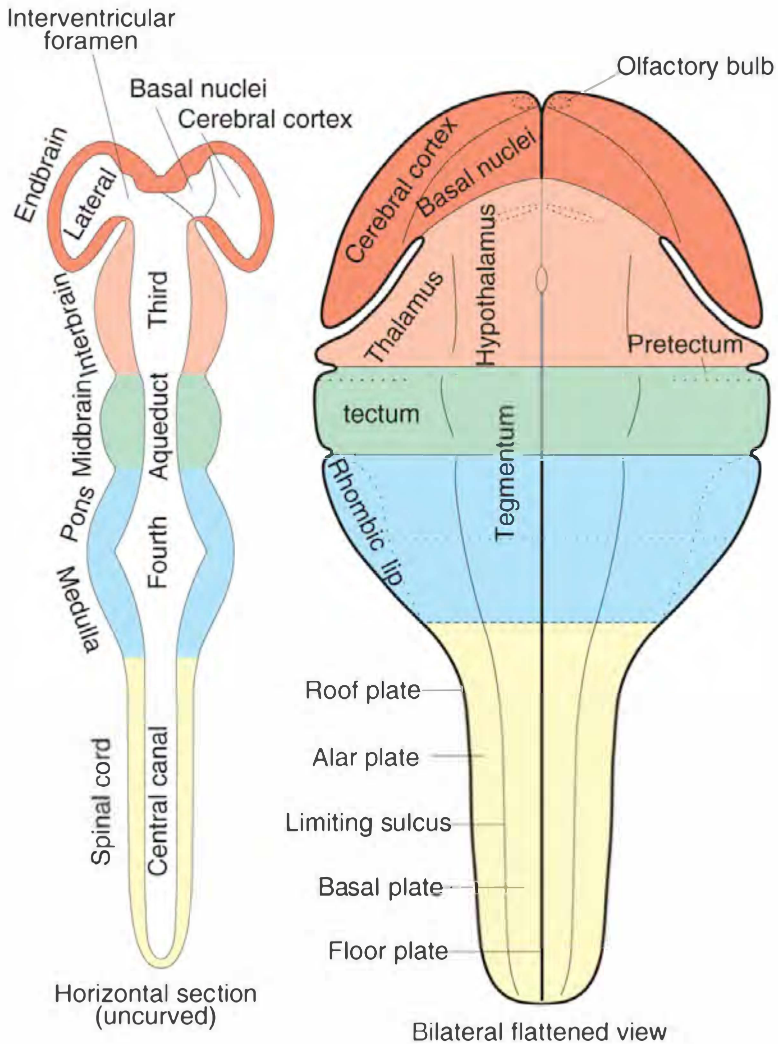
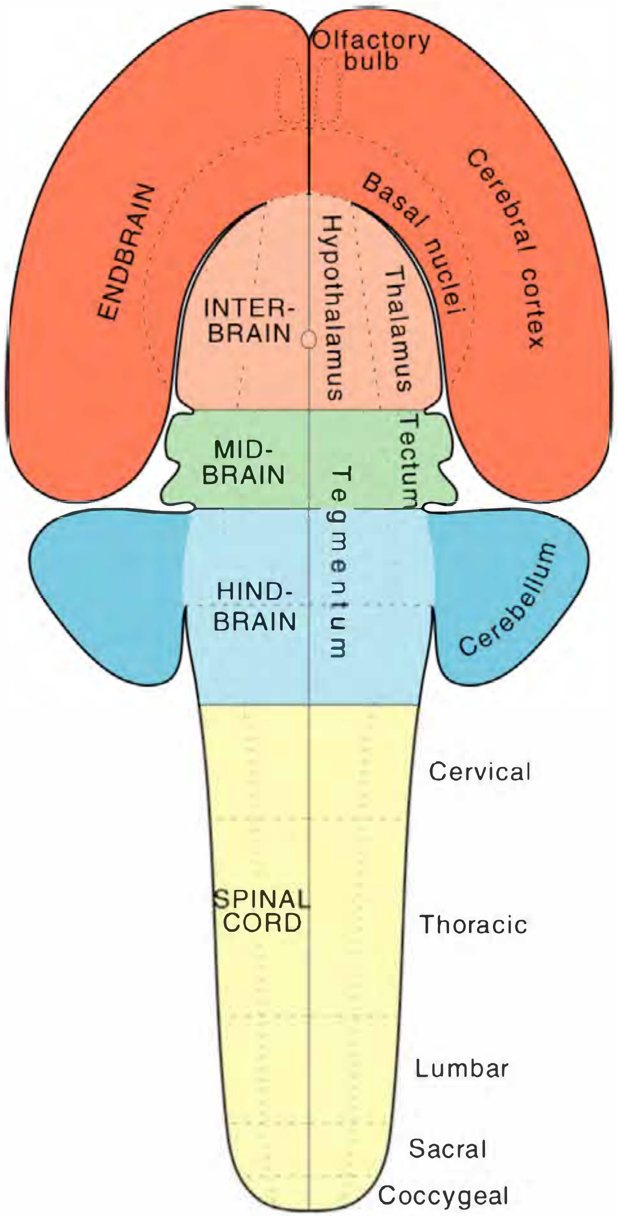
Cell Migration

Dieter Zimmermann
Institut für Pathologie und Molekularpathologie
Universitätsspital Zürich

HS 2017



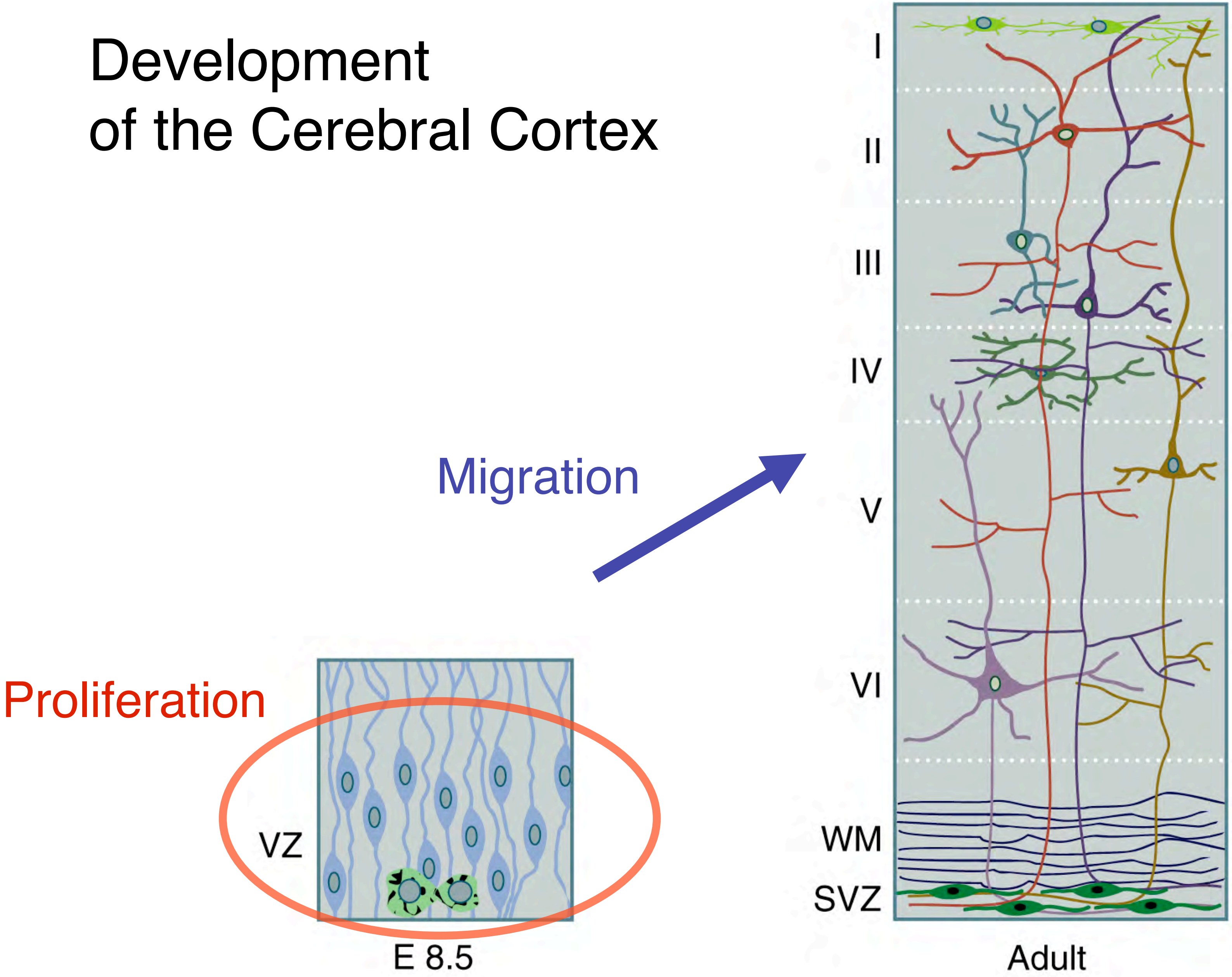
6 weeks (human)



adult (human)

Bregma: -0.94 mm
Interaural: 3.10 mm

Development of the Cerebral Cortex



VZ: Ventricular Zone   I-VI: Cortical Layers   WM: White Matter   SVZ: Subventricular Zone

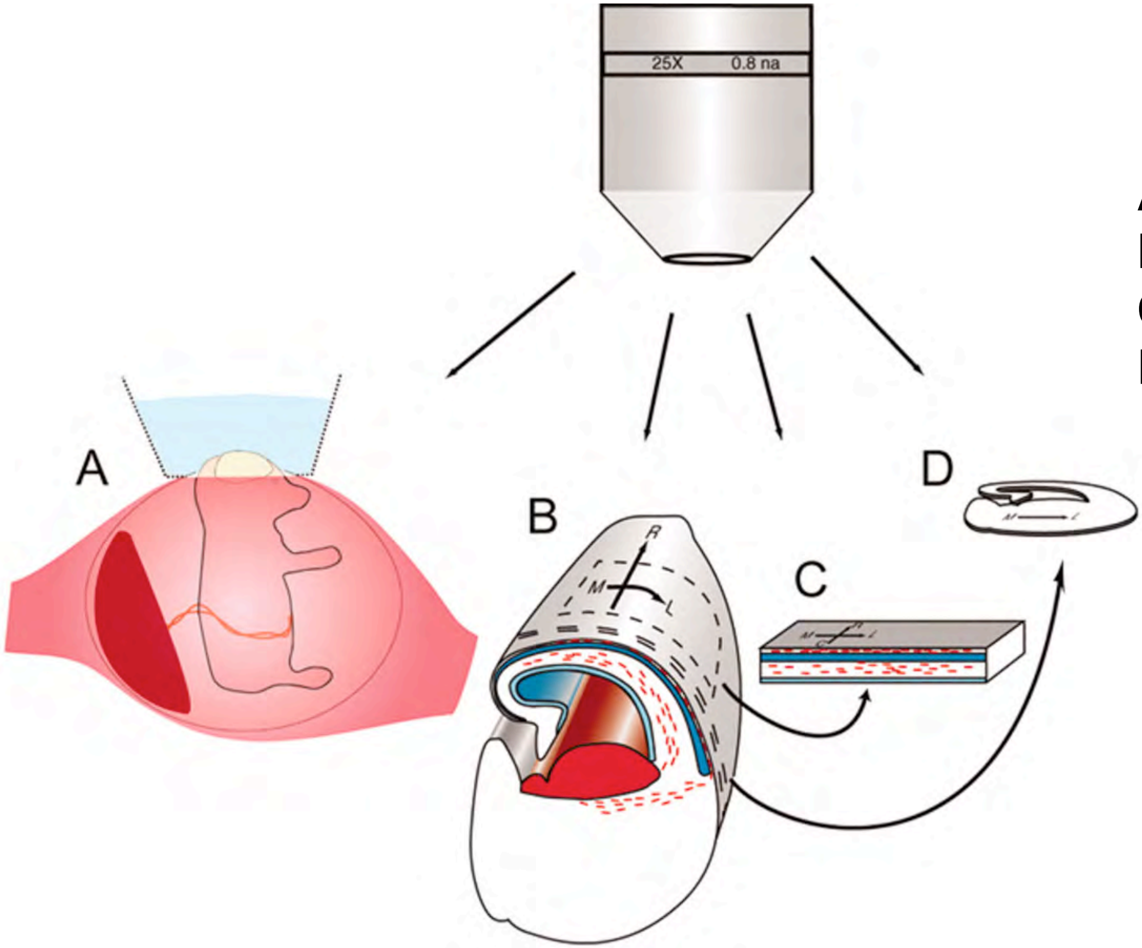
Cerebral Cortex July 2011;21:1465-1474

FEATURE ARTICLE

Strategies for Analyzing Neuronal Progenitor Development and Neuronal Migration in the Developing Cerebral Cortex

Holden Higginbotham, Yukako Yokota and E. S. Anton

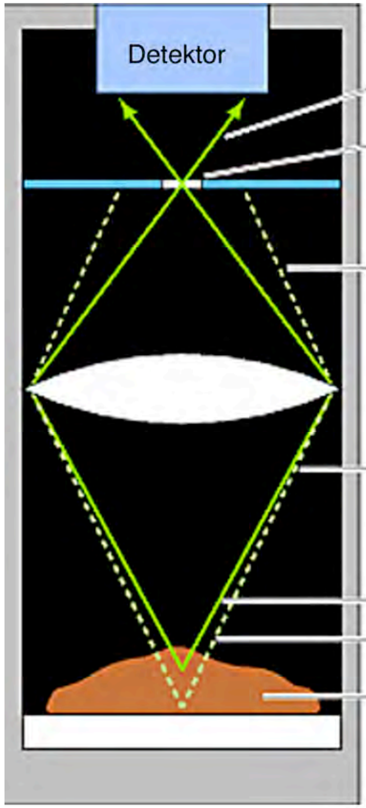
Imaging of cell migration with time-lapse video microscopy



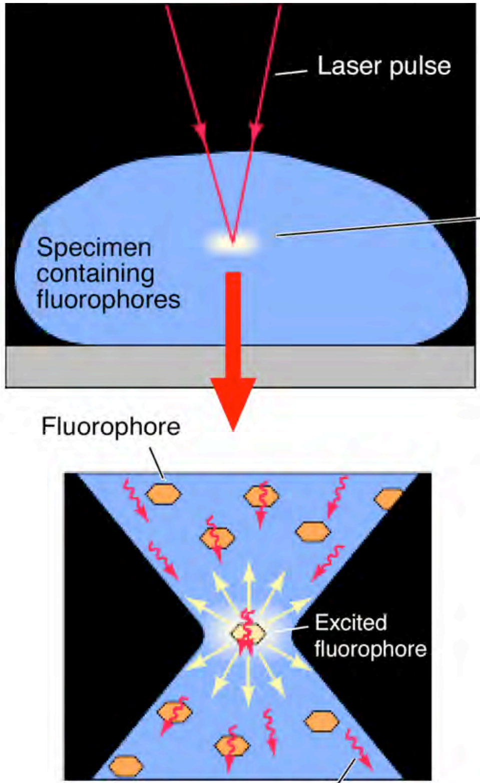
A. live in utero
B. in situ in whole brains
C. tangential cortical explants
D. organotypic coronal slices

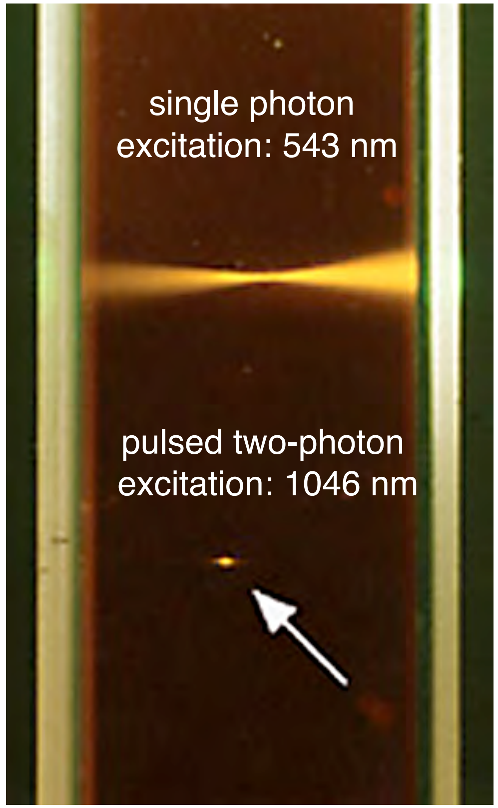
Requirements:
- Efficient labeling of cells with fluorescence markers (vital dyes)
- Detection with confocal or two-photon microscopy

Confocal Microscopy

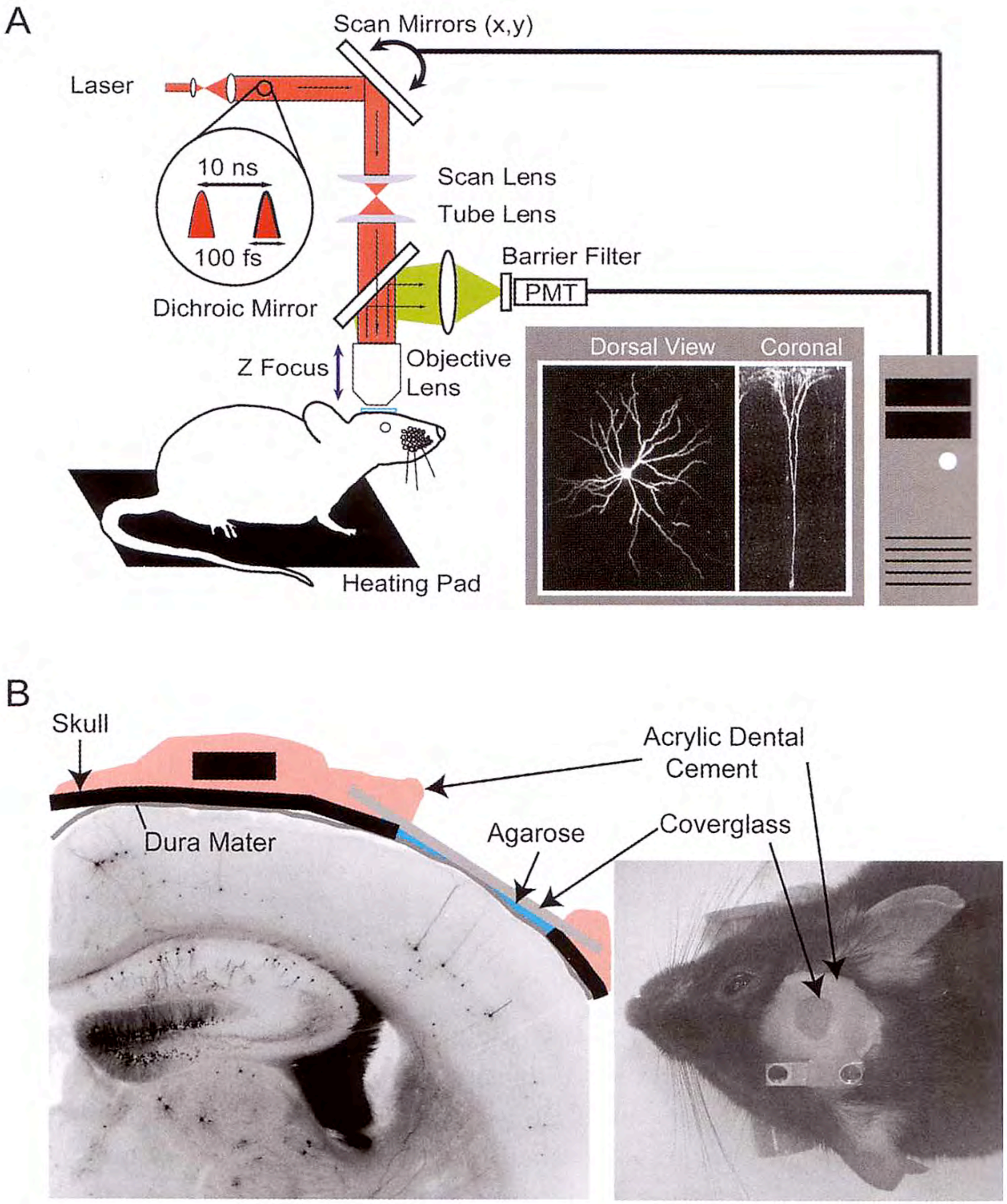


Two-Photon Microscopy

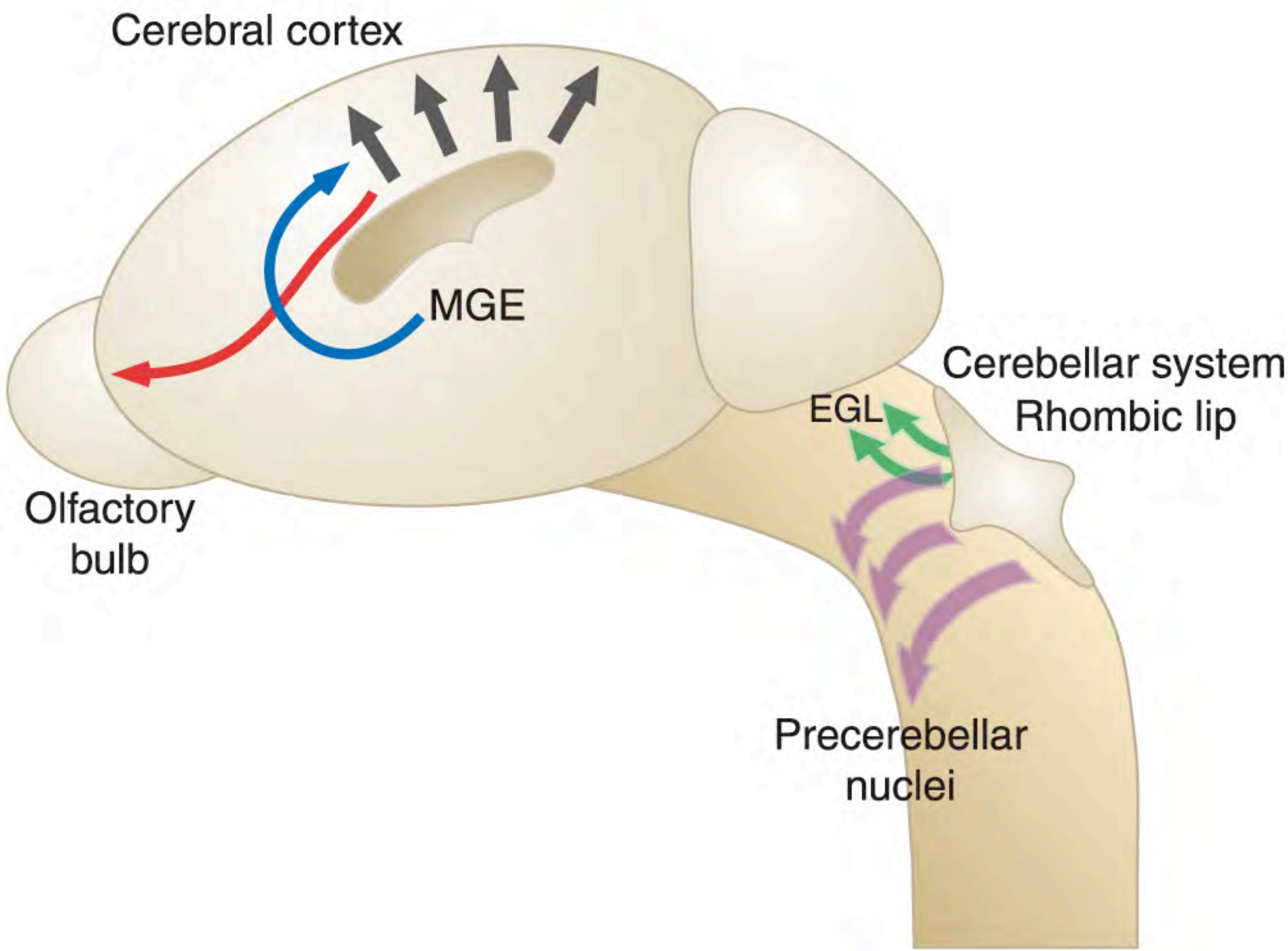




Safranin O


A
Scan Mirrors (x,y)
Laser
10 ns
100 fs
Scan Lens
Tube Lens
Barrier Filter
PMT
Dichroic Mirror
Z Focus
Objective Lens
Dorsal View
Coronal
Heating Pad
B
Skull
Acrylic Dental Cement
Dura Mater
Agarose
Coverglass

Migration Pathways in the Central Nervous System

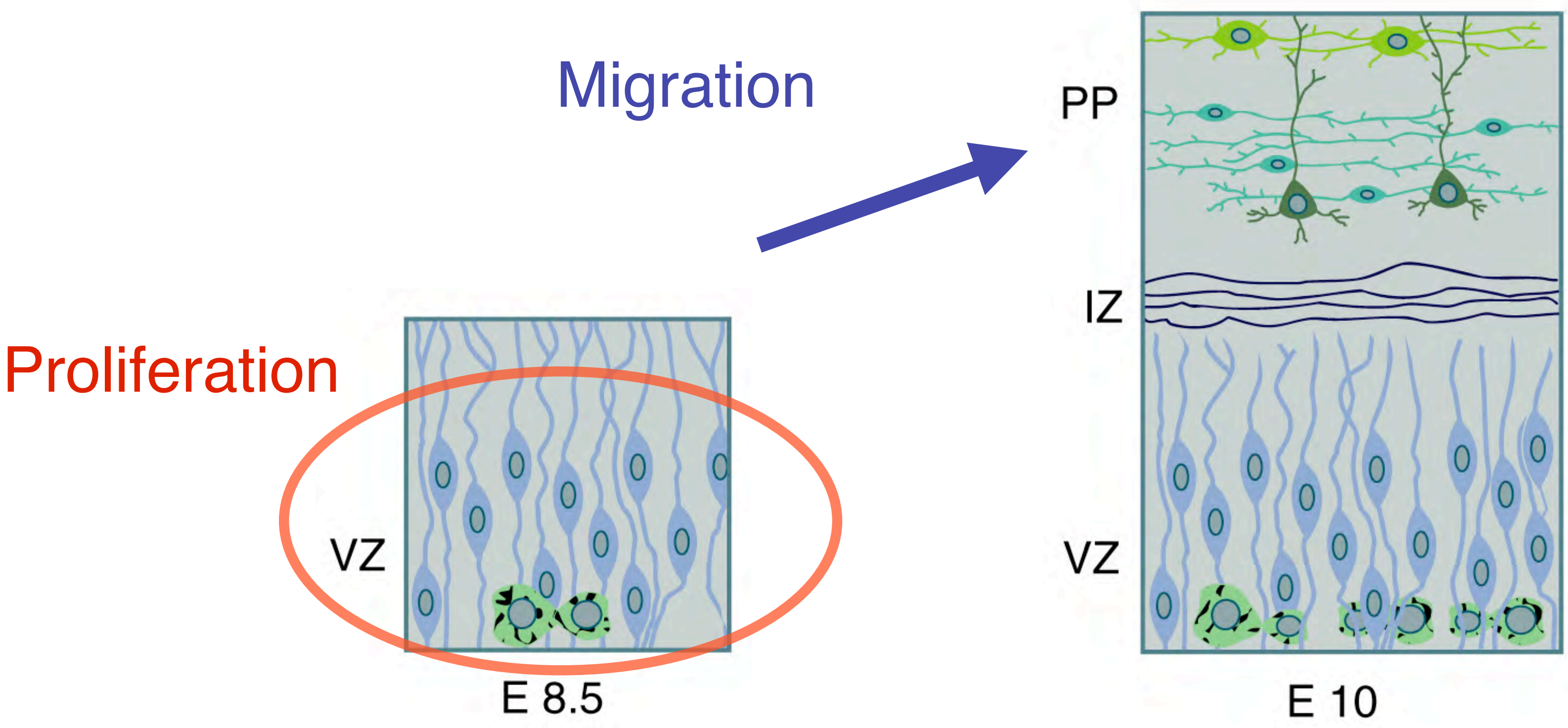


NATURE REVIEWS | NEUROSCIENCE VOLUME 3 | JUNE 2002 | 423

MODES OF NEURONAL MIGRATION IN THE DEVELOPING CEREBRAL CORTEX

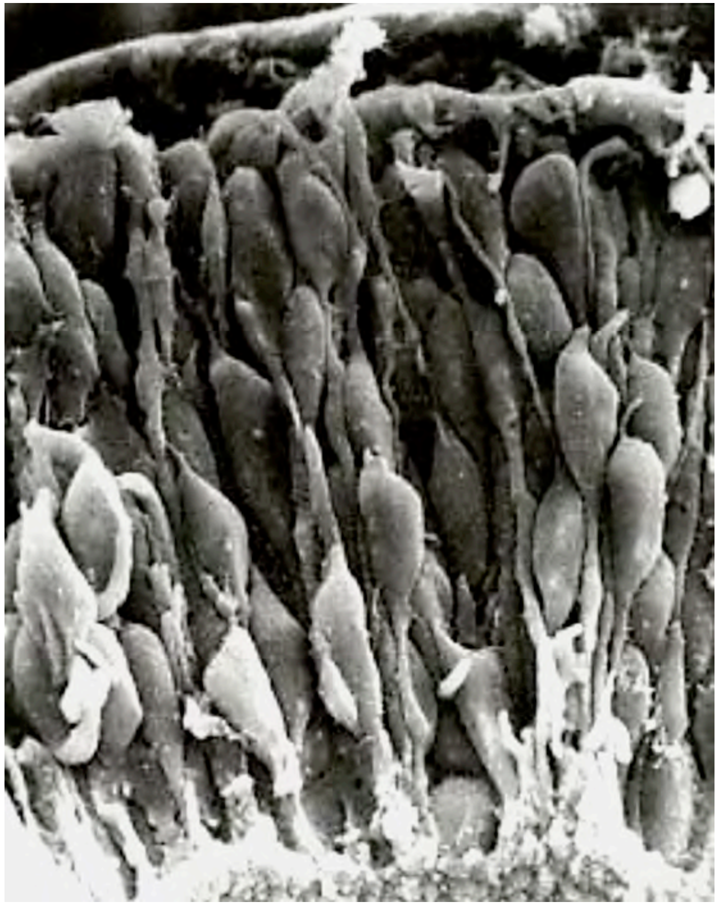
Bagirathy Nadarajah and John G. Parnavelas

Development
of the Cerebral Cortex



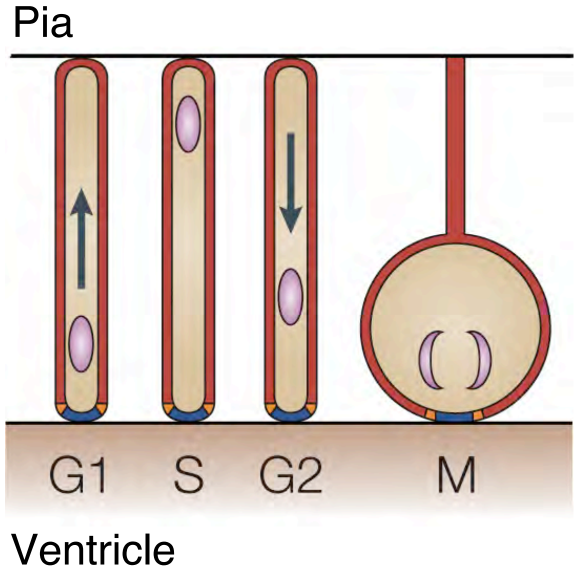
VZ: Ventricular Zone   PP: Preplate   IZ: Intermediate Zone

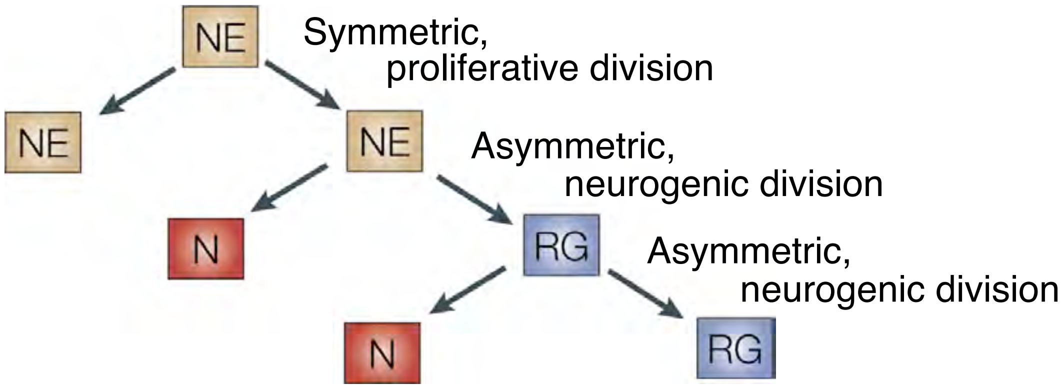
Early Neurogenesis in the Cerebral Cortex



One-cell-thick, pseudostratified neuroepithelium

Interkinetic nuclear migration

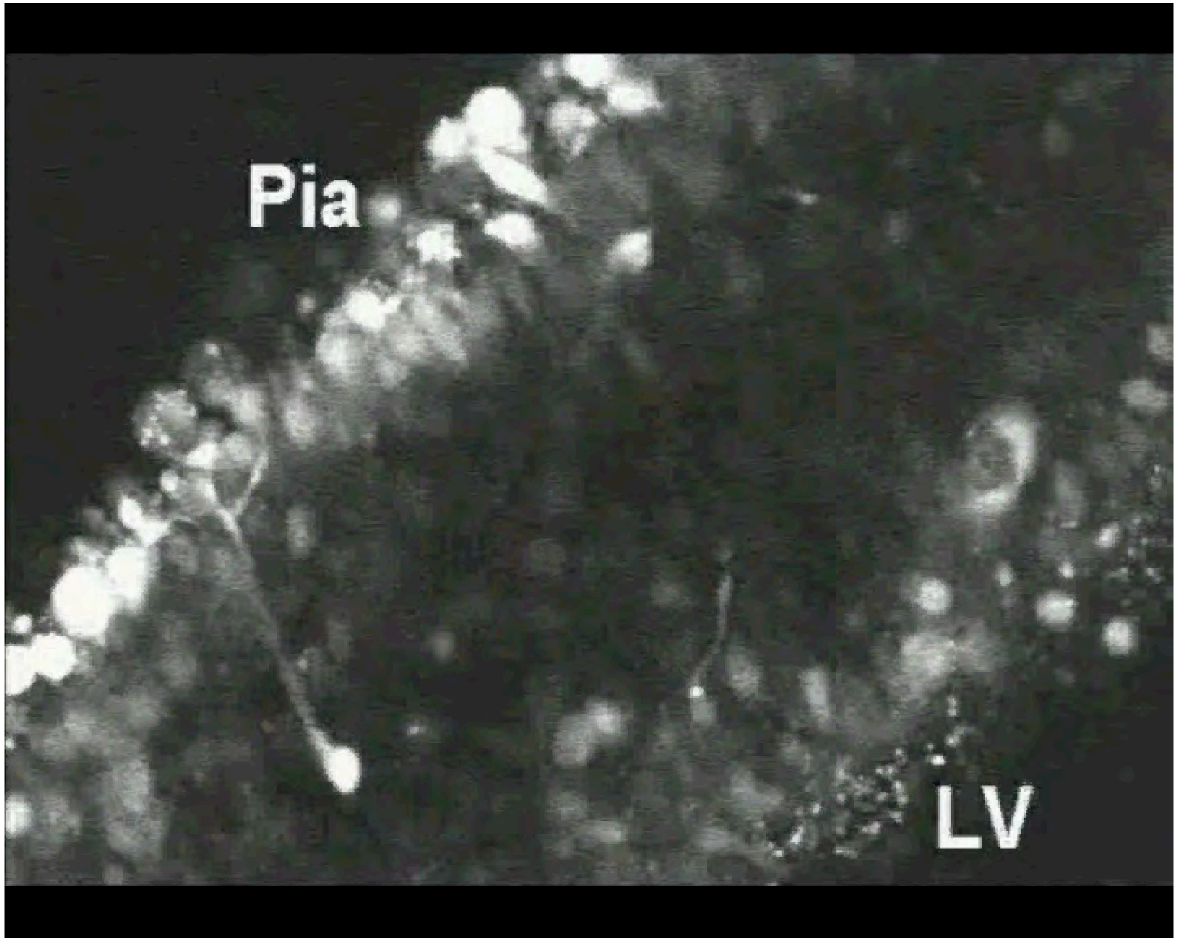


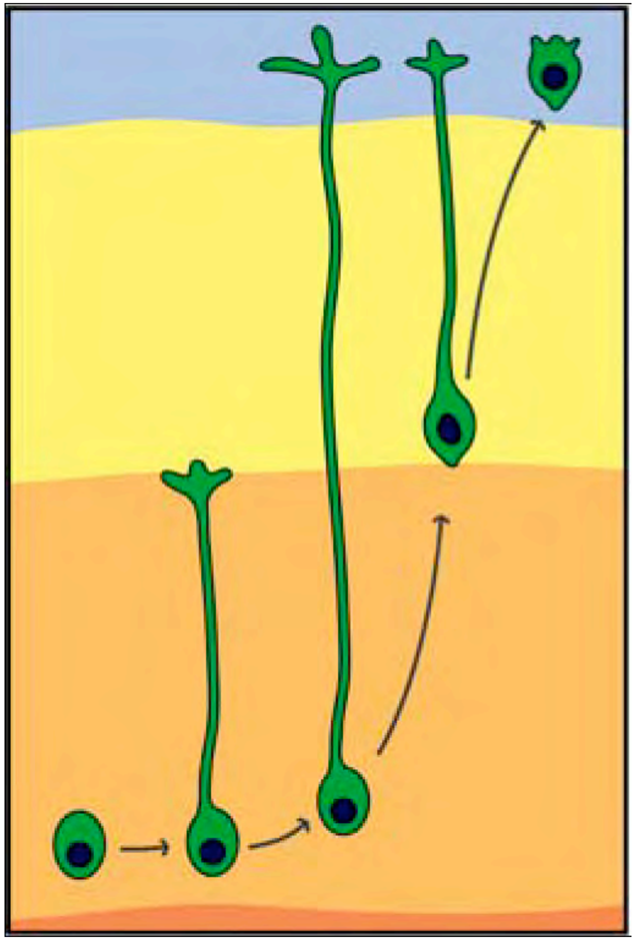


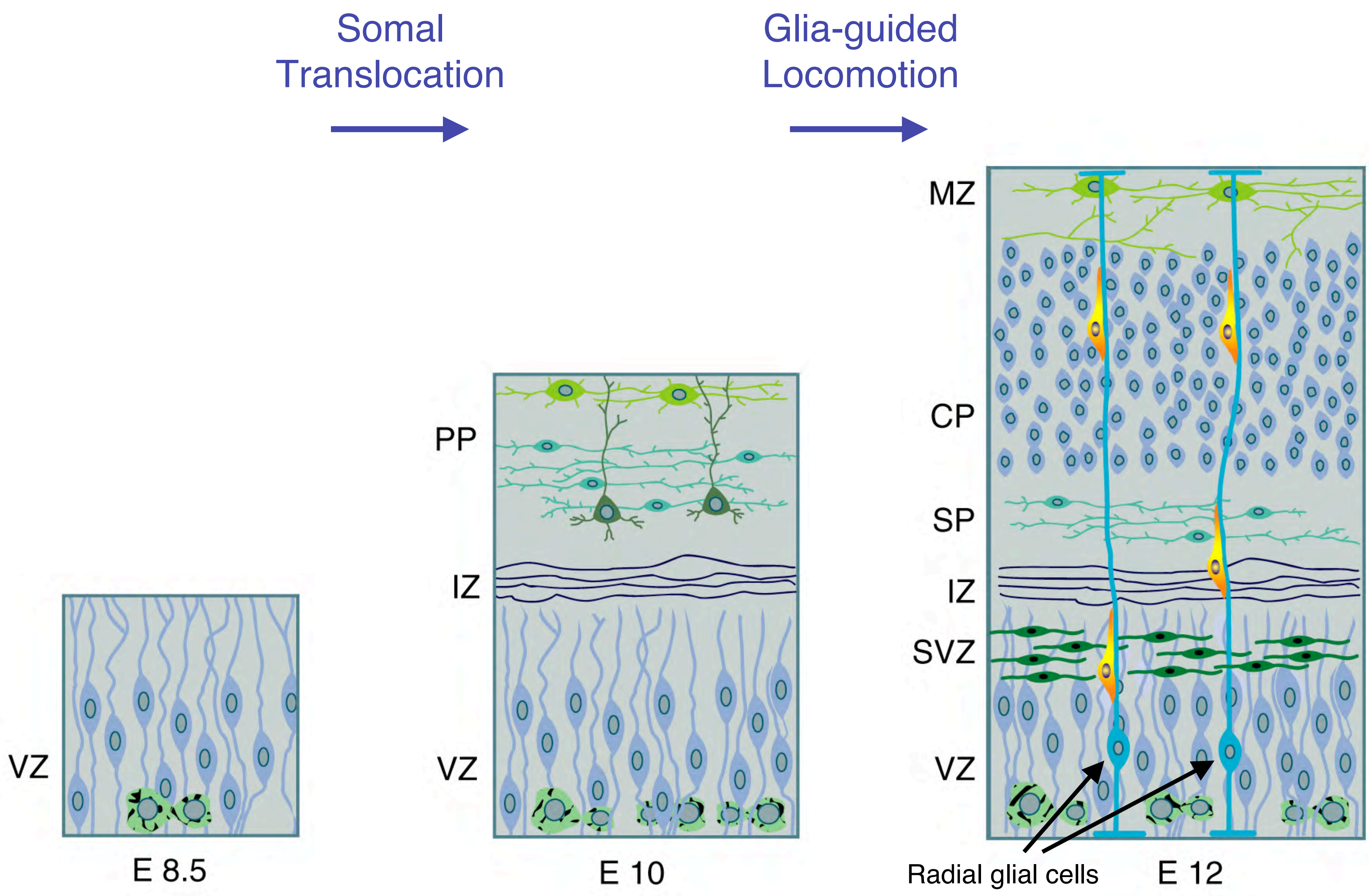
NE: neuroepithelial   N: neuronal cell   RG: radial glial cell

cell body leaves VZ and migrates to somwhere else like the cortical areas(?)

Somal Translocation

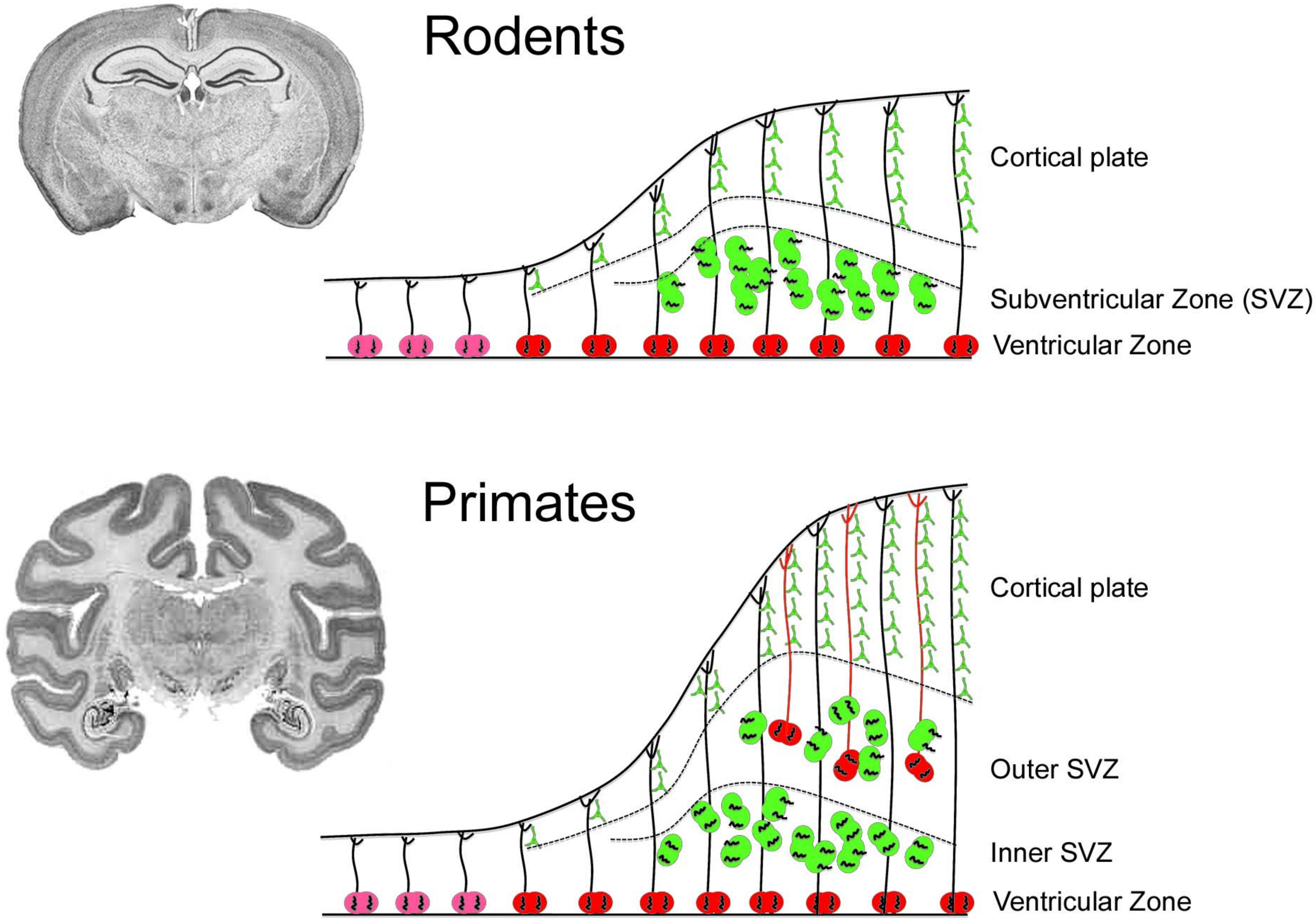






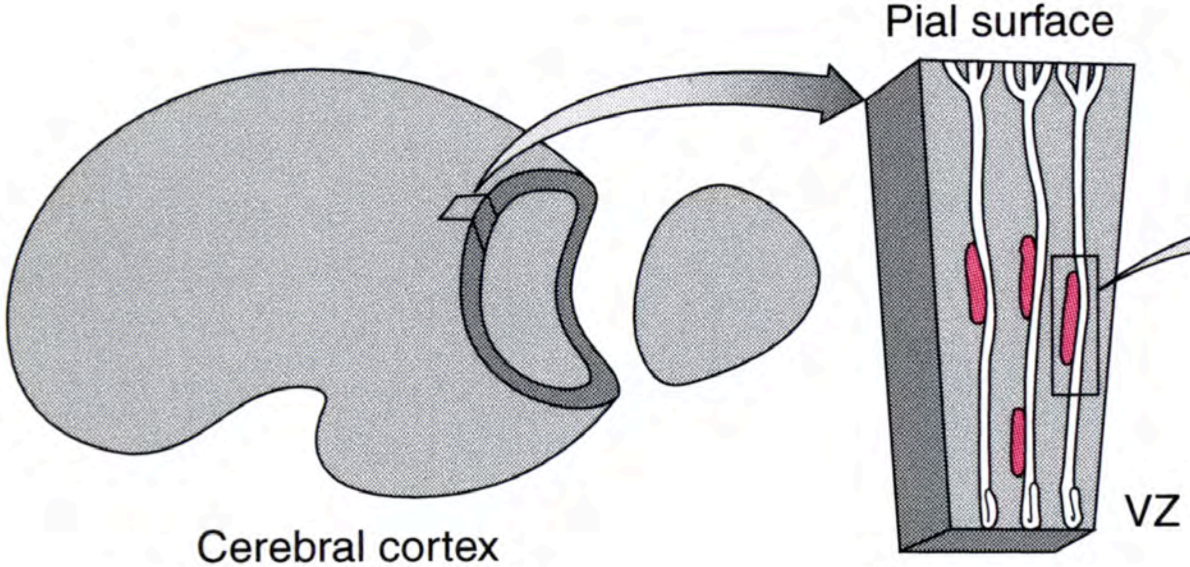
VZ: Ventricular Zone   PP: Preplate   IZ: Intermediate Zone

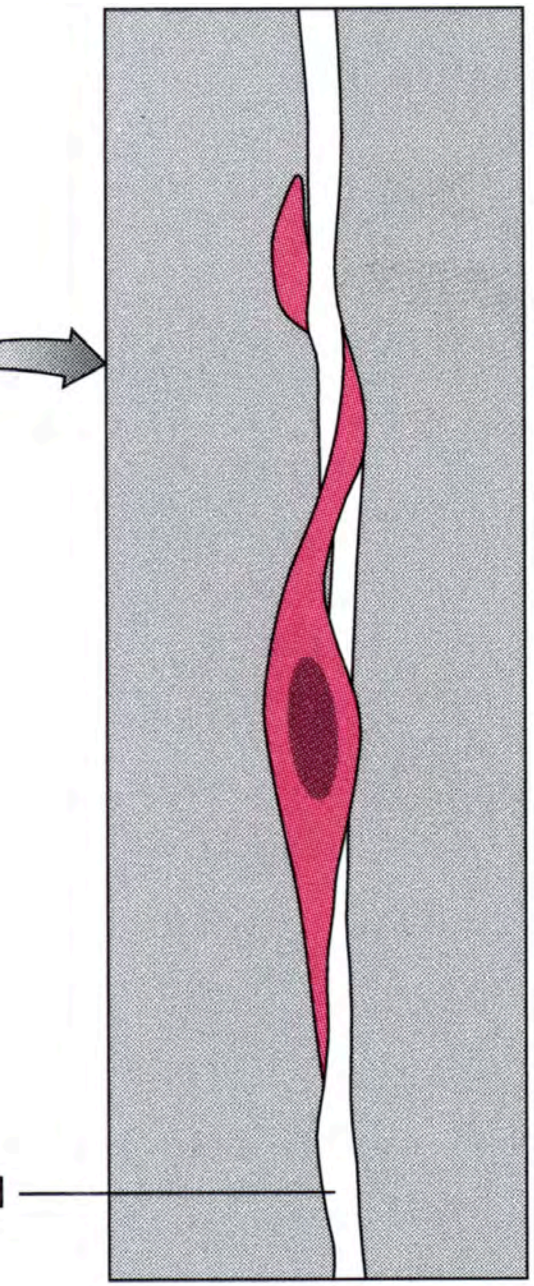
MZ: Marginal Zone   CP: Cortical Plate   SP: Subplate   SVZ: Subventricular Zone



Ref: Arnold Kriegstein 2011 (modified)

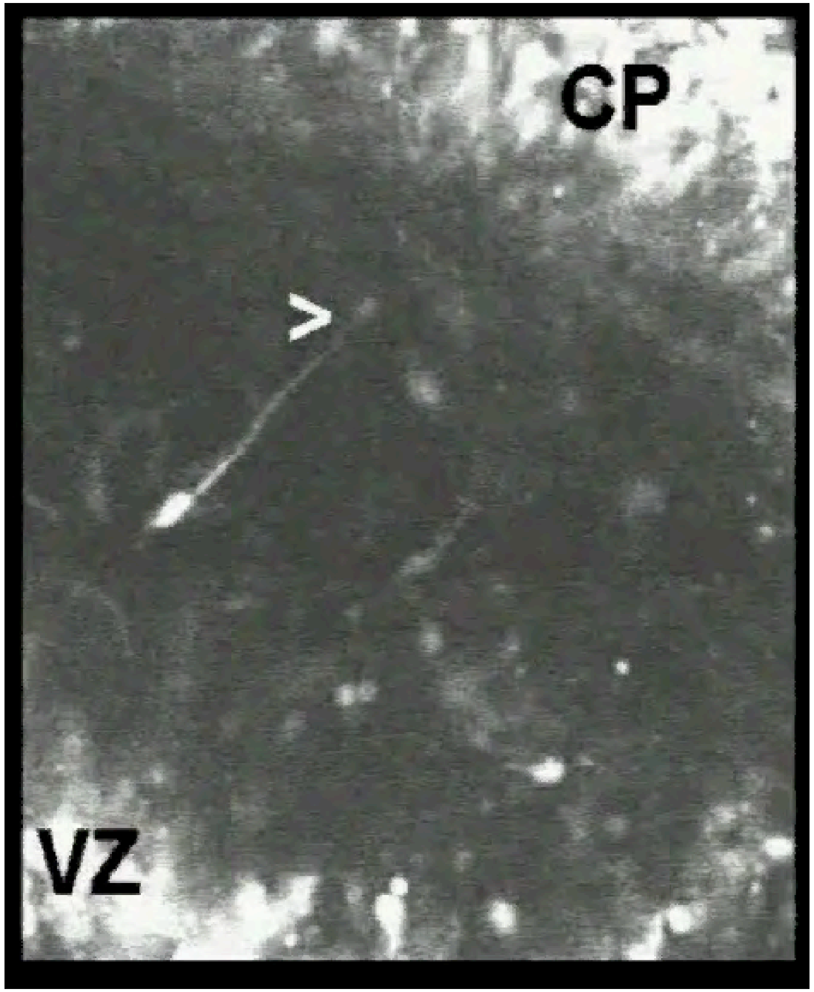
Glia-Guided Locomotion

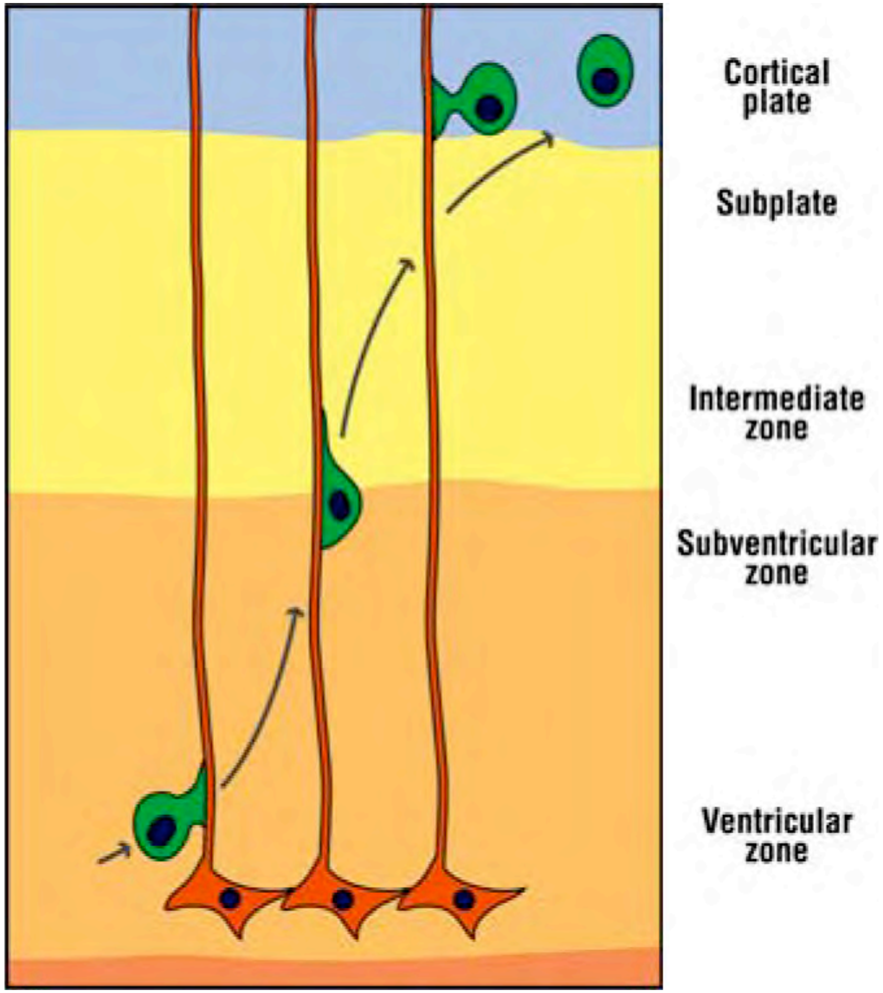




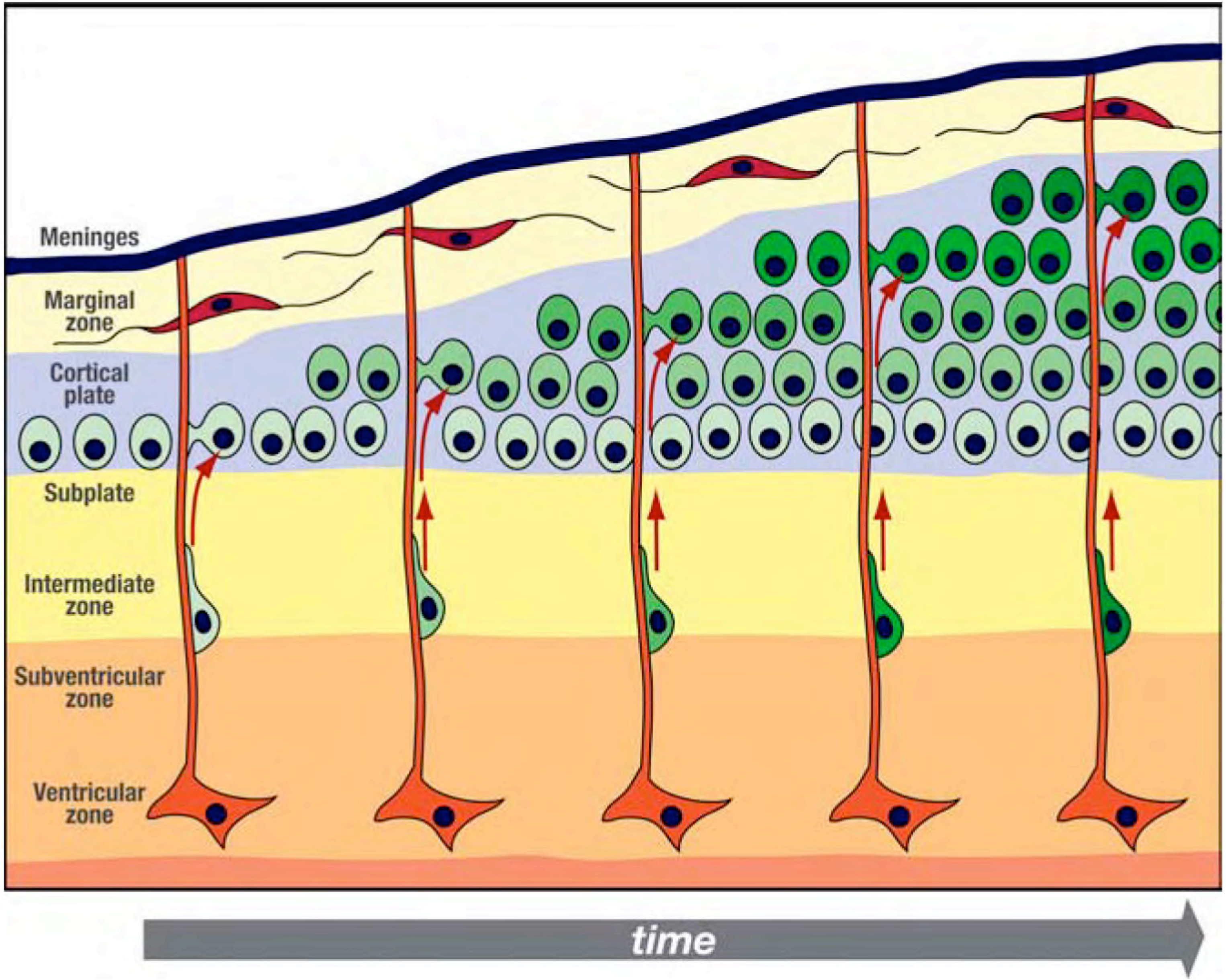
cells from VZ migrate along glia cells to the CP, they basically climb (?)

Glia-Guided Locomotion

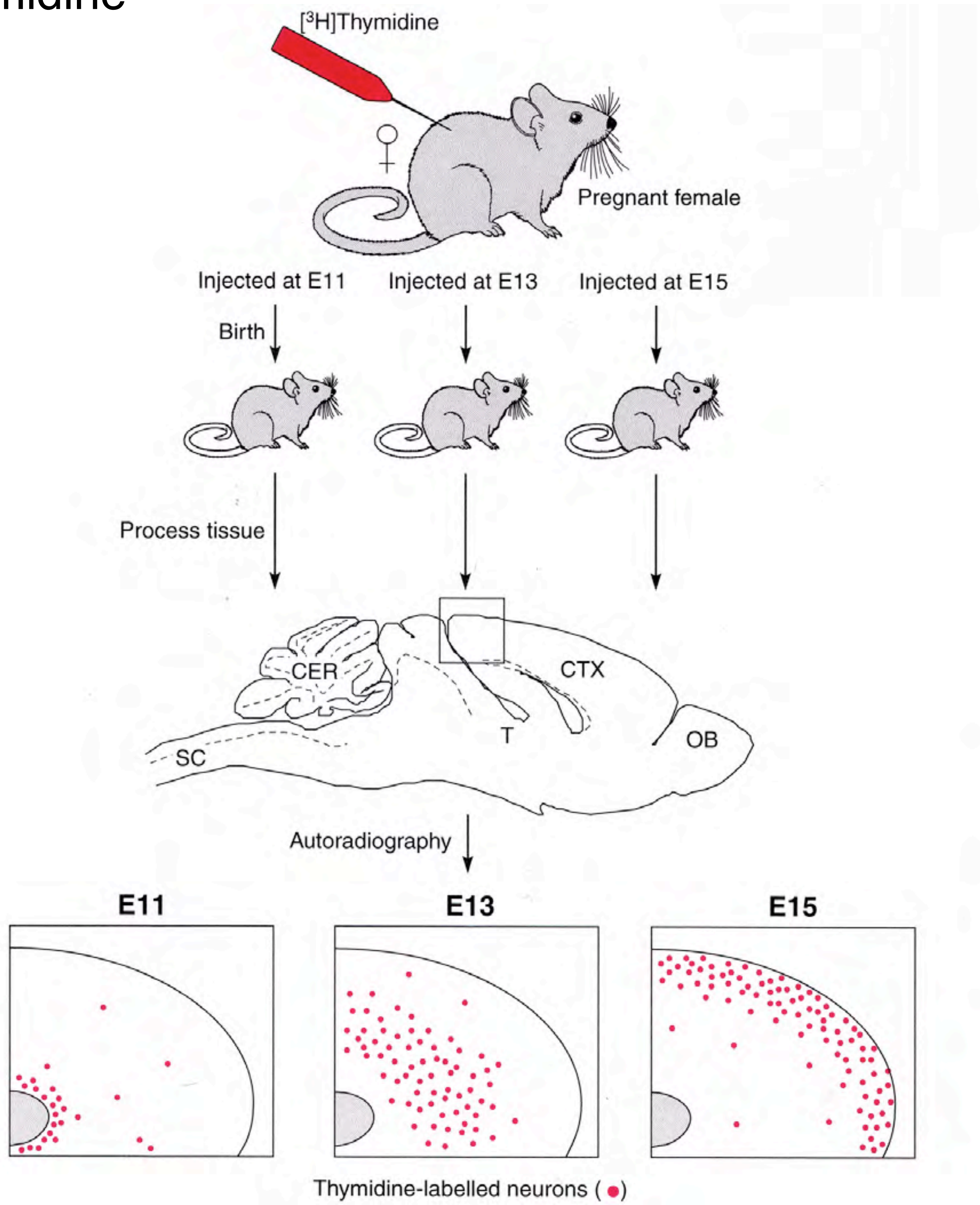




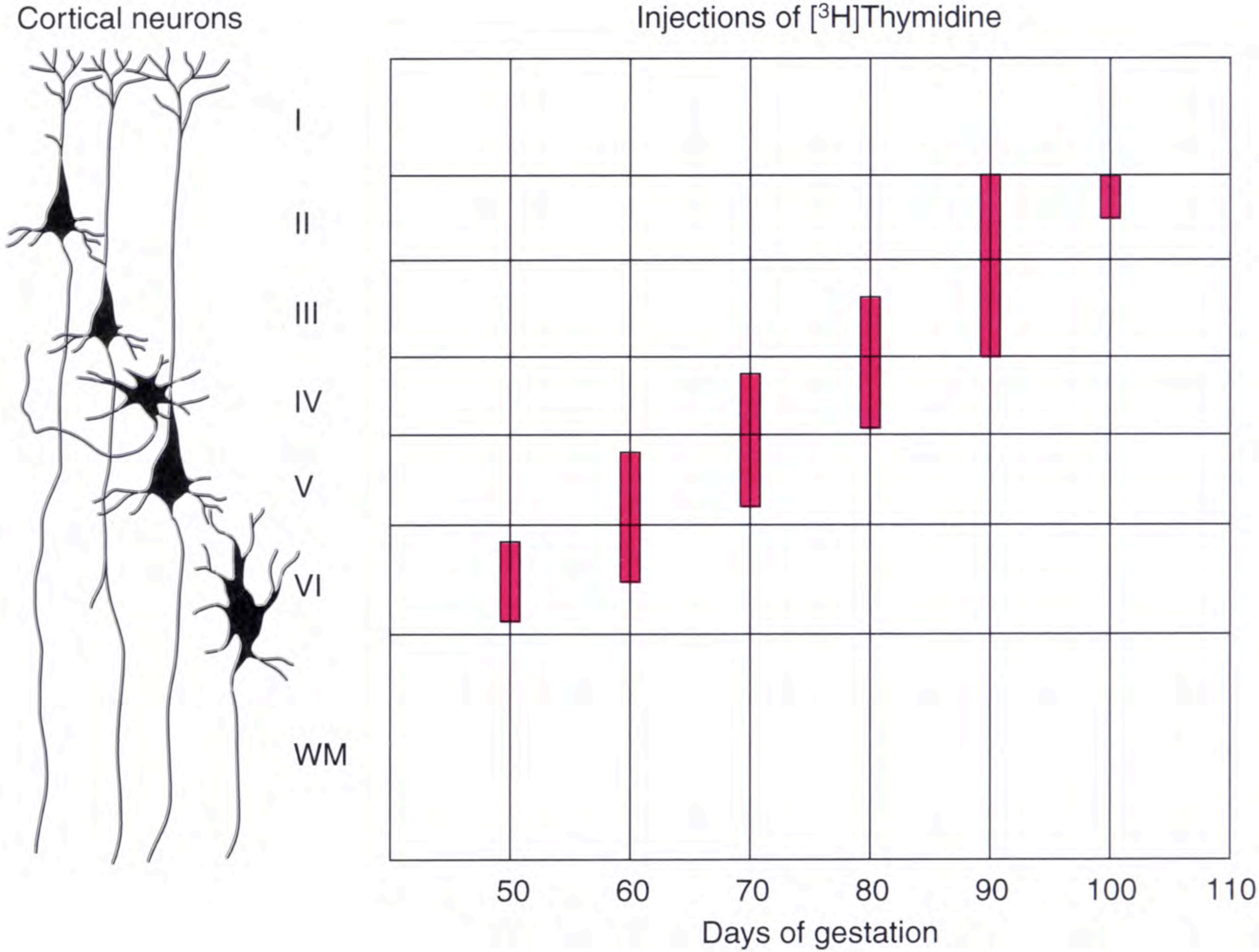
Inside-Out Development of the Cortical Plate



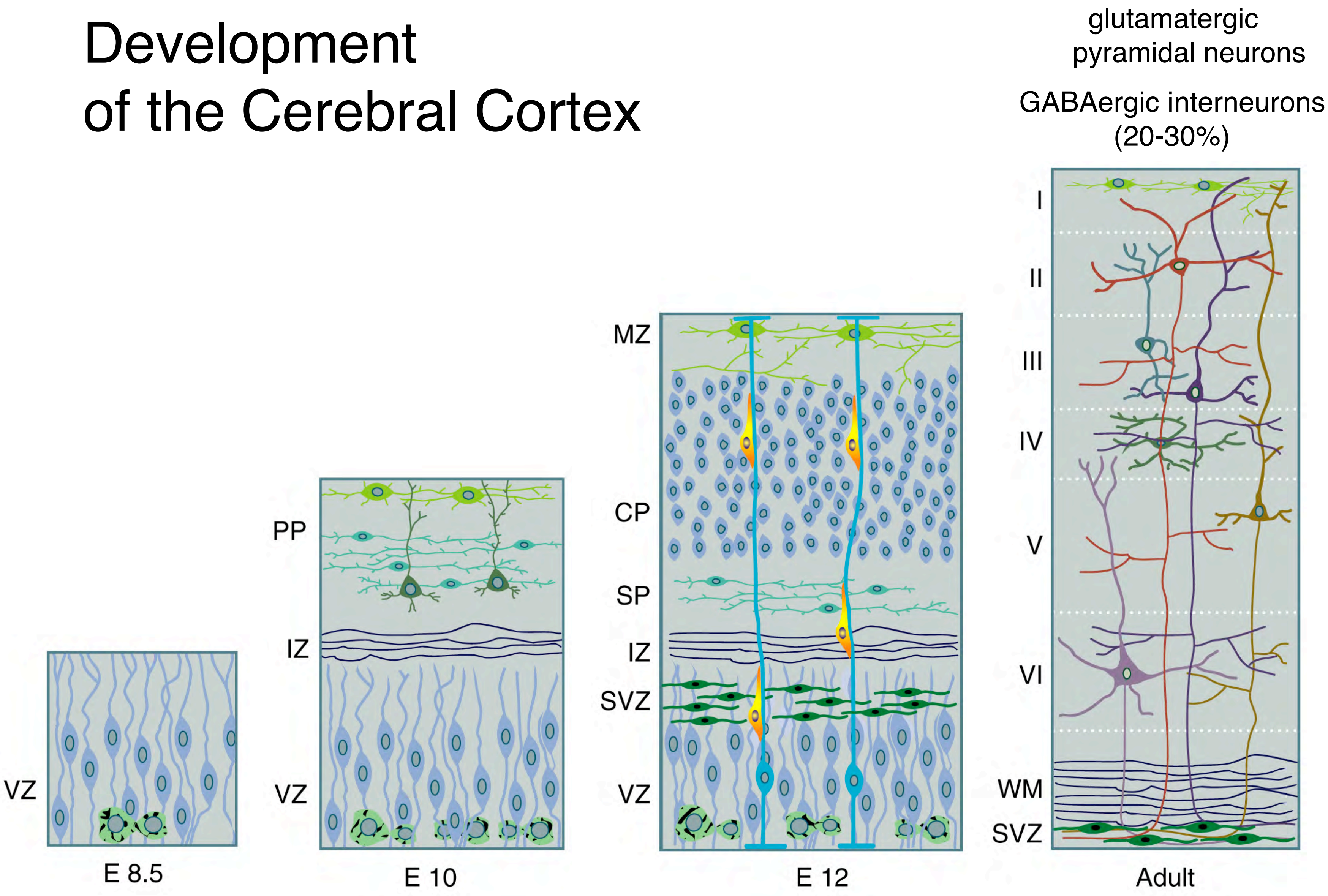
Birthdating with [^{3}H]-Thymidine



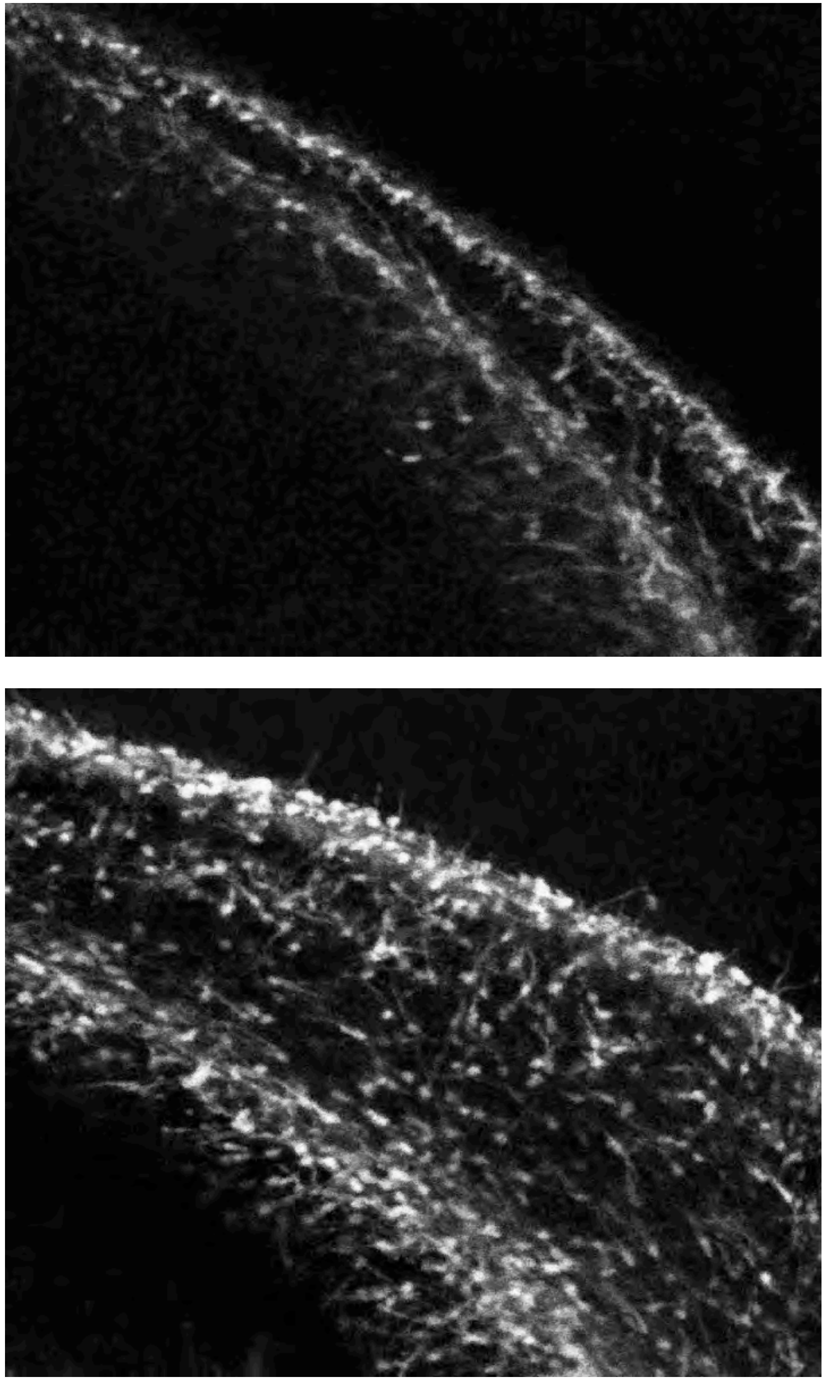
Birthdating with [^{3}H]-Thymidine (Monkey)



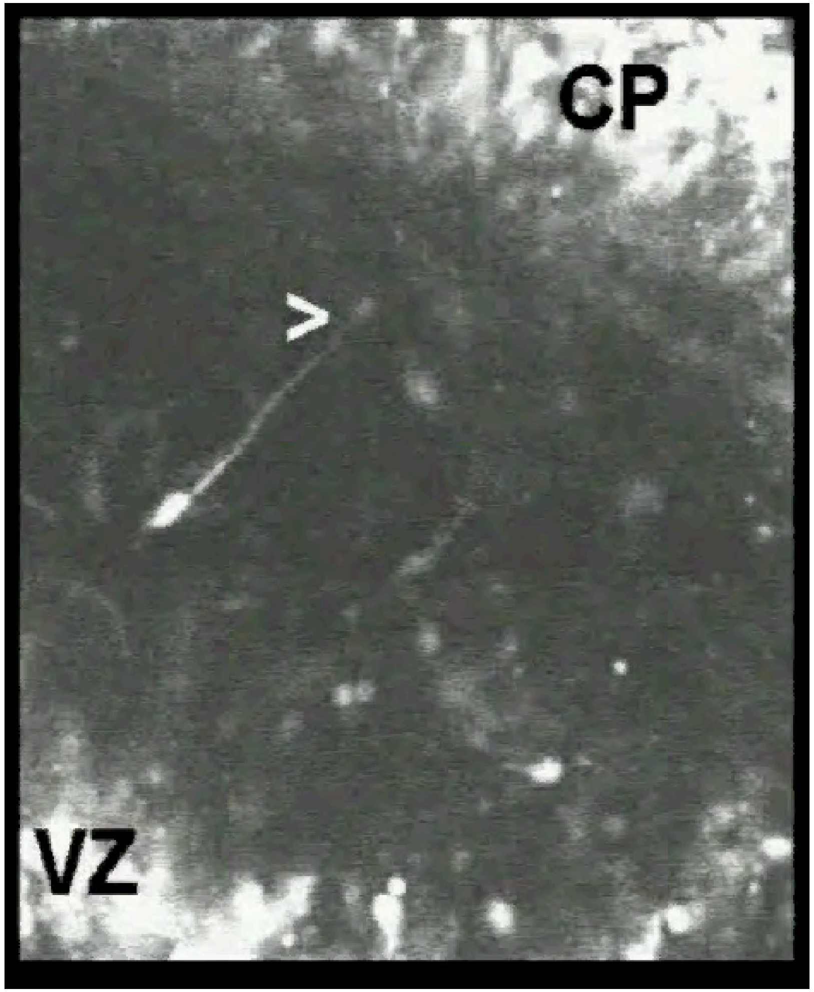
Development of the Cerebral Cortex



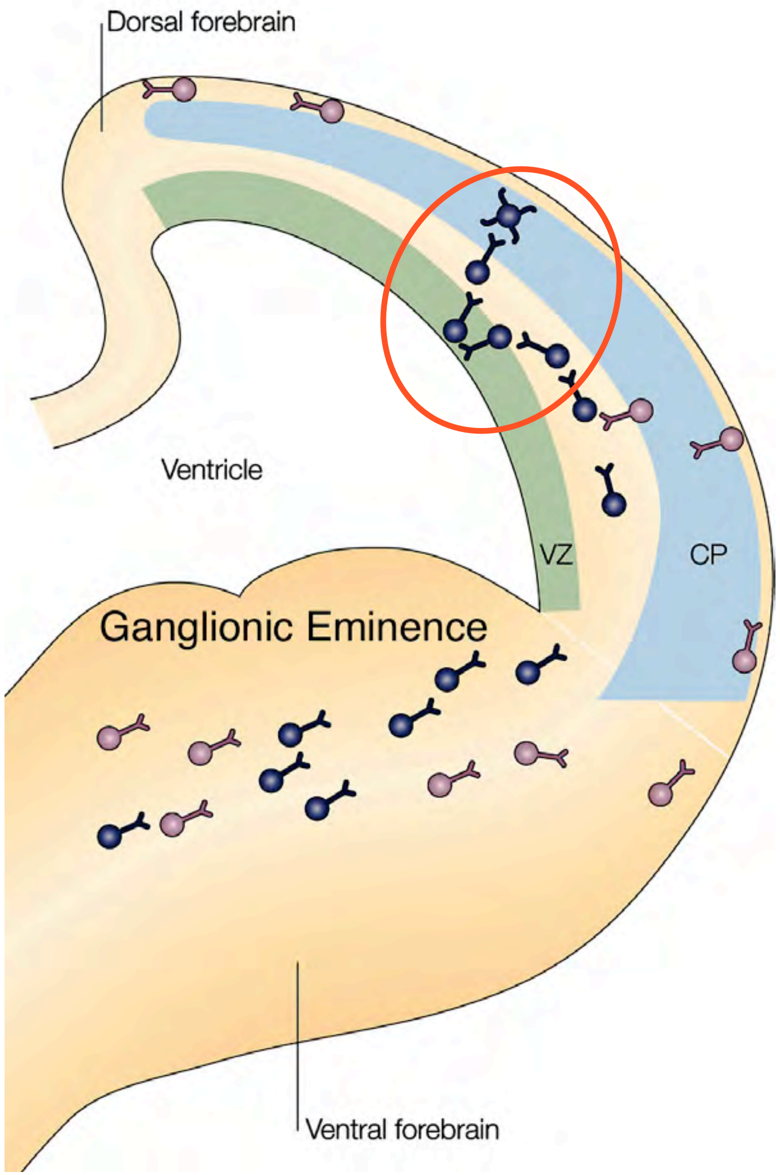
Tangential migration

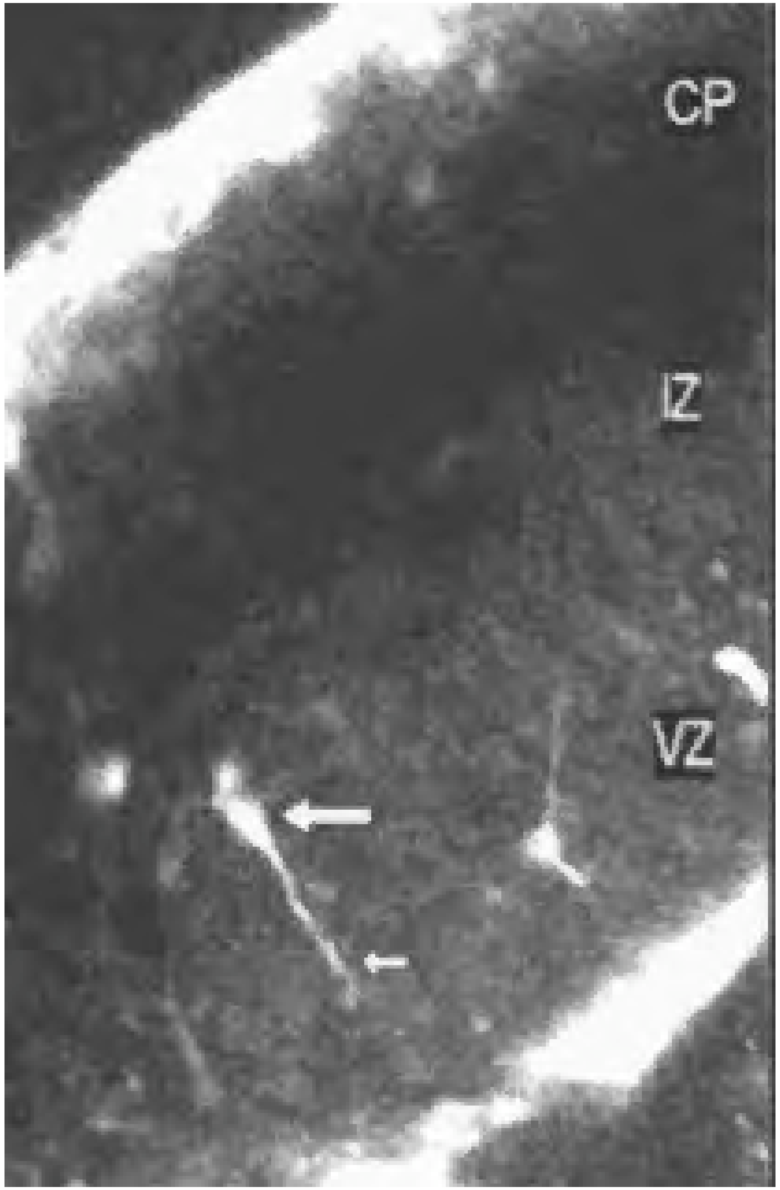


Radial migration

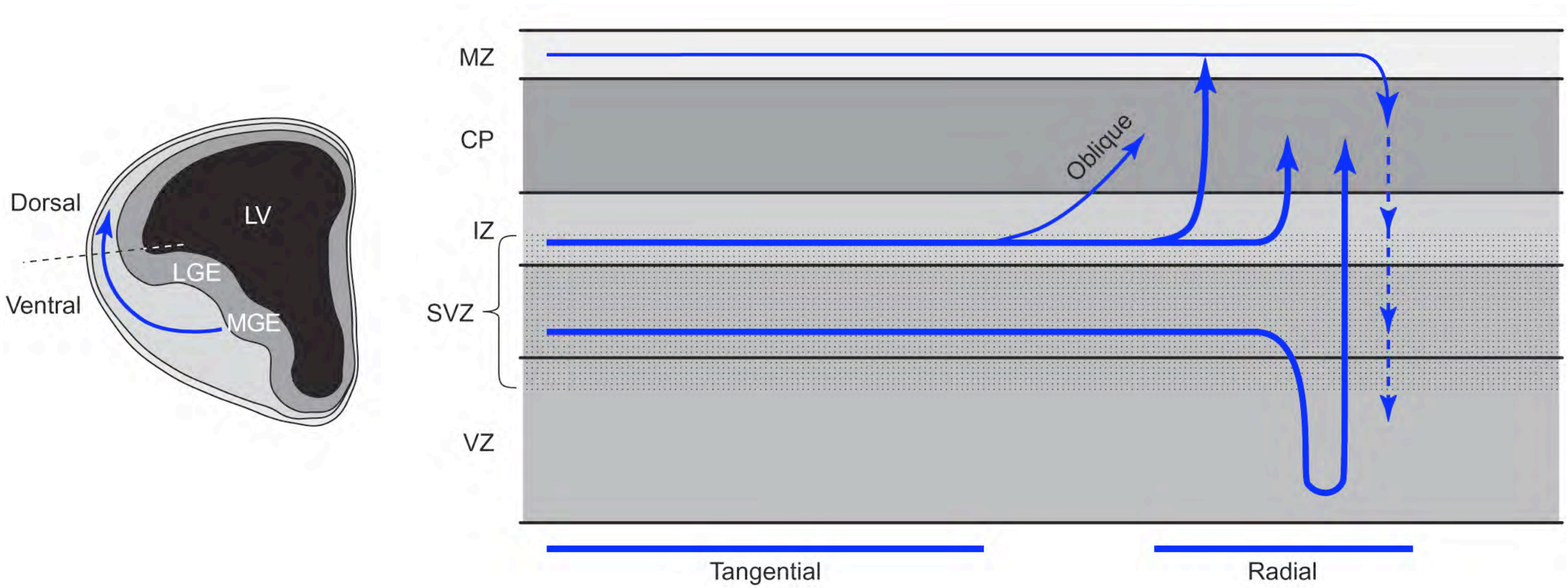


Ventricle-directed Migration

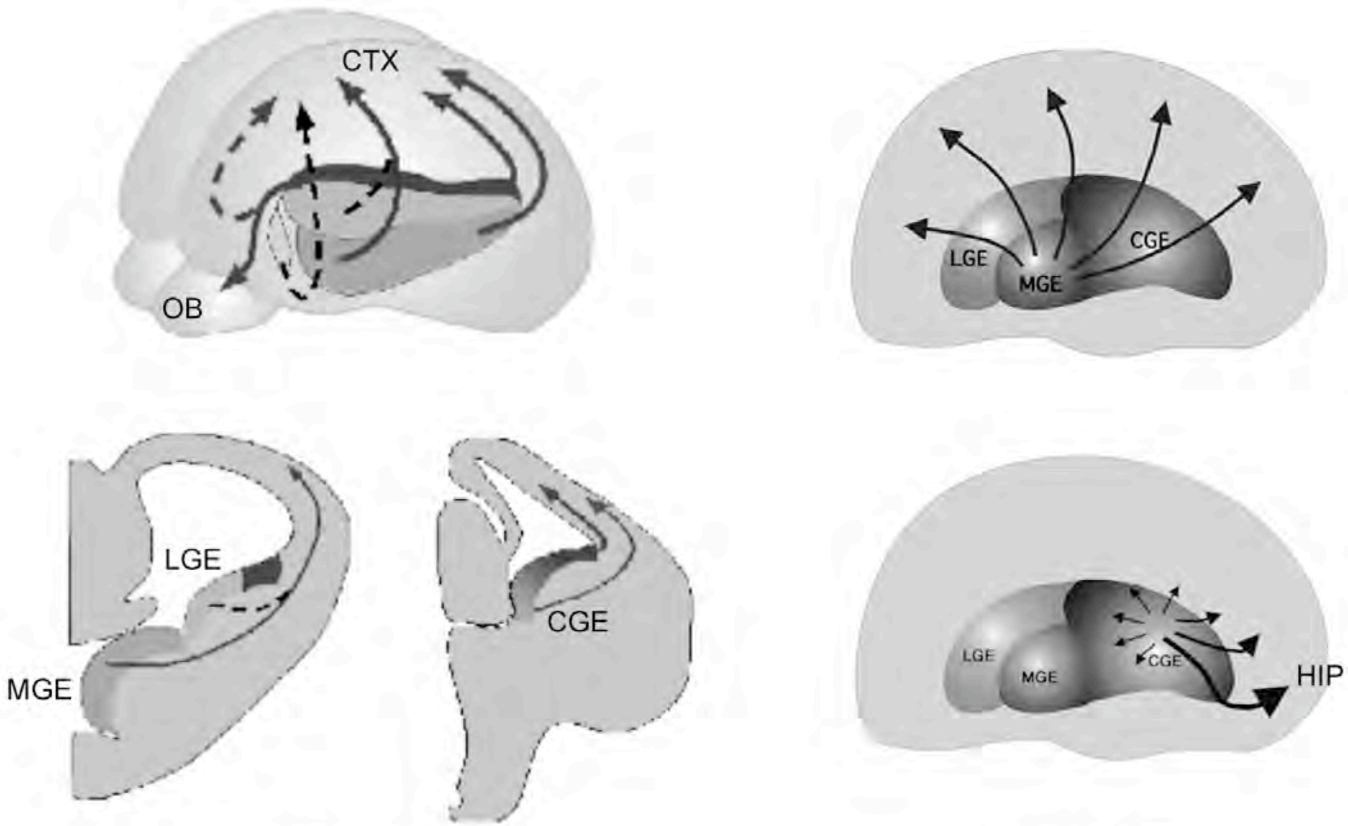




Final Positioning of Tangentially Migrating Neuronal Precursors



Pathways of Tangential Migration



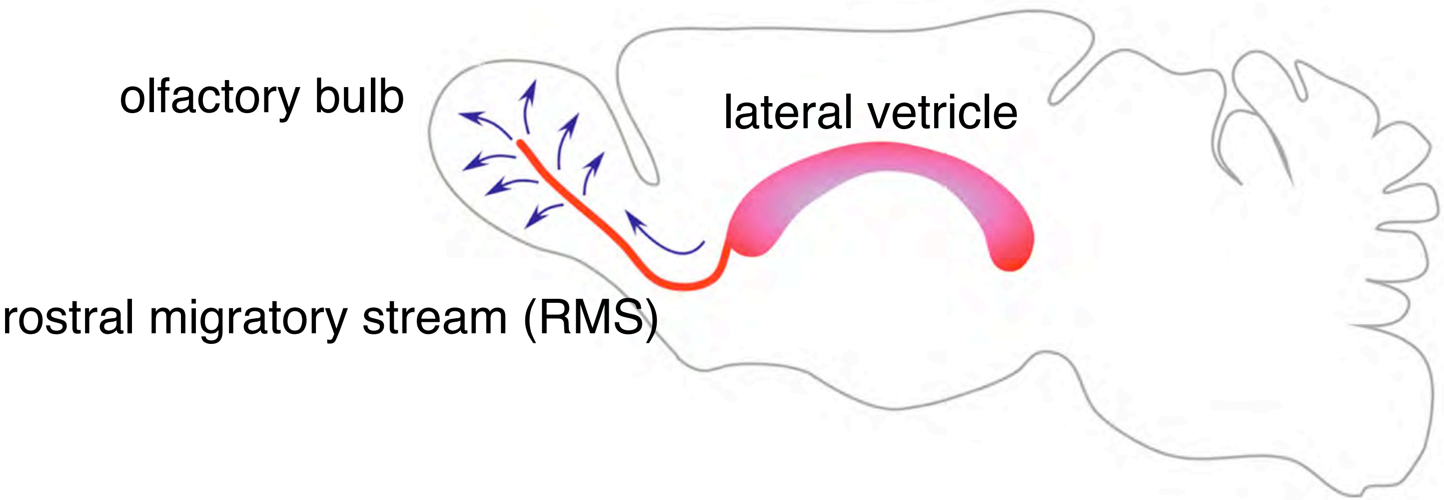
Coronal

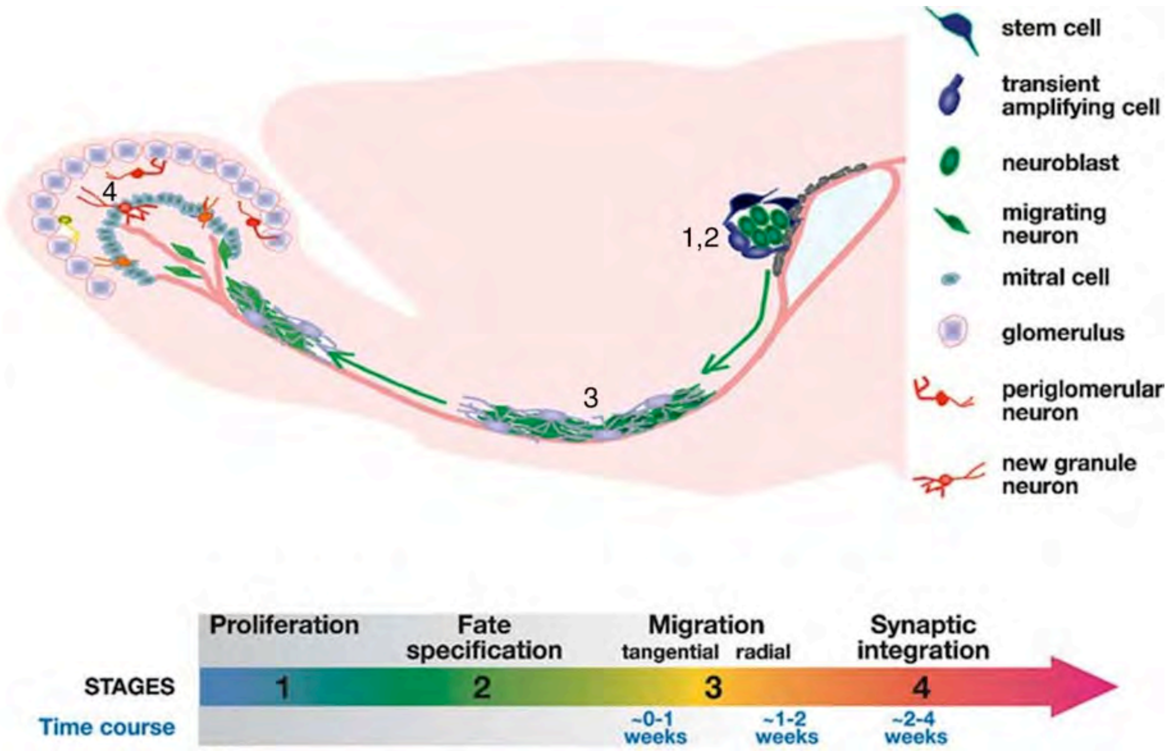
Saggital

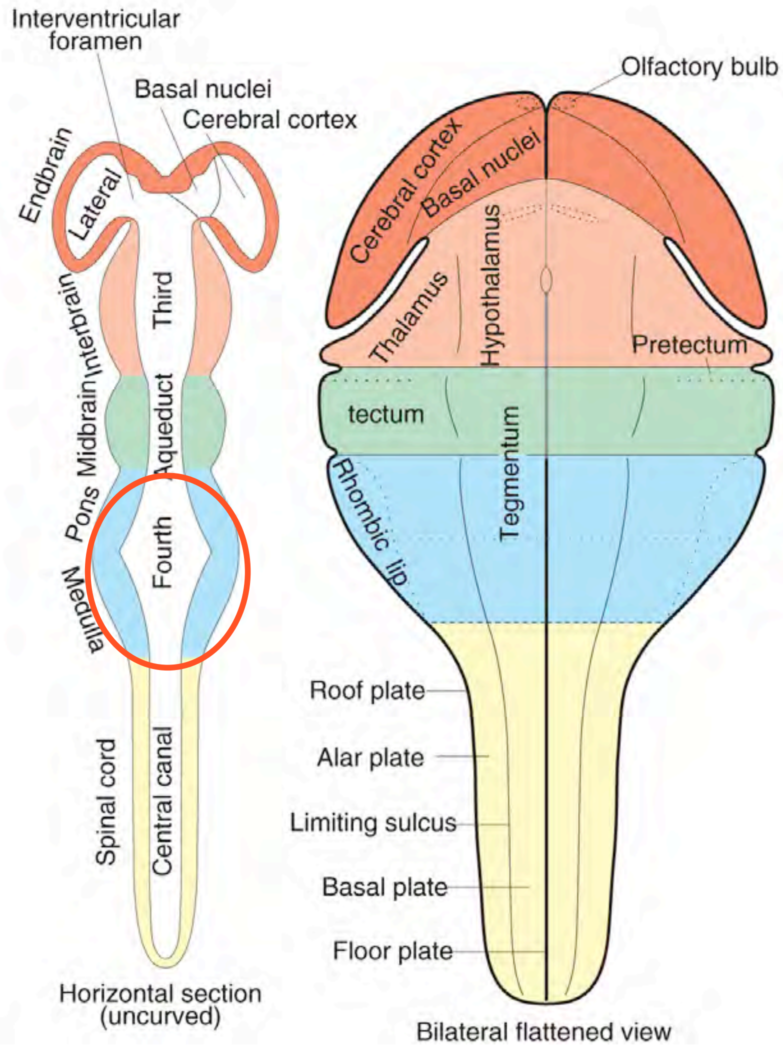
MGE: Medial Ganglionic Eminence
LGE: Lateral Ganglionic Eminence
CGE: Caudal Ganglionic Eminence

CTX: Cortex
OB: Olfactory Bulb
HIP: Hippocampus

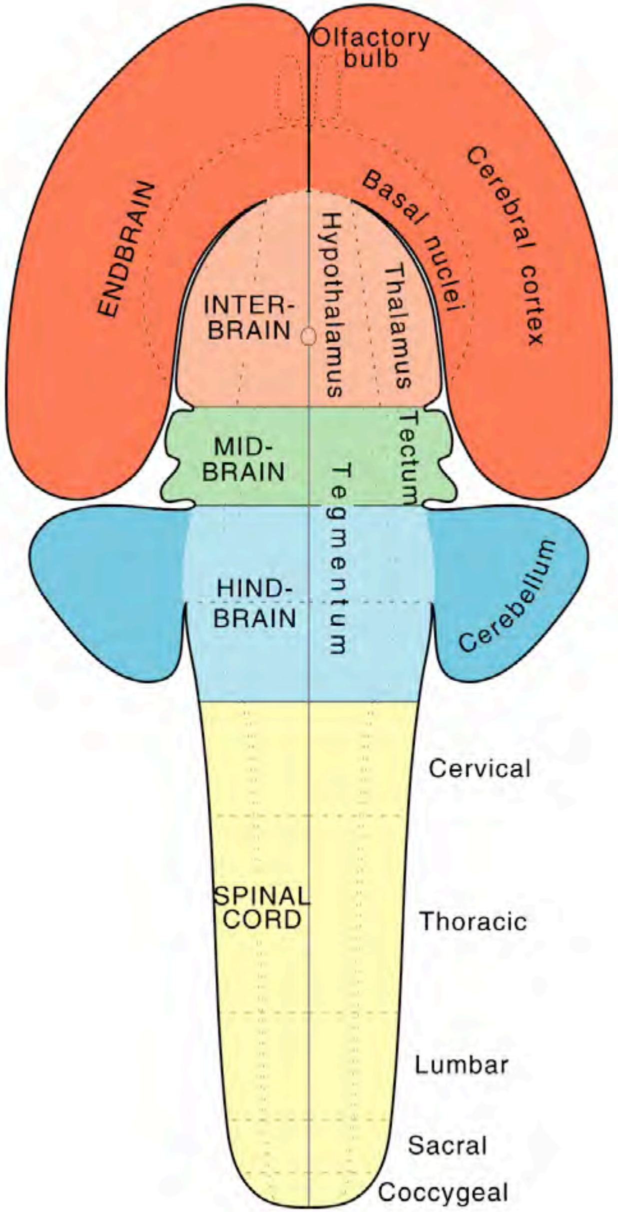
Migration of neuronal precursor cells to the olfactory bulb





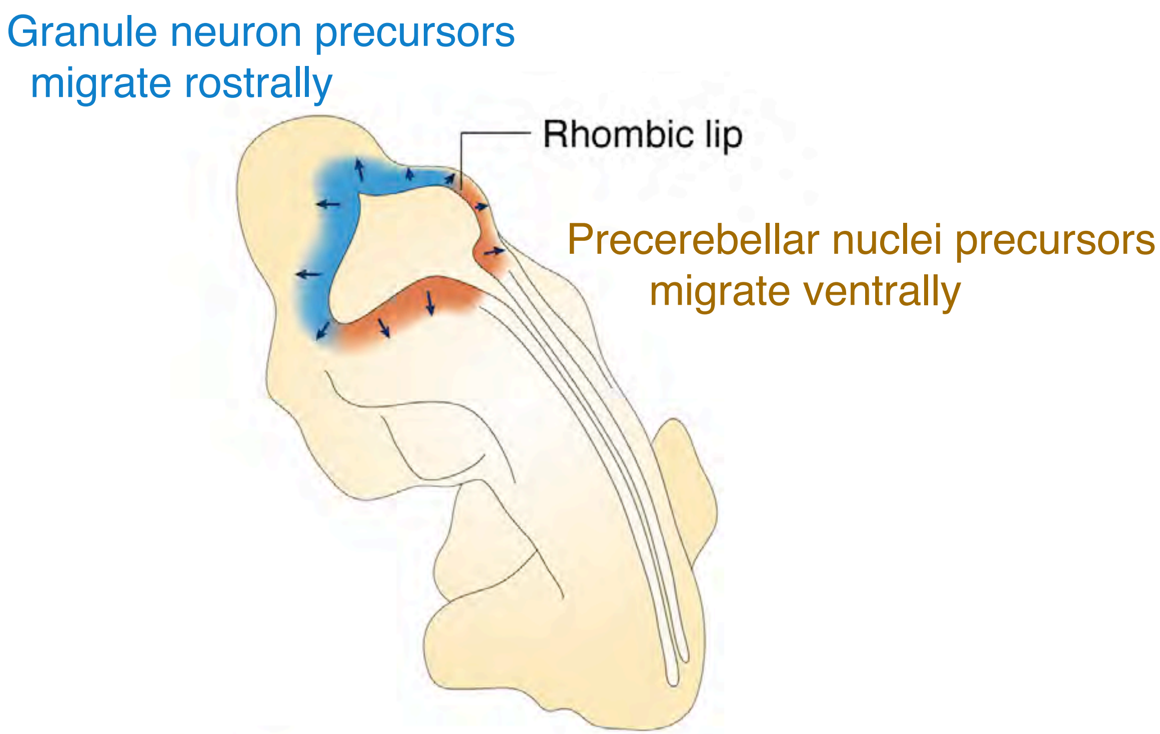


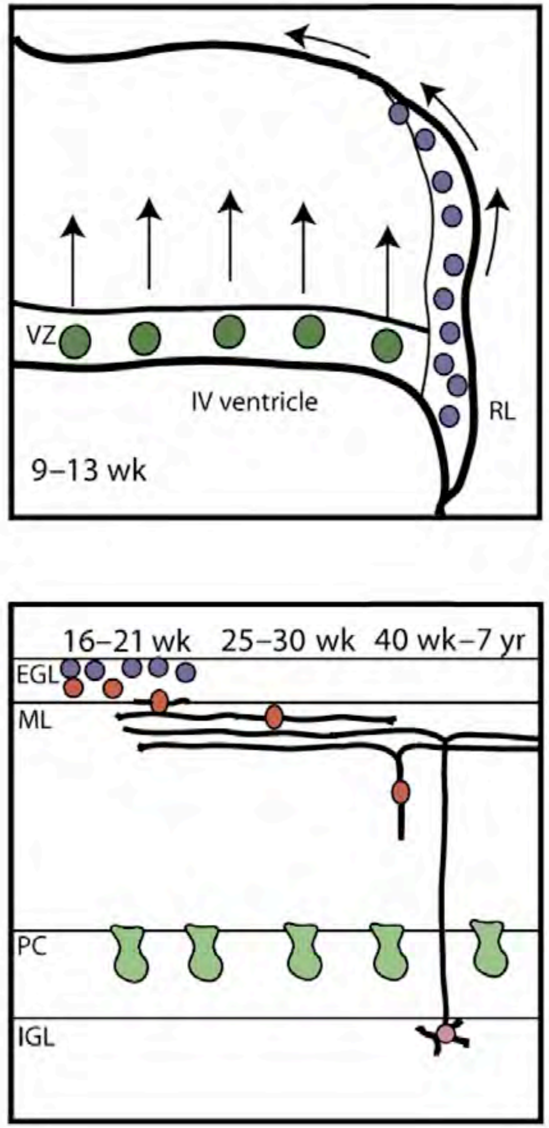
6 weeks (human)

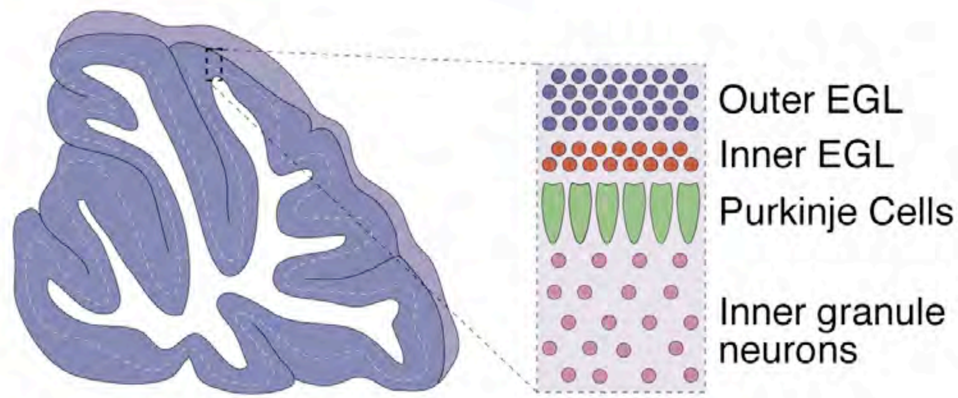


adult (human)

Migration in the Developing Cerebellum







EGL: external granule layer IGL: internal granular layer VZ: ventricular zone ML: molecular layer

Migration of neuronal precursor cells during brain development (Summary)

Cerebral cortex:

A. Radial migration

Formation of excitatory pyramidal neurons in the cortex

At least two major migration modes:

- somal translocation (early in development)
- glial guided locomotion along radial glia
  (up to 2 cm migration during human cortex development)

B. Tangential migration

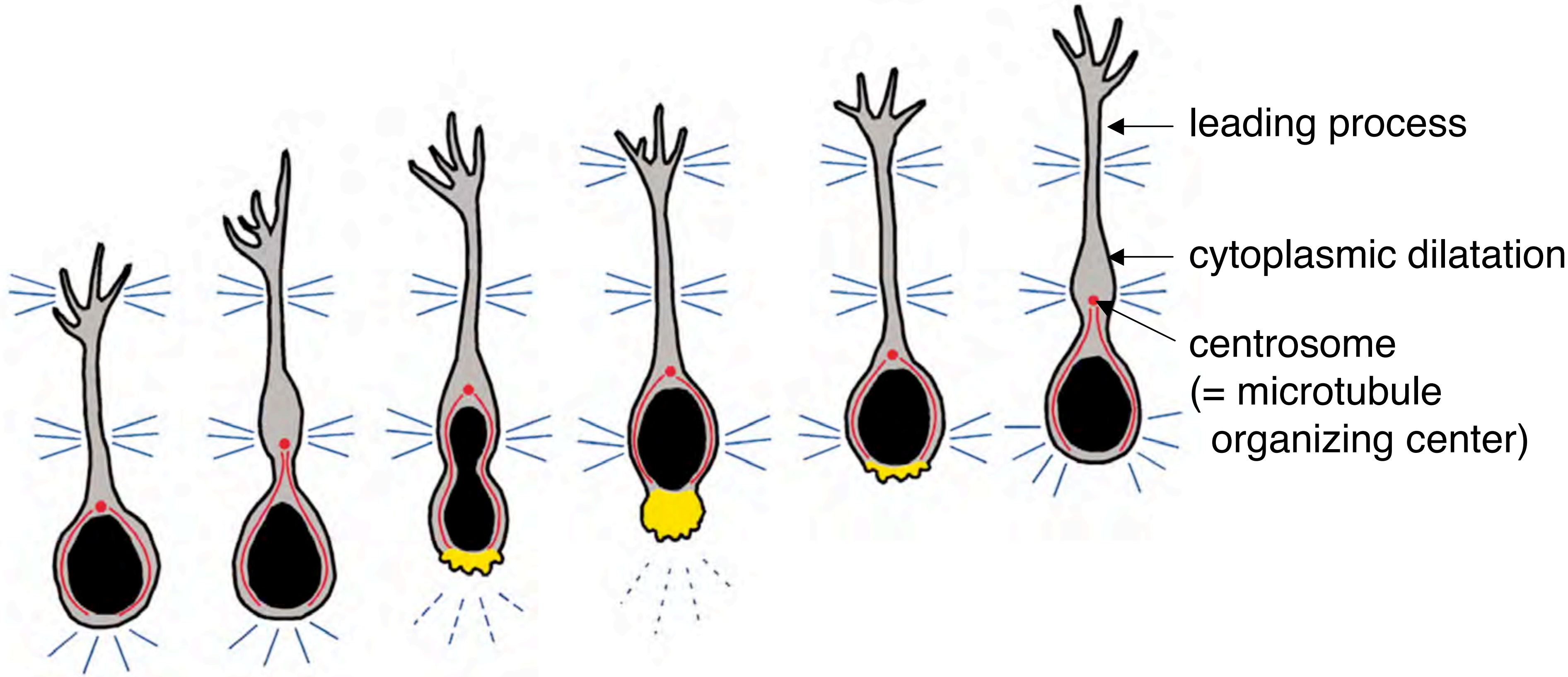
Immigration of inhibitory interneurons into the cortex and olfactory bulb

Cerebellum:

A. Radial migration of Purkinje precursor cells

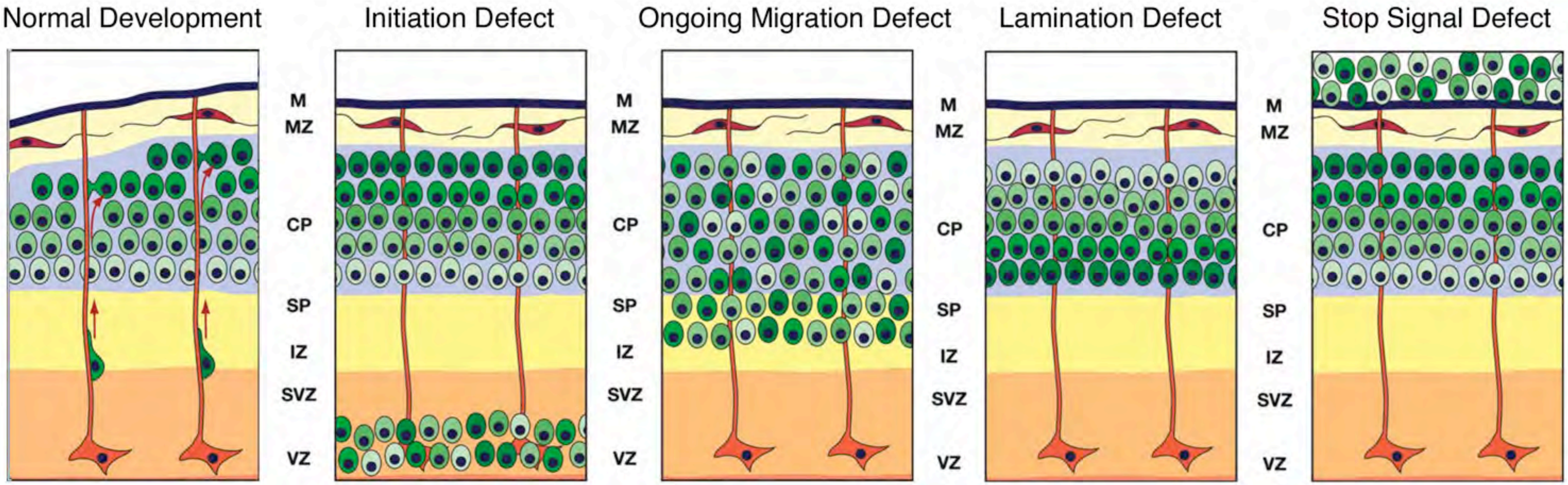
B. Tangential migration of cerebellar granule cell precursors and precursors of the precerebellar nuclei

Model of Saltatory Neuronal Migration



Requirements for movement:
- selective adhesion (e.g. through integrin-receptors)
- dynamic reorganization of the cytoskeleton
  (extension of leading process and nucleokinesis)

Cortical Migration Defects

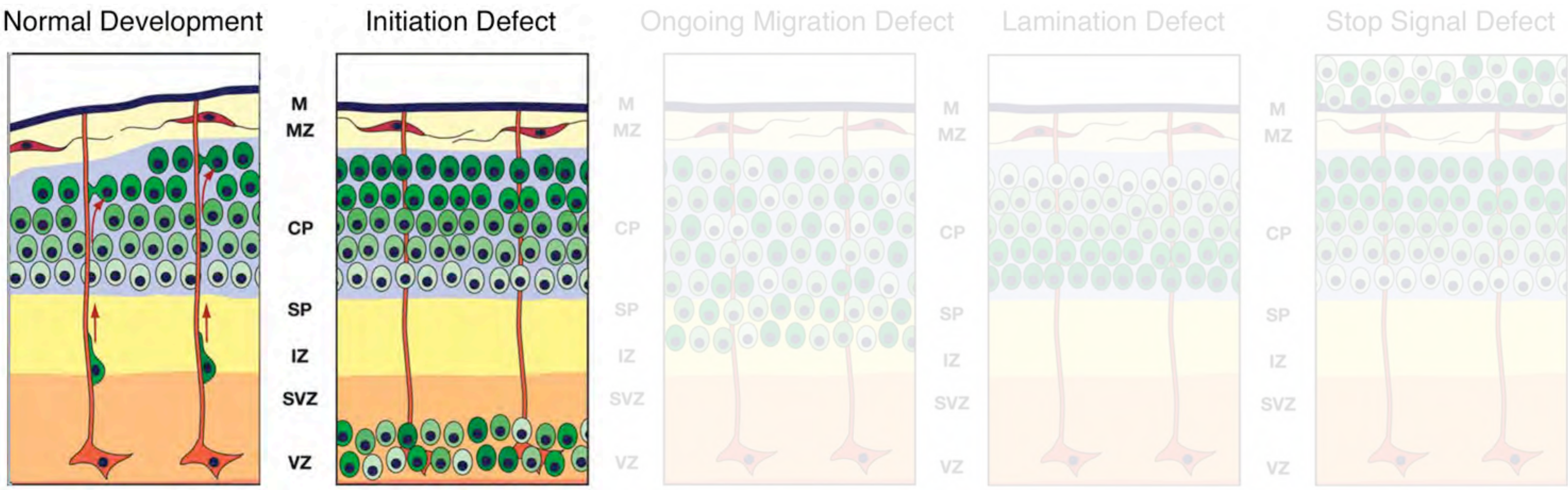


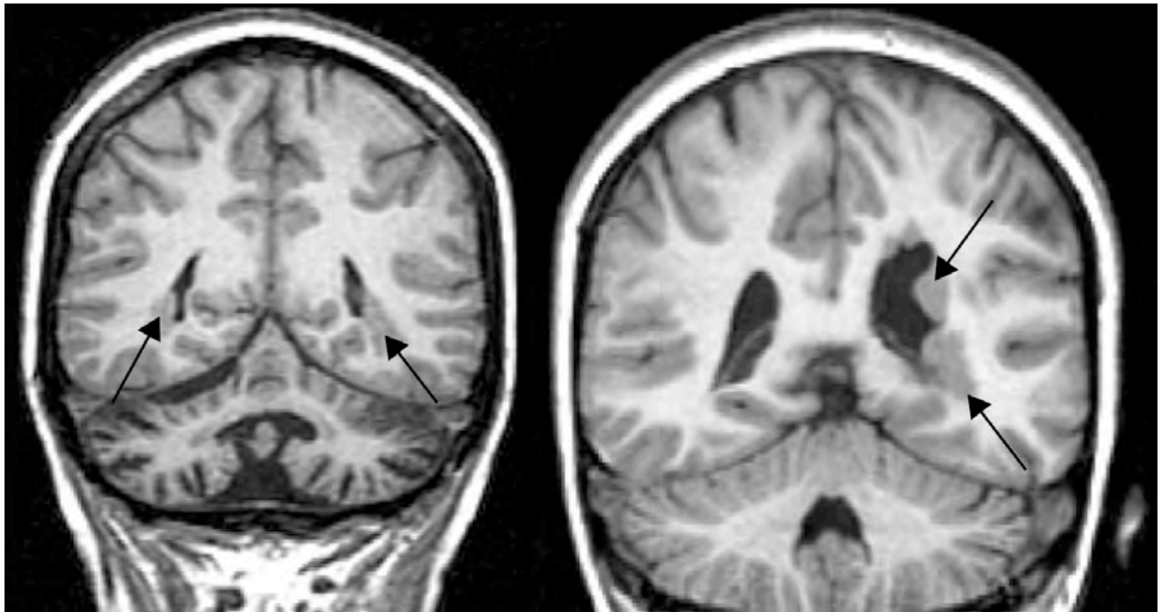
Annu. Rev. Cell Dev. Biol. 2004. 20:593–618

CORTICAL NEURONAL MIGRATION MUTANTS SUGGEST SEPARATE BUT INTERSECTING PATHWAYS

Stephanie Bielas, Holden Higginbotham, Hiroyuki Koizumi, Teruyuki Tanaka, and Joseph G. Gleeson

Cortical Migration Defects

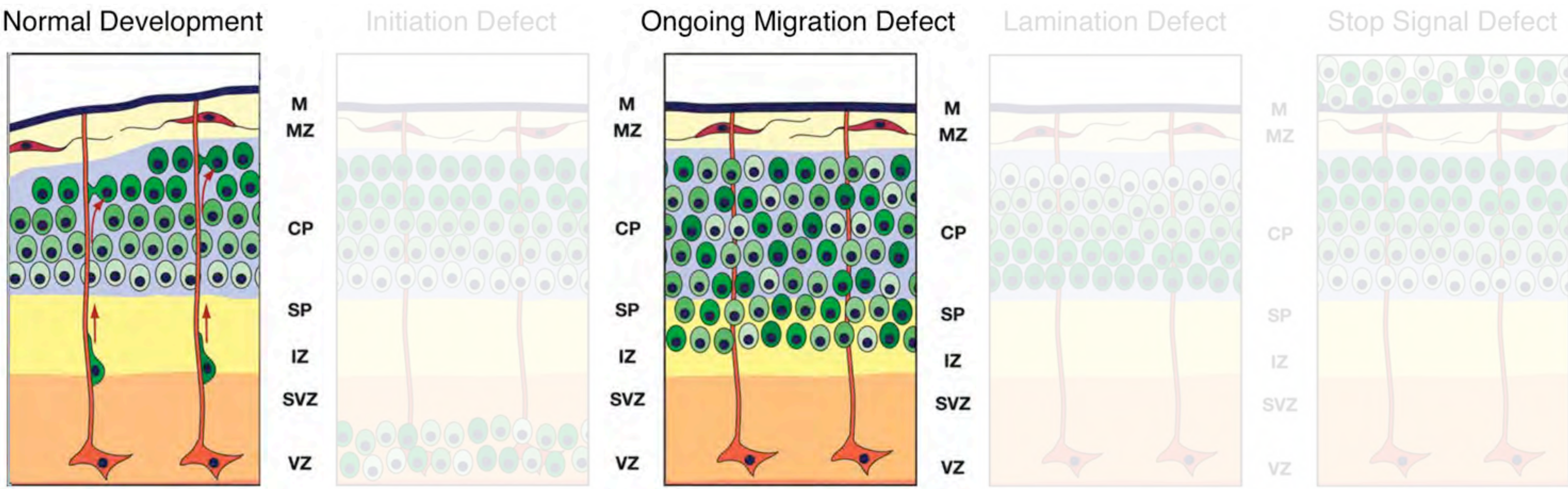


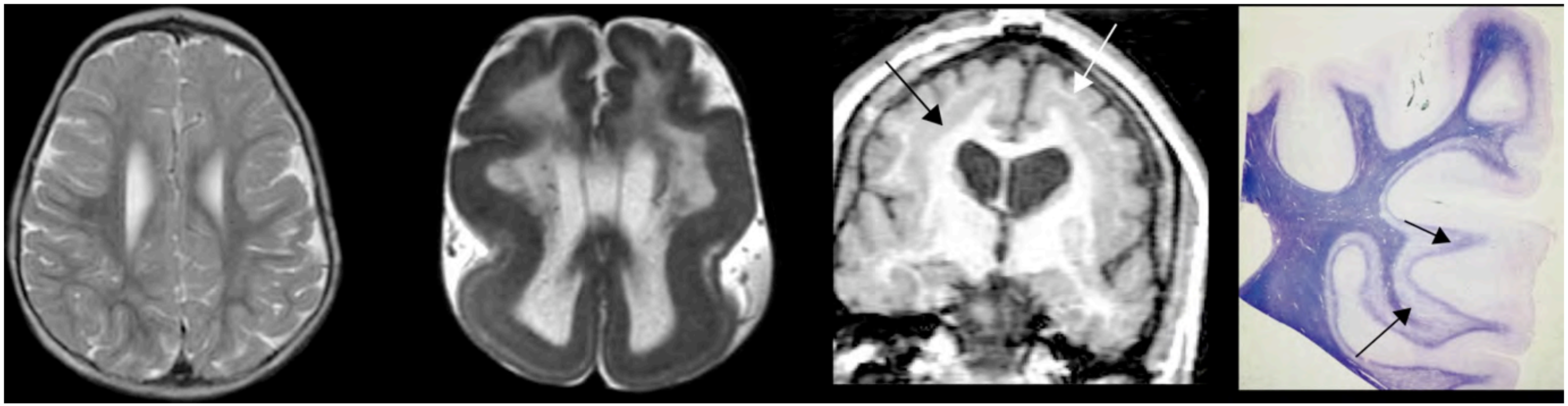


Human Disorder:
Periventricular Heterotopia

Mutated Genes:
- filamin A *(FLNA)*
  => actin-binding protein
- *Arfgef2*
  => vesicle trafficking
- etc

Cortical Migration Defects

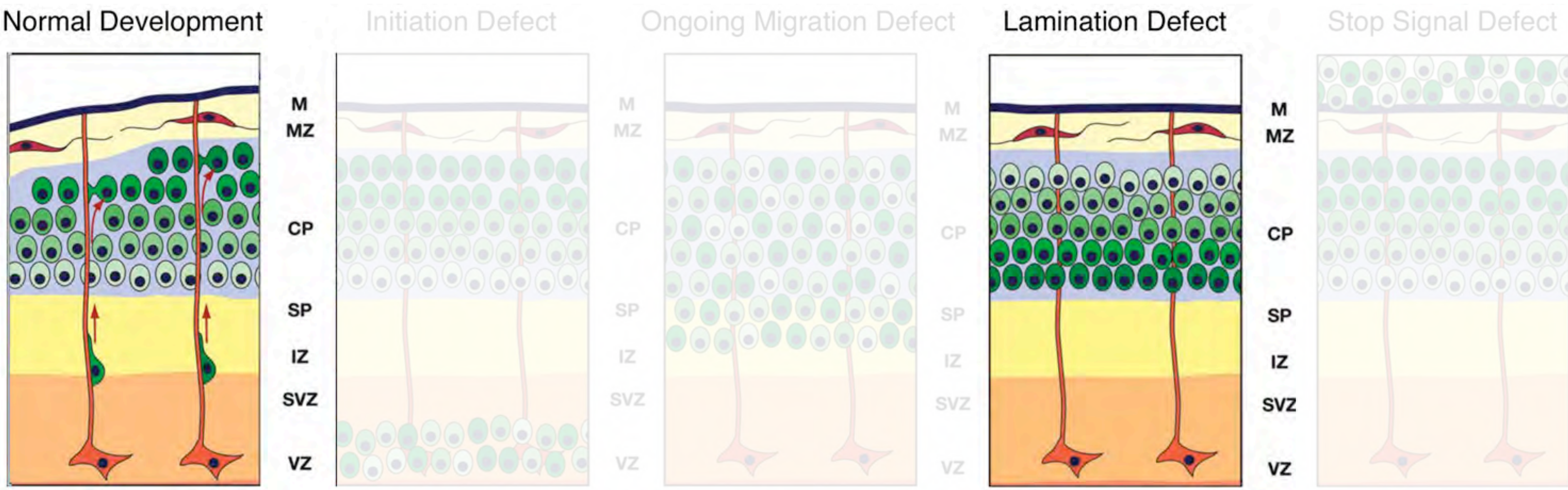


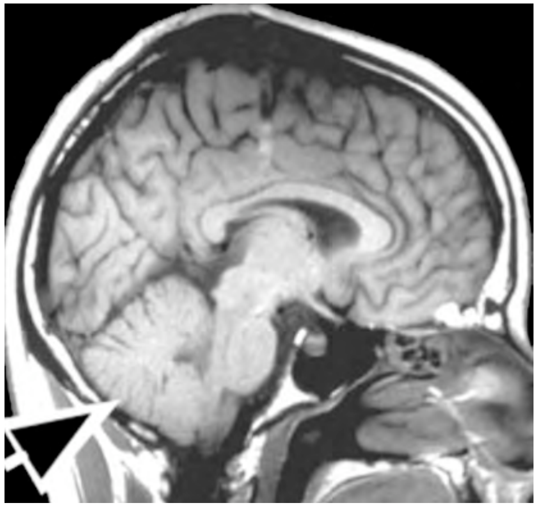


Normal

Human Disorder:
Lissencephaly / Subcortical Band Heterotopia (Double cortex)
Mutated Genes: *Dcx, Lis1, etc.*

Cortical Migration Defects



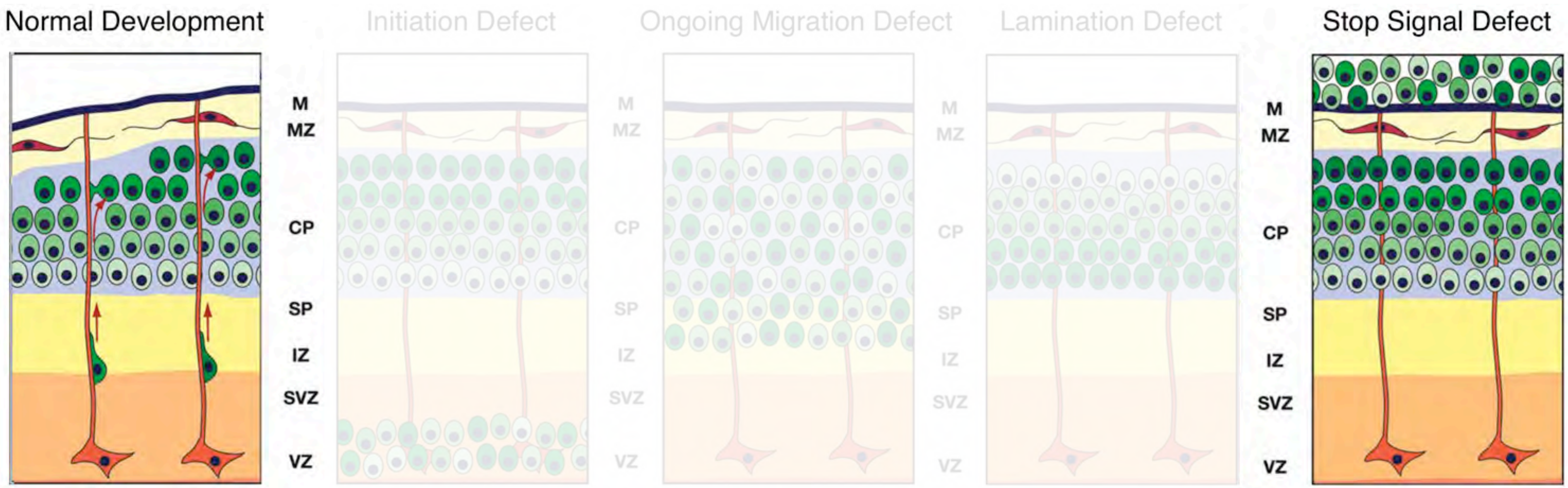


Normal

Human Disorder:
Lissencephaly /
Cerebellar
Hypoplasia

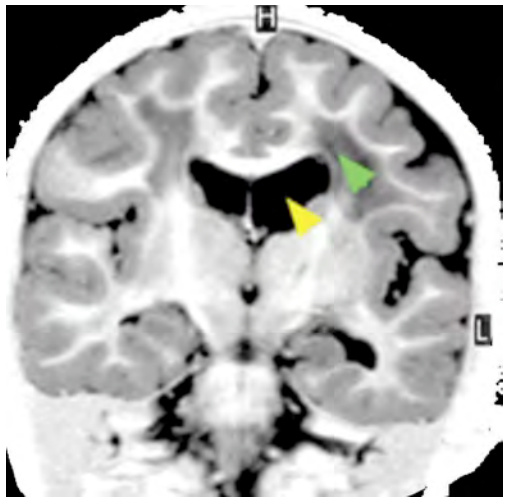
Mutated Gene:
Reelin *(RELN)*

Cortical Migration Defects

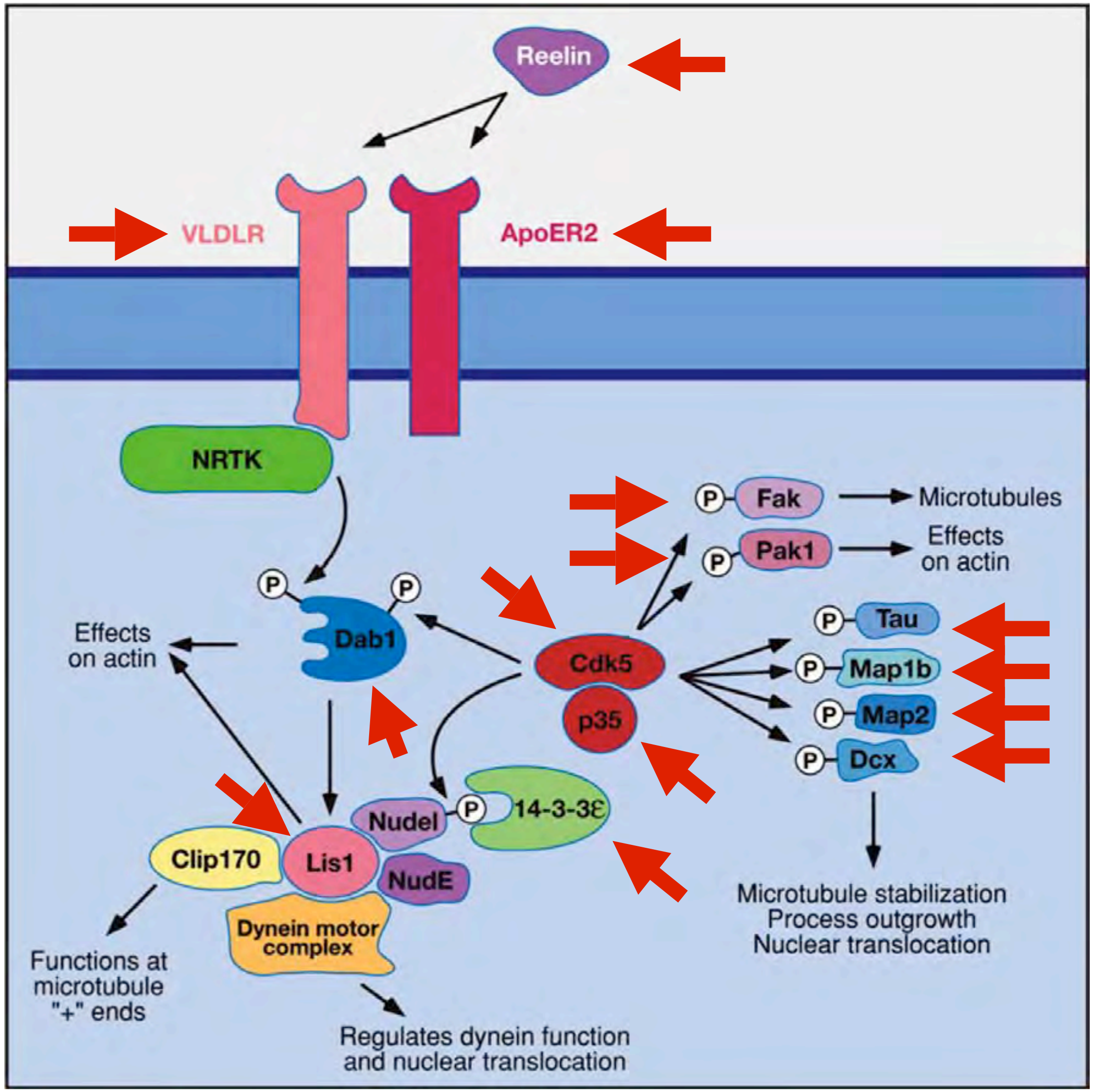


Human Disorder:
Cobblestone Lissencephaly

Mutated Gene:
- *POMT1*
- *POMGnT1*
- *Fukutin*



Functional Networks of Neuronal Migration Factors



Mutations leading to defects in the cortex development affect mostly genes involved in the assembly, stability and dynamics of the microtubule cytoskeleton.

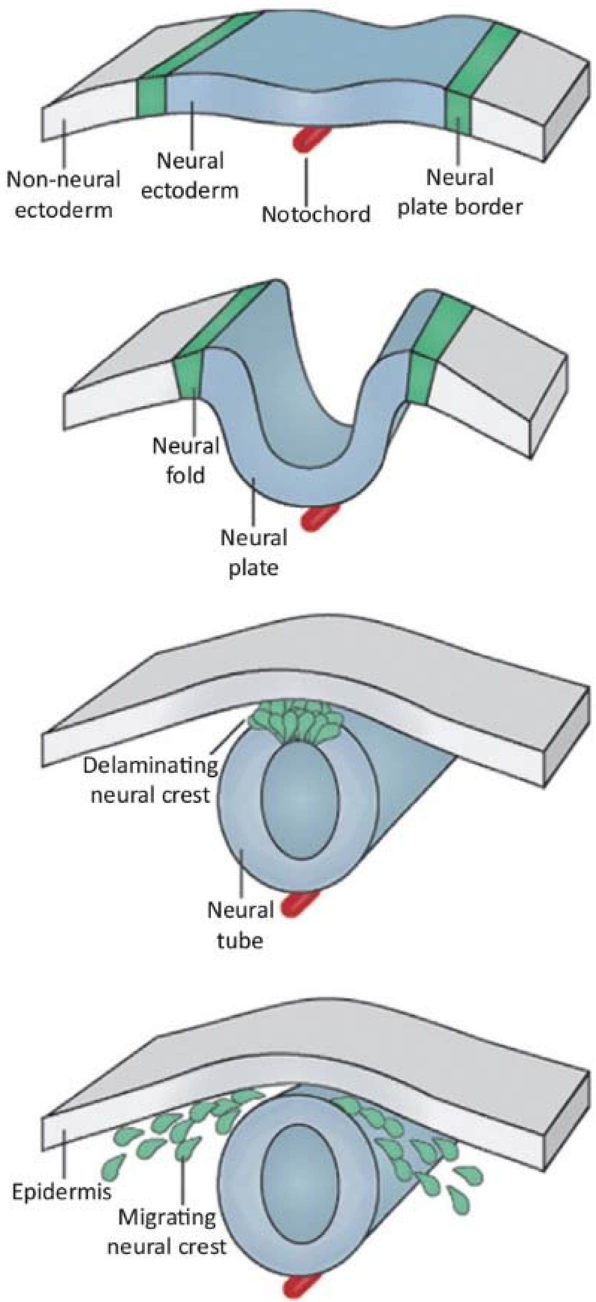
Review

Division of labor during trunk neural crest development

Laura S. Gammill *, Julaine Roffers-Agarwal

Developmental Biology 344 (2010) 555–565

Formation of the neural crest cells



Neural plate border specification

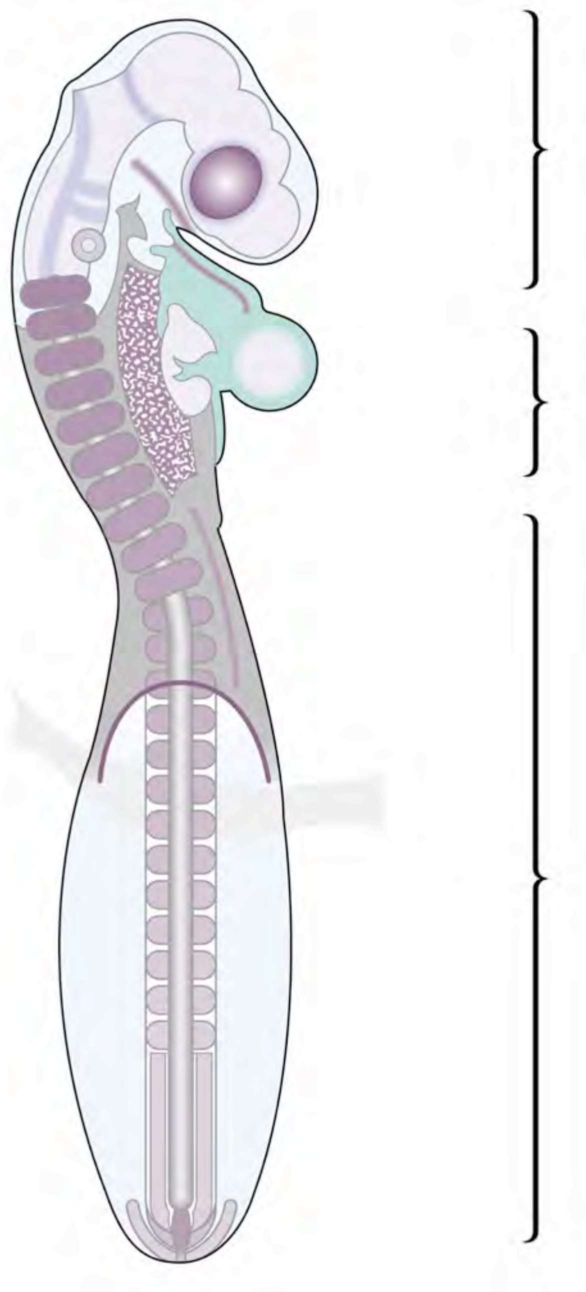
Neural crest specification

Neural crest epithelial to mesenchymal transition (EMT) / delamination

Neural crest migration

from: Martik & Bronner Trends in Genetics (2017) 33: 715-727

Neural crest cells and their derivatives

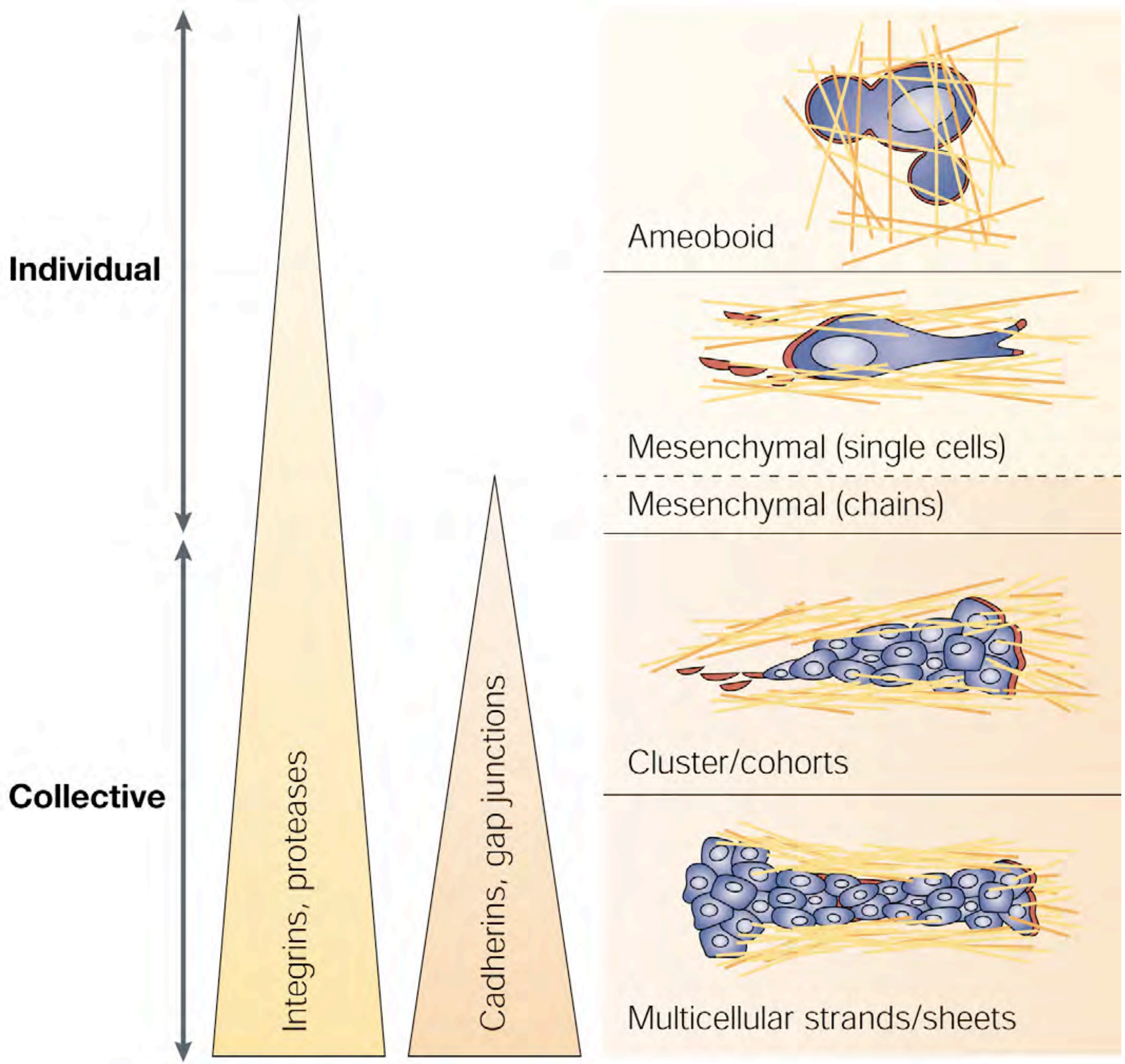


Cranial
Bone and cartilage
Connective tissues (teeth, eyes, ears)
Sensory neurons
Glial cells
Melanocytes

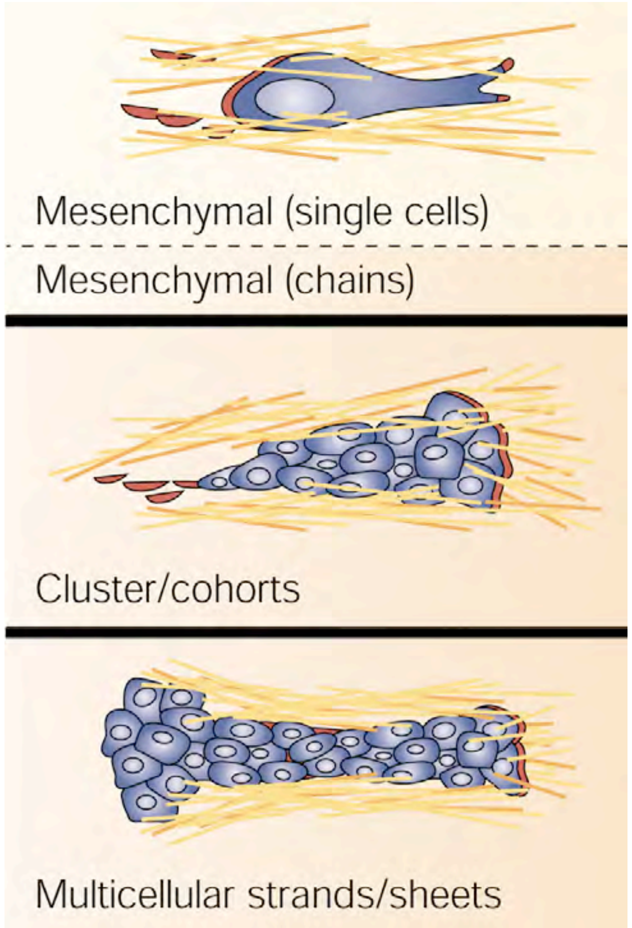
Vagal
Enteric neurons
Sensory neurons
Glial cells
Melanocytes
Smooth muscle
Cardiac tissues

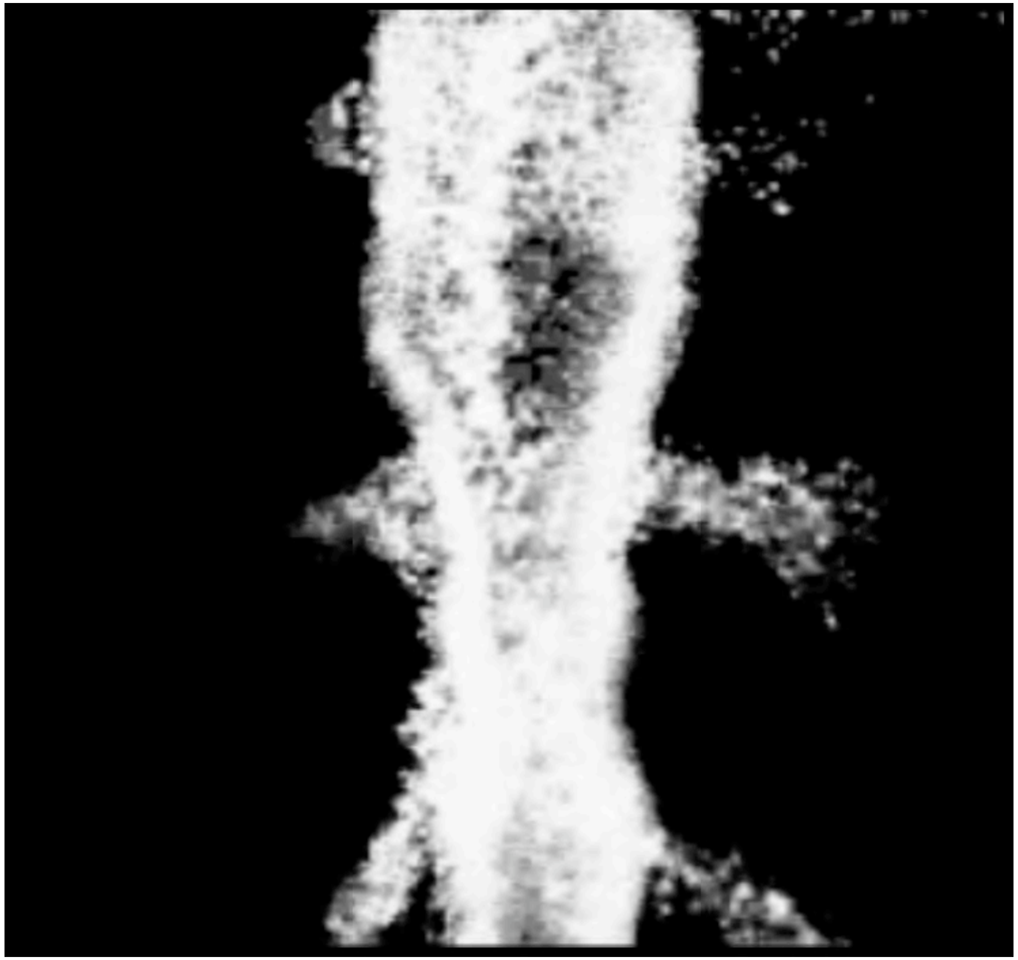
Trunk
Sensory neurons
Autonomic neurons
Chromaffin cells (adrenal medulla)
Glial cells
Melanocytes

Modes of cellular migration through the extracellular matrix

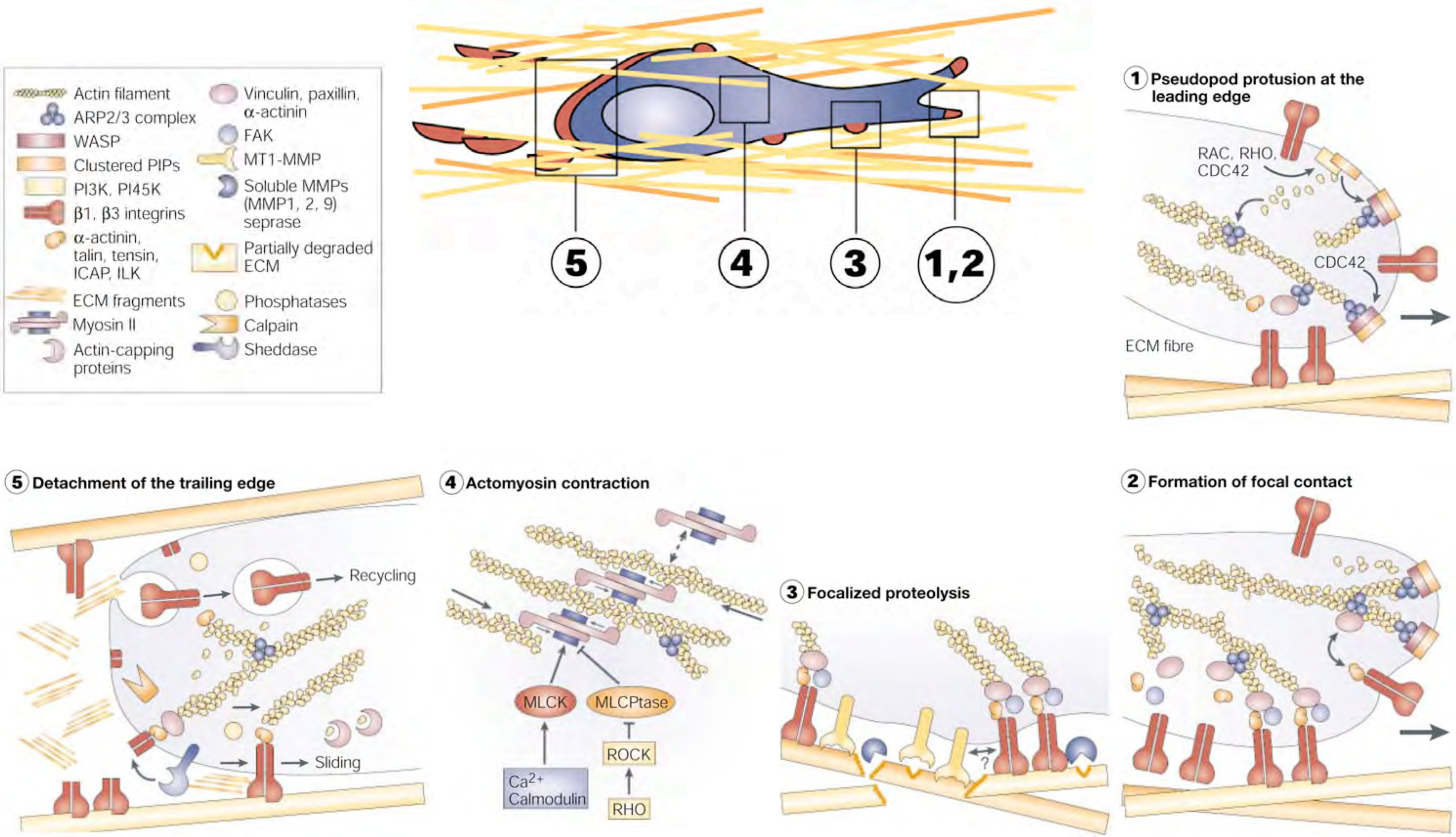


Neural Crest Cell Migration in Embryonic Chick Development

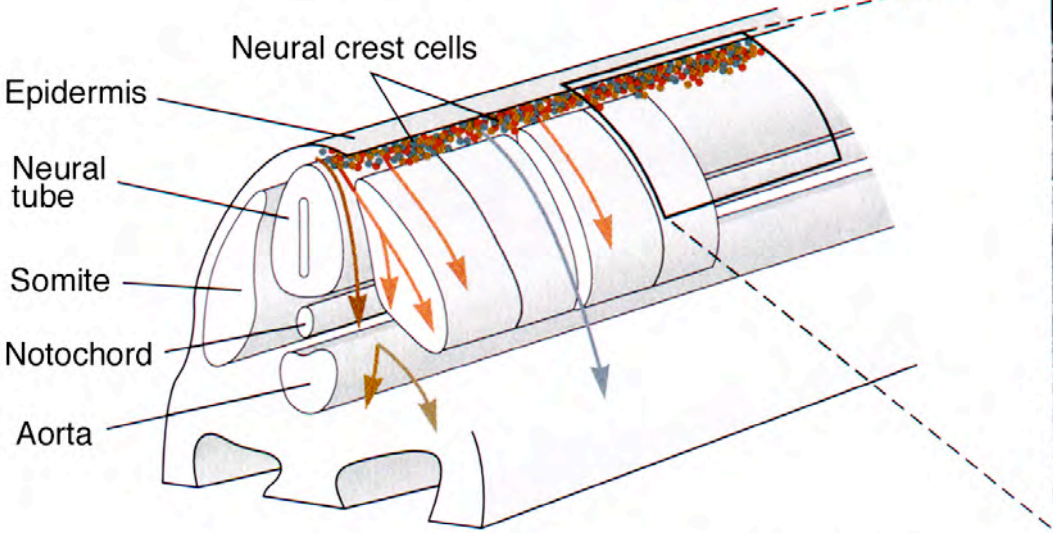


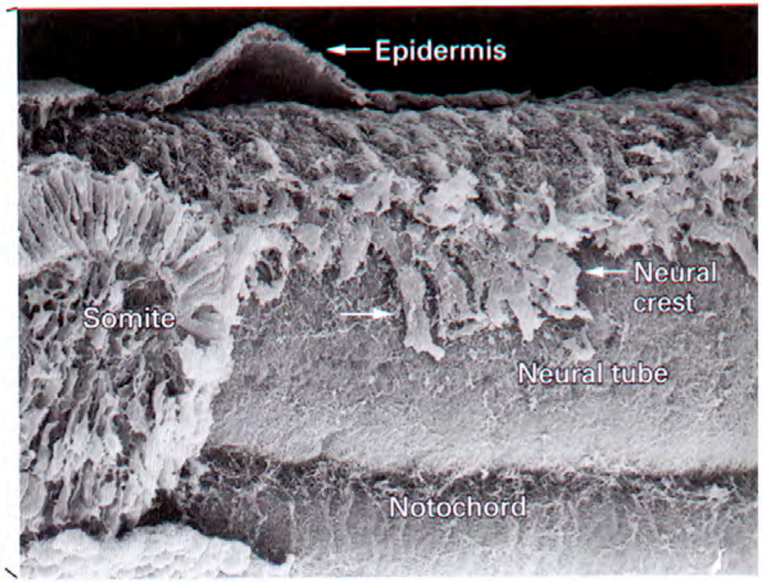


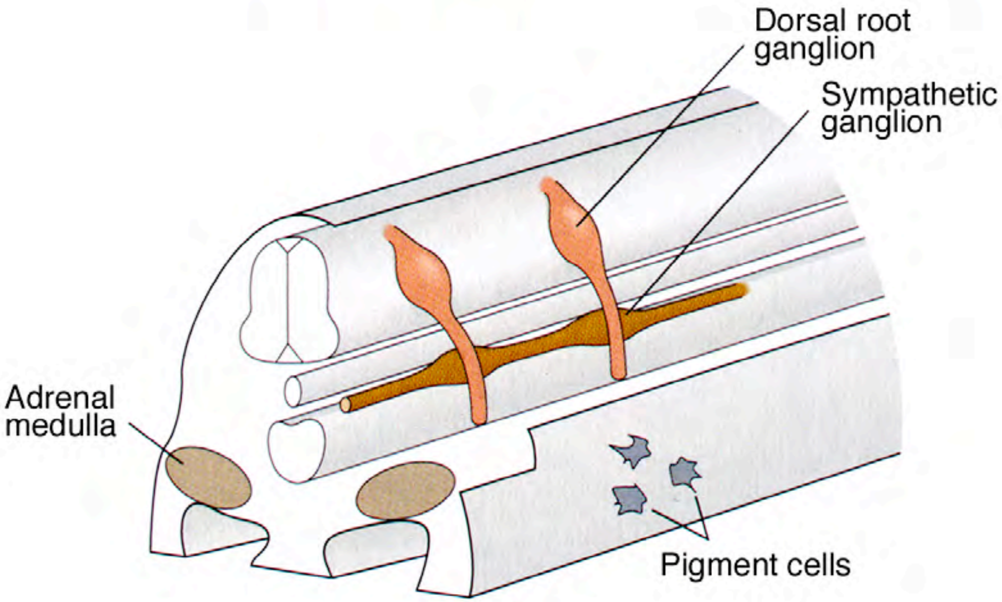
Mechanism of cell migration within extracellular matrices (model)



Migration of neural crest cells in the embryonic trunk

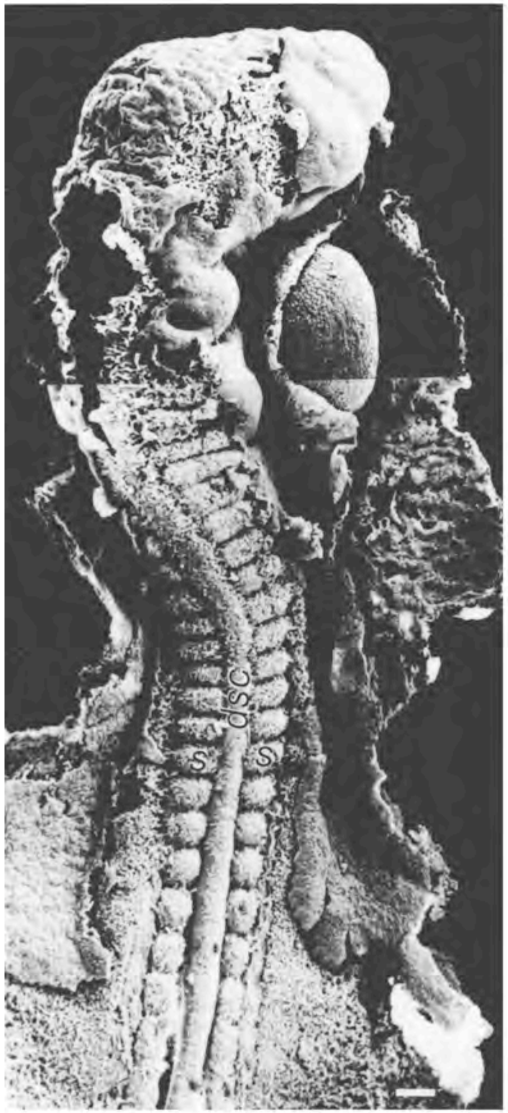






Ventral migration path:
- Dorsal root ganglia
- Sympathetic ganglia
- Medulla of the adrenal gland

Dorso-lateral migration path:
- Melanocytes (pigment cells)
  of the skin



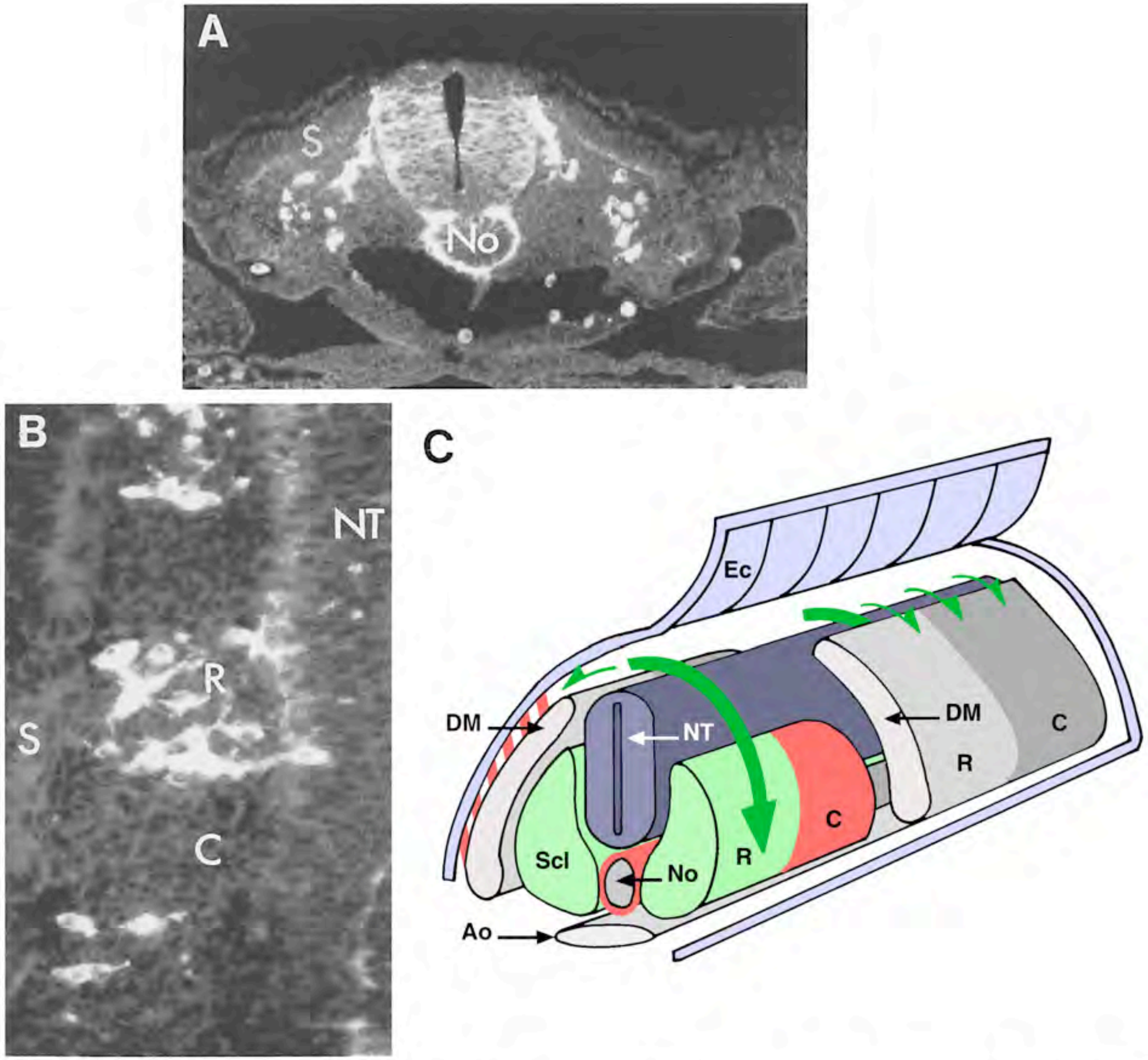
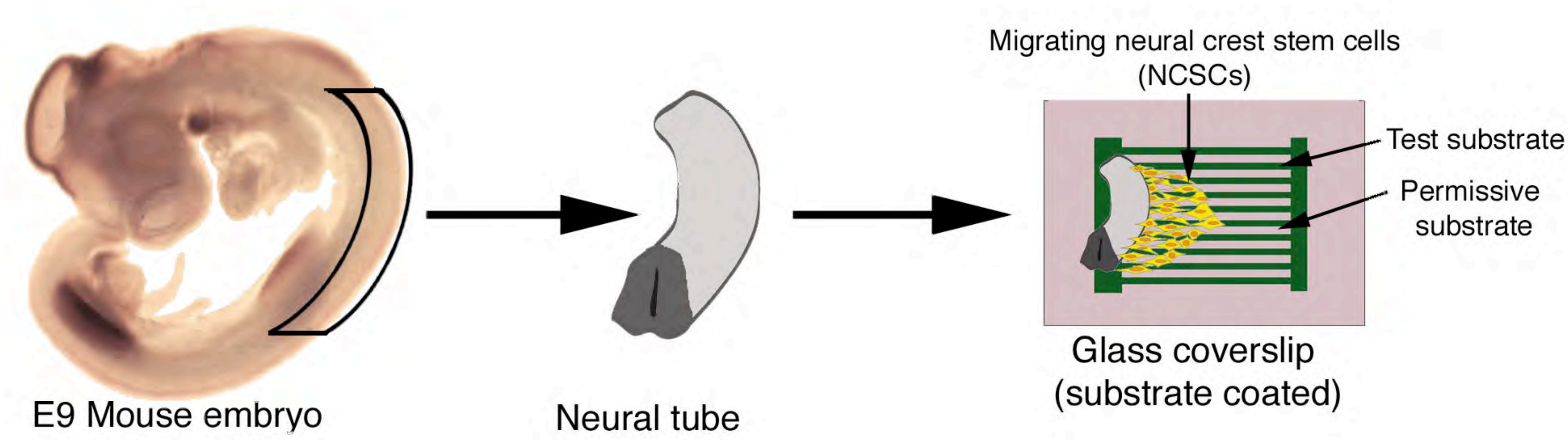
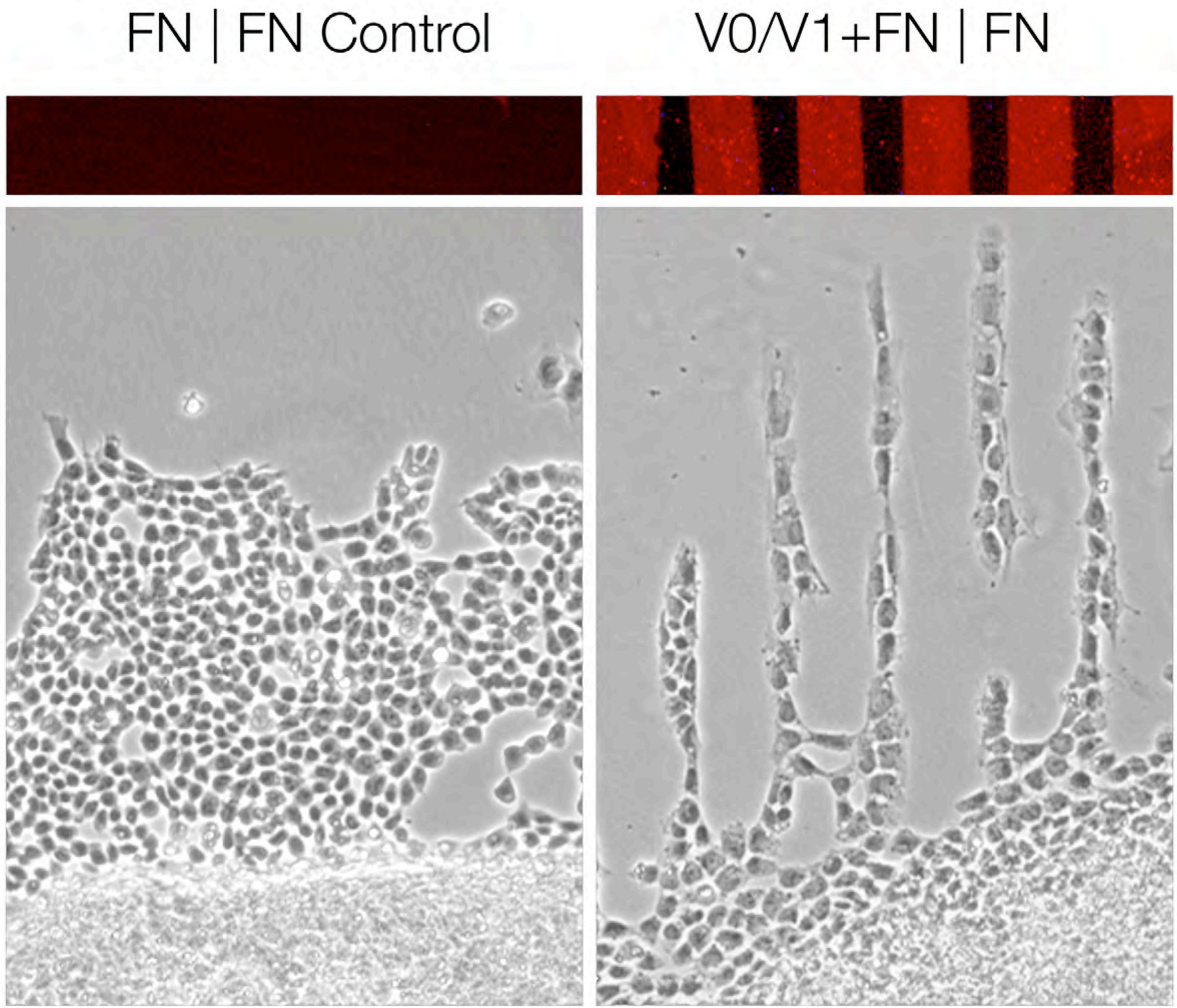


Fig. 3. HNK-1 antibody immunolabelling of neural crest cells. A) In transverse section, neural crest cells emerge from the neural tube (NT) and migrate through the rostral half of the sclerotome, with the exception of a region around the notochord (No). B) In longitudinal section, HNK-1 immunoreactive neural crest cells are visible in the rostral (R) but not caudal C) half of each somite (S). C) Three-dimensional summary diagram illustrating that trunk neural crest cells migrate ventrally through the rostral but not caudal half of each sclerotome. Those cells migrating dorsolaterally under the ectoderm (Ec) migrate in an unsegmented fashion. DM= dermomyotome; Ao = Aorta; Scl = sclerotome.

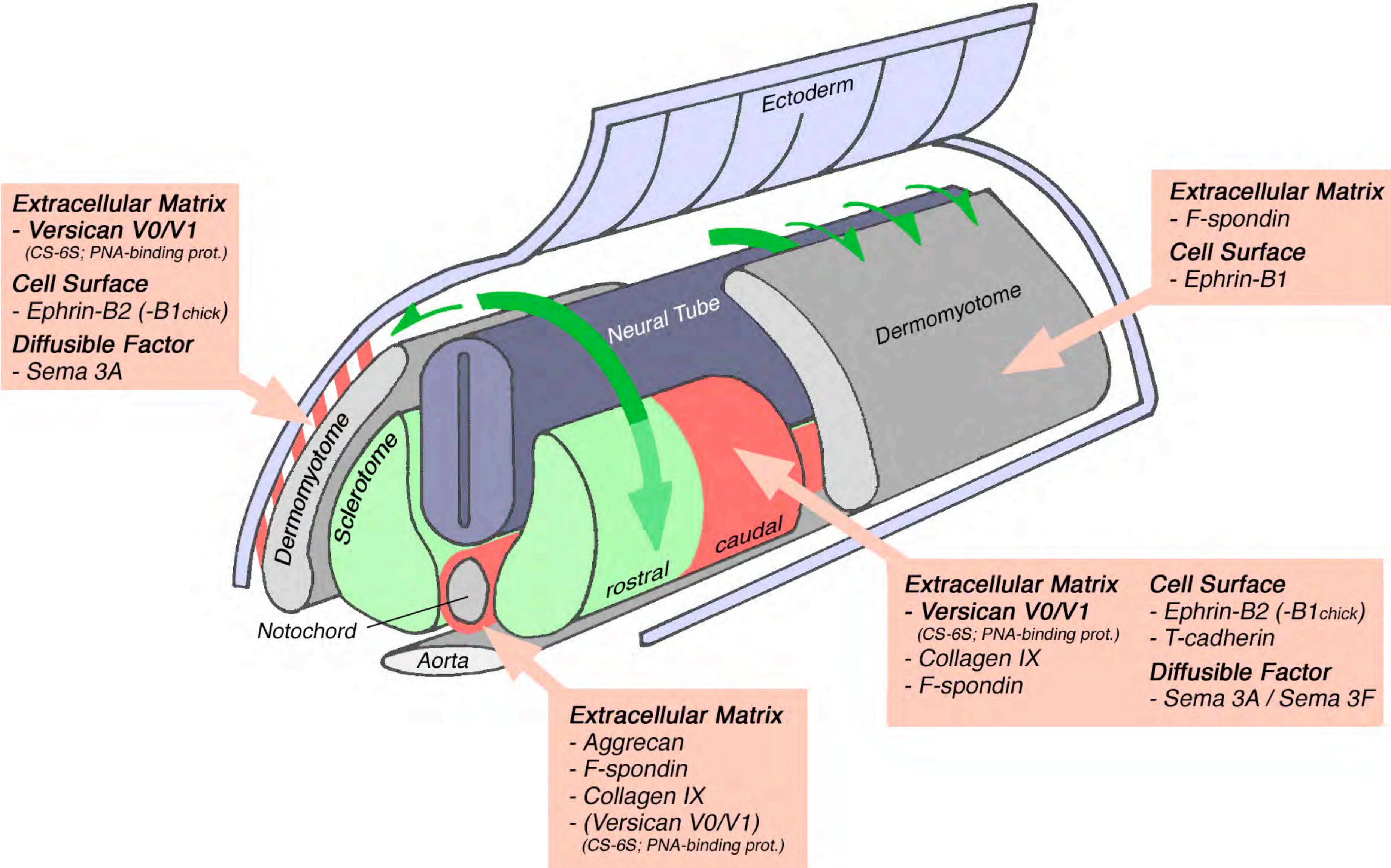
from: Bronner-Fraser, M. BioEssays 15, 221-230, 1993

Stripe choice assay




FN | FN Control
V0/V1+FN | FN

Inhibitors of neural crest cell migrations



Neural crest cell migration (Summary)

Neural crest cells emigrate from the dorsal neural tube shortly after its closure.

Some subpopulations migrate large distances giving rise to a wide variety of neural and non-neural tissues.

In the peripheral nervous system, sensory, sympathetic and enteric neurons as well as Schwann cells originate from the neural crest.

Cell surface and extracellular matrix molecules of the surrounding tissues guide neural crest cells to their targets.