

Coloration: a great system to study genotype-phenotype relationships

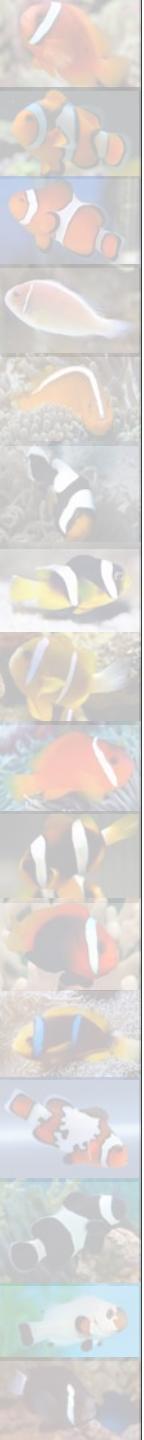
M1 – ENS
Module "Genomes and Phenotypes"
22/11/2018

Thibault Lorin



ENS

ÉCOLE NORMALE
SUPÉRIEURE

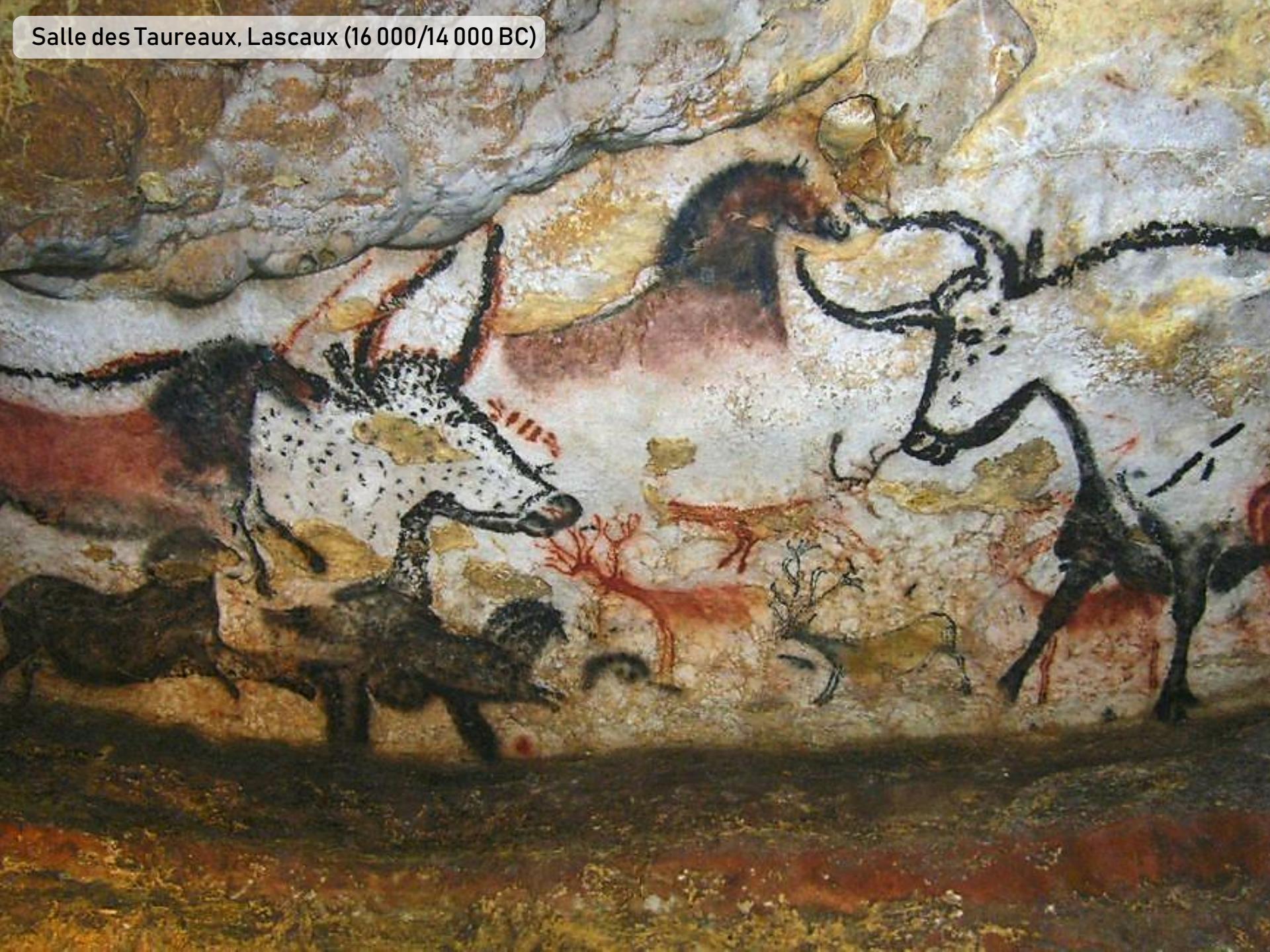


Laudet's lab



Volff's lab

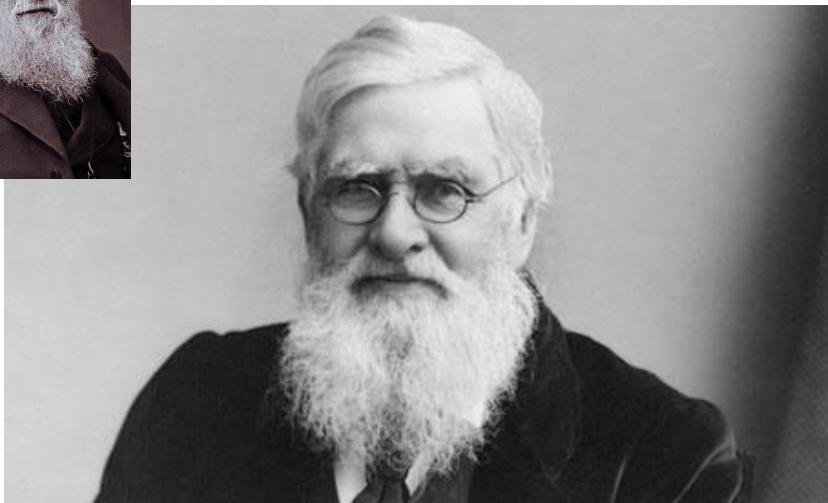
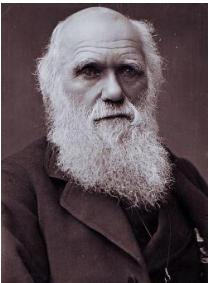
Salle des Taureaux, Lascaux (16 000/14 000 BC)



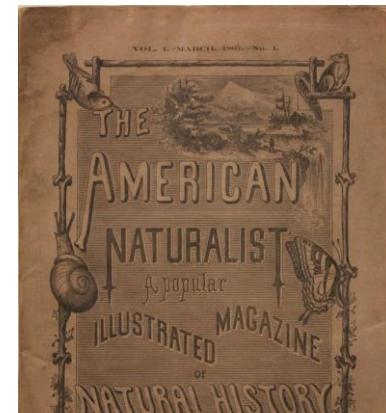
Introduction



Wallace and "coloration"



Alfred R. Wallace (1823-1913)

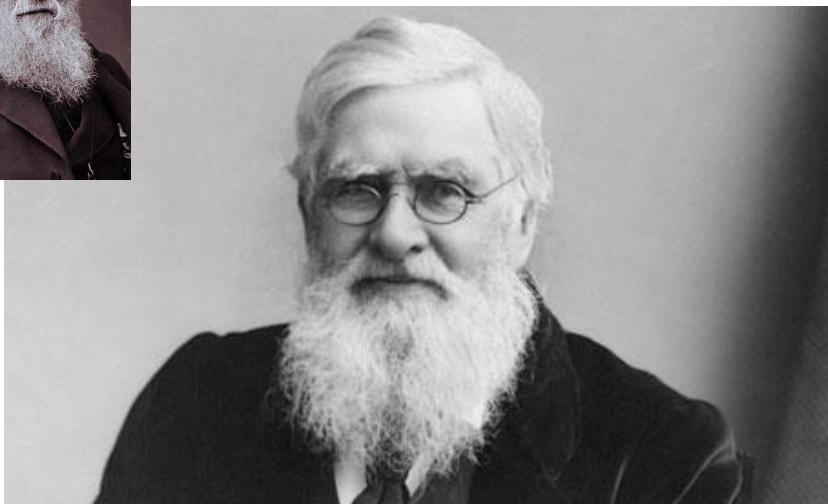
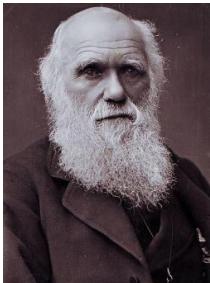


VOL. XI.—NOVEMBER, 1877.—No. 11.

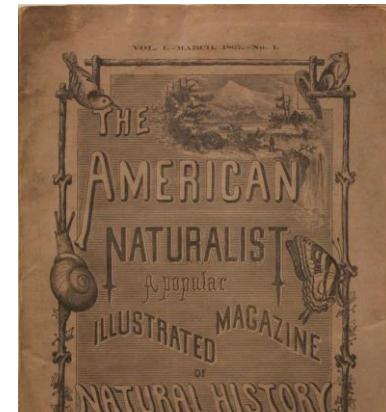
THE COLORS OF ANIMALS AND PLANTS.¹

BY ALFRED RUSSEL WALLACE.

Wallace and "coloration"



Alfred R. Wallace (1823-1913)



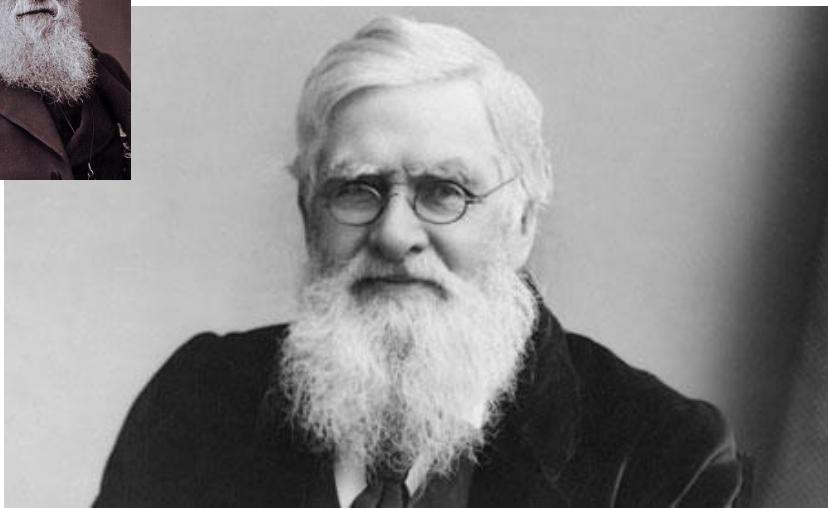
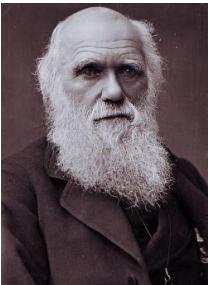
VOL. XI.—NOVEMBER, 1877.—No. 11.

THE COLORS OF ANIMALS AND PLANTS.¹

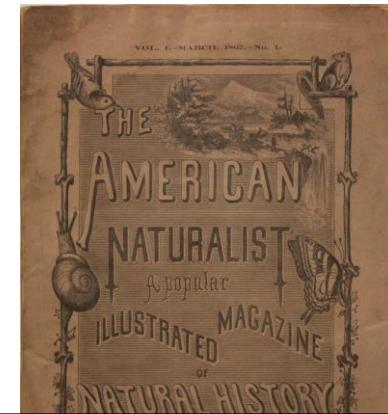
BY ALFRED RUSSEL WALLACE.

- Animals. { 1. Protective colors.
 2. Warning colors.
 3. Sexual colors.
 4. Typical colors.
Plants. 5. Attractive colors

Wallace and "coloration"



Alfred R. Wallace (1823-1913)



VOL. XI.—NOVEMBER, 1877.—No. 11.

THE COLORS OF ANIMALS AND PLANTS.¹

BY ALFRED RUSSEL WALLACE.



Camouflage

Animals.

- 1. Protective colors.
- 2. Warning colors.
- 3. Sexual colors.
- 4. Typical colors.



Intra- or Interspecific
communication colors

"Coloration" or "pigmentation"?



"Structural colors"

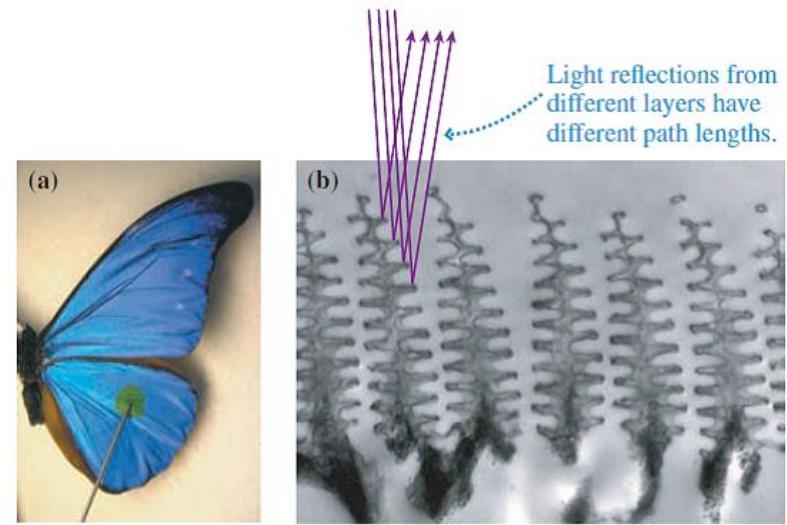
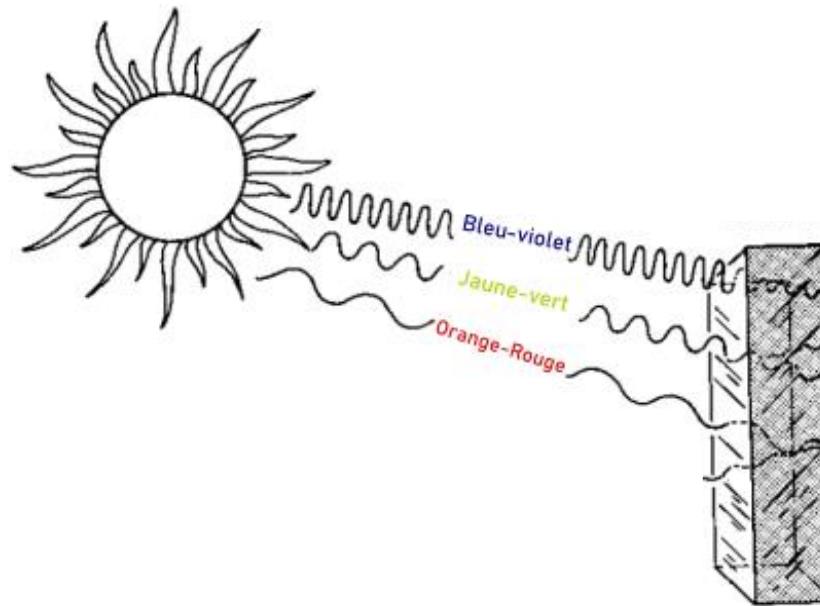


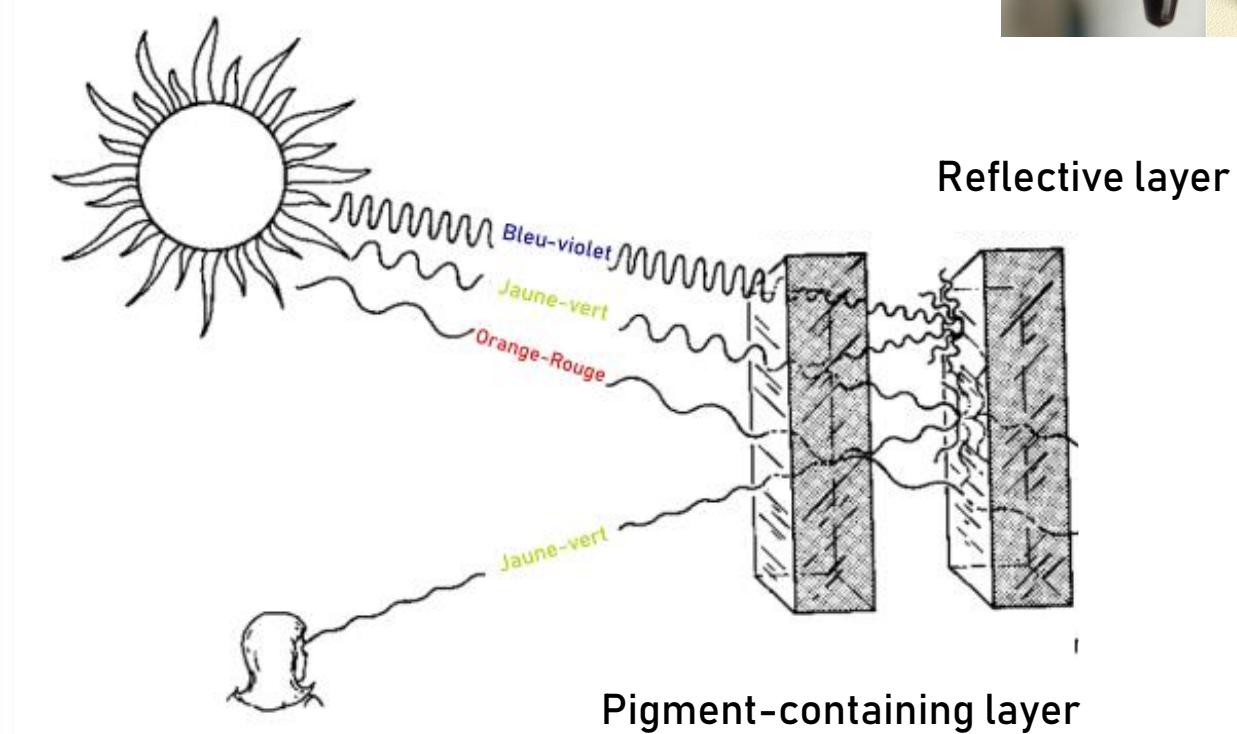
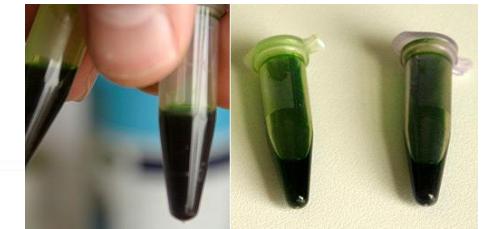
FIGURE P17.73

"Chemical" colors...



Pigment-containing layer

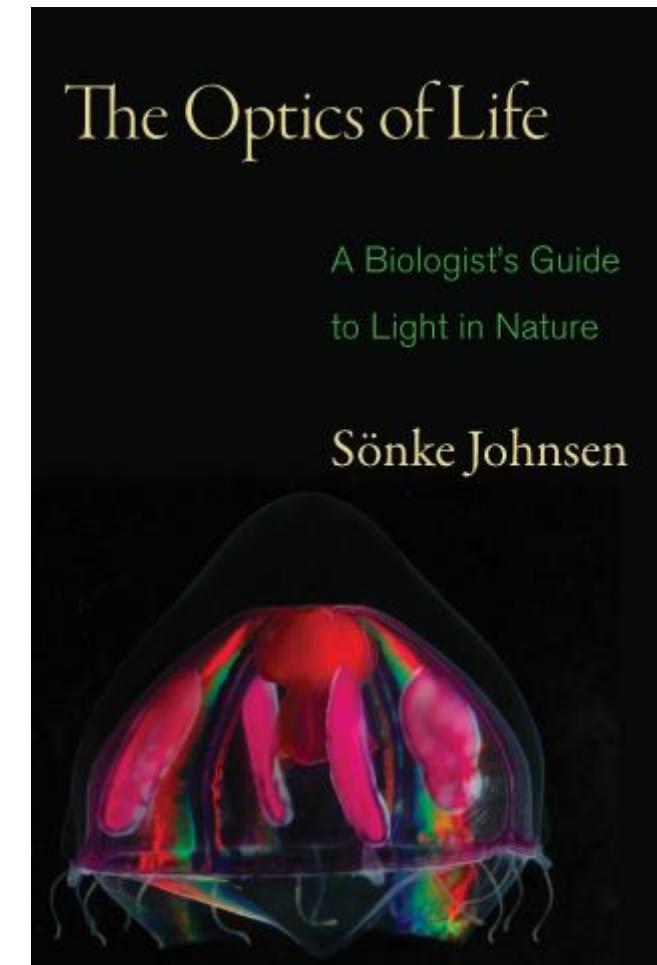
"Chemical" colors.... Need structural layers!



"Coloration" ≠ "pigmentation"



"Coloration" ≠ "pigmentation"



2011

Genotype-phenotype relationships

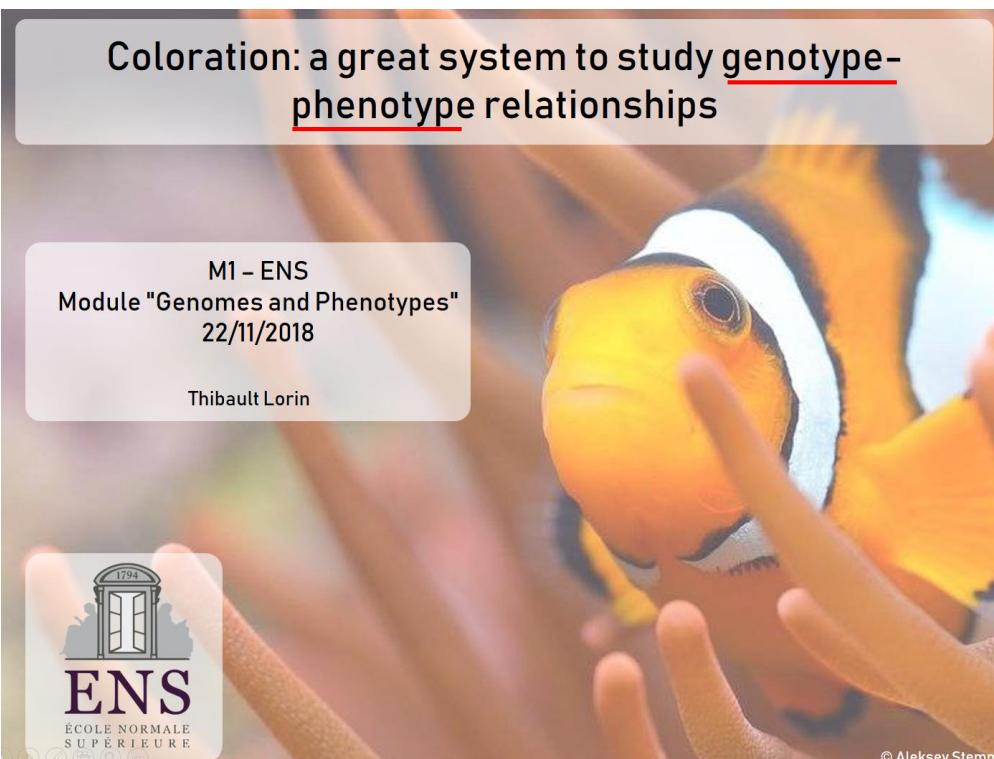
Coloration: a great system to study genotype-phenotype relationships

M1 – ENS
Module "Genomes and Phenotypes"
22/11/2018

Thibault Lorin



Relationships between genes and the phenotype, and their modulation by the environment



Genotype-phenotype relationships

(more detail and info here)



HYPOTHESIS AND THEORY
published: 19 May 2015
doi: 10.3389/fgene.2015.00179

The differential view of genotype–phenotype relationships

Virginie Orgogozo^{1*}, Baptiste Morizot² and Arnaud Martin³

¹ CNRS, UMR 7592, Institut Jacques Monod, Université Paris Diderot, Paris, France, ² Aix Marseille Université, CNRS, CEPERC UMR 7304, Aix en Provence, France, ³ Department of Molecular Cell Biology, University of California, Berkeley, CA, USA

Introduction

I. Coloration: a great system to study genotype-phenotype relationships

II. A case study: clownfish coloration



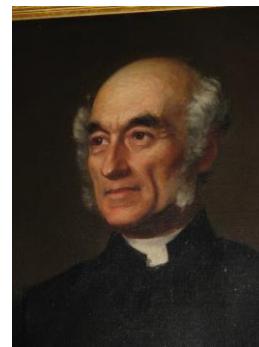
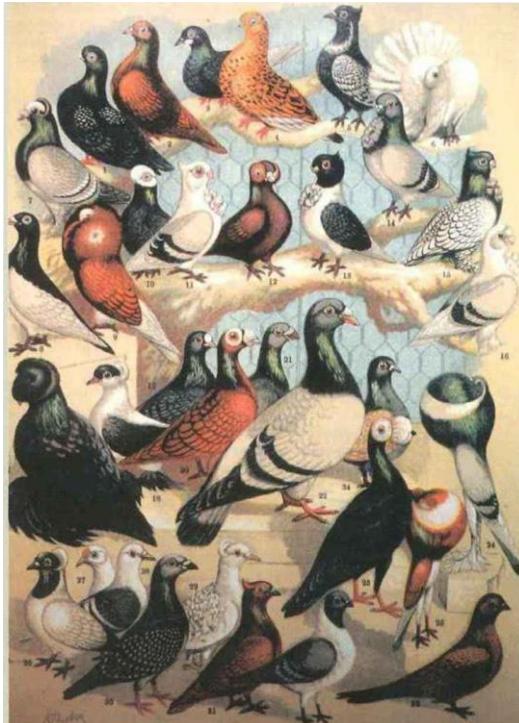
Introduction

I. Coloration: a great system to study genotype-phenotype relationships

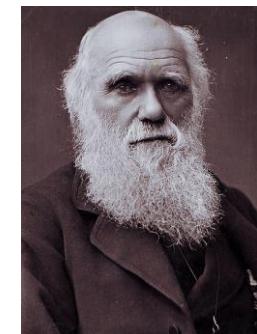
- a. Coloration in the History of Science
- b. Coloration in Vertebrates



Coloration and naturalists' interest



Whitwell Elwin



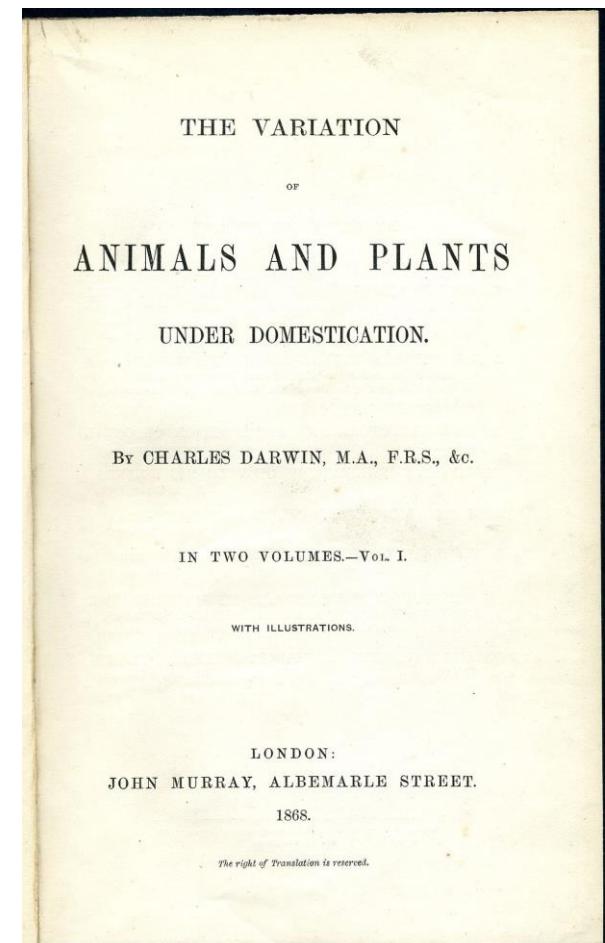
Charles Darwin

*"Everybody is interested in pigeons".
[A book like this would] "be reviewed
in every journal in the kingdom and
soon be on every table."*

Coloration and naturalists' interest

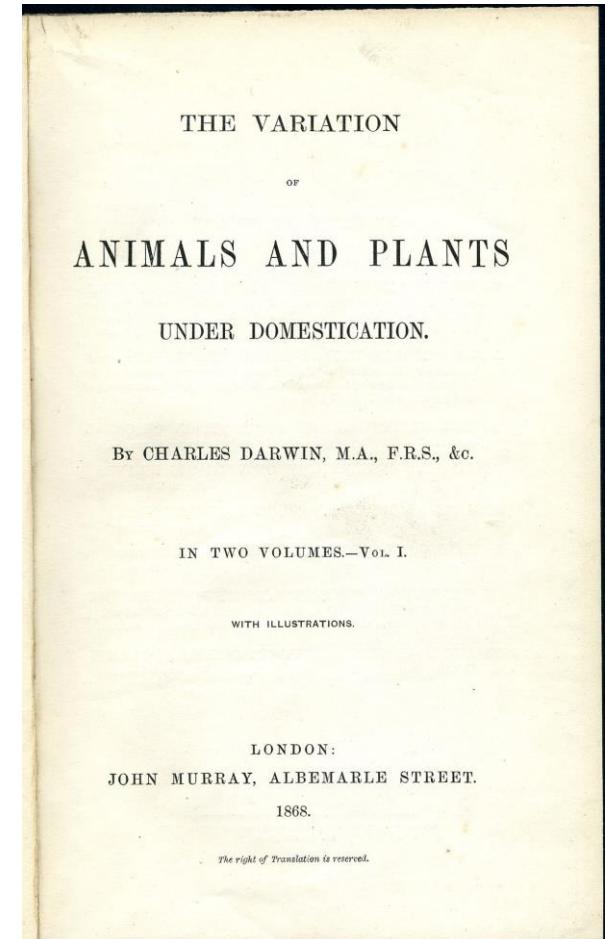
COLUMBA LIVIA or ROCK-PIGEON.											
GROUP I.			GROUP II.			GROUP III.			GROUP IV.		
1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	
Kali-Par.						Persian Tumbler					
Murasia.						Lotan Tumbler					
Bussorah.						Common Tumbler					
German P.				Bagadotin					Dove and pigeons		Char. V.
Lille P.			Dragon	Scanderoon	Trofno				Snowflakes,		
Dutch P.			Pigeon Cygne			Java Fau tail			Spotted,		
English Pouter.		English Carrier.	Raut.	Barb.	Fau tail.	Turbit	African Owl.	Short- Faced Tumbler.	Nim.		
								Indian Frill- back.	English Frill-back		
								Jacobs.	Leather,		
									Trumper.		

"I do not hesitate to affirm that some domestic races of the rock-pigeon differ fully as much from each other in external characters as do the most distinct natural genera."



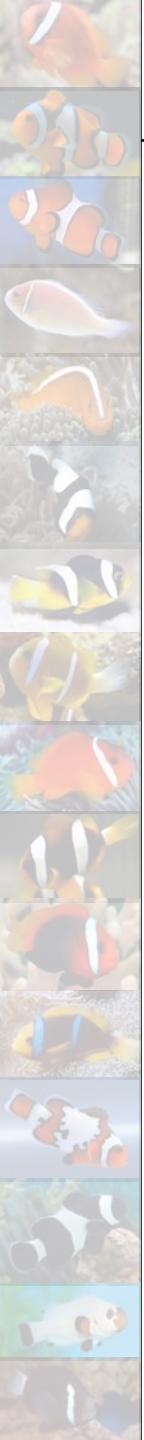
Coloration and naturalists' interest... also in plants!

Maize has varied in an extraordinary and conspicuous manner ... The whole ear is variable in shape ... The seeds are arranged in the ear in from 6 to even 20 rows, or are placed irregularly. The seeds are coloured - white, pale-yellow, orange, red, violet ...





Why study coloration?



Why study coloration?

→ Aesthetic

→ Profitable

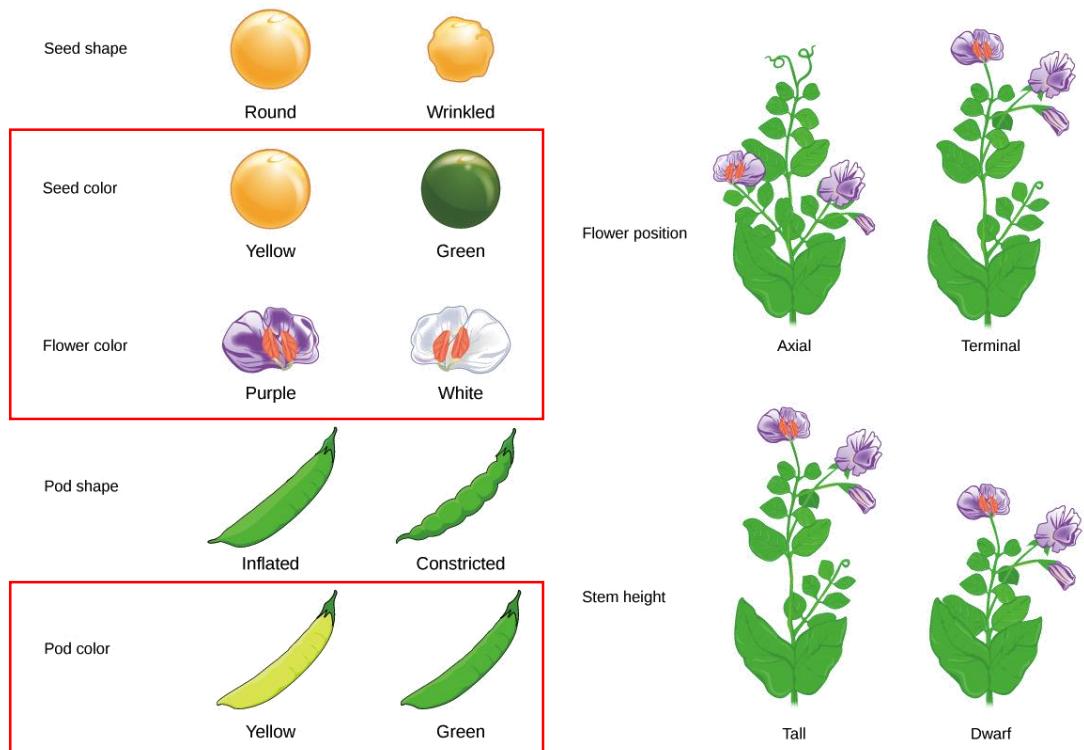
→ Convenient

Coloration and the History of the comprehension of GP relationship: Mendel

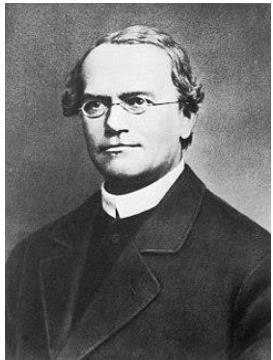


Gregor Mendel
(1822-1884)

"Father of
modern genetics"

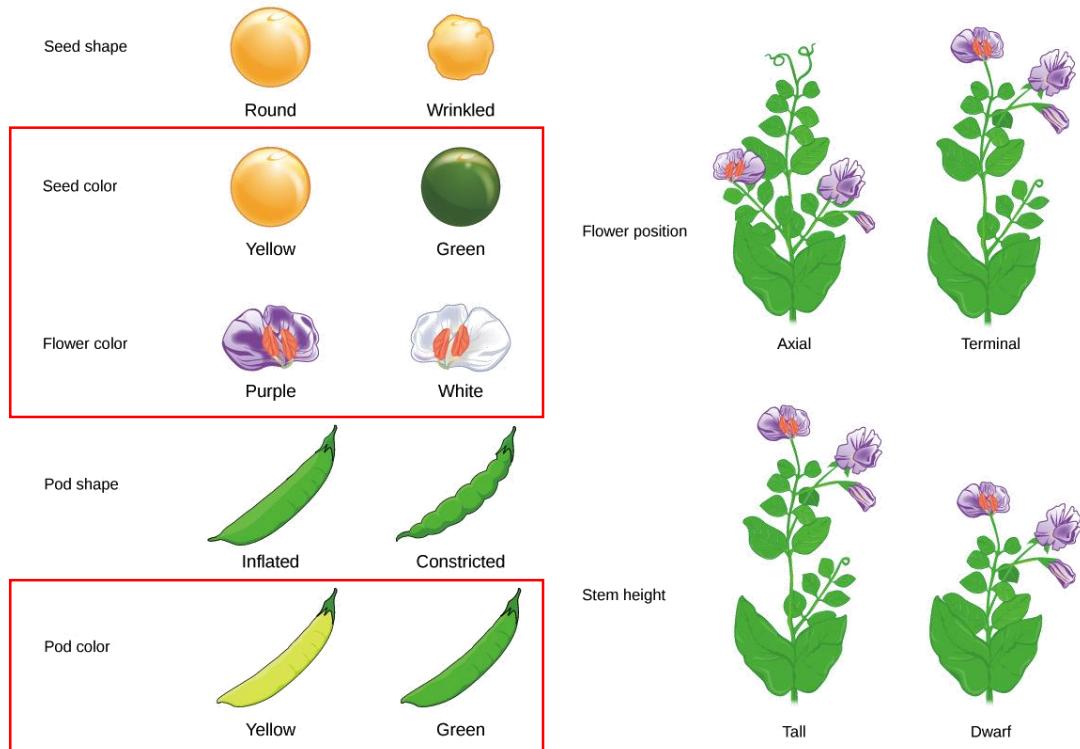


Coloration and the History of the comprehension of GP relationship: Mendel



Gregor Mendel
(1822-1884)

"Father of
modern genetics"



→ Coloration at the basis of the Mendel's Laws of Inheritance:
Law of Segregation, Law of Independent Assortment, Law of Dominance

Coloration and the History of the comprehension of GP relationship: Morgan



*Thomas Hunt
MORGAN
(1866-1945)*



1909

AMERICAN BREEDERS' ASSOCIATION.

365

WHAT ARE "FACTORS" IN MENDELIAN EXPLANATIONS?

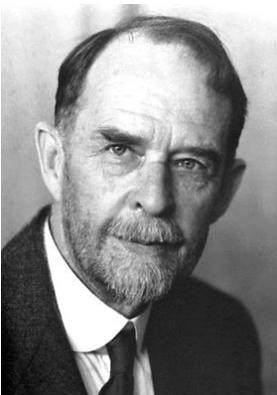
BY PROF. T. H. MORGAN.

Columbia University, New York, N. Y.

In the modern interpretation of Mendelism, facts are being transformed into factors at a rapid rate. If one factor will not explain the facts, then two are invoked; if two prove insufficient, three will sometimes work out. The superior jugglery sometimes necessary to account for the results may blind us, if taken too naively, to the common-place that the results are often so excellently "explained" because the explana-



Coloration and the History of the comprehension of GP relationship: Morgan



1910

→ Coloration at the basis of the discovery of heredity:
chromosomes carrying "genes" that allow inheritance

+ genetic linkage

120

SCIENCE

[N. S. VOL. XXXII. No. 812]

becoming manifest when conditions favoring transpiration are marked." The disease is therefore not due to the presence of parasitic organisms, but is what has been rather loosely called a physiological disorder.

In a short paper in the *Annales du Jardin Botanique de Buitenzorg* (2d Ser., Supp. III.) Professor Ramaley enumerates and discusses the European plants growing without cultivation in Colorado. In addition to an annotated list of species the author discusses the region included, and the mode of introduction and occurrence of the species. Botanists who have not given attention to these immigrants will be much surprised at the extent of the list.

PROFESSOR SARGENT continues his studies of the species of hawthorns in Pennsylvania in a paper entitled "Crataegus in Pennsylvania, II," published in the *Proceedings of the Academy of Natural Sciences of Philadelphia* (March, 1910). His first paper on the Pennsylvania hawthorns appeared about five years ago, since when much additional material has become available for study, resulting in a thick pamphlet of about one hundred pages. In this space the author enumerates and describes 110 species, of which 80 are described as new! Think of what the new editions of the botanical manuals will have to contain when these new species are added! We may have to grant the necessity of distinguishing these forms from one another in descriptive botany, but what an amount of work will have to be done by the taxonomists of the future in reducing these multitudinous forms to such categories as will be distinguishable by botanists, other than specialists in the hawthorns!

CHARLES E. BESSEY
THE UNIVERSITY OF NEBRASKA

SPECIAL ARTICLES

SEX LIMITED INHERITANCE IN DROSOPHILA

In a pedigree culture of *Drosophila* which had been running for nearly a year through a considerable number of generations, a male appeared with white eyes. The normal flies have brilliant red eyes.

The white-eyed male, bred to his red-eyed sisters, produced 1,237 red-eyed offspring, (F_1), and 3 white-eyed males. The occurrence of these three white-eyed males (F_1) (due evidently to further sporting) will, in the present communication, be ignored.

The F_1 hybrids, inbred, produced:

2,459 red-eyed females,
1,011 red-eyed males,
782 white-eyed males.

No white-eyed females appeared. The new character showed itself therefore to be sex limited in the sense that it was transmitted only to the grandsons. But that the character is not incompatible with femaleness is shown by the following experiment.

The white-eyed male (mutant) was later crossed with some of his daughters (F_1), and produced:

129 red-eyed females,
132 red-eyed males,
88 white-eyed females,
86 white-eyed males.

The results show that the new character, white eyes, can be carried over to the females by a suitable cross, and is in consequence in this sense not limited to one sex. It will be noted that the four classes of individuals occur in approximately equal numbers (25 per cent.).

An Hypothesis to Account for the Results.—The results just described can be accounted for by the following hypothesis. Assume that all of the spermatozoa of the white-eyed male carry the "factor" for white eyes " W "; that half of the spermatozoa carry a sex factor " X " the other half lack it, i. e., the male is heterozygous for sex. Thus the symbol for the male is " WWX ," and for his two kinds of spermatozoa $WX-W$.

Assume that all of the eggs of the red-eyed female carry the red-eyed "factor" R ; and that all of the eggs (after reduction) carry one X , each, the symbol for the red-eyed female will be therefore $RRXX$ and that for her eggs will be $RX-RX$.

When the white-eyed male (sport) is crossed with his red-eyed sisters, the following combinations result:

Coloration and the History of the comprehension of GP relationship

1917

EVIDENCE OF MULTIPLE FACTORS IN MICE AND RATS

C. C. LITTLE
HARVARD MEDICAL SCHOOL

THE object of this paper is to record certain data on the inheritance of two complex characters and analyze these data together with those obtained in certain analogous experiments by other investigators. This is done with a

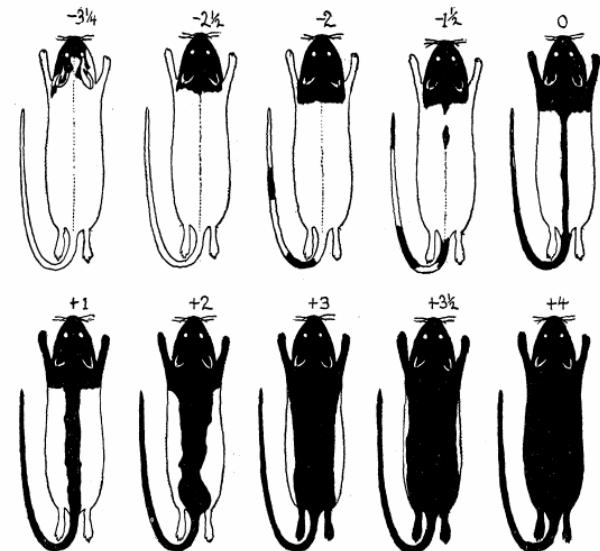


FIG. 2

"All indicate that in mammals the multiple factor hypothesis is steadily being strengthened as a scientific theory (...) of great interest and importance."

→ Coloration at the basis of the discovery of epistasis

Coloration and the History of genetics: a summary (in Vertebrates only)

Table 1 Timeline of some milestones and fundamental discoveries using pigmentation phenotypes

Date	Milestone	Representative reference
1700s	Establishment of laboratory mouse strains with 'fancy' coat color patterns	Morse (1978)
1902–1904	Demonstration of Mendelian inheritance in vertebrates using the albino locus	Castle and Allen (1903), Cuenot (1904)
1915	Establishment of genetic linkage in mammals using two pigmentation loci	Haldane <i>et al</i> (1915)
1917	Seminal papers on coat color genetics in laboratory animals	Wright (1917a, b, c, d)
1920s	Natural history studies linking vertebrate pigmentation to environmental variation	Sumner (1921, 1929a, b), Benson (1933), Dice and Blossom (1937)
1948	First mathematical treatment of clinal variation based on adaptive pigmentation traits	Haldane (1948)
1950s	First estimate of radiation-induced mammalian mutation rates at six coat color loci	Russell (1951), Russell and Major (1957)
1960s	Estimates of spontaneous mammalian mutation rates using coat color phenotypes	Schlager and Dickie (1966, 1969)
1986	Cloning of the first pigmentation gene	Shibahara <i>et al</i> (1986)
2000s	Linking mutations in pigmentation genes to adaptive phenotypic variation in the wild	

Coloration and the History of the comprehension of GP relationship: McClintock



*Barbara McClintock
(1902-1992)*

THE ORIGIN AND BEHAVIOR OF MUTABLE LOCI IN MAIZE

BY BARBARA McCLINTOCK

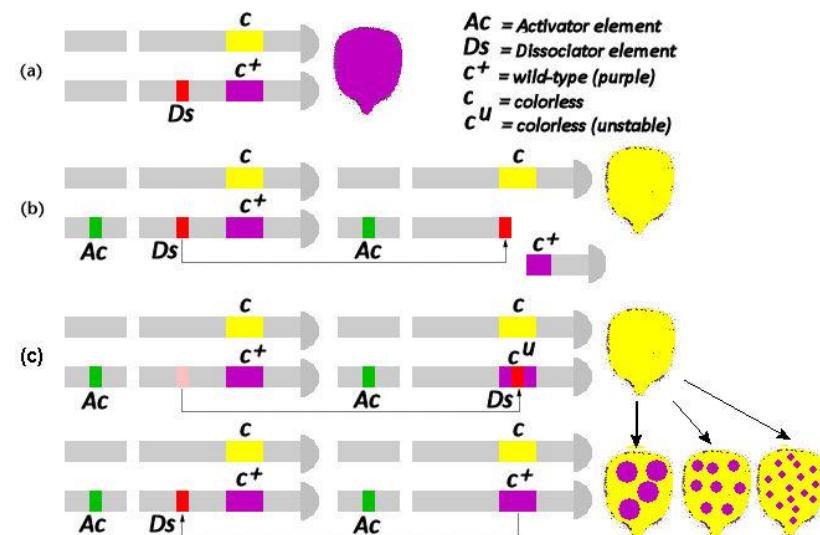
DEPARTMENT OF GENETICS, CARNEGIE INSTITUTION, COLD SPRING HARBOR, NEW YORK

Communicated April 8, 1950

In the course of an experiment designed to reveal the genic composition of the short arm of chromosome 9, a phenomenon of rare occurrence (or recognition) in maize began to appear with remarkably high frequencies in the cultures. The terms mutable genes, unstable genes, variegation,



Maize variegation



Coloration and the History of the comprehension of GP relationship: McClintock



*Barbara McClintock
(1902-1992)*

→ Coloration at the basis of the discovery of major genome sequences, transposable elements ("controlling elements")



Maize variegation

CLASS I - Retroelements (RNA intermediate)

Endogenous retrovirus (HIV, HERV)



Ty3/gypsy - BEL transposons



Ty1/copia retrotransposons



DIRS1-like retrotransposons



Non-LTR retrotransposons (L1, L2)



Penelope-like retrotransposons



Non-autonomous retrotransposons (SINEs)

(Alu, B2, B4)

CLASS II - DNA transposons

DDE transposons (piggyBac, Mariner, Transib)



Helitrons



Polintons / Mavericks



Non-autonomous DNA transposons (MITEs)
(MADE1)



More recently... "Color" is still a first-considered trait



Nature cover (1981)

Among all possible mutants used to describe the emergence of a new model system, guess which one was used?

Golden... a pigmentary mutant!

More recently... "Color" is still a first-considered trait



Nature cover (1981)

Among all possible mutants used to describe the emergence of a new model system, guess which one was used?

Golden... a pigmentary mutant!

Potential biases in the choice
of model systems?

Introduction

I. Coloration: a great system to study genotype-phenotype relationships

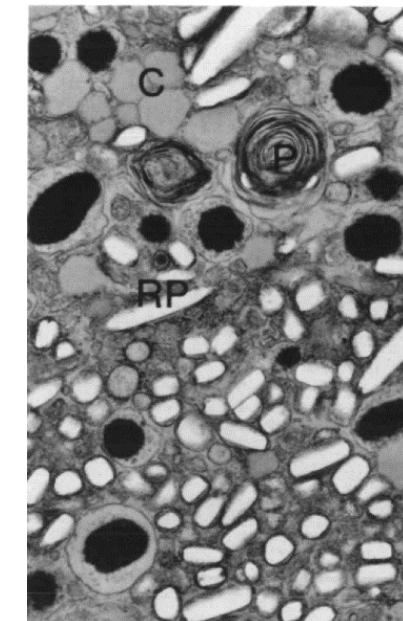
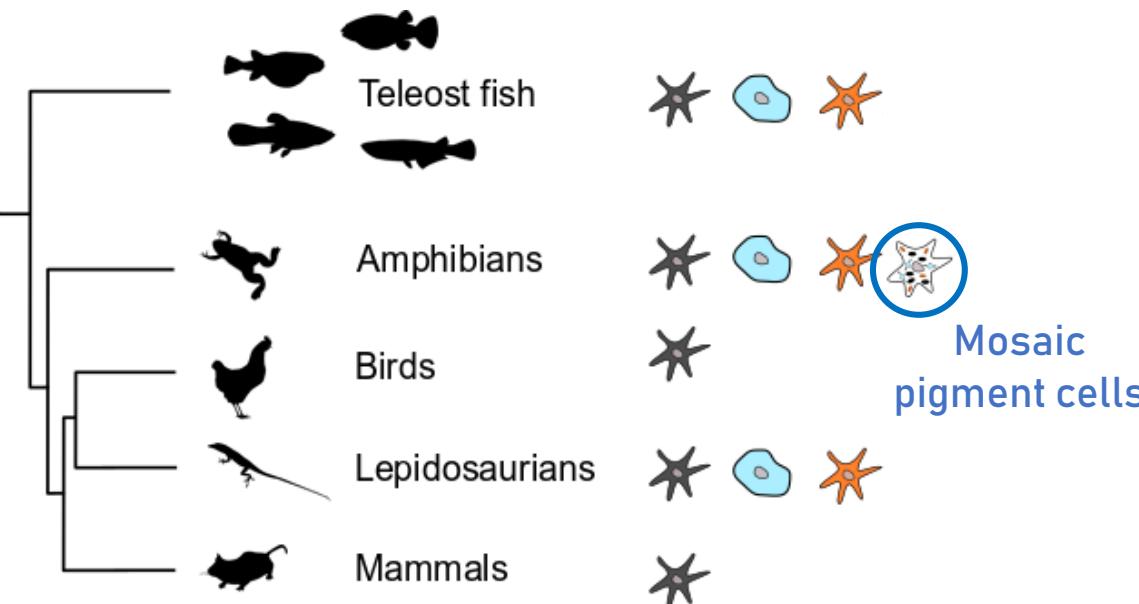
- a. Coloration in the History of Science
- b. Coloration in Vertebrates



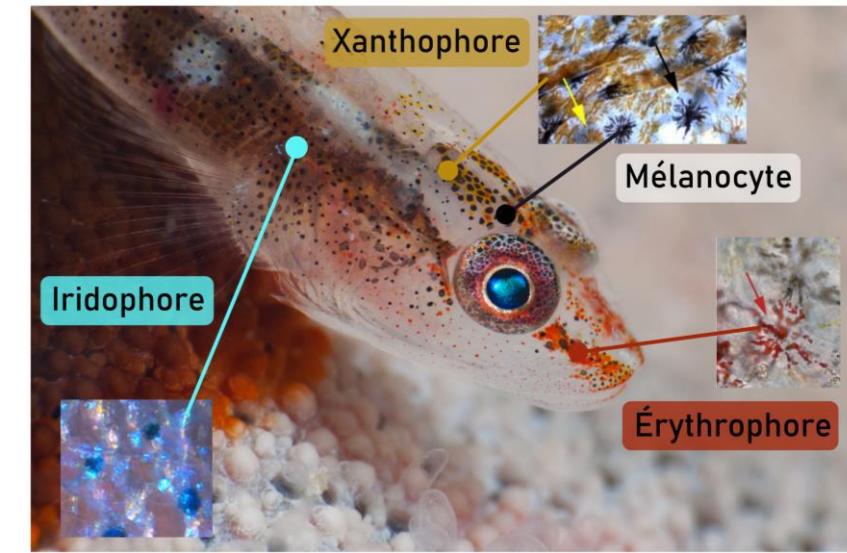
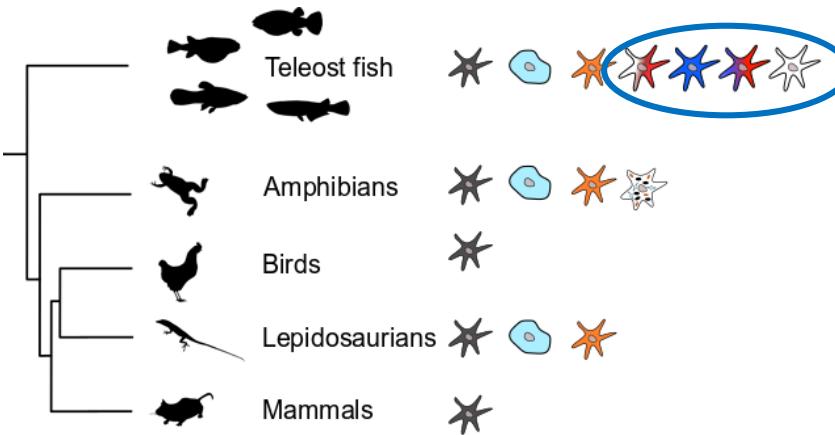
Developmental, cellular and molecular basis of pigmentation in Vertebrates



Developmental, cellular and molecular basis of pigmentation in Vertebrates

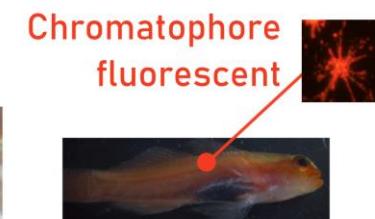
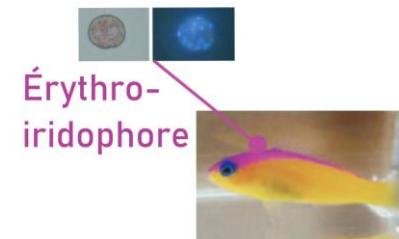
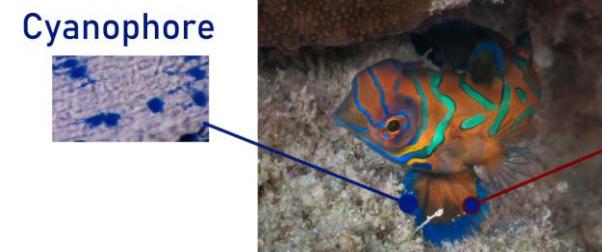
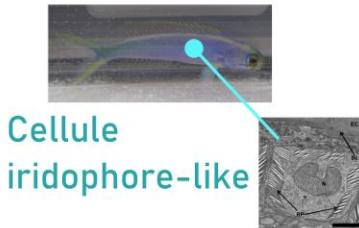
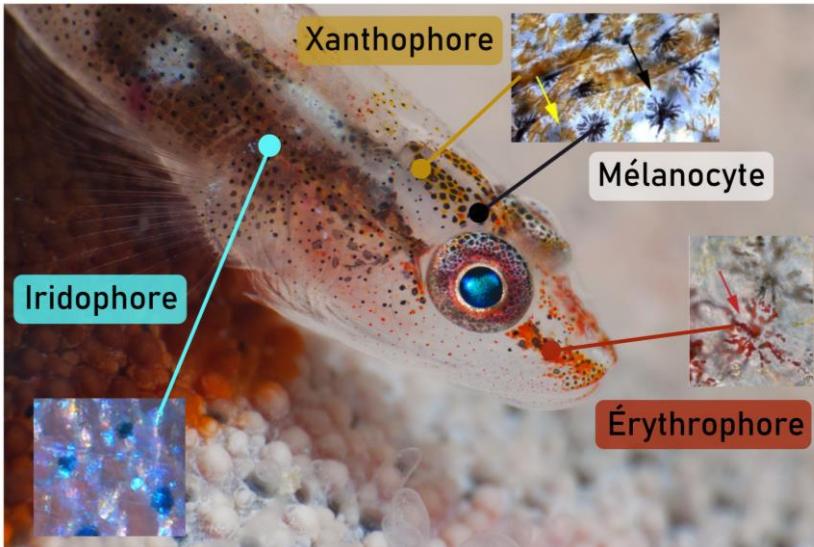


Developmental, cellular and molecular basis of pigmentation in Vertebrates

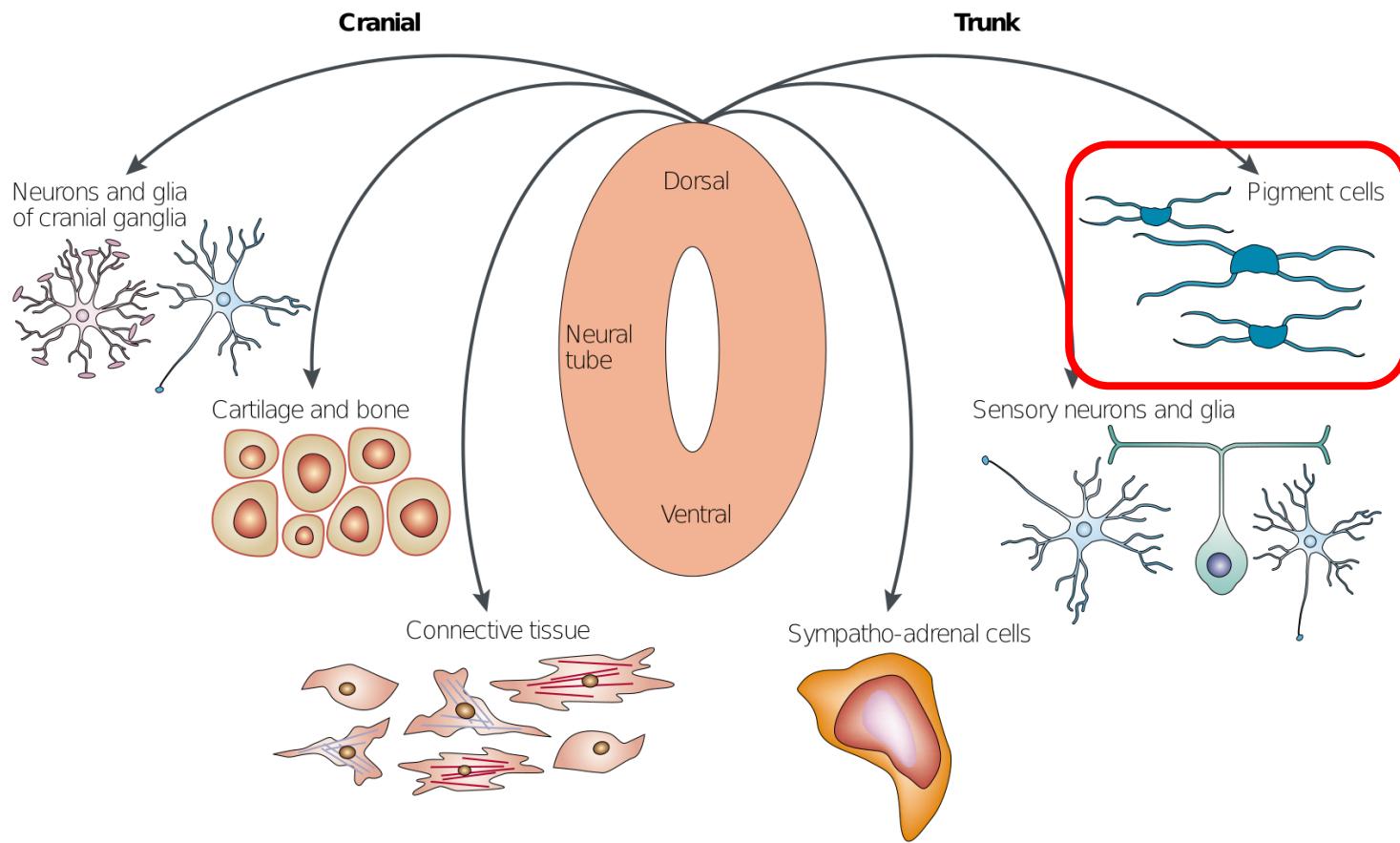


Picture: Germain Boussarie

Developmental, cellular and molecular basis of pigmentation in Vertebrates



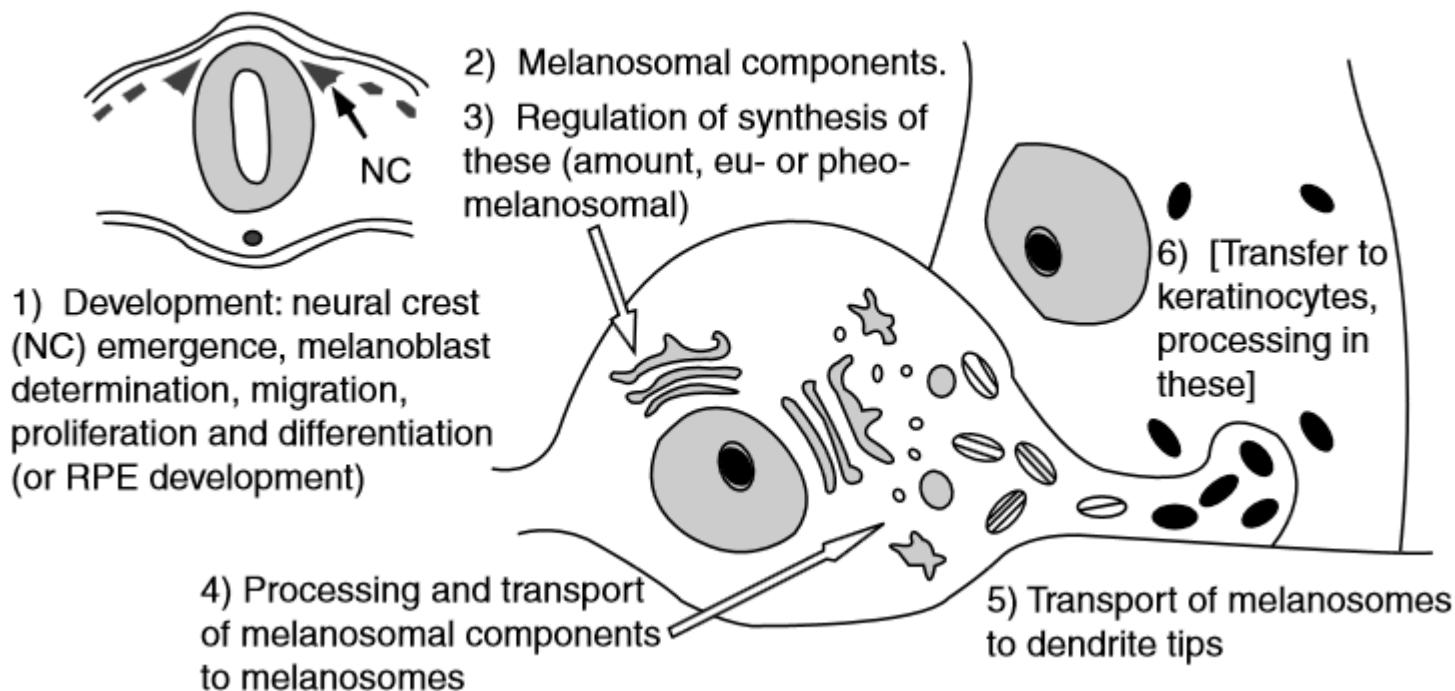
Pigment cells in vertebrates originate from the neural crest



PLANET
VIE

Les cellules des crêtes neurales : « la seule chose intéressante » chez les Vertébrés ?

Coloration is a very diverse trait

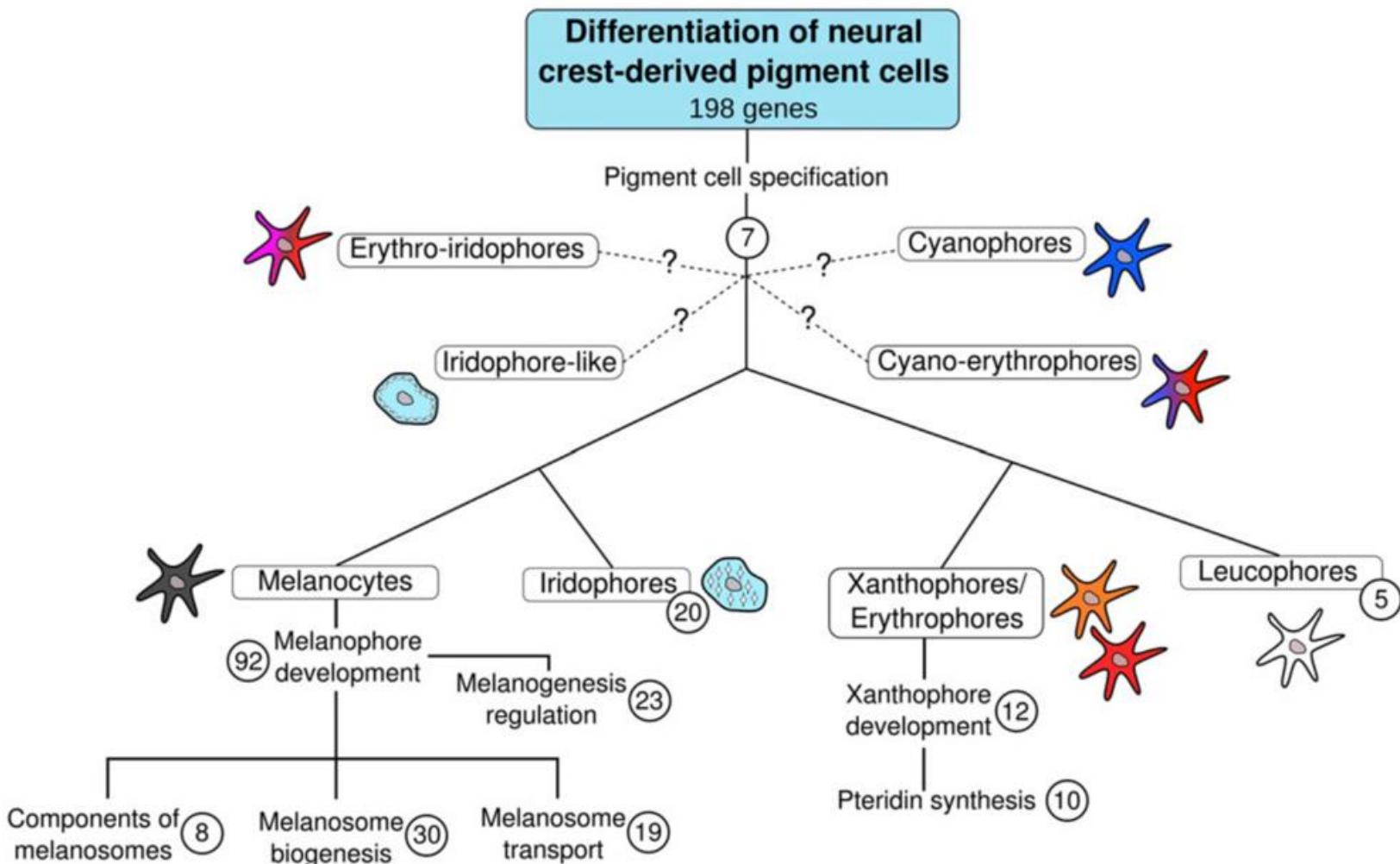


Coloration is a very diverse trait... endowed by a plethora of genes

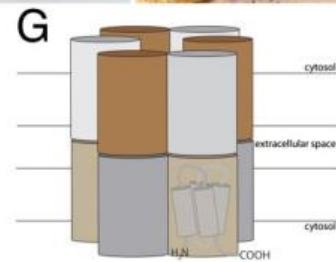
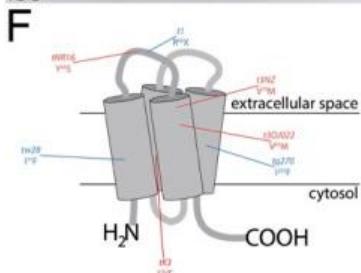
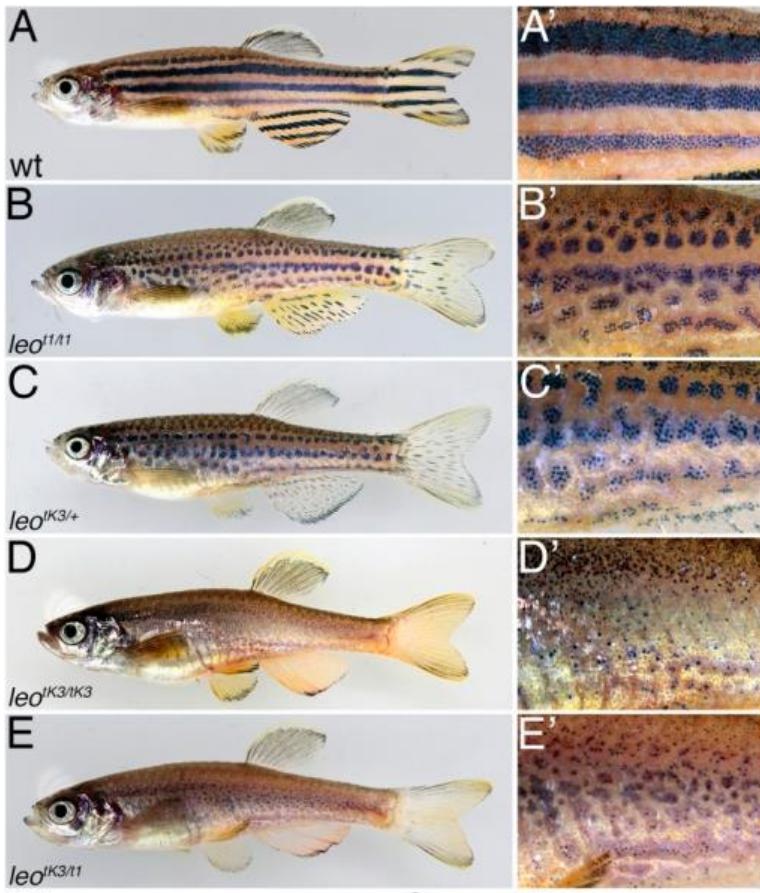
Table 1. Summary of the cloned mouse color genes

Symbol (old symbol)	Name (old name)	Chromosome	Function	Human symbol	Human chr'some	Syndrome
(a) Melanocyte development						
<i>Adam17</i>	A disintegrin and metalloprotease domain 17	12	Protease, processing various bioactive proteins	<i>ADAM17</i>	2p25	N
<i>Adamts20 (bt)</i>	A disintegrin and metalloprotease domain (reprolysin type) with thrombospondin type 1 motif, 20 (belted)	15	Metalloprotease. Melanoblast migration?	<i>ADAMTS20</i>	12q12	N
<i>Brcal</i>	Breast cancer 1	11	Development of various organs; tumor suppressor	<i>BRCA1</i>	17q21	BC
<i>Eda (Ta)</i>	Ectodysplasin-A (tabby)	X	Sweat gland, tooth and hair morphogenesis	<i>ED1</i>	Xq12-q13	EDA/HED
<i>Edn3 (ls)</i>	Endothelin 3 (lethal spotting)	2	Growth and differentiation factor	<i>EDN3</i>	20q13	HD, WSS
<i>Ednrb (s)</i>	Endothelin receptor type B (piebald spotting)	14	Growth factor receptor	<i>EDNRB</i>	13q22	HD, WSS
<i>Egfr (Dsk5)</i>	Epidermal growth factor receptor (dark skin 5)	11	Growth factor receptor	<i>EGFR</i>	7p12.3	N
<i>Fgf2r</i>	Fibroblast growth factor receptor 2	7	Growth factor receptor	<i>FGFR2</i>	10q26	CrS, Pfs
<i>Ikbkg</i>	Inhibitor of κB kinase, γ subunit (NEMO)	X	IκB kinase. Required for NFκB signaling	<i>IKBKG</i>	Xq28	IP, HED-ID, EDA-ID
<i>Kit (W)</i>	Kit oncogene (white spotting)	5	Growth factor receptor	<i>KIT</i>	4q11-q12	PS
<i>Kitl (Sl)</i>	Kit ligand (steel)	10	Growth and differentiation factor	<i>KITLG</i>	12q22	N
<i>Krt2-17 (Dsk2)</i>	Keratin 2-17 (dark skin 2)	15	Cytoskeleton	<i>KRT2A</i>	12q11-q13	IBS
<i>Lmx1a (dr)</i>	LIM homeobox transcription factor 1α (dreher)	1	Transcription factor	<i>LMX1A</i>	1q22-23	N
<i>Mcoln3 (Va)</i>	Mucolipin 3 (varintint-waddler)	3	Cation channel	<i>MCOLN3</i>	1p22.3	N
<i>Mitf (ml)</i>	Microphthalmia-associated transcription factor (microphthalmia)	6	Transcription factor	<i>MITF</i>	3p12-14	WS2
<i>Pax3 (Sp)</i>	Paired box gene 3 (splotch)	1	Transcription factor	<i>PAX3</i>	2q35	WS1, WS3
<i>Sfxn1 (f)</i>	Sideroflexin 1 (flexed tail)	13	Tricarboxylate carrier	<i>SFXN1</i>	5q35.3	N
<i>Snat2</i>	Snail homolog 2/Slug	16	Transcription factor	<i>SNAI2</i>	8q11	WS2
<i>Sox10 (Dom)</i>	SRY-box containing gene 10 (dominant megacolon)	15	Transcription factor	<i>SOX10</i>	22q13.1	WSS
<i>Sox18 (rg, Dcc1)</i>	SRY-box containing gene 18 (ragged, dark coat color 1)	2	Transcription factor	<i>SOX18</i>	20q13.33	N
<i>Wnt1</i>	Wingless-related MMTV integration site 1	15	Growth factor/morphogen	<i>WNT1</i>	12q13	N
<i>Wnt3a</i>	Wingless-related MMTV integration site 3A	11	Growth factor/morphogen	<i>WNT3A</i>	1q42	N
(b) Components of melanosomes and their precursors						
<i>Dct (slt)</i>	Dopachrome tautomerase (slt)	14	Melanosomal enzyme	<i>DCT</i>	13q31-q32	N
<i>Gpnmb</i>	Glycoprotein (transmembrane) NMB	6	Apparent melanosomal component	<i>GPNMB</i>	7p15	N
<i>Matp (uw)</i>	Membrane-associated transporter protein (underwhite)	15	Apparent transporter	<i>MATP</i>	5p	OCA4
<i>Rab38 (cht)</i>	RAB38, member RAS oncogene family (chocolate)	7	Targeting of Tyrp1	<i>RAB38</i>	11q14	N
<i>Sl (sj)</i>	Silver (silver)	10	Melanosome matrix	<i>SILV</i>	12q13-q14	N
<i>Tyr (c)</i>	Tyrosinase (color, albino)	7	Melanosomal enzyme	<i>TYR</i>	11q21	OCA1
<i>Tyrp1 (b)</i>	Tyrosinase-related protein 1 (brown)	4	Melanosomal protein	<i>TYRP1</i>	9p23	OCA3
(c) Melanosome construction/protein routing (HPS-related)						
<i>Ap3b1 (pe)</i>	Adaptor-related protein complex AP-3, β 1 subunit (pearl)	13	Organellar protein routing	<i>AP3B1</i> [HPS2]	15q15	HPS
<i>Ap3d (mh)</i>	Adaptor-related protein complex AP-3, δ subunit (mocha)	10	Organellar protein routing	<i>AP3D1</i>	19p13.3	N
<i>Vps33a (bf)</i>	Vacuolar protein sorting 33a (buff)	5	Organellar protein routing	<i>VPS33A</i>	12q24.31	N
<i>cno (cno)</i>	Cappuccino	5	Organelle biogenesis	<i>CNO</i>	4p16-p15	N
<i>Hps1 (ep)</i>	Hermansky-Pudlak syndrome 1 homolog (pale ear)	19	Organelle biogenesis and size	<i>HPS1</i>	10q24	HPS
<i>Hps3 (coa)</i>	Hermansky-Pudlak syndrome 3 homolog (cocoa)	3	Organelle biogenesis	<i>HPS3</i>	3q24	HPS
<i>Hps4 (le)</i>	Hermansky-Pudlak syndrome 4 homolog (light ear)	5	Organelle biogenesis and size	<i>HPS4</i>	22q11-q12	HPS
<i>Hps5 (ru2)</i>	Hermansky-Pudlak syndrome 5 homolog (ruby-eye 2)	7	Organelle biogenesis	<i>HPS5</i>	11p14	HPS
<i>Hps6 (ru)</i>	Hermansky-Pudlak syndrome 6 homolog (ruby-eye)	19	Organelle biogenesis	<i>HPS6</i>	10q24.31	HPS
<i>Lyst (bg)</i>	Lysosomal trafficking regulator (beige)	13	Organelle biogenesis and size	<i>LYST</i>	1q42	CHS

Coloration is a very diverse trait... endowed by a plethora of genes



Changes in "coding sequences" → changes in coloration: "direct GP relationship"



Example: gene cx41.8 in zebrafish

Cx41.8 1 MADNSLLGNFLEEVQEHSTSVDKVLTLIF **E**FRILVLGTRAEESWGDEQEDFTCDTEQPGCENVC **D**APPIAHIEFW **R** 80
 GJAS 1 MGDNDFLGNFLEEVHKHSTVVGKWLTVLFIFRMVLVLGTAEESSWGDEQADFRCDTIQPGCQNVYDQAFFISHIRYTWVL 80
 cons. M DWS LGNFLEEV. HST VGEVWLTVLFIFRMVLVLGTAEESSWGDEQ DF CDT QPGC.NVCYD.AFFI.HIR.WVL

Cx41.8 81 QIVP **R**STPSLIYMGHAMHIVRREEK **R**KELDDEGAQRDGCE---KYPEDDKNKED--EGGC **R**UHLRGALLQTY **G** **S** **L**IR 155
 GJAS 81 QIIPVSTPSLVYHGCHAMHITVREQEKRKLREAERAKEVRGSGSYEYPVAEKALSCWEEGNRRIALQGTLLNTVCSSELIR 160
 cons. QI.FVSTPSL.YMGHAMH VR .EKR. . . . G YP .K E G.G.R. L.G.LL.TVV SILLIR

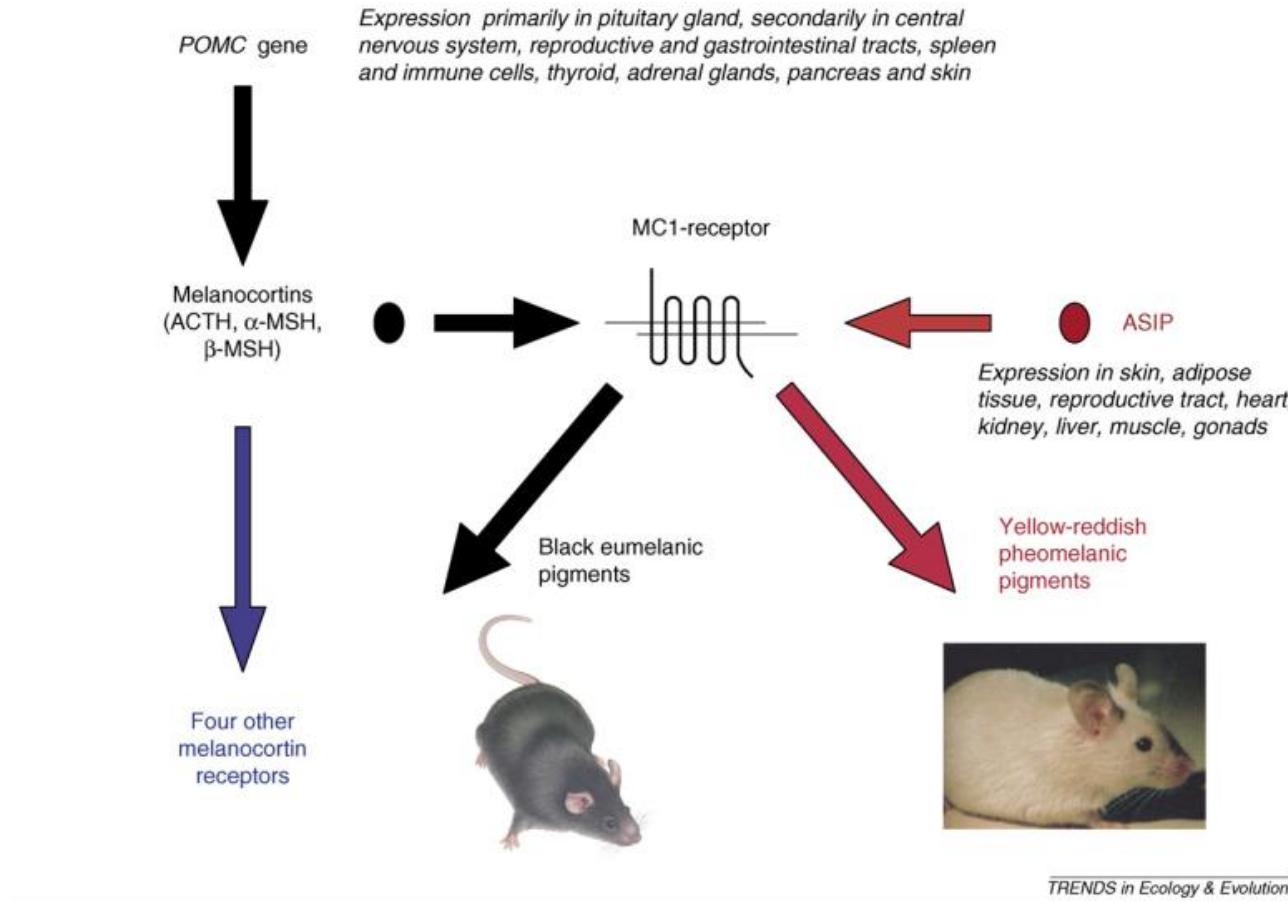
Cx41.8 156 TVMEVIF111QYLIYGVFLSALYVKAPPCHPVNCYISRPTEKKVF1VPMILAVAASVLLSIVELYHLANQQLRKTVHG 235
 GJAS 161 TTMEVGFIVQQYFYIGIFLTTLHVCRRSFCPHPVNCYVSRTIEKNVPIVPMILAVAASVLLSIVELYHLGNKKIRQRFV- 239
 cons. T MEV FI. QY IYG.FL..L VC. PCPHPVNCY. SRPEEKNVF1VPMILAVAAS.VLLS. ELYHL KK..R.

Cx41.8 236 YKASKQRPHTPSTMPALSPNPSTPMRACTPPPDFNQCLTSPPSSPTLQTHSLLHPTCPFFHDRLAHQQNSANMVTERHGG 315
 GJAS 240 -----KPRQHSMAKCQLSGDPGVQGSTTPPPDFNQCLENGPGKFFN-----PFSSNNMASQNTIONLVTEQVRCG 303
 cons. P . LS . .CTPPPFDNQCL P . PF . A QQN. N.VTE. RG

Cx41.8 316 QD-YLGVNFLS---FSQTPTETPNASCPSFLGSDFE-DKRRFSKSSGTSSMRPDDLV 370
 GJAS 304 QEQTPEGFIFIQVRYGKQP-EVPNGVSPGHLRPHGYHSDKRRLSKAS---SKARSDDLSV 358
 cons. Q. G . F. . Q P E FN . L . DKRR SK.S S. R DDL.V

But... The GP relationship is more complex than "one gene / one trait"

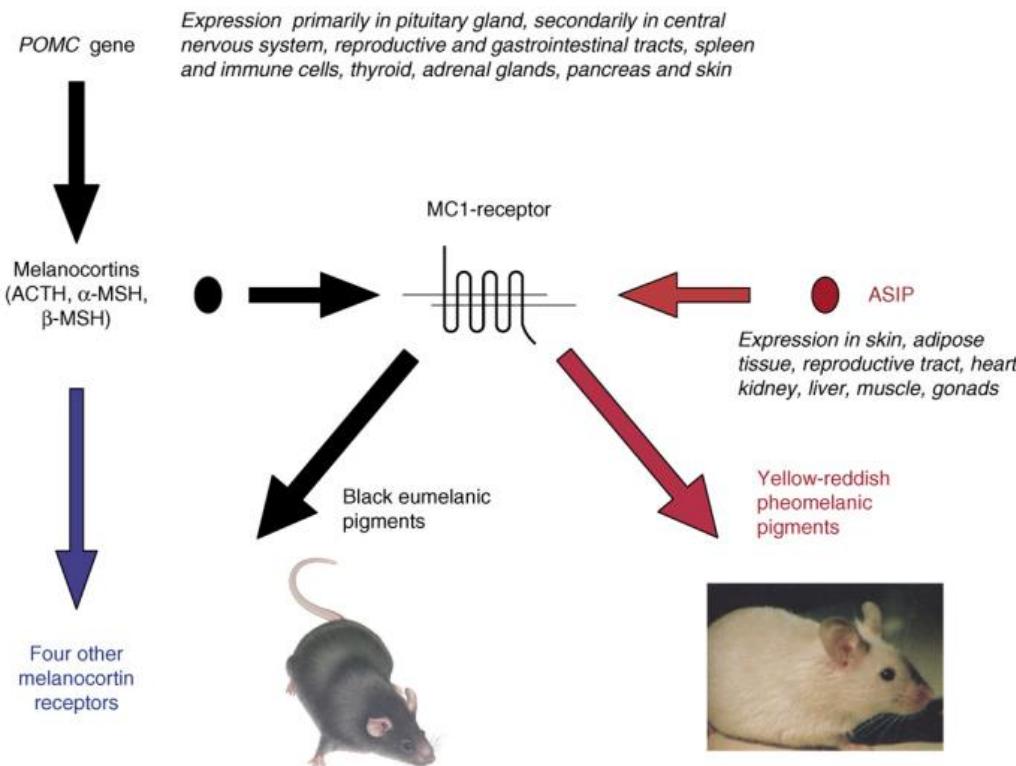
→ One gene / MULTIPLE traits: **Pleiotropy** of "color genes"



But... The GP relationship is more complex than "one gene / one trait"

→ One gene / MULTIPLE traits: Pleiotropy of "color genes"

→ MULTIPLE genes / one trait



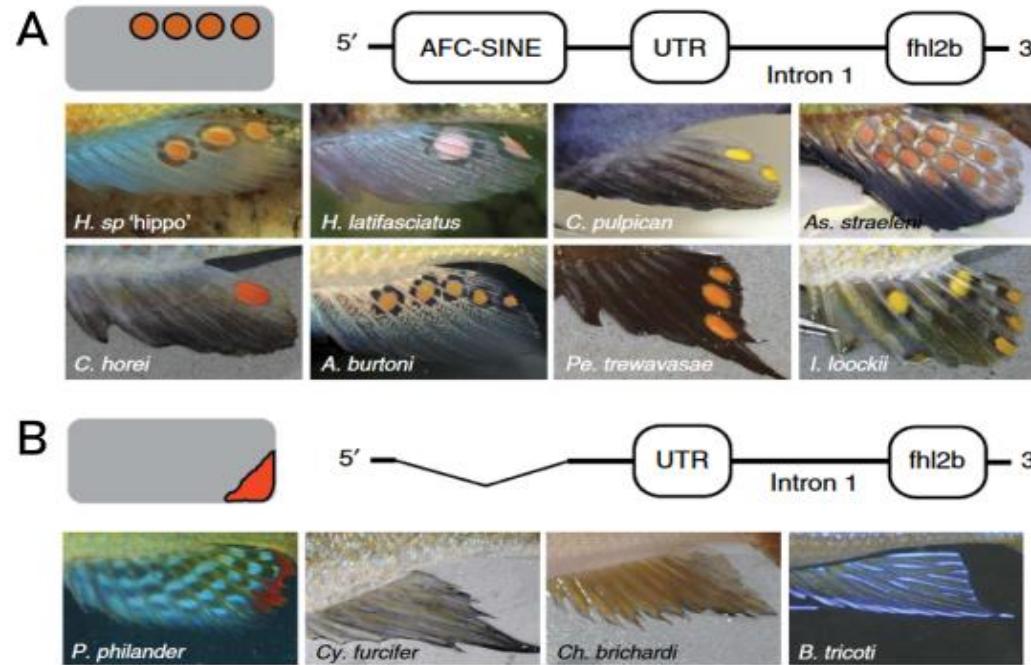
TRENDS in Ecology & Evolution

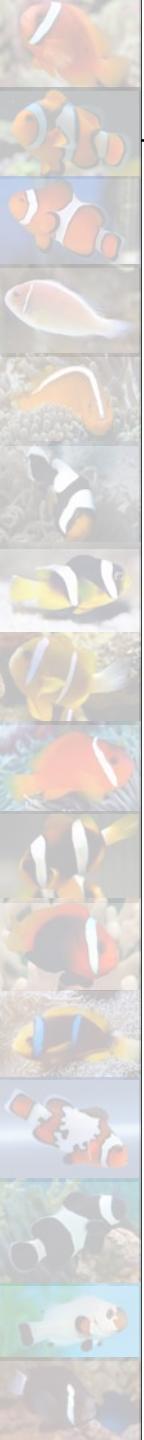
Ducrest et al. (2008) TREE

Coloration is sometimes due to regulatory sequences rather than "genes"



1. *Cis*-regulatory sequences

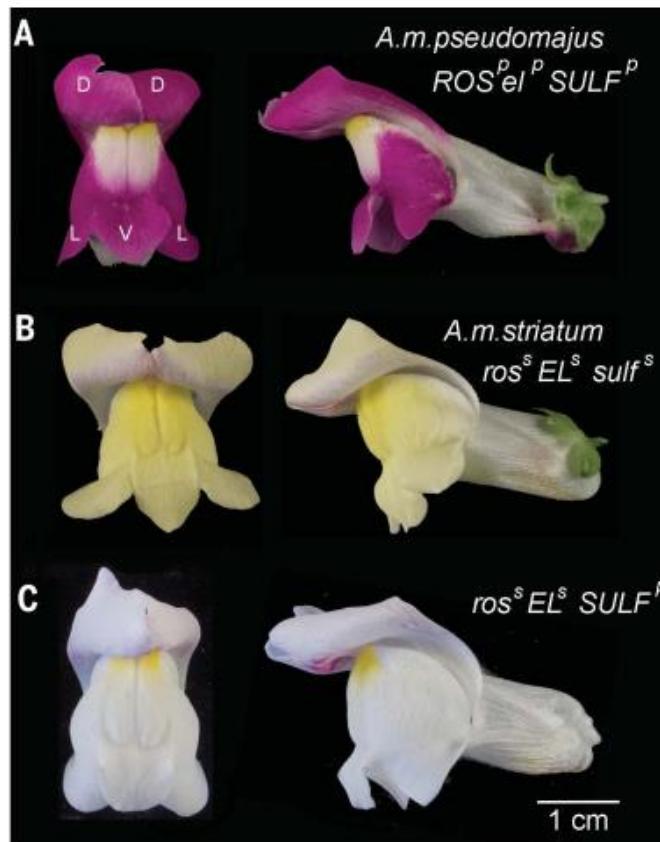


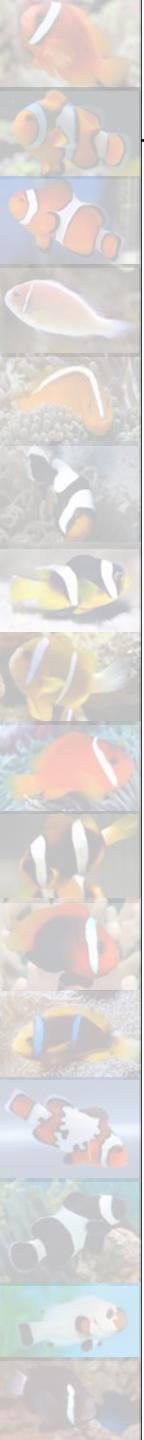


Coloration is sometimes due to regulatory sequences rather than "genes"



1. *Cis*-regulatory sequences
2. Non-coding RNAs / Epigenetics



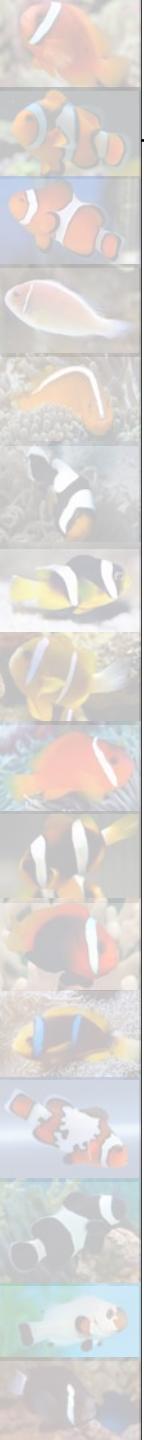


Why study coloration?

→ Profitable

→ Aesthetic

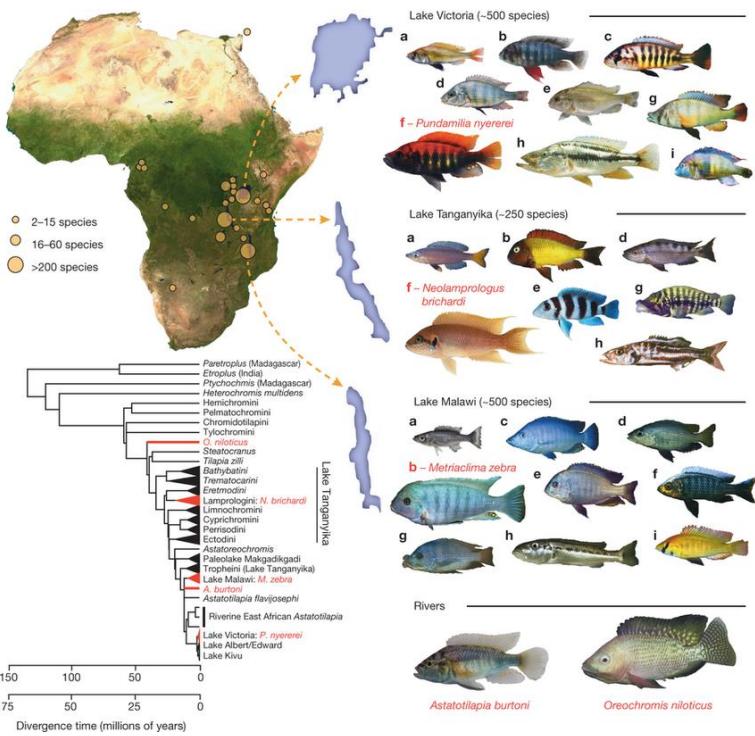
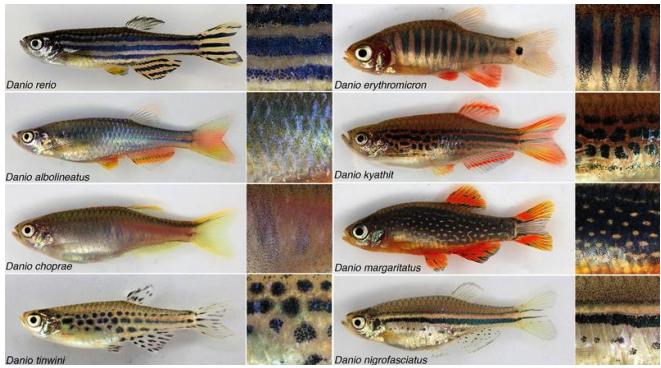
→ Convenient



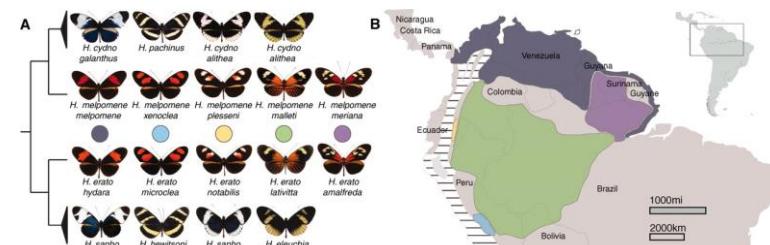
Why study coloration?

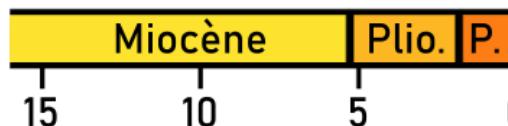
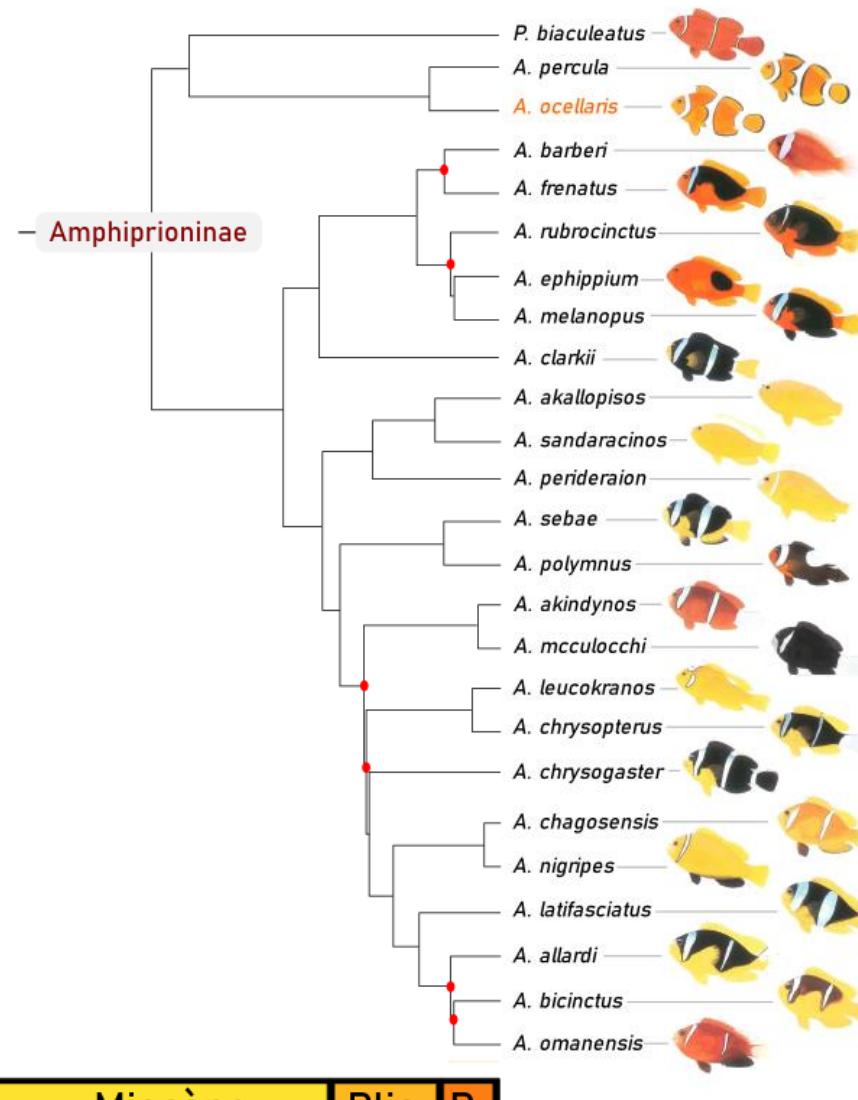
Coloration is a **fast-evolving trait**

Coloration is a fast-evolving trait



Gautier et al. (2018) *Current Biol.*





Adapted from Litsios *et al.* (2012), Litsios, Pearman *et al.* (2014) and Litsios and Salamin (2014)

Introduction

I. Coloration: a great system to study genotype-phenotype relationships

a. Coloration in the History of Science

b. Coloration in Vertebrates

- Many cell types and genes
- Not only genes
- Fast evolution



Introduction

I. Coloration: a great system to study genotype-phenotype relationships

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- b. Coloration in Vertebrates

II. A case study: clownfish coloration

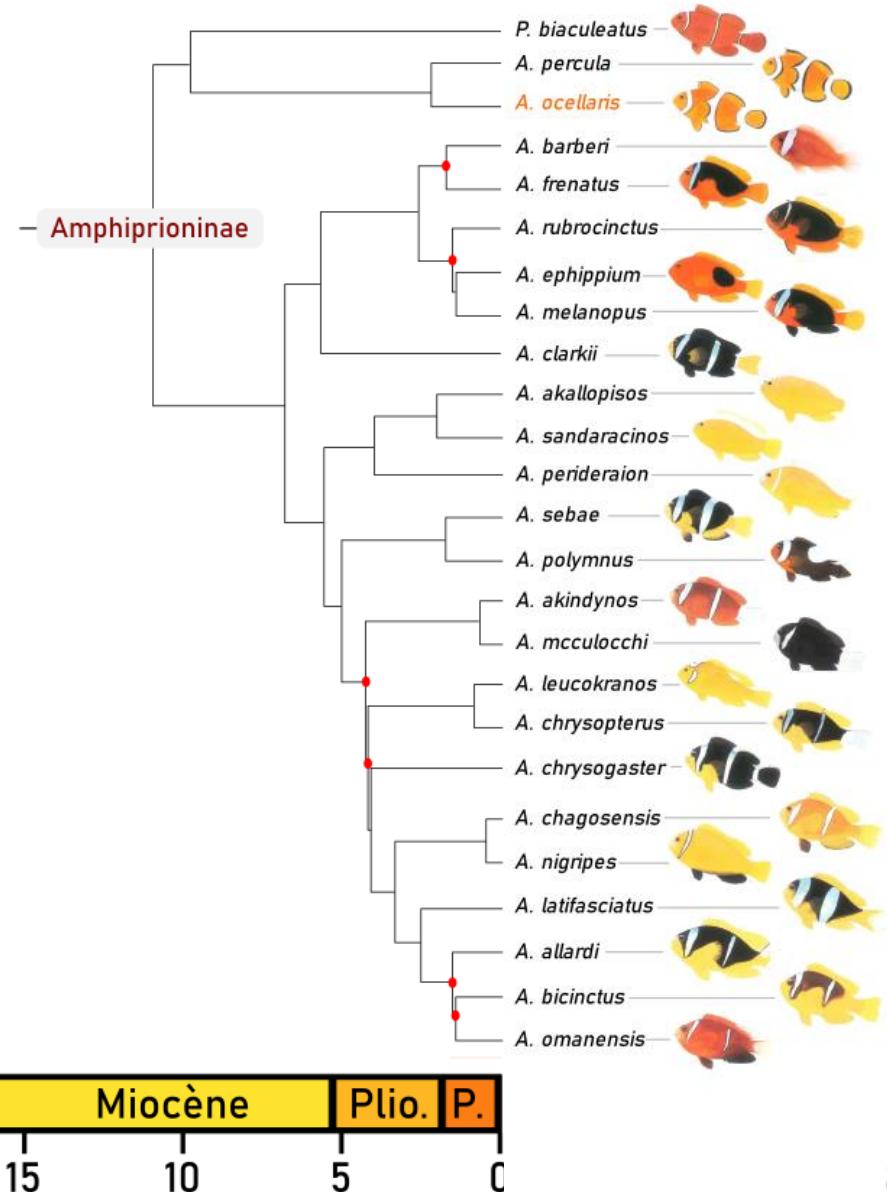
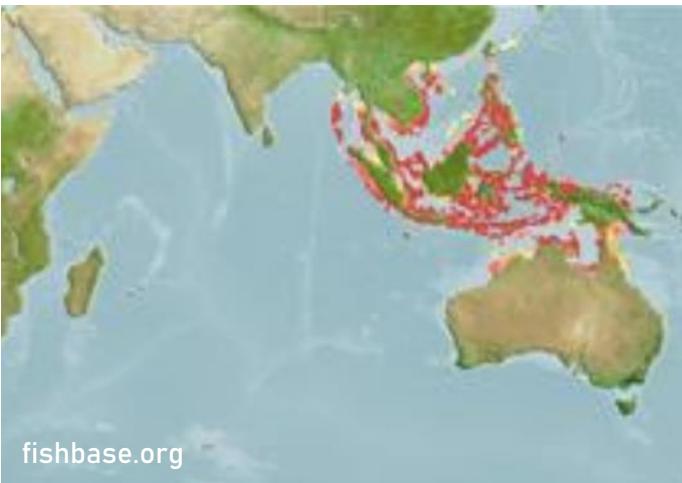
- a. Clownfish: a new model system
- b. Determinism of clownfish coloration





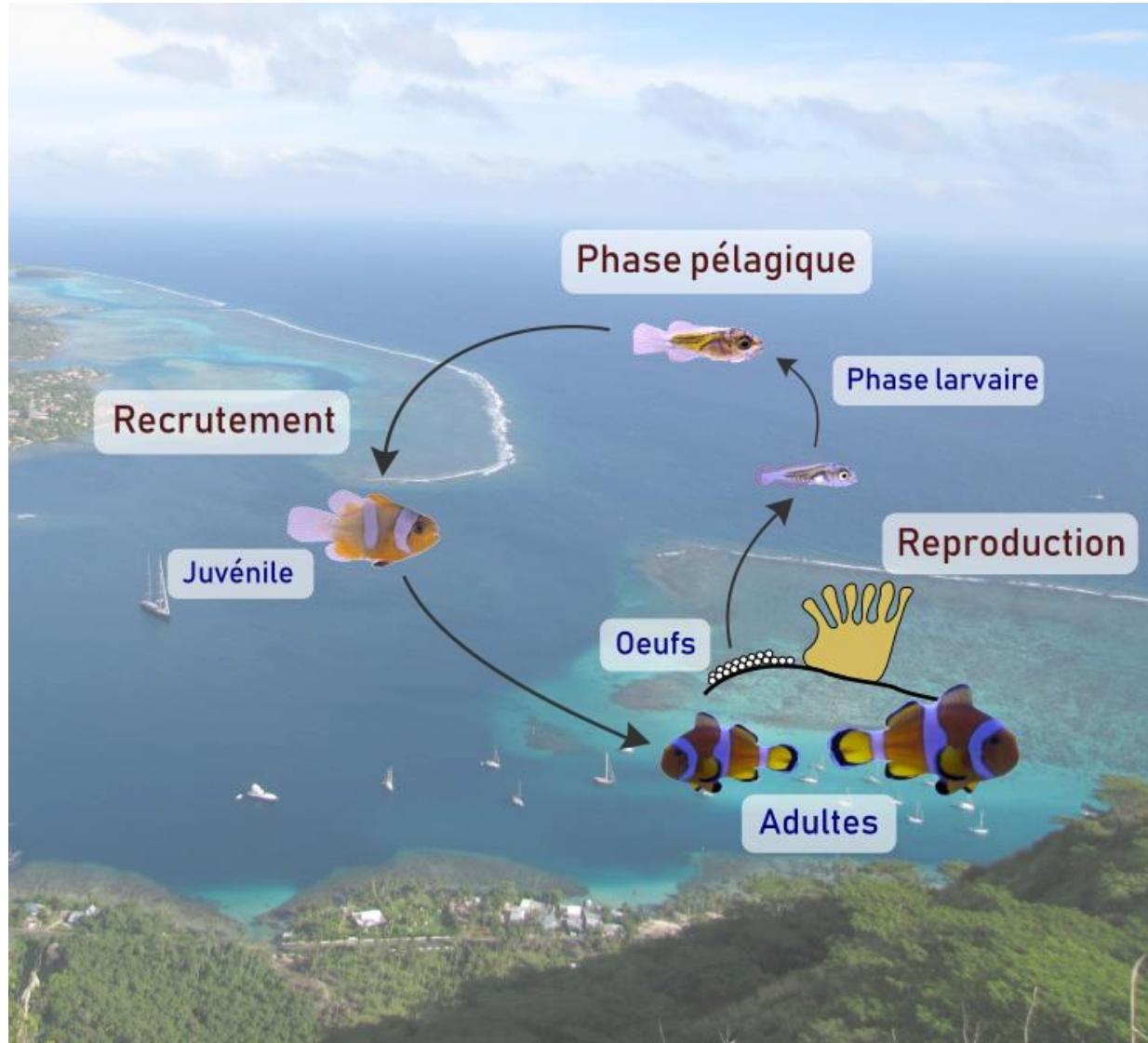
Why a new model system ?

Ecology and evolution of clownfish *Amphiprion ocellaris*

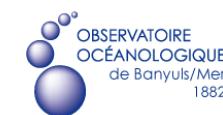
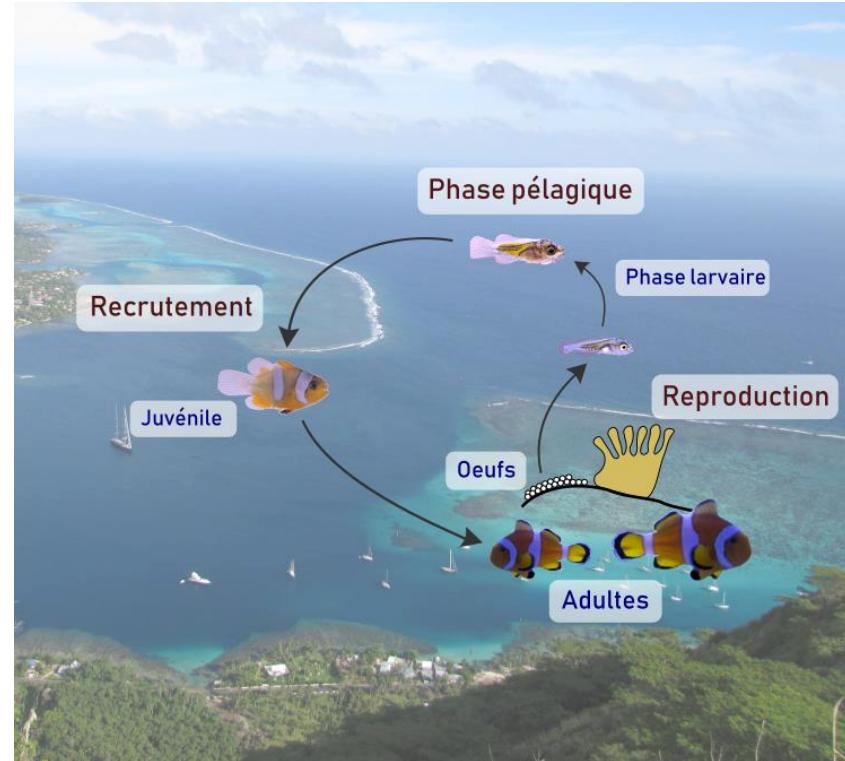
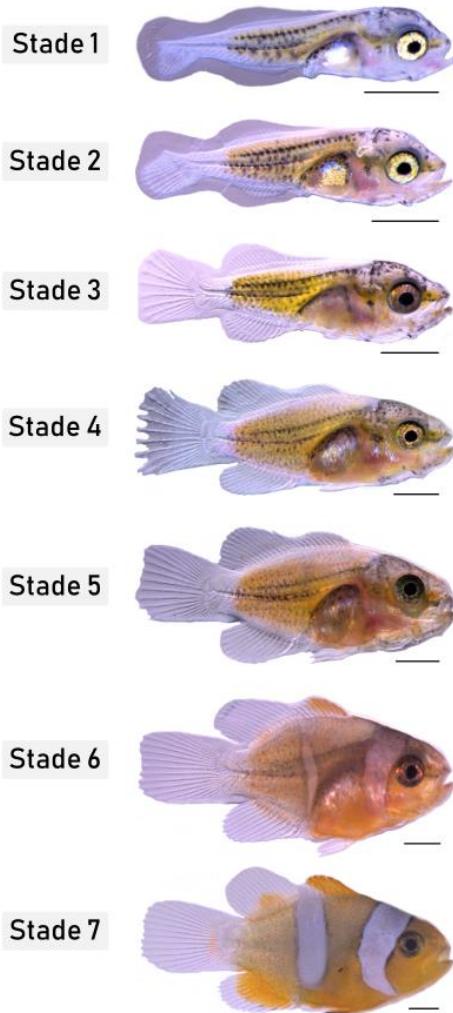


Topology adapted from Litsios *et al.* (2012), Litsios, Pearman *et al.* (2014) and Litsios and Salamin (2014)

Lifecycle of clownfish *A. ocellaris*



Pigmentary changes during *A. ocellaris* post-embryonic development



Introduction

I. Coloration: a great system to study genotype-phenotype relationships

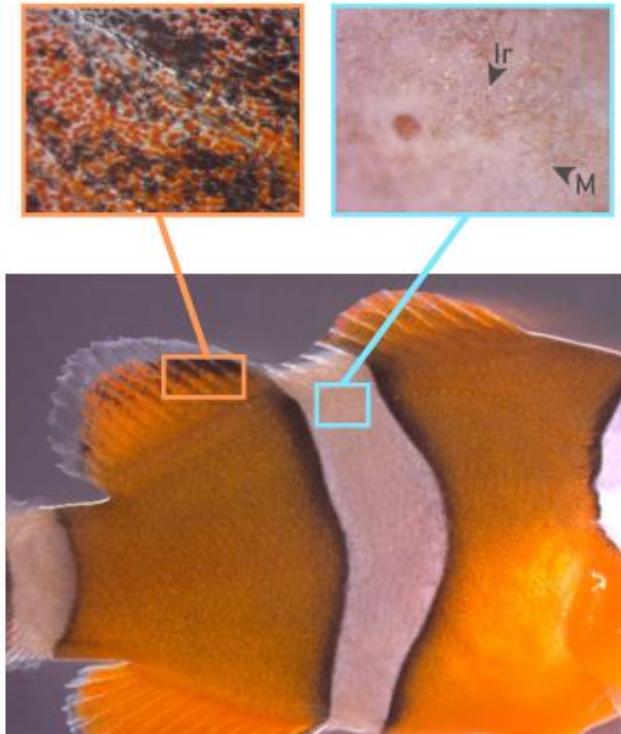
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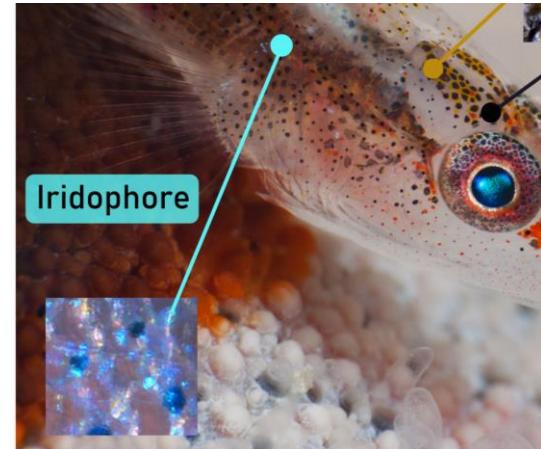
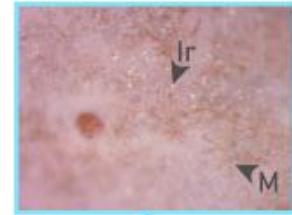
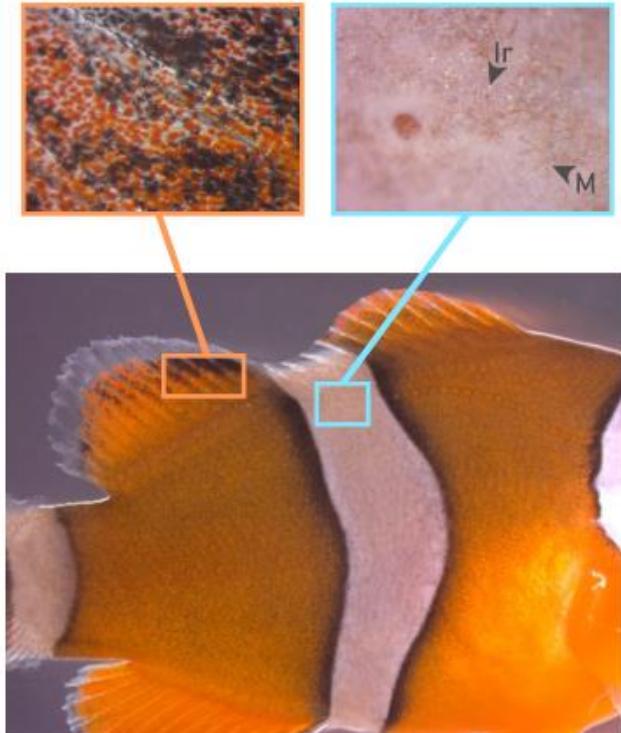


Cells present in each band in *A. ocellaris*

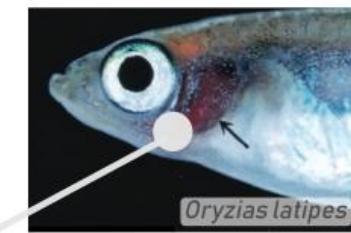


Pictures: N. Roux

Cells present in each band in *A. ocellaris*



?



Leucophore

Pictures: N. Roux

Cells present in each band in *A. ocellaris*



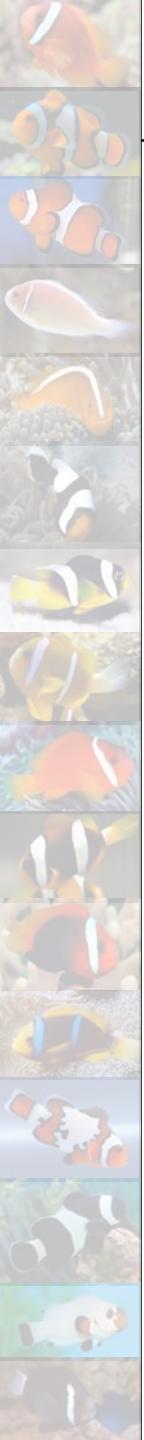
- Genetic determinism of white band
- Identify new candidates of white band

?

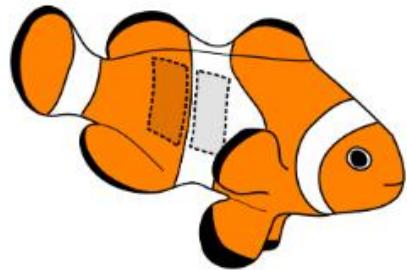
Pictures: N. Roux



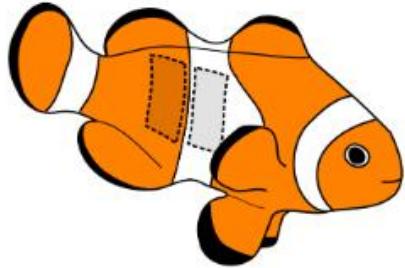
Leucophore



Comparison white vs. orange skin using RNA-Seq



Comparison white vs. orange skin using RNA-Seq



Unil
UNIL | Université de Lausanne

LBMc



Pauline Salis



Anna Marcionnetti



Nicolas Salamin

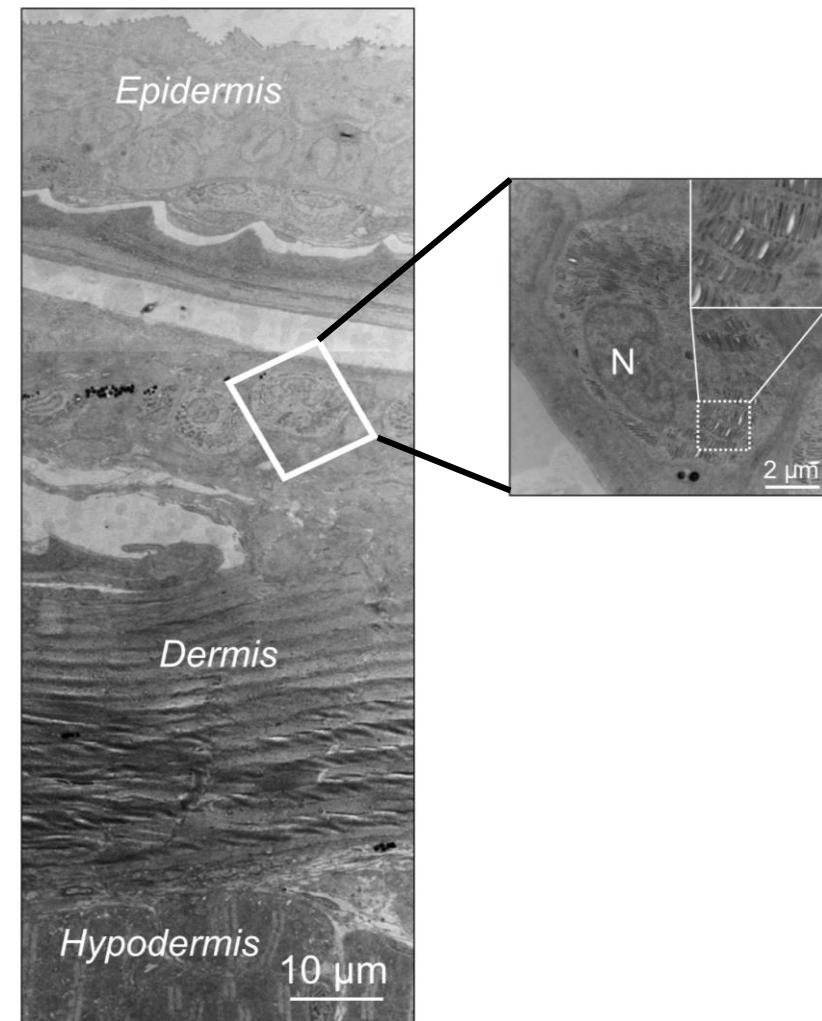
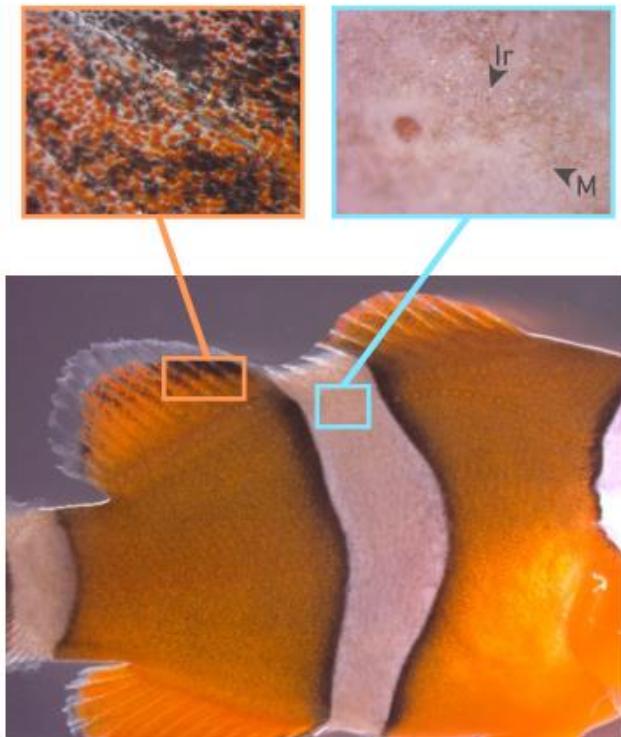


Carine Rey

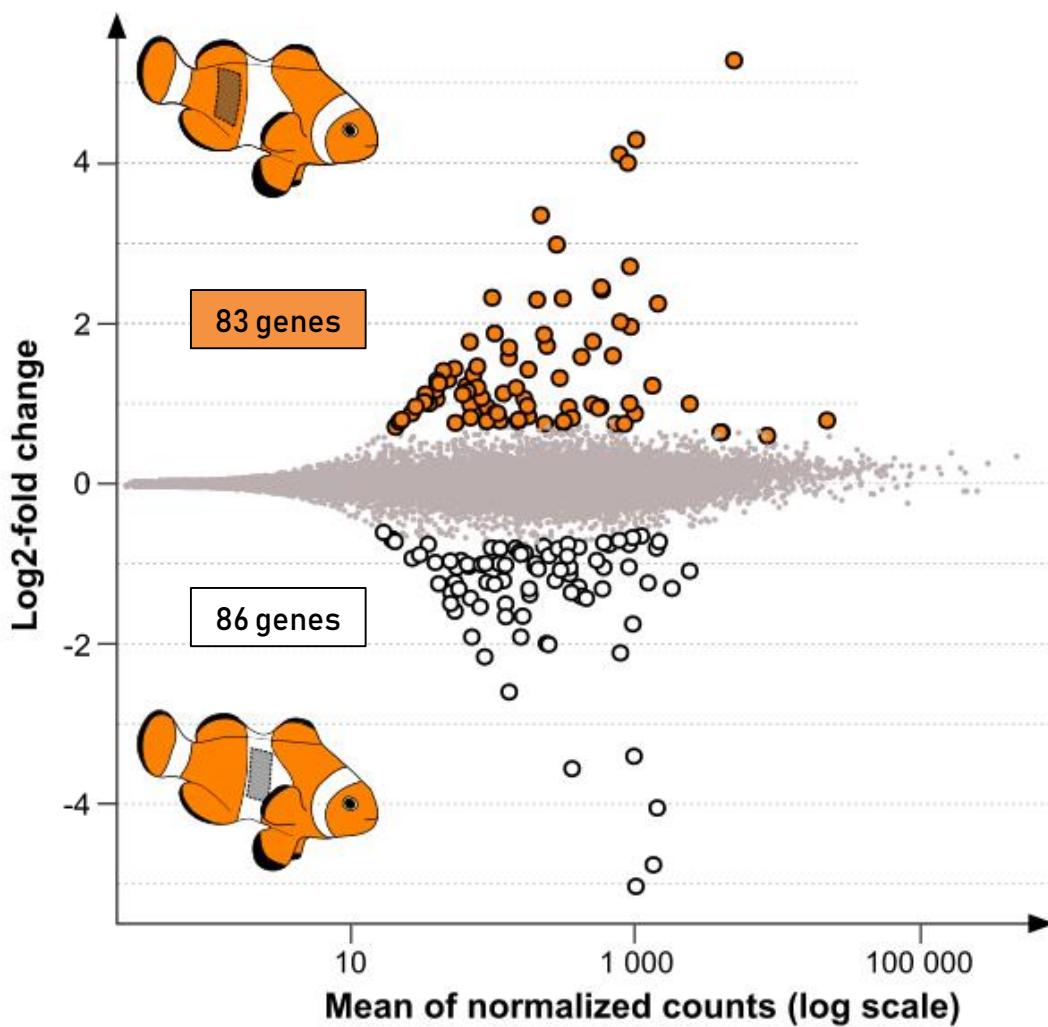


Marie Sémon

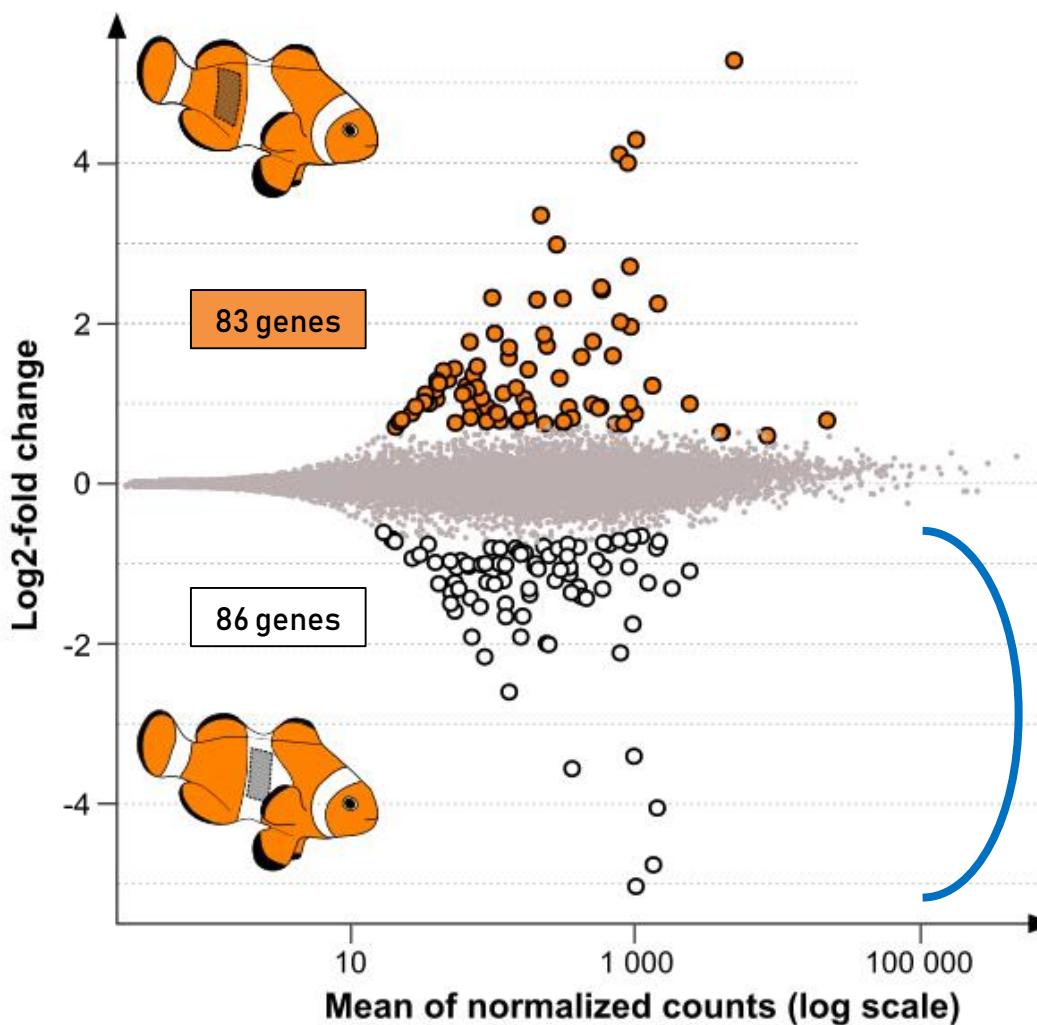
White skin of *A. ocellaris* harbors iridophores, not leucophores



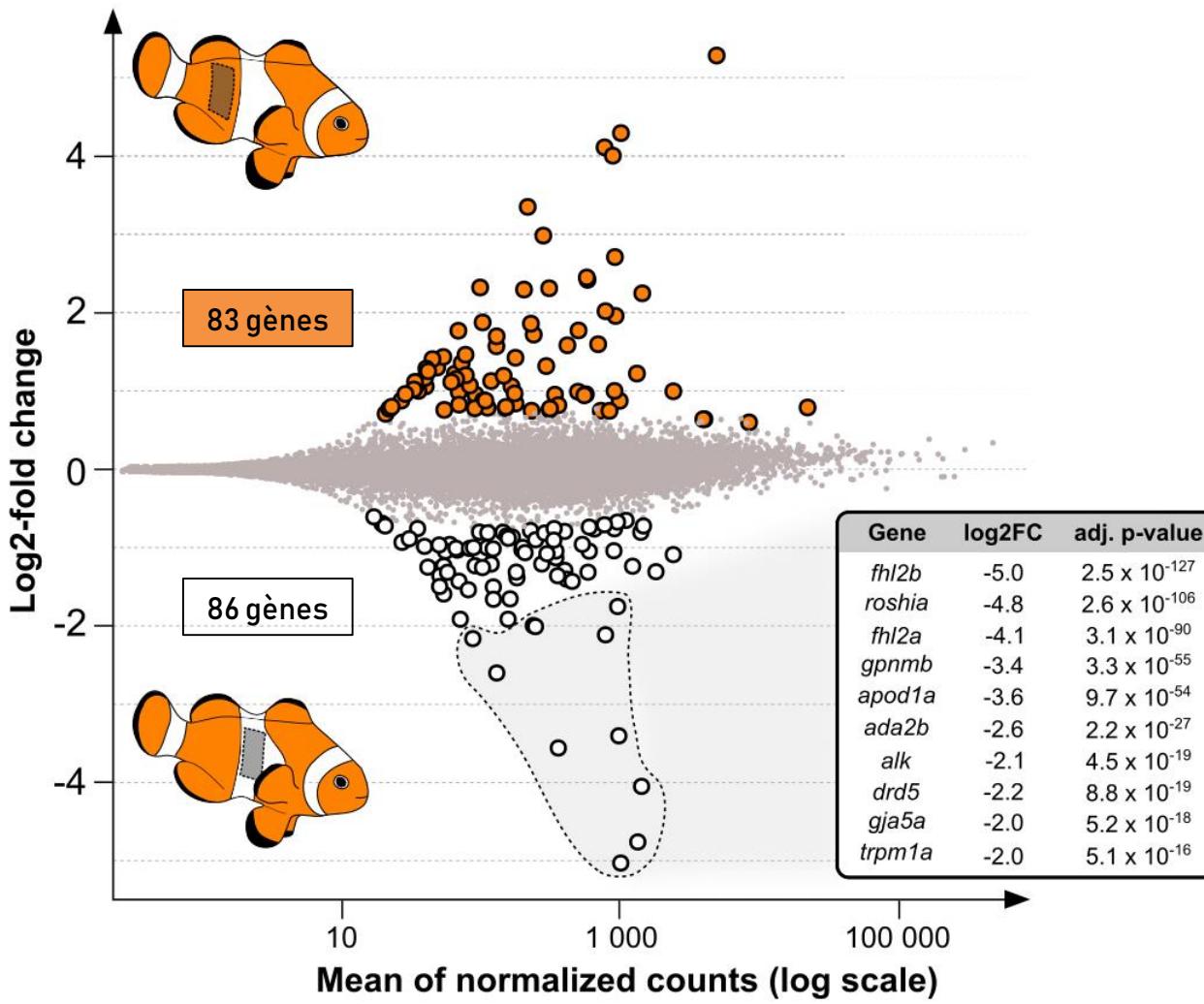
RNA-Seq comparison of white vs. orange skin



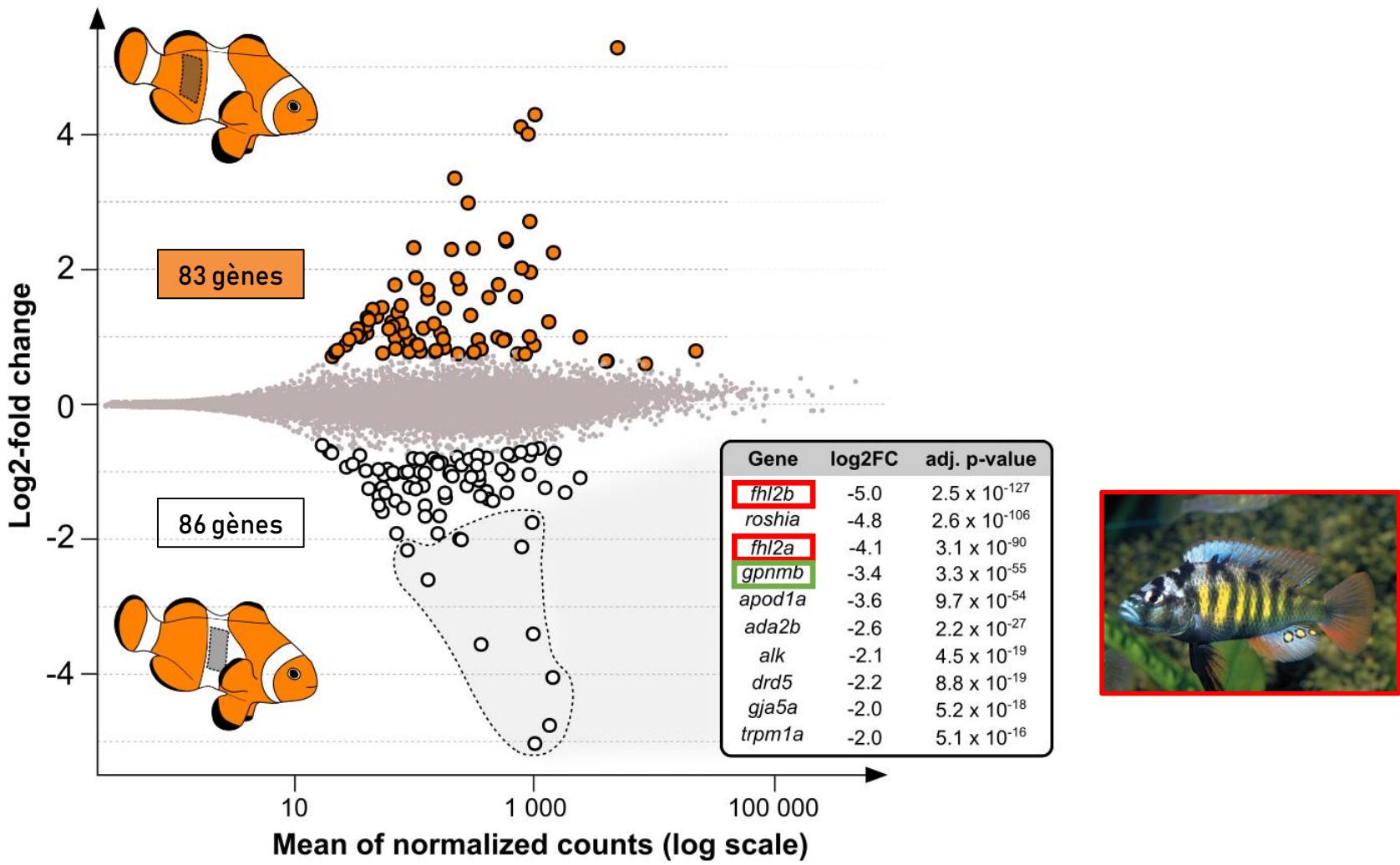
RNA-Seq comparison of white vs. orange skin



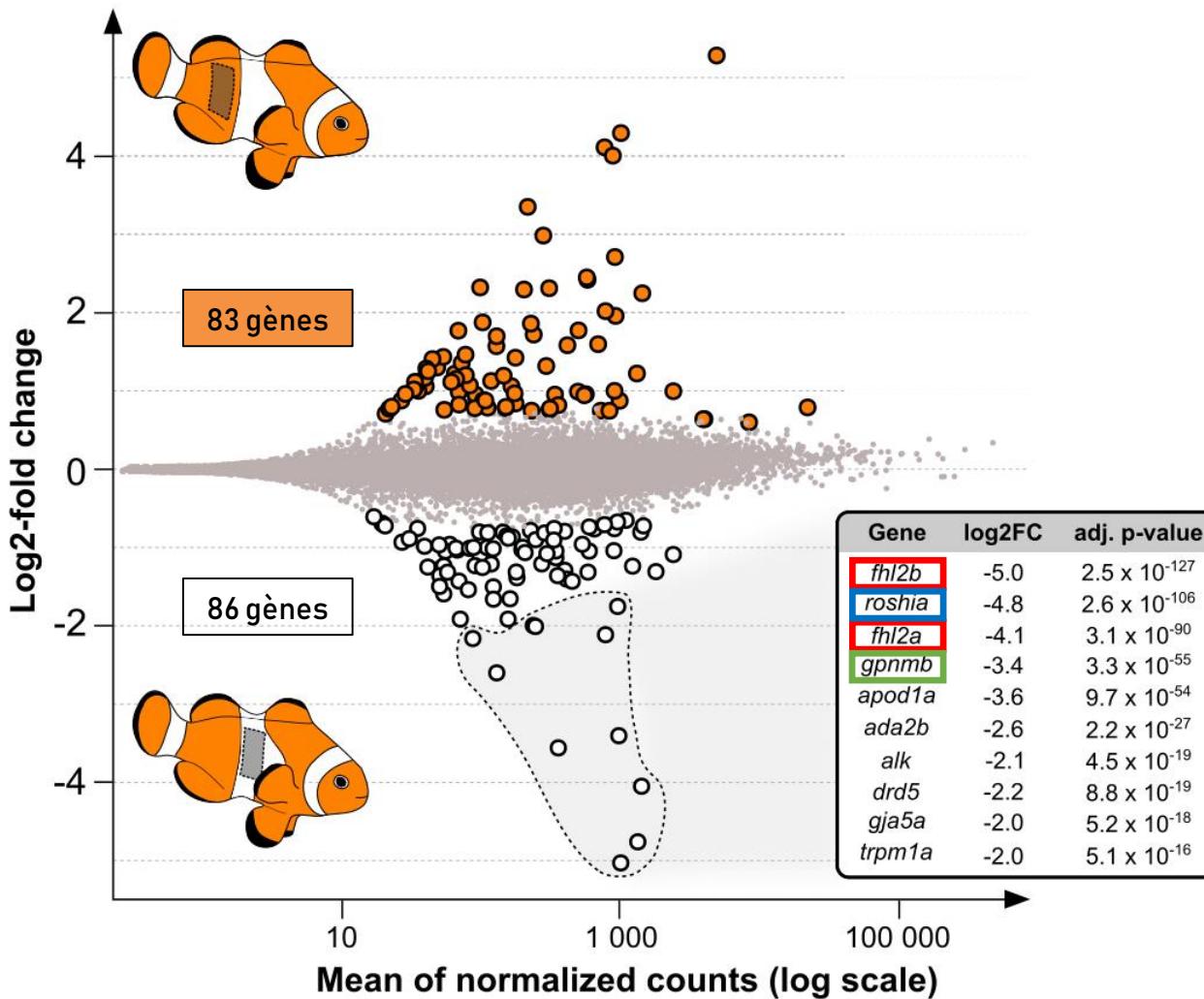
10 most DEGs in white skin



10 most DEGs in white skin



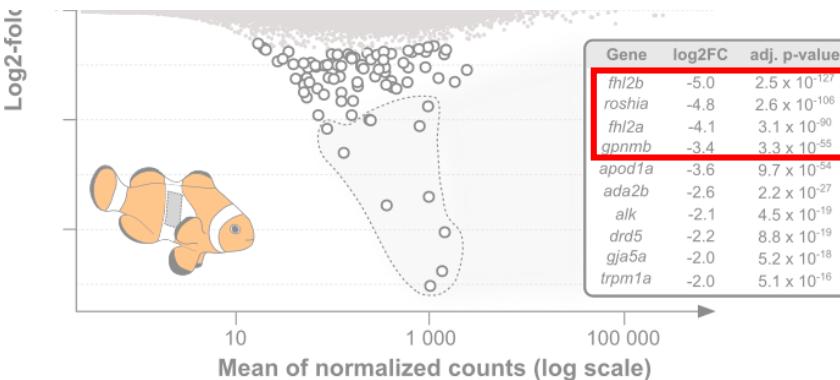
10 most DEGs in white skin



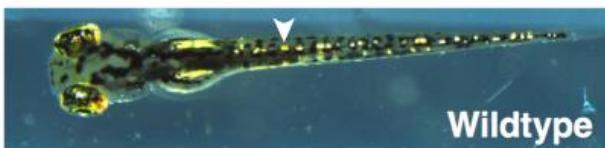
*non-annotated
→ roshi-a*



Functional validation of new candidate genes using CRISPR-Cas9 in *D. rerio*

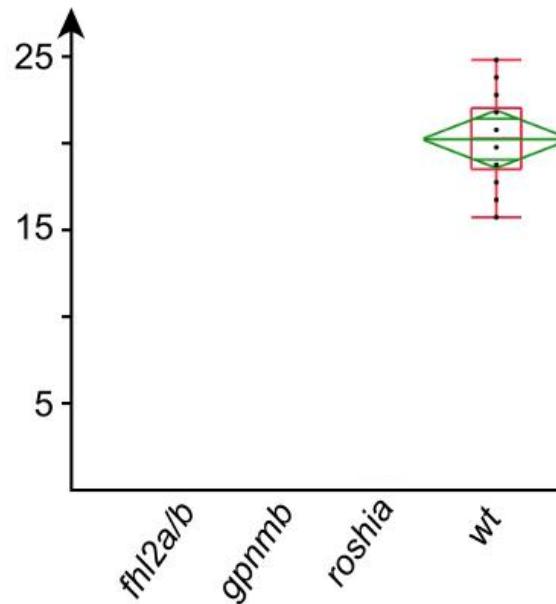


David Parichy



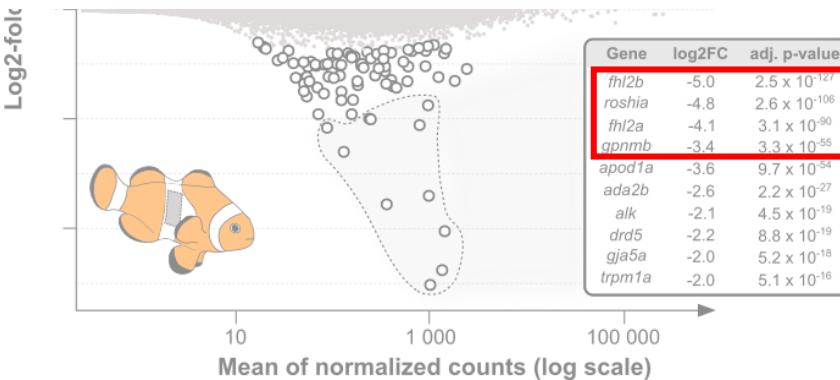
Wildtype

Iridophore
number

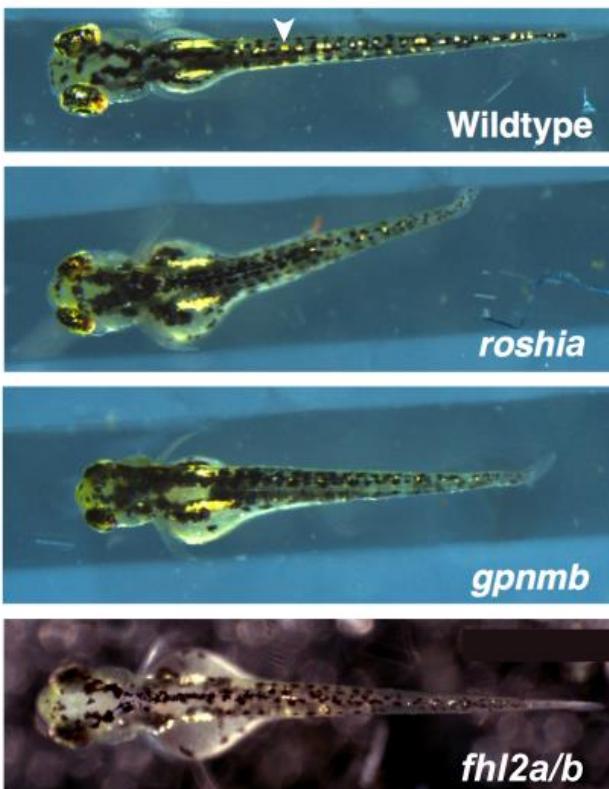


Victor Lewis

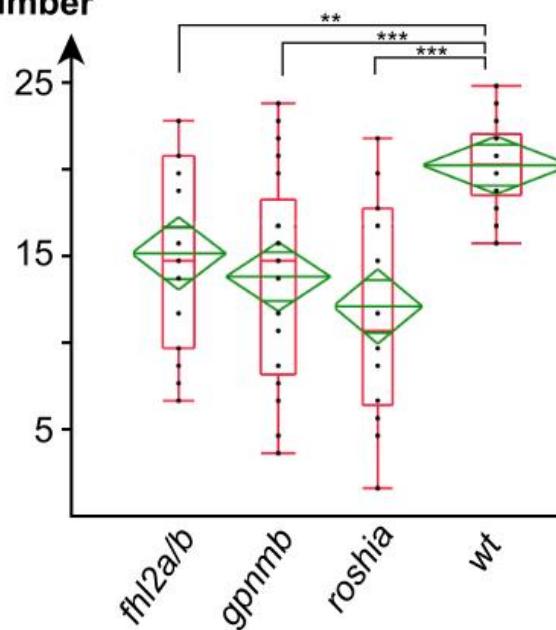
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Iridophore
number



Victor Lewis

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Conclusion



Evolution of GP relationships

The EVOLUTION of

Coloration: a great system to study genotype-phenotype relationships

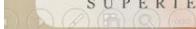
M1 – ENS
Module "Genomes and Phenotypes"
22/11/2018

Thibault Lorin



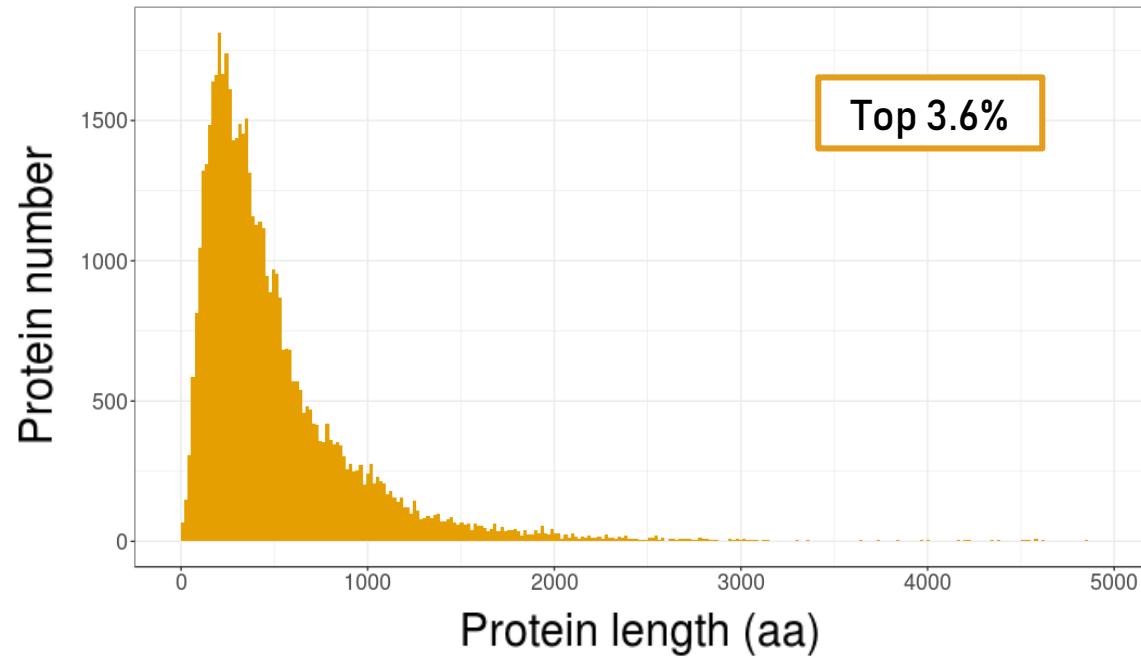
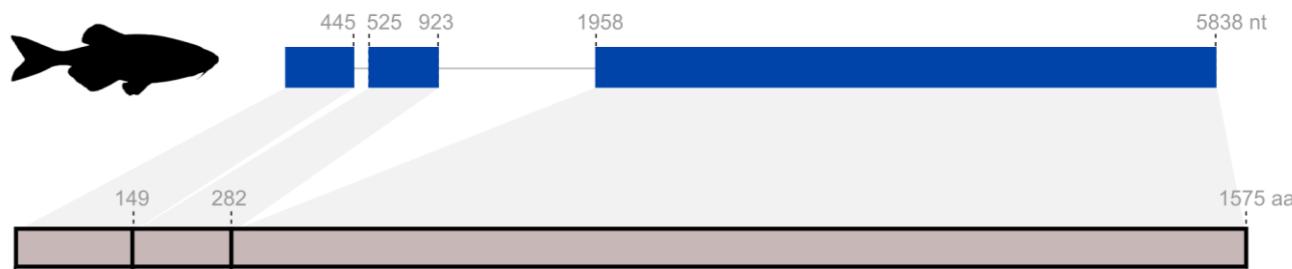
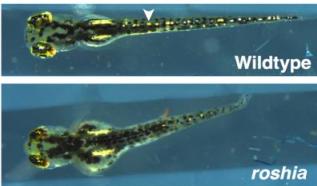
ENS

ÉCOLE NORMALE
SUPÉRIEURE

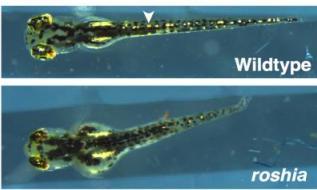


© Aleksey Stemmer

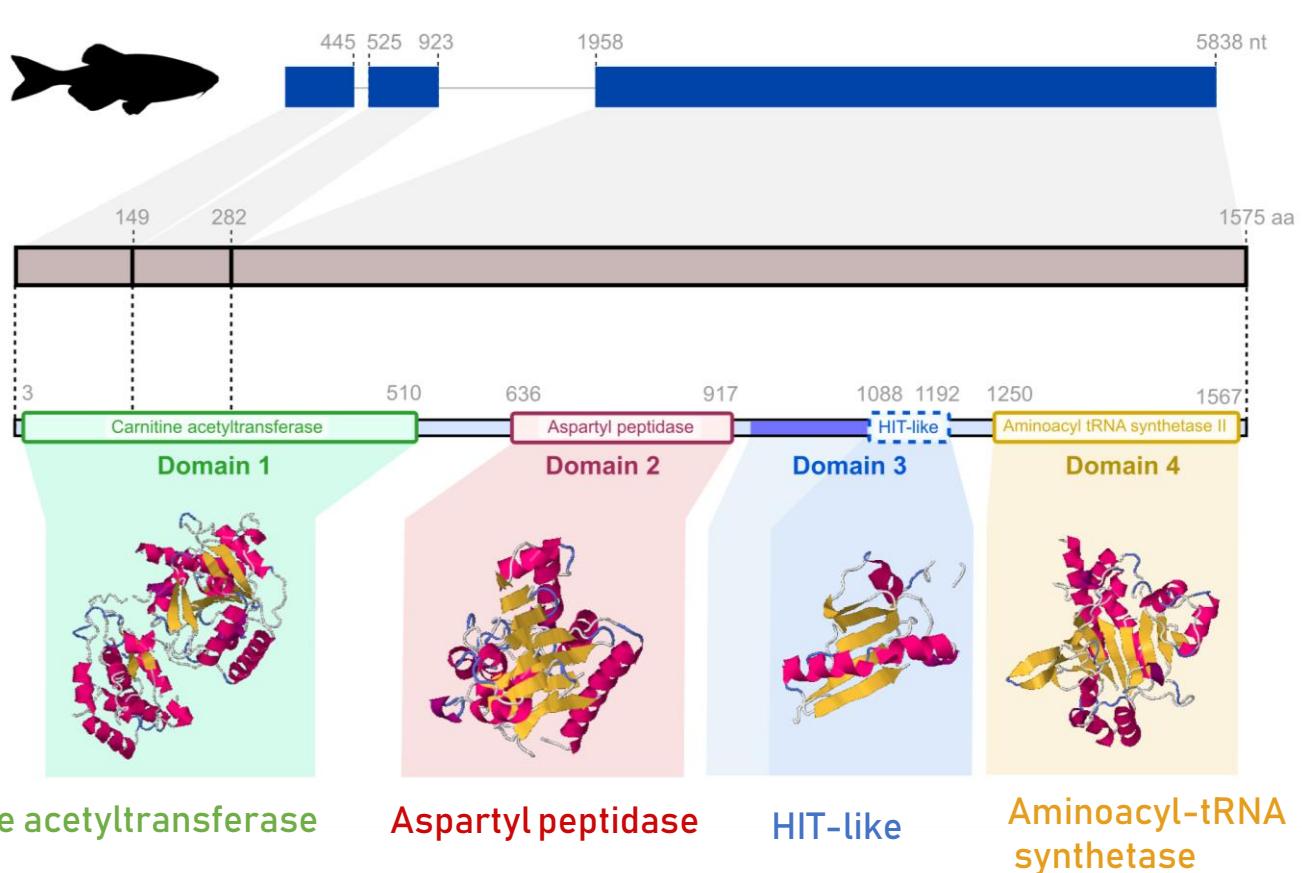
Structure and putative function of Roshi-a



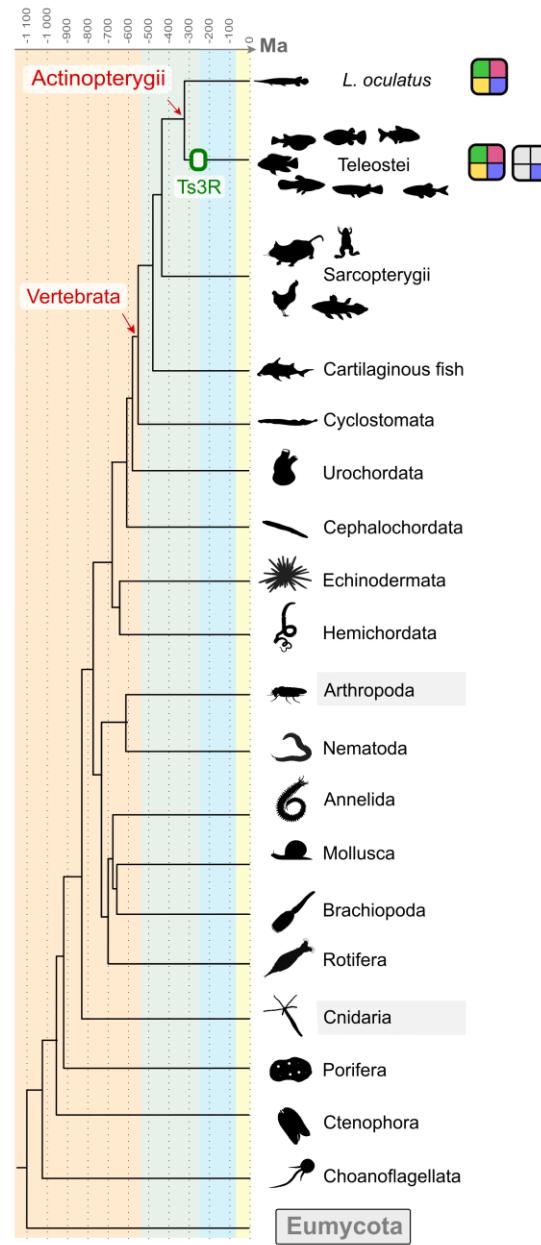
Structure and putative function of Roshi-a



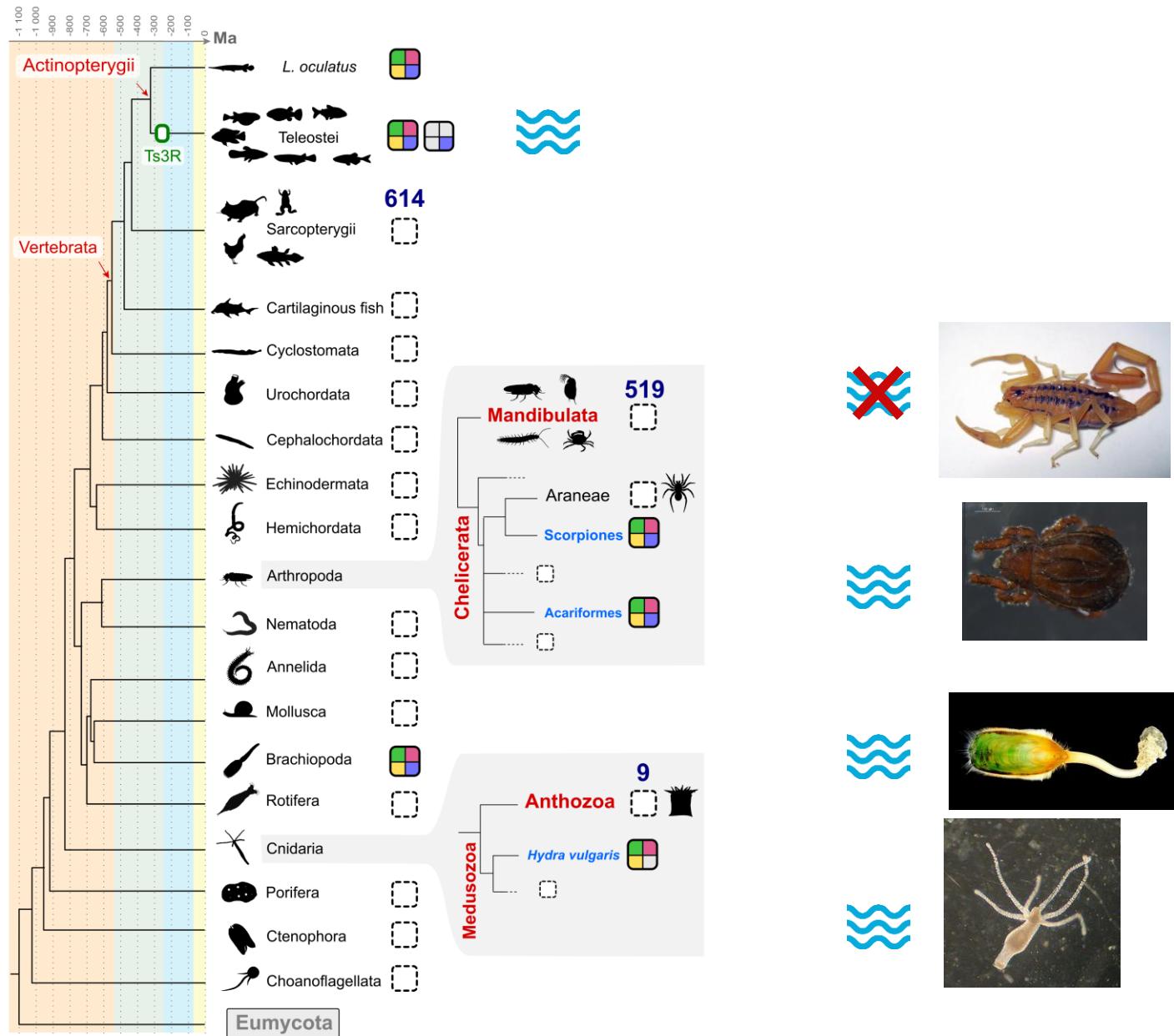
Roshi-a is "Long Putative Multifunctional Cytosolic Enzyme"



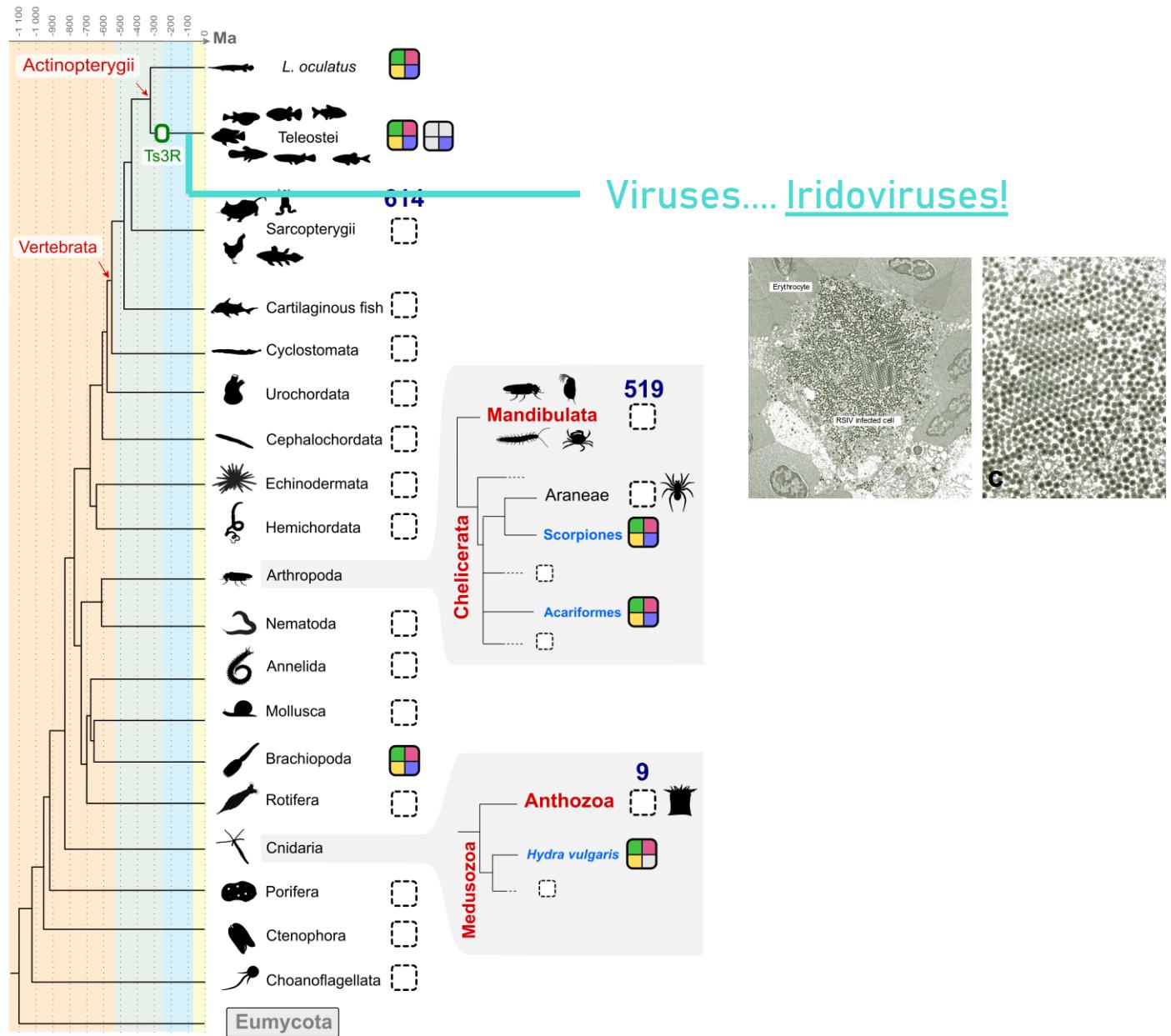
Roshi has a patchy distribution within animals



Roshi has a patchy distribution within animals

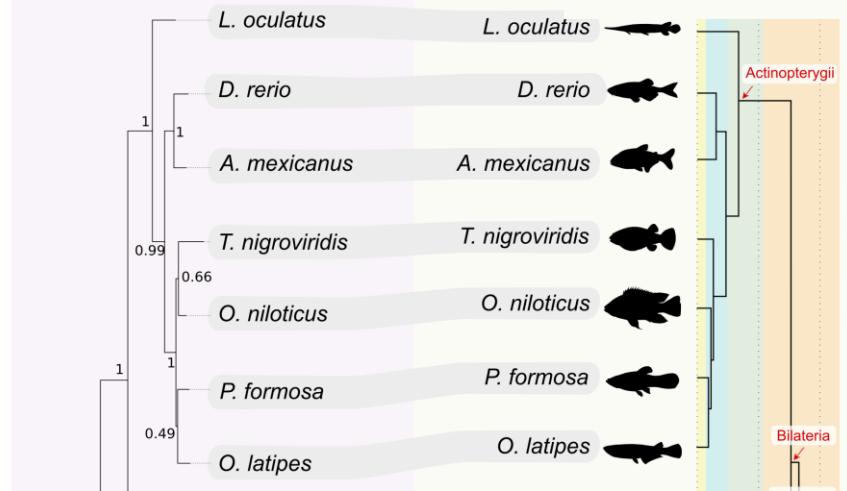


Roshi has a patchy distribution within animals

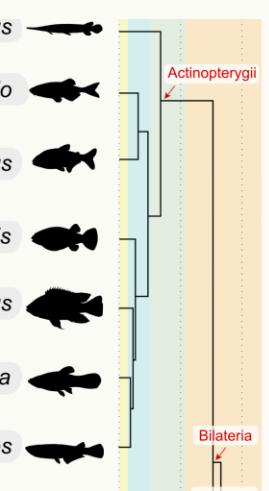


roshi gene tree does not correspond to species tree

Roshi protein phylogeny

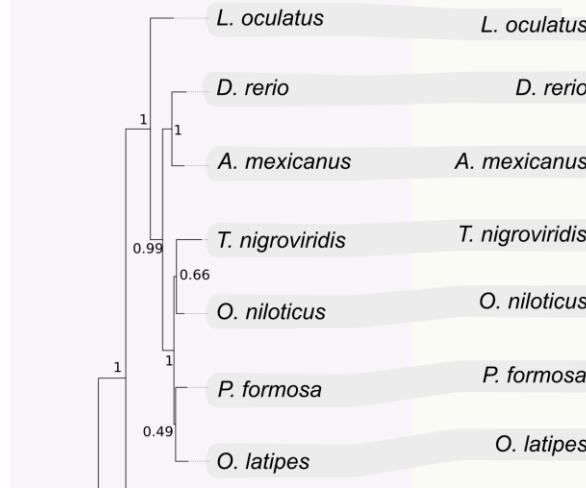


Species phylogeny

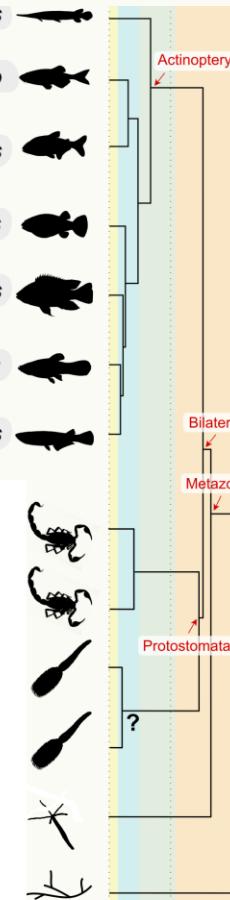


roshi gene tree does not correspond to species tree

Roshi protein phylogeny

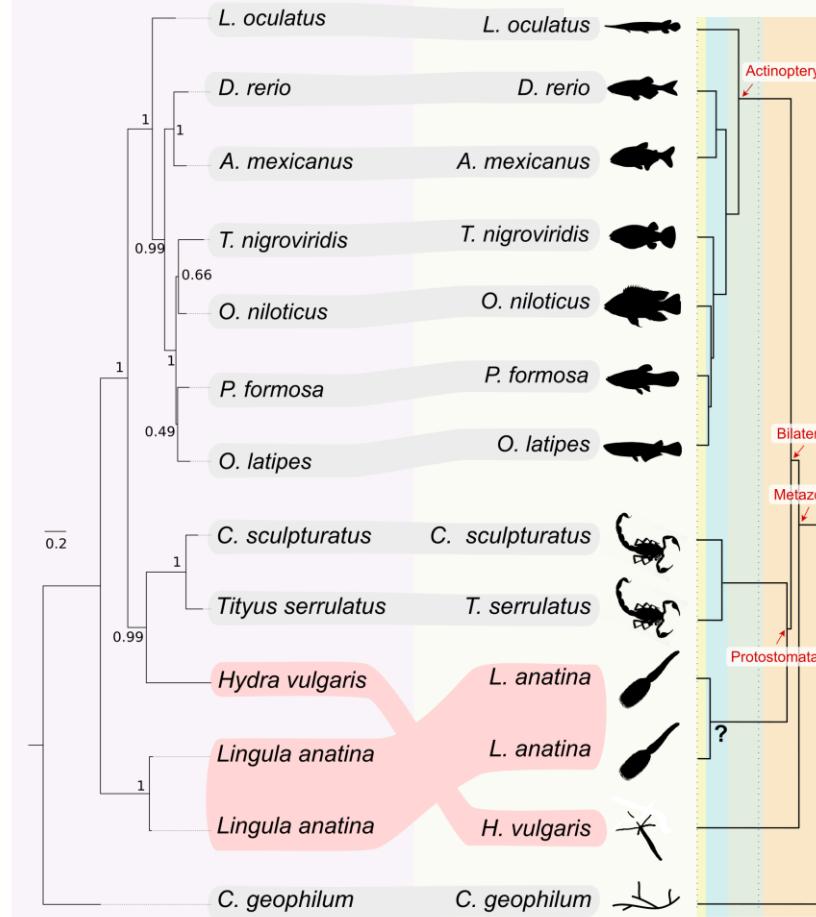


Species phylogeny



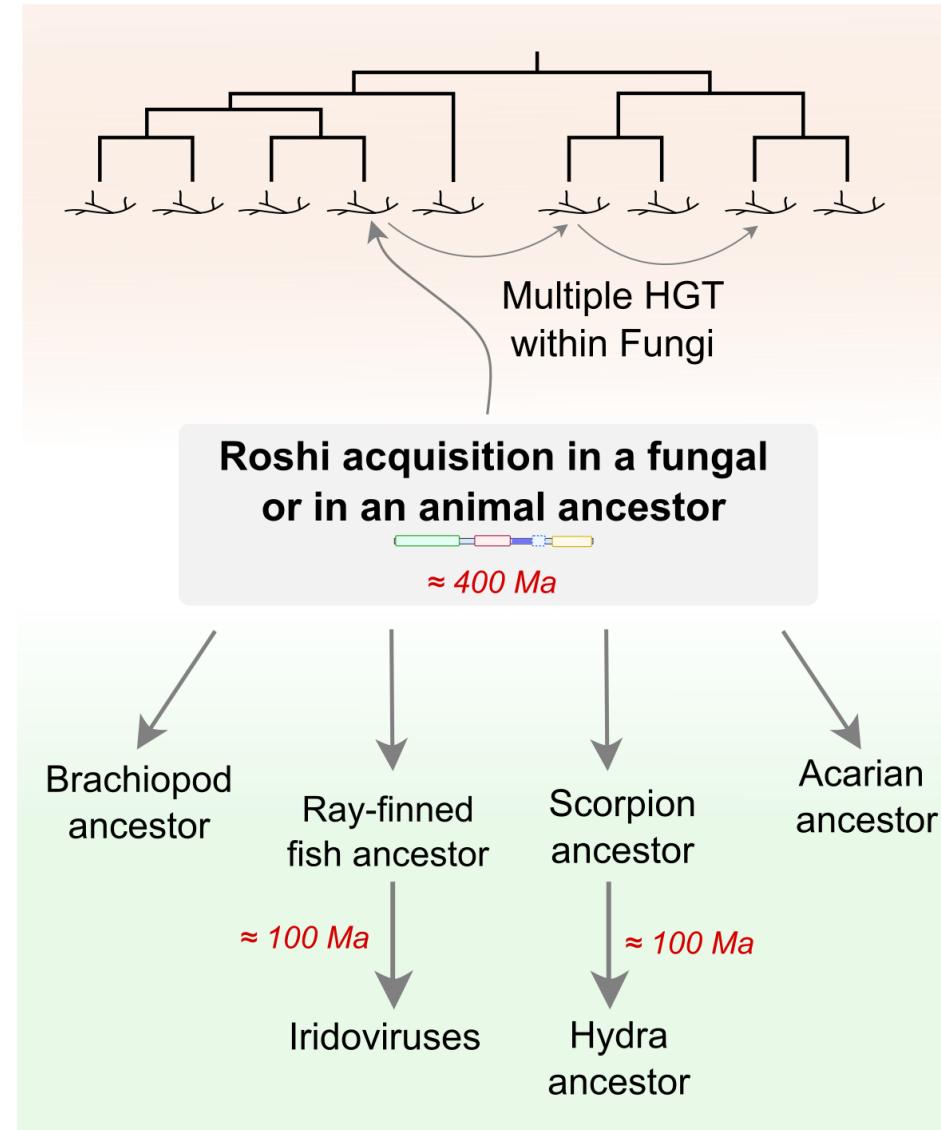
roshi gene tree does not correspond to species tree

Roshi protein phylogeny



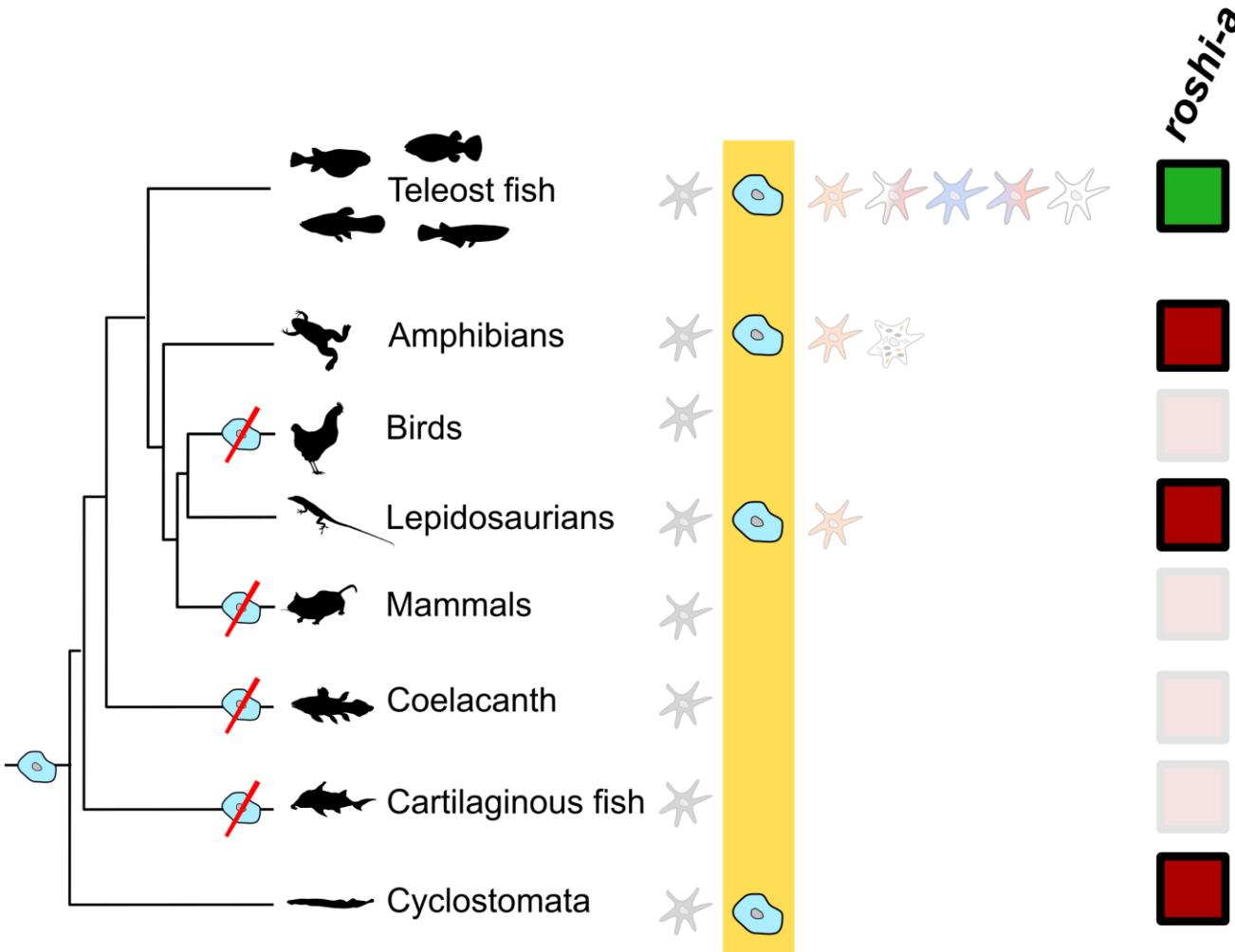
Species phylogeny

Hypothetical scenario for *roshi* evolution



Vincent Daubin

Roshi (among others) invite to reconsider the supposed monophyly of vertebrate iridophores



Evolution of GP relationships

The EVOLUTION of
Importance
of HGT?

Coloration: a great system to study genotype-phenotype relationships

M1 – ENS
Module "Genomes and Phenotypes"
22/11/2018

Thibault Lorin

ENS
ÉCOLE NORMALE SUPÉRIEURE

© Aleksey Stemmer



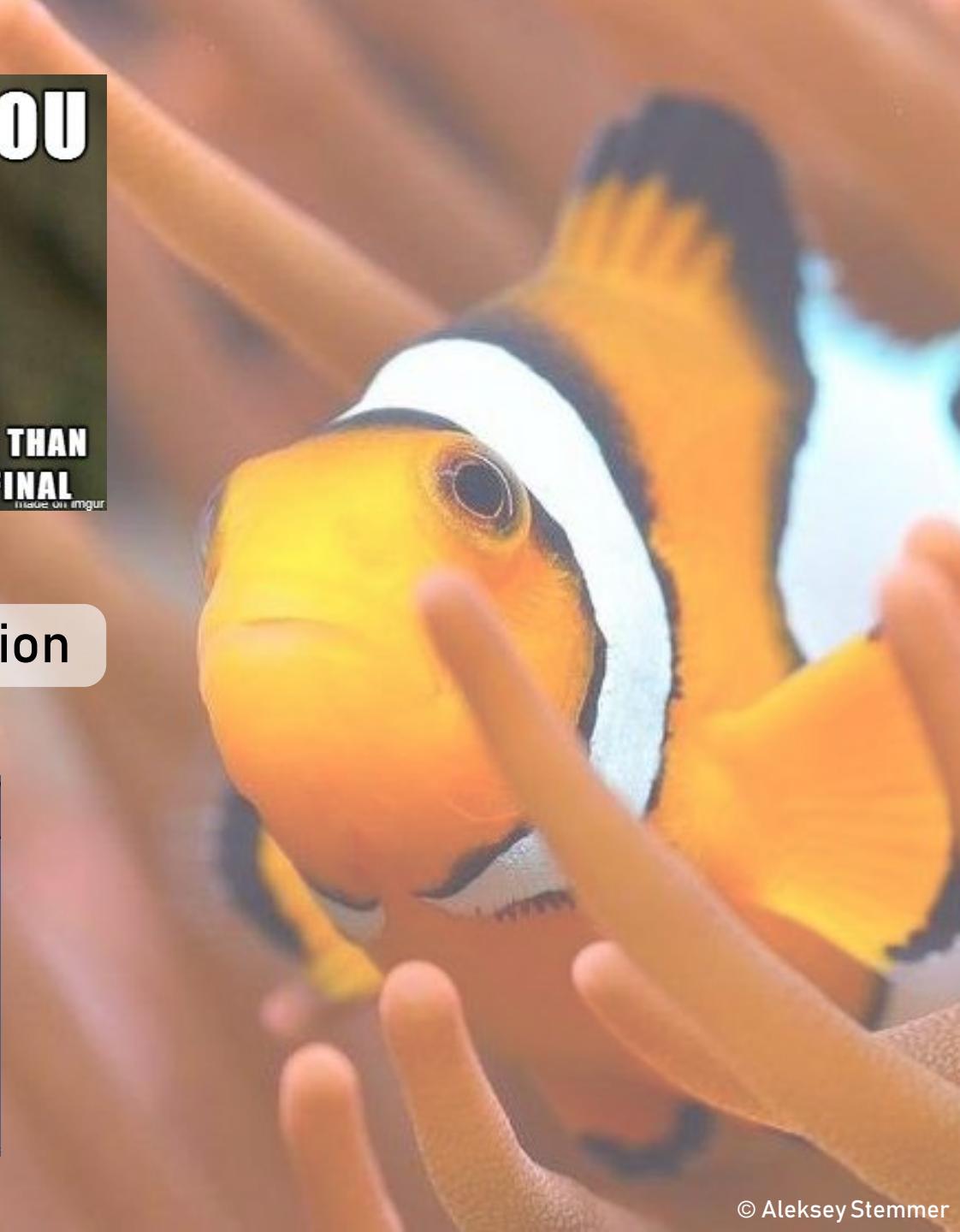
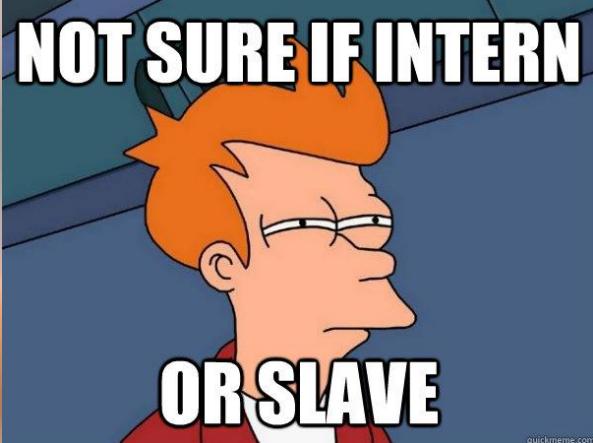
Thank you for your attention

WHAT IF I TOLD YOU

INTERNSHIPS WERE MORE IMPORTANT THAN
ANY GRADE, PROJECT, MIDTERM, OR FINAL

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Thank you for your attention

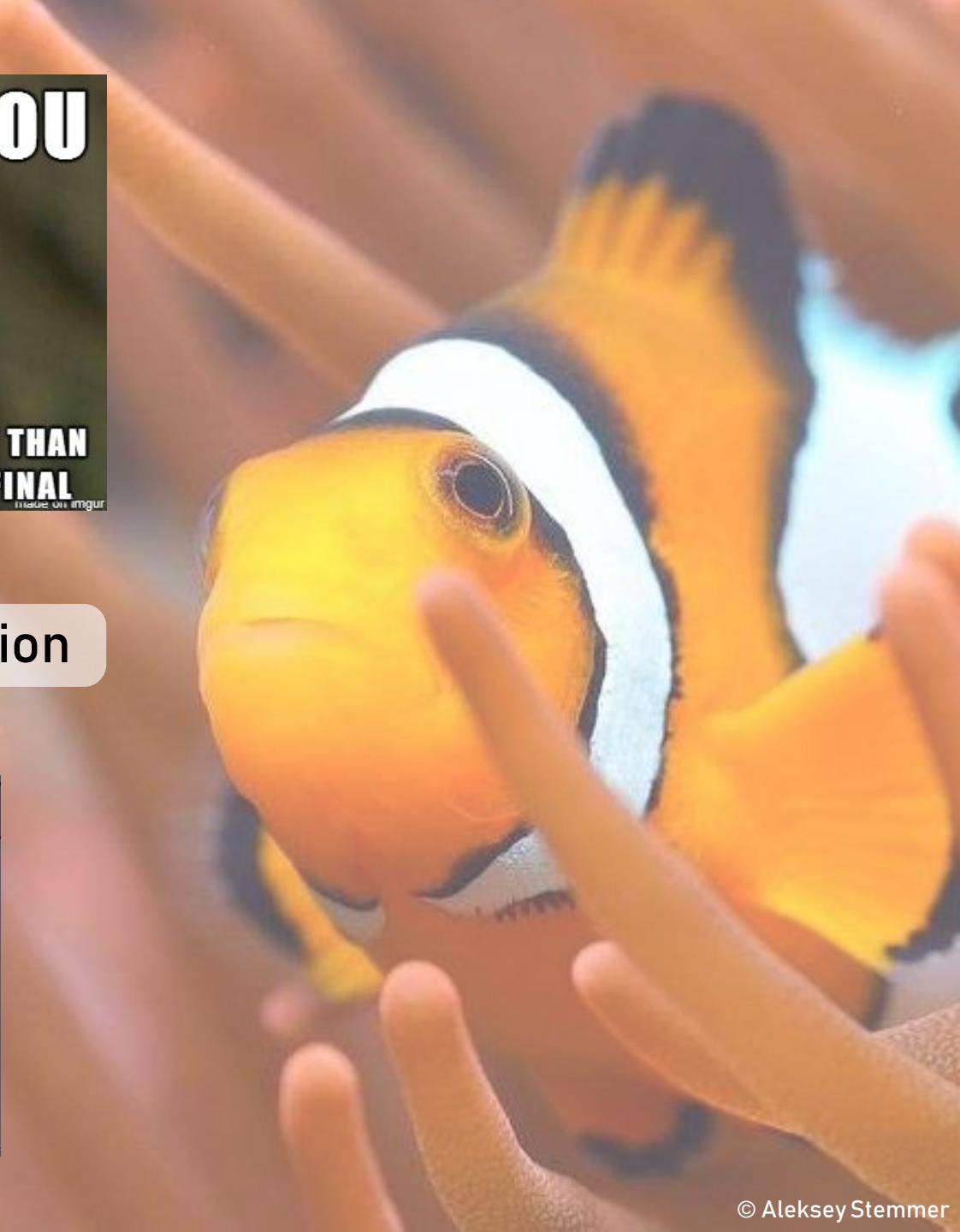
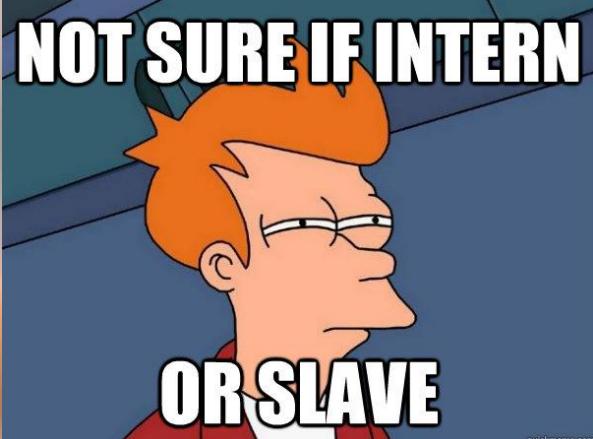


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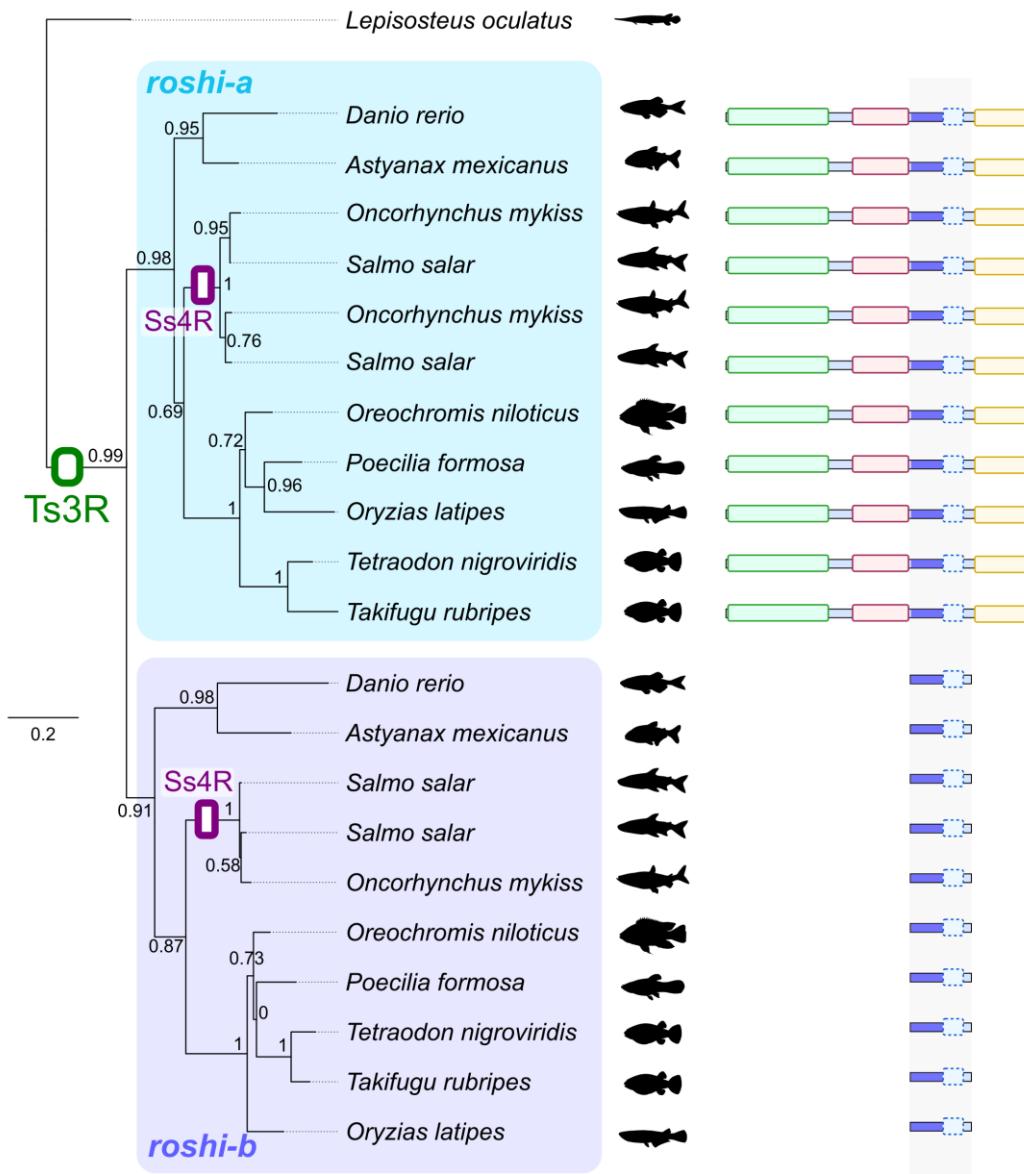
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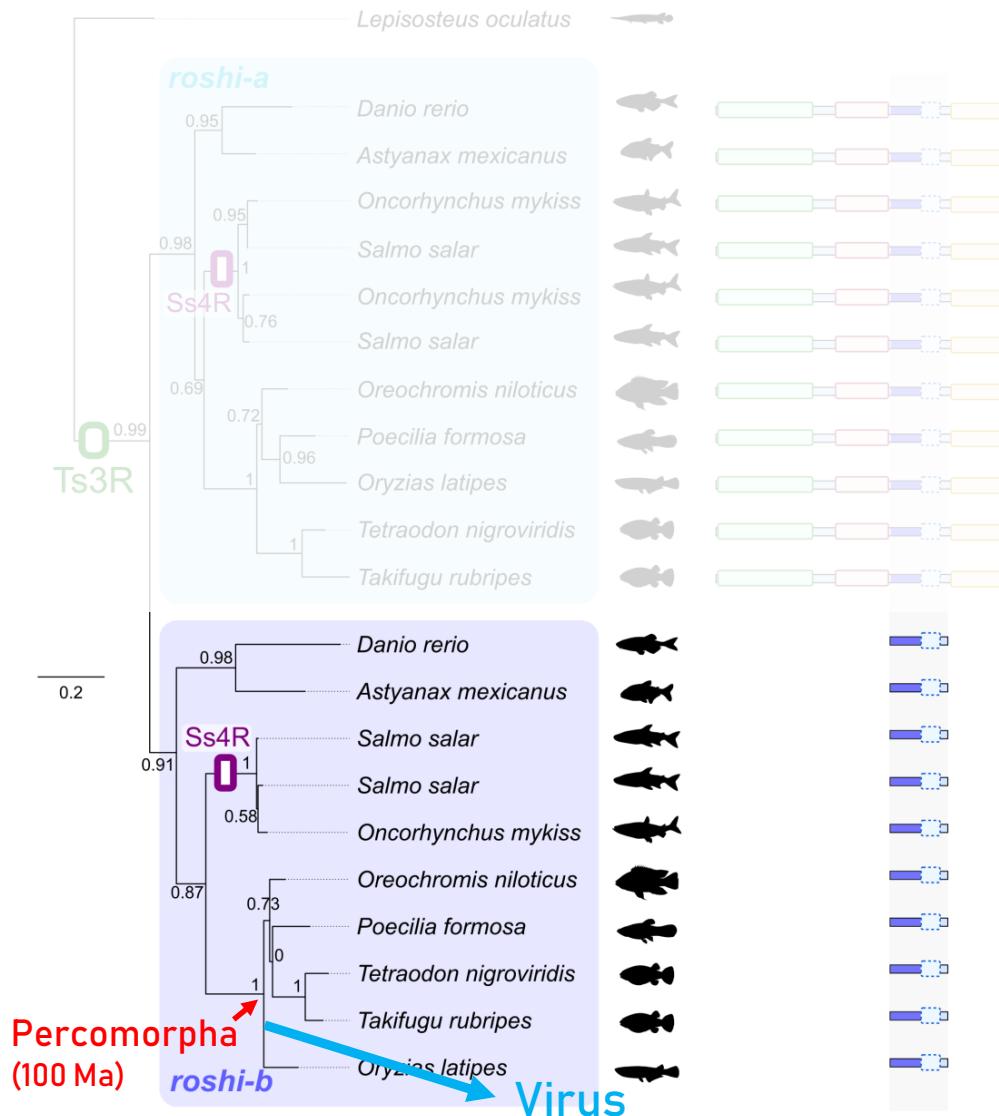
Thank you for your attention



Roshi a été dupliqué et retenu après la Ts3R

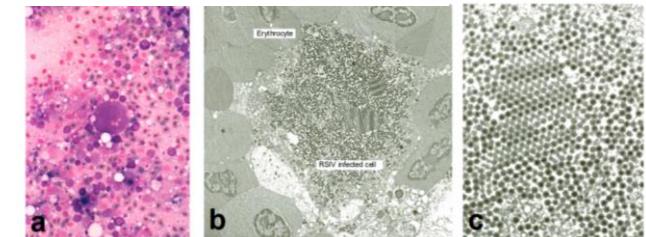


Roshi-b a été transféré à un virus de manière horizontale

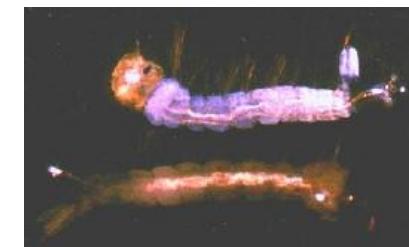


Séquences de Mégalocytivirus...

- Anémies
- Hémorragies
- Exophtalmie
- Gonflement de la rate

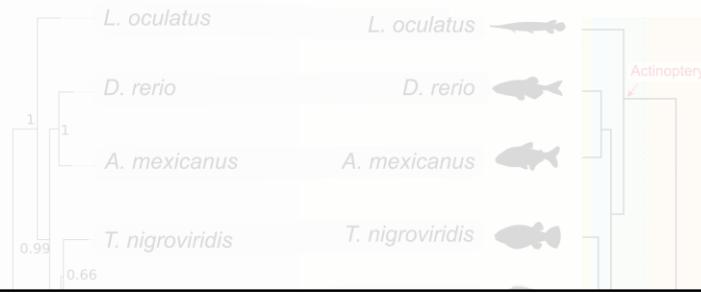


... qui sont des Iridovirus !



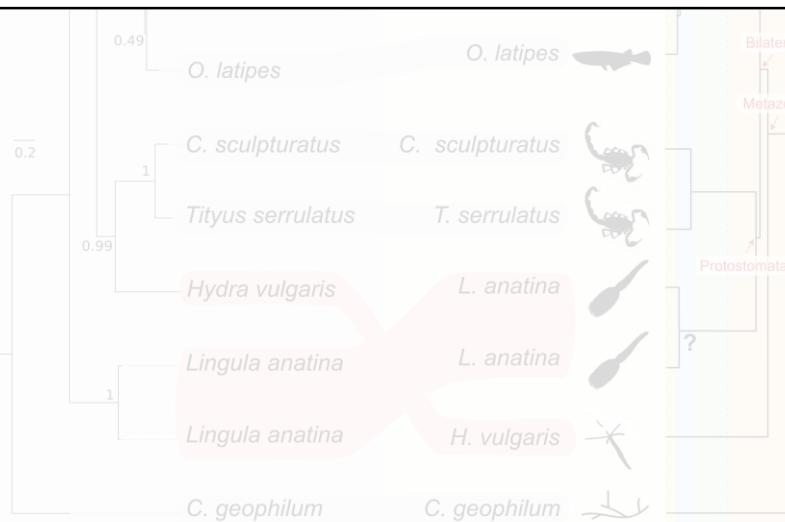
La phylogénie de *roshi* ne correspond pas à la phylogénie des espèces

Roshi protein phylogeny



Species phylogeny

Patron évolutif suggérant une transmission horizontale du gène



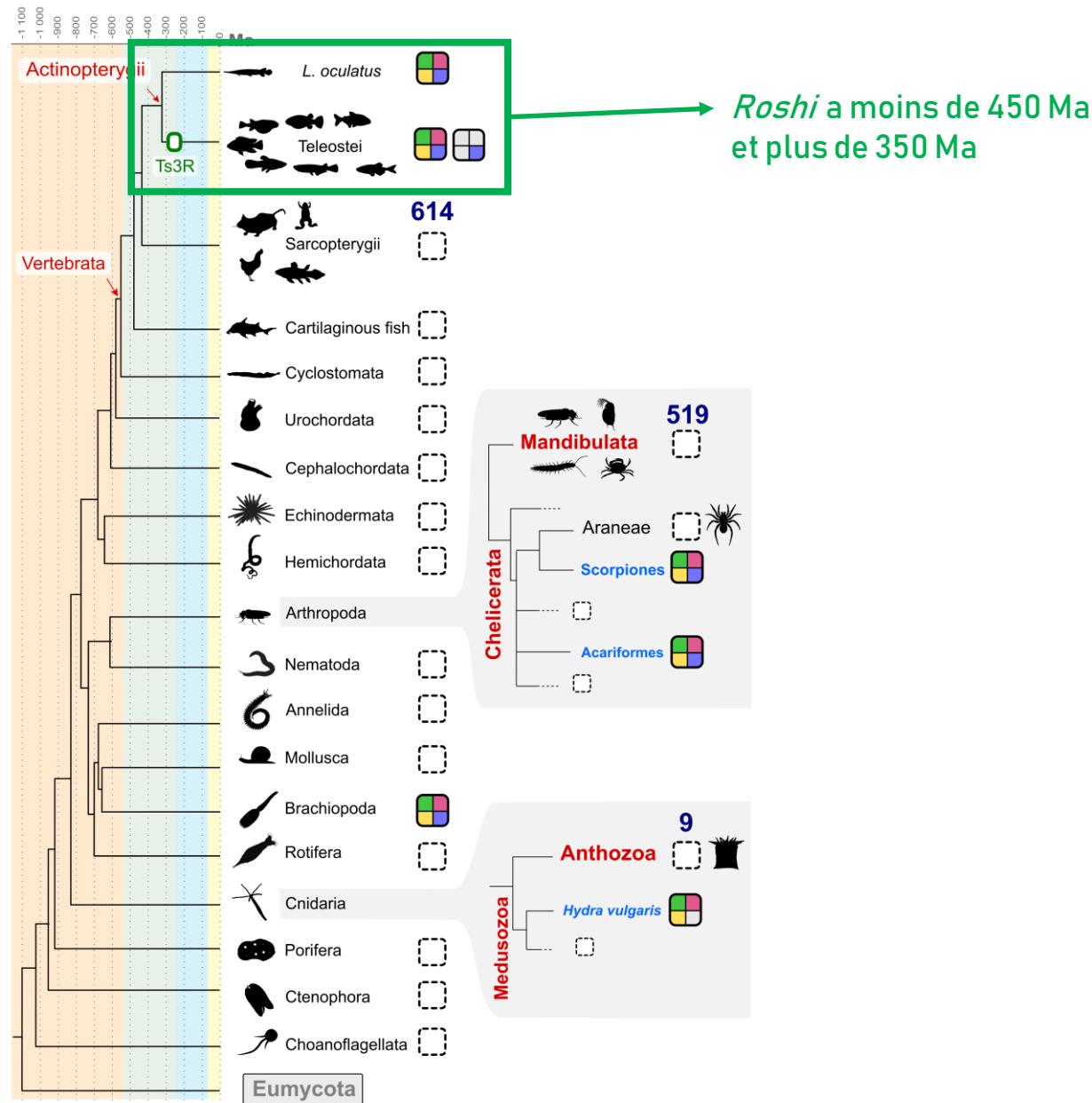
Transfert :

- de "qui" vers "qui" ?
- "quand" ?
- "comment" ?

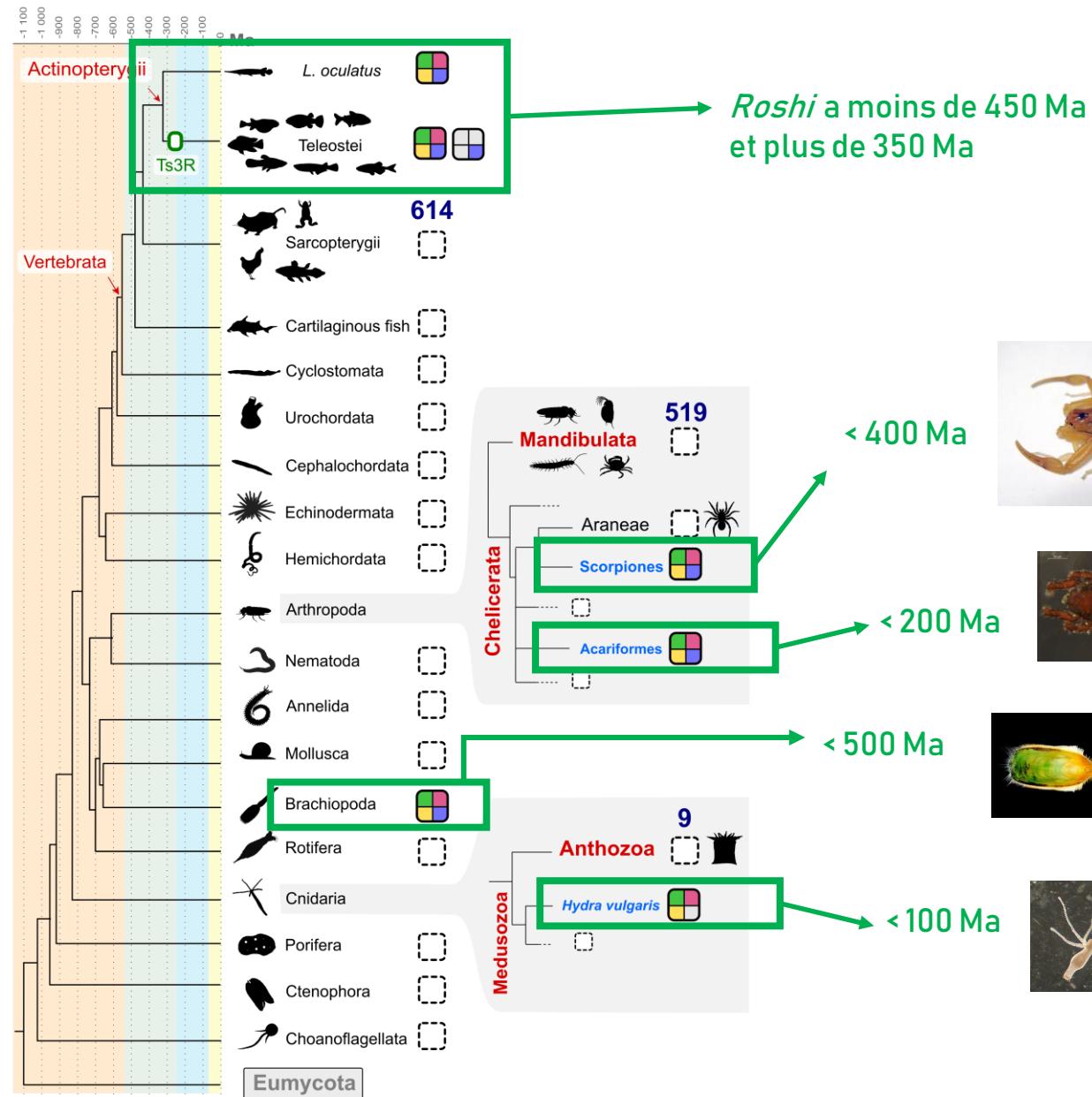


Vincent Daubin

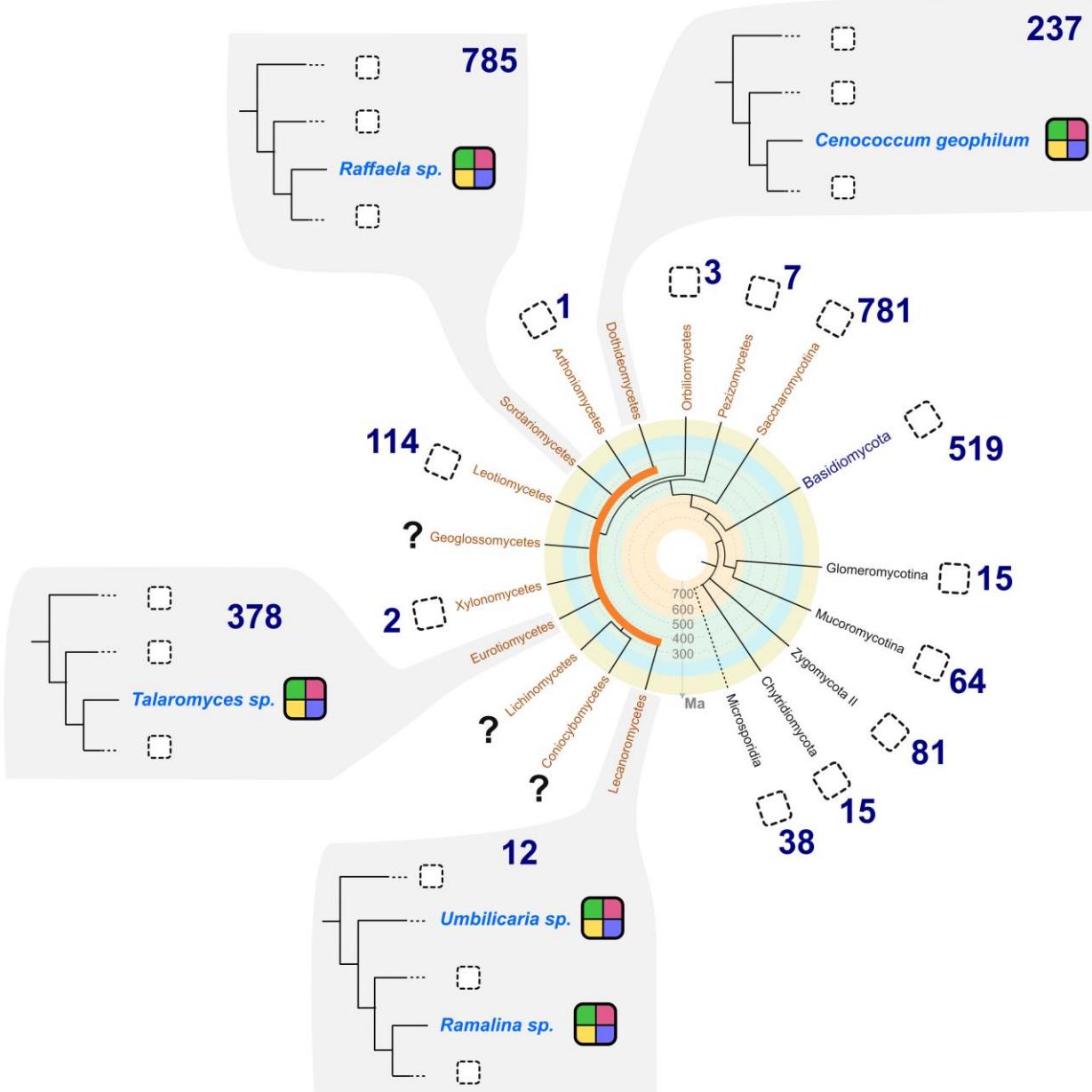
Estimation des âges de transfert de *roshi* chez les Animaux



Estimation des âges de transfert de *roshi* chez les Animaux



Distribution de *roshi* chez les Eumycètes



Quels sont les modes de transfert envisagés pour *Roshi* ?

1. Les HGT sont moins fréquents mais tout de même possibles chez les Eucaryotes

Moran *et al.* (2010) *Science*

Sun *et al.* (2015) *Sci Rep*

2. Les HGT "inter-Animaux" sont rares

Gilbert *et al.* (2012) *Mol Biol Evol*

Graham *et al.* (2012) *BMC Evol Biol*

Peccoud *et al.* (2017) *PNAS*

3. Les mécanismes de transfert reposent probablement sur des vecteurs viraux

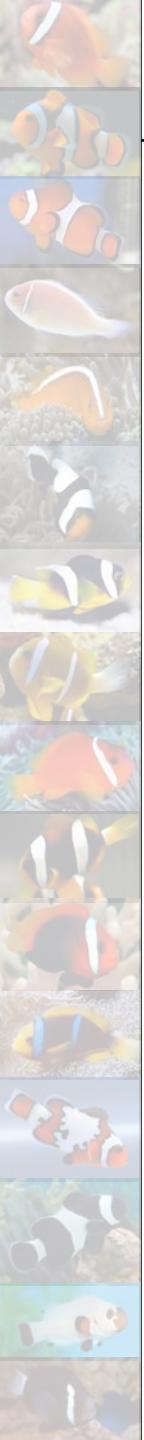
Gilbert *et al.* (2010) *Nature*

Gilbert and Cordaux (2017) *Curr Opin Virol*



Waddington *et al.* (2015)
Biol. Letters

- ✓ a. *Roshi-b* transféré horizontalement à des Iridovirus
- ✓ b. *Roshi* présent chez des Acariens
- ✓ c. Ecologie compatible (aquatique)



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4. Au sein des Champignons, les transferts horizontaux sont possibles

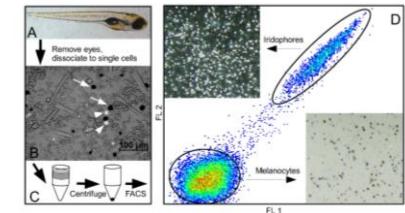
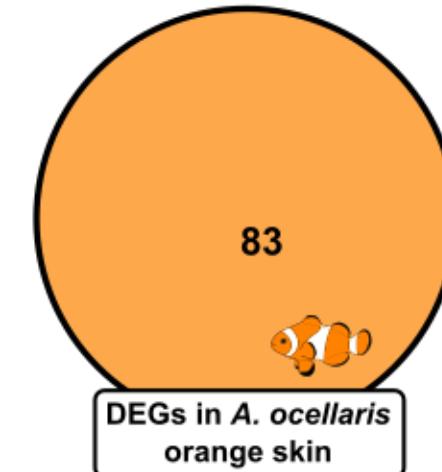
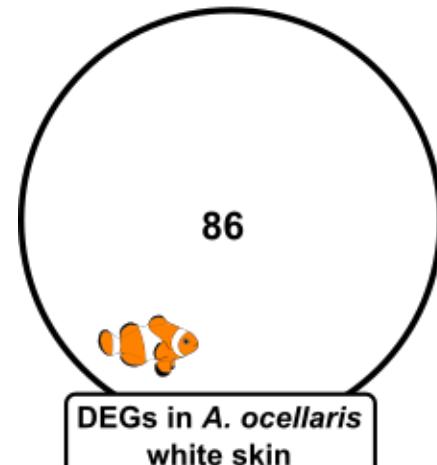
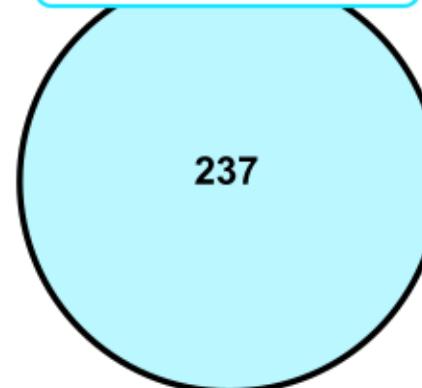
Fitzpatrick (2012) *FEMS Microbiol Lett*

Xie *et al.* (2008) *BMC Evol Biol*

La peau blanche a une "identité d'iridophores"

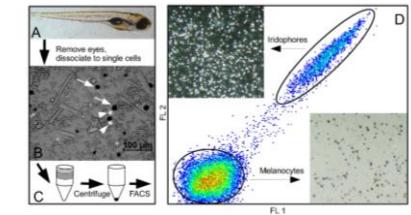
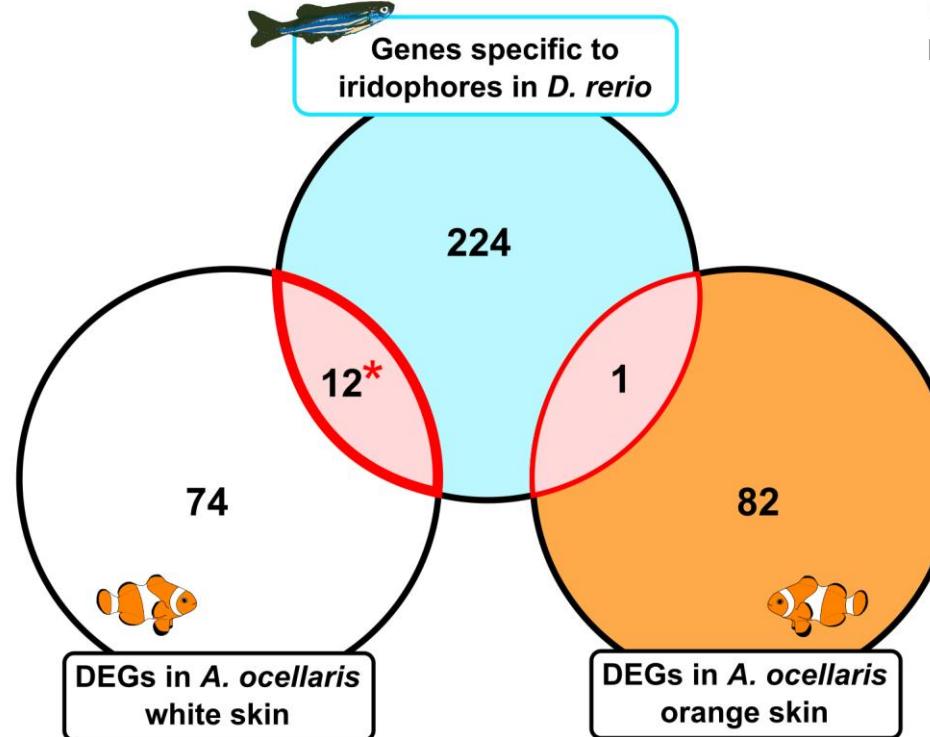


Genes specific to
iridophores in *D. rerio*



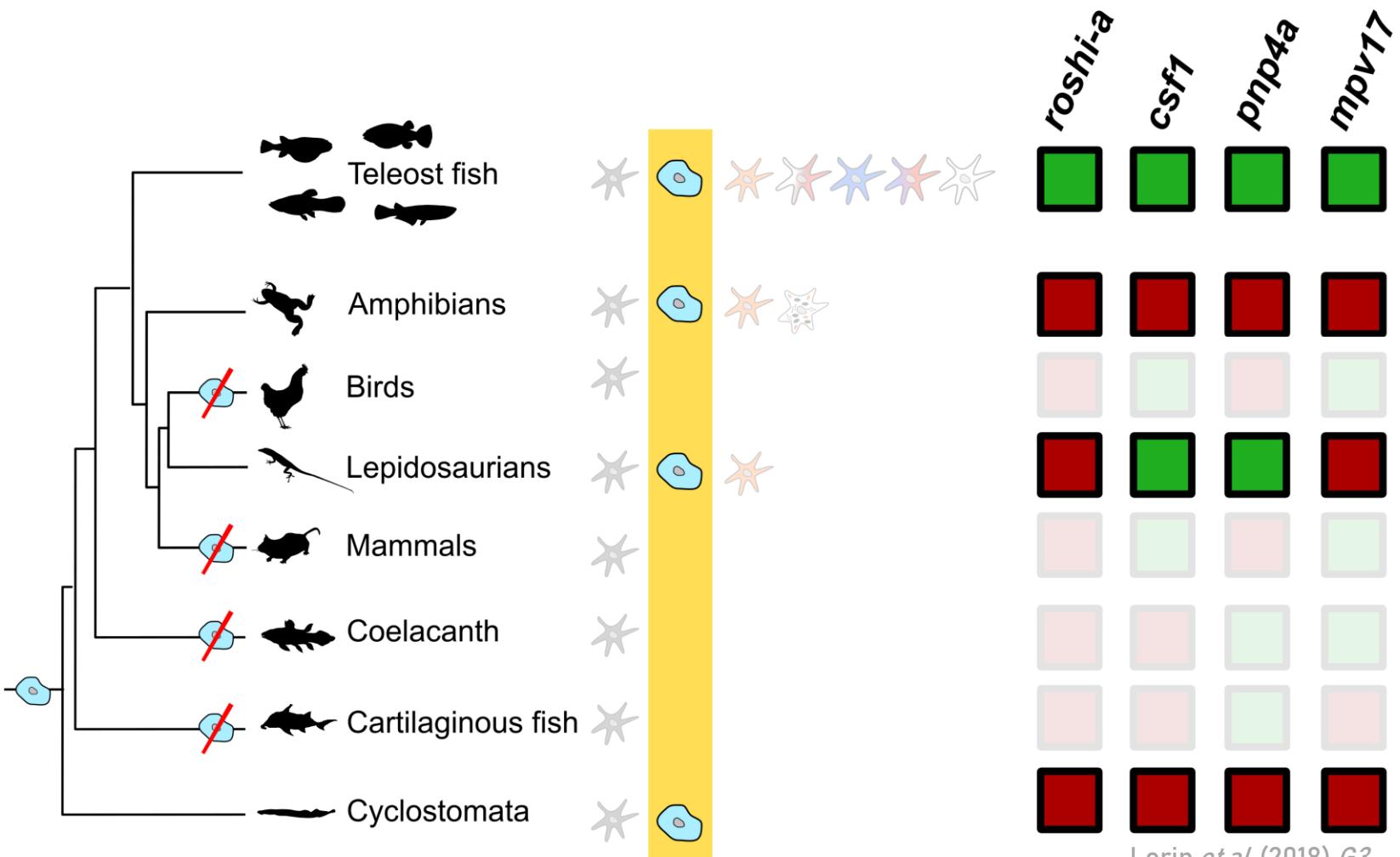
Higdon et al. (2013) Plos One

La peau blanche a une "identité d'iridophores"



Higdon et al. (2013) Plos One

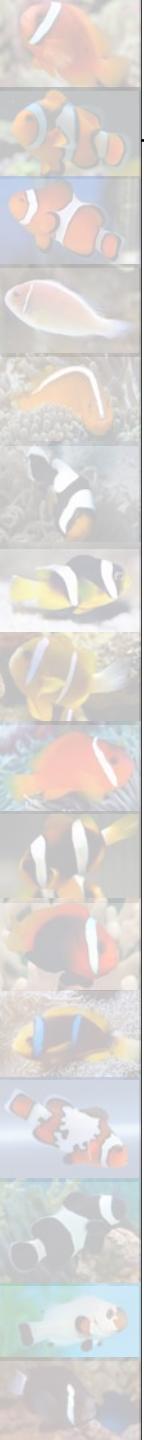
Roshi et d'autres gènes invitent à envisager l'évolution des iridophores chez les Vertébrés sous un nouvel angle

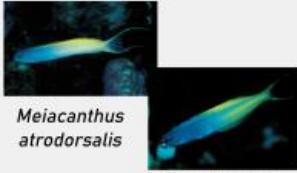


Lorin et al. (2018) G3

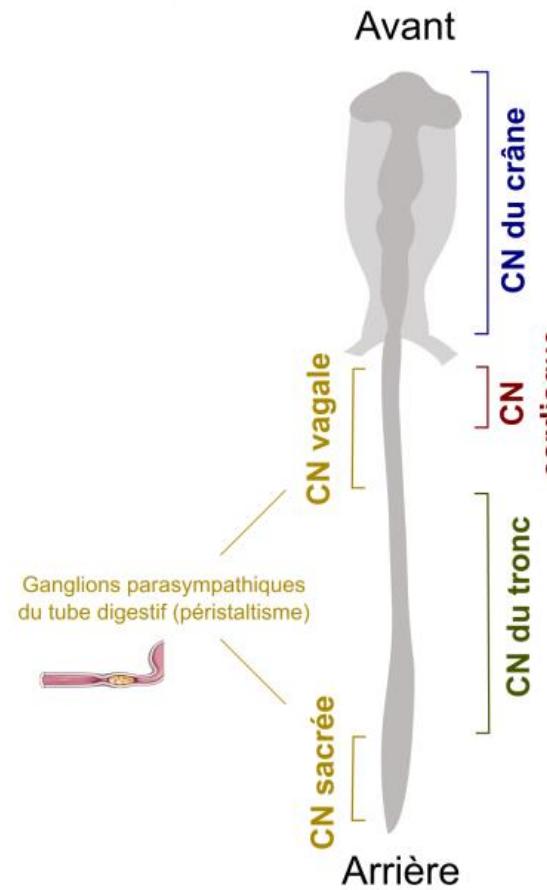
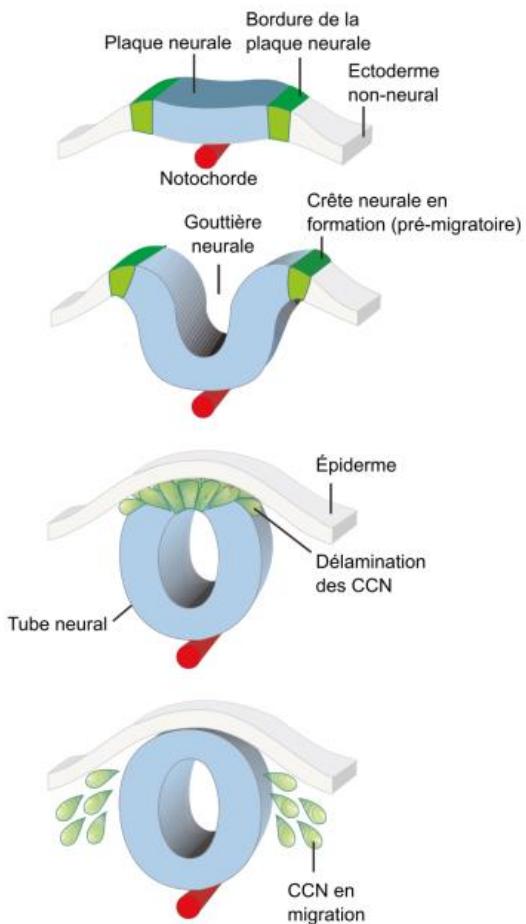
Wallace et la "coloration animale"

Une classification revisitée sur l'exemple des poissons coralliens



CAMOUFLAGE ("Protective colors")		COULEURS D'AVERTISSEMENT ("Warning colors")	COULEURS DE COMMUNICATION INTRA- OU INTERSPECIFIQUE ("Typical colors")
Cryptisme		Organismes naturellement protégés	Communication intraspécifique (hors sélection sexuelle)
Assortiment à l'arrière-plan		Aposématisme	Compétition intrasexuelle
Spécialisé	Généraliste	 <i>Pterois volitans</i> (Nelsen et al. 2014)	 <i>Chaetodon lunula</i> (Hamilton et al. 1971)
 <i>Hippocampus bargibanti</i> (Randall et al. 2005)	 <i>Antennarius commerson</i> (Randall et al. 2005)	Mimétisme müllerien	Signaux de regroupement
Countershading	Mascarade	 <i>Meiacanthus atrodorsalis</i>	 <i>Myripristis murdjan</i> (McRobert et al. 1998)
 <i>Chaetodon lunula</i> (Hamilton et al. 1971)	 <i>Juvénile de Platax orbicularis</i> (Randall et al. 2005)	 <i>Plagiotremus laudandus</i> (Randall et al. 2005)	Communication interspécifique
Coloration trompeuse	COULEURS SEXUELLES ("Sexual colors")	Organismes non-protégés	Confusion de prédateurs
 <i>Dascyllus aruanus</i> (Phillips et al. 2017)	Dimorphisme sexuel	Mimétisme batésien	 <i>Halichoeres brownfieldi</i> (Lönnstedt et al. 2013)
Transparence	 Femelle (en haut) et mâle (en bas) de Poisson-perroquet	 <i>Meiacanthus nigrolineatus</i> (peu comestible, à gauche) et <i>Ecsenius gravieri</i> (inoffensif) (Randall et al. 2005)	
Larve d' <i>Acanthurus triostegus</i> (Holzer, Besson et al. 2017)			

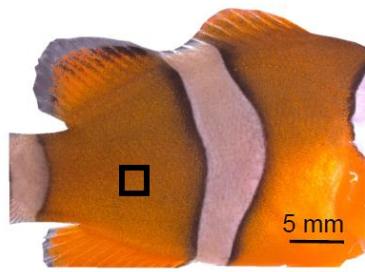
Les cellules pigmentaires proviennent de la crête neurale



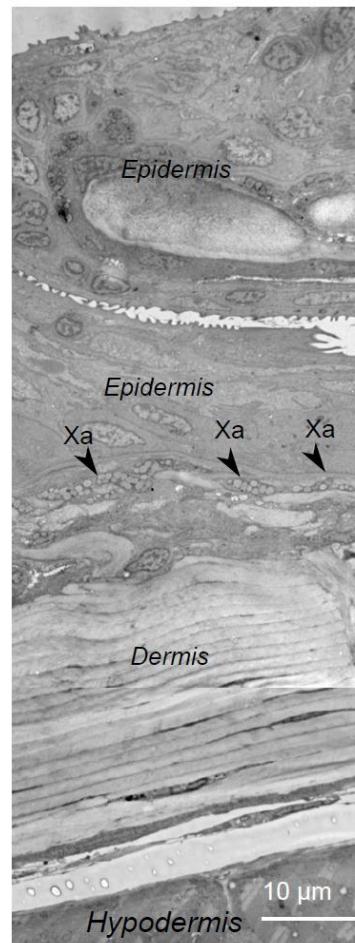
- Neurones et glie des ganglions crâniens
- Os et cartilage de l'avant de la tête
- Tissu conjonctif de la tête
- + mélanocytes odontoblastes + os de la mâchoire et de l'oreille interne + conjonctif de la thyroïde, du thymus...
- Conjonctif des grosses artères + mélanocytes + cartilage des arcs pharyngiaux/branchiaux
- Glande médullo-surrénale
- Système nerveux périphérique (cellules de Schwann, ganglions spinaux)
- Mélanocytes chez les Mammifères, autres cellules pigmentaires chez d'autres Vertébrés

Peau orange en microscopie

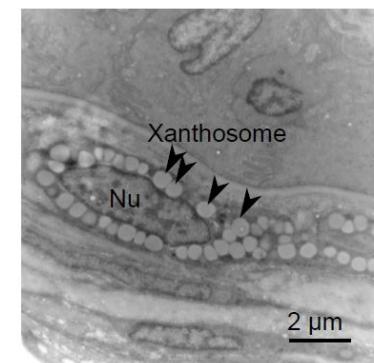
A.



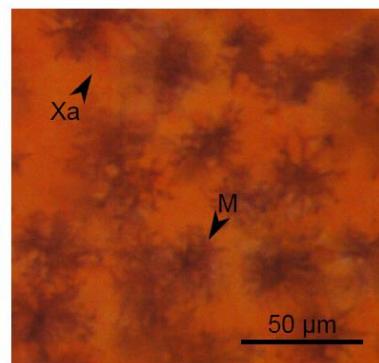
C.



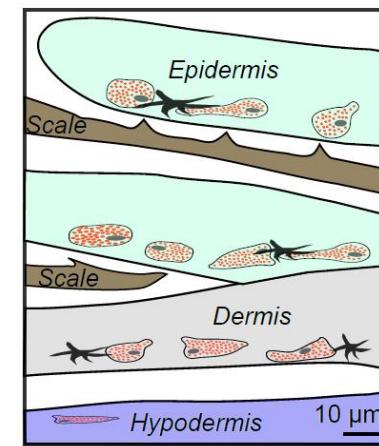
D.



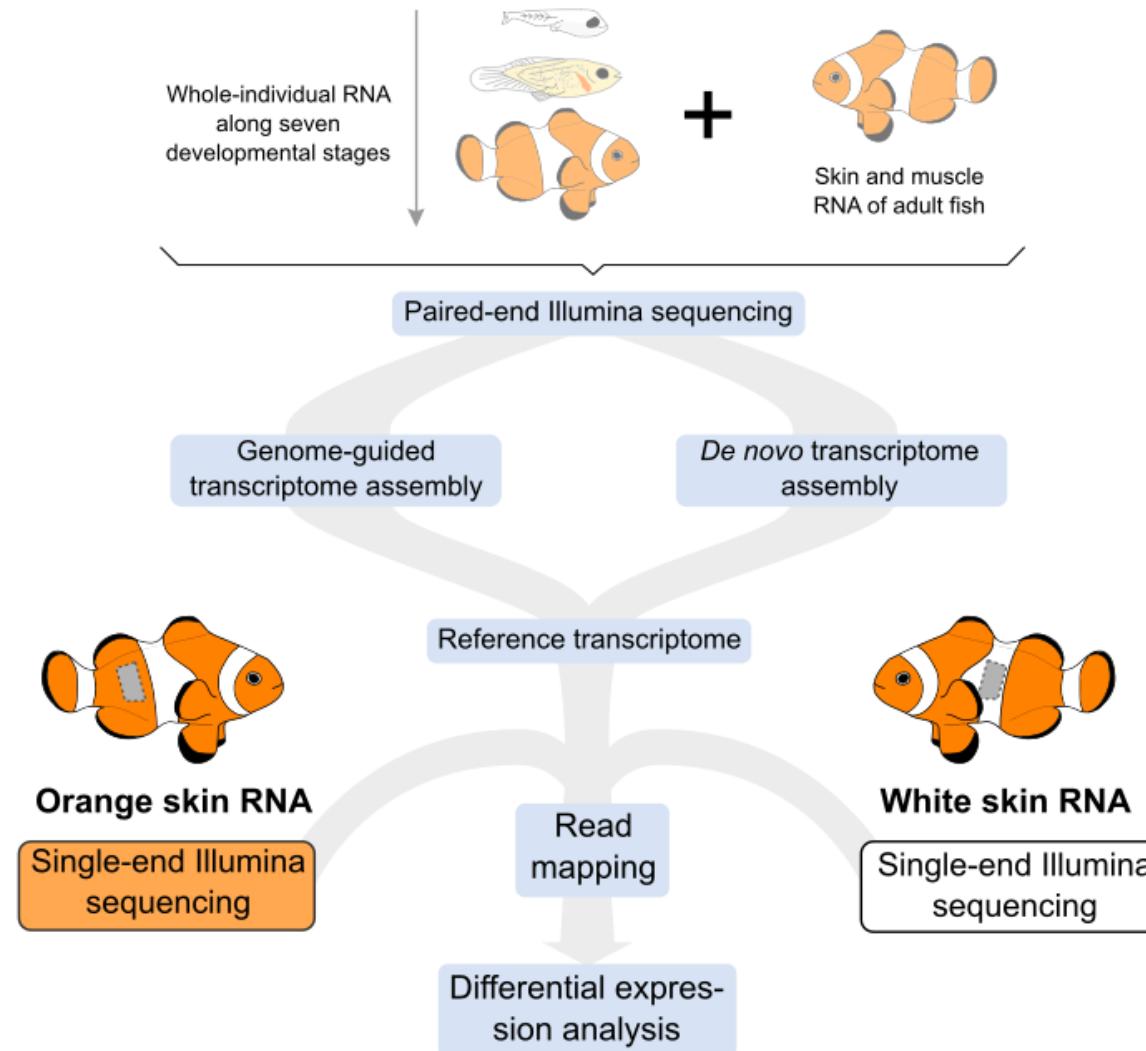
B.



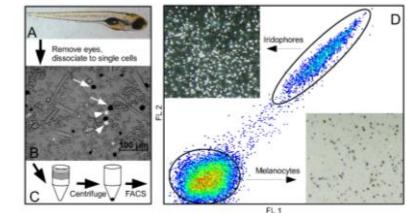
E.



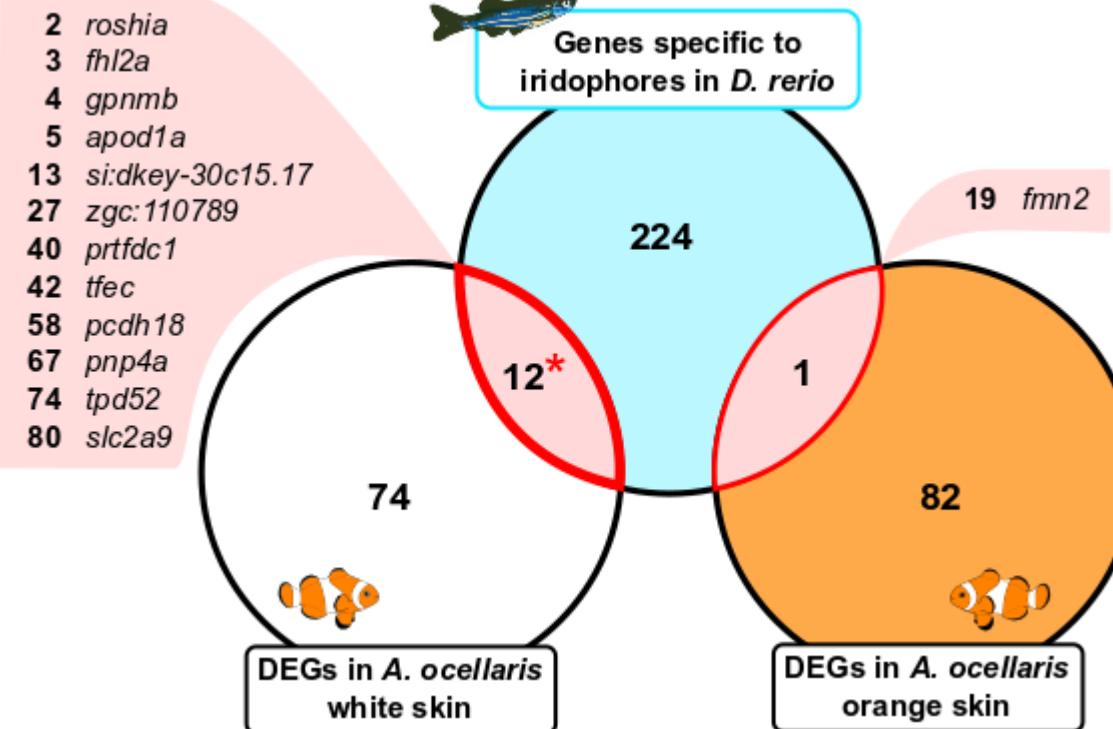
Pipeline utilisé pour l'analyse des différences d'expression



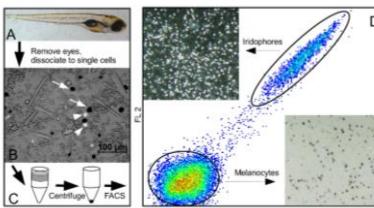
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Higdon et al. (2013) Plos One

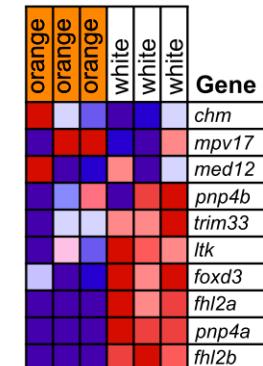
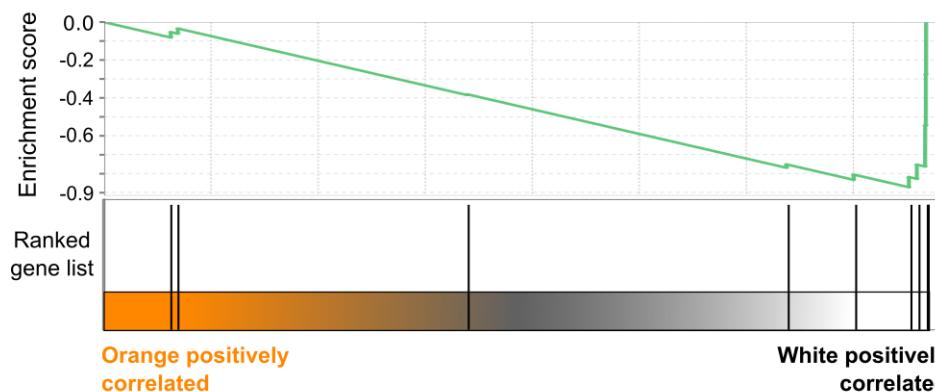
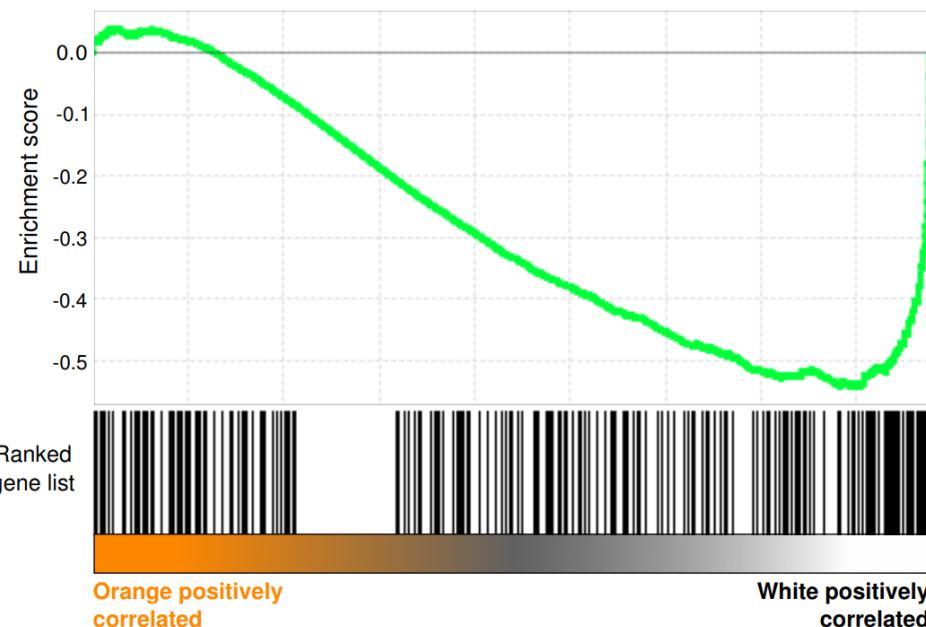


La peau blanche a une "identité d'iridophores"



Higdon et al. (2013) Plos One

Enrichment plot for **iridophore** markers - Higdon et al. (2013)



Megalocytivirus (Iridoviridae)

