Genetic bases of Phenotypic Plasticity

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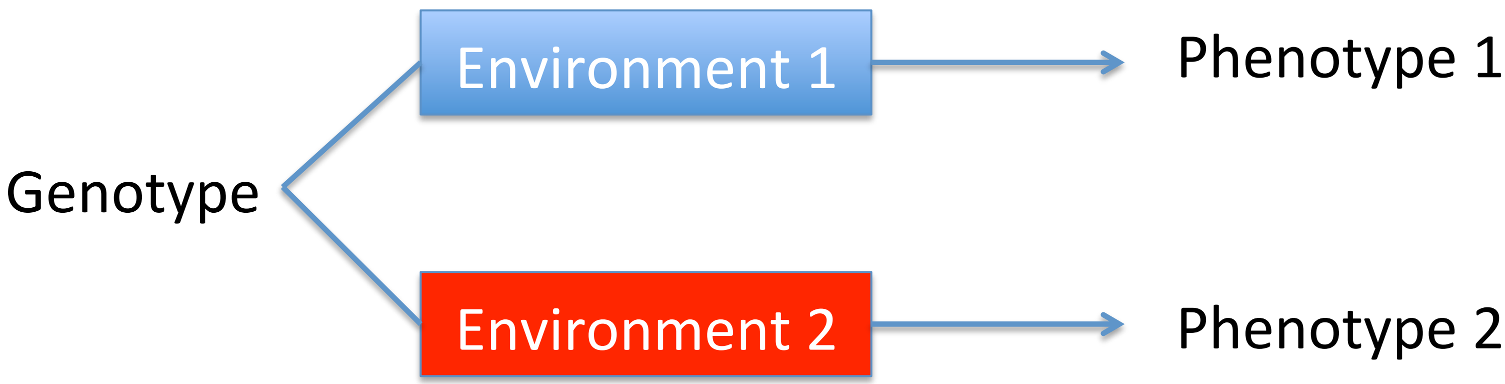
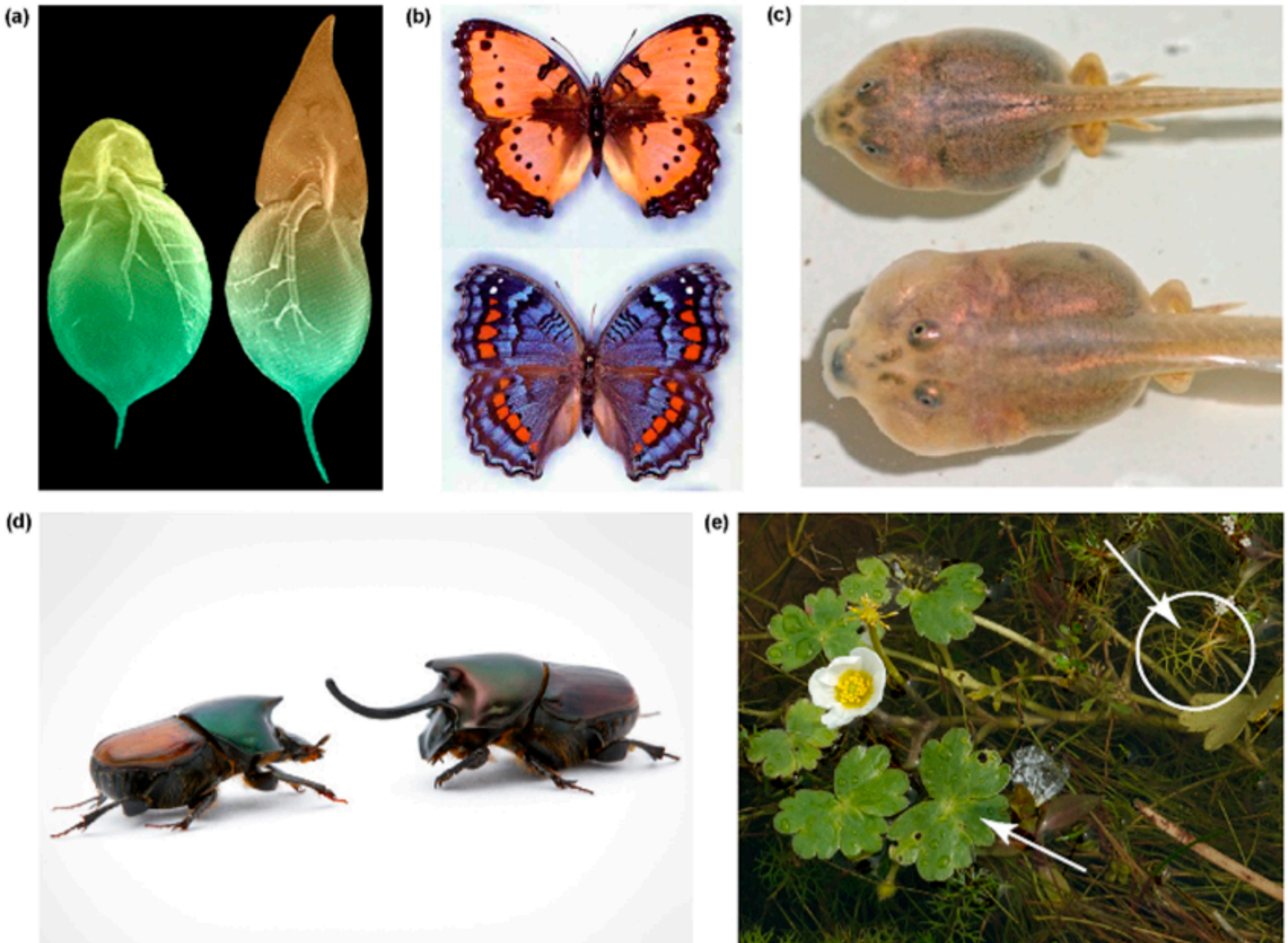
Phenotypic plasticity



« the property of a given genotype to produce different phenotypes in response to distinct environmental conditions » (Pigliucci, 2001)

Examples of phenotypic plasticity



(Pfennig *et al.,* 2010)

Phenotypic plasticity and adaptation to environmental fluctuations

Summer

Winter

Snow hare

Polyphenisms vs Polymorphisms

*''In order to make the term '**polymorphism**' more useful and precise, there is now a tendency to restrict it to **genetic polymorphism**. Since this would leave nongenetic variation of the phenotype without a designation, the term '**polyphenism**' is here proposed for it. Polyphenism is discontinuous when definite castes are present (certain social insects) or definite stages in the life cycle (larvae vs. adults; sexual vs. parthenogenetic) or definite seasonal forms (dry vs. wet; spring vs. summer). Polyphenism may be continuous, as in the cyclomorphosis of fresh-water organisms and some other seasonal variation.''*

(Mayr, 1963)

Canalization

Canalization describes the ability of a organism to maintain the wild-type phenotype despite genetic and environmental variations (Waddington 1942; see also Schmalhausen 1949).

Environmental canalization can be seen as the opposite of phenotypic plasticity (Flatt, 2005).

However, environmental canalization and phenotypic plasticity are not mutually exclusive:

- Polyphenisms can be robust (canalized): no intermediate phenotype observed between alternative morphs.

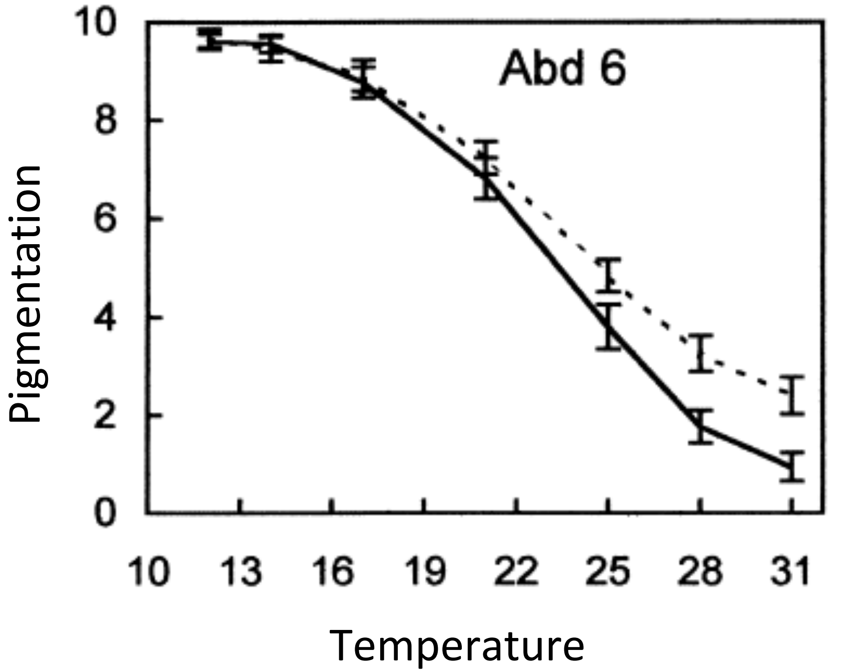
- A plastic molecular response to environmental variation can be used to maintain the phenotype.

Role in evolution: release of accumulated cryptic genetic variation upon decanalization.

The reaction norm: a major tool to represent phenotypic plasticity

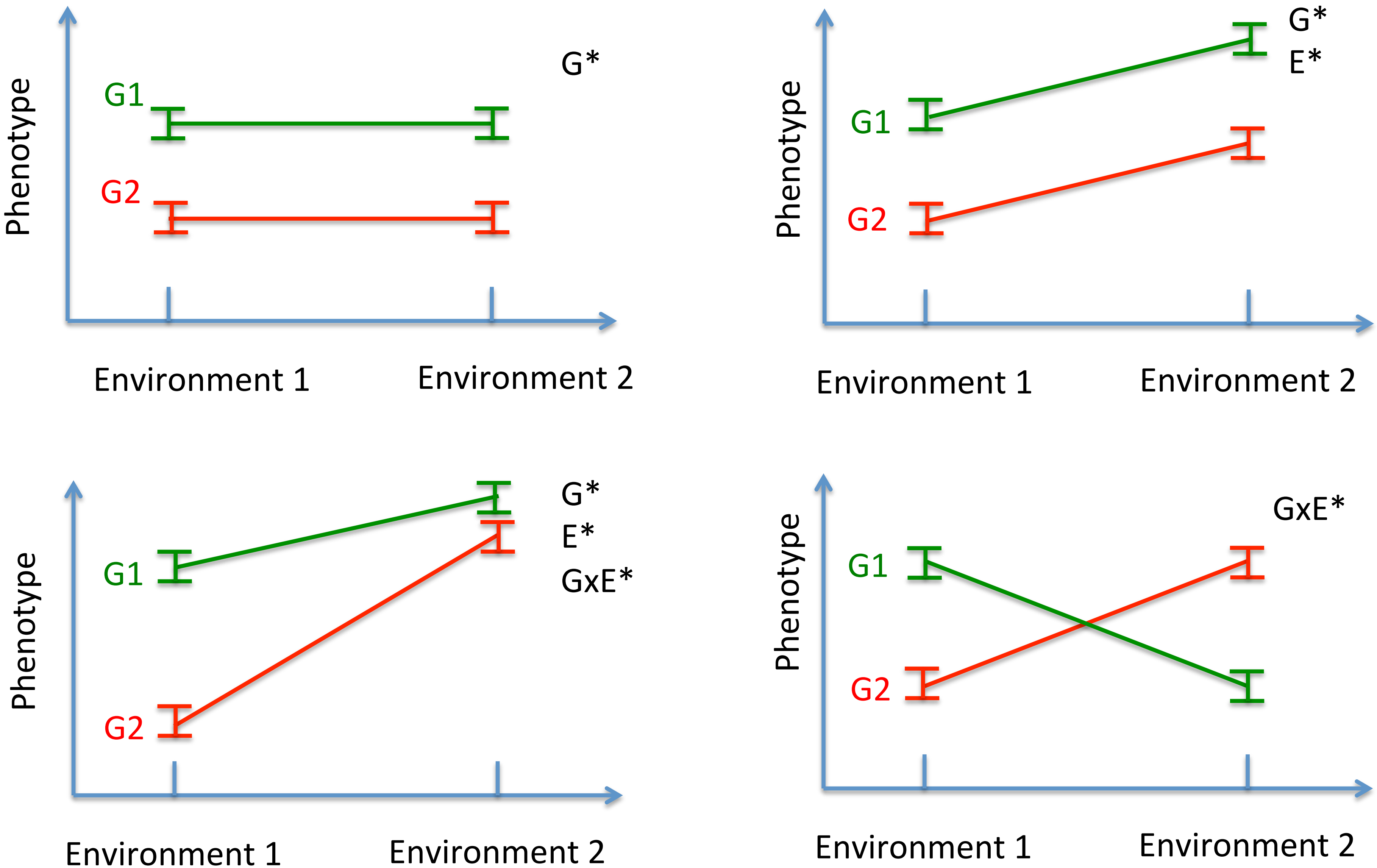
The reaction norm: *graph representing the phenotype as a function of the environment*

First drawn by Woltereck (1909) who however mis-interpreted them as the distinction between Genotype and Phenotype was made only in 1911 by Johannsen.



(Gibert P et al., 2000)

Analyses of reaction norms (using Analysis of Variance)



The genetics of phenotypic plasticity:

The idea that plasticity is under genetic control was initially developed by Bradshaw (1965)

Two genetic mechanisms were proposed (Via, 1995):

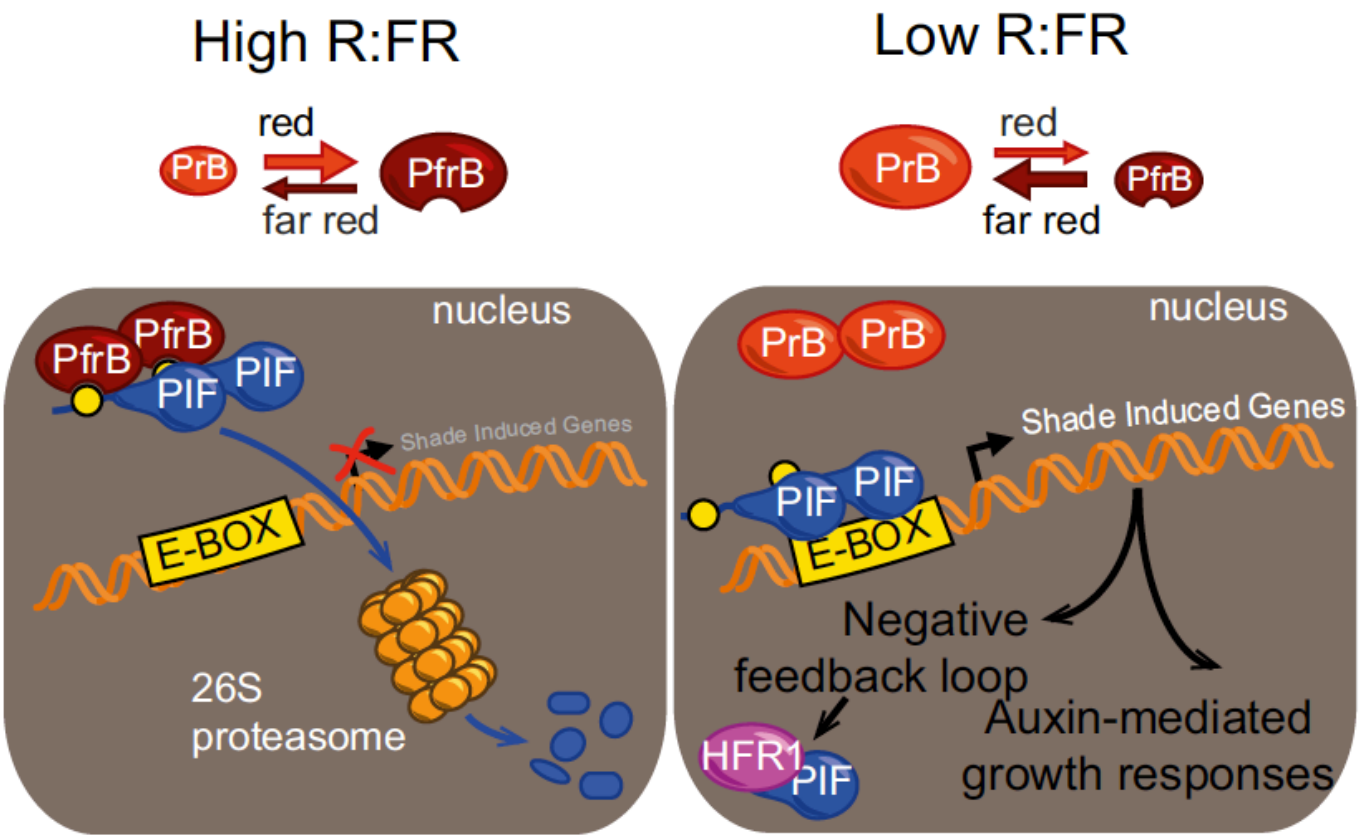
-allelic sensitivity

-gene regulation

But these to categories may blur.

How is the environmental cue perceived and integrated in gene regulatory network?

Shade avoidance in plants:
role of phytochromes in plants: detection of Red/Far Red ratio



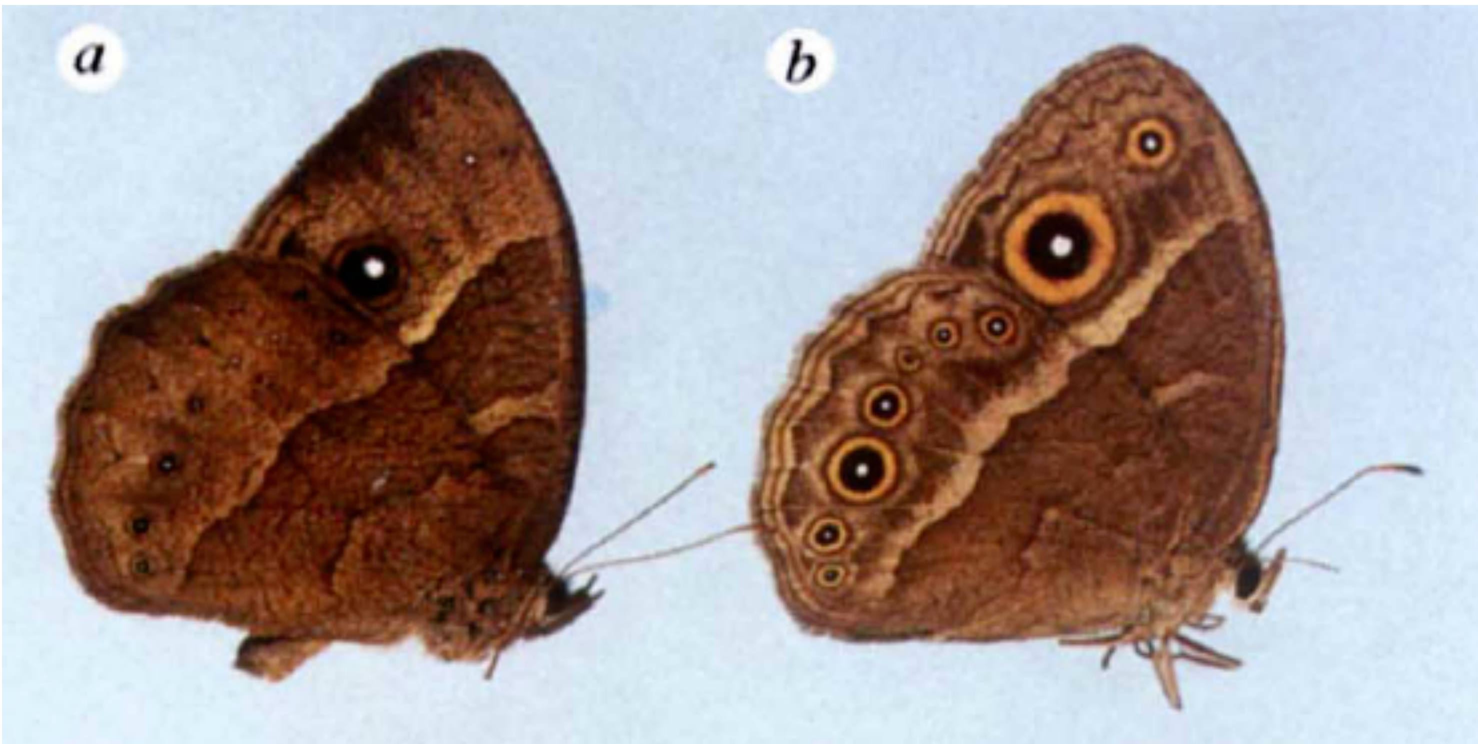
(Hersch et al., 2014)

Environmental conditions can strongly affect the transcriptome

Study of Drosophila adults transcriptome in 20 different environmental conditions: 15% of expressed genes show transcriptional plasticity (Zhou et al., 2012).

Environmental conditions modulate the expression of developmental regulatory genes:

Bicyclus anynana polyphenism



Dry season form
17°C

Wet season form
27°C

(Brakefield et al., 1996)

Distalless expression modulation in the butterfly *Bicyclus anynana* correlates with wing eyespot plasticity (Brakefield et al., 1996). Functional analyses show that *Distalless* is involved in eyespot formation (Monteiro et al., 2013).

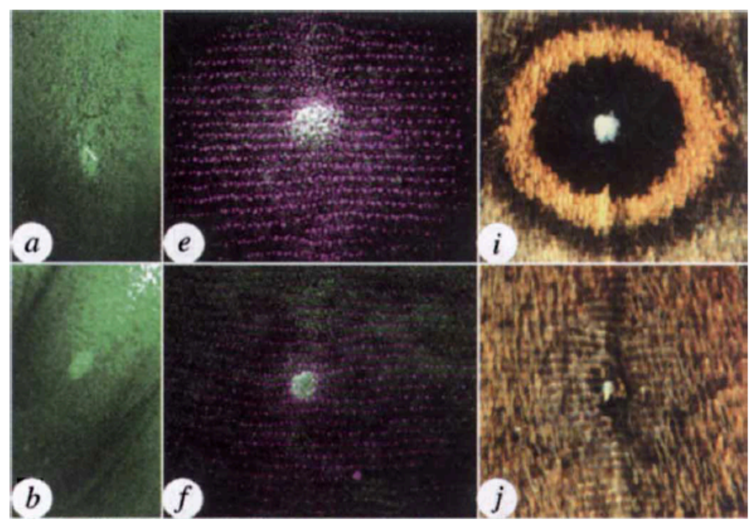
Late fith instar

24h after pupation

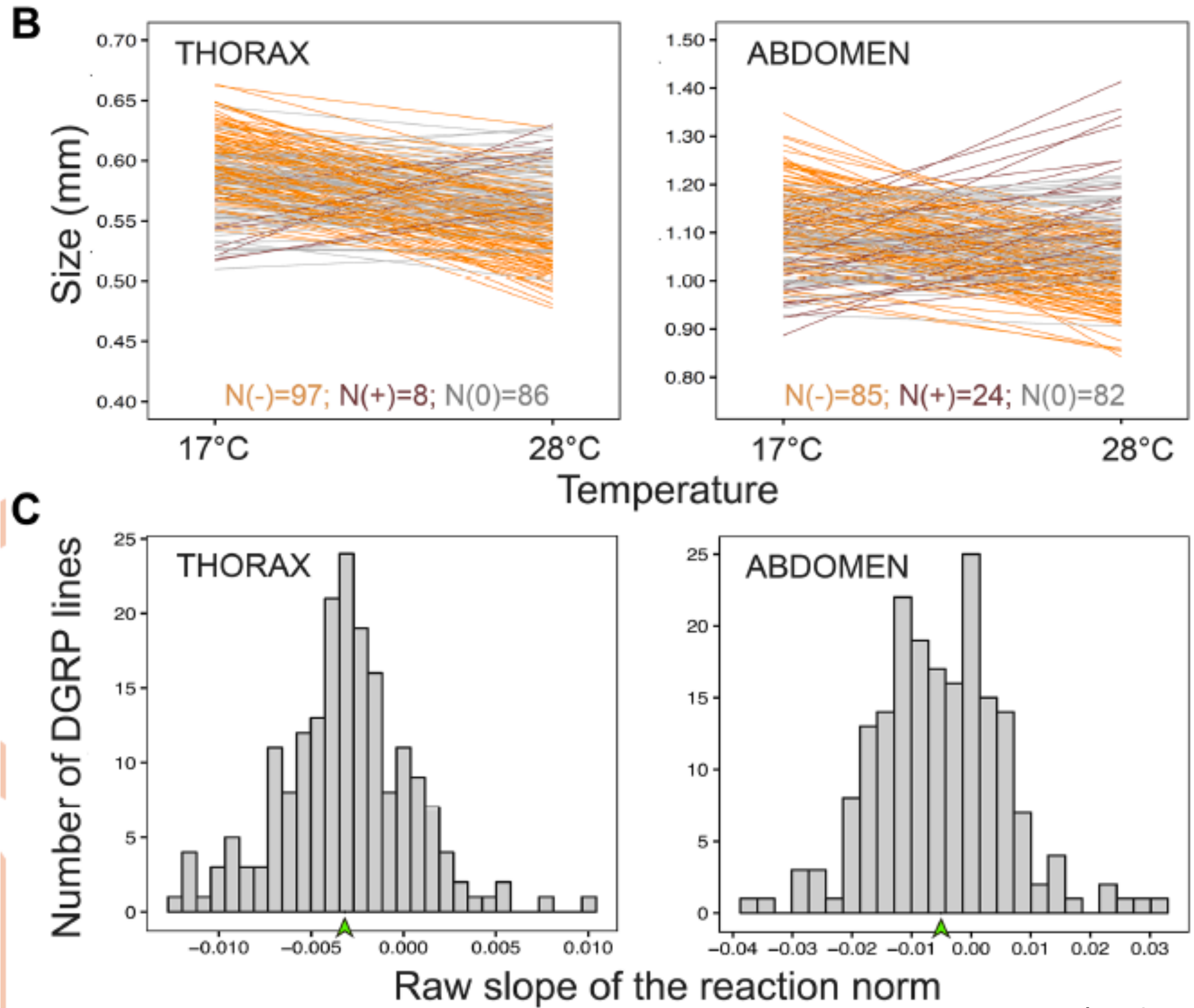
Adult phenotype

Wet-season form

Dry-season form

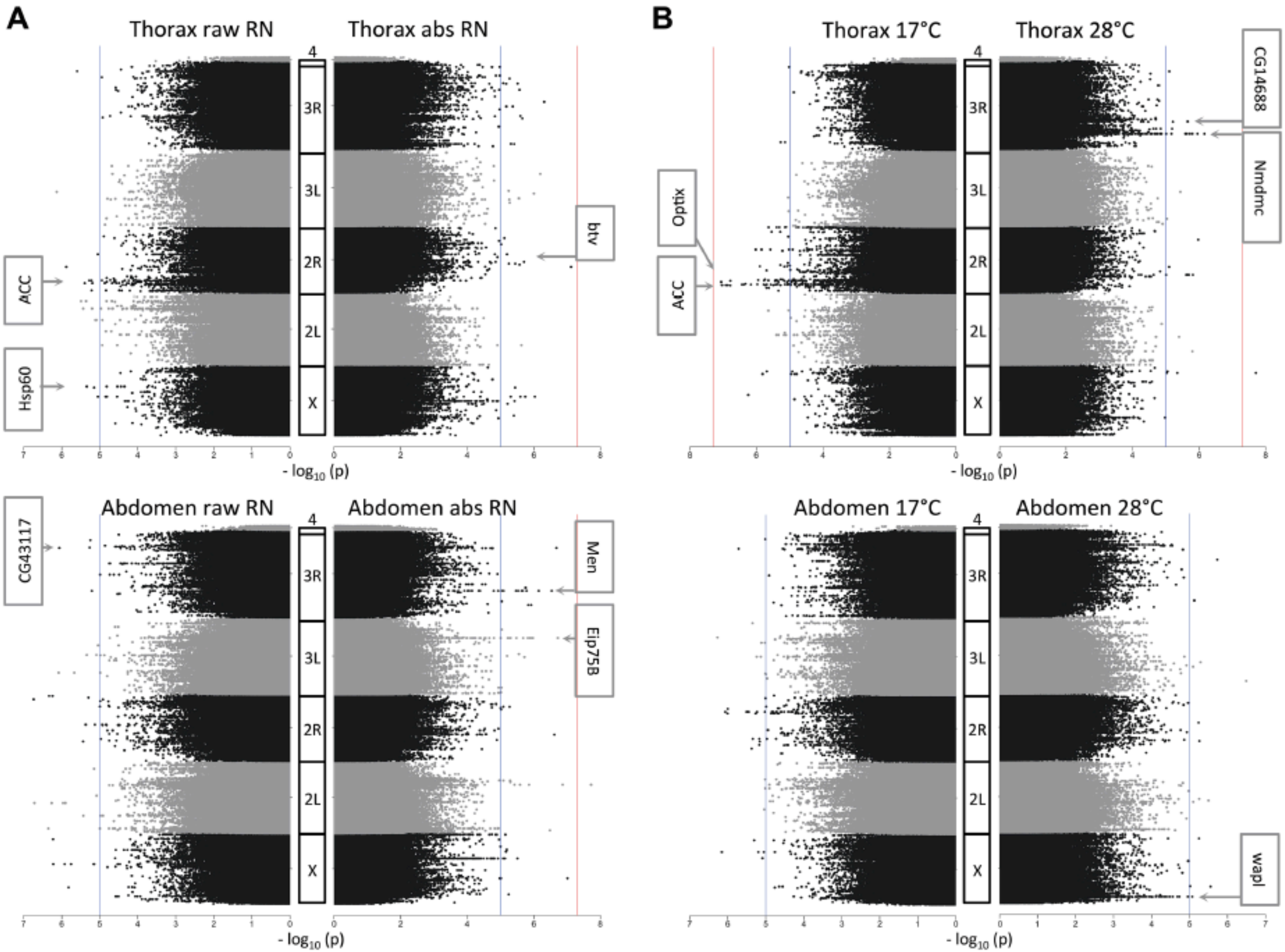


Mapping genetic variation for plasticity: example of size thermal plasticity in *Drosophila*



(Lafuente et al., 2018)

Identification of SNPs affecting size thermal plasticity or size



GWAS for plasticity of size

GWAS for size (Lafuente et al., 2018)

Epigenetic bases of phenotypic plasticity

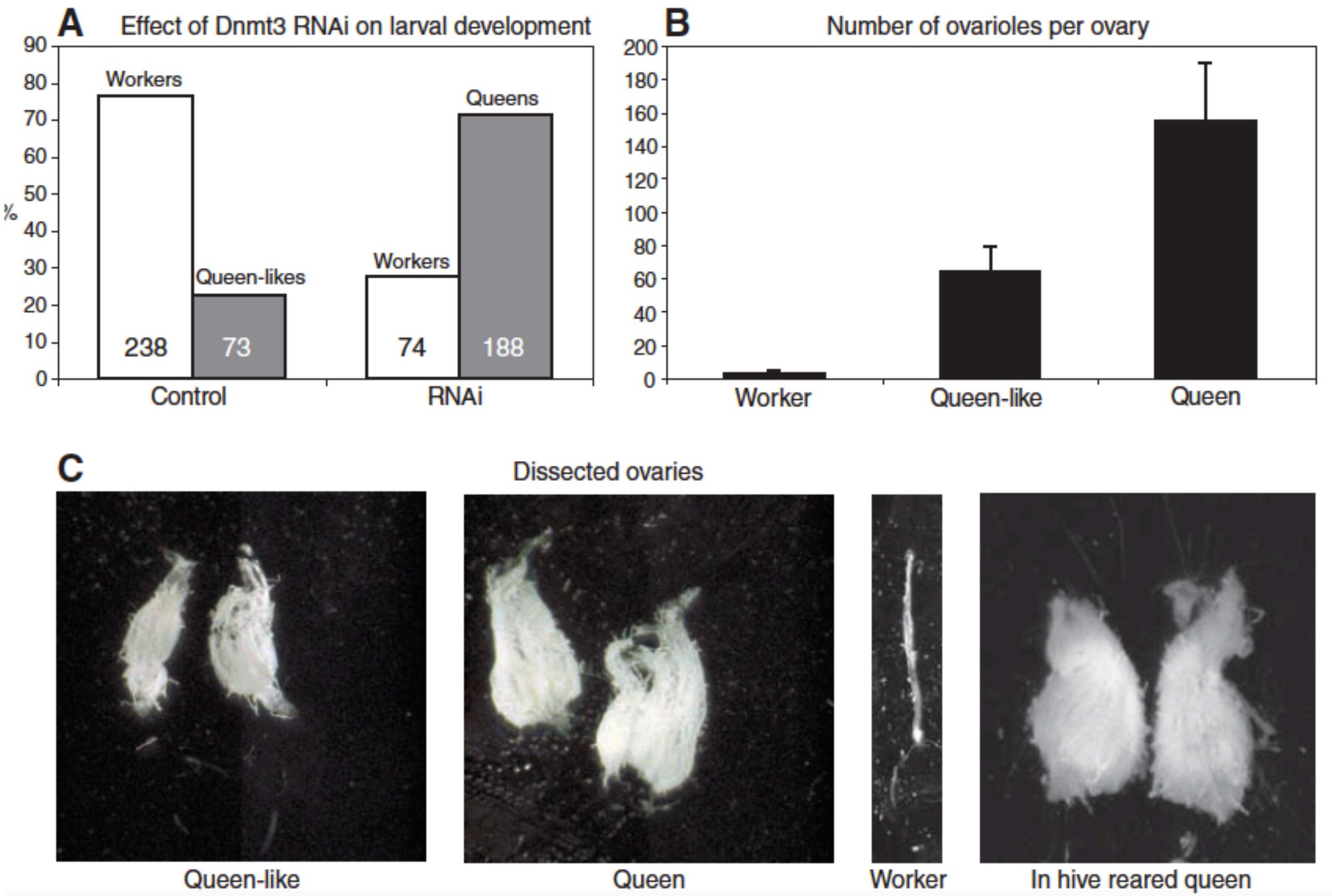
Epigenetics: The study of mitotically and/or meiotically heritable changes in gene function that cannot be explained by changes in DNA sequence" (Russo et al. 1996)

High fat diet induced chromatin remodeling in mouse liver (Leung et al., 2014).

Casts in the carpenter ant *Camponotus floridanus* and histone acetylation (Simola et al., 2012, 2016).

Honeybee casts and DNA methylation (Kucharski et al., 2008).

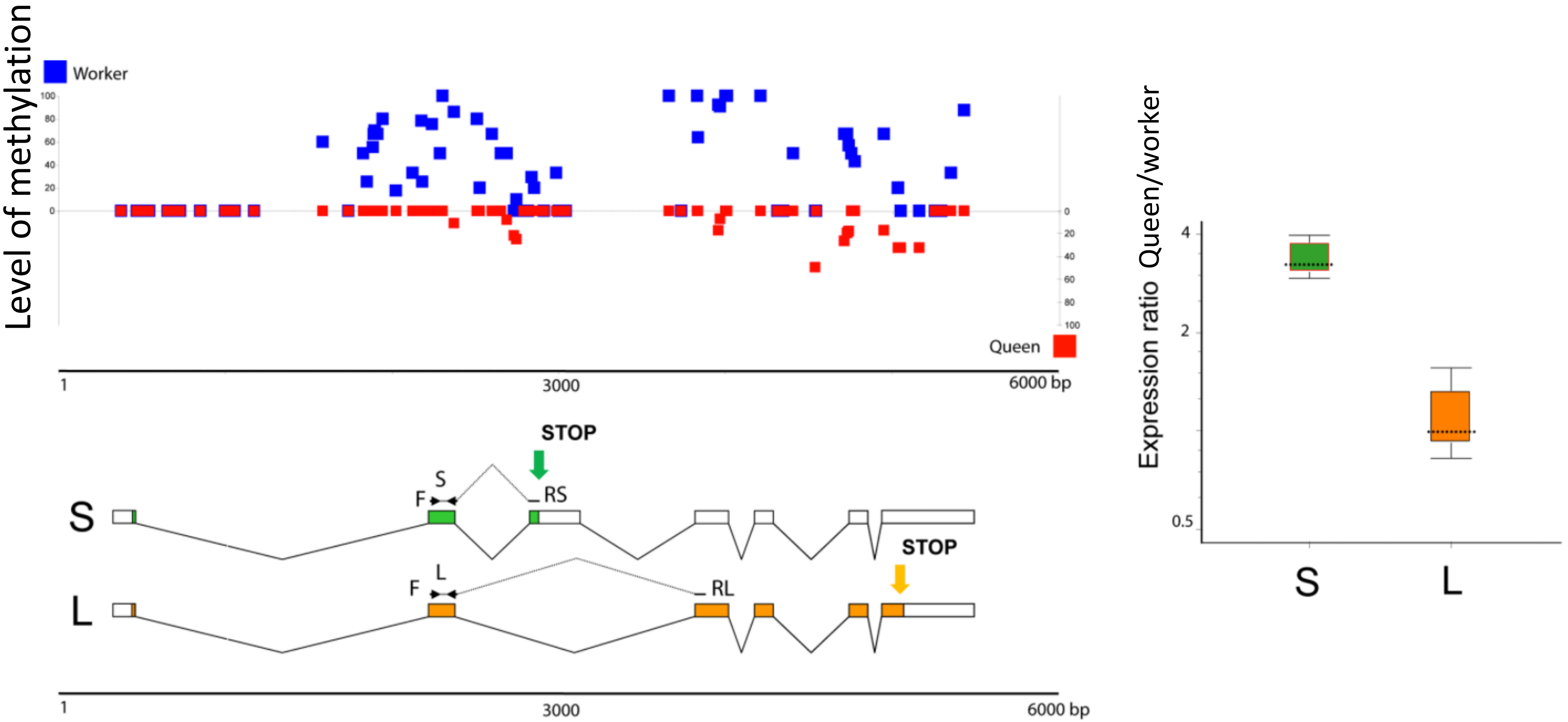
Effect of inactivation of DNA methyl transferase Dnmt3 in the honeybee



(Kucharski et al., 2008)

Difference of DNA methylation between honeybee casts

Over 550 genes show differential methylation in queen and worker brains.



exemple of the gene GB18602 in queen and worker brains

(Lyko et al., 2010)

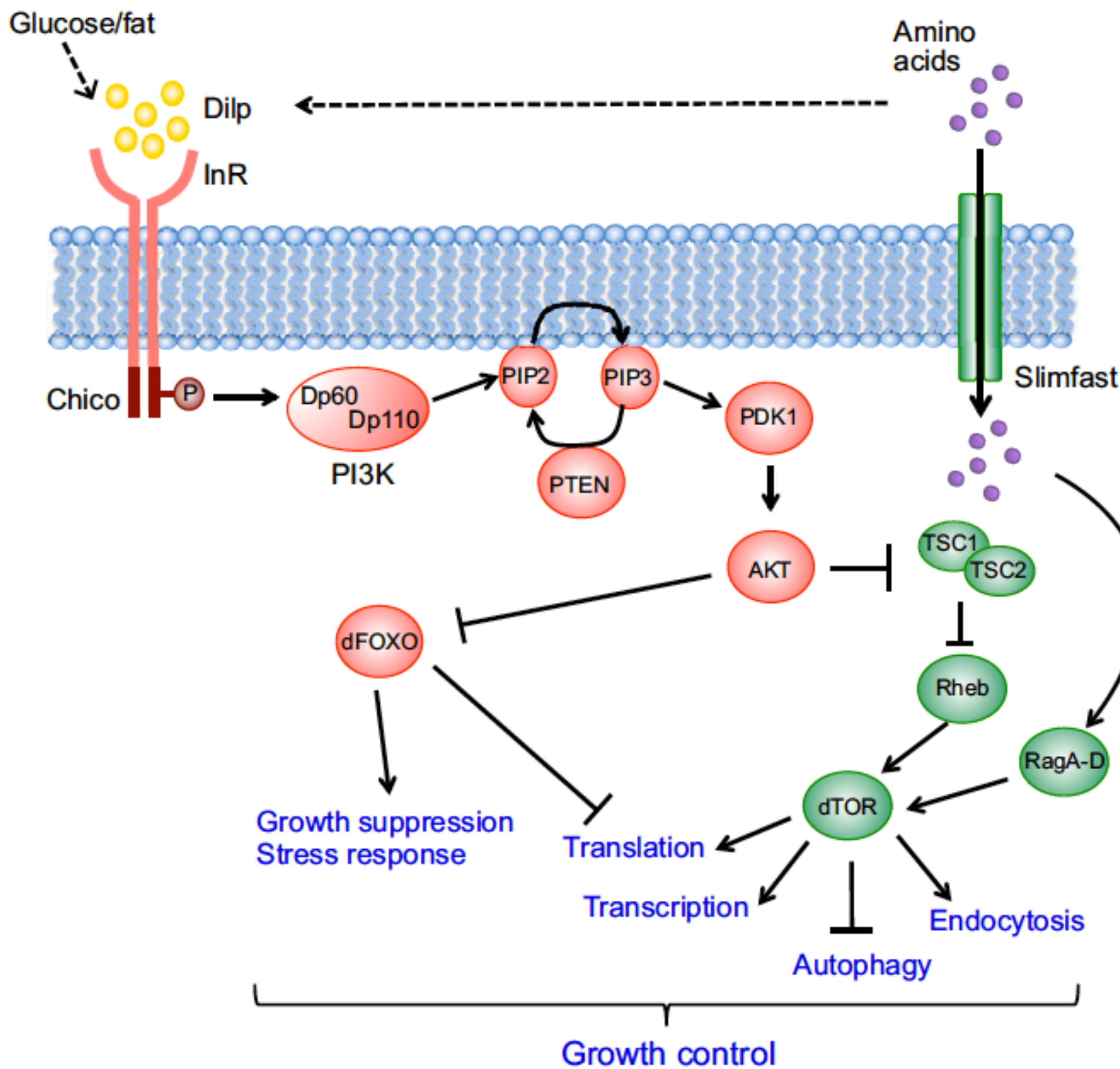
Hormonal bases of phenotypic plasticity

Corticotropin releasing hormone and reduction of developmental time in desiccating environment in amphibians (Denver, 1997).

Ecdysone and *Bicyclus anynana* eyespot plasticity (Monteiro et al., 2015).

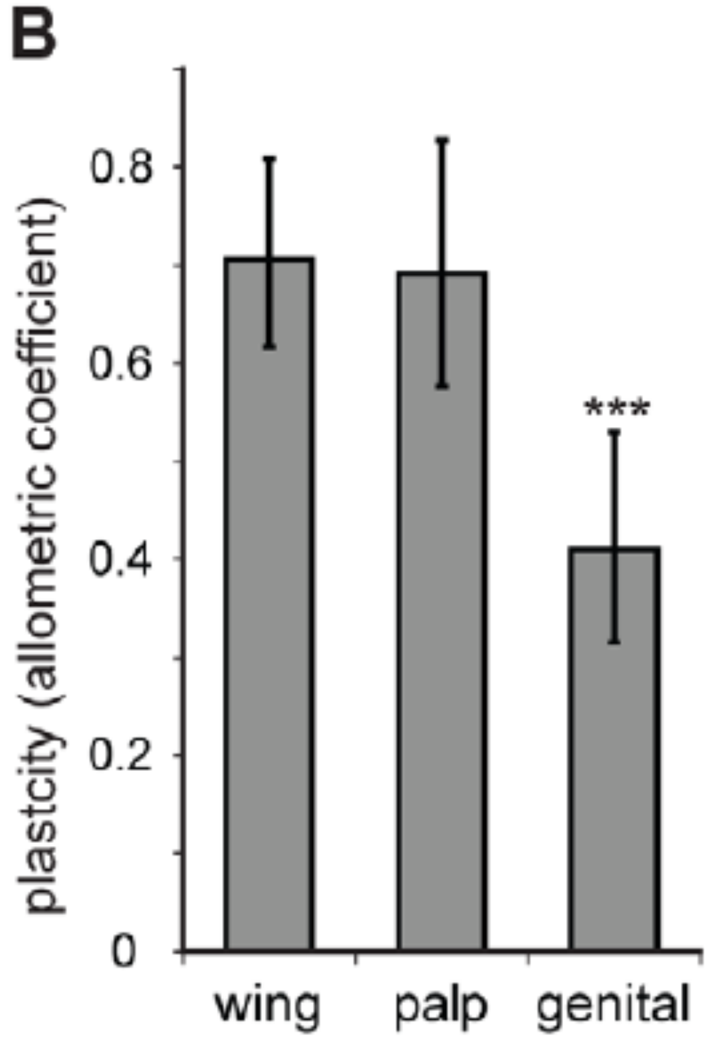
Insulin and nutritional plasticity in *Drosophila* (Tang et al., 2011).

The Insulin pathway in Drosophila



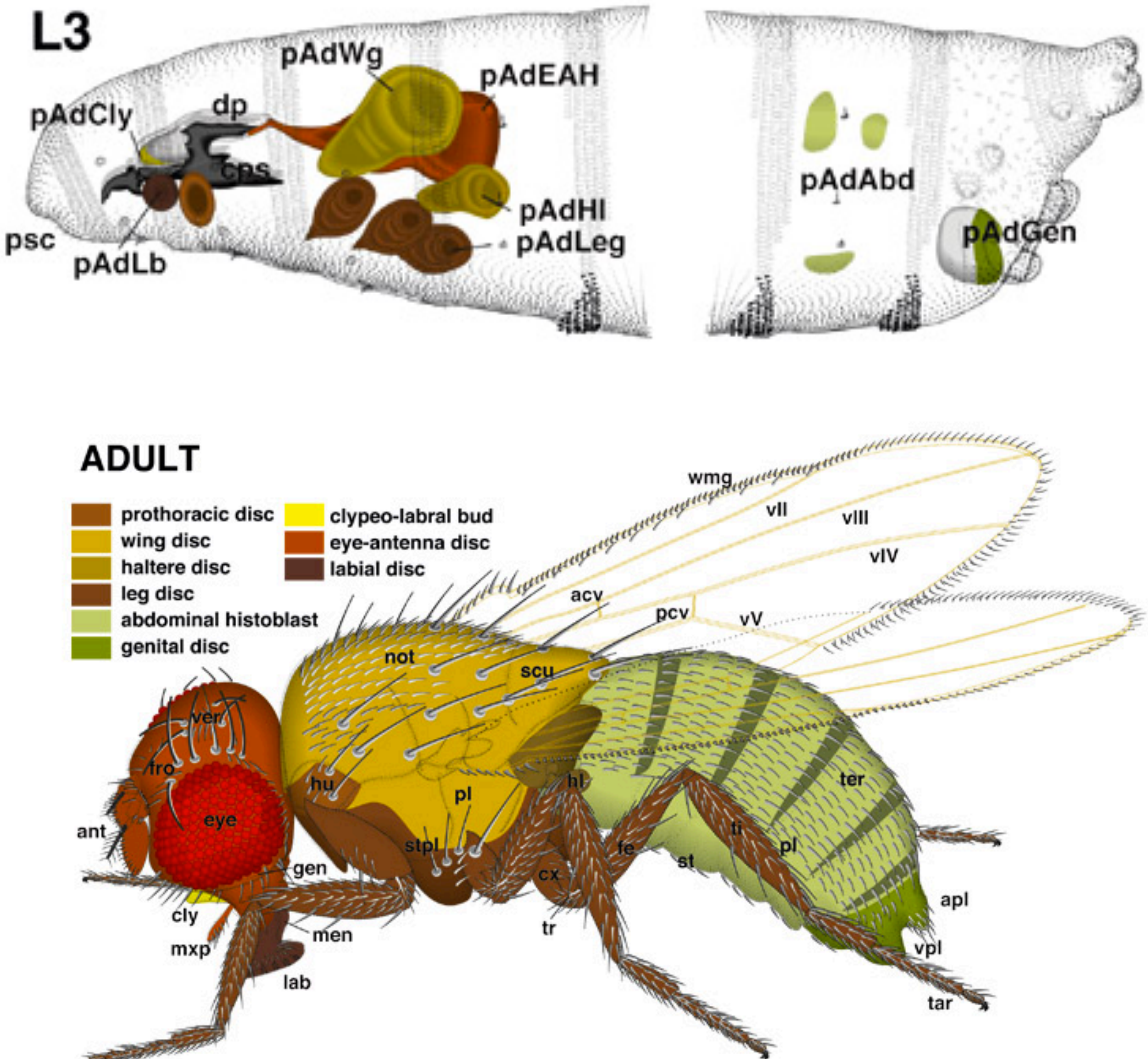
(Shim et al., 2013)

Nutritional plasticity differs between appendages in *Drosophila*



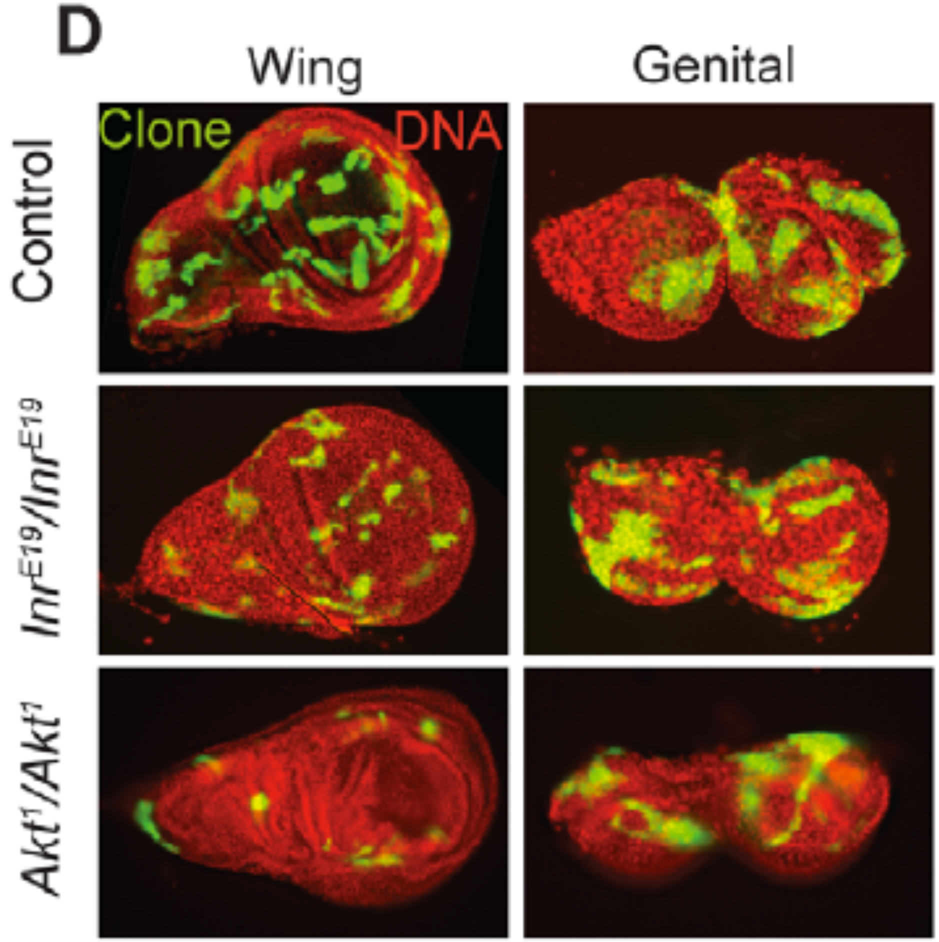
(Tang et al, 2011)

The imaginal discs of *Drosophila*



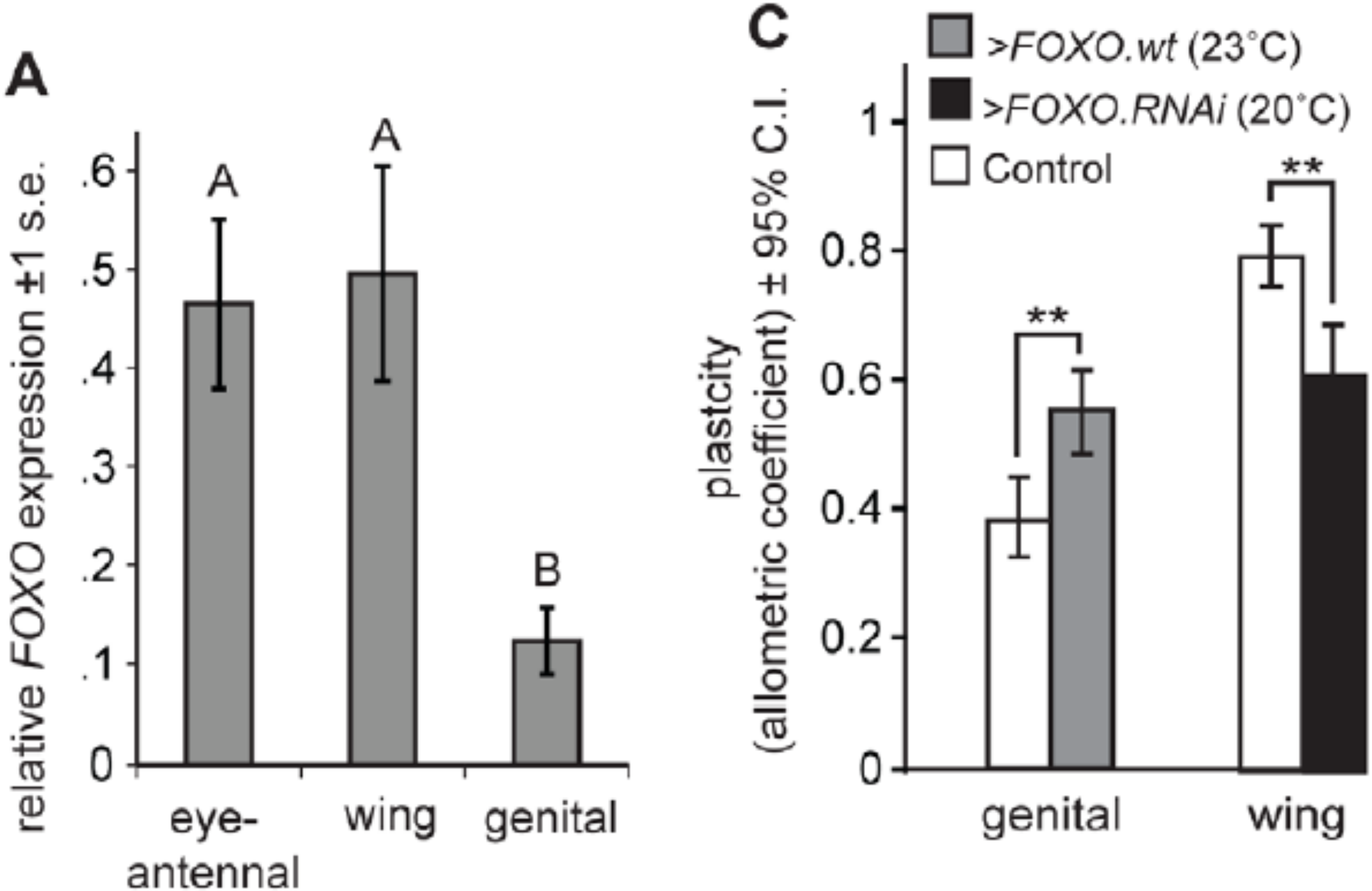
(Hartenstein, 1993)

Loss of activity of the insulin pathway has different effects depending on the appendage in *Drosophila*



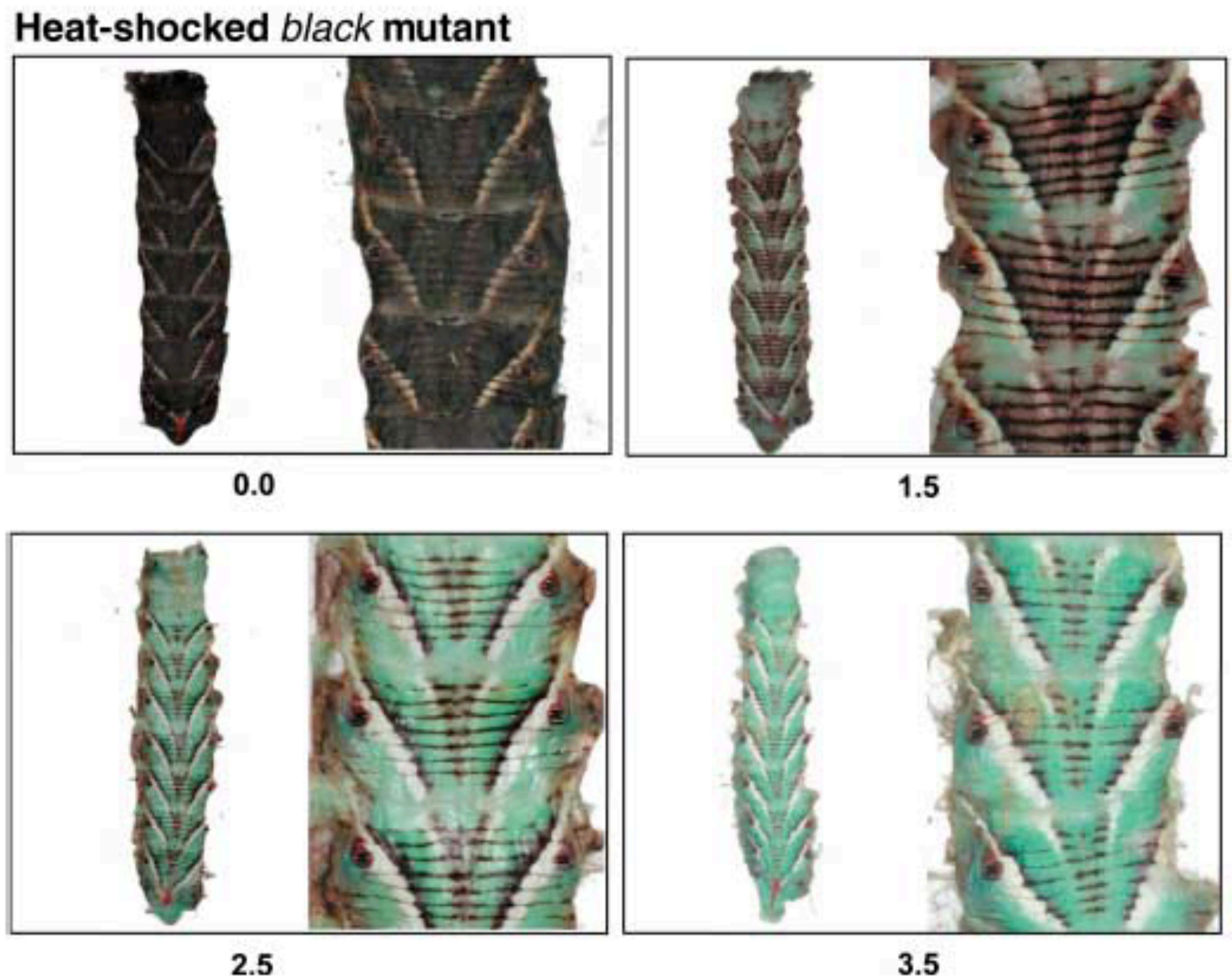
(Tang et al, 2011)

Differential expression of *foxo* explains the difference of nutritional plasticity between the wing and the genitals



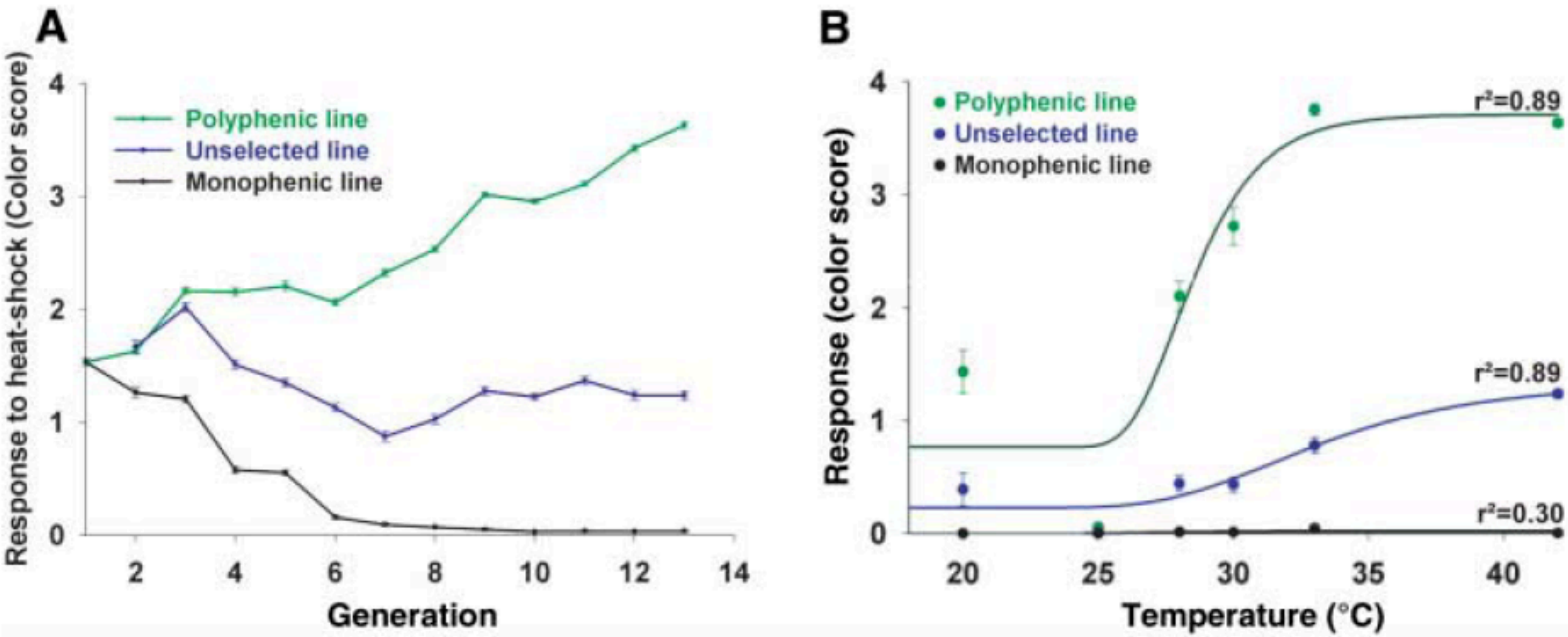
(Tang et al., 2011)

Artificial selection on phenotypic plasticity in *Manduca sexta*



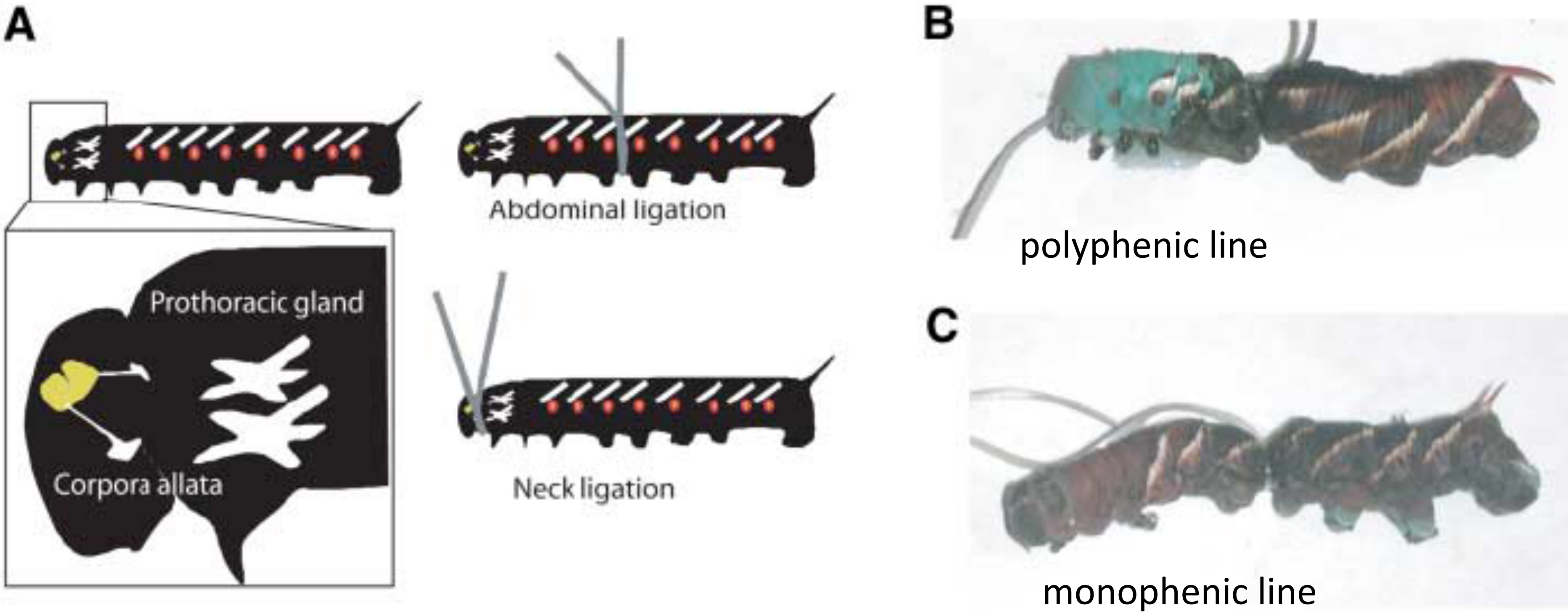
(Suzuki and Nijhout, 2006)

Artificial selection on phenotypic plasticity in *Manduca sexta*



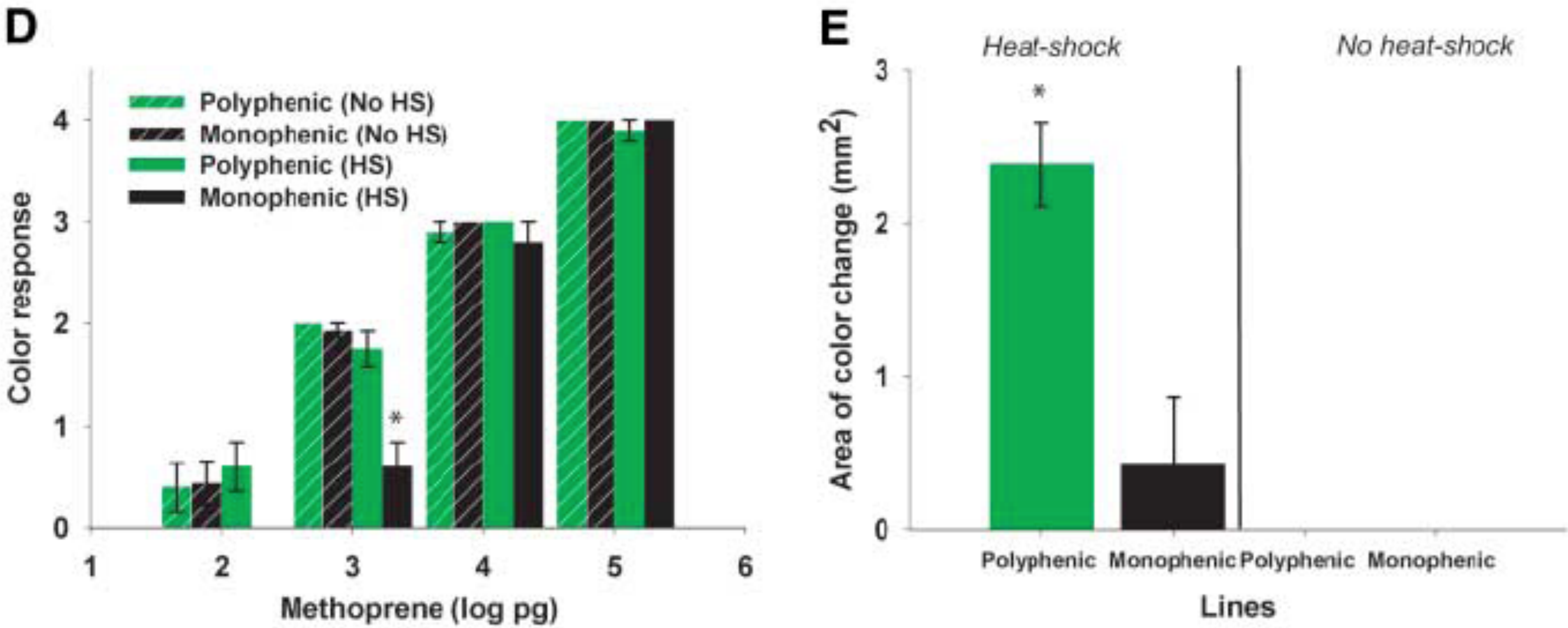
(Suzuki and Nijhout, 2006)

Artificial selection on phenotypic plasticity in *Manduca sexta*



(Suzuki and Nijhout, 2006)

Artificial selection on phenotypic plasticity in *Manduca sexta*



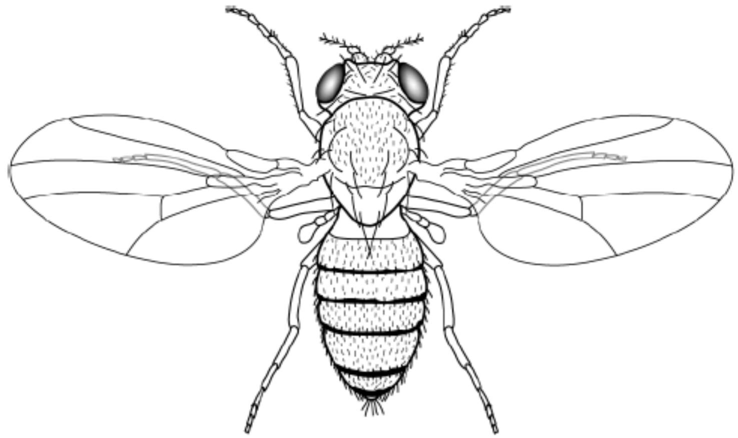
The monophenic line has a reduced JH sensitivity at high temperature.

The polyphenic line has a higher juvenile hormone (JH) titer at high temperature;

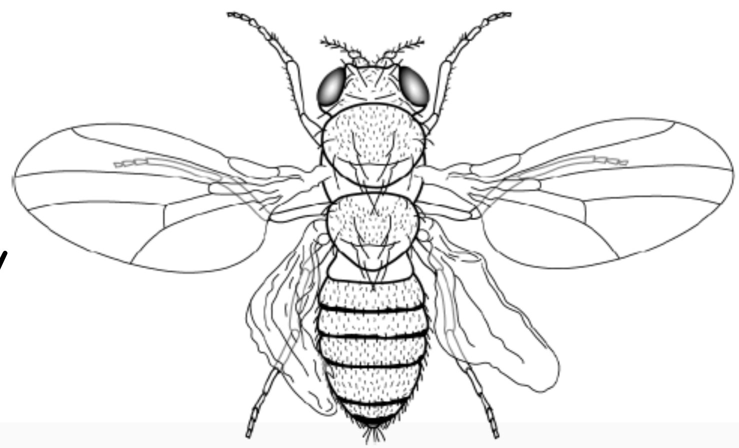
(Suzuki and Nijhout, 2006)

Genetic assimilation of ether induced Bithorax phenocopies

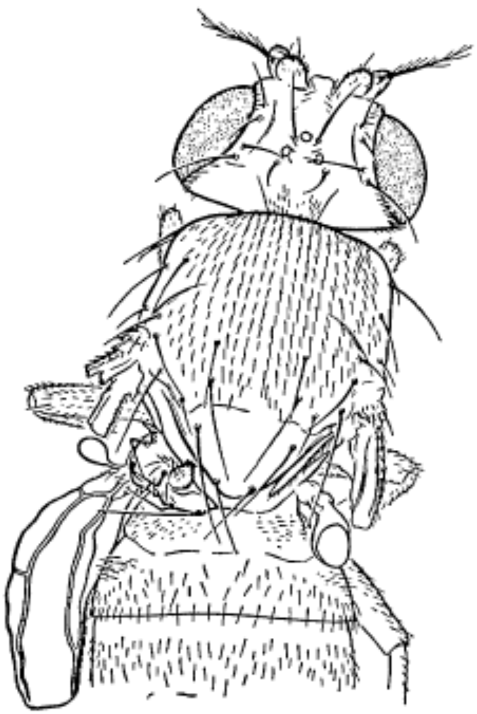
Wild-type fly

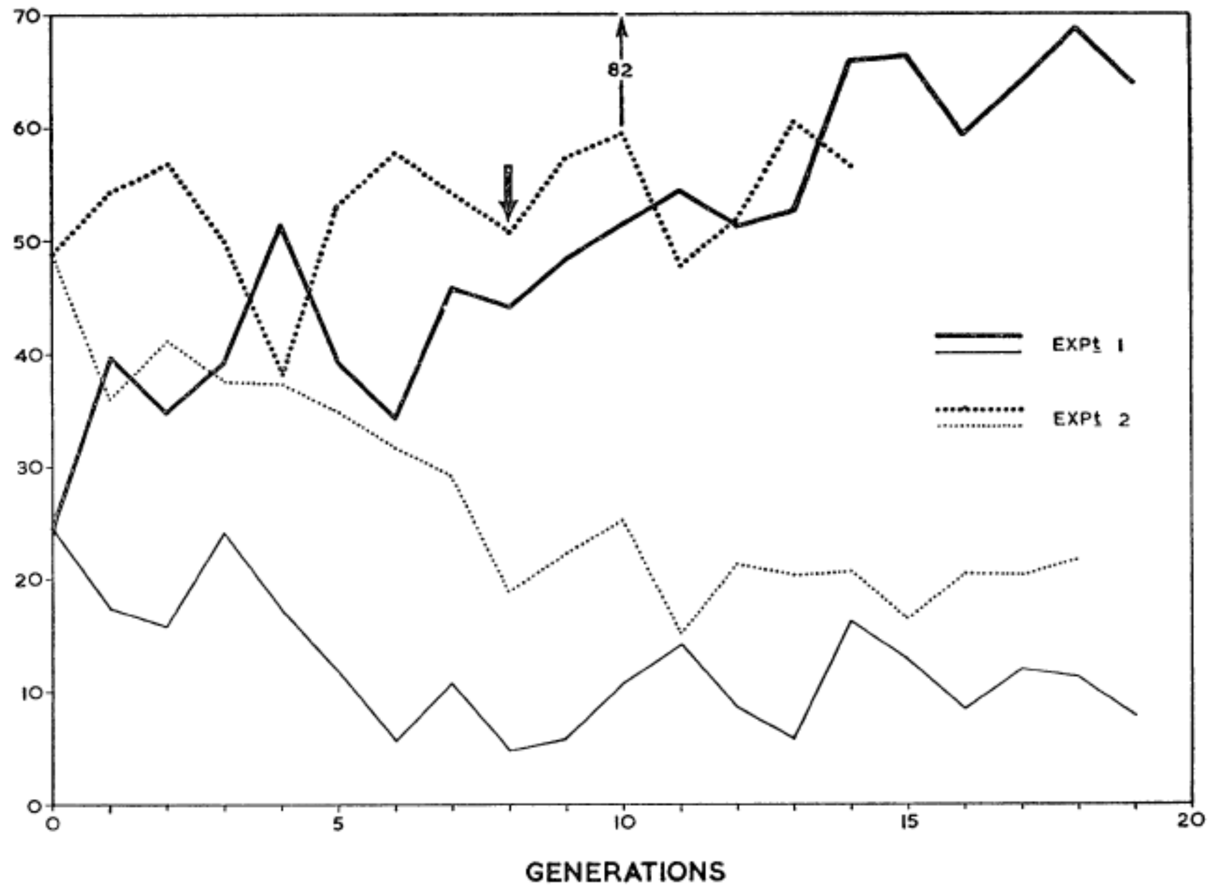


Bithorax phenocopy



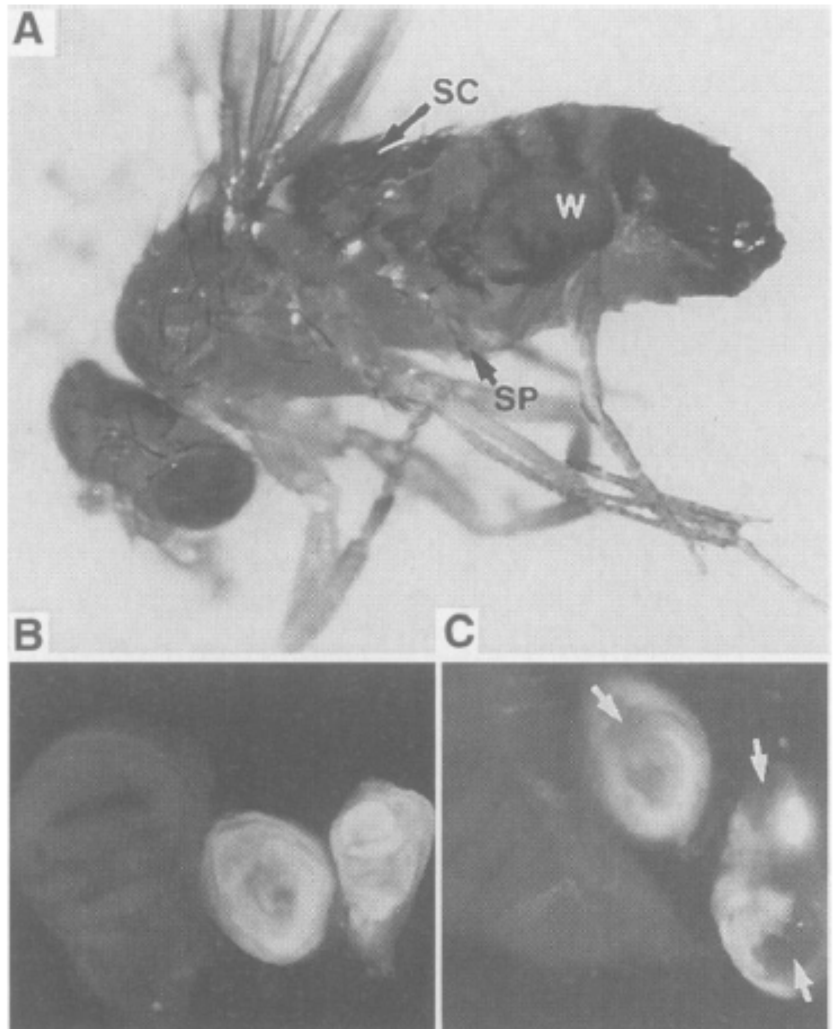
Selection for increased and decreased proportions of ether induced Bithorax phenocopies





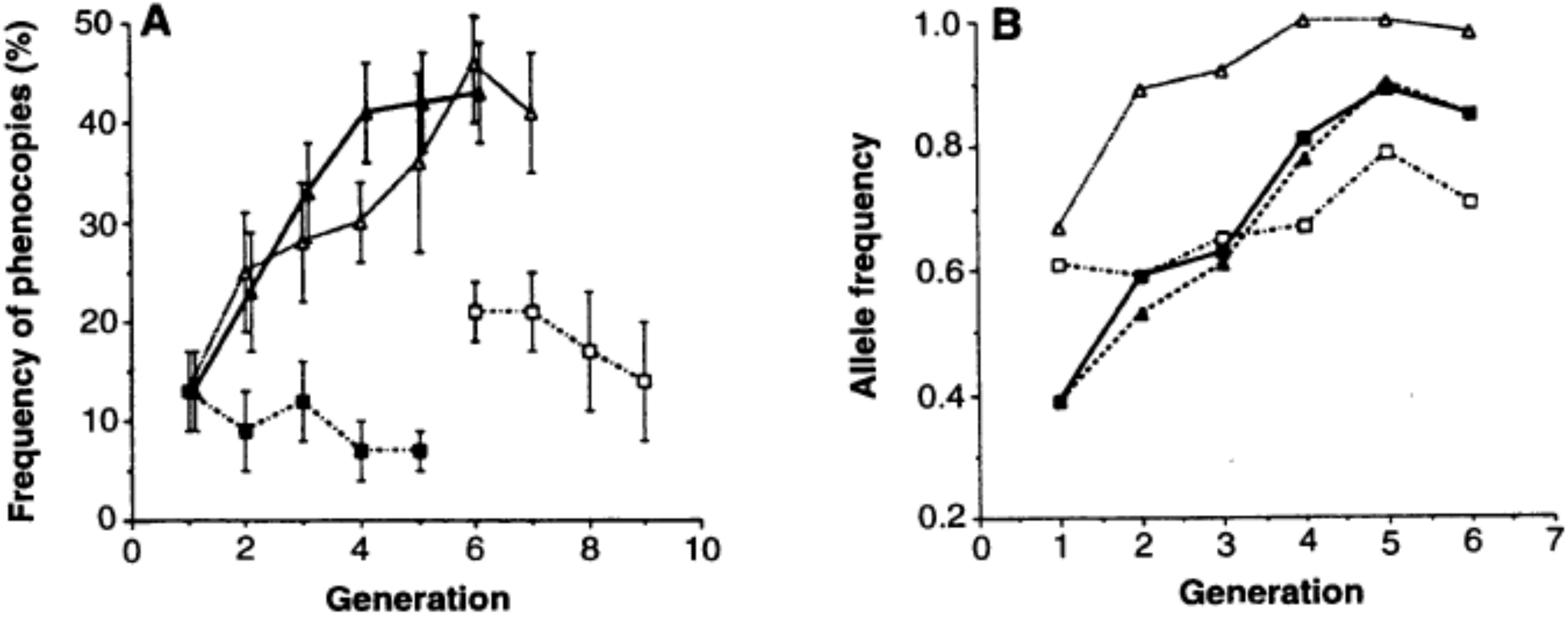
(Waddington, 1956)

Ether induced Bithorax phenocopies correspond to loss of expression of *Ubx*



(Gibson et Hogness, 1996)

Selection of *Ubx* alleles during genetic assimilation of the Bithorax phenotype



(Gibson et Hogness, 1996)

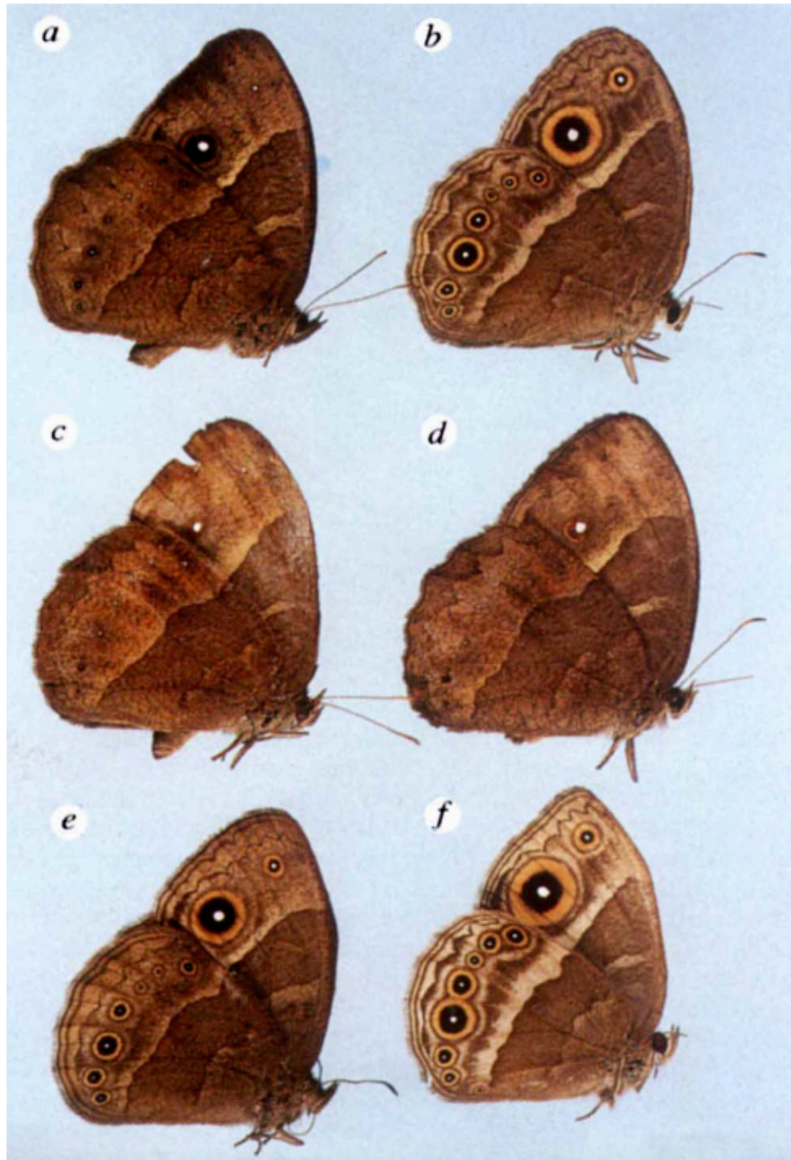
Genetic assimilation in the polyphenic butterfly *Bicyclus anynana*

17°C 27°C

WT line

Low line

High line



(Brakefield et al., 1996)

Genetic assimilation

Defined by Waddington (1952, 1959):

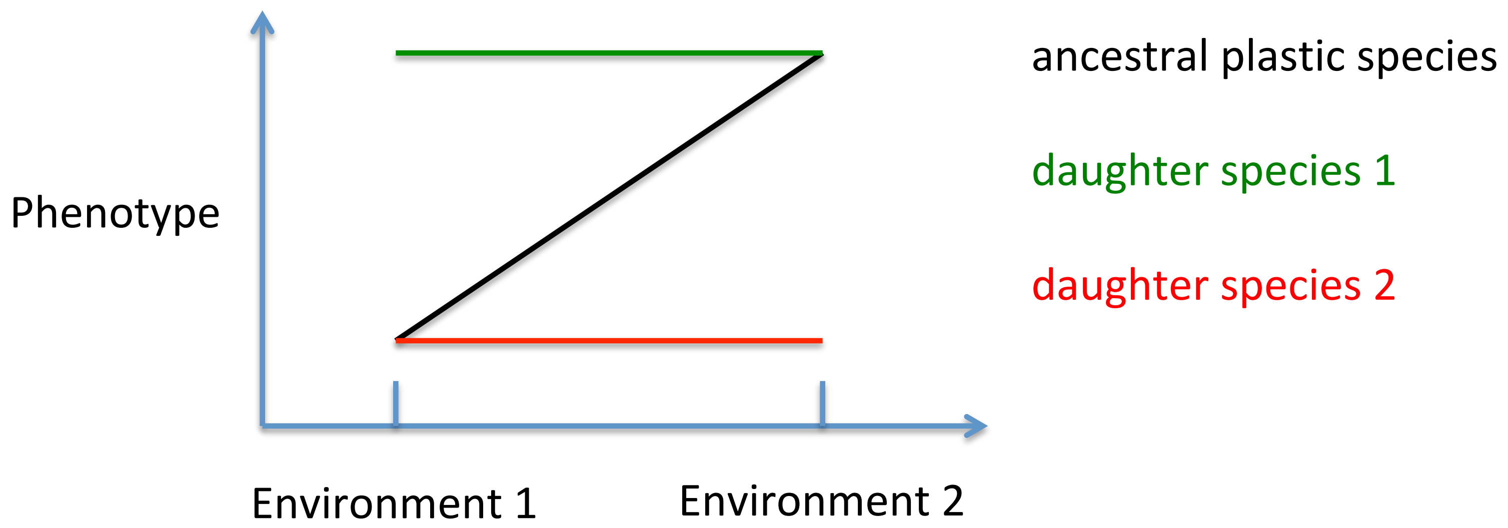
Environmental changes can reveal cryptic genetic variation and induce new phenotypes in some individuals.

This genetic variation can be selected allowing to fix a phenotype initially observed only in particular environmental conditions.

Some of Waddington's experiments were repeated with isogenic or outbred stocks and it was shown that genetic variation was necessary for genetic assimilation (Bateman, 1959).

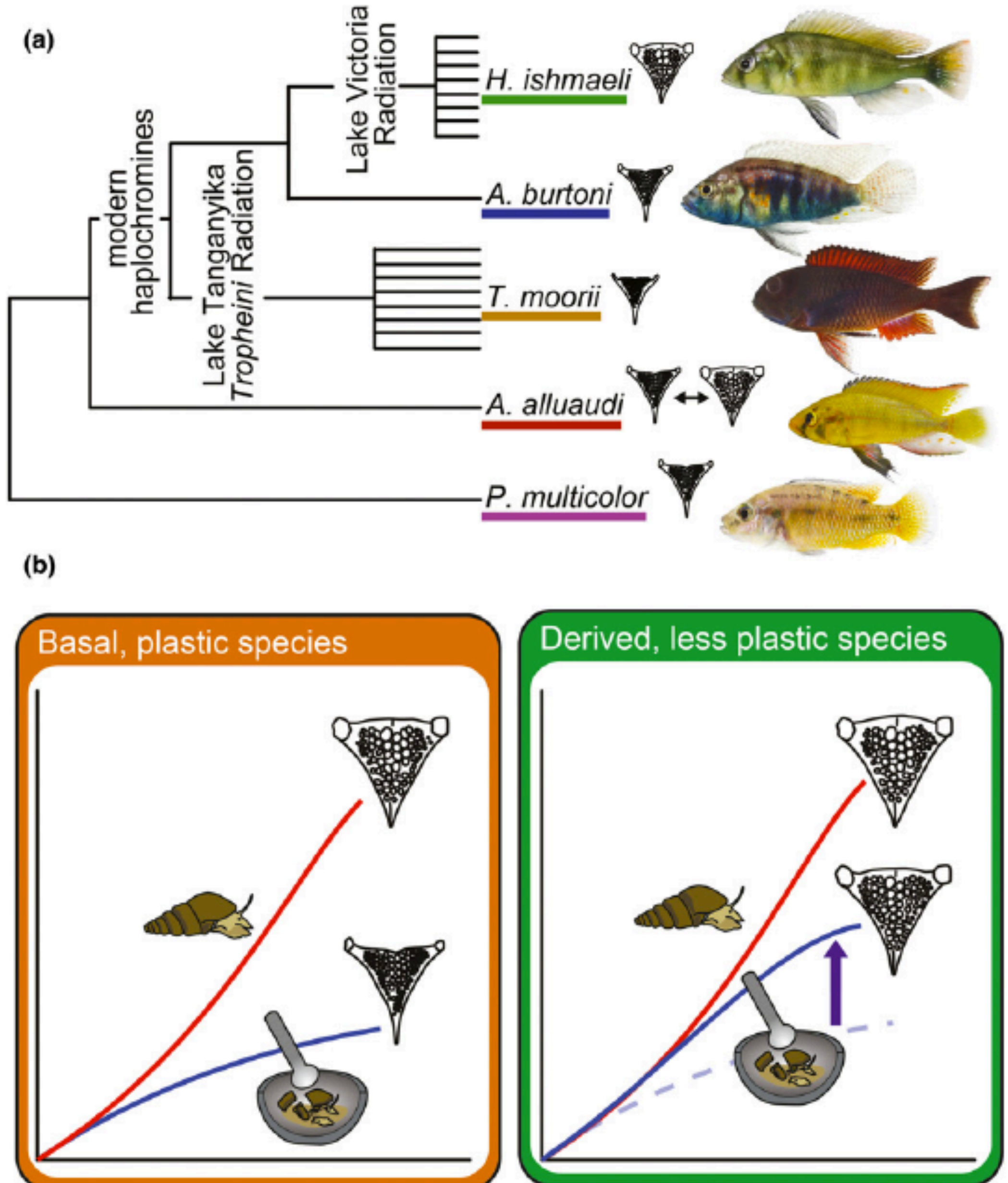
However, in a recent study, it was shown that de novo mutation induced by the environment (heatshock) can be involved in genetic assimilation (Fanti et al., 2017).

The idea that an ancestral plastic species can be at the origin of divergent species after fixation of the alternative morphs has been proposed by West-Eberhard as "*the flexible stem hypothesis*" (2003).



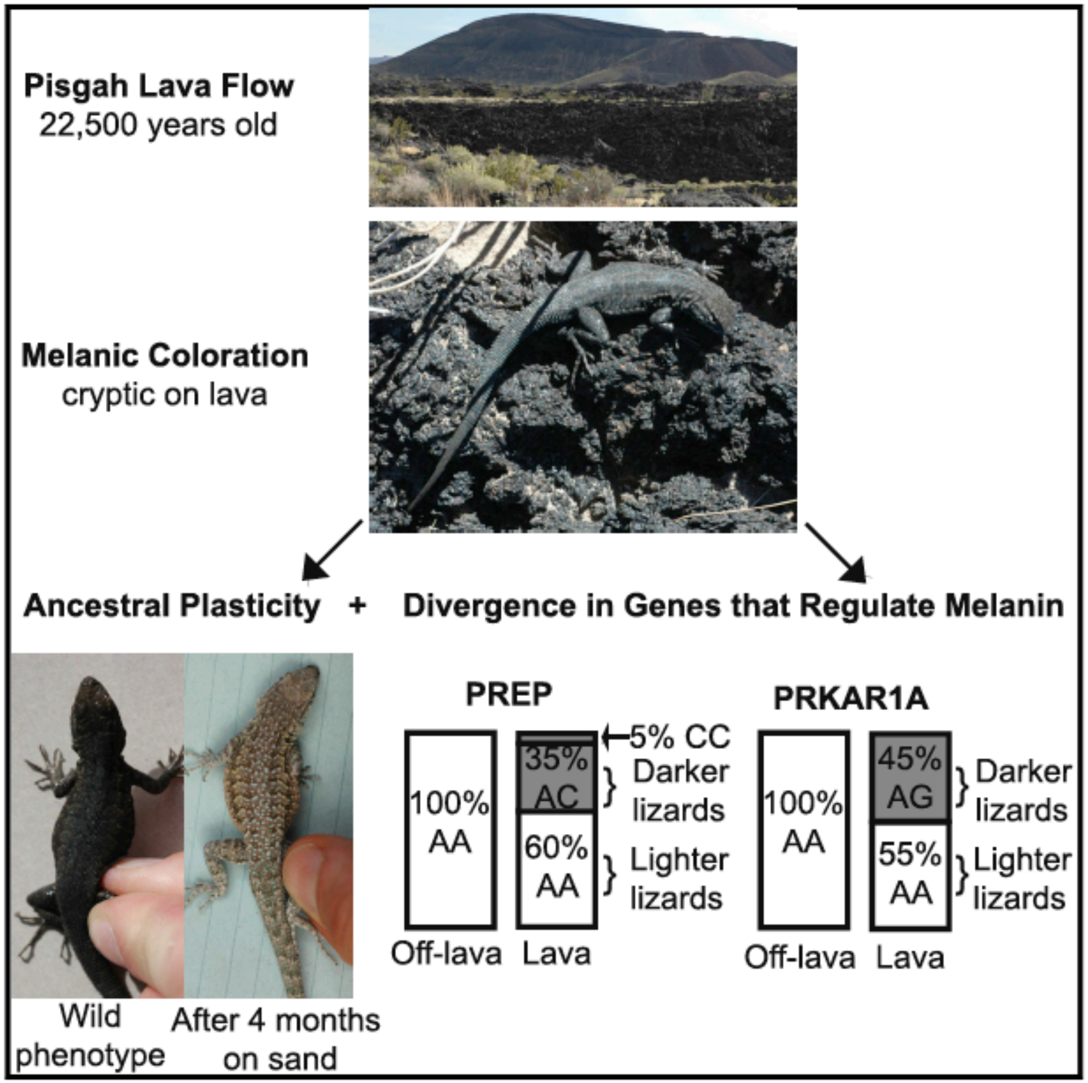
It is based on genetic assimilation discovered by Waddington.
The "*flexible stem hypothesis*" is also called "*plasticity first evolution*".

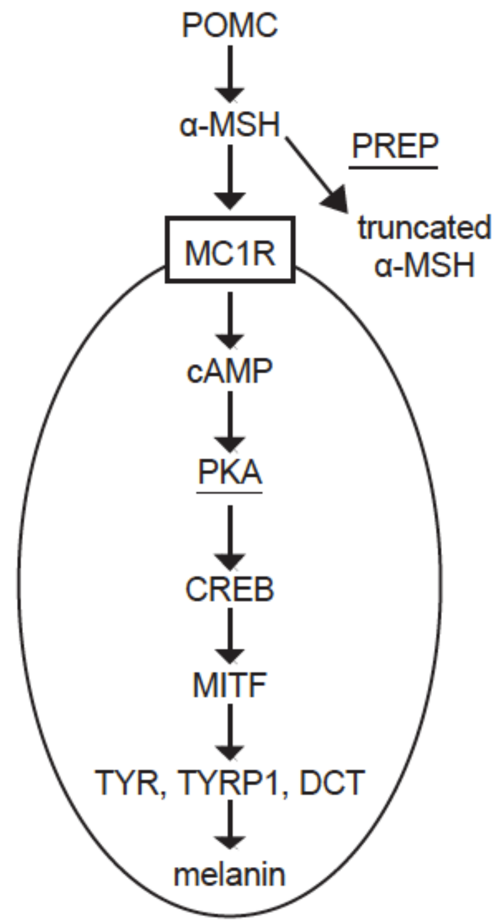
Plasticity first evolution in cichlid fishes



(Gunter et al., 2017)

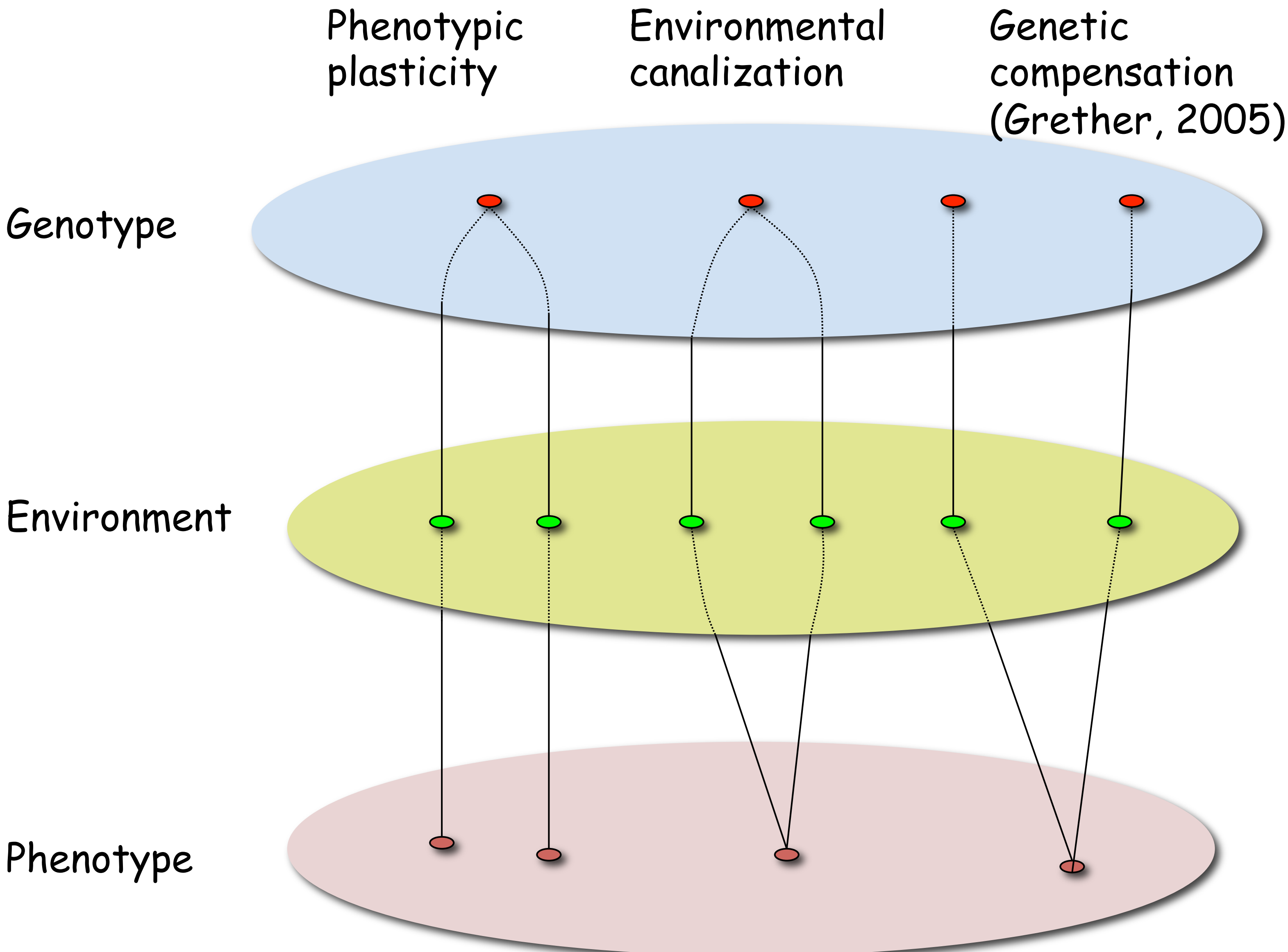
Plasticity first evolution in the lizard *Uta stansburiana*





(Corl et al., 2018)

The environment in the genotype-phenotype relation



Phenotypic plasticity is not always linked to differential gene expression

Influence of carotenoids present in the diet on pigmentation

(Price, 2006)

A study of the genetic bases of phenotypic plasticity: Pigmentation thermal plasticity in *Drosophila melanogaster*

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and Frédérique Peronnet

Developmental biology laboratory
CNRS-Sorbonne Université, IBPS
Paris

* equal contribution

Drosophila and temperature

In Drosophila temperature affects many traits:

Developmental rate,

Size,

Ovariole number,

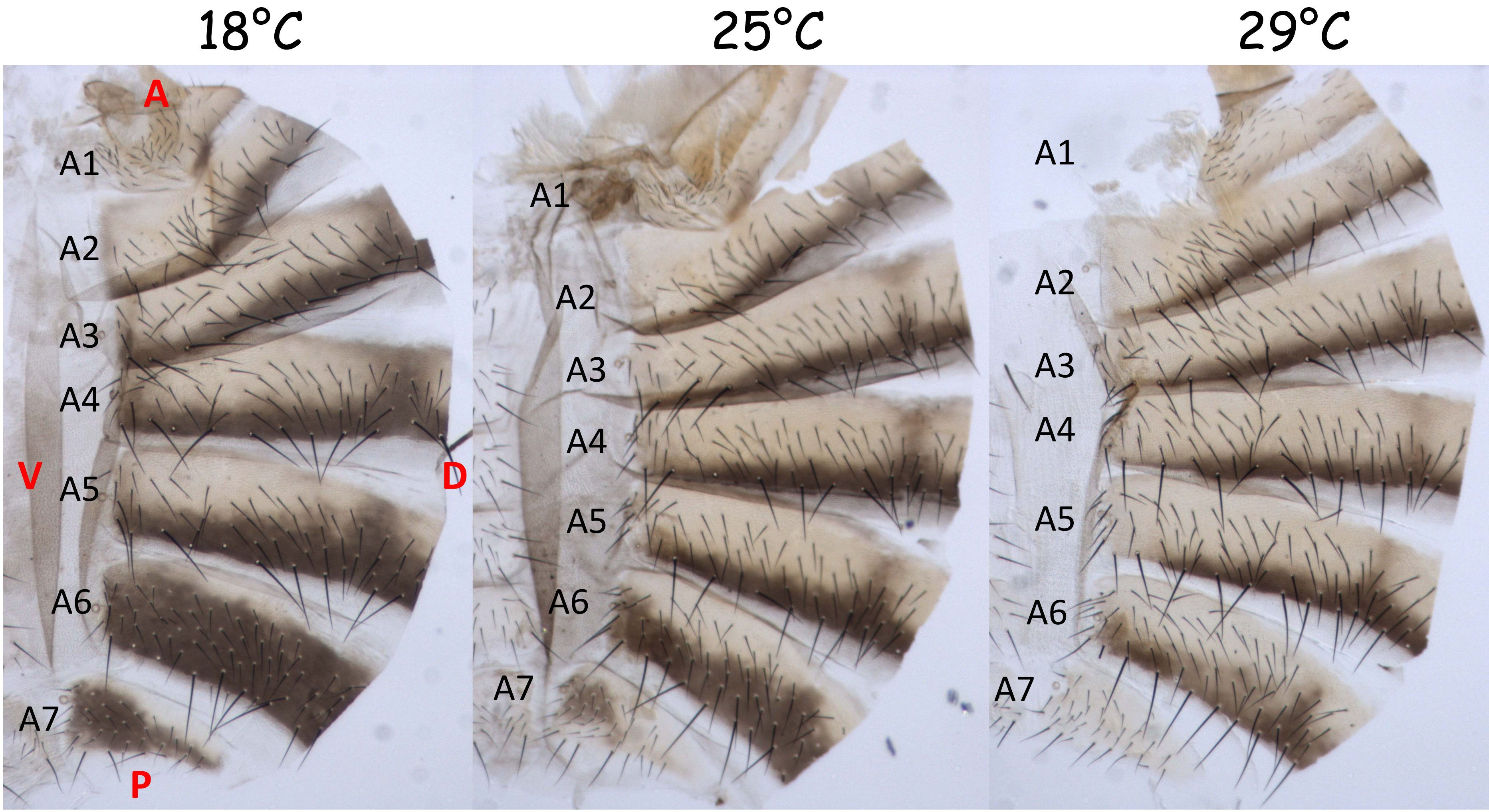
Bristle number,

Reproductive diapause,

Pigmentation

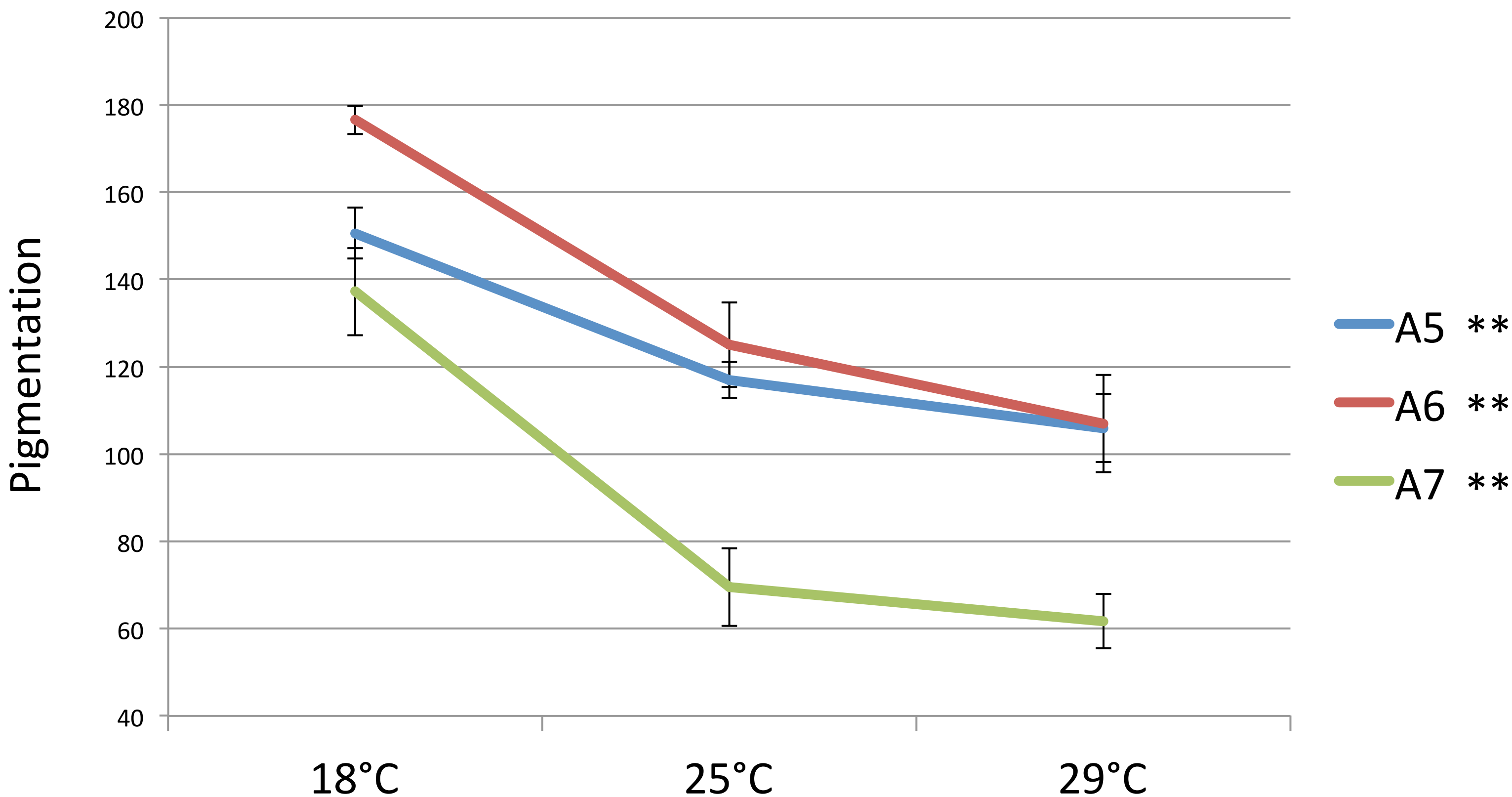
(Bouletreau-Merle et al., 2003; David et al., 2004; Schmidt et al., 2005; Trotta et al, 2006).

Temperature sensitivity of female abdominal pigmentation



Drosophila melanogaster, isogenic line w^{1118}

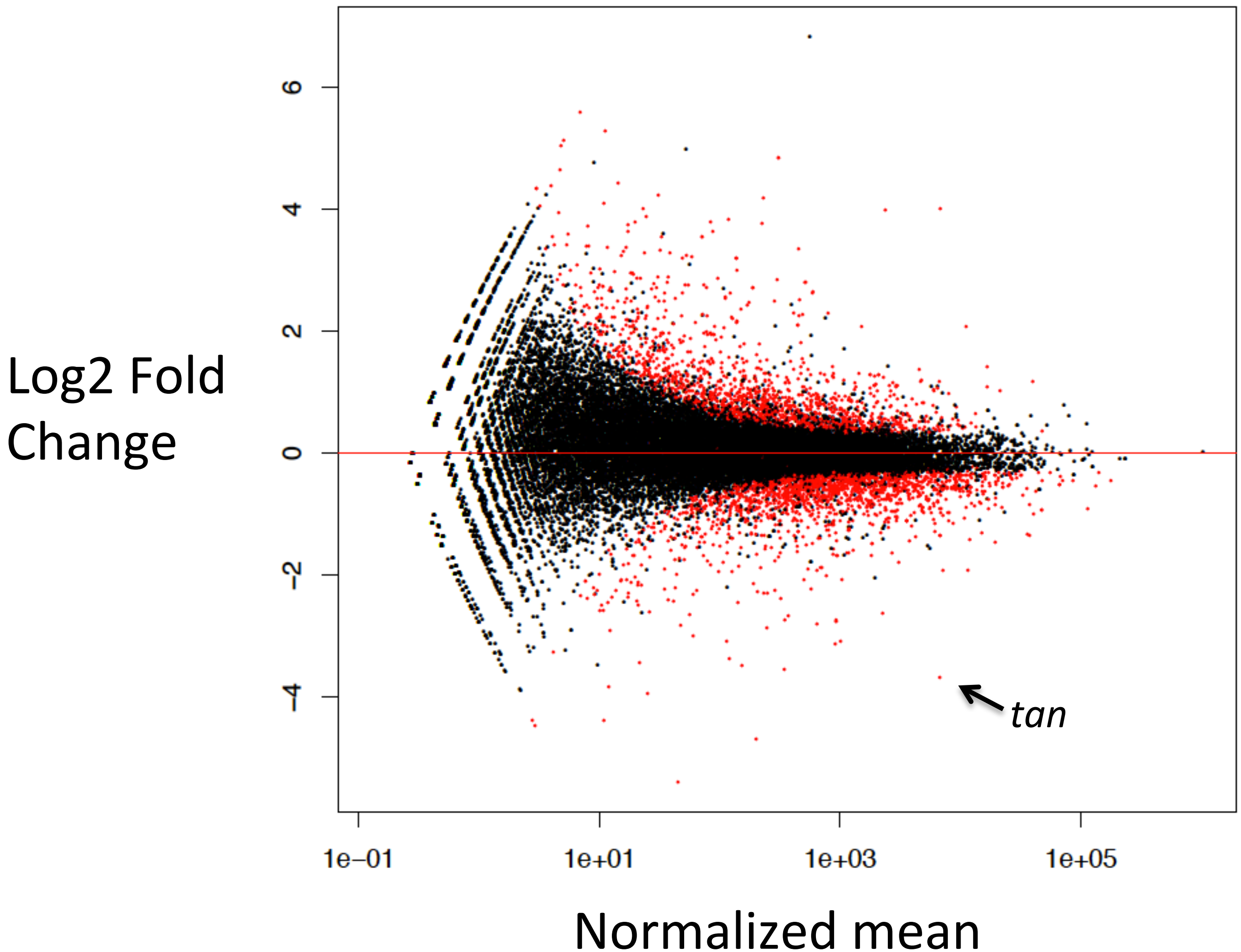
Reaction norms of female abdominal pigmentation



Quantification of pigmentation from mounted cuticles (ImageJ).

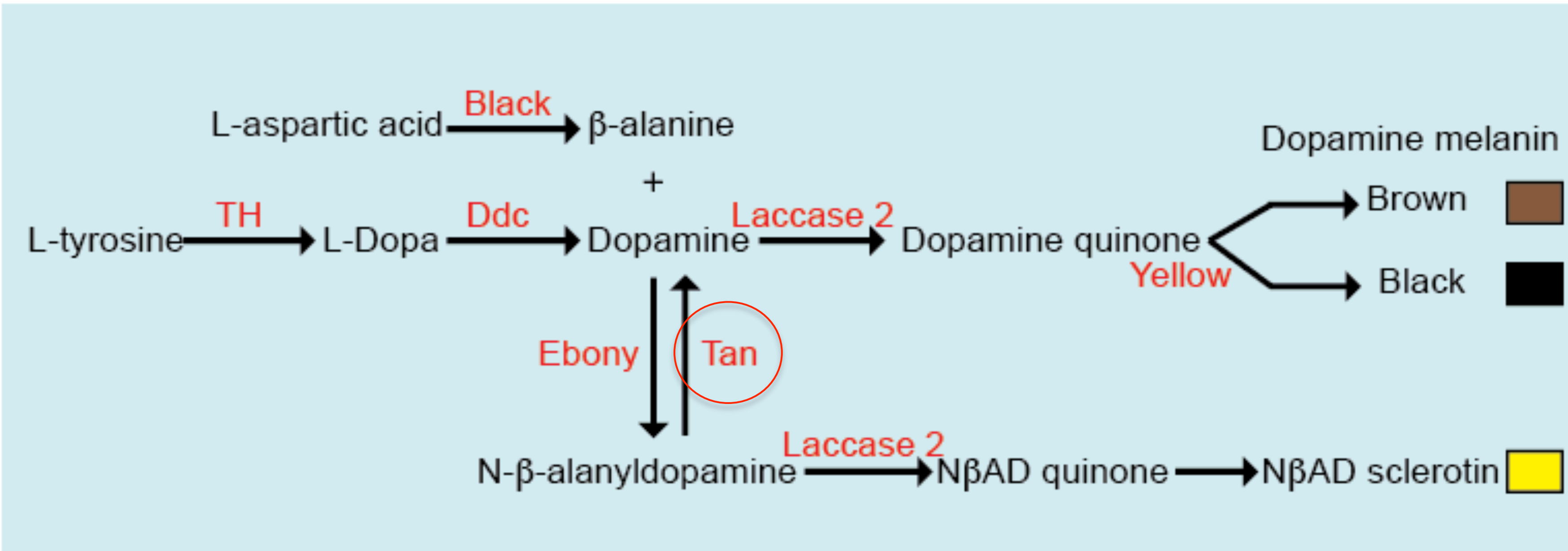
(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

Transcriptome analysis at 18°C and 29°C in young adult female posterior abdominal epidermis



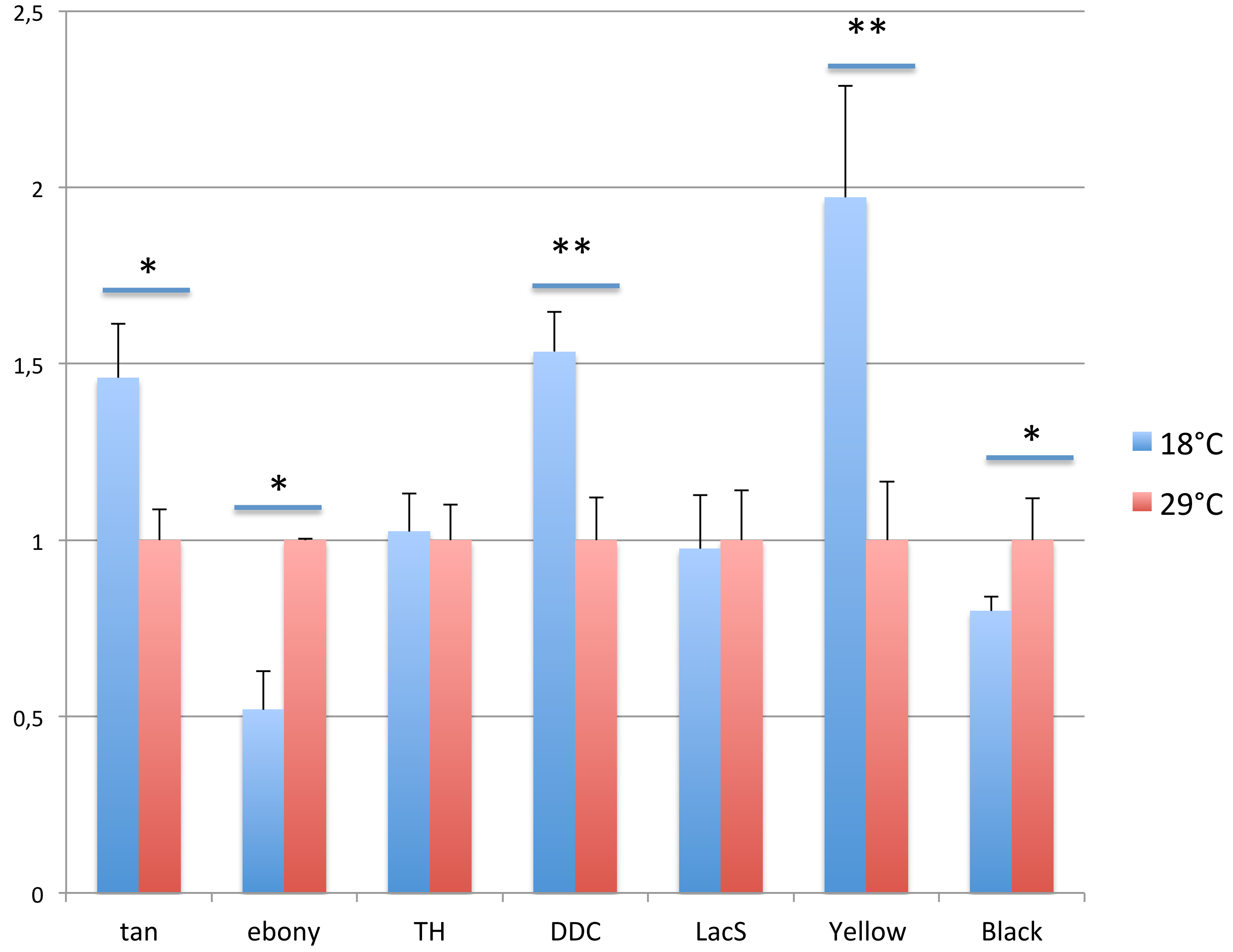
3000 transcripts=2097 genes ($p<0.05$), 200 transcripts ($p<1E-10$)

Cuticular pigment synthesis pathway



after Riedel et al., (2011)

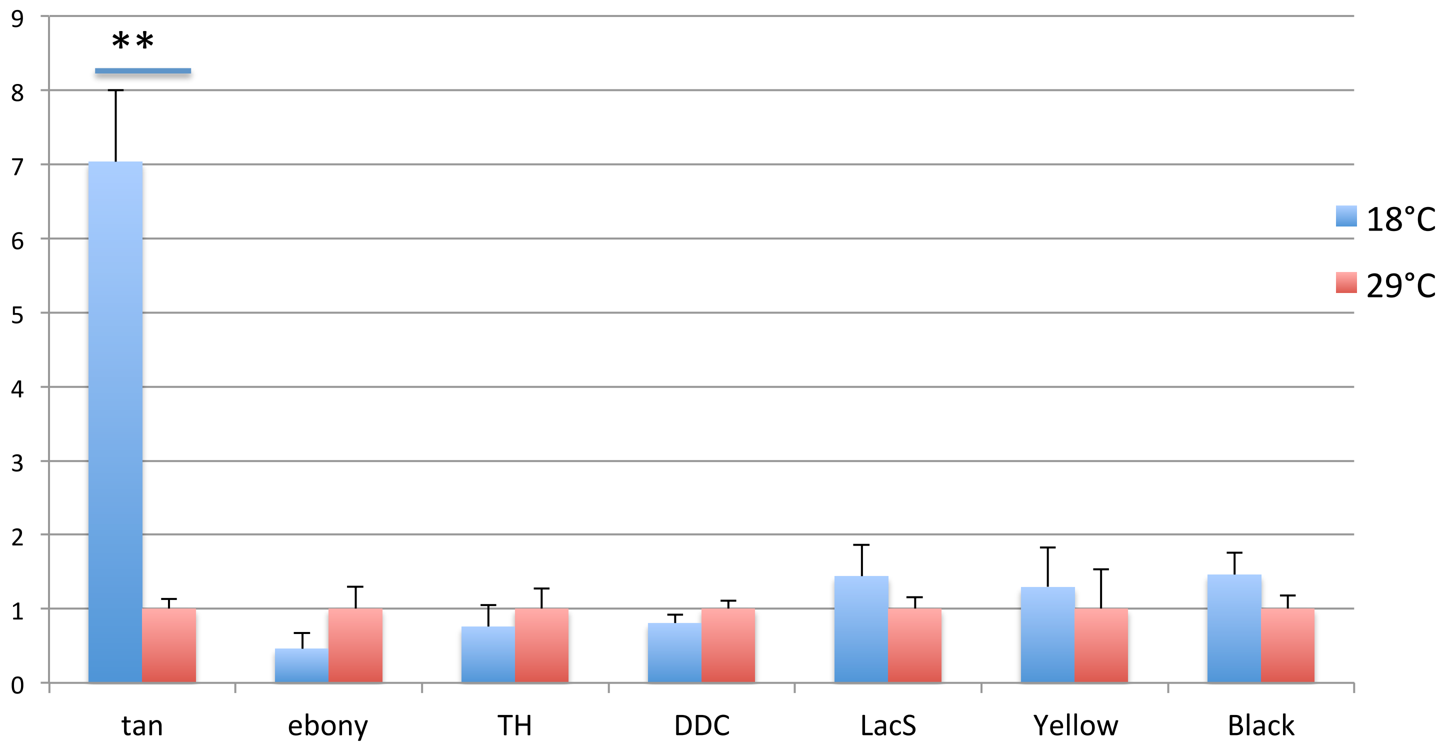
The expression of several pigmentation enzyme genes is modulated in pupal abdominal epidermis



RT-qPCR on 3 biological replicates, normalized with *Act5c* and *RP49*

(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

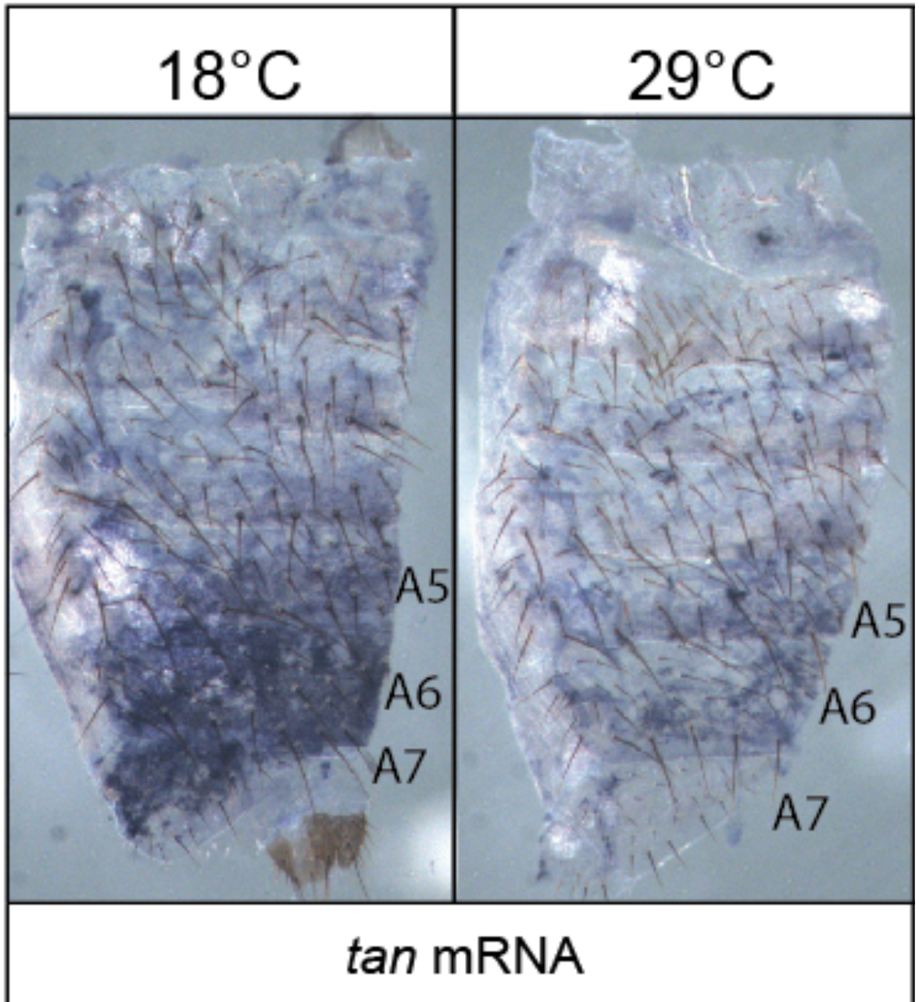
The expression of expression of *tan* is dramatically modulated by temperature in the abdominal epidermis of freshly hatched females



RT-qPCR on 3 biological replicates, normalized with *Act5c* and *RP49*

(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

tan expression is modulated by temperature

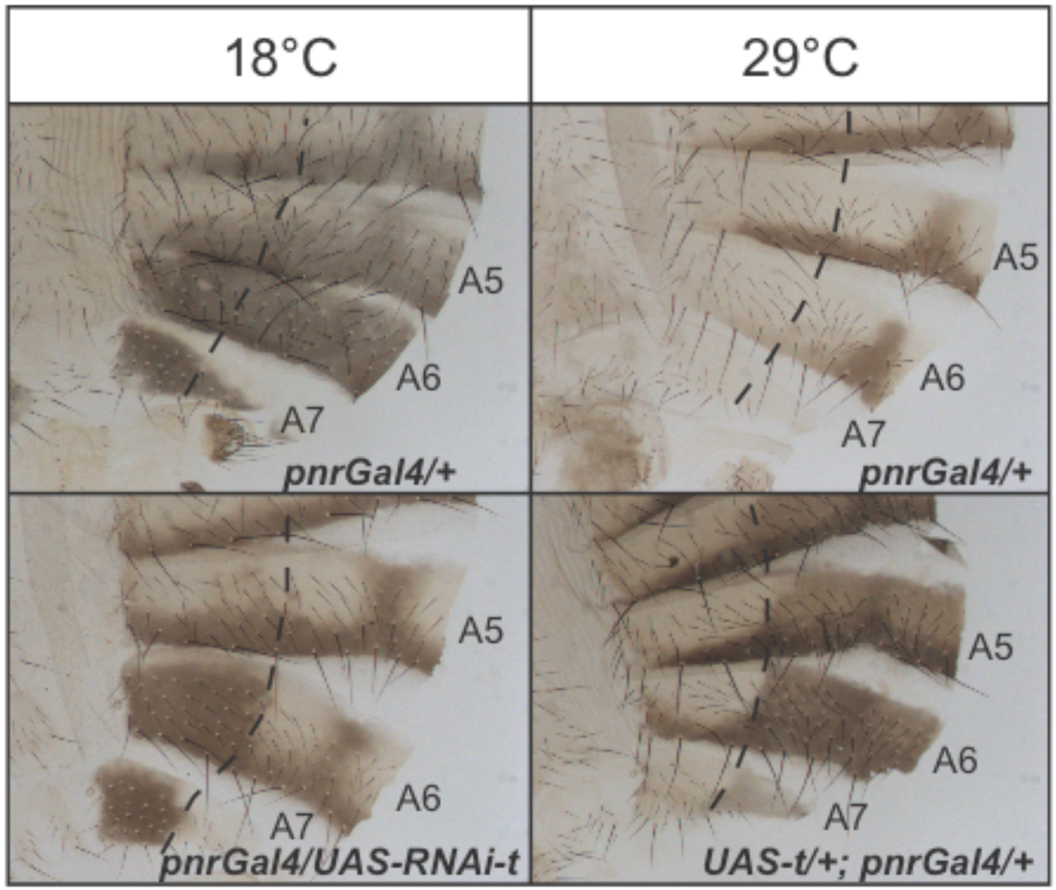


(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

Modulation of *tan* expression by temperature is essential for female abdominal pigmentation plasticity

control at 18°C

tan LOF at 18°C



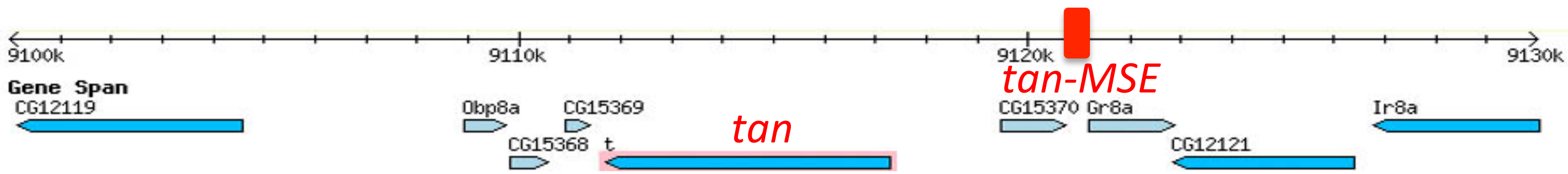
control at 29°C

tan GOF at 29°C

(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

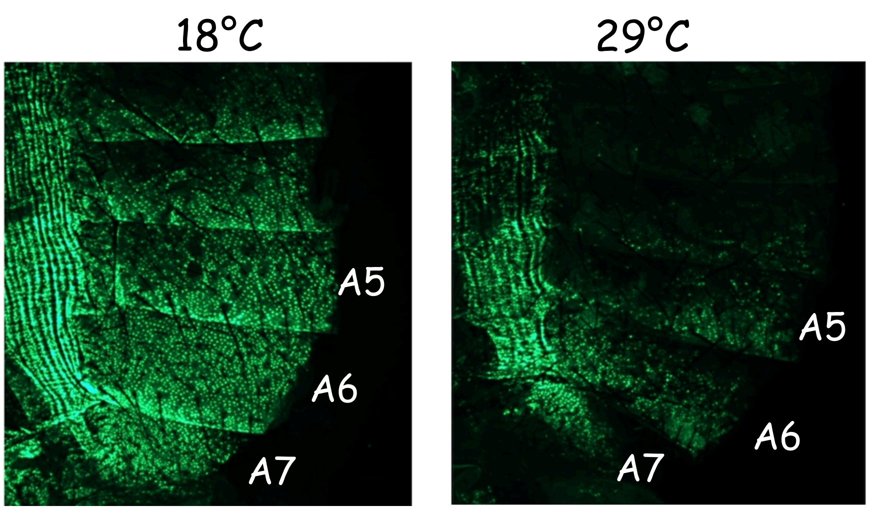
The effect of temperature on *tan* expression is mediated by the *tan-MSE* enhancer

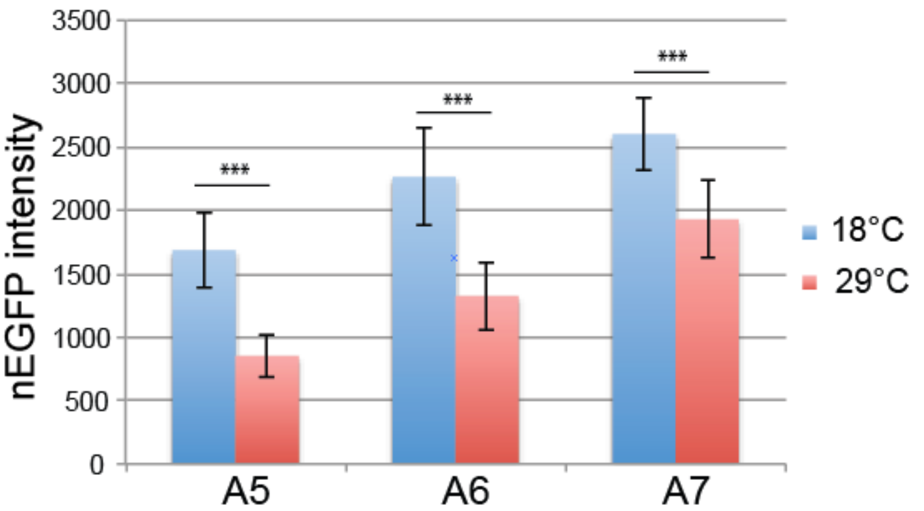
Structure of *tan* genomic region



after Jeong *et al.*, 2008

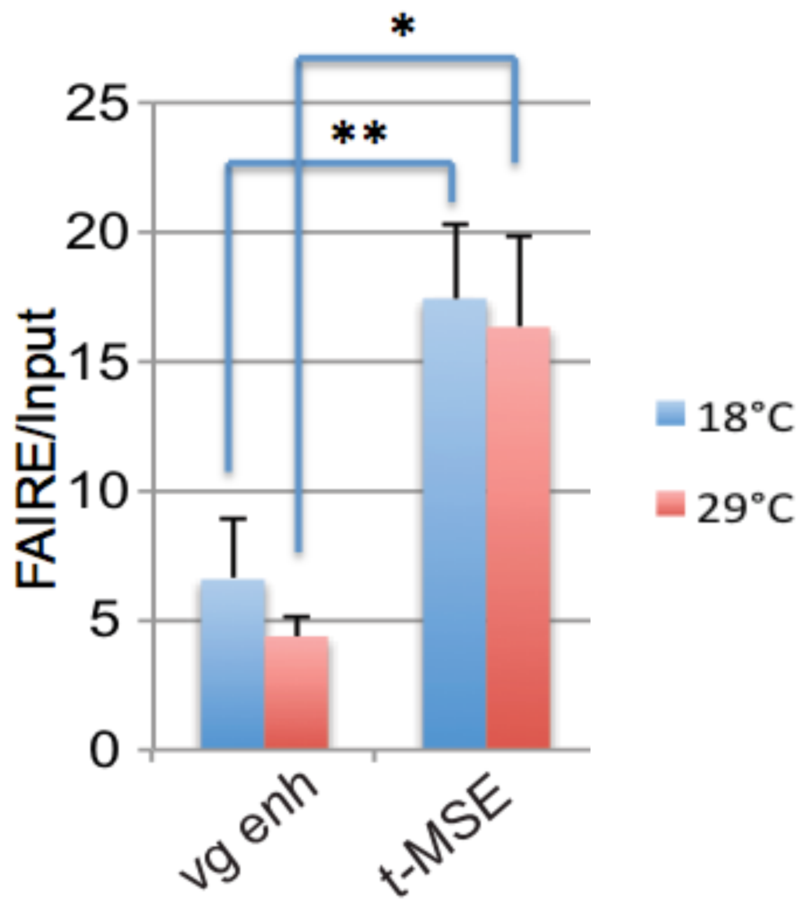
GFP expression in a *tan-MSE GFP* line is sensitive to temperature





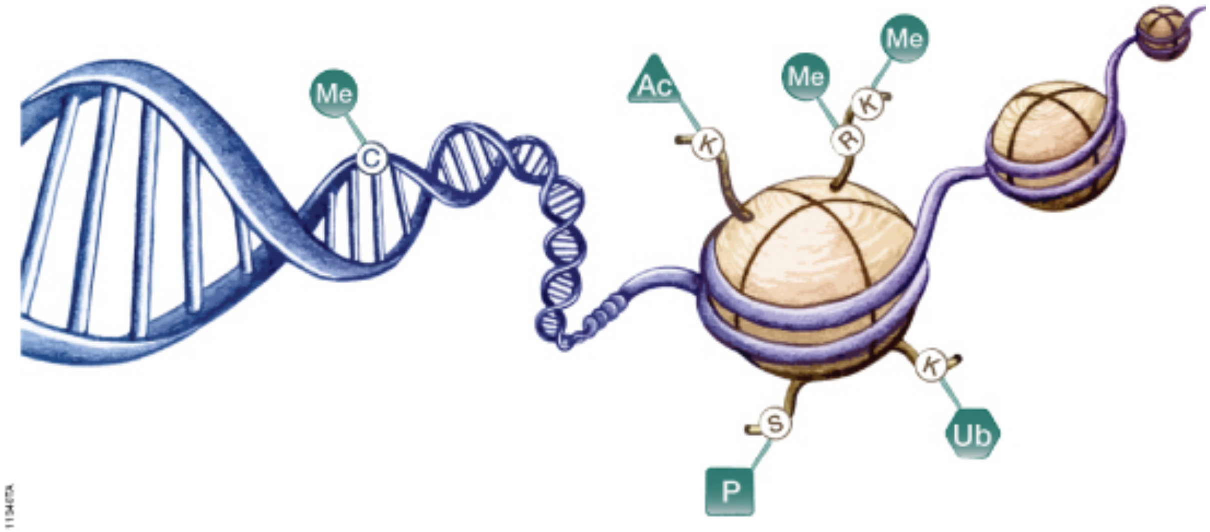
(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

FAIRE (Formaldehyde Assisted Isolation of Regulatory Element)-qPCR shows that *t_MSE* is less compacted than *vg* enhancer



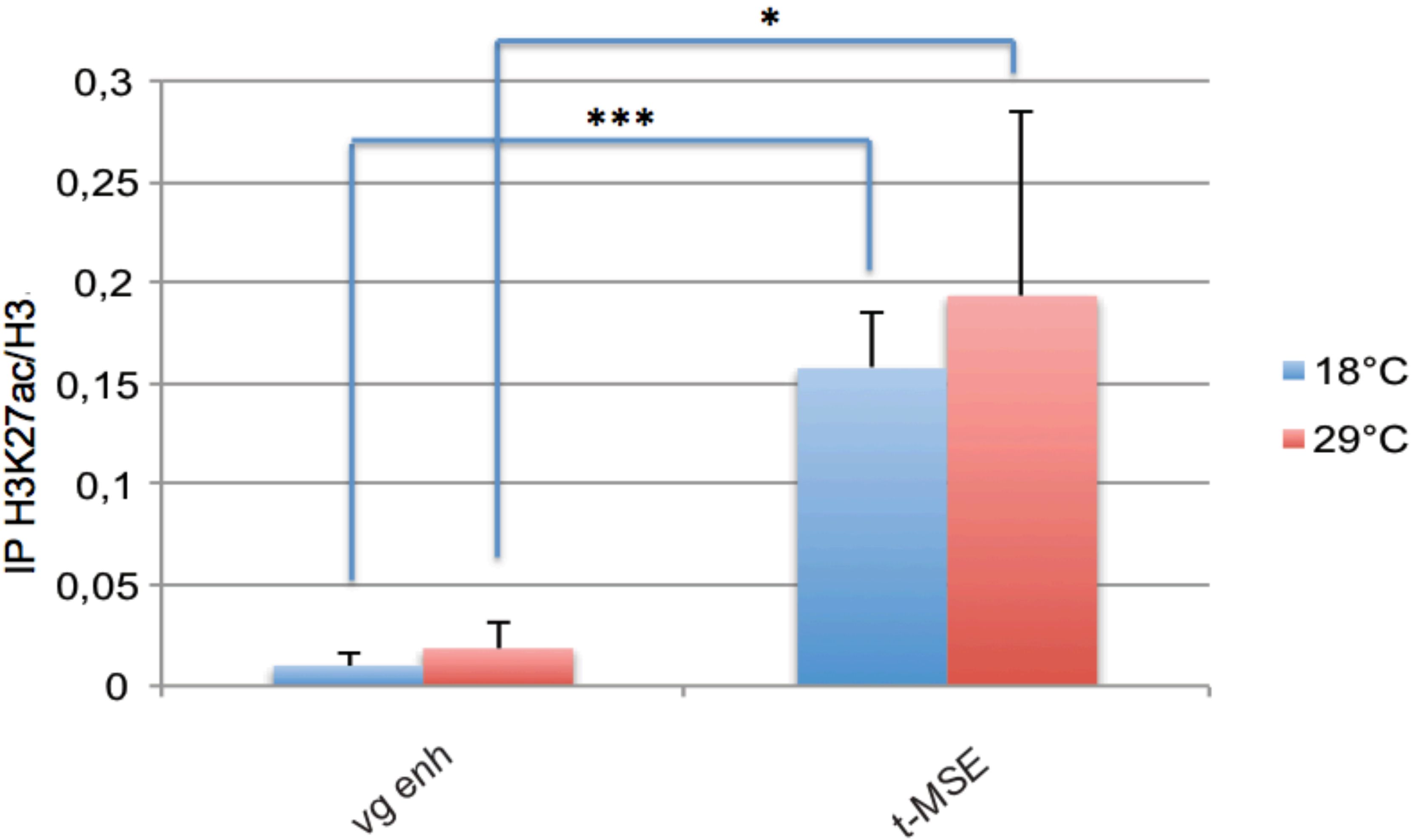
(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

Epigenetic marks analysed in *tan* region



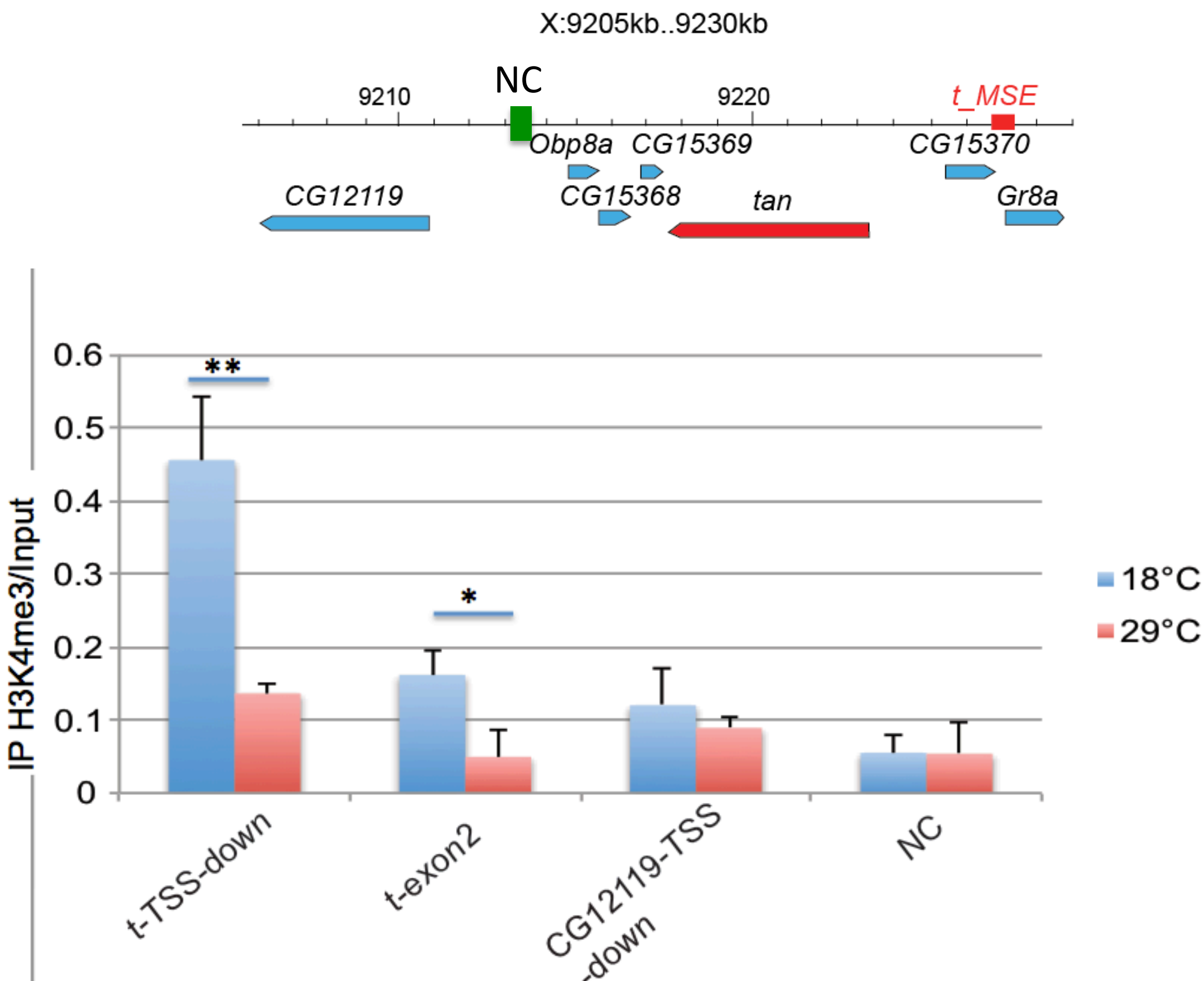
Mark	location	Indication
H3K4me3	Promoter	Active genes
H3K27ac	Enhancer	Active enhancer

t_MSE is enriched in H3K27ac, but this mark is not modulated by temperature



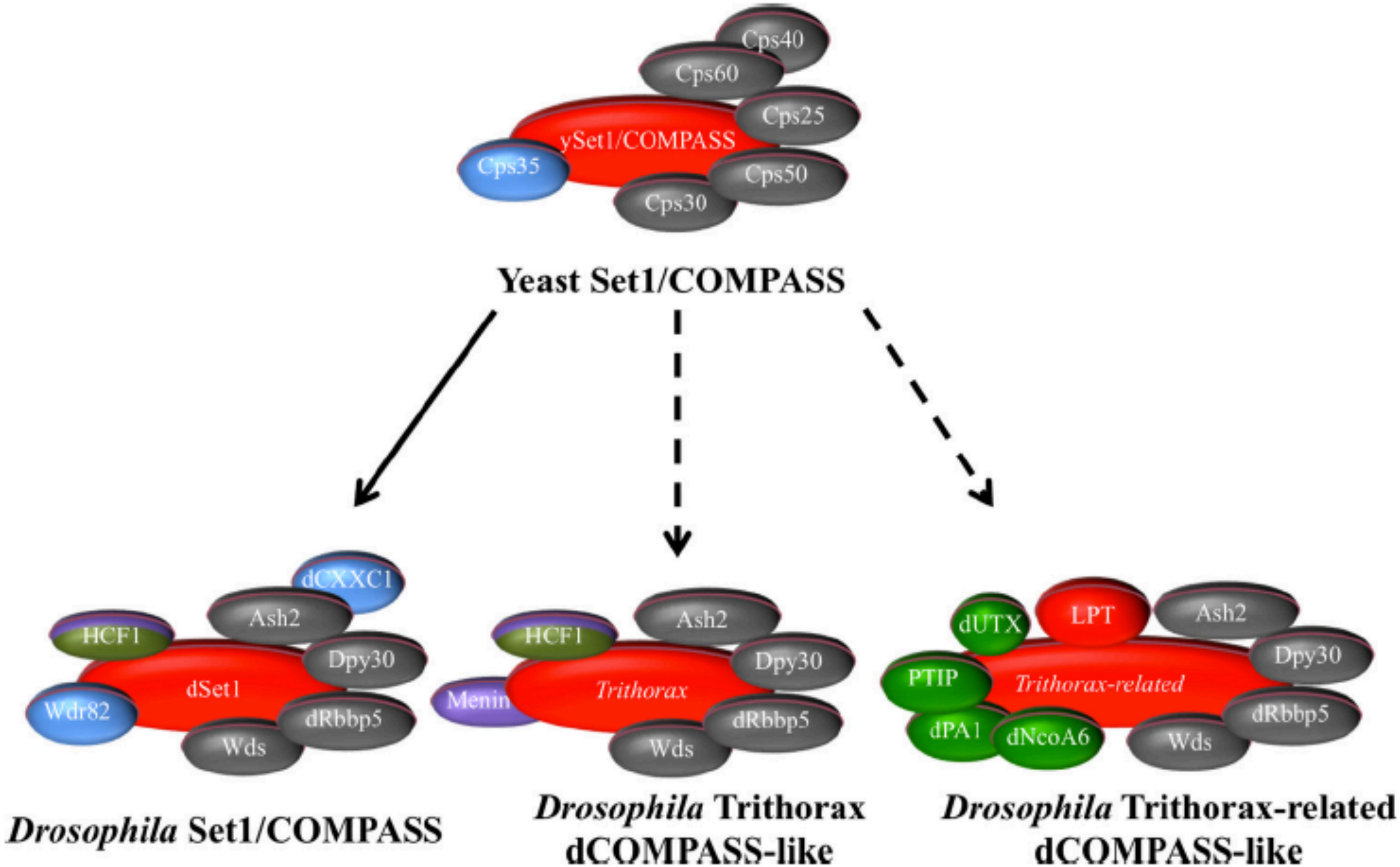
(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

H3K4me3 on *tan* promoter is strongly modulated by temperature



(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

Complexes involved in H3K4 methylation



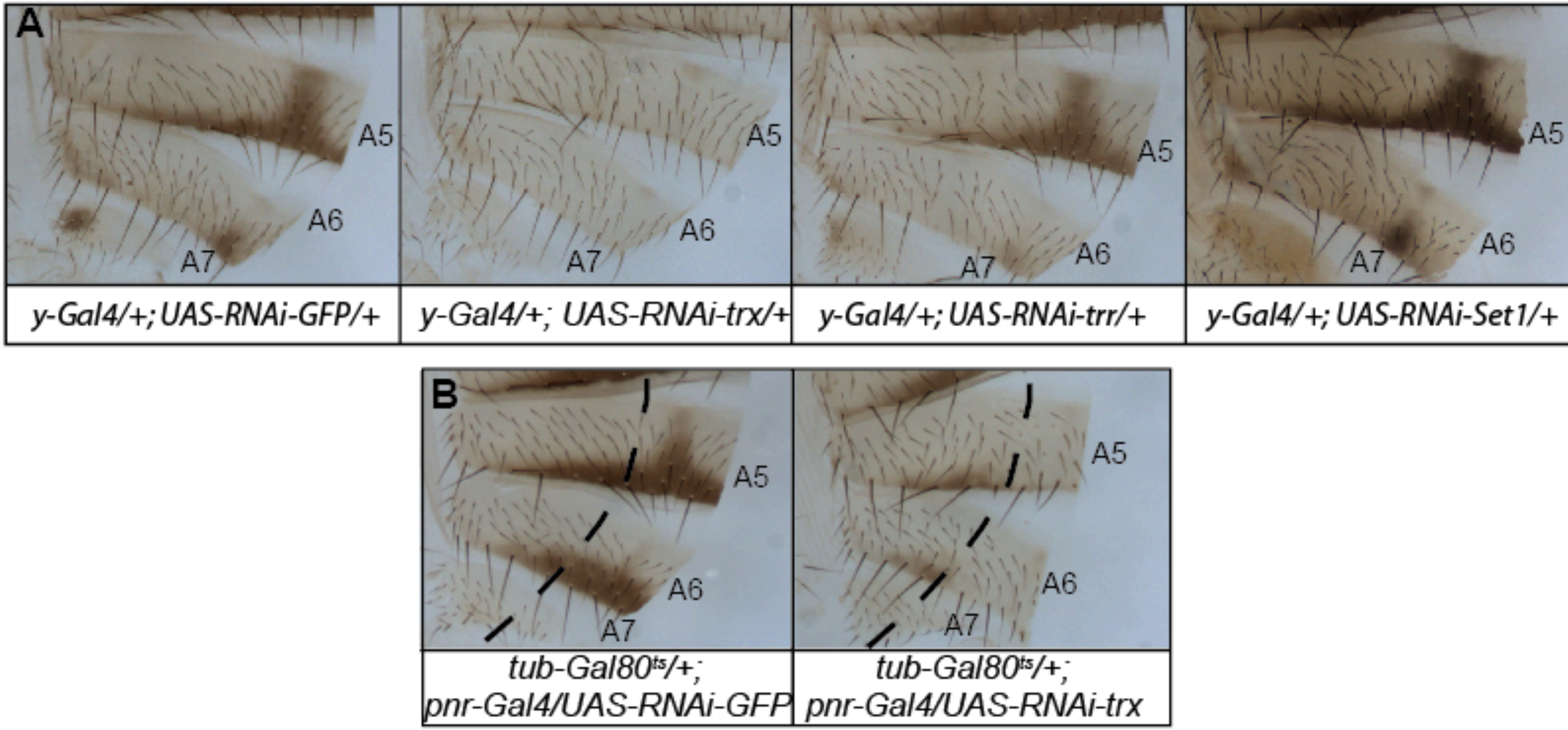
H3K4m2, 3

H3K4me1, 2, 3

H3K4me1

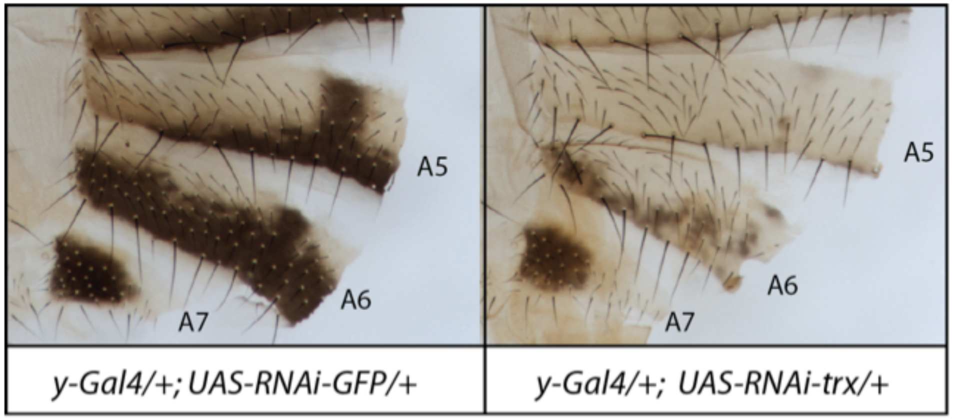
(Mohan et al., 2011; Herz, et al., 2012; Hallson et al., 2012; Tie et al;, 2014; Smith et al., 2004)

Female pigmentation phenotypes of H3K4 methyl-transferase LOF

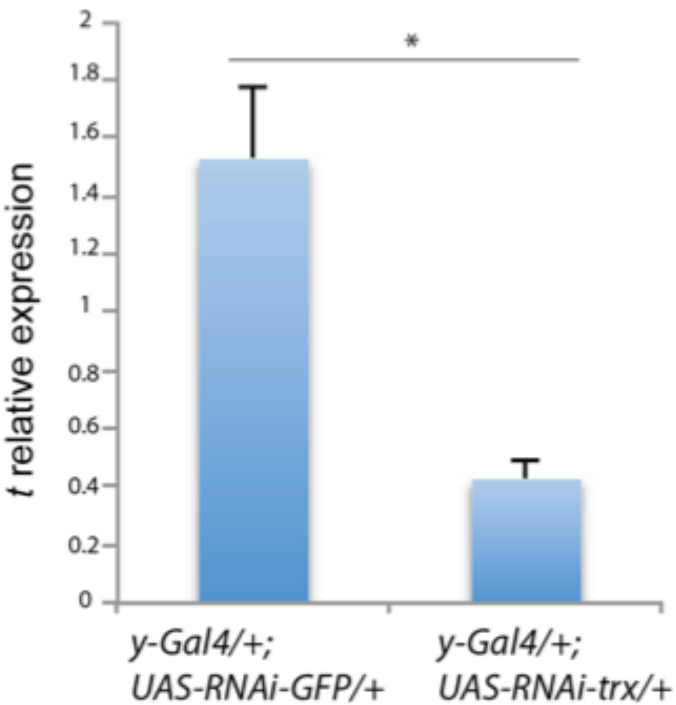


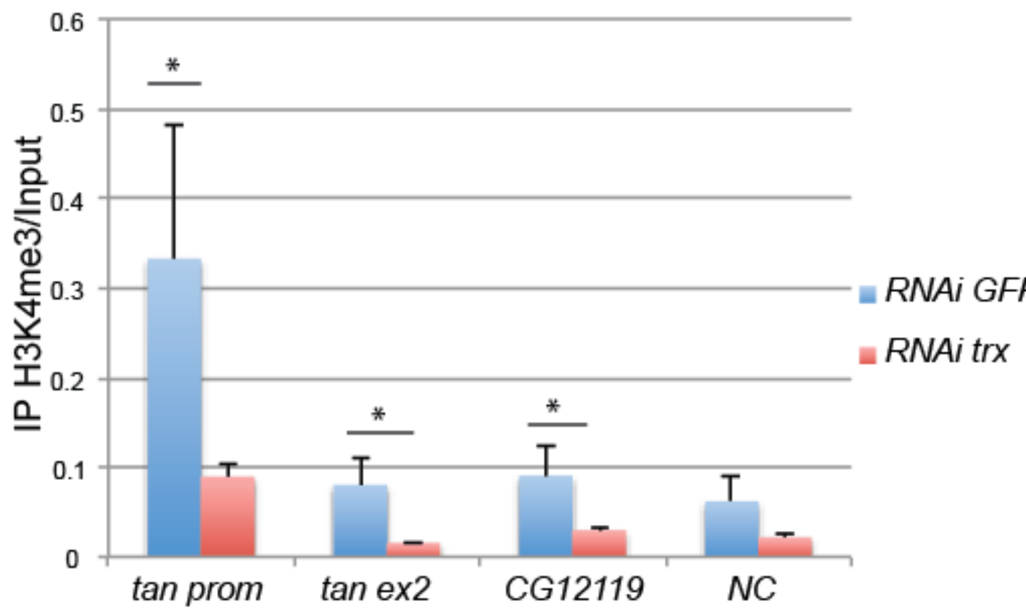
(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

The H3K4 methyl-transferase Trithorax is involved in female abdominal pigmentation and *tan* regulation



(18°C)





(Gibert, Mouchel-Vielh et al., PLoS Genetics, 2016)

Conclusions

tan temperature sensitive expression plays a major role in female abdominal pigmentation plasticity. Modulation of *yellow* expression by temperature is also involved (Gibert et al., Scientific Reports, 2017).

The effect of temperature is mediated at least partly by *t_MSE*. However we did not detect modification of chromatin structure on *t_MSE*.

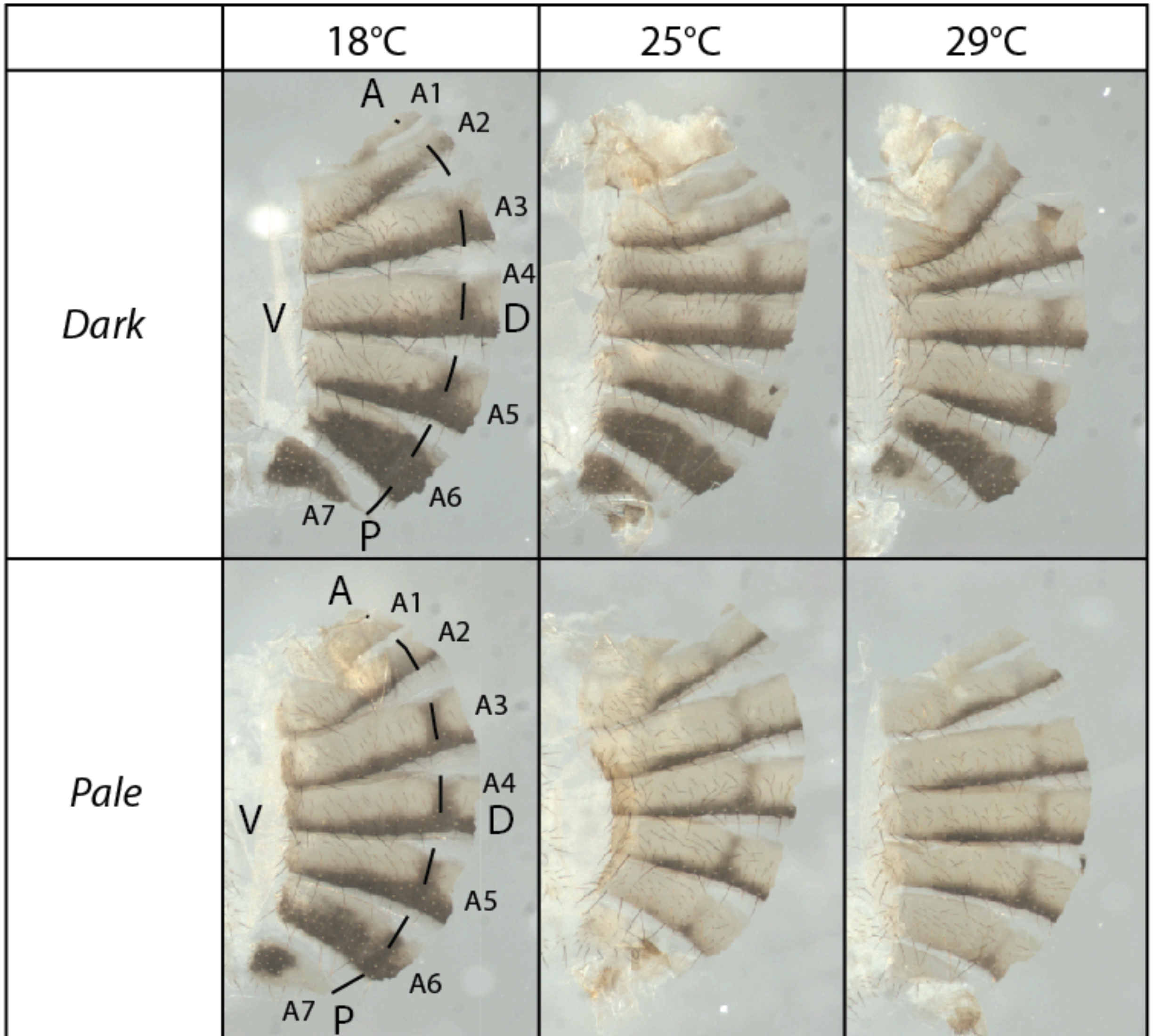
In contrast H3K4me3 level is strongly modulated by temperature on *tan* promoter.

The H3K4me3 methyl-transferase involved is likely Trithorax as it regulates female abdominal pigmentation, *tan* expression and H3K4me3 level on *tan* promoter.

25°C

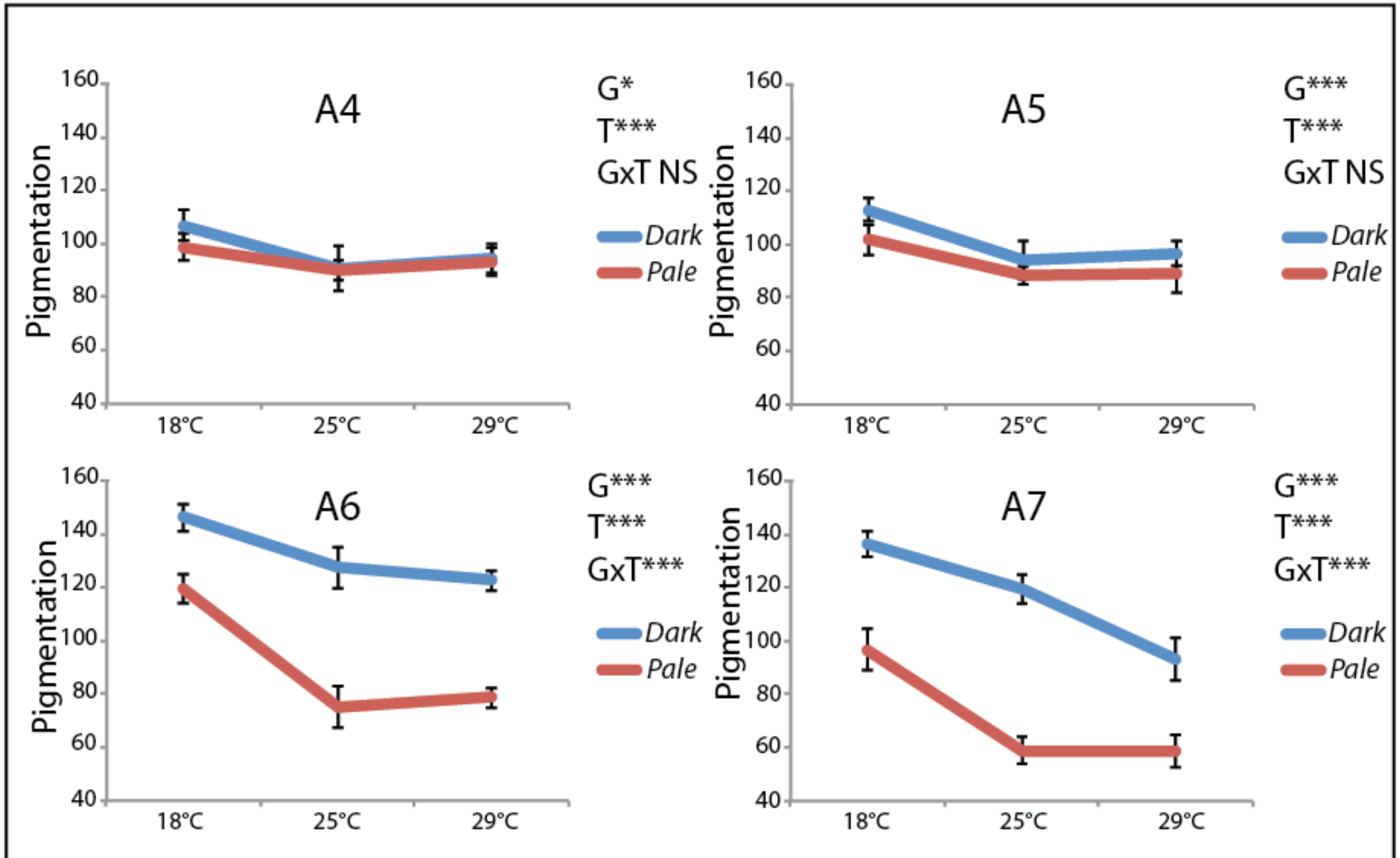
(De Castro *et al.*, PLOS Genetics, 2018)

Phenotypes of the *Dark* and *Pale* lines at different temperatures



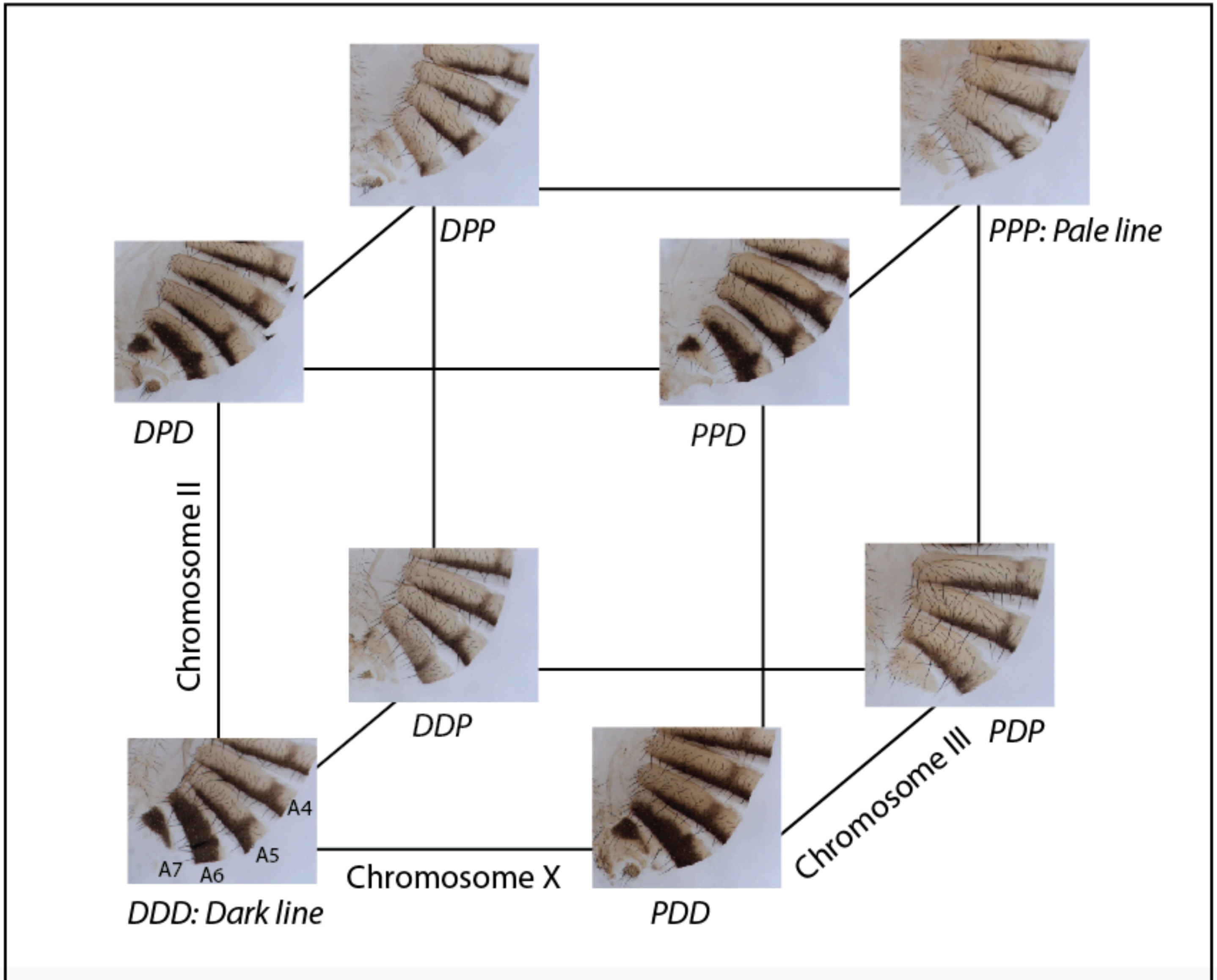
(De Castro *et al.*, PLOS Genetics, 2018)

Reaction norms of the *Dark* and *Pale* lines



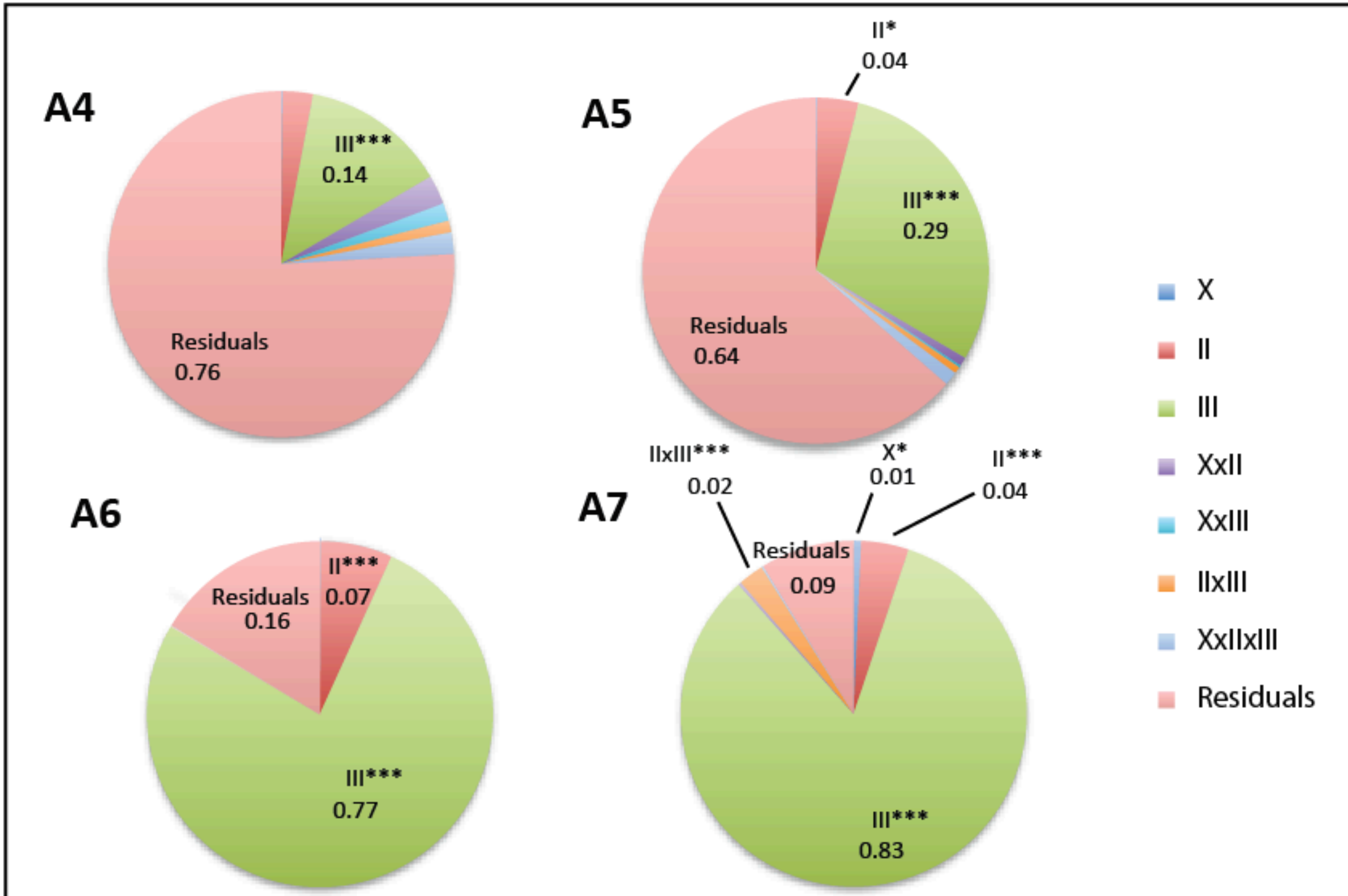
(De Castro *et al.*, PLOS Genetics, 2018)

Effects of the different chromosomes of the *Dark* and *Pale* lines on pigmentation



(De Castro *et al.*, PLOS Genetics, 2018)

The third chromosome plays a major role in the difference of pigmentation between the *Dark* and *Pale* lines



(De Castro *et al.*, PLOS Genetics, 2018)

bab, a major QTL for female abdominal pigmentation

Quantitative Trait Loci Responsible for Variation in Sexually Dimorphic Traits in *Drosophila melanogaster*

Artyom Kopp,* Rita M. Graze,† Shizhong Xu,‡ Sean B. Carroll* and Sergey V. Nuzhdin†,[1]

*Howard Hughes Medical Institute and Laboratory of Molecular Biology, University of Wisconsin, Madison, Wisconsin 53706, †Section of Evolution and Ecology, University of California, Davis, California 95616 and ‡Department of Botany and Plant Sciences, University of California, Riverside, California 92521

2003

OPEN ACCESS Freely available online PLoS GENETICS

Composite Effects of Polymorphisms near Multiple Regulatory Elements Create a Major-Effect QTL

Ryan D. Bickel[1,2]*, Artyom Kopp[3], Sergey V. Nuzhdin[2]

1 School of Biological Science, University of Nebraska – Lincoln, Lincoln, Nebraska, United States of America, 2 Program in Molecular and Computational Biology, Department of Biological Sciences, University of Southern California, Los Angeles, California, United States of America, 3 Department of Evolution and Ecology, University of California Davis, Davis, California, United States of America

2011

OPEN ACCESS Freely available online PLOS | GENETICS

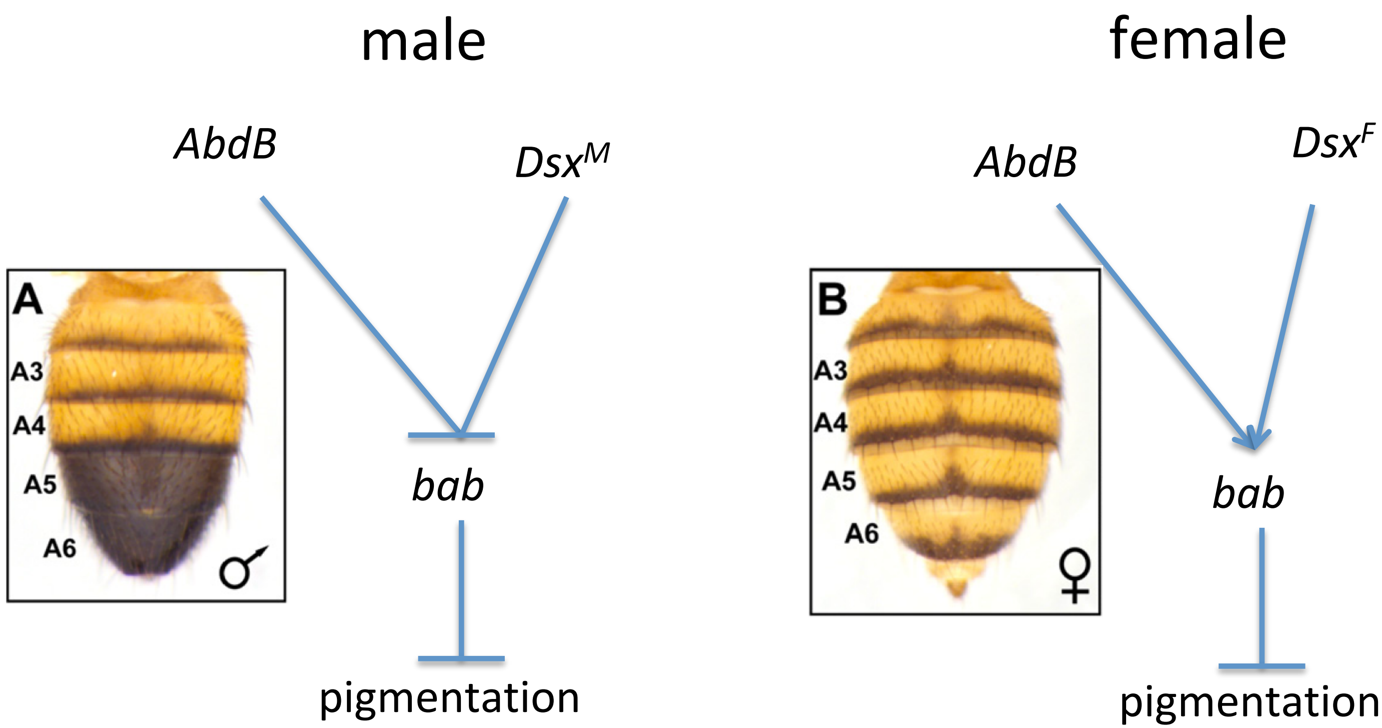
Recurrent Modification of a Conserved *Cis*-Regulatory Element Underlies Fruit Fly Pigmentation Diversity

William A. Rogers[1], Joseph R. Salomone[1], David J. Tacy[1], Eric M. Camino[1], Kristen A. Davis[1], Mark Rebeiz[2], Thomas M. Williams[1,3]*

1 Department of Biology, University of Dayton, Dayton, Ohio, United States of America, 2 Department of Biological Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, 3 Center for Tissue Regeneration and Engineering at Dayton, University of Dayton, Dayton, Ohio, United States of America

2013

bab and sex-specific pigmentation



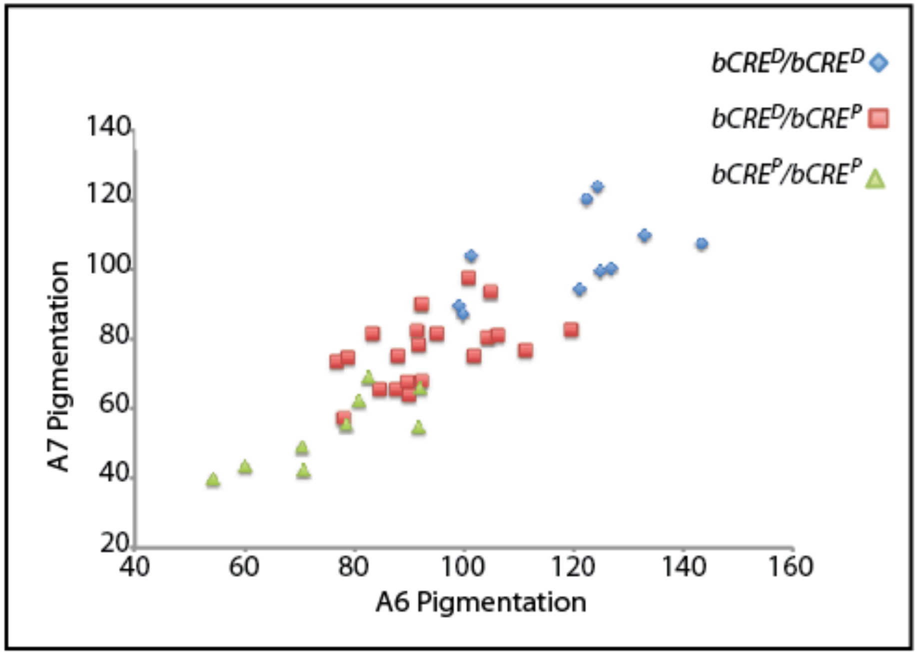
(Williams et al., 2008)

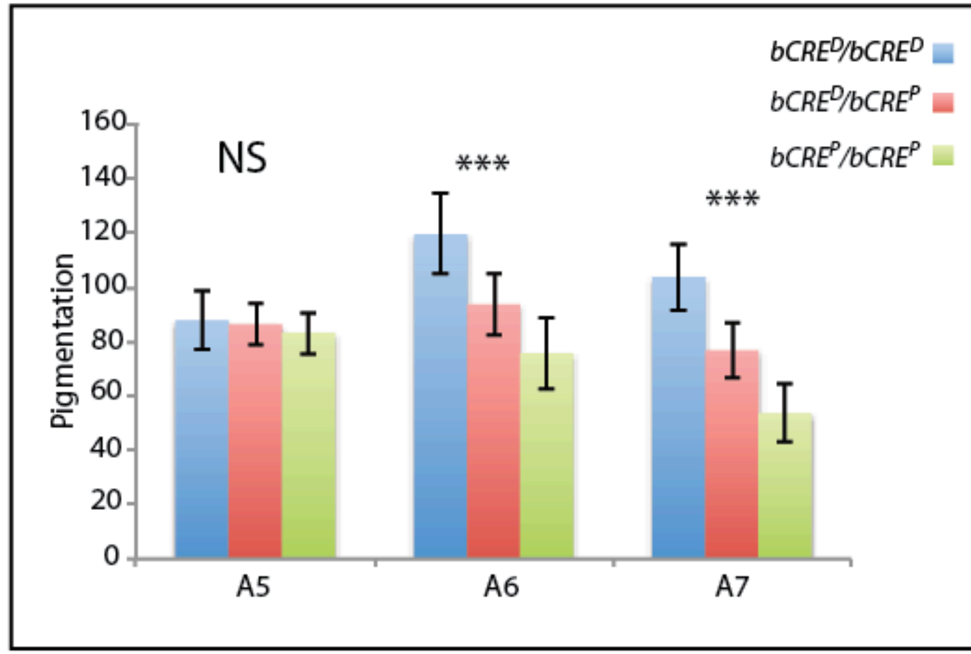
bab dimorphic CRE in w^{1118}, *Dark* and *Pale*

```
Canton/w    TTTTAAGACCATAAATTCAGCTCACTCTCTCTCTCGCTCTTTCTCTTTGCCATTTTAA 480
Dark        TTTTAAGACCATAAATTCAGCTCACTCTCTCTCTCGCTCTTTCTCTTTGCCATTTTAA 480
Pale        TTTTAAGACCATAAATTCAGCTCACTCTCTCTCTCGCTCTTTCTCTTTGCCATTTTAA 480
            **********************************************************

              AbdB1          AbdB2                         AbdB3
Canton/w    CTTTTATTACTCTTAATATAAAAAAGCTGGCTAGATGCGGGCCAGCTGTAAAAATGCACG 540
Dark        CTTTTATTACTCTTAATATAAAAAAGCTGGCTAGATGCGG-------------------- 520
Pale        CTTTTATTACTCTTAATATAAAAAAGCTGGCTAGATGCGGGCCAGCTGTAAAAATGCACG 540
            ****************************************

                 AbdB4
Canton/w    CGGTCATAAAAAGTTGCAGGAGGCATGTTGCCAGTTGCCTGCAACCGGCAACATTCGCAG 600
Dark        ------------------------------------GCCTGCAACCGGCAACATTCGCAG 544
Pale        CGGTCATAAAAAGTTGCAGGAGGCATGTTGCCAGTTGCCTGCAACCGGCAACATTCGCAG 600
                                                ************************

                           AbdB5          D                        Dsx1
Canton/w    AACAGCAGCAACATCGTAAAATAACTTCTTGCTCTGCGGTCTGAGTTTGGCCGCAACAAT 660
Dark        AACAGCAGCAACATCGTAAAATAACTTCTTGCTCTGCGGTCTGAGTTTGGCCGCAACAAT 604
Pale        AACAGCAGCAACATCGTAAAATAACTTCTTCCTCTGCGGTCTGAGTTTGGCCGCAACAAT 660
            ****************************** *****************************

                     AbdB6
Canton/w    GTTGCTGCATTTATTCGTATTATTATTACATTTTAATGAATAATTCTAATTATATGCAAC 720
Dark        GTTGCTGCATTTATTCGTATTATTATTACATTTTAATGAATAATTCTAATTATATGCAAC 664
Pale        GTTGCTGCATTTATTCGTATTATTATTACATTTTAATGAATAATTCTAATTATATGCAAC 720
            ************************************************************

                                  AbdB7
Canton/w    TTGAATAAGCCCGCCGATGCCAATAAAAAGCGGCGTGGCAAAGTGGAGTGGACTGGGTTT 780
Dark        TTGAATAAGCCCGCCGATGCCAATAAAAAGCGGCGTGGCAAAGTGGAGTGGACTGGGTTT 724
Pale        TTGAATAAGCCCGCCGATGCCAATAAAAAGCGGCGTGGCAAAGTGGAGTGGACTGGGTTT 780
            ************************************************************

                                    AbdB8
Canton/w    GTGTGGCGCCCCTGCTAGTGGCACATAAAAATTGGCGCAAGTTAATTGTGGTAGTTATTT 840
Dark        GTGTGGCGCCCCTGCTAGTGGCACATAAAAATTGGCGCAAGTTAATTGTGGTAGTTATTT 784
Pale        GTGTGGCGCCCCTGCTAGTGGCACATAAAAATTGGCGCAAGTTAATTGTGGTAGTTATTT 840
            ************************************************************

                                 AbdB9    AbdB10
Canton/w    GCTGTTTTGCCATTTGGTCATTTTACAATTTTACCATTTCAGCCACAACTTTTCGCACTG 900
Dark        GCTGTTTTGCCATTTGGTCATTTTACAATTTTACCATTTCAGCCACAACTTTTCGCACTG 844
Pale        GCTGTTTTGCCATTTGGTCATTTTACAATTTTACCATTTCAGCCACAACTTTTCGCACTG 900
            ************************************************************
```

(De Castro *et al.*, PLOS Genetics, 2018)

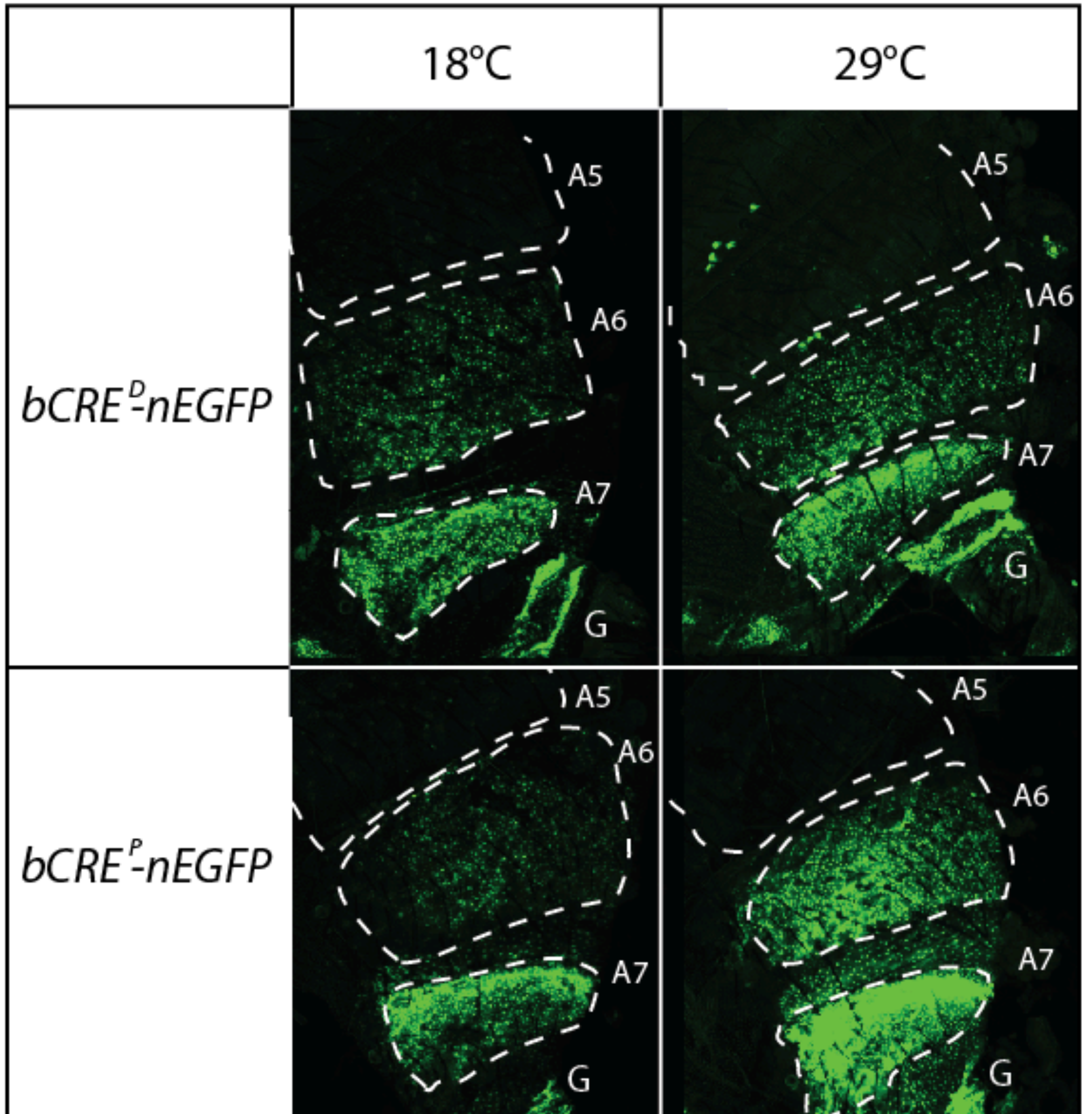
Genotyping of the F2 of a *Dark x Pale* cross shows that the *bab* locus is linked to the pigmentation phenotype





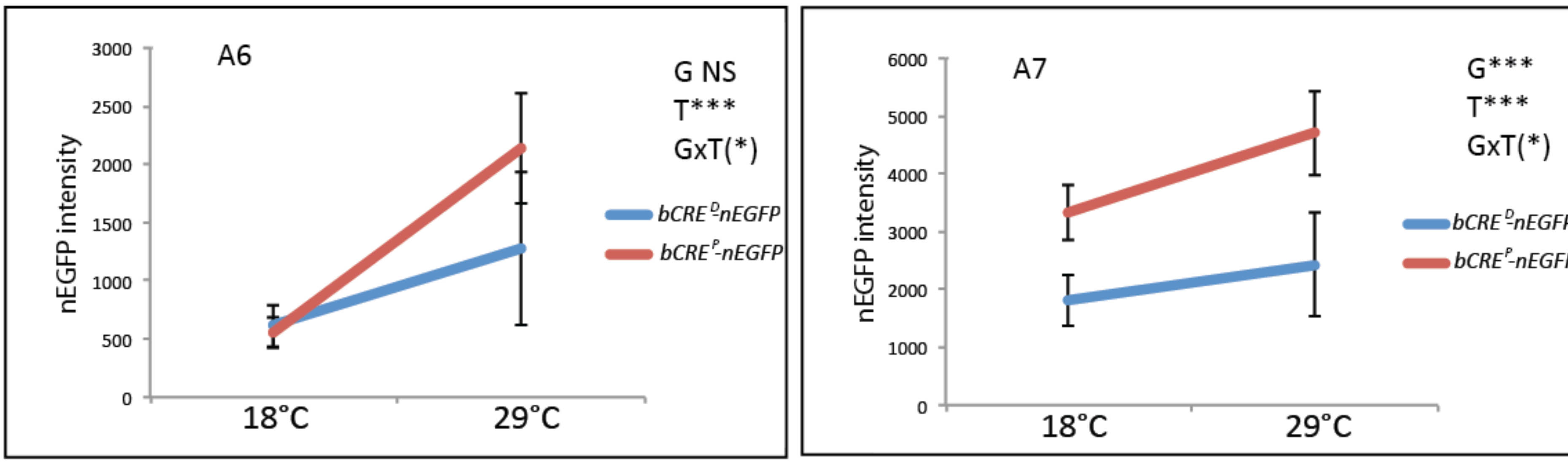
(De Castro *et al.*, PLOS Genetics, 2018)

Comparison of the activities of *bab* dimorphic enhancers from the *Dark* and *Pale* lines



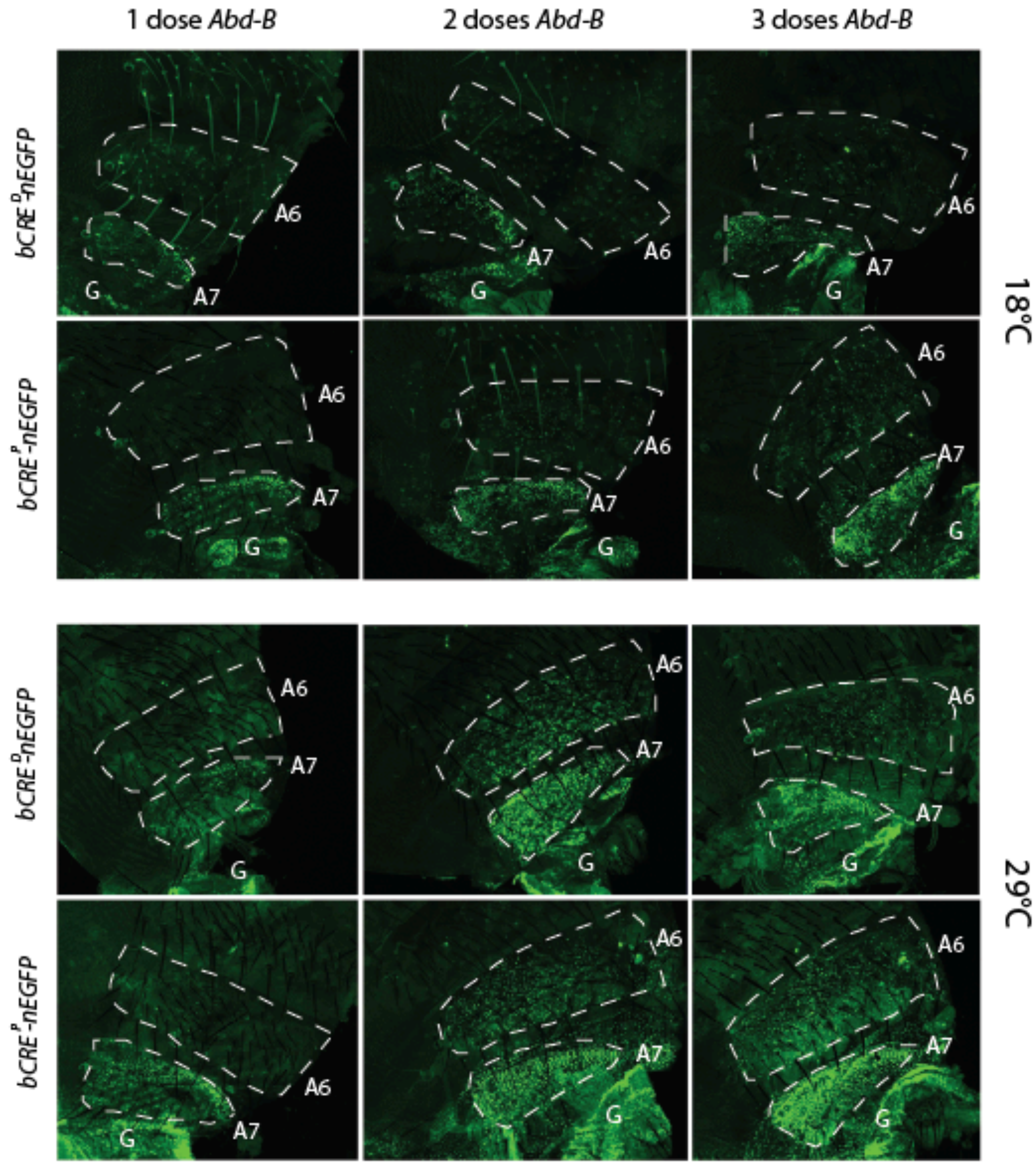
(De Castro *et al.*, PLOS Genetics, 2018)

Comparison of the activities of *bab* dimorphic enhancers from the *Dark* and *Pale* lines



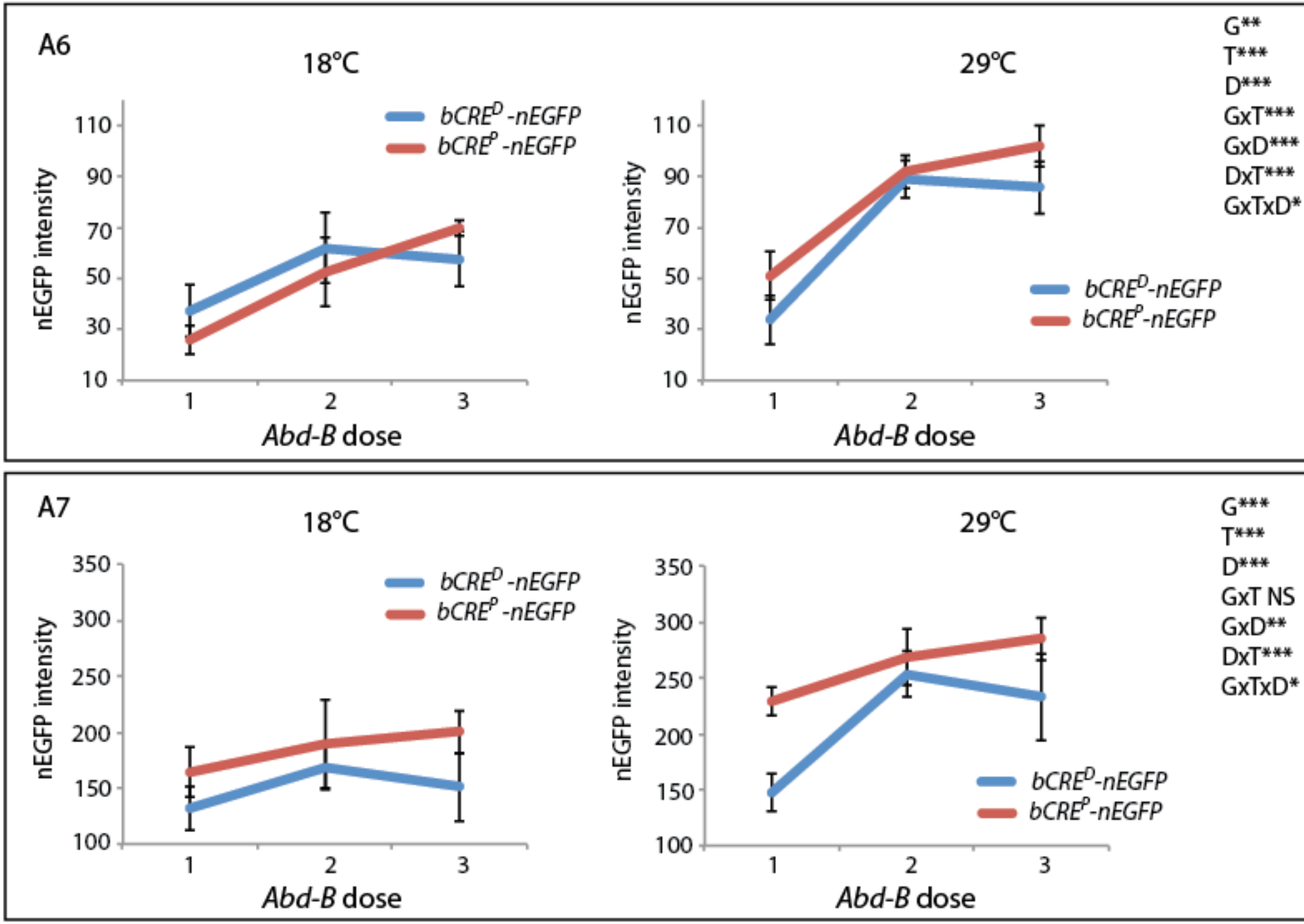
(De Castro *et al.*, PLOS Genetics, 2018)

Impact of genetic variation in the enhancer on its activation by AbdB



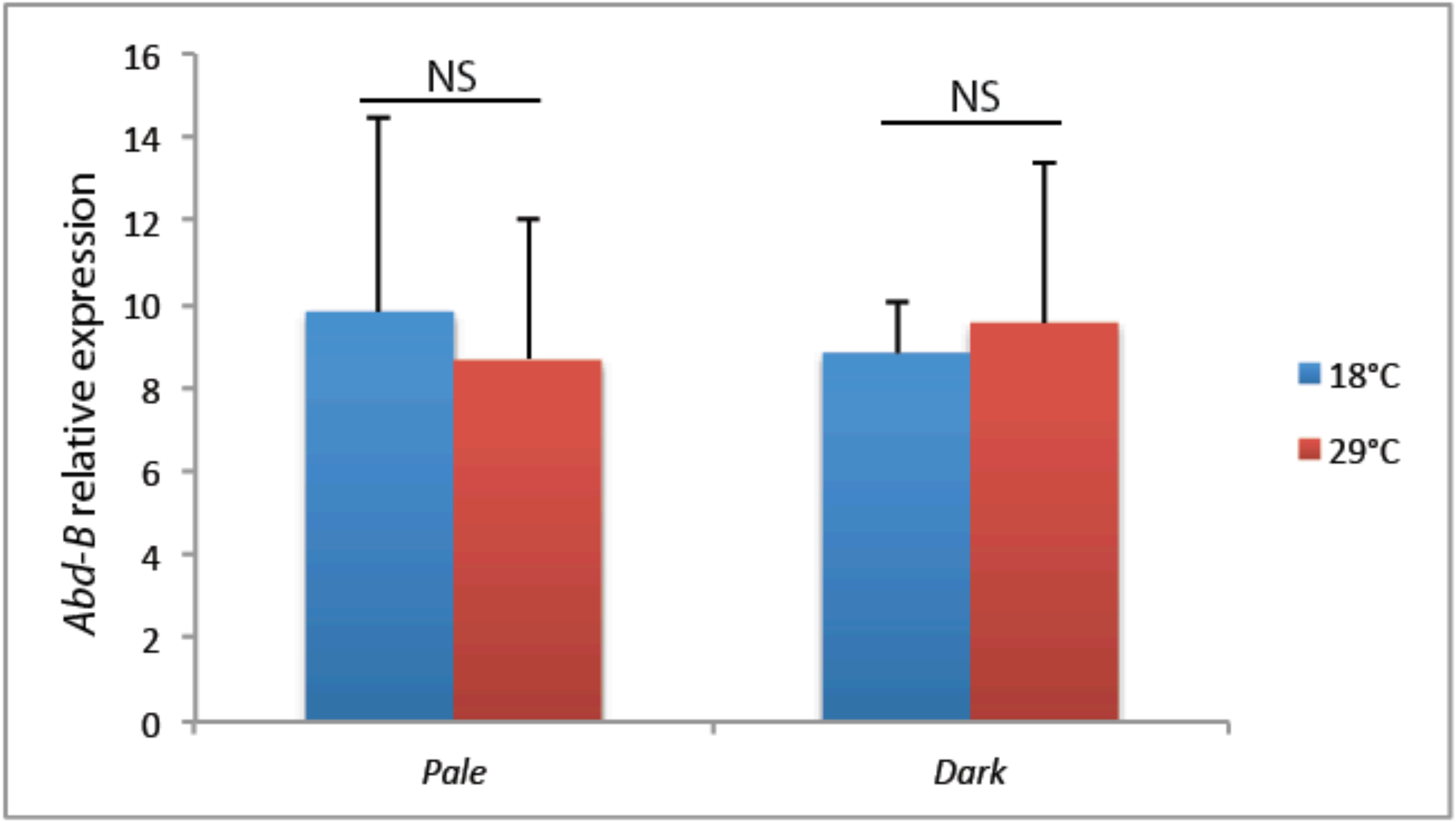
(De Castro *et al.*, PLOS Genetics, 2018)

Impact of genetic variation in the enhancer on its activation by AbdB



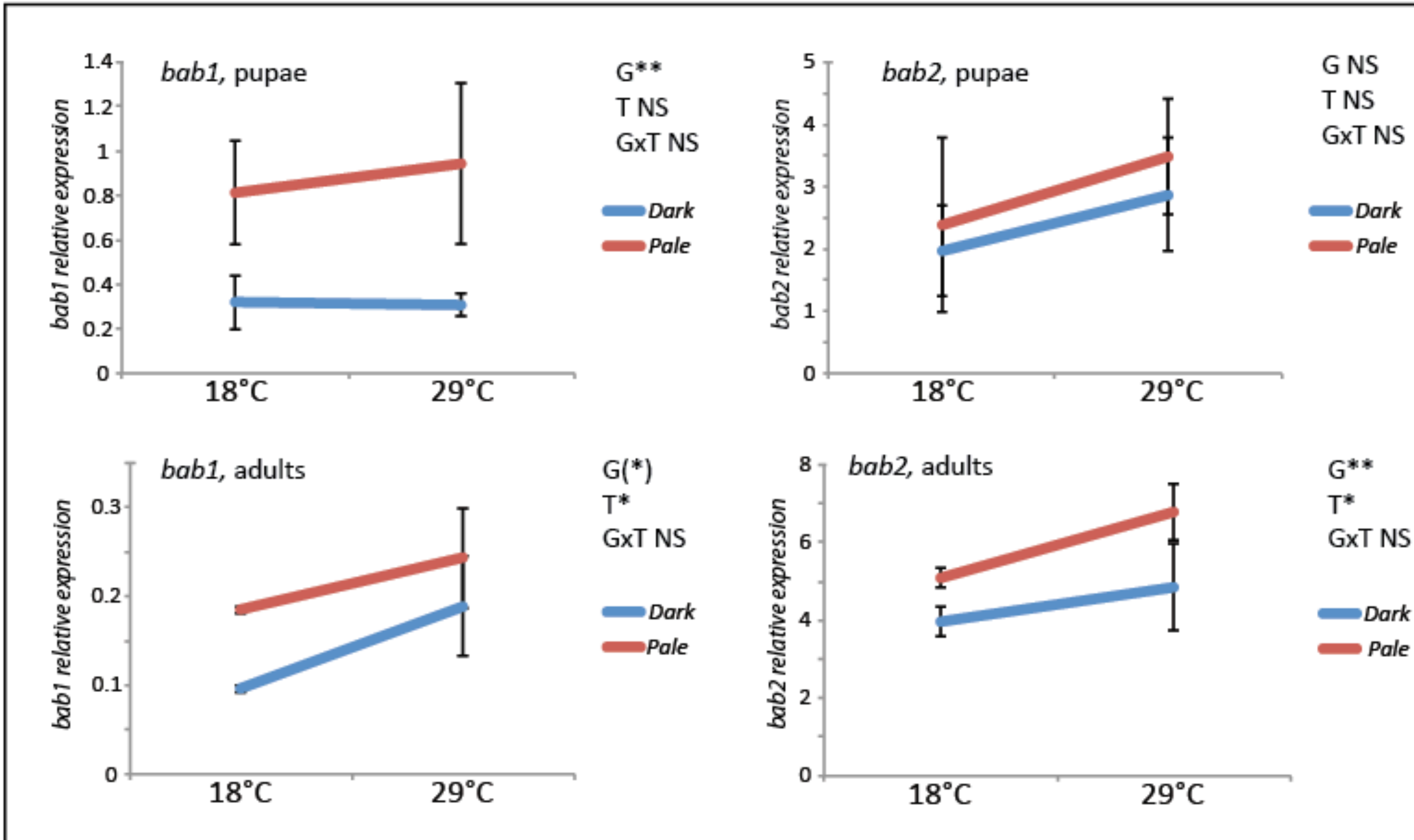
(De Castro *et al.*, PLOS Genetics, 2018)

AbdB expression is not modulated by temperature



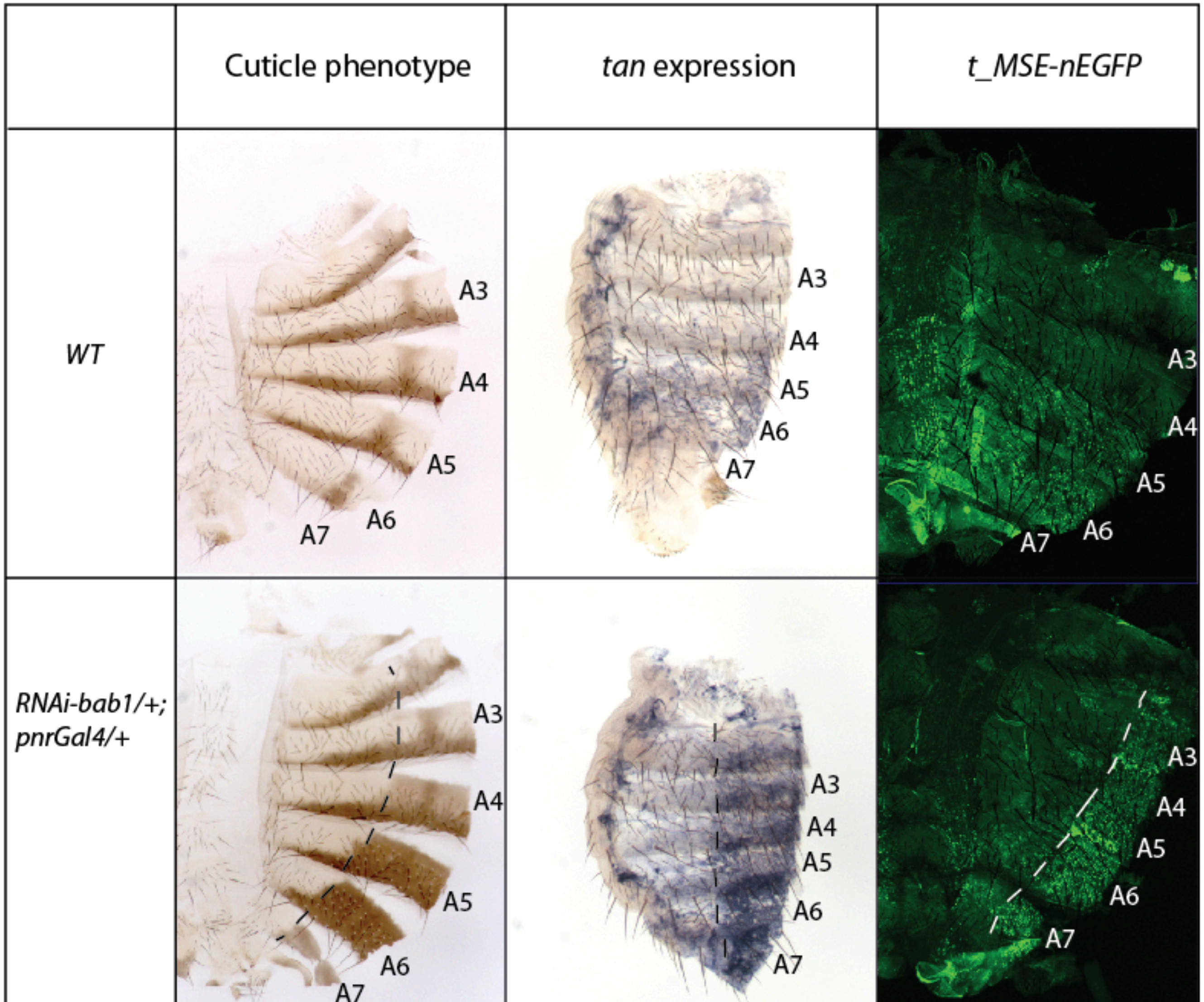
(De Castro *et al.*, PLOS Genetics, 2018)

bab1 and *bab2* expressions are different between the *Dark* and *Pale* lines and modulated by temperature



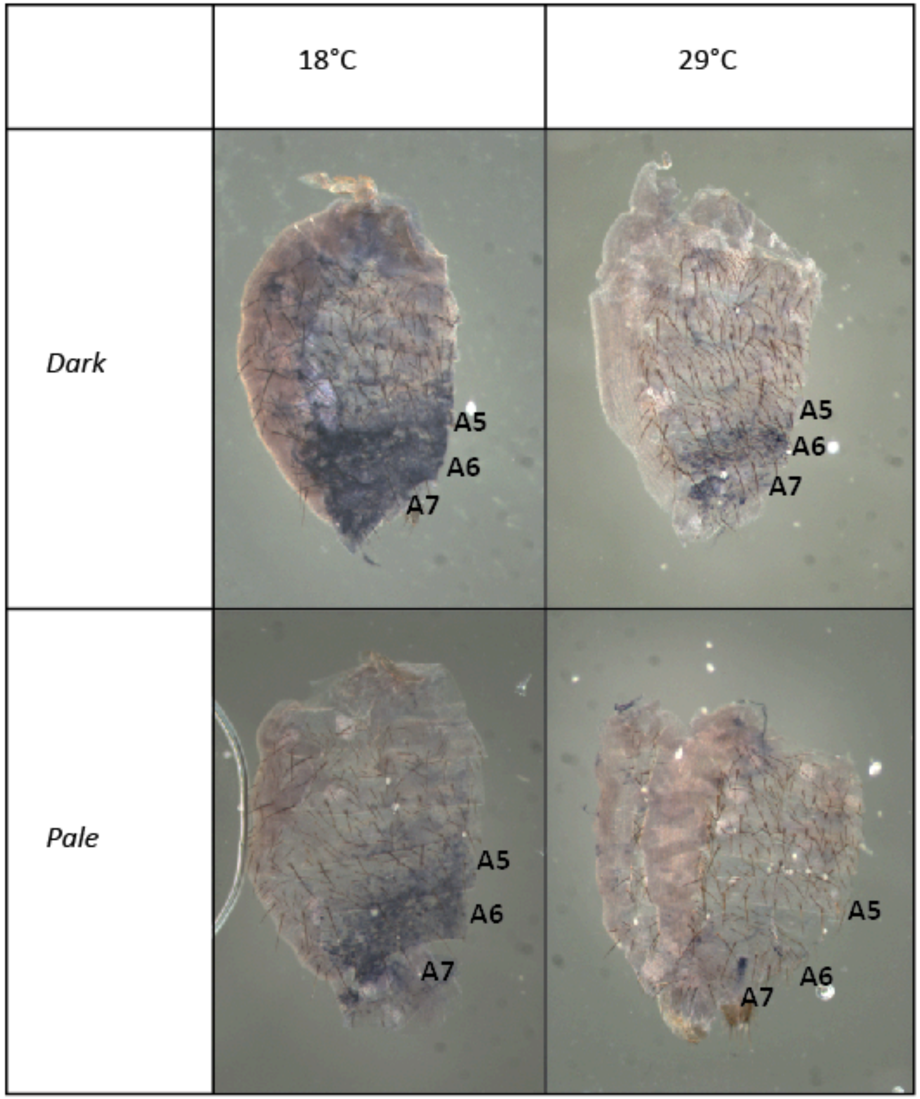
(De Castro *et al.*, PLOS Genetics, 2018)

bab represses *tan via* the *t_MSE*



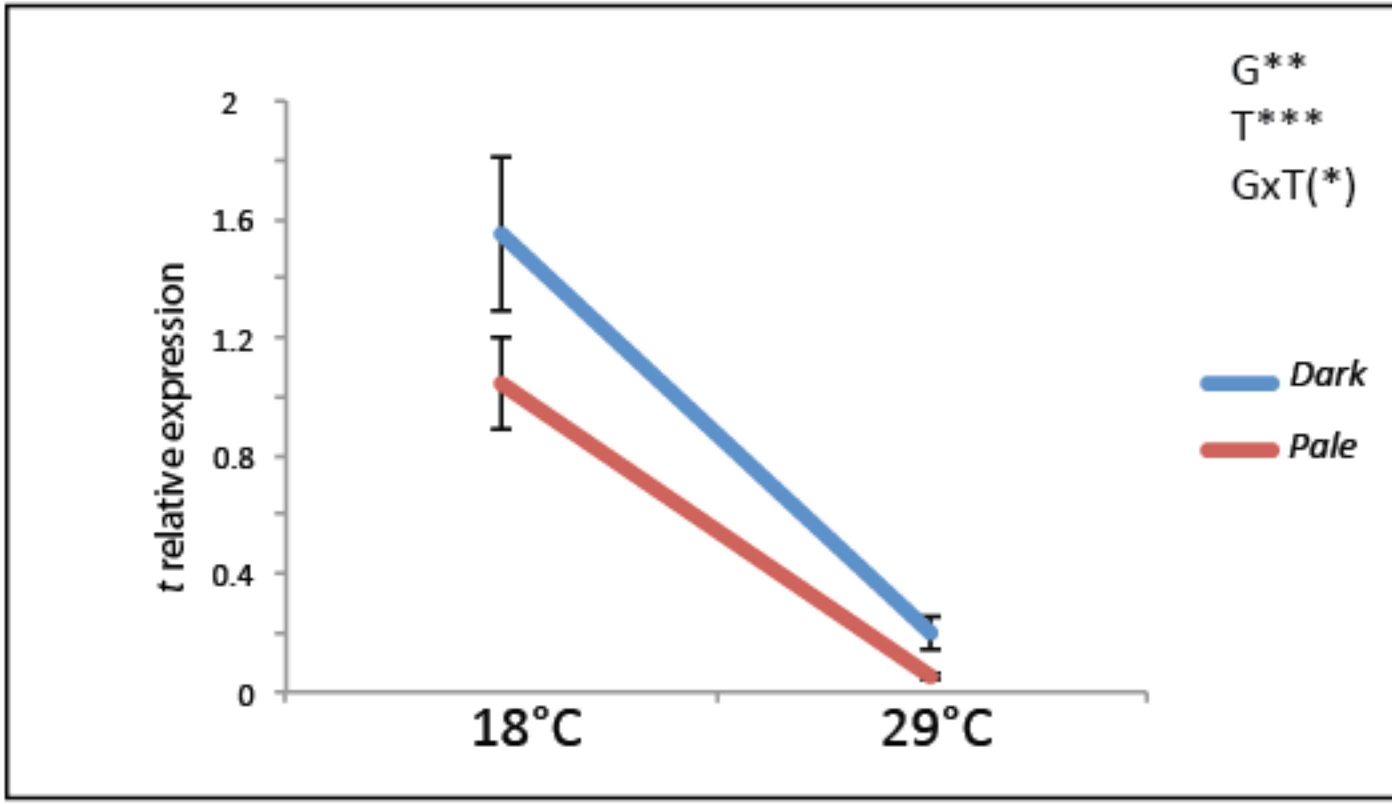
(De Castro *et al.*, PLOS Genetics, 2018)

Analysis of *tan* expression in the *Dark* and *Pale* lines



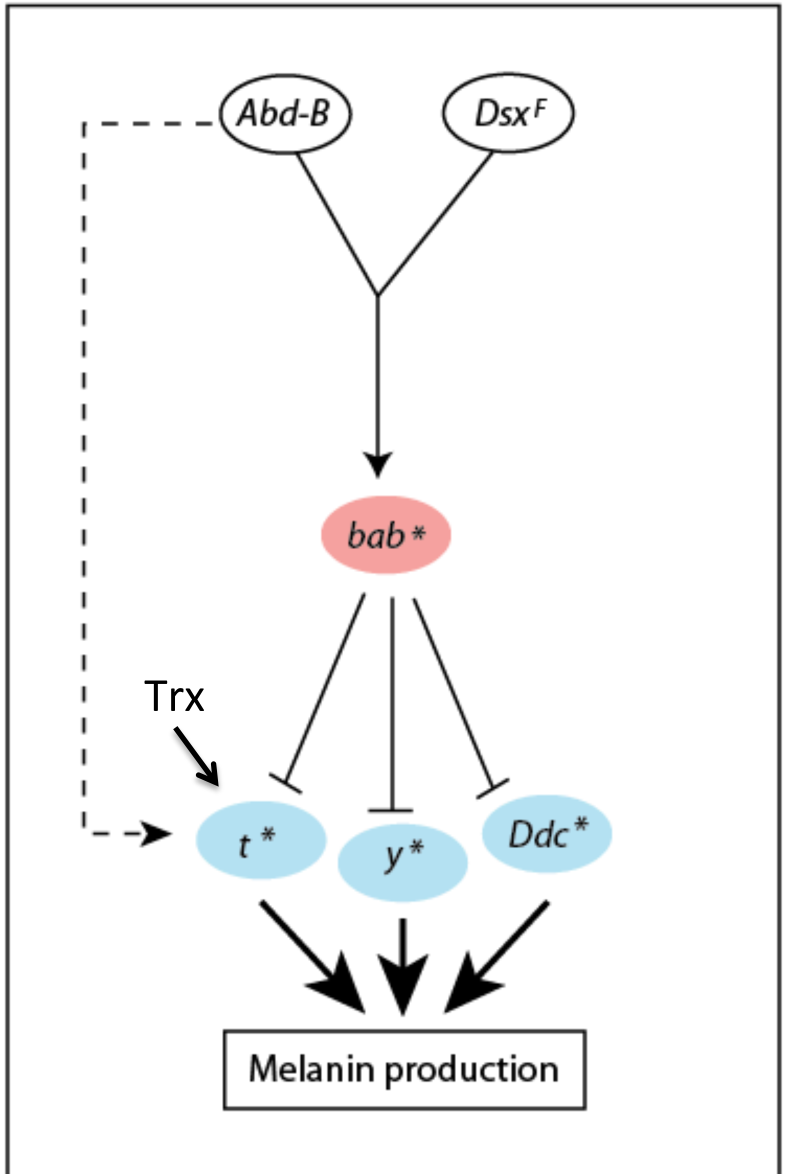
(De Castro *et al.*, PLOS Genetics, 2018)

Analysis of *tan* expression in the *Dark* and *Pale* lines



(De Castro *et al.*, PLOS Genetics, 2018)

Model



(De Castro *et al.*, PLOS Genetics, 2018)

Interestingly, genetic variation in *tan t-MSE* and *bab* dimorphic element is involved in within and between *Drosophila* species pigmentation variation (Bastide et al., 2013; Yassin et al., 2016; Jeong et al., 2008; Rogers et al., 2013).

This suggests that the temperature sensitivity of these regulatory sequences turns them into evolutionary hotspots by facilitating the selection of the genetic variation they carry.

Acknowledgments

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Bart Deplancke (EPFL)

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