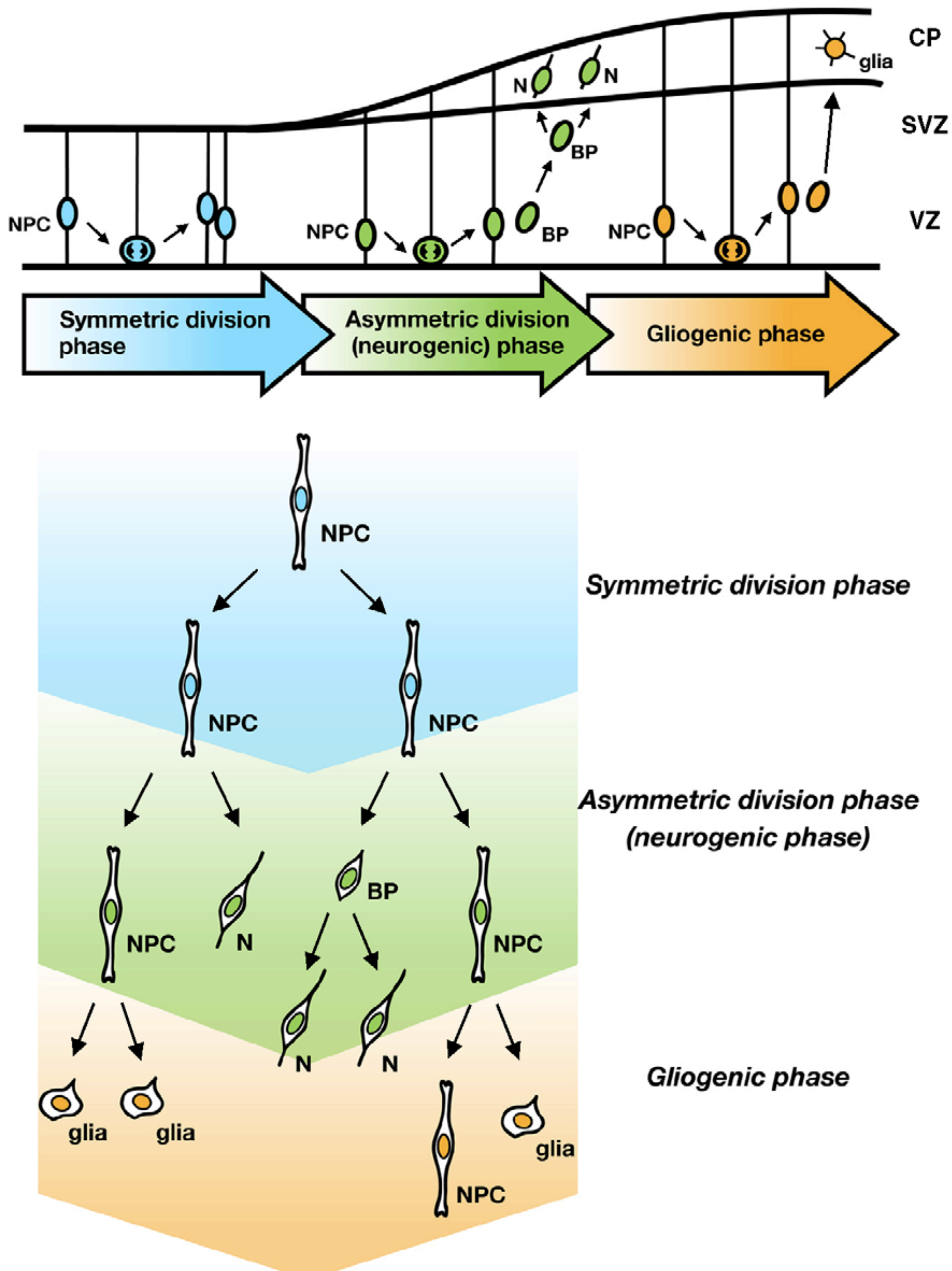
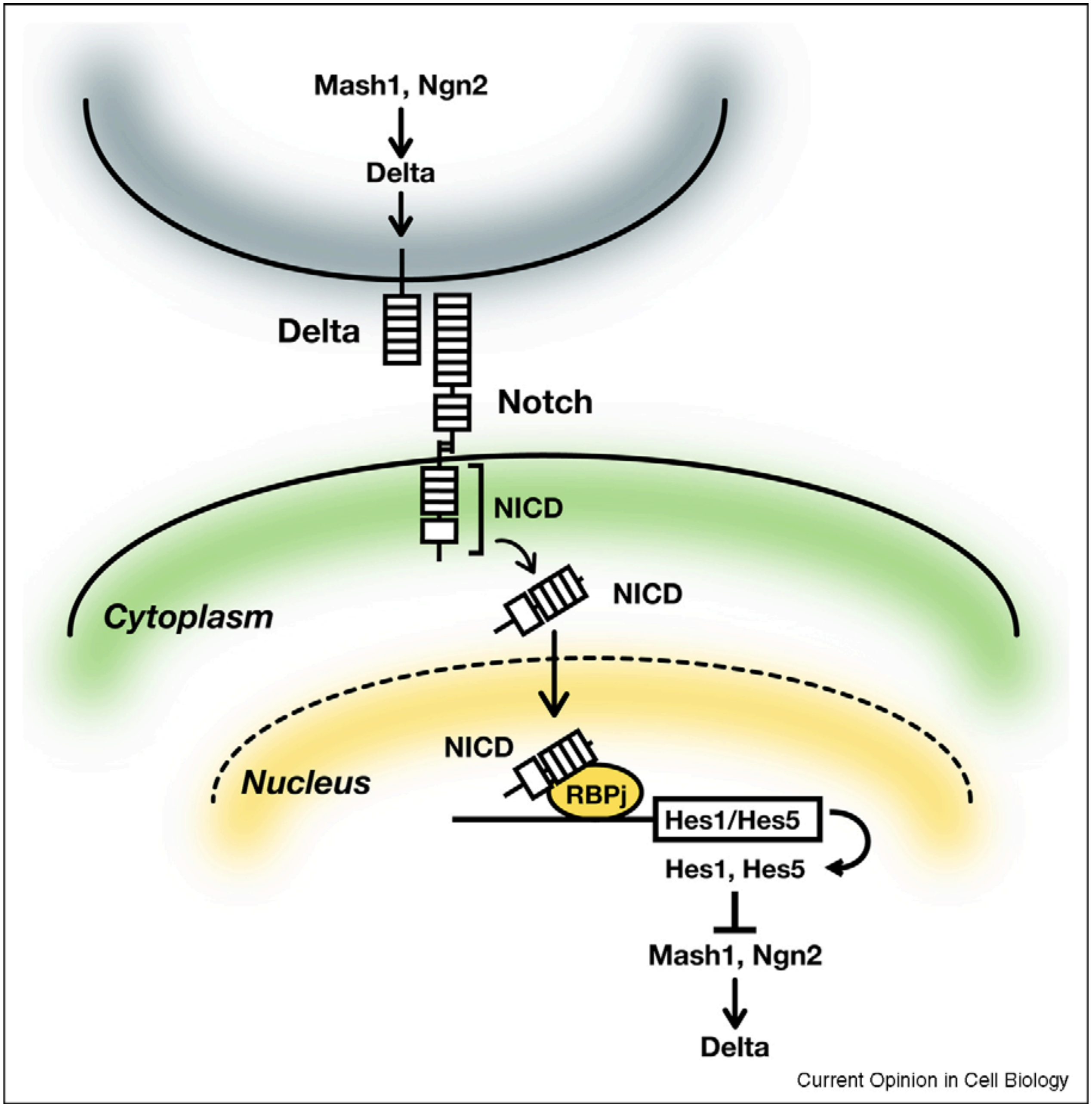
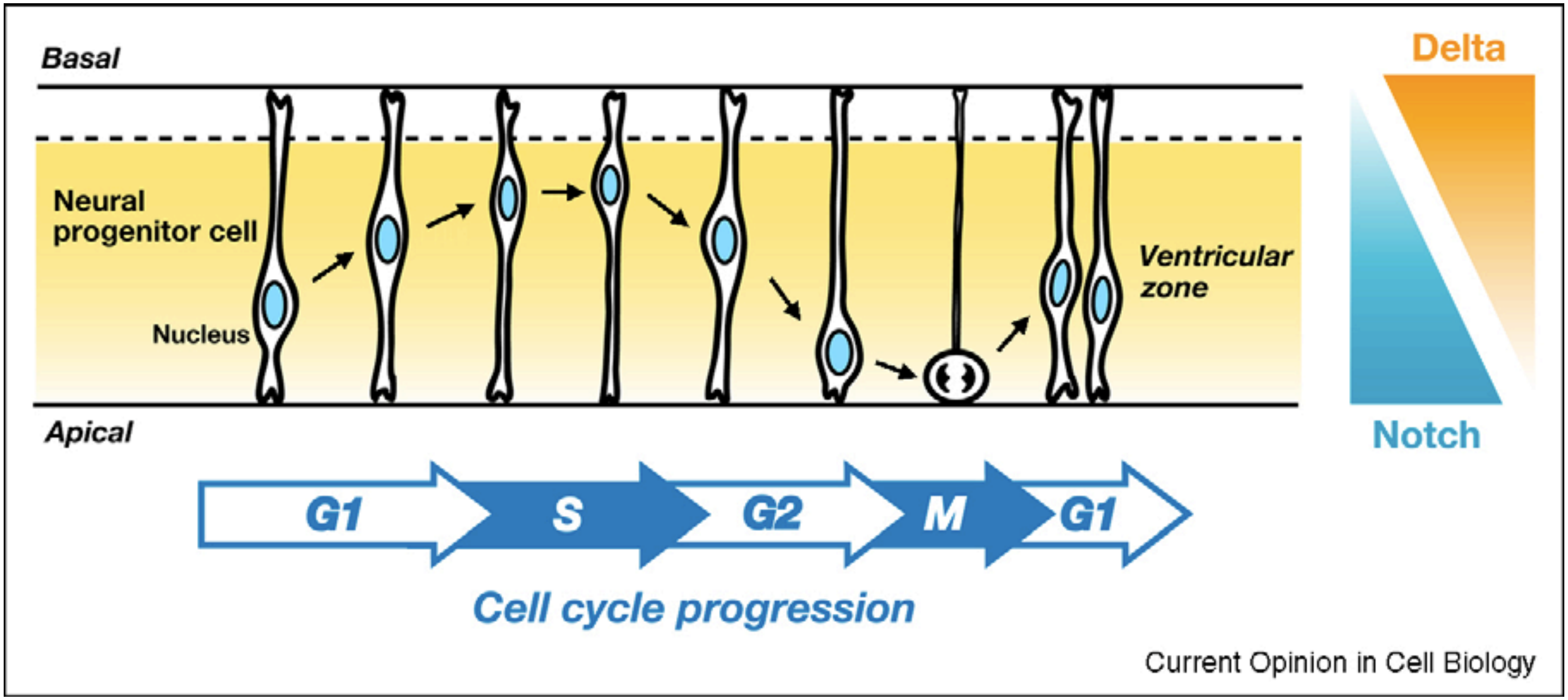
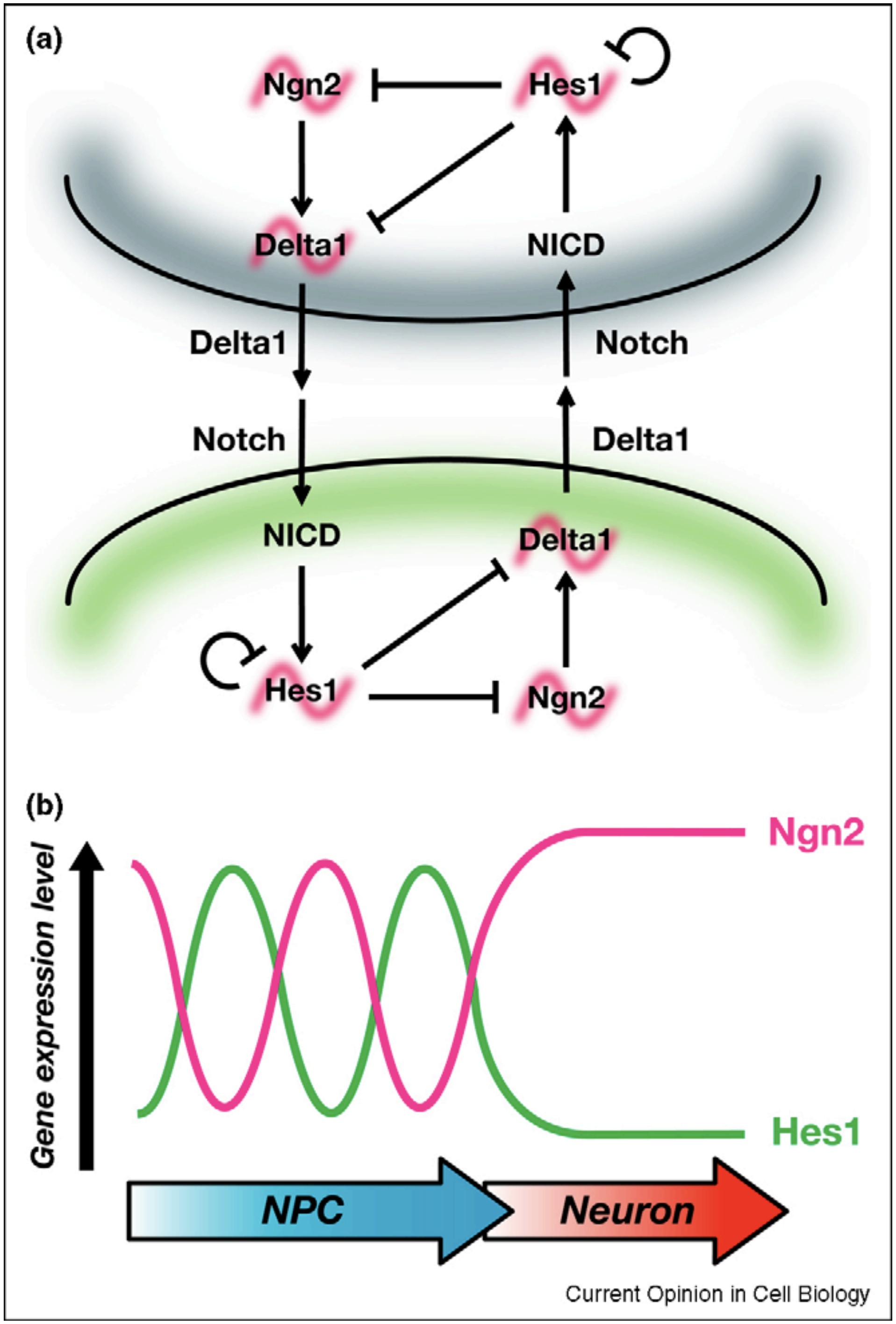


Current Opinion in Cell Biology


Mash1, Ngn2
Delta
Delta
Notch
NICD
NICD
Cytoplasm
NICD
Nucleus
RBPj
Hes1/Hes5
Hes1, Hes5
Mash1, Ngn2
Delta
Current Opinion in Cell Biology



Basal
Delta
Neural
progenitor cell
Nucleus
Ventricular
zone
Apical
Notch
G1
S
G2
M
G1
Cell cycle progression
Current Opinion in Cell Biology


(a)
Ngn2
Hes1
Delta1
NICD
Delta1
Notch
Notch
Delta1
NICD
Delta1
Hes1
Ngn2
(b)
Gene expression level
Ngn2
Hes1
NPC
Neuron
Current Opinion in Cell Biology

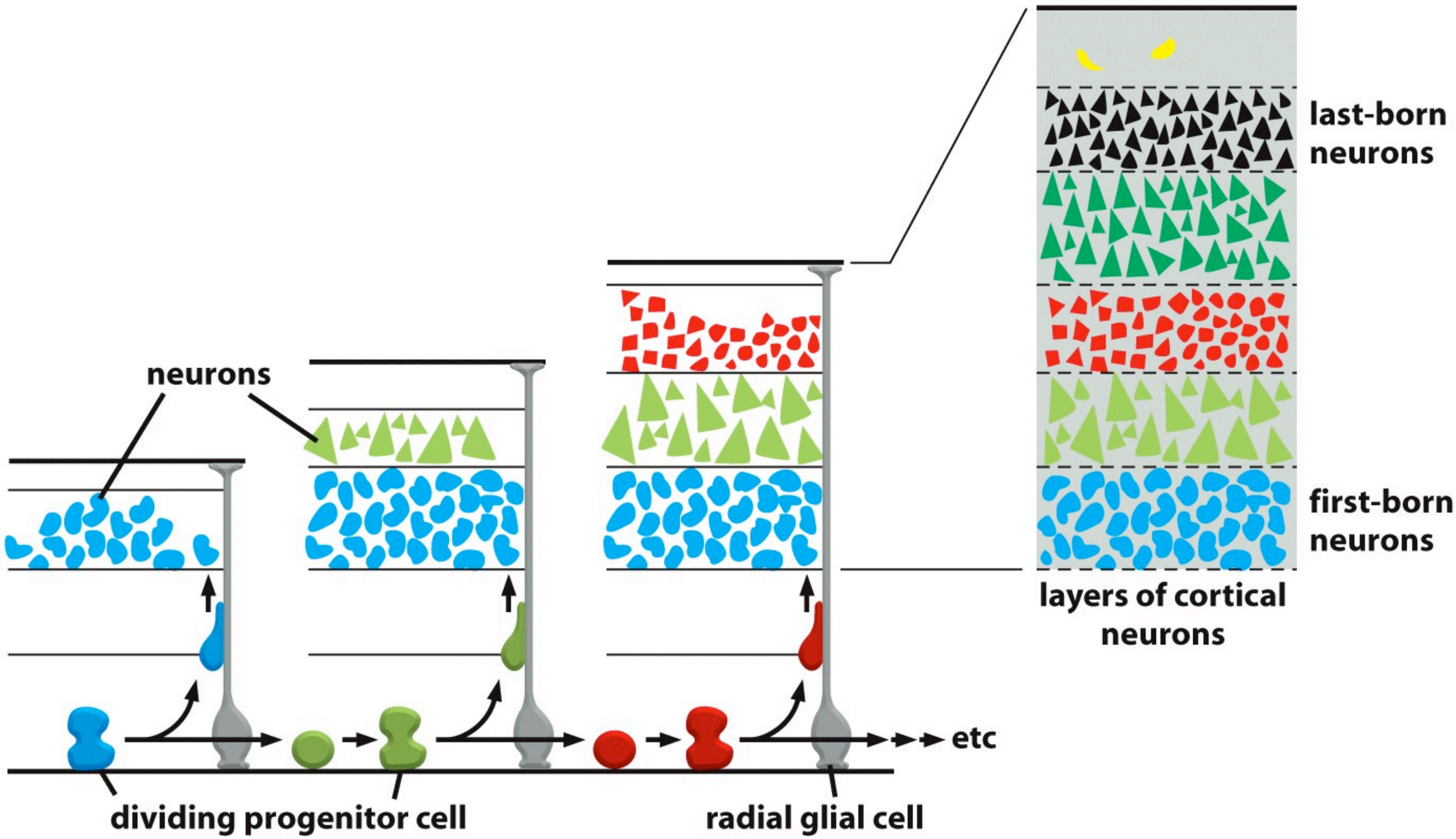


Figure 22-99 *Molecular Biology of the Cell* (© Garland Science 2008)

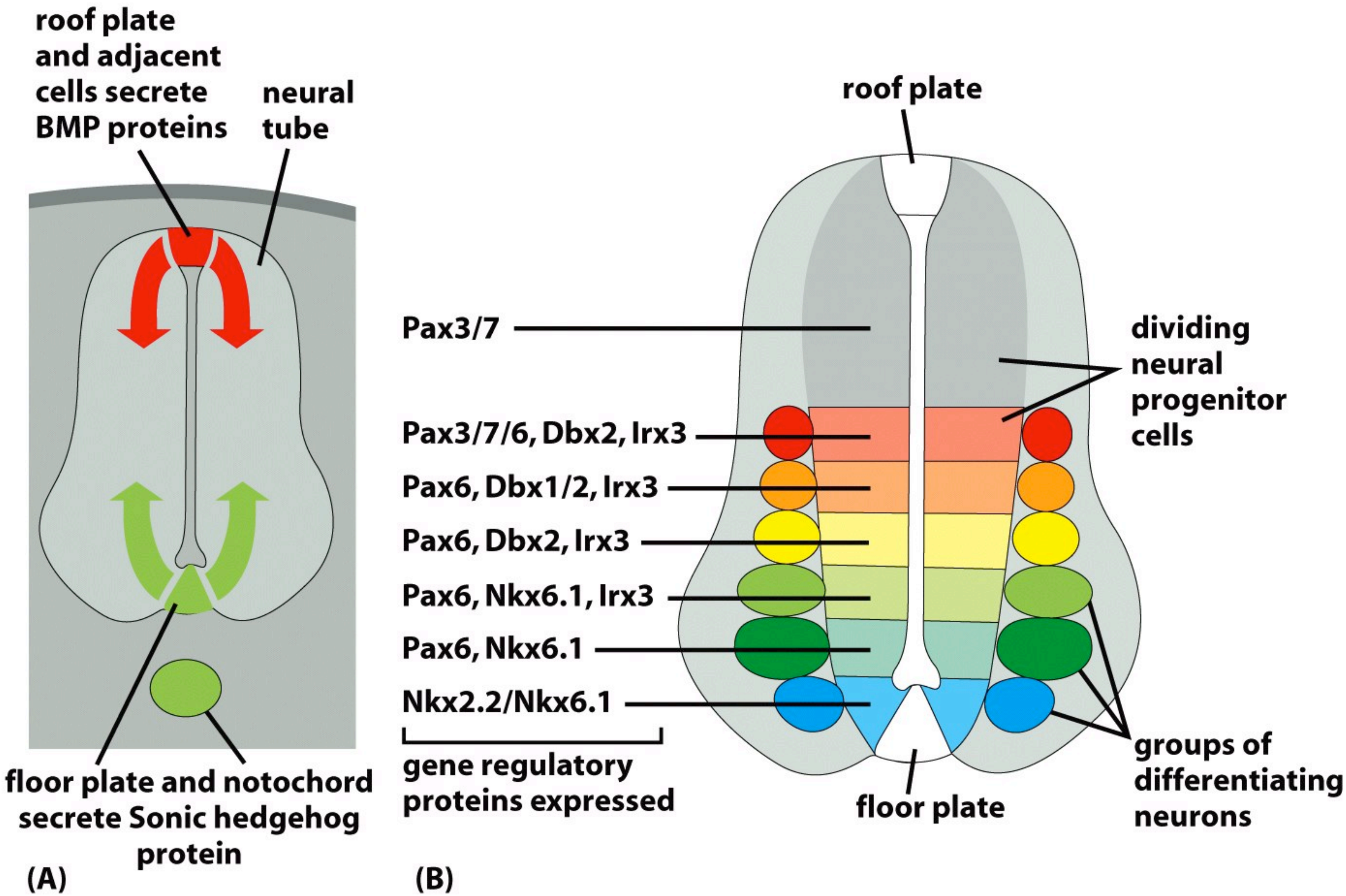
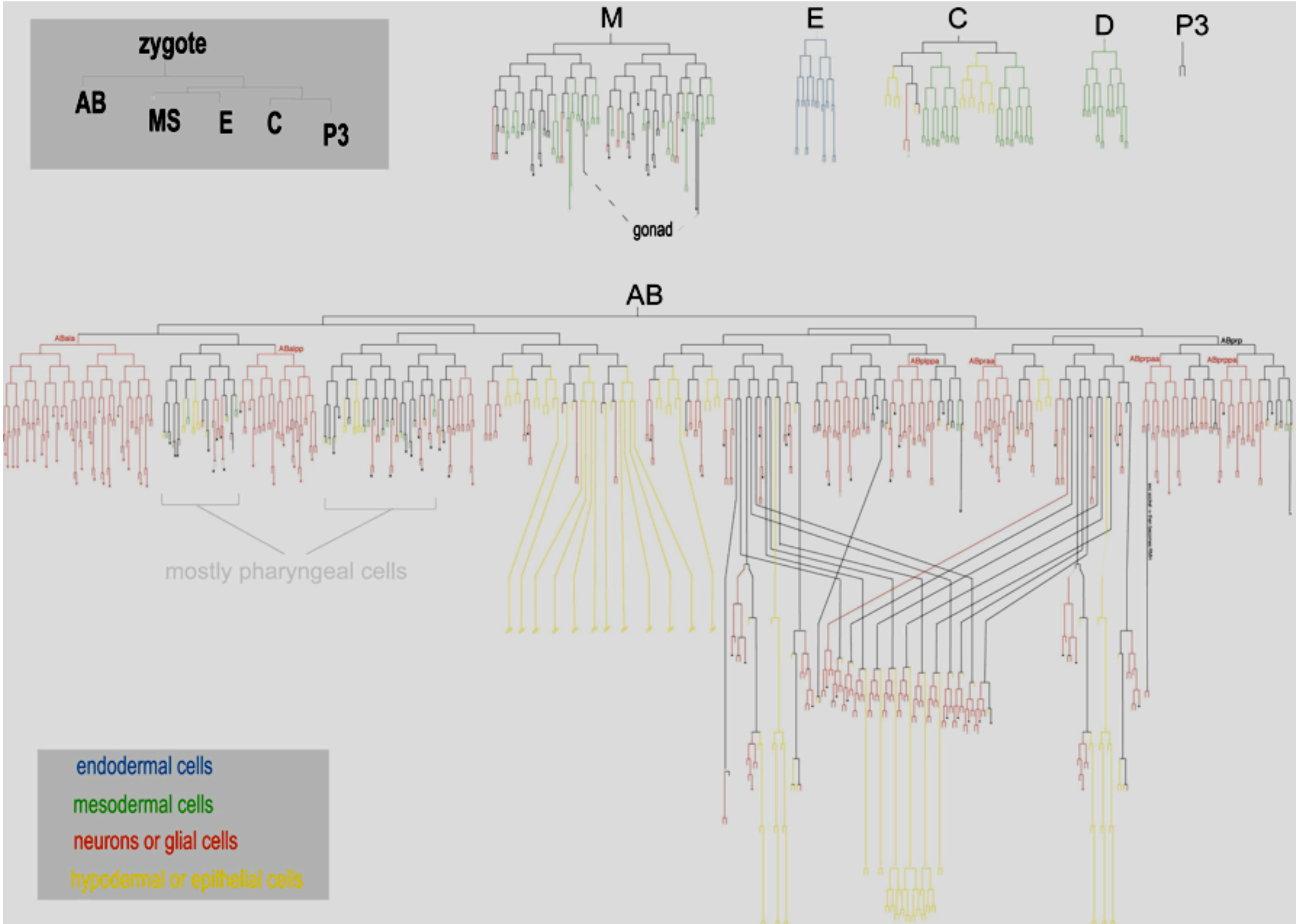


Figure 22-80 *Molecular Biology of the Cell* (© Garland Science 2008)


zygote
AB
MS
E
C
P3
M
E
C
D
P3
gonad
AB
mostly pharyngeal cells
endodermal cells
mesodermal cells
neurons or glial cells
hypodermal or epithelial cells

302 neurons
118 classes (types)

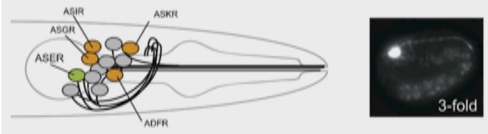
Defect	Gene name	Gene class	Neurons affected	Reference
All known features lost	*ceh-36*	Homeobox	AWC sensory neurons	Lanjuin et al., 2003; Koga and Ohshima, 2004
	ceh-37	Homeobox	AWB sensory neurons	Lanjuin et al., 2003
	che-1	Zn finger	ASE sensory neurons	Chang et al., 2003; Uchida et al., 2003
	egl-44, *egl-46*	Zn-finger and TEF-type	HOB sensory neurons	Yu et al., 2003
	lin-11	LIM homeobox	AWA sensory neurons AVG interneuron	Sarafi-Reinach et al., 2001; Hutter, 2003
	lim-4	LIM homeobox	AWB sensory neurons	Sagasti et al., 1999
	mec-3	LIM homeobox	Touch neurons	Way and Chalfie, 1988; Zhang et al., 2002
	odr-7	Nuclear hormone receptor	AWA sensory neurons	Sengupta et al., 1994
	ttx-1[a]	Homeobox	AFD sensory neurons	Satterlee et al., 2001
	ttx-3	LIM homeobox	AIY interneurons	Hobert et al., 1997
	unc-30	Homeobox	D-type motorneurons	Jin et al., 1994
	unc-86	POU homeobox	Many	Finney et al., 1988; Finney and Ruvkun, 1990; Sze et al., 2002
	unc-130	Forkhead	ASG sensory neurons	Sarafi-Reinach and Sengupta, 2000
Subfeatures lost	*ceh-2*	Homeobox	M3 motorneuron	Aspock et al., 2003
	ceh-10	Homeobox	CAN neuron[b]	Forrester et al., 1998
	ceh-14	Homeobox	AFD sensory neurons	Cassata et al., 2000
	ceh-17	Homeobox	ALA, SIA neurons	Pujol et al., 2000
	ceh-23	Homeobox	AIY interneurons	Altun-Gultekin et al.,2001
	egl-5	HOX cluster	HSN motorneurons	Desai et al., 1988
	egl-43, *ham-2*	Zn finger	HSN motorneurons	Baum et al., 1999
	fax-1	Nuclear hormone receptor	AVK interneurons	Much et al., 2000

302 neurons
118 classes (types)

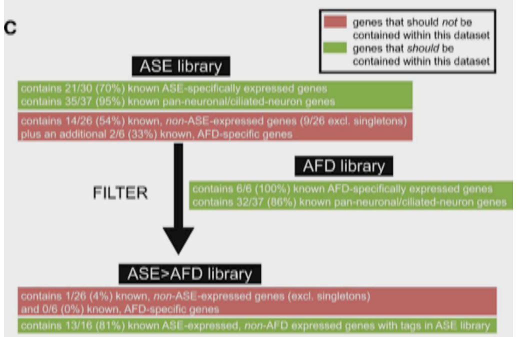
Defect	Gene name	Gene class	Neurons affected	Reference
Subfeatures lost	*lin-11*	LIM homeobox	AIZ interneurons, VC motorneurons	Hobert et al., 1998
	lin-39, mab-5	HOX cluster	Q neuroblasts	Kenyon, 1986; Clark et al., 1993
	lim-4	LIM homeobox	RID motorneuron	Tsalik et al., 2003
	lim-6	LIM homeobox	DVB motorneuron, RIS interneuron	Hobert et al., 1999; Tsalik et al., 2003
	ttx-3	LIM homeobox	AIA interneurons	Altun-Gultekin et al., 2001
	unc-3	Zn finger	ASI, ventral cord motorneurons	Prasad et al., 1998
	unc-42	Homeobox	Command interneurons, RMD motorneurons, ASH sensory neurons	Baran et al., 1999; Brockie et al., 2001
	zag-1	Zn finger	Many neurons	Clark and Chiu, 2003; Wacker et al., 2003
Alternative or "default" program executed	*ahr-1*	Zn finger	RMED/V vs. RMEL/R motorneurons	Huang et al., 2004
	ceh-36, cog-1, lim-6	Homeobox	ASEL vs. ASER	Chang et al., 2003; Johnston and Hobert, 2003; Chang et al., 2004
	die-1	Zn finger		
	lsy-6, mir-273	miRNA		
	cfi-1	ARID	URA vs.CEM sensory neurons	Shaham and Bargmann, 2002
	egl-5, mab-5	HOX gene	Male sensory rays	Lints et al., 2004
	mab-18	Pax gene		
	egl-44	TEF-family	Represses touch fate	Wu et al., 2001
	egl-46, sem-4	Zn finger		Wu et al., 2001; Toker et al., 2003
	mec-3, unc-86	Homeobox	FLP vs. touch neurons	Mitani et al., 1993
	pag-3	Zn finger	BDU vs. ALM	Jia et al., 1996
	unc-4	Homeobox	VA vs. VB motorneurons DA vs. DB motorneurons [c]	Winnier et al., 1999; Esmaeili et al., 2002
	unc-55	Nuclear hormone receptor	DD vs. VD motorneurons	Zhou and Walthall, 1998
	vab-7	Homeobox	DA vs. DB motorneurons	Esmaeili et al., 2002

C. elegans gustatory neuron

A B



C



D

Number of genes and tags in SAGE libraries		
Complete ASE library	1 tag ("singleton")	2501 genes
	>1 to <10 tags	4494 genes
	10 tags to <100 tags	1191 genes
	100 tags or more (743 max.)	31 genes
	Total (excluding singletons)	5716 genes
ASE>AFD library	1 ASE-only tag ("singleton")	974 genes
	>1 to <10 ASE-only tags	590 genes
	10 ASE-only tags or more (32 max.)	11 genes
	3 fold enrichment ASE vs. AFD	254 genes
	>3 fold to 10 fold enrichment ASE vs. AFD	326 genes
	>10 fold enrichment ASE vs. AFD (max. 36)	16 genes
	>1 to >3 fold enrichment ASE vs. AFD (p<0.05)	105 genes
	Total (excluding singletons)	1302 genes

E

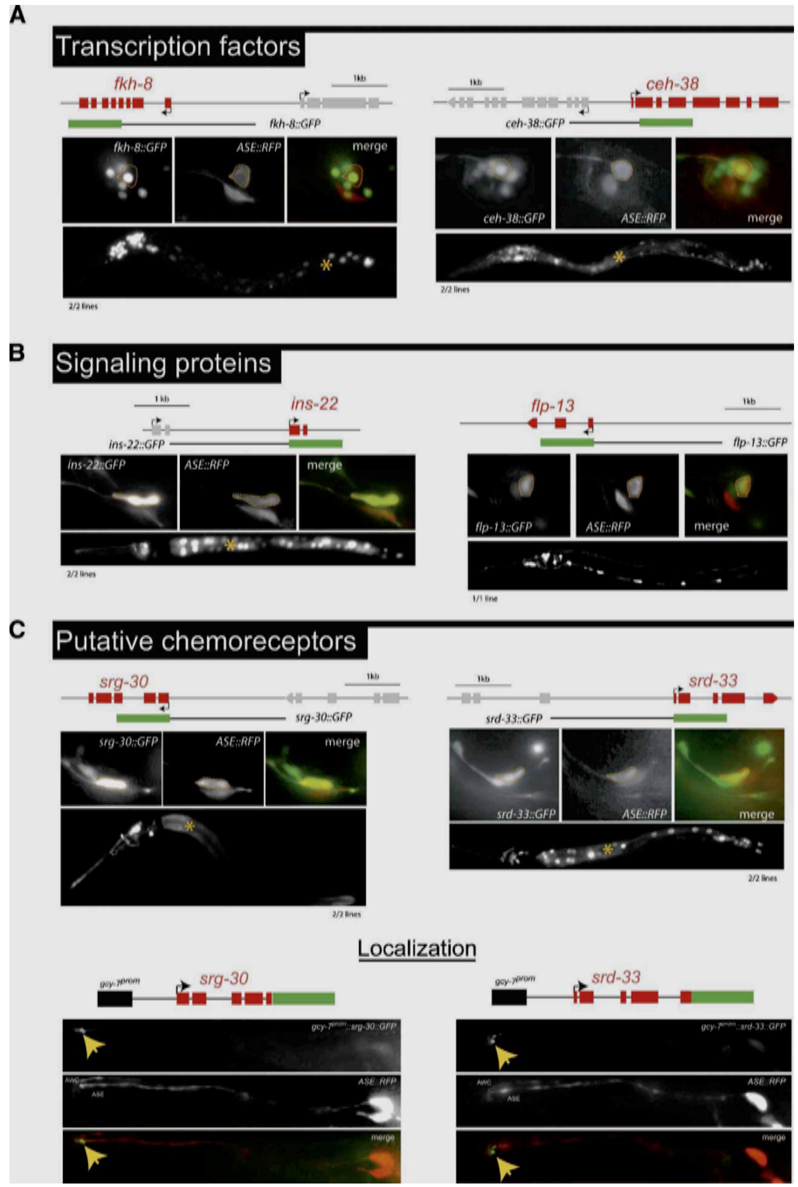
Classification of genes in ASE>AFD library
(singletons excluded)

Gene class	Type	# of genes
Transcription factors	C2H2 Zn finger	18
	C4 Zn finger (*nhr*-type)	28
	Homeobox	7
	Others	14
	Total	68
Putative chemoreceptors	7TMR-type	11 (41)[1]
	Degenerin-type	3
	TRP-channel-type	1
	Total	15
Neurotransmitter/neurohormone receptors	GPCR or kinase	7
	ionotropic receptor	7
	Total	14
Neurotransmitters/neurohormones	*flp*-type	5
	nlp-type	5
	ins-type	1
	Total	11 (12)[2]
Ion channels (excluding ligand-gated ion channels, DEGs and TRPs; see above)	Ca^{++} channels	4
	K^{+} channels	4
	Total	8

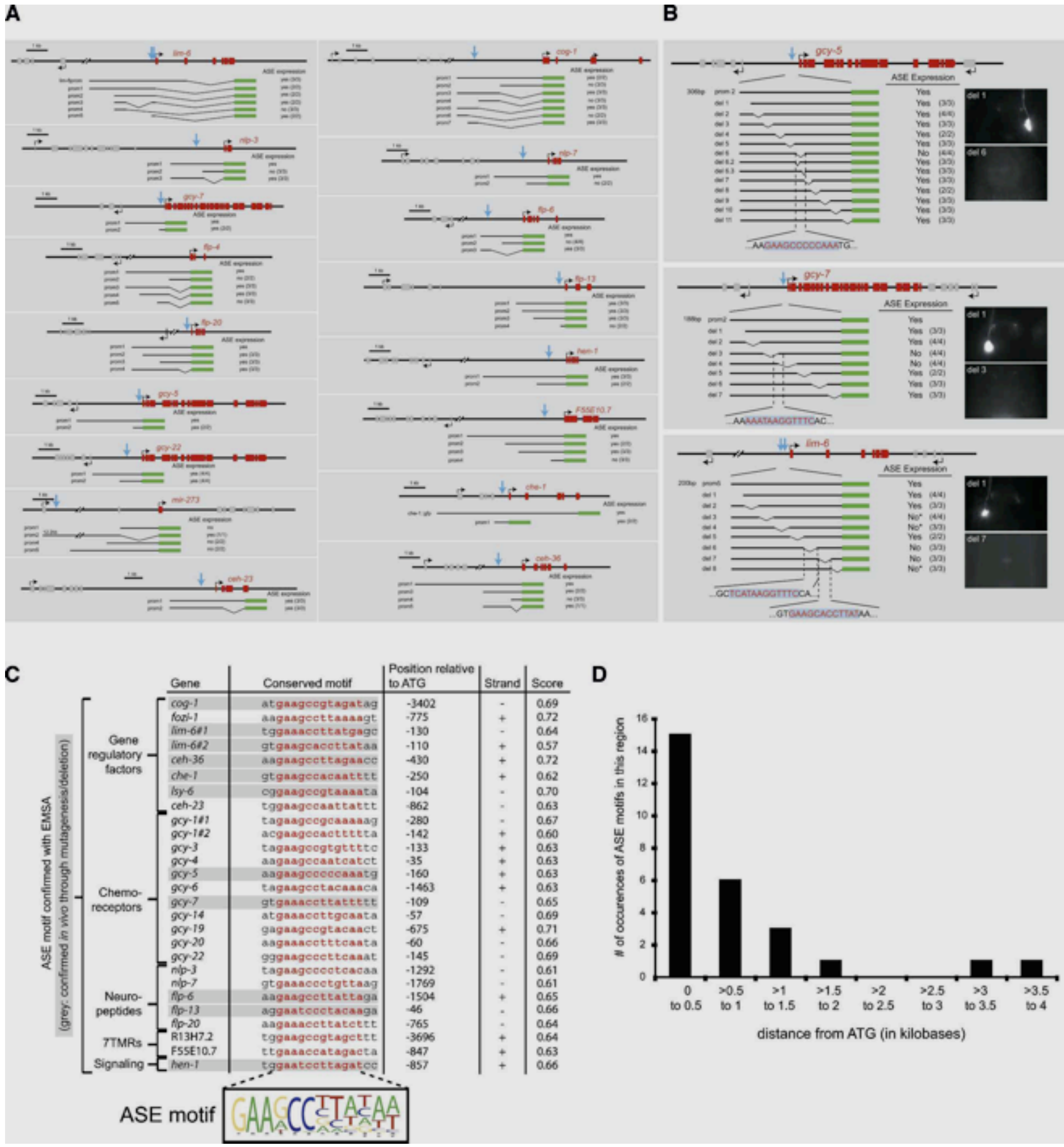
F

Natural antisense transcripts (NATs) in the ASE transcriptome	
Number of NATs (excluding singletons)	Total: 126
Enriched NATs in ASE vs. AFD	exclusive to ASE: 13 (non-singletons)
	3x enriched: 18
	Total: 31
Relation of ASE-enriched NATs with corresponding sense transcripts in ASE	Correlated: 17/31 Anti-correlated: 14/31
Possible origin of NATs	20/31 NATs <200 bp tail-to-tail orientation to neighboring transcript *or* located on opposite strand in intron of other transcript

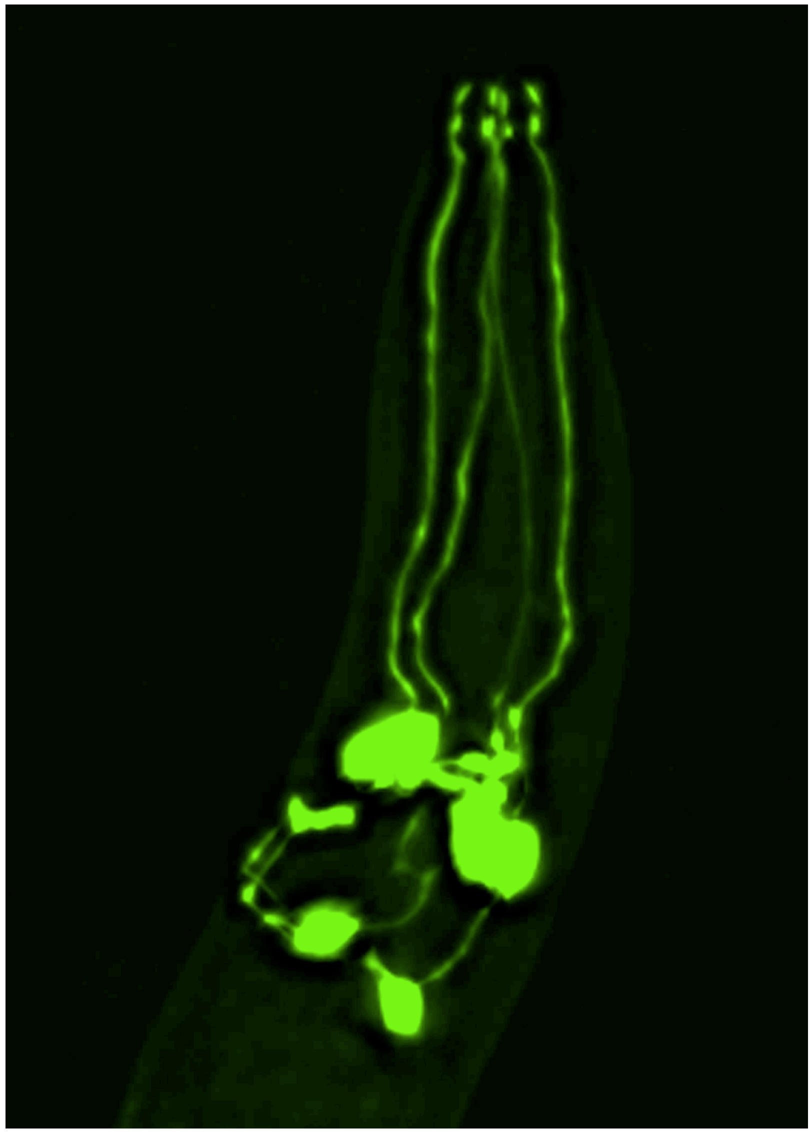
C. elegans gustatory neuron



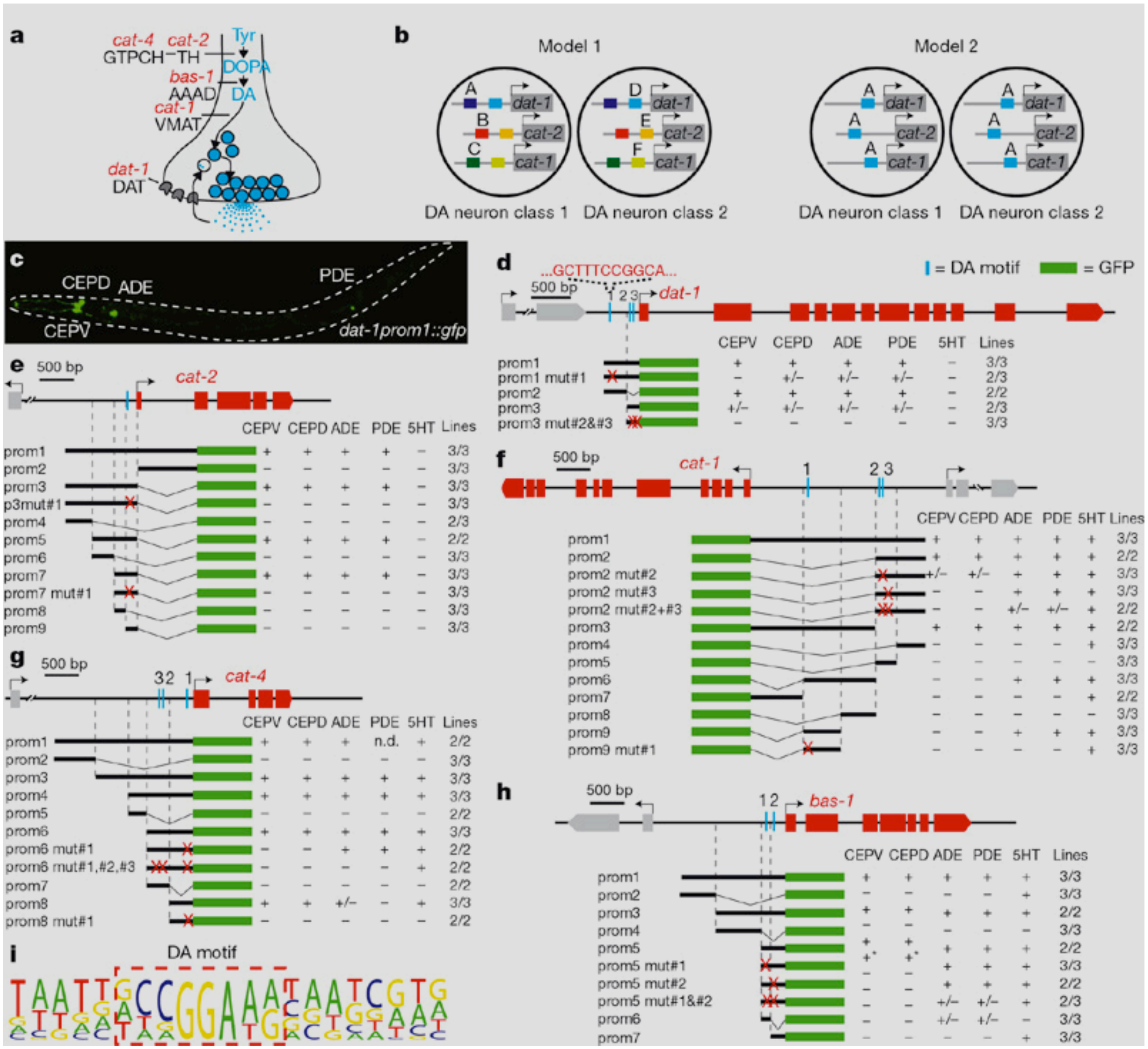
C. elegans gustatory neuron



C. elegans DA neurons

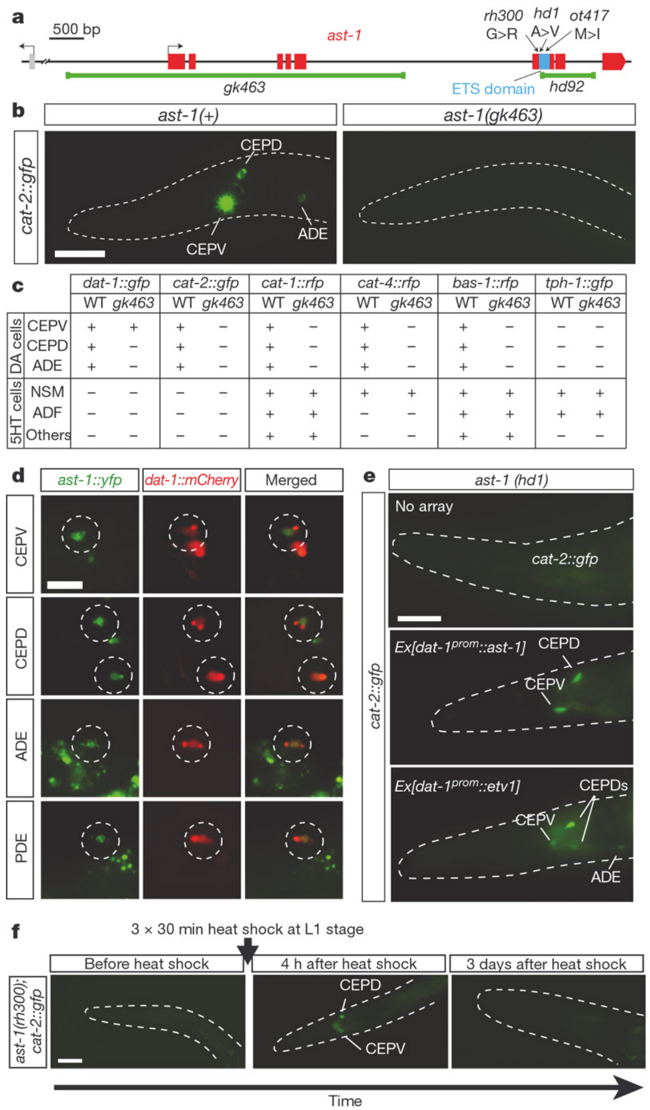


Characterization of the DA motif in *C. elegans*



N Flames & O Hobert
Nature **000**, 1-5 (2009)
doi:10.1038/nature07929

ast-1 is required to induce and maintain DA neuron differentiation.

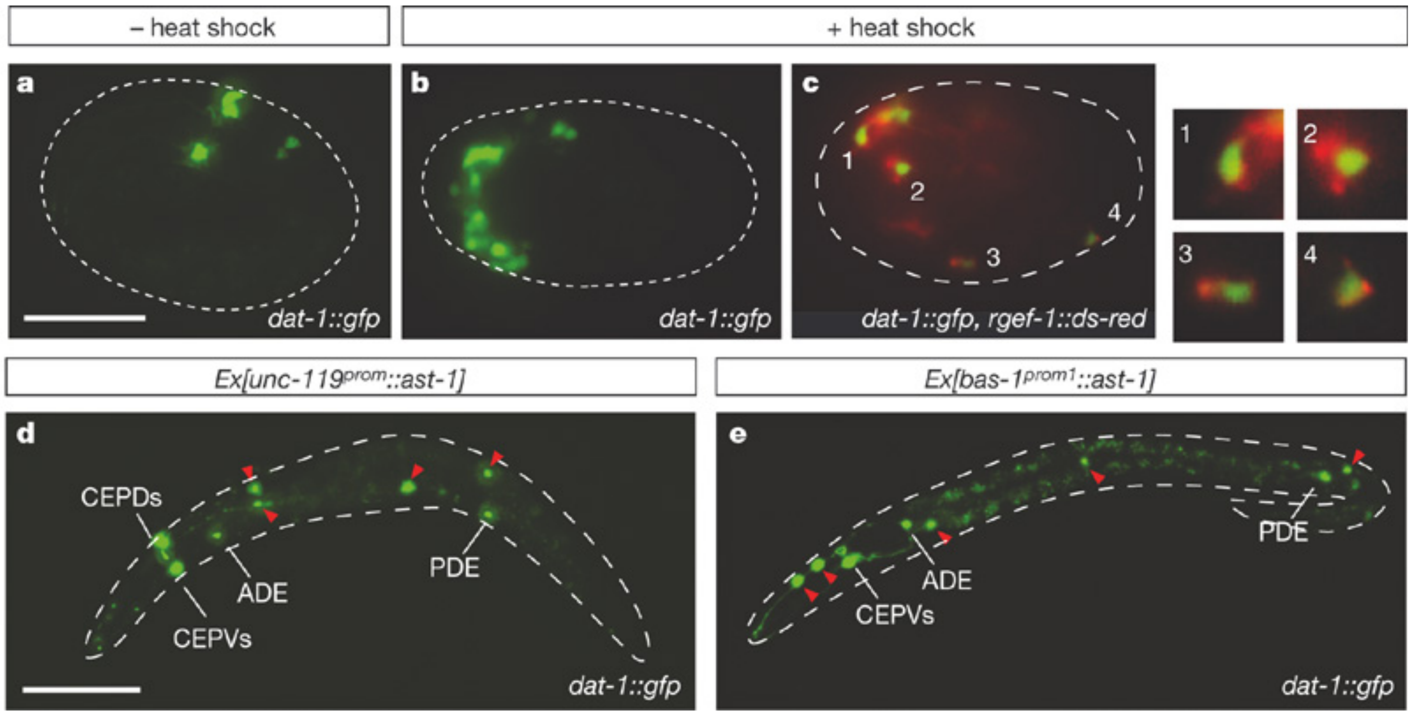


		dat-1::gfp		cat-2::gfp		cat-1::rfp		cat-4::rfp		bas-1::rfp		tph-1::gfp	
		WT	gk463	WT	gk463	WT	gk463	WT	gk463	WT	gk463	WT	gk463
DA cells	CEPV	+	+	+	−	+	−	+	−	+	−	−	−
	CEPD	+	−	+	−	+	−	+	−	+	−	−	−
	ADE	+	−	+	−	+	−	+	−	+	−	−	−
5HT cells	NSM	−	−	−	−	+	+	+	+	+	+	+	+
	ADF	−	−	−	−	+	+	−	−	+	+	+	+
	Others	−	−	−	−	+	+	−	−	+	+	−	−

N Flames & O Hobert *Nature* **000**, 1-5 (2009) doi:10.1038/nature07929

nature

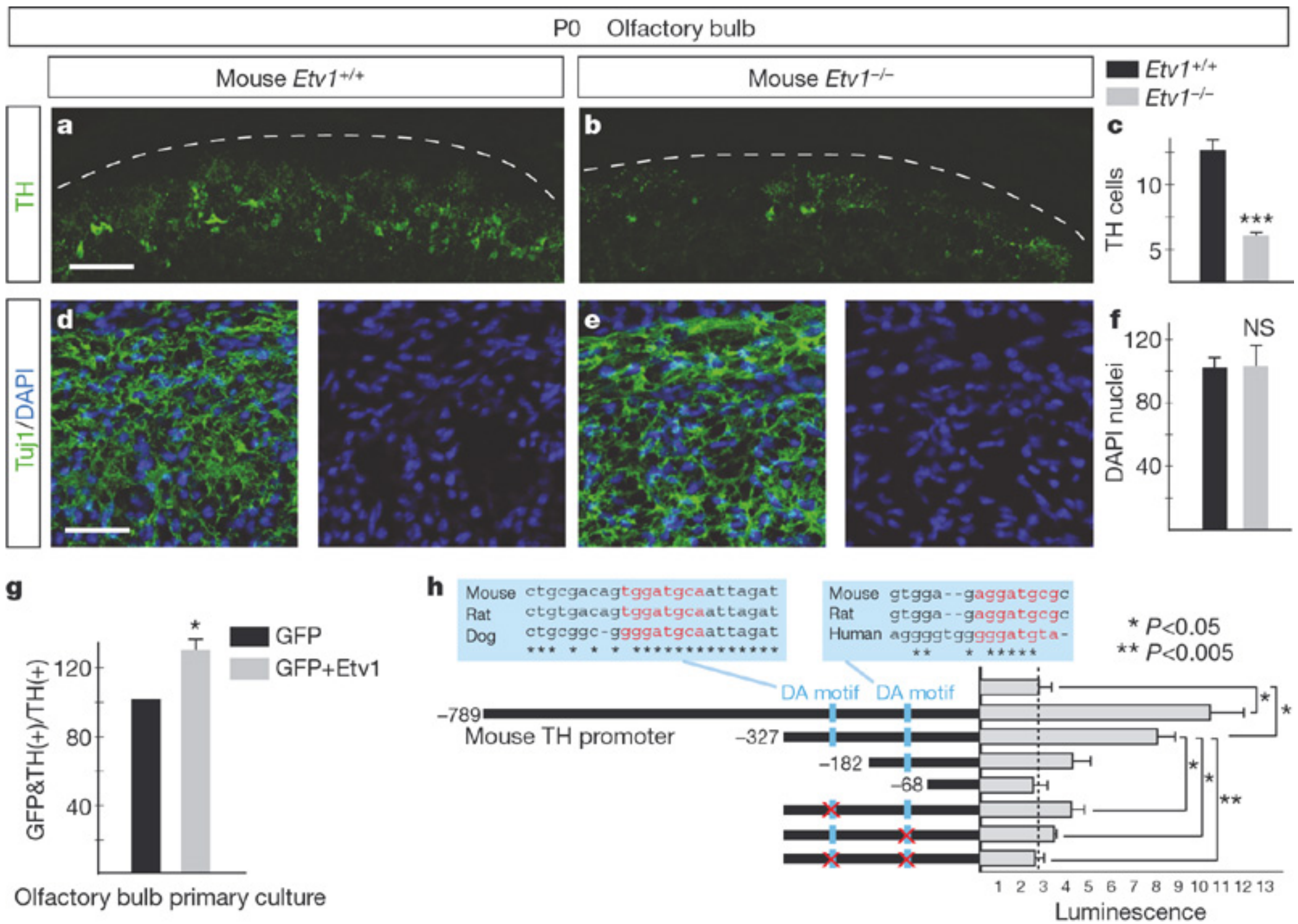
Ectopic *ast-1* expression can induce DA cell fate.



N Flames & O Hobert *Nature* **000**, 1-5 (2009) doi:10.1038/nature07929

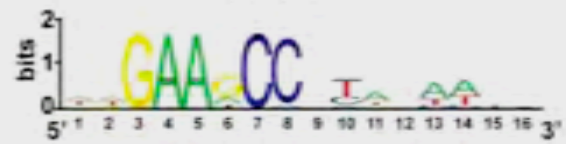
nature

Mouse Etv1 is necessary for the olfactory bulb DA neuron specification



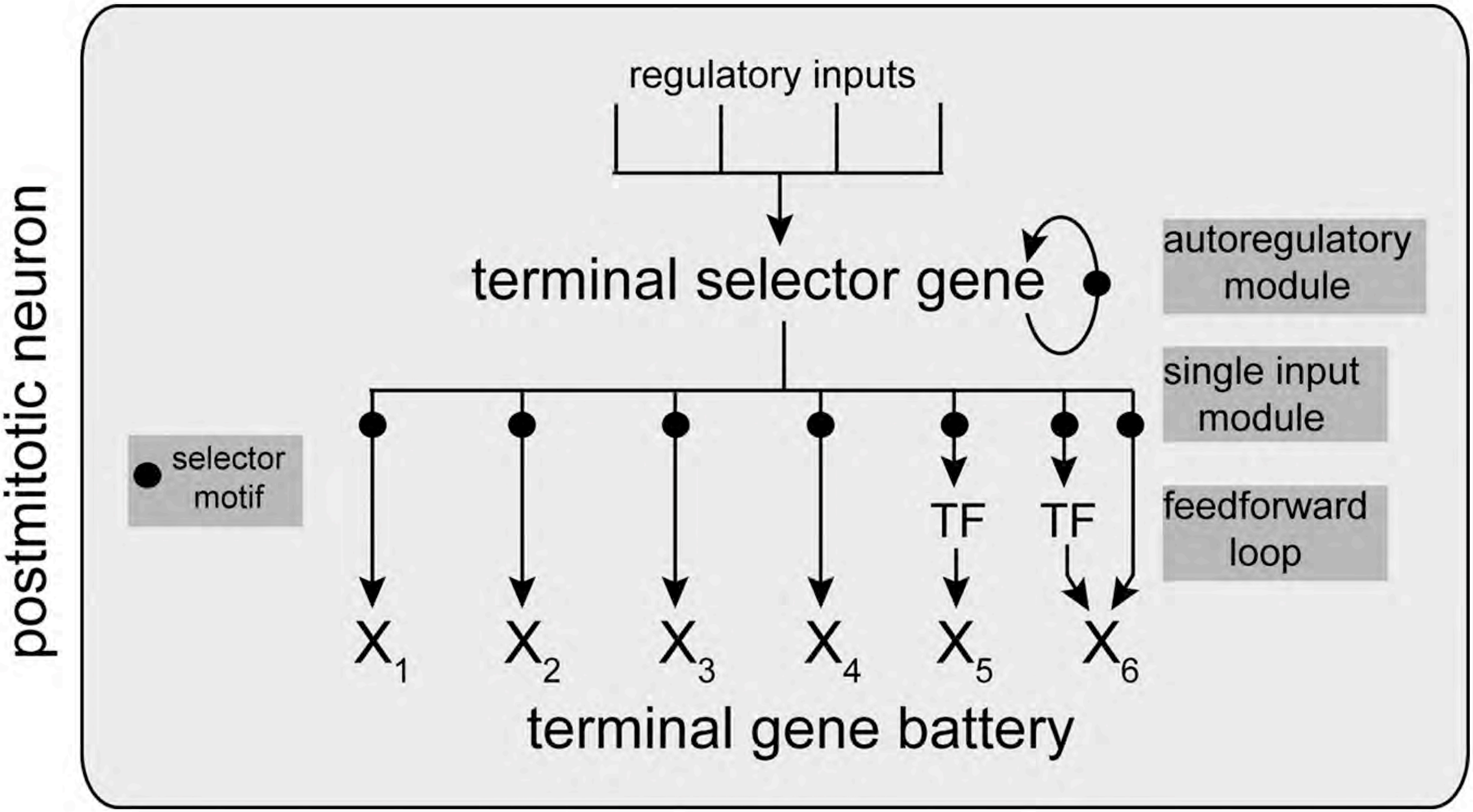
N Flames & O Hobert *Nature* **000**, 1-5 (2009) doi:10.1038/nature07929

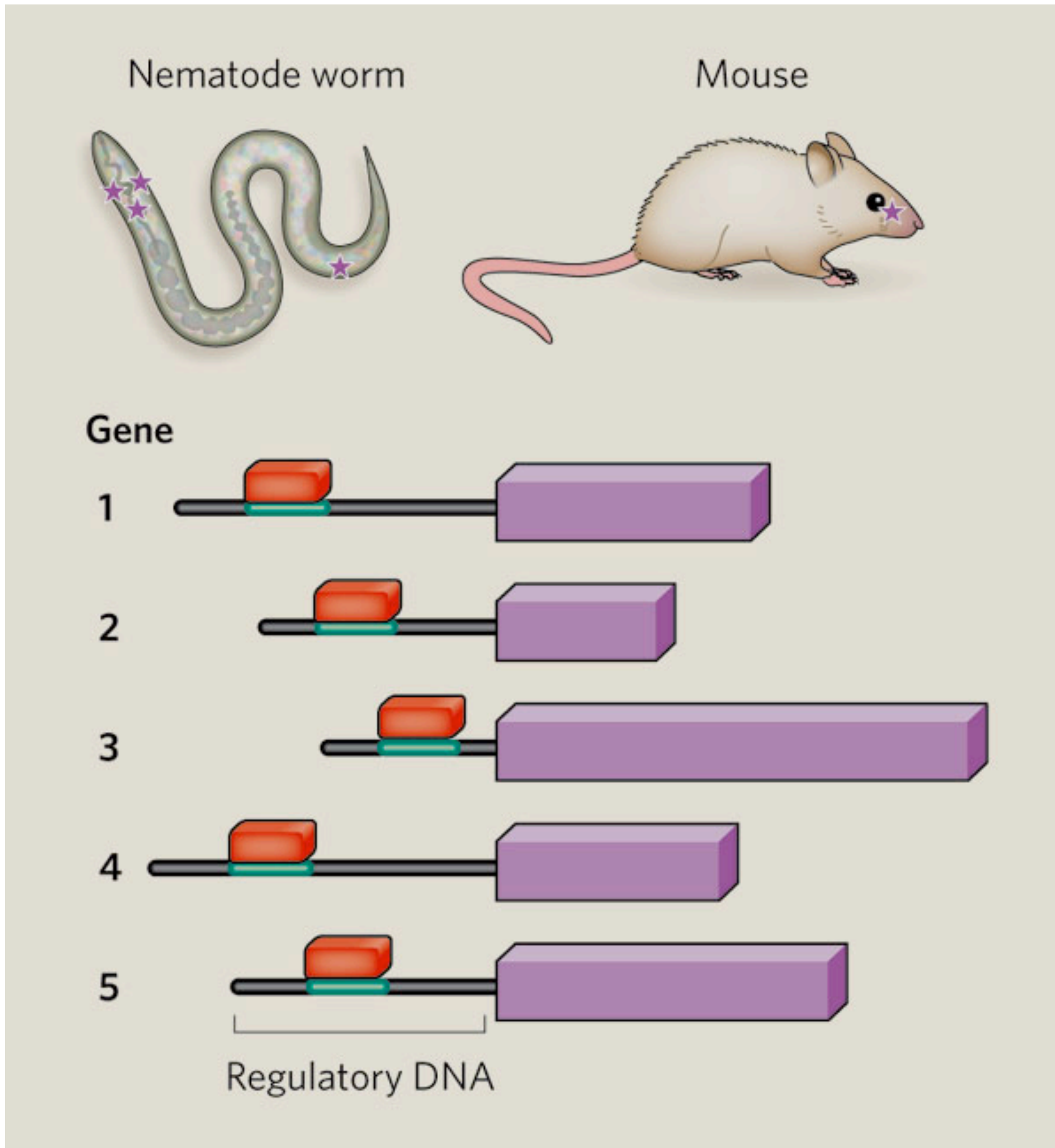
Table 1. Examples of neuronal terminal selector genes in *C. elegans*

Terminal selector gene	Neuron class	Selector motif	Sufficiency of motif
CHE-1 zinc finger transcription factor	ASE sensory neurons	ASE motif 	Yes
TTX-3/CEH-10 LIM/Prd homeodomain dimer	AIY interneurons	AIY motif 	Yes
AST-1 ETS-type transcription factor	All dopaminergic neurons	DA motif 	Yes
MEC-3/UNC-86 LIM/POU homeodomain dimer	Mechanosensory neurons		Yes
UNC-30 Prd-type homeodomain	GABAergic ventral cord motorneurons		ND

See text for references. ND, not determined.

Serial analysis of gene expression (SAGE)
ASE- two bilaterally symmetric sensory neurons
AIY – two bilaterally symmetric interneurons for processing sensory information


postmitotic neuron
regulatory inputs
terminal selector gene
autoregulatory module
single input module
selector motif
feedforward loop
TF
TF
X1
X2
X3
X4
X5
X6
terminal gene battery


Nematode worm
Mouse
Gene
1
2
3
4
5
Regulatory DNA

Synapse biology

- Eighteenth century -Luigi Galvani's description of "animal electricity"
- He induced the contraction of limb muscles when he inserted a metal hook into the medulla of the frog and attached the other end to an iron railing
- Charles Sherrington coined the term ''synapse'' to refer to the special connections from one nerve cell to another that facilitated the transmission of nervous impulses

Synapse Biology

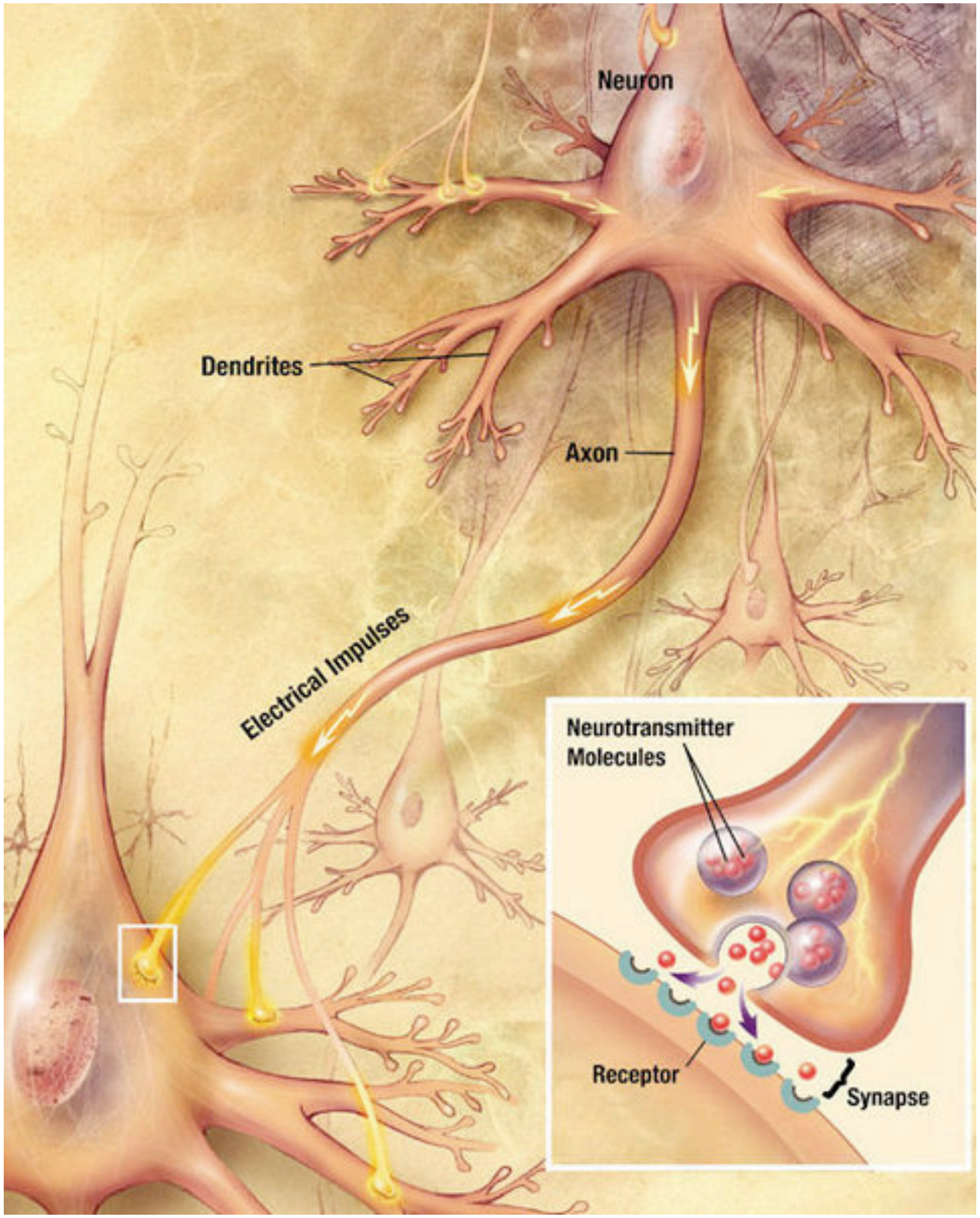
- Santiago Ramo´n y Cajal (1852-1934) was able to visualize the morphology of individual cells in the context of the nervous system using Golgi's silver nitrate stain

Synapse Biology

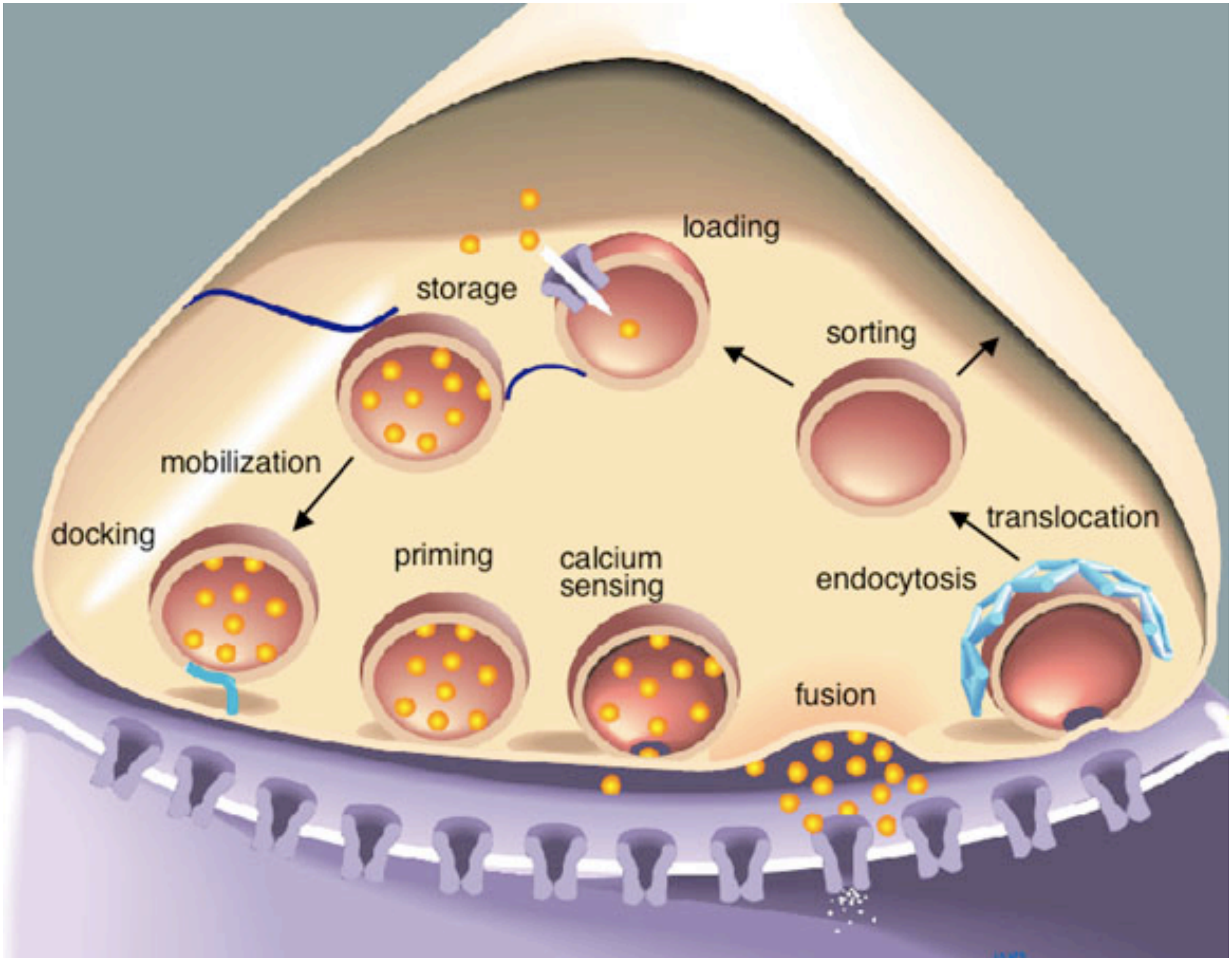
- Two general categories of synapses: electrical synapses and chemical synapses
- Electrical synapses are gap junctions that allow bidirectional propagation of signals
- Chemical synapses allow communication between discontinuous neurons via the highly regulated secretion of chemical intermediate signals

Synapse biology

- Although sponges (Phylum Porifera) are the only metazoans (so far) without a nervous system, it was found that sponges express a nearly complete set of postsynaptic protein homologues that are hypothesized to assemble into synaptic-like scaffolds. Although sponges do not have neurons, these postsynaptic-like structures are hypothesized to act as chemosensory structures capable of responding to environmental cues (Sakaryaet al., 2007, A post-synaptic scaffold at the origin of the animal kingdom. PLoS ONE 2, e506.)



The worm book



The worm book