# Integration of BMP, JAK/STAT and EGFR signaling in the Drosophila egg chamber during anterior-posterior fate determination

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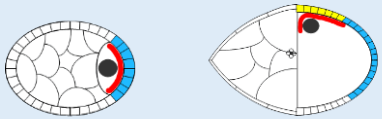
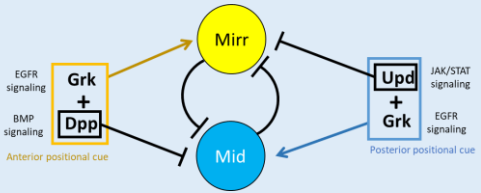
## Introduction

- Drosophila follicular epithelium, which eventually gives rise to the eggshell, becomes patterned as it develops
- The EGFR ligand Gurken (Grk) localized at the oocyte nucleus is required for the establishment of AP and DV axes of the follicular epithelium



Stage 8 Stage 10A

**Grk induces different cell fate determinant genes in follicle cells at different positions.** Grk induces *midline* (*mid*, Blue) at posterior follicle cells and *mirror* (*mirr*, Yellow) at anterior follicle cells. *mid* and *mirr* expressions do not overlap.

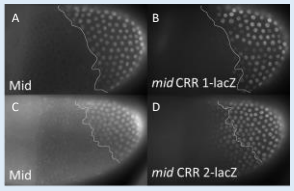


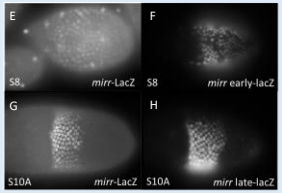

**Known regulatory inputs to *mid*, *mirr*.** By genetic analyses, It was shown that Grk signaling activates *mid* in presence of BMP (Dpp) signaling and *mirr* in presence of JAK/STAT (Upd) signaling, while these signals also independently repress the expression of the other target. *mid* and *mirr* were shown to repress each other's expression.

### Questions

- How could the same signaling ligand activates one target and repress the other?
- Are the putative CRRs responsive to the known regulatory inputs to *mirr* and *mid*?
- Is the regulation of *mid* and *mirr* by the positional cues/Signaling ligands direct?

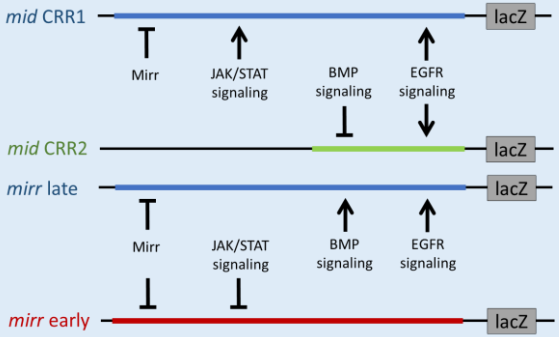
## Putative *mid*, *mirr cis*-regulatory regions (CRRs) for follicle cell expression



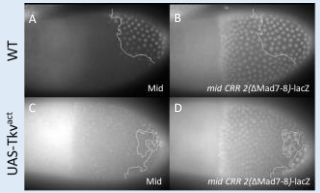

To understand how the multiple signaling inputs are integrated, we generated lacZ reporters of *mid* and *mirr* to map the CRRs. "*mid* CRR1" (B) has an expression domain similar to that of the endogenous Mid (A, C); "*mid* CRR2"(D) displays an expression pattern that is more expanded anteriorly. Similar to the expression of *mirr* enhancer trap (E, G), "*mirr* Early" CRR expresses in lateral follicle cells in early stage (F); "*mirr* late" CRR" drives expression in anterior follicle cells at late stage (H).

## Regulation of *mid* and *mirr* CRRs by known regulatory inputs



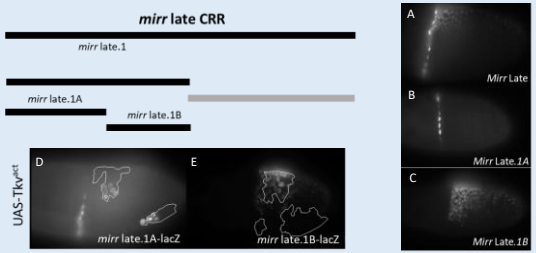

*mirr* and *mid* CRR lacZ reporter's response to JAK STAT and BMP signaling. GFP marks cells expressing UAS-Tkv$^{act}$ (ectopic BMP signaling) or UAS-hop (ectopic JAK/STAT signaling). *mid* CRR1 is responsive to JAK/STAT signaling but not to BMP signaling; mid CRR 2 is responsive to BMP signaling but not to JAK/STAT signaling. "*mirr* early" CCR is responsive to JAK/STAT signaling but not BMP signaling . "*mirr* late" CCR is responsive to BMP signaling but not JAK/STAT signaling .

## Is *mid* directly regulated by BMP pathway?




Removing the putative MAD binding sites from *mid* CCR 2 (B, D) result in loss of repression by UAS-Tkv$^{act}$ (D) and expansion of expression domain driven by the *mid* CRR 2 (B) compared to the wild type *mid* CRR 2.

## Defining the minimal *mirr* CRRs by deletion mapping




*mirr* late CRR (A) was further dissected into *mirr* late.1A and mirr late.1B. *mirr* late.1A drives expression at the anterior ventral side at the ventral belt (B); *mirr* late 1B drives expression at the anterior dorsal side (C). *mirr* late.1A respond to BMP signaling at the ventral side (D) and *mirr* late.1B respond to BMP signaling at the dorsal side (E).

### Summary

- *Cis*-regulatory regions of *mid* and *mirr*, can be broken down into modules. Elements that respond to different known signaling ligands can be dissected apart from each other.
- Removing the elements that respond to BMP signaling from a *mid cis*-regulatory region resulted in changes in the boundary of its expression domain.