Comment et pourquoi le cerveau gyre-t-il ?

Homa Adle-Biassette,

Hôpital Lariboisière , U1141

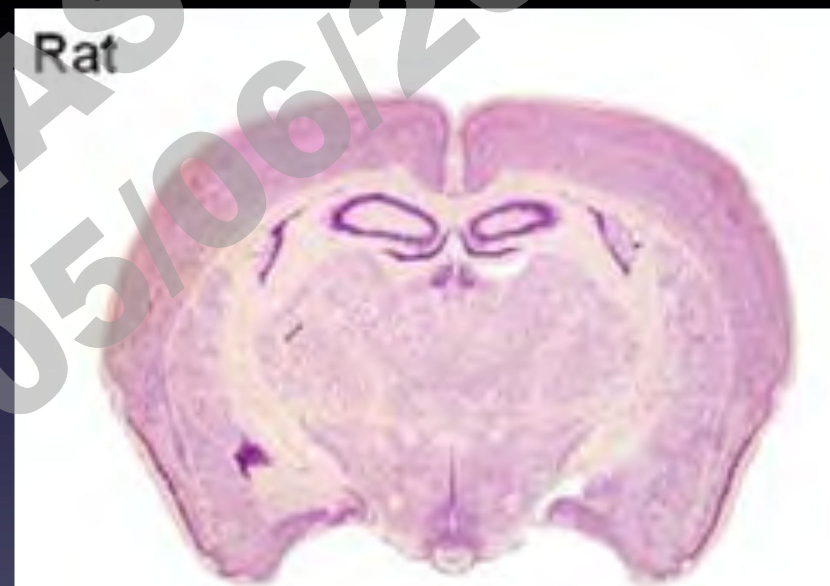
Jeannette Nardelli, Pierre Gressens, Sara Cipriani,

Fabien Guimiot, Anne-Lise Delezoide

INSERM U1141 et BDD Hôpital Robert Debré

SOFFOET Juin 2015

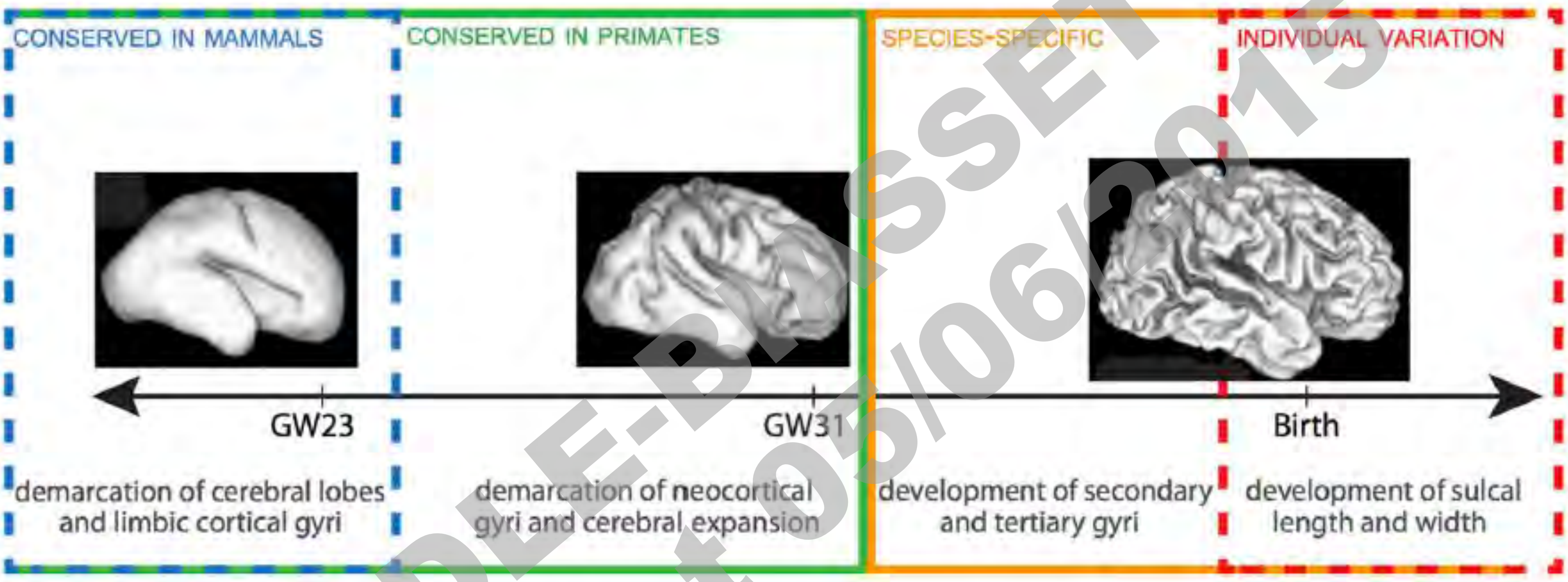
Poids du cerveau et du corps, surface cerveau



Gyration apparaît avant l'augmentation significative du volume cortical

Maturation- Gyrification

Gyrification



- Degré de gyrencéphalie stabilisé vers 1 an chez l'homme et le macaque

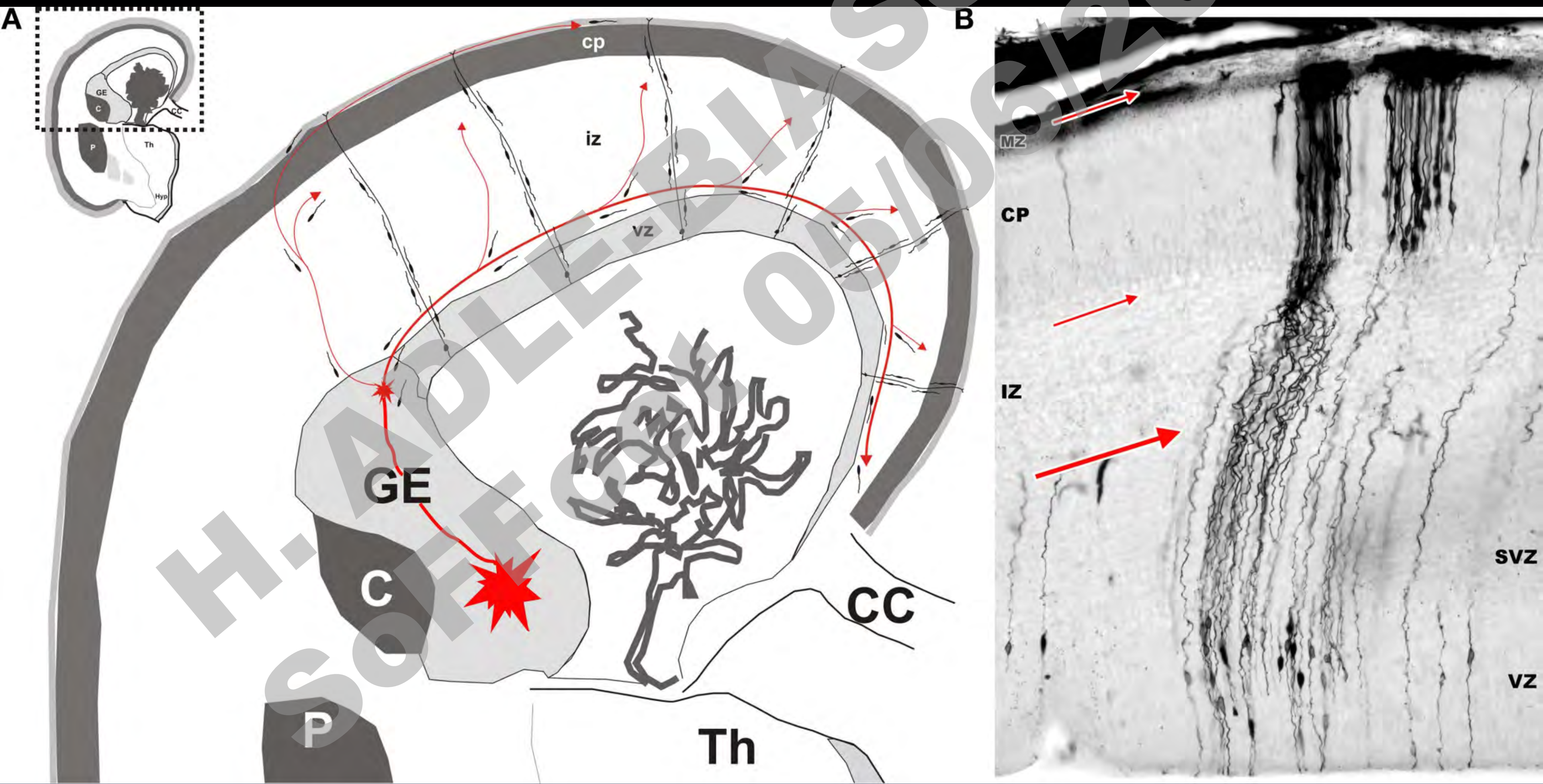
frontiers in HUMAN NEUROSCIENCE
HYPOTHESIS AND THEORY ARTICLE

Conical expansion of the outer subventricular zone and the role of neocortical folding in evolution and development

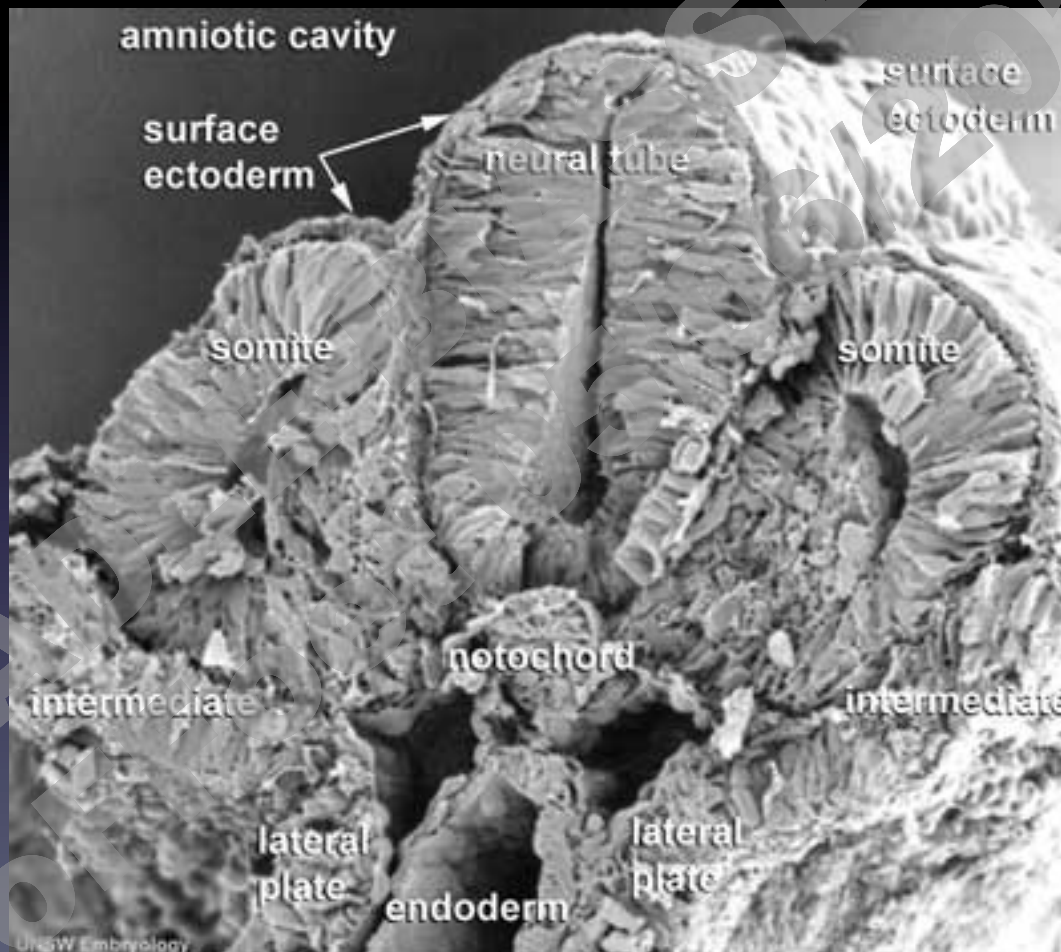
Eric Lewitus, Iva Kelava and Wieland B. Huttner*

Origines et patrons de migration des deux types de neurones corticaux

Petanjek 2009



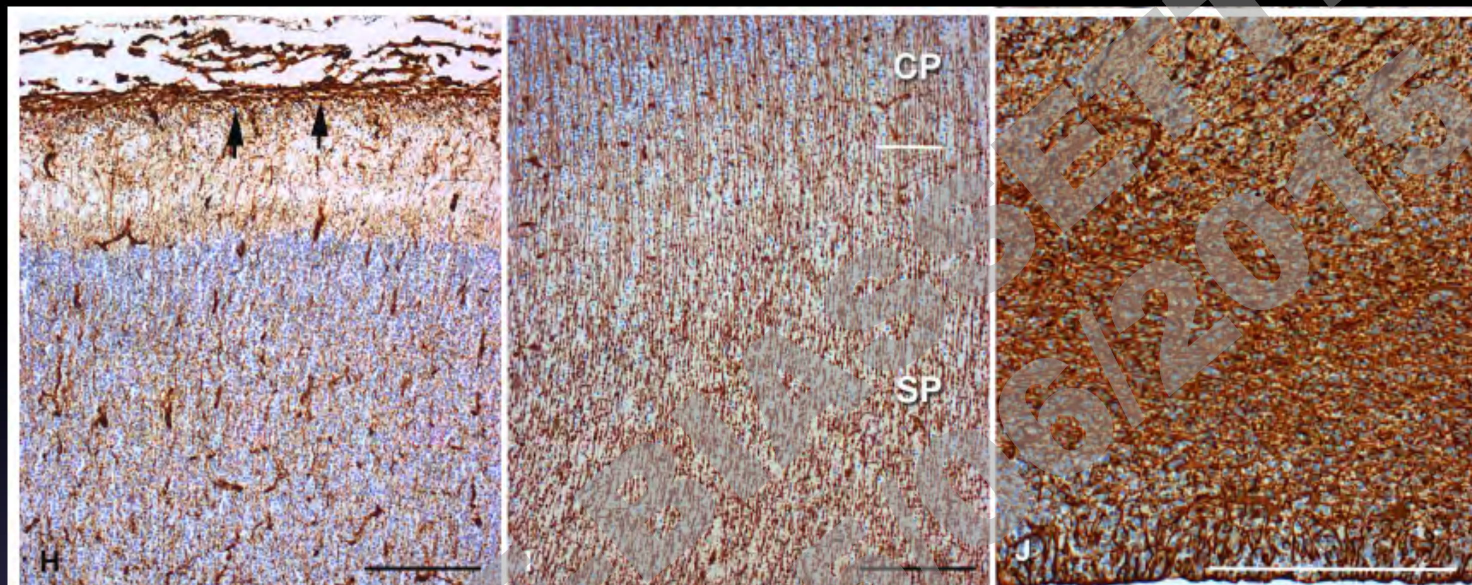
Neurogenèse

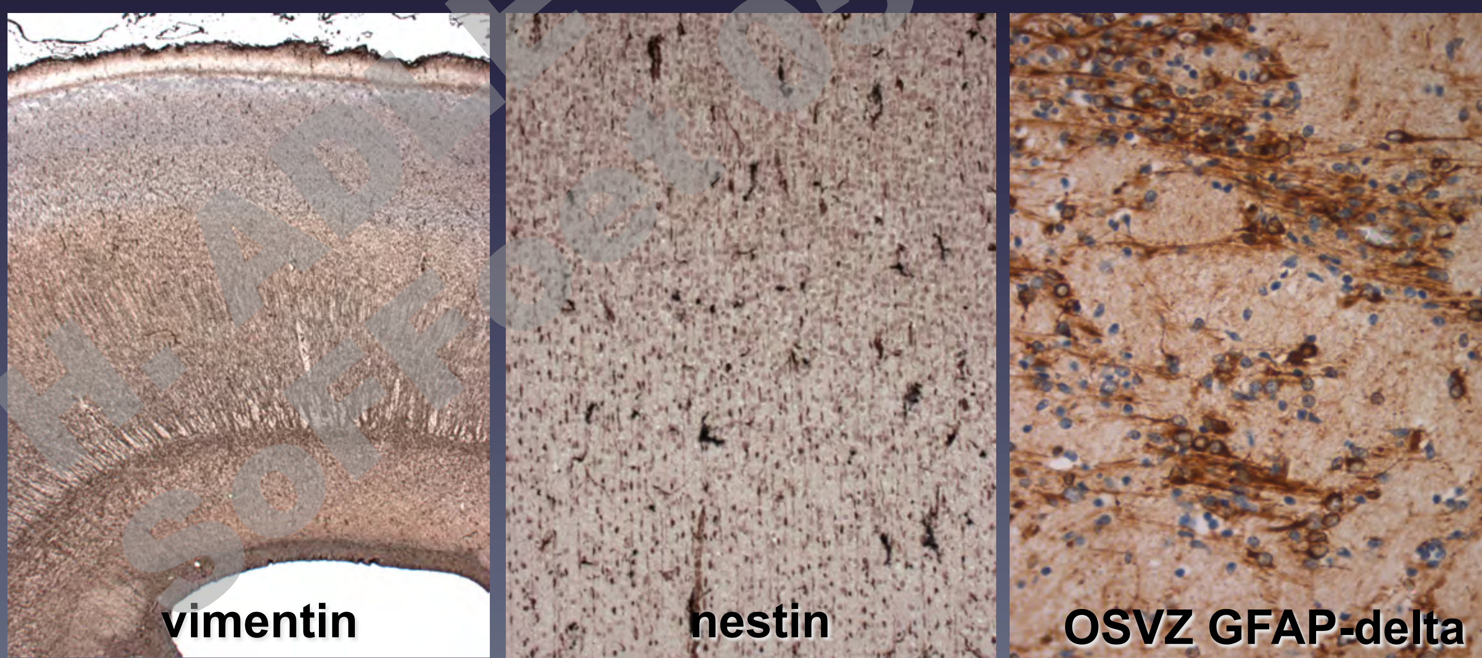


Cellules neuroépithéliales => glie radiaire

- NSC => Glie radiaire
  - forkhead box G1 (FOXG1)
  - LIM homeobox 2 (LHX2)
  - paired box 6 (PAX6)
  - empty spiracles homologue 2 (EMX2)
- Caractéristiques moléculaires communs
  - Nestine
  - Antigènes reconnus par Ac anti-RC1 et RC2

Glie radiaire





Evolution of the neocortex: a perspective from developmental biology

Pasko Rakic

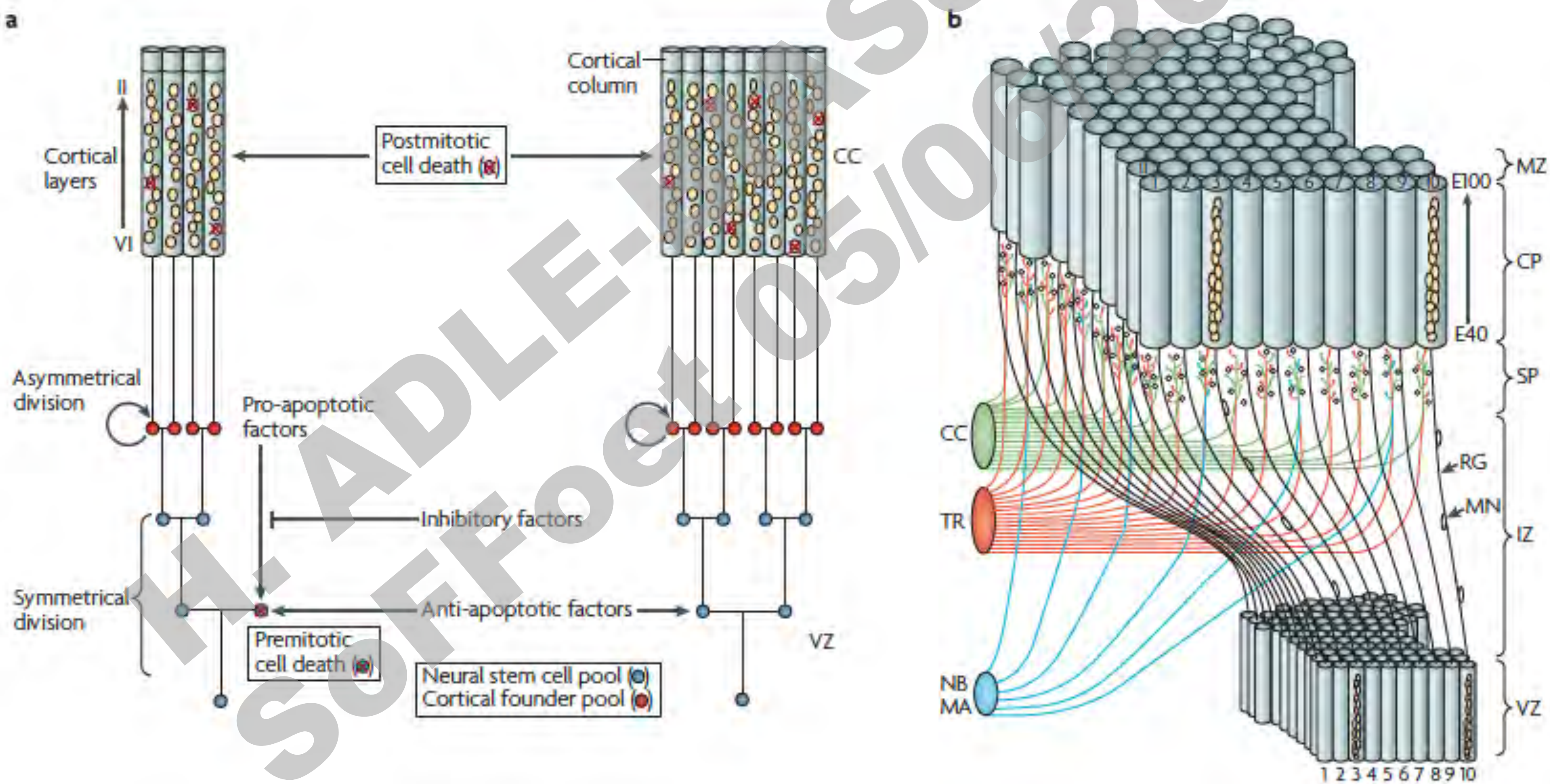


Figure 3 | Enlargement of cortical surface by decrease in programmed cell death or increase in proliferation. a | Brain sections of a wild type mouse and that of a

Golgi 1979 (Schemche & Rakic)

nature Vol 464|25 March 2010|doi:10.1038/nature08845

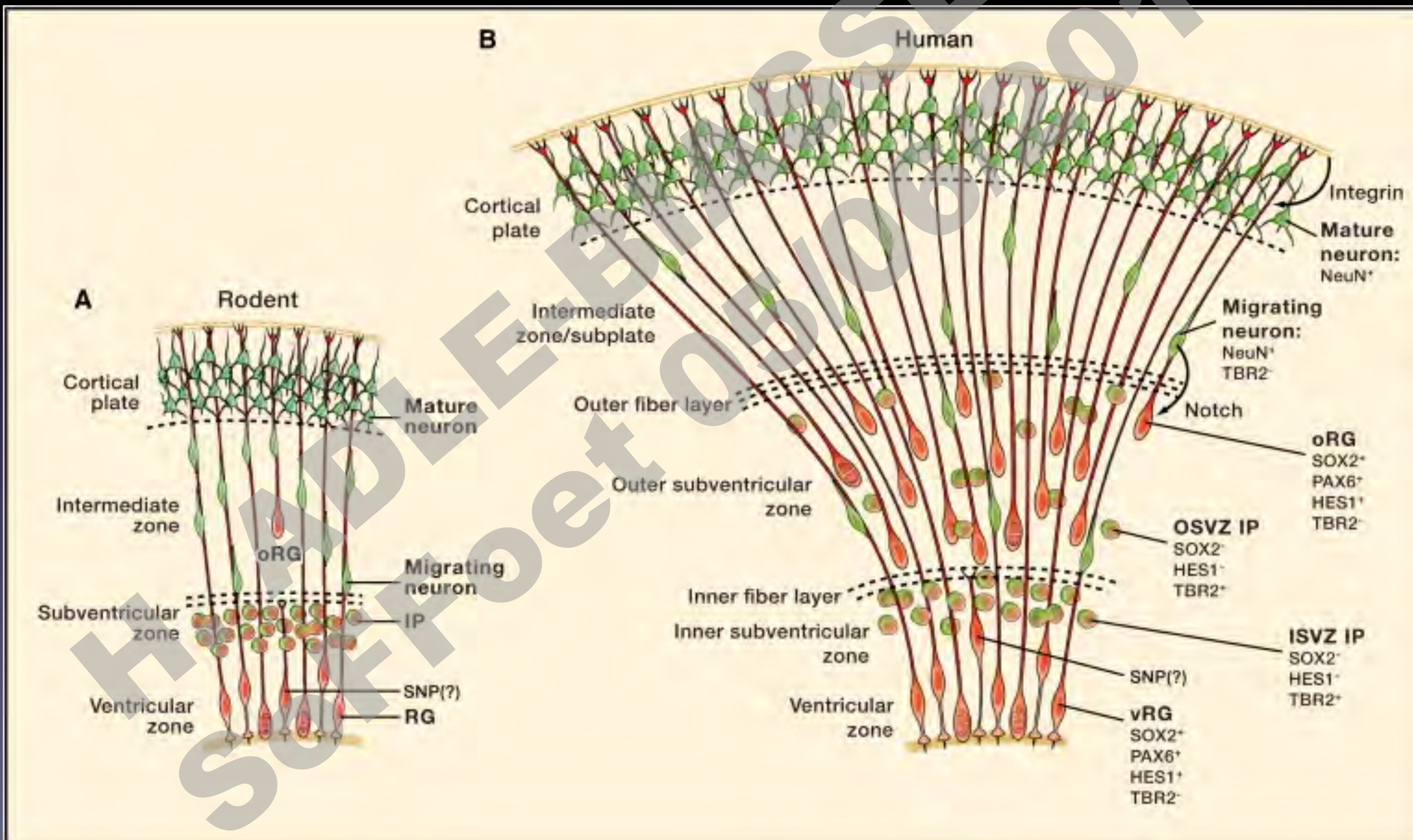
ARTICLES

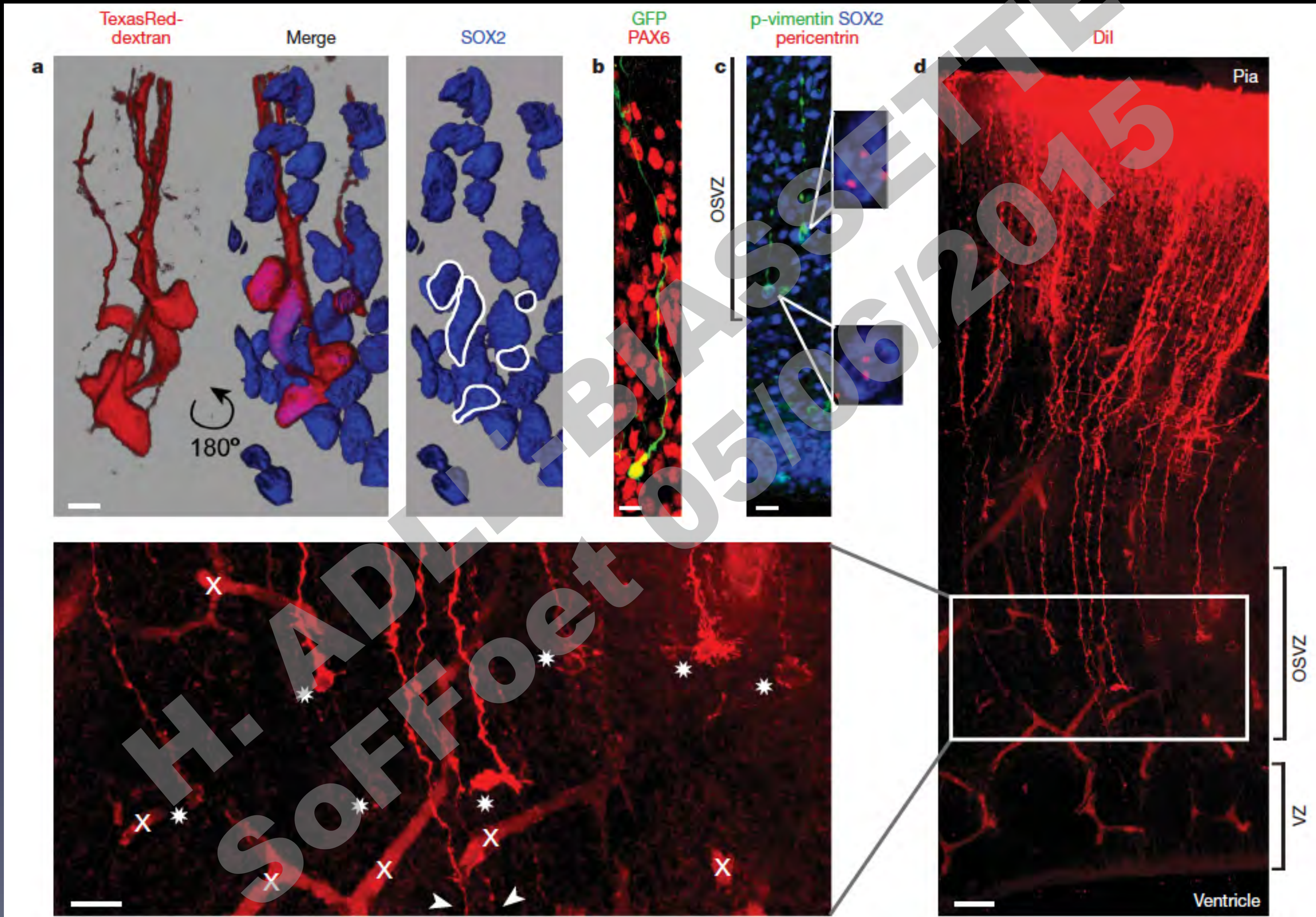
Neurogenic radial glia in the outer subventricular zone of human neocortex

David V. Hansen[1,2]*, Jan H. Lui[1,2,3]*, Philip R. L. Parker[1,2,4] & Arnold R. Kriegstein[1,2]

Development and Evolution of the Human Neocortex

Jan H. Lui,[1,2,3] David V. Hansen,[1,2,4] and Arnold R. Kriegstein[1,2,*]




TexasRed-dextran
Merge
SOX2
GFP
PAX6
p-vimentin SOX2
pericentrin
DiI
a
b
c
d
180°
OSVZ
Pia
OSVZ
VZ
Ventricle


nature Vol 464 | 25 March 2010 | doi:10.1038/nature08845

ARTICLES

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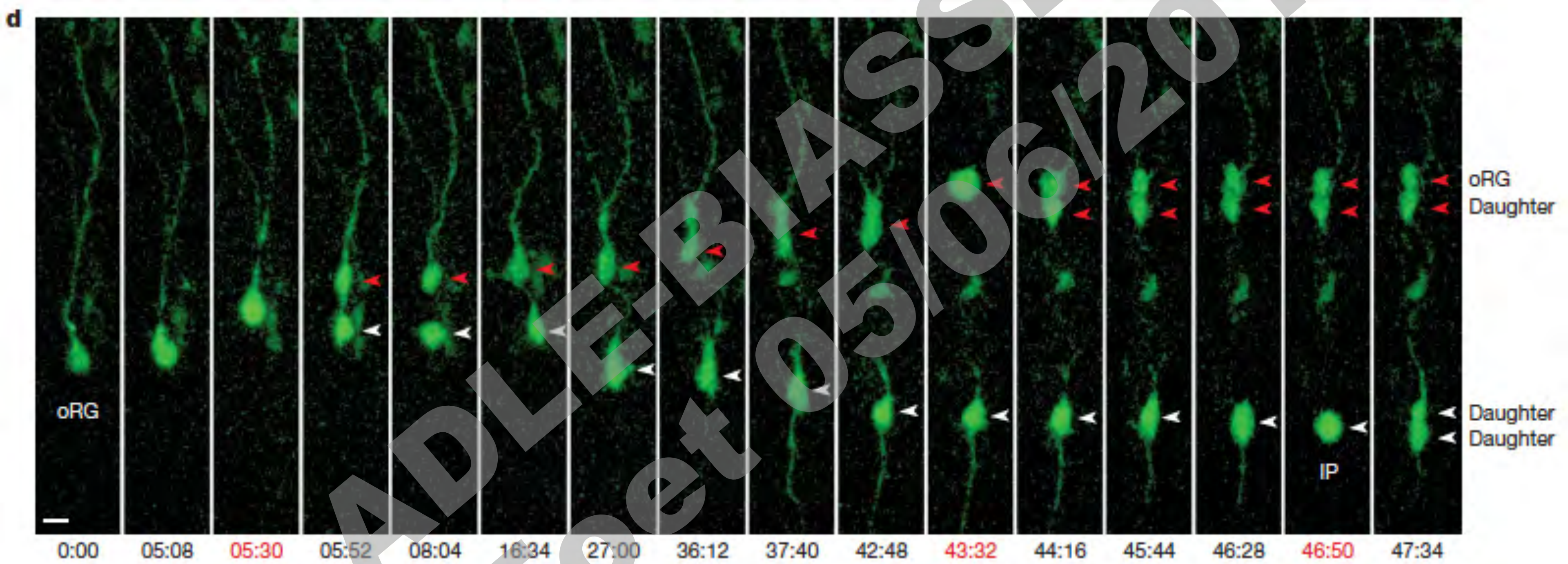
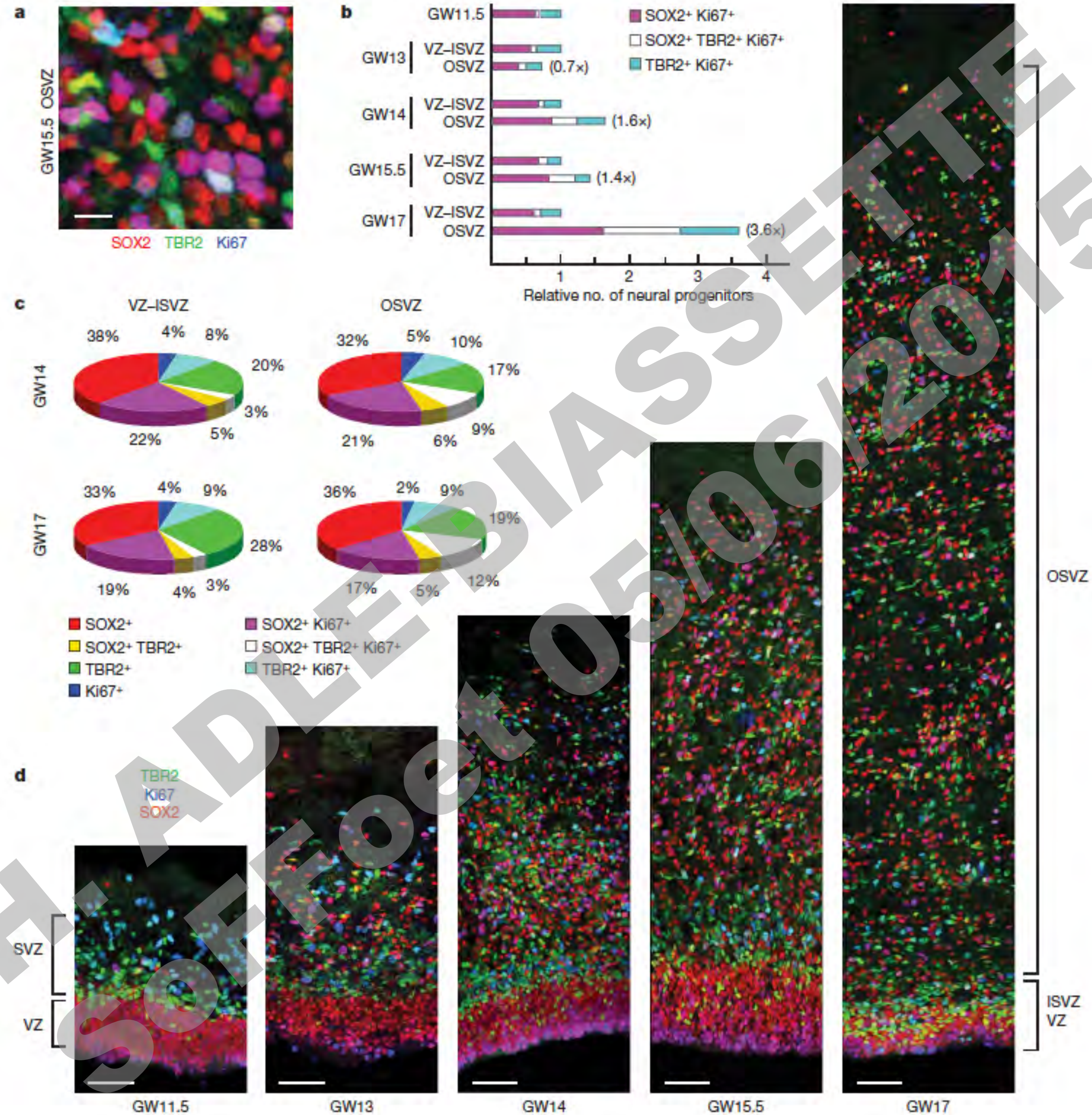


- oRGC s'autorenouvellent
- produisent des progéniteurs intermédiaires (IP) qui se multiplient

Compartiments provisoires

Figure 1 | **The Boulder Committee's 1970 schematic model of human neocortical development, and a proposed revision. A** | The Boulder Committee's original summary diagram of neocortical development. **B** | Our revised version.


a
GW15.5 OSVZ
SOX2 TBR2 Ki67
b
GW11.5
GW13
GW14
GW15.5
GW17
VZ–ISVZ
OSVZ
(0.7×)
(1.6×)
(1.4×)
(3.6×)
SOX2+ Ki67+
SOX2+ TBR2+ Ki67+
TBR2+ Ki67+
1
2
3
4
Relative no. of neural progenitors
c
VZ–ISVZ
OSVZ
GW14
38%
4%
8%
20%
3%
5%
22%
32%
5%
10%
17%
9%
6%
21%
GW17
33%
4%
9%
28%
3%
4%
19%
36%
2%
9%
19%
12%
5%
17%
SOX2+
SOX2+ TBR2+
TBR2+
Ki67+
SOX2+ Ki67+
SOX2+ TBR2+ Ki67+
TBR2+ Ki67+
d
TBR2
Ki67
SOX2
SVZ
VZ
OSVZ
ISVZ
VZ
GW11.5
GW13
GW14
GW15.5
GW17

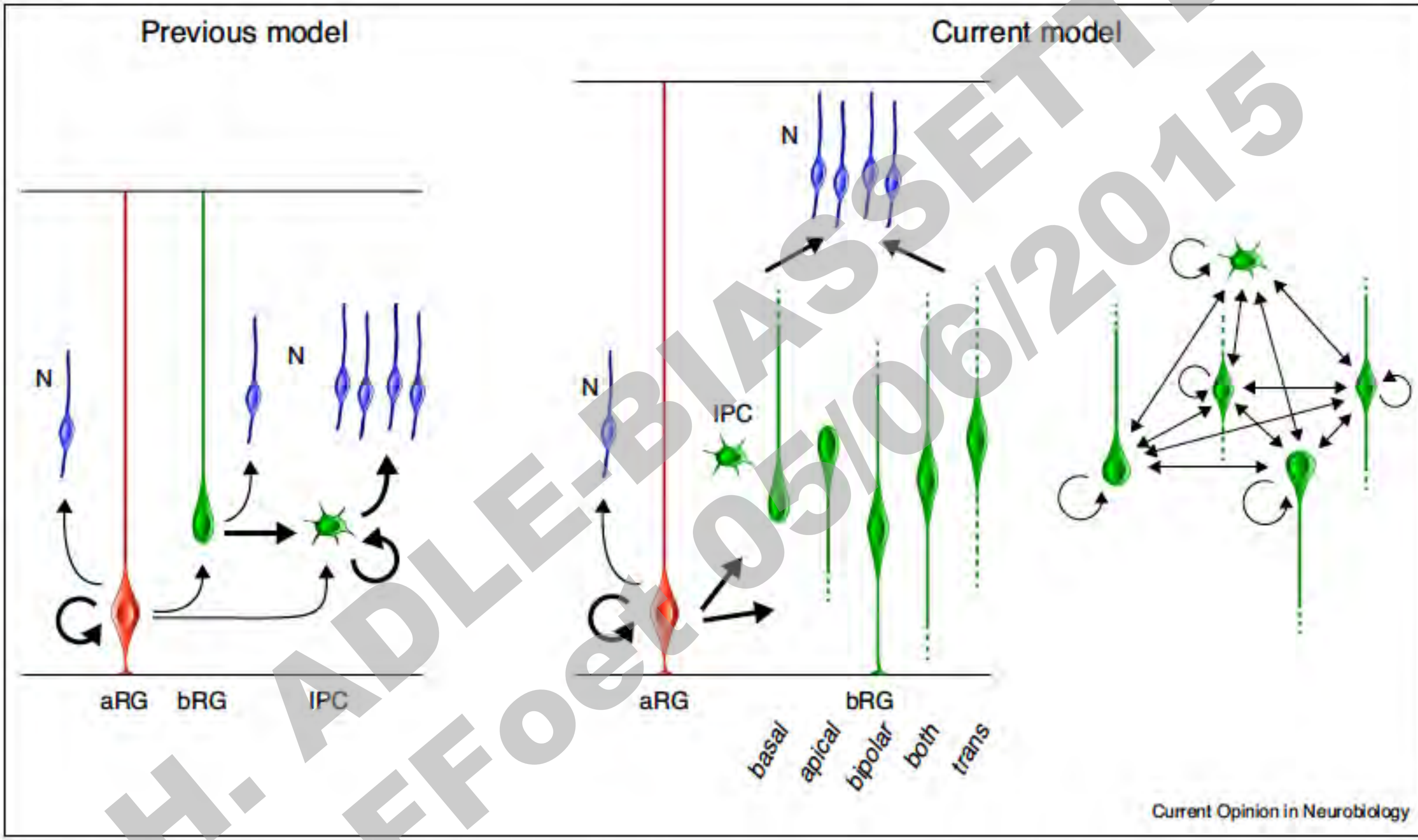
Topologie des gyri

- Reflète l'activité mitotique des progéniteurs de l'OSVZ *(chat, ferret, singe, homme)*

- bRG : corrélation avec gyrification (nouvel unité radial Reillo 2011)
  - Ferret, homme: OSVZ
  - Souris et rat :
    - SVZ (=ISVZ chez l'homme morphologiquement)
    - Progéniteurs moins abondants

- IP : surface et épaisseur corticale
  - Marmoset: primate relativement lissencéphale
  - Agouti : rongeur relativement gyrencéphalique

Figure 2

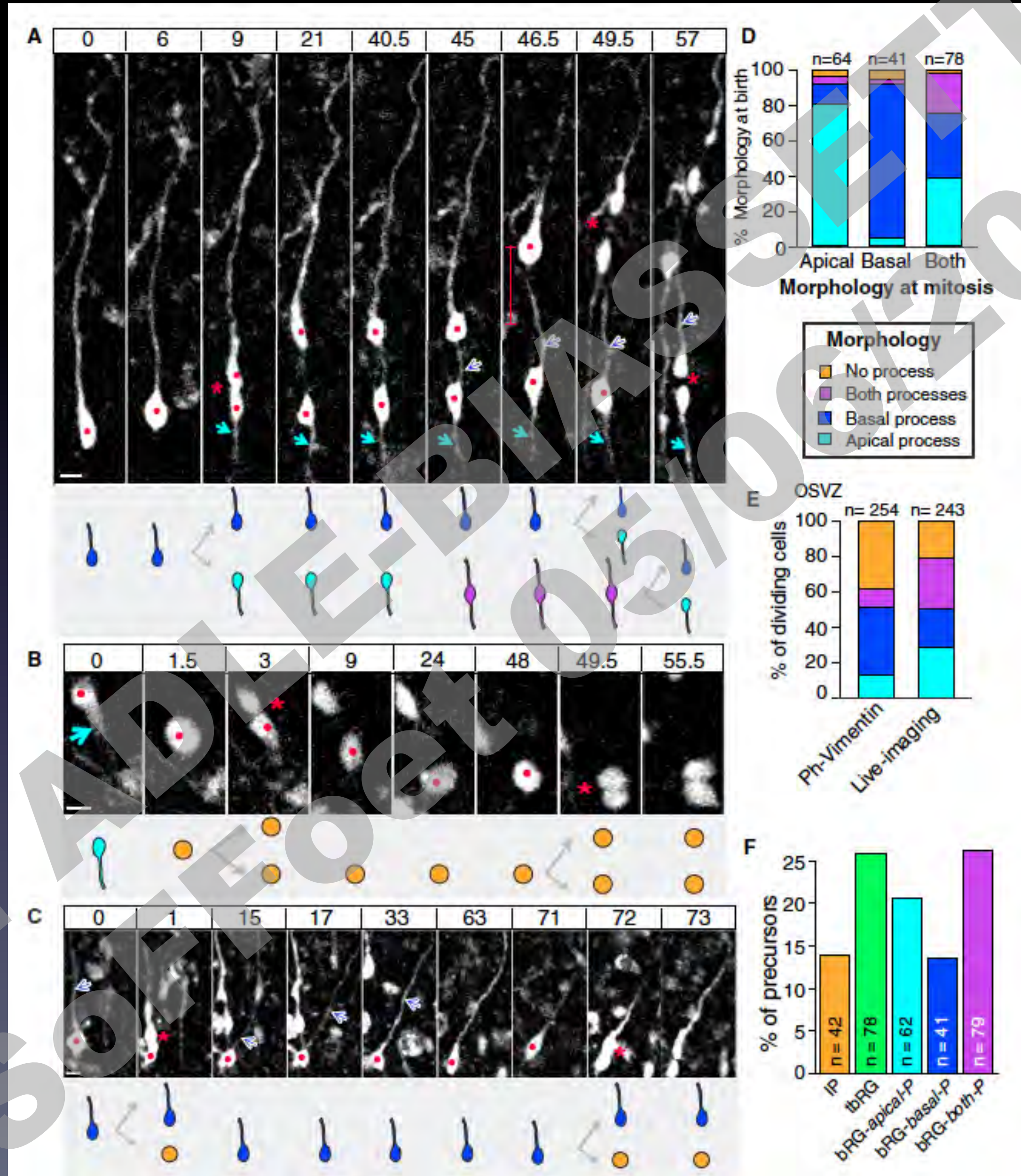


Models of corticogenesis. The prevailing model (left) acknowledged only the existence of aRG, bRG and multipolar IPCs, and proposed that most cortical neurons (N) are generated by IPCs, derived by self-amplification, aRGCs or bRGCs [23,32]. The current model (right) distinguishes 5 different classes of bRGCs depending on the nature of their radial processes [28**,29**]. IPCs and every type of bRGCs self-renew and can generate virtually any other type of bRGCs or IPCs (far right). In this model, cortical neurons are generated by all basal progenitors, but most abundantly by bipolar RGCs.

Neuron
Article

Precursor Diversity and Complexity of Lineage Relationships in the Outer Subventricular Zone of the Primate

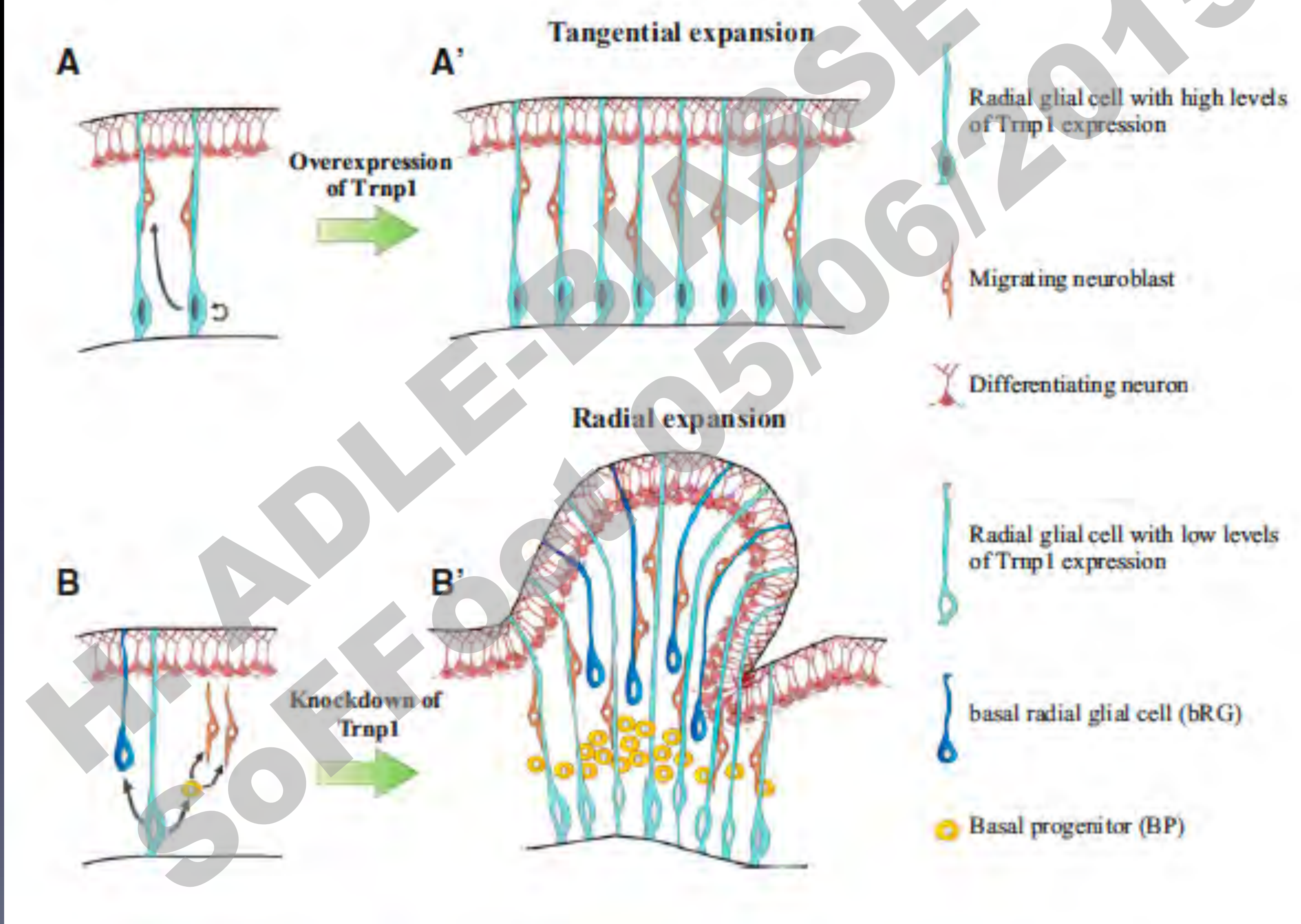
Marion Betizeau,[1,2] Veronique Cortay,[1,2] Dorothée Patti,[1,2] Sabina Pfister,[3] Elodie Gautier,[1,2] Angèle Bellemin-Ménard,[1,2] Marielle Afanassieff,[1,2] Cyril Huissoud,[1,2,4] Rodney J. Douglas,[3] Henry Kennedy,[1,2] and Colette Dehay[1,2,*]

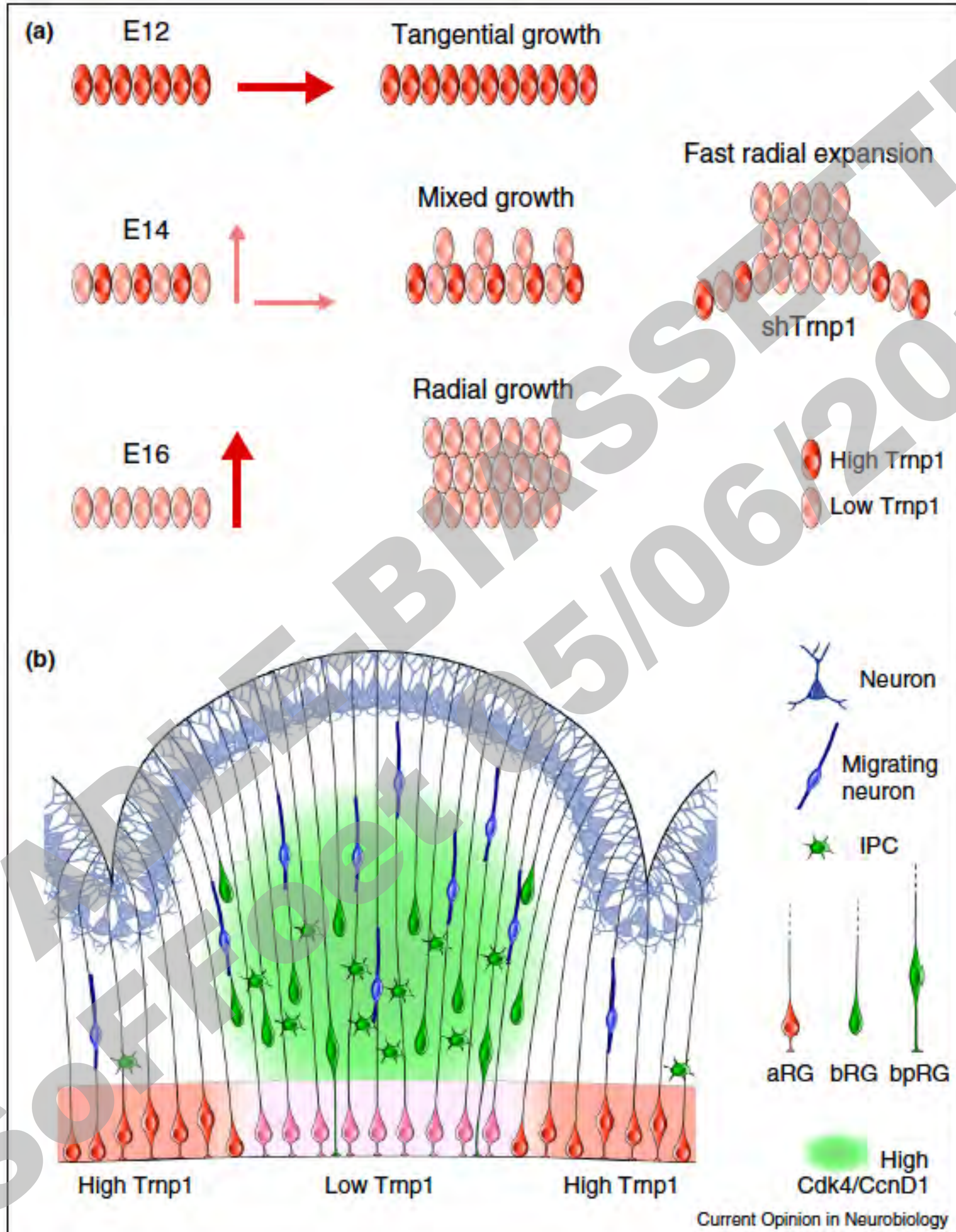


Trnp1 Regulates Expansion and Folding of the Mammalian Cerebral Cortex by Control of Radial Glial Fate

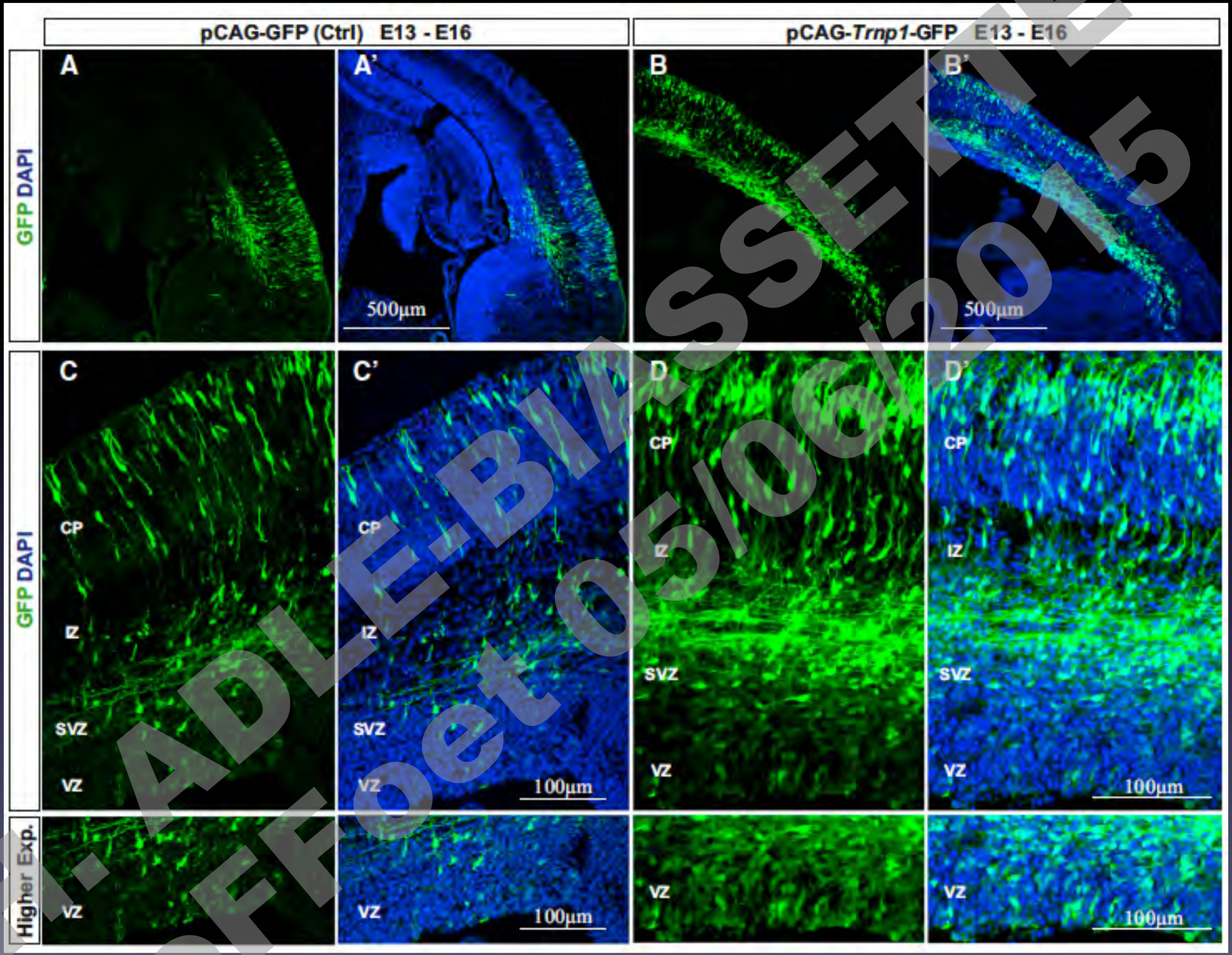
Cell

Ronny Stahl,[1,2,3] Tessa Walcher,[3] Camino De Juan Romero,[5] Gregor Alexander Pilz,[3] Silvia Cappello,[3] Martin Irmler,[4] José Miguel Sanz-Aquela,[6] Johannes Beckers,[4,7] Robert Blum,[1,9] Víctor Borrell,[5] and Magdalena Götz[1,2,3,8,*]

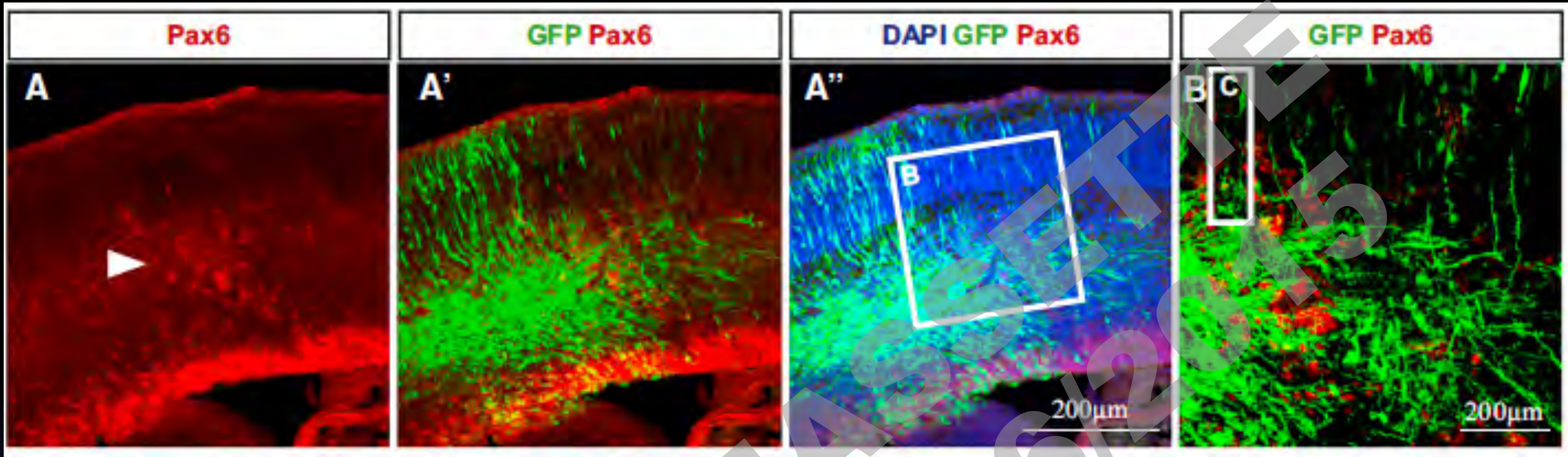


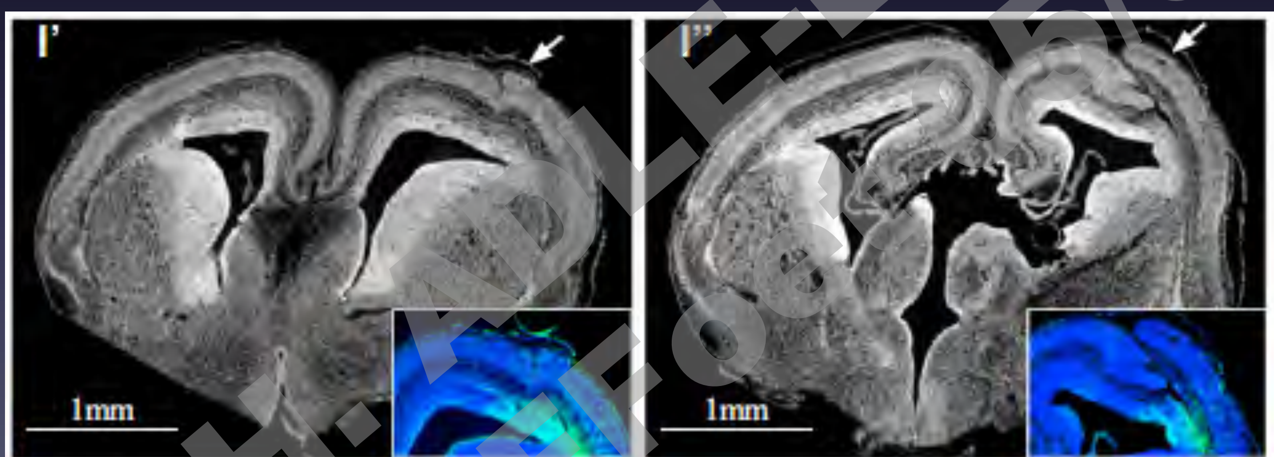

(a)
E12
Tangential growth
E14
Mixed growth
Fast radial expansion
shTrnp1
E16
Radial growth
High Trnp1
Low Trnp1
(b)
Neuron
Migrating neuron
IPC
aRG
bRG
bpRG
High Cdk4/CcnD1
High Trnp1
Low Trnp1
High Trnp1
Current Opinion in Neurobiology

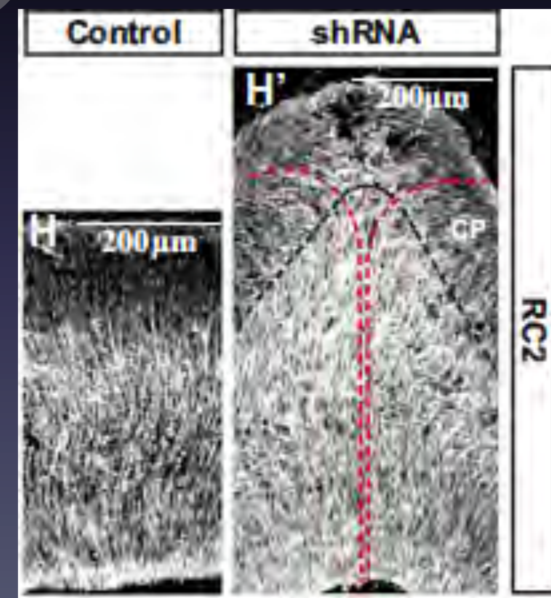
TMF regulated nuclear protein



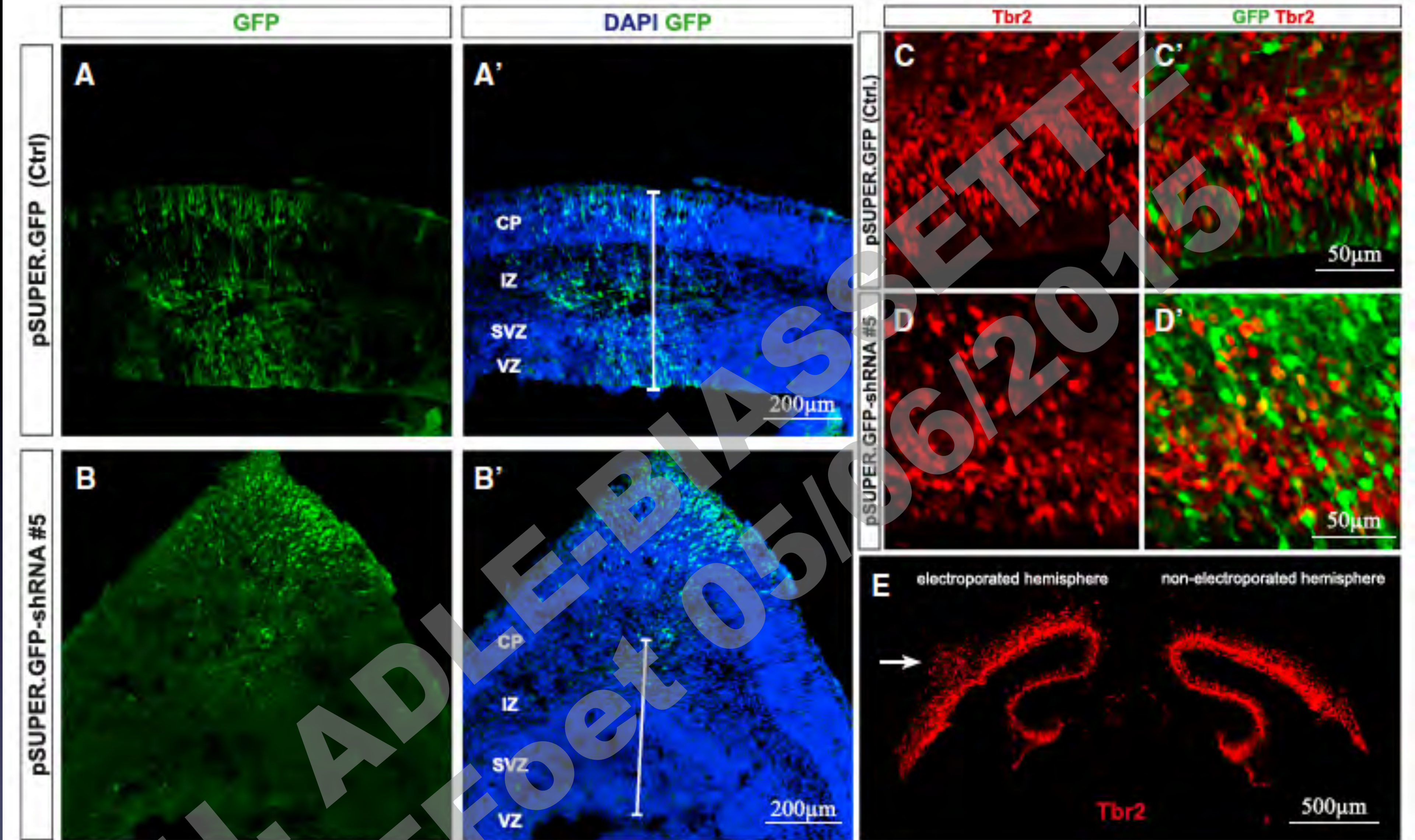
High Trnp1 levels promote NSC self-renewal & tangential expansion







Lower levels promote RG, with a potent increase of the number IP & bRG leading to folding of the otherwise smooth murine cortex



lower levels promote RG, with a potent increase of the number IP & bRG leading to folding of the otherwise smooth murine cortex

Topologie de gyration

Comparaison développement humain normal et pathologique et autres espèces

- Types de progéniteurs et abondance
- Dynamique du cycle cellulaire
- Organisation glie radiaire
- Profil expression des gènes

Mécanismes ?

- Expansion conique des zones germinatives ?

Et/ou

- Distribution des connections ?

Topologie des gyri

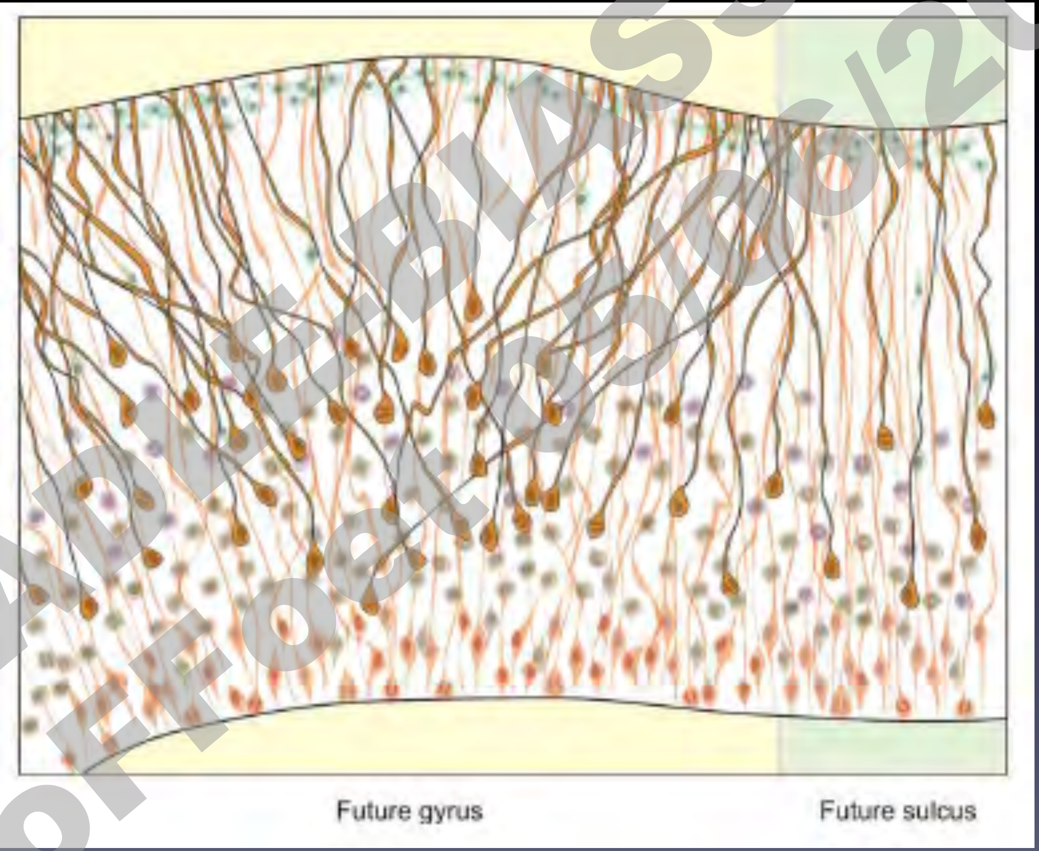
- Divergence conique des fibres de la glie radiaire (pas le nombre de neurones)

=> ↑ exponentielle dans les régions prospective de gyration

  - Pachygyrie (baisse surface) sans baisse de neurones
  - Microcéphalie à gyration conservée

- N'existe pas chez les lissencéphales

Expansion conique de la glie radiaire basale



Gyrification
Matrice extracellulaire

- Signalisation / Intégrine : nombre de bRG mais pas IPC
- Fibres thalamiques plus denses dans SVZ (division O et ISVZ) => facteurs prolifératifs
- Vaisseaux SVZ souris => niche proliférative
- Transcriptome : MEC OSVZ/VZ et OSVZ humain / SVZ souris

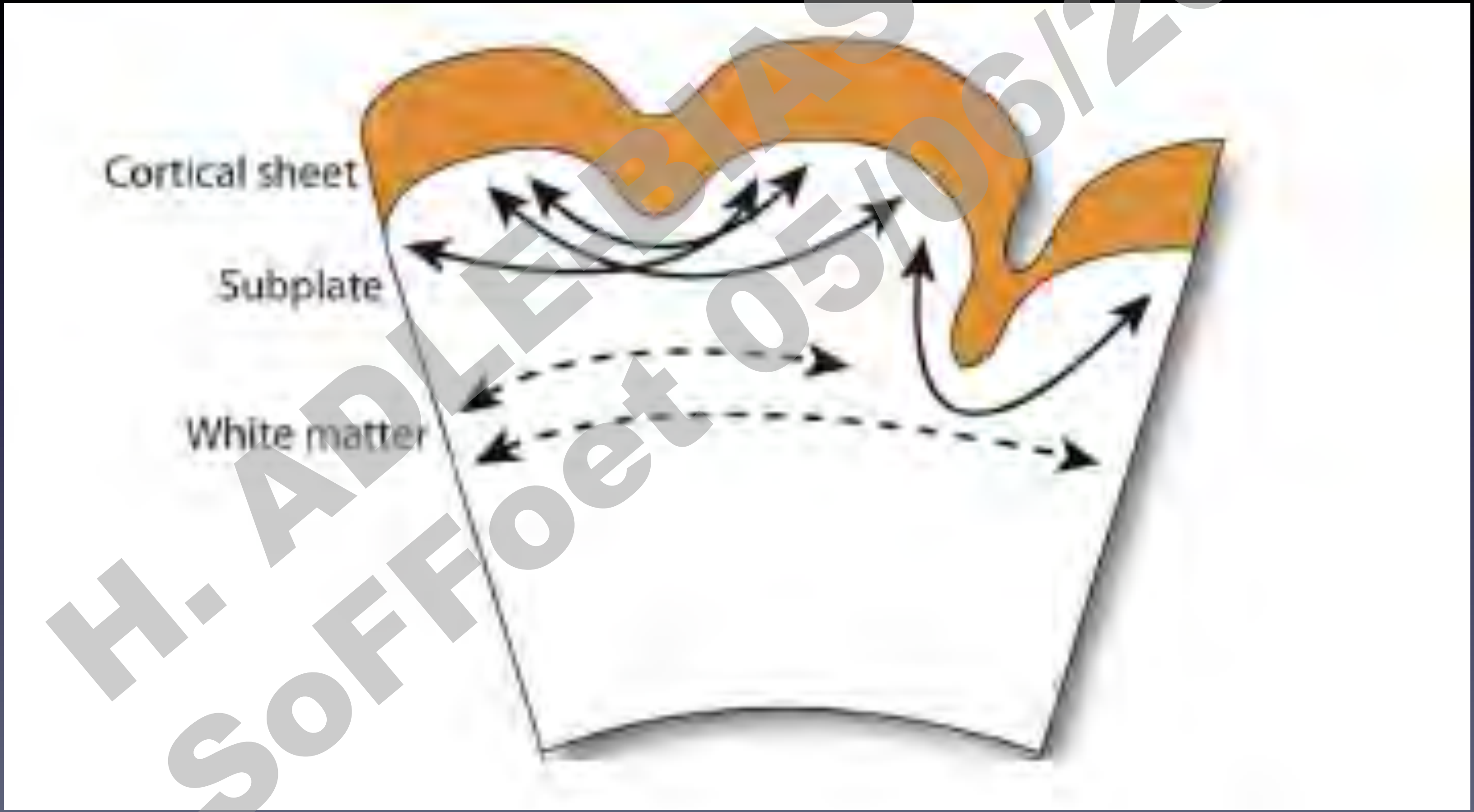
Topologie de gyrification

Rôle des tensions axonales et plasticité corticale tardive

- Faisceaux cortico-corticaux et –souscorticaux se forment lors du développement de la pré-plaque
- Puis formation de sous-plaque: fx cortico-thalamique et cortico-corticaux
- Effort pour minimiser les distances entre les connections (tension radiale dans les gyri régulé par les connections)
  - Forces tangentielles cortico-cortical forte
  - Et faible: radiale cortico-souscorticale

Topologie de gyrification

Rôle des tensions axonales et plasticité corticale tardive



Conclusions

- Subdivision de la ZSV (OSVZ et ISVZ)
- Expansion OSVZ
- ↑ de capacité proliférative des progéniteurs « apolaires »
- ↑ de vascularisation des zones germinatives corticales
- ↑ signalisation MEC aux progéniteurs sous-ventriculaires
- Tensions axonales corticales

Table 1. Differences between Developing Human and Mouse Neocortex

Quantitative Differences*

- Number of neurons and surface area ~1000 x larger
- Number or ontogenetic (radial) columns ~ 1000x higher
- Length of cell cycle length (~ 3- 4 x longer)
- Duration of cortical neurogenesis ~ 20 x longer
- Subplate Zone occupies several-fold larger portion of the embryonic cerebral wall
- Configuration gyrencephalic rather than lissencephalic
- Birth occurs during later stages of cortical development
- Lower density of neurons, larger neuropil, higher dendritic and axonal branching
- Tempo of cortical maturation in relation to onset of reproduction very different
- Very prolonged neoteny with cortical maturation surpassing puberty and adolescence

Qualitative Differences

- Introduction of new genes, gene variants, regulatory elements, and expression patterns
- Introduction of new neuronal types (e.g. Predecessors, VEN -Spindle cells; ISN)
- Distinct upper stratum of the outer subventricular zone (OSVZ)
- Subset of GABAergic interneurons originate from the dorsal VZ/SVZ
- Neuronal migration to thalamus from the GE absent in all examined mammals (CGT)
- Transient Subpial Granular Layer (SGL, absent in rodents and carnivores)
- Distinct Radial Glial Cells (early GFAP+ and differentiated and genetically distinct)
- Modification of common cytoarchitectonic areas (e.g. layer IV in A17)
- Introduction of new cytoarchitectonic areas (e.g. **A22, 28, 44, 45, 46**)
- Absence of neuronal turnover and resistance to regeneration

*The quantitative statements above are only an approximation of the level of an order of magnitude to highlight how large the differences are. The inclusion of all the references and precise numbers and measurements that may differ due to the individual variations within species as well as the

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Jeannette Nardelli
Anne-Lise Delezoide
Fabien Guimiot
Pierre Gressens

Vienne: Gabor Kovacs

Barcelone: Isidro Ferrer

Amsterdame: Eleonora Aronica

DEVELAGE

Inserm
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