Role of axial patterning genes in growth regulation during eye development

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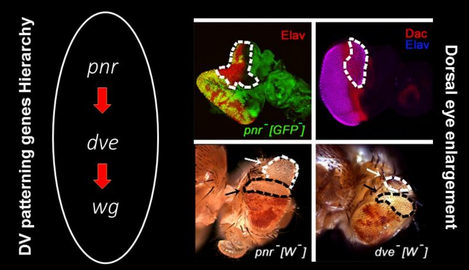
Abstract

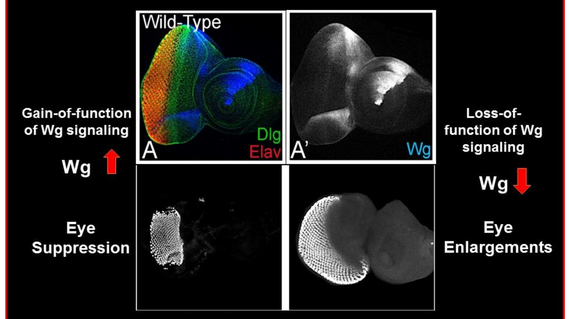
An important question in developmental biology is that how axial patterning genes work with growth and patterning to form any three-dimensional organ. In any multicellular organism, Organogenesis, requires axial patterning i.e. formation of Antero-Posterior (AP), Dorso-Ventral (DV), Proximo-Distal (PD) axes. Any deviation in these axes during development leads to genetic birth defects. We use *Drosophila melanogaster* (a.k.a fruit fly), eye as our model. As the genetic machinery between flies and human is conserved, any insights generated in flies can be extrapolated into humans. In *Drosophila*, DV patterning marks first lineage restriction event where expression of dorsal, ventral fate selectors forms dorsal & ventral compartments in eye respectively. We have identified *defective proventriculus (dve)*, an ortholog of SATB *homeobox 1* (in humans), as a new member of DV patterning gene hierarchy. Our previous data establishes dorsal gene hierarchy & states that *dve* acts downstream of *pannier (pnr,* GATA-1 transcription factor), and upstream of Wingless *(wg)*, Loss-of-function of both *dve* or *pnr* results in dramatic dorsal eye enlargements. Furthermore, Wingless, also exhibits similar eye enlargement phenotypes and has also been shown to play a role in growth. Our data also suggests that Wg is downstream target of Hippo pathway (highly conserved) and that the pathway promotes cell differentiation by downregulating wingless. Hereby, I propose to investigate the role of *dve* and *pnr* in growth and patterning during *Drosophila* eye development. I will test whether these two fundamental processes works independently or in coordination with each other to form an eye. The proposed study will help in elucidating how cell fate specification, pattern formation and growth are involved in organ formation. Our study will have significant bearing on developmental mechanisms, patterning events, growth regulation during organogenesis, and helps us in understanding the etiology of growth related birth defects in eye.

Loss-of-function phenotypes of both *dve* and dorsal eye fate selector gene *pannier (pnr)* exhibits growth phenotypes

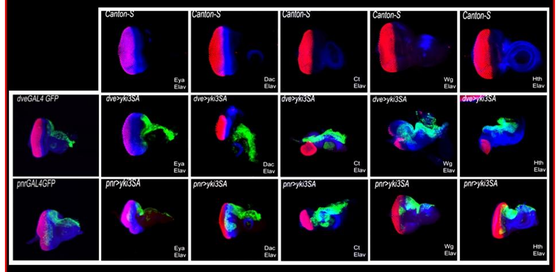


Oros et al., 2010 ,puli *et al.*, in prep.

Role of Wingless in eye development

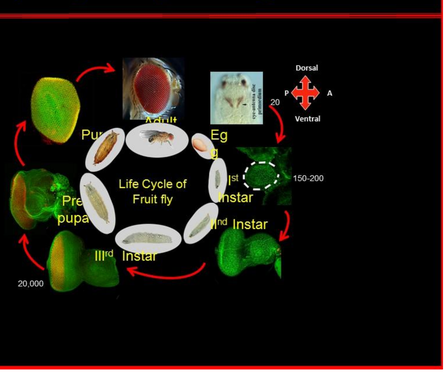


In-activating Hippo signaling in *dve* and *pnr* expression domain

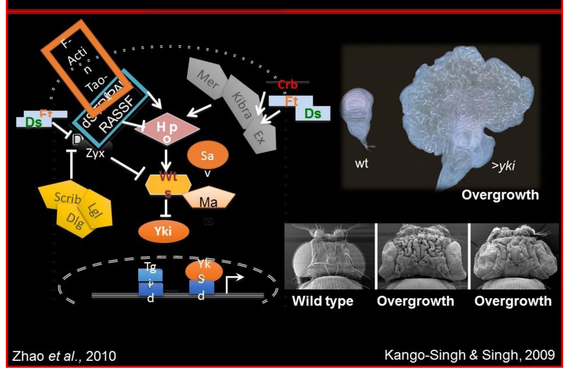


Supression of Eyes Absent (Eya) and Dacshund (Dac)
Induction of Cut (Ct), Wingless (Wg) and Homothorax (Hth)

Drosophila eye development along the time axis

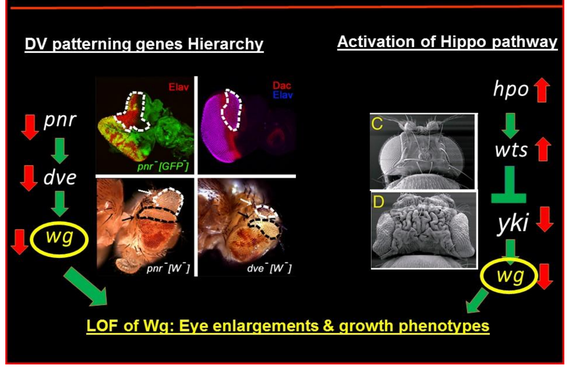


Hippo Signaling Pathway

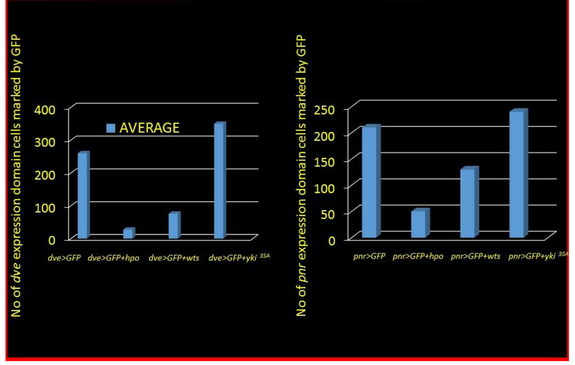


Zhao *et al.*, 2010 Kango-Singh & Singh, 2009

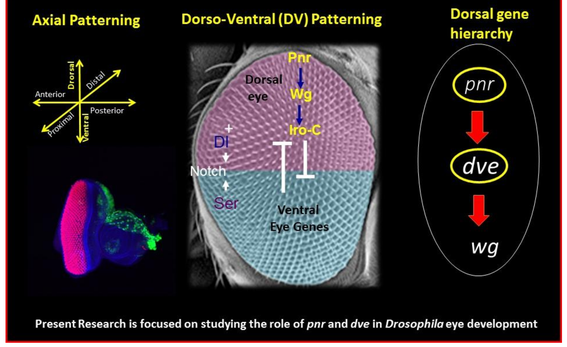
Wg is downstream target of both of these signaling pathways



Quantitative Analysis of *dve* and *pnr* expressing cells

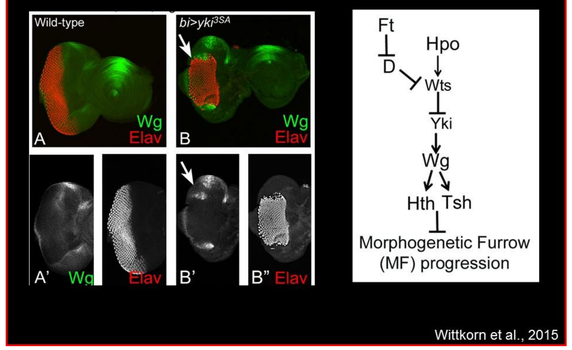


Pattern formation in the Eye



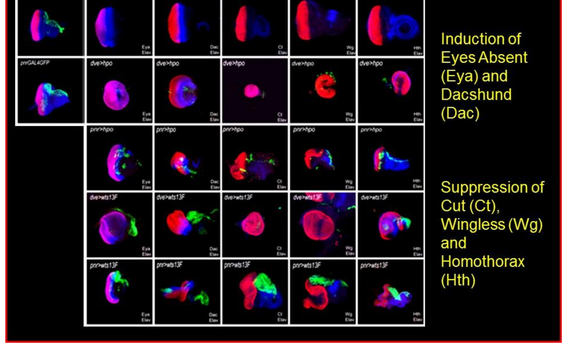
Present Research is focused on studying the role of *pnr* and *dve* in *Drosophila* eye development

Wingless is the downstream target of Hippo pathway in eye

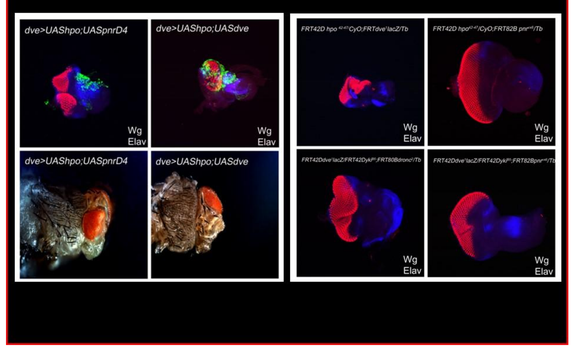


Wittkorn et al., 2015

Activating Hippo signaling in *dve* and *pnr* expression domain



Genetic Epistasis and Trans-Heterozygous studies



Conclusions:

- *dve* and *pnr* plays important role in growth regulation during eye development.
- *dve* and *pnr* may suppress hippo signaling in their expression domain to determine head specific fate.
- LOF of *dve* and *pnr* may activate ectopic hippo signaling in dorsal cells which results in downregulation of wingless in these cells and leads to change of head to eye specific fate.
- Both these pathways may interact with each other by regulating Wg signaling

Acknowledgements: We would like to thank Hugo Bellen, Madhuri Kango-Singh, Bloomington Stock Center & DSHB for the reagents. NG is supported by Department of Biology graduate prog at University of Dayton.