From egg to embryo to organism…

Positional information

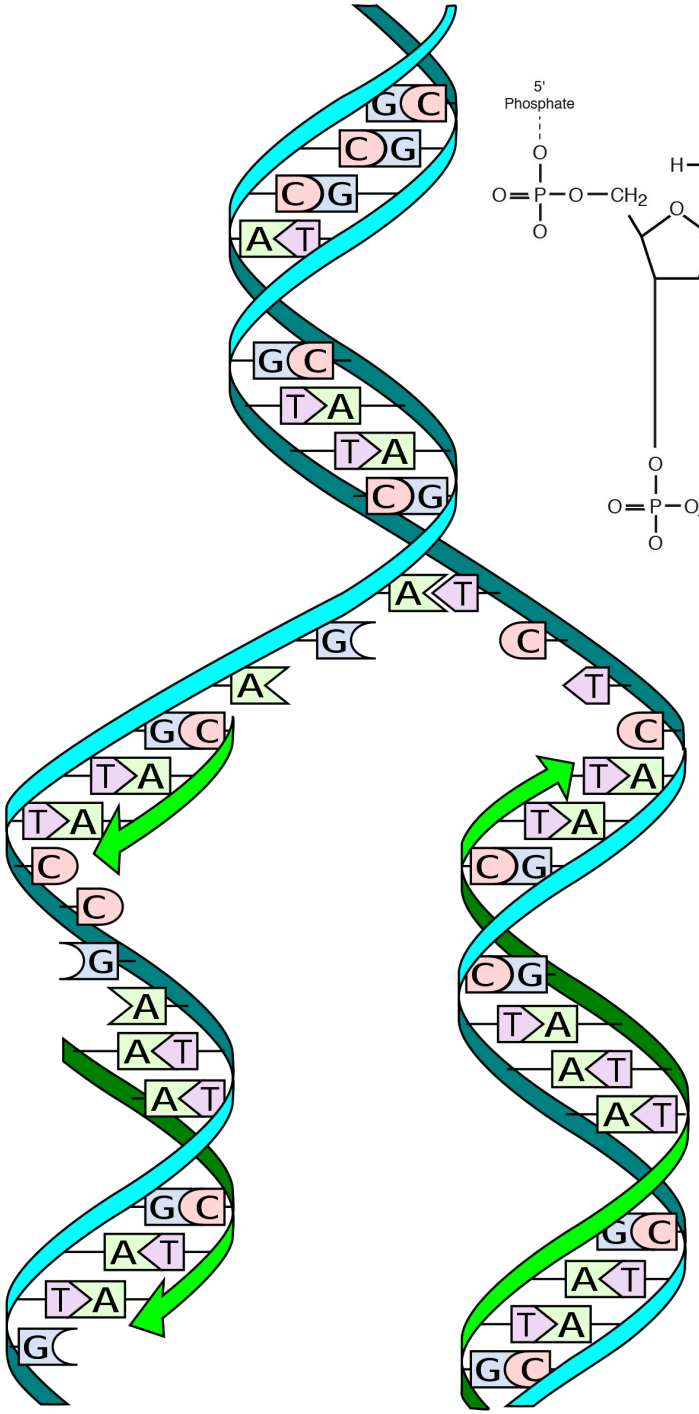
Size and shape of organs and tissues

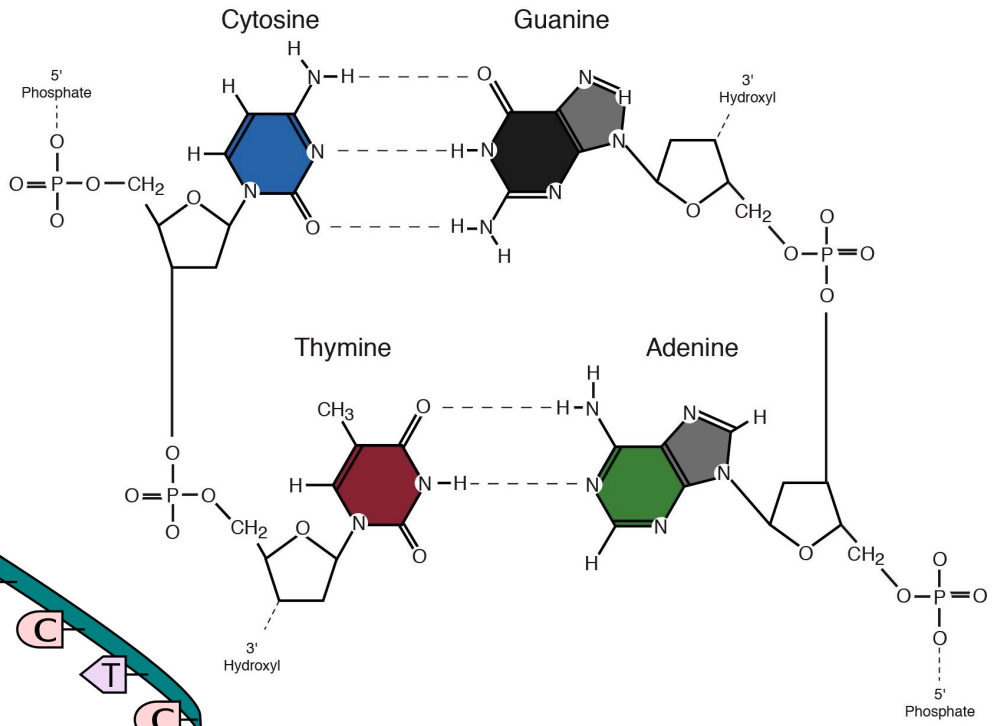
Physiological connections

Improvised use of basic cellular mechanisms

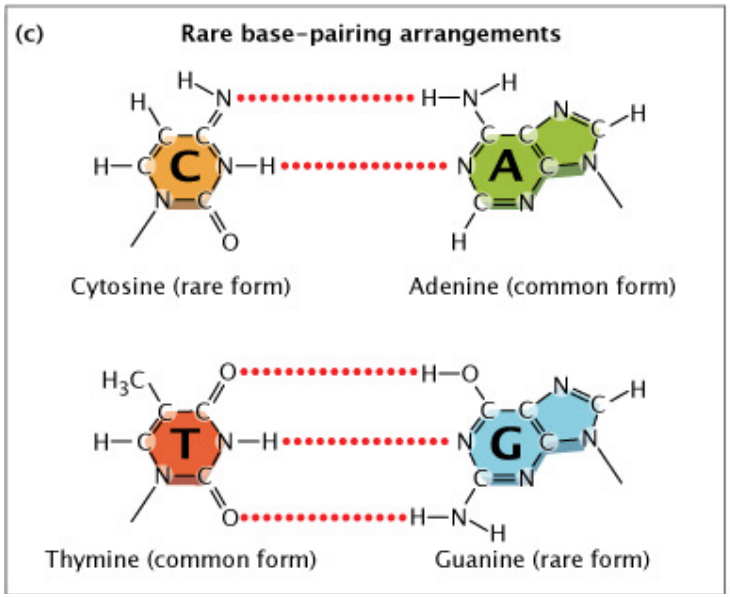
Complex regulatory circuits controlling cell division

Spatio-temporal regulation of gene expression





Variations in DNA copying mechanism



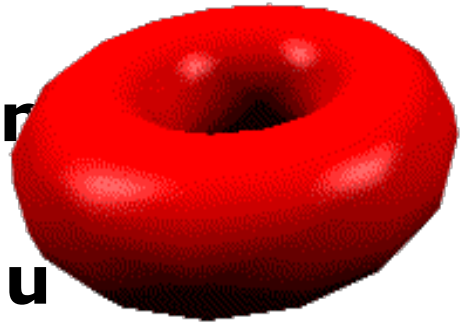
Structure–Function relationship

Genetic variations cause structural changes.

Function emerges

New function is the substrate for natural selection.

Normal Human Beta Chain (first 7 codon

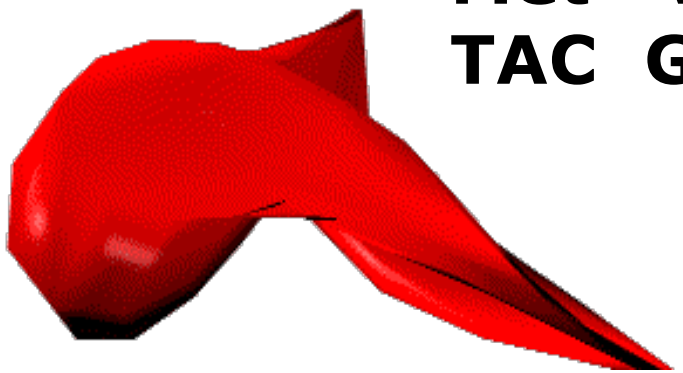


Met	Val	His	Leu	Thr	Pro	Glu
TAC	GTG	CAC	CTG	ACT	CCT	GAG

Sickle cell hemoglobin (Hemoglobin S) results when, glutamic acid that is normally present in the 7th position on the beta globin chain is substituted with valine.

Sickle Cell Hemoglobin (first 7 codons)

Met	Val	His	Leu	Thr	Pro	Val
TAC	GTG	CAC	CTG	ACT	CCT	GTG



- **Sickle Cell Anemia vs Malaria**

Generation of endless forms/most beautiful

Every time we pass on our genetic information to the next generation, some new variations are introduced. Depending on the environment, some will survive, some will not.

Diversity is key for survival

Sustenance of life on earth for the past 3.7 billion years has been possible due to the process, in which each individual becomes different from the rest.

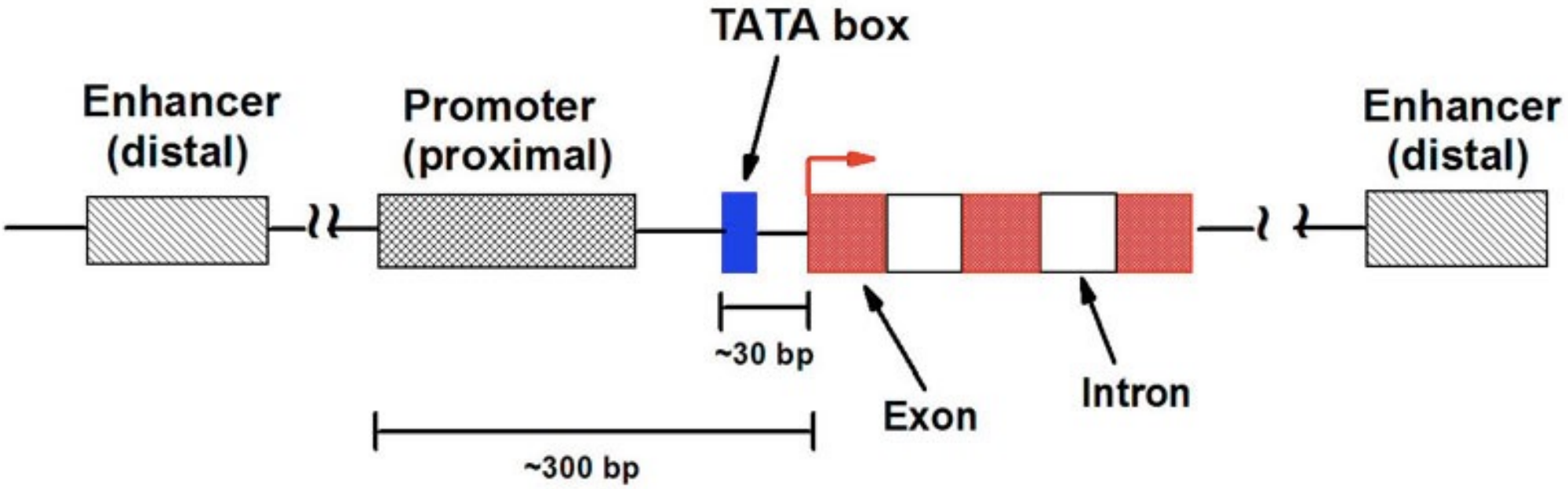
This ensures that, at least, a group of individuals of a population survive in any given environment.

More the genetic diversity of a population, more is the chances of its survival and continuance.

Evolution of Developmental Mechanisms

Morphogen gradients –
Signaling Pathways
Master regulatory genes

Typical structure of a Eukaryotic gene

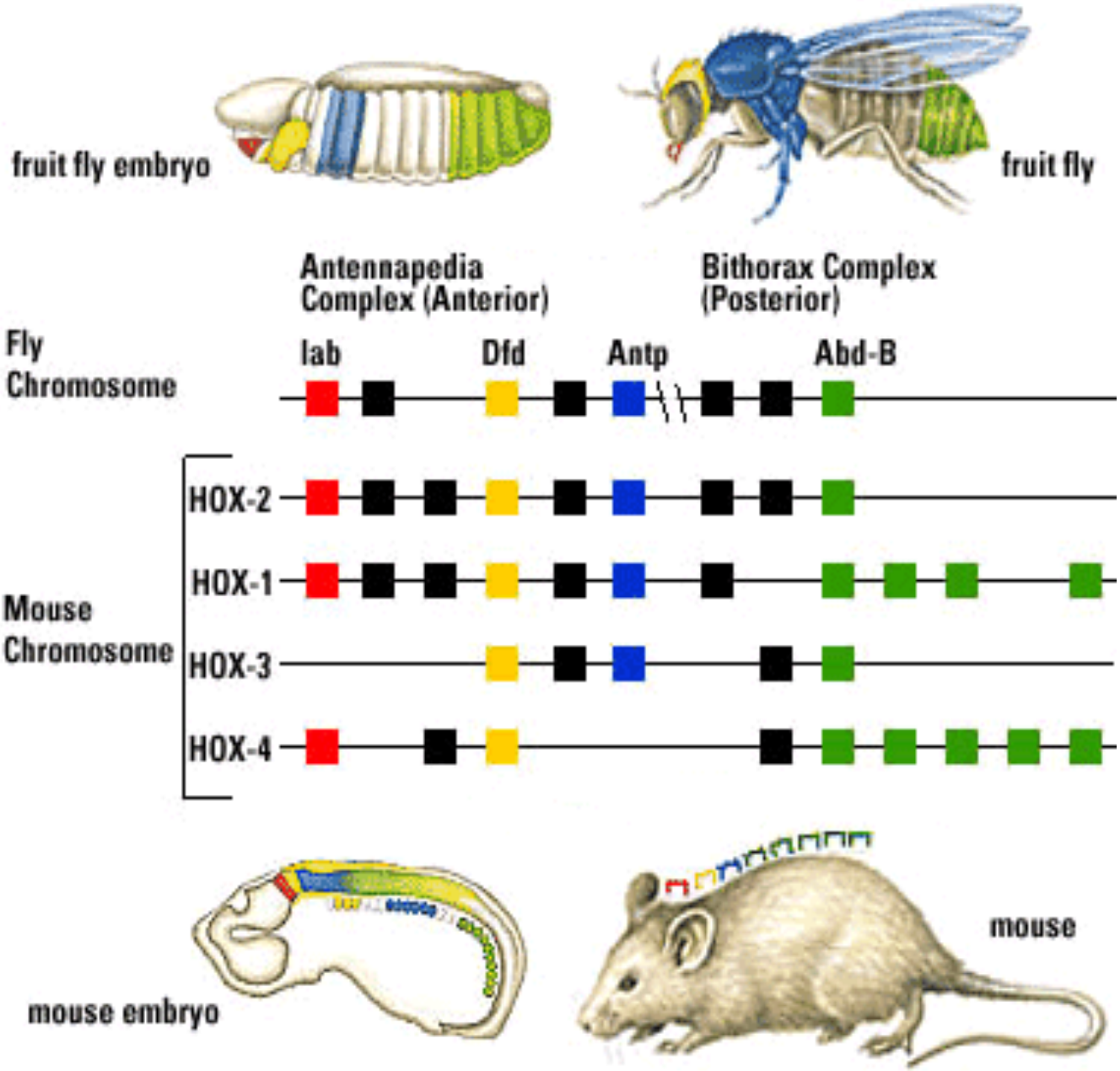


DNA has information not only to make a specific protein, but also when, where and how much

Several models linking gene evolution to changes in adult body plan

- Changes in the number of genes (duplication and divergence) –
- Changes in domain of gene expression
- Changes in gene that give the protein new properties
- Changes in cofactors that interact and provide specificity to gene functions
- Changes in downstream-responsive elements

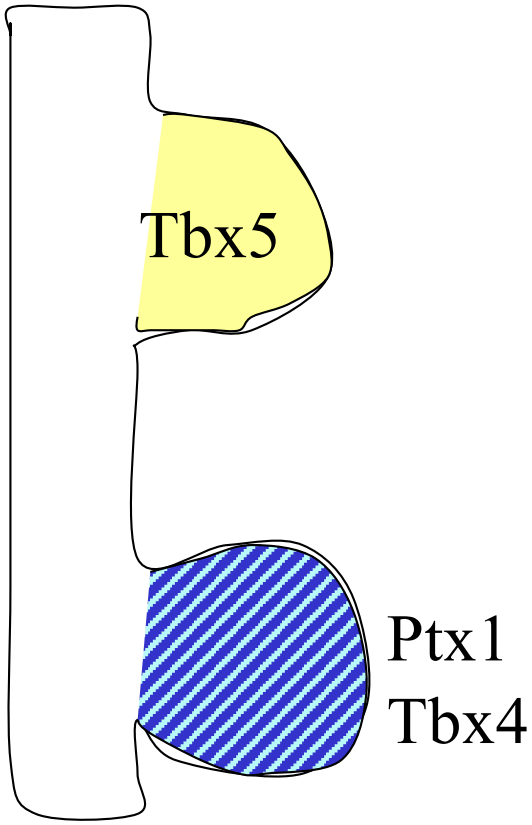
Comparison of Hox genes in fly and mouse embryos



Organization of Hox genes, their sequences and function – all are conserved from flies to mice to human.

Regulation of gene expression

Fore Limb Vs Hind Limb

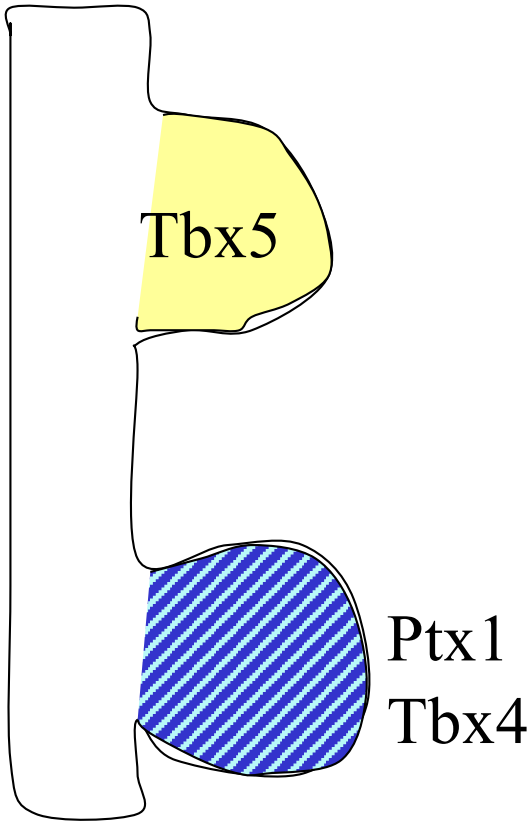


Hoxc4 Hoxc5

Hoxc6 Hoxc8

Hoxc9 Hoxc10 Hoxc11

Fore Limb Vs Hind Limb



Hoxc4 Hoxc5

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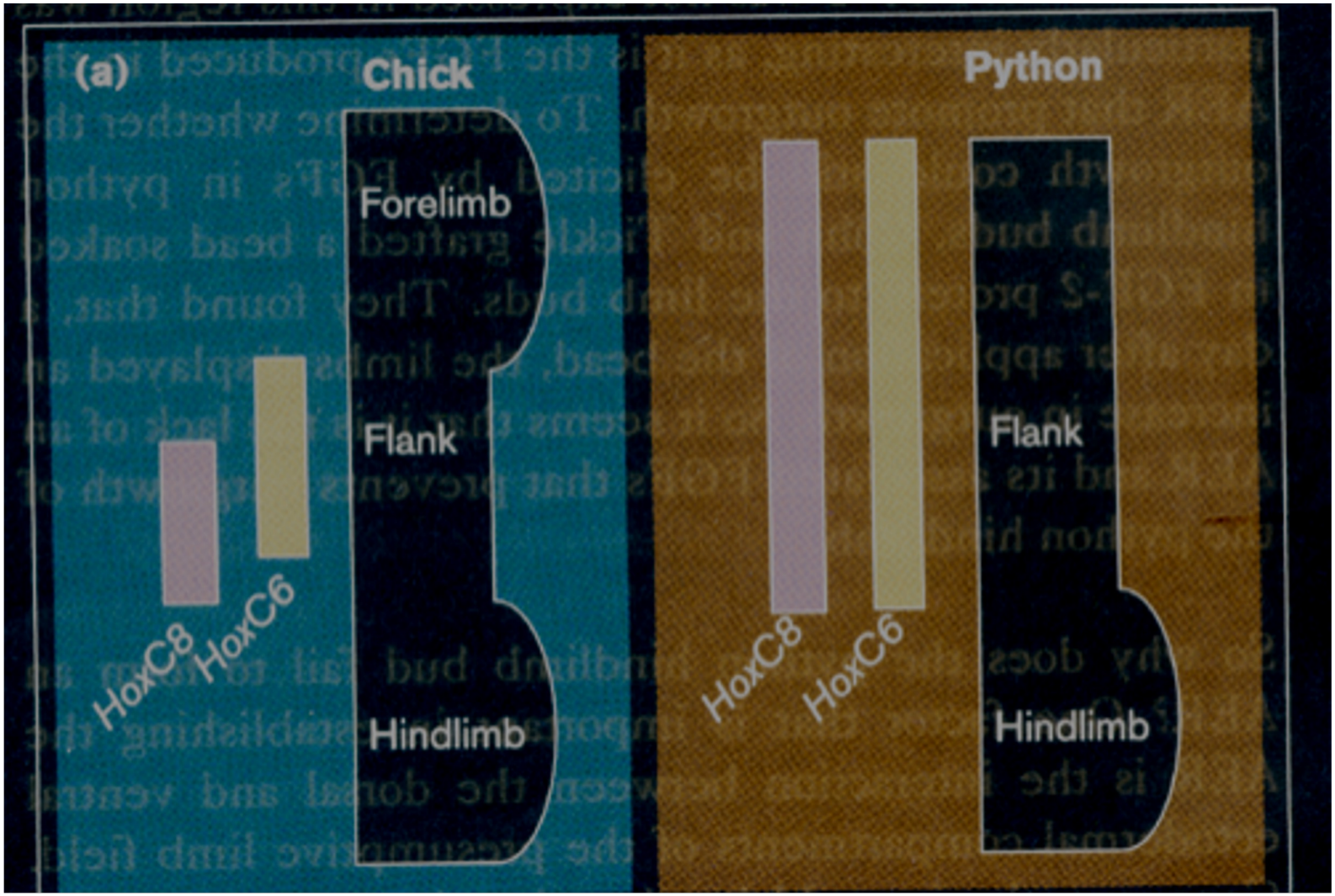

(a)
Chick
Forelimb
Flank
Hindlimb
HoxC8
HoxC6
Python
Flank
Hindlimb
HoxC8
HoxC6

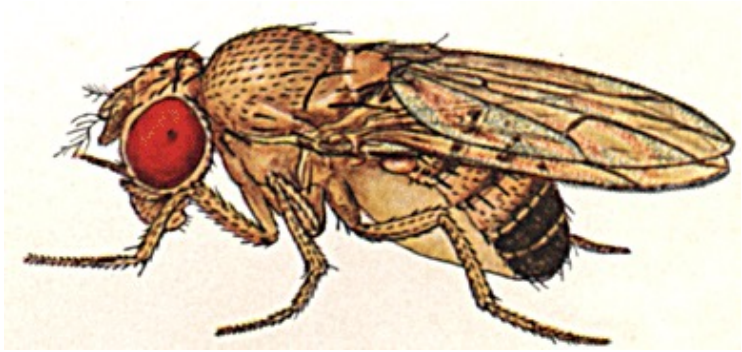
Phylum Arthropoda

Common brine shrimp (*Artemia*)
Class Crustacea

Butterfly

Class Insecta

Order lepidoptera

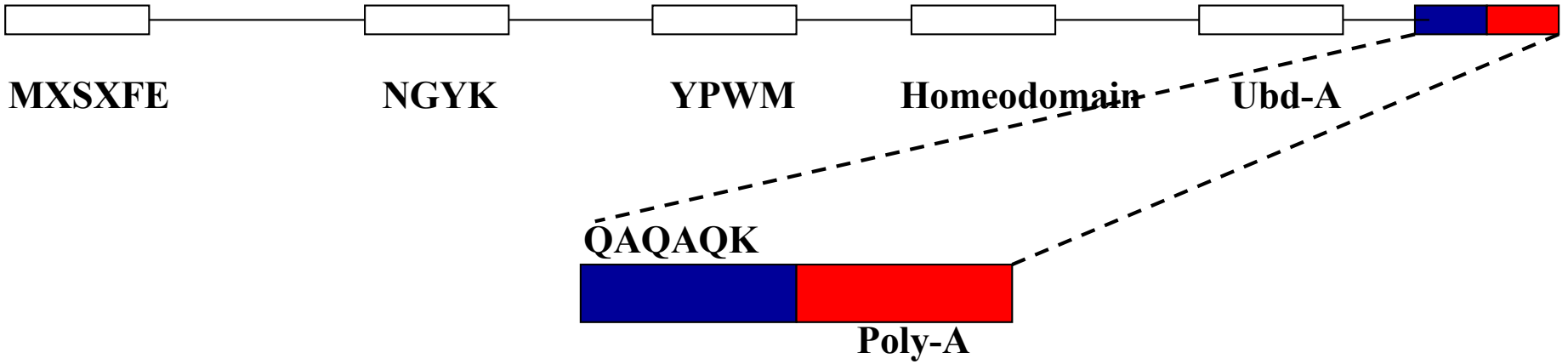


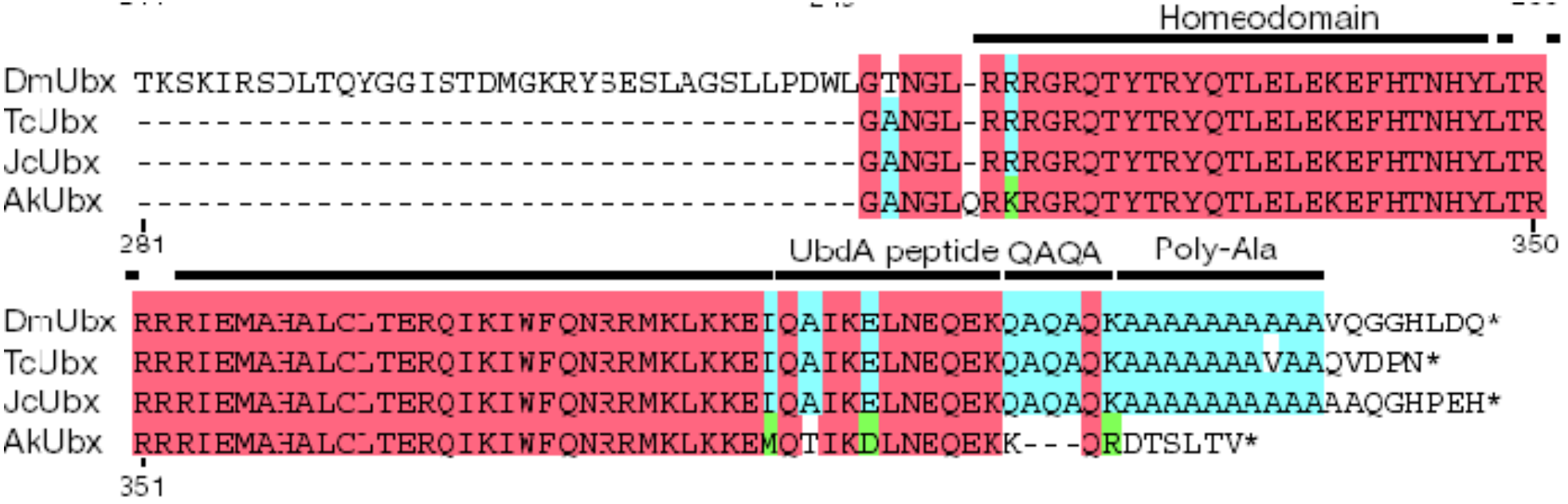
Drosophila

Class Insecta

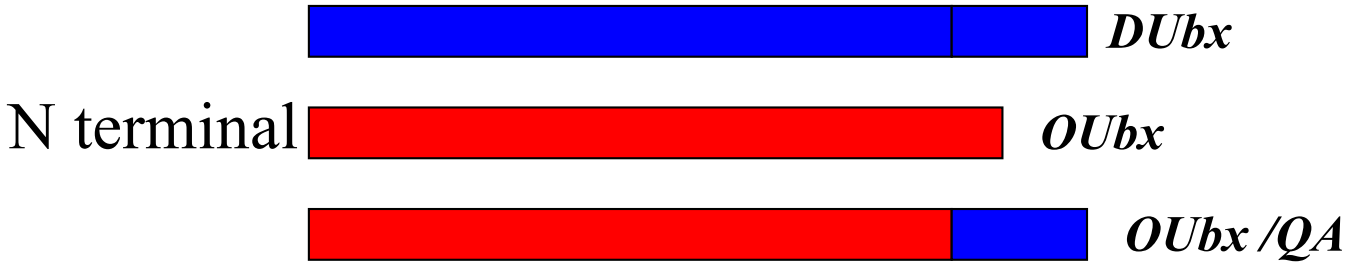
Order Diptera

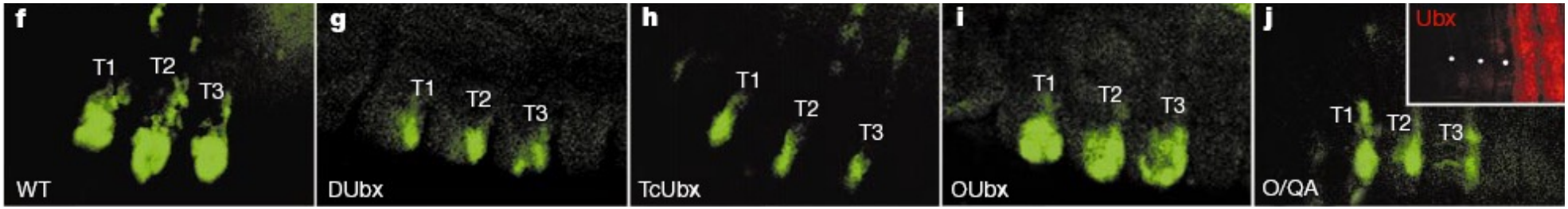
Evolution of C-terminal domain of the insect Ubx vis-à-vis suppression of abdominal leg development





Evolution of C-terminal domain of the insect Ubx vis-à-vis suppression of abdominal leg development





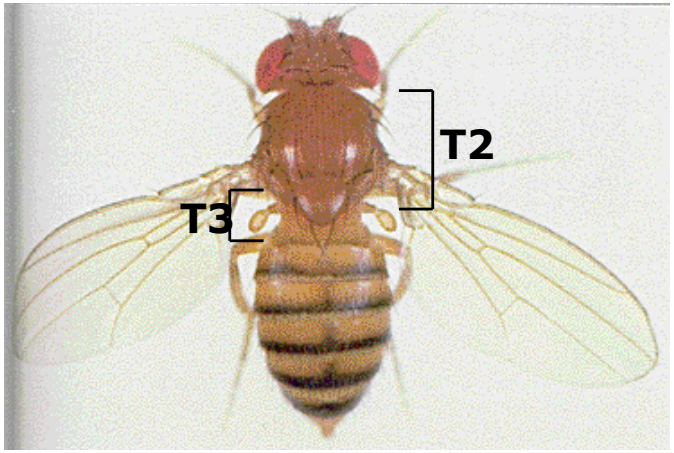
Galant R, Carroll SB.Nature. 2002 Feb 21;415(6874):910-3.
Ronshaugen et al Nature. 2002 Feb 21;415(6874):914-7.

Several models linking Hox evolution to changes in adult body plan

- Changes in the number of Hox gene (duplication and divergence)
- Changes in domain of Hox gene expression
- Changes in Hox gene that gives the protein new properties
- Changes in cofactors that interact and provide specificity to Hox proteins
- Changes in Hox-responsive elements of downstream genes

wing vs haltere in *Drosophila*

No *Ubx* in T3

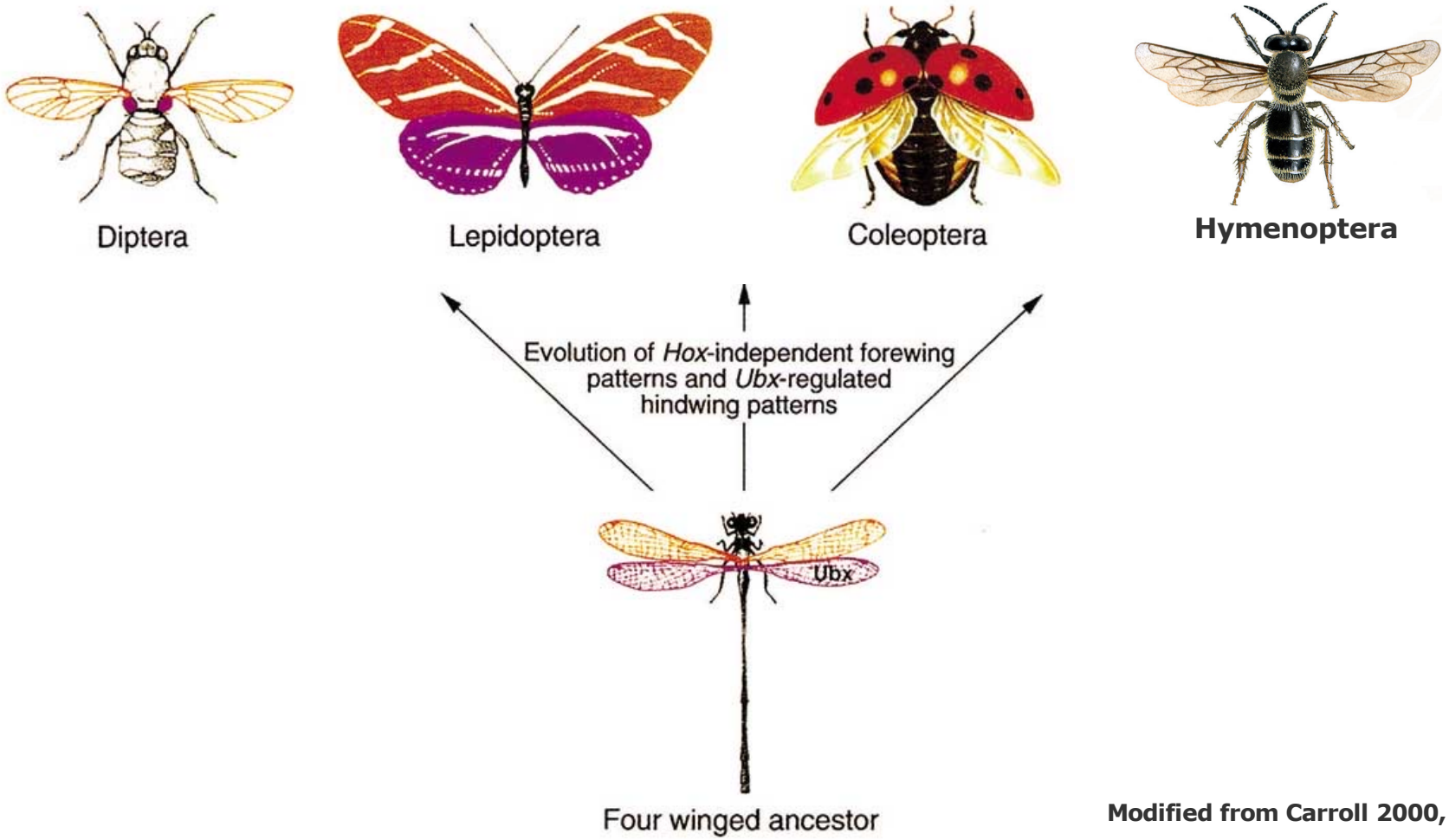


Wildtype

Ubx in both T2 and T3

Ed Lewis, Antonio Garica-Bellido, Gines Morata, Ernesto Sanchez-Herrero and many others

Evolution of Insect wing number and morphology



Modified from Carroll 2000,

Several models linking Hox evolution to changes in adult body plan

- **Changes in the number of Hox gene (duplication and divergence) – *all insects have the same number of Hox genes and only one Ubx***

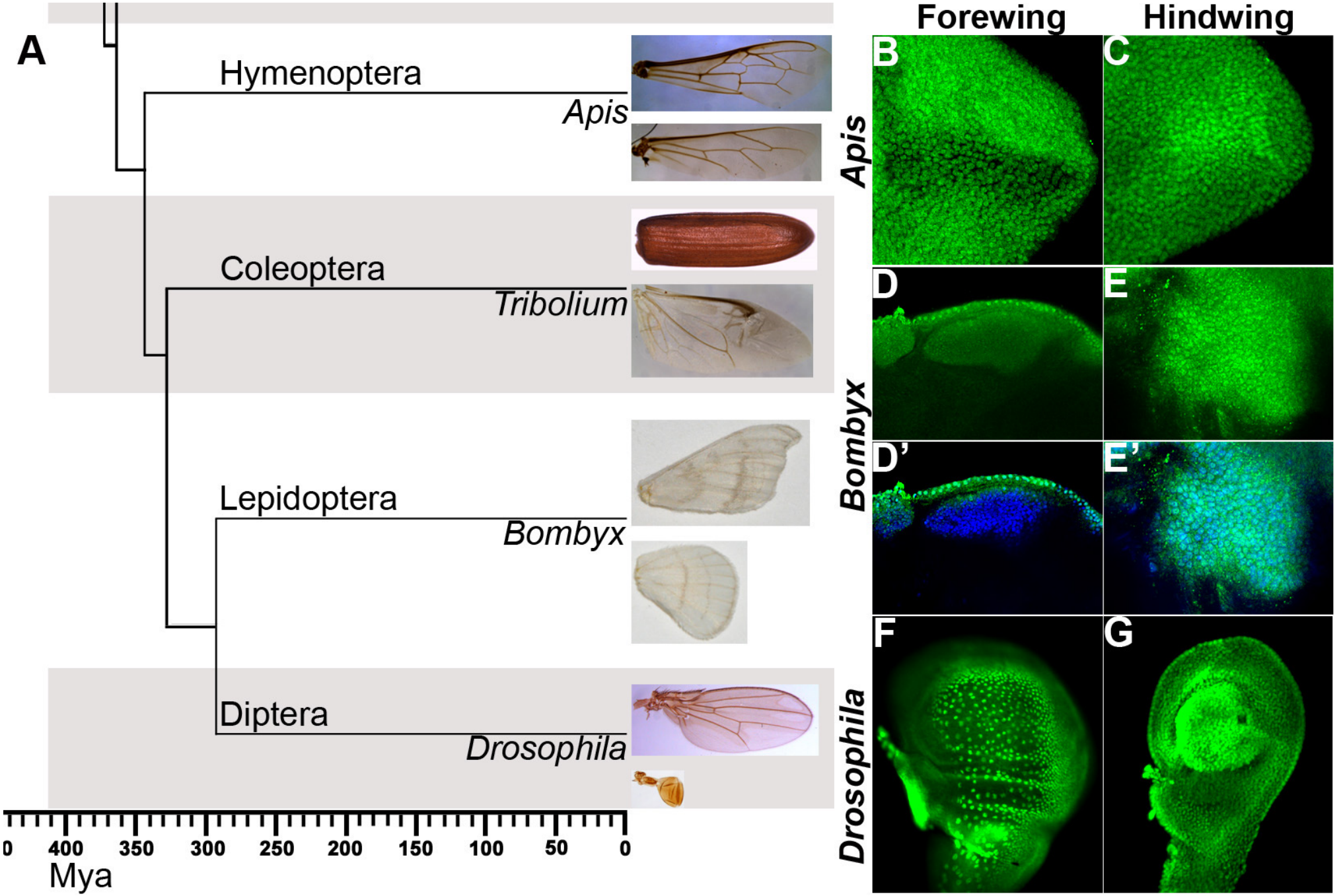
- **Changes in domain of Hox gene expression**

- **Changes in Hox gene that gives the protein new properties**

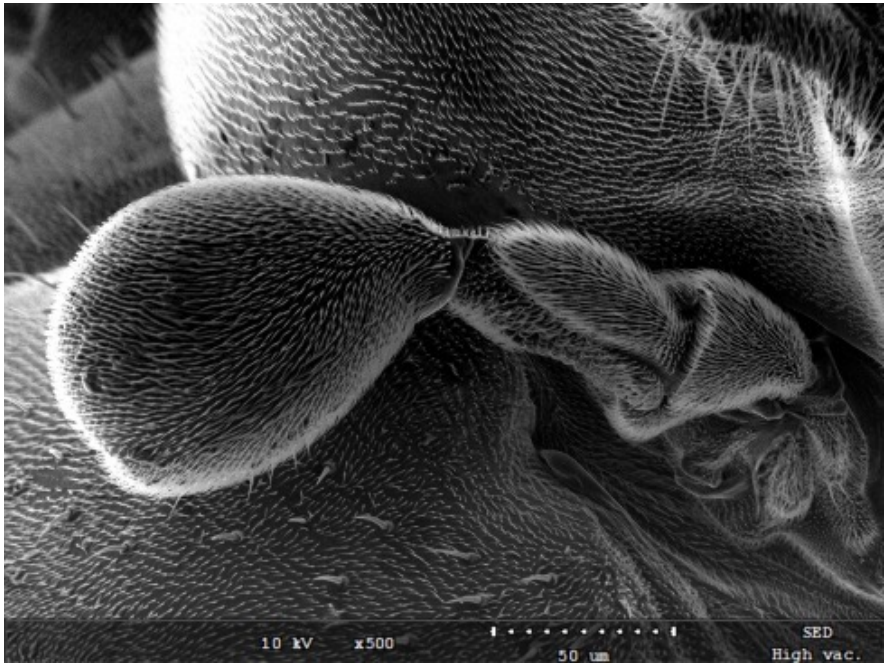
- **Changes in cofactors that interact and provide specificity to Hox proteins**

- **Changes in Hox-responsive elements of downstream genes**

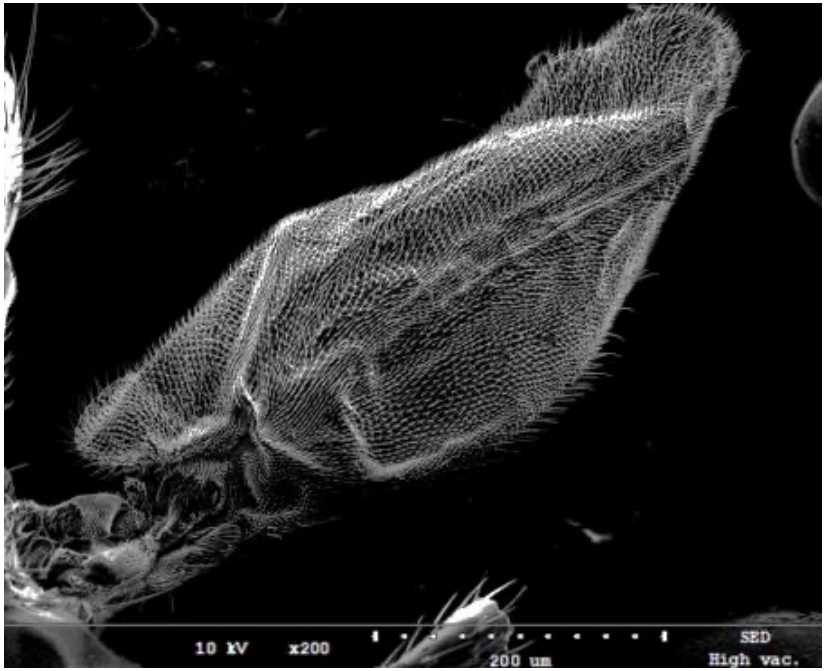
Ubx is expressed in the developing hindwing of all insects

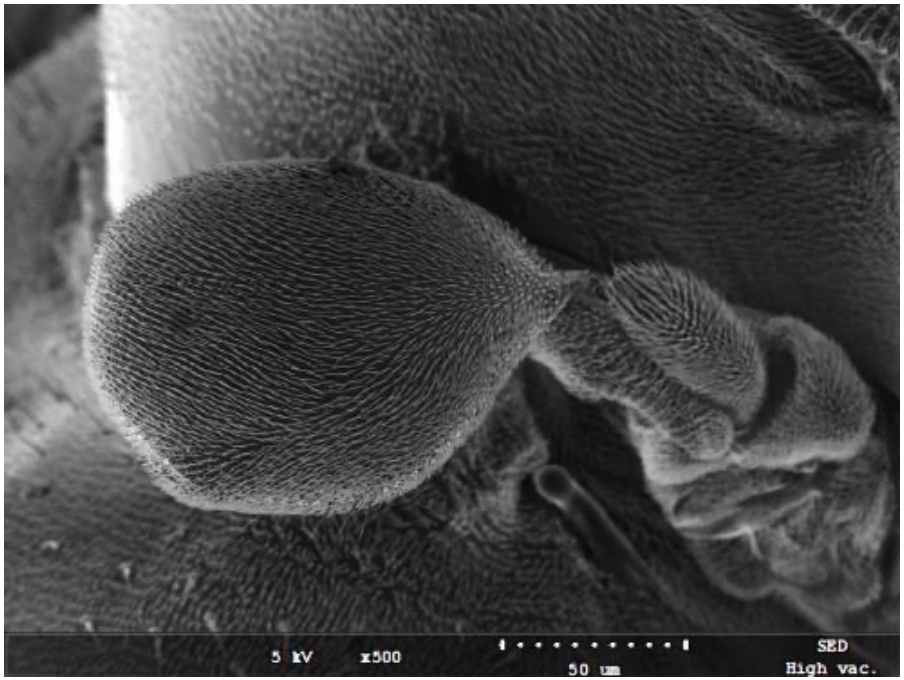


Wild Type



Ubx-mutant





Ubx-mutant,
rescued by *Drosophila* Ubx

Samir lab

Ubx-mutant,
rescued by *Tribolium* Ubx

Ubx-mutant,
rescued by *Bombyx* Ubx

Samir lab

Identification of direct targets of Ubx in *Drosophila*, *Apis*, and *Bombyx* by ChIP-chip or ChIP-seq method

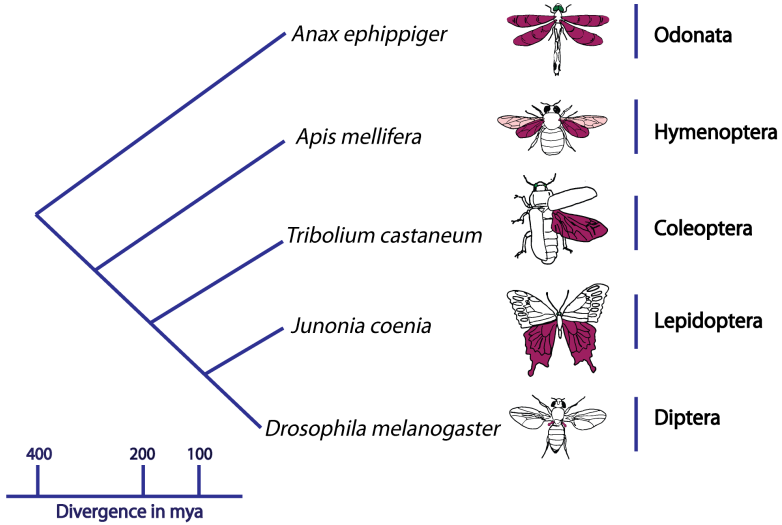
Tribolium

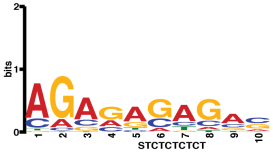
Apis √√

Bombyx √√

Drosophila √√

A Differences in Ubx-binding motifs – *Drosophila* vs *Apis*

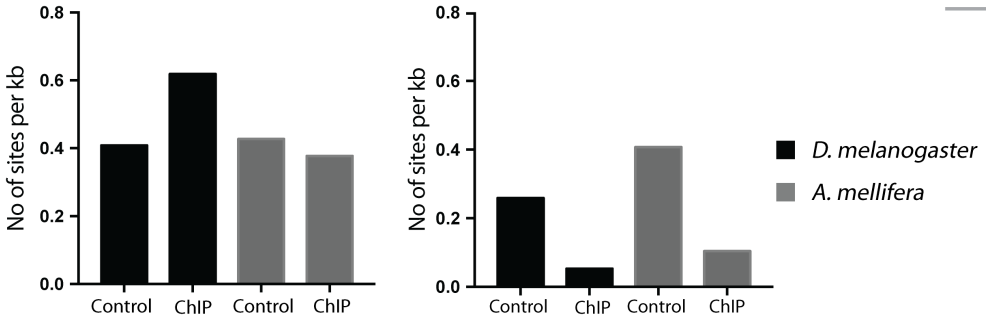


Enriched motif from de-novo analysis		p Value	
		D. melanogaster	*A. mellifera*
	TAAAT motif	1e-106	Not enriched
	Pho/Phol	1e-52	1e-419
	Trl/GAGA	1e-35	1e-27
	Brk	1e-46	1e-17

C

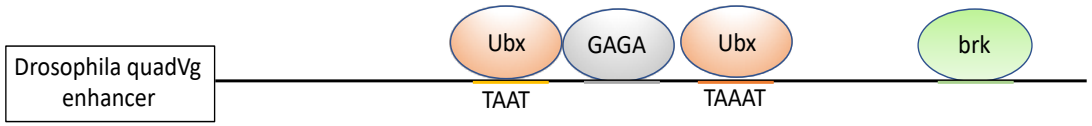
TAAAT motif

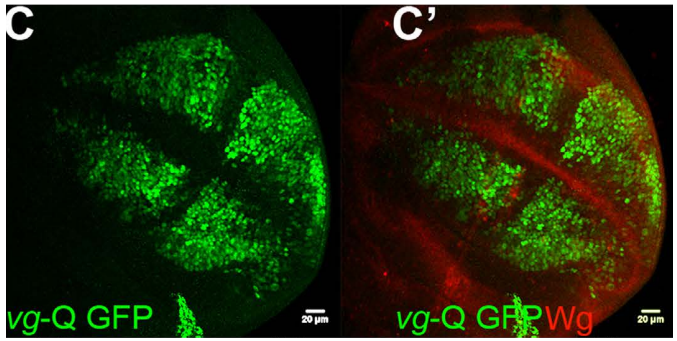
TAAT motif



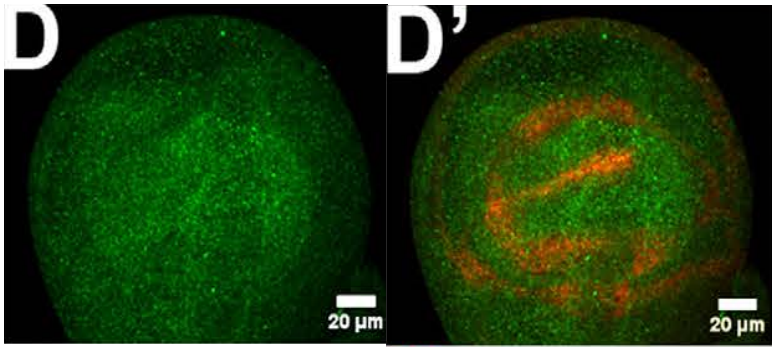
Soumen Khan

Assessing the importance of the TAAT vs TAAAT motifs in the regulation of a target of Ubx (Vg – negatively regulated in *Drosophila*

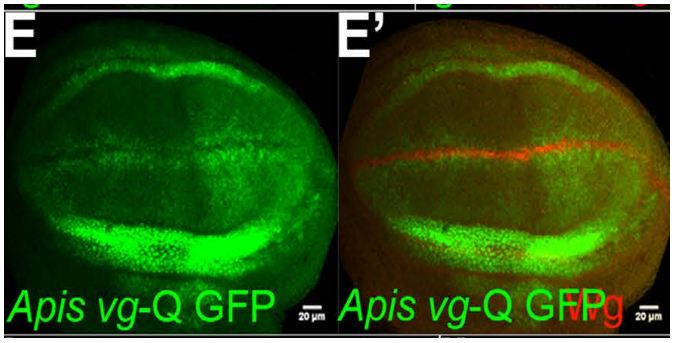




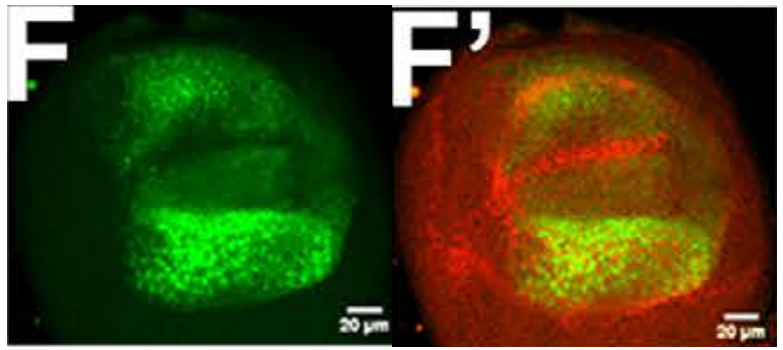
vg-Q GFP in the wing discs



vg-Q GFP in the haltere discs



Apis vg-Q GFP in the wing discs



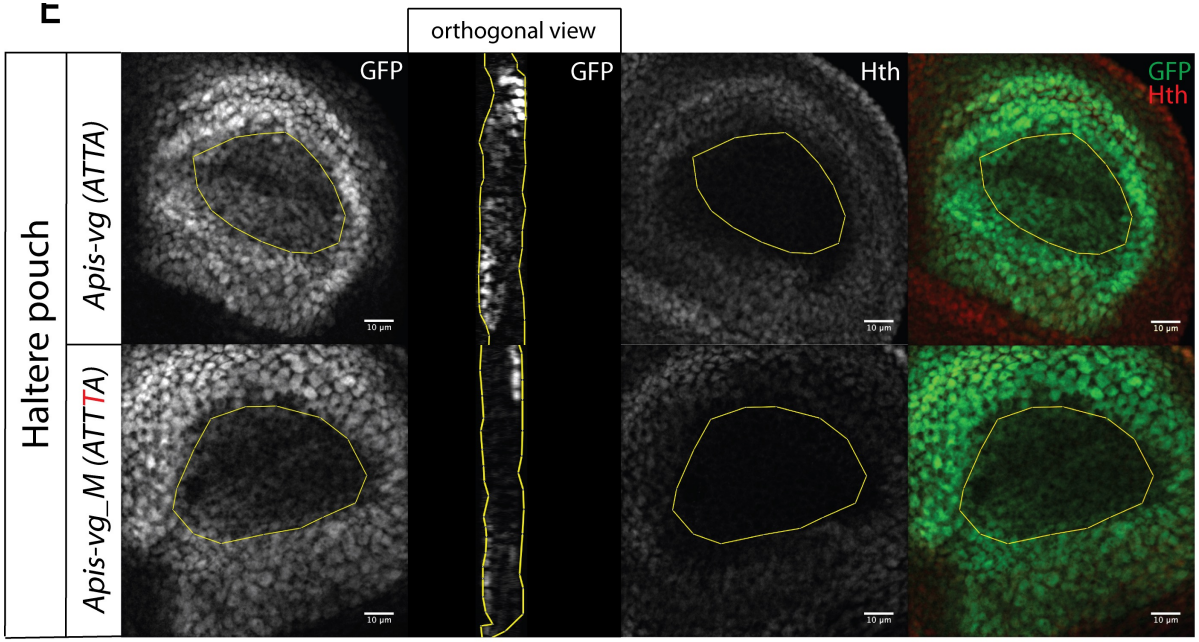
Apis vg-Q GFP in the haltere discs

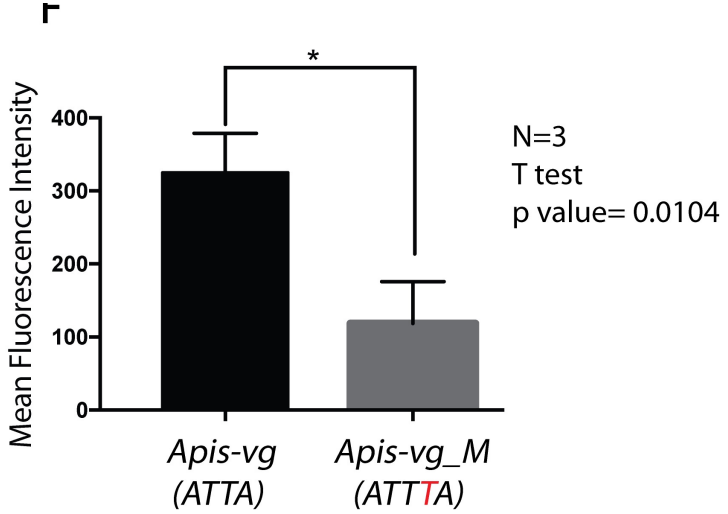
Prasad et. al, 2016

TAAAT and not TAAT motif is sufficient to suppress *Apis-vg* enhancer

Apis-vg (ATTA) GCTCTTATTAATTGCGAGC

Apis-vg_M (ATTTA) GCTCTTATTTATTGCGAGC





Soumen Khan

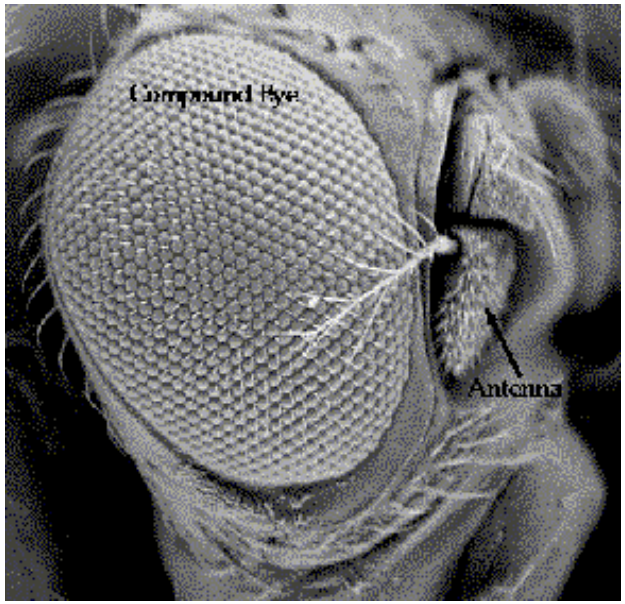
Conserved spatio-temporal gene regulation, but divergence of downstream events

We now know so much about how eye develops and in exactly the same position in a species that

we can induce eye development on legs…

…or virtually anywhere!

Eye development in *Drosophila*, mouse and human is regulated by a similar protein (Pax6)



Work from Walter Gehrig's laboratory

new eye could be induced by expressing Pax-6 gene either from *Drosophila* or mouse or human

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THANK YOU