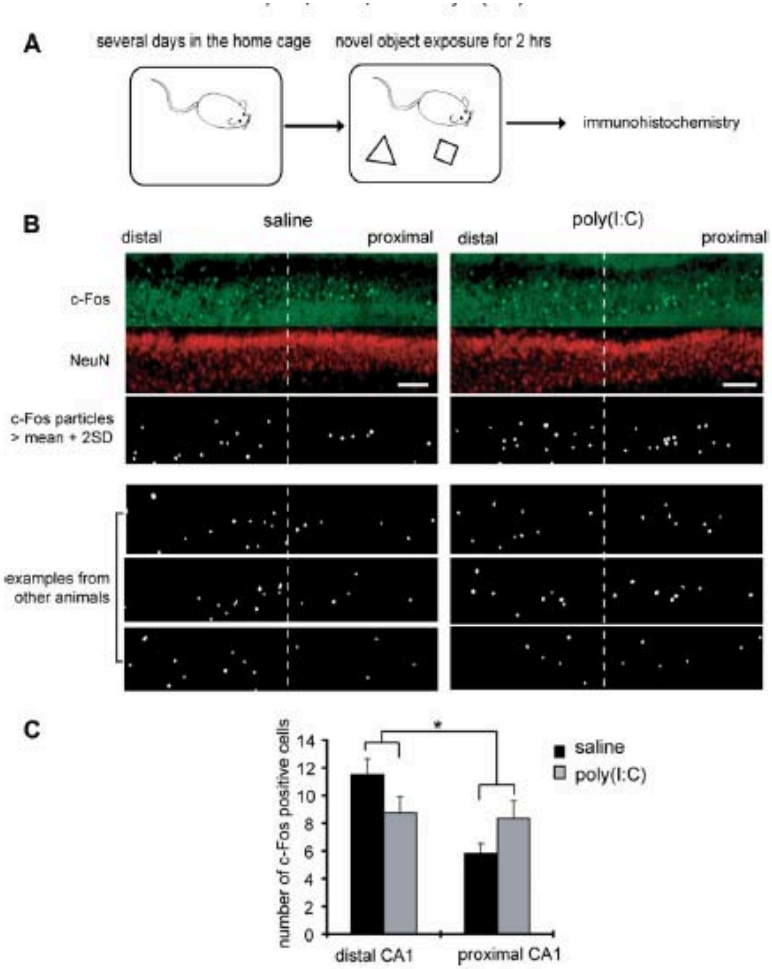

Distal= novel object recognition
Projette sur le cortex enthorhinal latéral (LEC)

Dans le contrôle nette différence d'activité entre distal (objet) et proximal. Différence perdue dans le poly-IC

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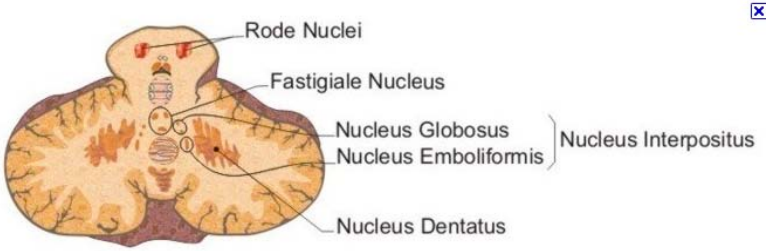
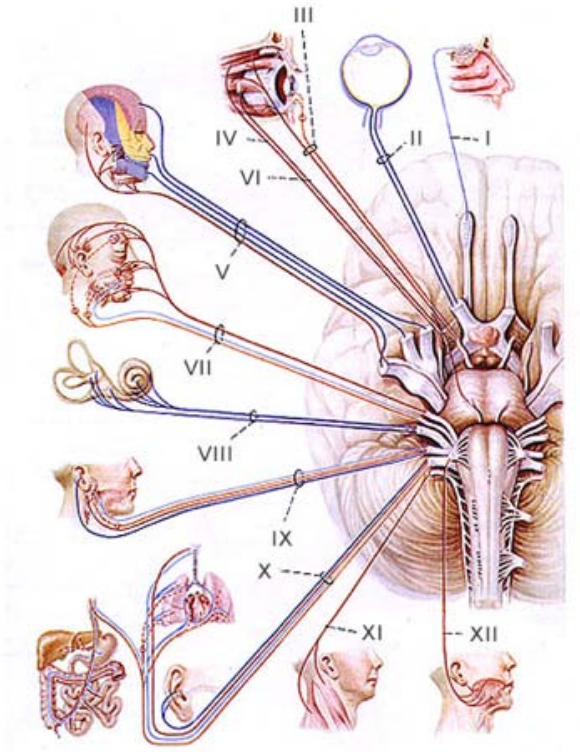
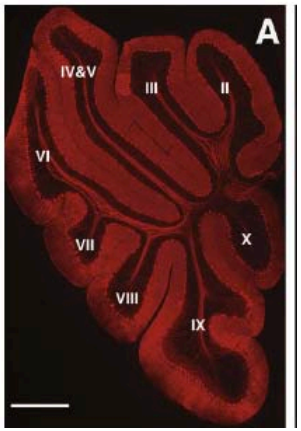
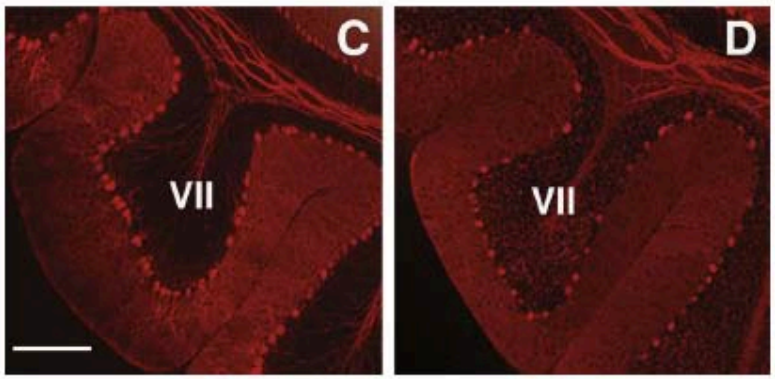


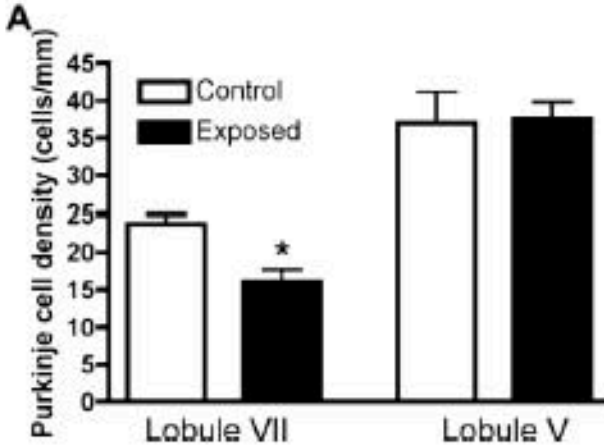




Nouveau né

contrôle Infection





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