UNIVERSITY OF OXFORD

University of Essex

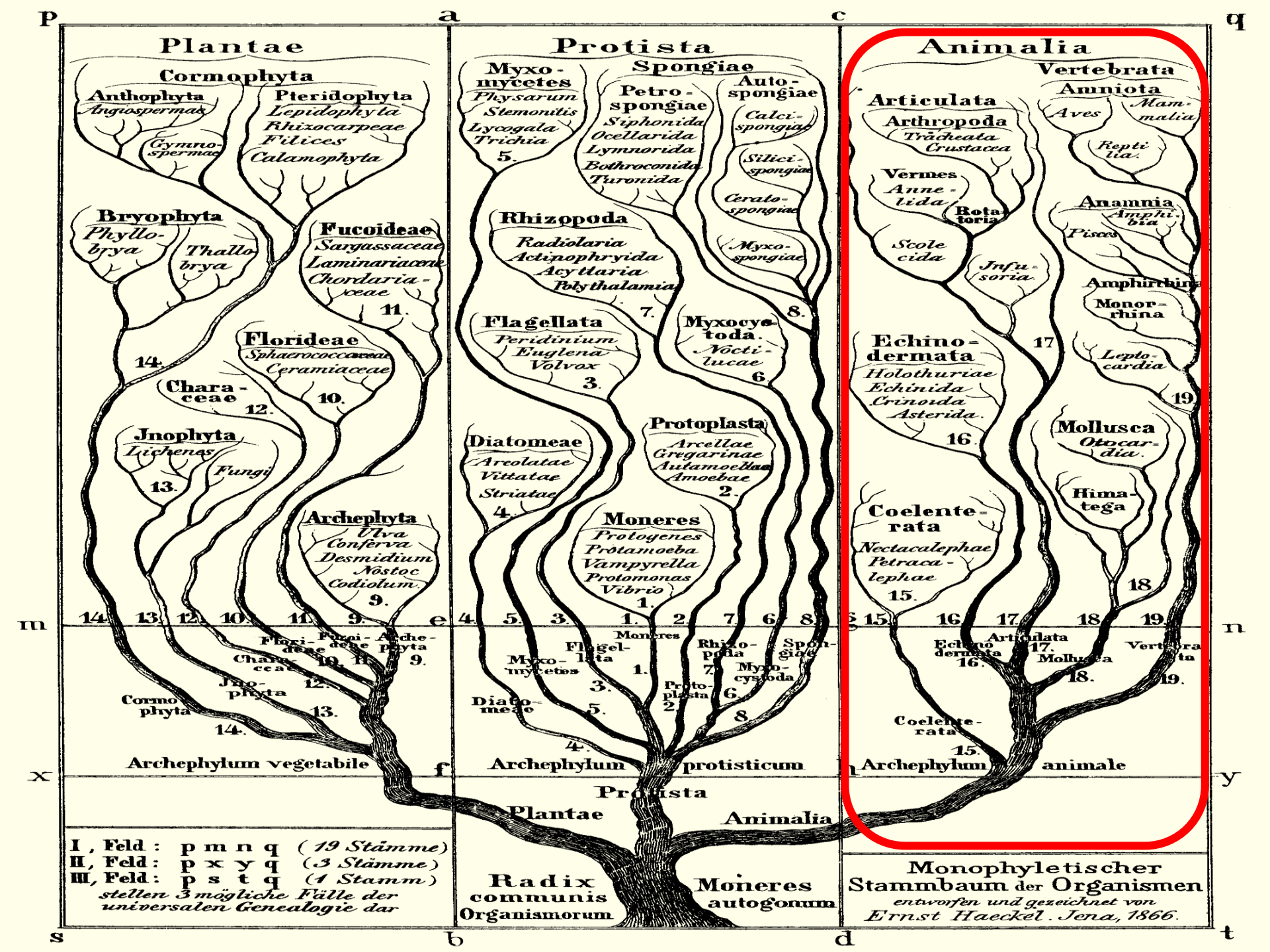
RECONSTRUCTING ANCESTRAL GENOMES TO UNDERSTAND MAJOR TRANSITIONS

Jordi Paps

@JordiPaps

Public

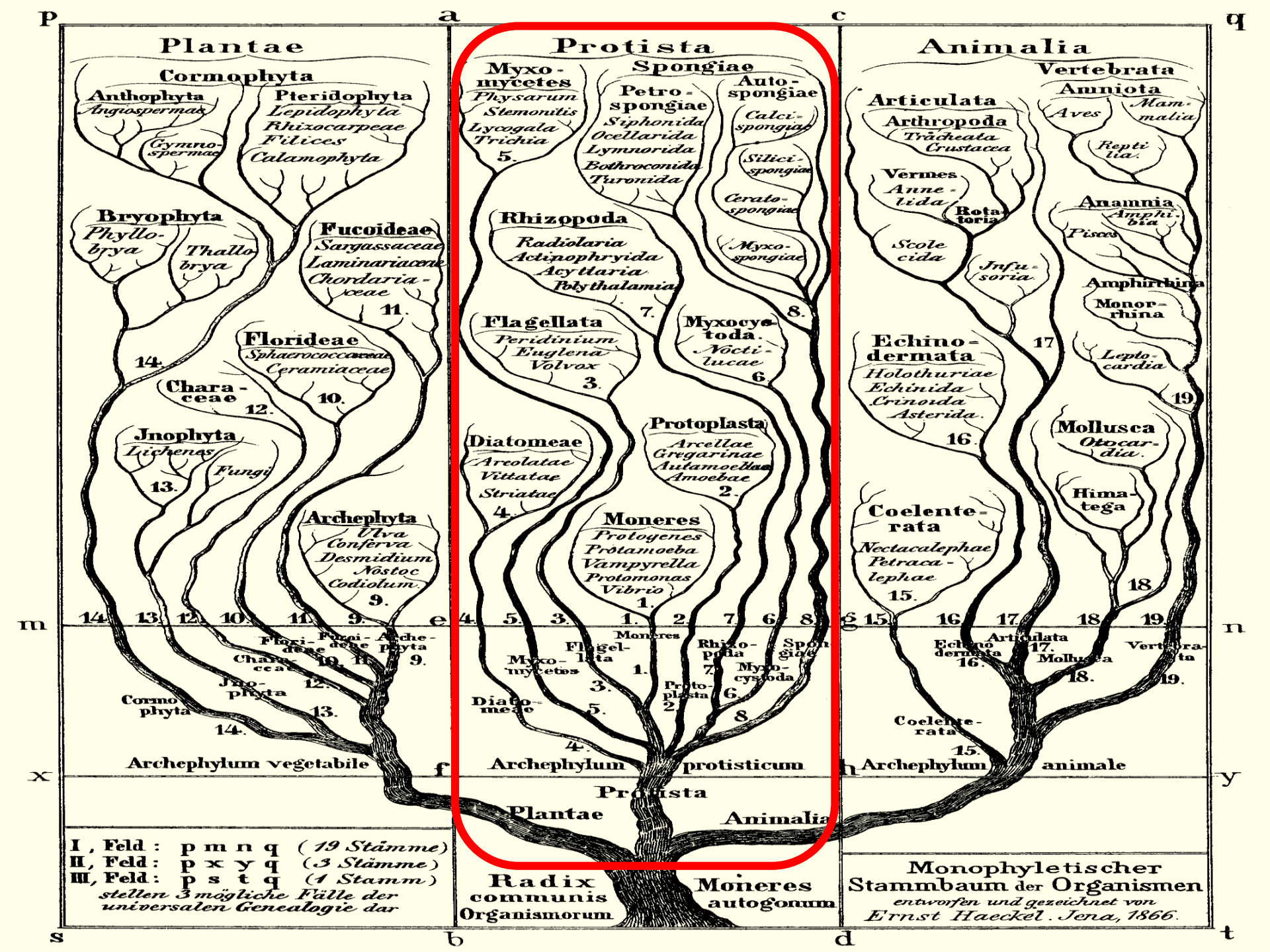
University of BRISTOL


Plantae
Cormophyta
Anthophyta
Angiospermae
Gymnospermae
Pteridophyta
Lepidophyta
Rhizocarpeae
Filices
Calamophyta
Bryophyta
Phyllobrya
Thallobrya
Fucoideae
Sargassaceae
Laminariaceae
Chordariaceae
11.
Florideae
Sphaerococcaceae
Ceramiaceae
10.
14.
Characeae
12.
Thallophyta
Lichenes
Fungi
13.
Archephyta
Ulva
Conferva
Desmidium
Nostoc
Codiolum
9.
14. 13. 12. 10. 11. 9.
Archephylum vegetabile
Protista
Myxomycetes
Physarum
Stemonitis
Lycogala
Trichia
5.
Spongiae
Petrospongiae
Siphonida
Ocellarida
Lymnorida
Bothroconida
Turonida
Autospongiae
Calcispongiae
Silicispongiae
Cerato-spongiae
Myxospongiae
8.
Rhizopoda
Radiolaria
Actinophryida
Acyttaria
Polythalamia
7.
Flagellata
Peridinium
Euglena
Volvox
3.
Myxocytoda
Noctilucae
6.
Protoplasta
Arcellae
Gregarinae
Autamoebae
Amoebae
2.
Diatomeae
Arcolatae
Vittatae
Striatae
4.
Moneres
Protogenes
Protamoeba
Vampyrella
Protomonas
Vibrio
1.
4. 5. 3. 1. 2. 7. 6. 8.
Archephylum protisticum
Protista
Plantae
Animalia
Radix communis Organismorum
Moneres autogonum
Animalia
Vertebrata
Amniota
Aves
Mammalia
Reptilia
Articulata
Arthropoda
Tracheata
Crustacea
Vermes
Annelida
Rotatoria
Scolecida
Infusoria
Anamnia
Amphibia
Pisces
Amphirhina
Monorhina
Leptocardia
19.
Echinodermata
Holothuriae
Echinida
Crinoida
Asterida
16.
17.
Mollusca
Otocardia
Himatega
18.
Coelenterata
Nectacalephae
Petracalephae
15.
15. 16. 17. 18. 19.
Archephylum animale
I, Feld: p m n q (19 Stämme)
II, Feld: p x y q (3 Stämme)
III, Feld: p s t q (1 Stamm)
stellen 3 mögliche Fälle der universalen Genealogie dar
Monophyletischer Stammbaum der Organismen
entworfen und gezeichnet von
Ernst Haeckel. Jena, 1866.
p
a
c
q
m
e
g
n
x
f
h
y
s
b
d
t

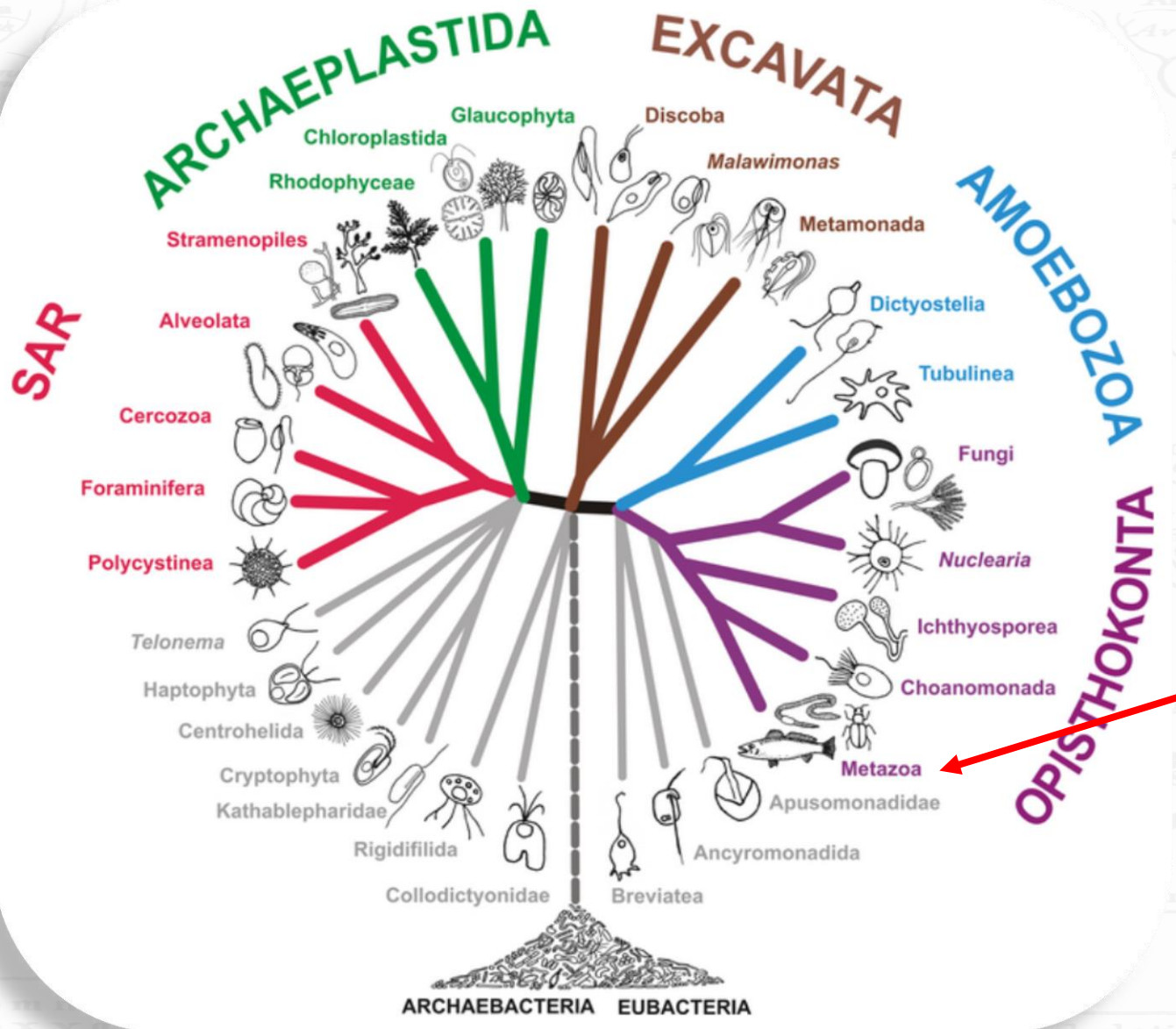
Animals

The Origin of the Animal Kingdom

Public


p
a
c
q
Plantae
Cormophyta
Anthophyta
Angiospermae
Gymno-
spermae
Pteridophyta
Lepidophyta
Rhizocarpeae
Filices
Calamophyta
Bryophyta
Phyllo-
brya
Thallo-
brya
Fucoideae
Sargassaceae
Laminariaceae
Chordaria-
ceae
11.
Florideae
Sphaerococcaceae
Ceramiaceae
10.
14.
Chara-
ceae
12.
Jnophyta
Lichenes
Fungi
13.
Archephyta
Ulva
Conferva
Desmidium
Nostoc
Codiolum
9.
Protista
Myxo-
mycetes
Physarum
Stemonitis
Lycogala
Trichia
5.
Spongiae
Petro-
spongiae
Siphonida
Ocellarida
Lymnorida
Bothroconida
Turonida
Auto-
spongiae
Calci-
spongiae
Silici-
spongiae
Cerato-
spongiae
Myxo-
spongiae
8.
Rhizopoda
Radiolaria
Actinophryida
Acyttaria
Polythalamia
7.
Flagellata
Peridinium
Euglena
Volvox
3.
Myxocyto-
toda.
Noctilucae
6.
Diatomeae
Arcolatae
Vittatae
Striatae
4.
Protoplasta
Arcellae
Gregarinae
Autamoebae
Amoebae
2.
Moneres
Protogenes
Protamoeba
Vampyrella
Protomonas
Vibrio
1.
Animalia
Vertebrata
Amniota
Aves
Mam-
malia
Reptilia.
Articulata
Arthropoda
Tracheata
Crustacea
Vermes
Anne-
lida
Rota-
toria
Scole-
cida
Infu-
soria
Anamnia
Amphi-
bia
Pisces
Amphirhina
Monor-
rhina
17
Echino-
dermata
Holothuriae
Echinida
Crinoida
Asterida.
16.
Lepto-
cardia
19.
Mollusca
Otocar-
dia.
Hima-
tega
18.
Coelente-
rata
Nectacalephae
Petraca-
lephae
15.
m
n
e
g
14. 13. 12. 10. 11. 9. 4. 5. 3. 1. 2. 7. 6. 8. 15. 16. 17. 18. 19.
Flagi-
dese
Fungi
Archephyta
Chara-
ceae
Jno-
phyta
Corno-
phyta
Moneres
Flagel-
lata
Myco-
mycetes
Diato-
meae
Proto-
plasta
Rhizo-
poda
Spon
giae
Myxo-
cystoda
Articulata
Echino-
dermata
Mollusca
Verte-
brata
Coelente-
rata
x
y
f
h
Archephylum vegetabile
Archephylum protisticum
Archephylum animale
Protista
Plantae
Animalia
I, Feld: p m n q (19 Stämme)
II, Feld: p x y q (3 Stämme)
III, Feld: p s t q (1 Stamm)
stellen 3 mögliche Fälle der universalen Genealogie dar
Radix
communis
Organismorum
Moneres
autogonum
Monophyletischer
Stammbaum der Organismen
entworfen und gezeichnet von
Ernst Haeckel. Jena, 1866.
s
b
d
t

Where?

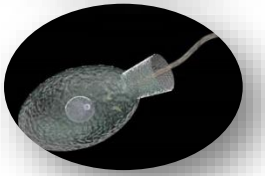


Adl *et al* 2012

Public

Opisthokonta

Animals

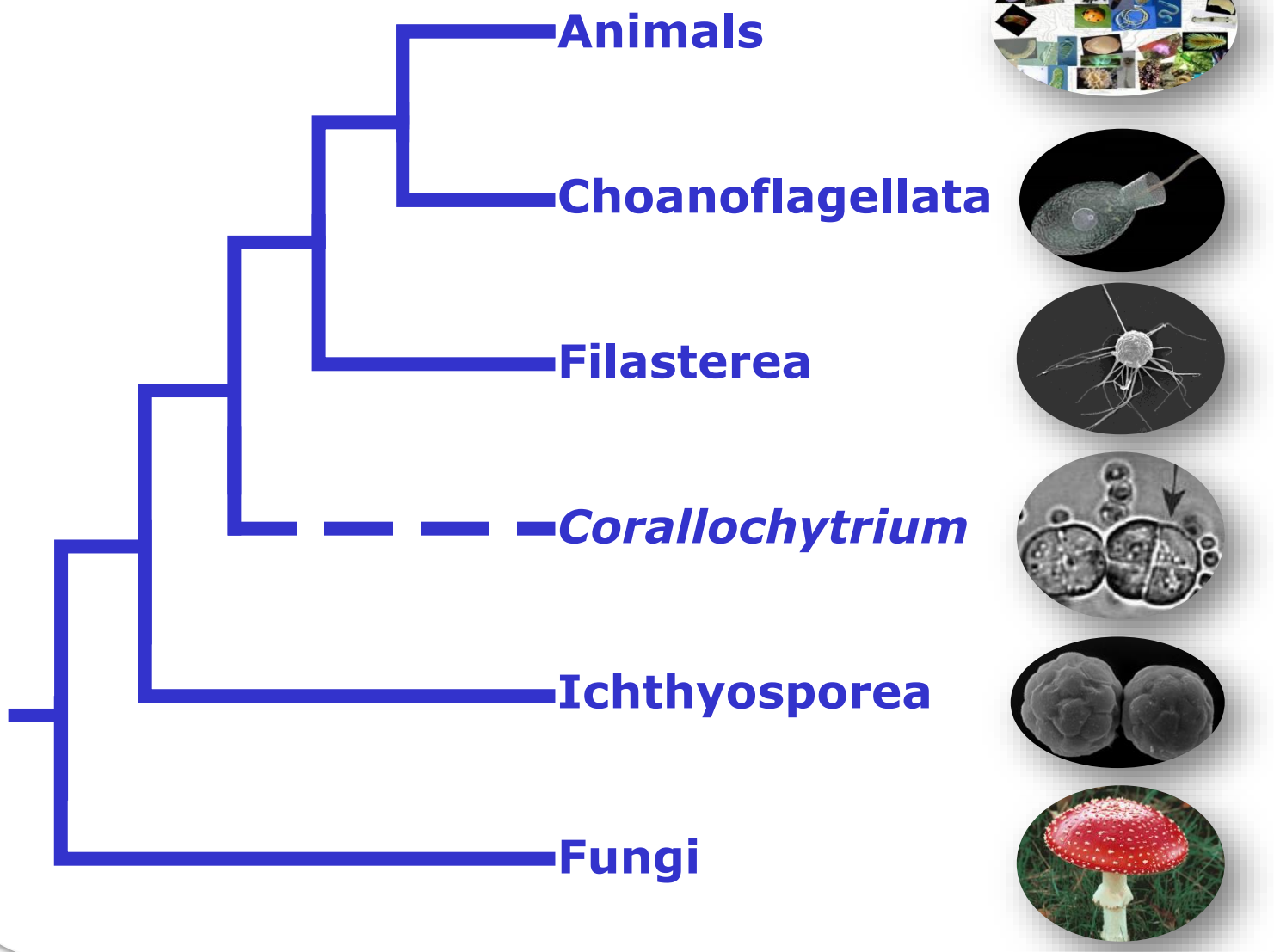


Choanoflagellata

Fungi

Public

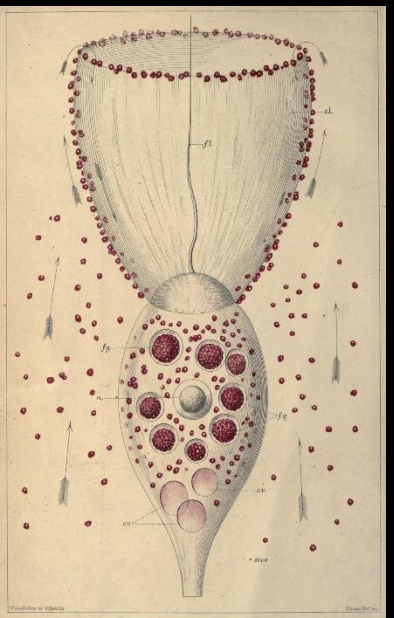
Opisthokonta

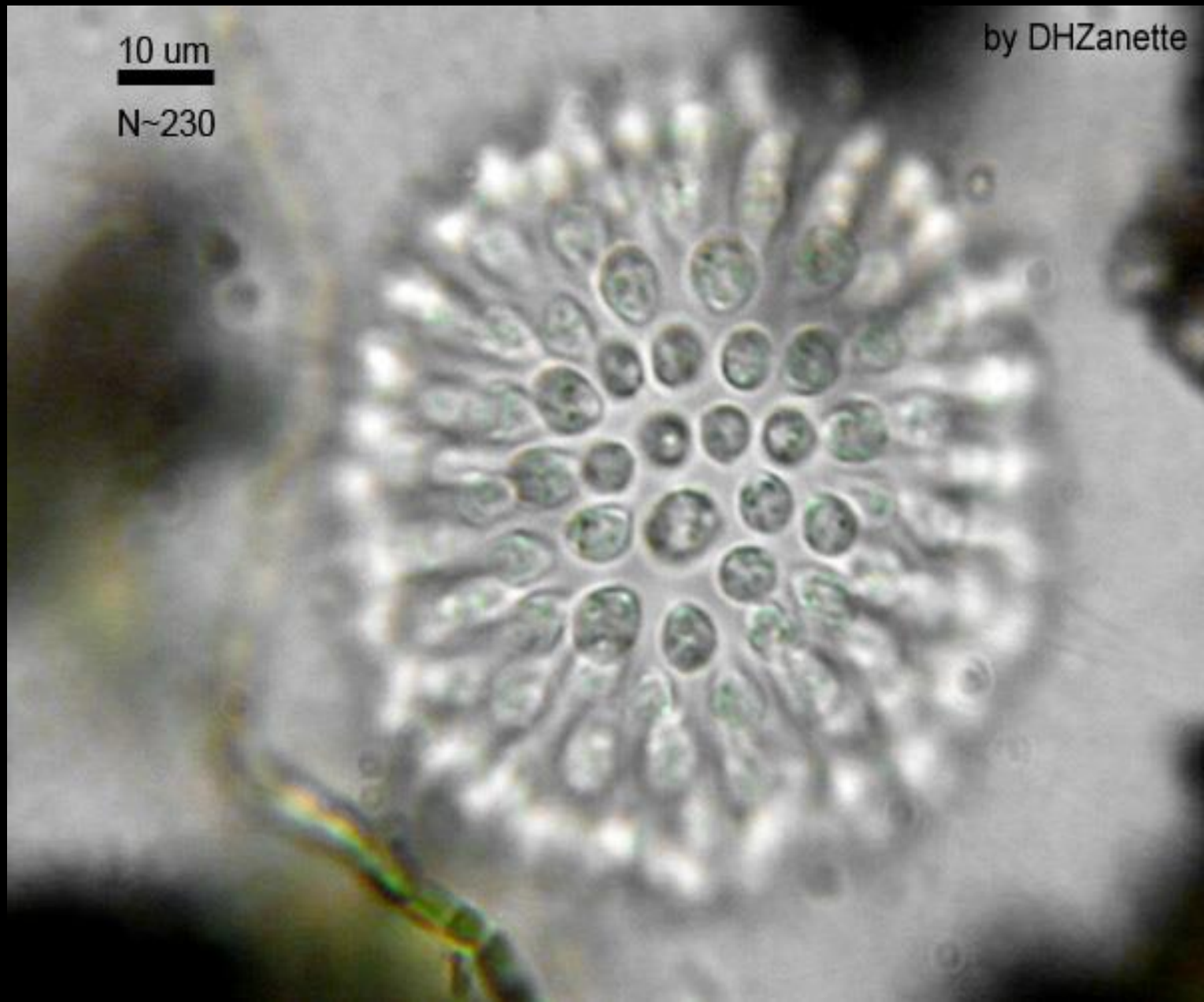


Public

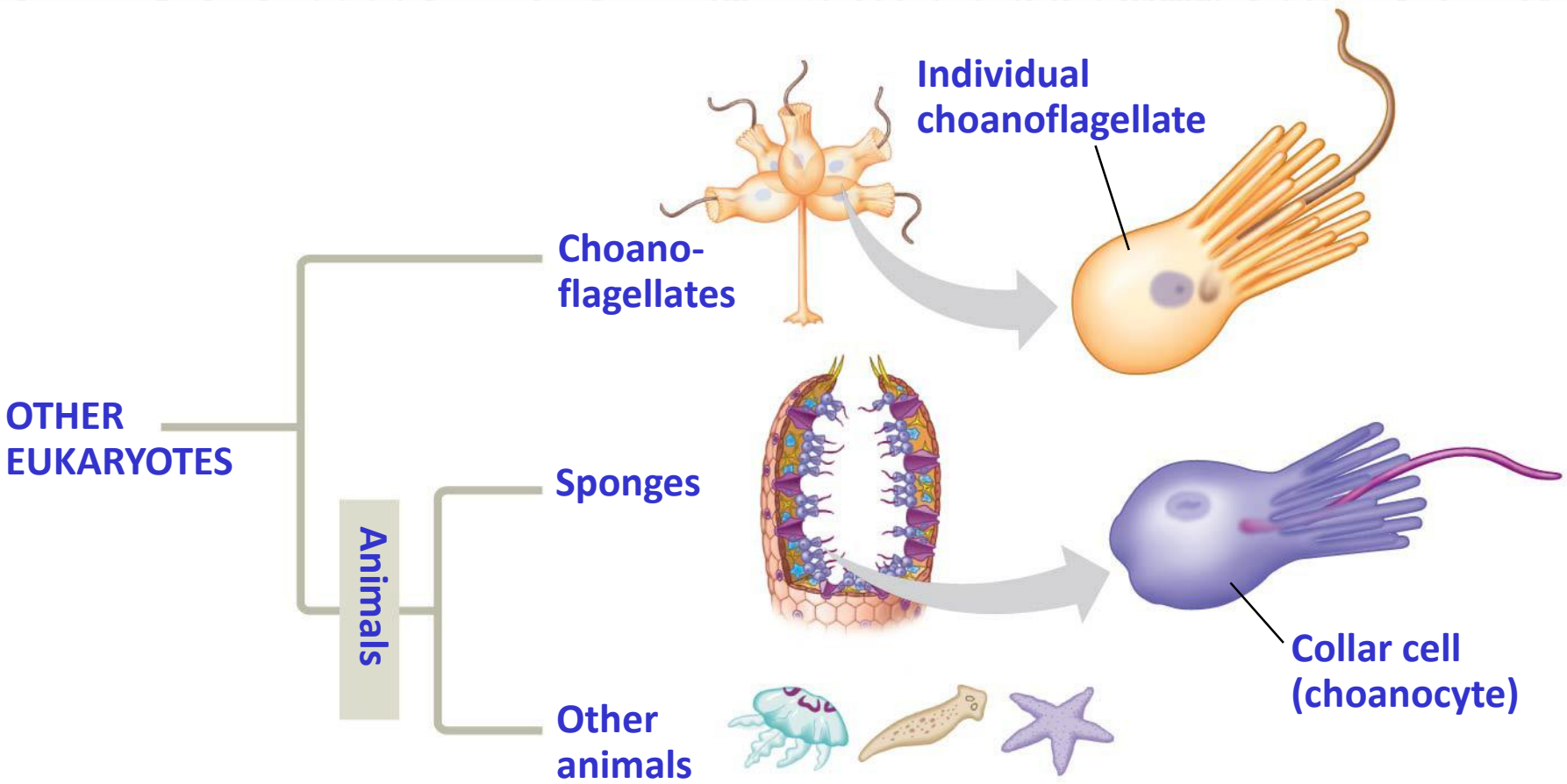
Choanoflagellata

Nicole King



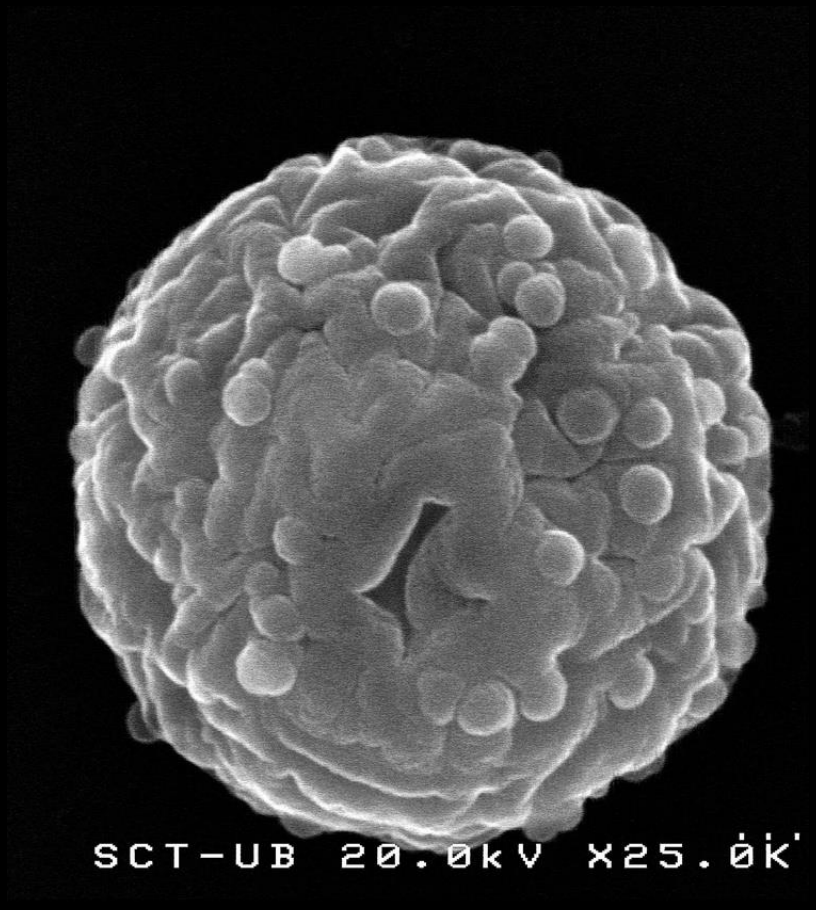


Origin of Multicellular Animals



- **Morphological** and **molecular** evidence points to **choanoflagellates** as the closest living relatives to animals

Filasterea (*Capsaspora*)



Ichthyosporea (*Sphaeroforma*)

Iñaki Ruiz-Trillo

When?

EON	ERA	PERIOD		
Phanerozoic	Cenozoic	Quaternary	Pleistocene	1.806
		Tertiary – Neogene	Pliocene	5.332
			Miocene	23.03
		Tertiary – Paleogene	Oligocene	33.9
			Eocene	55.8
			Paleocene	65.5
	Mesozoic	Cretaceous		145.5
		Jurassic		199.6
		Triassic		251
	Paleozoic	Permian		299
		Carboniferous – Pennsylvanian		318.1
		Carboniferous – Mississippian		359.2
		Devonian		416
		Silurian		443.7
		Ordivician		488.3
		Cambrian		542
Precambrian – Proterozoic	Neoproterozoic	Ediacaran		630
		Cryogenian		850
		Tonian		1000
	Mesoproterozoic	Stenian		1200
		Ectasian		1400
		Calymmian		1600
	Paleoproterozoic	Statherian		1800
		Orosirian		2050
		Rhyacian		2300
		Siderian		2500
Precambrian – Archean	Neoarchean			2800
	Mesoarchean			3200
	Paleoarchean			3600
	Eoarchean			4000
Hadean				4567

560 Mya Ediacaran biota

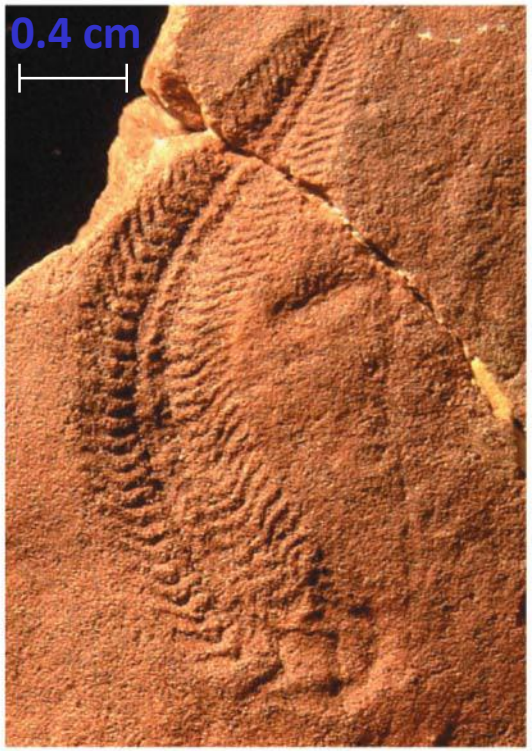
2,000 Mya Oldest eukaryote fossils

4,000 Mya Origin of life

Ediacaran biota

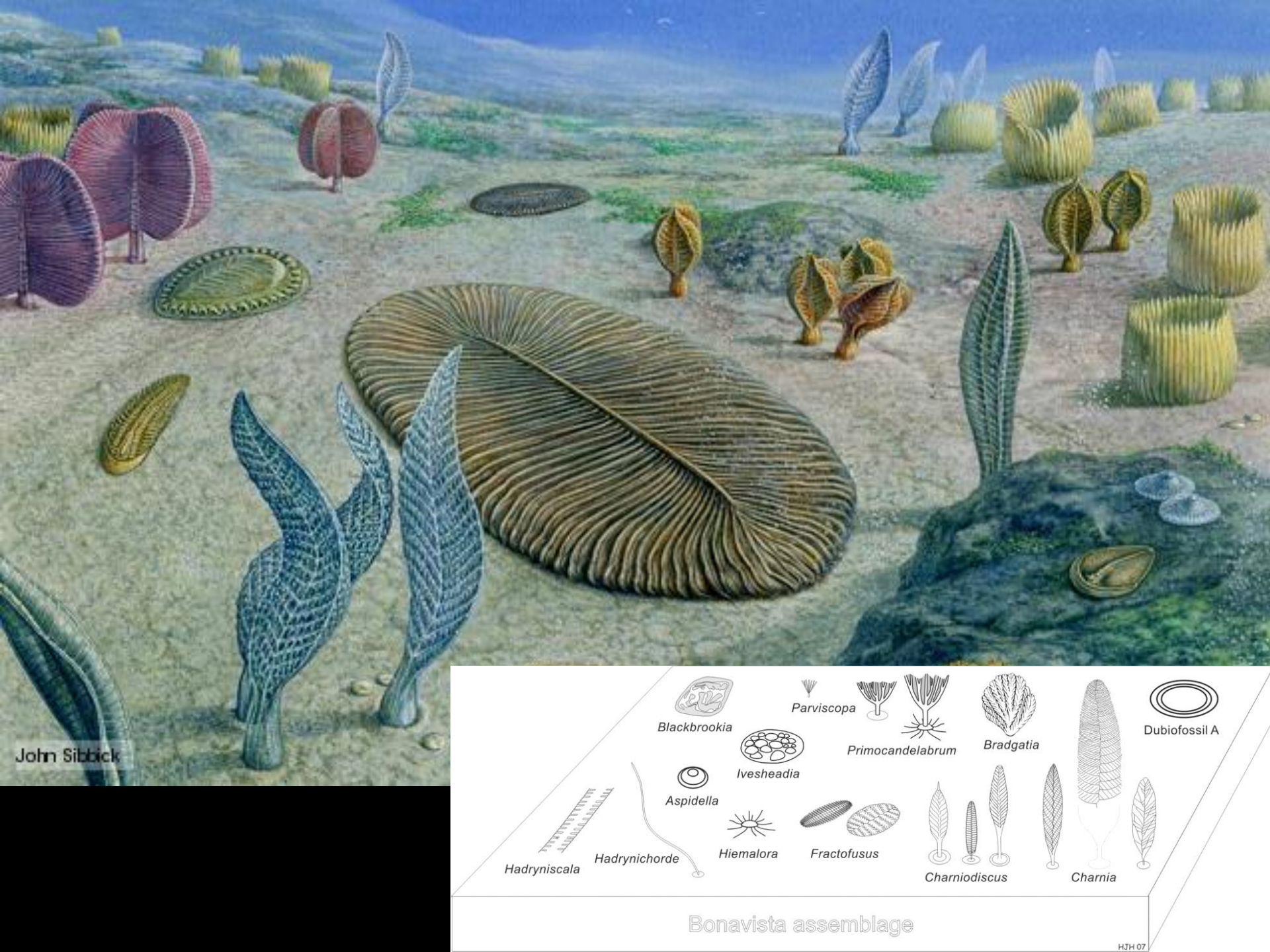
- **Ediacaran biota** (560 million years ago) composed by **multicellular organisms**. Strong debate about their nature: **animals or not?**

(a) ***Mawsonites spriggi***



(b) ***Spriggina floundersi***

Public


John Sibbick
Blackbrookia
Parviscopa
Primocandelabrum
Bradgatia
Dubiofossil A
Ivesheadia
Aspidella
Hadryniscala
Hadrynichorde
Hiemalora
Fractofusus
Charniodiscus
Charnia
Bonavista assemblage
HJH 07

When?

EON	ERA	PERIOD		
Phanerozoic	Cenozoic	Quaternary	Pleistocene	1.806
		Tertiary – Neogene	Pliocene	5.332
			Miocene	23.03
		Tertiary – Paleogene	Oligocene	33.9
			Eocene	55.8
			Paleocene	65.5
	Mesozoic	Cretaceous		145.5
		Jurassic		199.6
		Triassic		251
	Paleozoic	Permian		299
		Carboniferous – Pennsylvanian		318.1
		Carboniferous – Mississippian		359.2
		Devonian		416
		Silurian		443.7
		Ordivician		488.3
		Cambrian		542
Precambrian – Proterozoic	Neoproterozoic	Ediacaran		630
		Cryogenian		850
		Tonian		1000
	Mesoproterozoic	Stenian		1200
		Ectasian		1400
		Calymmian		1600
	Paleoproterozoic	Statherian		1800
		Orosirian		2050
		Rhyacian		2300
		Siderian		2500
Precambrian – Archean	Neoarchean			2800
	Mesoarchean			3200
	Paleoarchean			3600
	Eoarchean			4000
Hadean				4567

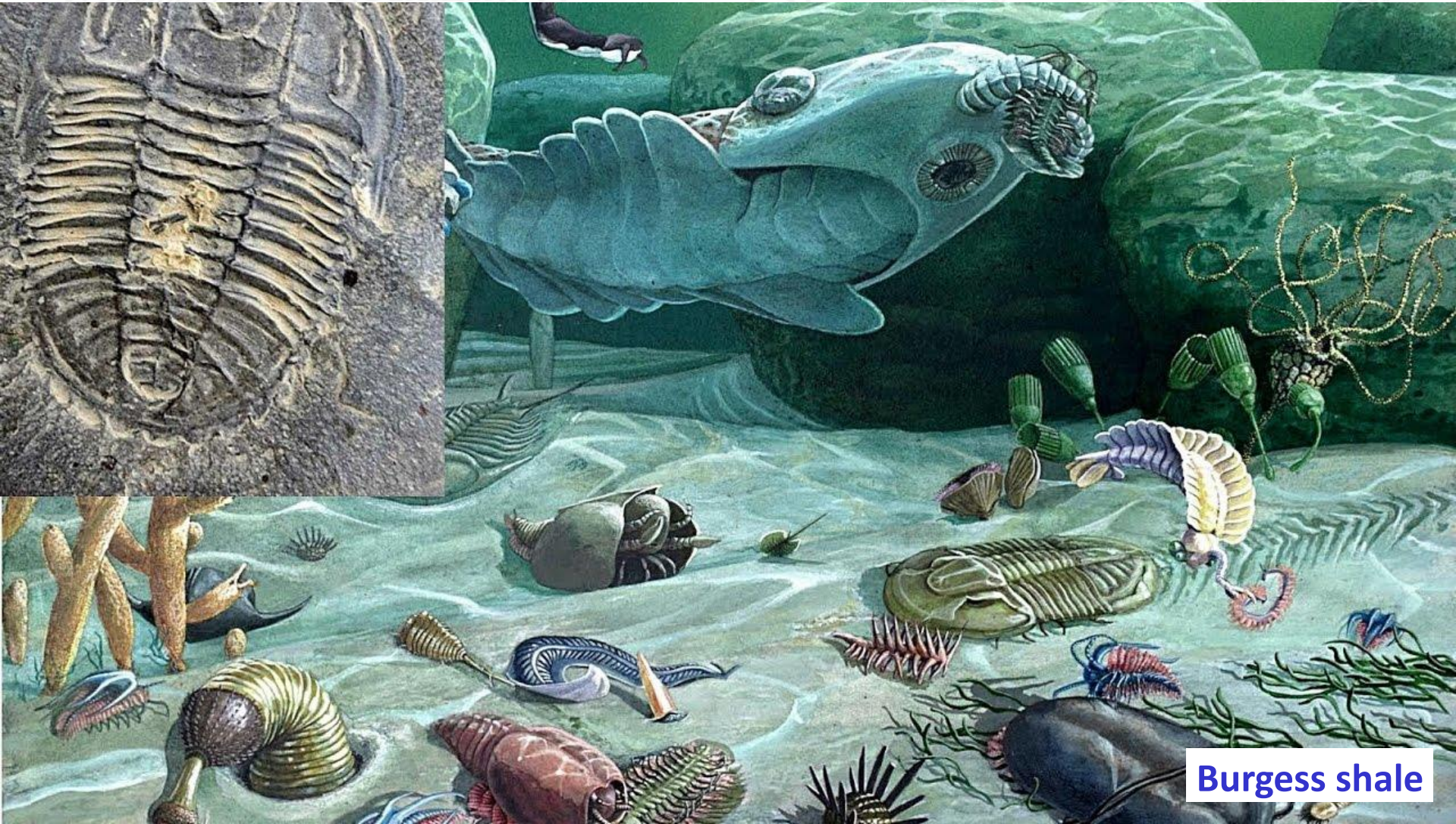
542 Mya Cambrian explosion

560 Mya Ediacaran biota

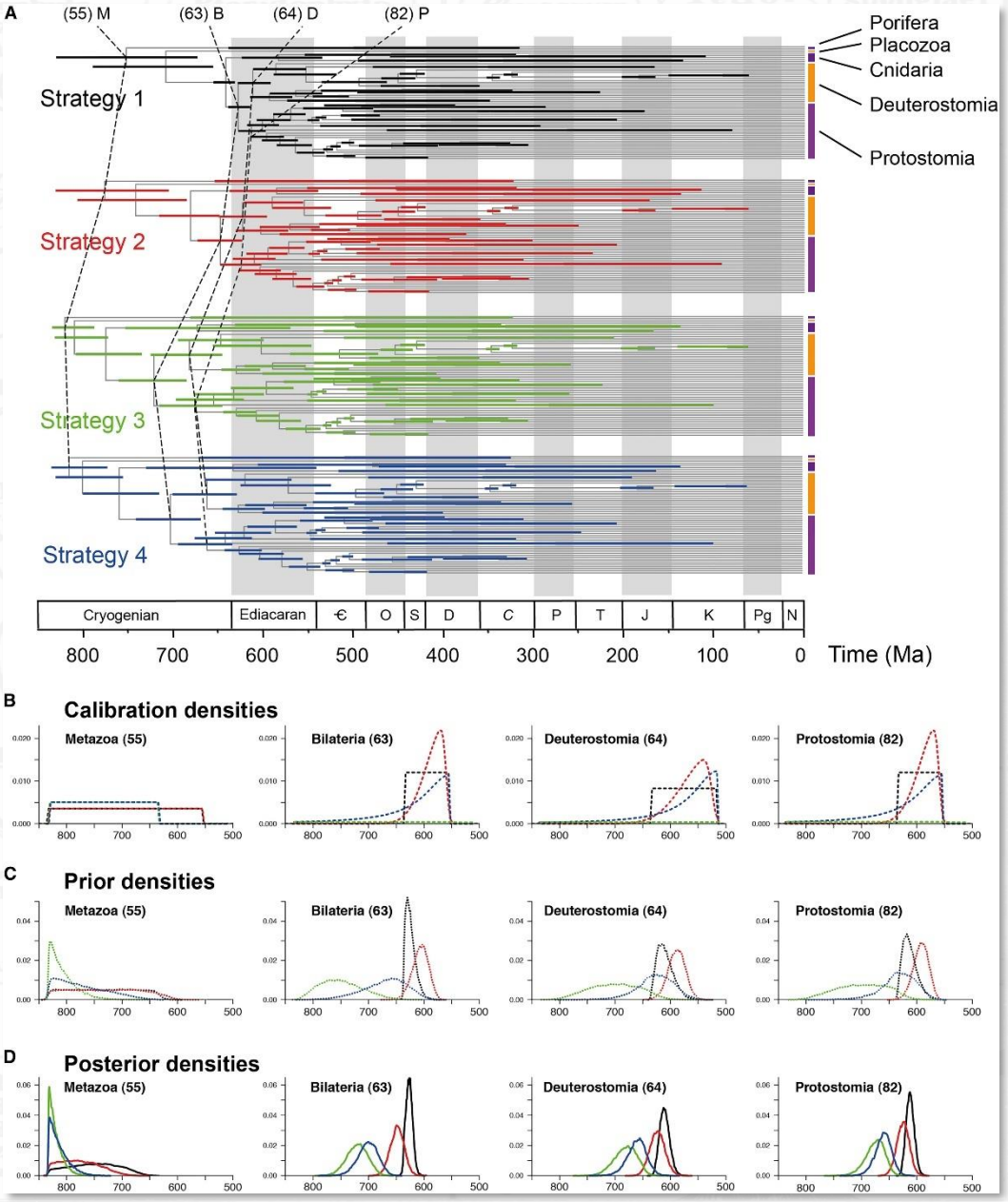
2,000 Mya Oldest eukaryote fossils

4,000 Mya Origin of life

The **Cambrian explosion** (535 to 525 Mya): **sudden fossil appearance** of all the major groups of **extant groups animals**



When?

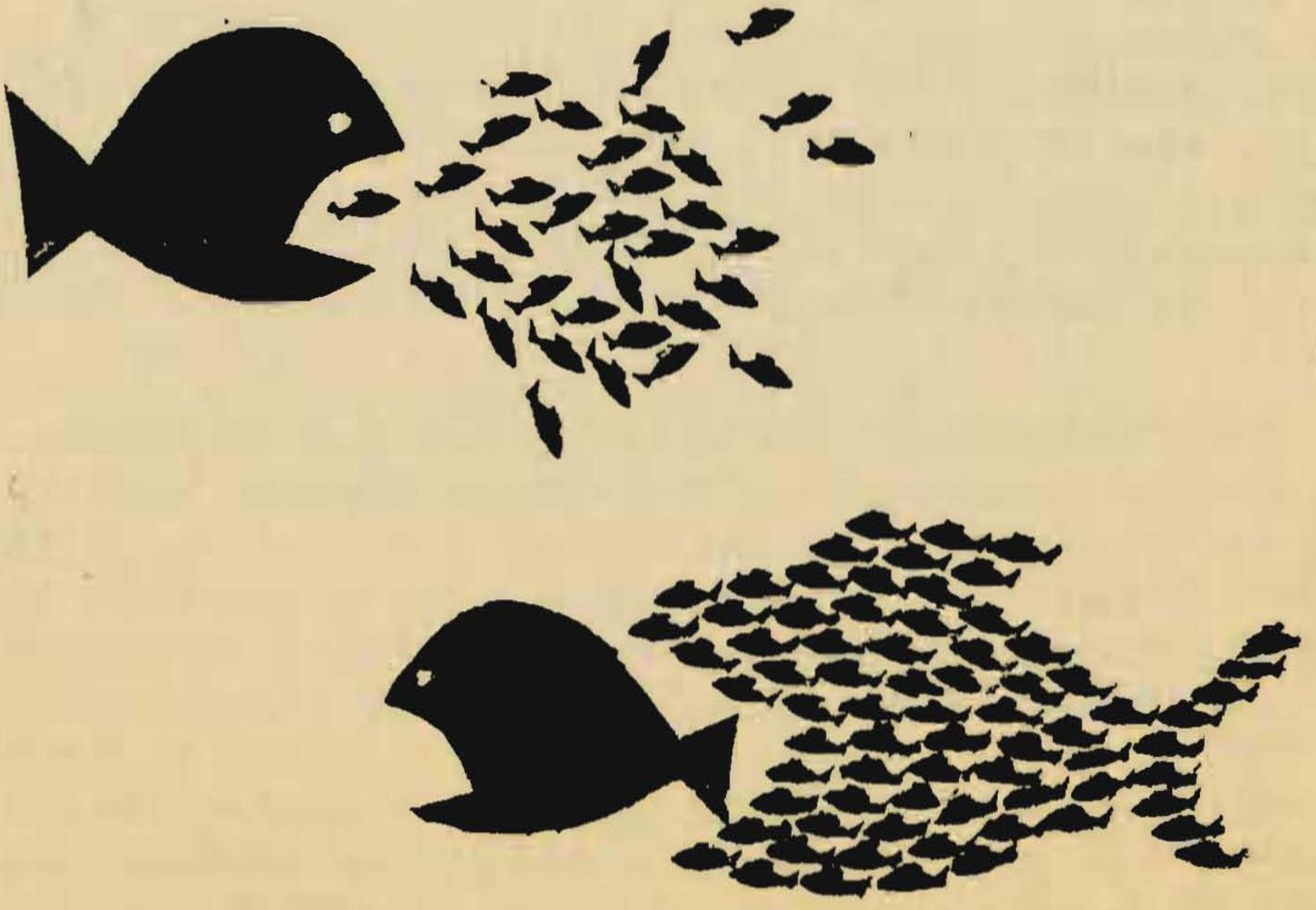


833–650 Ma

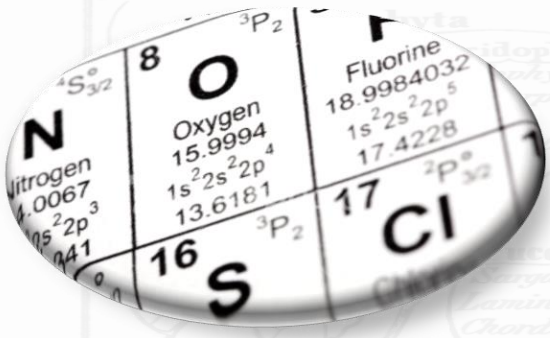
Dos Reis *et al* 2015

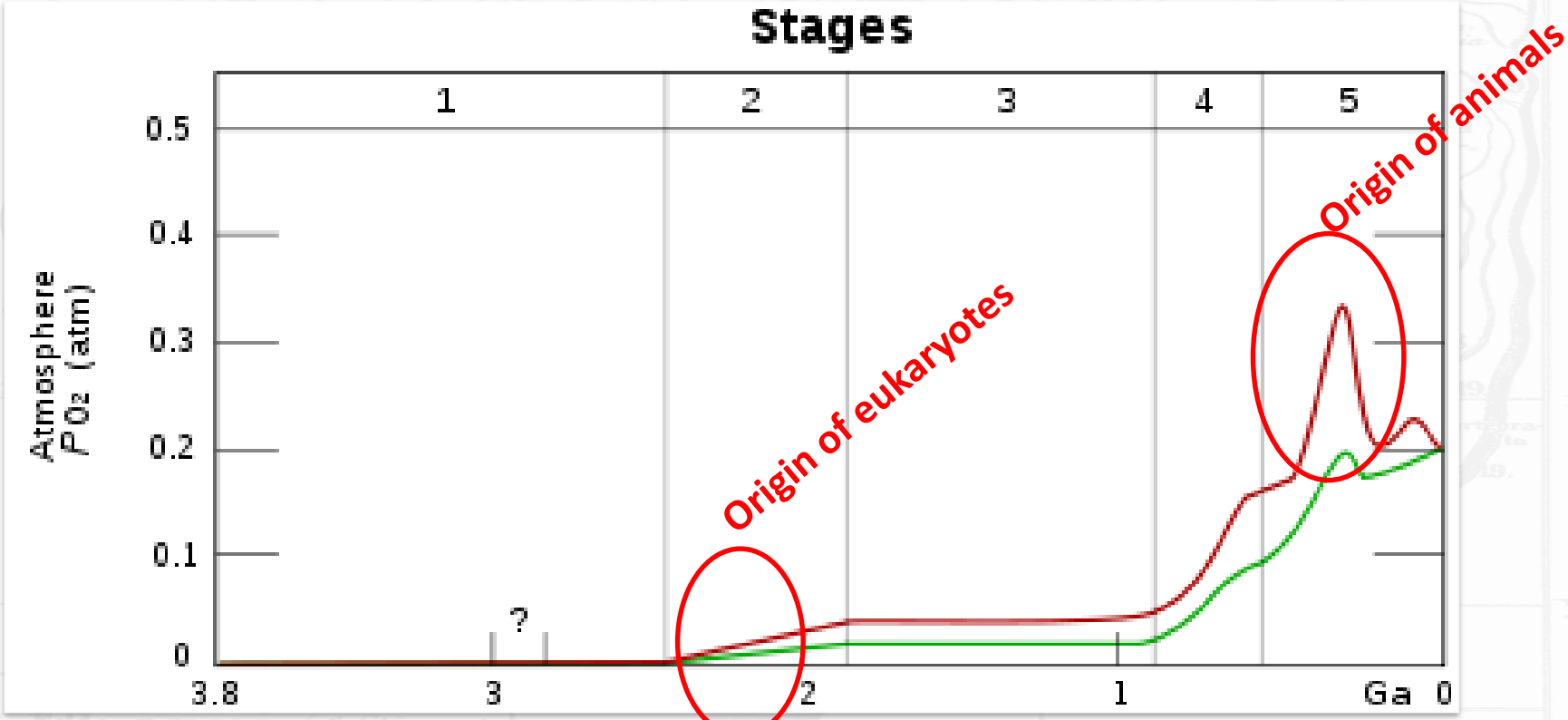
Public

Ecology



Environment

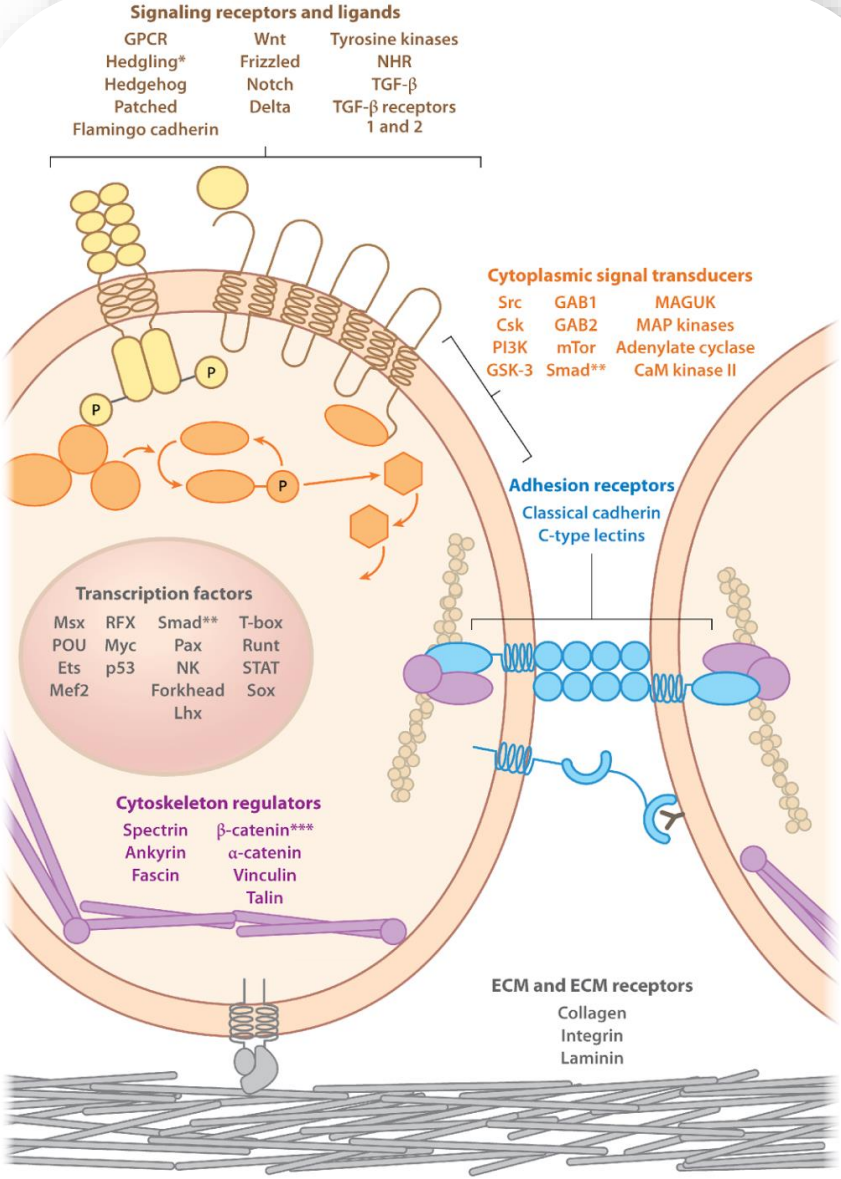




Public

Genome

Triggers



Richter DJ, King N. 2013.
Annu. Rev. Genet. 47:509–37

- **Gene regulation** (TFs,and signalling pathways)
- **Cell adhesion**
- **Cell type specialization**
- **Cell cycle**
- **Immunity**

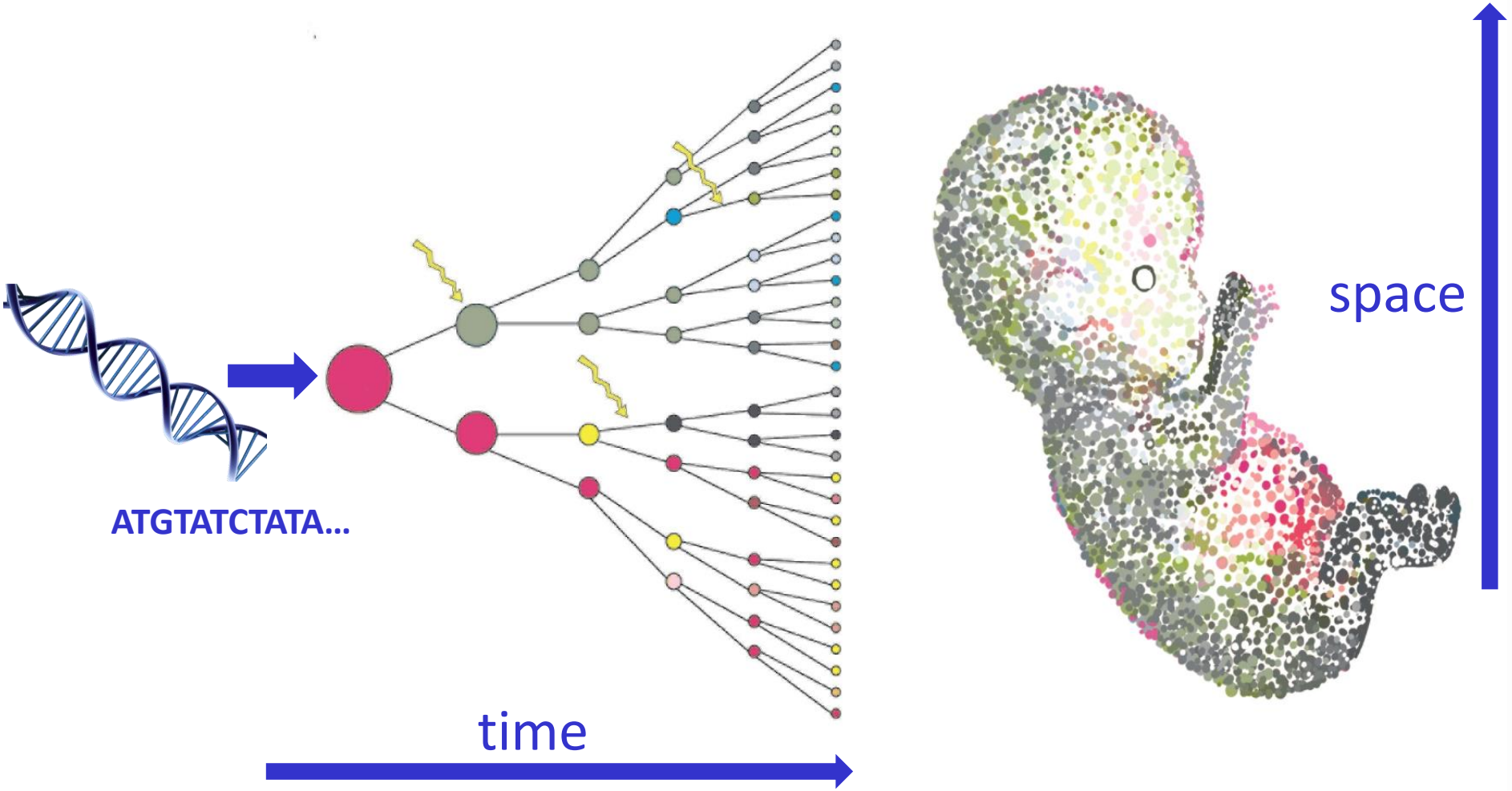
How to make a baby?

Public

How to make a baby…

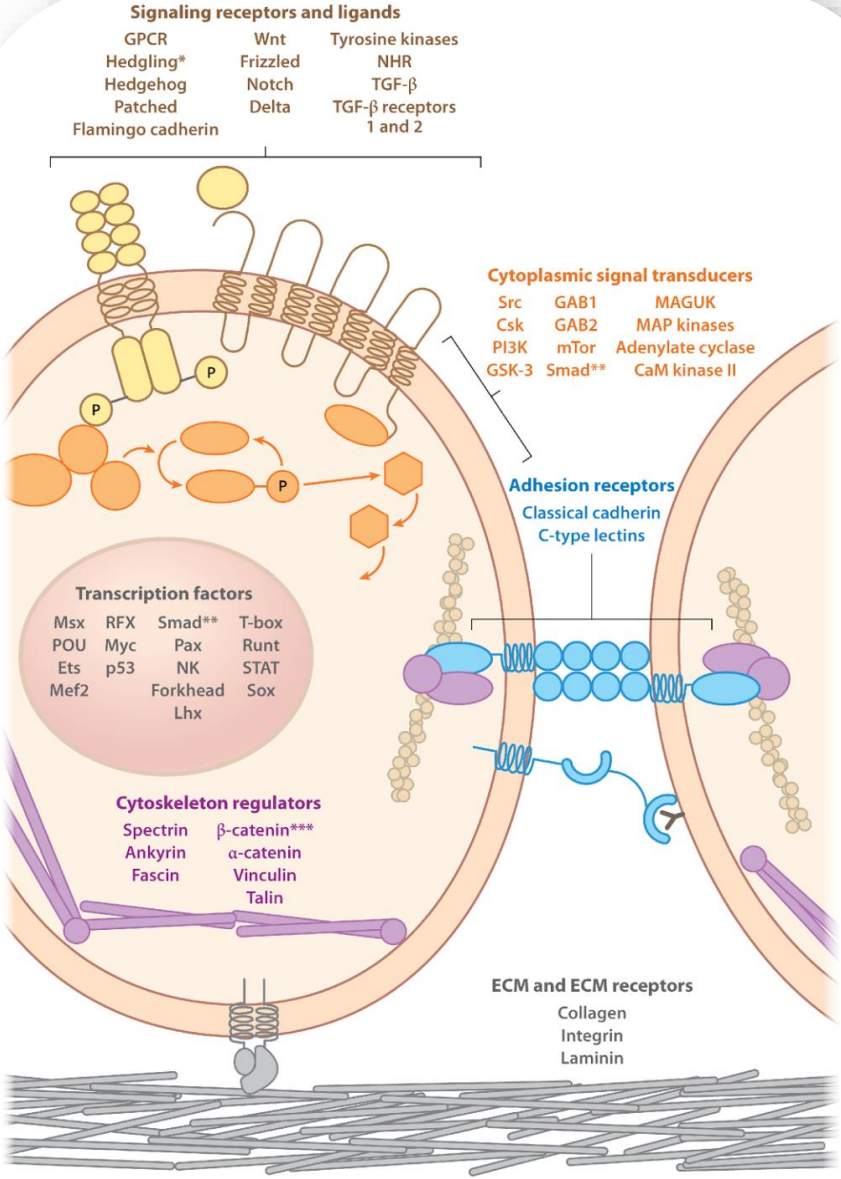
Public

Development converts info from 1D (DNA) to 4D



Public

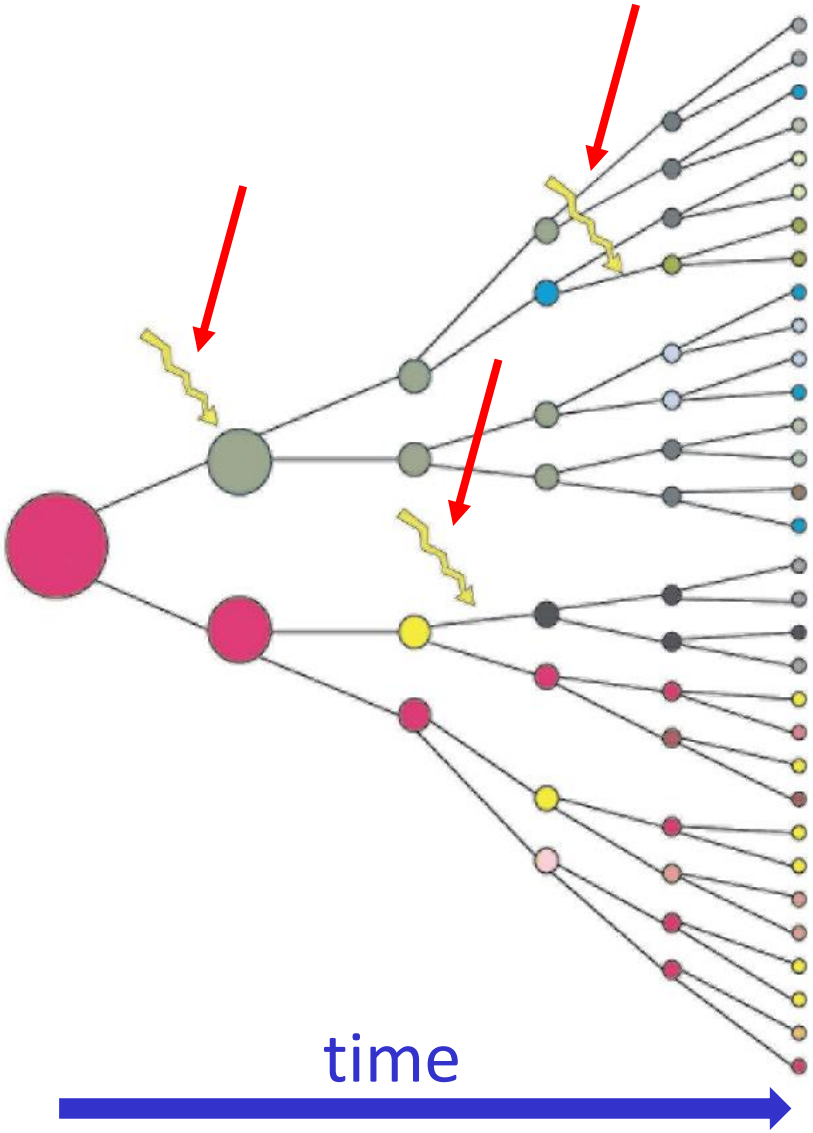
Genome

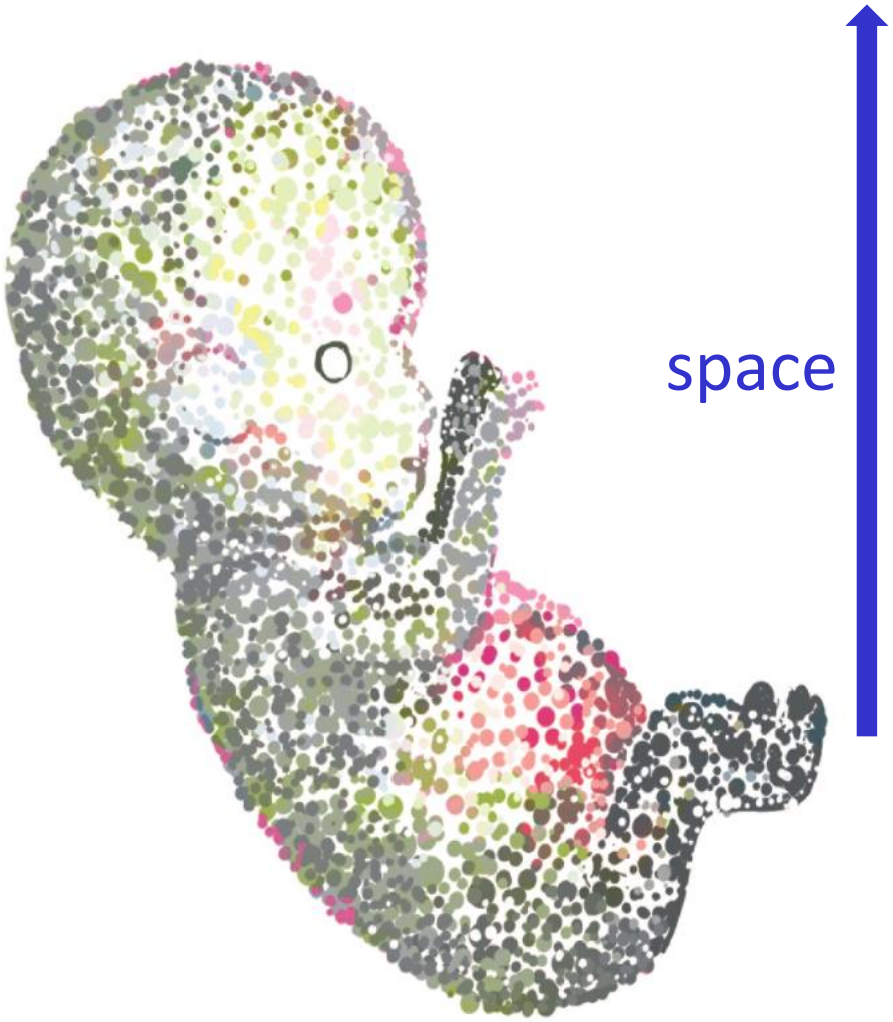


Richter DJ, King N. 2013.
Annu. Rev. Genet. 47:509–37

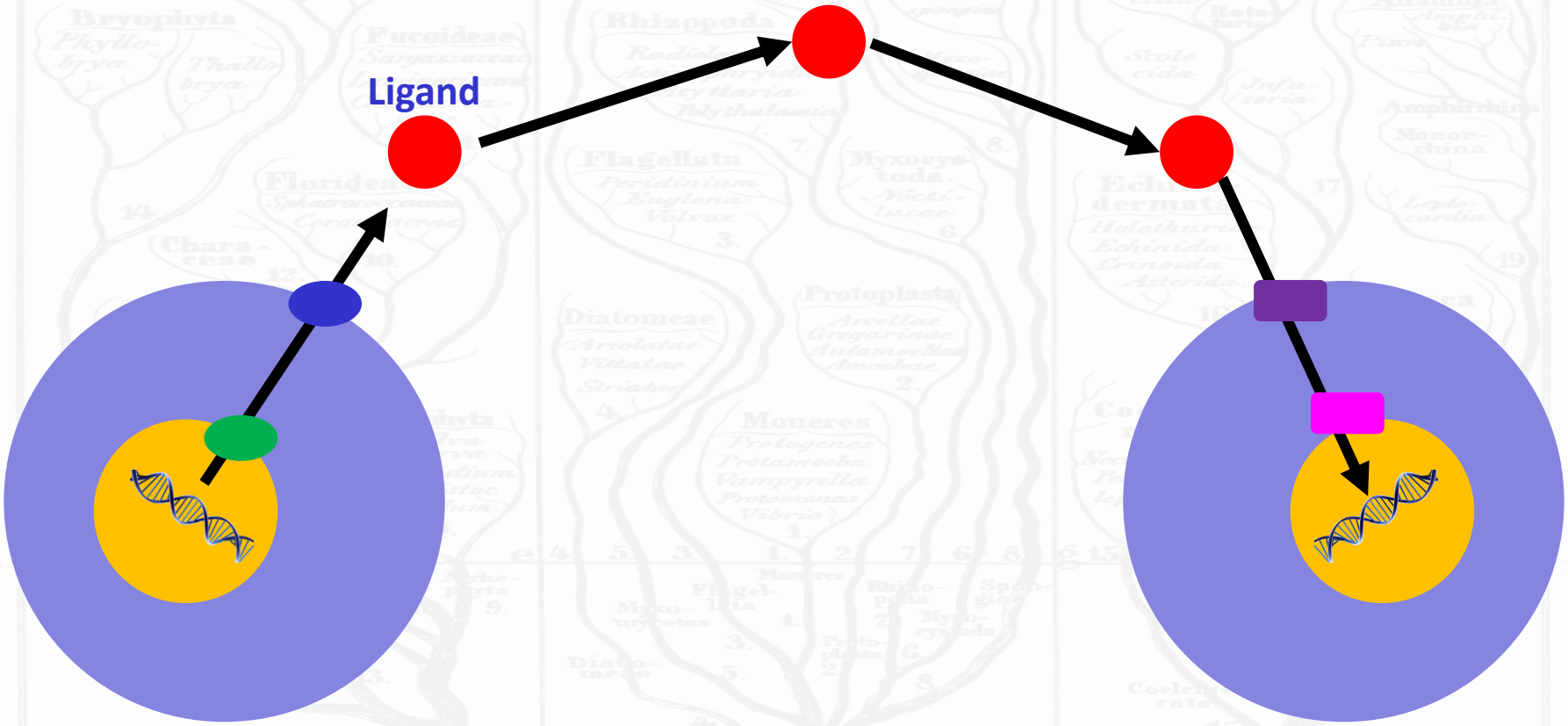
- **Gene regulation** (TFs,and signalling pathways)
- **Cell adhesion**
- **Cell type specialization**
- **Cell cycle**
- **Immunity**

Differential gene expression



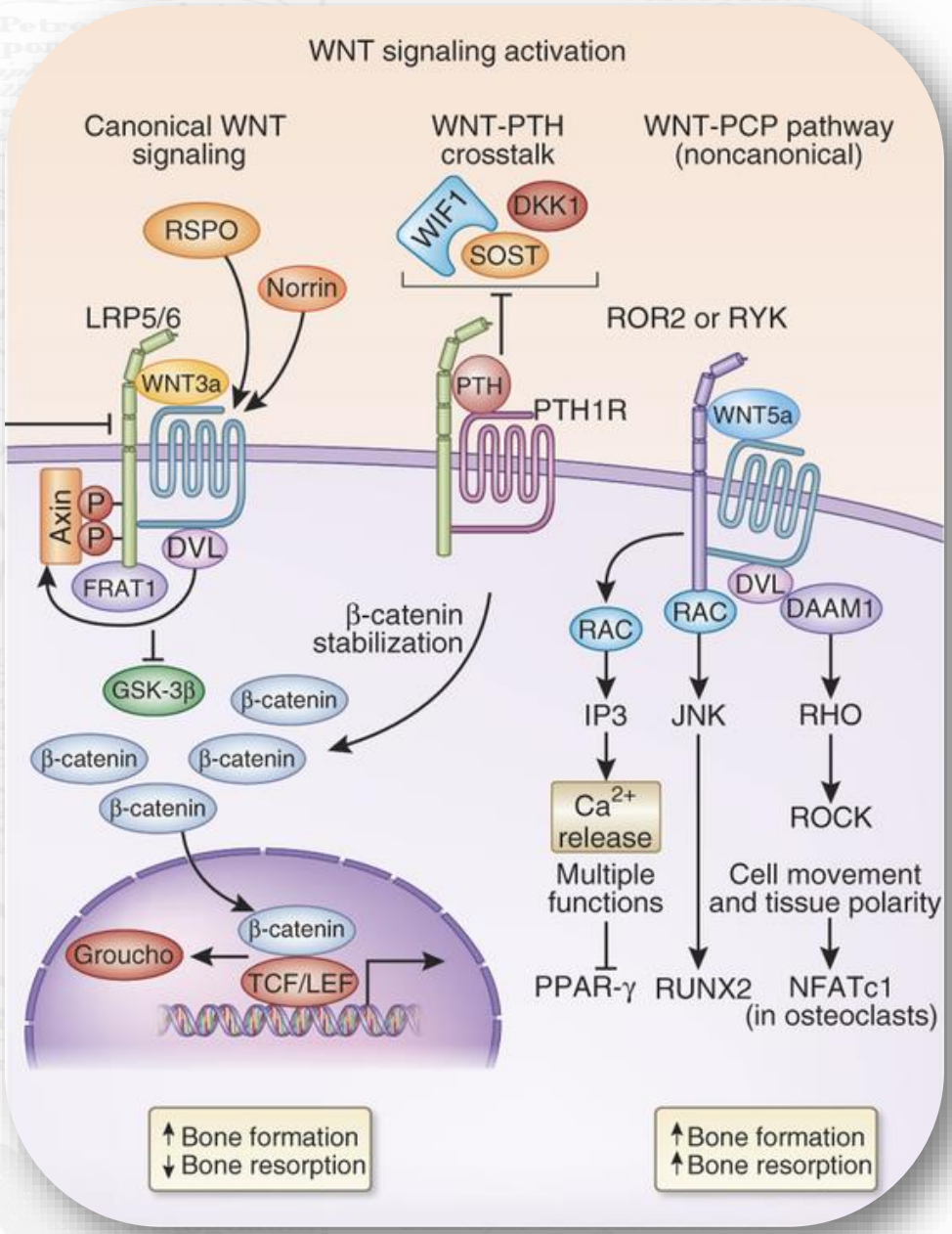


Signalling pathways: cell communication

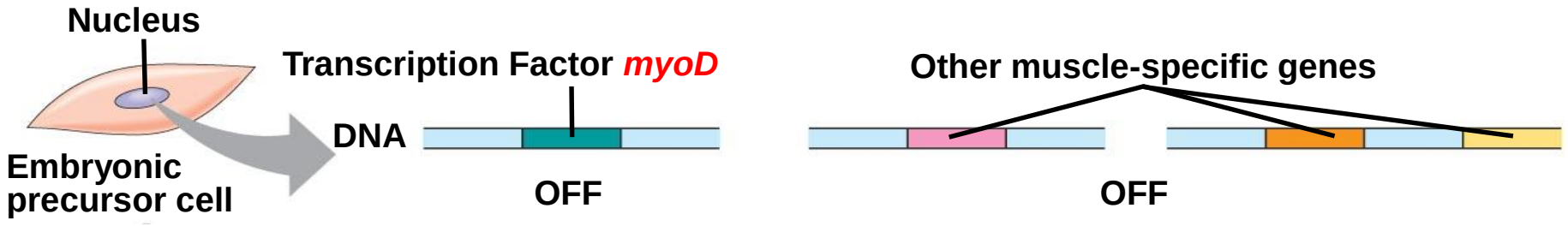


Public

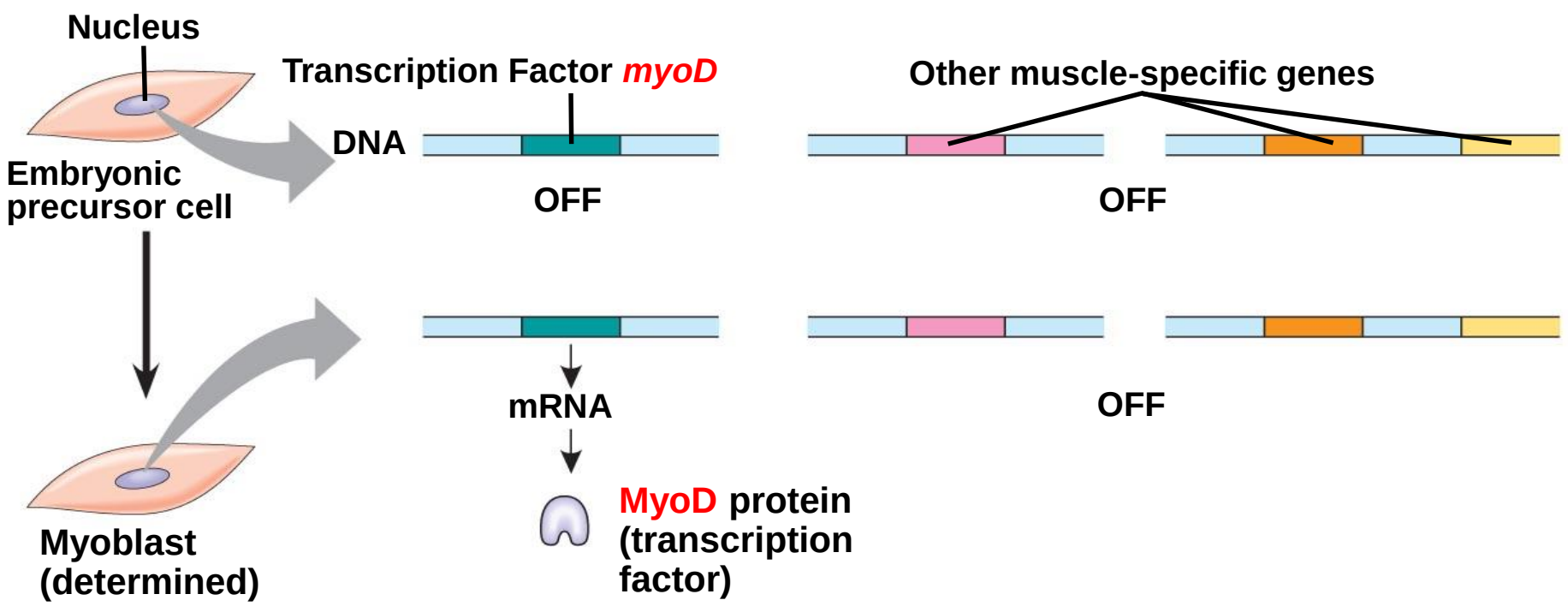
Signalling pathways: Wnt



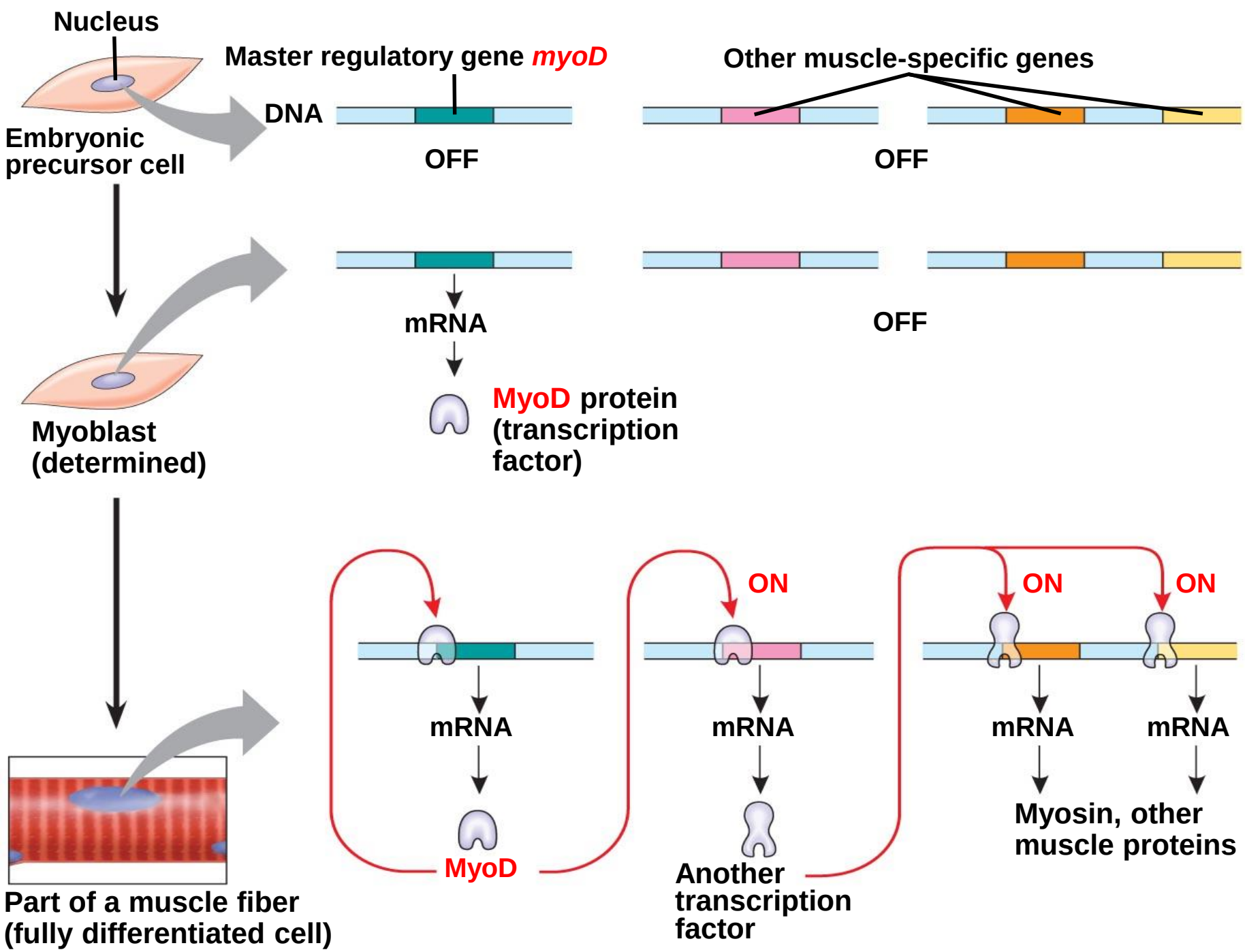
Public



Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings.

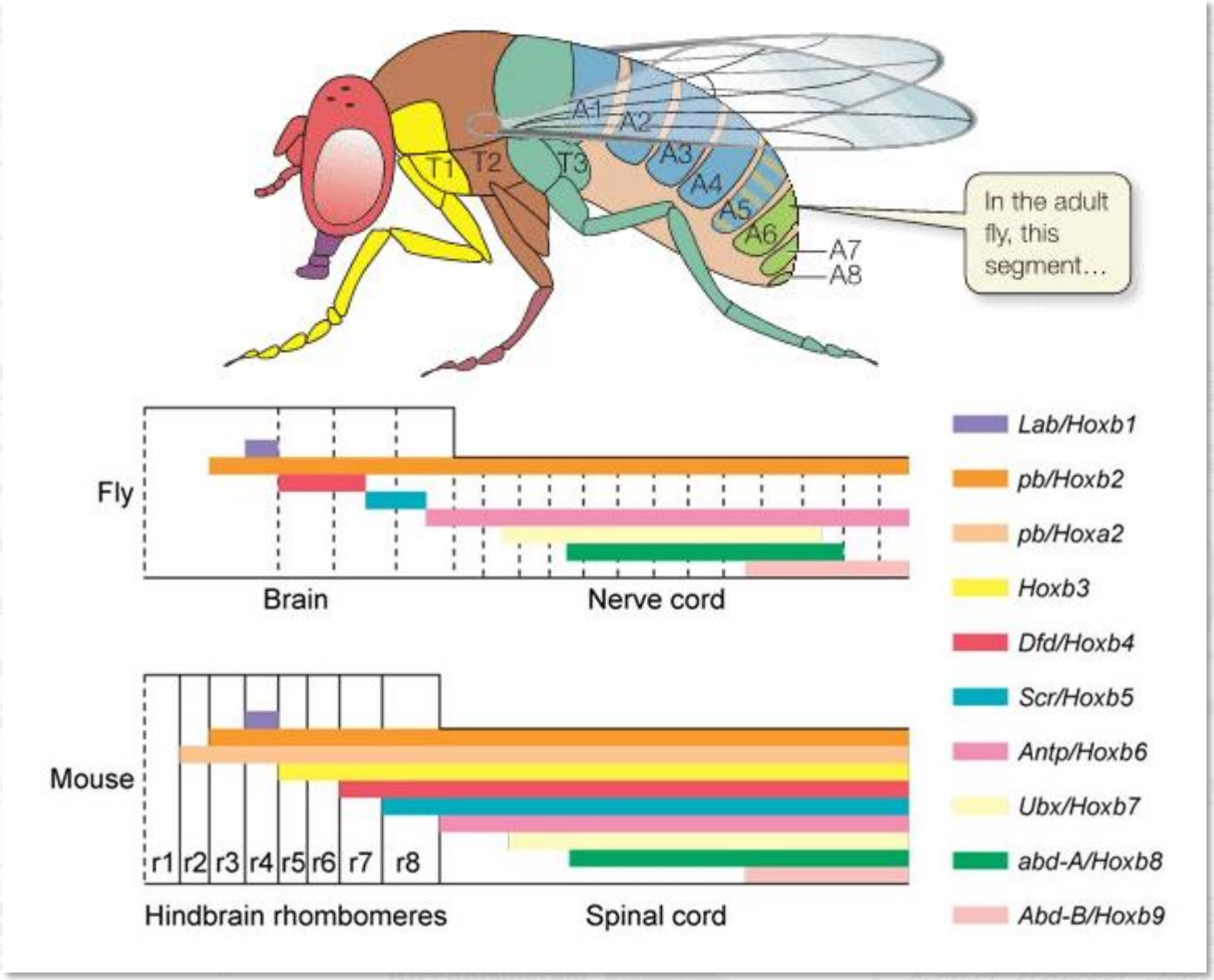


Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings.



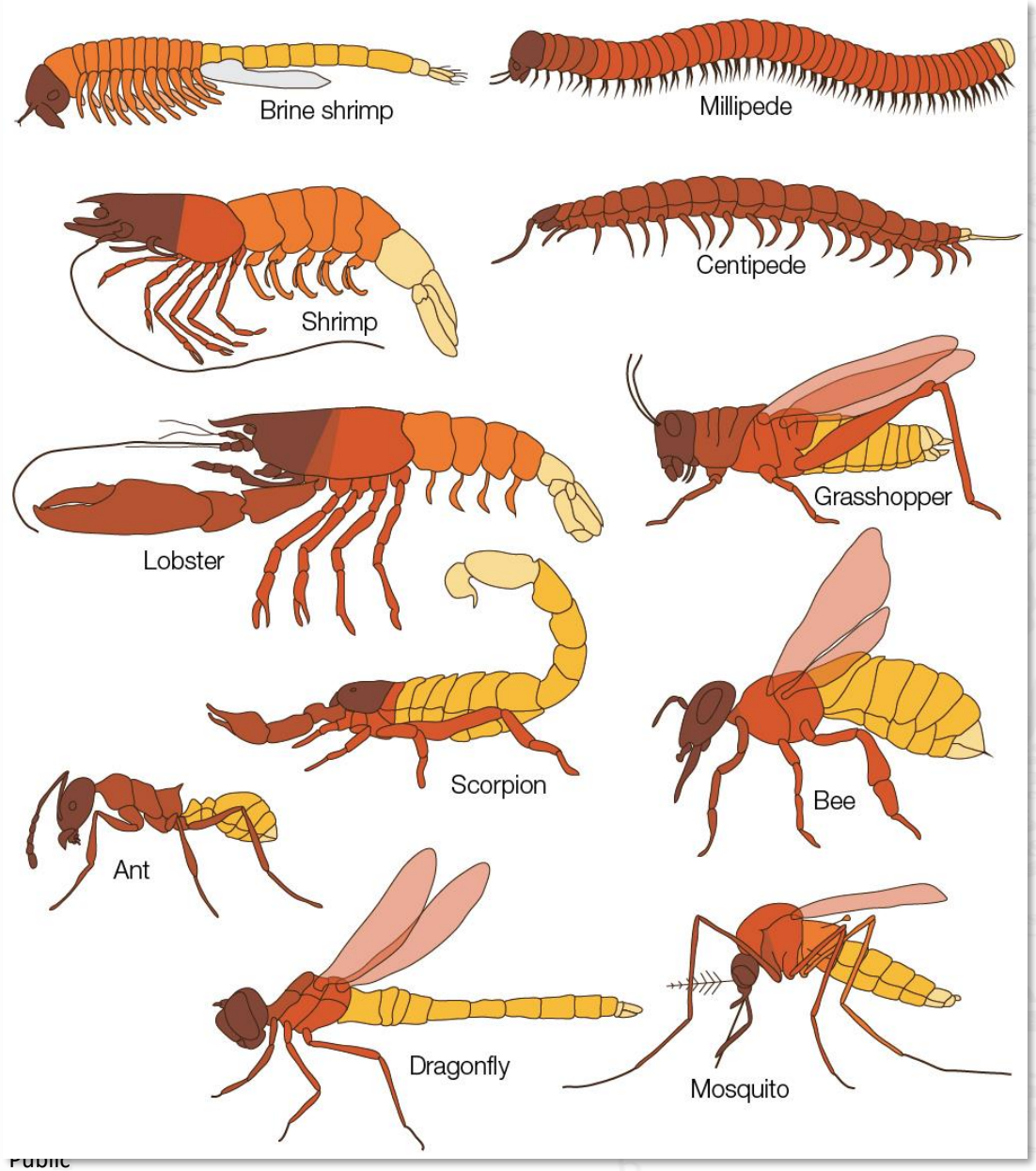
Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings.

Transcription Factors (TFs): Hox genes



Public

Transcription Factors (TFs): Hox genes

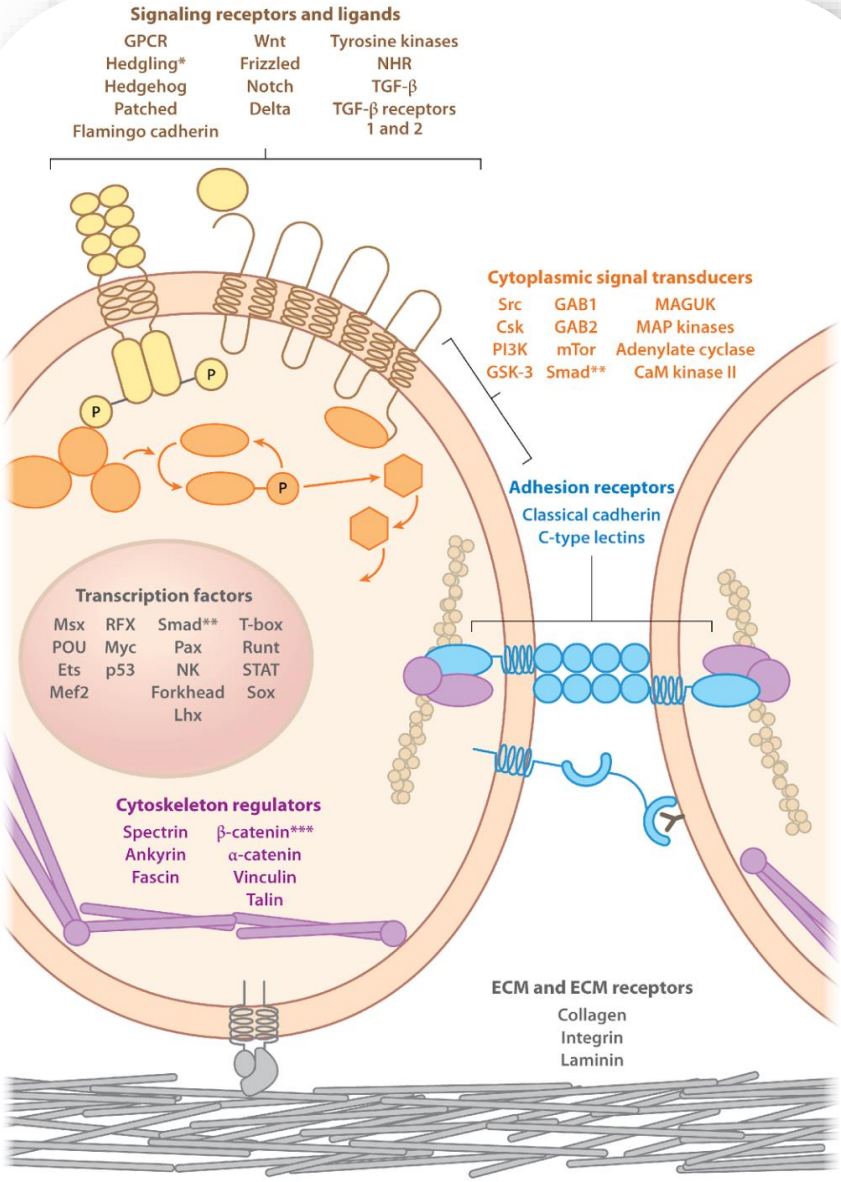


Learn genetics

http://learn.genetics.utah.edu/content/basics/hoxgenes/

Public

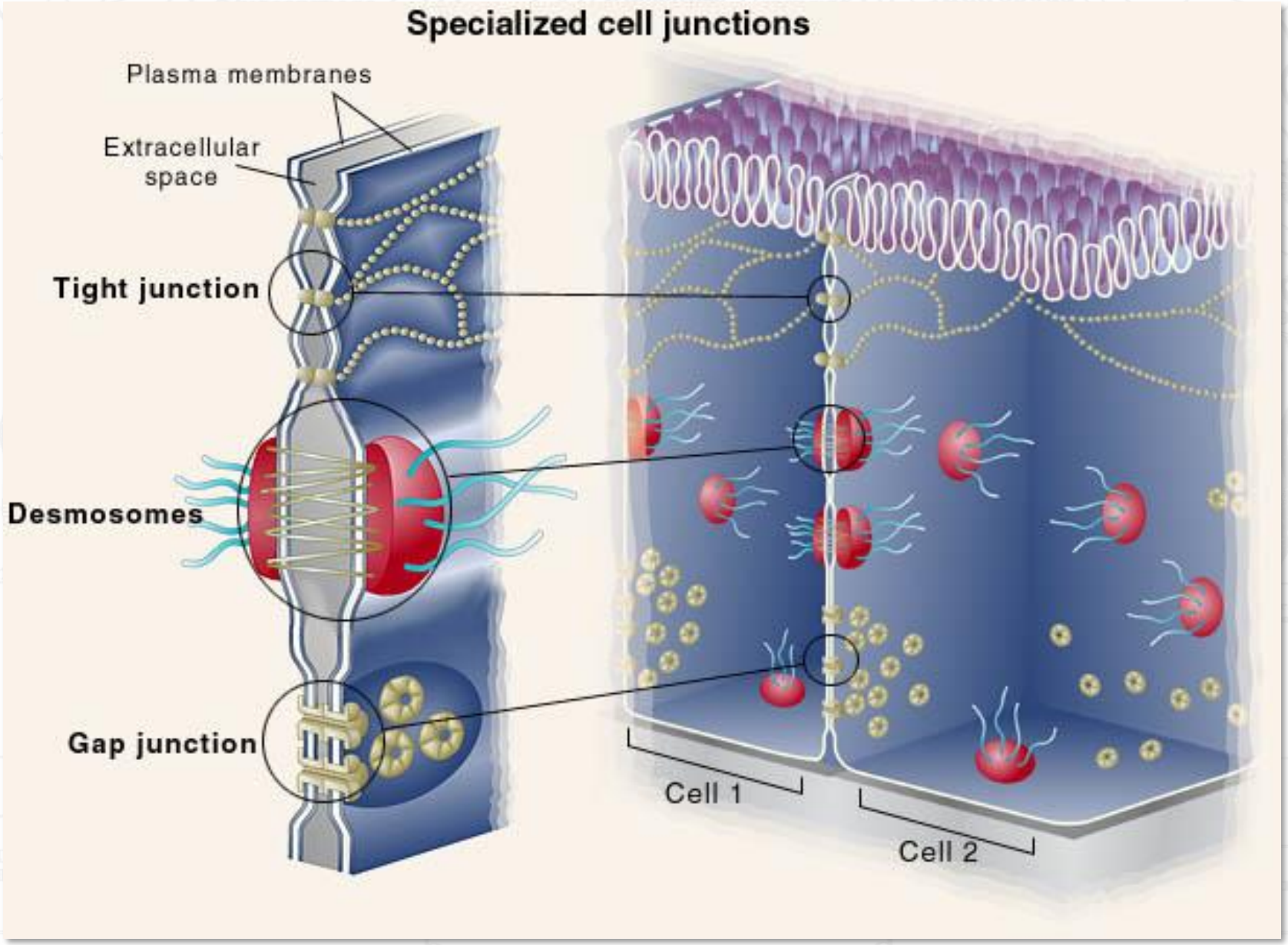
Genome



Richter DJ, King N. 2013.
Annu. Rev. Genet. 47:509–37

- **Gene regulation** (TFs,and signalling pathways)
- **Cell adhesion**
- **Cell type specialization**
- **Cell cycle**
- **Immunity**

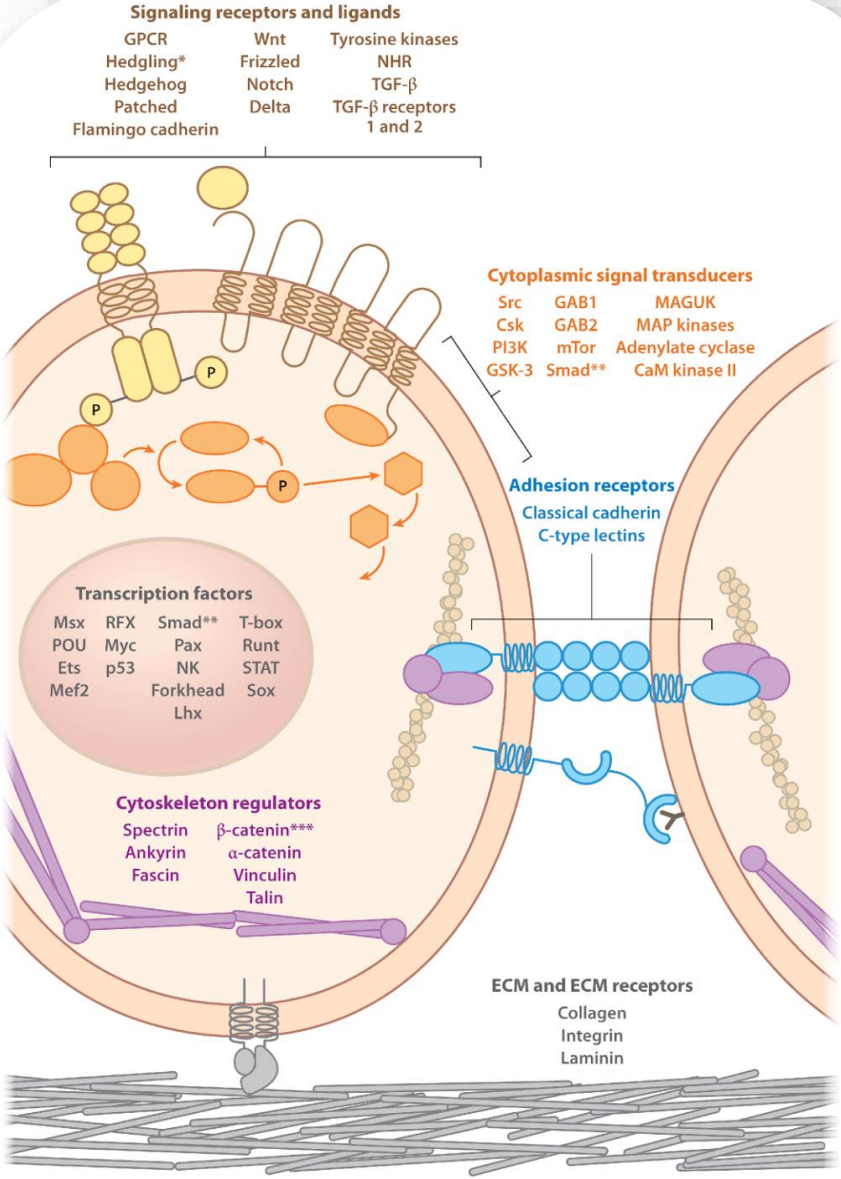
Cell adhesion



Public

Genome

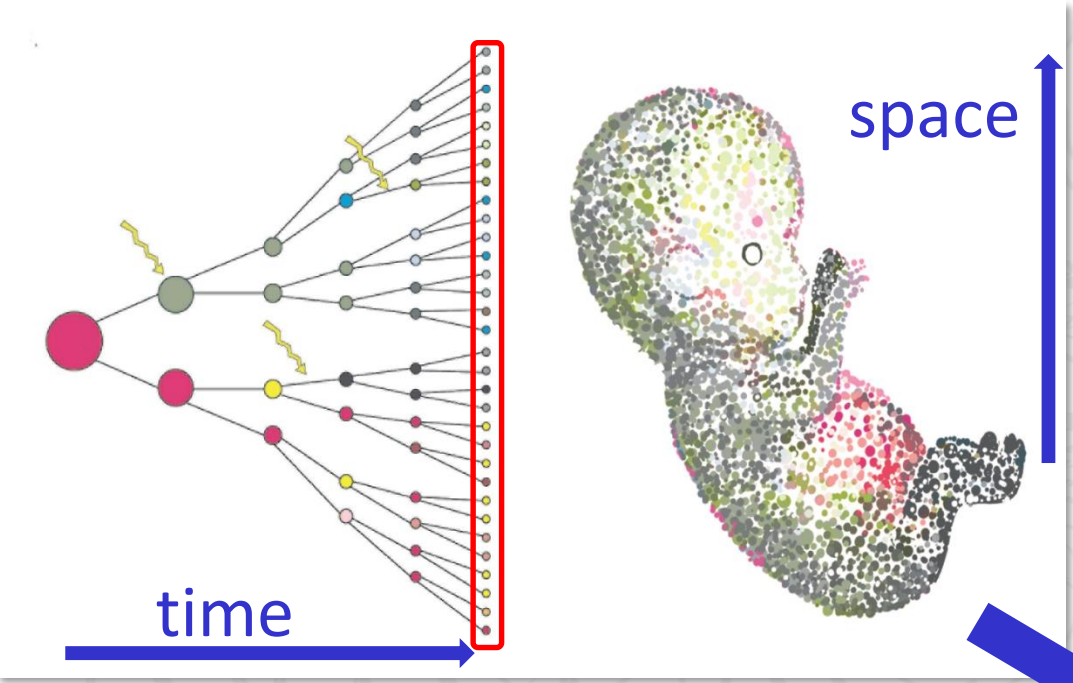
Triggers

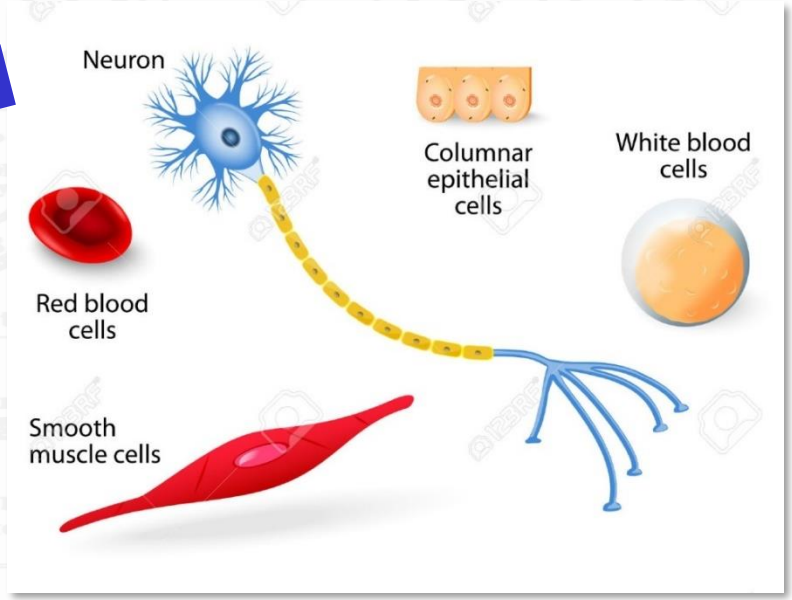


Richter DJ, King N. 2013.
Annu. Rev. Genet. 47:509–37

- **Gene regulation** (TFs,and signalling pathways)
- **Cell adhesion**
- **Cell type specialization**
- **Cell cycle**
- **Immunity**

Cell types

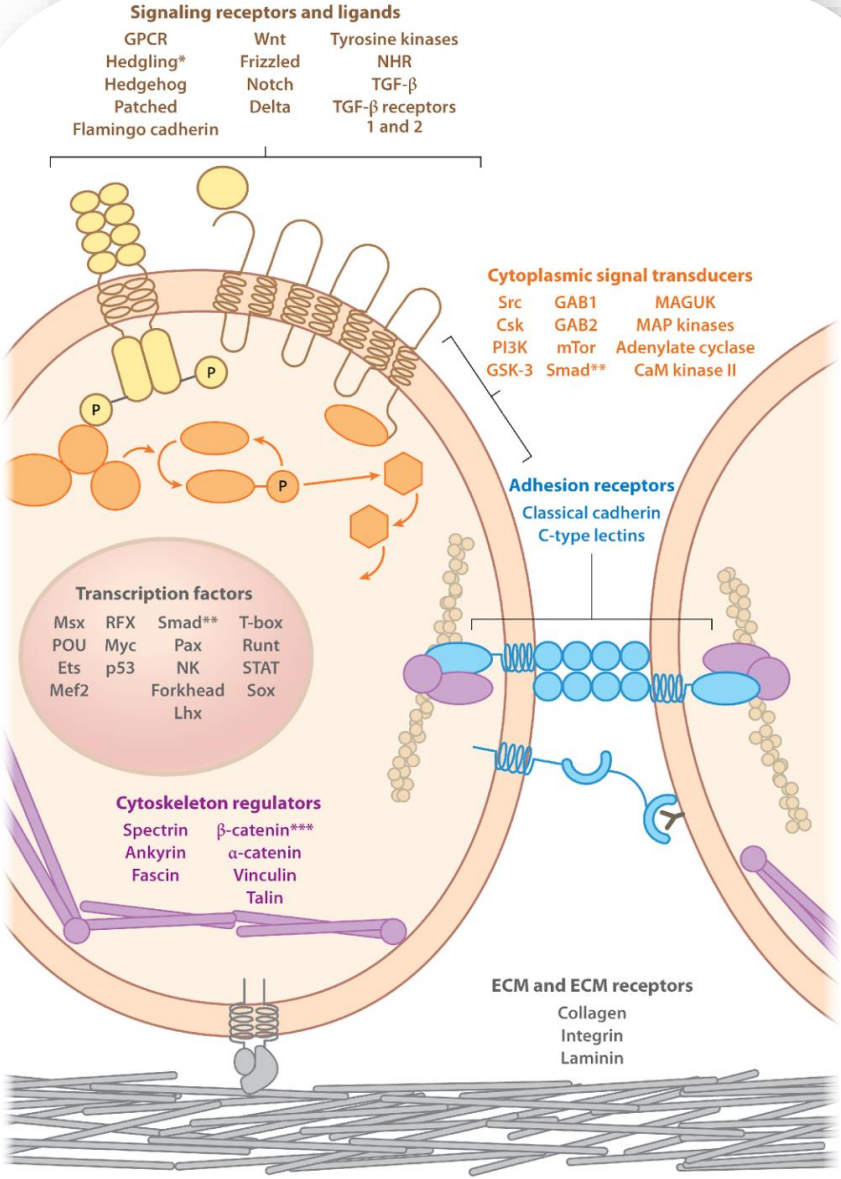




Public

Genome

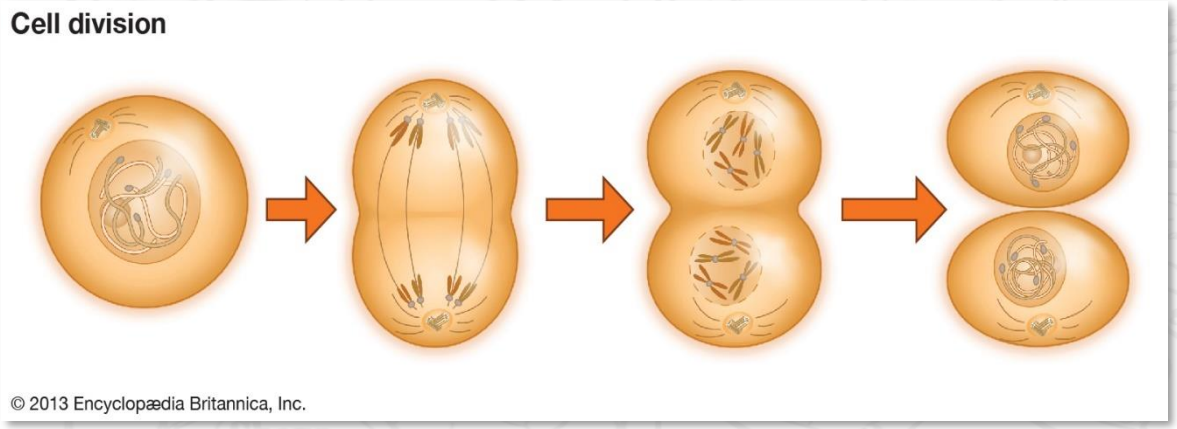
Triggers

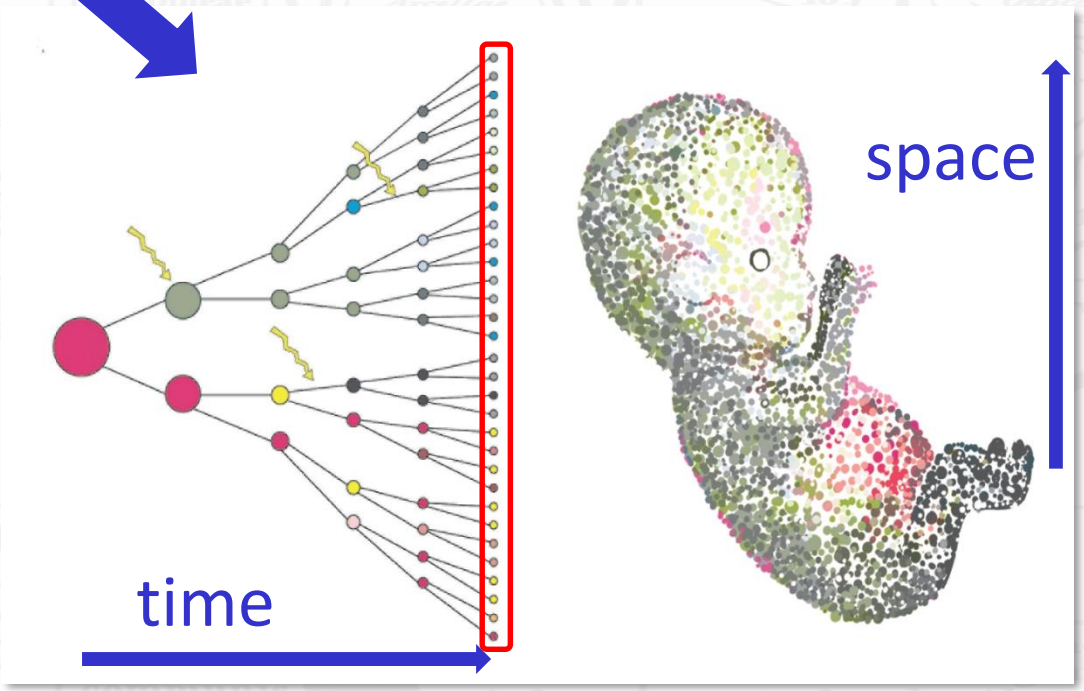


Richter DJ, King N. 2013.
Annu. Rev. Genet. 47:509–37

- **Gene regulation** (TFs,and signalling pathways)
- **Cell adhesion**
- **Cell type specialization**
- **Cell cycle**
- **Immunity**

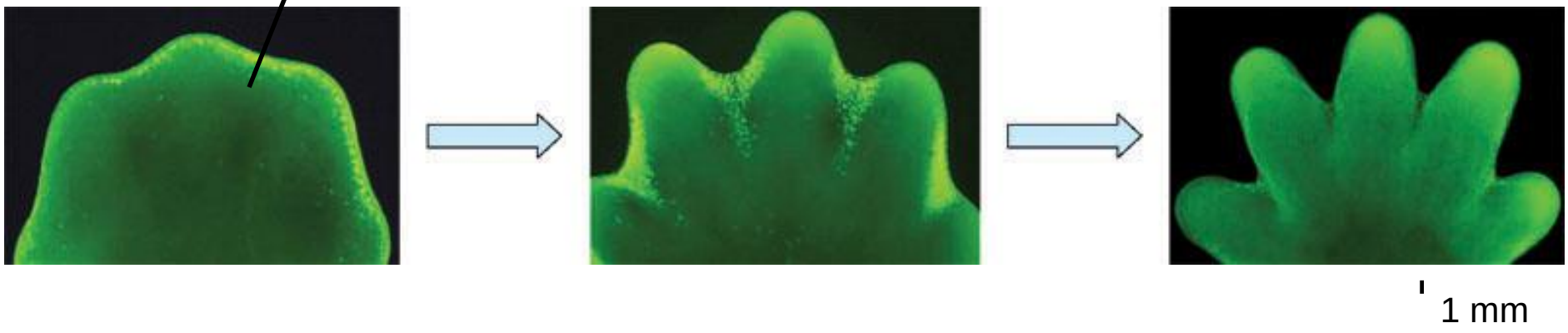
Cell cycle





Public

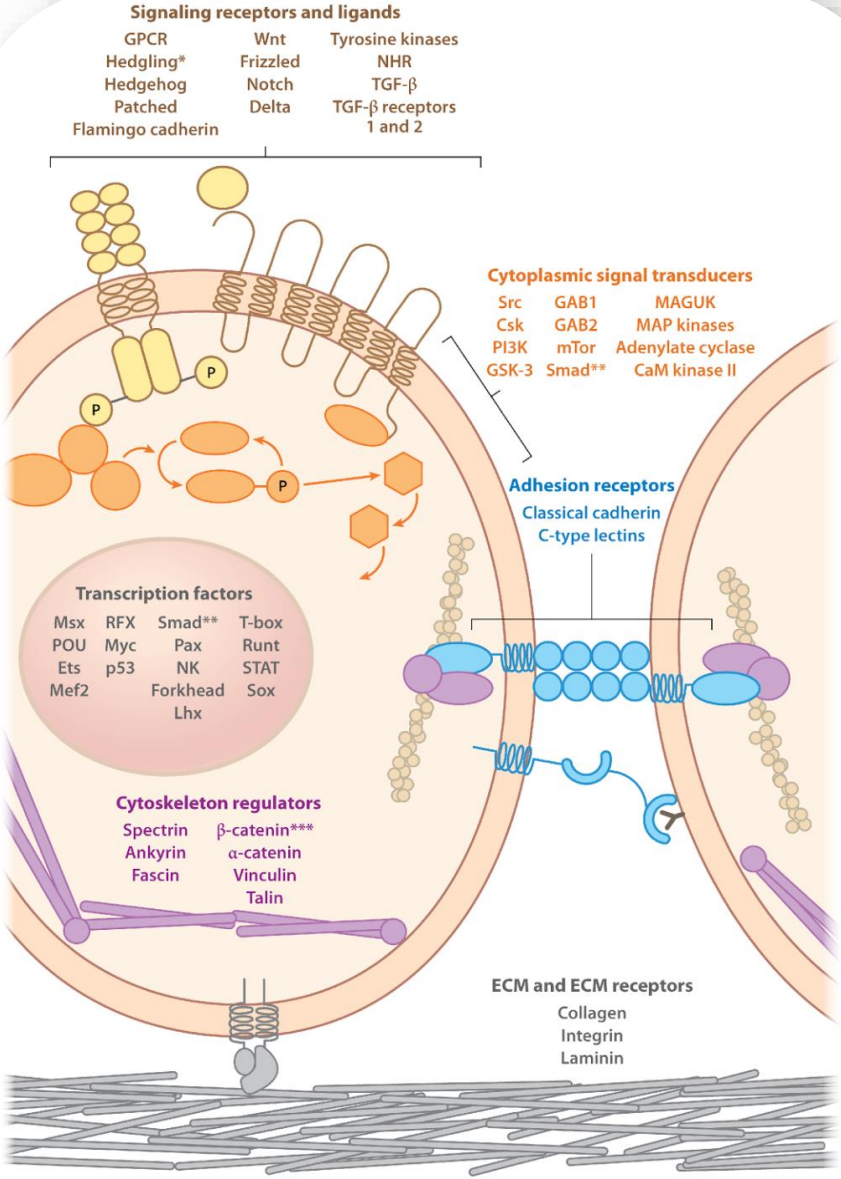
Programmed cell death: apoptosis



Public

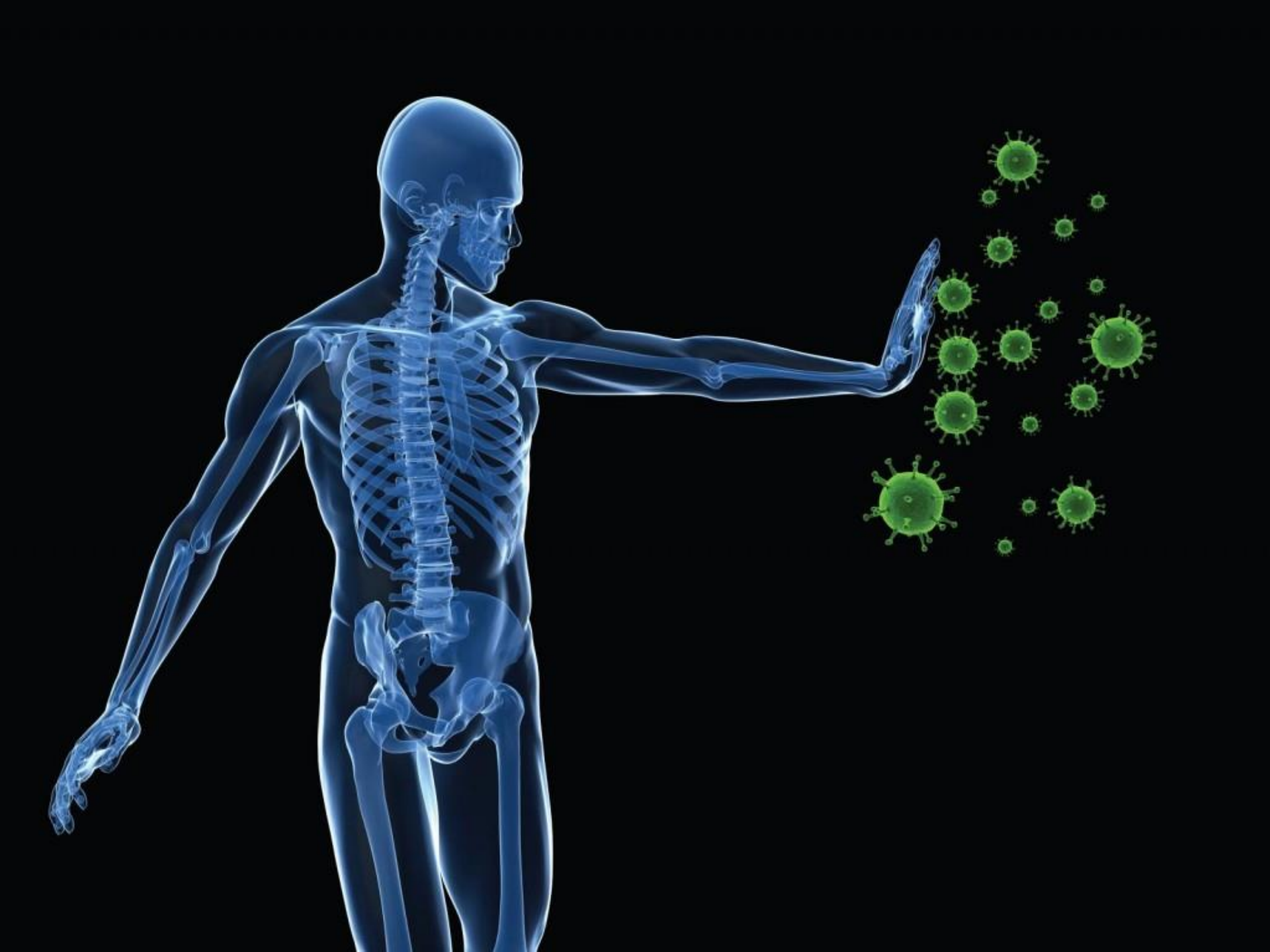
Genome

Triggers

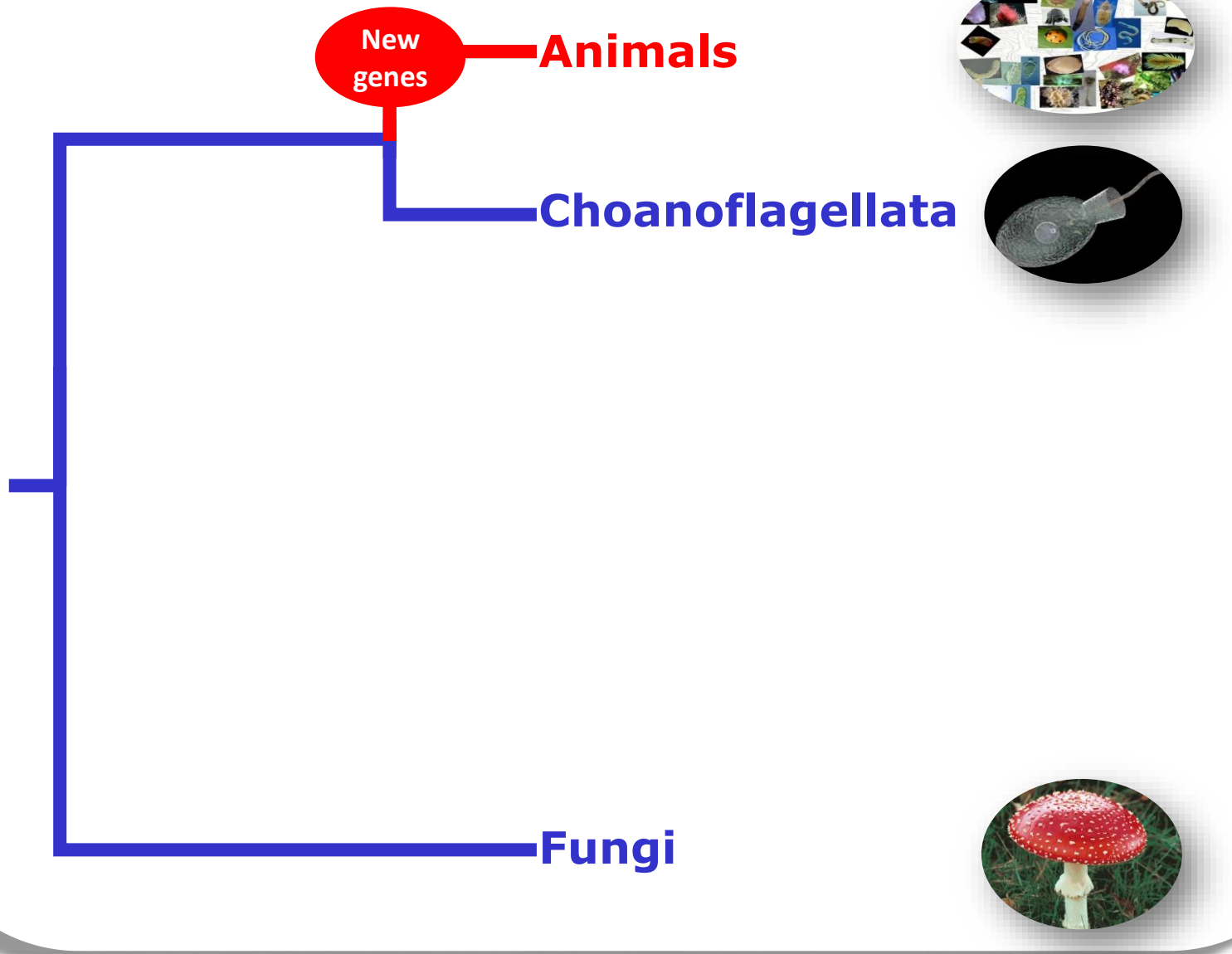


Richter DJ, King N. 2013.
Annu. Rev. Genet. 47:509–37

- **Gene regulation** (TFs,and signalling pathways)
- **Cell adhesion**
- **Cell type specialization**
- **Cell cycle**
- **Immunity**



Genomic Novelties



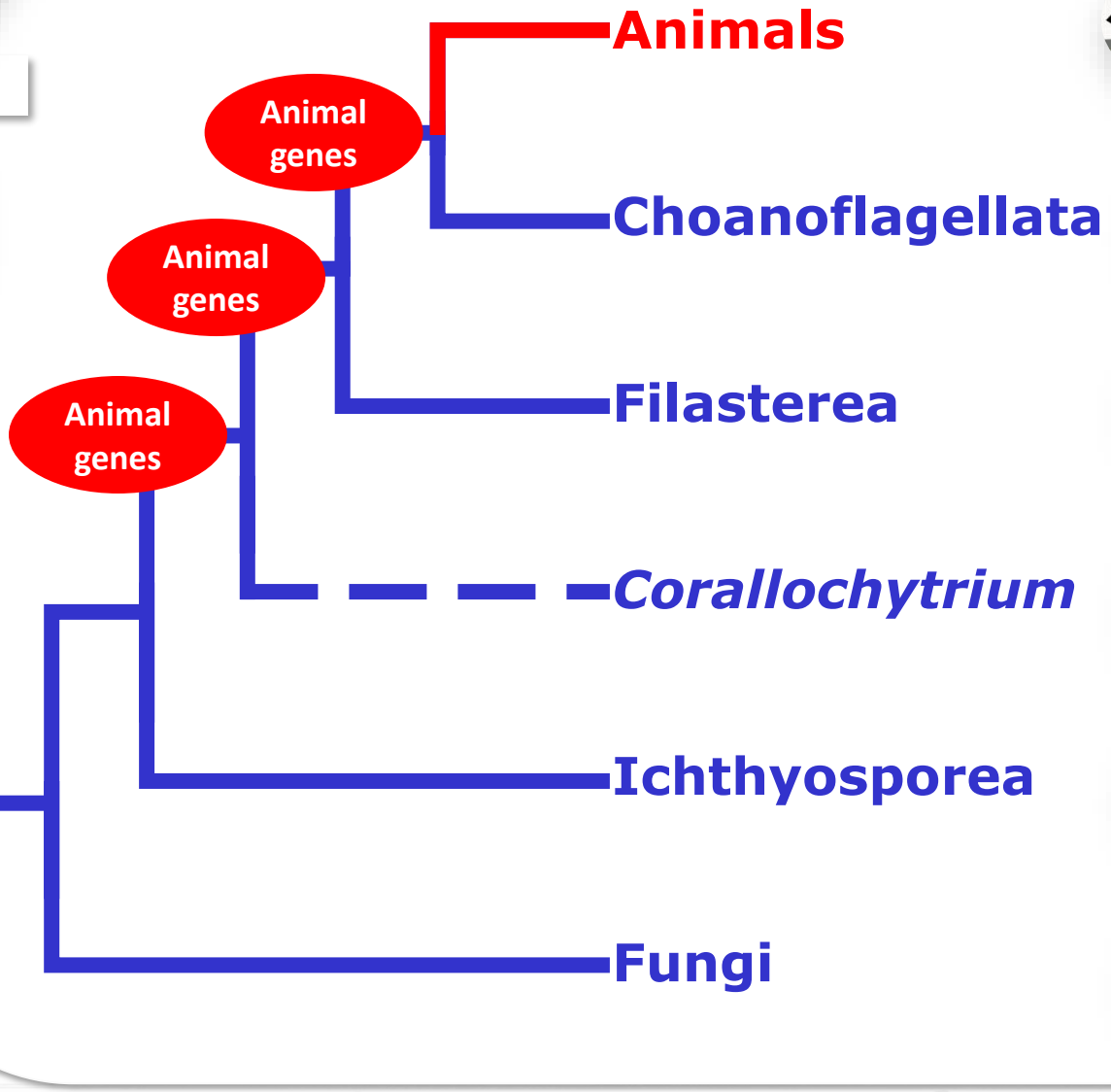
Public

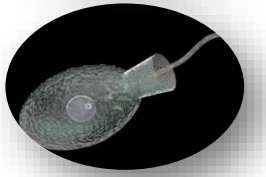
Nicole King

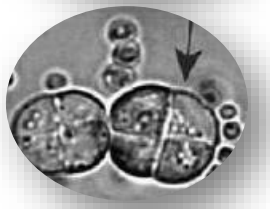
Iñaki Ruiz-Trillo

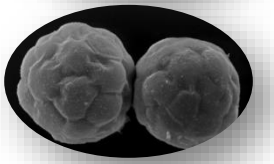
Genomic Tinkering

Old vs New





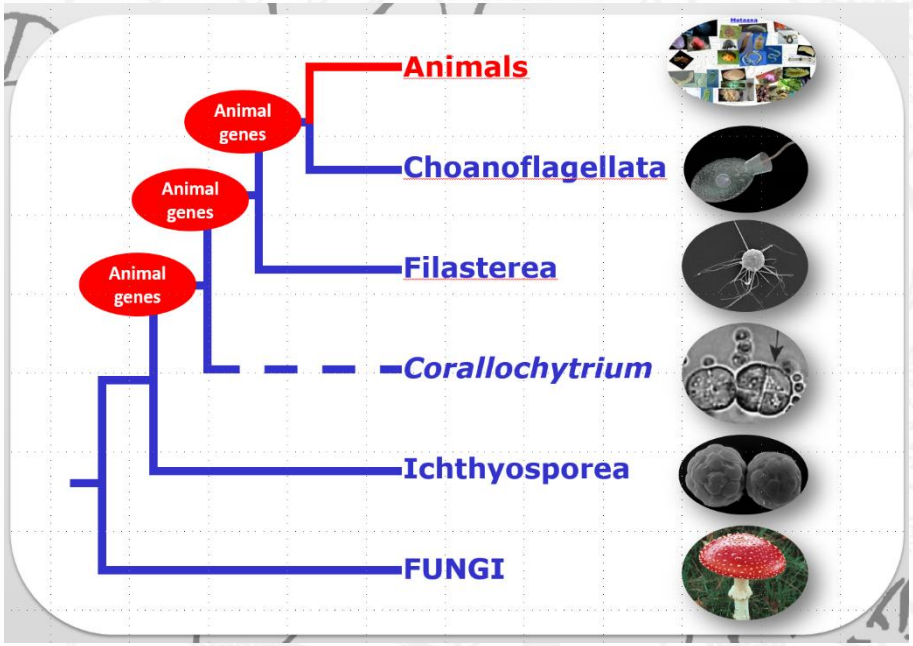


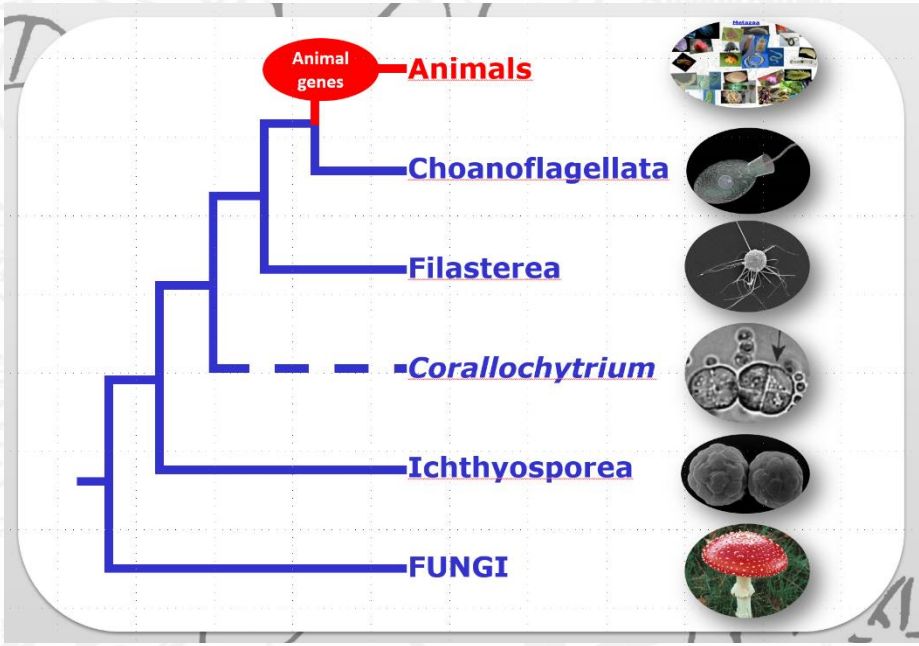


Public

Old vs new

?





Public

Compare genomes to profile the role of novelty in Animal Origins

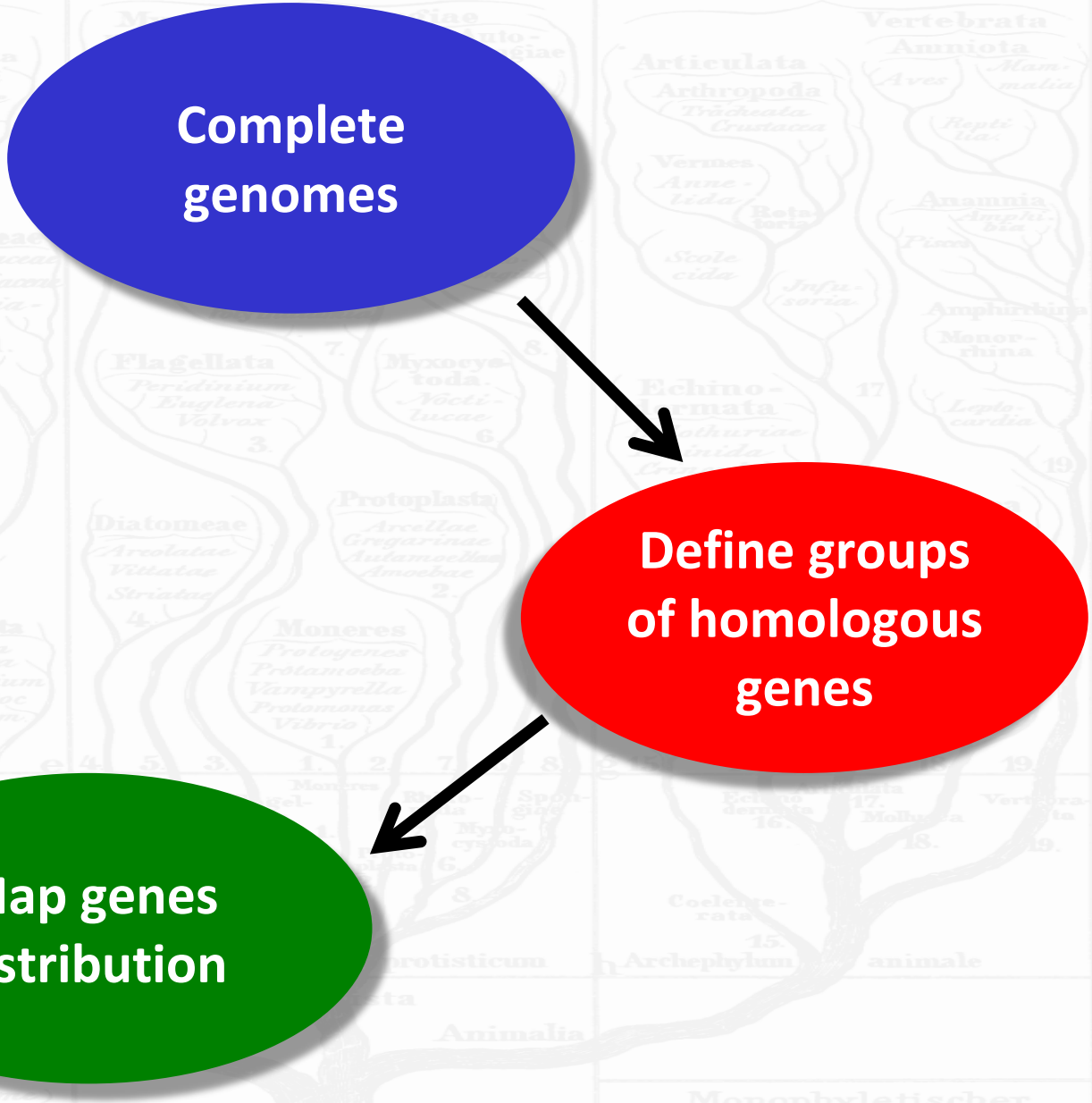
UNIVERSITY OF OXFORD

Peter WH Holland

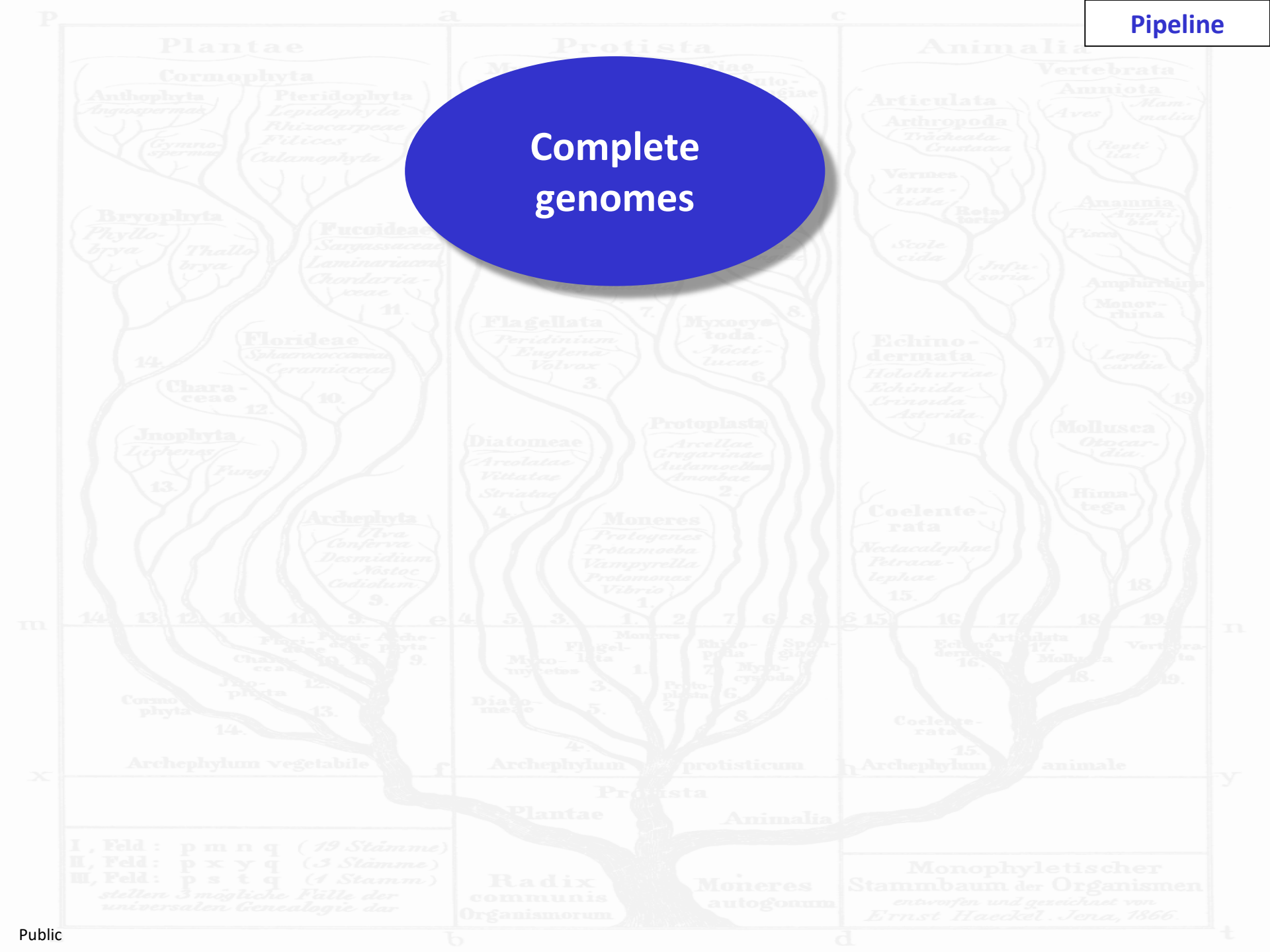
Public

The Pipeline

Public


Complete genomes
Define groups of homologous genes
Map genes distribution

Public

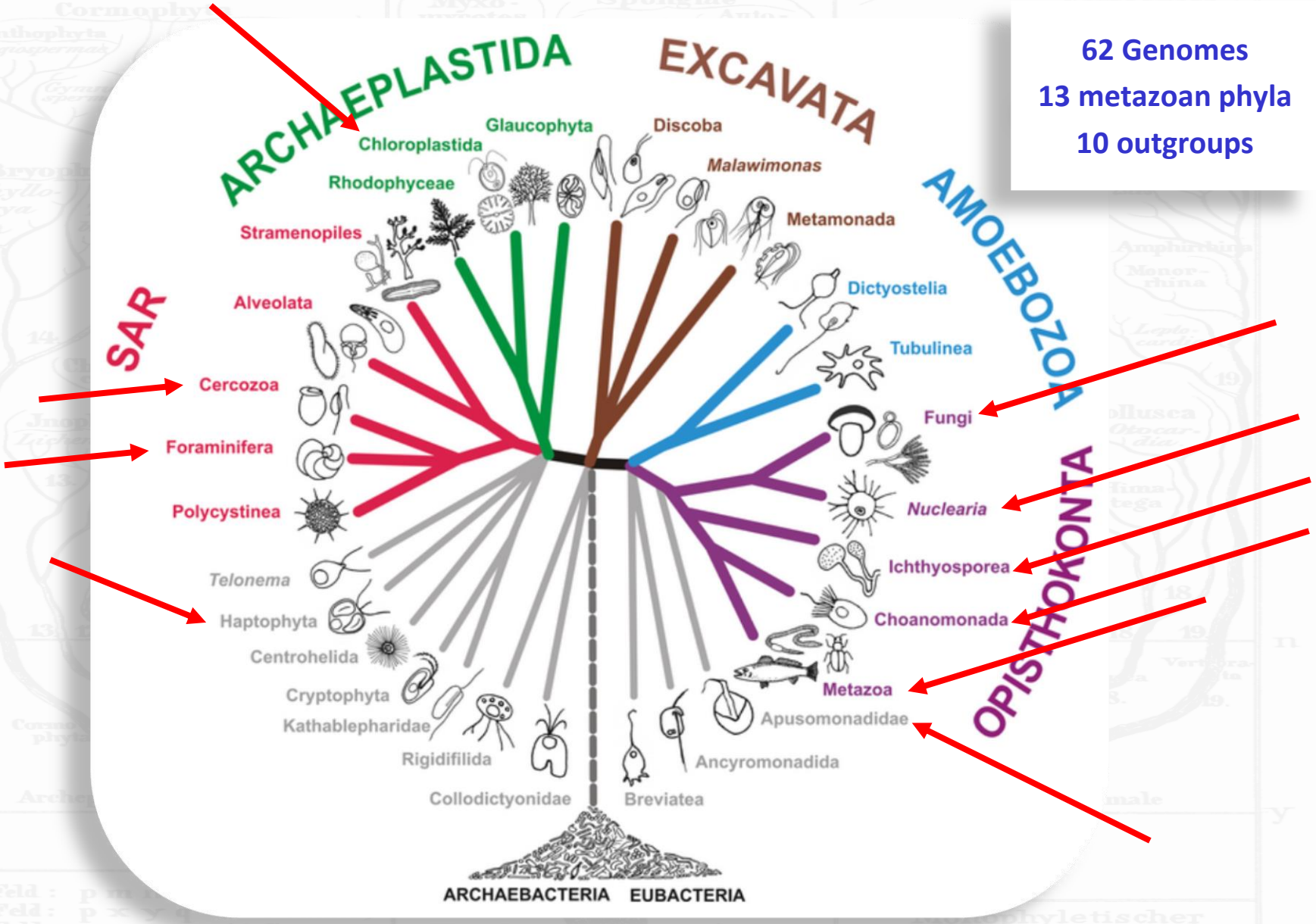


Public

Eukaryotes

Pipeline

62 Genomes
13 metazoan phyla
10 outgroups



Adl *et al* 2012

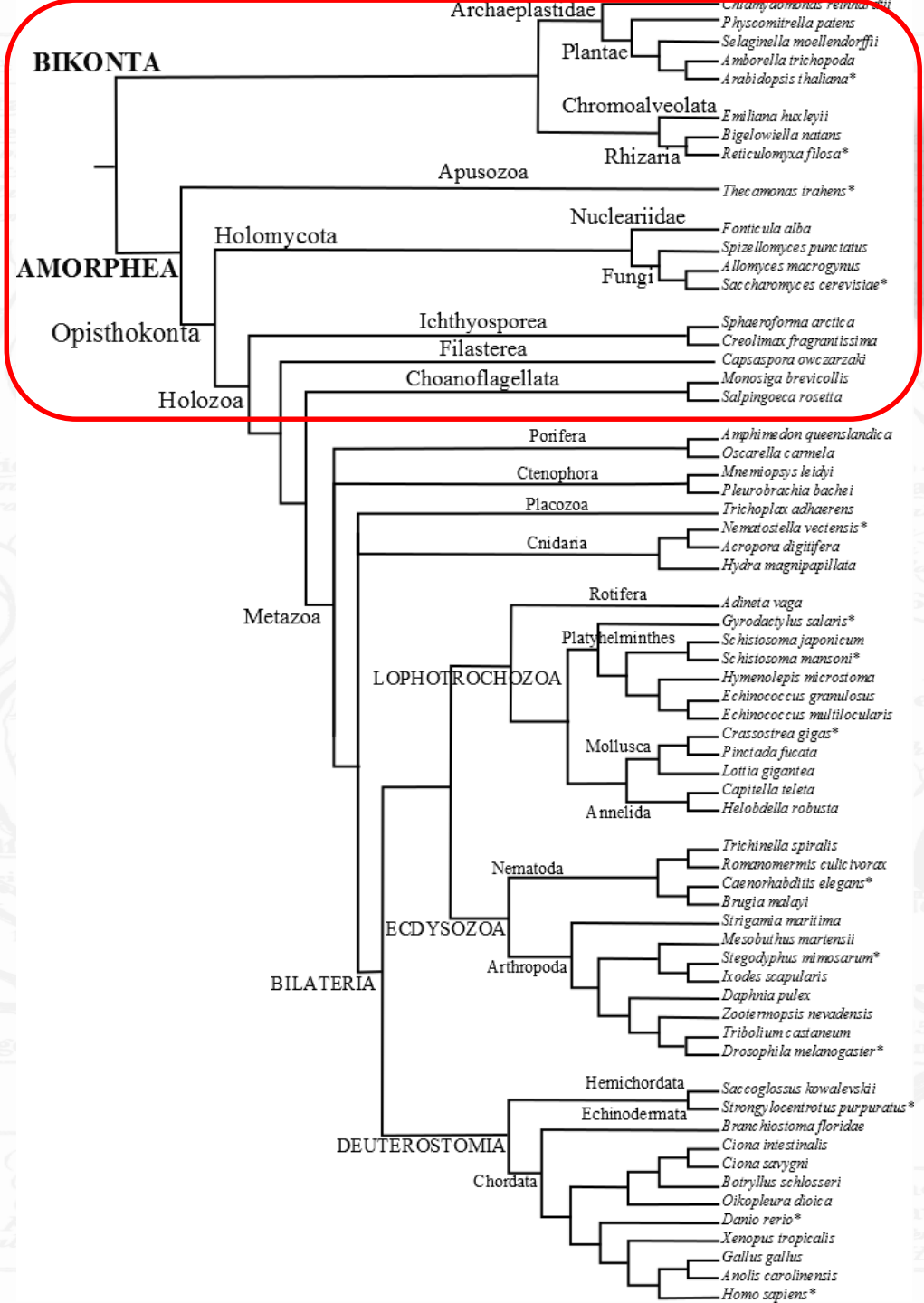
Public

Animals Origins

62 Genomes

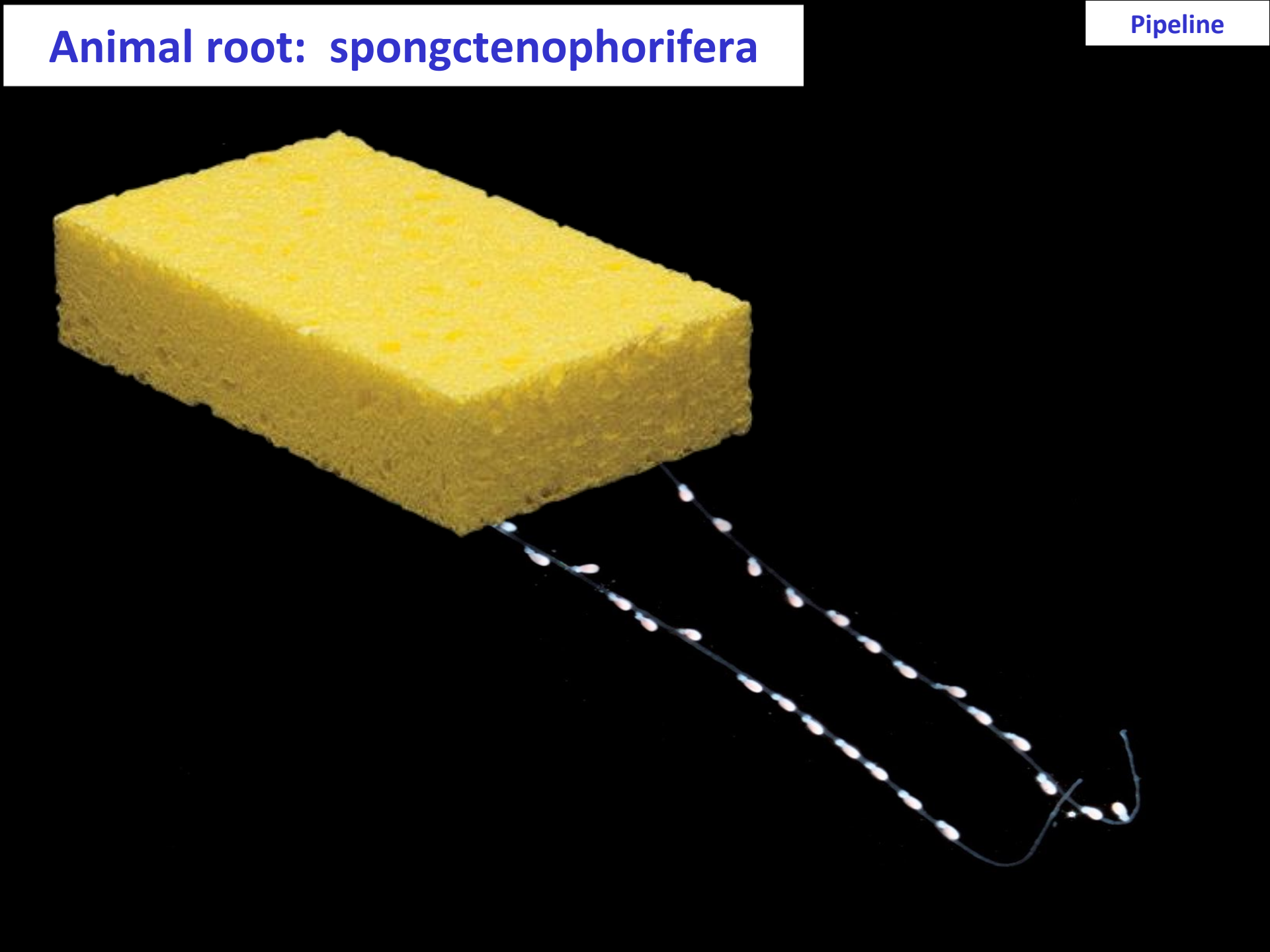
13 metazoan phyla

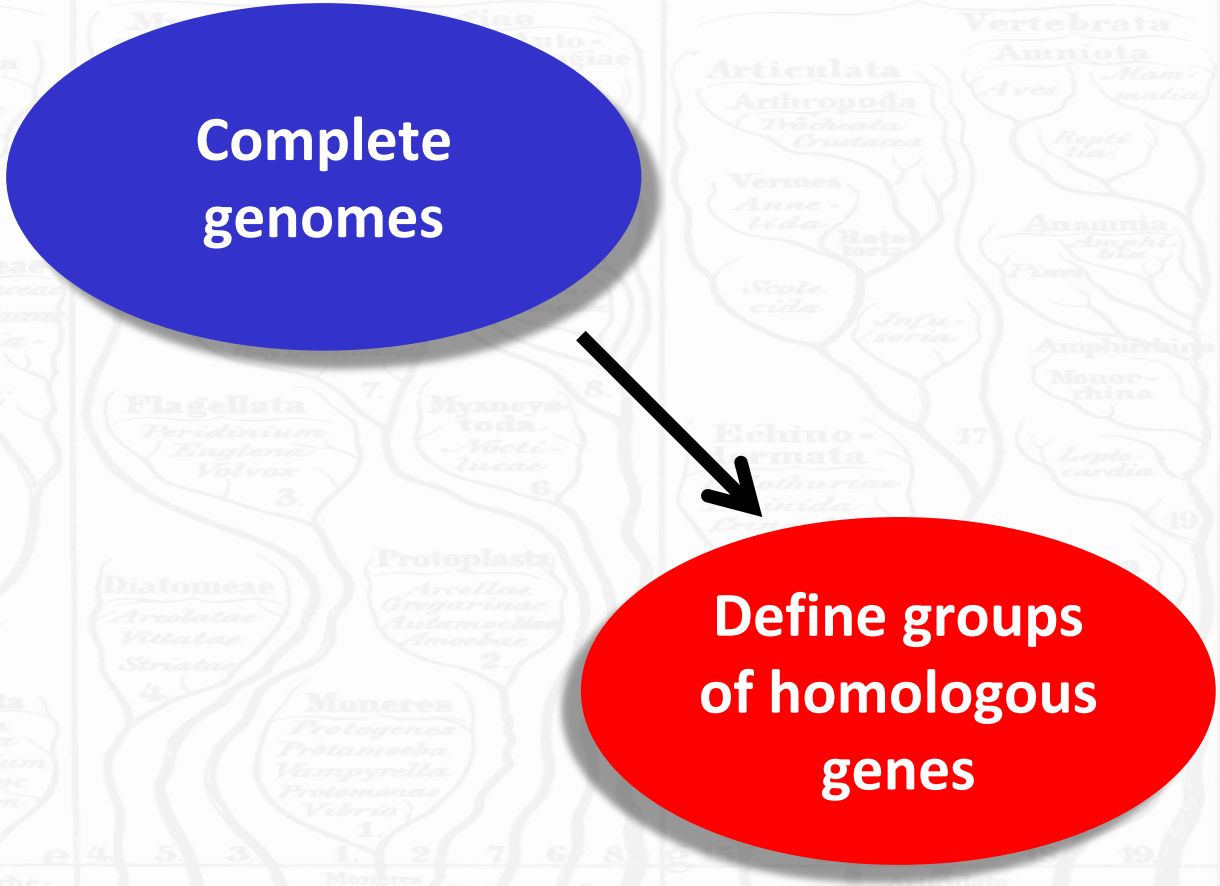
10 outgroup lineages



Public

Animal root: spongctenophorifera





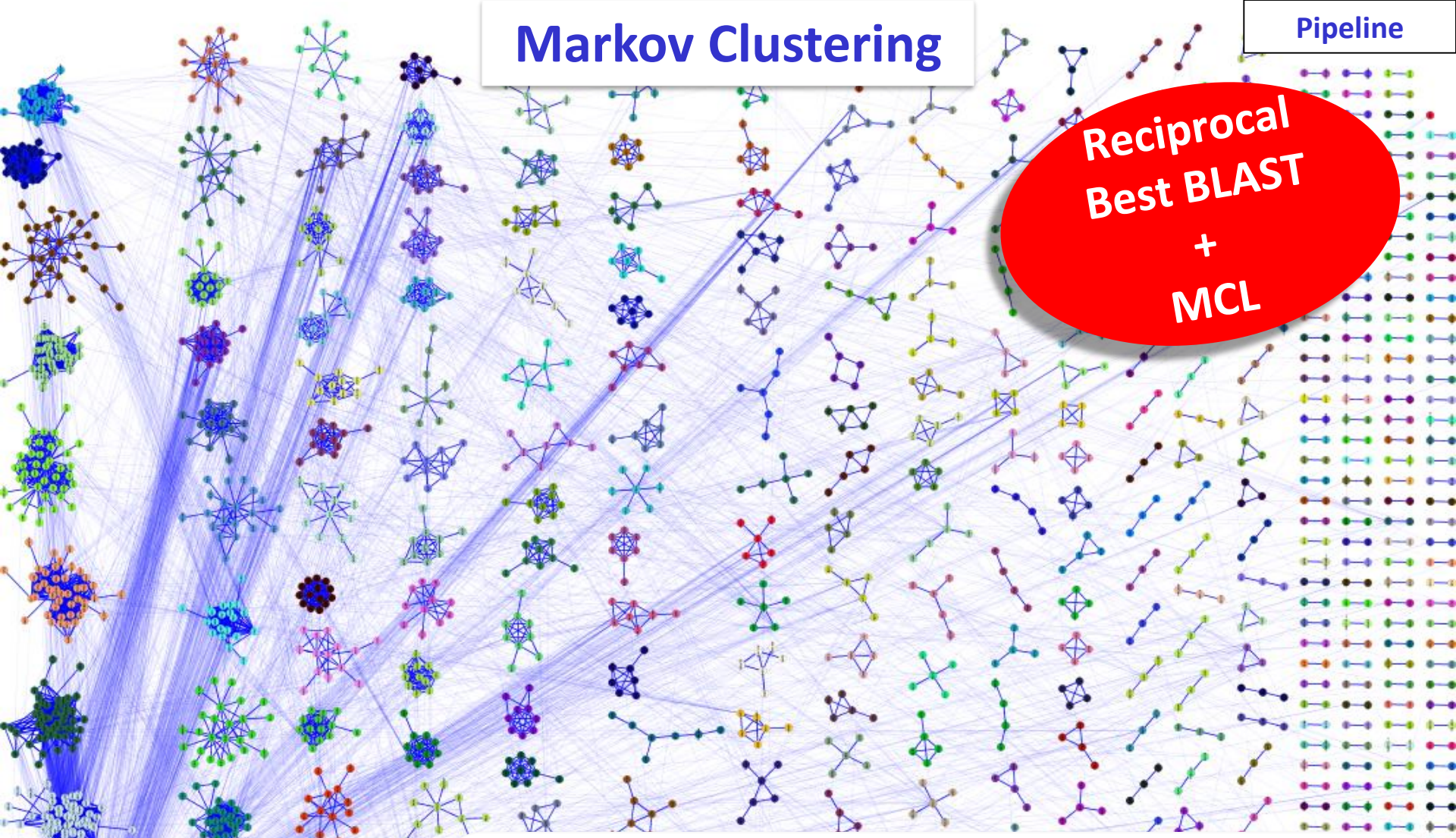
Public

Homology assignment

	Speed	Accuracy	Orthology/Paralogy
Phylostratigraphy one spp query one-way BLAST	+++	+	**None** (assumes one-to-one)
Reciprocal Best BLAST All spp vs all Two-way BLAST RBB/RBD/RBH…	++	++	**BLAST e-value** (i.e. Inparanoid) **Gene trees**
Reciprocal BLAST + HMM All spp vs all Two-way BLAST MCL	+	+++	**BLAST e-value** (i.e. OrthoMCL) **Gene trees**

Public

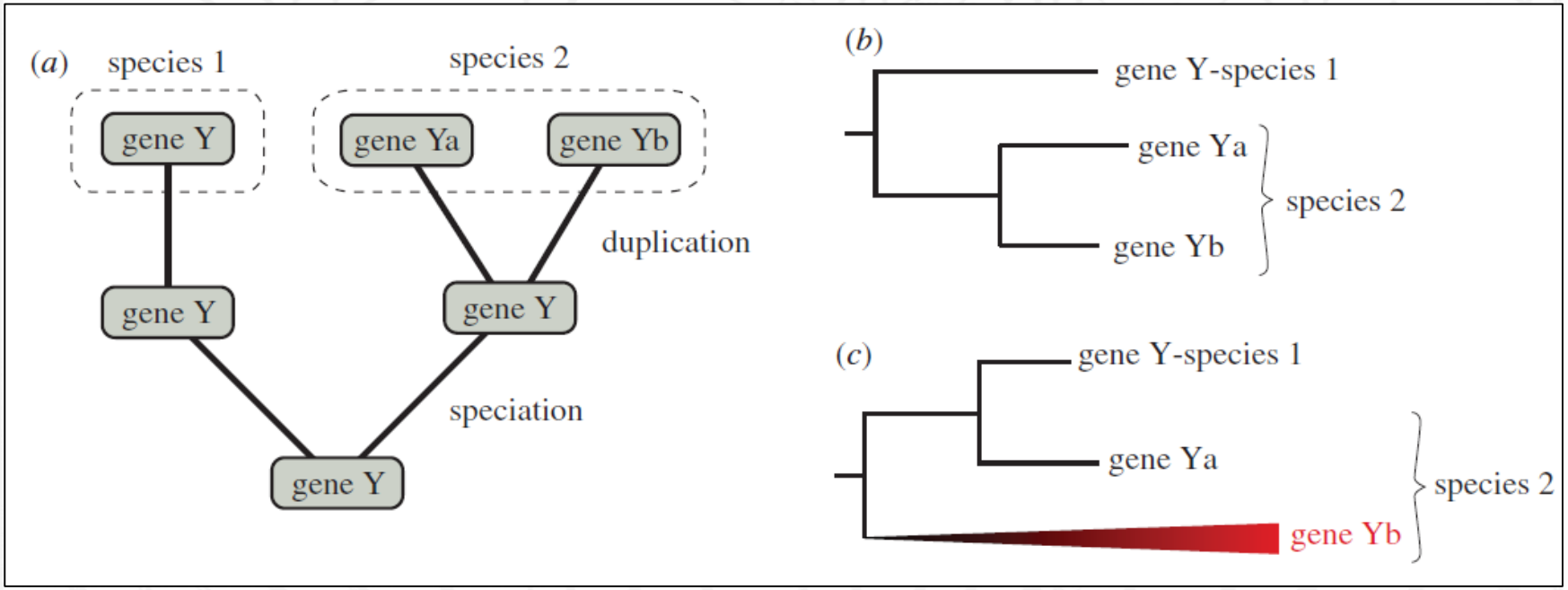
Markov Clustering



Reciprocal Best BLAST + MCL

- 1,500,000 genes in the 62 genomes
- 2,000,000,000,000 one vs one comparisons
- 268,440 homology groups (HG)

Why no orthology/paralogy? Assymetric evolution



PHILOSOPHICAL TRANSACTIONS B

rstb.royalsocietypublishing.org

Review

Cite this article: Holland PWH, Marlétaz F, Maeso I, Dunwell TL, Paps J. 2017 New genes from old: asymmetric divergence of gene duplicates and the evolution of development. *Phil. Trans. R. Soc. B* **372**: 20150480. http://dx.doi.org/10.1098/rstb.2015.0480

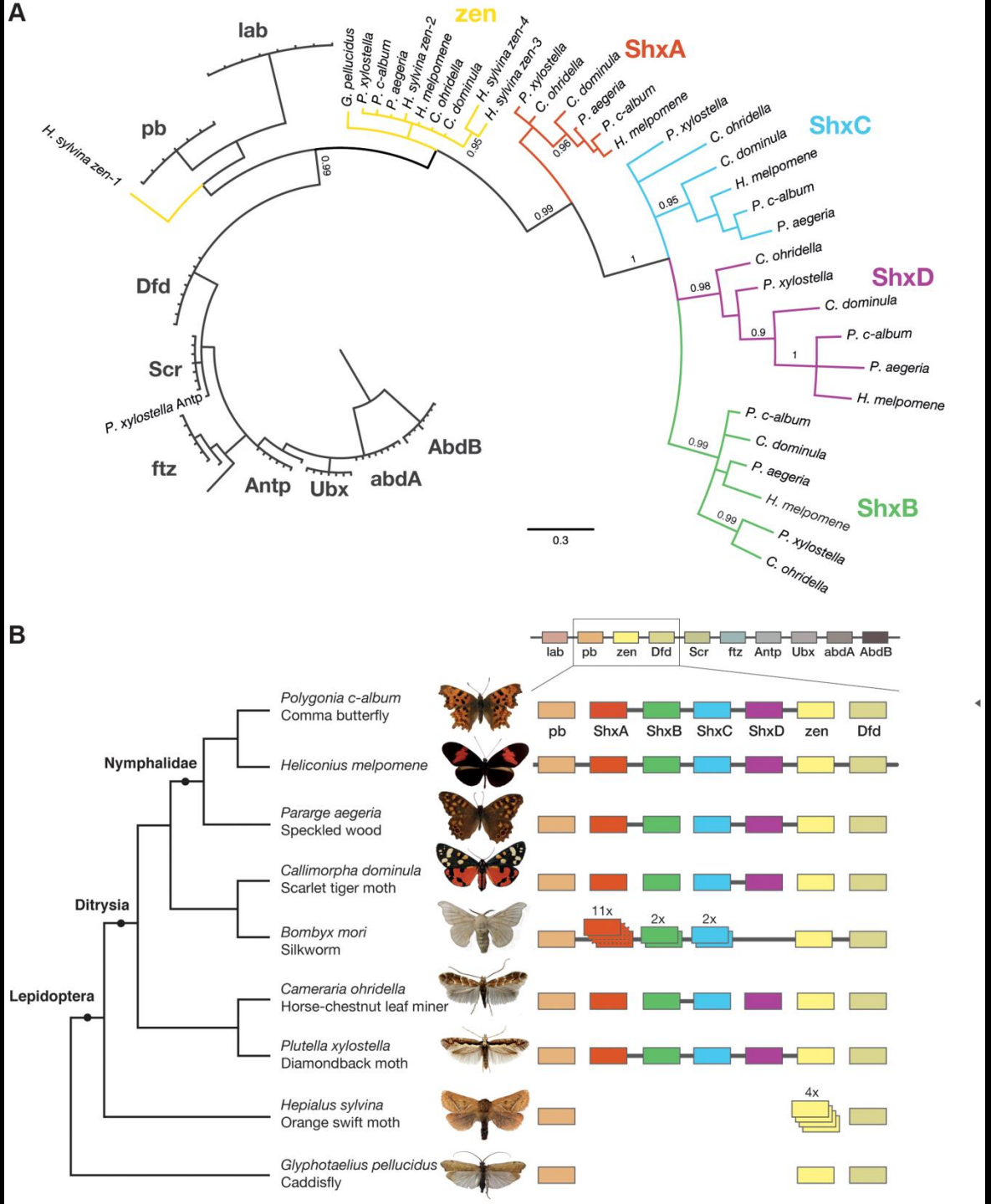
New genes from old: asymmetric divergence of gene duplicates and the evolution of development

Peter W. H. Holland[1], Ferdinand Marlétaz[1,2], Ignacio Maeso[1,3], Thomas L. Dunwell[1] and Jordi Paps[1,4]

[1]Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK
[2]Molecular Genetics Unit, Okinawa Institute of Science and Technology Graduate University, Onna, Okinawa 904-0495, Japan
[3]Centro Andaluz de Biología del Desarrollo, Consejo Superior de Investigaciones Científicas/Universidad Pablo de Olavide, 41013 Sevilla, Spain
[4]School of Biological Sciences, University of Essex, Colchester, Essex, UK

PWHH, 0000-0003-1533-9376

Public



Ferguson et al 2014

Homeobox Superfamily

⬇

Class ANTP

⬇

Subclass HOXL

⬇

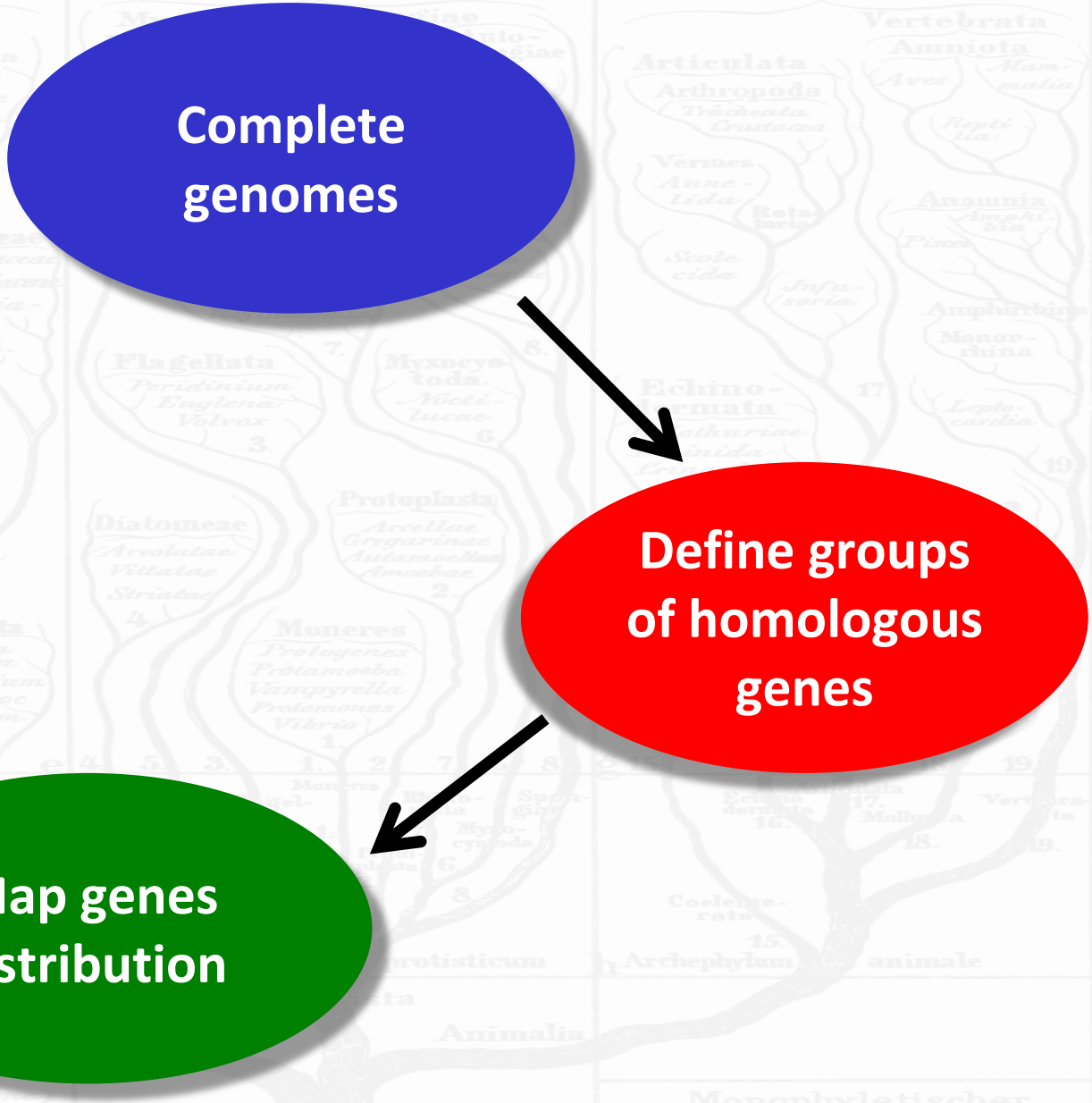
Family *Hox1*

Classes	Families
ANTP(767)	HOXL subclass Cdx(22) Evx(17) Gbx(15) Gsx(13) Hox1(21) Hox2(13) Hox3(25) Hox4(24) Hox5(19) Hox6-8(55) Hox9-13(15)(96) Meox(14) Mnx(15) Pdx(6) NKL subclass Abox(5) Ankx(1) Barhl(16) Bari(4) Barx(10) Bsx(10) Dbx(15) Dlx(35) Emx(22) En(19) Hhex(10) Hlx(9) Hx(1) Lbx(14) Lcx(1) Msx(22) Msxlx(3) Nanog(15) Nedx(5) Nk1(17) Nk2.1(18) Nk2.2(15) Nk3(14) Nk4(19) Nk5/Hmx(25) Nk6(19) Nk7(4) Noto(10) Ro(5) Tlx(19) Vax(12) Ventx(18)
PRD(458)	Alx(16) AprdA(1) AprdB(1) AprdC(1) AprdD(2) AprdE(1) Argfx(3) Arx(14) CG11294(3) Dmbx(8) Dprx(8) Drgx(9) Dux(42) Esx(2) Gsc(14) Hbn(3) Hesx(5) Hopx(5) Isx(5) Leutx(1) Mix(7) Nobox(5) Obox(36) Otp(12) Otx(24) Pax2/5/8(12) Pax3/7(24) Pax4/6(24) Phox(17) Pitx(20) Prop(8) Prrx(14) Rax(14) Repo(4) Rhox(39) Sebox(3) Shox(12) Tprx(5) Uncx(16) Vsx(18)
LIM(104)	Isl(14) Lhx1/5(17) Lhx2/9(19) Lhx3/4(15) Lhx6/8(18) Lmx(21)
POU(112)	Hdx(6) Pou1(6) Pou2(24) Pou3(29) Pou4(21) Pou5(12) Pou6(15)
HNF(23)	Ahnfx(1) Hmbox(10) Hnf1(12)
SINE(48)	Six1/2(18) Six3/6(17) Six4/5(13)
TALE(147)	Atale(1) Irx(44) Meis(23) Mkx(8) Pbx(29) Pknox(14) Tgif(28)
CUT(58)	Acut(1) Cmp(5) Cux(17) Onecut(24) Satb(11)
PROS(16)	Prox(16)
ZF(83)	Adnp(9) Azfh(1) Tshz(16) Zeb(14) Zfhx(21) Zhx/Homez(22)
CERS(26)	Cers(26)

- All human genome: 9,415 homology groups
- All fruit fly genome: 7,681 homology clusters

Zhong and Holland 2011

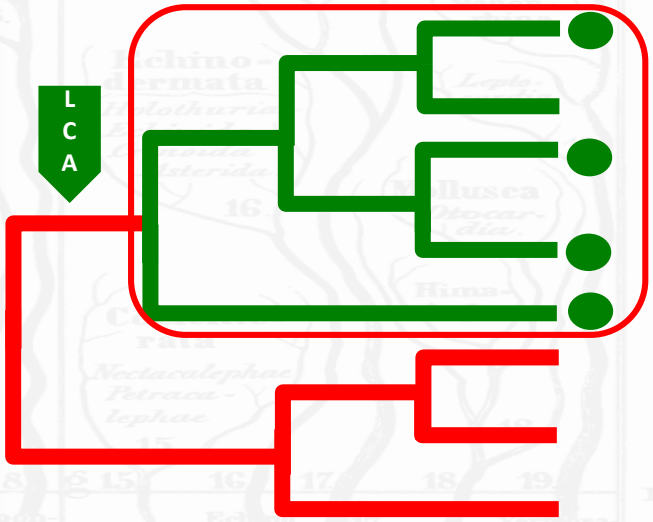
Public


Complete genomes
Define groups of homologous genes
Map genes distribution

Public

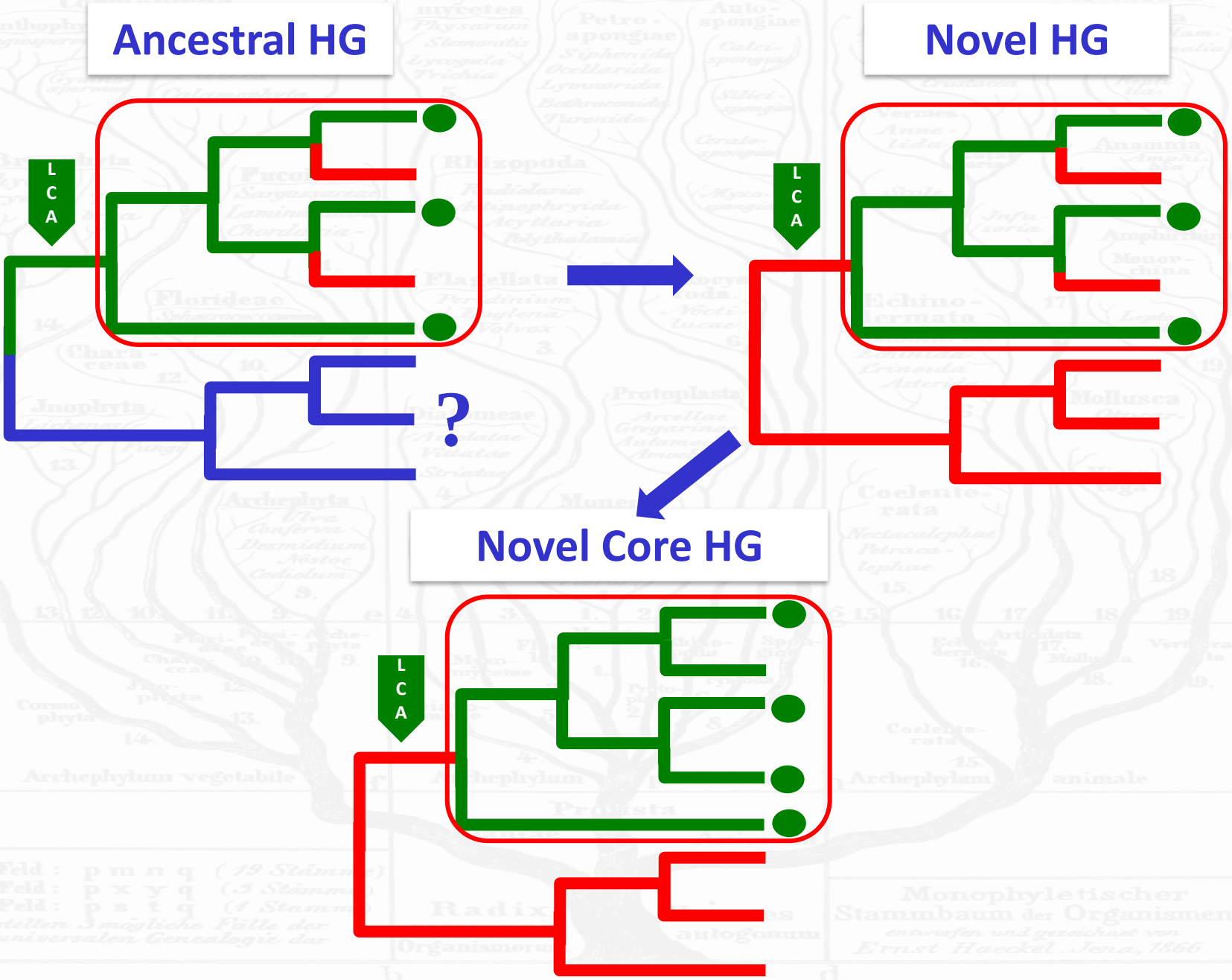
Phylogenetically-Aware Parsing Script

```
jordi@zoo-paralog: ~/ACTG/0_Analyses/03_Analyses
Tree:
Eukaryota
Amorphea
  Opisthokonta
    Holozoa
      Metazoa
        Diploblastica_(paraphyletic)
          Cnidaria
            Anthozoa
              Acropora_digitifera_(Adig) => 24
              Nematostella_vectensis_(Nvec) => 23
            Medusozoa
              Hydra_magnipapillata_(Hmag) => 25
          Placozoa
              Trichoplax_adhaerens_(Tadh) => 22
          Ctenophora
            Tentaculata_Lobata
              Mnemiopsys_leidyi_(Mley) => 20
            Tentaculata_Cydippida
              Pleurobrachia_bachei_(Pbac) => 21
          Porifera
            Homoscleromorpha
              Oscarella_carmela_(Ocar) => 19
            Demospongiae
              Amphimedon_queenslandica_(Aque) => 18
        Bilateria
          Deuterostomia
            Hemichordata
              Enteropneusta
                Saccolossus_kowaleski_(Skow) => 50
            Chordata
              Cephalochordata
                Branchiostoma_floridae_(Bflo) => 52
              Urochordata
                Botryllus_schlosseri_(Bsch) => 55
                Ciona_intestinalis_(Cint) => 53
                Ciona_savygni_(Csav) => 54
                Oikopleura_dioica_(Odio) => 56
              Vertebrata
                Anolis_carolinensis_(Acar) => 60
                Gallus_gallus_(Ggal) => 59
                Danio_rerio_(Drer) => 57
                Homo_sapiens_(Hsap) => 61
                Xenopus_tropicales_(Xtro) => 58
            Echinodermata
              Echinoidea
                Strongylocentrotus_purpuratus_(Spur) => 51
          Ecdysozoa
            Nematoda
              Chromadorea
                Caenorhabditis_elegans_(Cele) => 40
                Brugia_malayi_(Bmal) => 41
              Enoplea
                Romanomermis_culicivorax_(Rcul) => 39
                Trichinella_spiralis_(Tspi) => 38
```



Public

Types of gene groups



Public

Limitations

- Based on **protein-coding** genes, neglecting the role of **non-coding genes** (e.g., non-coding RNAs), **transposable elements**, and **regulatory elements** (e.g., enhancer, promoters, etc.).

- Based on **BLAST**, ignoring **gene fusions** and **fissions**, **alternative splicing**, etc. Limited to the **detection power** of the algorithm.

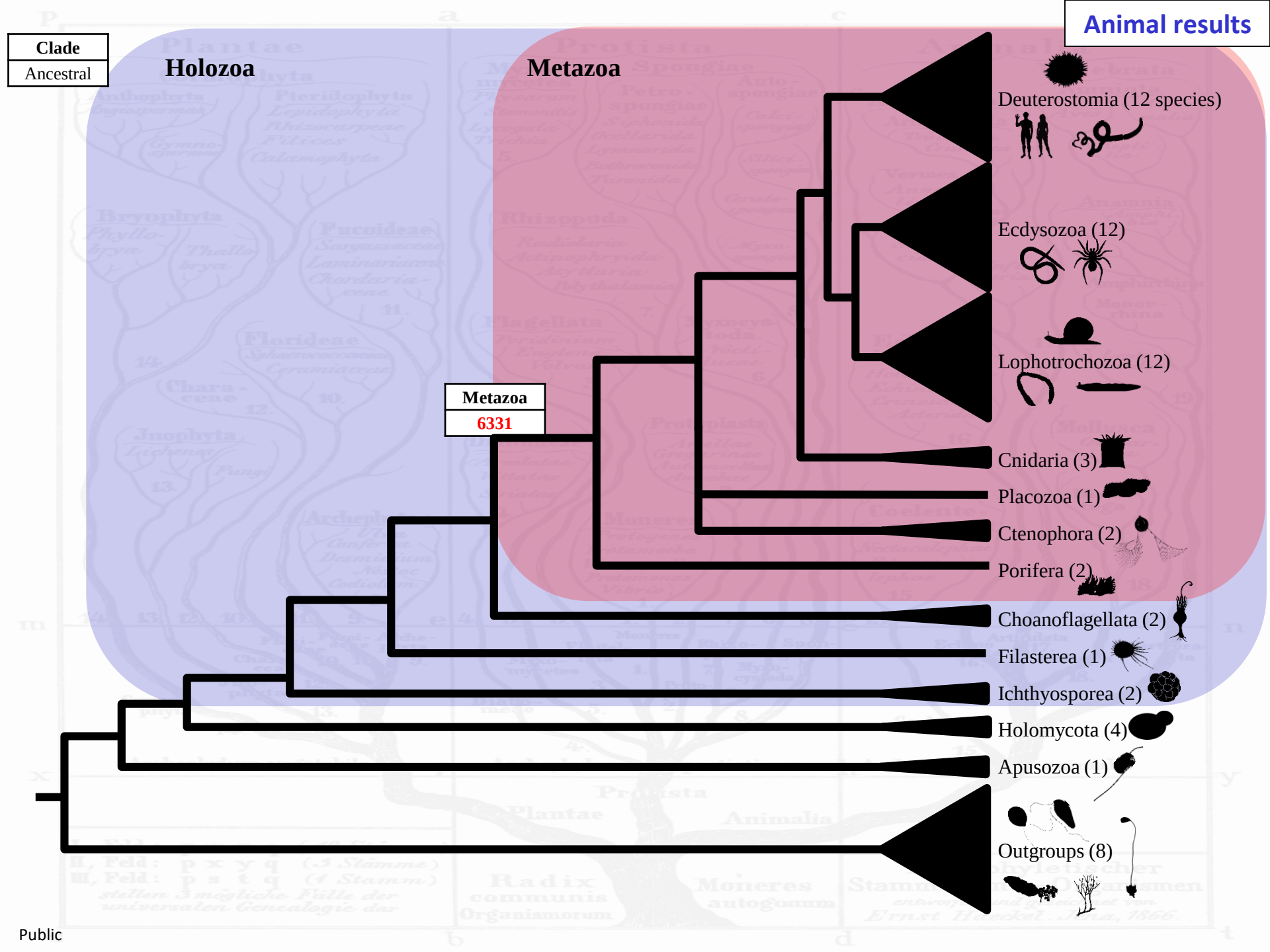
- **Robust taxon sampling**, but still far from complete.

Public

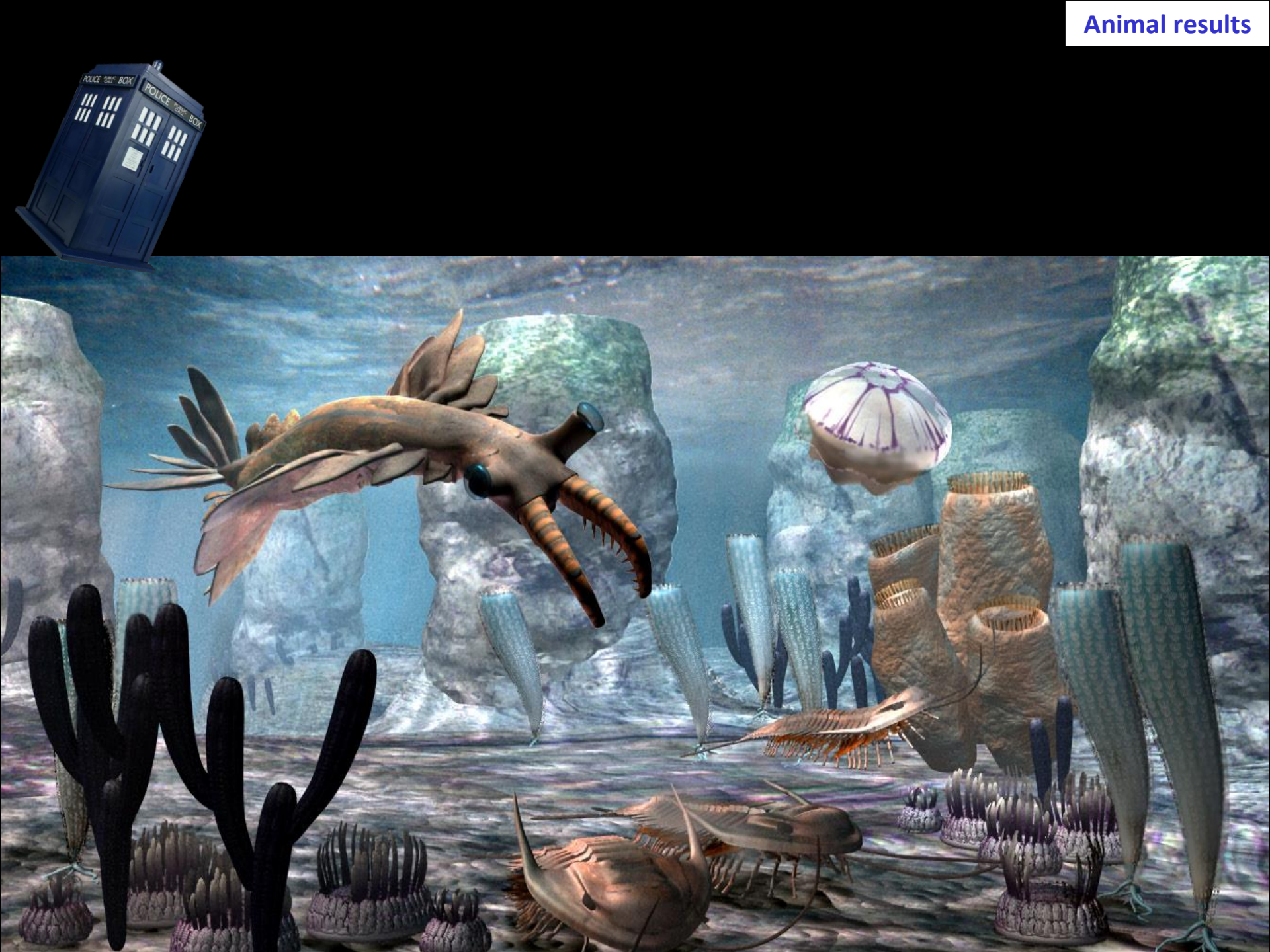
THE GENOME OF THE FIRST ANIMAL

Public

Animal results

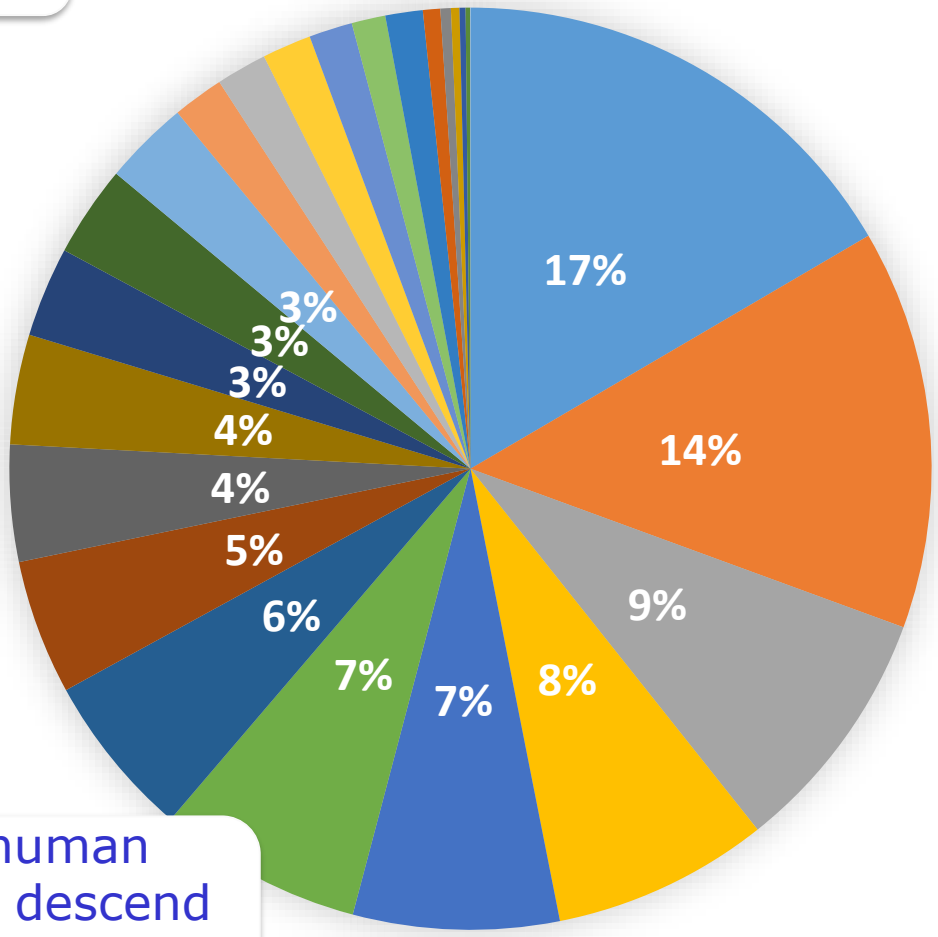


Public


POLICE PUBLIC BOX
POLICE PUBLIC BOX

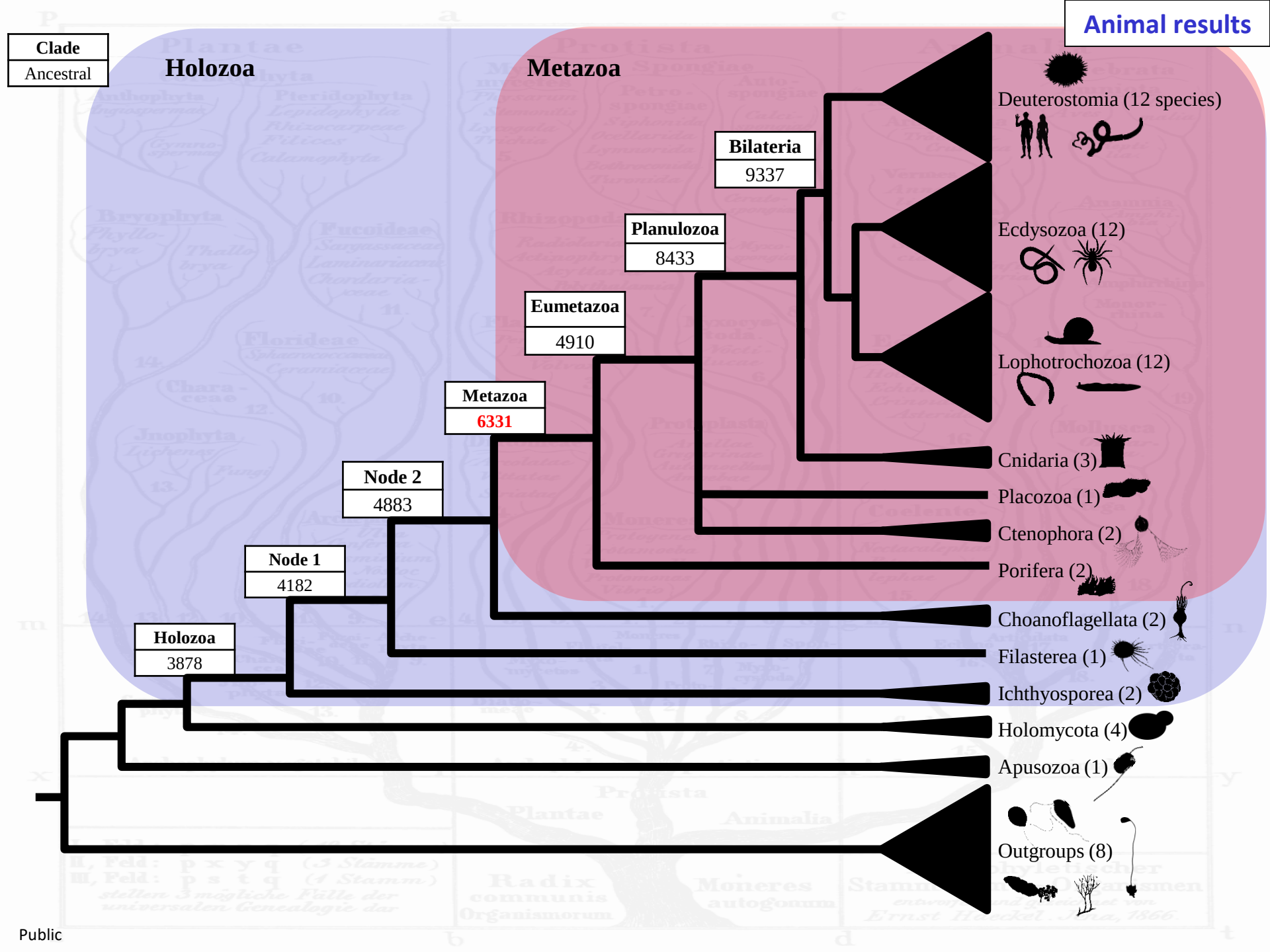
6331 homology groups in the first animal

- **Gene regulation**
- **Metabolism**



- **60%** of modern human and fruit fly genes descend from these homology groups.

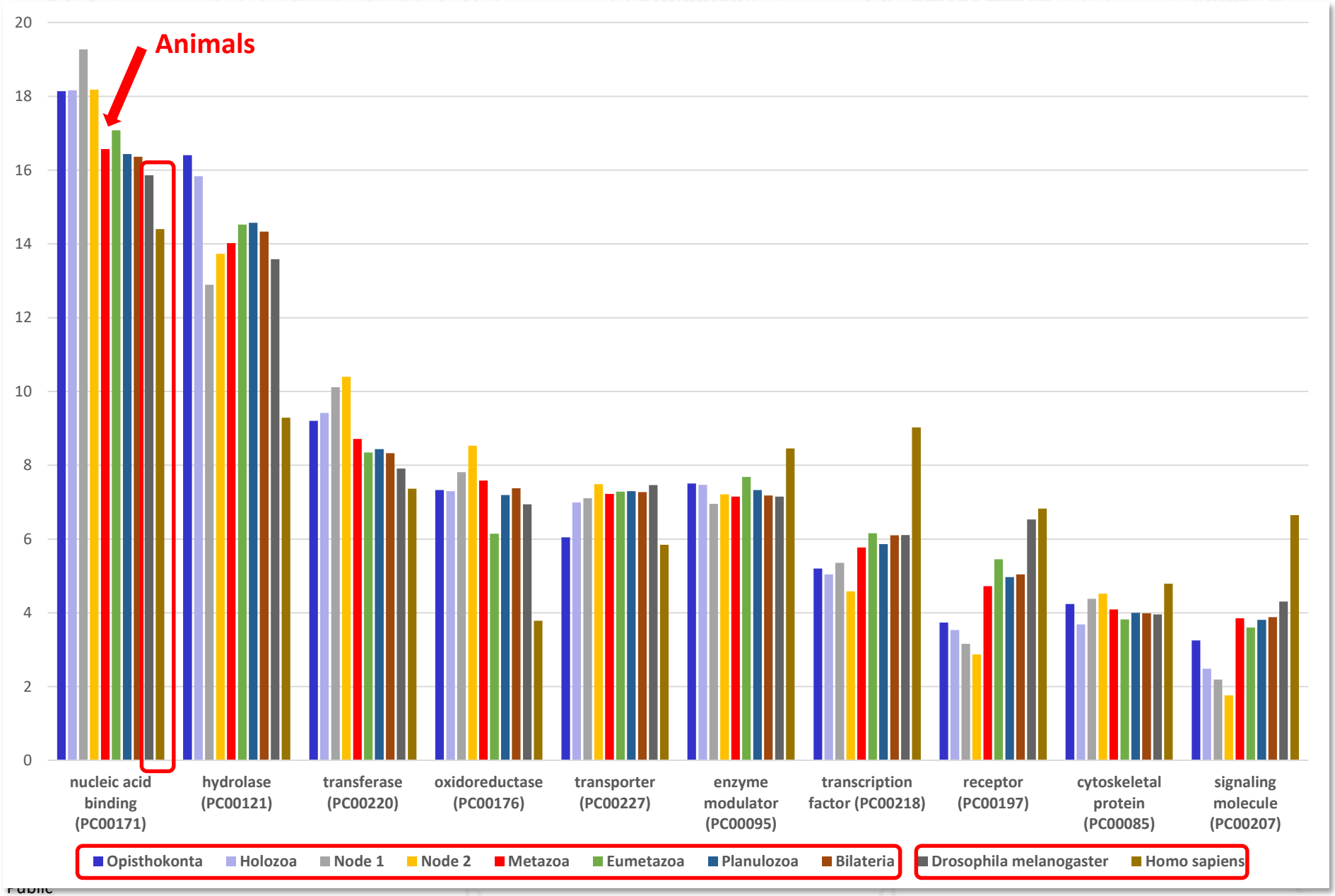
Public


Clade
Ancestral
Holozoa
Metazoa
Bilateria
9337
Planulozoa
8433
Eumetazoa
4910
Metazoa
6331
Node 2
4883
Node 1
4182
Holozoa
3878
Deuterostomia (12 species)
Ecdysozoa (12)
Lophotrochozoa (12)
Cnidaria (3)
Placozoa (1)
Ctenophora (2)
Porifera (2)
Choanoflagellata (2)
Filasterea (1)
Ichthyosporea (2)
Holomycota (4)
Apusozoa (1)
Outgroups (8)

Public

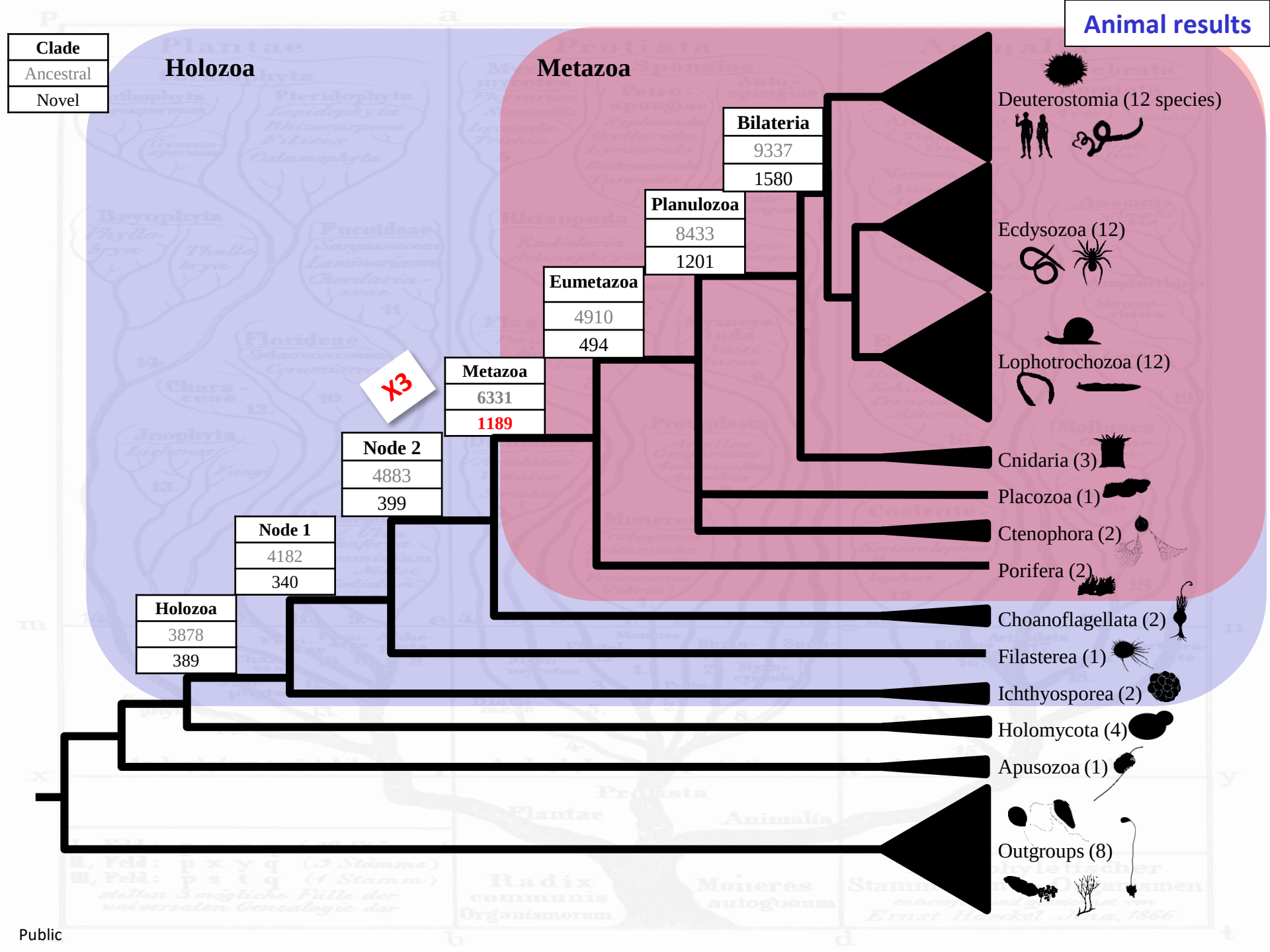
Evolution of Ancestral HG

Animal results



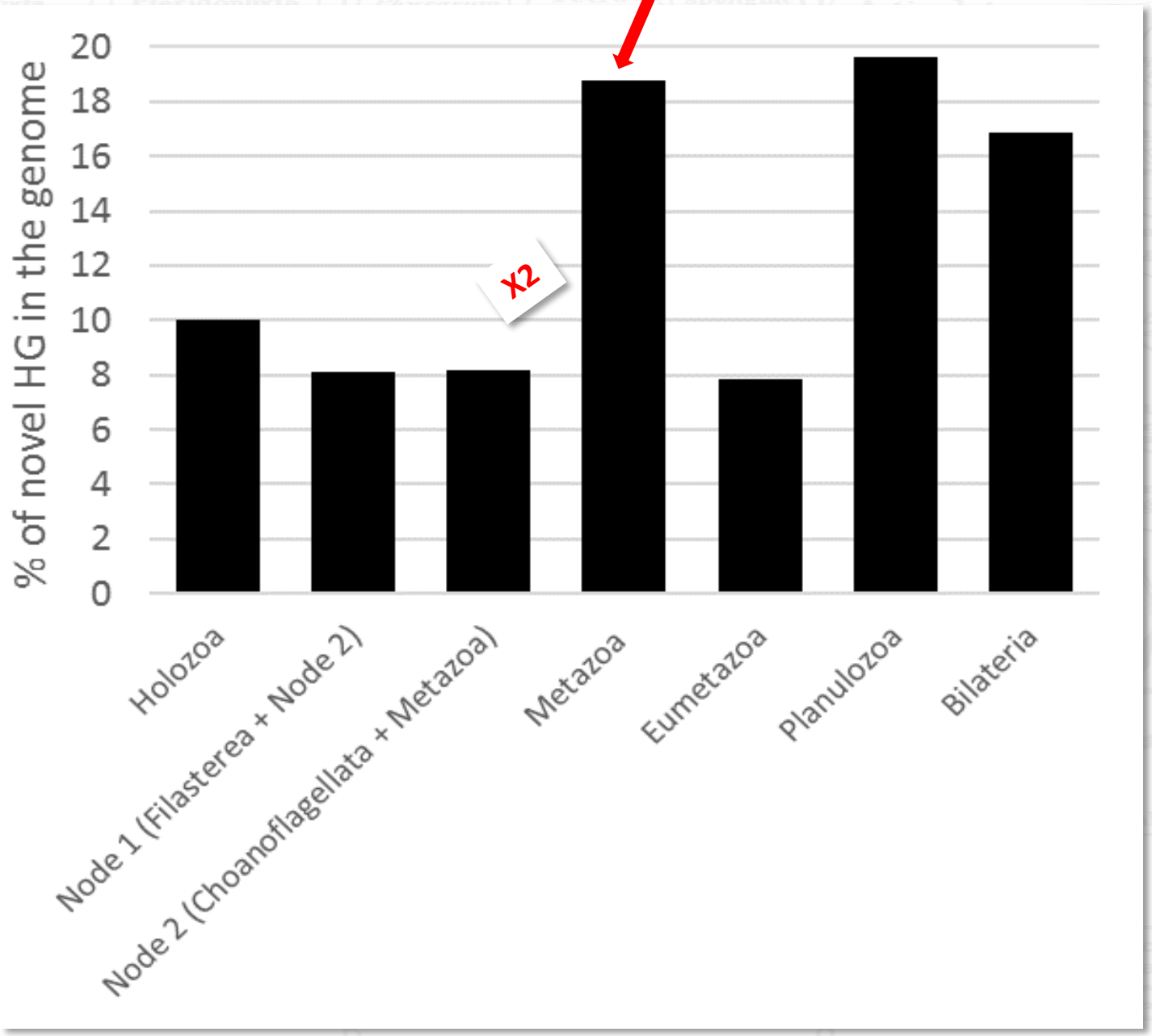
A GENOMIC EXPLOSION OF NOVELTY

Public


Clade
Ancestral
Novel
Holozoa
Metazoa
Holozoa
3878
389
Node 1
4182
340
Node 2
4883
399
Metazoa
6331
1189
X3
Eumetazoa
4910
494
Planulozoa
8433
1201
Bilateria
9337
1580
Deuterostomia (12 species)
Ecdysozoa (12)
Lophotrochozoa (12)
Cnidaria (3)
Placozoa (1)
Ctenophora (2)
Porifera (2)
Choanoflagellata (2)
Filasterea (1)
Ichthyosporea (2)
Holomycota (4)
Apusozoa (1)
Outgroups (8)

Public

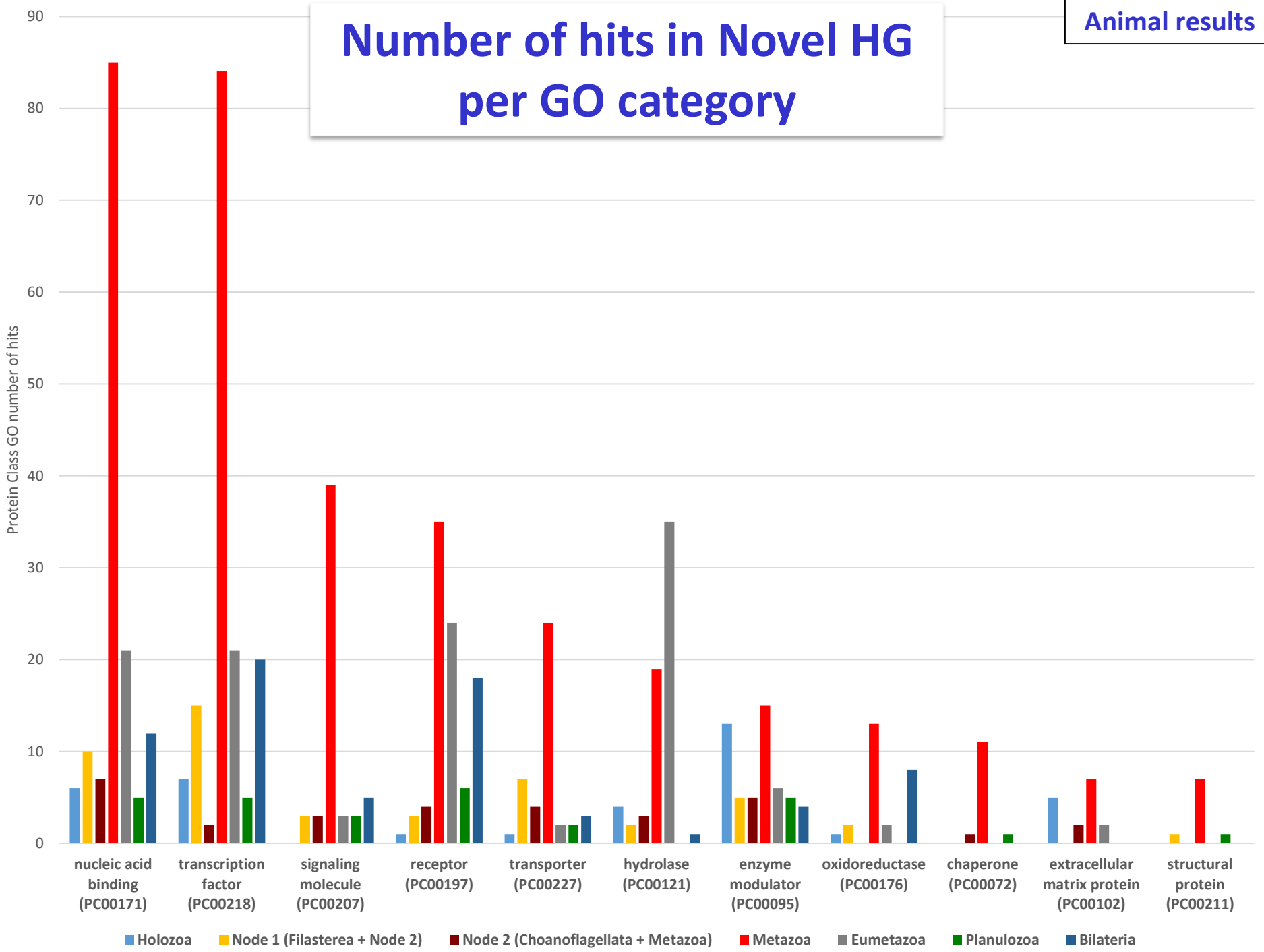
% Novelty



Public

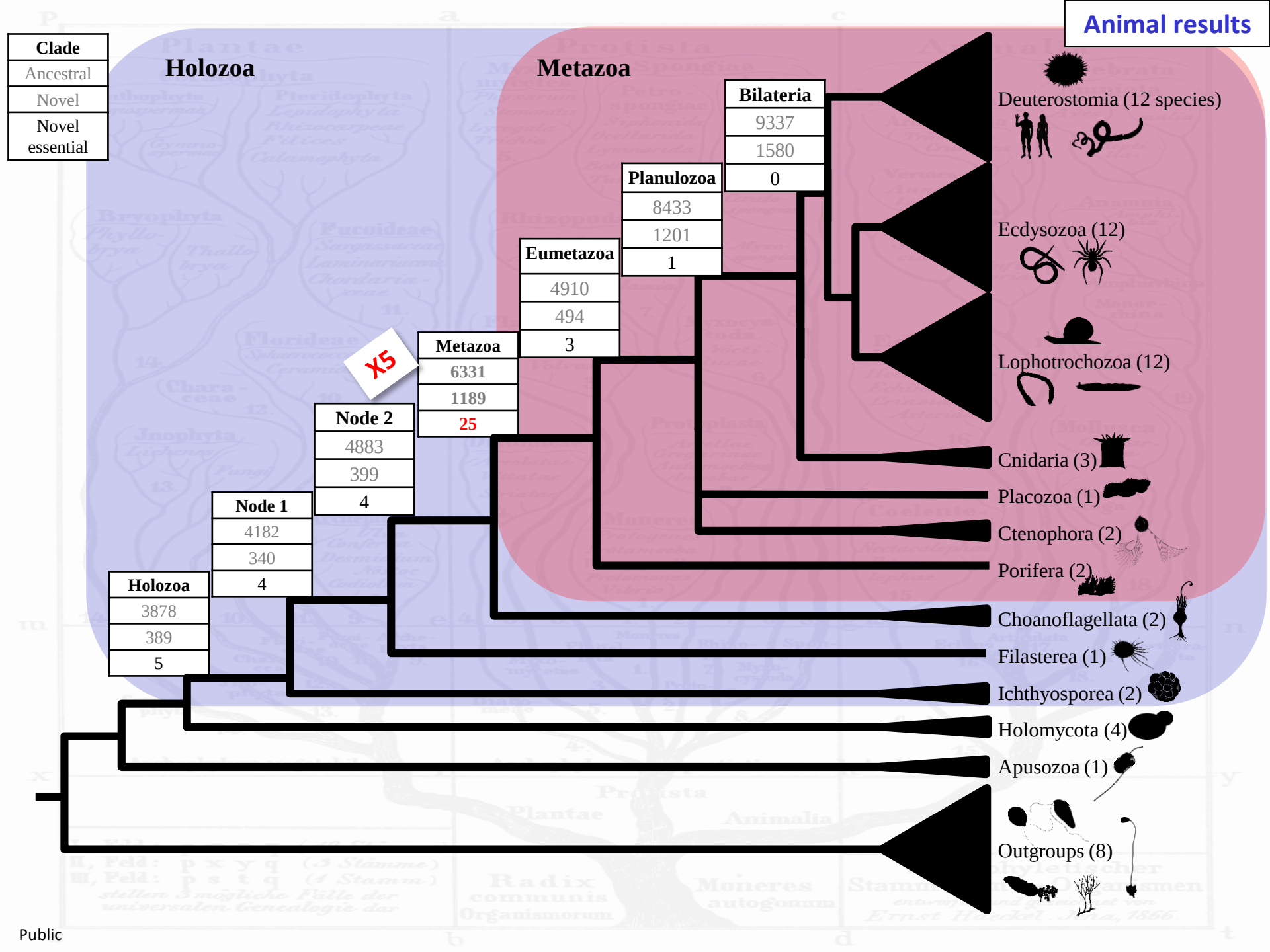
Animal results

Number of hits in Novel HG per GO category



25 ESSENTIAL NEW ANIMAL HOMOLOGY GROUPS

Public


Clade
Ancestral
Novel
Novel essential
Holozoa
Metazoa
Holozoa
3878
389
5
Node 1
4182
340
4
Node 2
4883
399
4
X5
Metazoa
6331
1189
25
Eumetazoa
4910
494
3
Planulozoa
8433
1201
1
Bilateria
9337
1580
0
Deuterostomia (12 species)
Ecdysozoa (12)
Lophotrochozoa (12)
Cnidaria (3)
Placozoa (1)
Ctenophora (2)
Porifera (2)
Choanoflagellata (2)
Filasterea (1)
Ichthyosporea (2)
Holomycota (4)
Apusozoa (1)
Outgroups (8)

Public

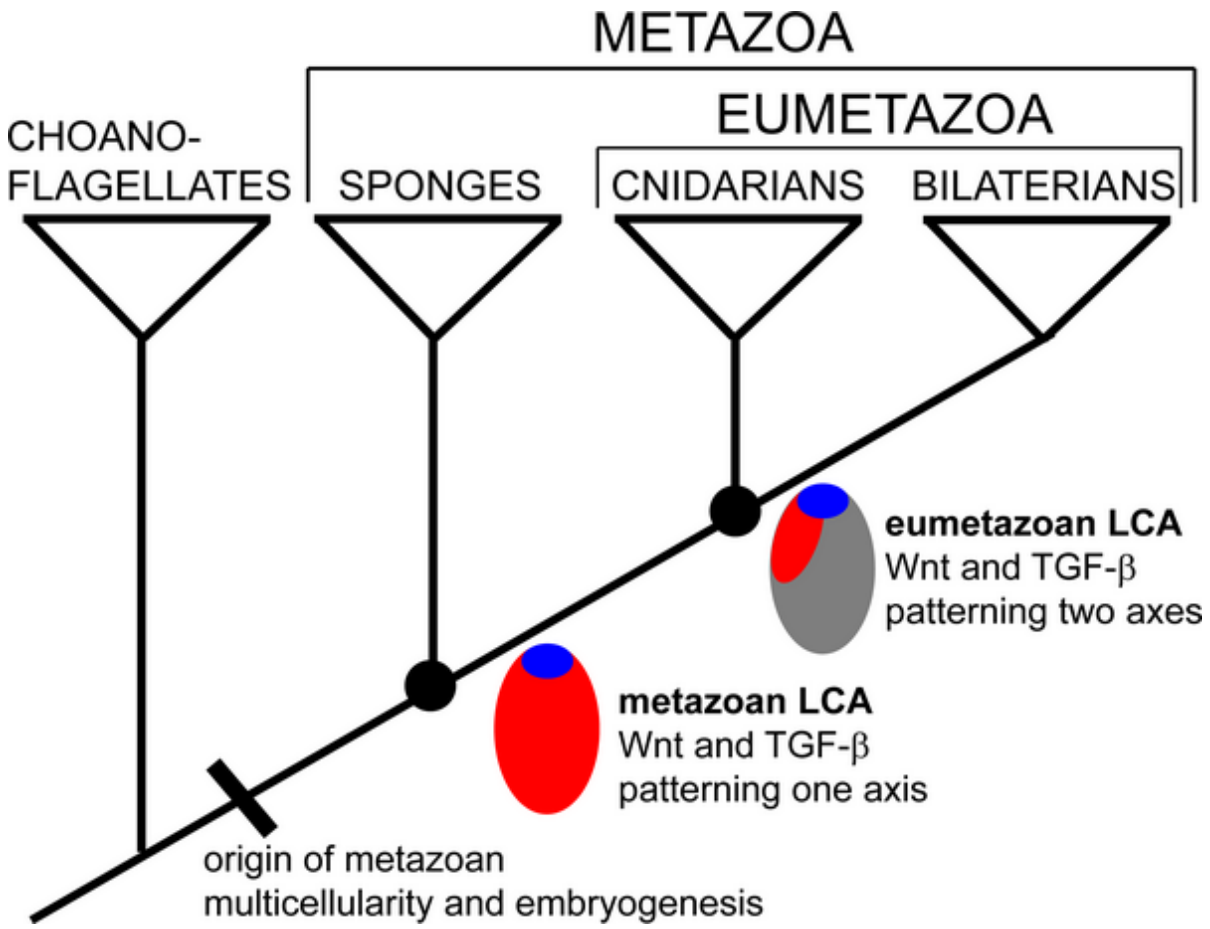
Summary of metazoan novelties

8 HG involved in signalling pathways

Signalling pathways		Fruitfly genes examples
Wnt	• **Wnt**	*wingless*
	• **Frizzled**	*frizzled, smoothened*
	• **pangolín/TCF-LEF**	*pangolin*
	• **armadillo/beta-catenin**	*armadillo*
TGF-Beta/BMP	• **TGF-Beta/BMP**	*decapentaplegic, screw, activin beta*
	• **SMAD**	*mothers against decapentaplegic*
	• **TFG-Beta Receptor**	*punt, saxophone, wishful thinking*
	• **MAPKKK**	*sunday driver*

Public

Wnt and TFG-Beta

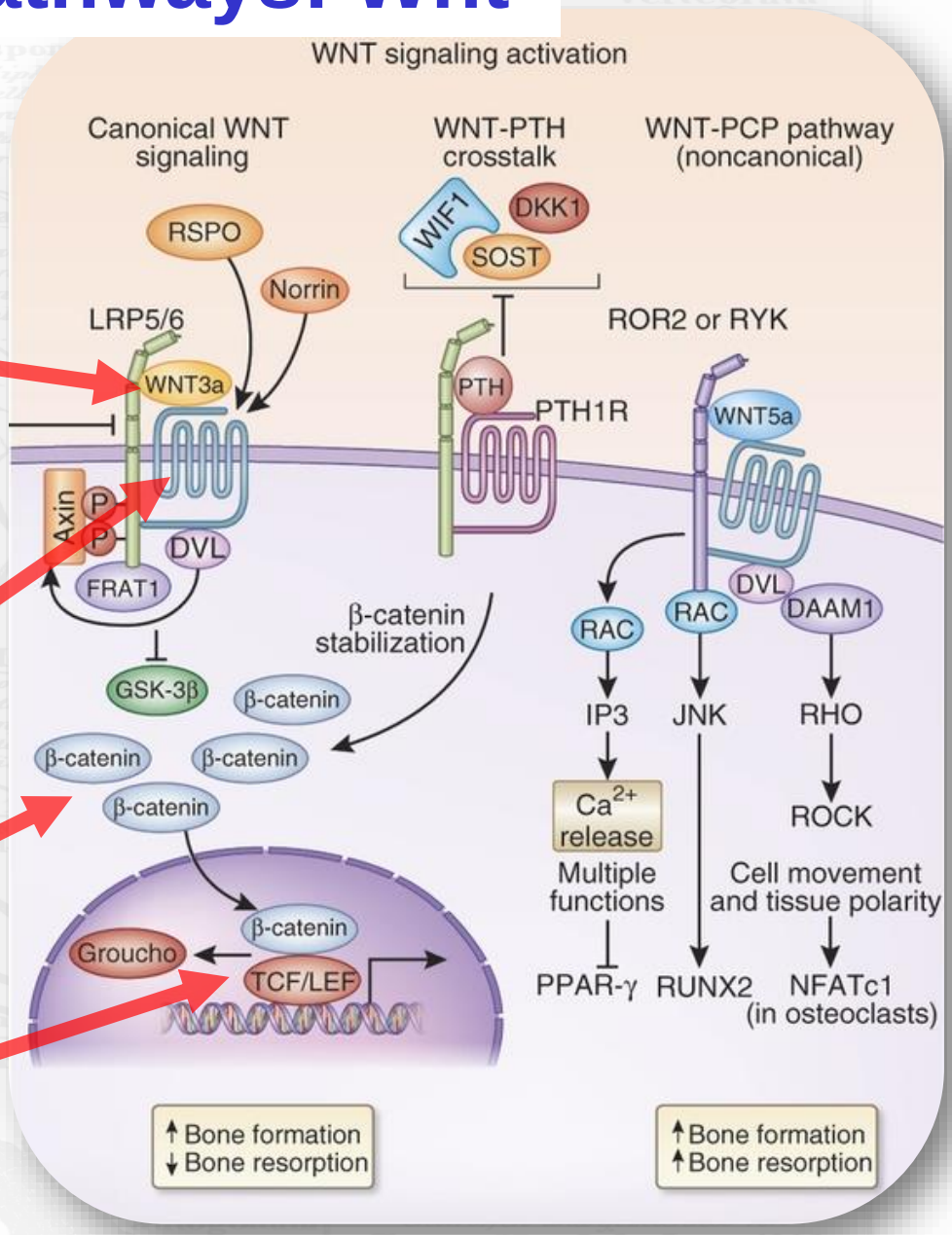


Adamska *et al* 2007

Public

Signalling pathways: Wnt

Wnt	Ligand
Frizzled	GPCR **receptor of Wnt**, activates *Dishevelled* in cytosol
Armadillo/beta -catenin	Translocation to nucleus
Pangolin LEF/TCF	Gene activation

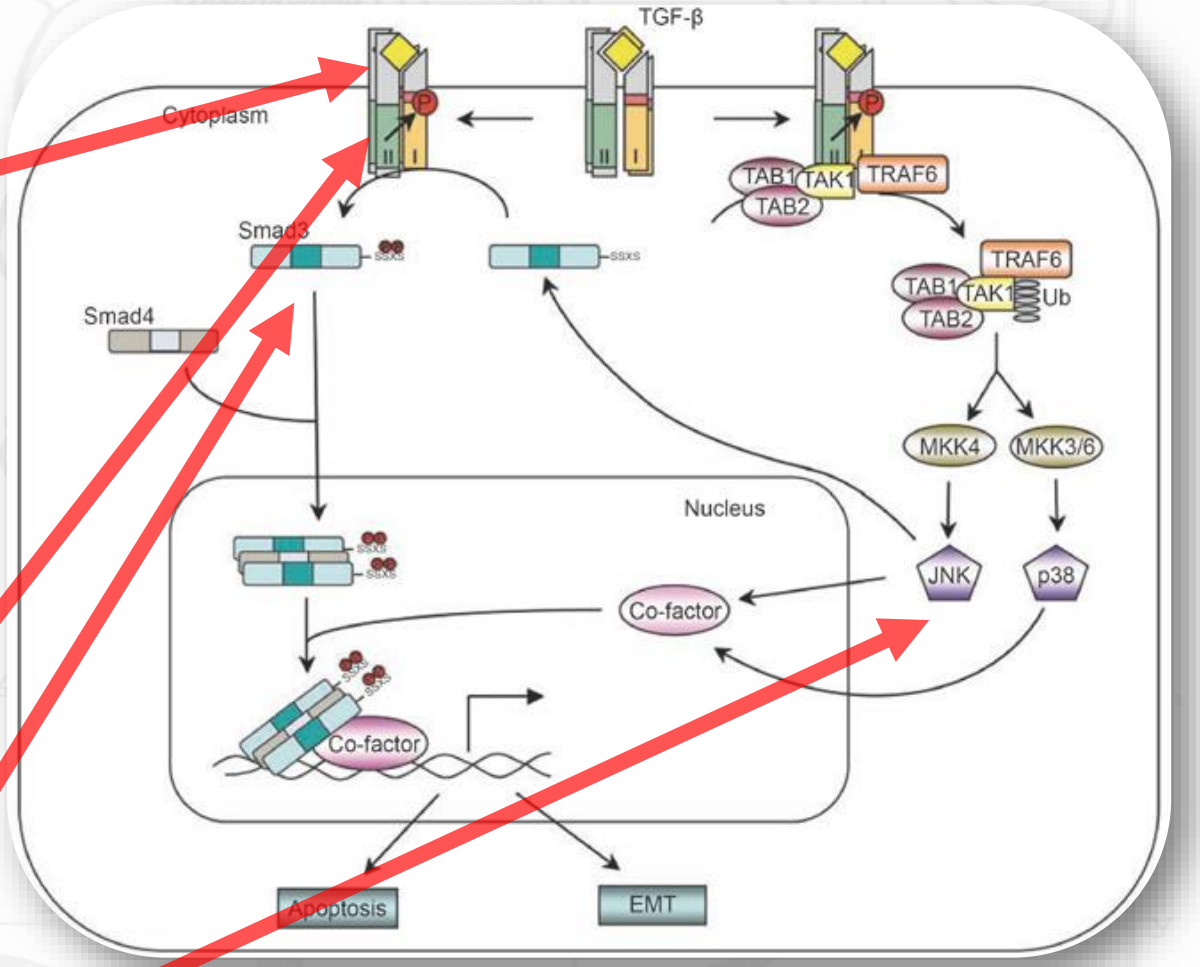


Public

TGF-Beta / BMP

Animal results

TGF-β / BMP Growth differentiation factor / inhibin / myostatin	Cell signalling proteins, involved in **growth, development, tissue homeostasis** and **immune system.** Cellular processes in adult and embryo (cell growth, differentiation, apoptosis, cellular homeostasis...), growth factors such as cytokines and as metabologen. TGFβ ligands bind to a **type II receptor -> phosphorylates a type I receptor** -> phosphorylates receptor-regulated **SMADs** (R-SMADs) which can now bind the coSMAD SMAD4 -> R-SMAD/coSMAD act as TFs in the nucleus
TGF Beta Recept / Activin Recept / BMP Recept	Transmembrane receptor
SMAD	Signal transductor of extracellular TGF beta ligands)
MAP kinase kinase kinase (MAPK8IP3, Sunday driver)	serine/threonine-specific protein kinase, **JNK**



Summary of metazoan novelties

7 HG comprising Transcription Factors

	Transcription Factors	Fruitfly genes examples
Homeobox	• **NKL subclass of the ANTP Class**	*tinman, distalless, ems*
	• **SIX Class**	*sine oculis, optix*
	• **POU Class**	*pou proteins, nubbi, ventral veins lacking*
bHLH	• **hes/hairy**	*hairy, hey, deadpan, clockwork orange*
	• **bHLH-PAS**	*single-minded, spineless, trachealess*
	• **twist/hand**	*twist, hand, target of Poxn, taxi, atonal*
• **ETS**		*ets65A, anterior open, pointed*

Public

Homeobox genes

Animal results

Classes	Families
ANTP(767)	HOXL subclass Cdx(22) Evx(17) Gbx(15) Gsx(13) Hox1(21) Hox2(13) Hox3(25) Hox4(24) Hox5(19) Hox6-8(55) Hox9-13(15)(96) Meox(14) Mnx(15) Pdx(6) NKL subclass Abox(5) Ankx(1) Barhl(16) Bari(4) Barx(10) Bsx(10) Dbx(15) Dlx(35) Emx(22) En(19) Hhex(10) Hlx(9) Hx(1) Lbx(14) Lcx(1) Msx(22) Msxlx(3) Nanog(15) Nedx(5) Nk1(17) Nk2.1(18) Nk2.2(15) Nk3(14) Nk4(19) Nk5/Hmx(25) Nk6(19) Nk7(4) Noto(10) Ro(5) Tlx(19) Vax(12) Ventx(18)
PRD(458)	Alx(16) AprdA(1) AprdB(1) AprdC(1) AprdD(2) AprdE(1) Argfx(3) Arx(14) CG11294(3) Dmbx(8) Dprx(8) Drgx(9) Dux(42) Esx(2) Gsc(14) Hbn(3) Hesx(5) Hopx(5) Isx(5) Leutx(1) Mix(7) Nobox(5) Obox(36) Otp(12) Otx(24) Pax2/5/8(12) Pax3/7(24) Pax4/6(24) Phox(17) Pitx(20) Prop(8) Prrx(14) Rax(14) Repo(4) Rhox(39) Sebox(3) Shox(12) Tprx(5) Uncx(16) Vsx(18)
LIM(104)	Isl(14) Lhx1/5(17) Lhx2/9(19) Lhx3/4(15) Lhx6/8(18) Lmx(21)
POU(112)	Hdx(6) Pou1(6) Pou2(24) Pou3(29) Pou4(21) Pou5(12) Pou6(15)
HNF(23)	Ahnfx(1) Hmbox(10) Hnf1(12)
SINE(48)	Six1/2(18) Six3/6(17) Six4/5(13)
TALE(147)	Atale(1) Irx(44) Meis(23) Mkx(8) Pbx(29) Pknox(14) Tgif(28)
CUT(58)	Acut(1) Cmp(5) Cux(17) Onecut(24) Satb(11)
PROS(16)	Prox(16)
ZF(83)	Adnp(9) Azfh(1) Tshz(16) Zeb(14) Zfhx(21) Zhx/Homez(22)
CERS(26)	Cers(26)

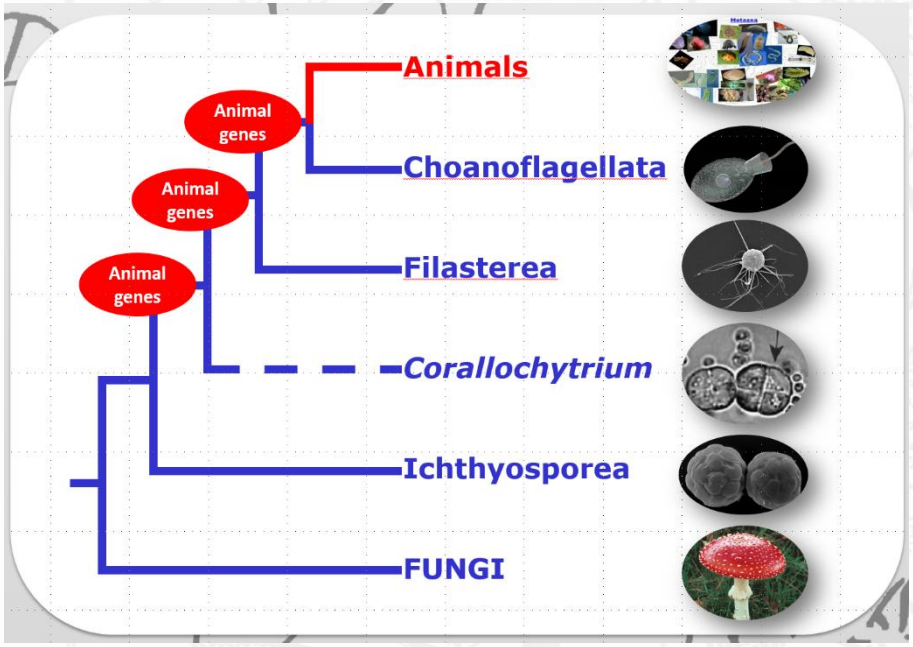
Zhong and Holland 2011

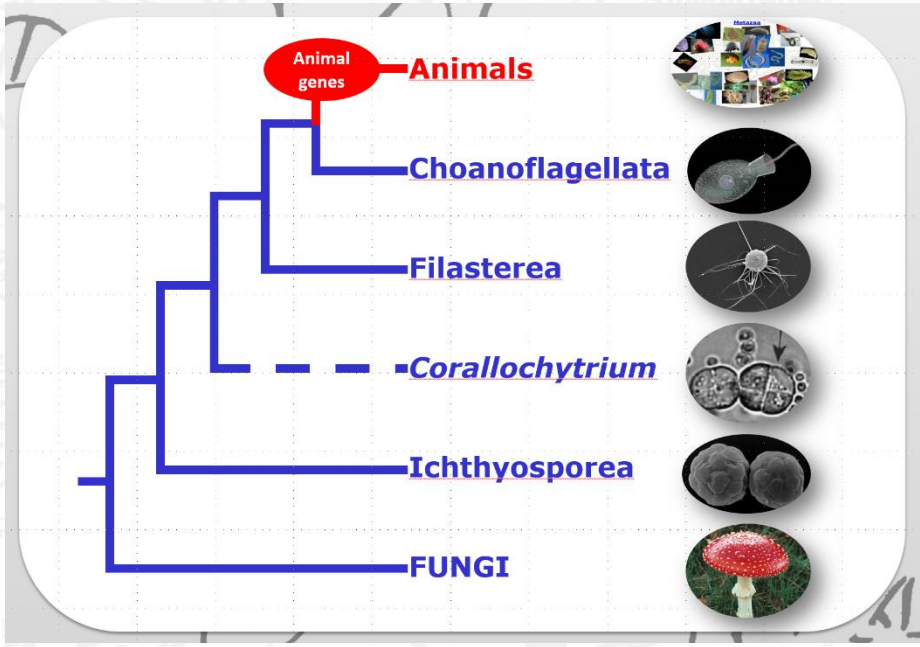
Public

Transcripts polyadenilation	
• Cytoplasmic Polyadenylation Element Binding (CPEB)	Binds the polyA tail of mRNA and regulates their translation
Cell adhesion	
• Alpha-catenin • Fermitin • Liprin	Activation of the integrin pathway and other cell-extracellular matrix interactions via focal adhesions
Cell cycle	
• RUN	Cell prolifera
• MADD/GEF	Cell apoptos
Receptors	
• Nuclear Hormone Receptors	
• Neurotransmitter Receptors	
Synaptic exocytosis	
• Calcium activated protein for secretion (CAPS) • Rab3-interacting molecules (RIM)	Regulate the fusion of vesicles with the cell membrane, neuroendrocine cells and presynaptic neurons respectively

Public

Old vs new





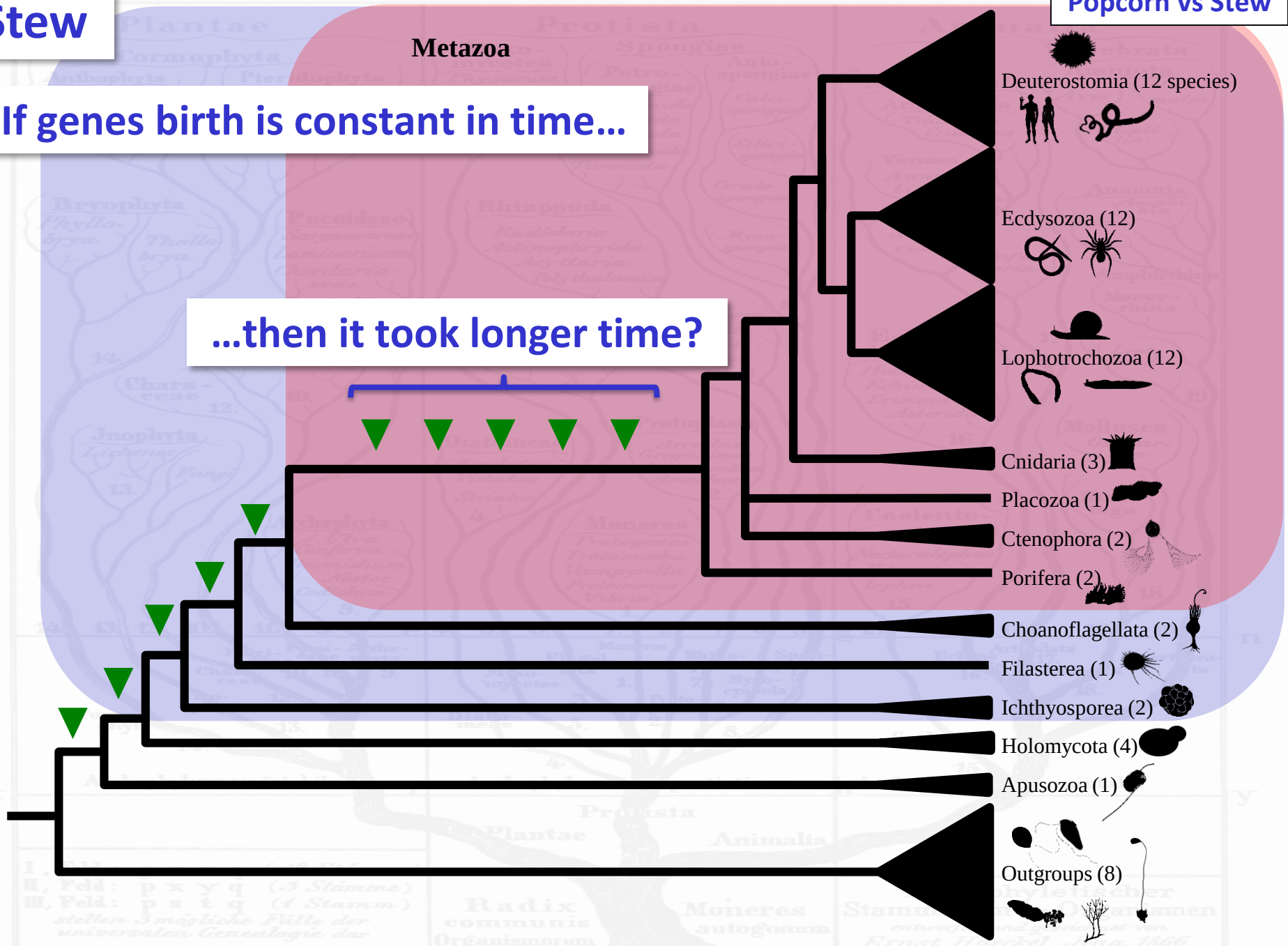
Public

Animal Origins: Stew vs Popcorn

Public

Stew

Popcorn vs Stew



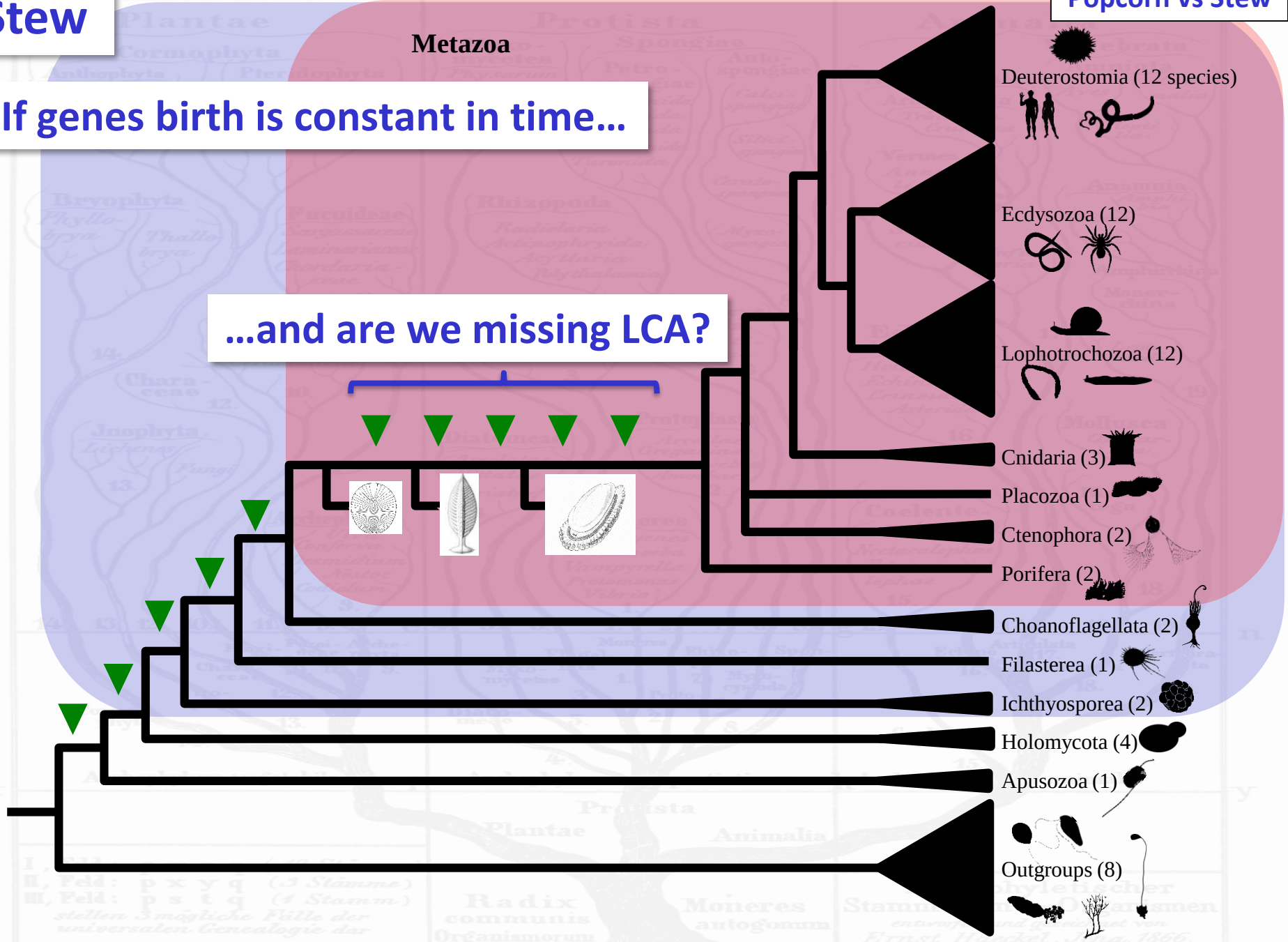
Public

Stew

Popcorn vs Stew

- If genes birth is constant in time…

…and are we missing LCA?

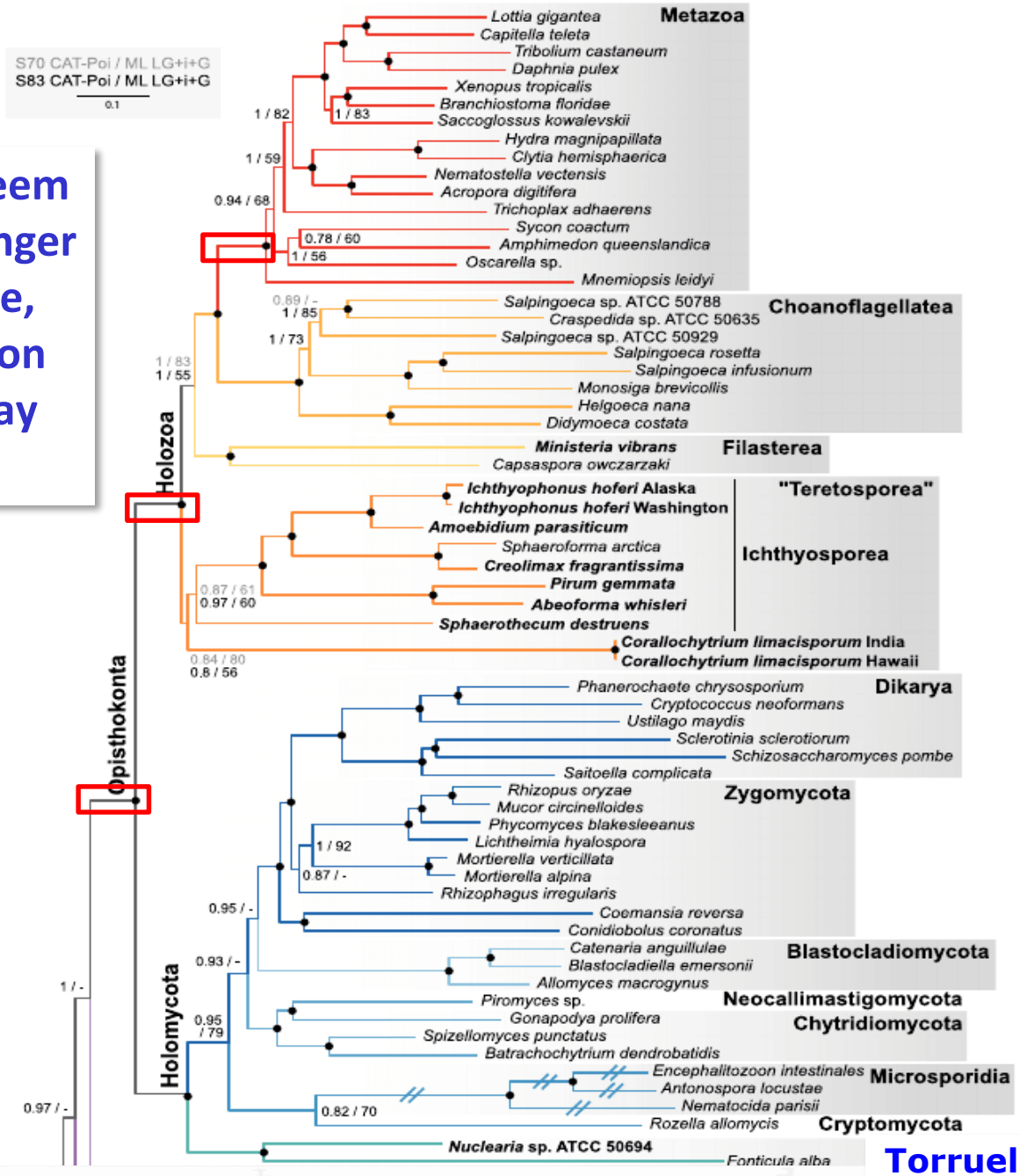


Public

Stew

Popcorn vs Stew

Trees do not seem to support a longer period of time, but substitution saturation may mask it.



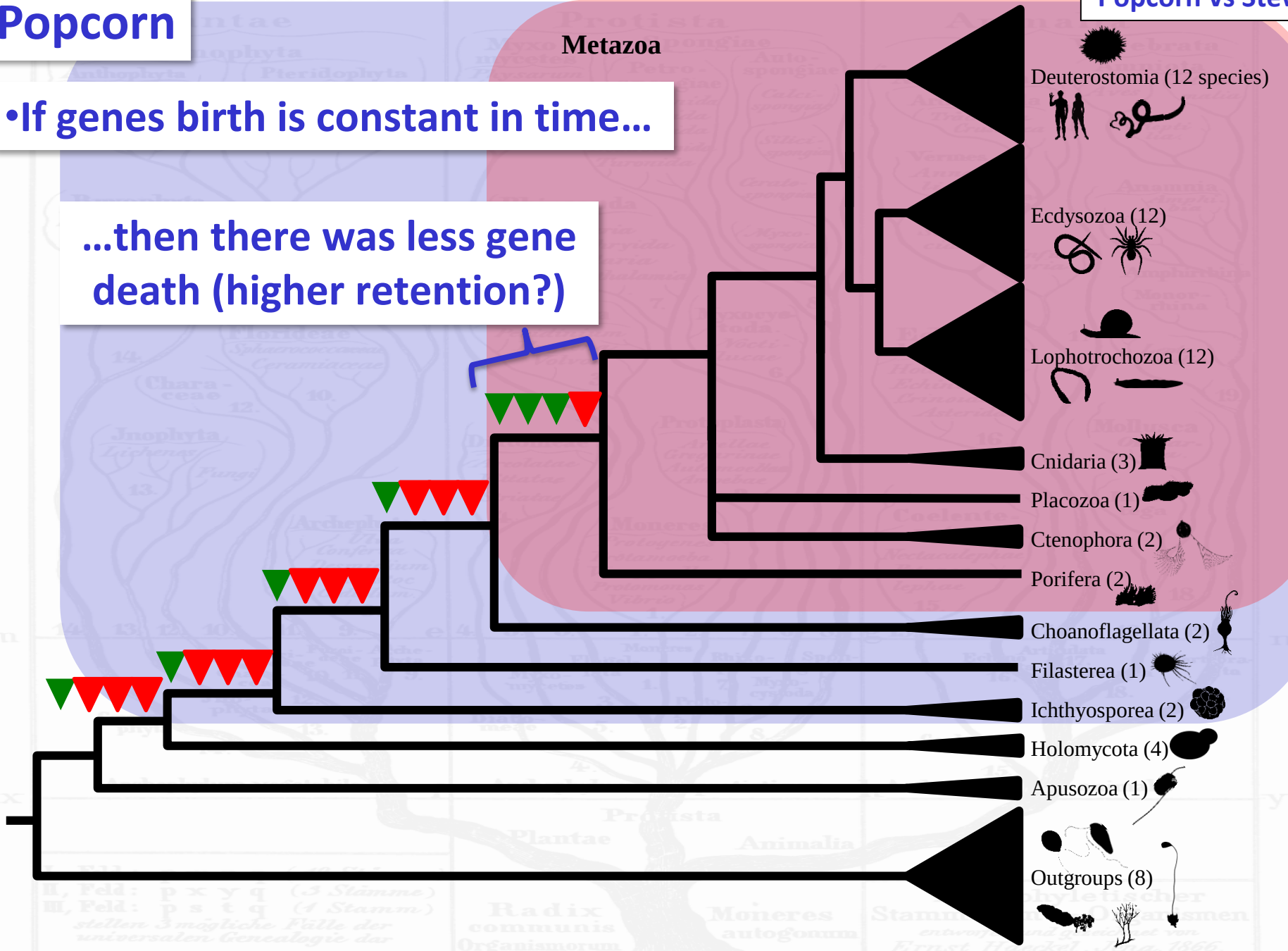
Torruella et al 2015

Public

Popcorn

- If genes birth is constant in time…

…then there was less gene death (higher retention?)



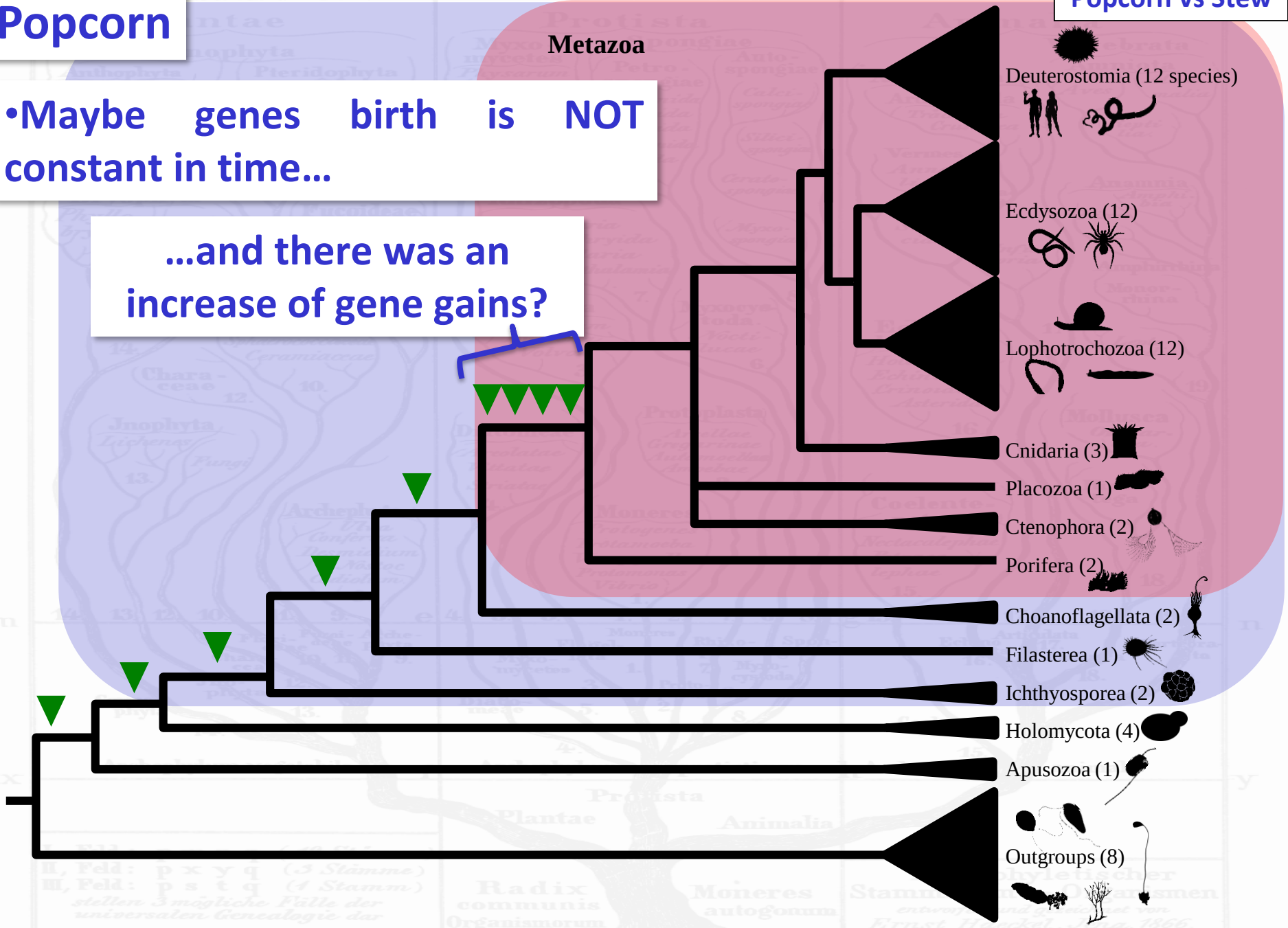
Public

Popcorn

Popcorn vs Stew

- Maybe genes birth is NOT constant in time…

…and there was an increase of gene gains?



Public

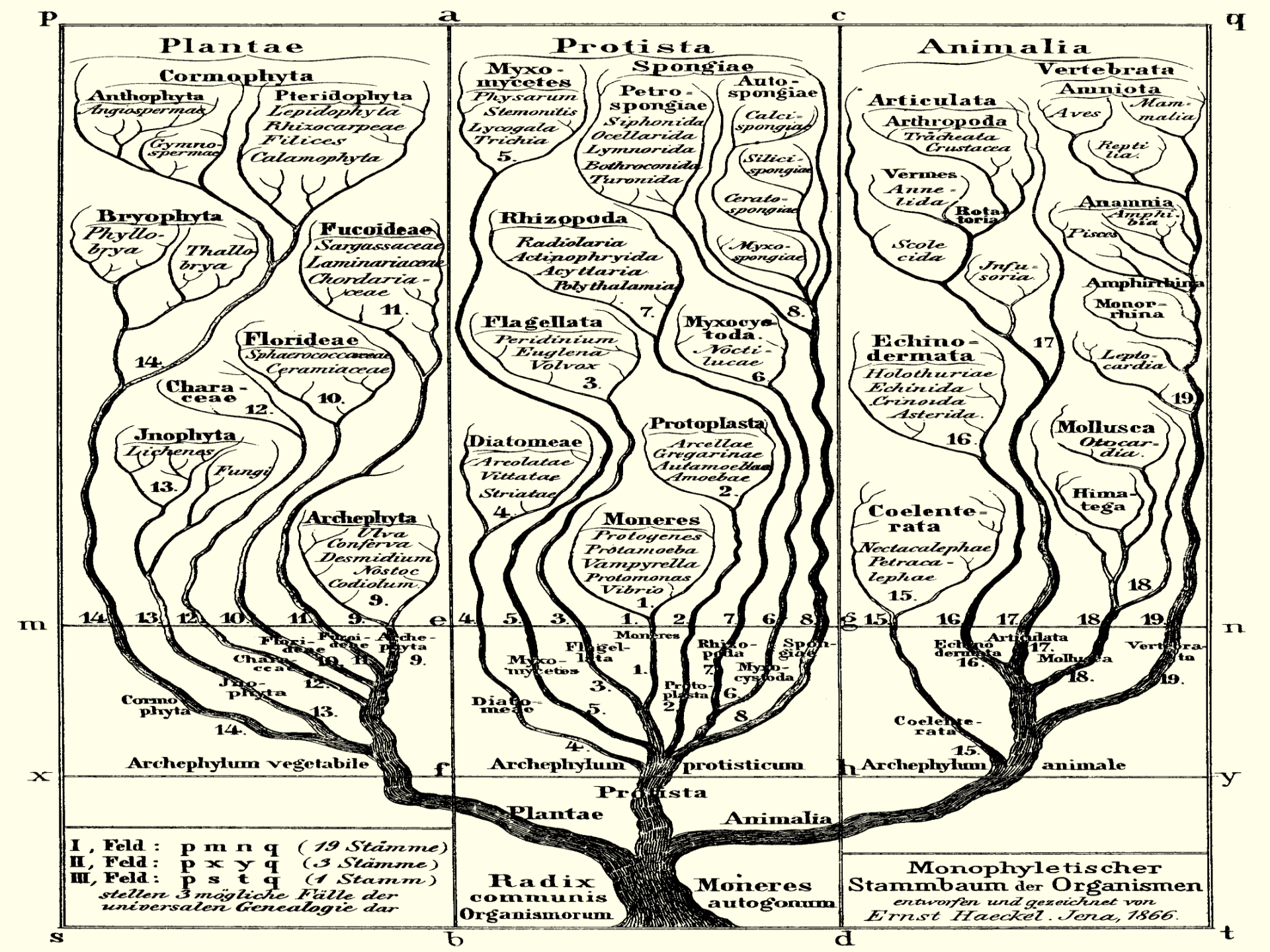
To sum up…

- **The reconstruction of the first animal genome** shows a (*boring*) list of **6381 homology groups**. Predominant functions include **gene regulation and metabolism**, its composition is similar to other **LCA and modern metazoan genomes**.

- **The origin of animals**, compared to other nodes, shows a **surge in the level of gene novelties**, specially for **gene regulation**.

- There is a **core set of 25 homology groups**, never lost since the origin of animals, formed by some **iconic systems** (i.e. Wnt, Nk homeobox), but also by other **novel genes** never linked before to animal origins with relevant functions related to multicellularity.

Public


p
a
c
q
Plantae
Cormophyta
Anthophyta
Angiospermae
Gymnospermae
Pteridophyta
Lepidophyta
Rhizocarpeae
Filices
Calamophyta
Bryophyta
Phyllobrya
Thallobrya
Fucoideae
Sargassaceae
Laminariaceae
Chordariaceae
11.
Florideae
Sphaerococcaceae
Ceramiaceae
10.
14.
Characeae
12.
Jnophyta
Lichenes
Fungi
13.
Archephyta
Ulva
Conferva
Desmidium
Nostoc
Codiolum
9.
Protista
Myxomycetes
Physarum
Stemonitis
Lycogala
Trichia
5.
Spongiae
Petrospongiae
Siphonida
Ocellarida
Lymnorida
Bothroconida
Turonida
Autospongiae
Calcispongiae
Silicispongiae
Cerato-spongiae
Myxospongiae
8.
Rhizopoda
Radiolaria
Actinophryida
Acyttaria
Polythalamia
7.
Flagellata
Peridinium
Euglena
Volvox
3.
Myxocytoda
Noctilucae
6.
Diatomeae
Arcolatae
Vittatae
Striatae
4.
Protoplasta
Arcellae
Gregarinae
Autamoebae
Amoebae
2.
Moneres
Protogenes
Protamoeba
Vampyrella
Protomonas
Vibrio
1.
Animalia
Vertebrata
Amniota
Aves
Mammalia
Reptilia
Articulata
Arthropoda
Tracheata
Crustacea
Vermes
Annelida
Rotatoria
Scolecida
Infusoria
Anamnia
Amphibia
Pisces
Amphirhina
Monorrhina
Leptocardia
19.
17.
Echinodermata
Holothuriae
Echinida
Crinoida
Asterida
16.
Mollusca
Otocardia
Himatega
18.
Coelenterata
Nectacalephae
Petracalephae
15.
m
e
g
n
14.
13.
12.
10.
11.
9.
4.
5.
3.
1.
2.
7.
6.
8.
15.
16.
17.
18.
19.
Archephyta
Florideae
Characeae
Jnophyta
Cormophyta
Myxomycetes
Flagellata
Diatomeae
Protoplasta
Rhizopoda
Myxocystoda
Spongiae
Coelenterata
Echinodermata
Articulata
Mollusca
Vertebrata
x
f
h
y
Archephylum vegetabile
Archephylum protisticum
Archephylum animale
Protista
Plantae
Animalia
I, Feld: p m n q (19 Stämme)
II, Feld: p x y q (3 Stämme)
III, Feld: p s t q (1 Stamm)
stellen 3 mögliche Fälle der universalen Genealogie dar
Radix communis Organismorum
Moneres autogonum
Monophyletischer Stammbaum der Organismen
entworfen und gezeichnet von
Ernst Haeckel. Jena, 1866.
s
b
d
t