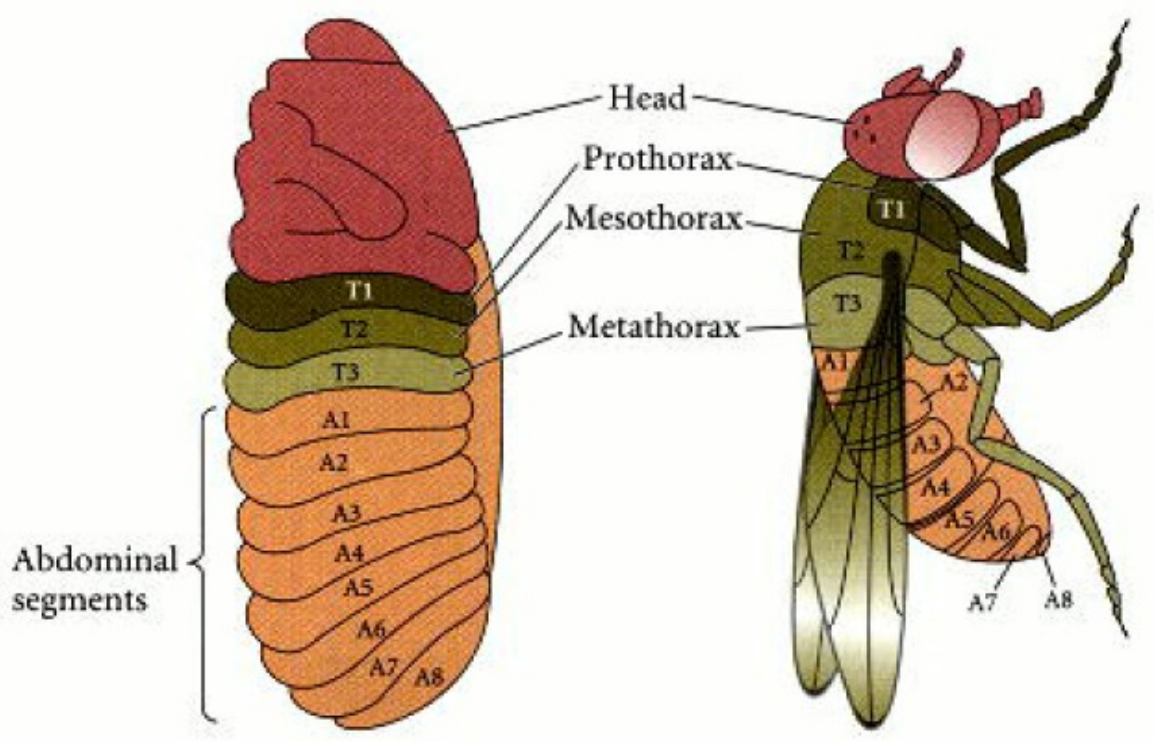
A missing piece of Drosophila shell game: How do heterodimers work?

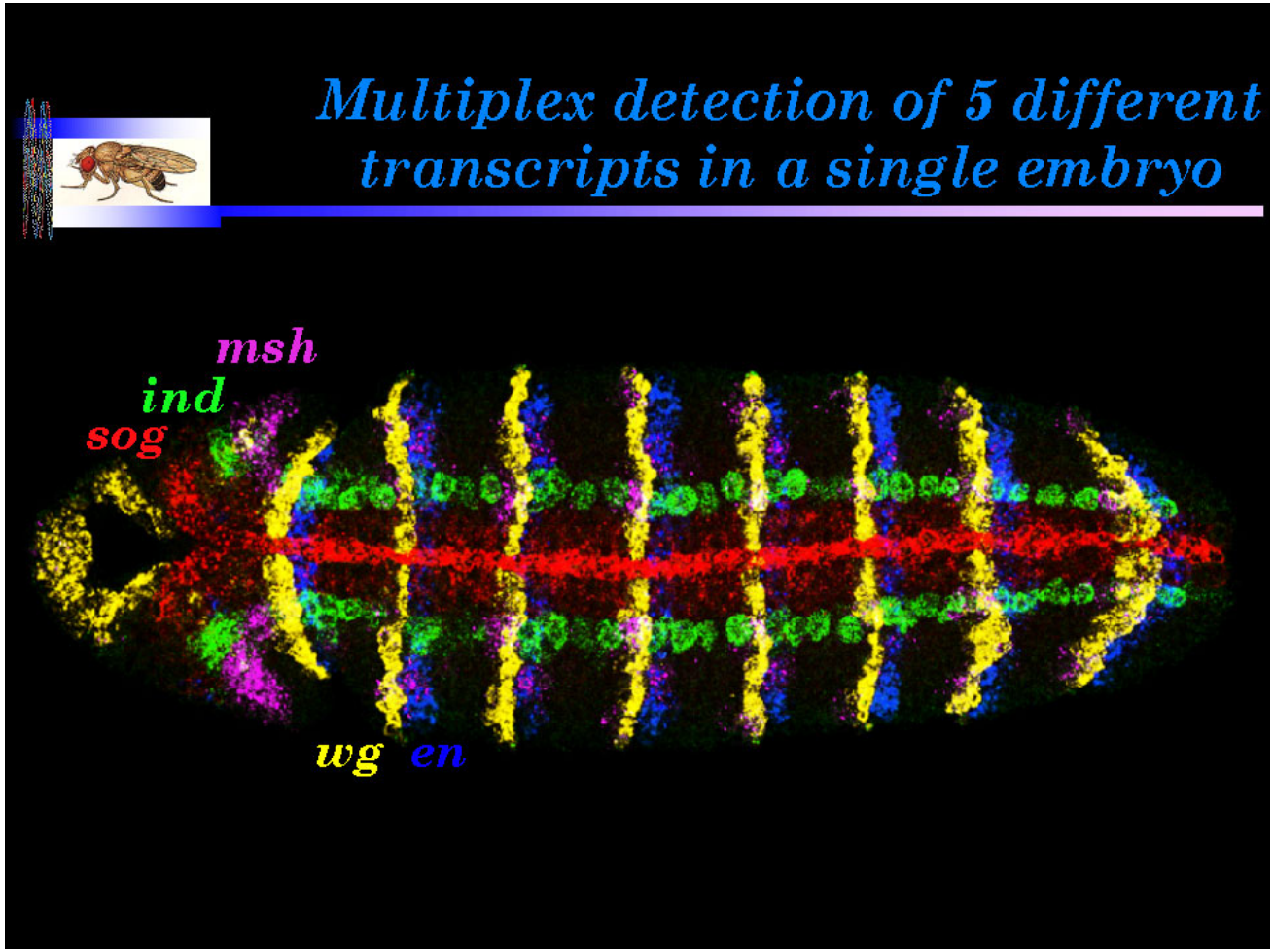
Cui Tiange

Smart cells or tractable cells?



Scott F. Gilbert, Developmental Biology (6th ed.): 2000

Gene patterning



Kosman et al., Science: 2004

“Form giving substances”

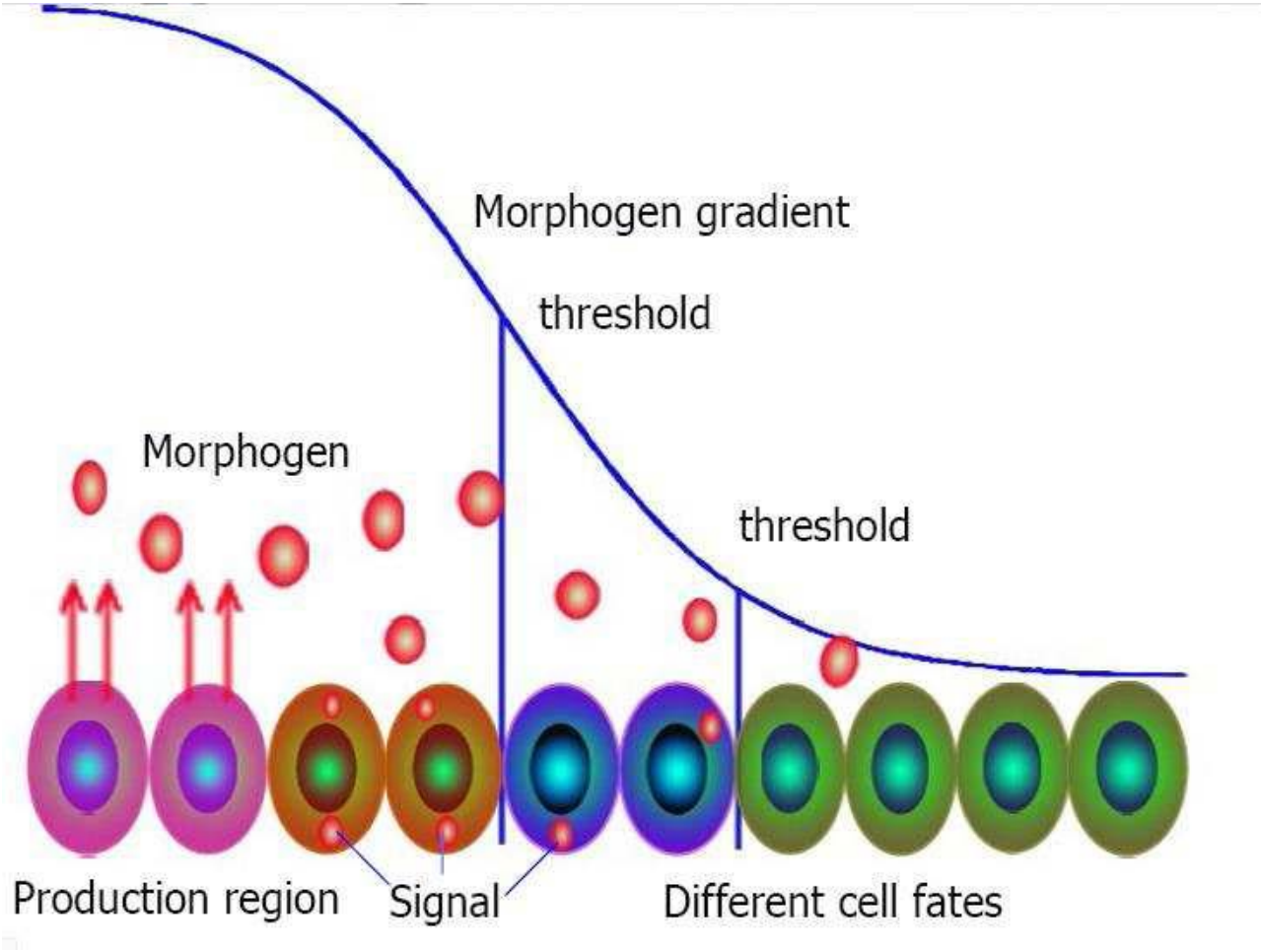
“A system of chemical substances, called ***morphogens***, reacting together and diffusing through a tissue, is adequate to account for the main phenomena of morphogenesis.”

— Dr. Turing, 1952

Alan M. Turing

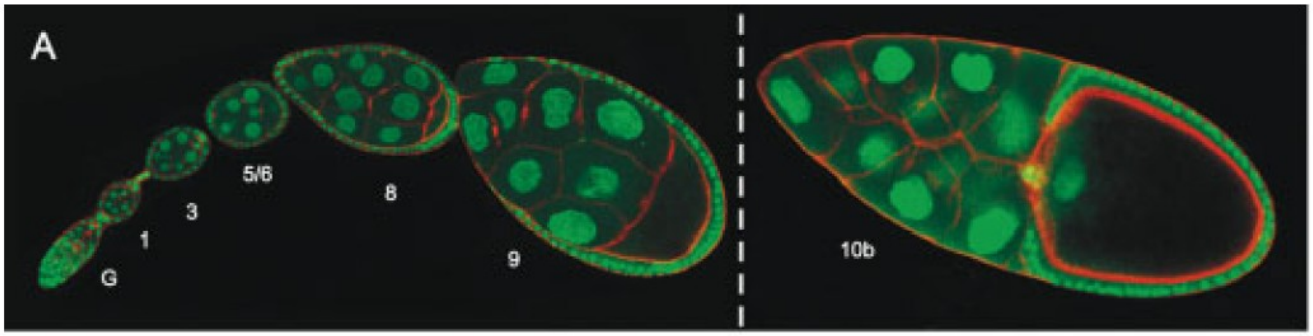
(1912-1954)

Morphogen



Jinzhi Lei, NSFC 10601029: 2007

Drosophila Oogenesis



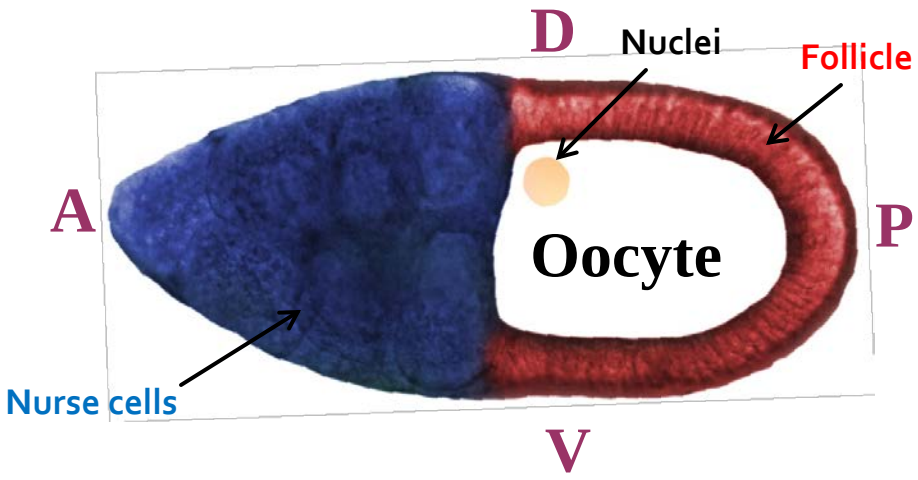
B

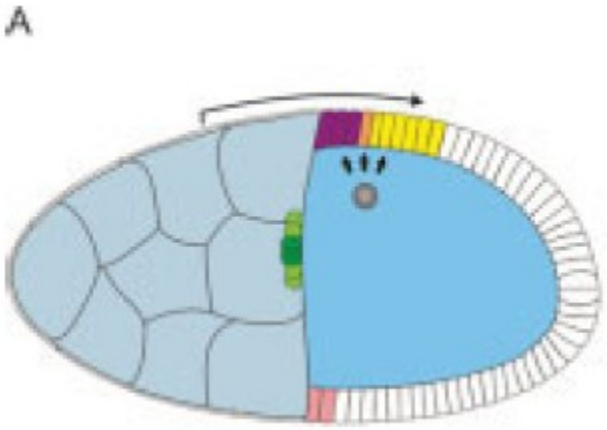
C

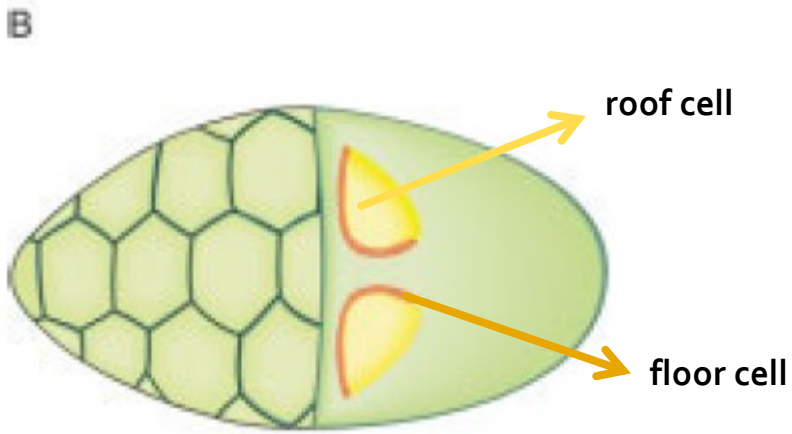
Stage	Up to 1	2	3	4	5	6	7	8	9	10a	10b	11-13	14
Time (hrs)	~40	8	8	6	5	3	6	6	6	6	4	3.5	>2

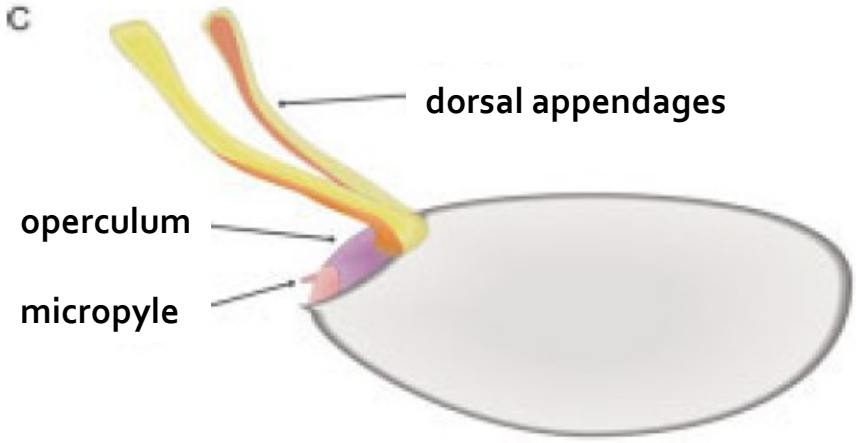
Badovinac and Bilder, Dev. Dynamics: 2005

Eggshell patterning



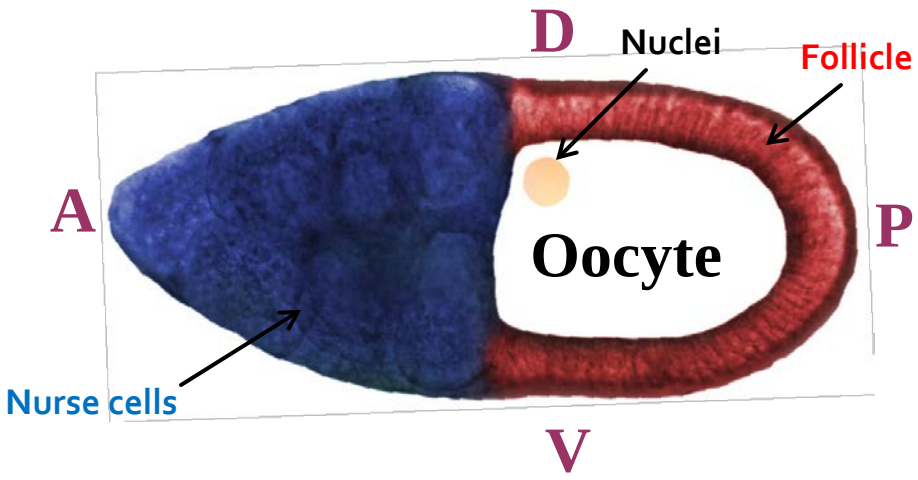


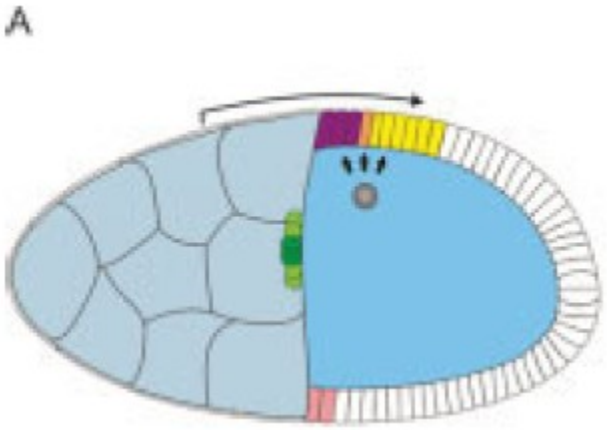


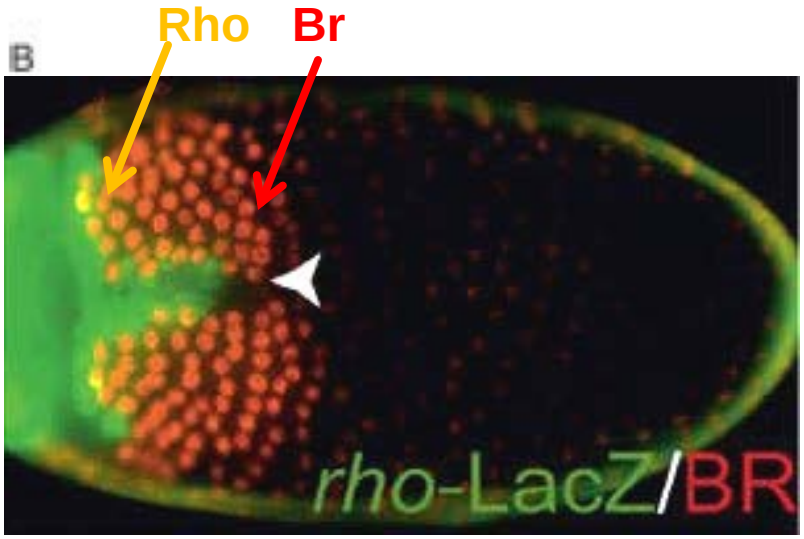


Badovinac and Bilder, Dev. Dynamics: 2005

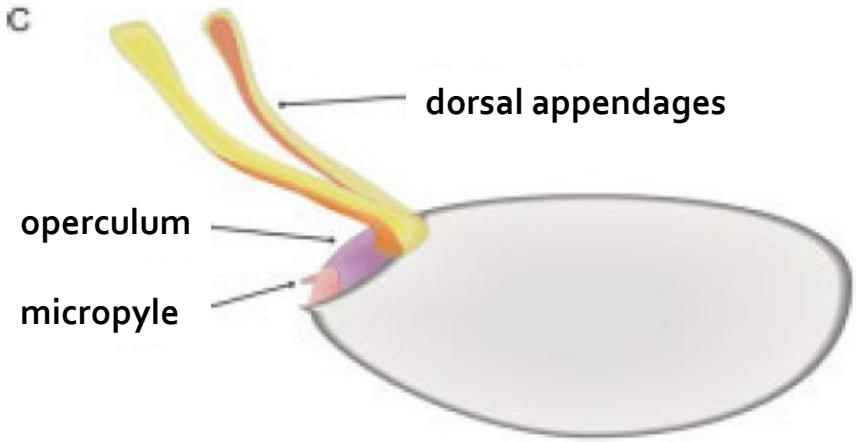
Eggshell patterning





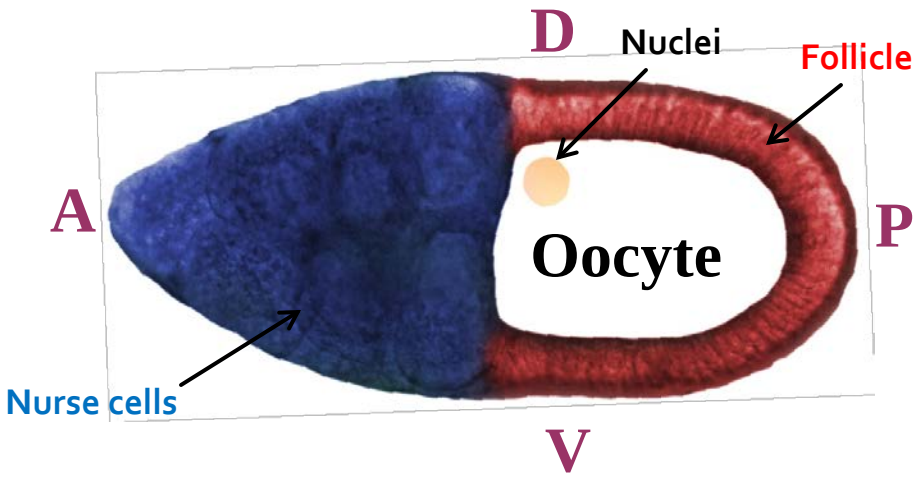


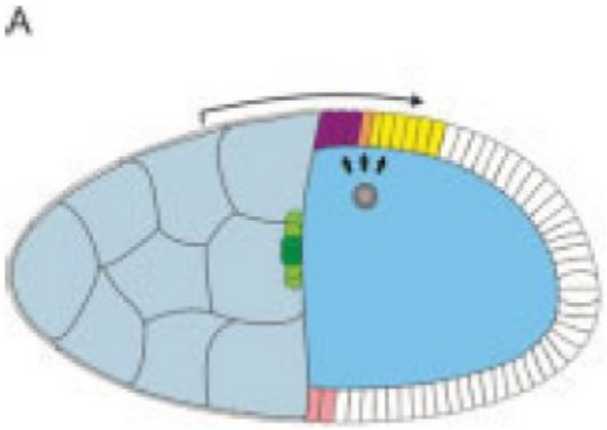
Yakoby et al., Dev. Cell: 2008

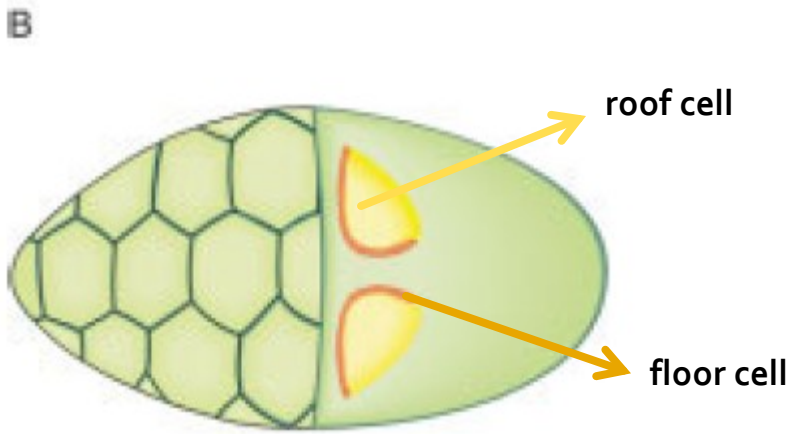


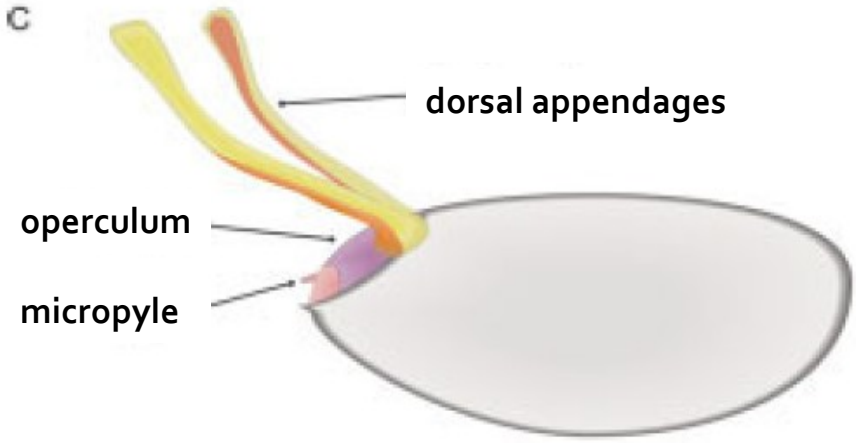
Badovinac and Bilder, Dev. Dynamics: 2005

Eggshell patterning









Badovinac and Bilder, Dev. Dynamics: 2005

Combination of signaling pathways

EGFR signaling pathway

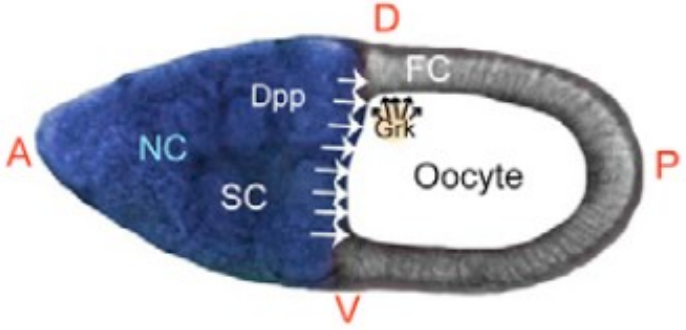
Reeves et al., Dev. Cell : 2006

Activated gradient: Dorsal | Ventral

BMP signaling pathway

Activated gradient:

Anterior – Posterior

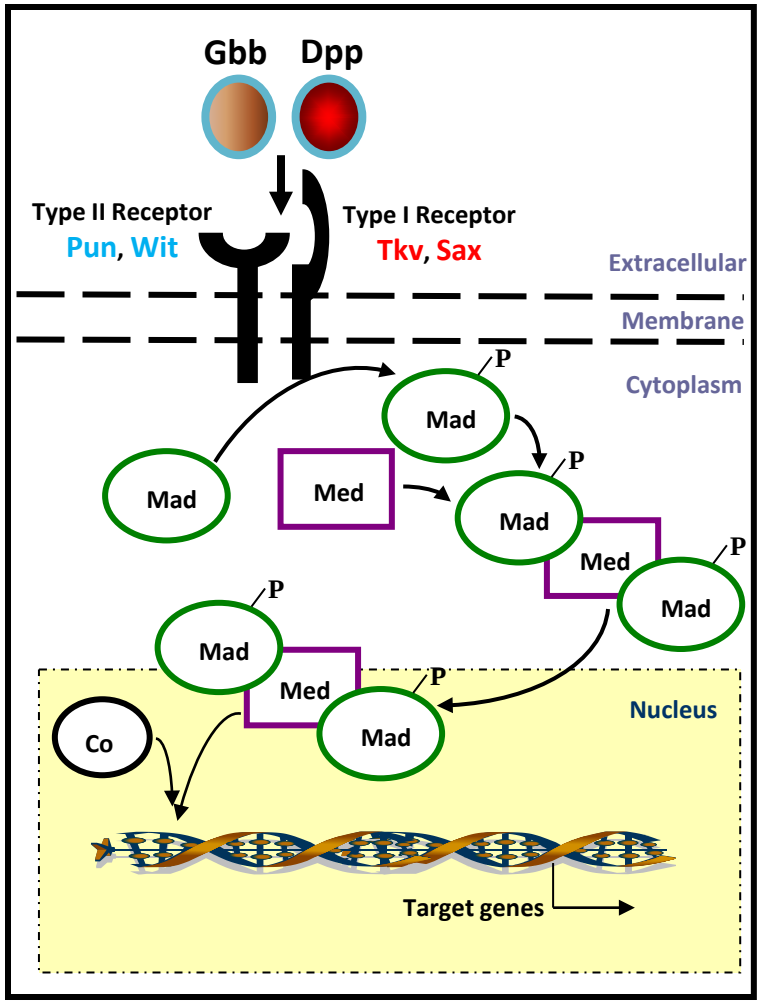


Yakoby et al., Development: 2008

BMP signaling pathway

- Three major ligands of *Drosophila* BMP pathway :

  - *Decapentaplegic* (***Dpp***)
  - *Screw* (***Scw***)
  - *Glass bottom boat – 6oA* (***Gbb***)



by Robert Marmion

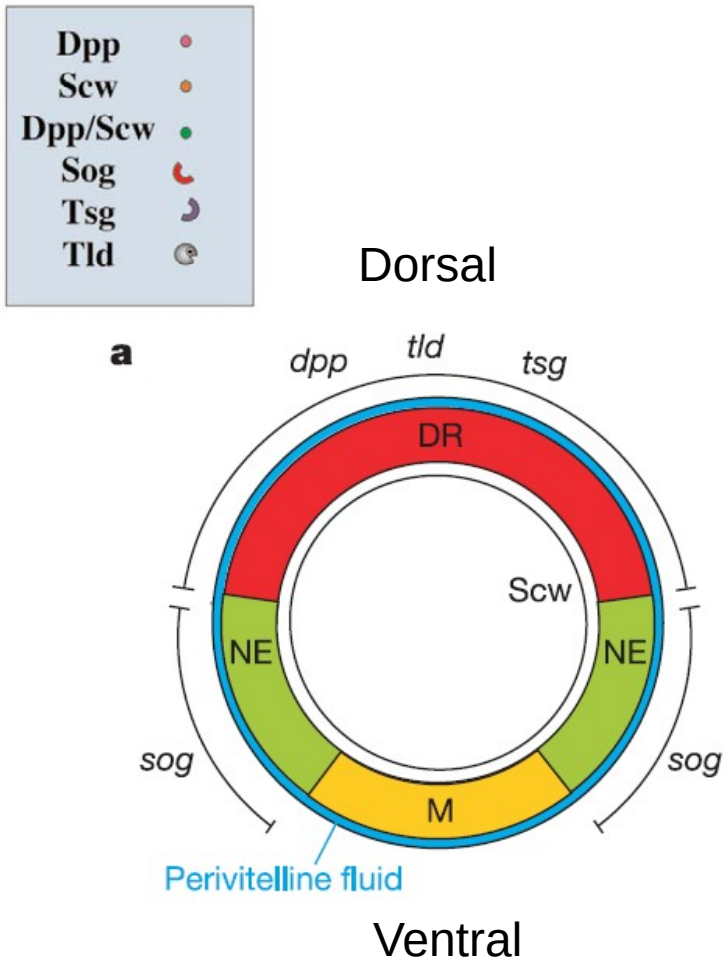
Homodimers & Heterodimers

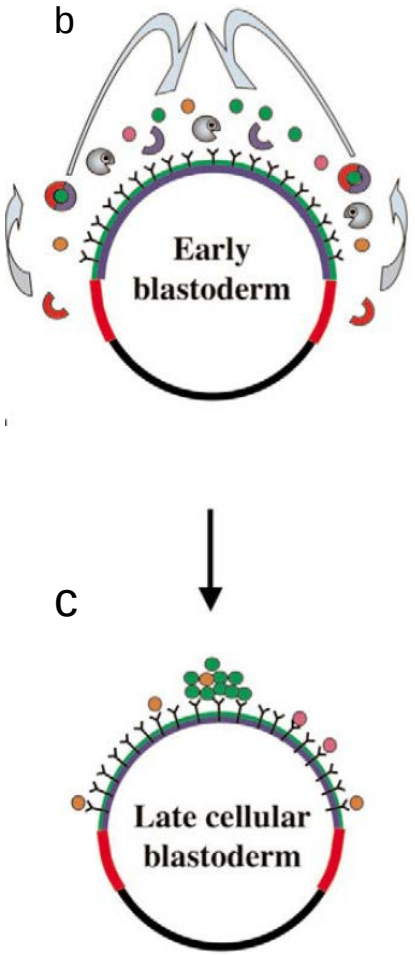
- DPP/DPP homodimers
- GBB /GBB homodimers
- SCW/SCW homodimers

- DPP/GBB heterodimers
- DPP/SCW heterodimers
- GBB/SCW heterodimers

Embryo patterning

DPP/SCW heterodimers

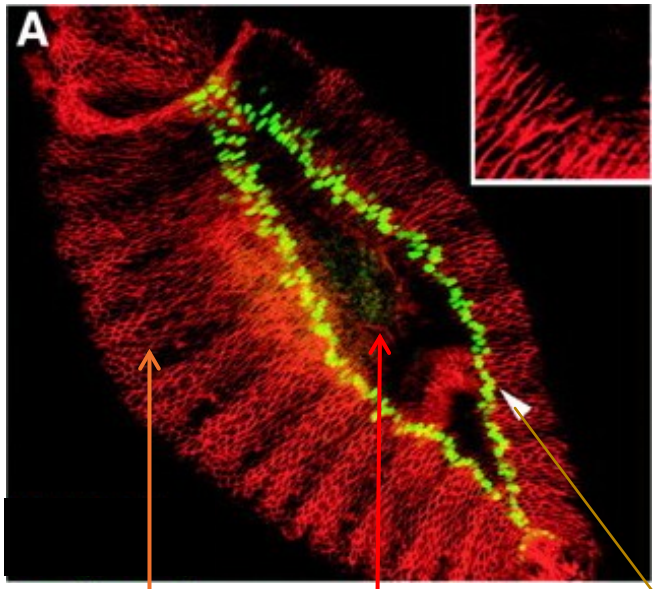




Avigdor Eldar et al., Nature: 2002

O'Connor et al., Development: 2006

Different cell fates

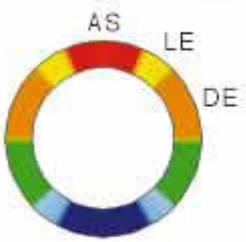


Dorsal ectoderm
DE

Amnioserosa
AS

Leading edge cells
LE

PATTERNING BY GRADIENTS

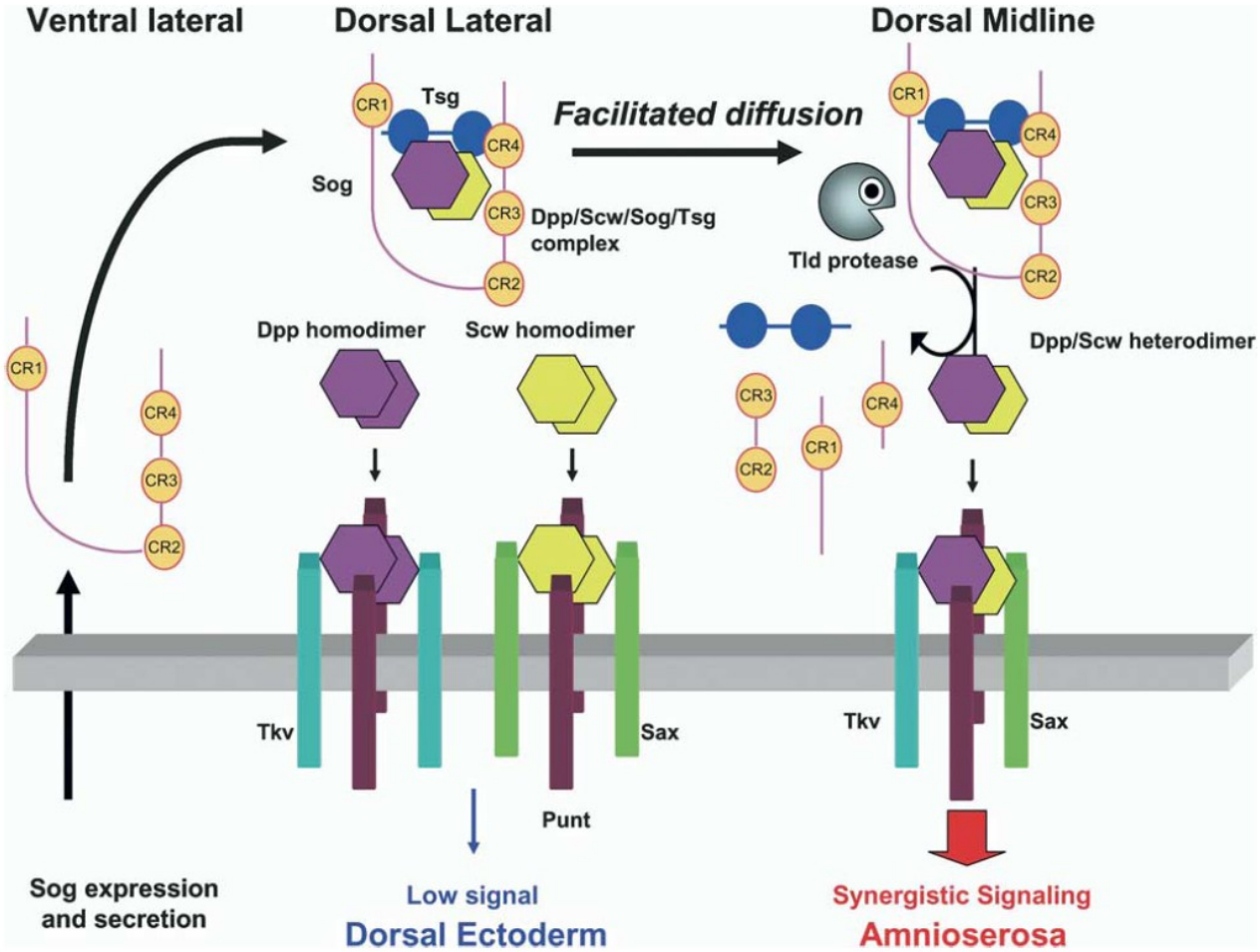


blastoderm stage

expected in D-V mutant

Stronach and Perrimon, Development: 2001

Schematic Model



Shimmi et al., Cell : 2005

Brief Summary

- In *embryo*

DPP → Dorsal midline

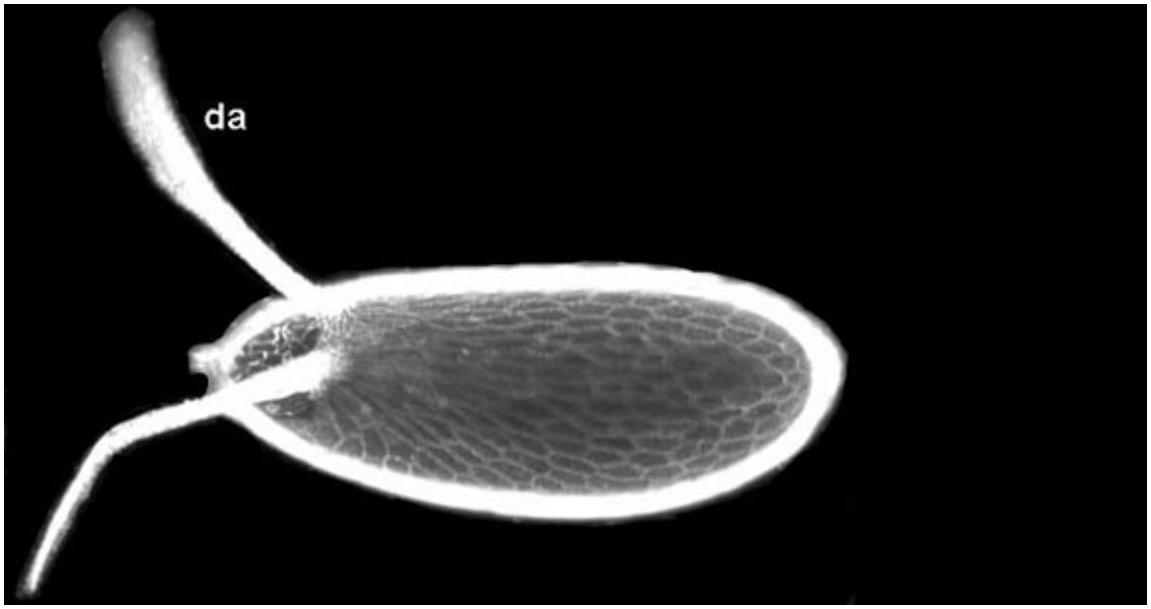
SCW → Uniformly

DPP/SCW heterodimers → **Dorsal midline**

↓

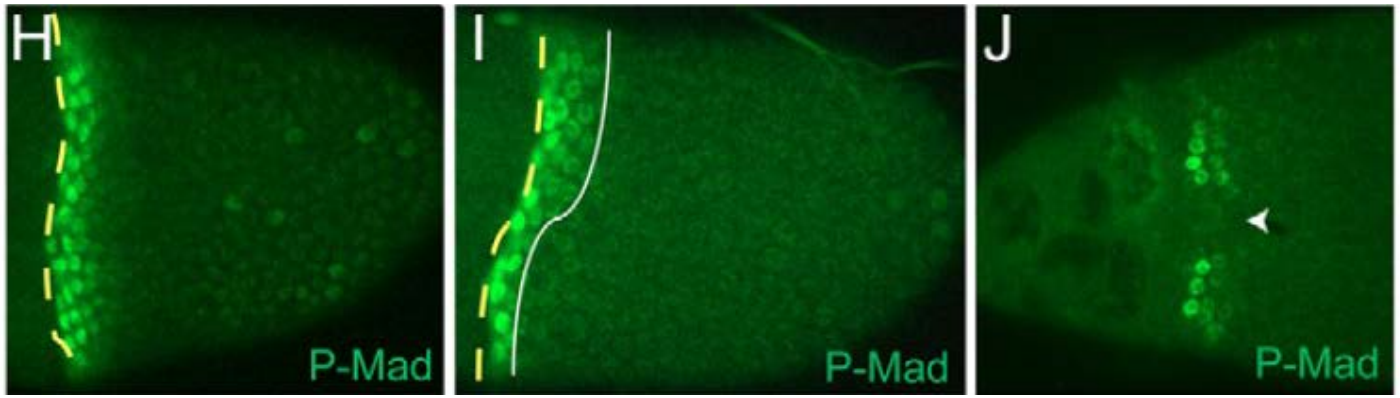
High level signal → **Amnioserosa**

Let's go back to eggshell



Gertrud Schupbach

Dynamics of Dpp signaling

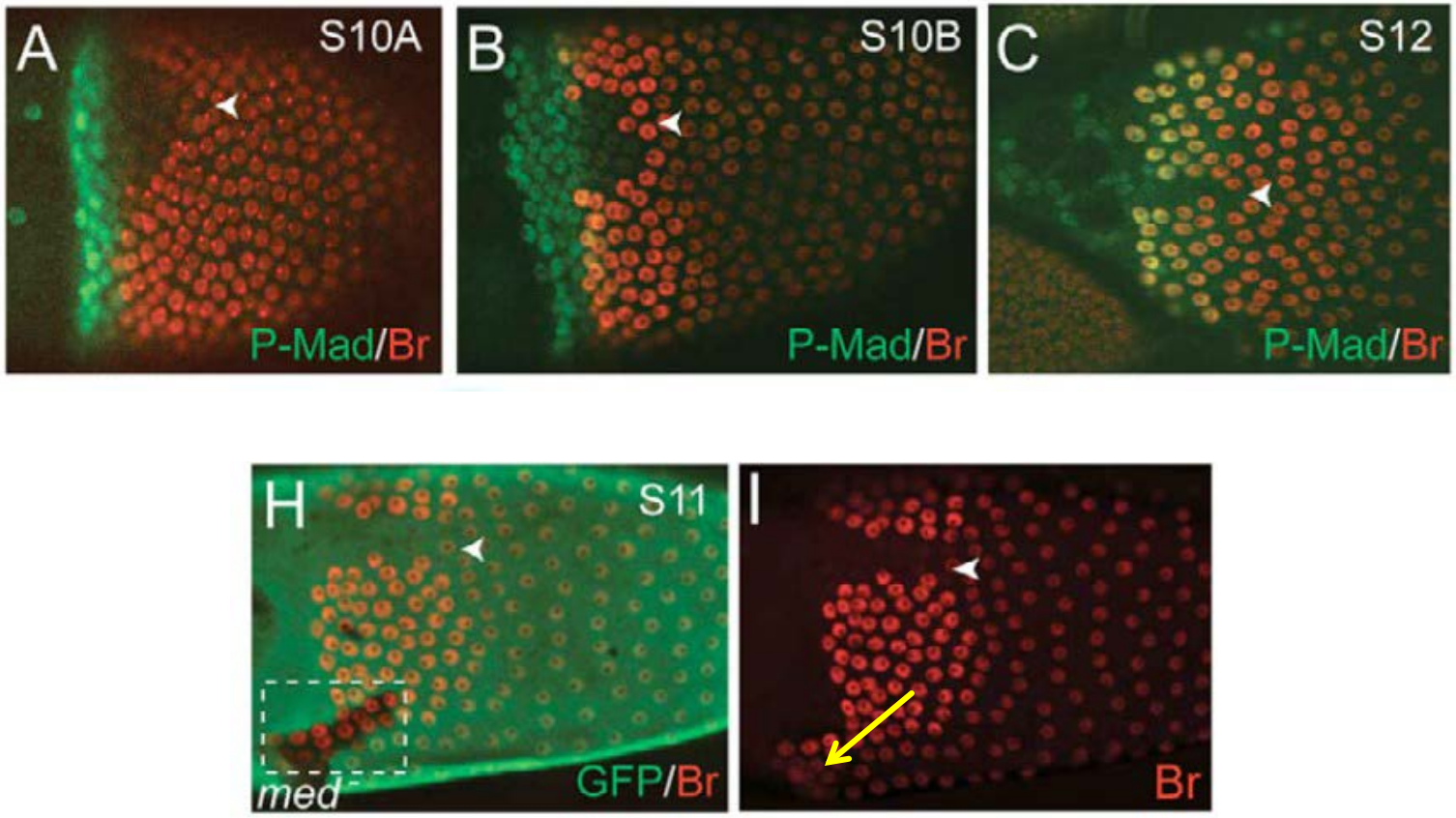


Lateral view

Dorsal view

Yakoby et al., Development: 2008

Correlation between Dpp and Br



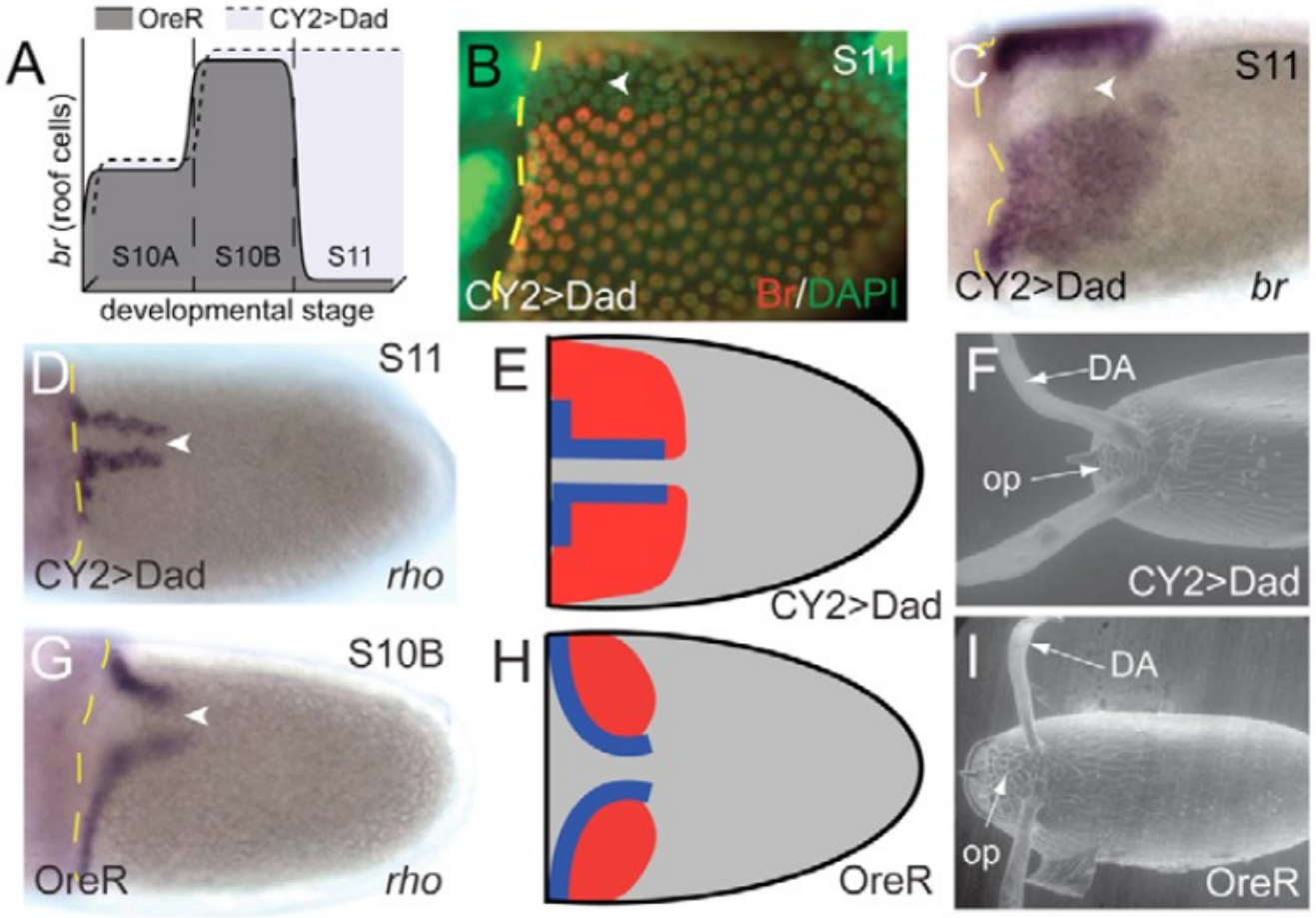
Dpp

⊥

Br

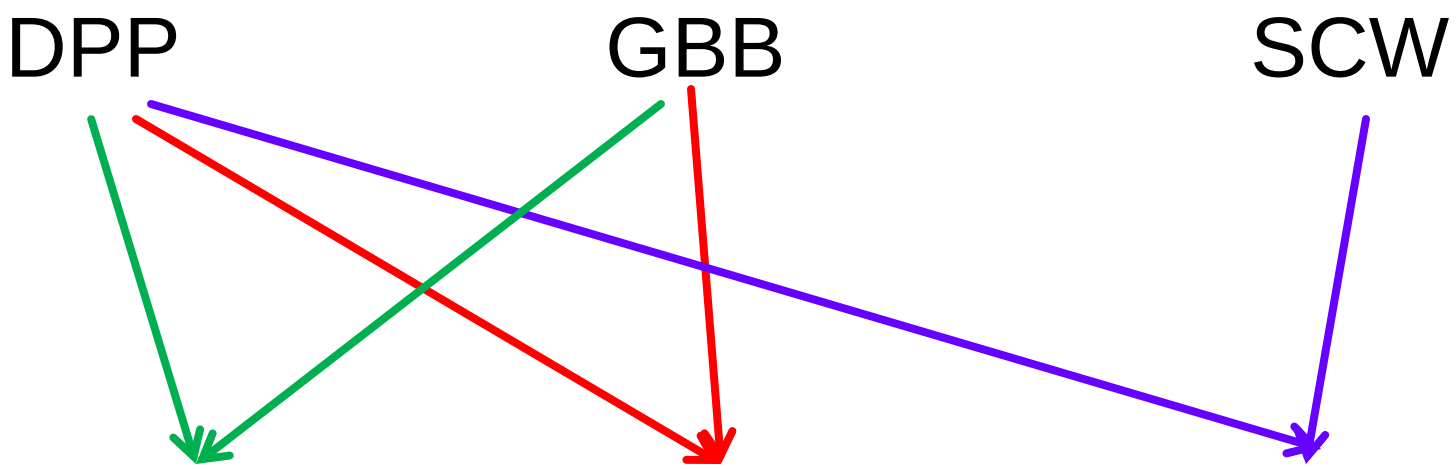
Yakoby et al., Development: 2008

Correlation between Dpp and DA



Yakoby et al., Development: 2008

DPP/GBB heterodimers in oogenesis?



DPP/GBB heterodimer

Eggshell patterning ?

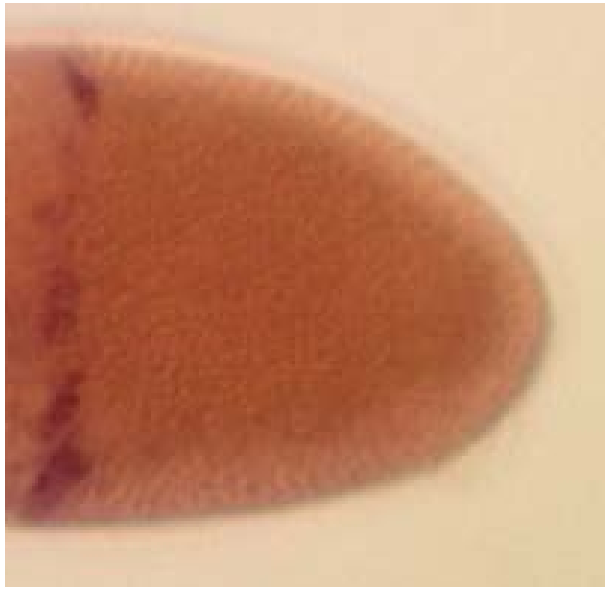
DPP/GBB heterodimer

Wing patterning

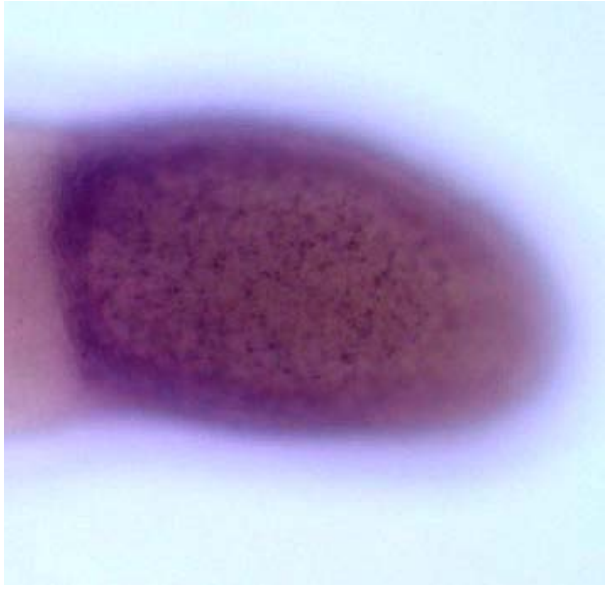
DPP/SCW heterodimer

Embryo patterning

Dynamics of Dpp and Gbb

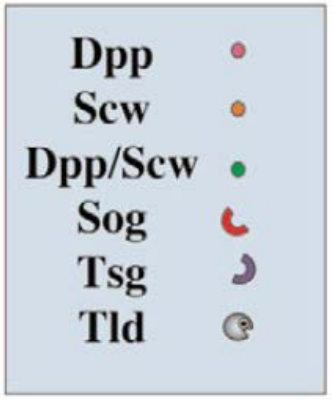


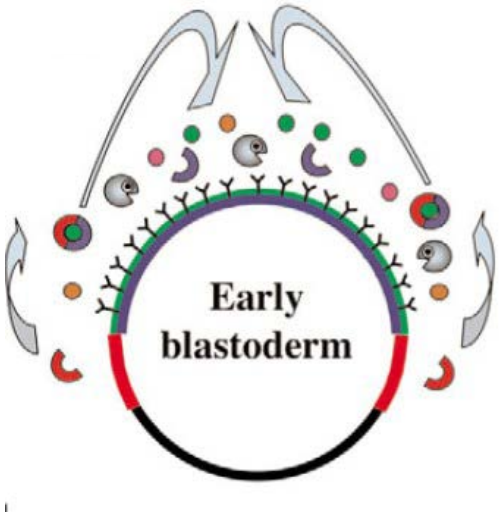
Dpp



Gbb

Dynamics of *Tsg* and *Sog*

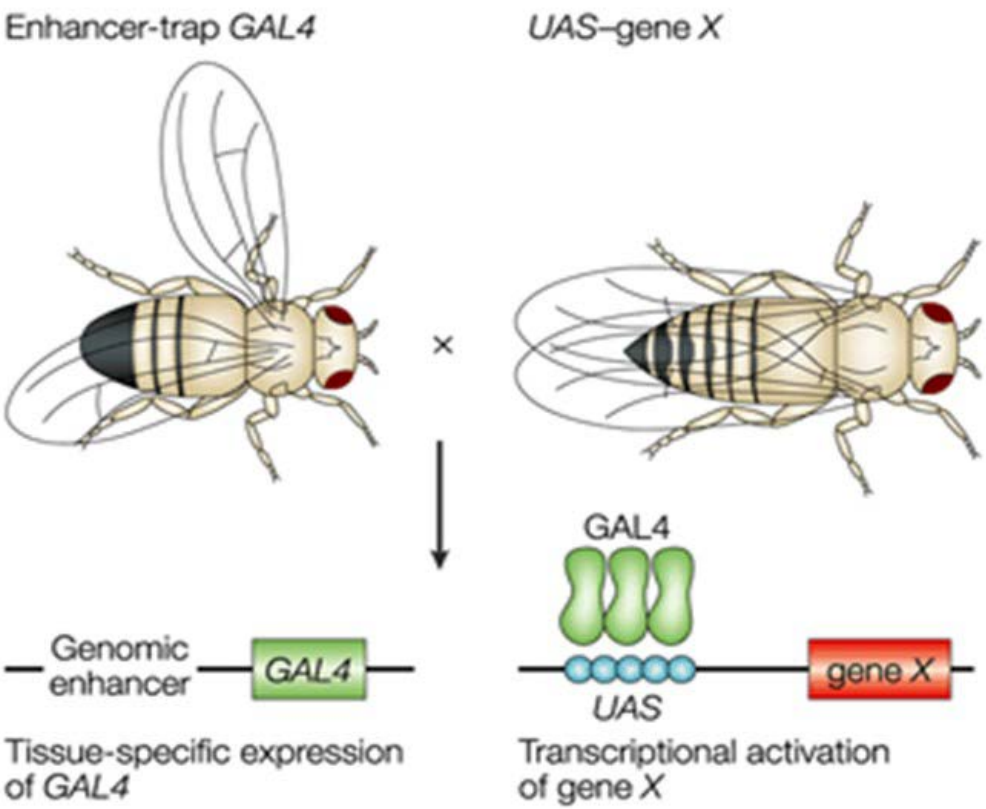




Yakoby et al., Dev. Cell 2008

O'Connor et al., Development: 2006

Overexpression : *UAS/Gal4* system



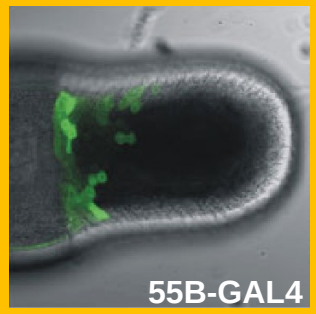
- UAS- Upstream Activation Sequence

Nature Reviews | Genetics (2002)

My Drosophila Lines:

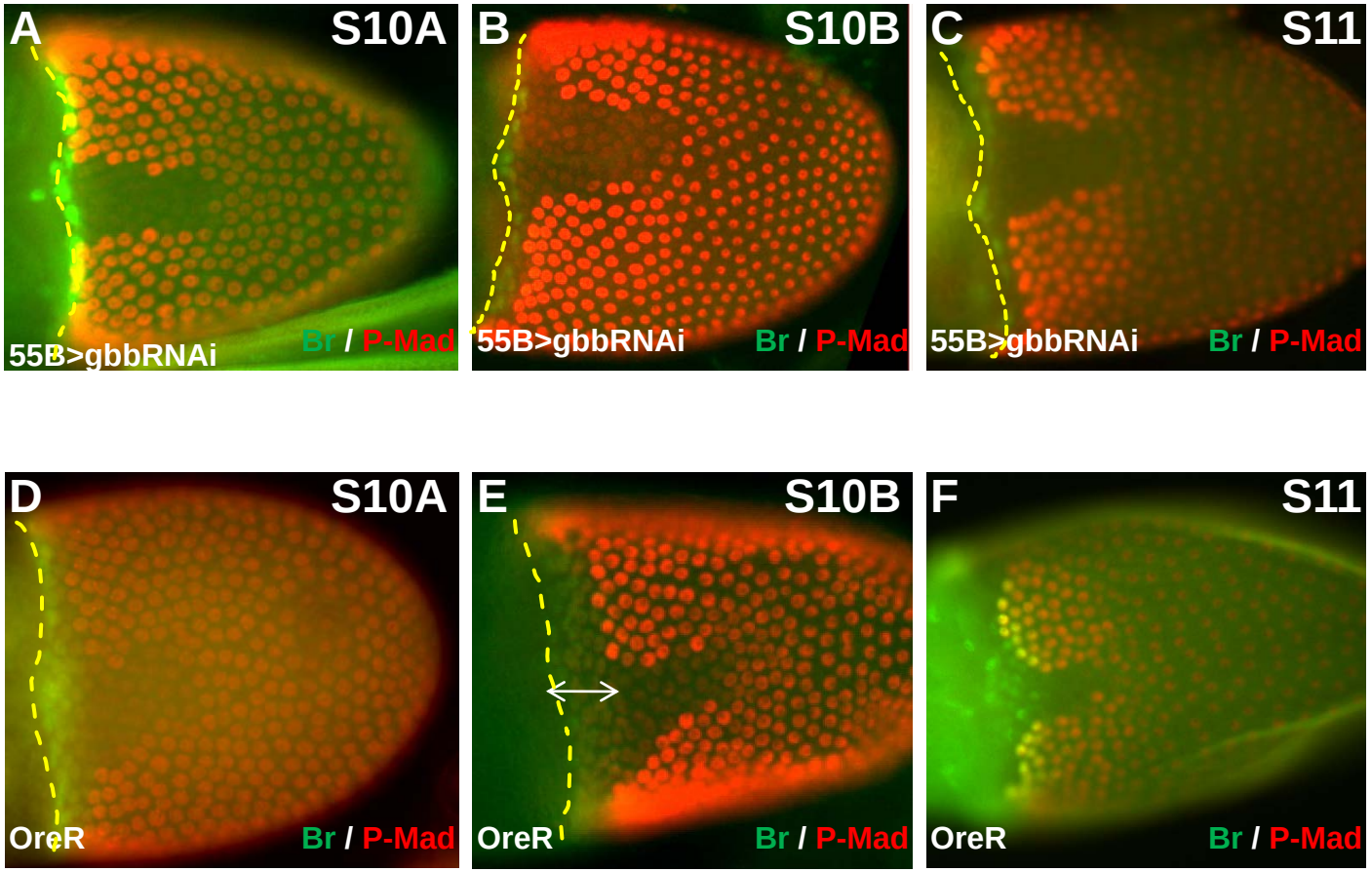
55B-Gal4 > gbbRNAi

Cy2-Gal4 > gbbRNAi

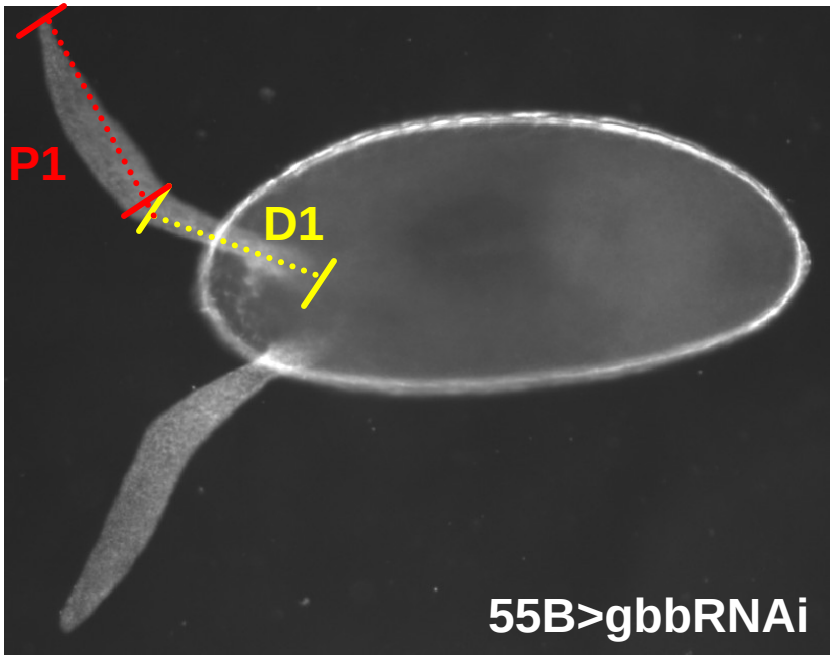


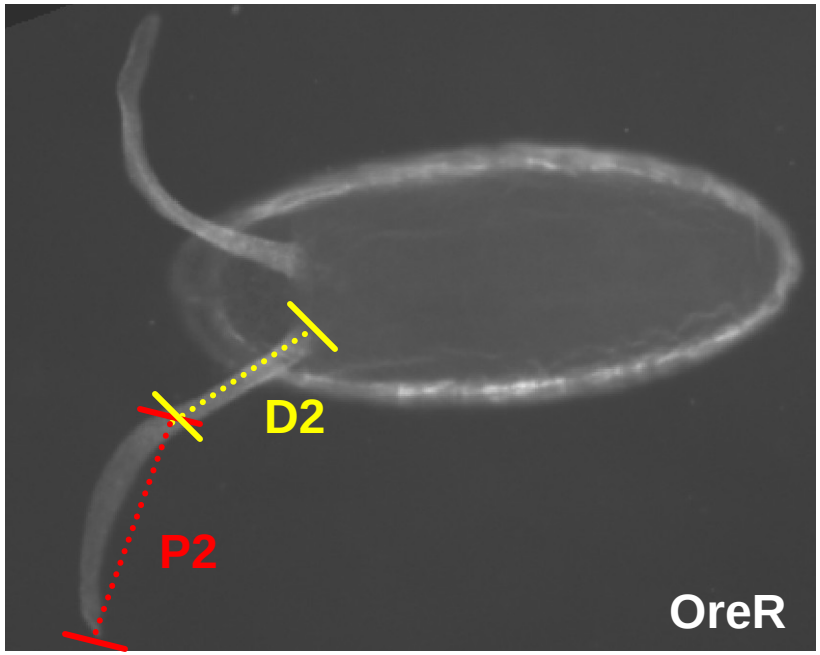
Yakoby et al., Genesis: 2006

55B-Gal4 > gbbRNAi *VS* OreR



Eggshell structure comparison

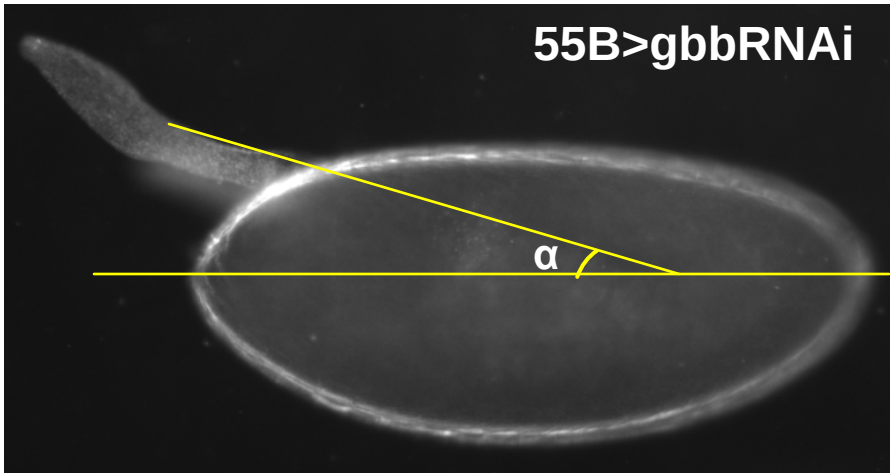


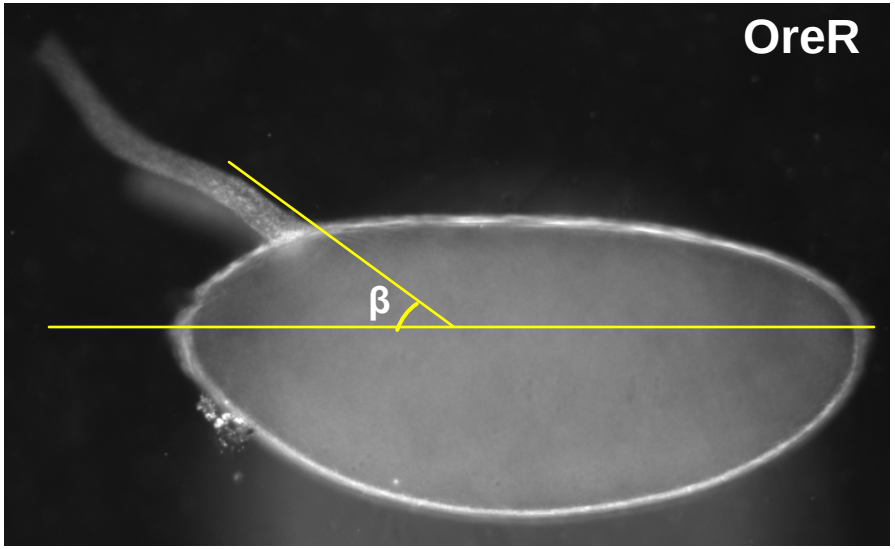


Larger pedal → 10% reduction from P2 to P1

Shorter dorsal appendage → 26% reduction from (P2+D2) to (P1+D1)

Angle difference of Dorsal Appendage





Reduction in operculum

$$\overline{\angle \alpha} < \overline{\angle \beta}$$

Conclusion

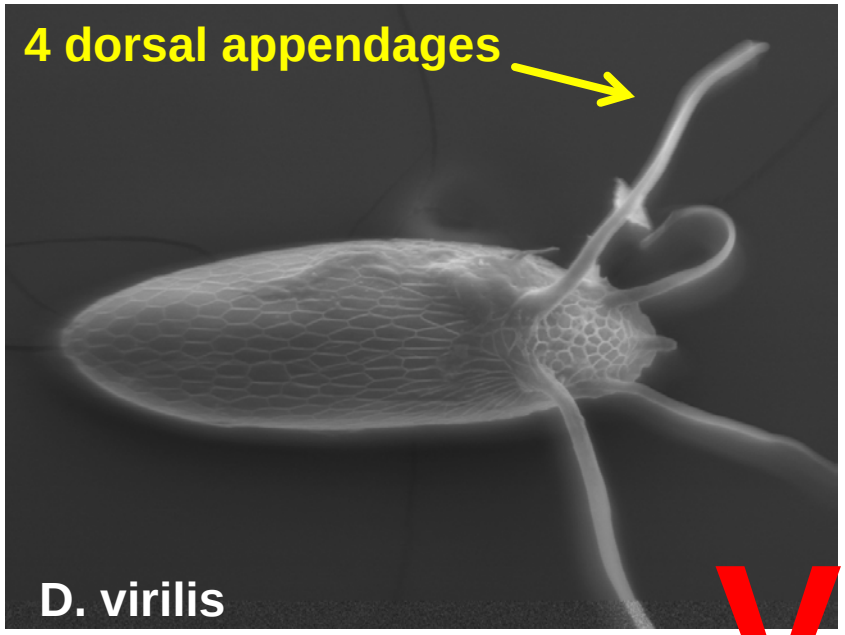
- Heterodimers can produce a synergistic high level signal to affect the *Drosophila* patterning.

- Lacking of *Gbb* signaling can lead to changes of eggshell morphology.

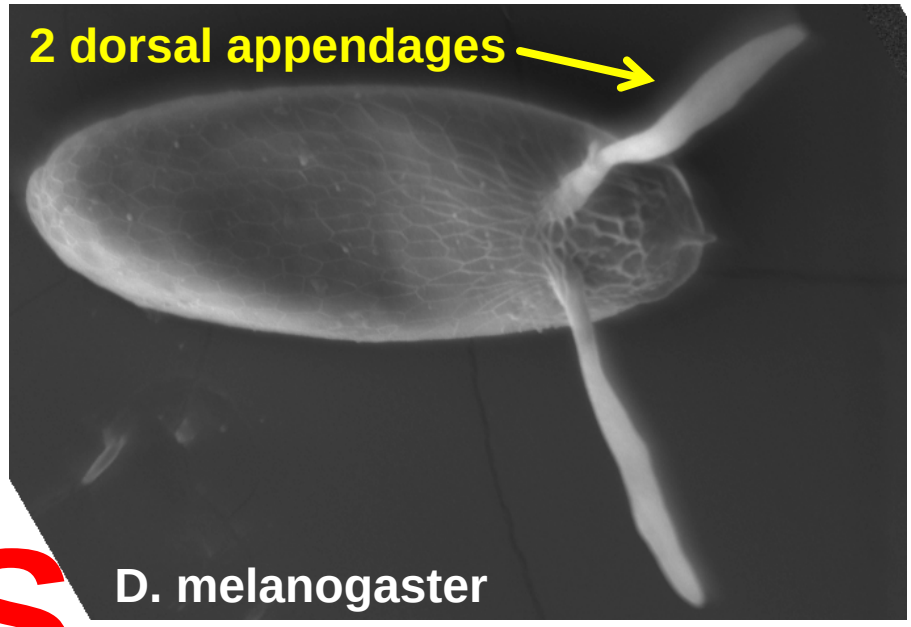
Future work

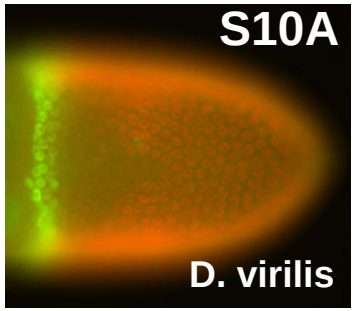
- GBB's function in BMP signaling pathway.
- GBB's function in eggshell's patterning and morphology.
- Clarify the mechanism for ligands' migration.

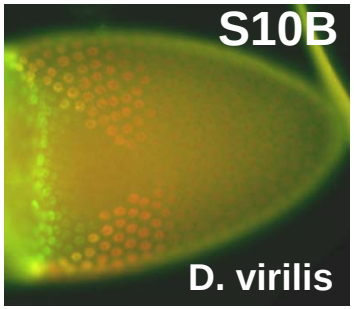
Regulation through species

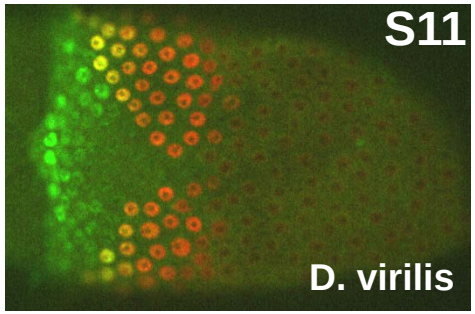


VS









Matthew Niepielko: 2009

Acknowledgement

- Nir Yakoby
- Matthew Niepielko
- Robert Marmion
- Kenneth Kim
- And all the other brilliant lab members!

RUTGERS
CAMDEN

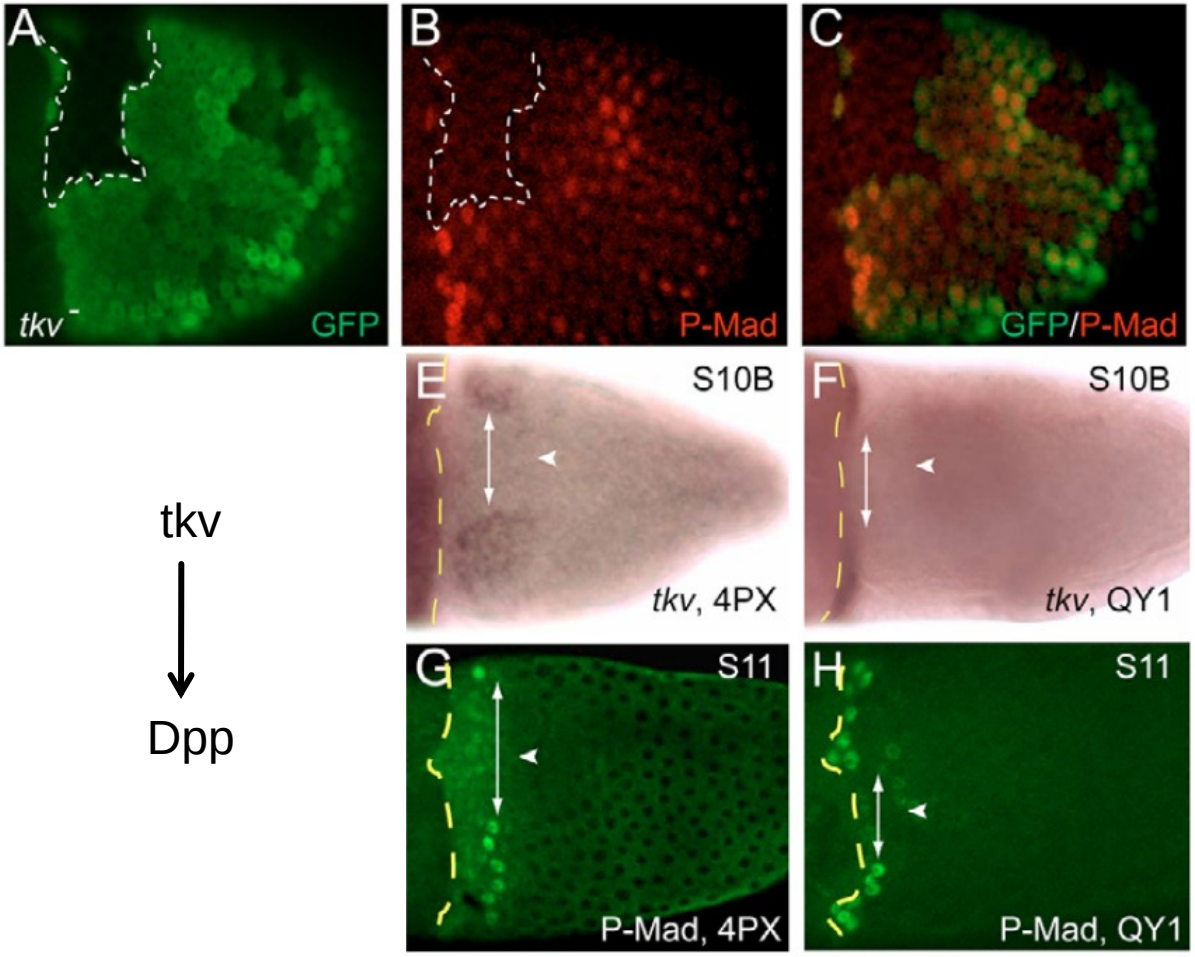
A missing piece of Drosophila shell game: How do heterodimers work?

—— *Tiange Cui*

THANK YOU !

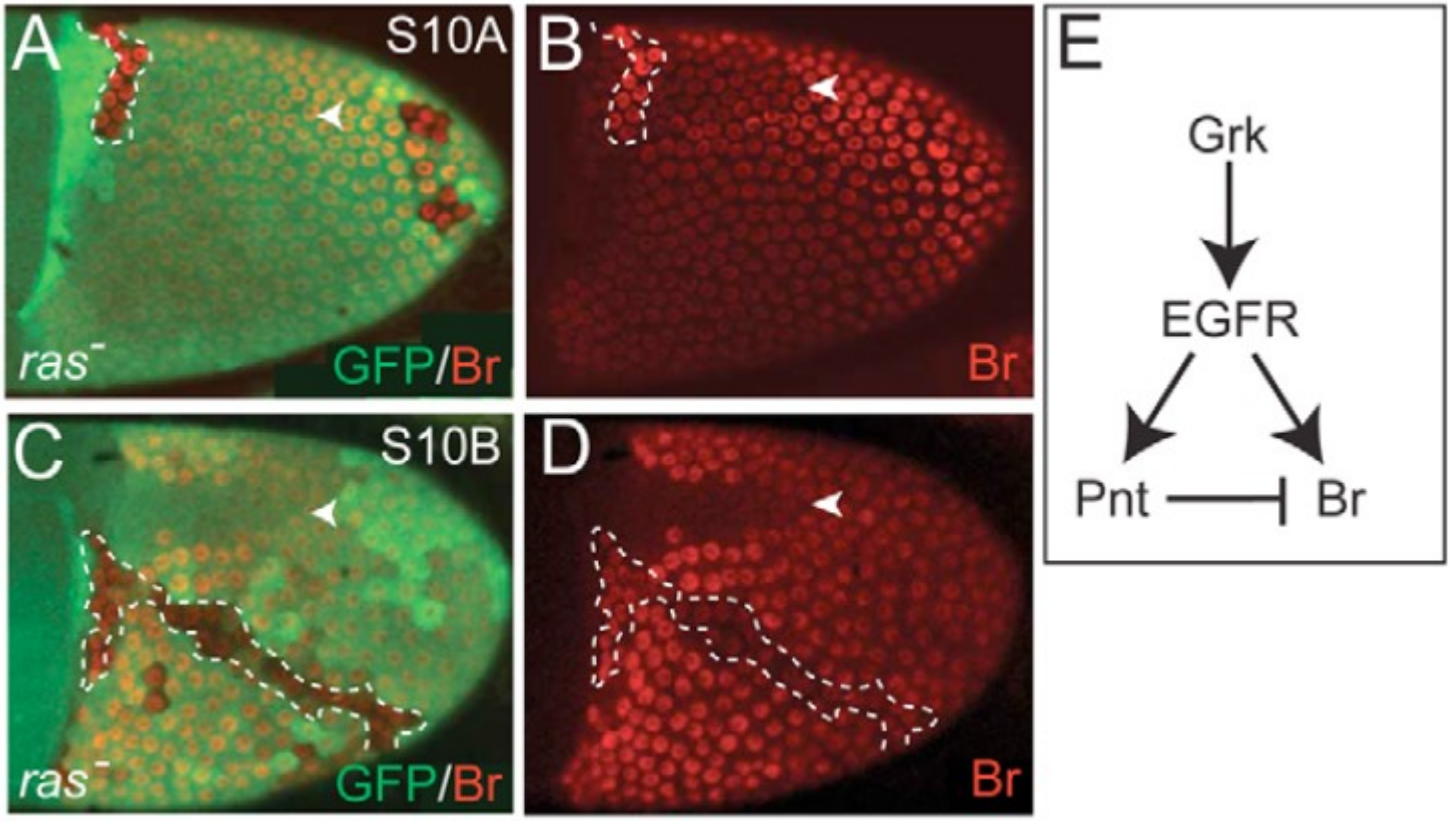
Questions?

What's the role of *tkv* ?



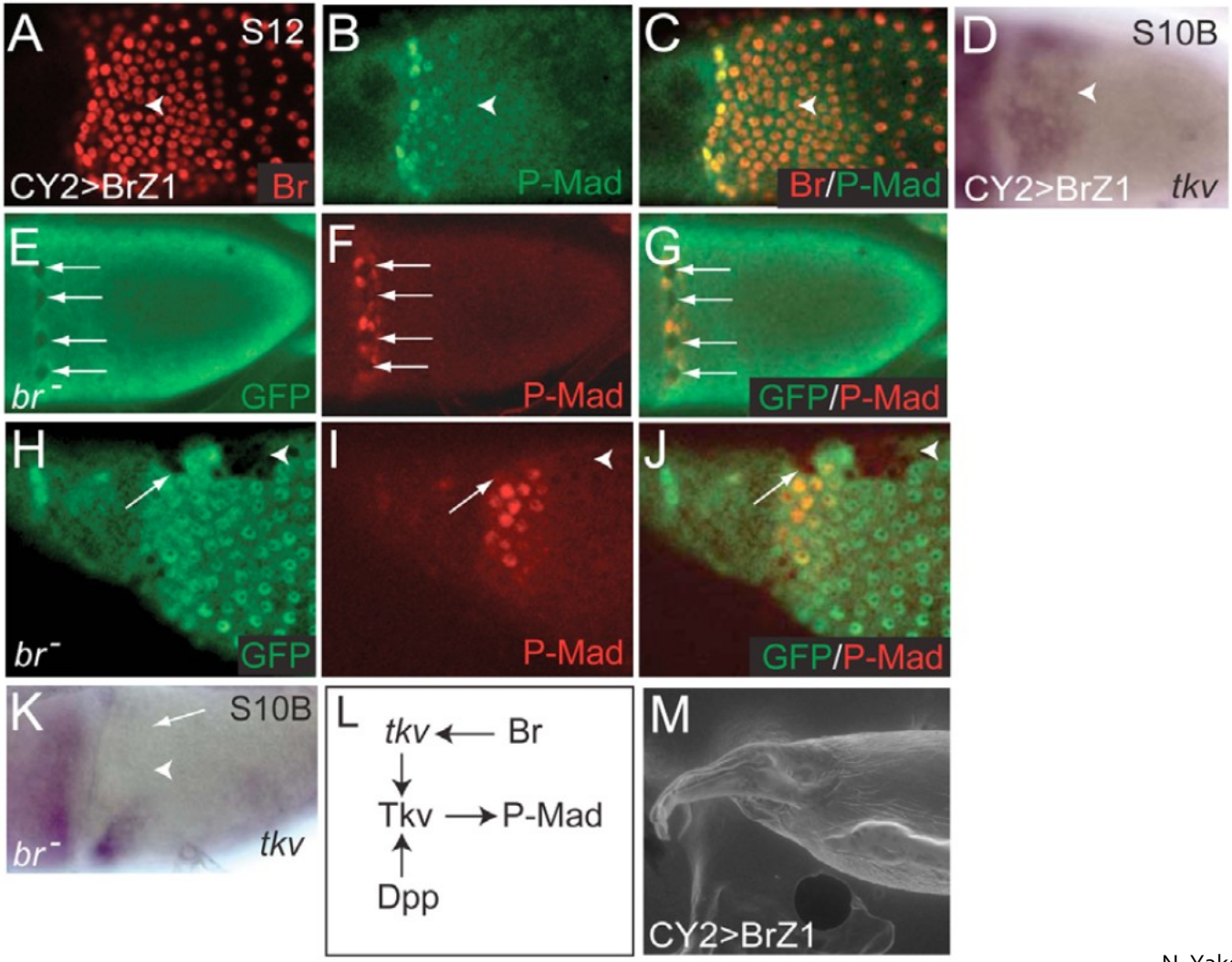
N. Yakoby et al., Development: 2008

Correlation between EGFR and Br



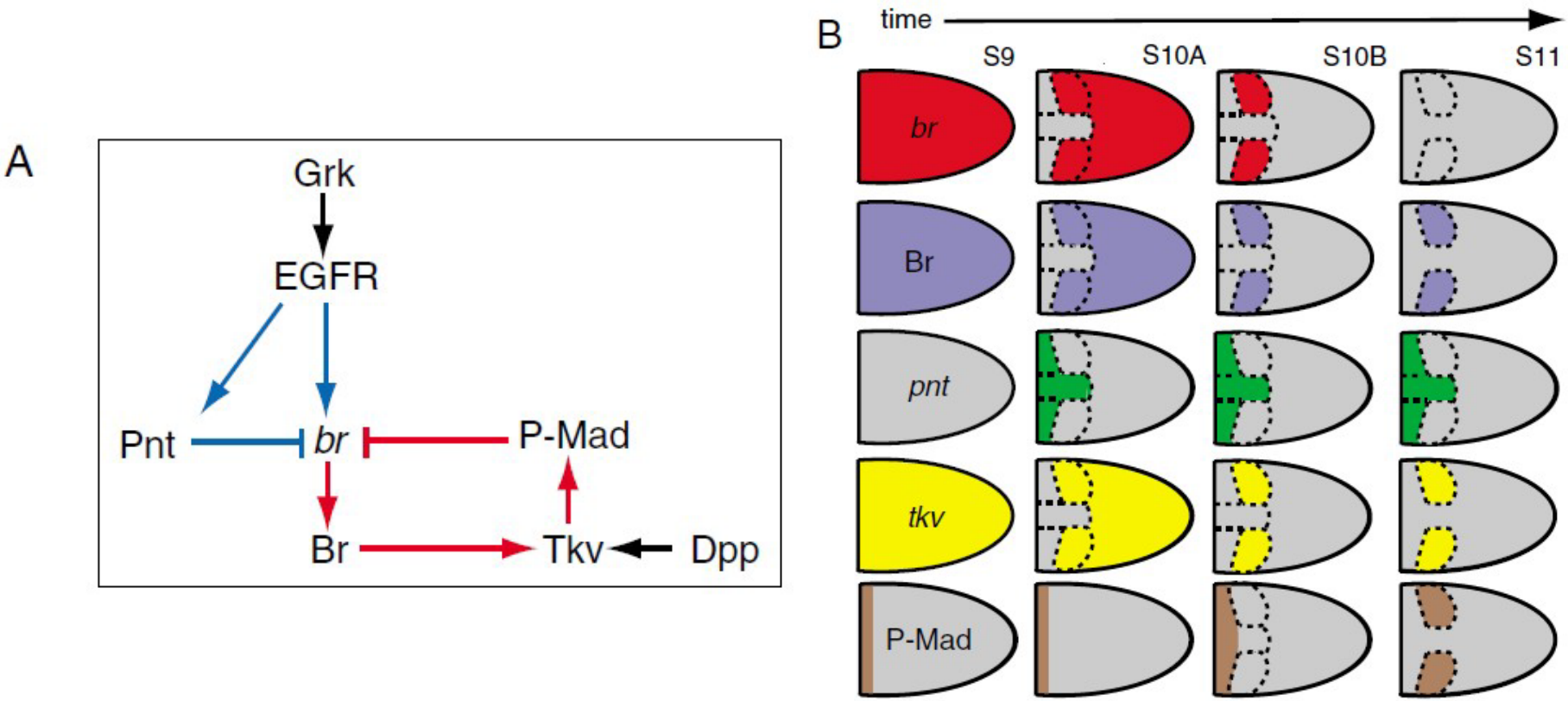
N. Yakoby et al., Development: 2008

Correlation between Br and tkv



N. Yakoby et al., Development: 2008

Our Model



N. Yakoby et al., Development: 2008