Dr Nandor Nagy (Semmelweis Univ.):

Neural crest cells

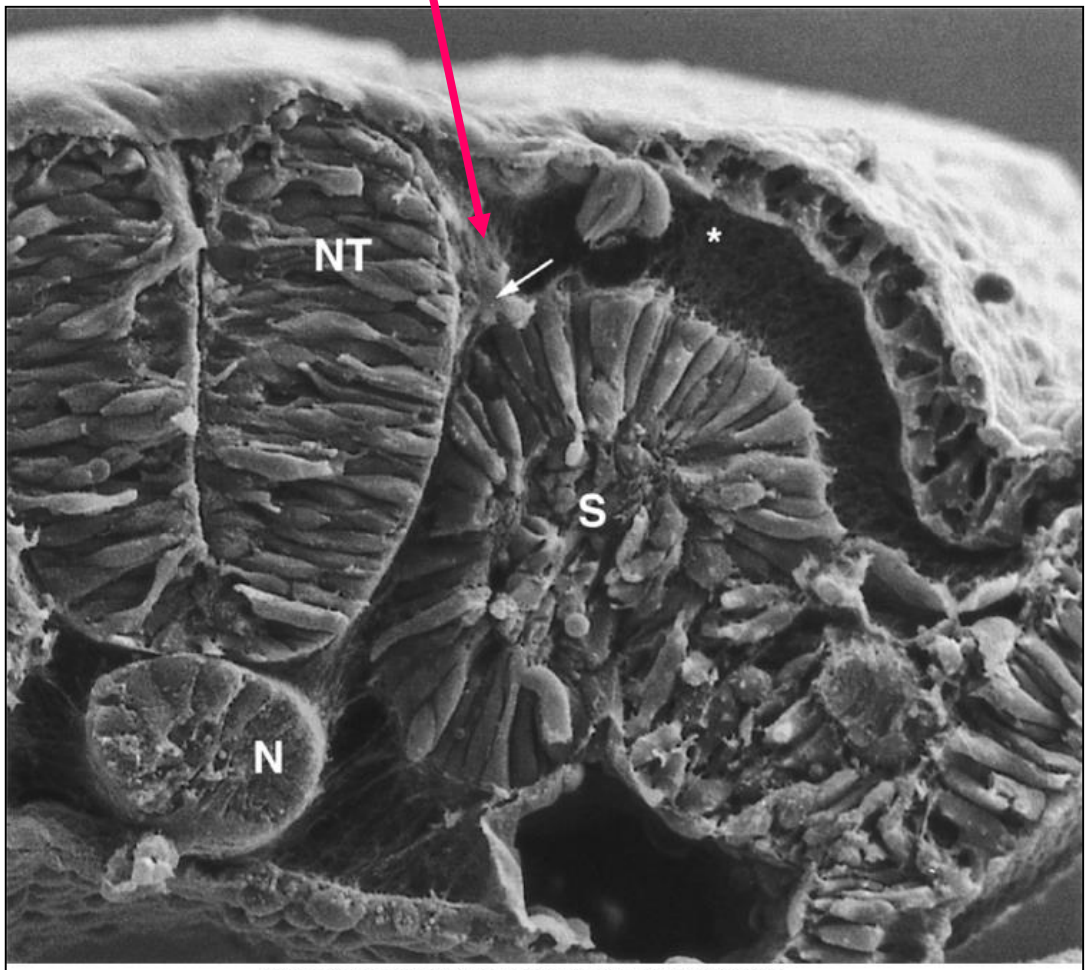
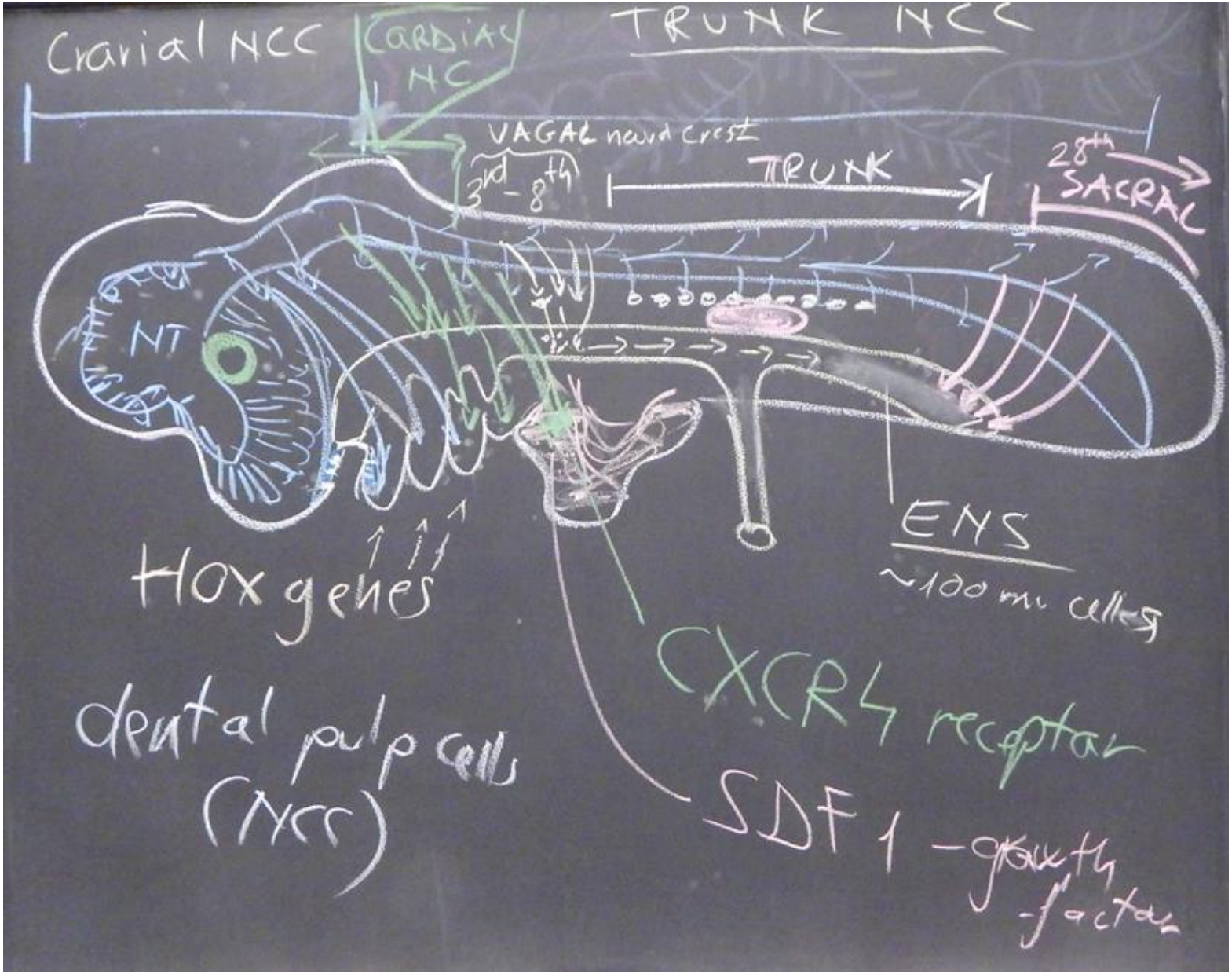
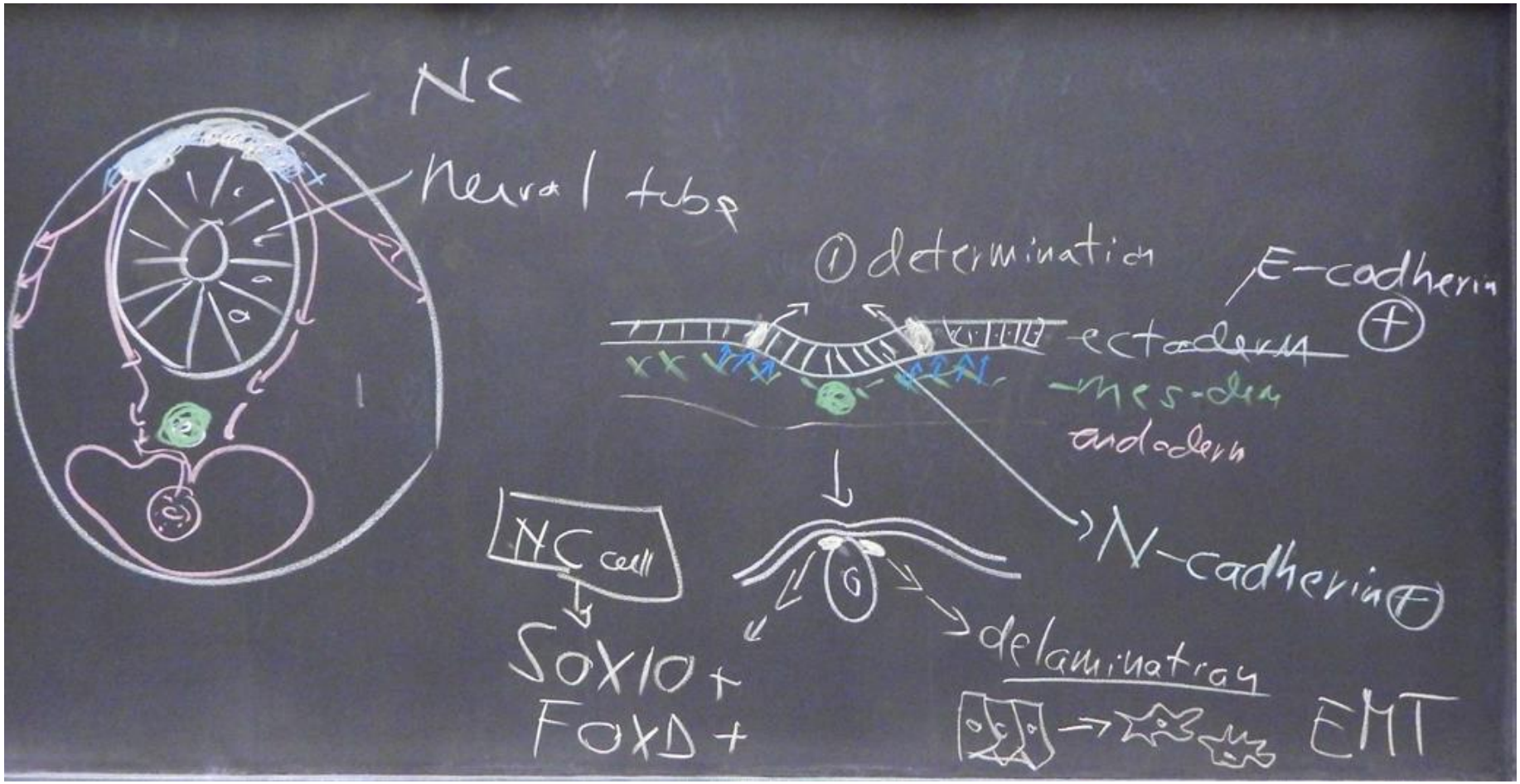


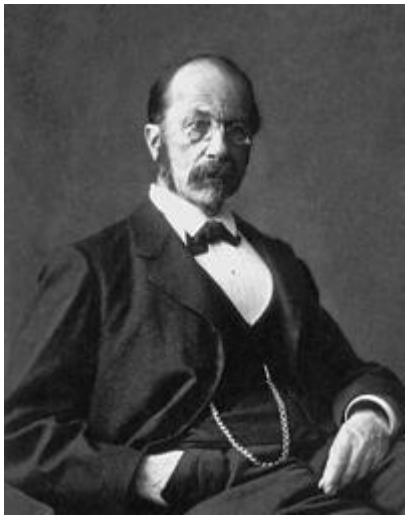
Figure 12-2 Scanning electron micrograph of a chick embryo, showing the early migration of neural crest cells (arrow) out of the neural tube (NT). The subectodermal pathway of neural crest migration (*) is relatively cell-free, but contains a fine mesh of extracellular matrix molecules. N, notochord; S, somite. (Courtesy K. Tosney, Ann Arbor, Mich.)

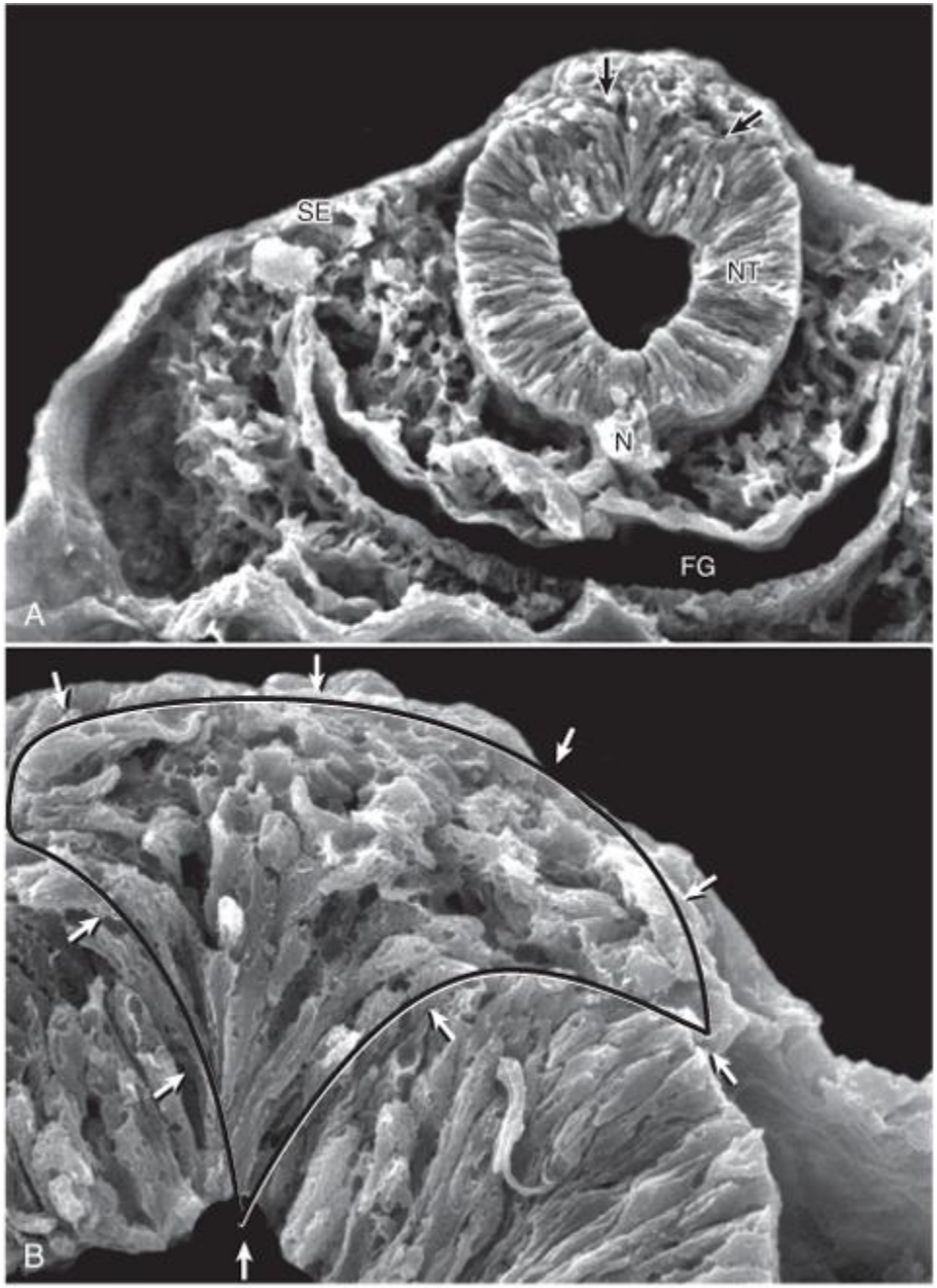

Cranial NCC
CARDIAC NC
TRUNK NCC
VAGAL neural crest
3rd - 8th
TRUNK
28th SACRAL
NT
ENS
~100 mn cells
Hox genes
CXCR4 receptor
dental pulp cells (NCC)
SDF 1 - growth factor


NC
neural tube
① determination
E-cadherin
+
ectoderm
mesoderm
endoderm
N-cadherin
+
NC cell
SOX10+
FOXD+
delamination
EMT

First discovery by His in the chiken embryo (1868).

Mediodorsal cells immigrate laterally to invade spinal ganglia.
He named them „ganglionic crest” cells.





Schoenwolf et al: Larsen's Human Embryology, 4th Edition.

Neural crest and the placodes, two transient ectodermal cell populations in the embryo

Neural crest cells give advantages to Vertebrates

Most of the morphological and functional differences between vertebrates and other chordates occur in the head and are derived embryologically from muscularized hypomere, neural crest, and epidermal (neurogenic) placodes. In the head, the neural crest functions as mesoderm and forms connective, skeletal, and muscular tissue. Both the neural crest and the epidermal placodes form special sense organs and other neural structures. These structures may be homologous to portions of the epidermal nerve plexus of protochordates. The transition to vertebrates apparently was associated with a shift from a passive to an active mode of predation, so that many of the features occurring only in vertebrates became concentrated in the head.(Gans és Northcutt, Science 1983)

Characterictics of the vertebrate „New Head”:

Special composite sense organs, complex visual organ is important in predation

Jaws for predation!

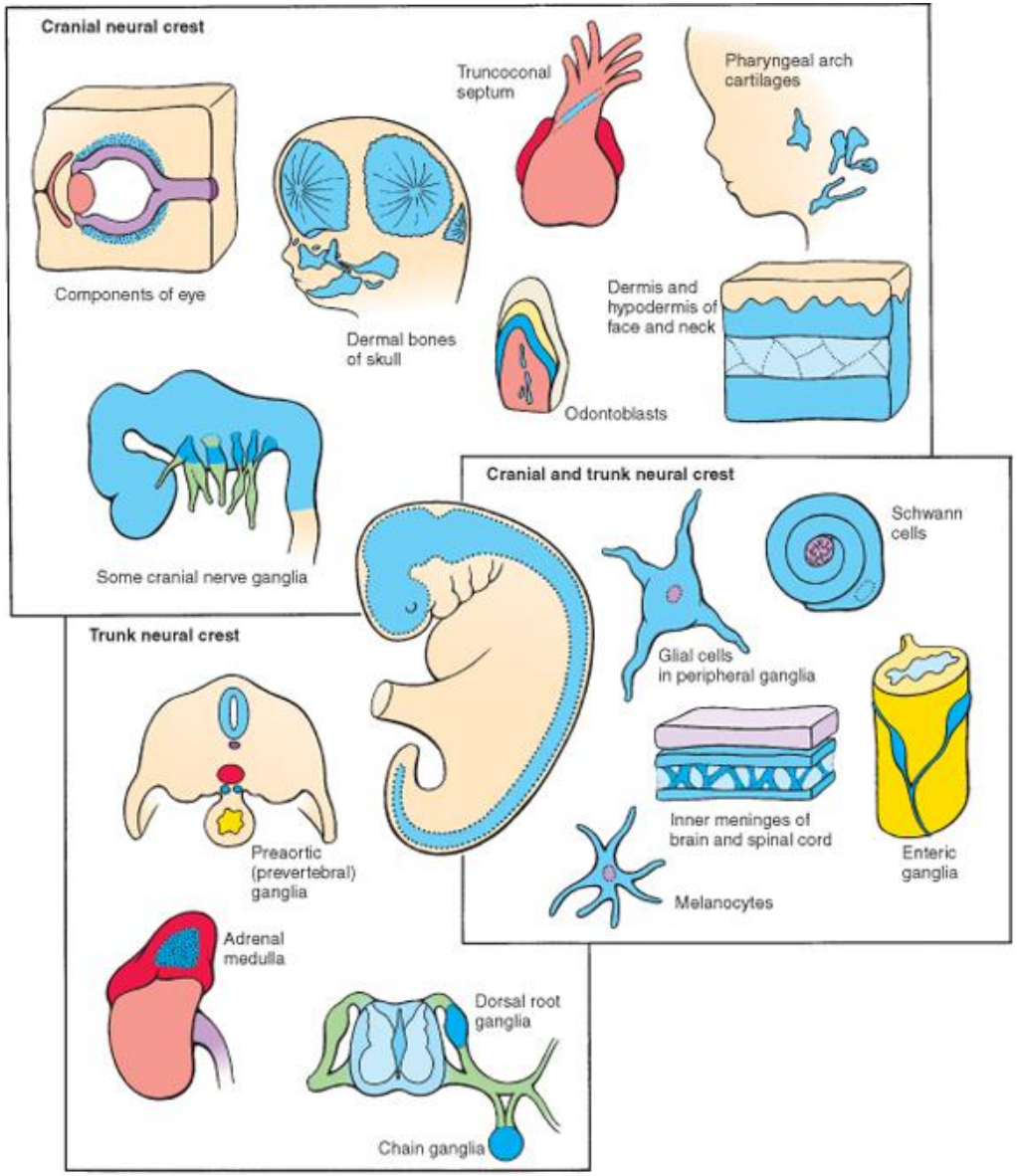
Complex viscerocranium and chondrocranium development

Derivatives:

- peripheral nervous system
  - sympathetic, parasympathetic, sensory, autonome
  - Schwann cells
- melanocytes

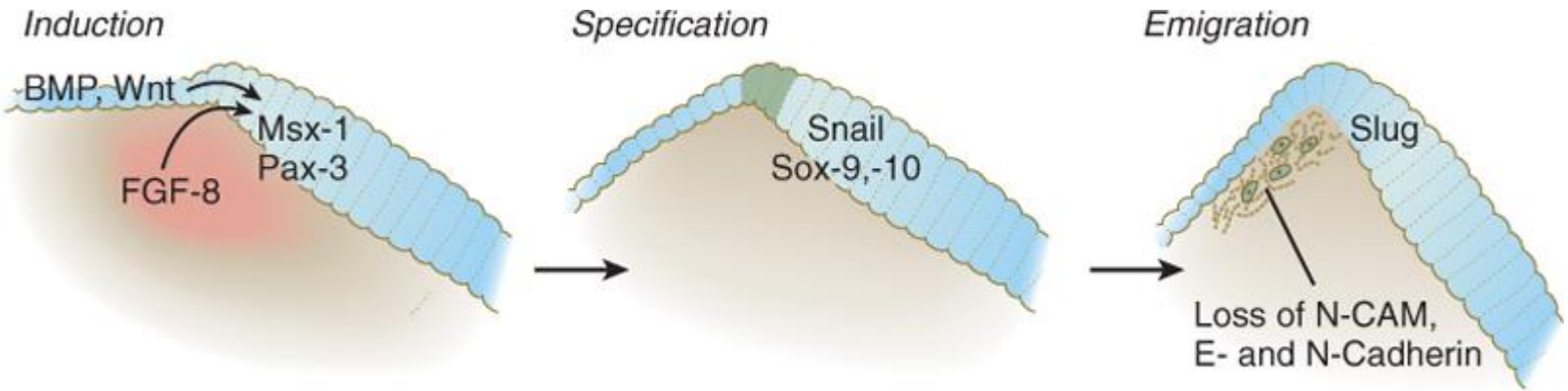
- cartilage and bone in the head, smooth muscle, myofibroblast and fibroblast , mesectoderm
- endocrine cells (adrenal medulla)
- meninges
- vessel wall (not endothelia) in the head region

- Heart :
aortico-pulmonal, conotruncal septum



Schoenwolf et al: Larsen's Human Embryology, 4th Edition.

Neural crest induction, current modell



Signals from ectoderm: BMP, Wnt
from mesoderm FGF-8 (amphibian data)
high conc. of BMP: epidermal ectoderm, low: neural ectoderm
medium BMP conc. defines neural crest

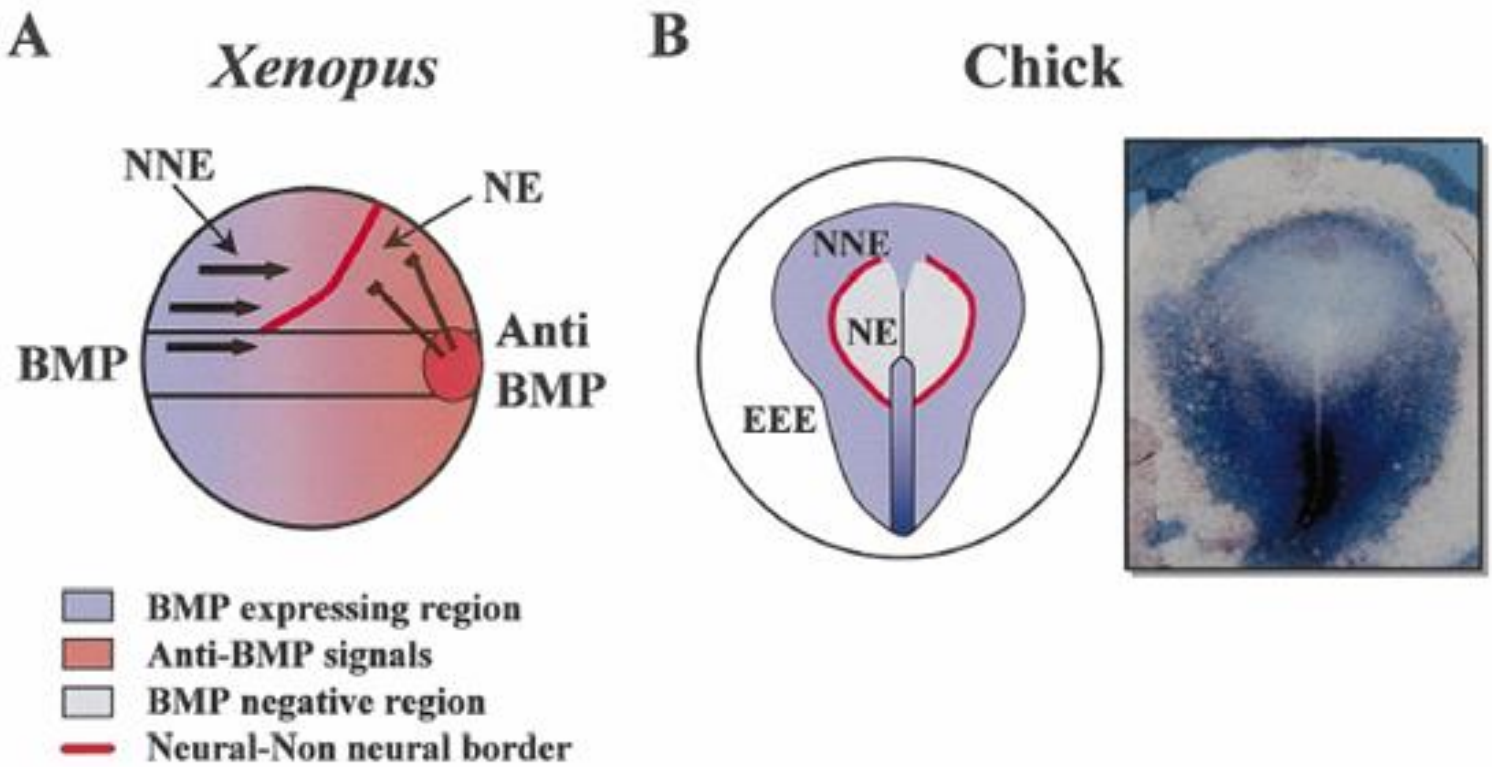
Msx-1, Pax-3 expression starts (characteristic for NC cells)

snail-1 and slug (snail-2) expression starts which is needed for EMT (epithelio-mesenchymal transition)

slug is expressed at gastrulation as well!

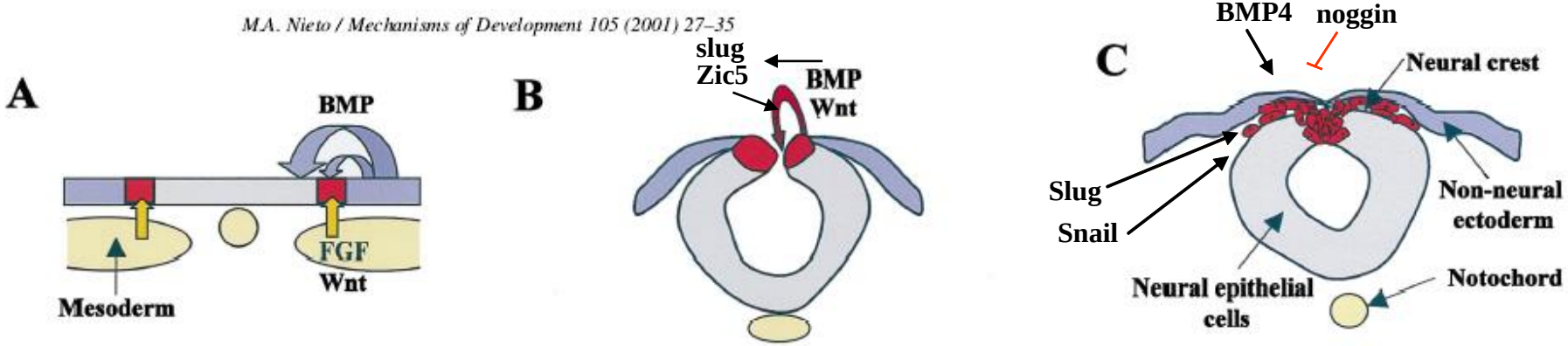
Changes in adhesion properties (adhesion molecules)

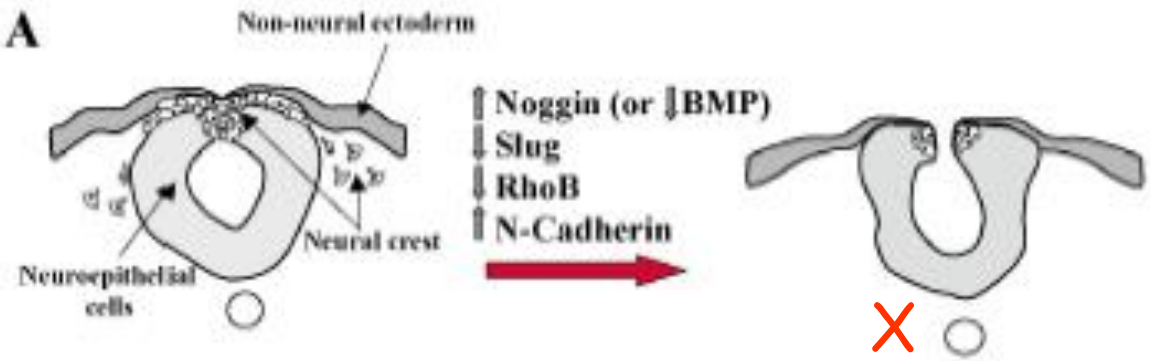
Determination of neural crest cells starts at the border of neural, non-neural ectoderm



Delamination

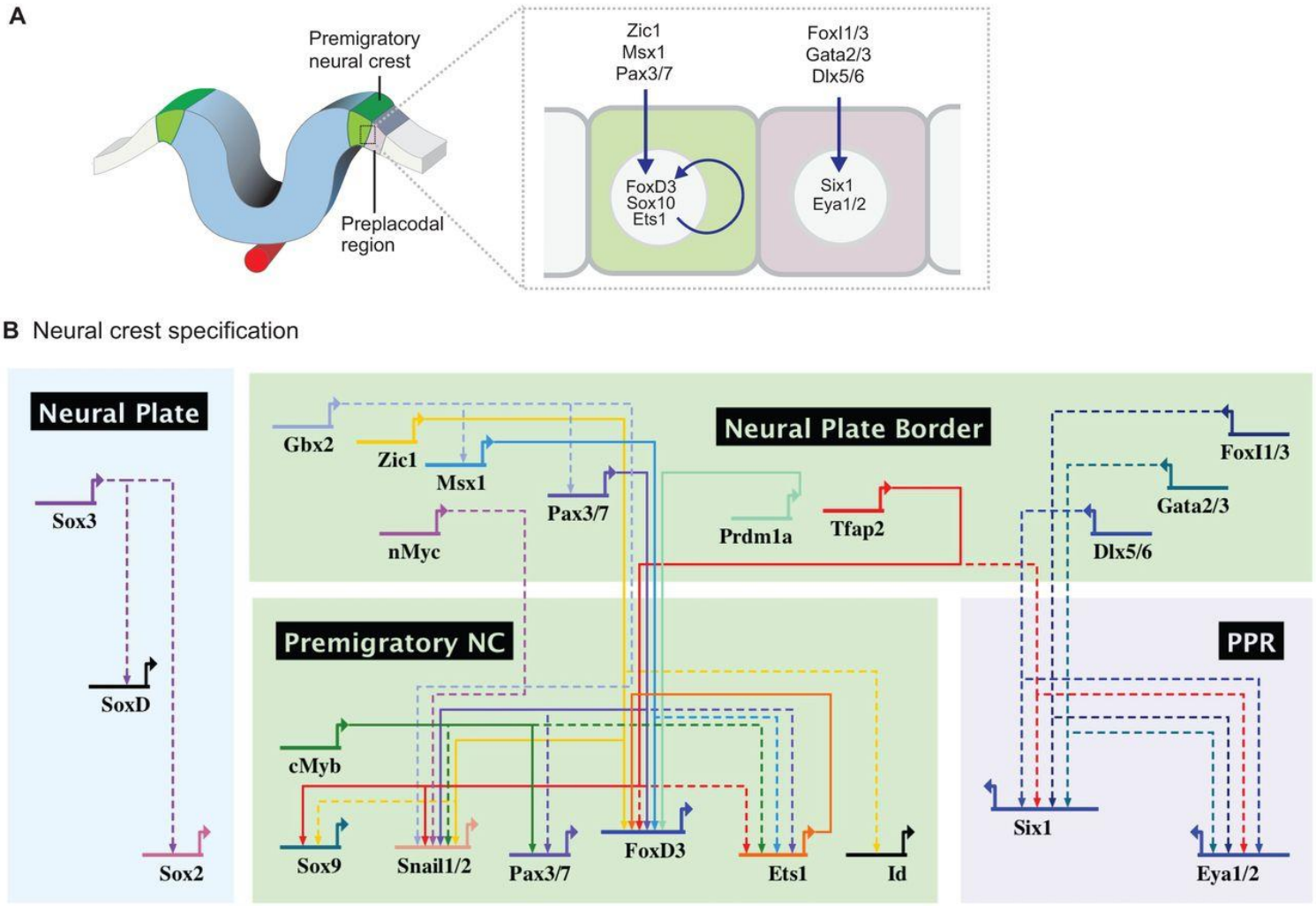
- epithelial – mesenchymal transition (EMT)
- E and N-cadherin, NCAM ↓ , cadherin 7 and 11 expr. ↑
- rhoB (small GTPase): before migration, role: in reorganisation of the actin sceleton and cell shape
- determination: noggin-BMP, Slug and Snail act on adhesion molecule genes





Mech. of Development 105 (2001) 27-35

Gene regulatory interactions controlling specification of the neural crest.



Marcos Simões-Costa, and Marianne E. Bronner
Development 2015;142:242-257

Quail-chick chimera fate mapping studies 1.

N.M. Le Douarin / Mechanisms of Development 121 (2004) 1089–1102

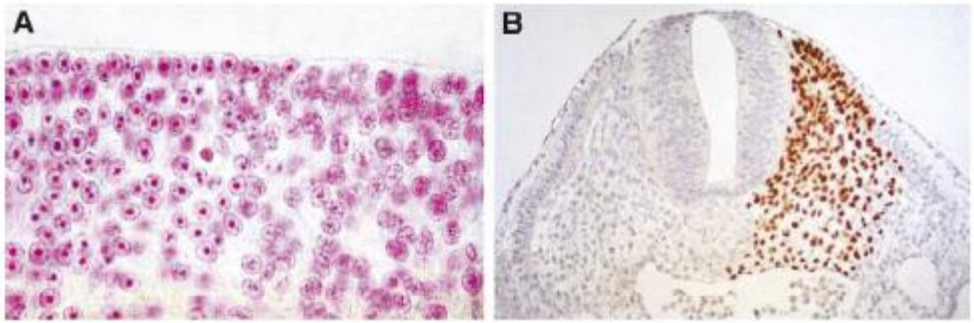
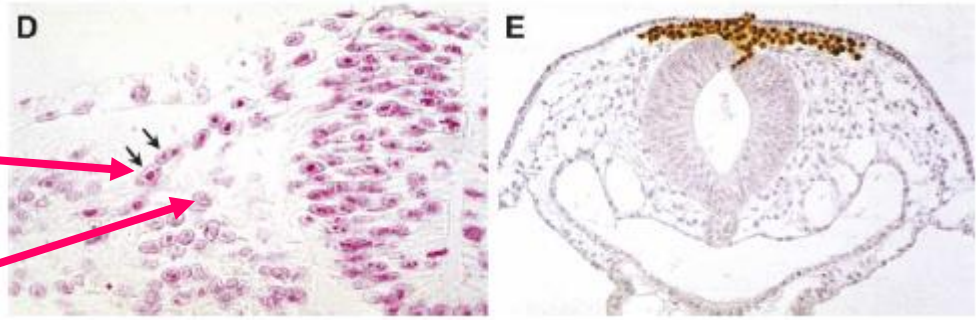


Fig. 1. The quail-chick marker system (A,B): two means for recognizing quail from chick cells. (A) Feulgen staining of DNA shows a large mass of heterochromatin in the centre of the nucleus, which is associated with the nucleolus in quail cells (left). In chick cells, the heterochromatin is evenly distributed (right). (B) Staining of quail cells (half a somite on the right) grafted into a chick embryo with a monoclonal antibody raised against a quail nuclear antigen (produced by Carlson and Carlson, University of Michigan).

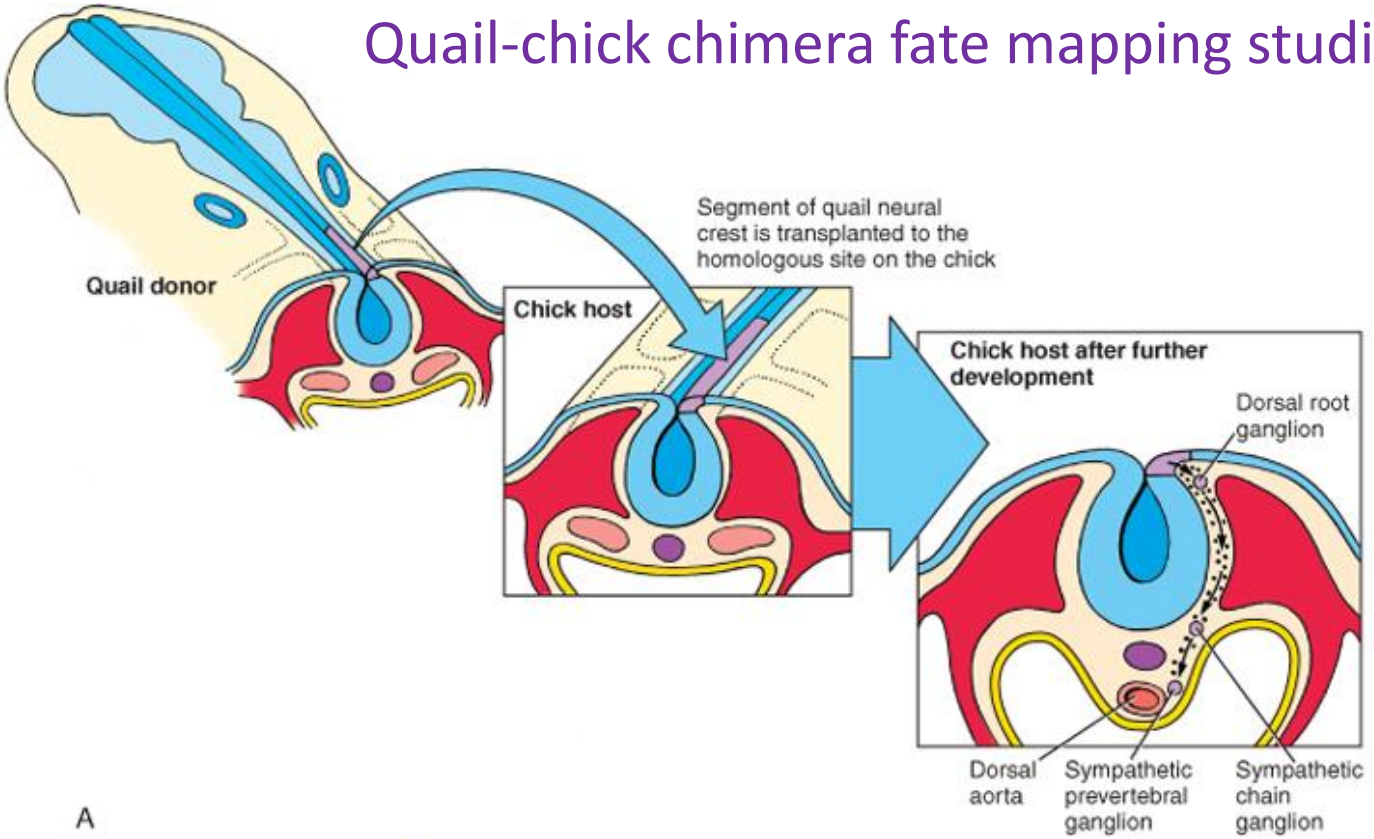
(D,E) NCC migrating from a neural tube quail graft at the trunk level (D) or from a neural fold (right) graft at the cephalic level. Note that a unilateral NC fold graft expands on both sides during migration.

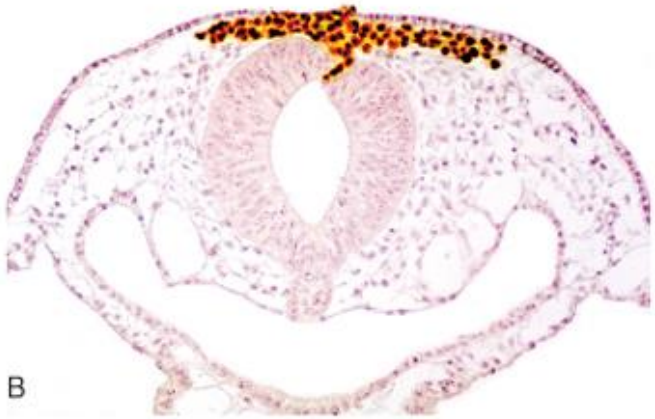
heterochromatin is different in quail nuclei, lot of heterochromatin associated to the nucleolus

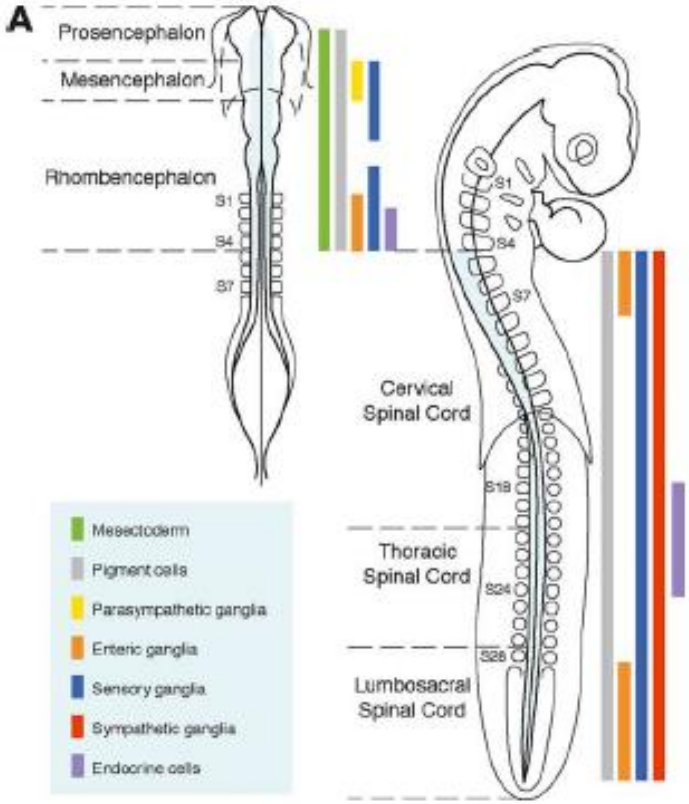
dispersal heterochromatin in chicken nuclei



Quail-chick chimera fate mapping studies 2.







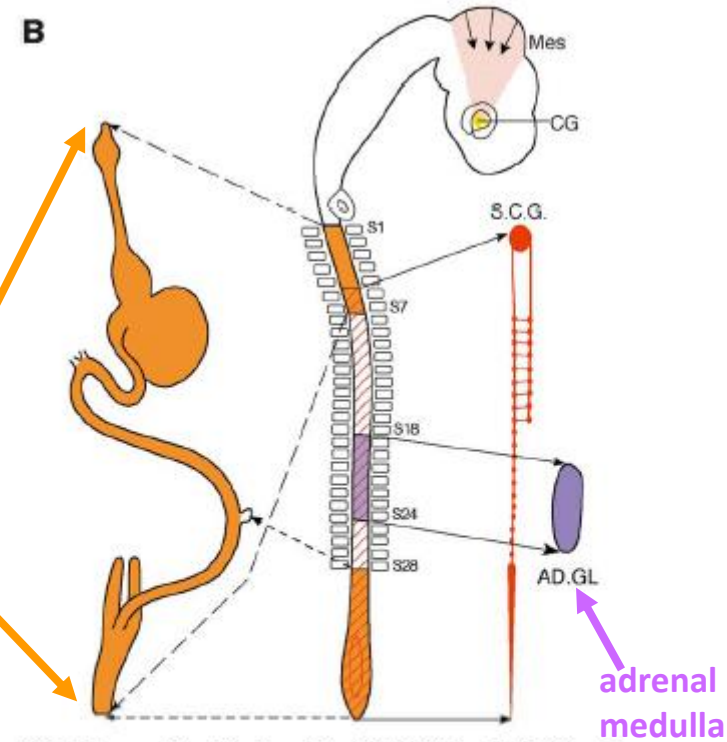
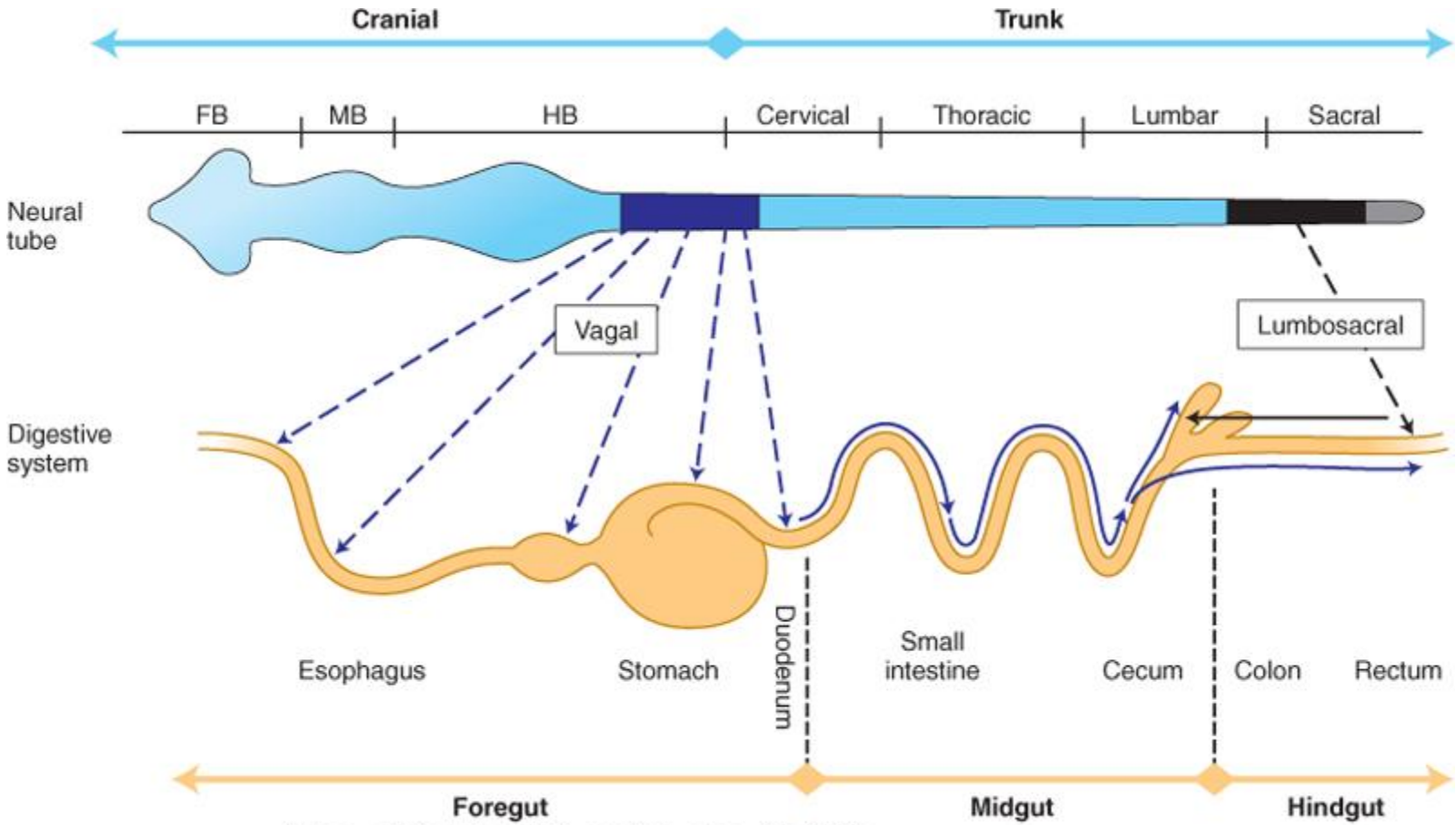
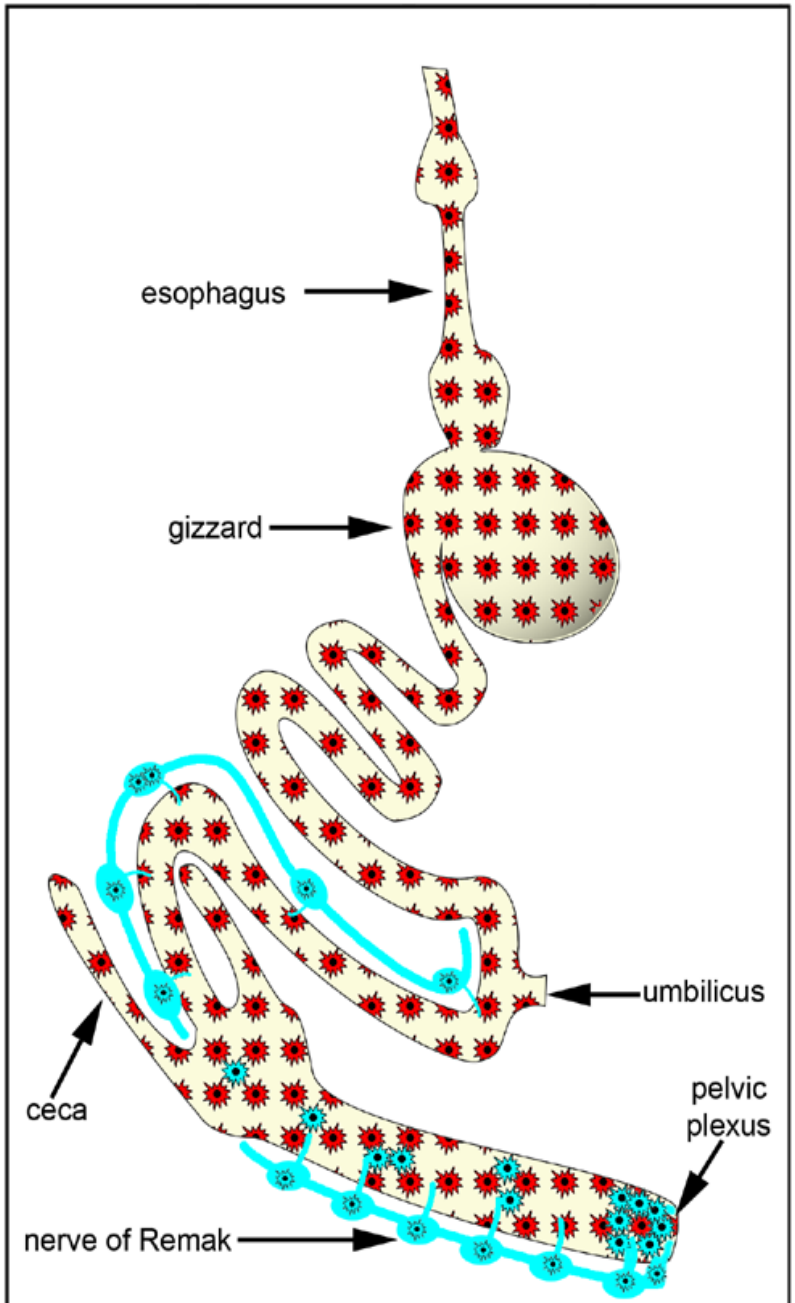
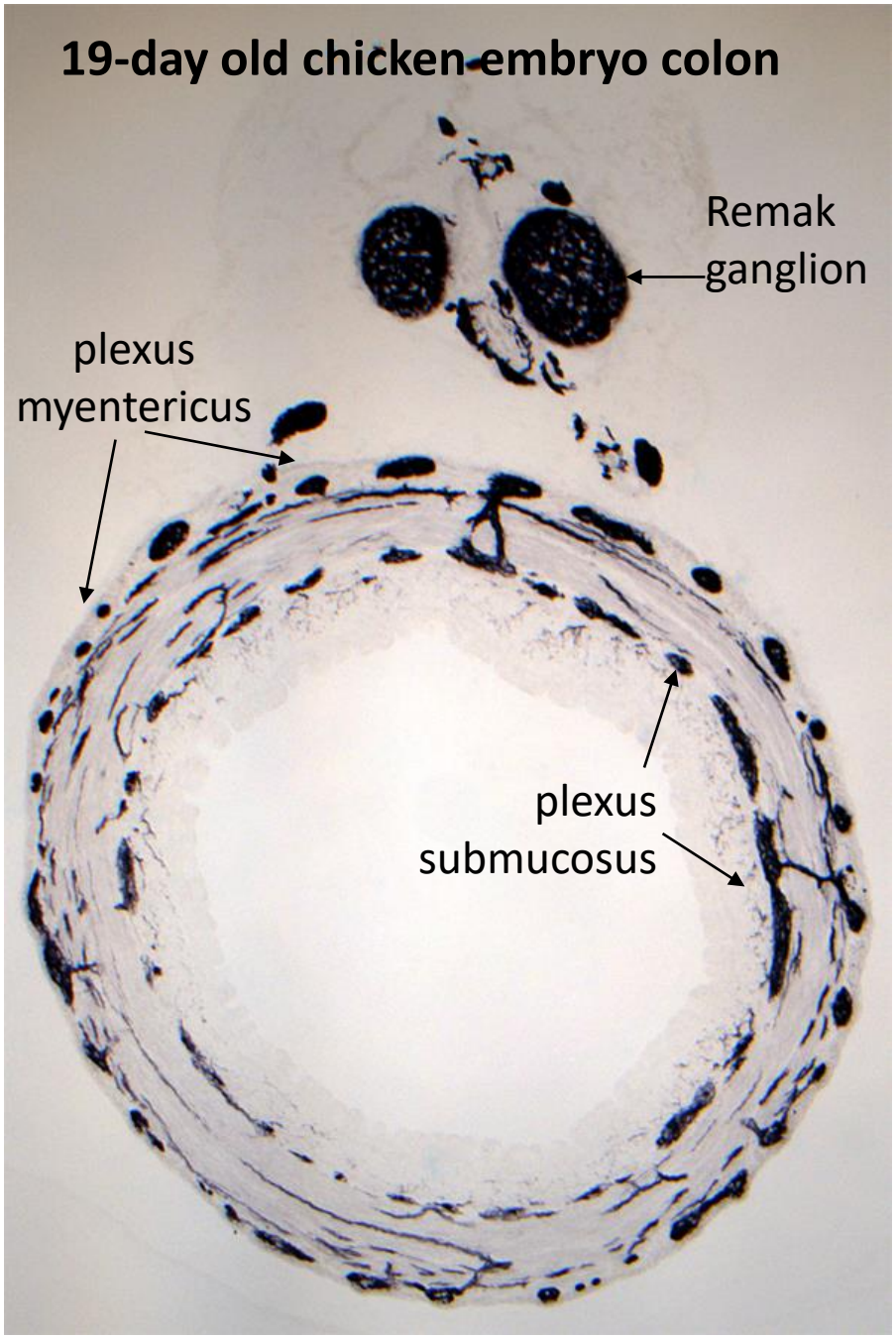


Fig. 2. Fate map of the derivatives of the NC. (A) The levels of origin of the main derivatives of the NC are indicated along the neural axis at two developmental stages: 7 somite stage (ss) and 28 ss. (B) The origin of ganglia of the ENS is indicated in yellow, that of the autonomic sympathetic chains in red and that of endocrine (adrenal medulla) in violet. AD. GL, adrenal gland; Mes, mesencephalon, CG, ciliary ganglia, SCG, superior cervical ganglion.





Goldstein and Nagy, 2008, vol 64. Ped Res



Neural crest divisions

cranial

trunk

6th somite

Circumpharyngeal

pharynx

heart, great vessels

intestine

Topography

Cranial

craniofacialis (ecto-) mesenchyme, cartilage, bone, conn. tissue, nerve, glia

Cardiac

arterial wall, septum aorticopulmonale

Enteric

vagal, sacral, parasympathetic elements

Trunk

melanocytes, spinal ganglia, sympathetic ganglia

Cranial neural crest

Migration begins before neural tube closure

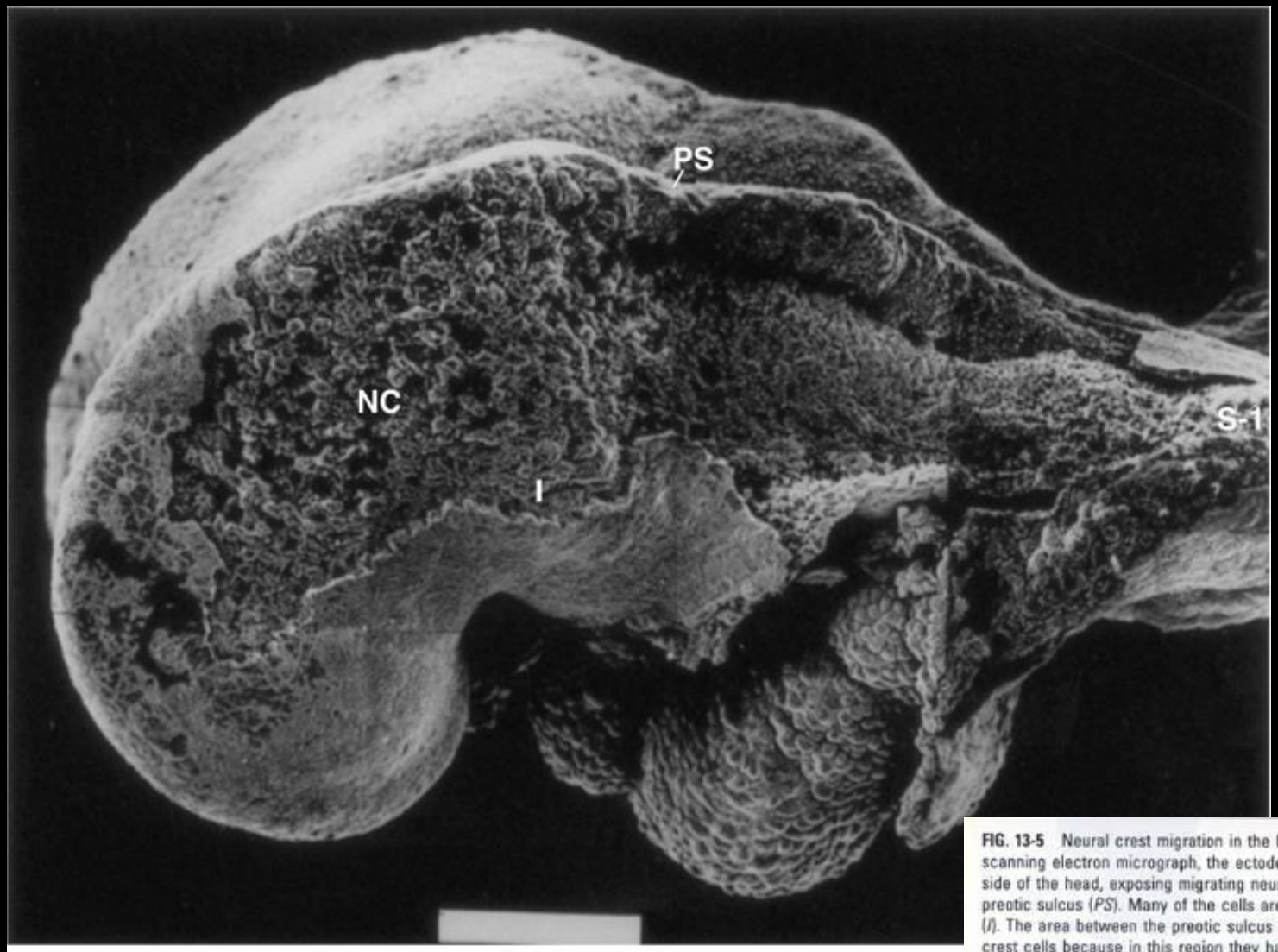
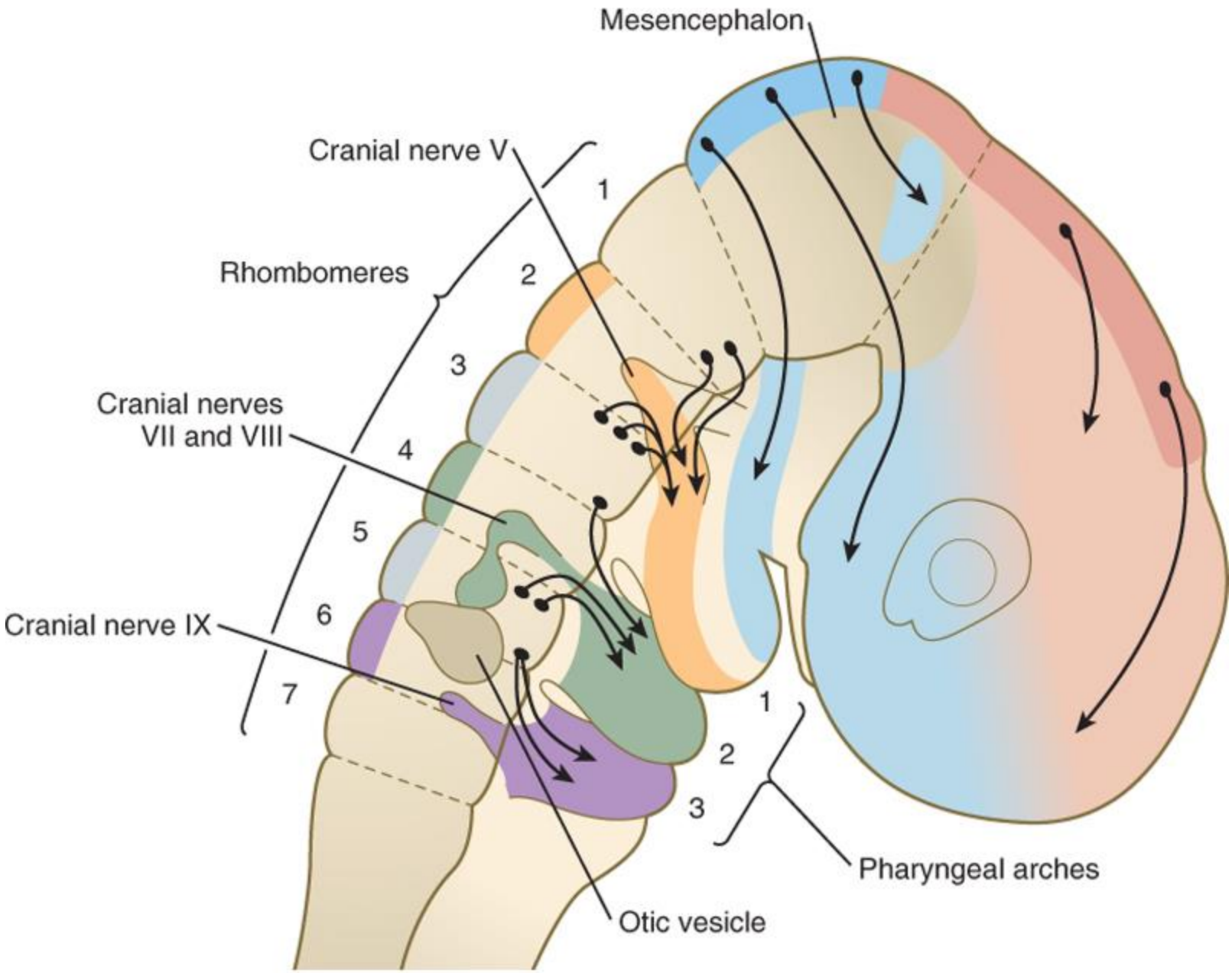
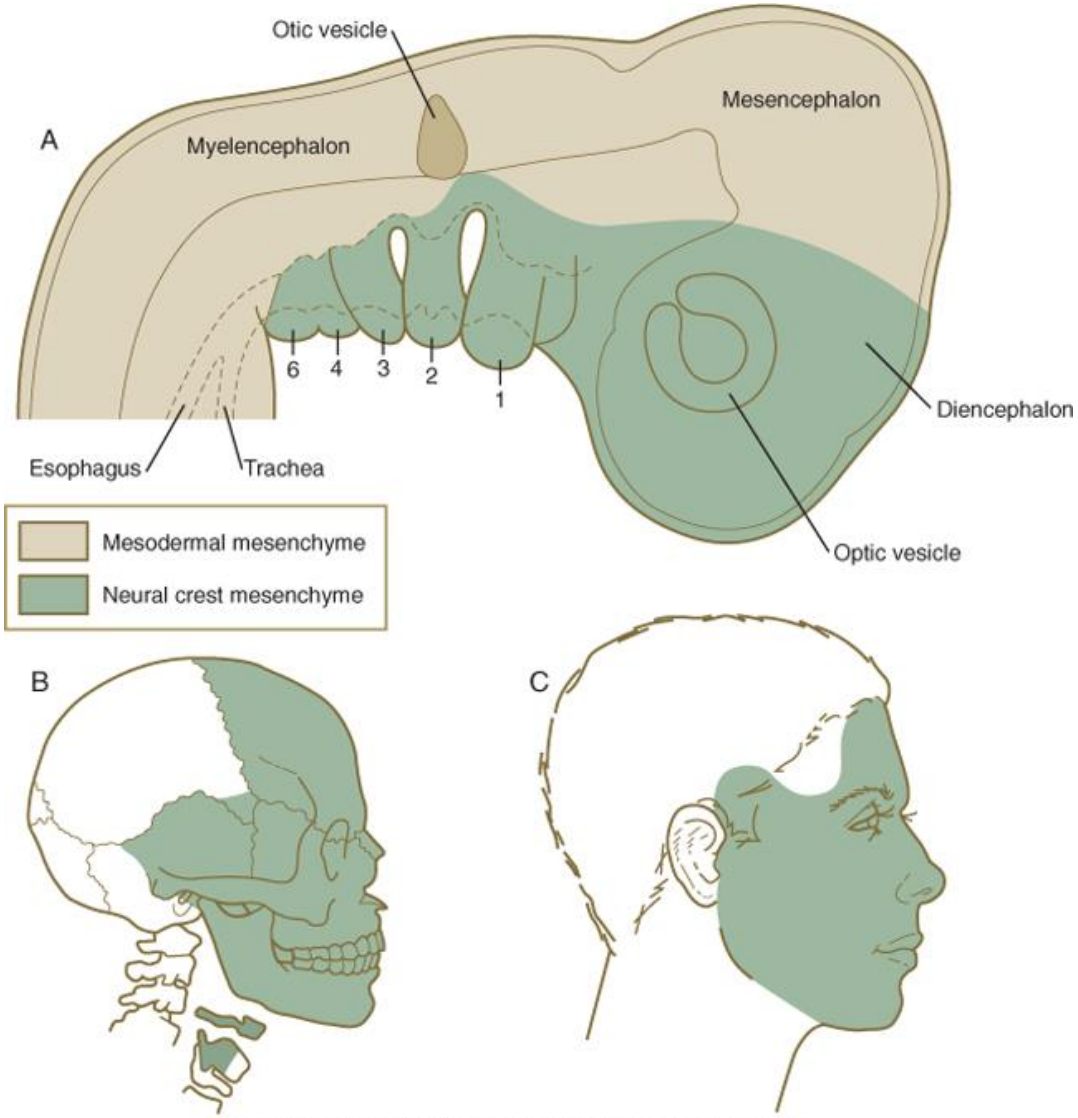


FIG. 13-5 Neural crest migration in the head of a 7-somite rat embryo. In this scanning electron micrograph, the ectoderm was removed from a large part of the side of the head, exposing migrating neural crest (*NC*) cells cranial (to the left) to the preotic sulcus (*PS*). Many of the cells are migrating toward the first pharyngeal arch (*I*). The area between the preotic sulcus and the first somite (*S-1*) is devoid of neural crest cells because in this region they have not begun to emigrate from the closing neural folds. The white bar at the bottom represents 100 μm.
(Based on studies from Tan and Morriss-Kay [1985].)

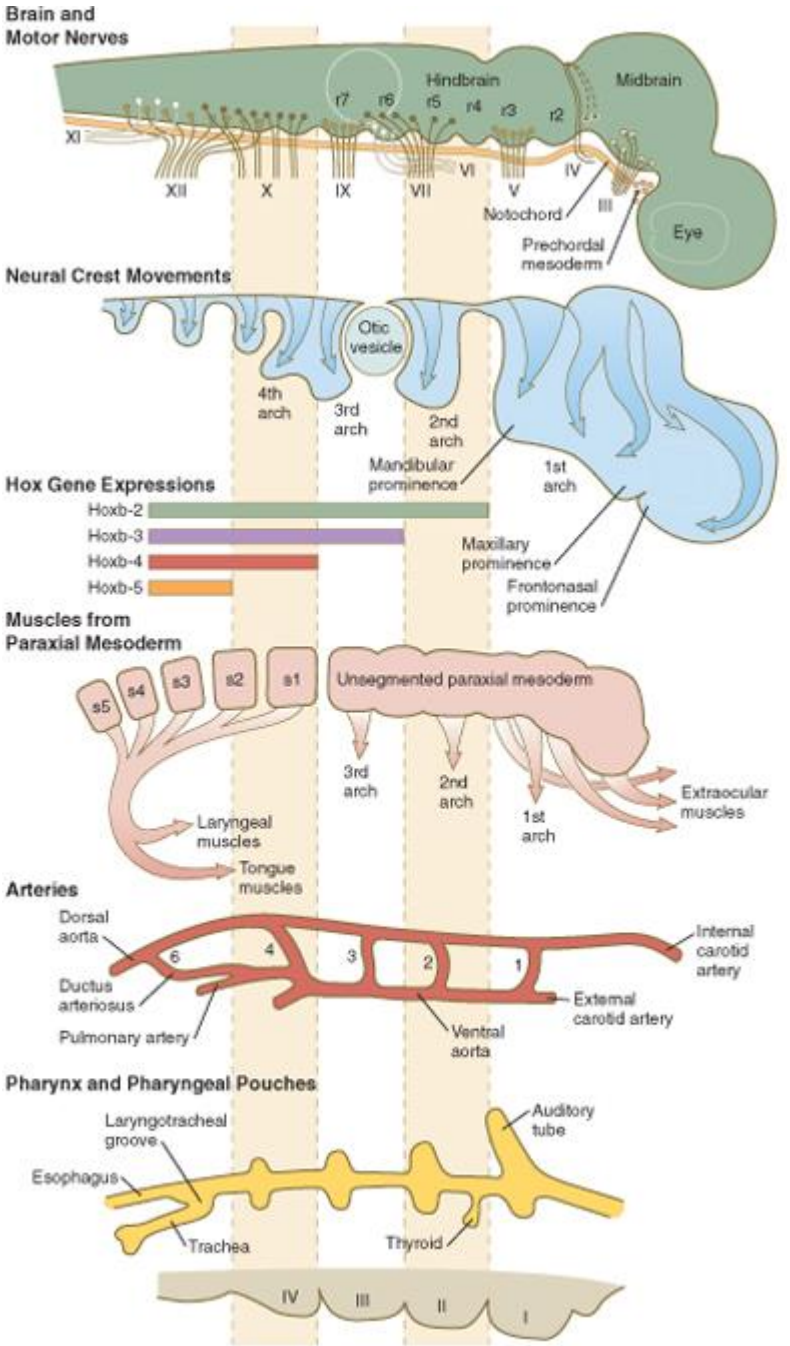




5th and 6th prosomere level do not give rise to neural crest only 1-4 prosomeres.

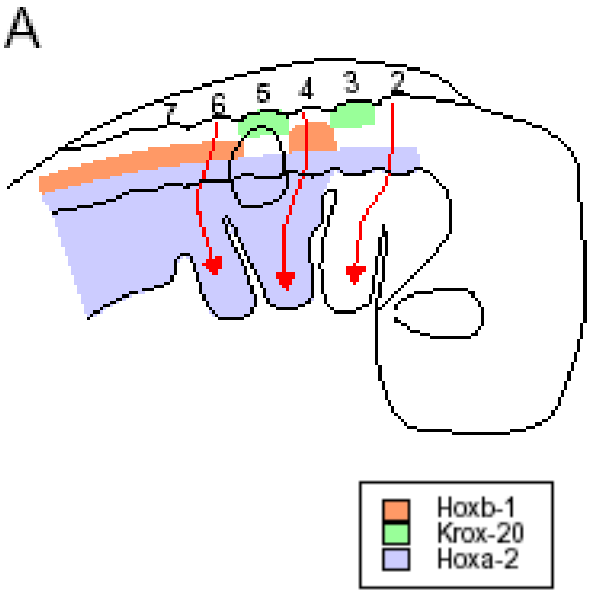
NC from hindbrain levels colonise 1st-3rd pharyngeal arches.
Each rhombomeric and mesencephalic crest cell „remember" to the segmental code.

In the pharyngeal region,
the pathways of crest cell migration are closely correlated with Hoxb gene expr.
Cells of the cranial crest may be patterned with level –specific instructions, whereas cells of the trunk crest are not.

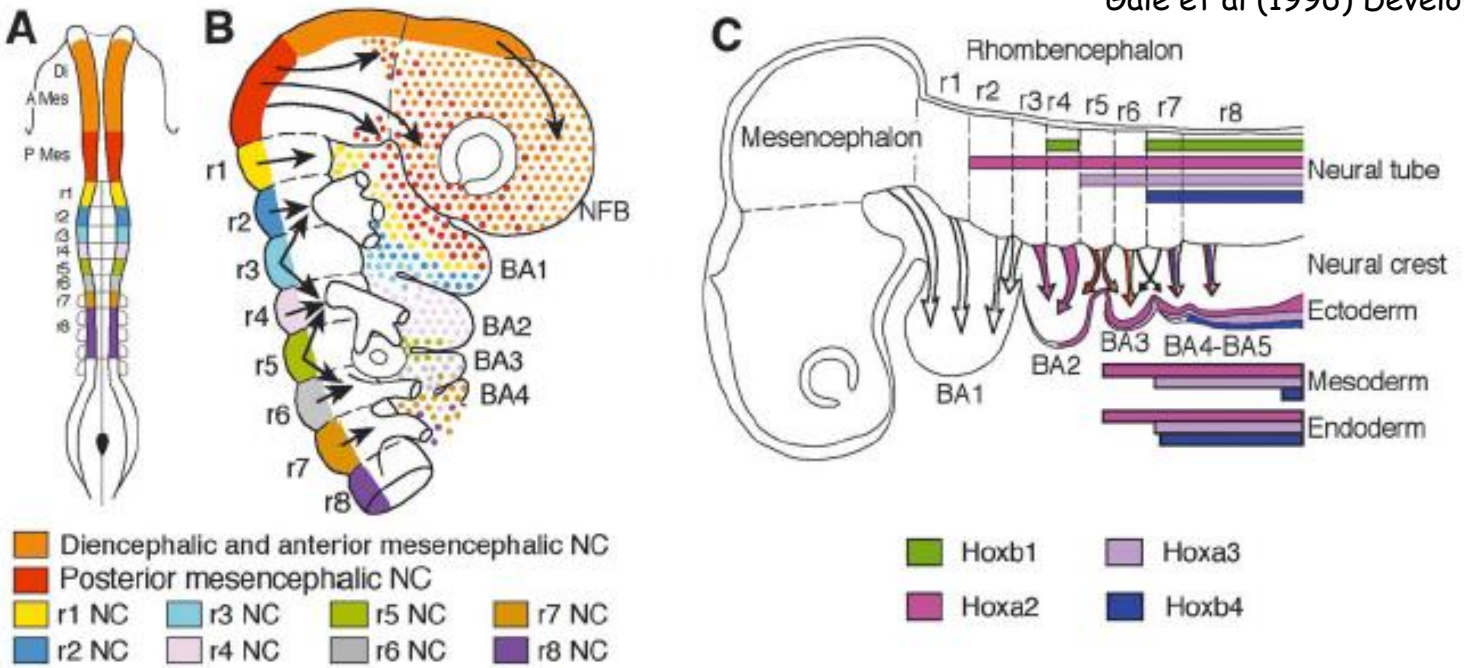


Migration in the head region

- Migration takes place between the surface ectoderm and neural epithelium, mesenchymal morphology
- cartilage, bone, smooth muscle forms
- Hox genes determines segments and NC cells do not mix between these segments

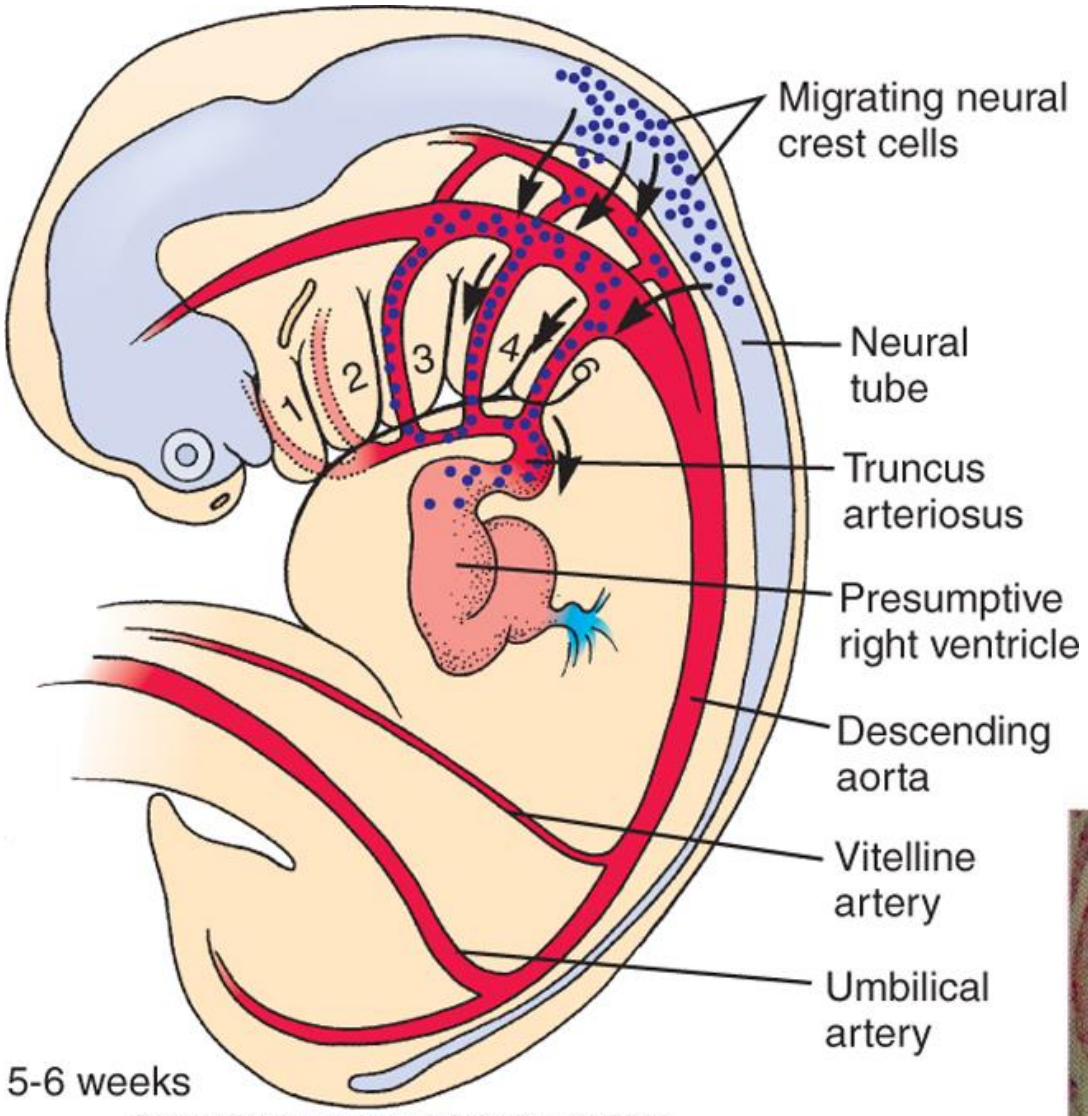


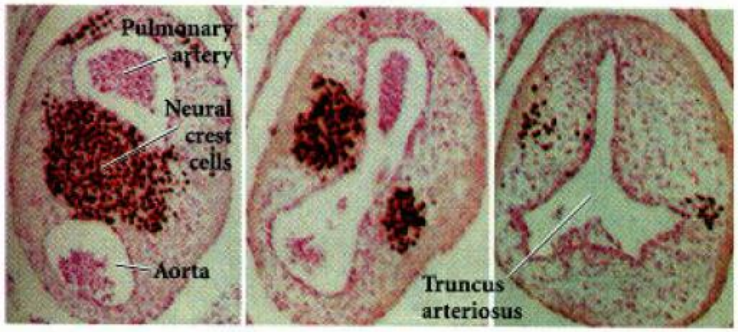
Gale et al (1996) Development. 122: 783-793.

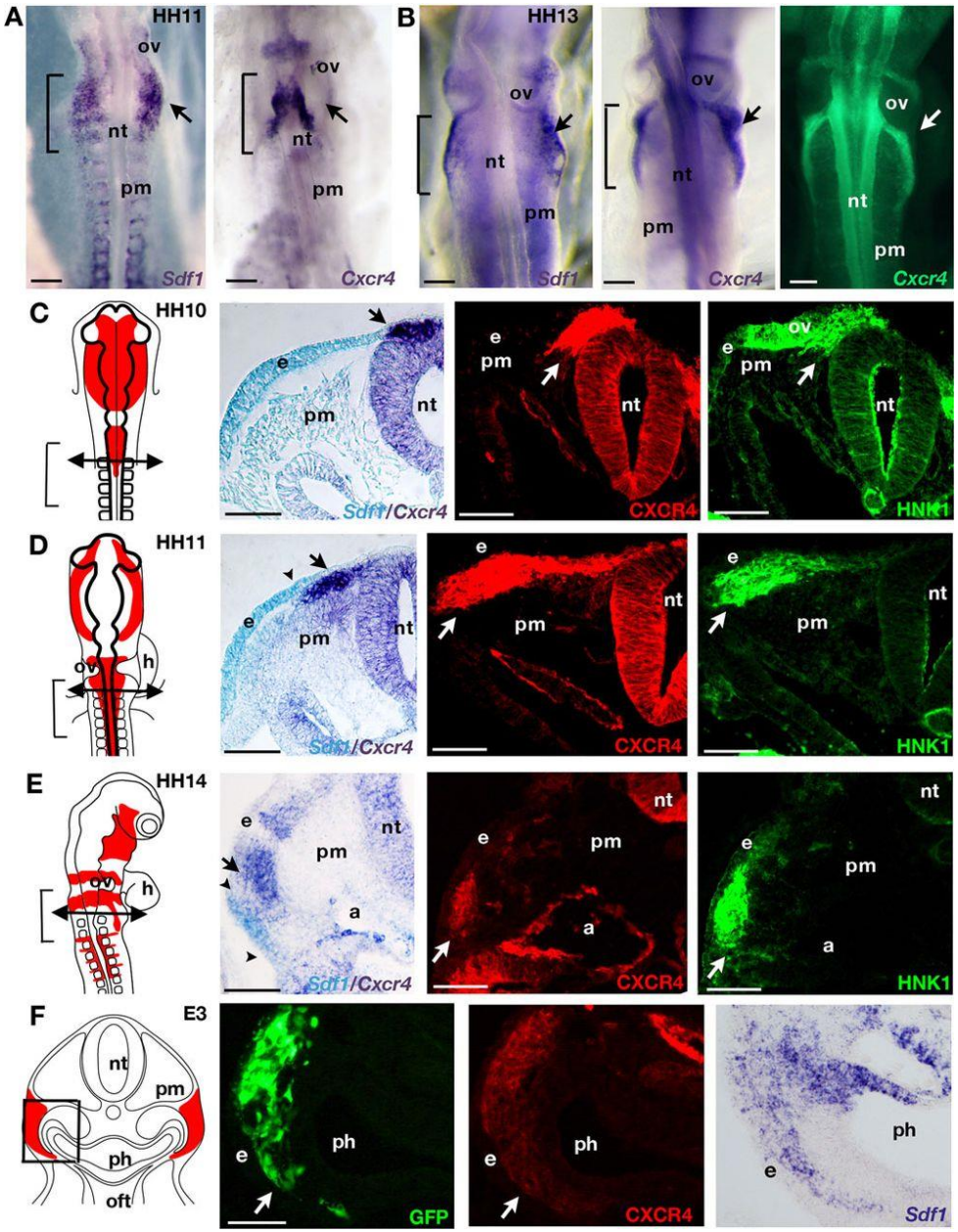


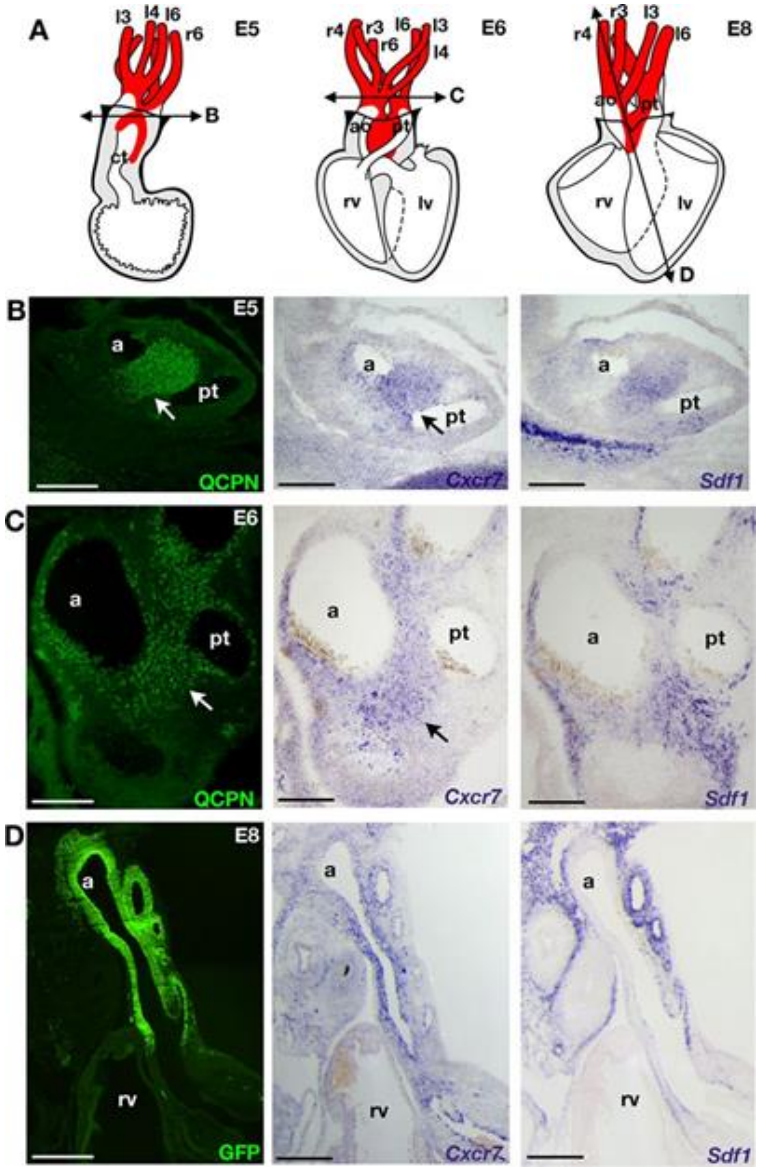
N.M. Le Douarin / Mechanisms of Development 121 (2004) 1089–1102

NC in heart development







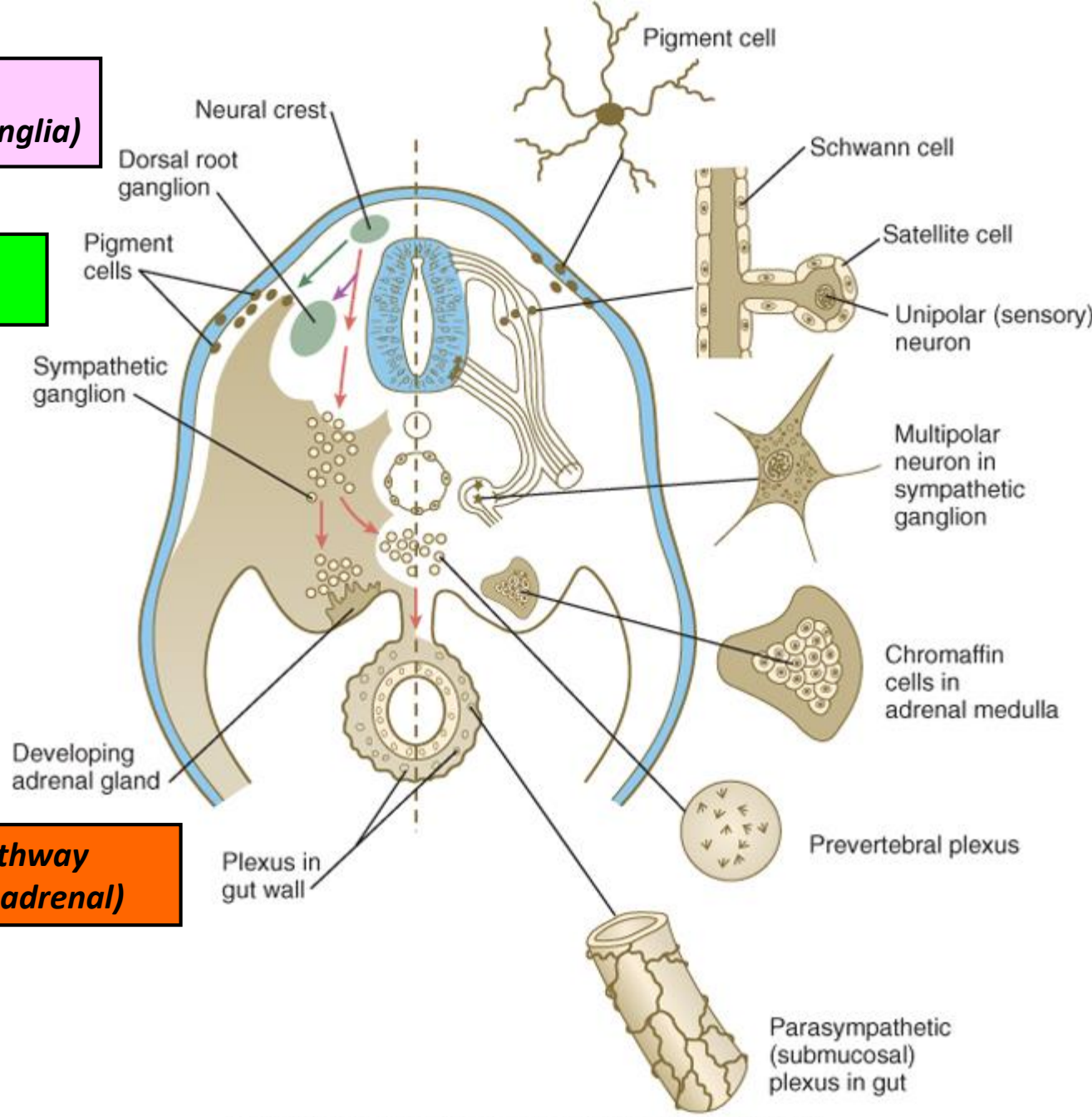


Misregulation of SDF1-CXCR4 Signaling Impairs Early Cardiac Neural Crest Cell Migration Leading to Conotruncal Defects, Volume: 113, Issue: 5, Pages: 505-516, DOI: (10.1161/CIRCRESAHA.113.301333)

ventrolateral pathway (anterior somite: sensory ganglia)

dorsolateral pathway (melanocytes)

ventral pathway (sympathico-adrenal)



Migration in the trunk

- Role of BMP4

- Ventromedial pathway:
  - rostral part of somite
  - ephrin B1 caudally, non favorable
  - In posterior scelotome (semaforins, chondroitin-sulphate)
  - Derivatives: spinal ganglia, sympathetic ggl., Schwann cells, chromaffin cells
  - Development is in concert with somite development and differentiation

- Dorsolateral pathway:
  - Between somite and ectoderm
  - 24 h after ventromedial cells
  - Derivatives: melanocytes
  - endothelin-3

- Glicoproteins on cell surface regulate which pathway to take
- ECM constitution regulates migration: tenascin, thrombospondin stimulate, F-spondin, collagen IX inhibit migration
- Perinotochordal mesenchyme (chondroitin-sulfate)

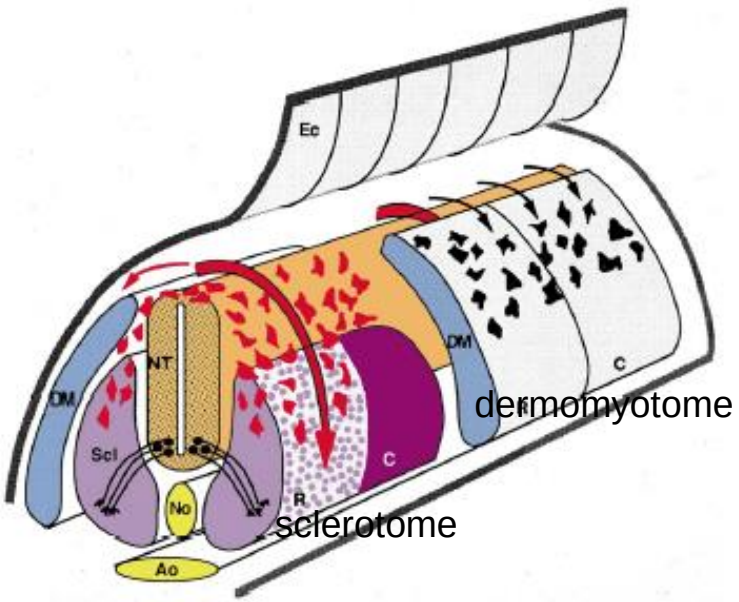
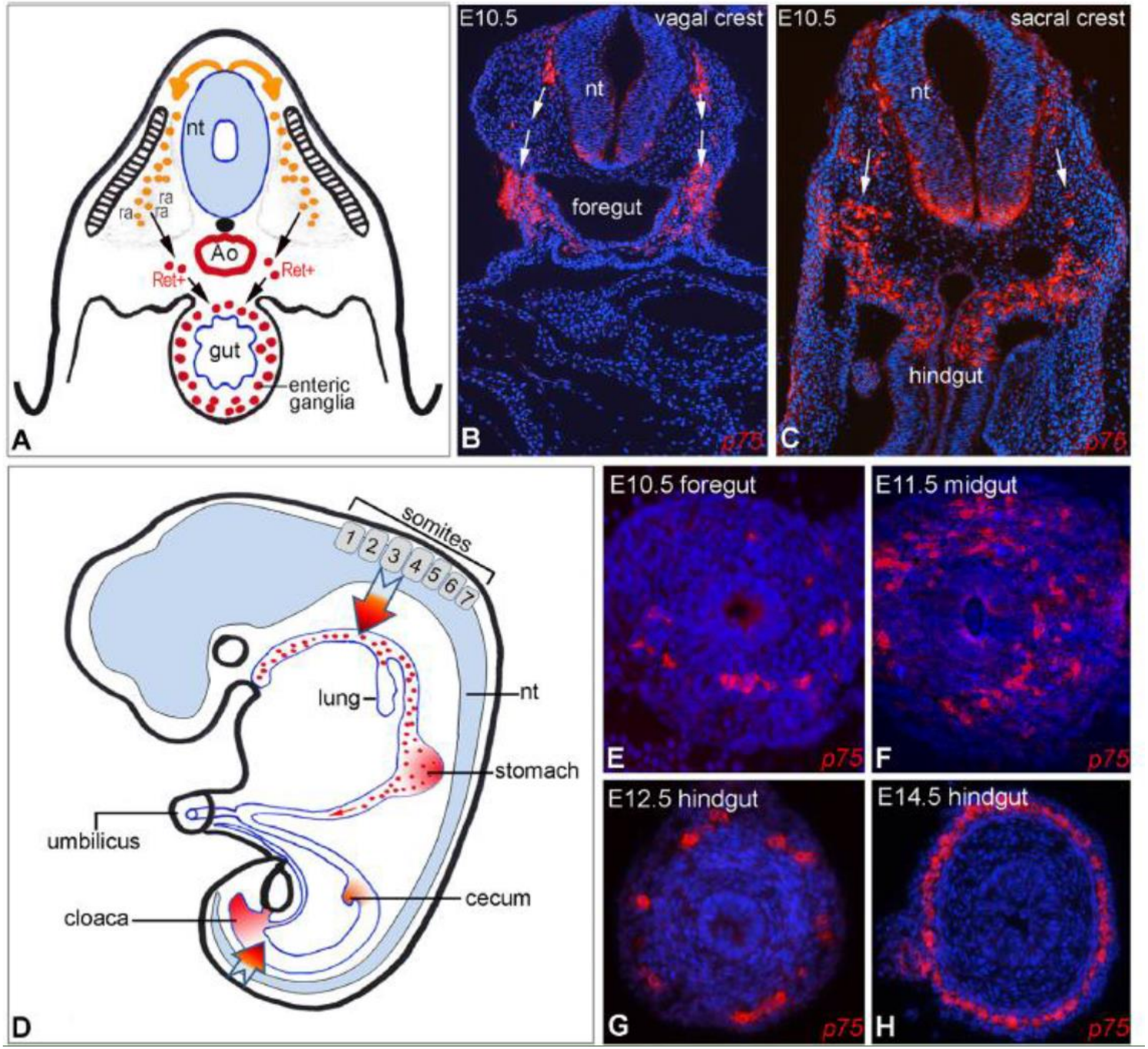
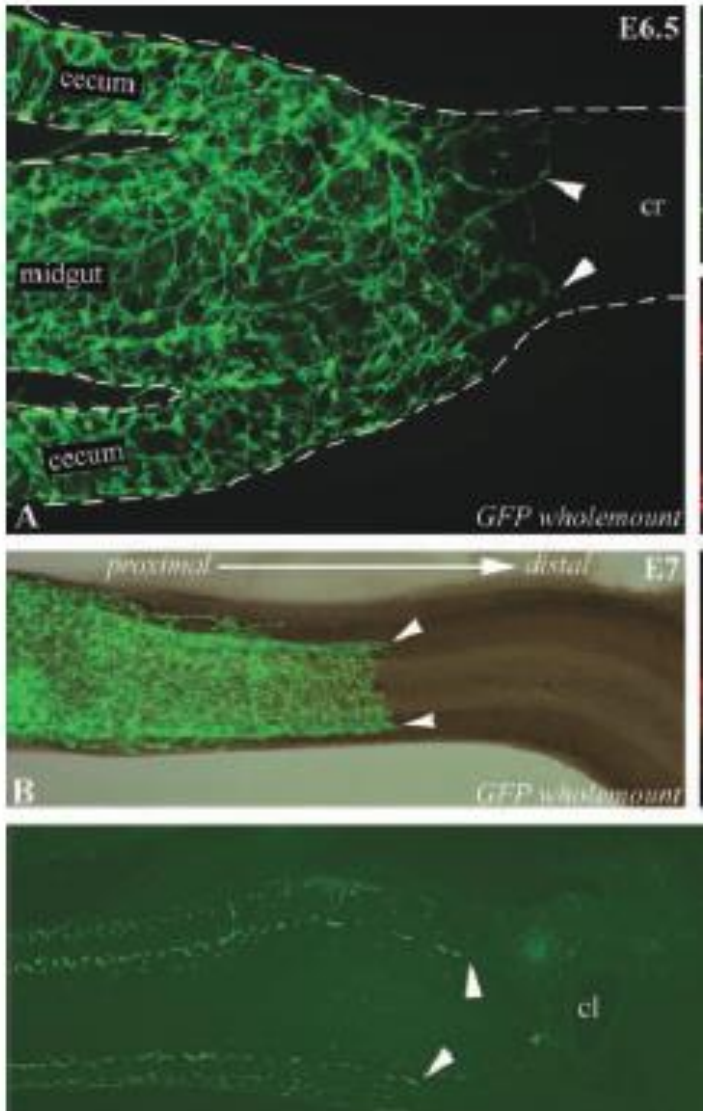


Fig. 1. Avian trunk neural crest cells travel on two distinct pathways after emigration from the neural tube. Schematic diagram of a longitudinal view of the trunk region of an avian embryo. Some trunk neural crest cells (red) emerge from the dorsal neural tube and travel ventromedially, through the rostral, but not caudal, somitic sclerotome. Other neural crest cells (black) migrate dorsolaterally in a uniform manner between the somites and overlying ectoderm. DM, dermomyotome; Scl, sclerotome; No, notochord; Ao, aorta; Ec, ectoderm; NT, neural tube; R, rostral; C, caudal.

Krull (2001) MOD, 105:37-45.


nt
ra
ra
ra
Ao
Ret+
Ret+
gut
enteric ganglia
A
E10.5
vagal crest
nt
foregut
B
p75
E10.5
sacral crest
nt
hindgut
C
p75
somites
1 2 3 4 5 6 7
lung
nt
stomach
umbilicus
cecum
cloaca
D
E10.5 foregut
E
p75
E11.5 midgut
F
p75
E12.5 hindgut
G
p75
E14.5 hindgut
H
p75

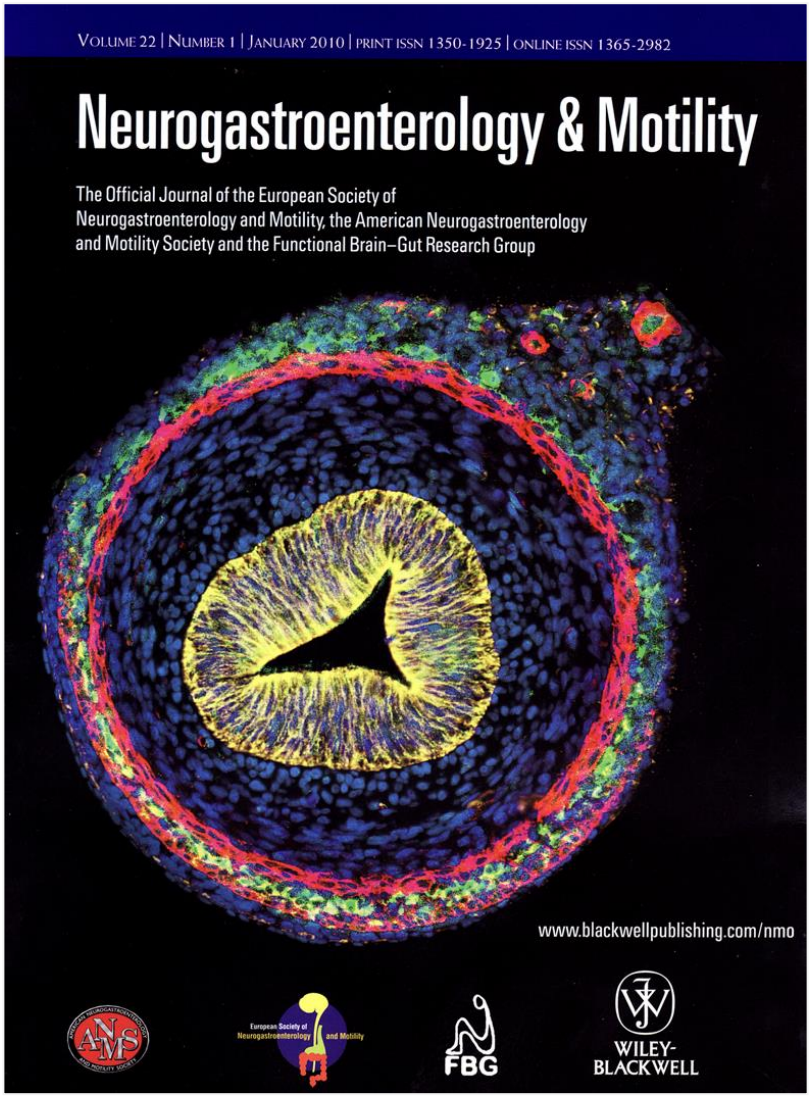


DEVELOPMENTAL DYNAMICS 241:842–851, 2012

RESEARCH ARTICLE

Immunophenotypic Characterization of Enteric Neural Crest Cells in the Developing Avian Colorectum

Nandor Nagy,[1,2] Alan J. Burns,[3] and Allan M. Goldstein[1]*



12 week old human embryo colon

Cover image by Nagy N and Goldstein A.M, 2010