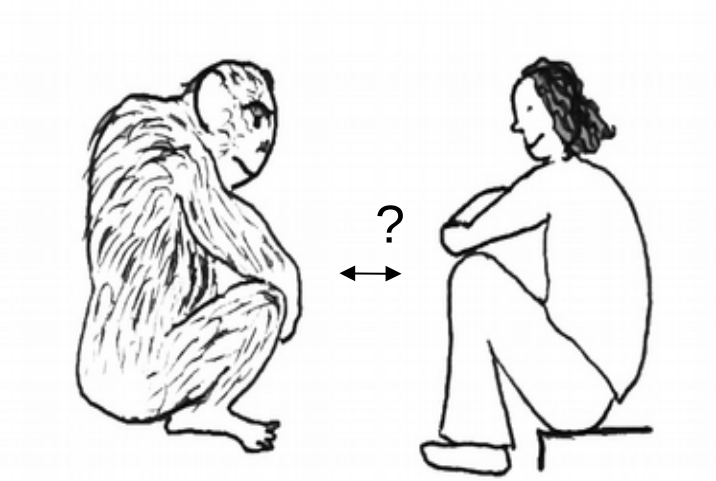
Développement et évolution des caractères morphologiques

Virginie Courtier-Orgogozo
Institut Jacques Monod, Paris

What makes us different?

between individuals

between species



Where do we come from?

What are the mutations responsible for phenotypic differences?

Genomic approach

identifies rapidly-evolving genomic regions, new genes, deleted genes

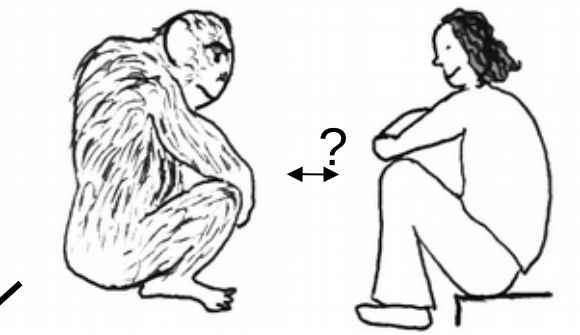
?

Genomes

CCTCCTCCATACCCAAATGGATGGTACGGCATTCTTGAATCATCAAAGCT
TAGAGCGGGGGAATCGAAGCATATATCATGTCTAGGCGAGCAACTTATAG
TGTTCCGTTCCCAAGCTGGTGAAGTTTATATCTTGGATGCGTATTGCCCG
CACTTGGGCGCTAATTTGAGTAAGGGAGGTCGAGTTATAGGAGATAATAT
TGAATGTCCCTTTCACCACTGGAGCTTTAGAGGCAGTGATGGCATGTGTA
CCAATATTCCCTACAGCAGCAATATACACTCATCTACAAAAACTAAAAAA
TGGACCTCCACCGAAGTGAATGGATTCATATTTCTTTGGTACAATGTCGA
AGAATCTGAAGTTCCGTGGAATATACCAAAATCAGTTGGTGTTGCAAAAA

CCTCCTCCATACCCAAATGGATGGTACGGCATTCT**C**GAATCATCAAAGCT
TAGAGCGGGGGAATCGAAGCATATATCATGTCTAGGCGAGCAACTTATAG
TGTTCCGTTCCCAAGCT**C**GTGAAGTTTATATCTTGGAT**T**CGTATTGCCCG
CACTTGGGCGCTAATTNGAGTAAGGGAGGTCGAGTTATAGGAGATAATAT
TGAATGTCCCTTTCACCACTGGAGCTTTAGAGGCAGTGATGGCATGTGTA
CCAATATTCCCTACAGCAGCAATATACACTCATCTACAAAAACTAAAAAA
TGGAC**T**TCCACC**T**AAGTGAATGGATTCATATTTCT**C**TGGTACAATGTCGA
AGAATCTGAAGTTCCGTGGAATATACCAAAATCAGTTGGTGTTGCAAAAA

Phenotypic differences

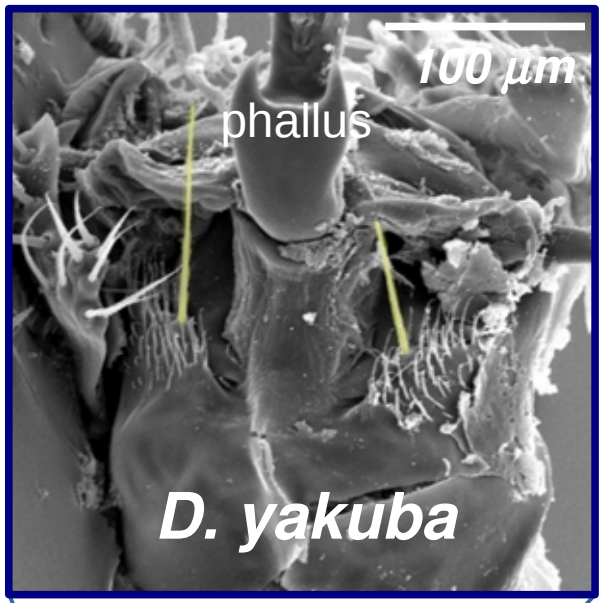


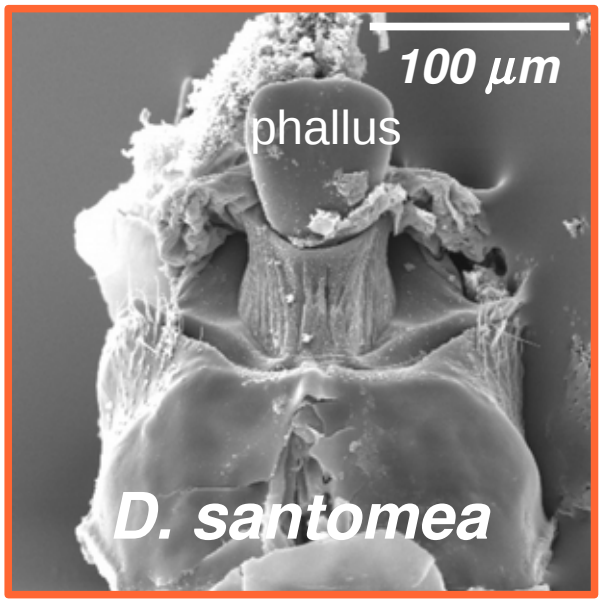
Phenotypic approach

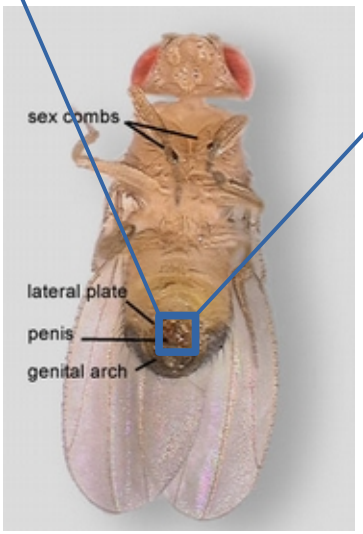
identifies the gene(s) and the mutation(s) responsible for a phenotypic change

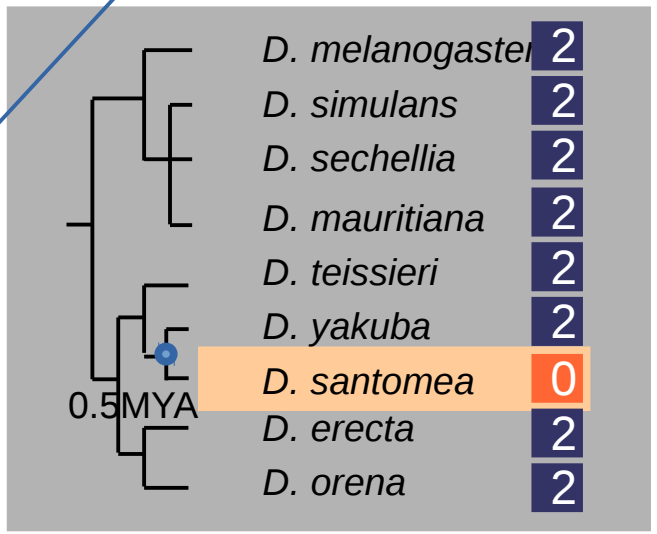
Evolutionary loss of bristles in *D. santomea*

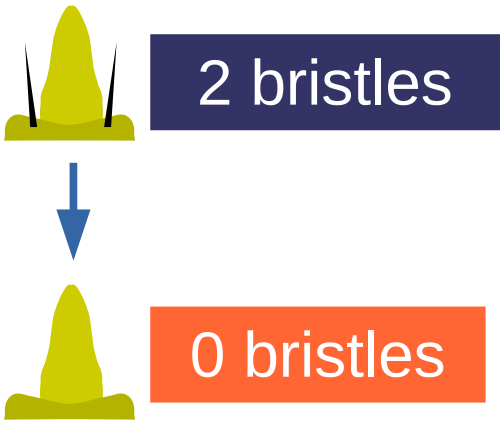
D. santomea has lost sex bristles



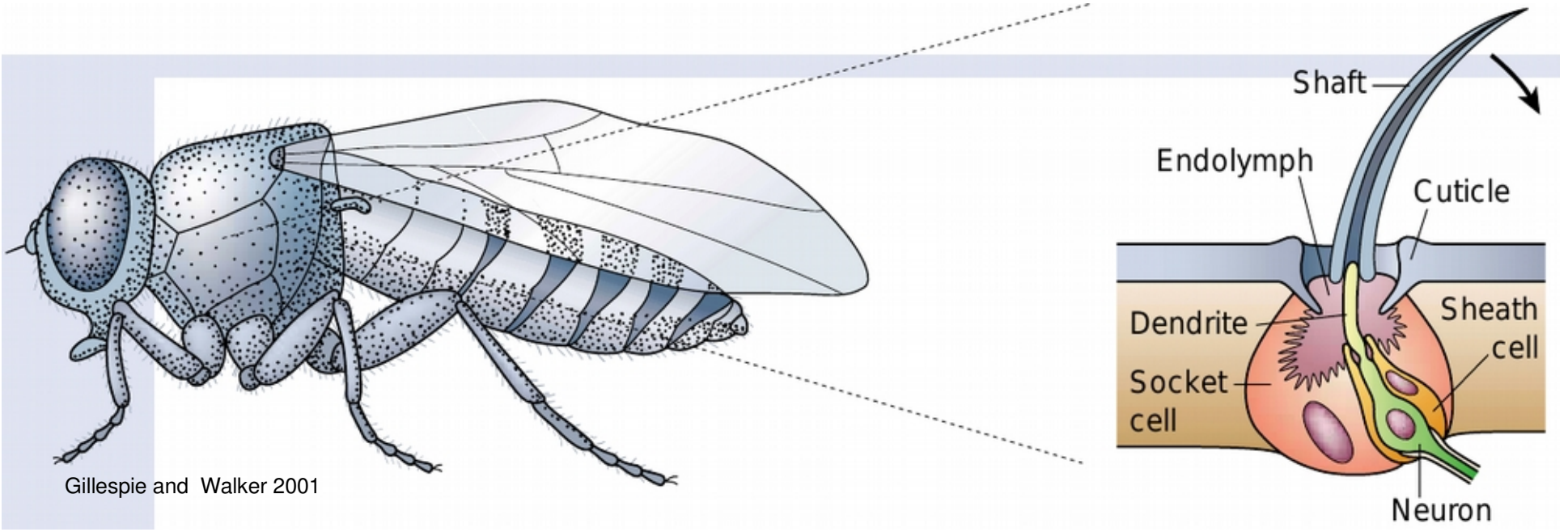




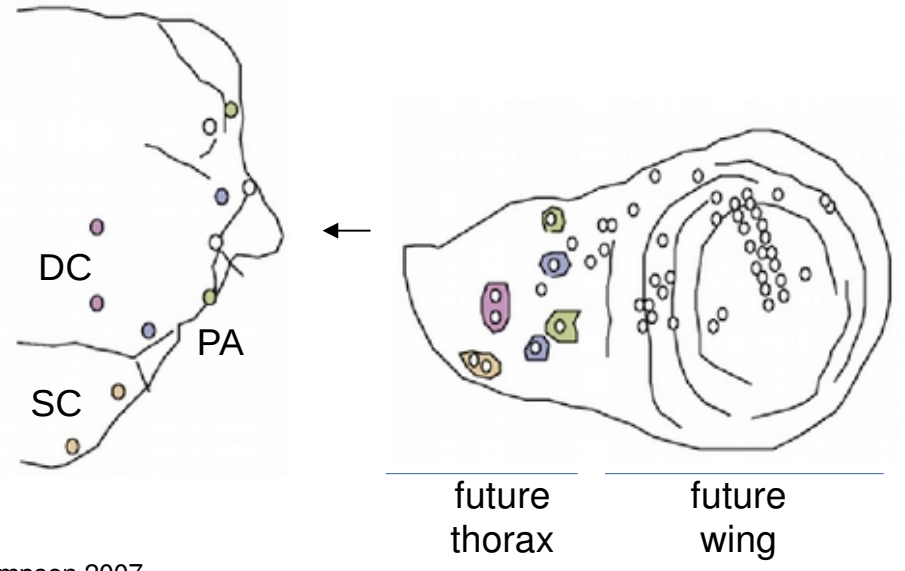




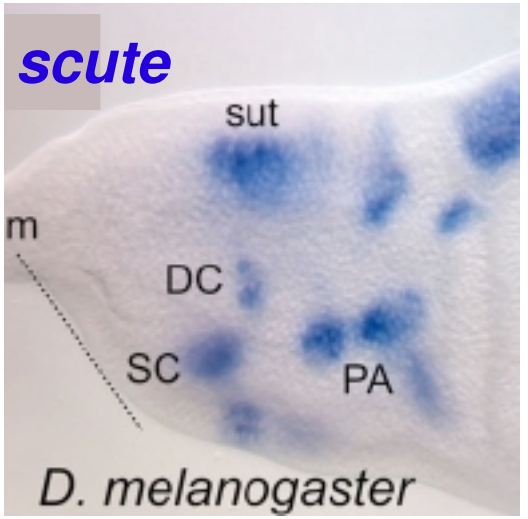
Bristle development



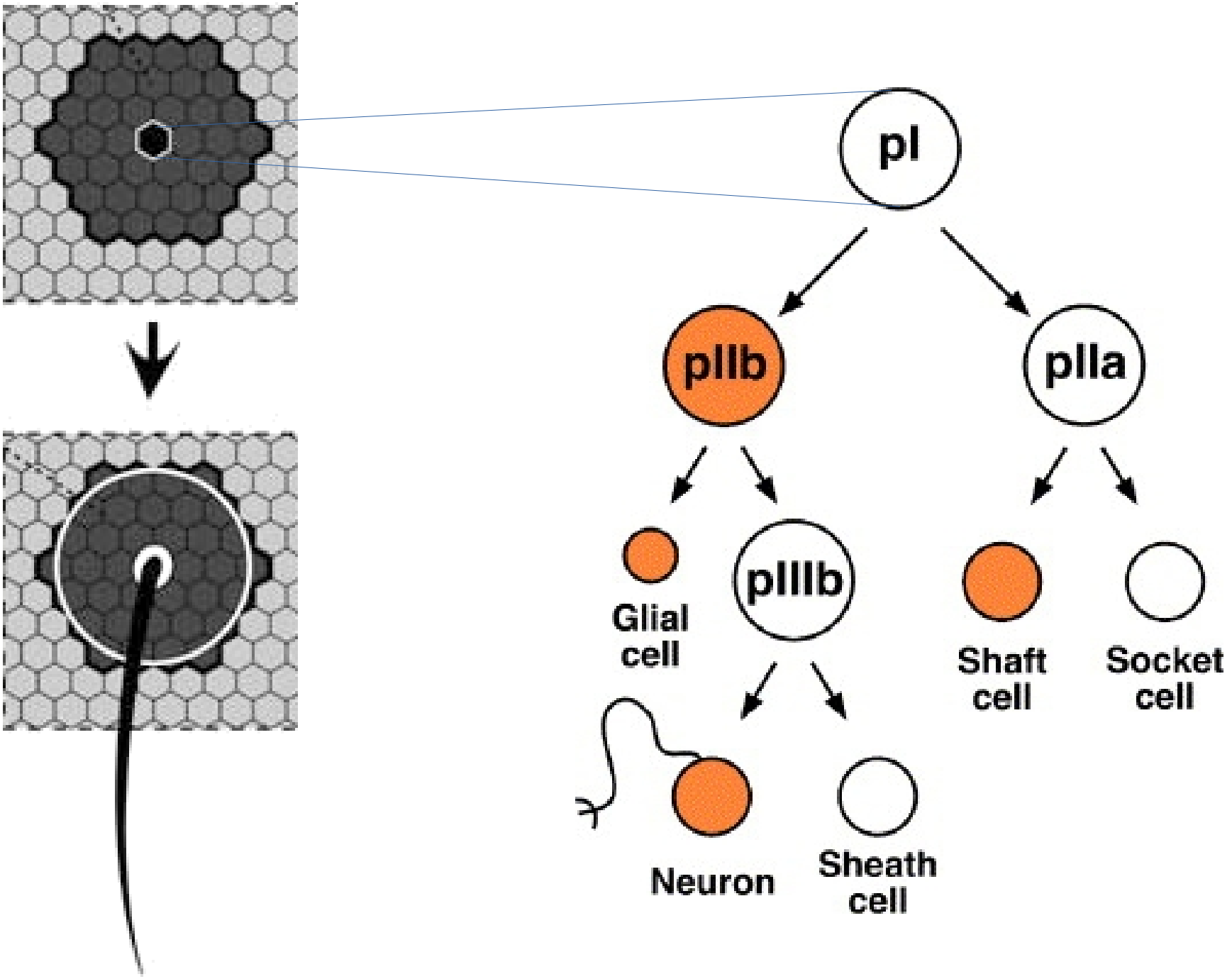
Gillespie and Walker 2001



Simpson 2007

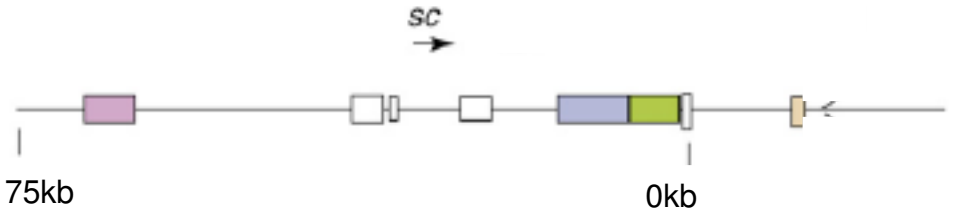


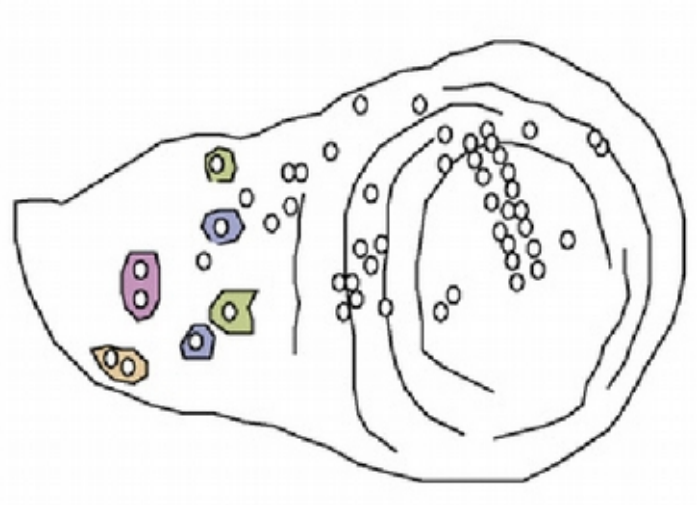
Marcellini 2006 - PloS Biology



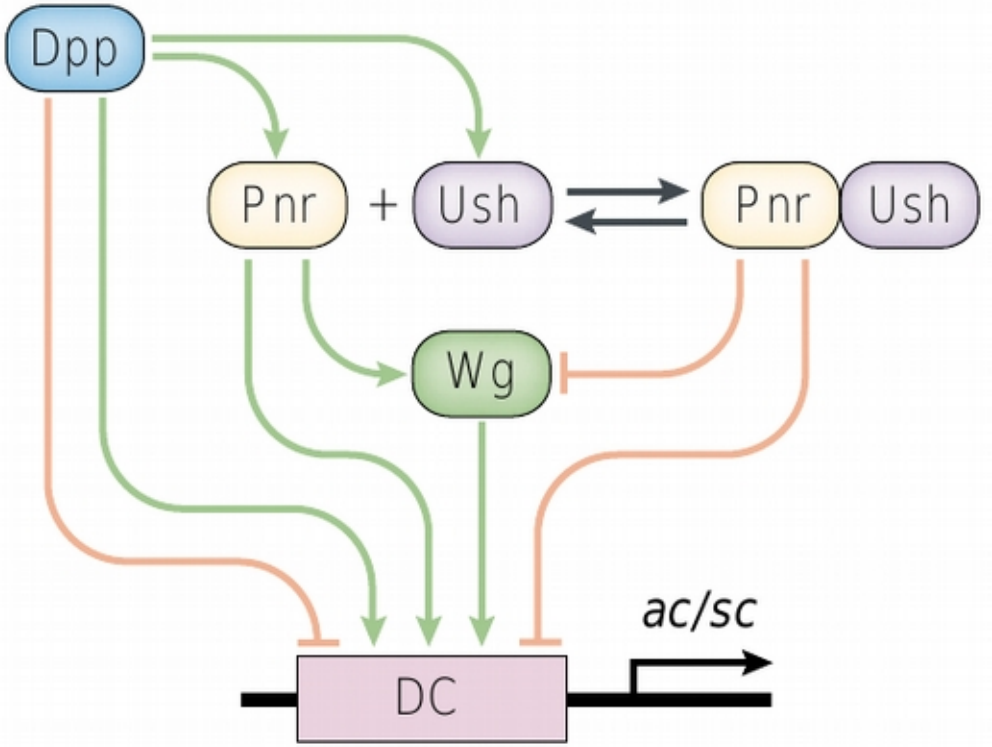
Lewis - Imaginal discs

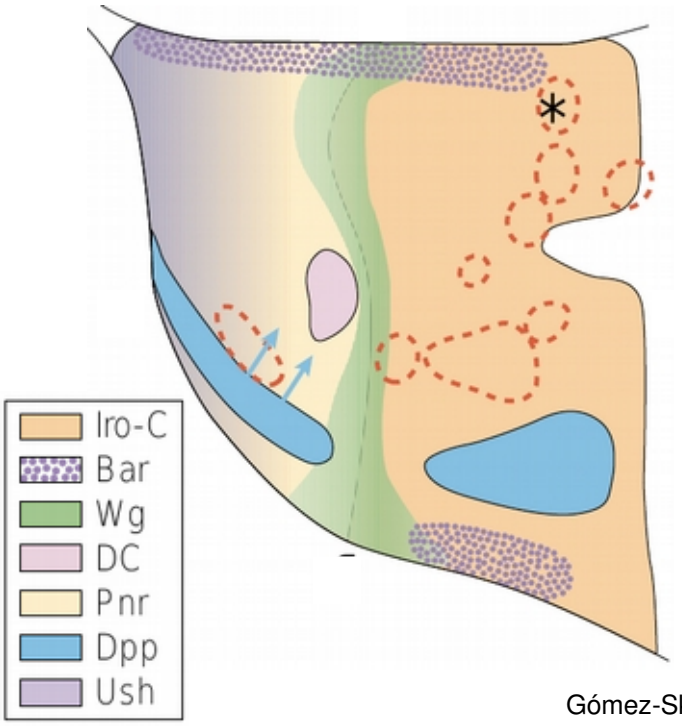
scute cis-regulatory elements are "master switches"





Simpson 2007

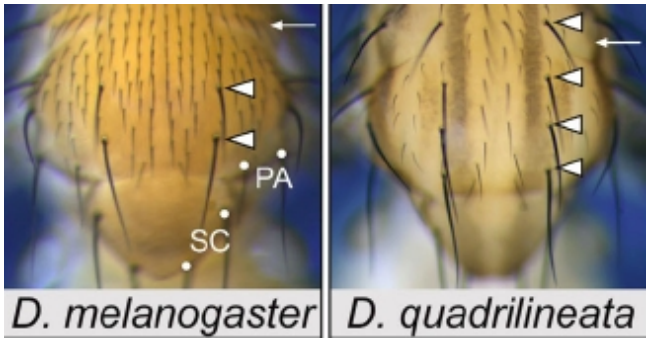


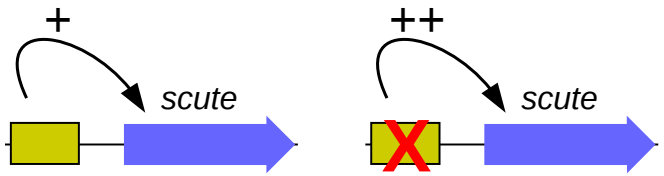


Gómez-Skarmeta 2003

Evolution of fly bristle pattern

Cis-regulatory element (CRE) in *scute*



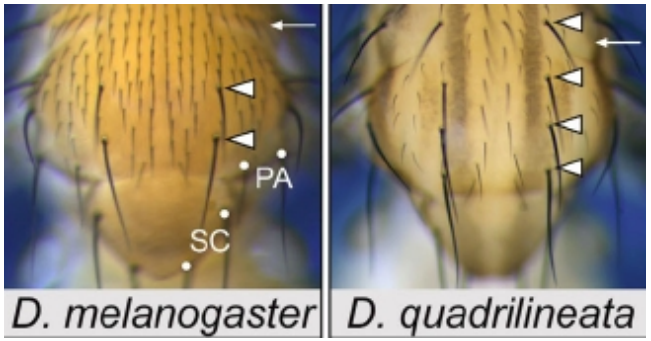


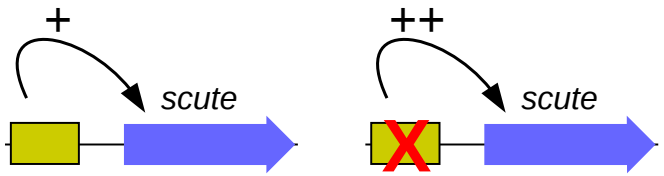
Marcelini and Simpson 2006 PloS Biology

Genetic evolution is predictable

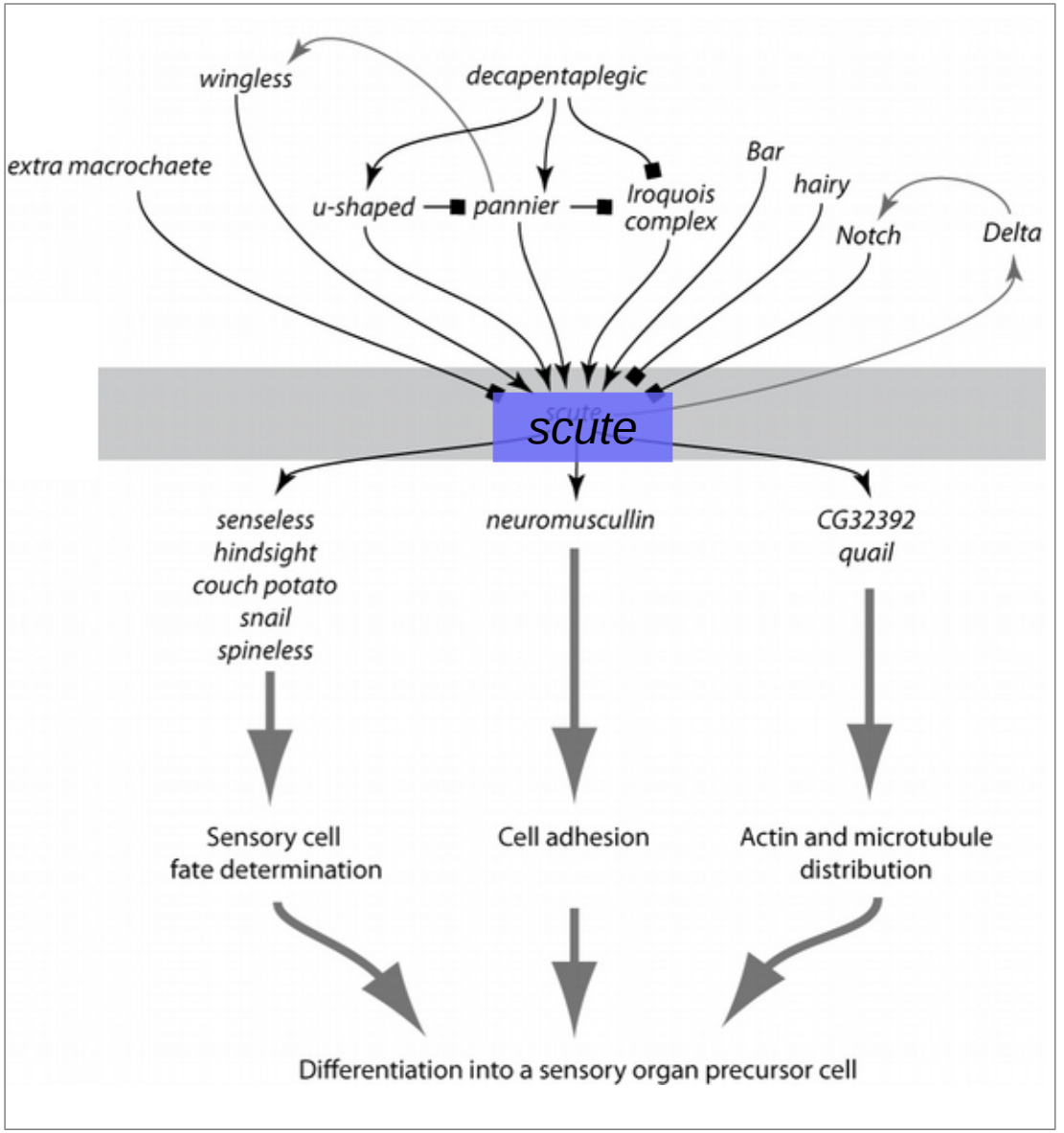
Evolution of fly bristle pattern

Cis-regulatory element (CRE) in *scute*



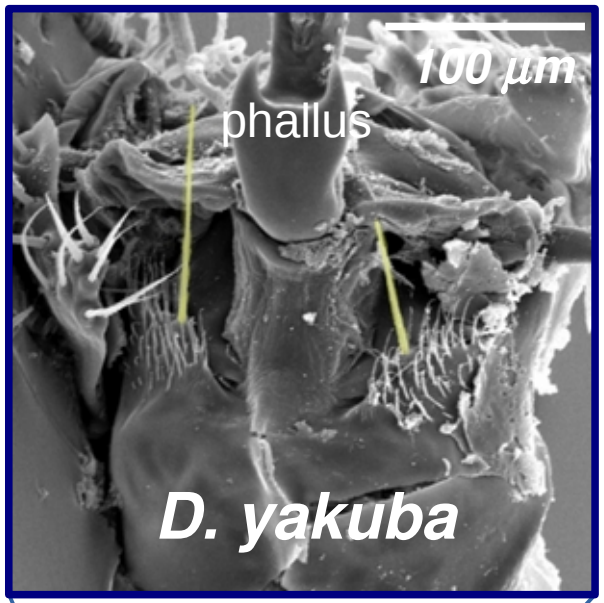


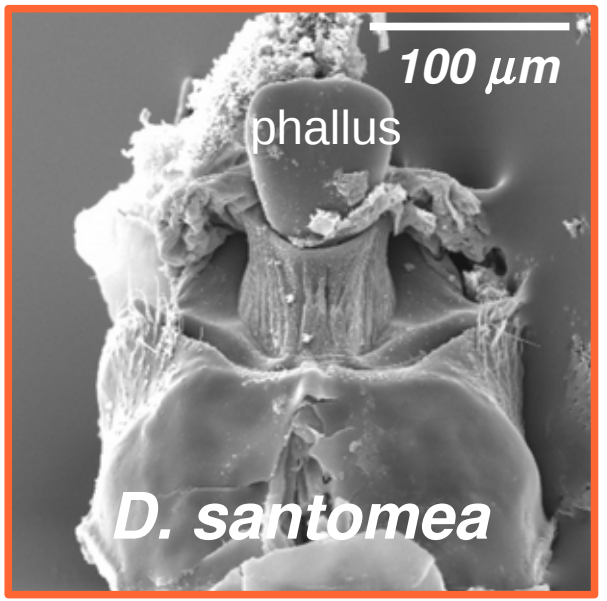
Marcelini and Simpson 2006 PloS Biology

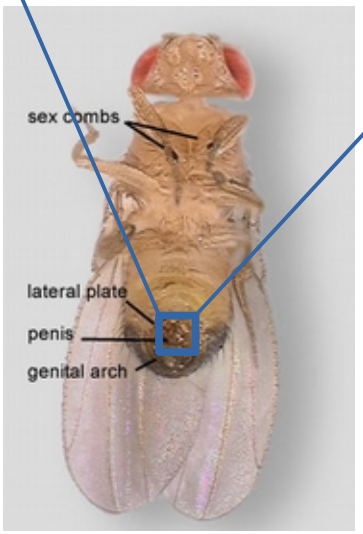


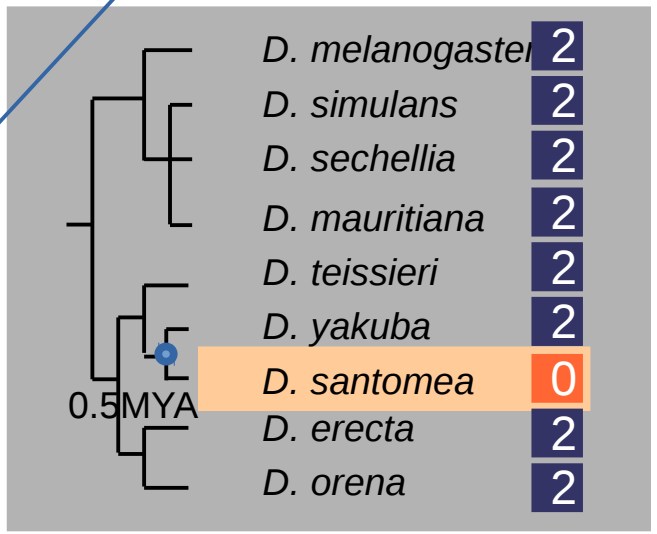
Stern and Orgogozo 2009 Science

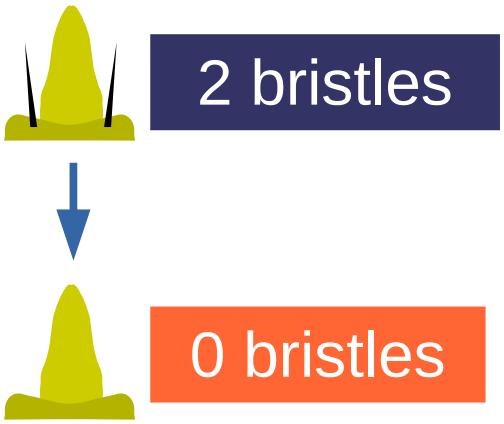
D. santomea has lost sex bristles



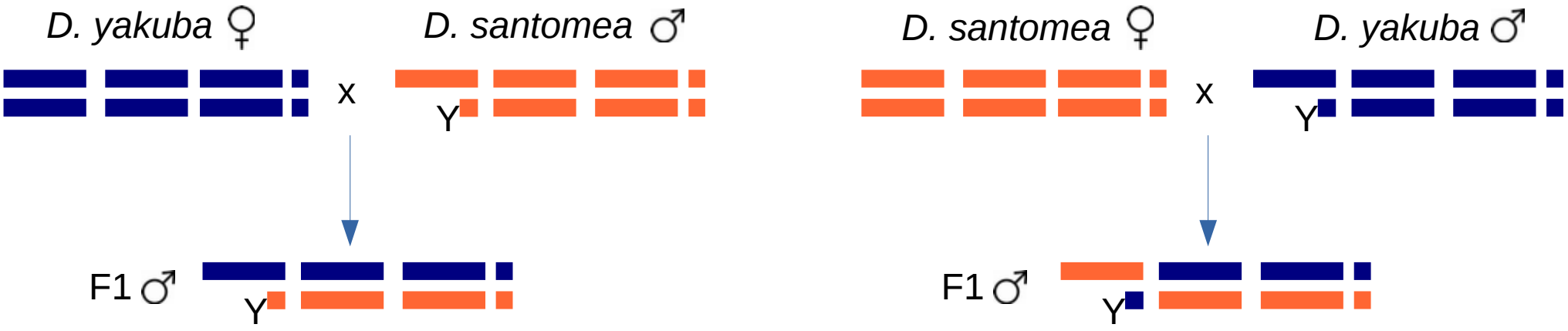




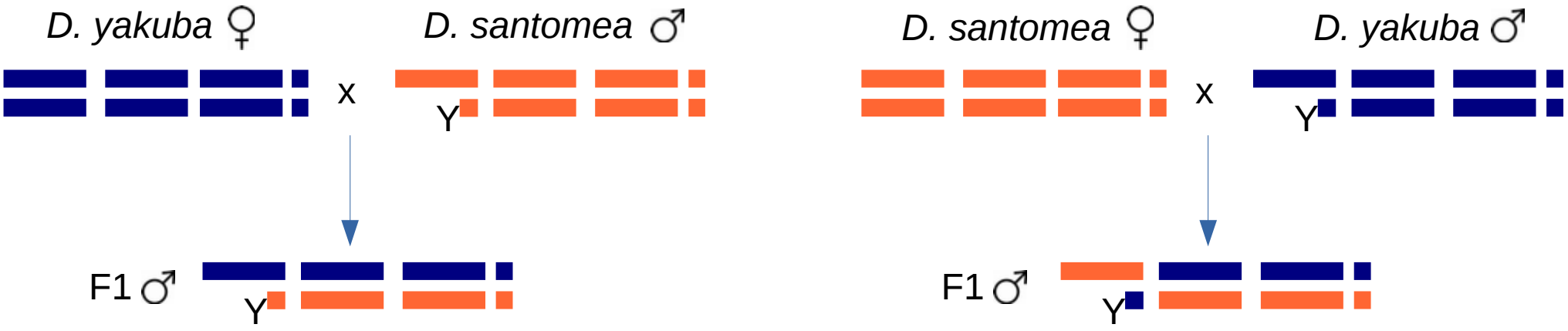




Is the causing mutation X-linked?

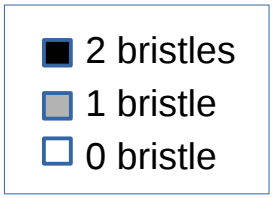


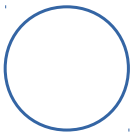
Is the causing mutation X-linked?



The causing mutation is X-linked

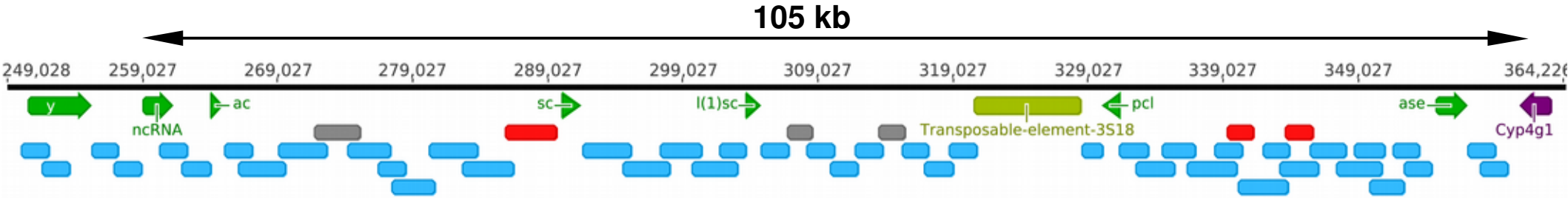
n = 35





n = 8

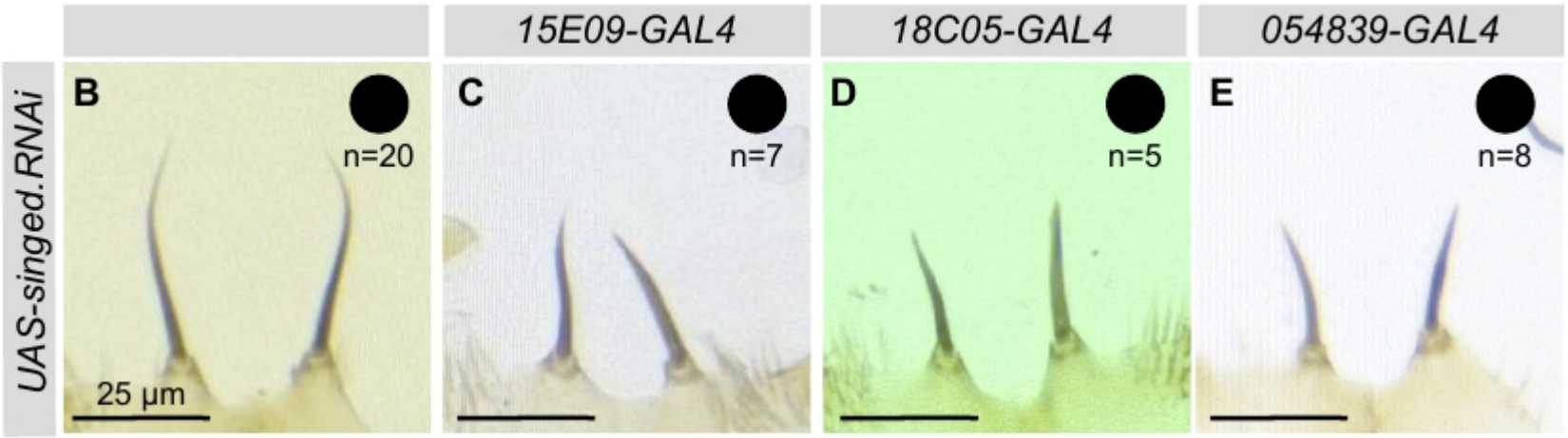
Screening a 100-kb region



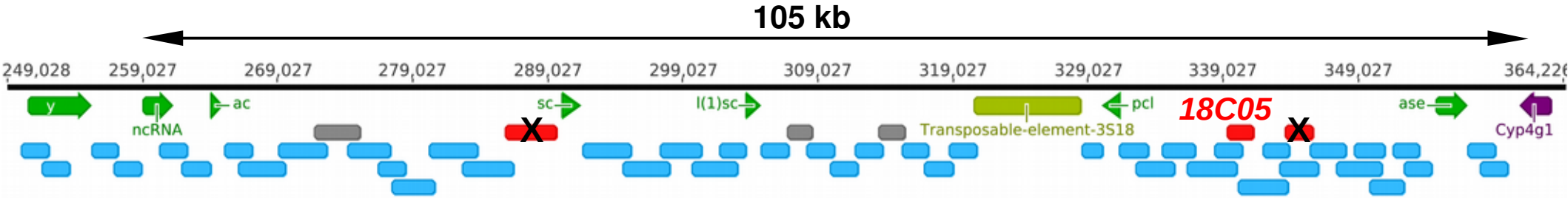
drives expression in developing genital bristles
drives no expression
not tested yet

screen of *D. melanogaster* *GAL4* lines

x *UAS-RNAi-singed , UAS-Dicer2*



18C05 drives expression independently of *scute*



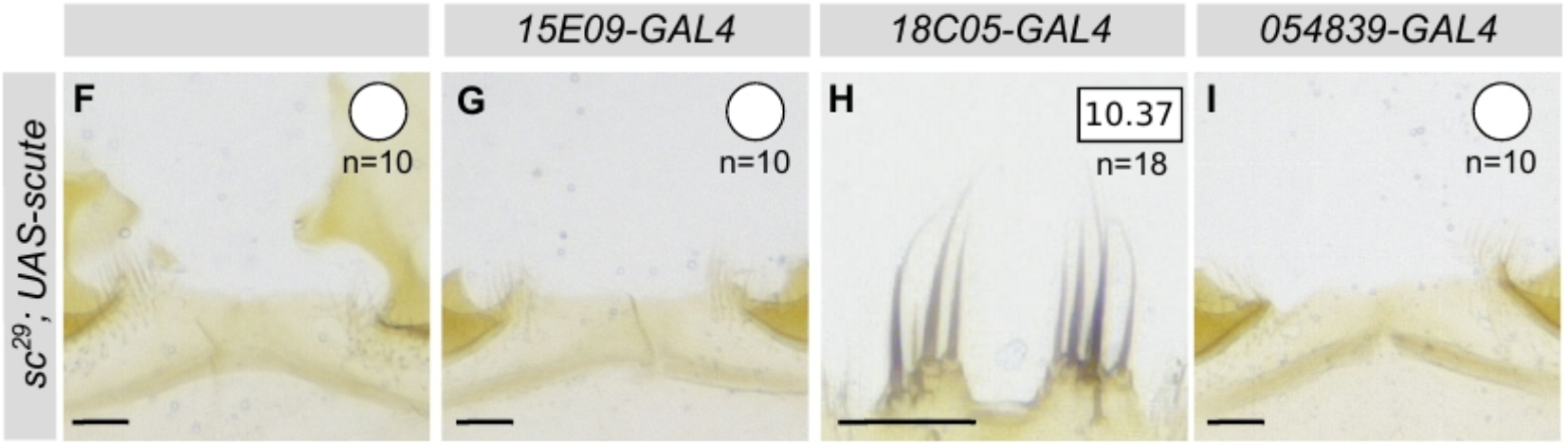
drives expression in developing genital bristles

drives no expression

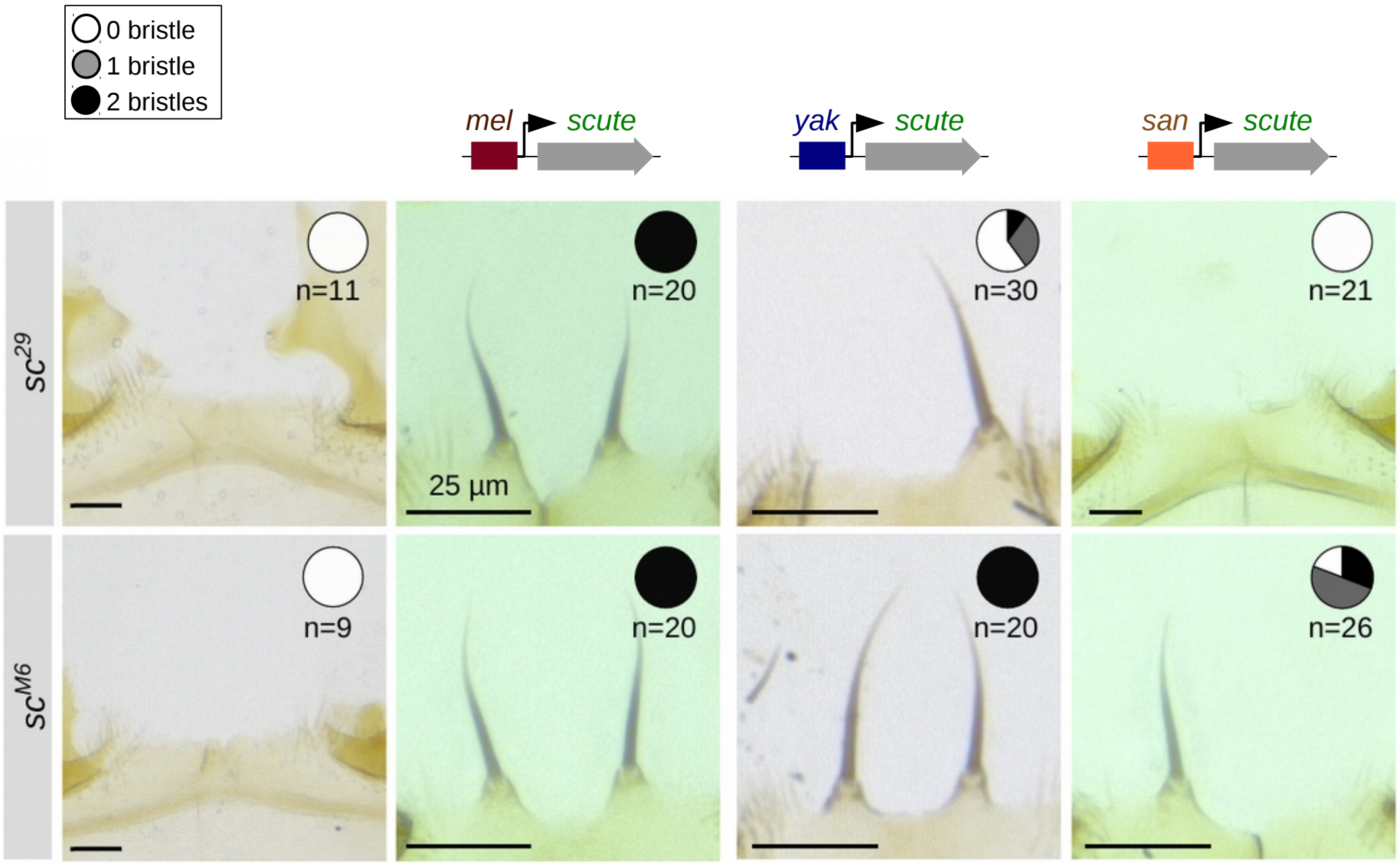
not tested yet

x

sc^{29} ; *UAS-scute*

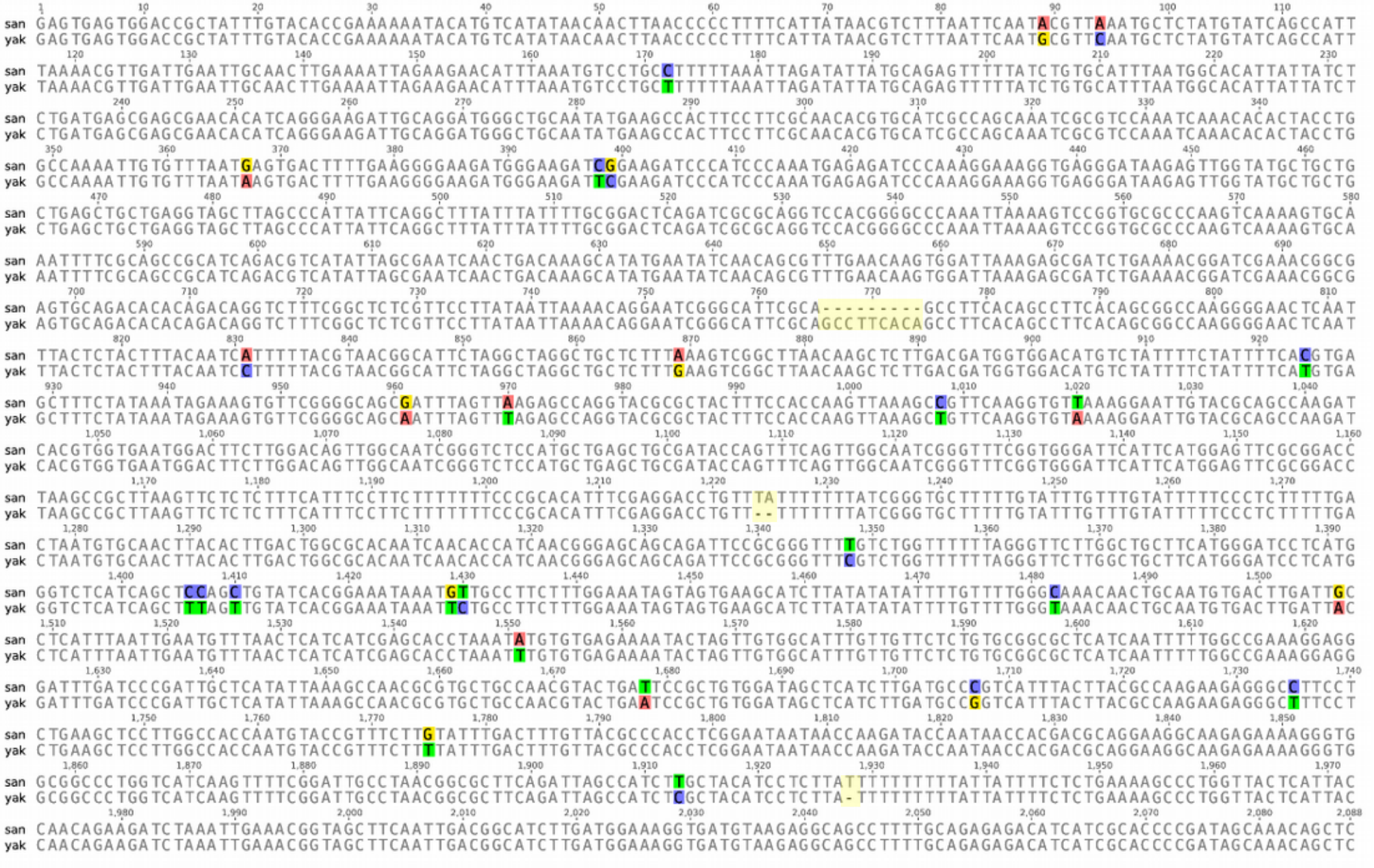


Mutation(s) in *18C05* cause loss of bristles

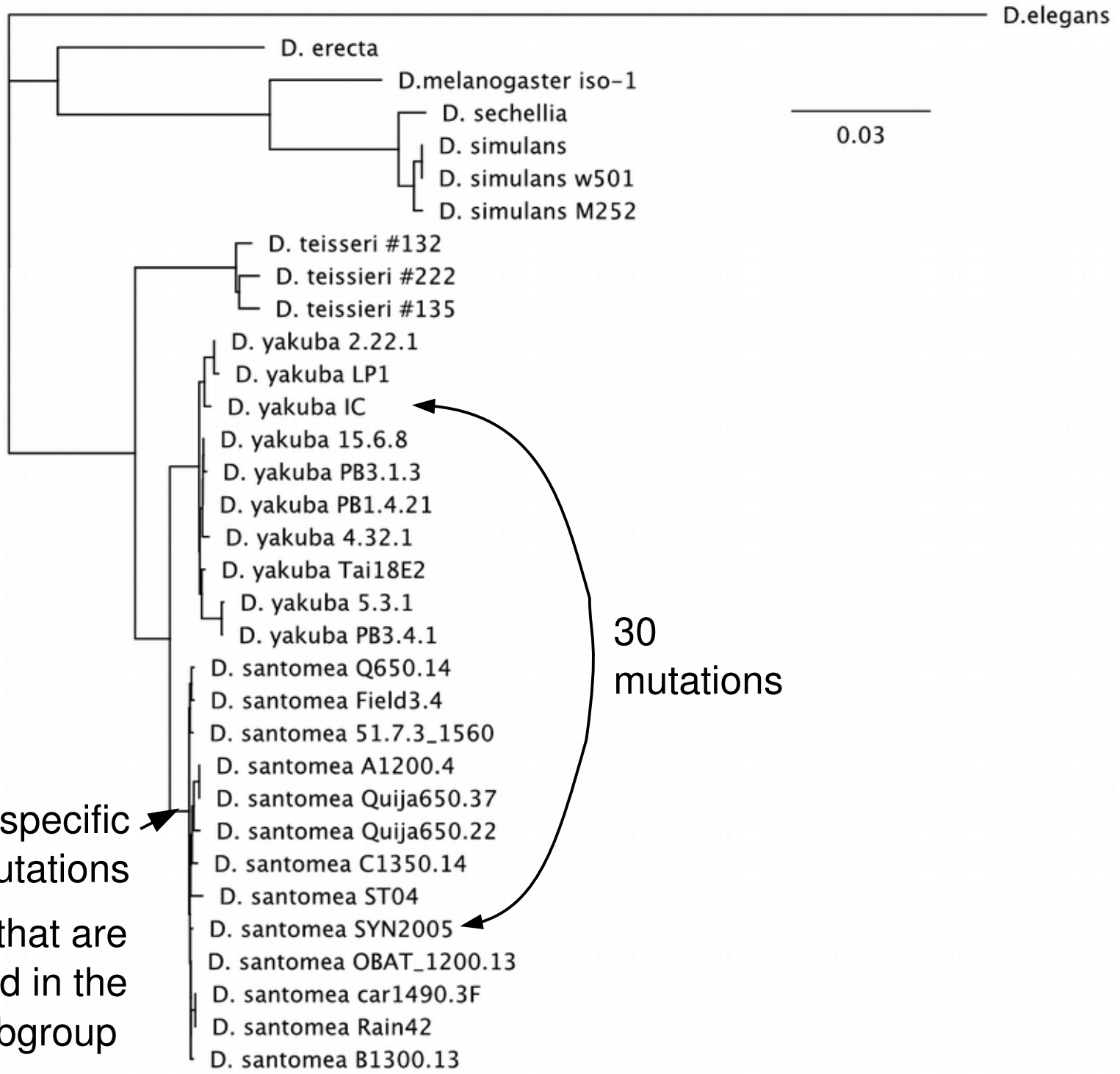


D. melanogaster transgenics

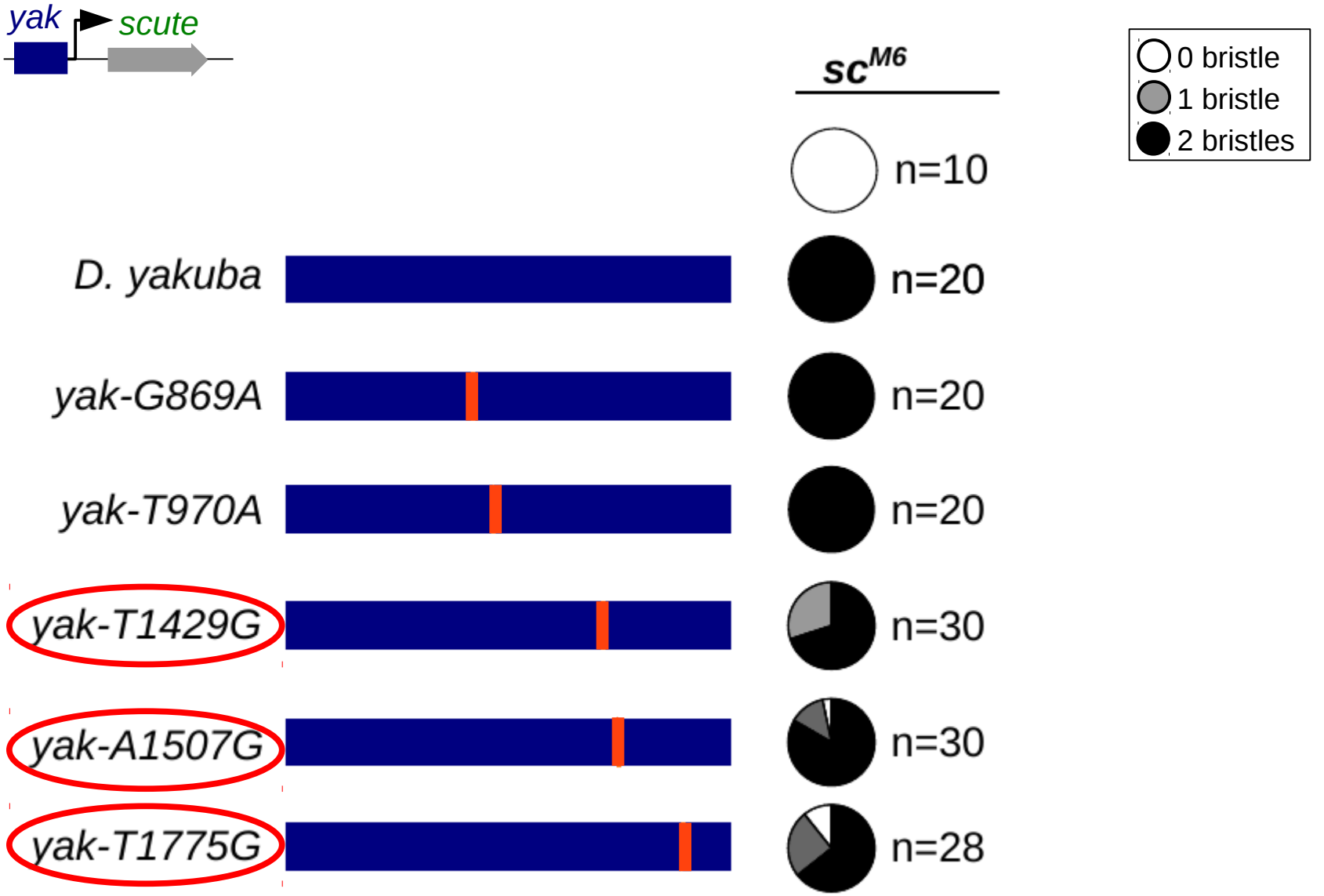
27 SNPs and 3 indels between *D. santomea* and *D. yakuba*



18C05 alignment



3 mutations affect genital bristle number



T1775G mutation disrupts an AbdB binding site

D. yakuba

1775

ACCGTTTCTTT**T**TATTTGACTT

TGGAAAAGAAA**A**ATAAACTGAA

0.91

T1775G

D. santomea

1775

ACCGTTTCTTG**G**TATTTGACTT

TGGCAAAGAAC**C**ATAAACTGAA

0.78

JASPAR
Binding Score

T1775G mutation disrupts an AbdB binding site

D. yakuba

1775

ACCGTTTCTTTTATTTGACTT

TGGAAAAGAAAATAAACTGAA

0.91

T1775G

D. santomea

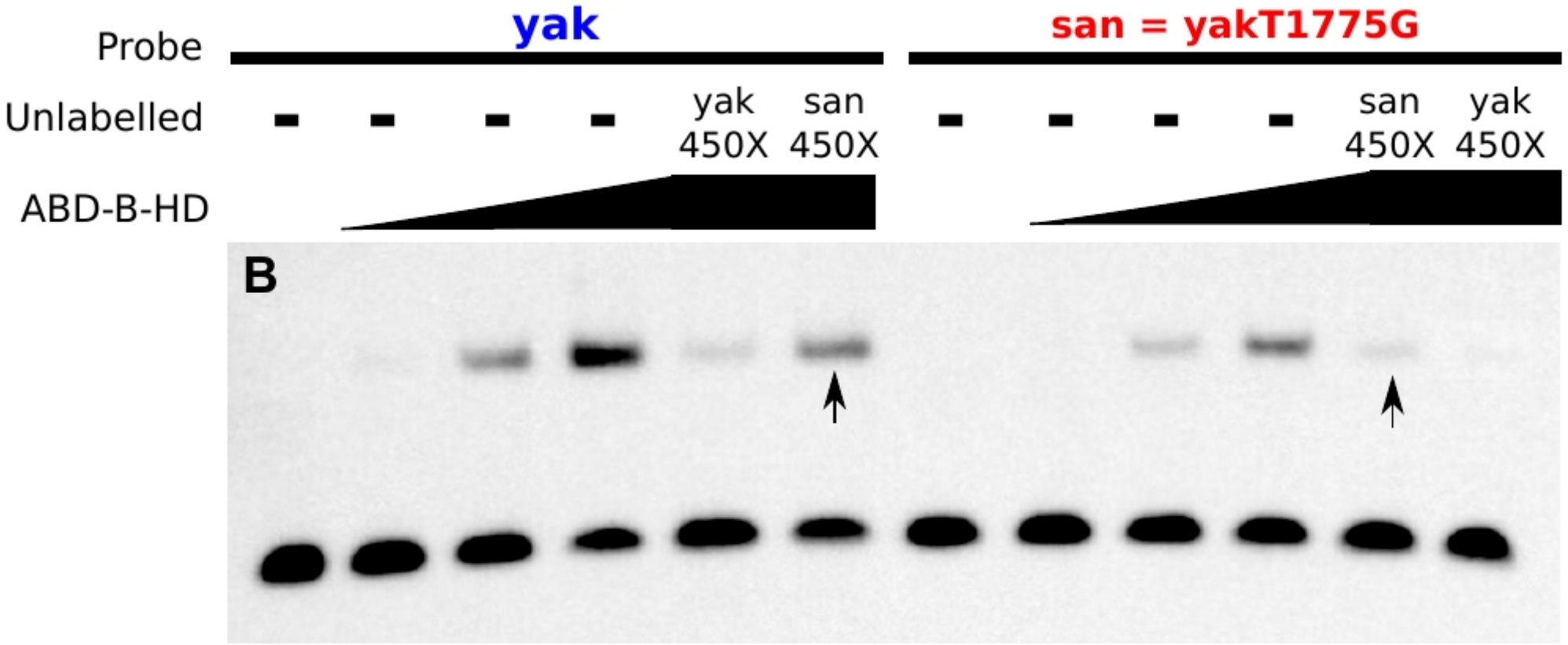
1775

ACCGTTTCTTGTATTTGACTT

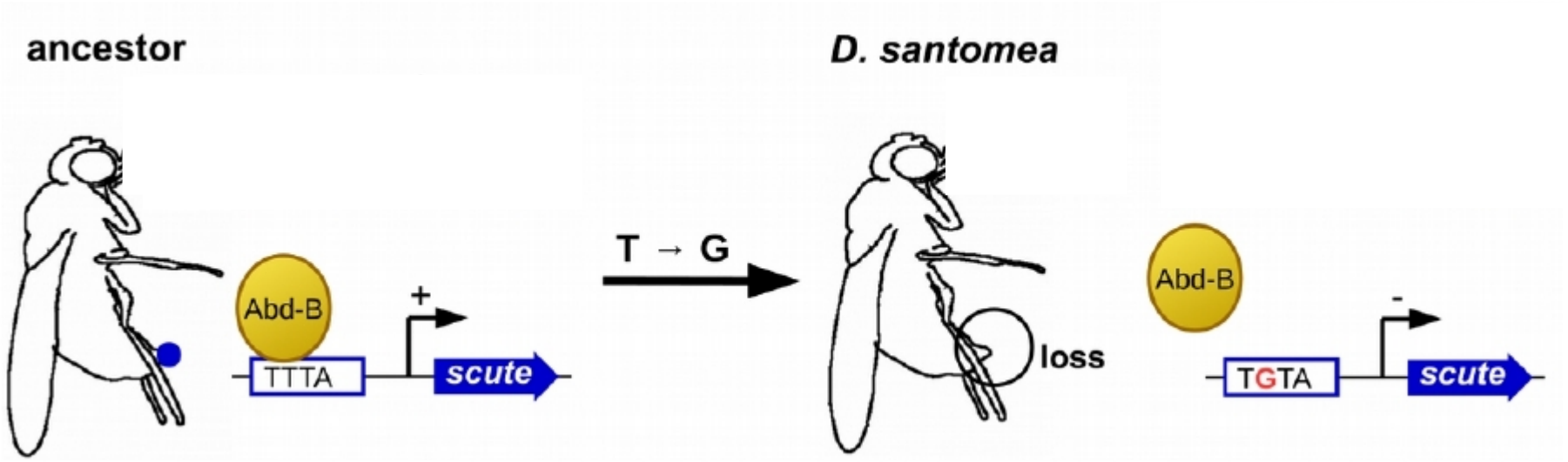
TGGCAAAGAACATAAACTGAA

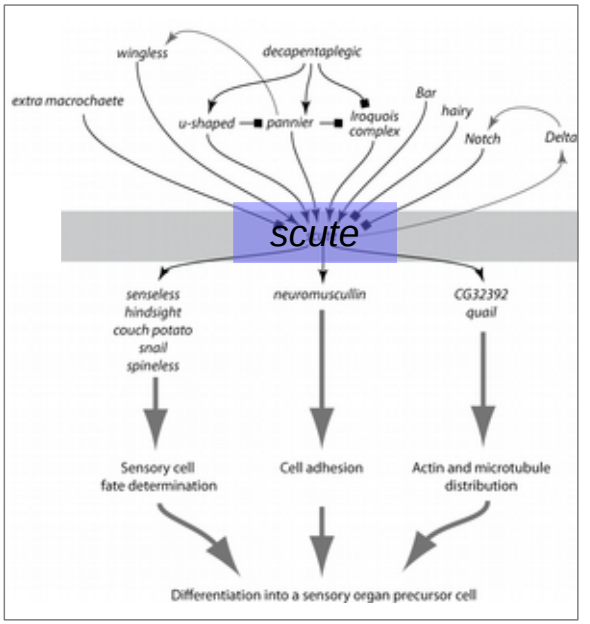
0.78

JASPAR Binding Score



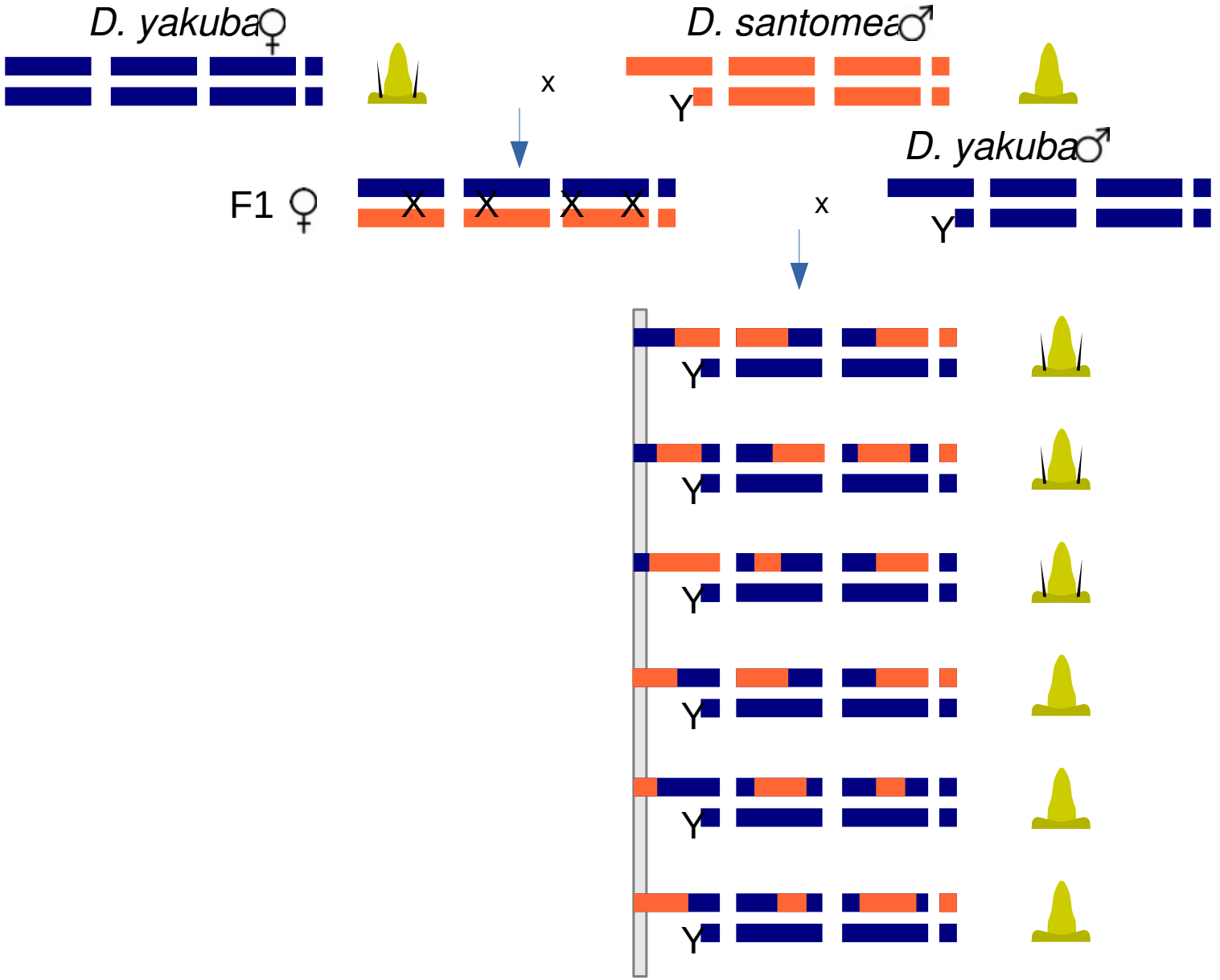
D. santomea lost genital bristles via 3 mutations in *scute*





QTL mapping

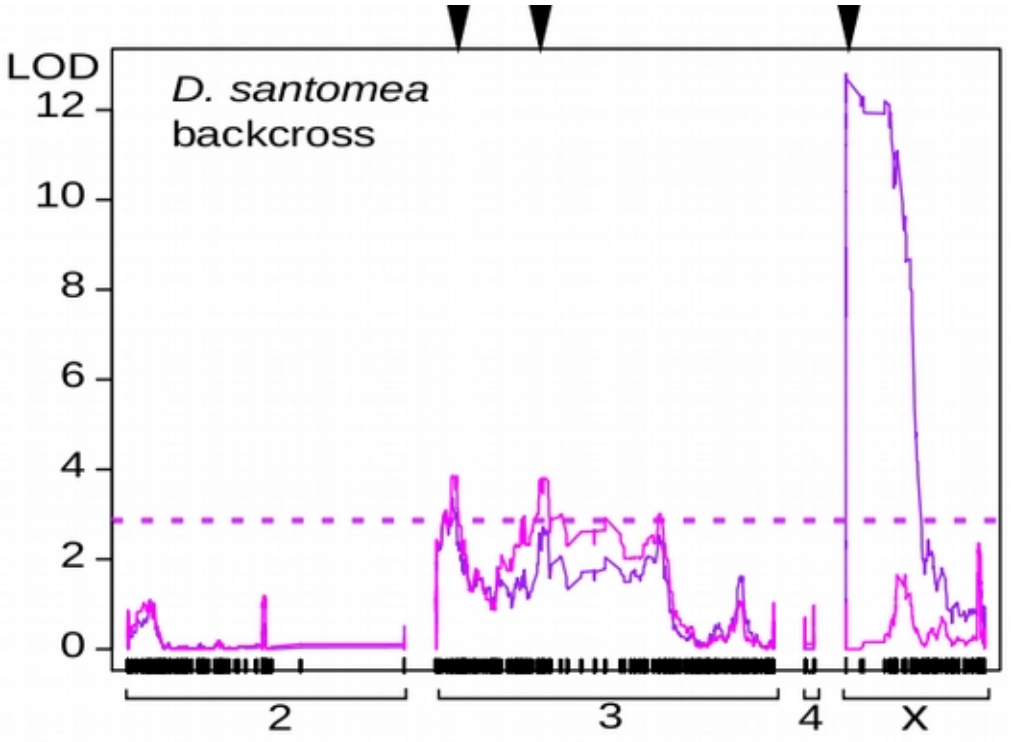
***D. yakuba* backcross**

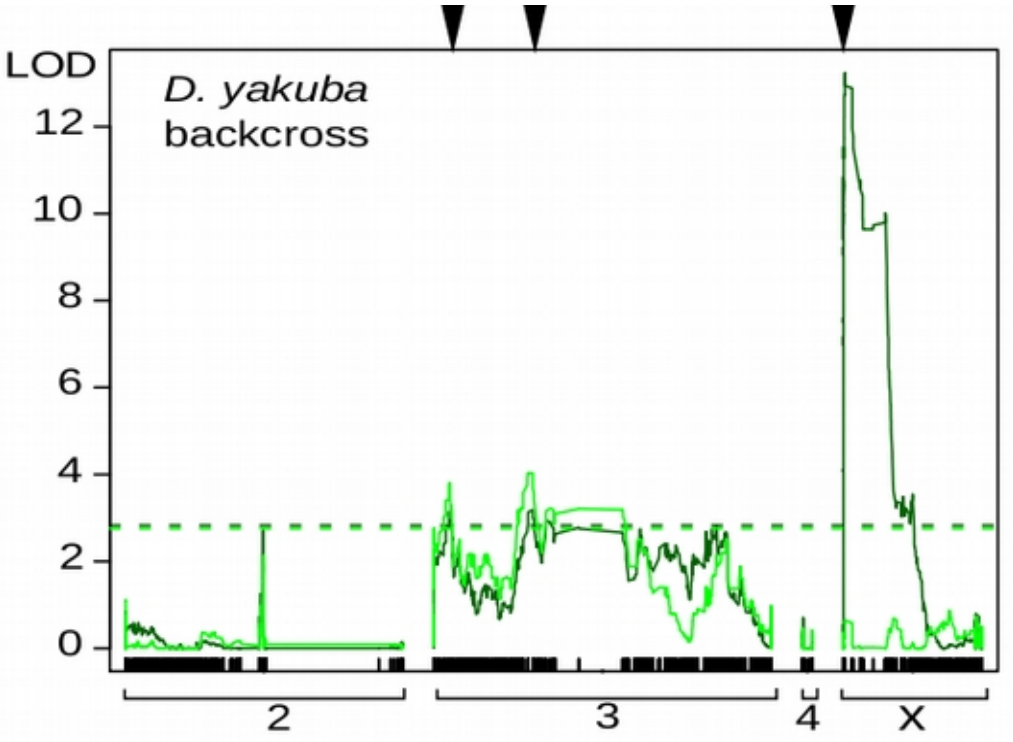


Genomic region associated with the phenotype

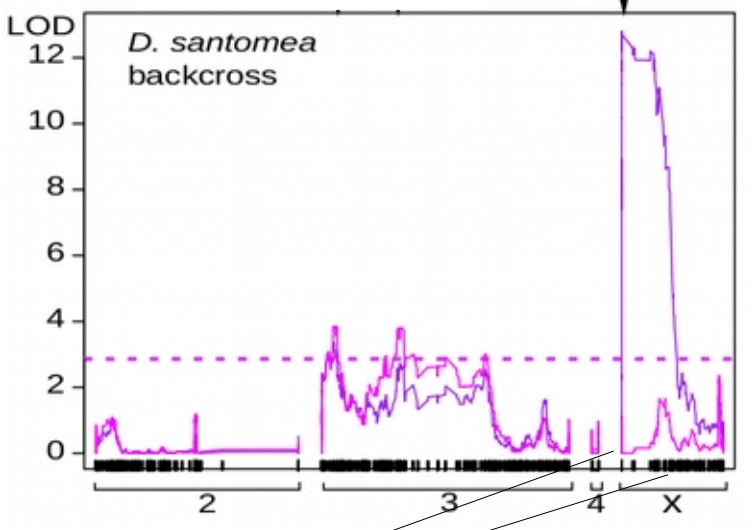
QTL mapping

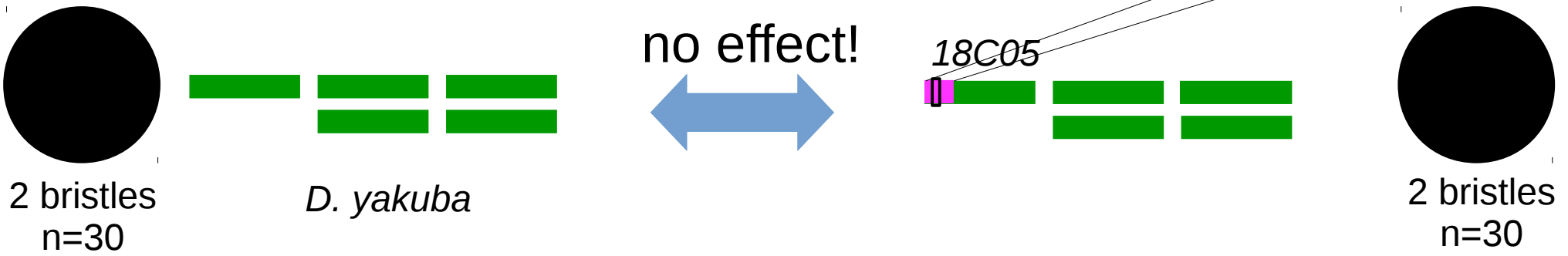
One major QTL at the tip of the X chromosome
Two minor QTL on the 3rd chromosome





Introgression of *18C05* (*scute*)



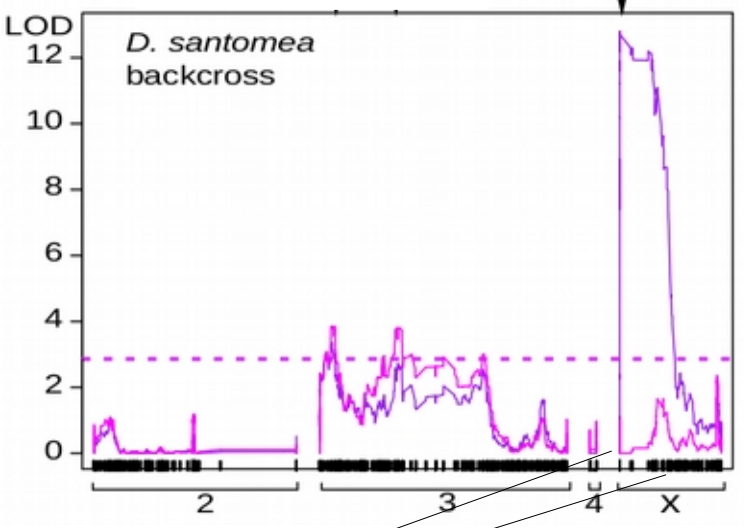


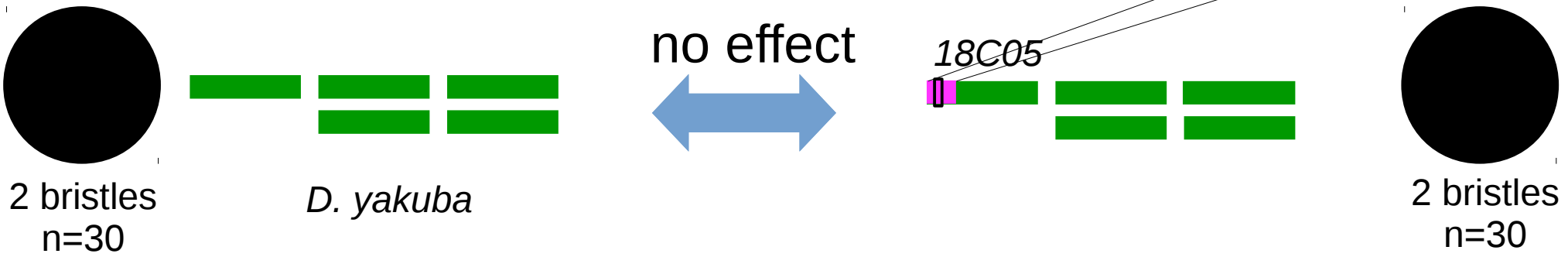
2 bristles
n=30

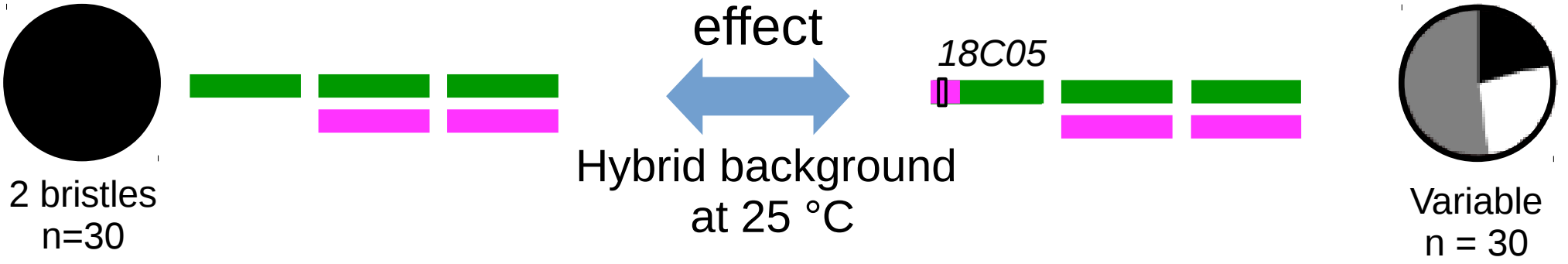
D. yakuba

2 bristles
n=30

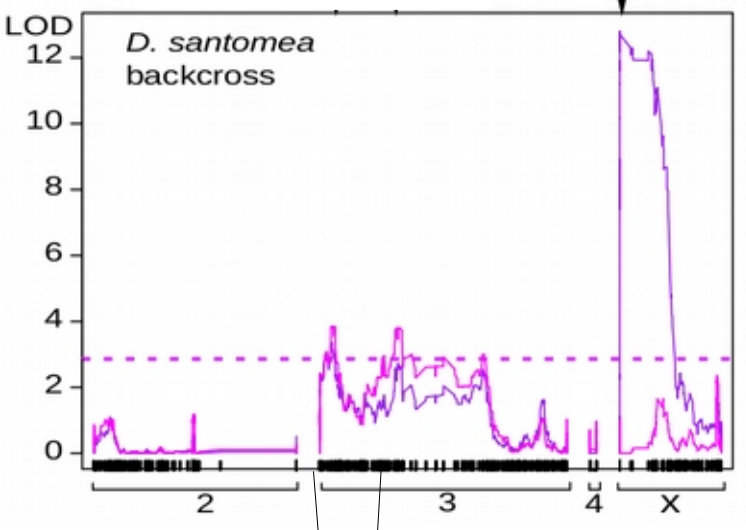
Introgression of *18C05* (*scute*)

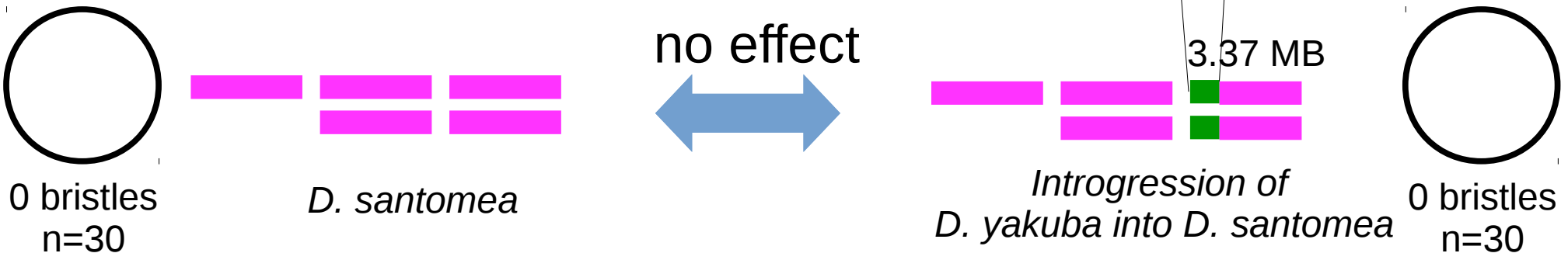


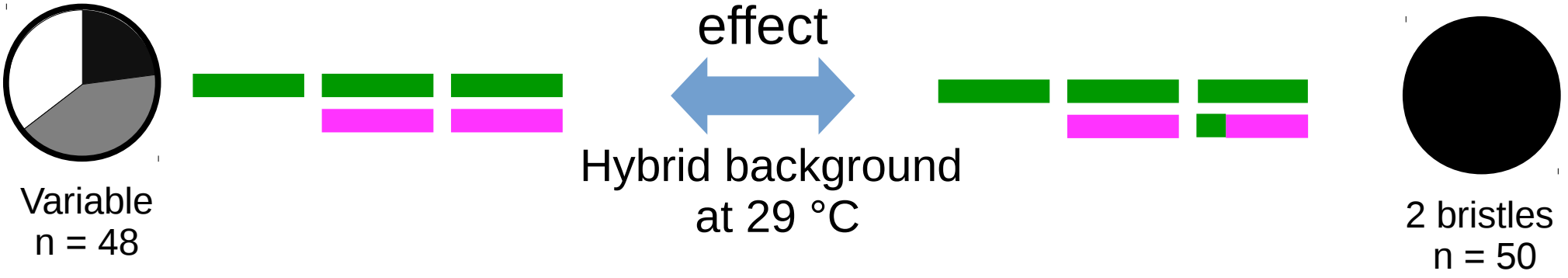




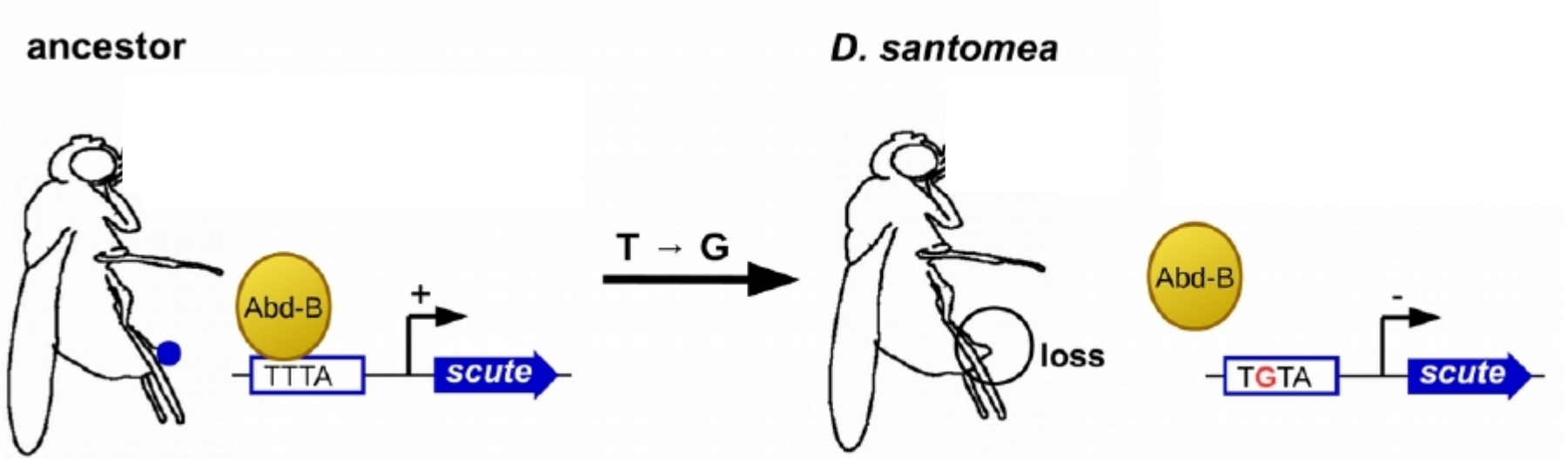
Introgression of 3L







D. santomea lost genital bristles via mutations in *scute*



.. and in at least 2 other genes on 3L.

The *scute* locus has no effect alone.

Sensitive genetic and environment backgrounds help to magnify the QTL effects.

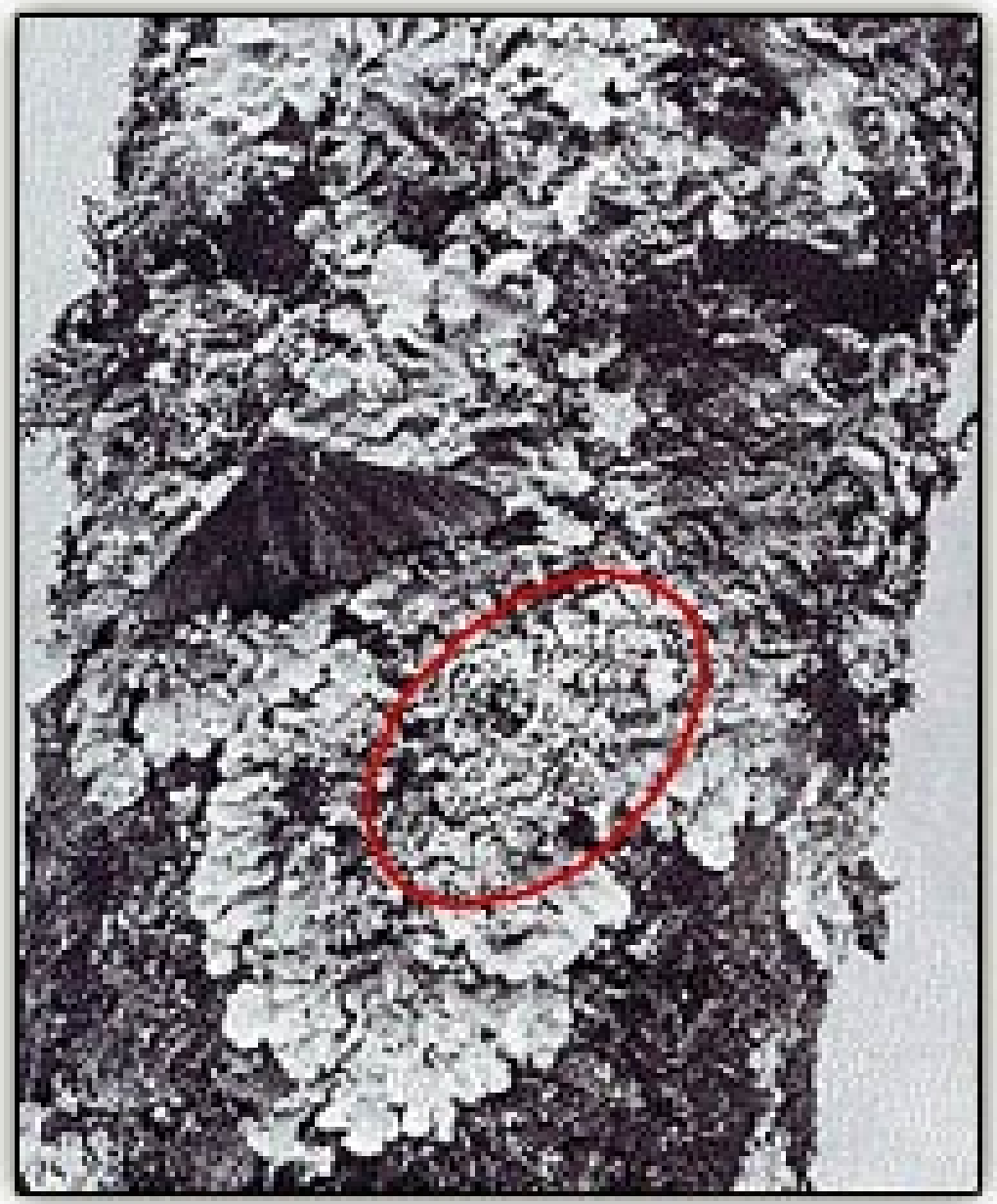
Evo-devo in butterflies

(slides modified from A. Martin)

Butterfly Alphabet by Kjell Sandvell

Mimicry : natural selection for resemblance

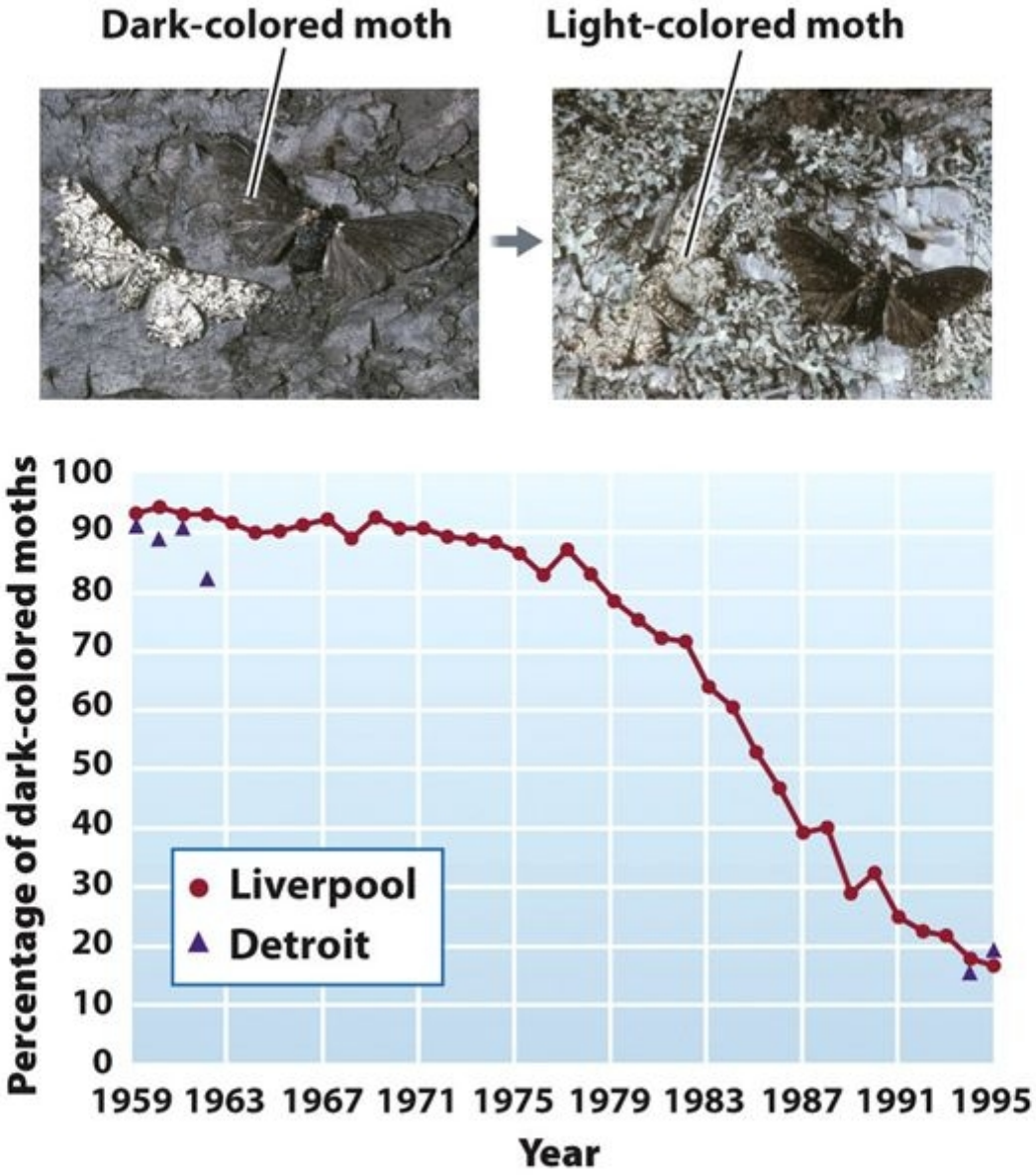
Monarch Viceroy



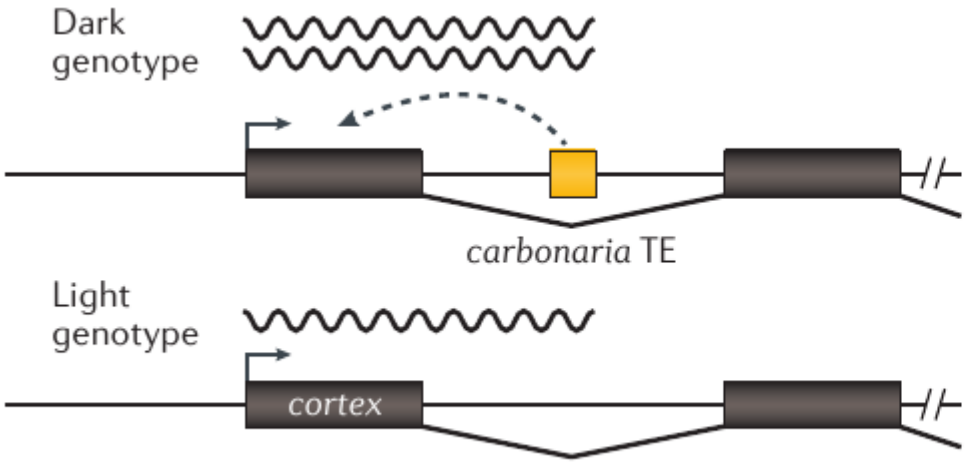
On these expanded membranes nature writes, as on a tablet, the story of the modification of species

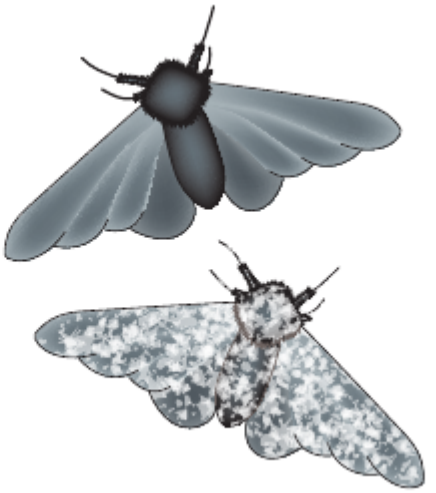
Henry Walter Bates (1863)

A CASE OF DIRECTIONAL SELECTION

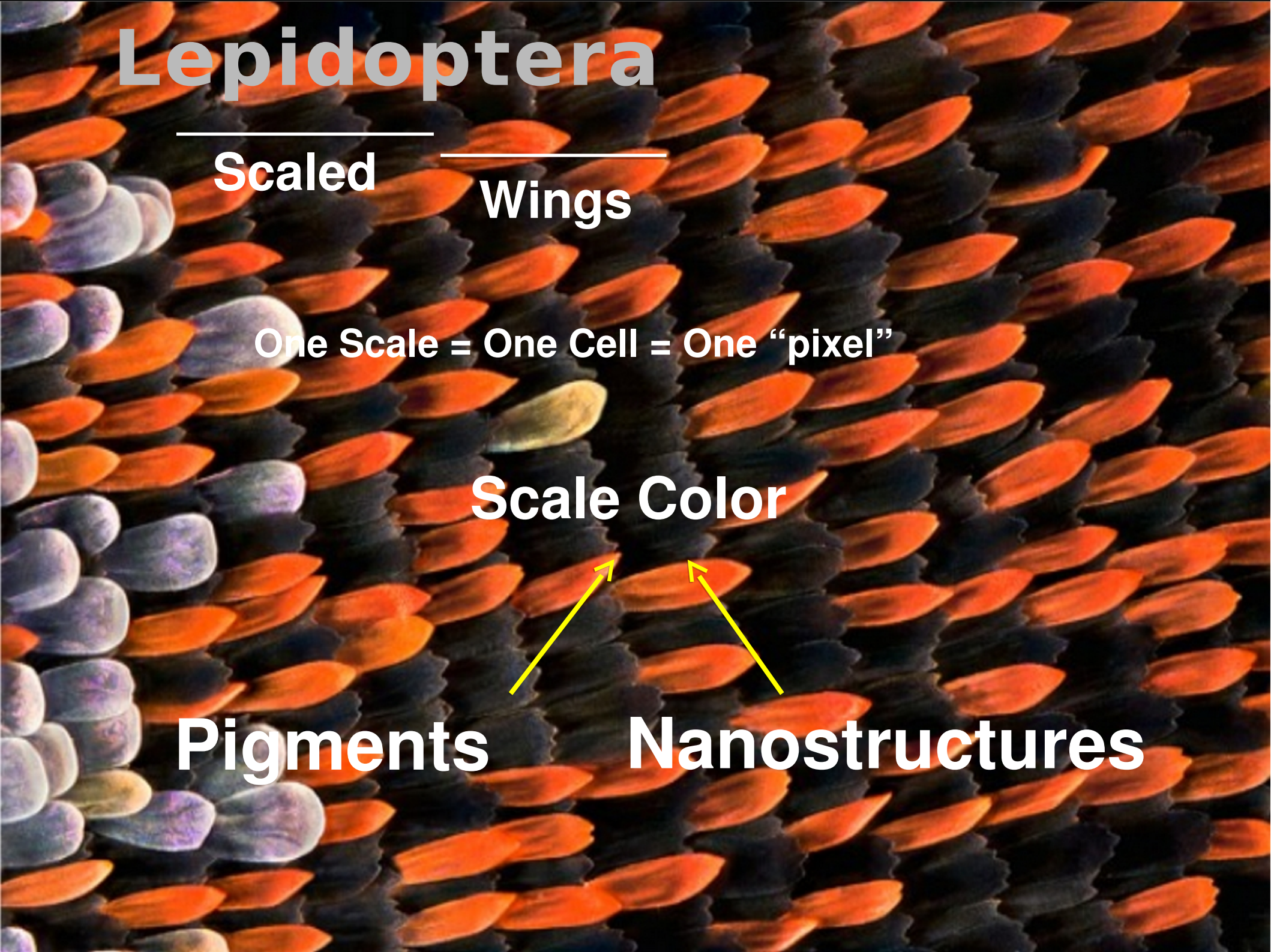


Discover Biology, 5/e Figure 18.8

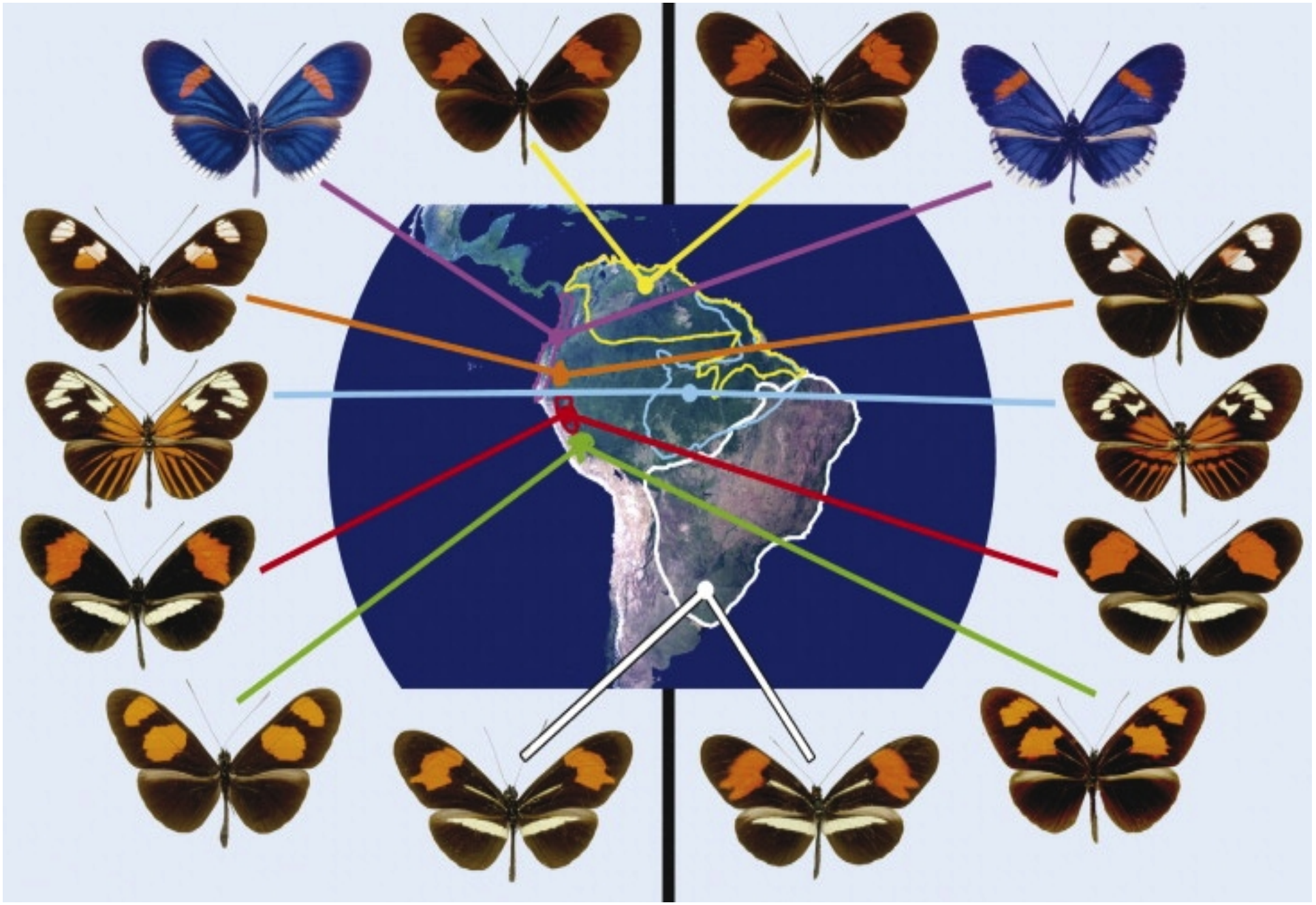




Upregulates cortex, resulting in increased darker coloration

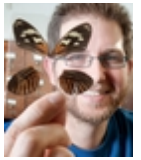

Lepidoptera
Scaled
Wings
One Scale = One Cell = One “pixel”
Scale Color
Pigments
Nanostructures

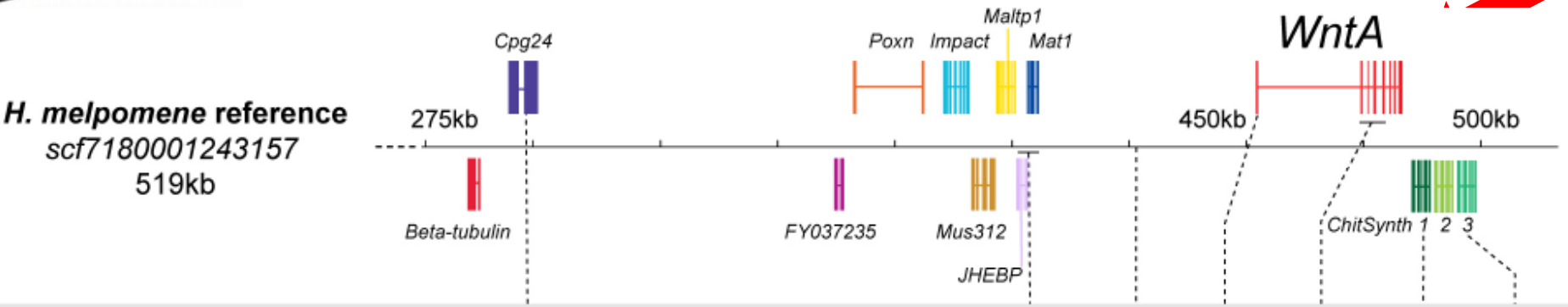
Heliconius clade



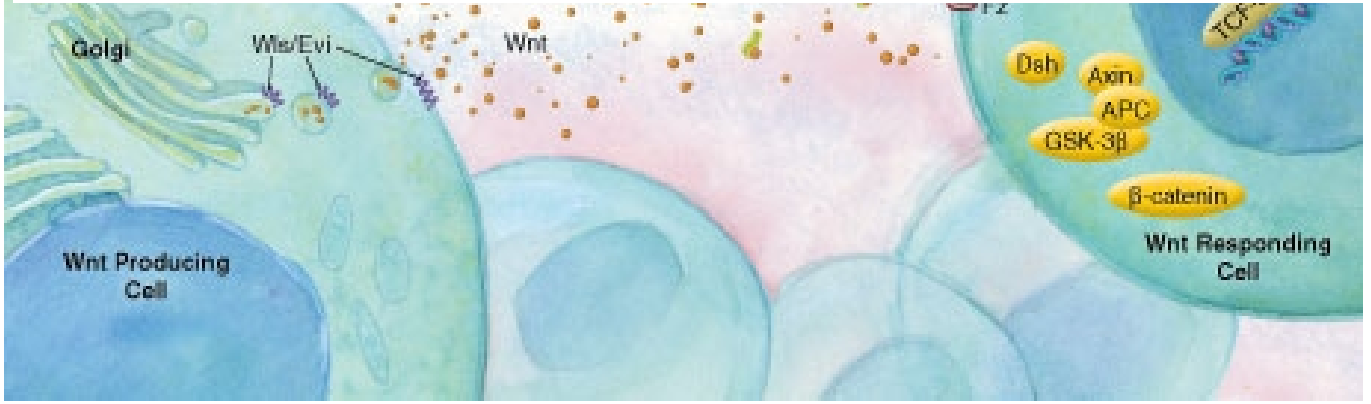
Forward genetics

Crosses: Riccardo Papa
Brian Counterman ,
Owen McMillan

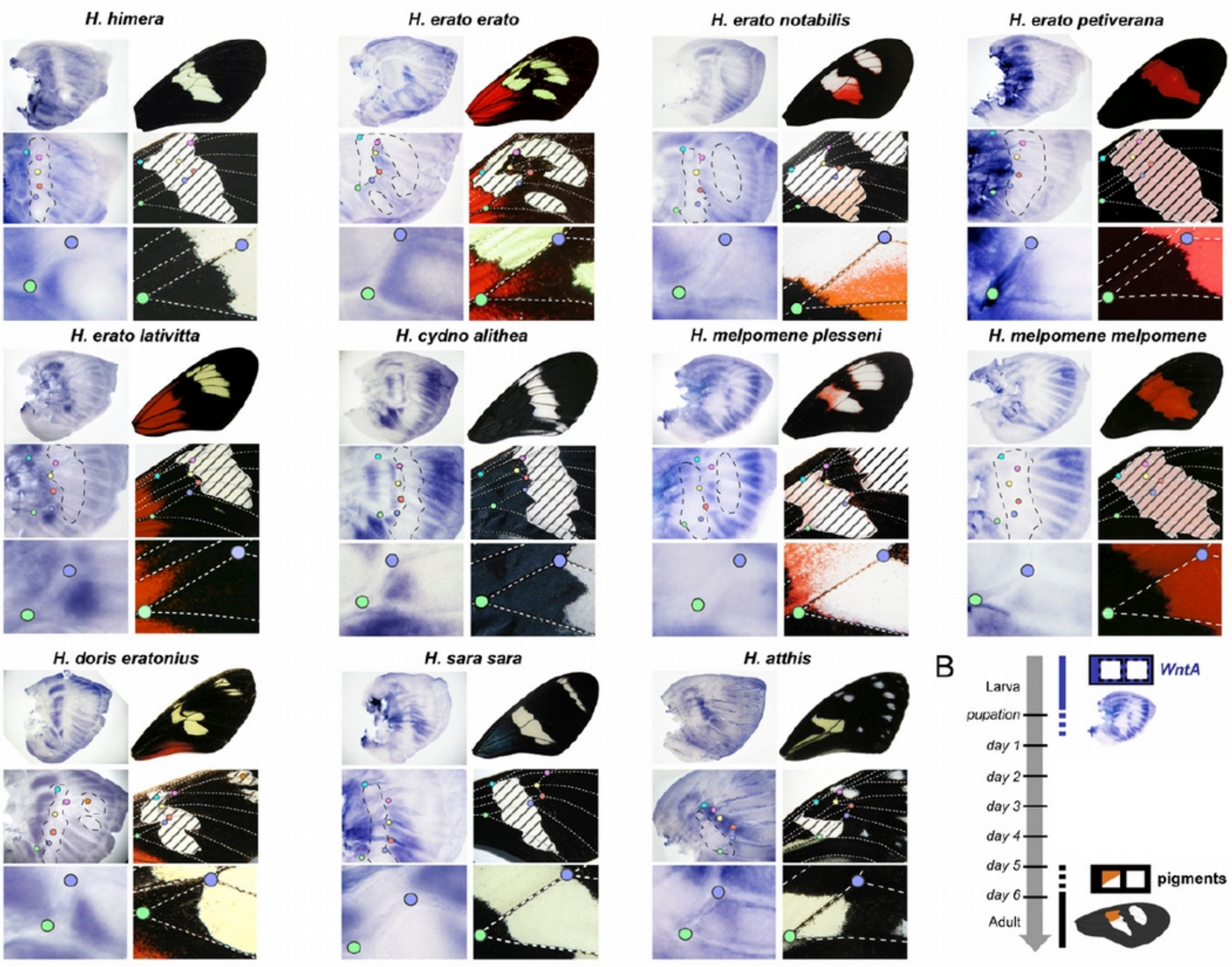



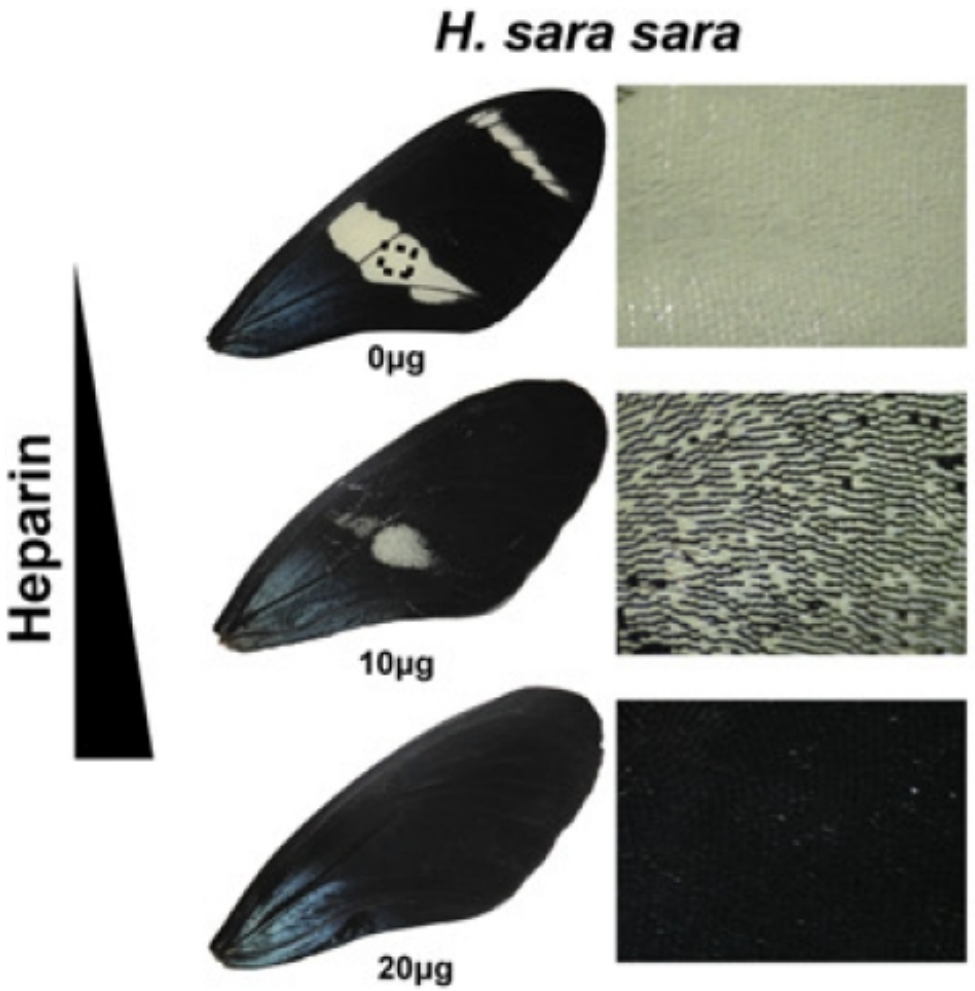
									N
Sd	*H. himera* x *H. erato etylus* and *notabilis*	2		2	1	0	0	0	1	348
Ac	*H. melpomene melpomene* x *H. melpomene malleti*	2		0					0	51
Ac	*H. cydno galanthus* x *H. cydno alithea* and *H. pachinus*	0					0		0	129



Martin et al., PNAS 2012


H. himera
H. erato erato
H. erato notabilis
H. erato petiverana
H. erato lativitta
H. cydno alithea
H. melpomene plesseni
H. melpomene melpomene
H. doris eratonius
H. sara sara
H. atthis
B
Larva
pupation
day 1
day 2
day 3
day 4
day 5
day 6
Adult
WntA
pigments

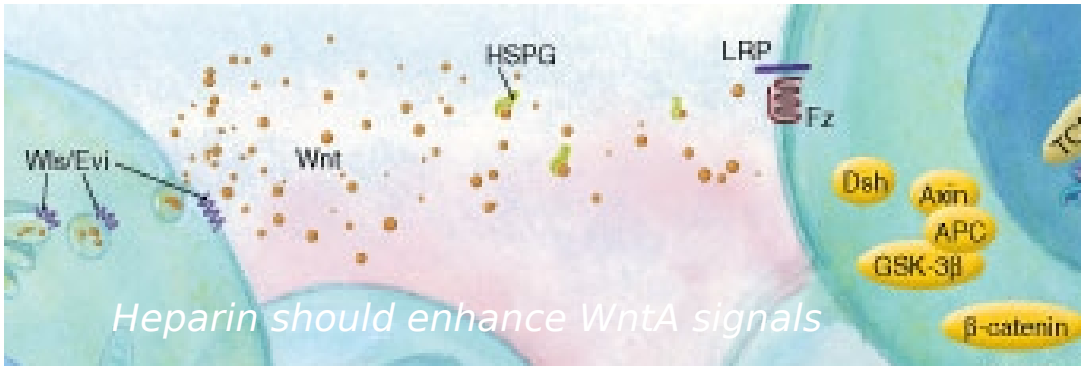
Pharmaceutical *WntA* gain-of-function assay



Development 124, 2623-2632 (1997)
Printed in Great Britain © The Company of Biologists Limited 1997
DEV5125

Genetic evidence that heparin-like glycosaminoglycans are involved in *wingless* signaling

Richard C. Binari[1], Brian E. Staveley[1], Wayne A. Johnson[2], Ranga Godavarti[3], Ram Sasisekharan[3] and Armen S. Manoukian[1,*]

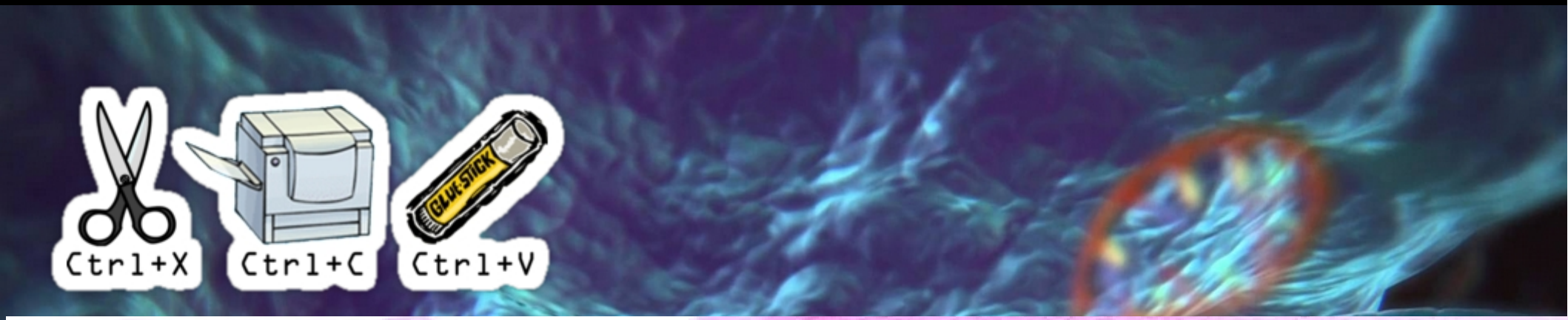


heparin-like GAGs

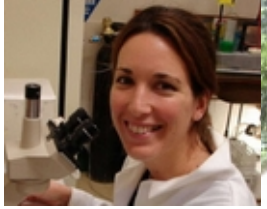
Martin et al., PNAS 2012

CRISPR-Cas9

Clustered regularly-interspaced short palindromic repeats



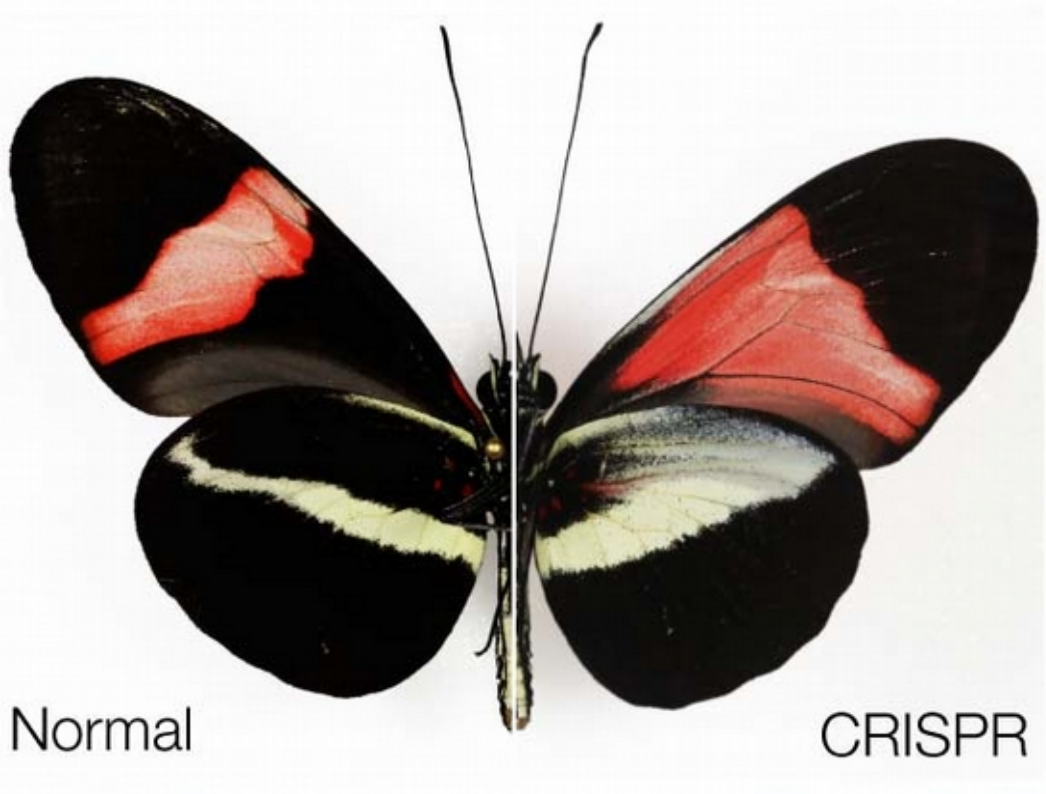
Done by Carolina Concha
Richard Wallbank

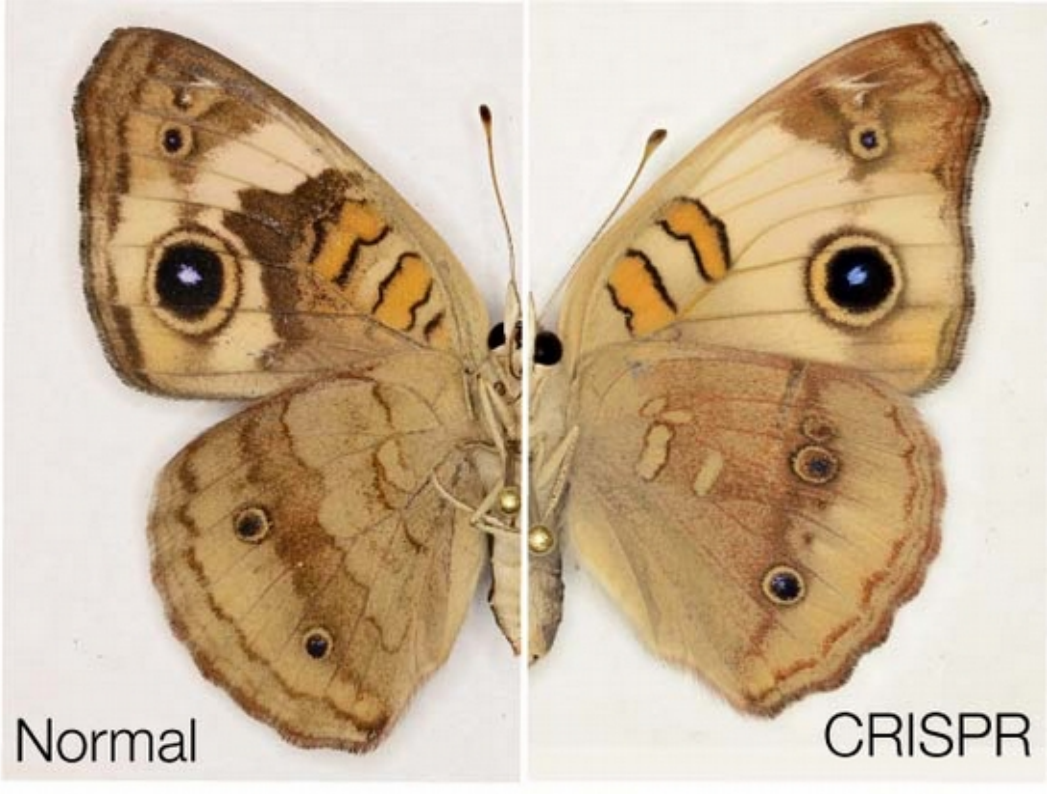


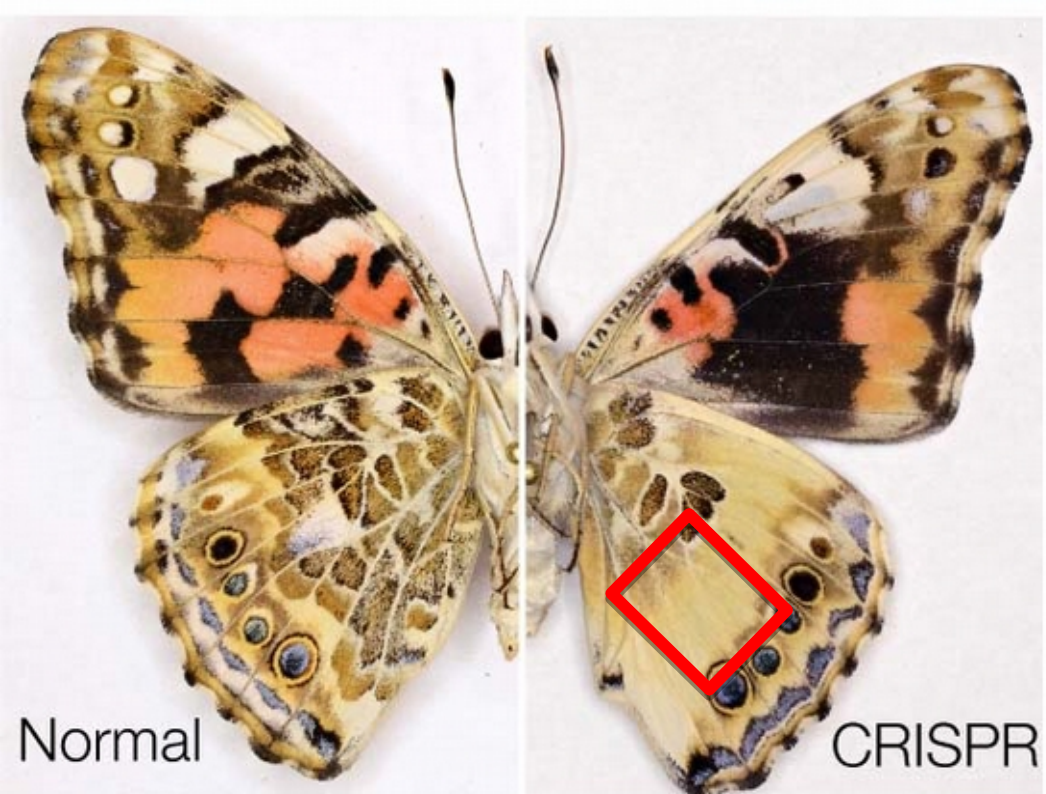
WntA knock-out

WT **_WntA_ CRISPR**

removal of black/yellow boundaries


Normal
CRISPR


Normal
CRISPR


Normal
CRISPR


Normal
CRISPR

Methods to identify the genes and the mutations responsible for phenotypic evolution

Two types of approaches

Genetic mapping

Candidate gene

no a priori, fewer bias
long and tedious
rarely ends with identification of the gene

only with strains/species which produce fertile hybrids

Based on an a priori idea
can be fast and efficient

will only find known genes

<u>In both cases genes with small effect are more difficult to identify</u>

Various methods

Genetic

which chromosome (ex: autosomal versus sex)
QTL mapping
Genetic association studies
Candidate Gene
Complementation tests

General biology

General knowledge of the genes involved in the phenotype
Similarity with a known phenotype
Correlation with a change in gene expression level/pattern

Final test of protein activity

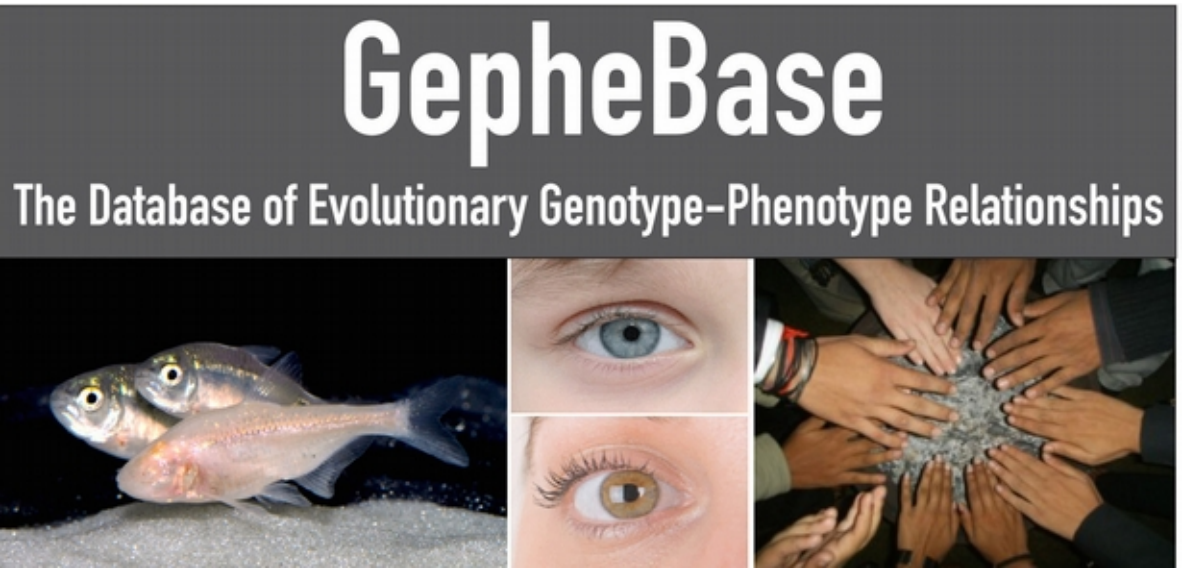
in vitro in *E. coli*, by transgenesis in the studied species or the closest model organism (ex: *beta-defensin* of dogs tested in mouse)

Final test of cis-regulatory regions

- with reporter constructs, transgenesis, comparison of both regions
- comparison of allele expression levels in hybrids (pyrosequencing)
- CRISPR-mediated targeted mutation

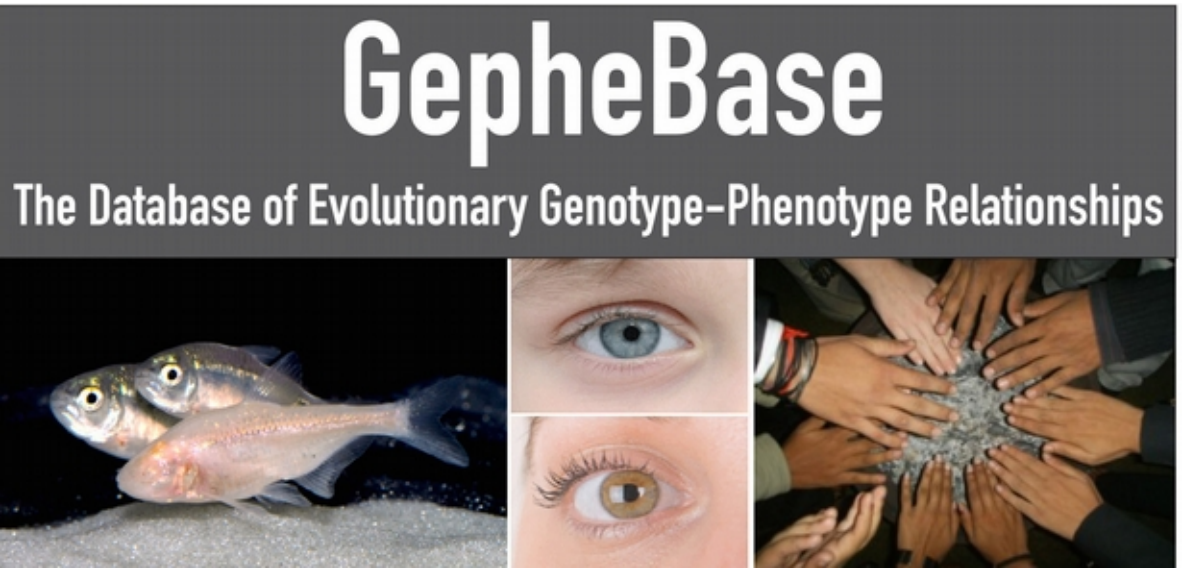
Evolution repeats itself

www.gephebase.org



Virginie Courtier-Orgogozo
Arnaud Martin (Washington DC)
Laurent Arnoult (former postdoc)
Stéphane Prigent (former postdoc)

www.gephebase.org



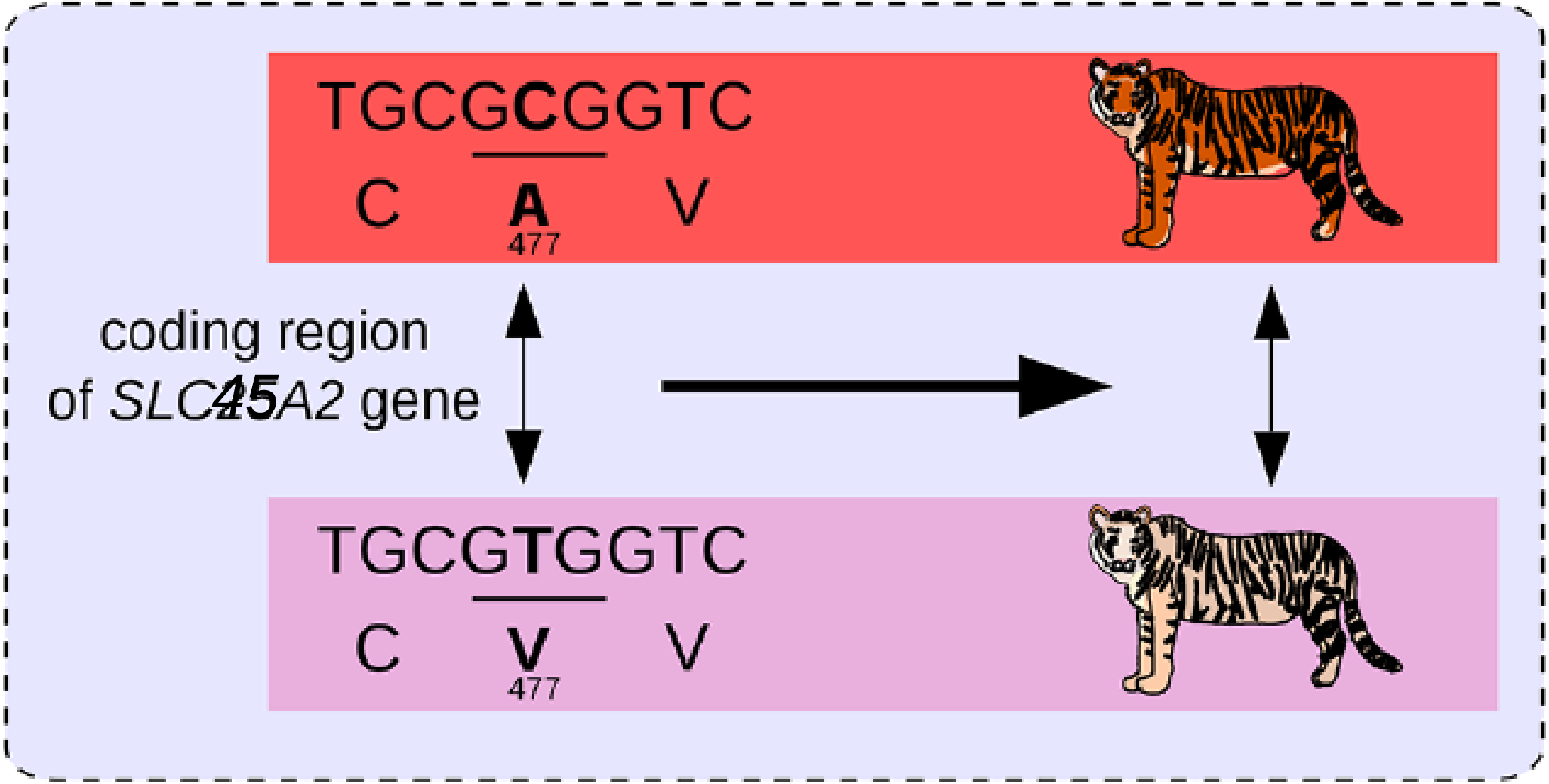
Includes Natural, Domesticated and Experimental Variation
but NO *LAB MUTANTS* and NO *CLINICAL TRAITS*

>1600 genes and mutations
associated with
natural phenotypic changes
in animals and plants

Virginie Courtier-Orgogozo
Arnaud Martin (Washington DC)
Laurent Arnoult (former postdoc)
Stéphane Prigent (former postdoc)

Ge-phe

a Genetic VARIATION *causing* a Phenotypic VARIATION

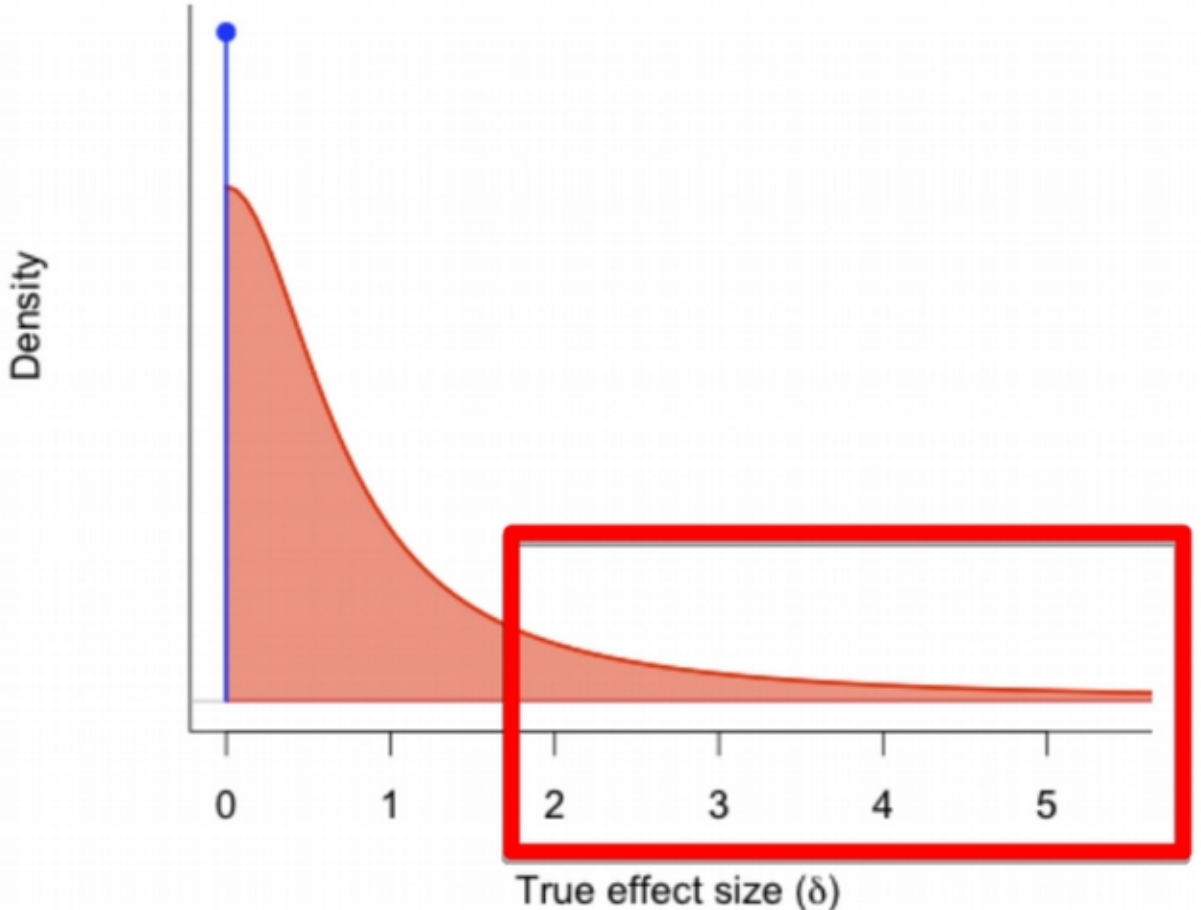


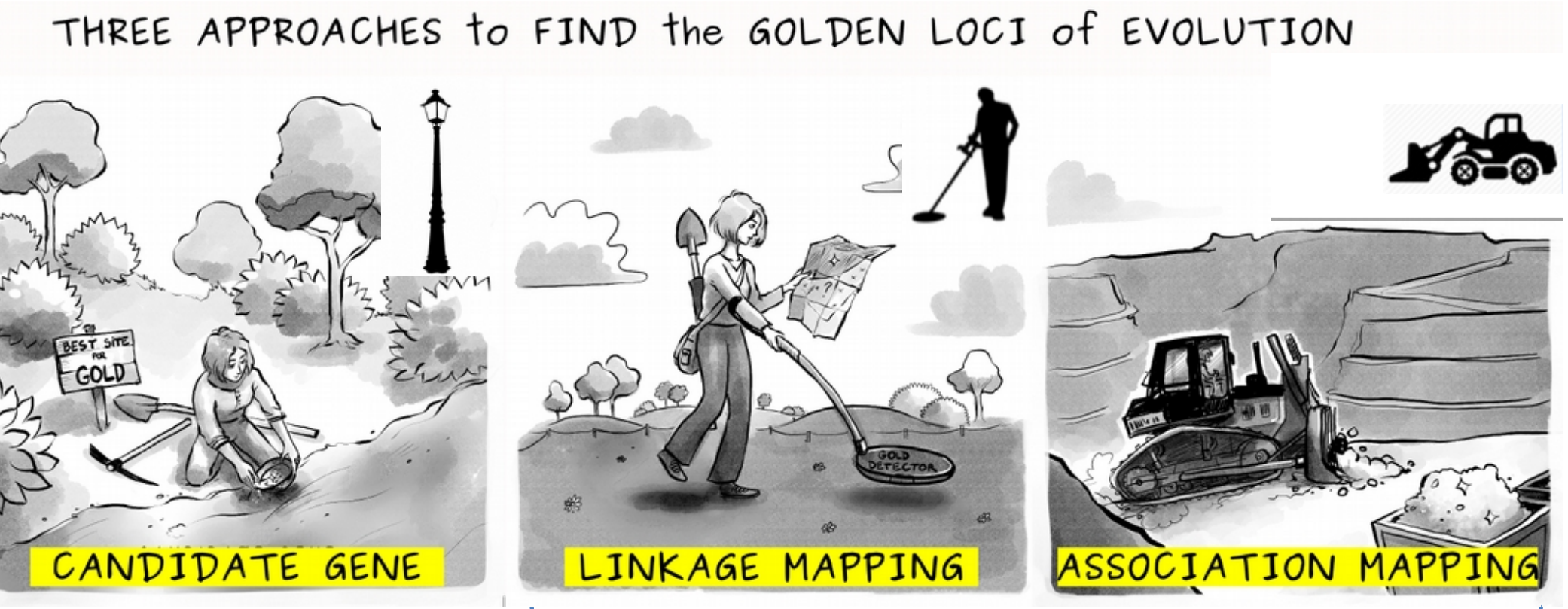
Orgogozo, Morizot & Martin *Frontiers Genet.* 2015

THE QTN PROGRAM AND THE ALLELES THAT MATTER FOR EVOLUTION: ALL THAT'S GOLD DOES NOT GLITTER

Matthew V. Rockman[1,2]

The shiny
"**large effect**" loci we can document experimentally





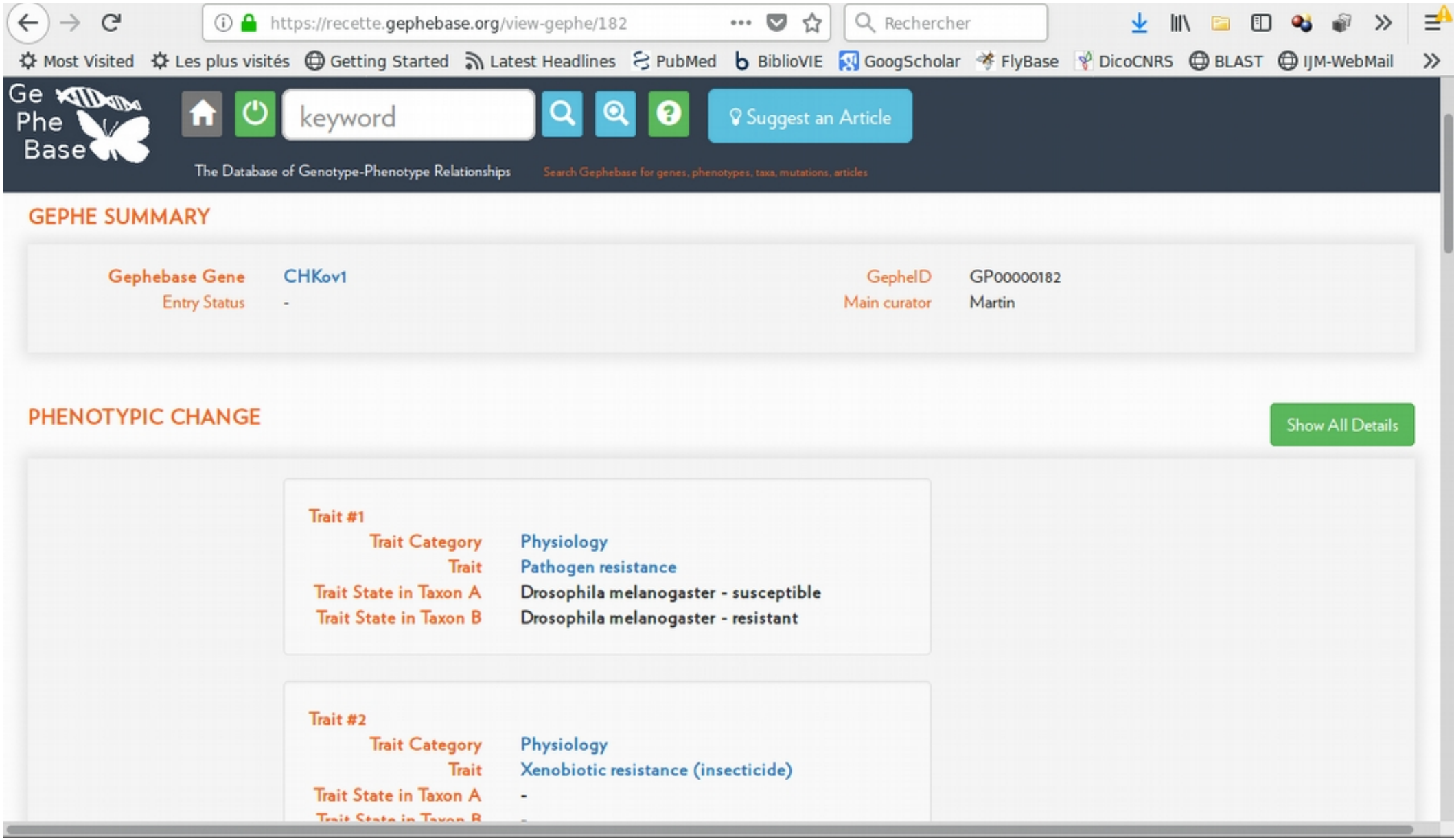
REVERSE GENETICS
From genes to traits

FORWARD GENETICS
From traits to genes

Little Ascertainment Bias, but Micro-Evolution only:

Requires the intermixing of two gene pools or lineages

CHKov1


https://recette.gephebase.org/view-gephe/182
Rechercher
Most Visited
Les plus visités
Getting Started
Latest Headlines
PubMed
BiblioVIE
GoogScholar
FlyBase
DicoCNRS
BLAST
IJM-WebMail
Ge Phe Base
keyword
Suggest an Article
The Database of Genotype-Phenotype Relationships
Search Gephebase for genes, phenotypes, taxa, mutations, articles
GEPHE SUMMARY
Gephebase Gene CHKov1
Entry Status -
GepheID GP00000182
Main curator Martin
PHENOTYPIC CHANGE
Show All Details
Trait #1
Trait Category Physiology
Trait Pathogen resistance
Trait State in Taxon A Drosophila melanogaster - susceptible
Trait State in Taxon B Drosophila melanogaster - resistant
Trait #2
Trait Category Physiology
Trait Xenobiotic resistance (insecticide)
Trait State in Taxon A -

Generic Gene Name	**CHKov1**
Synonyms	CG10618
String	-
Sequence Similarities	-
GO - Molecular Function	-
GO - Biological Process	-
GO - Cellular Component	-

UniProtKB Drosophila melanogaster	Q961V7
GenebankID or UniProtKB	AY047531

Presumptive Null	**No**
Molecular Type	**Coding**
Aberration Type	**Insertion**
Insertion Size	**1-10 kb**
Molecular Details of the Mutation	**Insertion of a Doc TE element resulting in novel; seemingly functional short protein**
Experimental Evidence –	Linkage Mapping :
Main Reference –	Successive increases in the resistance of Drosophila to viral infection through a transposon insertion followed by a Duplication. (2011) :
Authors	Magwire MM; Bayer F; Webster CL; Cao C; Jiggins FM
Abstract	To understand the molecular basis of how hosts evolve resistance to their parasites, we have investigated the genes that cause variation in the susceptibility of Drosophila melanogaster to viral infection. Using a host-specific pathogen of D. melanogaster called the sigma virus (Rhabdoviridae), we mapped a major-effect polymorphism to a region containing two paralogous genes called CHKov1 and CHKov2. In a panel of inbred fly lines, we found that a transposable element insertion in the protein coding sequence of CHKov1 is associated with increased resistance to infection. Previous research has shown that this insertion results in a truncated messenger RNA that encodes a far shorter protein than the susceptible allele. This resistant allele

ADVANCED SEARCH

	Field	Term	
AND	Trait Category	Morphology	✖
AND	Taxon and Synonyms	"Mammalia"	✖
AND	Molecular Type	Cis-regulatory	✖
AND	Aberration Type	Deletion	✖
AND	Aberration Size	10-99 bp	✖

+ Add search criteria

☐ Group Mutations

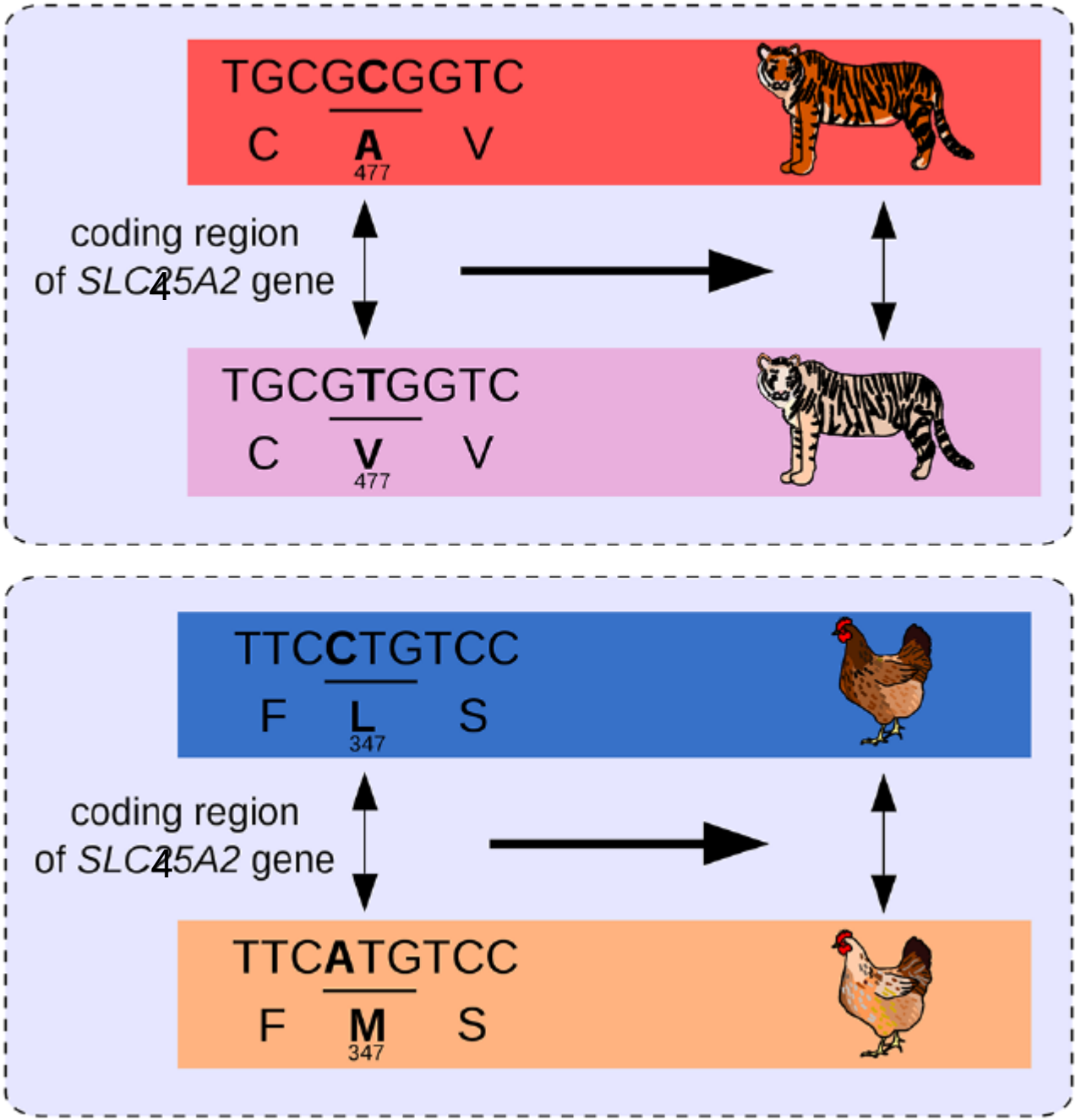
☐ Group Genes

Submit

Since 2015:
hard to keep up with all the publications...

The Wrinkled-Seed Character of Pea Described by Mendel Is Caused by a Transposon-like Insertion in a Gene Encoding Starch-Branching Enzyme

Repeated evolution



Also in:
Humans
Horses
Quails
Chickens
Mice
Pigeons

Orgogozo et al 2015 Frontiers Genetics

Repeats in..

.. the genes responsible for natural evolution

Ex : *hemoglobin* in dogs and humans in Tibet
(Wang et al 2014 GBE)

.. the genes responsible for experimental evolution

Ex : *sulfate transporter SUL1* in yeasts in low sulfate
(Gresham et al 2008 PloS Genetics)

.. the phenotypes evolving in certain environments

Ex : flying marsupial phalanger and placental flying squirrel

Orgogozo 2015 Interface Focus

For a given phenotypic change the underlying gene is predictable

Color vision

opsin

Hypoxia resistance

hemoglobin

Pesticide Resistance

VKORC1

Flowering Time

FRIGIDA

Pigmentation

SLC45A2

Loss of seed dispersal

Sh1

Drosophila bristle pattern

scute

Bone Skeleton

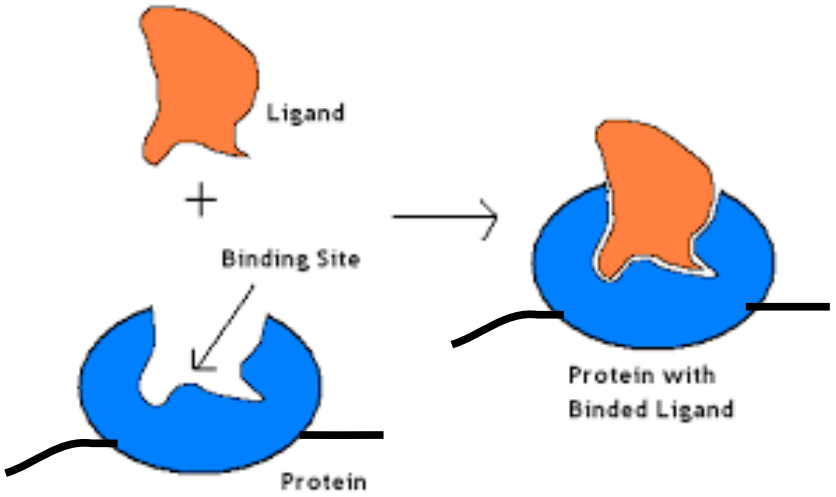
GDF6

Lactase Persistence

lactase

Genetic predictions broader than the gene level

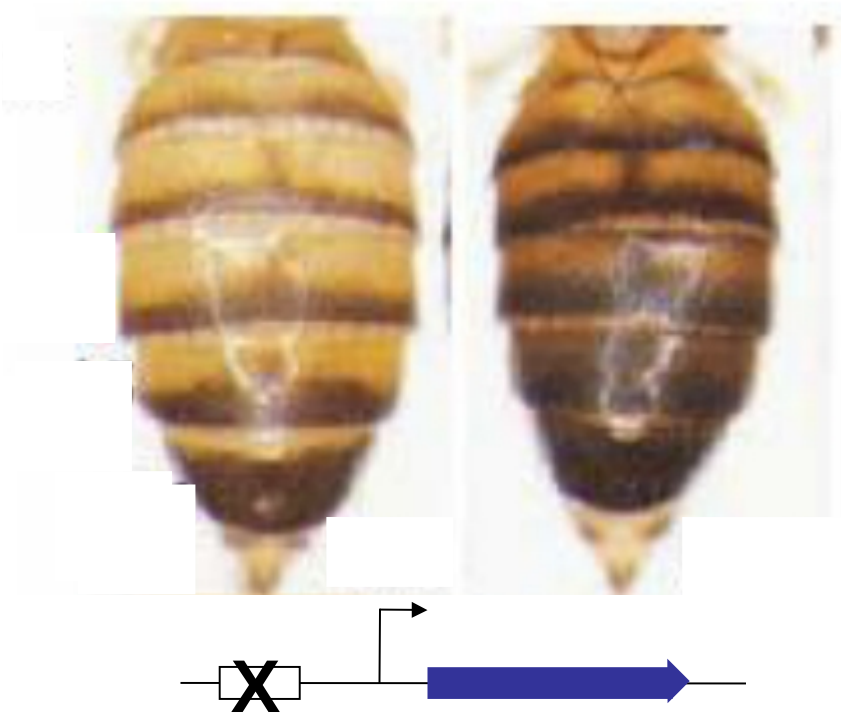
Morphological evolution is likely to involve ***ligand-coding genes****.*



19 signaling genes represent 20% of the cases where an animal morphological change has been mapped to a gene (80/391)

Martin and Orgogozo 2017 in press

Drosophila pigmentation evolution is likely to involve ***cis-regulatory mutations****.*



32 cases, 9 genes, all cis-regulatory.

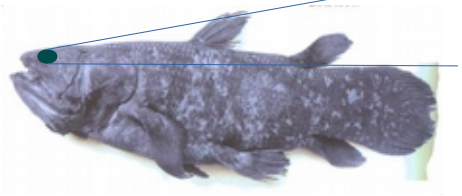
Massey and Wittkopp 2016

There are genetic paths of least resistance

Why is the set of genes causing evolution limited?

There are specialized genes in a genome

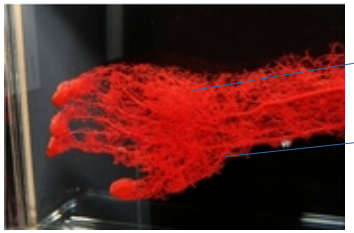
Color vision



a specialized tissue
specialized molecules

mutations in *opsin* genes

Hypoxia resistance



a specialized tissue
specialized molecules

mutations in *haemoglobin* genes

McCracken 2009

Specialized genes are usually genes that interact with external parameters

Specialized loci in the genome

Proteins that interact with external molecules

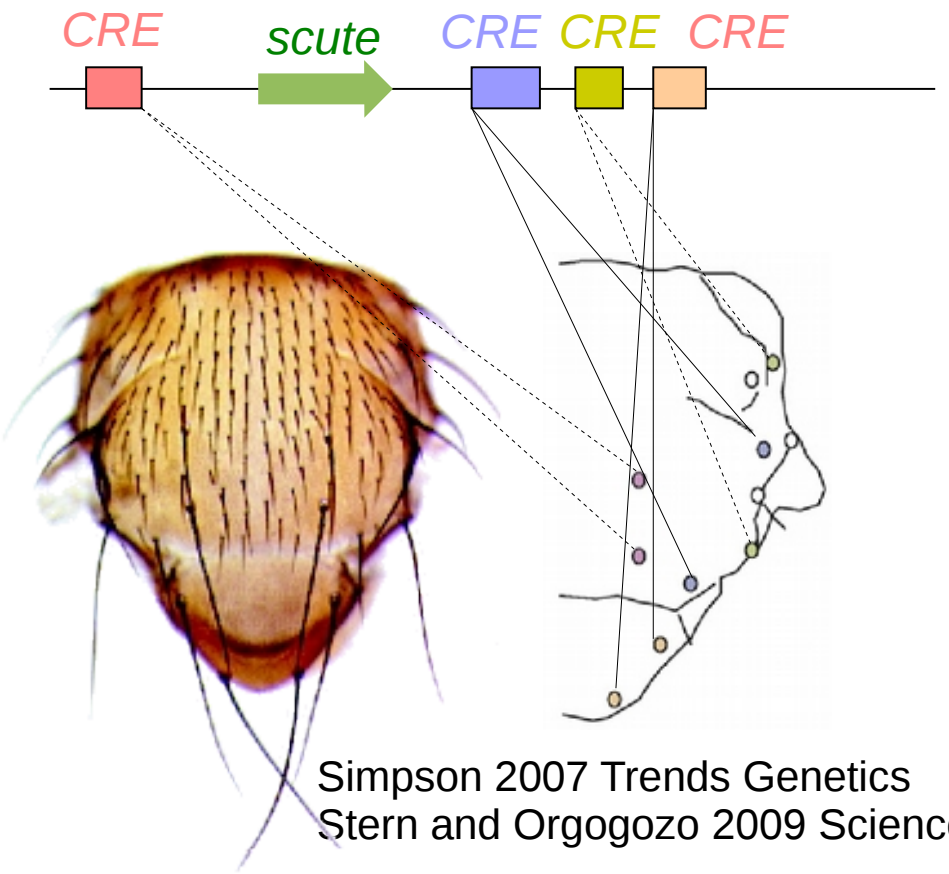
oxygen, photons, insecticide, cholesterol...

Specialized loci in the genome

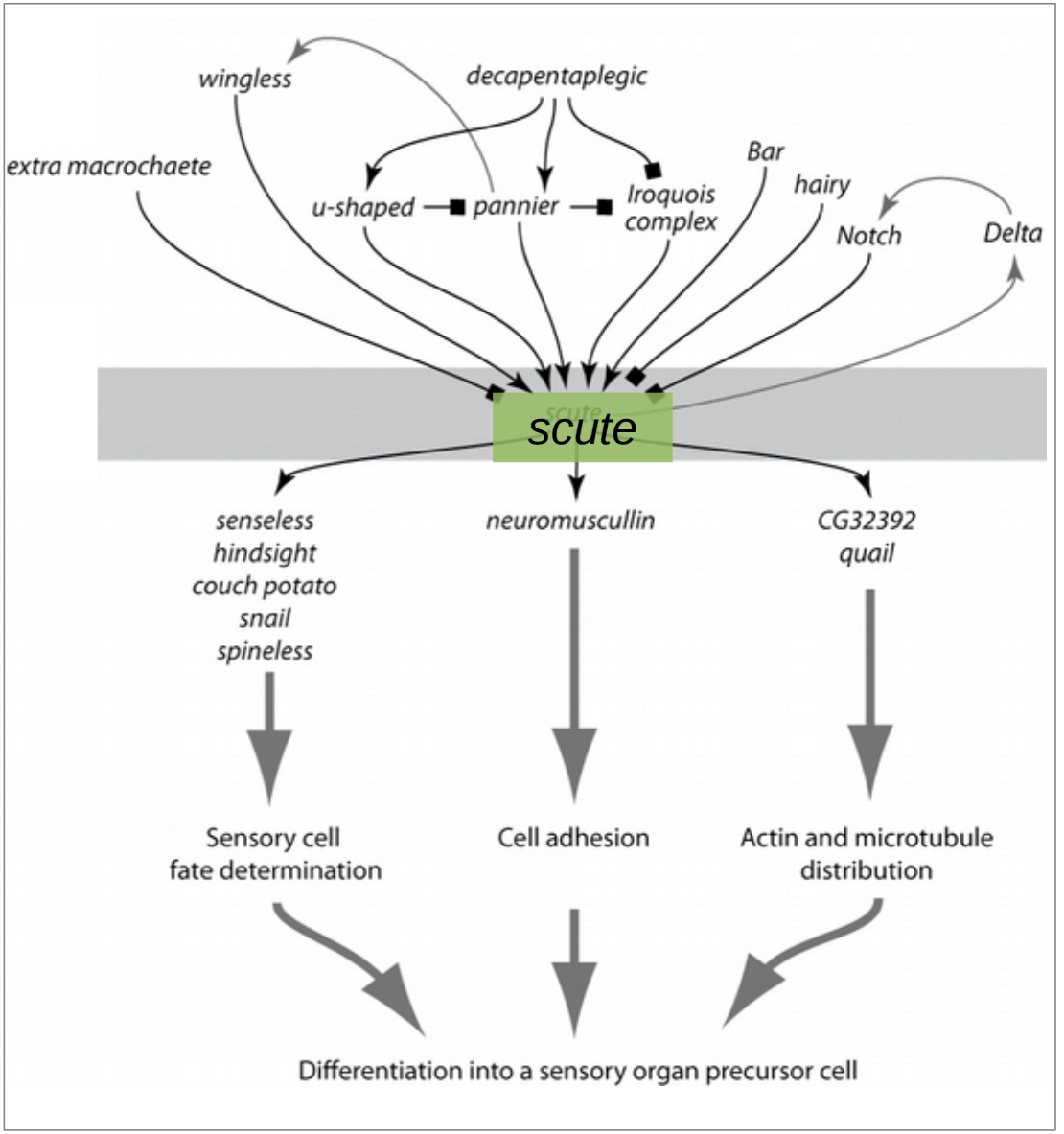
Proteins that interact with external molecules

oxygen, photons, insecticide, cholesterol...

Cis-regulatory elements of “developmental switch genes”



Simpson 2007 Trends Genetics
Stern and Orgogozo 2009 Science

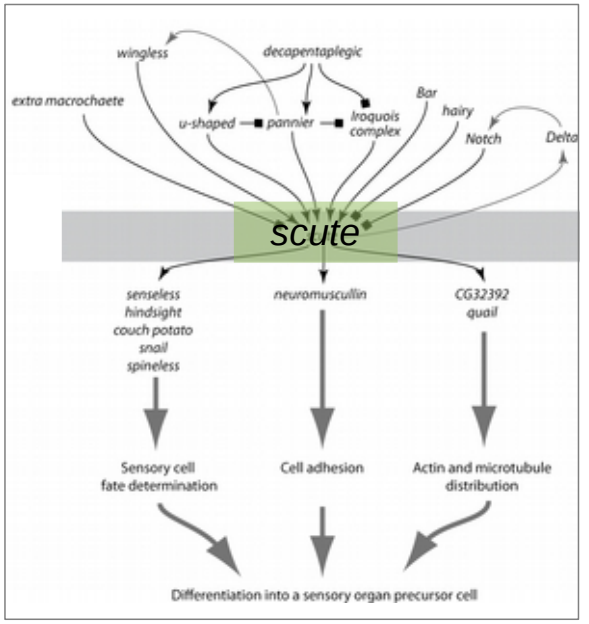


From random processes can emerge predictability

Many unpredictable processes at a low level

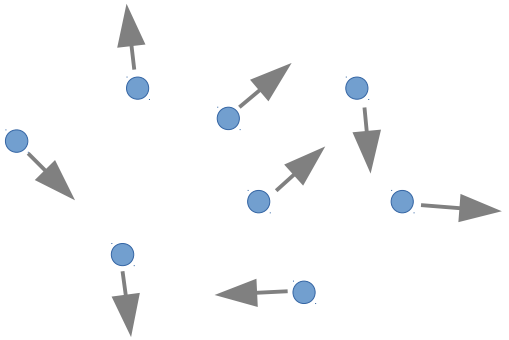
Predictable Evolution at the genetic level

Mutations in DNA
Chromosome segregation during meiosis
Assortative mating
Gamete competition during fecondation
Life history traits
Genetic linkage
Environmental changes (meteorite, etc.)
...



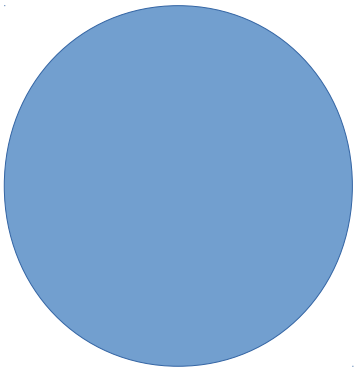
From random processes can emerge predictability

Microscopic world

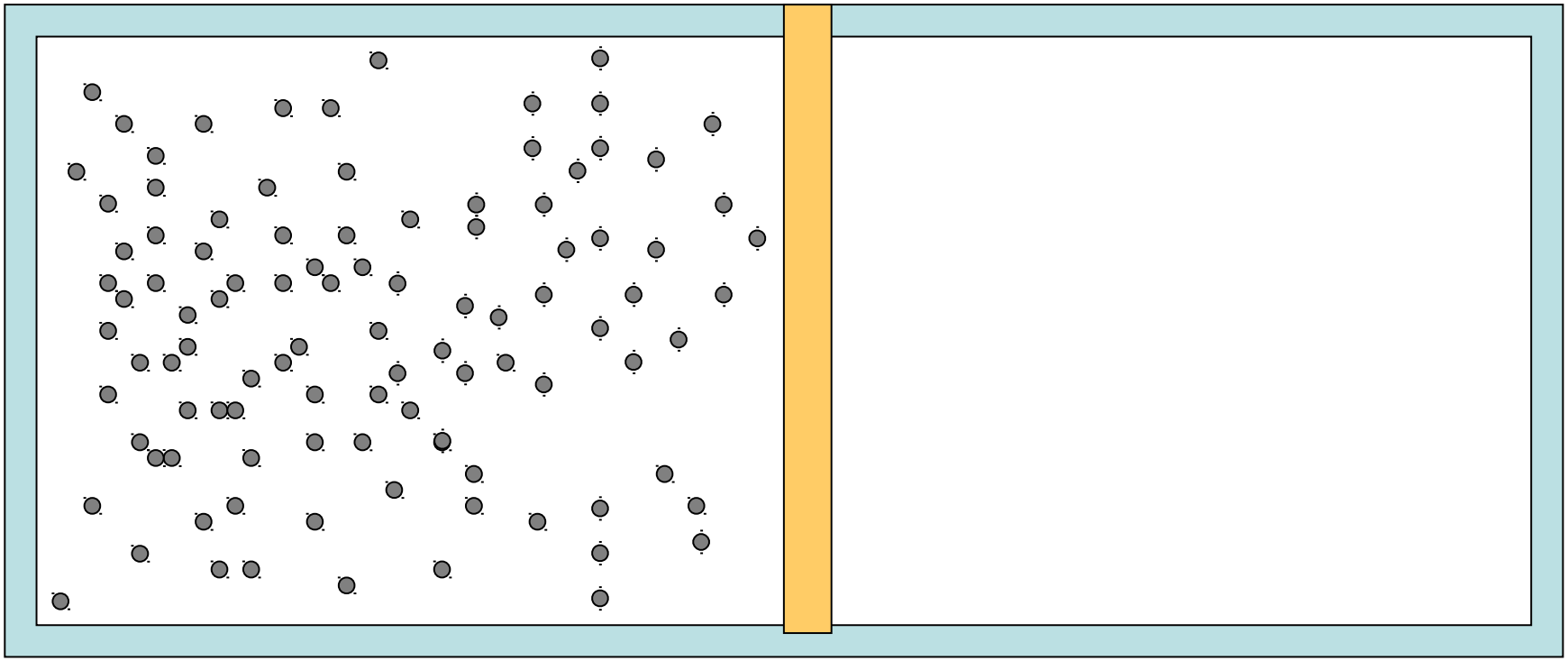


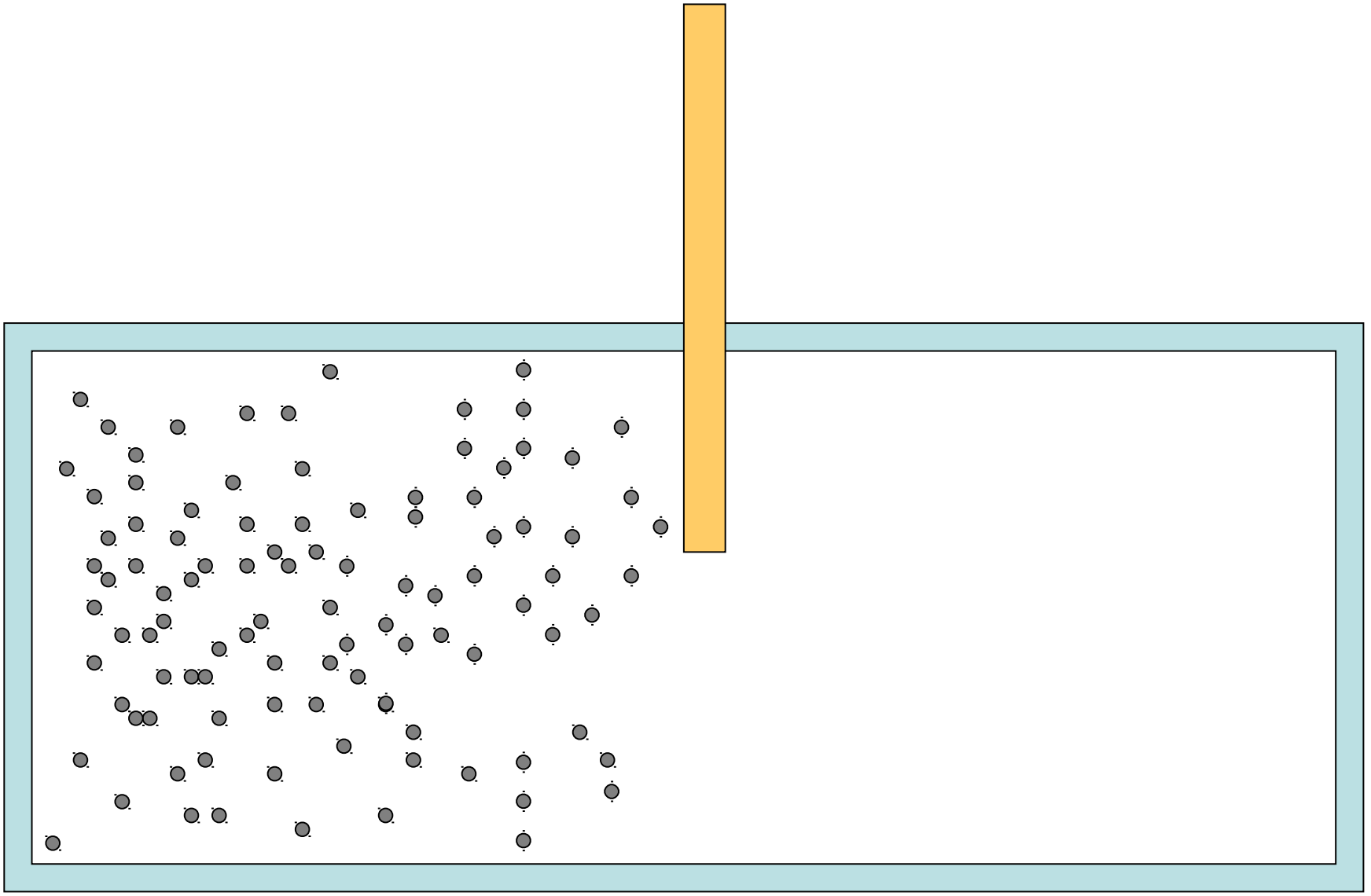
Position, mass, velocity of each particle

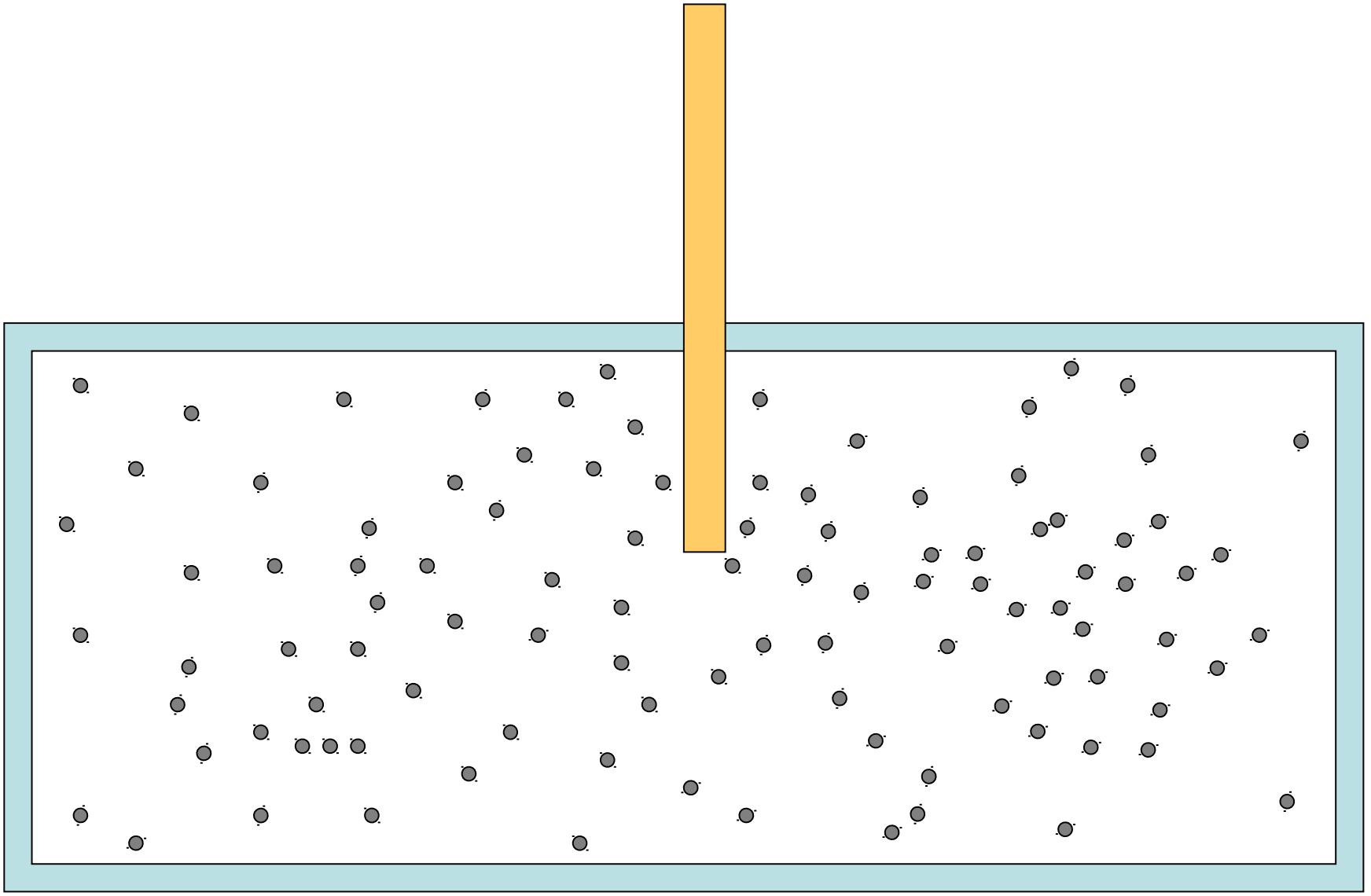
Macroscopic world



Pressure, Volume, Temperature,
Number of moles





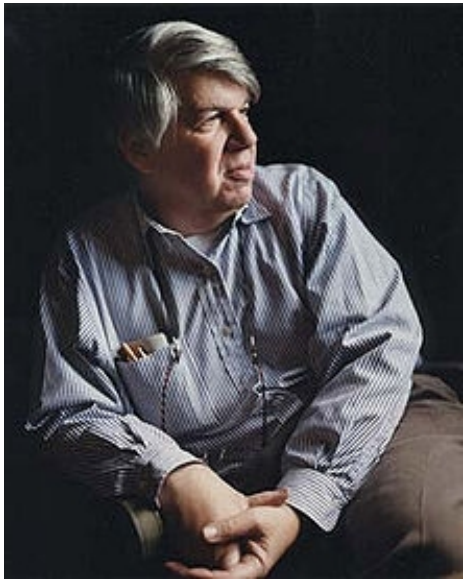


After a few seconds

Evolution:
unconstrained and unpredictable?

[past and present organisms are]
a subset of workable, but basically fortuitous, survivals among a much larger set that could have functioned just as well, but either never arose, or lost their opportunities, by historical happenstance.

Stephen Jay Gould, 2002



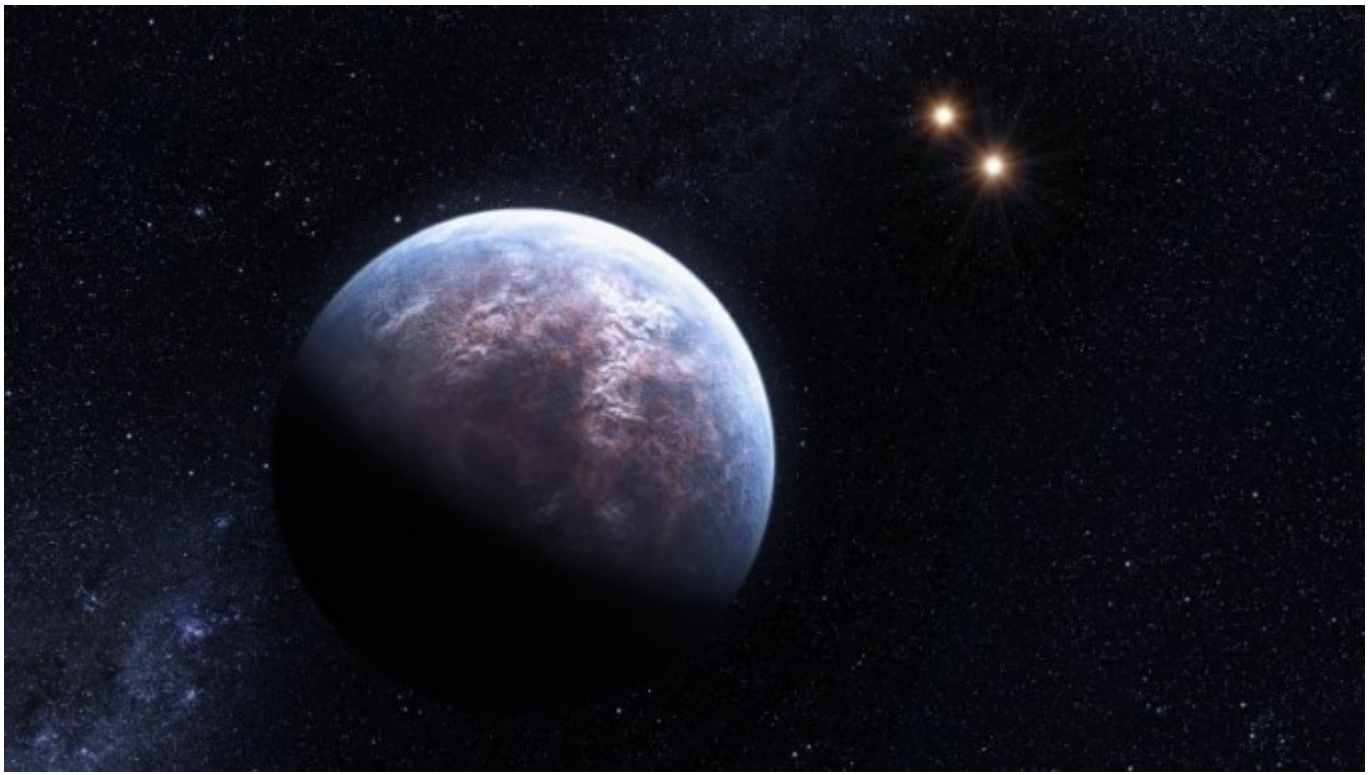
It is hard to realize that the living world as we know it is just one among many possibilities; that its actual structure results from the history of the earth.

1977

Evolution and Tinkering

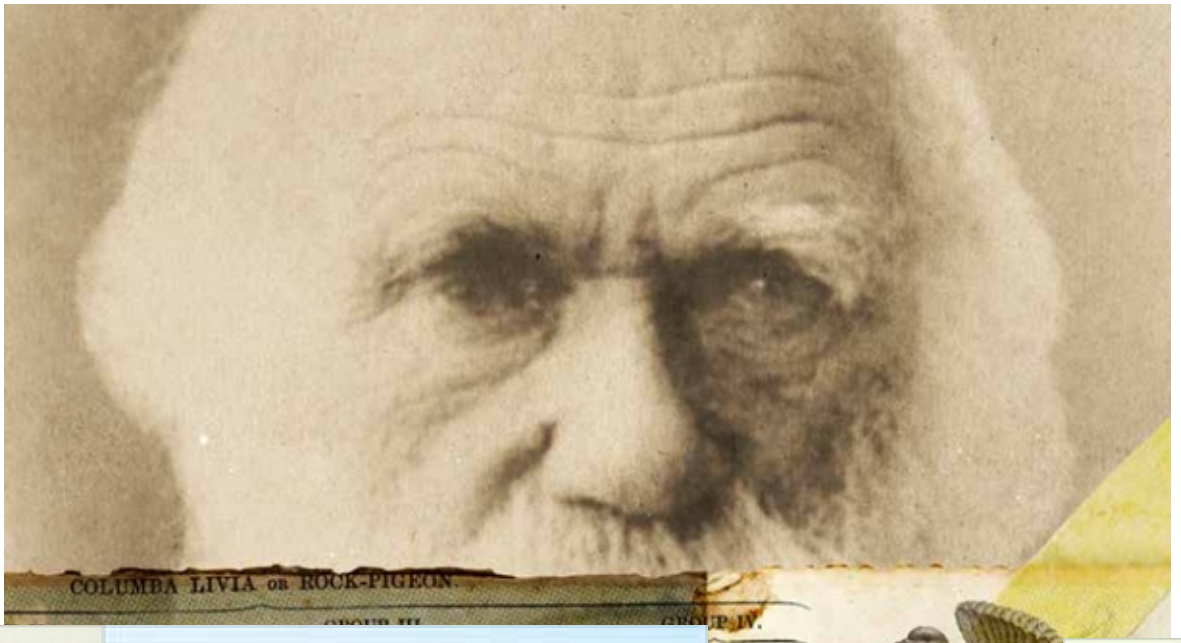
François Jacob

Would life evolve again, would it produce similar living beings?



evolution

- **How?**
- **Why?** (1) rather than nothing
- **Why?** (2) rather than another change



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RICHARD DAWKINS

THE SELFISH GENE

30th Anniversary edition

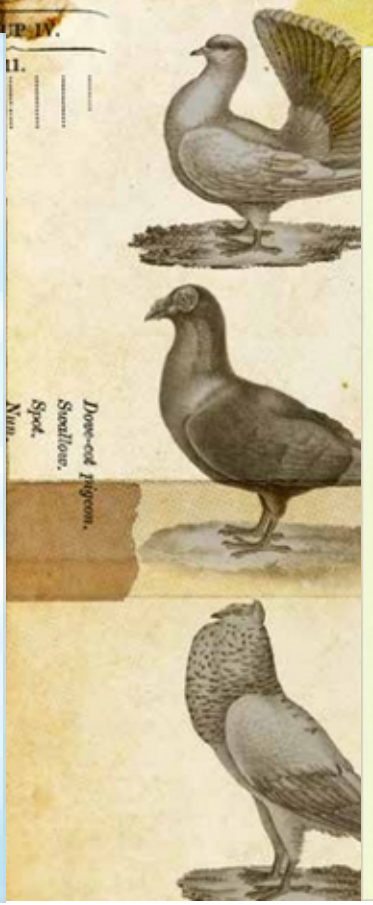
WITH A NEW INTRODUCTION BY THE AUTHOR

HOW THE SNAKE LOST ITS LEGS

Curious Tales from the Frontier of Evo-Devo

LEWIS I. HELD, JR.

CAMBRIDGE



'Compelling . . . masterful . . . outstandingly good.'
Richard Dawkins, *TLS*

WHY EVOLUTION IS TRUE

JERRY A. COYNE

Genital evolution
Alexis Lalouette

Left-right asymmetry
Michael Lang
Bénédicte Lefèvre

Glue evolution
Flora Borne

Virginie.courtier@ijm.fr
@Biol4Ever

Collaborators

Gephebase
Arnaud Martin
Baptiste Morizot

Fly anatomy
Jean David

Morphometrics
François Graner

Genotyping
David L. Stern

Fly crosses
Daniel Matute

INSTITUT JACQUES MONOD
cnrs
université PARIS DIDEROT PARIS 7
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FONDATION RECHERCHE MÉDICALE