

# Molecular Basis of Odor Perception in the Mouse

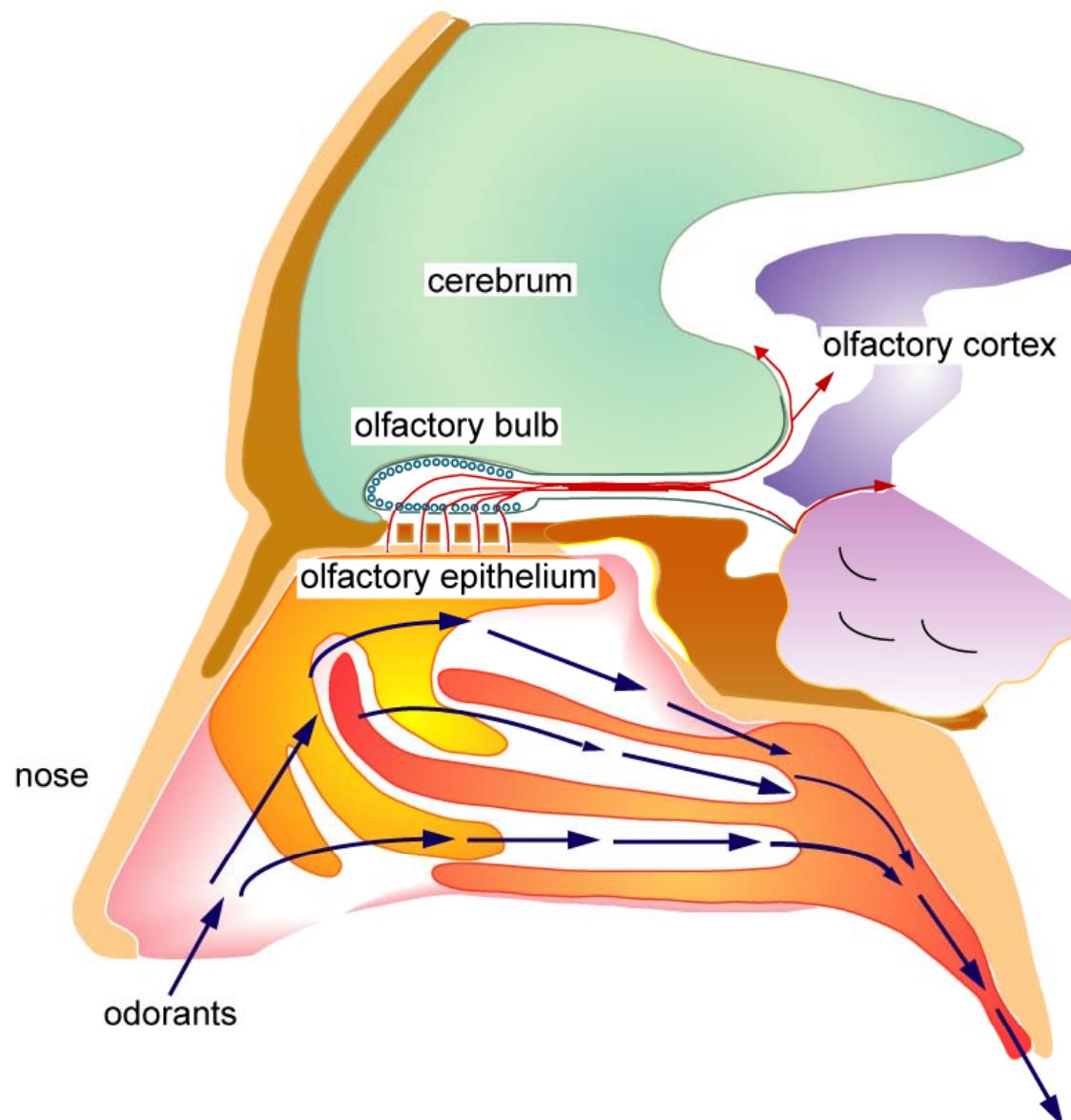


Hitoshi Sakano  
The University of Tokyo

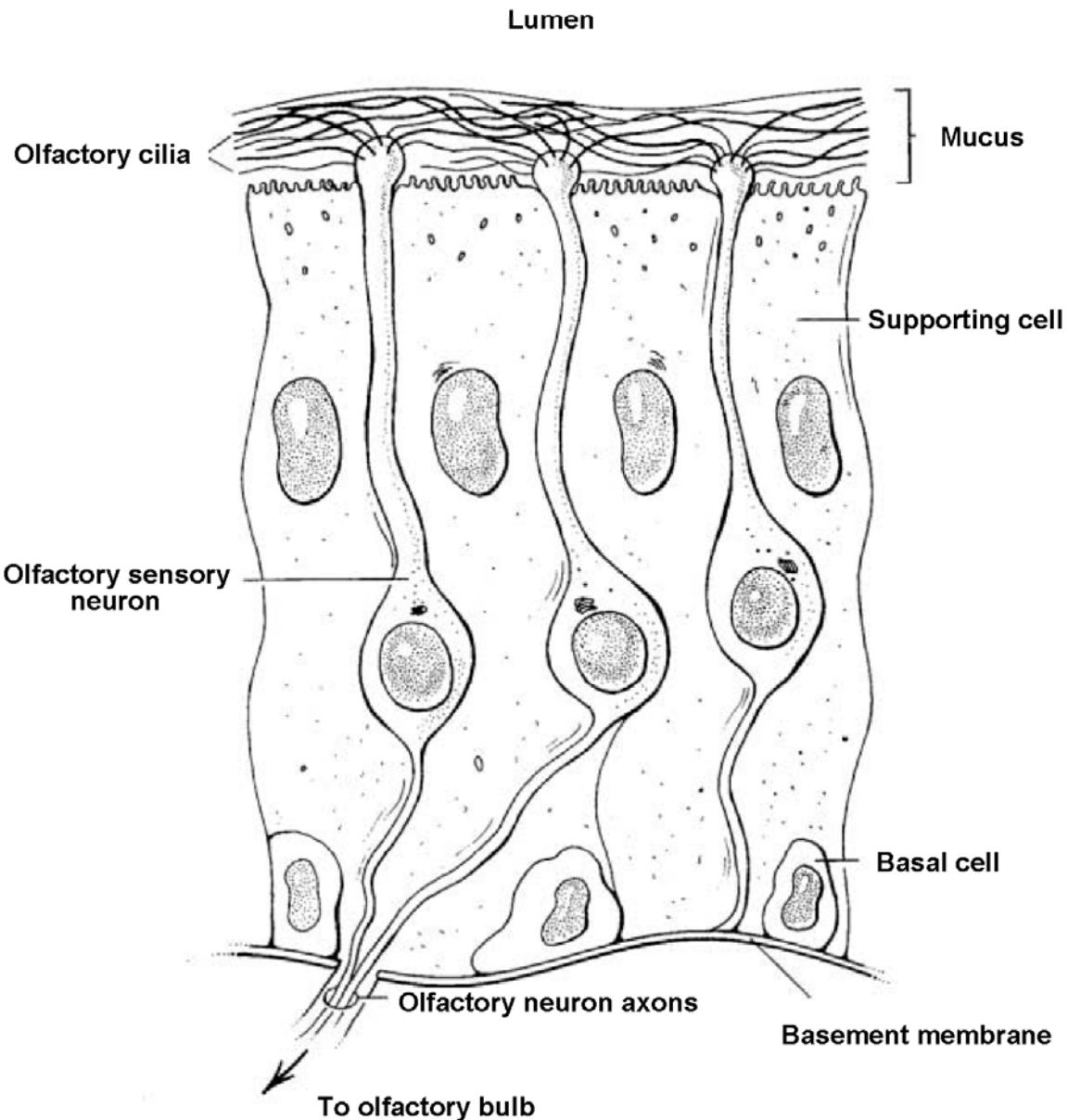
「#:このマークが付してある著作物は、第三者が有する著作物ですので、同著作物の再使用、同著作物の二次的著作物の創作等については、著作権者より直接使用許諾を得る必要があります。」

2009. 7. 16 俯瞰講義 © 駒場

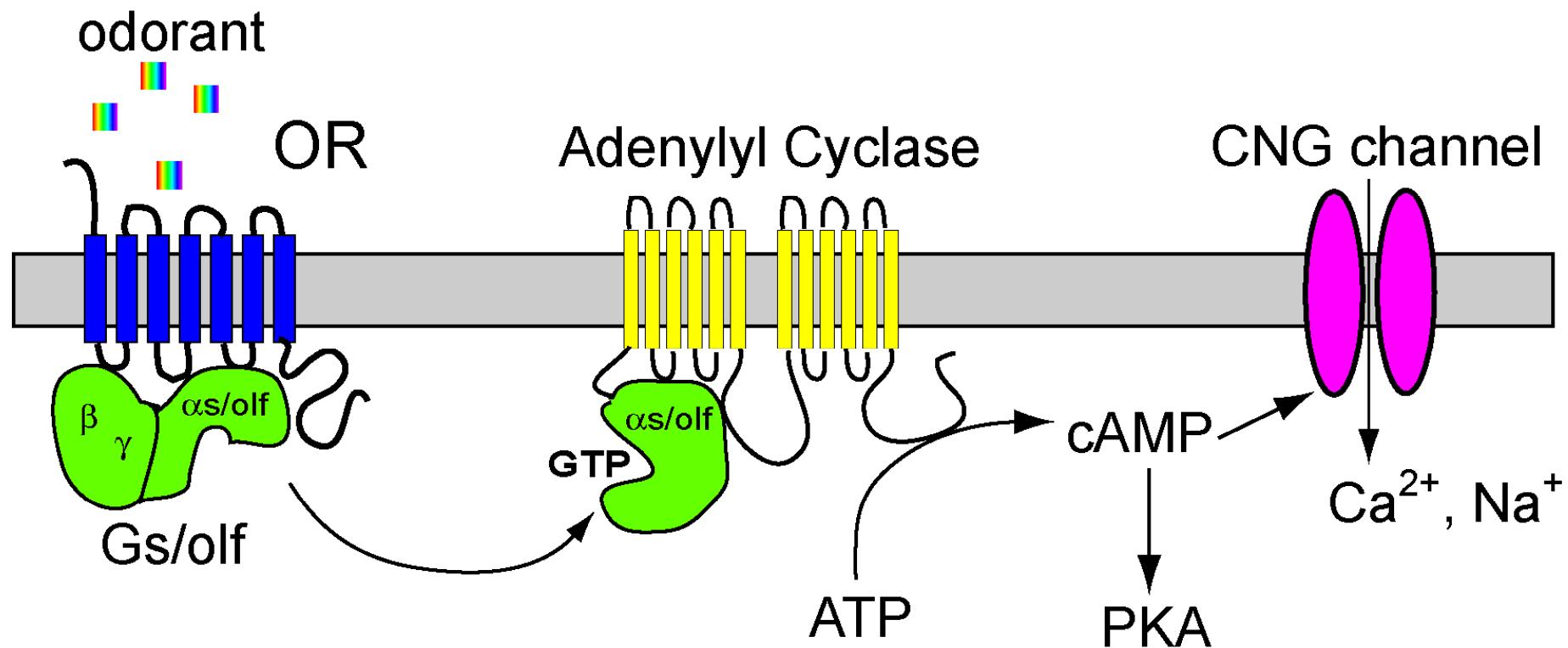
# Human Olfactory System



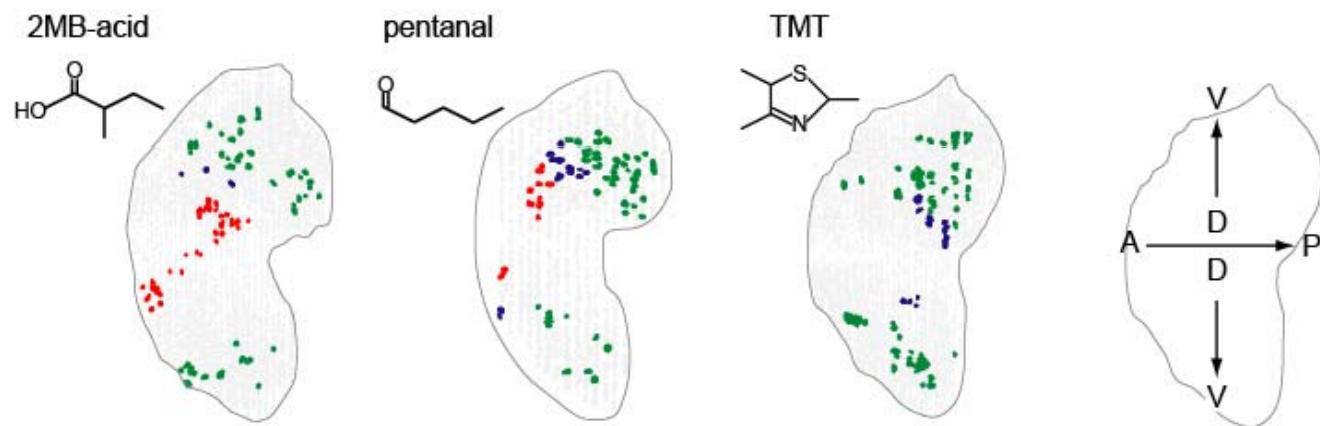
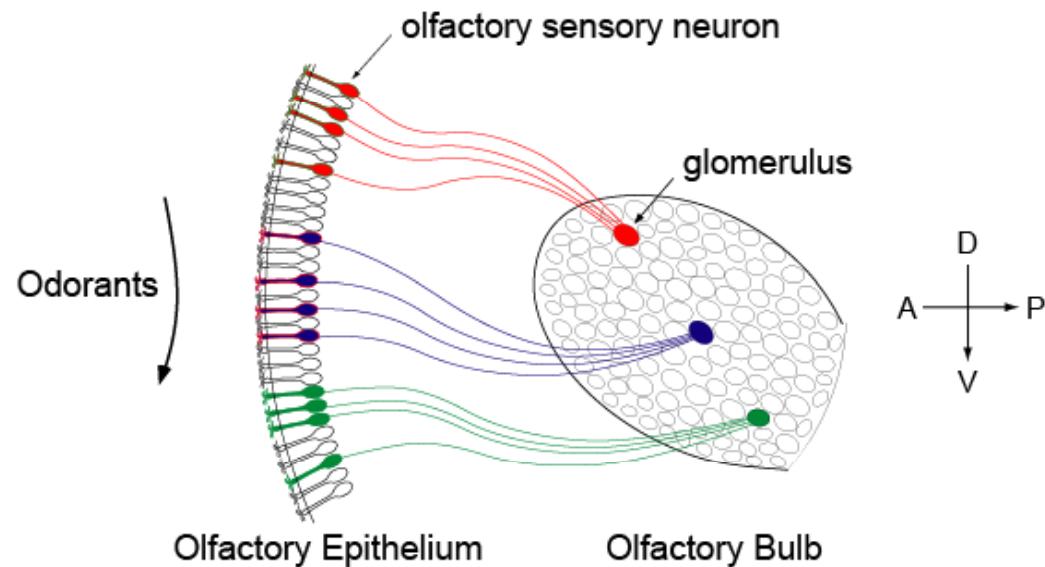
# Olfactory Neuroepithelium



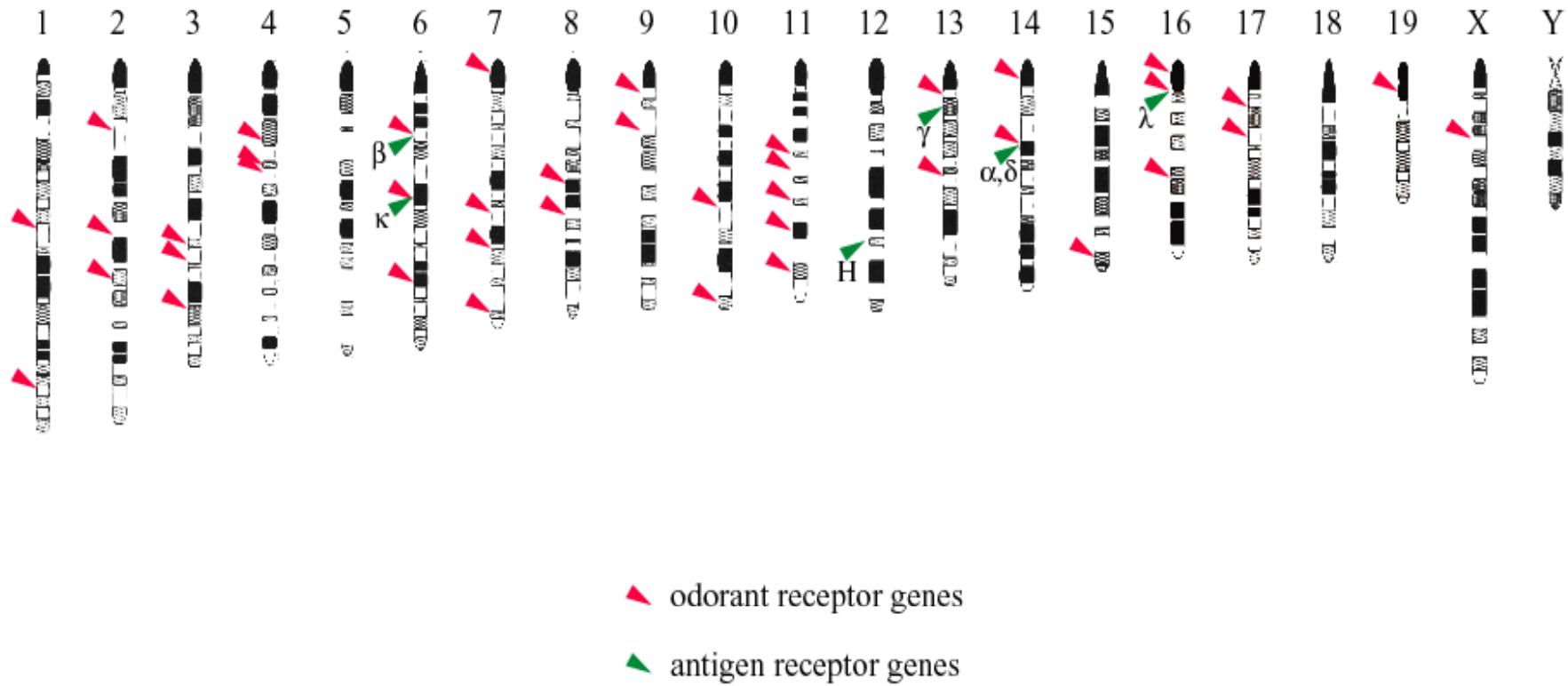
# Olfactory Signal Transduction



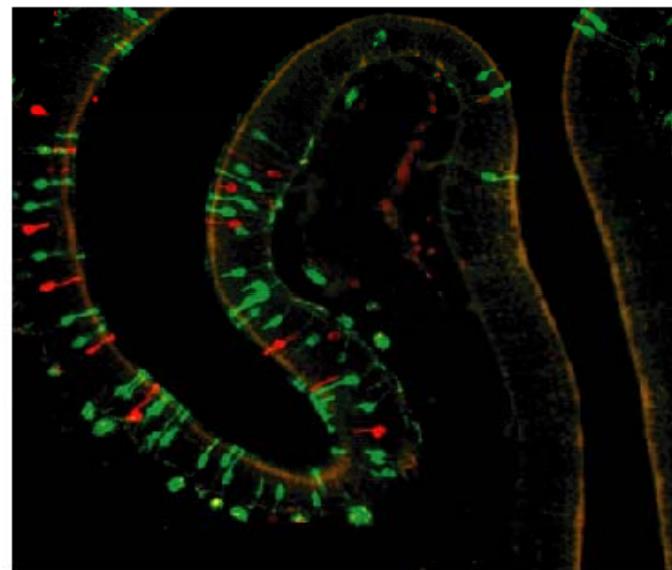
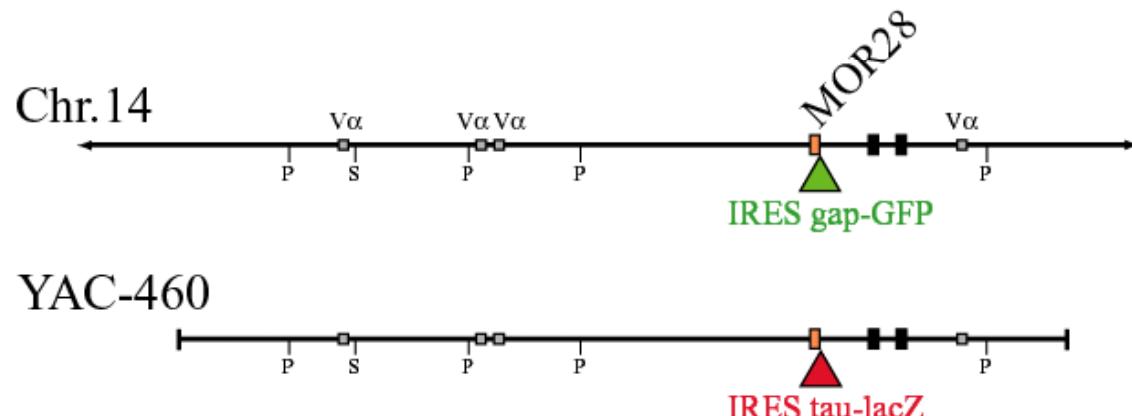
# Conversion of olfactory signals



# Distribution of the Mouse OR Gene Clusters



# Exclusion Between the Transgenic and Endogenous *MOR28* Genes



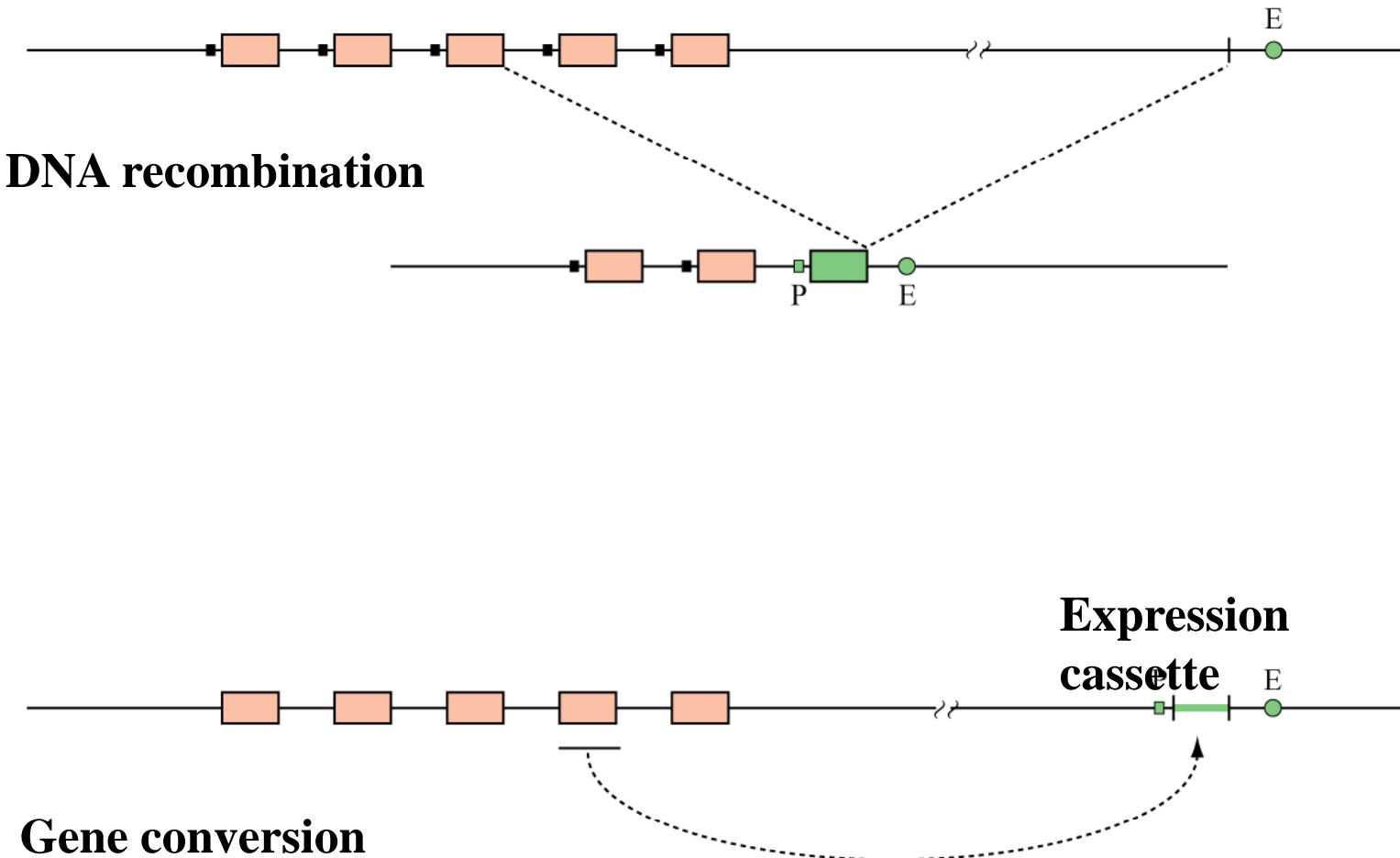
Olfactory epithelium

Serizawa *et al.*, *Nature Neurosci.* 7, 687 (2000)

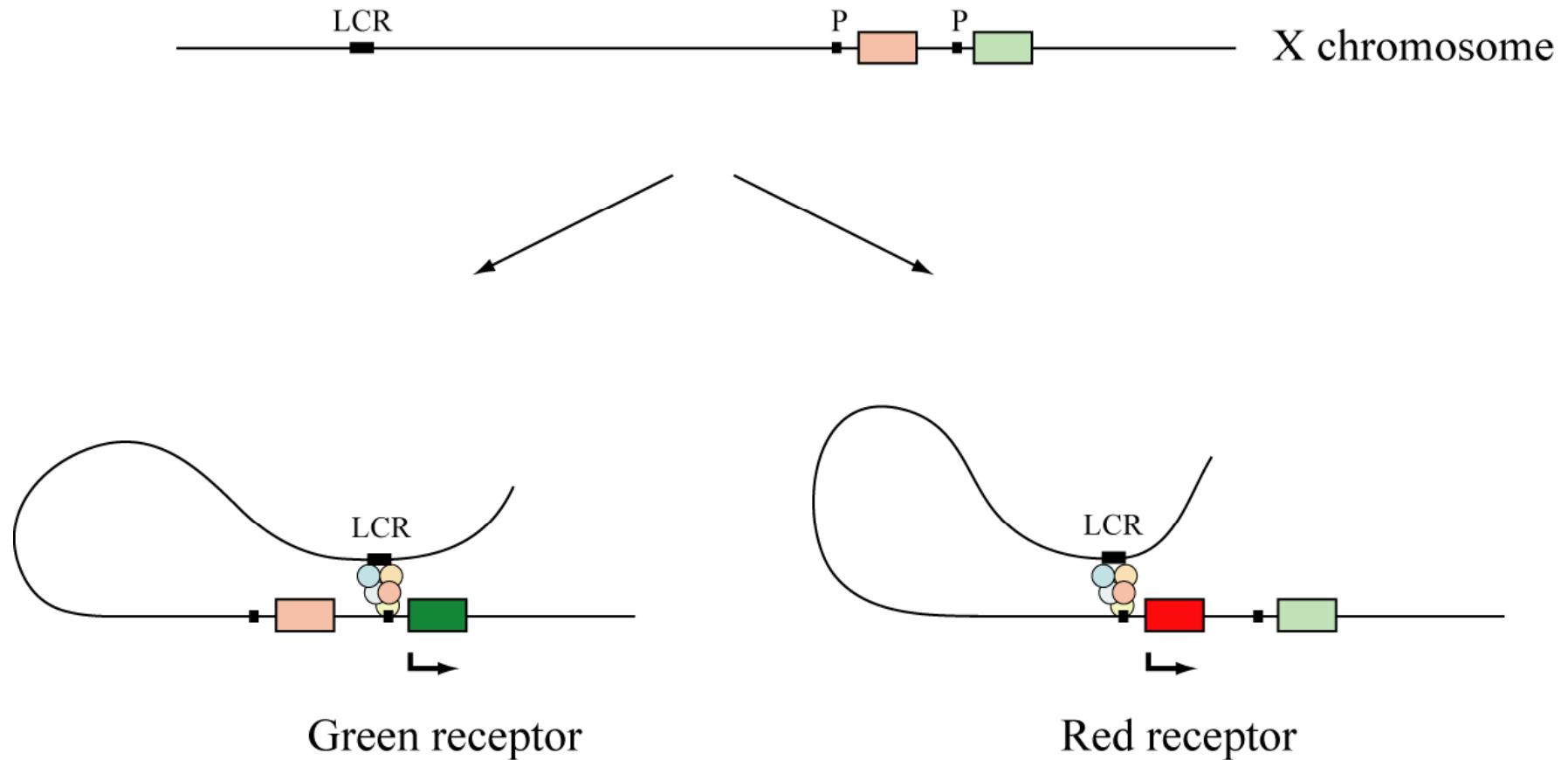
7

‡[http://www.nature.com/neuro/journal/v3/n7/full/nn0700\\_687.html](http://www.nature.com/neuro/journal/v3/n7/full/nn0700_687.html)

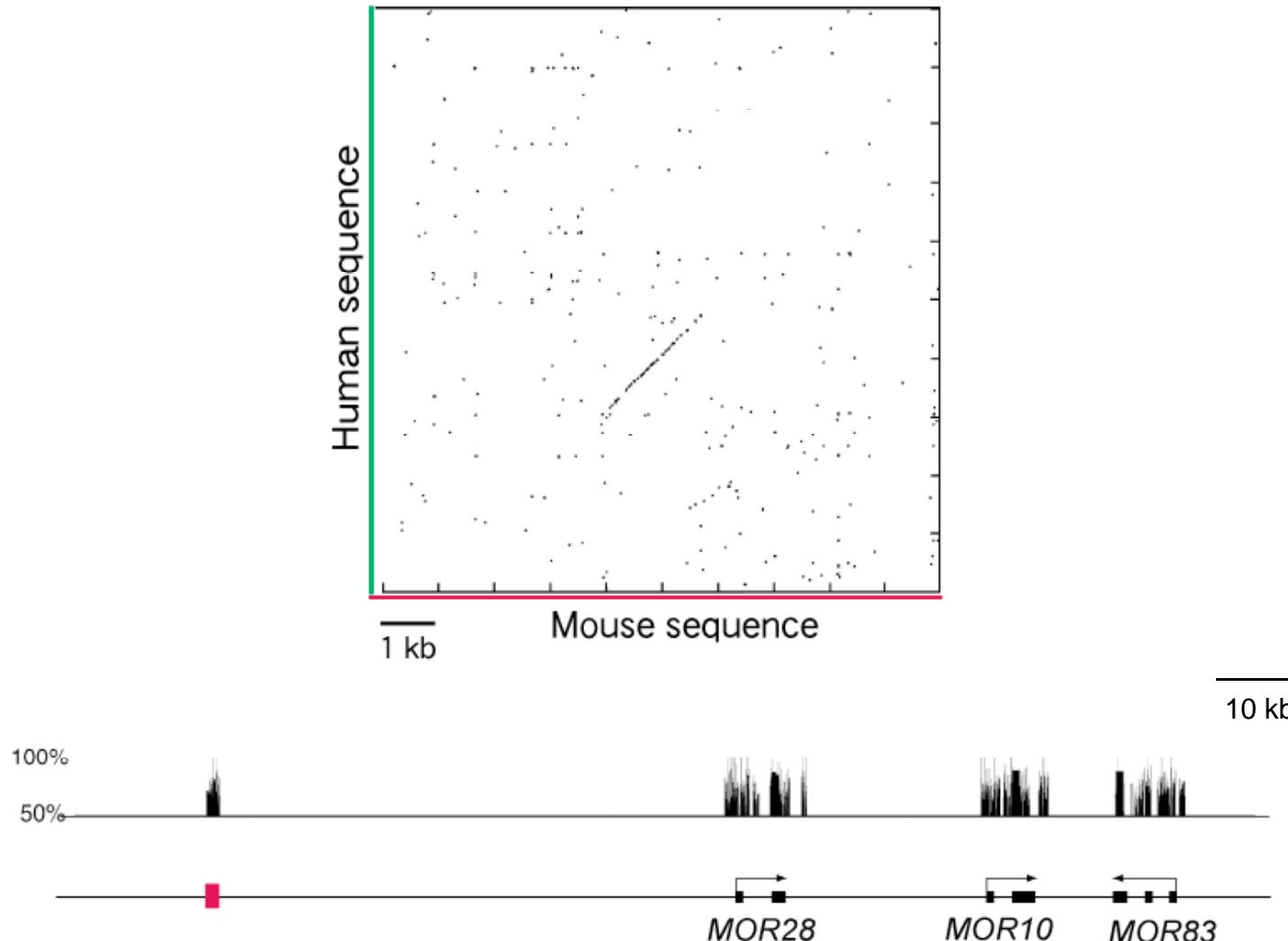
# Single Gene Choice by Somatic DNA Rearrangement



# Mutually Exclusive Activation of Visual Pigment Genes

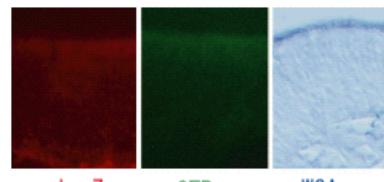
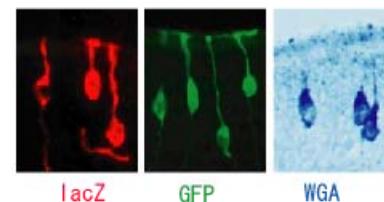
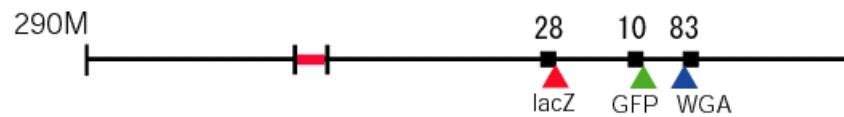
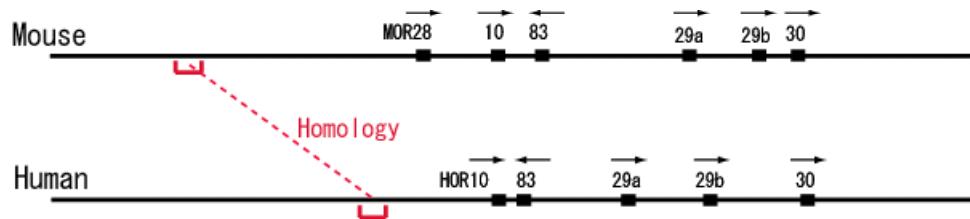


# Identification of the Homology (H) Region



# From Serizawa *et al.*, SCIENCE 302:2088(2003) :  
<http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=302&firstpage=2088&resourcetype=HWCIT>  
Reprinted with permission from AAAS.

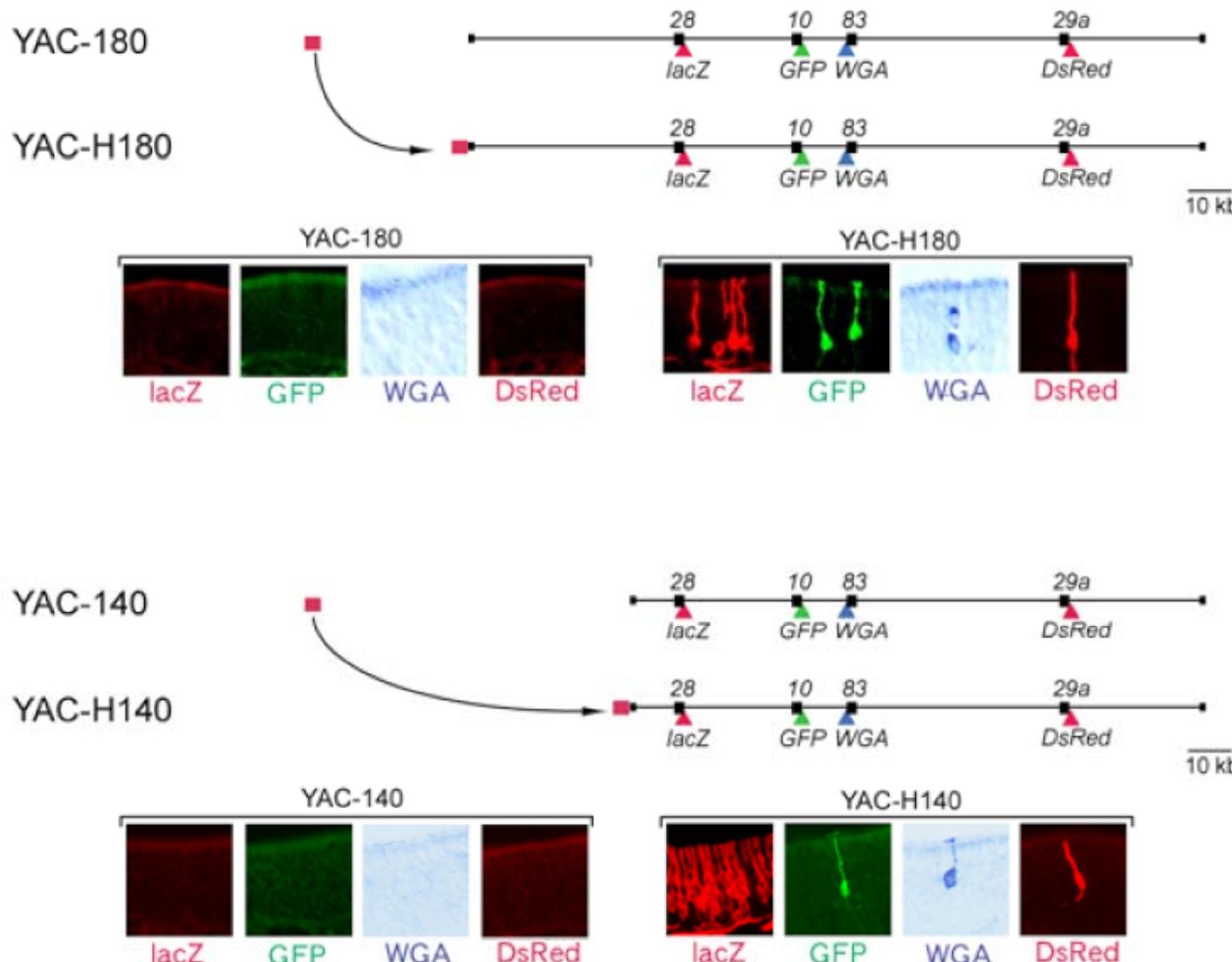
# H-Region is Necessary for *MOR28* Expression



‡ From Serizawa *et al.*, SCIENCE 302:2088(2003) :  
<http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=302&firstpage=2088&resourcetype=HCIT>

Reprinted with permission from AAAS.

# H-Region Reactivates Truncated Constructs



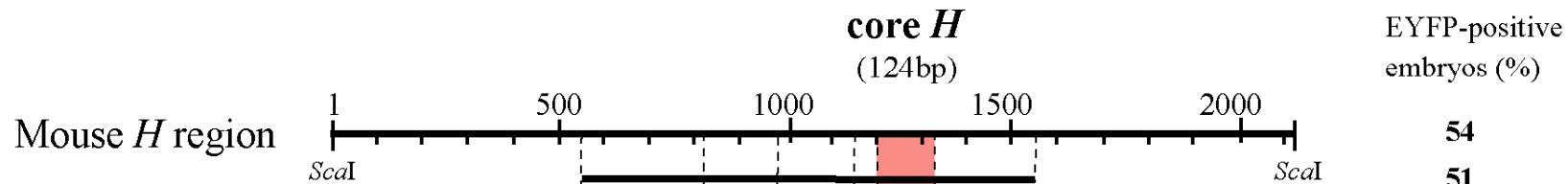
From Serizawa *et al.*, SCIENCE 302:2088(2003) :

‡ [http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&search\\_id=1&FIRSTINDEX=0&volume=302&firstpage=2088&resourcetype=HWCIT](http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&search_id=1&FIRSTINDEX=0&volume=302&firstpage=2088&resourcetype=HWCIT) 12

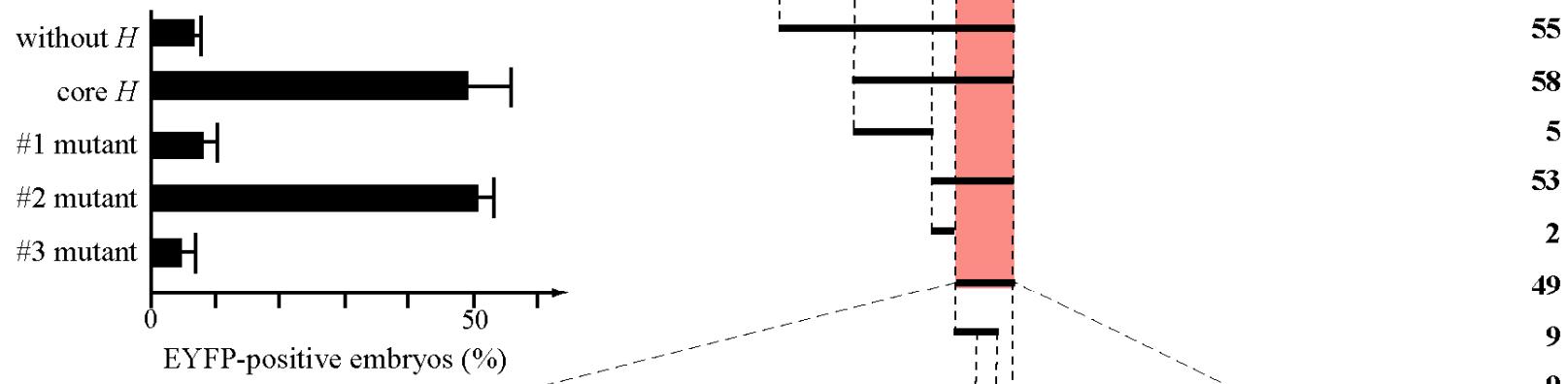
Reprinted with permission from AAAS.

# Dissection of the essential sequences of the mouse *H* region

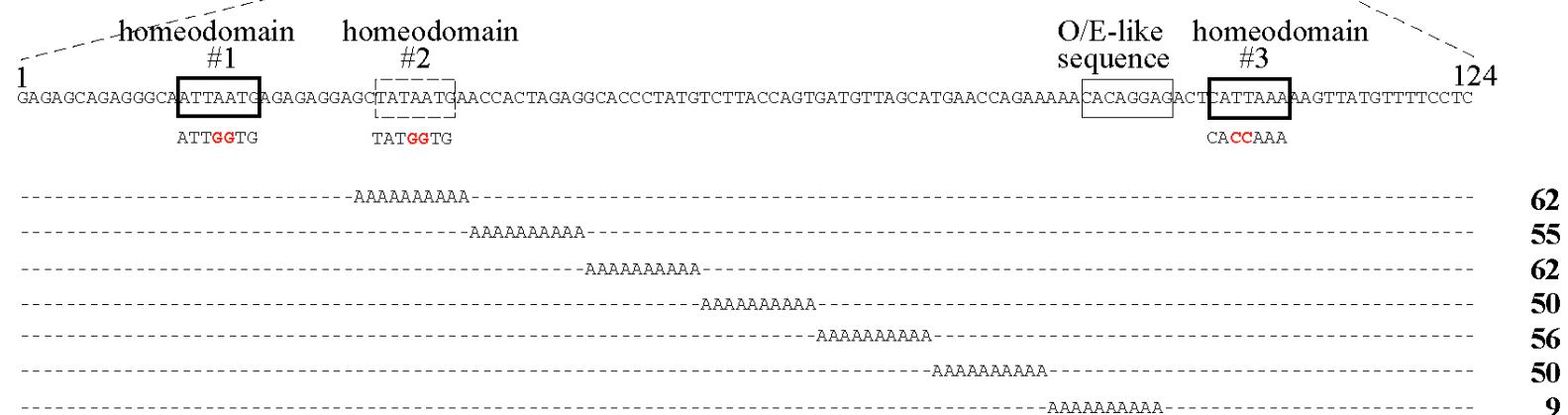
A



B



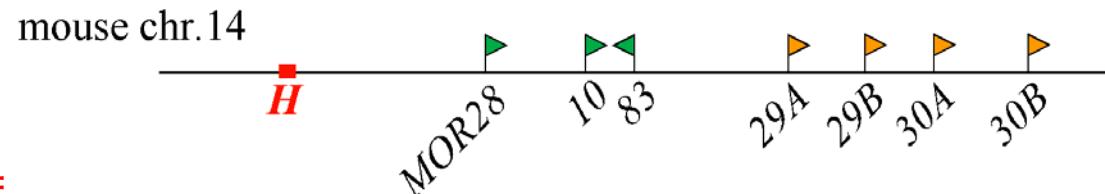
C



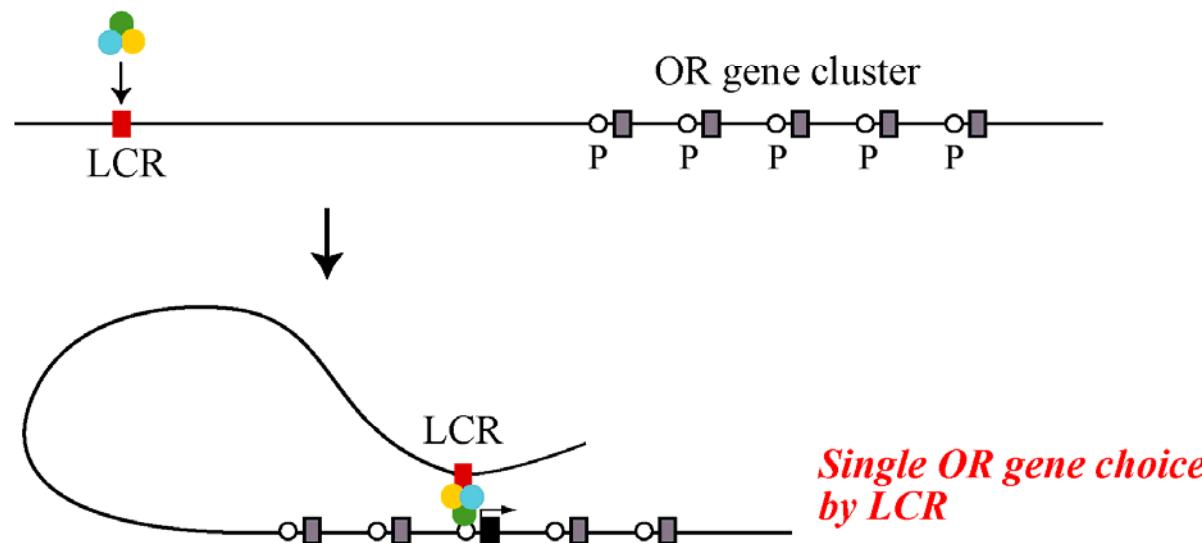
† PNAS vol.104, no.50, Decembe 11 2007 "Deletion of the core-H region in mice abolishes the expression of three proximal odorant receptor genes in cis" Hirofumi Nishizumi et al., P.20069, Fig.2, Copyright (2007) National Academy of Sciences, U.S.A. 13

# Single OR gene choice by LCR

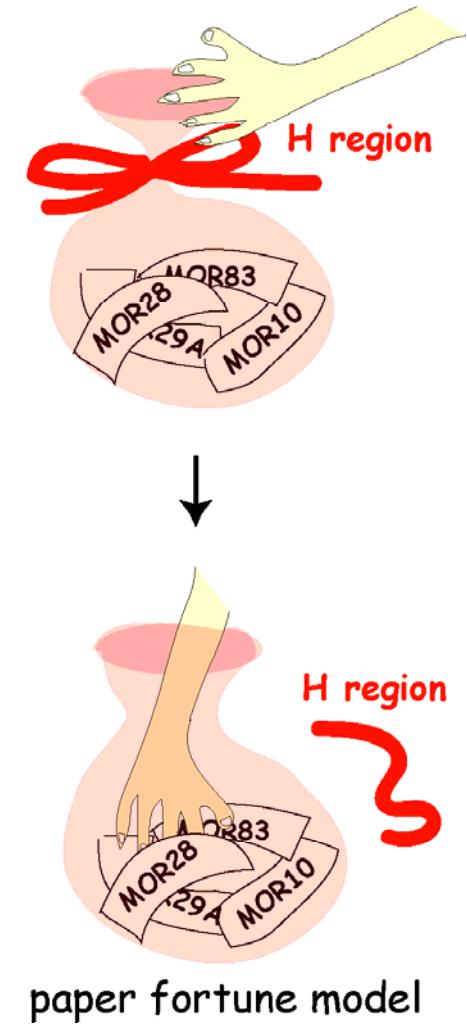
A



B



C



# From Serizawa *et al.*, SCIENCE 302:2088(2003) :

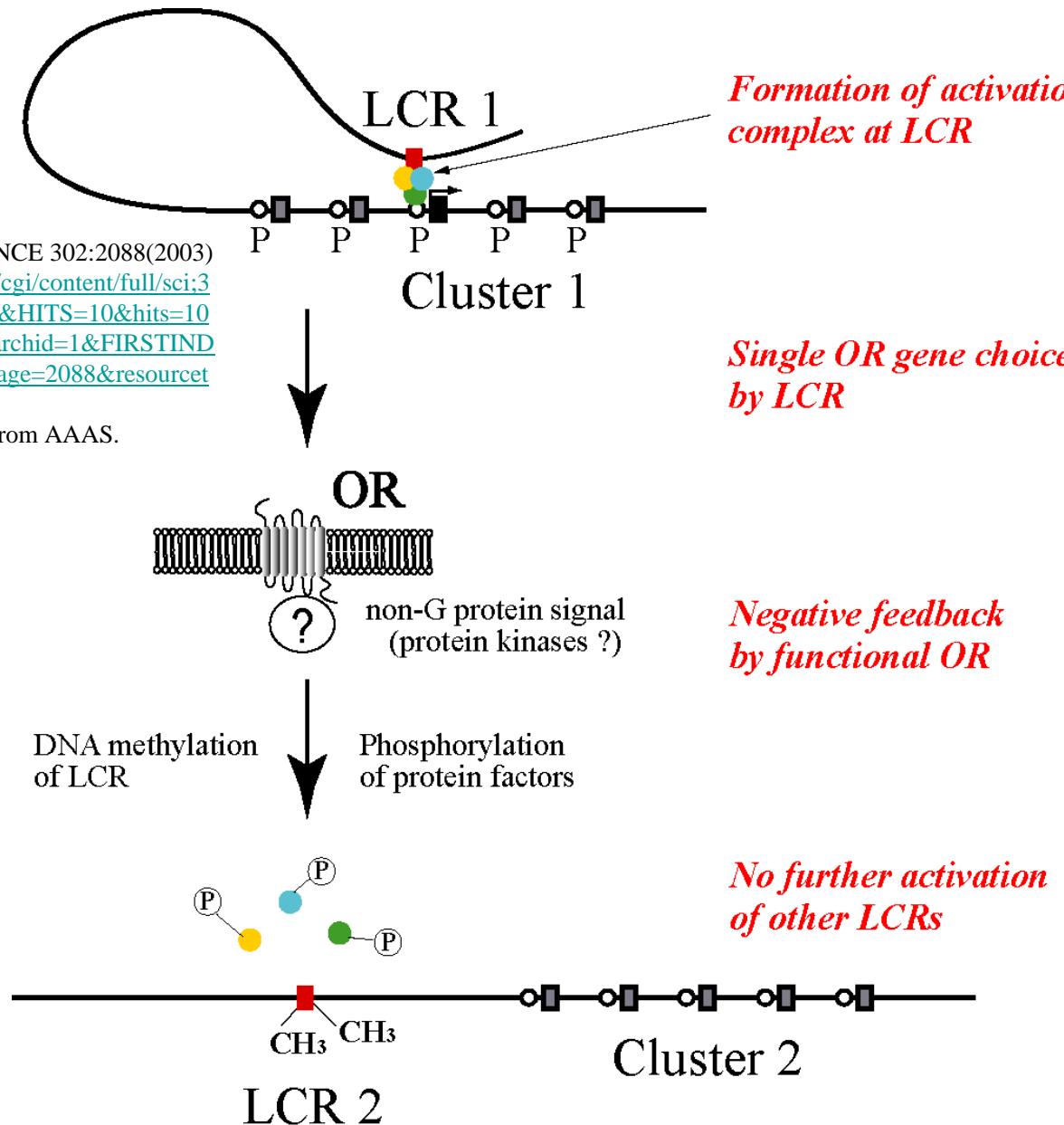
[http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RE\\_SULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=302&firstpage=2088&resourcetype=HW\\_CIT](http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RE_SULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=302&firstpage=2088&resourcetype=HW_CIT)

Reprinted with permission from AAAS.

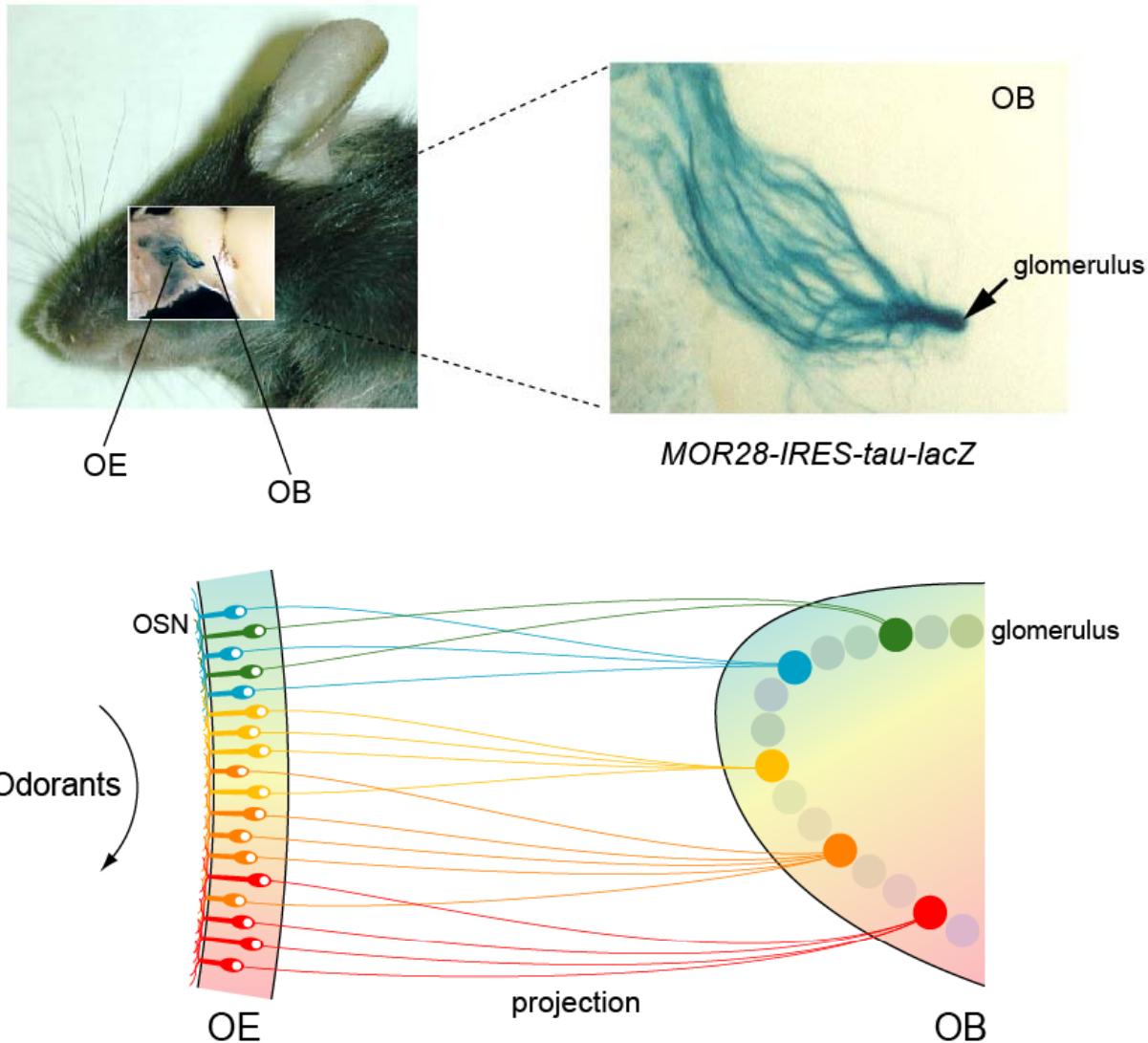
# Maintenance of One Neuron – One Receptor Rule

From Serizawa *et al.*, SCIENCE 302:2088(2003)  
<http://www.sciencemag.org/cgi/content/full/sci;302/5653/2088?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=302&firstpage=2088&resource-type=HW CIT>

Reprinted with permission from AAAS.

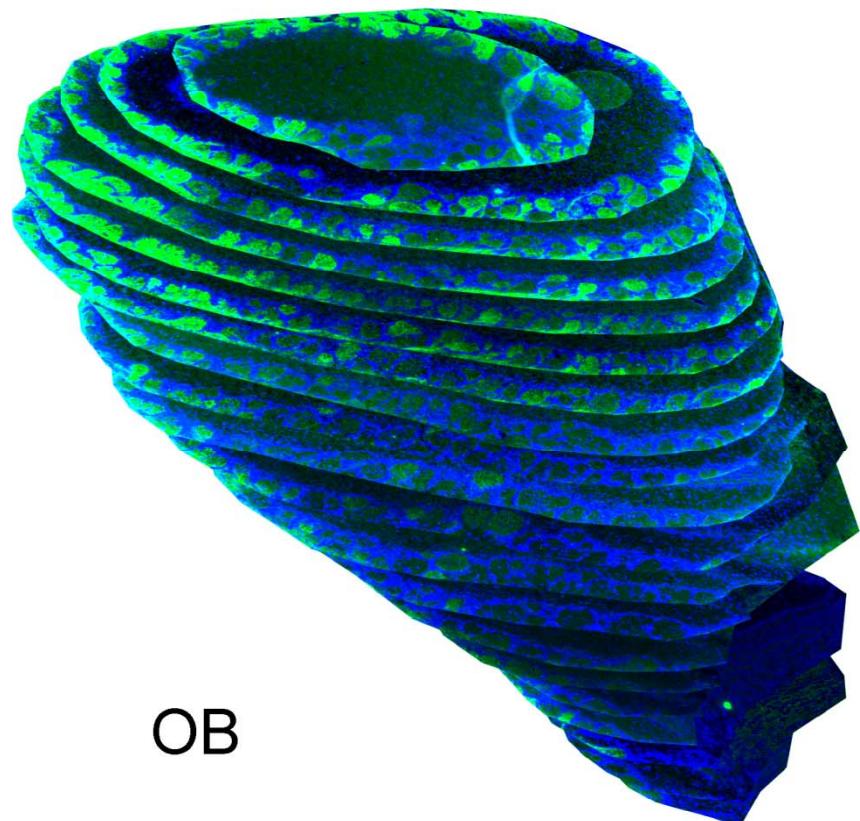


# OR instructed axonal projection



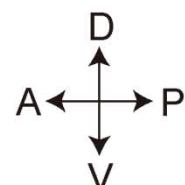
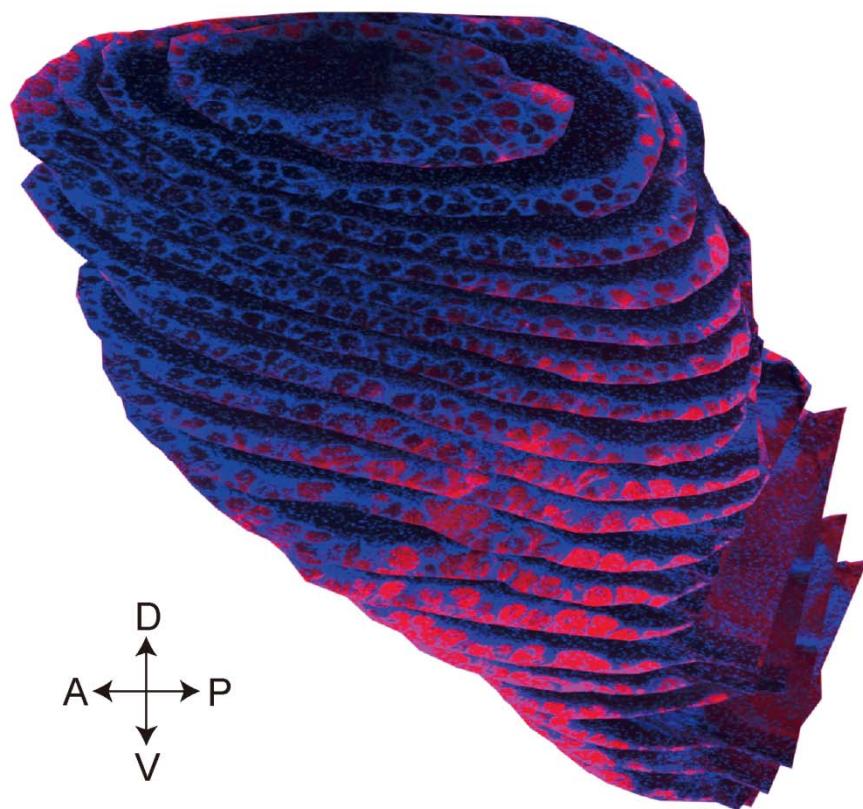
Graded and complementary detection of Robo-2 and Nrp-2 in the glomerular map along the D/V axis of the OB

Robo-2

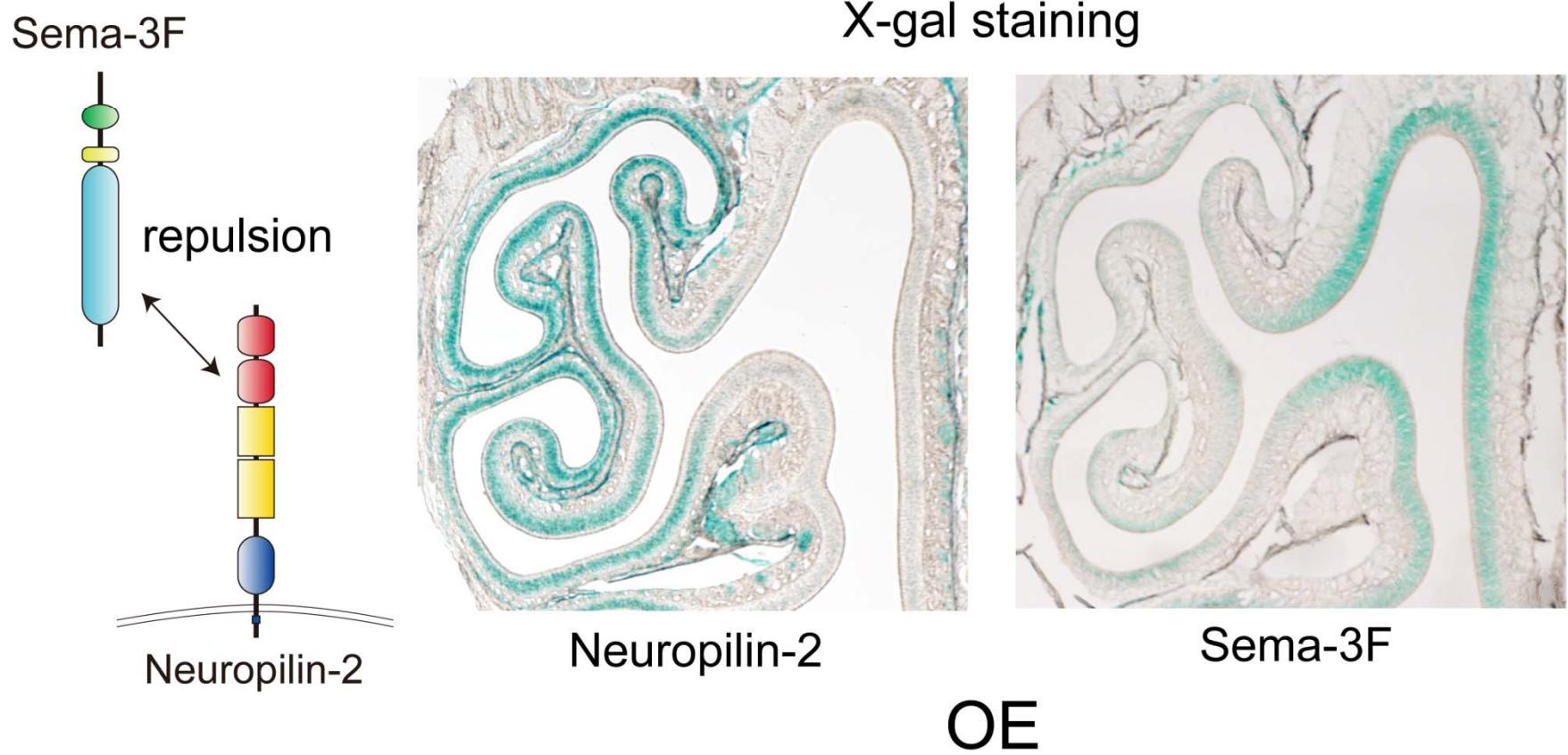


OB

Nrp-2



# Complementary expression of Neuropilin-2 and Sema-3F

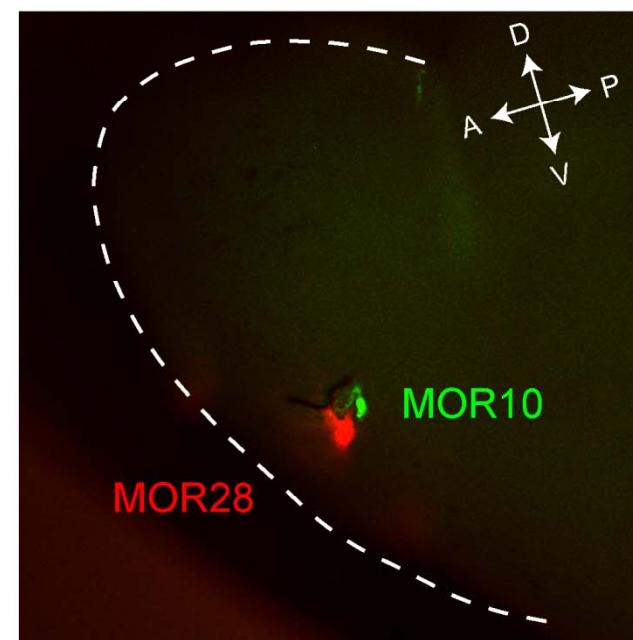
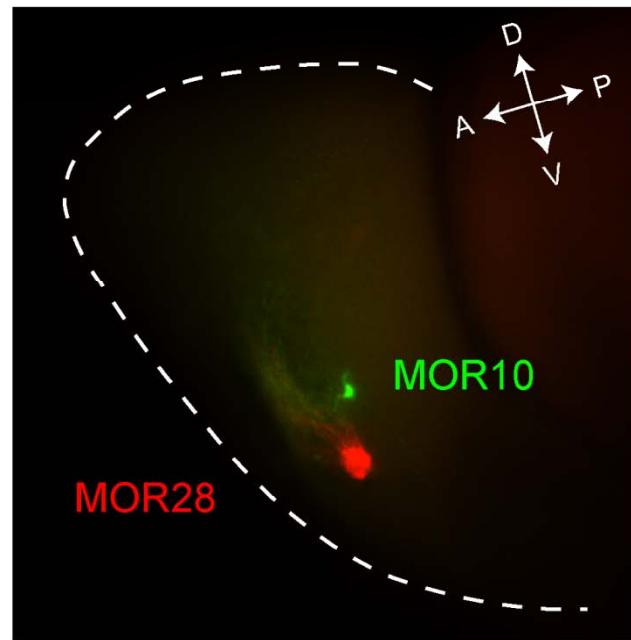
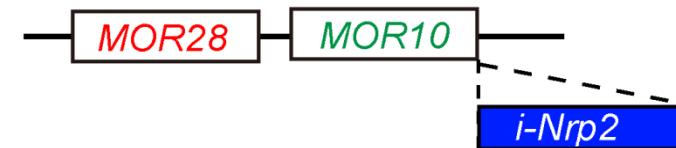


# Gain of function for Nrp2

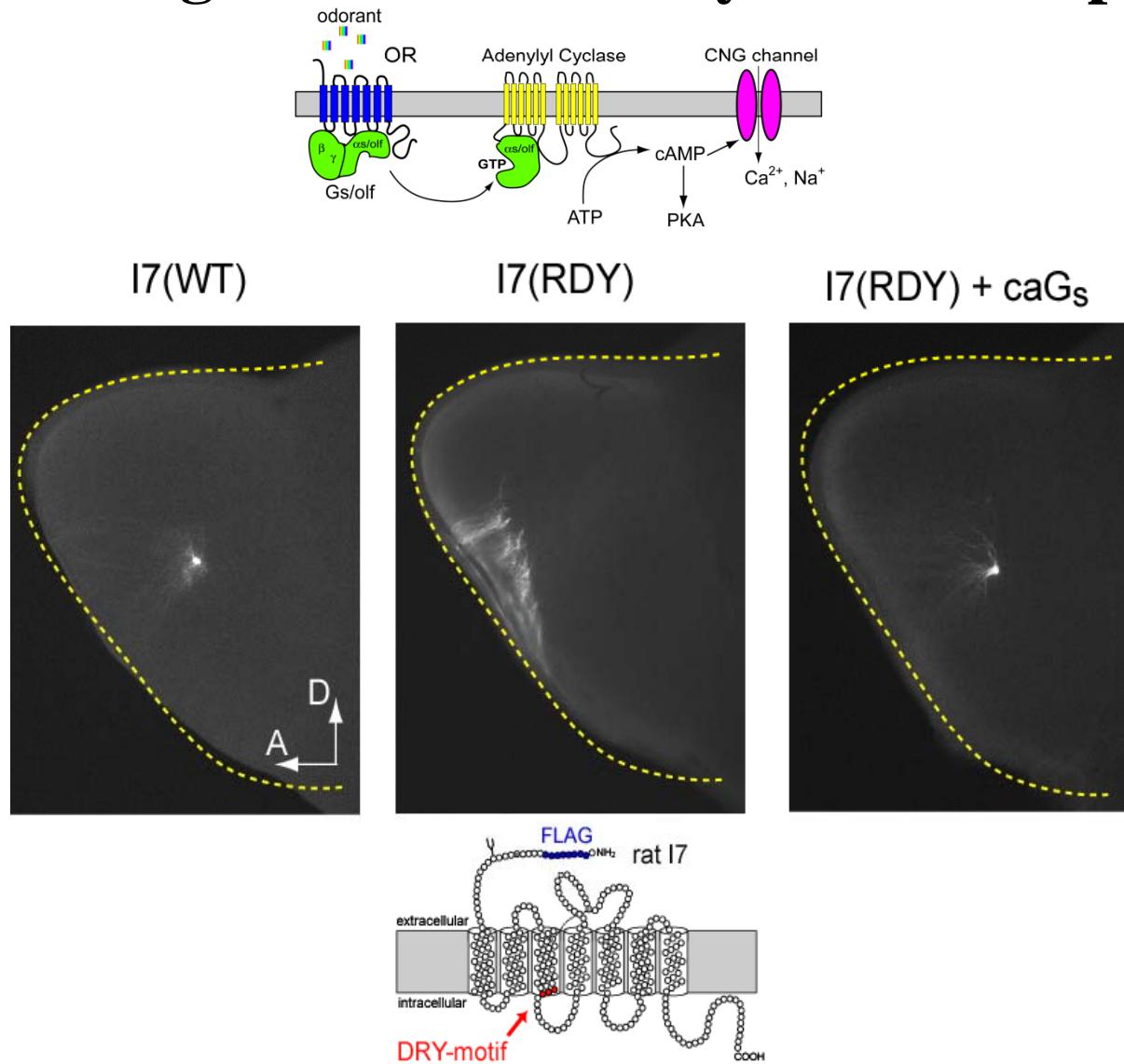
BAC



BAC (+Nrp2)



# G protein signals are necessary for axonal projection



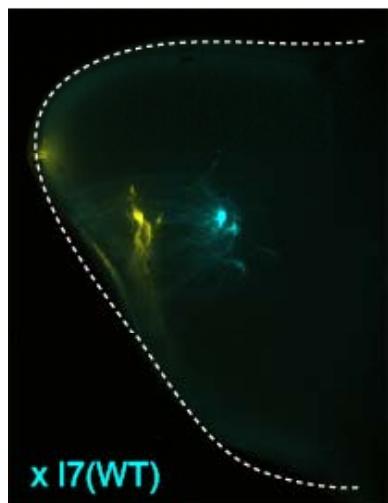
‡ From Imai et al., SCIENCE 314:657(2006)

<http://www.sciencemag.org/cgi/content/full/sci;314/5799/657?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=314&firstpage=657&resourcetype=HWCIT>

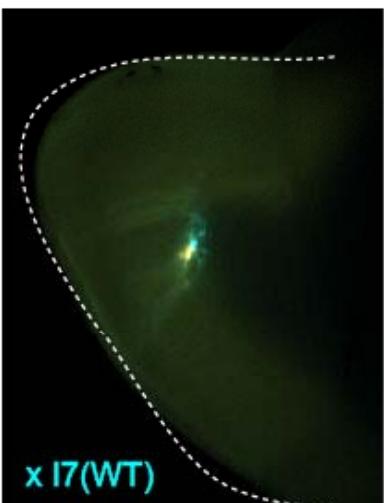
Reprinted with permission from AAAS.

# cAMP signals regulate glomerular positioning along the A/P axis

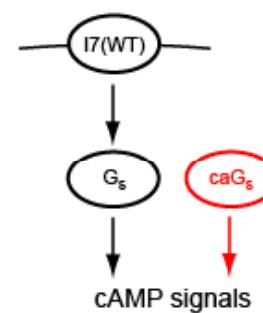
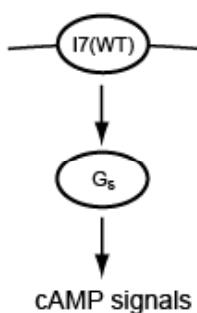
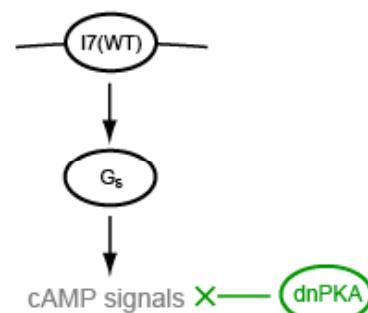
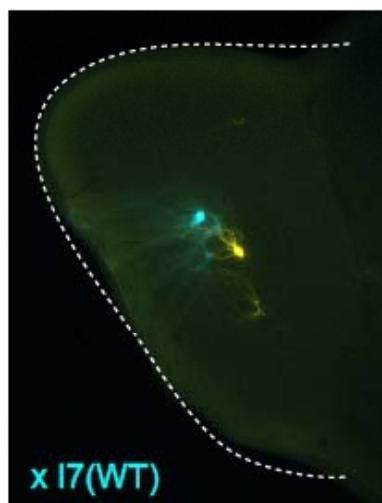
I7(WT) + dnPKA



I7(WT)



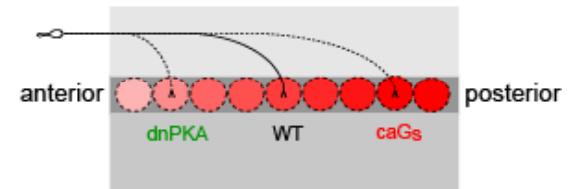
I7(WT) + caG<sub>s</sub>



G<sub>s</sub>

cAMP  
signals

low → high

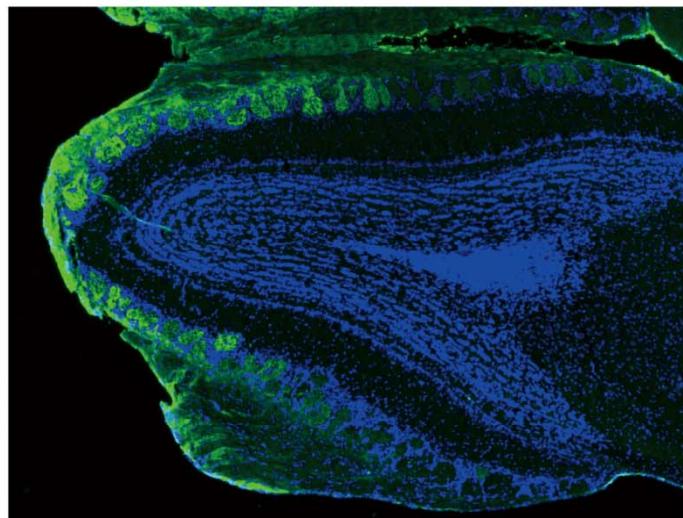


‡ From Imai et al., SCIENCE 314:657(2006)

<http://www.sciencemag.org/cgi/content/full/sci;314/5799/657?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&searchid=1&FIRSTINDEX=0&volume=314&firstpage=657&resourcetype=HWCIT>

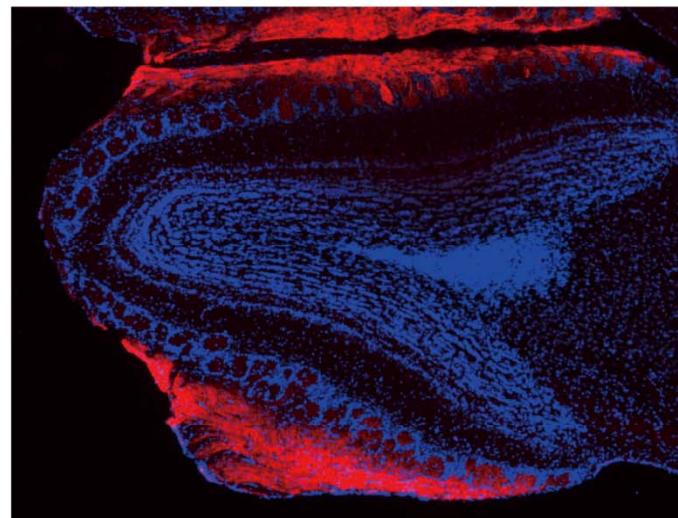
Reprinted with permission from AAAS.

# Complementary expression of Plexin-A1 and Neuropilin-1



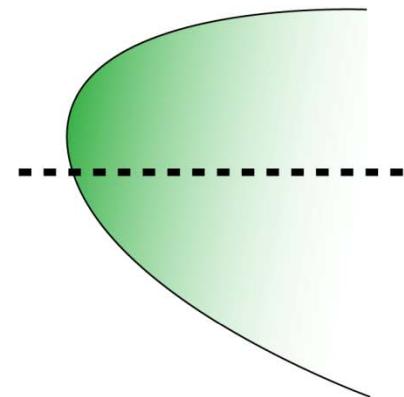
Plexin-A1

M  
A ← → P  
L

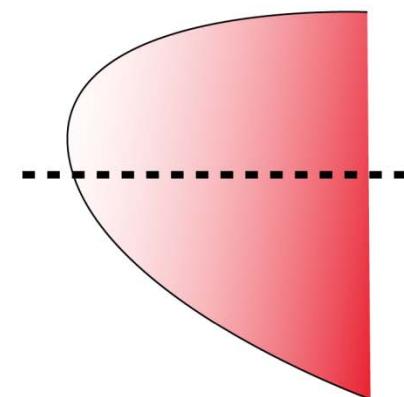


Neuropilin-1

OB

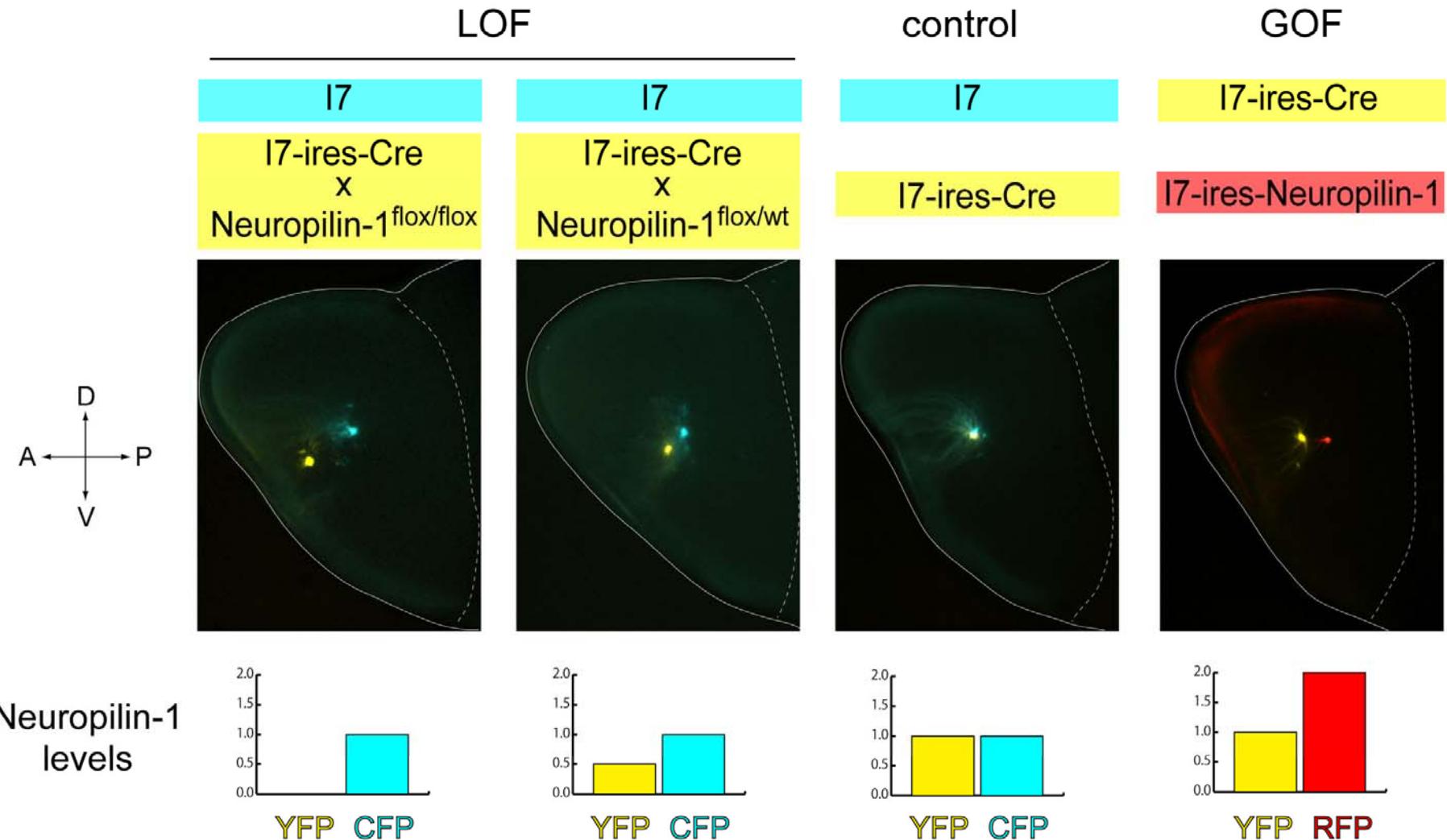


D  
A ← → P  
V



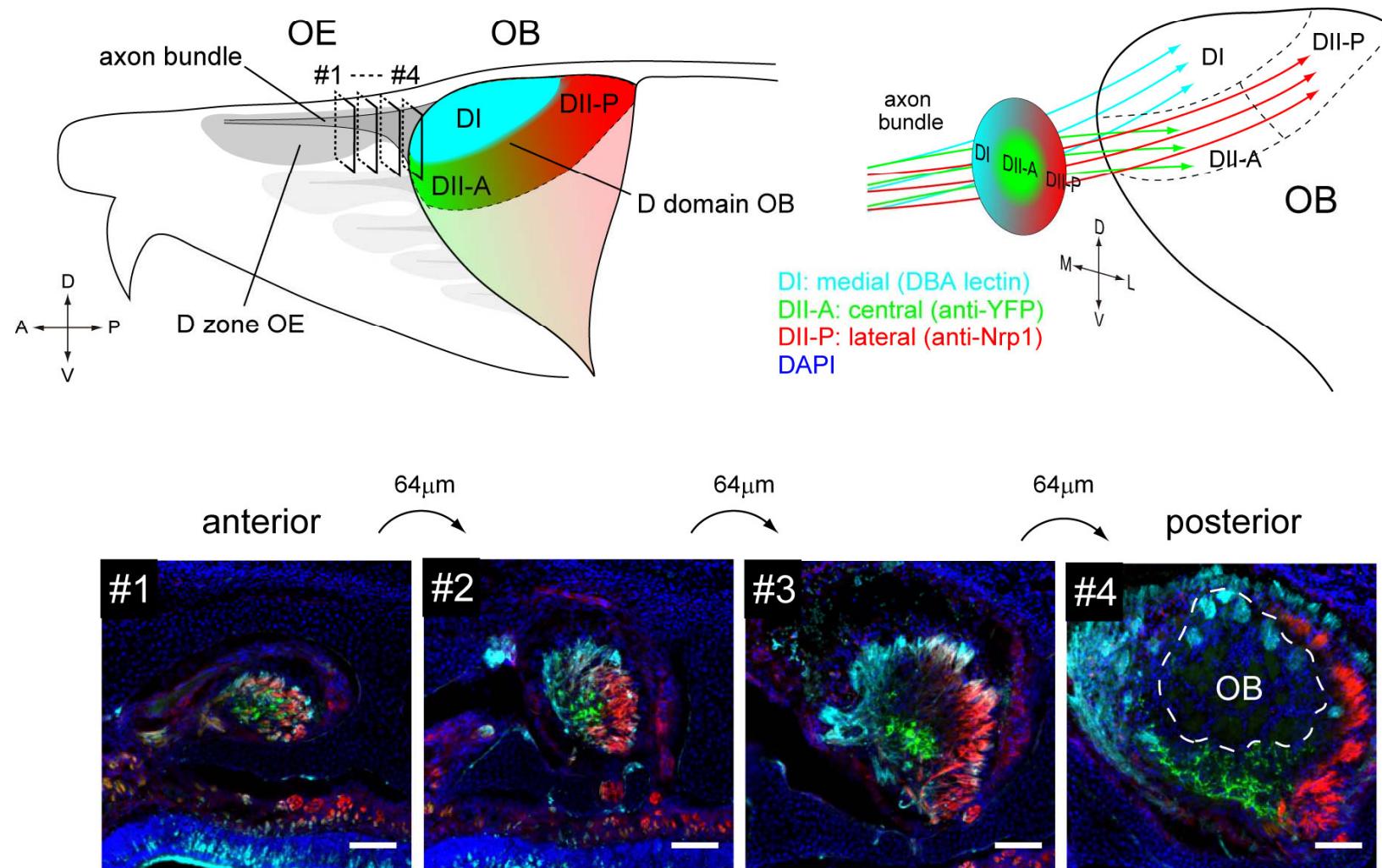
22

# Nrp1 level determines A-P positioning



‡ From Imai *et al.*, SCIENCE 325:585(2009)  
<http://www.sciencemag.org/cgi/content/abstract/325/5940/585>  
Reprinted with permission from AAAS.

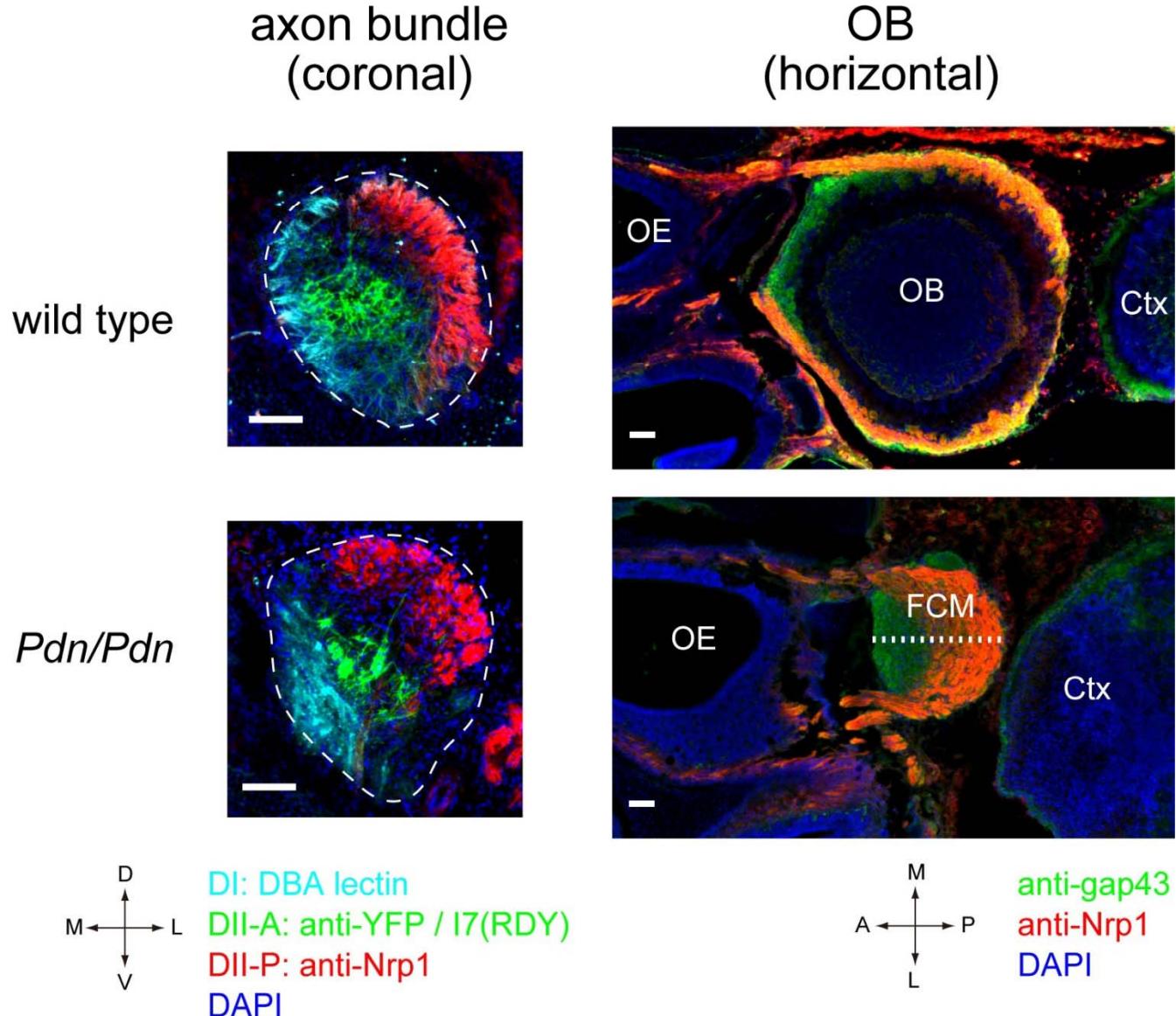
# Pre-target axon sorting of OSNs



coronal sections of the axon bundle from D zone

‡ From Imai *et al.*, SCIENCE 325:585(2009)  
<http://www.sciencemag.org/cgi/content/abstract/325/5940/585>  
Reprinted with permission from AAAS.

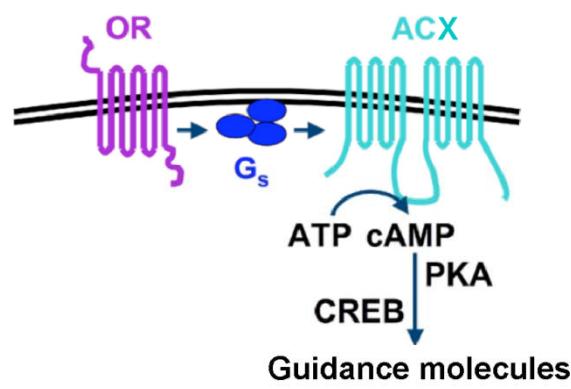
# Pre-target axon sorting in the OB-less mutant



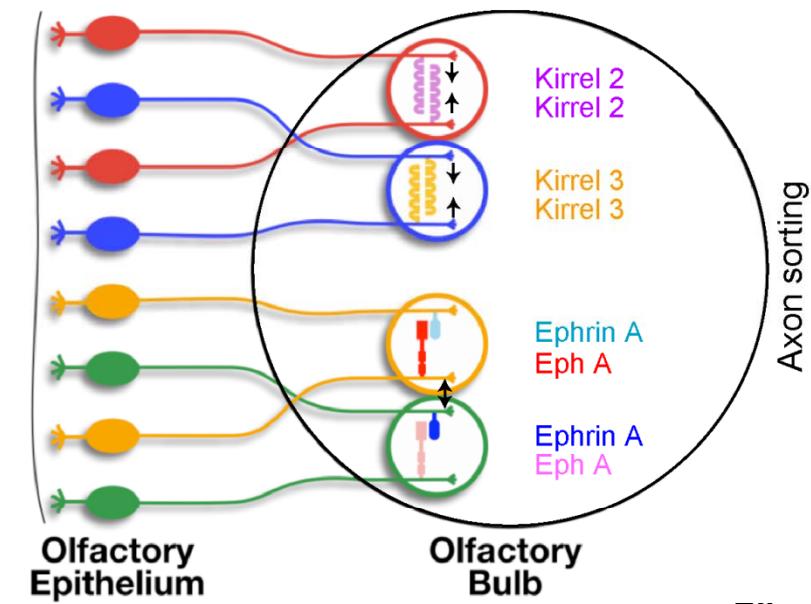
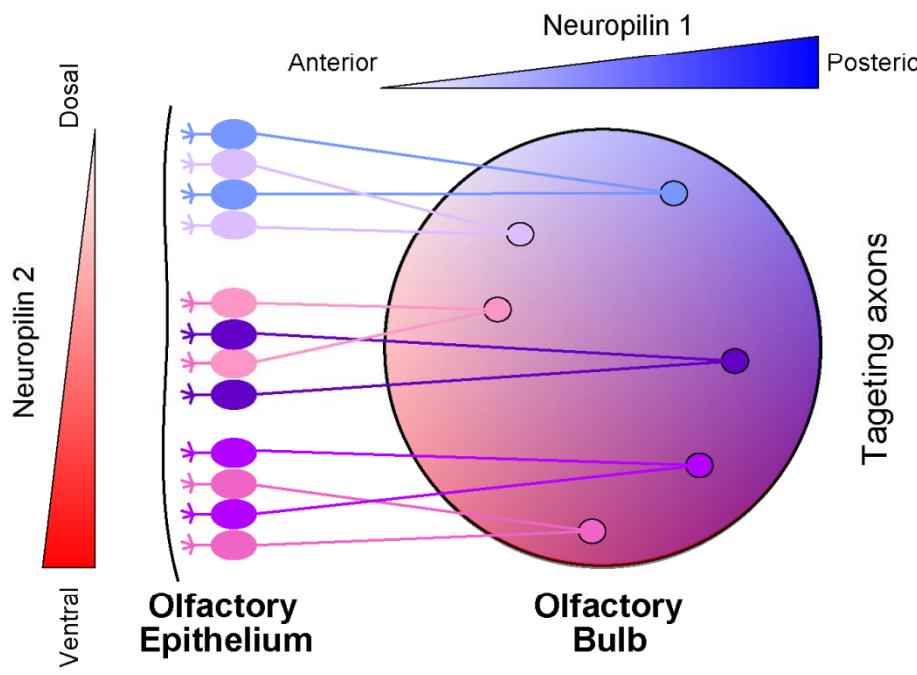
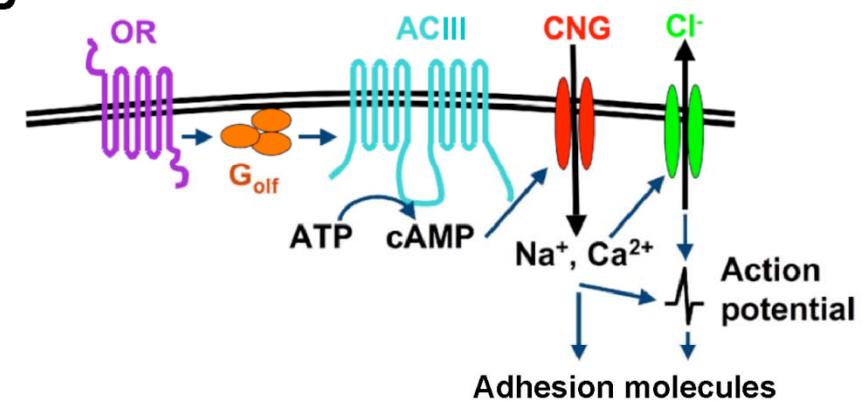
‡ From Imai *et al.*, SCIENCE 325:585(2009)  
<http://www.sciencemag.org/cgi/content/abstract/325/5940/585>  
Reprinted with permission from AAAS.

# Two Step Model for Glomerular Map Formation

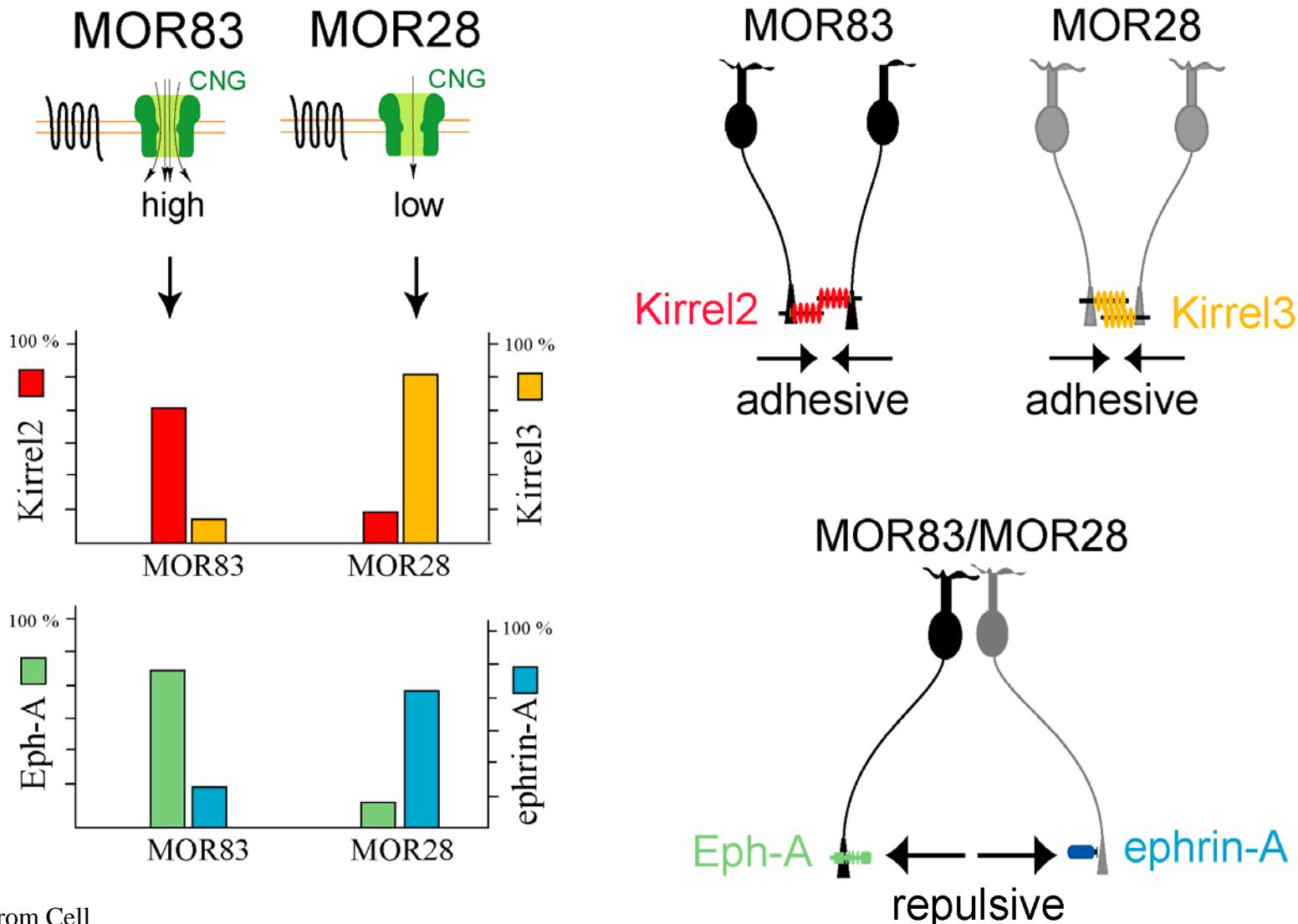
**A**



**B**



# OR-specific and activity-dependent segregation of axon termini

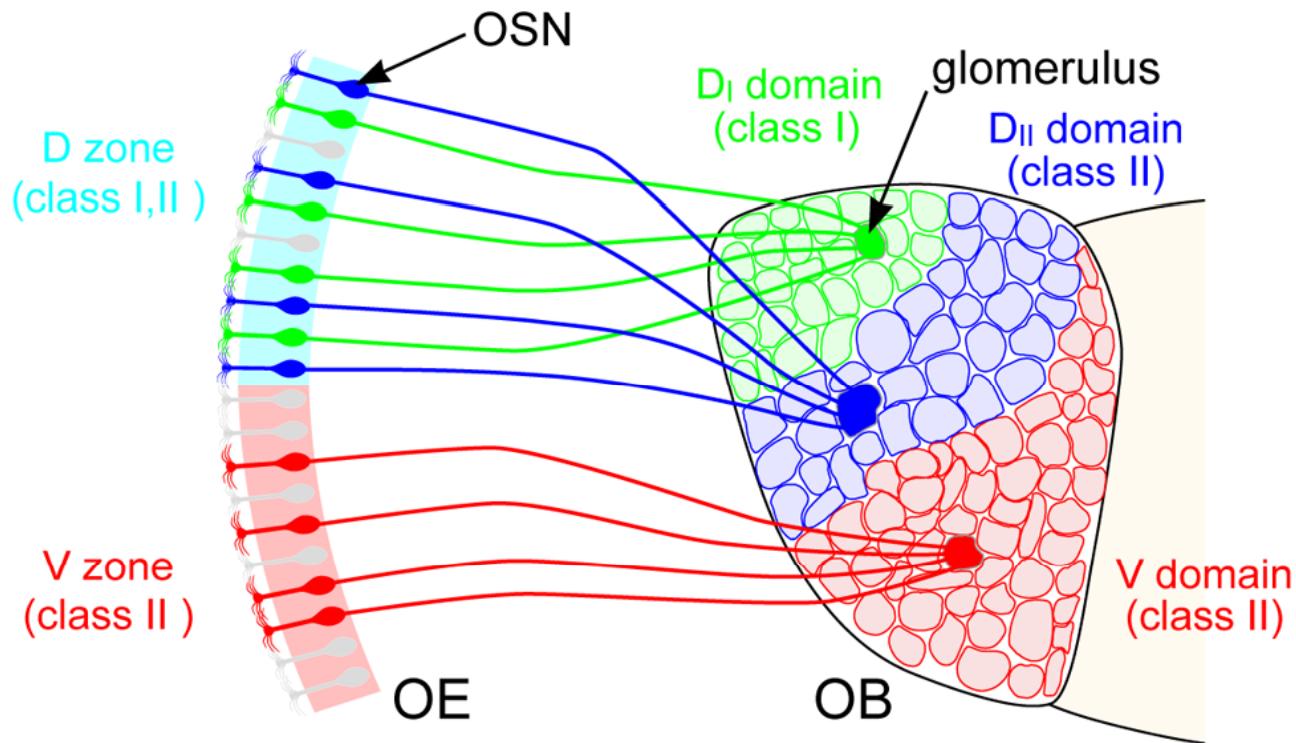


‡ Reprinted from Cell

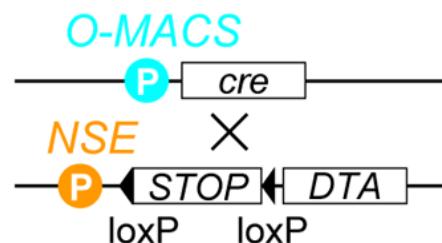
<http://www.sciencedirect.com/science/journal/00928674>

Volume 127, Issue 5, Shou Serizawa et al., A Neuronal Identity Code for the Odorant Receptor-Specific and Activity-Dependent Axon Sorting, Fig.8, Copyright (2006)National Academy of Sciences, U.S.A.

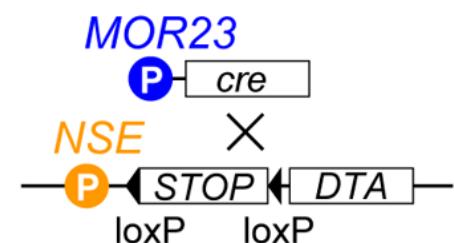
# Domain-specific glomerular ablation



$\Delta D$



$\Delta II$



Kobayakawa *et al.* *Nature* **450**, 503 (2007)