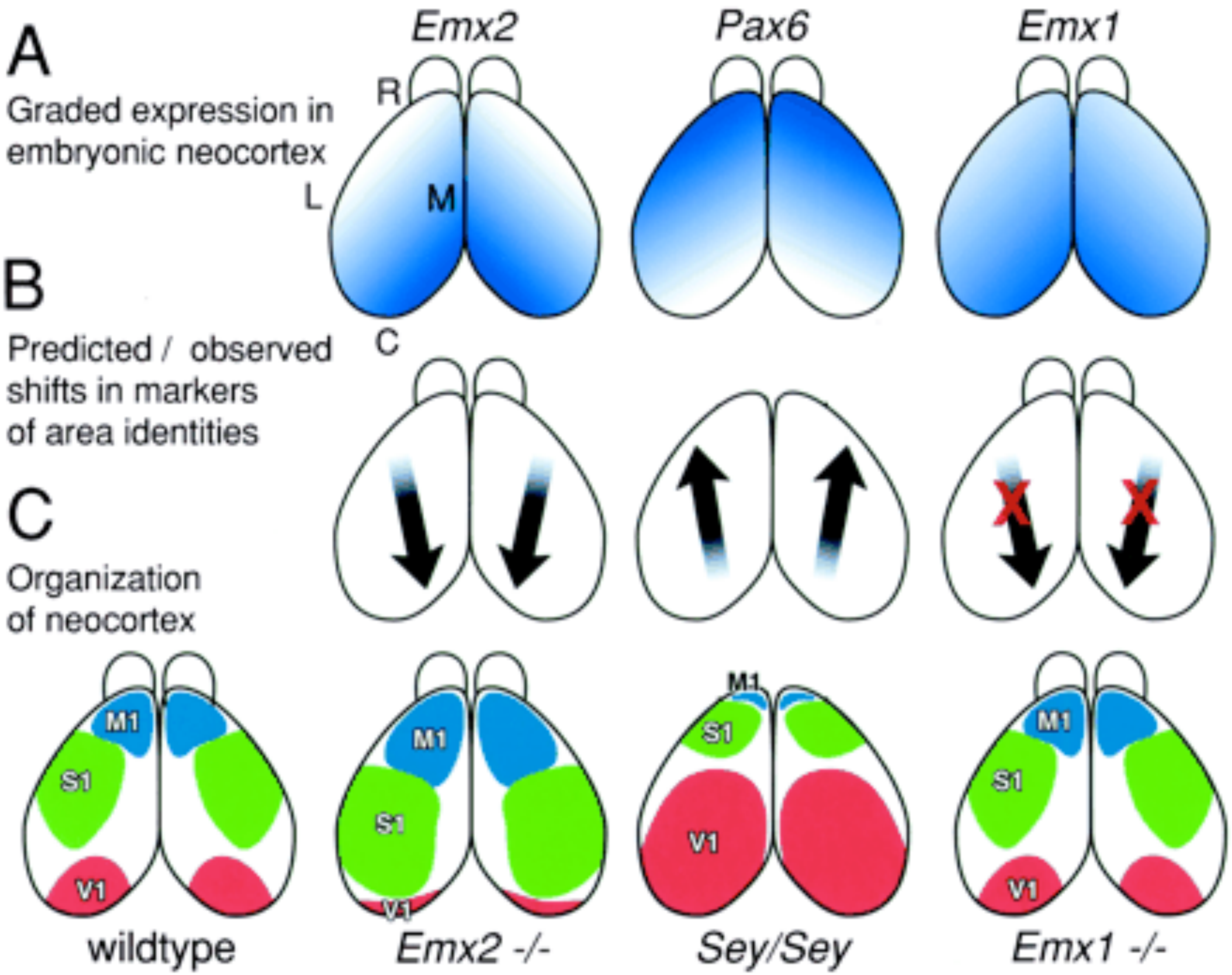
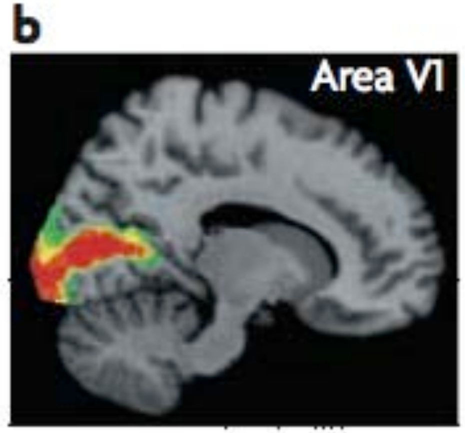
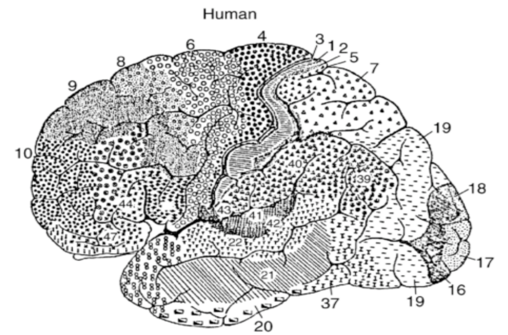
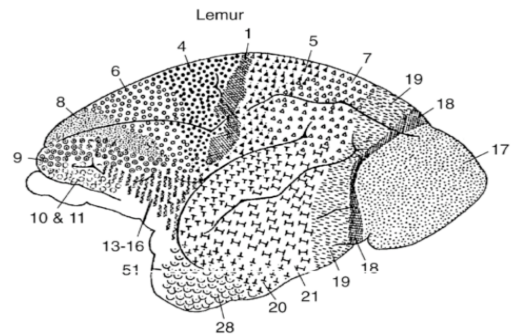
Cours du 10 octobre 2011

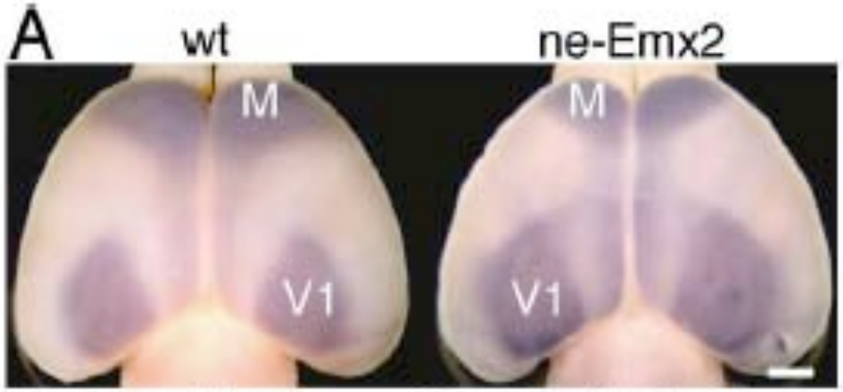

A
Graded expression in
embryonic neocortex
B
Predicted / observed
shifts in markers
of area identities
C
Organization
of neocortex
Emx2
Pax6
Emx1
R
L
M
C
M1
S1
V1
wildtype
Emx2 -/-
Sey/Sey
Emx1 -/-


b
Area VI


Human


Lemur

Hamasaki et al. Neuron, vol 43, p359–372, 2004



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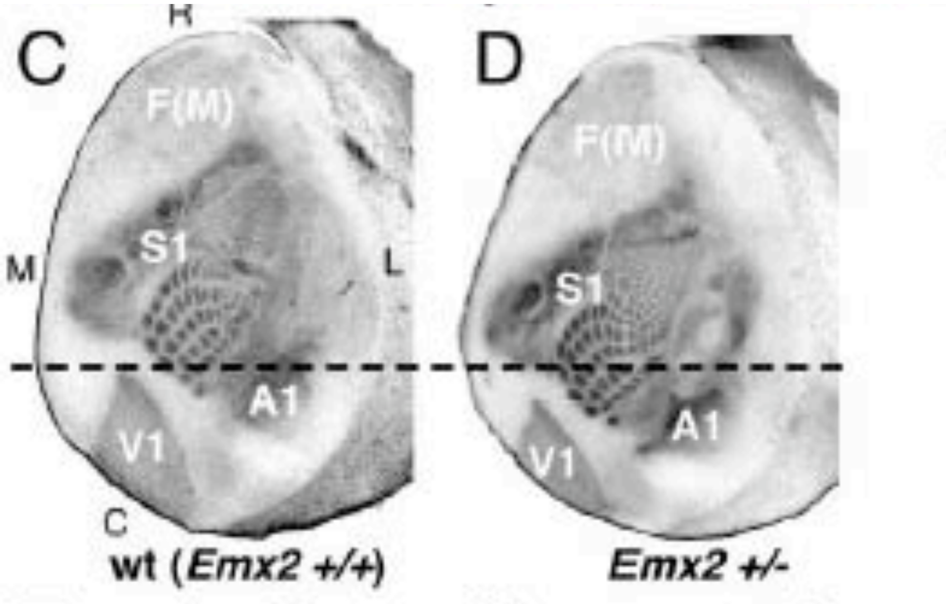

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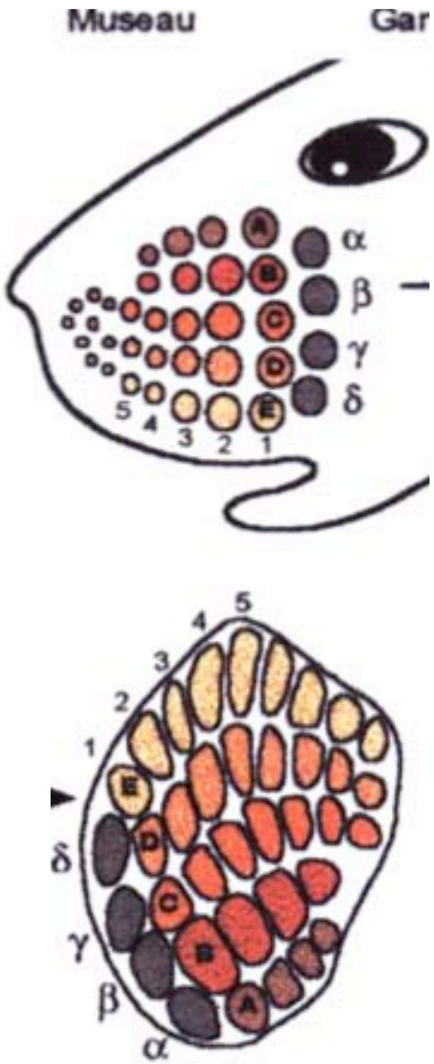
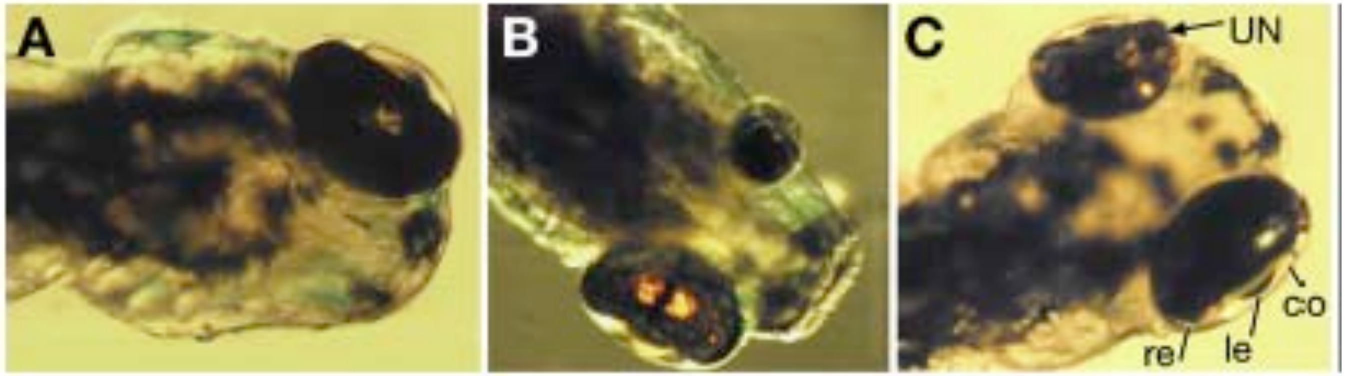


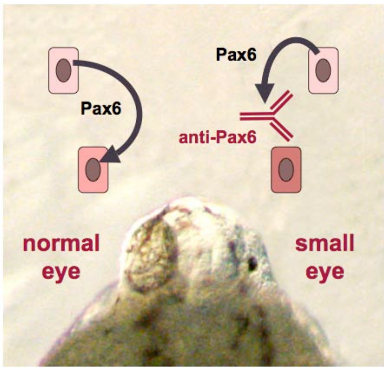
Hsp90 Selectively Modulates Phenotype in Vertebrate Development

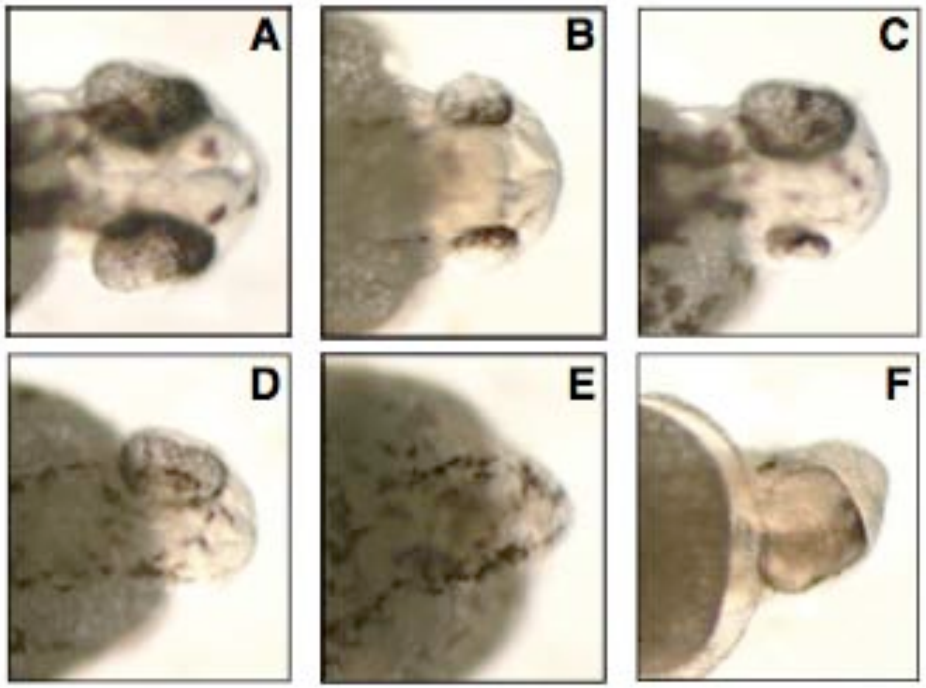
March 2007 | Volume 3 | Issue 3 | e43

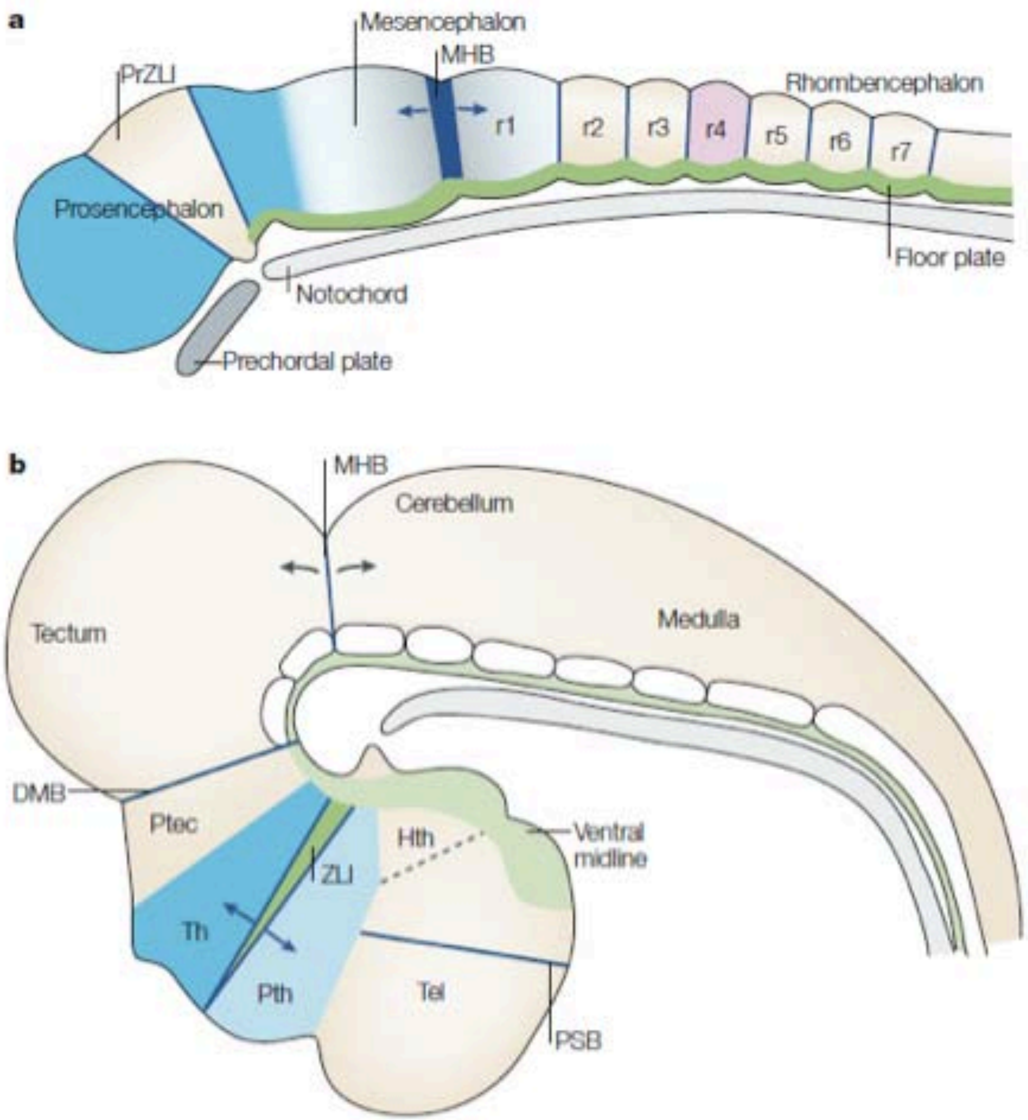
Patricia L. Yeyati*, Ruth M. Bancewicz, John Maule, Veronica van Heyningen*

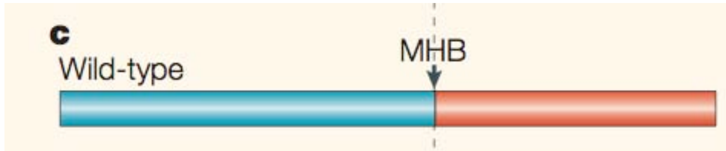
PLoS Genetics | www.plosgenetics.org

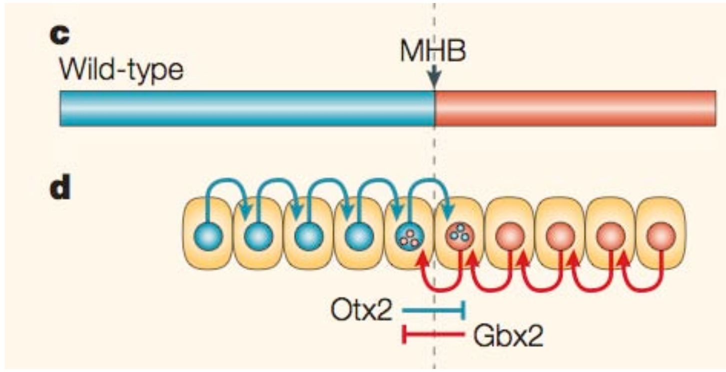


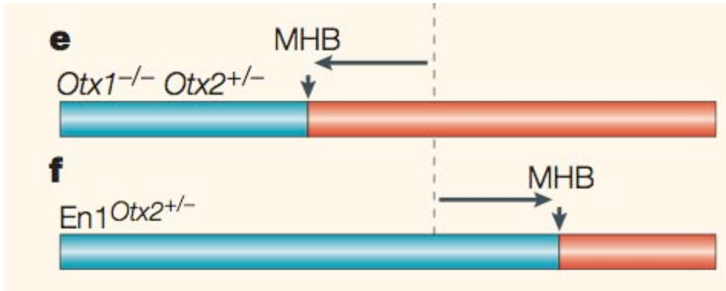




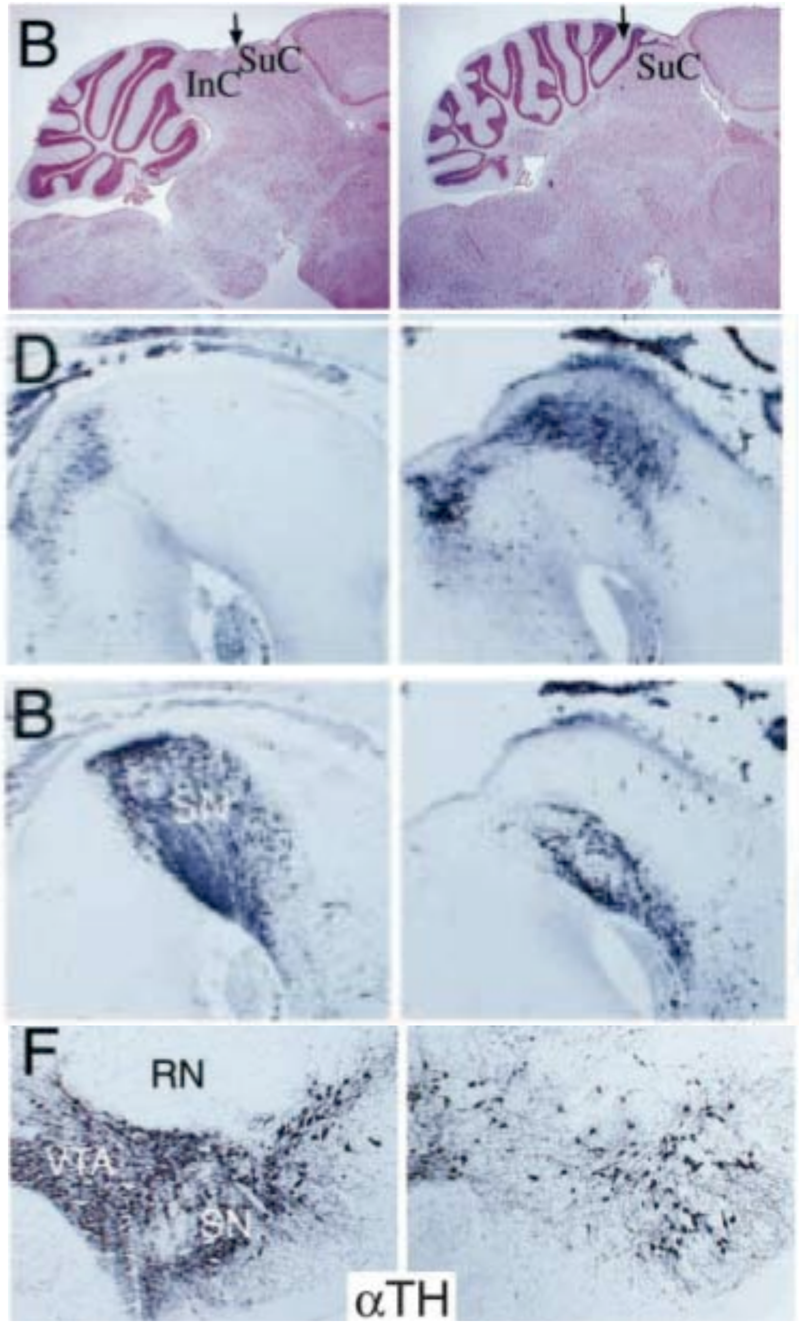

a
Mesencephalon
MHB
PrZLI
Rhombencephalon
r1
r2
r3
r4
r5
r6
r7
Prosencephalon
Floor plate
Notochord
Prechordal plate
b
MHB
Cerebellum
Tectum
Medulla
DMB
Ptec
Hth
Ventral
midline
ZLI
Th
Pth
Tel
PSB


c
Wild-type
MHB


c
Wild-type
MHB
d
Otx2
Gbx2


e
MHB
Otx1−/− Otx2+/−
f
MHB
En1Otx2+/−

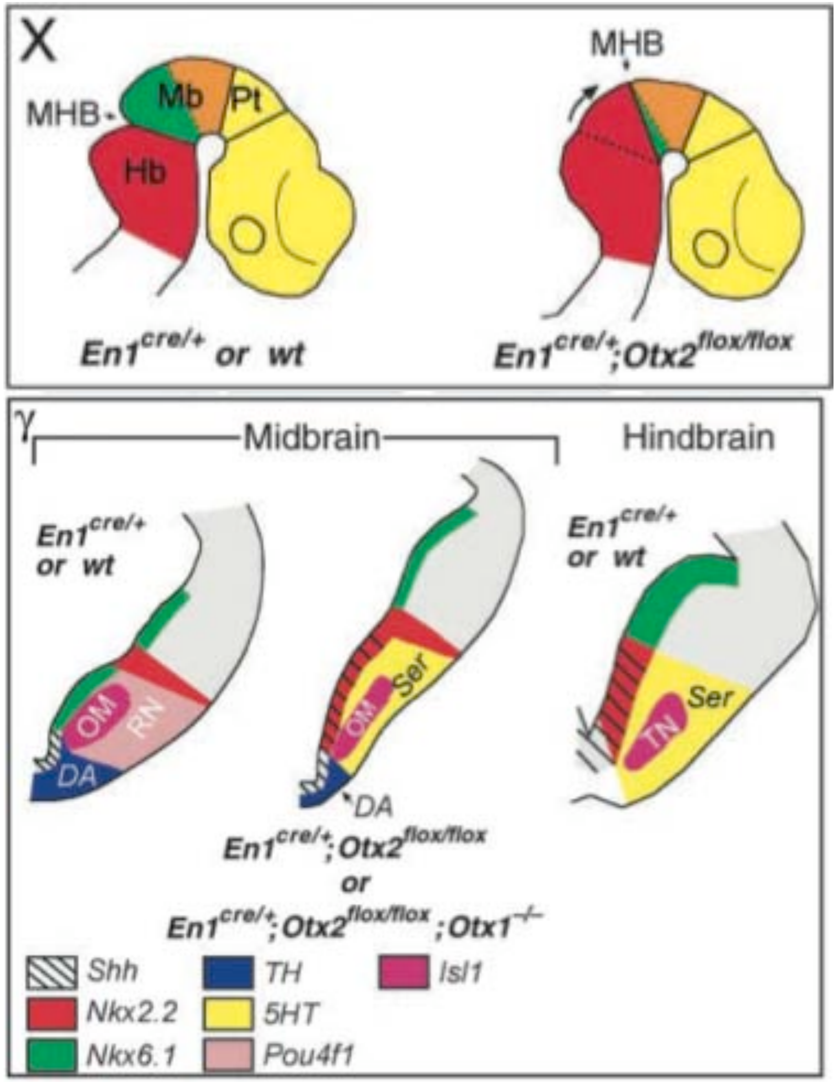
Elimination de Otx2 dans le domaine En1



Otx2 regulates the extent, identity and fate of neuronal progenitor domains in the ventral midbrain

Puelles E, Annino A, Tuorto F, Usiello A, Acampora D, Czerny T, Brodski C, Ang SL, Wurst W, Simeone A

Development
2004 vol. 131 (9) pp. 2037-48

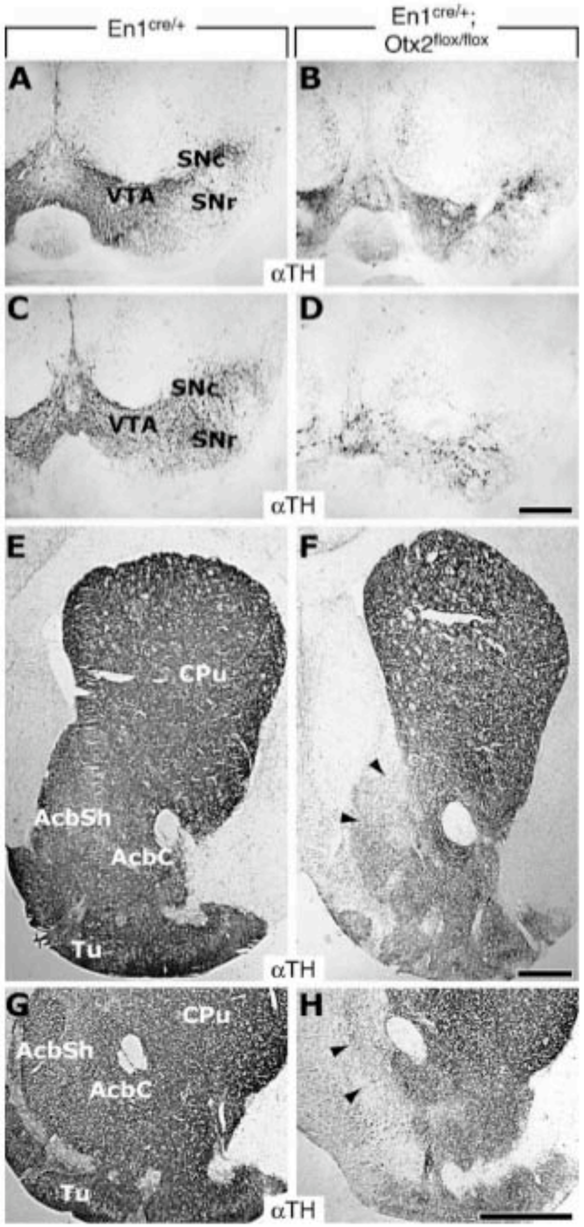


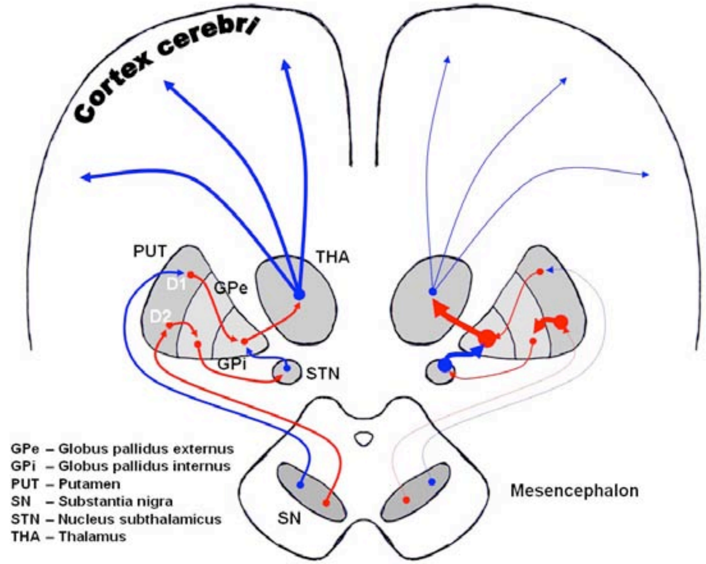
TN Trochlear OM Oculomotor

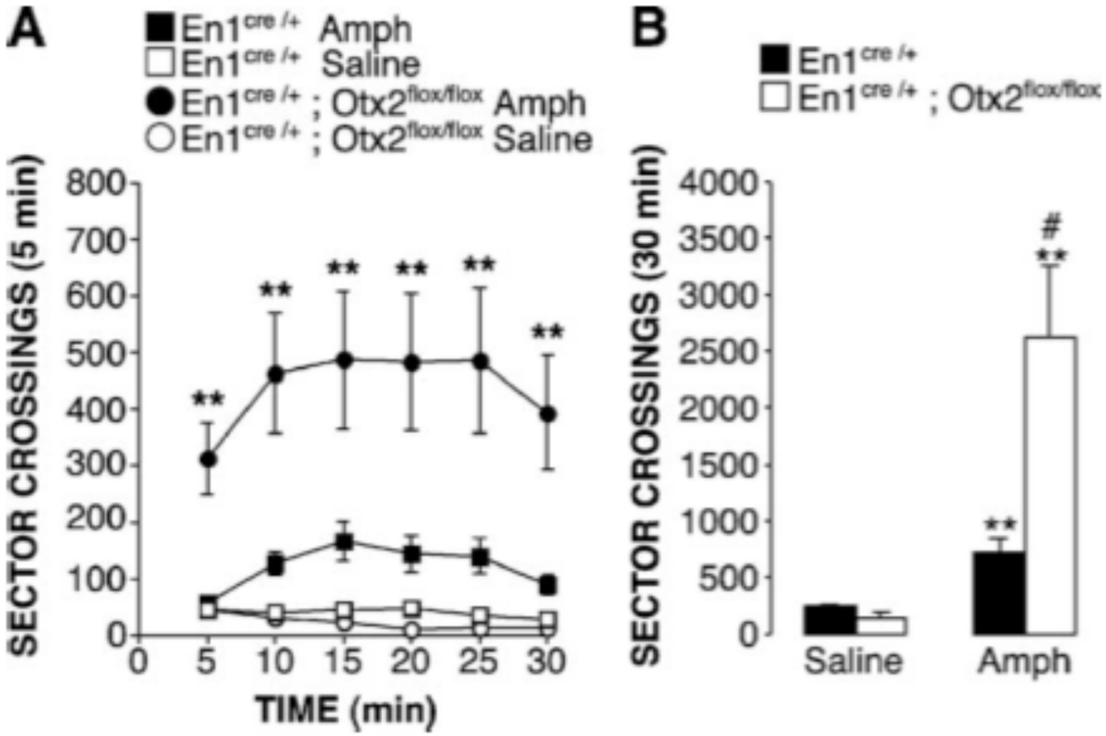
Altered dopaminergic innervation and amphetamine response in adult Otx2 conditional mutant mice

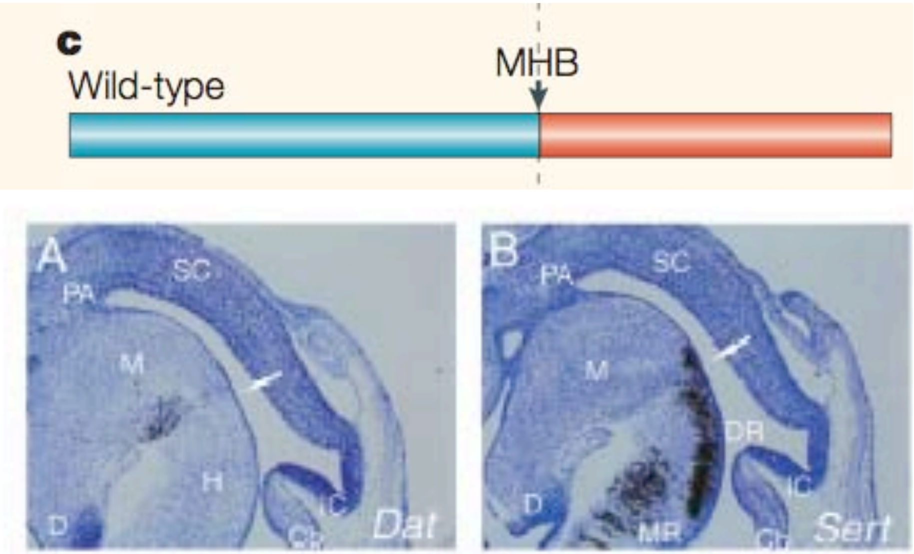
Borgkvist A, Puelles E, Carta M, Acampora D, Ang SL, Wurst W, Goiny M, Fisone G, Simeone A, Usiello A

Mol Cell Neurosci
2006 vol. 31 (2) pp. 293-302





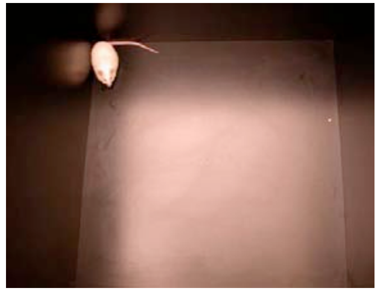


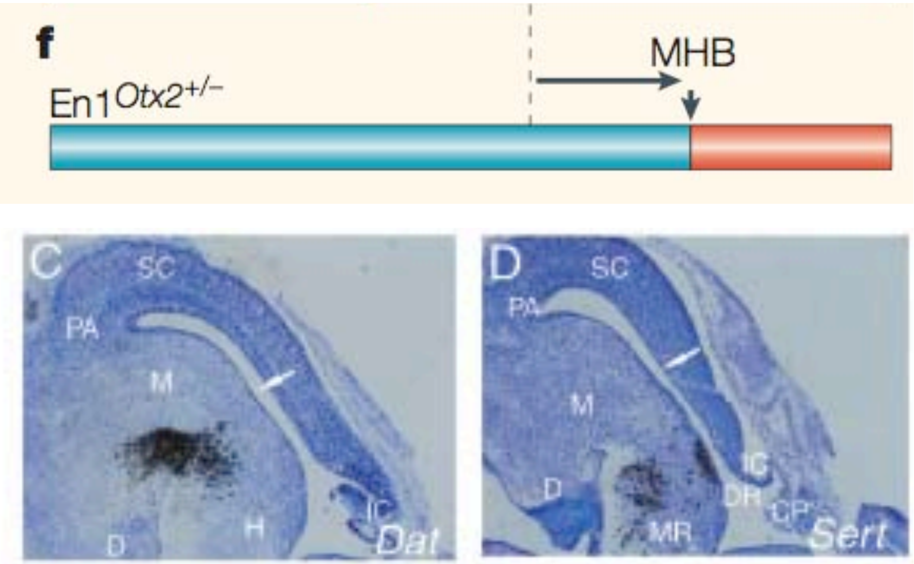


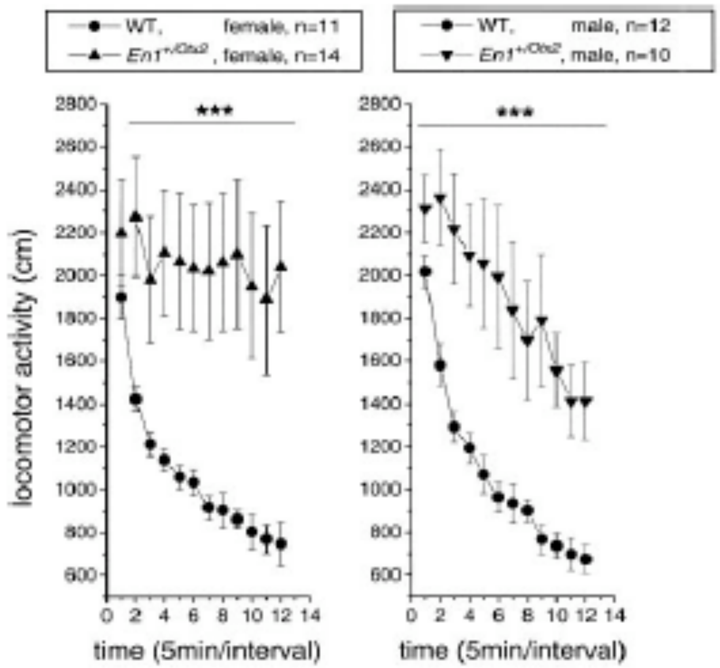
The Journal of Neuroscience, May 15, 2003 • 23(10):4199–4207 • 4199

Location and Size of Dopaminergic and Serotonergic Cell Populations Are Controlled by the Position of the Midbrain–Hindbrain Organizer

Claude Brodski,[1*] Daniela M. Vogt Weisenhorn,[1*] Massimo Signore,[2*] Inge Sillaber,[1] Matthias Oesterheld,[1] Vania Broccoli,[3] Dario Acampora,[2] Antonio Simeone,[2] and Wolfgang Wurst[1]



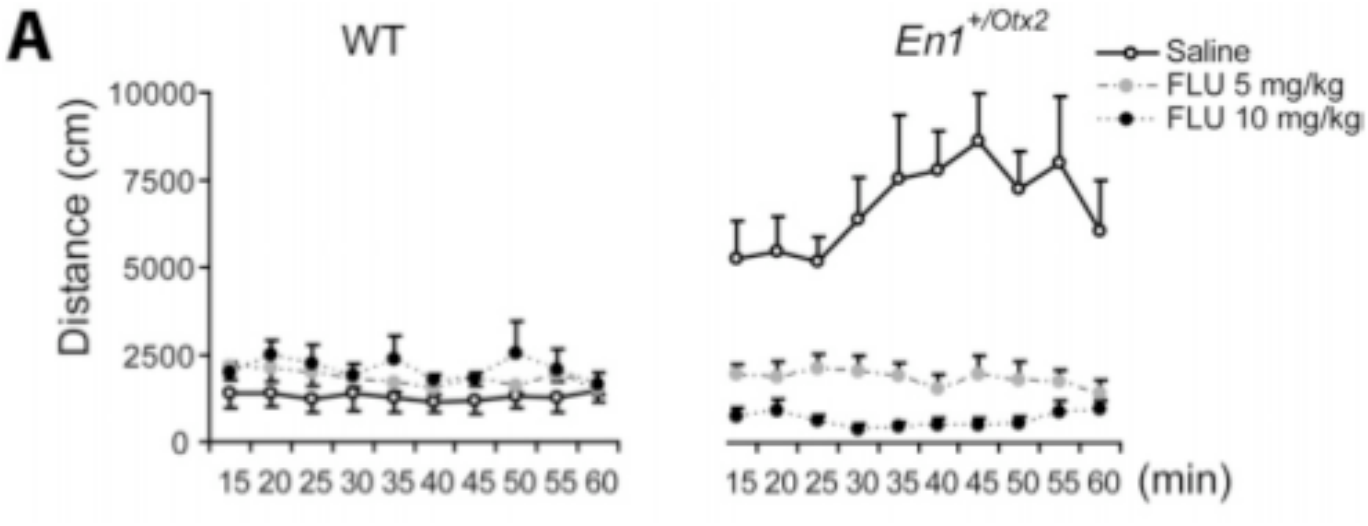


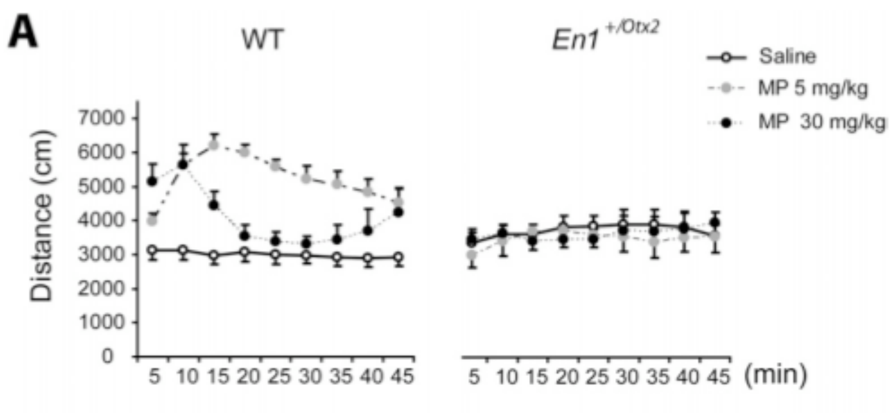


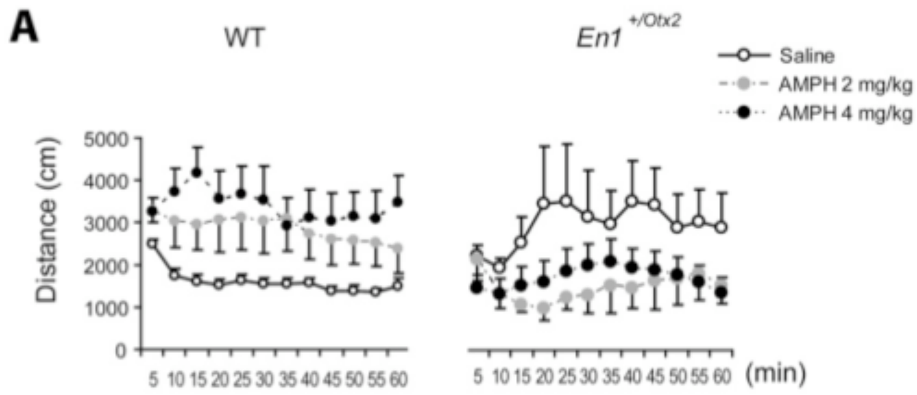
CRITICAL ROLE OF THE EMBRYONIC MID–HINDBRAIN ORGANIZER IN THE BEHAVIORAL RESPONSE TO AMPHETAMINE AND METHYLPHENIDATE

H. TILLEMAN,[a] O. KOFMAN,[b] L. NASHELSKY,[a] U. LIVNEH,[b] N. ROZ,[e] I. SILLABER,[c] A. BIEGON,[d] M. REHAVI[e] AND C. BRODSKI[a]*

Neuroscience 163 (2009) 1012–1023







COMPARTMENTS AND THEIR BOUNDARIES IN VERTEBRATE BRAIN DEVELOPMENT

Clemens Kiecker and Andrew Lumsden

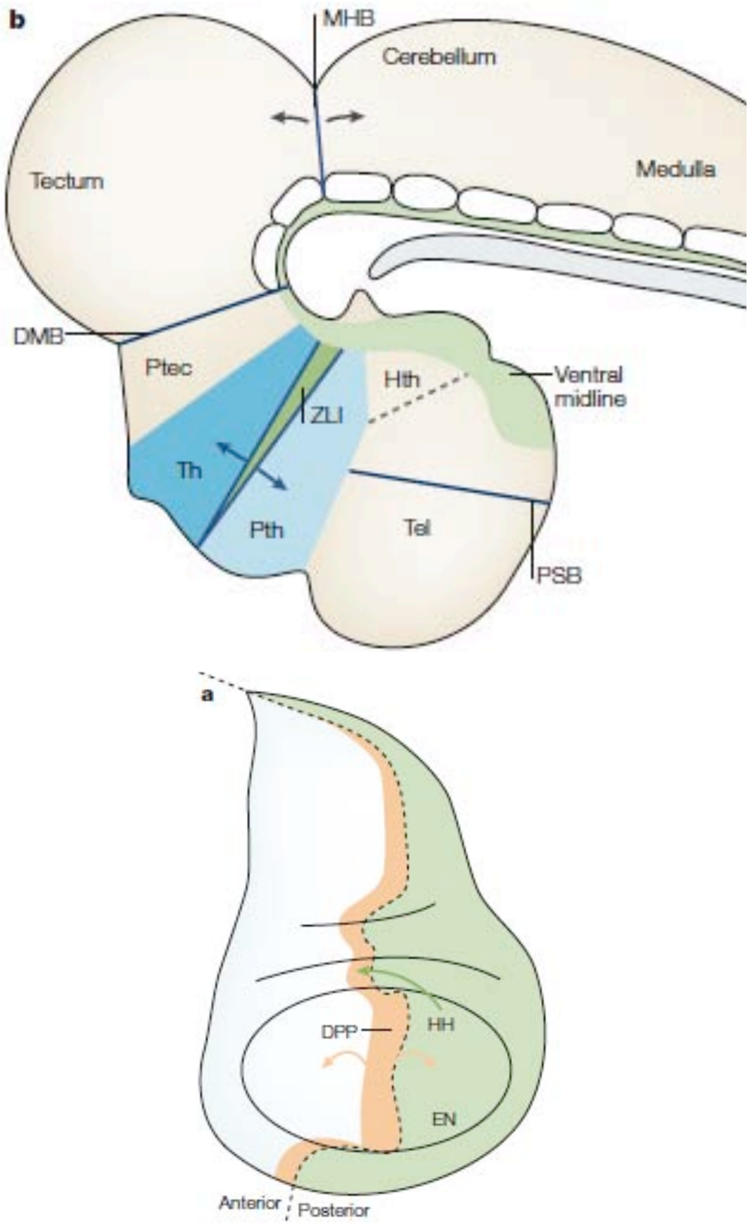


Table 1 | **Boundaries in the developing vertebrate brain**

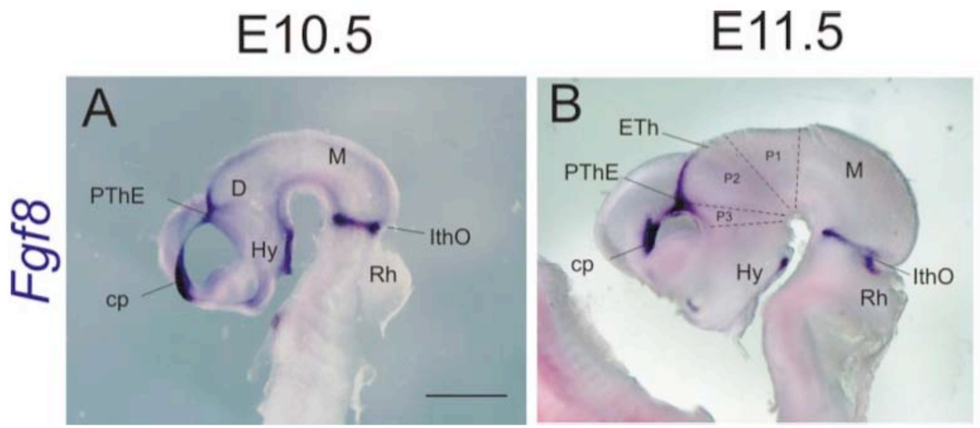
Regional interface	Cell lineage restriction	Signalling function
Anterior neural border (ANB)	?	+ (anti-WNT, FGFs)
Pallial–subpallial boundary (PSB)	+ (Ventricular zone only)	None detected
Telencephalon–diencephalon	–	None detected
Zona limitans intrathalamica (ZLI)	+ (Two boundaries with lineage restriction anteriorly and posteriorly; does not extend into roof plate)	+ (SHH, WNTs?, FGFs?)
Thalamus–pretectum	–	None detected
Diencephalic–midbrain boundary (DMB)	+	None detected
Midbrain–hindbrain boundary (MHB)	+ (Might be leaky; possibly two boundaries dorsally)	+ (FGFs, WNT1)
Rhombomeres	+ (Except floor plate; ventricular zone only)	+ (WNT1, WNT3A?, WNT8B?, WNT10B?)
Spinal cord	–	Anteroposterior: – Dorsoventral: +

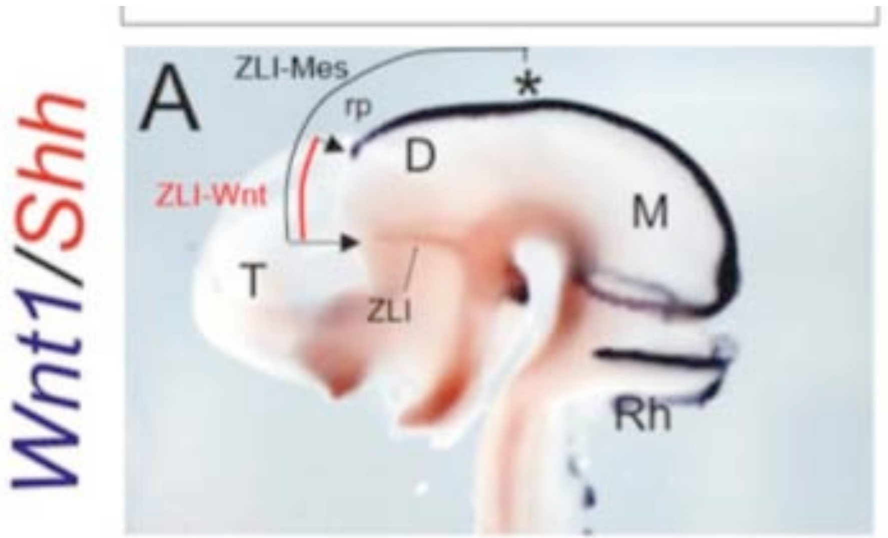
FGF, fibroblast growth factor; SHH, sonic hedgehog.

Wizenmann et al., Neuron, 64: 355-366, 2009
Layalle et al., Development 138: 2315-2323, 2011

The development of the thalamic motor learning area is regulated by Fgf8 expression

J Neurosci
2009 vol. 29 (42) pp. 13389...

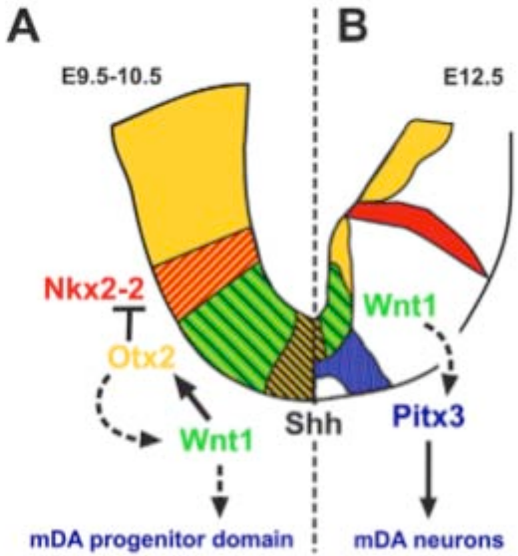




A Wnt1-regulated genetic network controls the identity and fate of midbrain-dopaminergic progenitors in vivo

Prakash N, Brodski C, Naserke T, Puelles E, Gogoi R, Hall A, Panhuysen M, Echevarria D, Sussel L, Weisenhorn DM, Martinez S, Arenas E, Simeone A, Wurst W

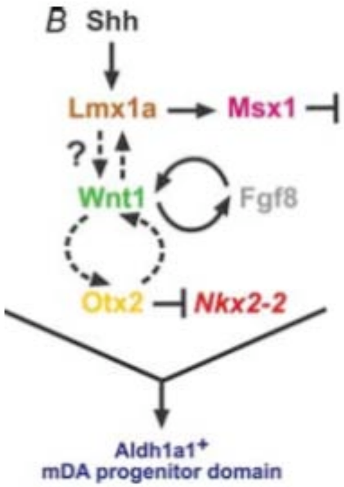
Development
2006 vol. 133 (1) pp. 89-98



Genetic networks controlling the development of midbrain dopaminergic neurons

Prakash N, Wurst W

The Journal of Physiology
2006 vol. 575 (Pt 2) pp. 403-10



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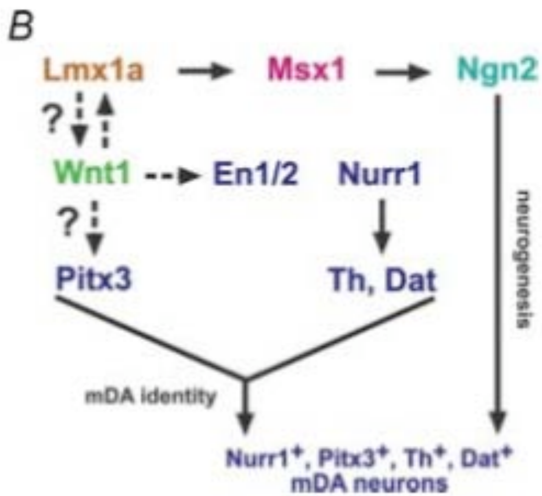


12,5

En1 and Wnt signaling in midbrain dopaminergic neuronal development

Alves Dos Santos MT, Smidt M

Neural Dev
2011 vol. 6 pp. 23

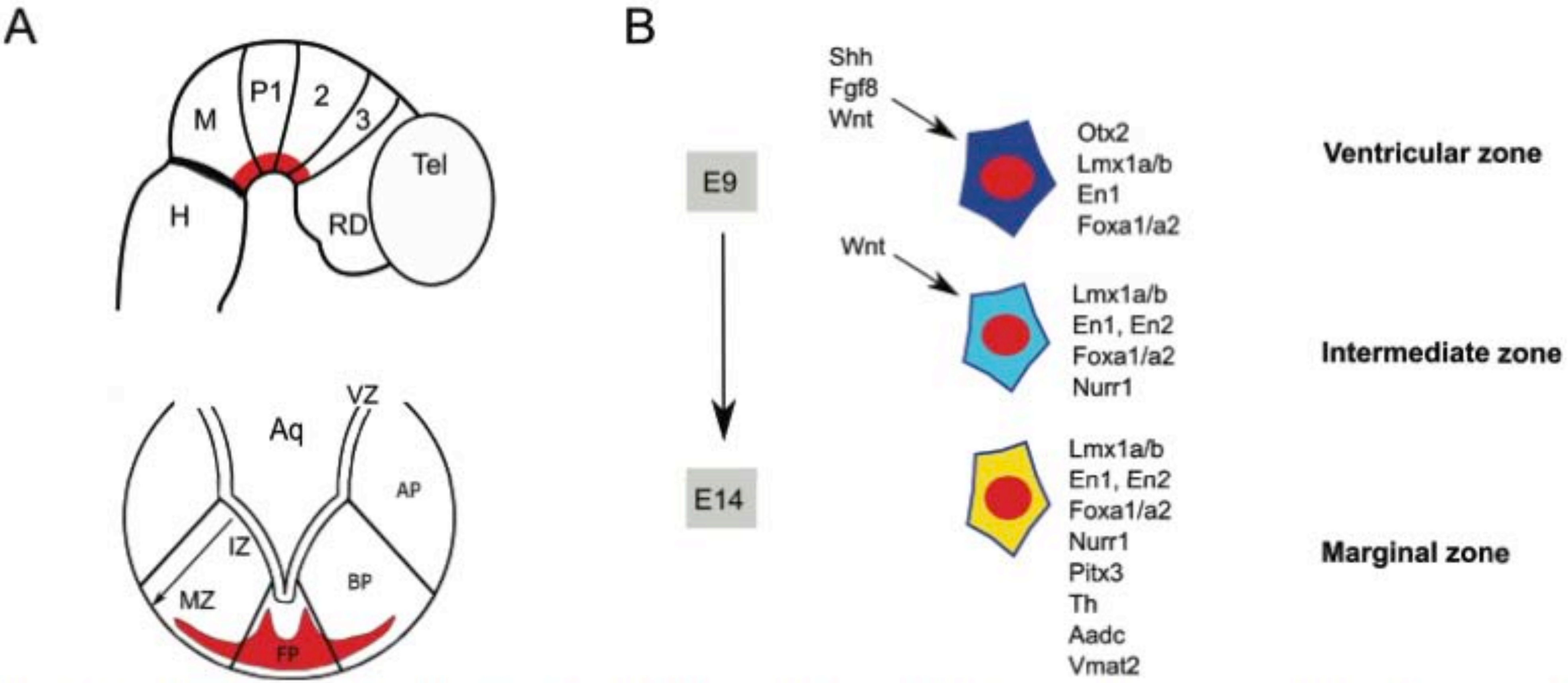


Figure 1 Spatial and temporal developmental stages leading to mesodiencephalic dopaminergic neurogenesis. (A) Sagittal and coronal

En1 and Wnt signaling in midbrain dopaminergic neuronal development

Alves Dos Santos MT, Smidt M

Neural Dev
2011 vol. 6 pp. 23

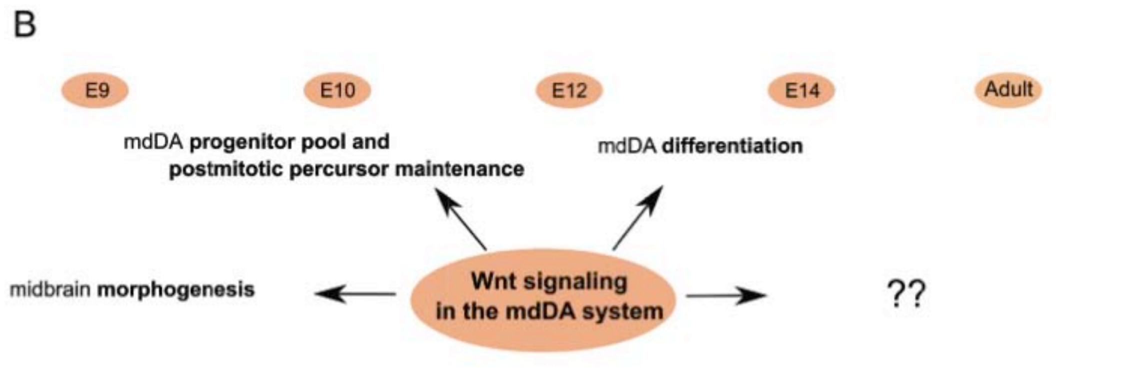


Figure 4 Wnt signaling during the central nervous system and mesodiencephalic dopaminergic neuron development. (A) Wnt signaling

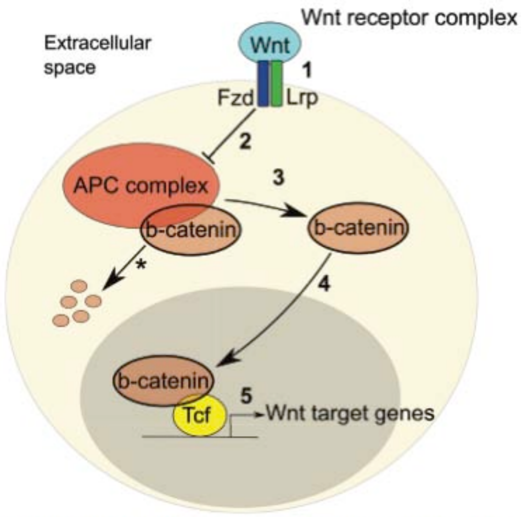


Figure 3 Canonical Wnt signaling mechanism. (1) Wnts bind to

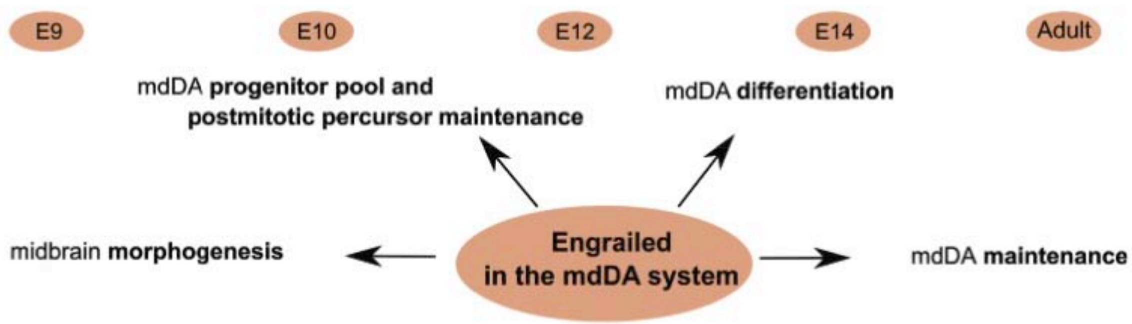
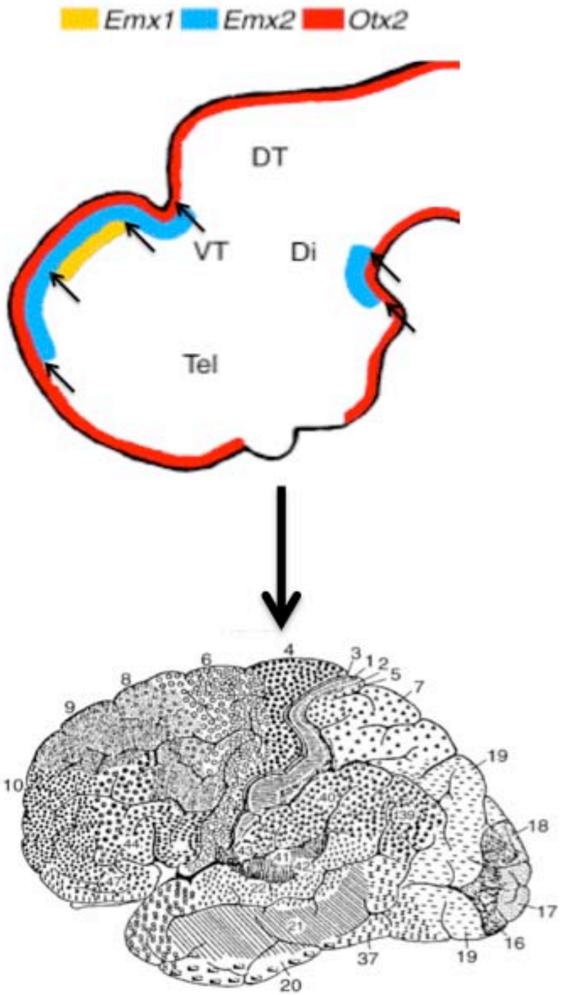


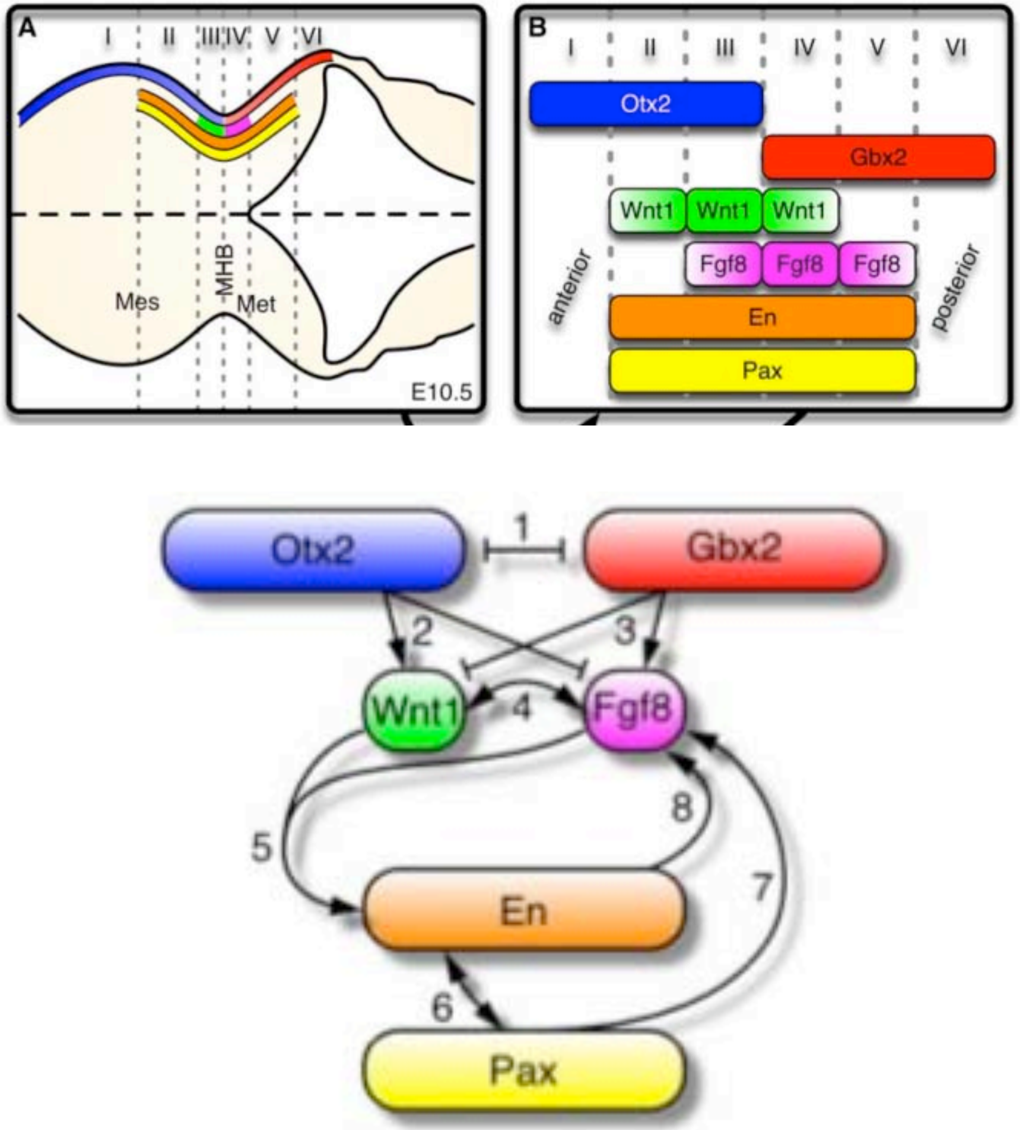
Figure 2 The impact of the engrailed genes in the development of the central nervous system and the mesodiencephalic dopaminergic system. (A) Engrailed proteins are key players in diverse processes during embryonic development of the central nervous system (CNS), including patterning, axonal guidance and neuron specification. **(B)** Engrailed proteins are essential in mesodiencephalic dopaminergic (mdDA) neuron development from an early stage, where they are involved in morphogenesis and mdDA neurogenesis, and in the adult, where they play a role in mdDA neuron maintenance E, embryonic day.

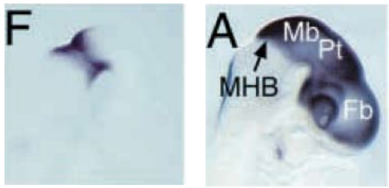
Spatial Analysis of Expression Patterns Predicts Genetic Interactions at the Mid-Hindbrain Boundary

PLoS Computational Biology | Volume 5 | Issue 11 | e1000569

Dominik M. Wittmann[1,2], Florian Blöchl[1], Dietrich Trümbach[3,4], Wolfgang Wurst[3,4], Nilima Prakash[3], Fabian J. Theis[1,2,5]*







E10

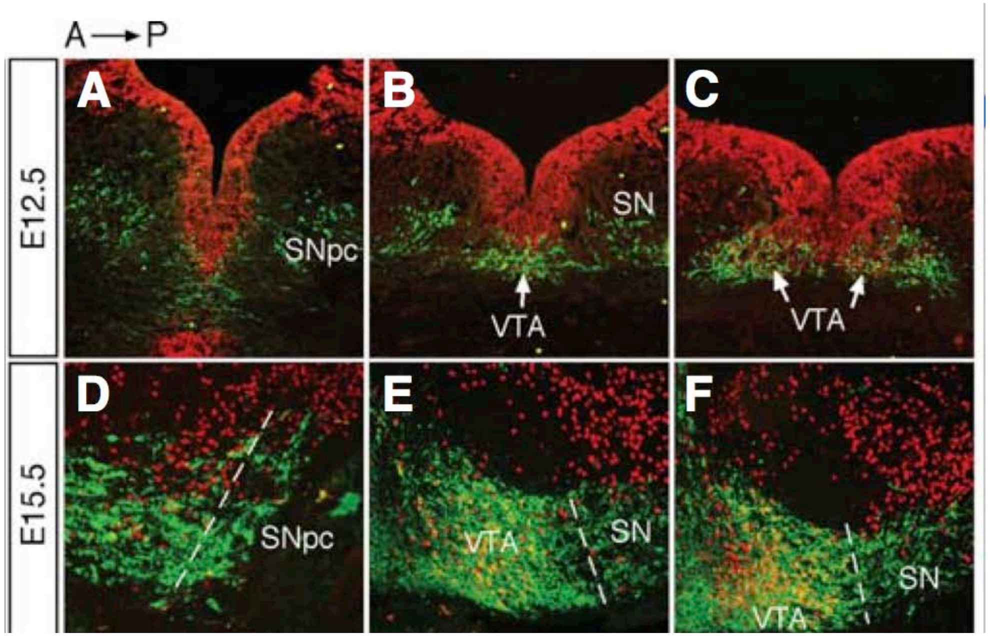
Otx2 expression is restricted to dopaminergic neurons of the ventral tegmental area in the adult brain

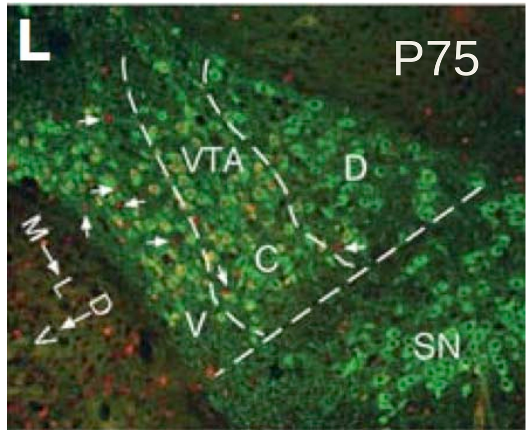
Di Salvio M, Di Giovannantonio LG, Omodei D, Acampora D, Simeone A

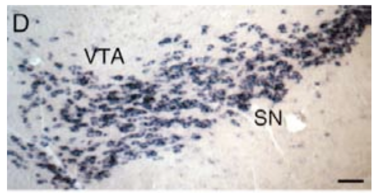
Int J Dev Biol
2010 vol. 54 (5) pp. 939-45

Otx2

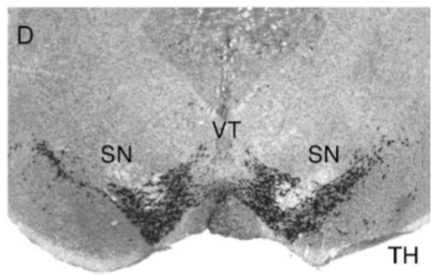
TH

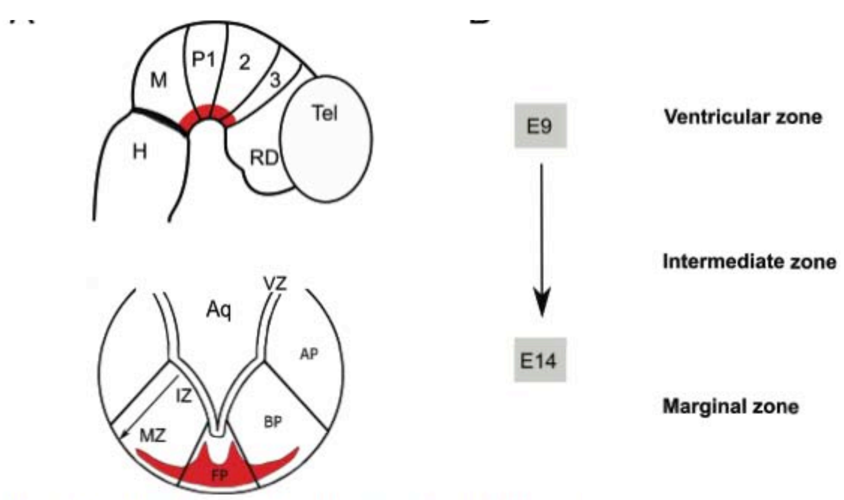






En1





Engrailed genes are cell-autonomously required to prevent apoptosis in mesencephalic dopaminergic neurons

Albéri L, Sgadò P, Simon H

Development
2004 vol. 131 (13) pp. 3229-36

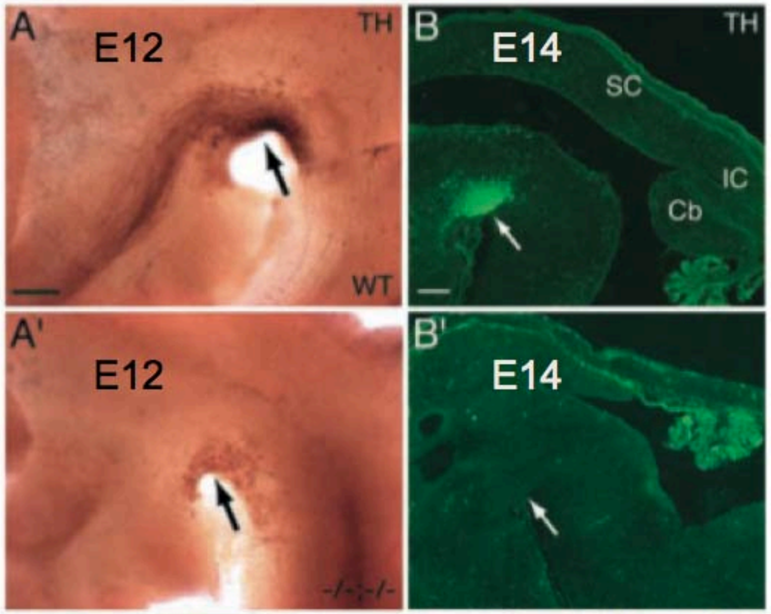
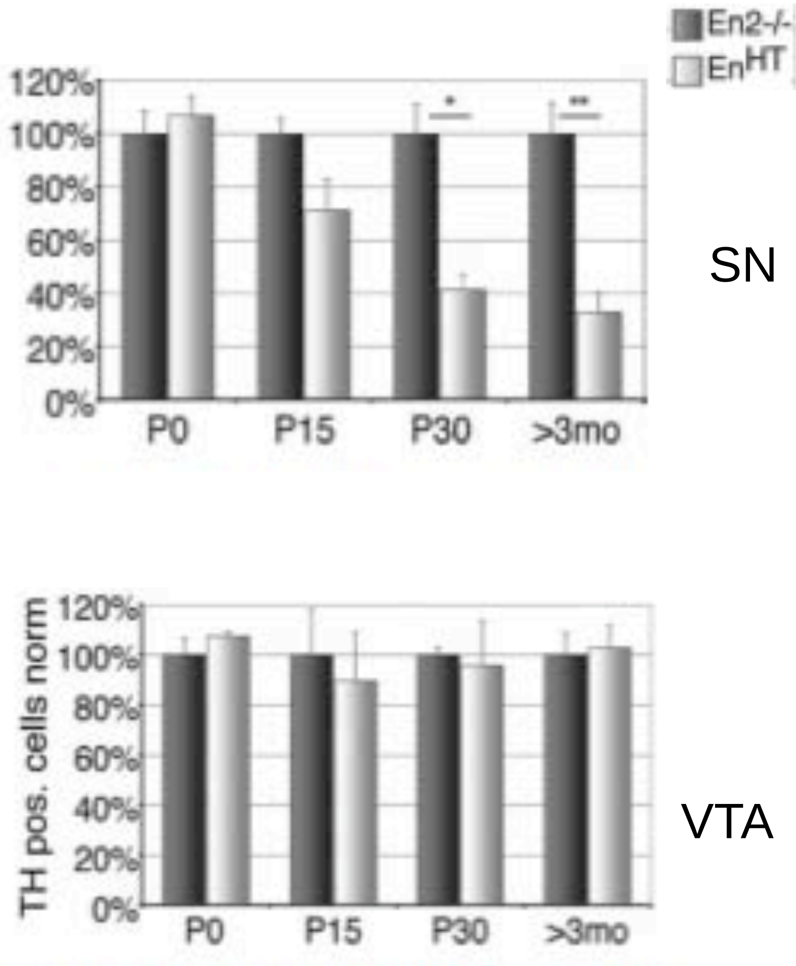


Fig. 1. Loss of midbrain dopaminergic neurons in engrailed double mutant embryo by apoptosis. (A) E12 whole-mount preparation of isolated neural tube. TH-positive neurons are located in the mesencephalic flexure (arrow) of wild-type (A) and mutant (A′) embryo. The TH domain in the mutant is smaller than the wild type and there are no axons heading in rostral direction. (B) Midsagittal sections of E14 embryos. In the wild type (B), mDA neurons have continued to differentiate and start to form the SNC and VTA (arrow). In the mutant embryos (B′), no TH-positive cells are detectable in the ventral midbrain. Additionally, the anlage for the cerebellum (Cb), inferior colliculus (IC) and superior colliculus (SC) are absent. (C-E) Transverse sections of E12 En1^{+}/tlz;*En2*$^{-/-}$ ventral

Slow progressive degeneration of nigral dopaminergic neurons in postnatal Engrailed mutant mice

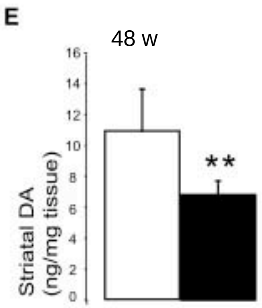
Sgadò P, Albéri L, Gherbassi D, Galasso SL, Ramakers GM, Alavian K, Smidt MP, Dyck RH, Simon H

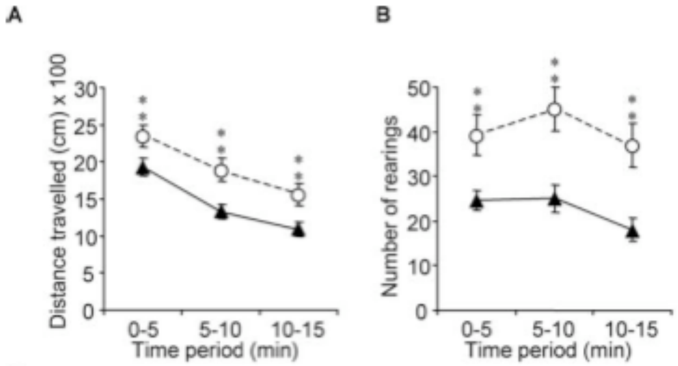
Proc Natl Acad Sci USA
2006 vol. 103 (41) pp. 15242-7

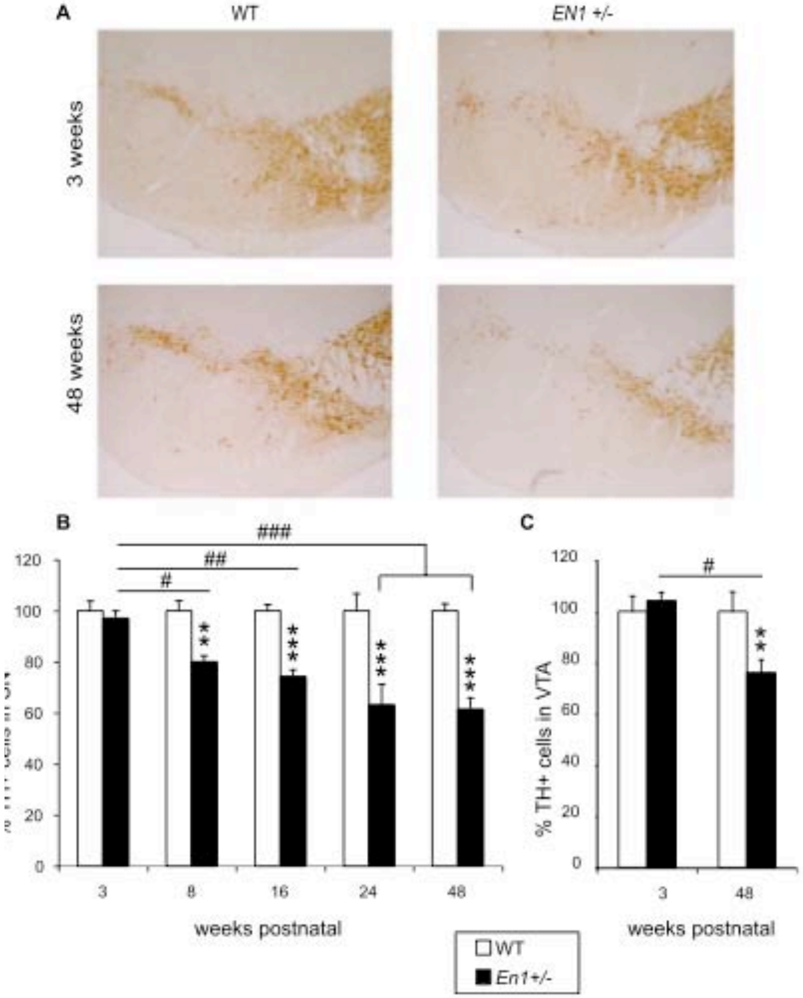


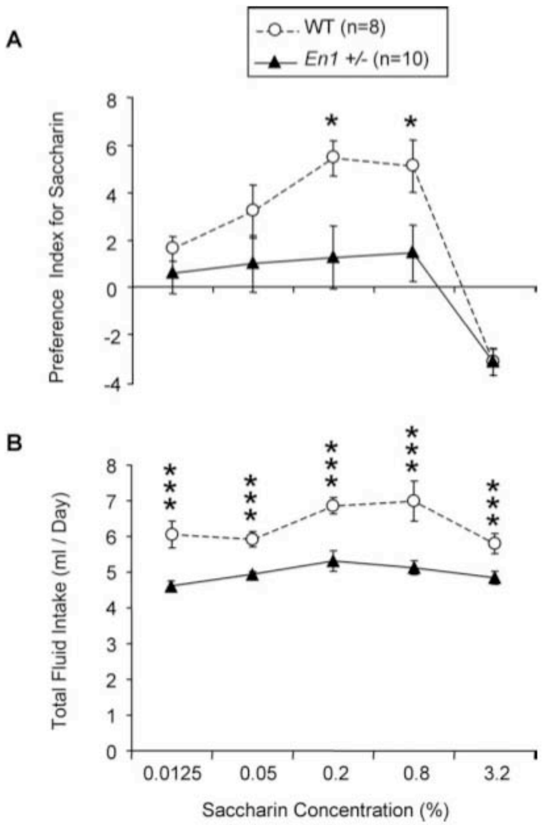
Progressive loss of dopaminergic neurons in the ventral midbrain of adult mice heterozygote for Engrailed1

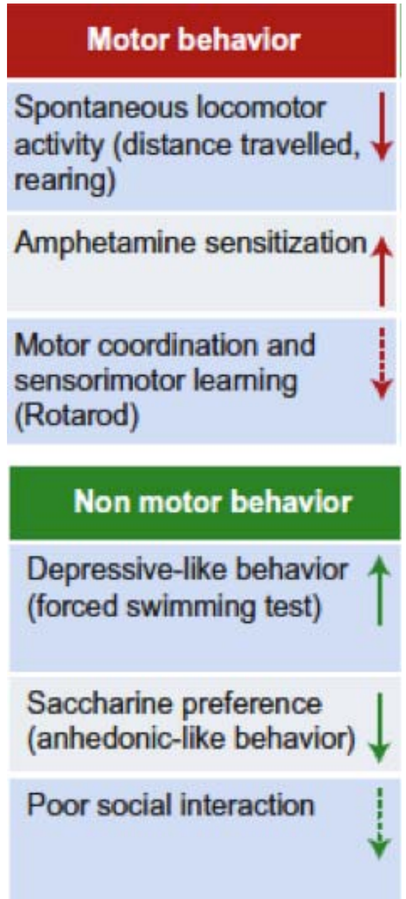
Sonnier L, Le Pen G, Hartmann A, Bizot JC, Trovero F, Krebs MO, Prochiantz A











J Neurosci
2007 vol. 27 (5) pp. 1063-71

The transcription factor orthodenticle homeobox 2 influences axonal projections and vulnerability of midbrain dopaminergic neurons

Chung CY, Licznerski P, Alavian K, Simeone A, Lin Z, Martin E, Vance J, Isacson O

Brain
2010 vol. 133 (Pt 7) pp. 202...

Otx2 controls neuron subtype identity in ventral tegmental area and antagonizes vulnerability to MPTP

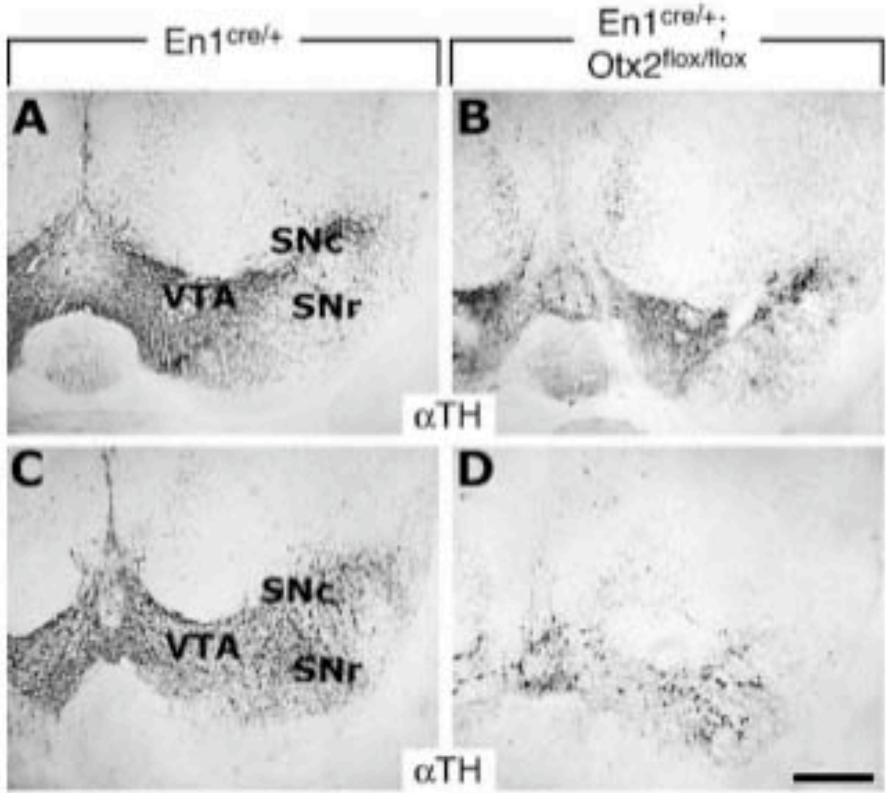
Di Salvio M, Di Giovannantonio LG, Acampora D, Prosperi R, Omodei D, Prakash N, Wurst W, Simeone A

Nature Neuroscience
2010 vol. 13 (12) pp. 1481-8

Altered dopaminergic innervation and amphetamine response in adult Otx2 conditional mutant mice

Borgkvist A, Puelles E, Carta M, Acampora D, Ang SL, Wurst W, Goiny M, Fisone G, Simeone A, Usiello A

Mol Cell Neurosci
2006 vol. 31 (2) pp. 293-302



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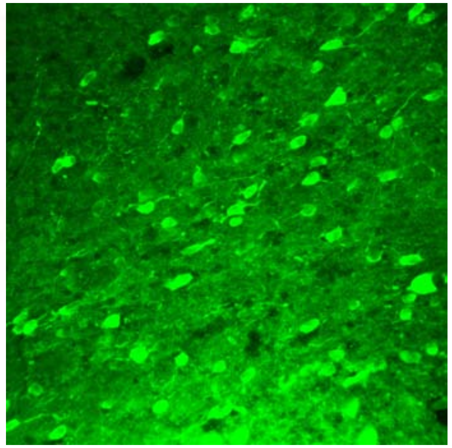
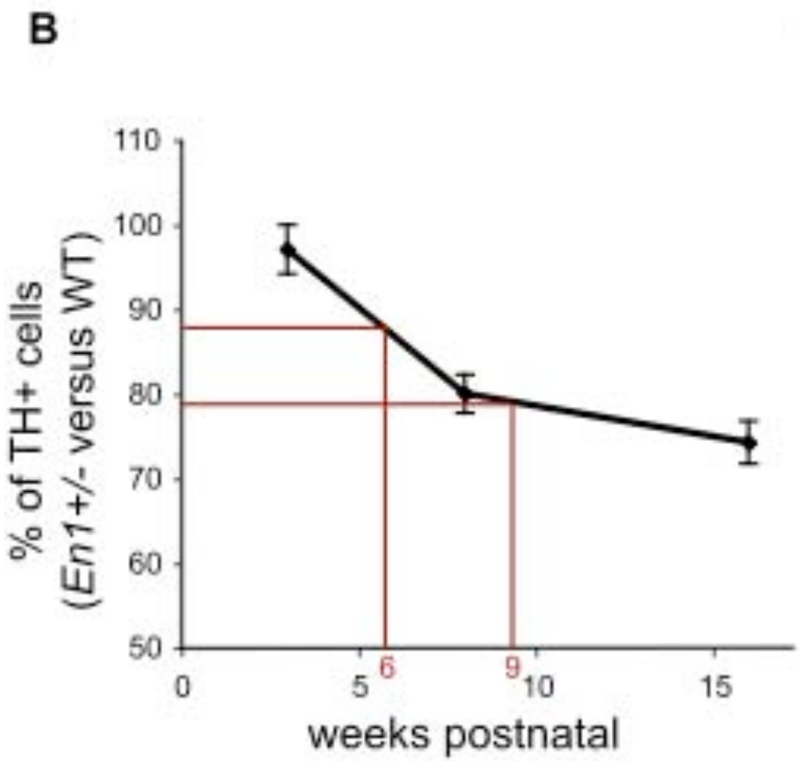
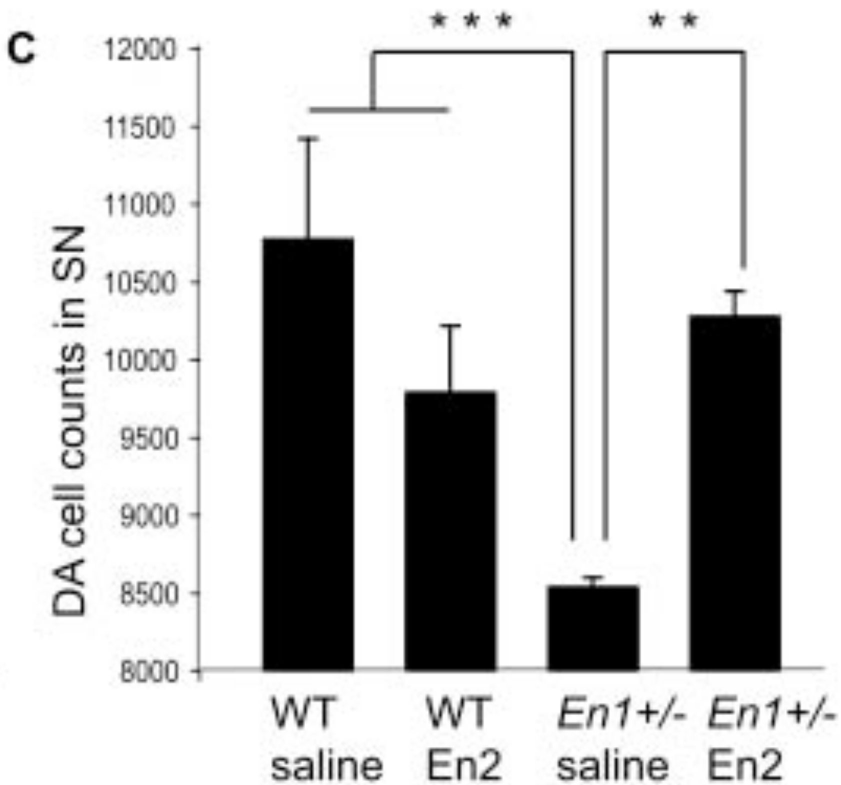
J Neurosci
2007 vol. 27 (5) pp. 1063-71

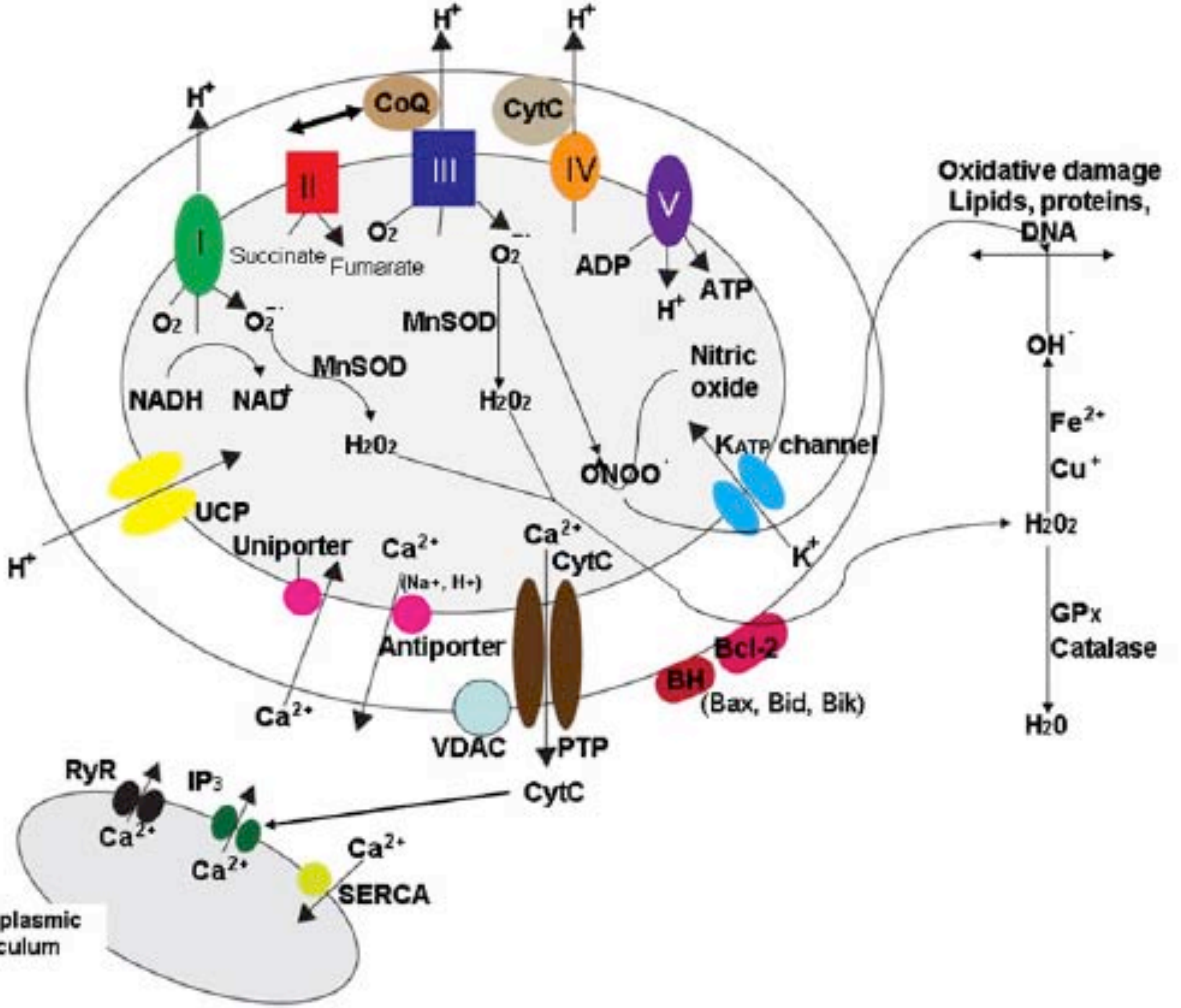






Mitochondria in Neuroplasticity and Neurological Disorders

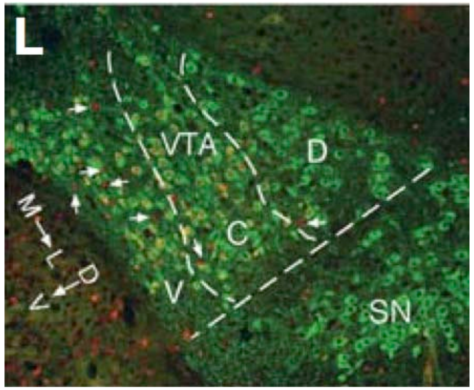
Mark P. Mattson,[1,*] Marc Gleichmann,[1] and Aiwu Cheng[1]



Otx2 controls neuron subtype identity in ventral tegmental area and antagonizes vulnerability to MPTP

Di Salvio M, Di Giovannantonio LG, Acampora D, Prosperi R, Omodei D, Prakash N, Wurst W, Simeone A

Nature Neuroscience
2010 vol. 13 (12) pp. 1481-8



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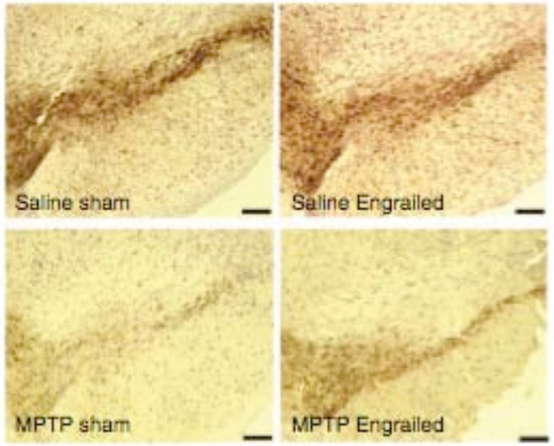
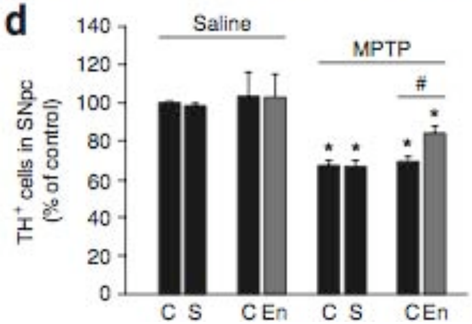
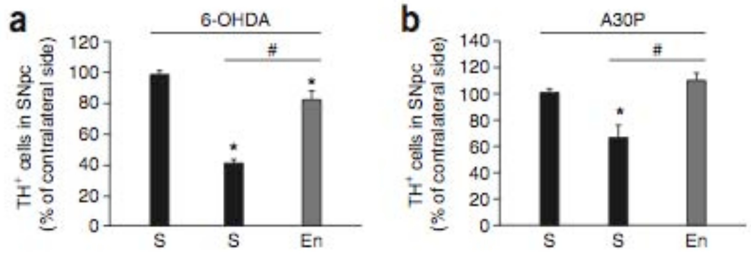
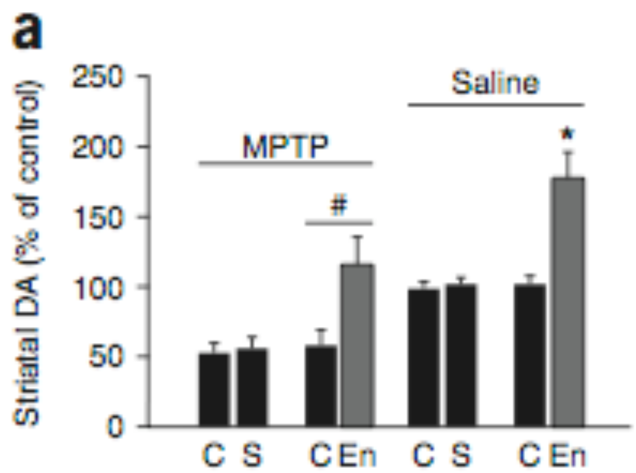


d







Engrailed protects mouse midbrain dopaminergic neurons against mitochondrial complex I insults

Alvarez-Fischer D, Fuchs J, Castagner F, Stettler O, Massiani-Beaudoin O, Moya KL, Bouillot C, Oertel WH, Lombès A, Faigle W, Joshi RL, Hartmann A, Prochiantz A

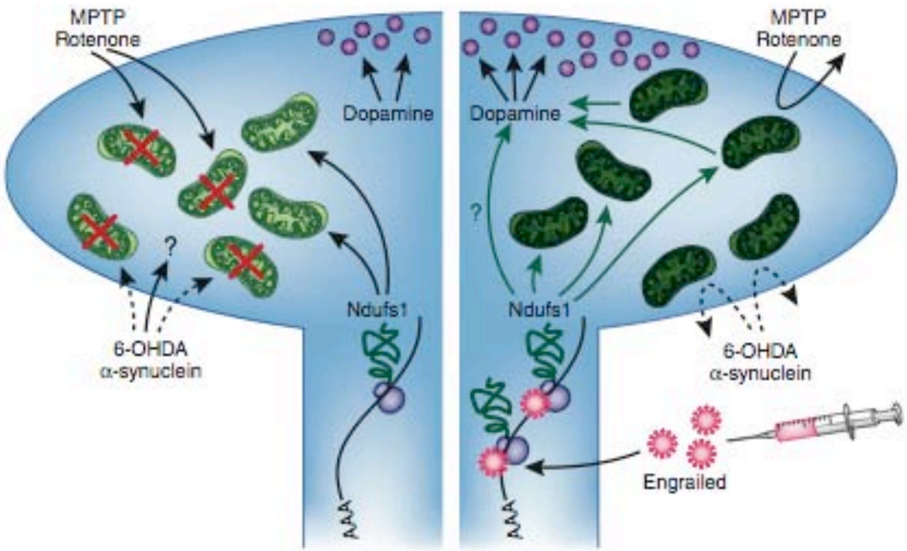
Nature Neuroscience
2011 vol. 14 (10) pp. 1260-...

Regulation of complex I by Engrailed is complex too

Nature Neuroscience
2011 vol. 14 (10) pp. 1221-2

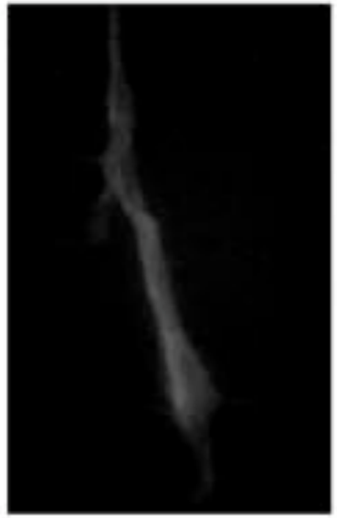
Sanders LH, Greenamyre JT

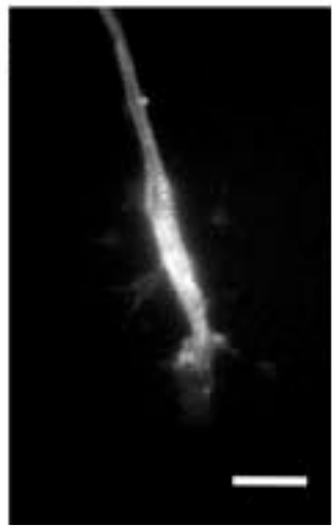
NEWS AND VIEWS



Katie Vicari

Figure 1 A dopaminergic nerve terminal, before and after Engrailed treatment. Left, normally, MPTP and rotenone produce selective dopaminergic degeneration by binding to mitochondrial complex I and generating reactive oxygen species and inhibiting respiration. 6-Hydroxydopamine (6-OHDA) and α-synuclein may also exert their toxicities, in part, by targeting mitochondria. Right, after treatment with Engrailed, the homeobox protein enters dopaminergic neurons and binds the mRNA translational machinery, where it enhances the synthesis of the Ndufs1 subunit of complex I. Under these conditions, nigrostriatal neurons become resistant to the classical complex I inhibitors (MPTP and rotenone), as well as to 6-OHDA and α-synuclein. In addition, upregulation of Ndufs1 is also responsible, by an unknown mechanism, for elevating dopamine. Solid arrows indicate known toxic effects of rotenone and MPTP on complex I; dashed arrows indicate potential direct or indirect effects of 6-OHDA and α-synuclein on complex I.





Model-based gene selection shows engrailed 1 is associated with antipsychotic response

Webb BT, Sullivan PF, Skelly T, van den Oord EJ

Haplotype analysis of the engrailed-2 gene in young-onset Parkinson's disease

Rissling I, Strauch K, Höft C, Oertel WH, Möller JC

Association of transcription factor polymorphisms PITX3 and EN1 with Parkinson's disease

Haubenberger D, Reinthaler E, Mueller J, Pirker W, Katzenschlager R, Froehlich R, Bruecke T, Daniel G, Auff E, Zimprich A

Autism-associated haplotype affects the regulation of the homeobox gene, ENGRAILED 2

Benayed R, Choi J, Matteson PG, Gharani N, Kamdar S, Brzustowicz LM, Millonig JH

Intronic single nucleotide polymorphisms of engrailed homeobox 2 modulate the disease vulnerability of autism in a han chinese population

Haplotype analysis of the engrailed-2 gene in young-onset Parkinson's disease

Rissling I, Strauch K, Höft C, Oertel WH, Möller JC

Department of Neurology, Philipps University, Marburg, Germany.