

T-box transcriptional control of *Drosophila* wing development

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Motivation

- Human development is exquisitely sensitive to T-box protein levels.
- Under or over-expression can lead to defective development and cancer in humans.

Project Description

- Three T-box factors are expressed in the fly wing and lead to distinct phenotypes when mutated
- How do endogenous T-box factors interact to control wing development?
 - Identify target genes
 - Identify how T-box mutations affect target gene expression
 - Identify how misexpression of T-box factors affects gene expression

Context

- The expression of at least 8 T-box factors during mouse limb formation complicate these experiments.
- Similar pathways control fly wing and mammalian forearm development.
- Fly model allows:
 - easily scorable phenotypes
 - routine methods to drive expression of genes that are normally not expressed in this tissue
 - ease of creating new fly lines with mutated genes

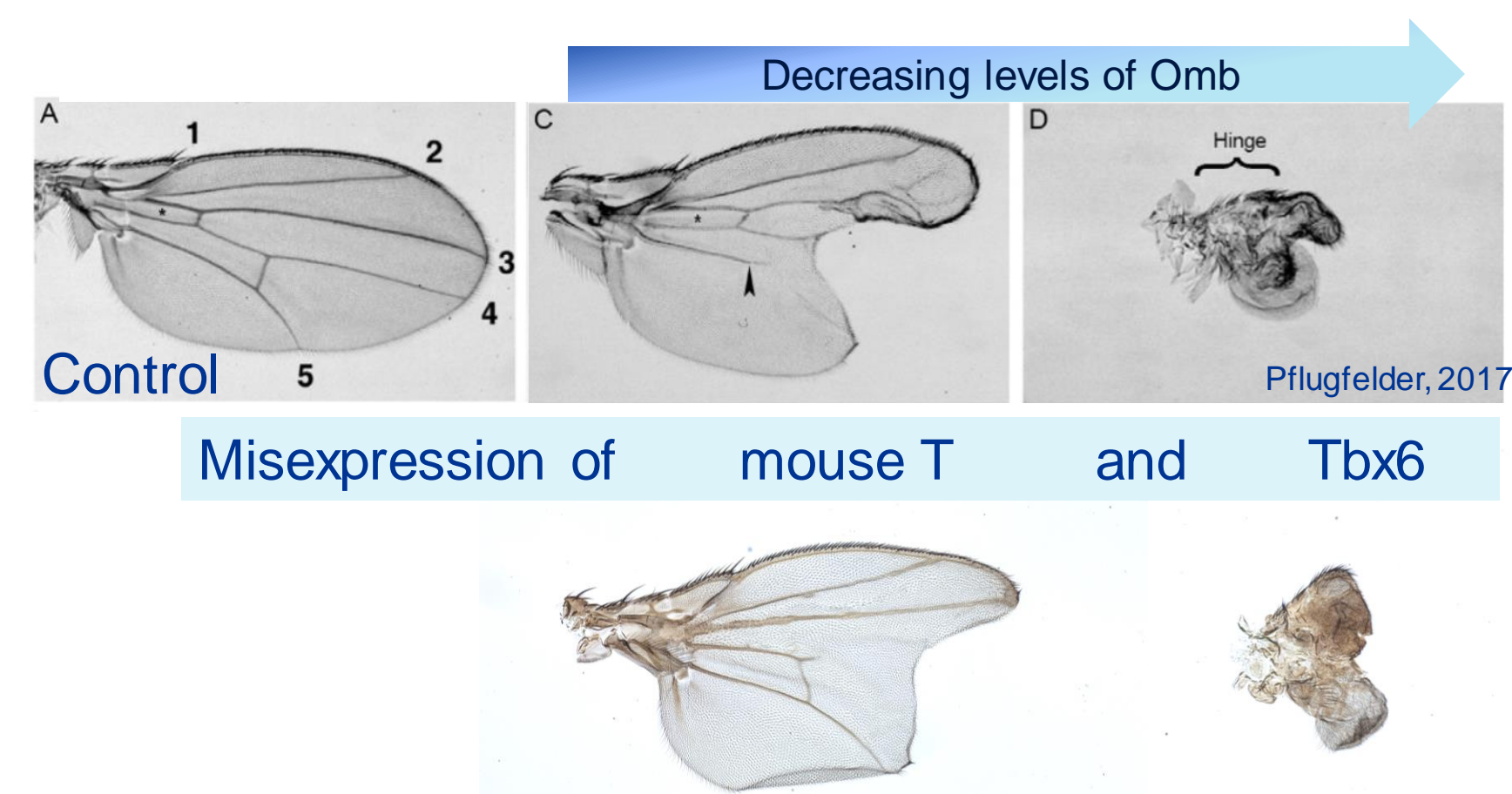


Figure 1. Scorable phenotypes for wing formation. Omb is a fly T-box factor, while T and Tbx are mammalian T-box factors.

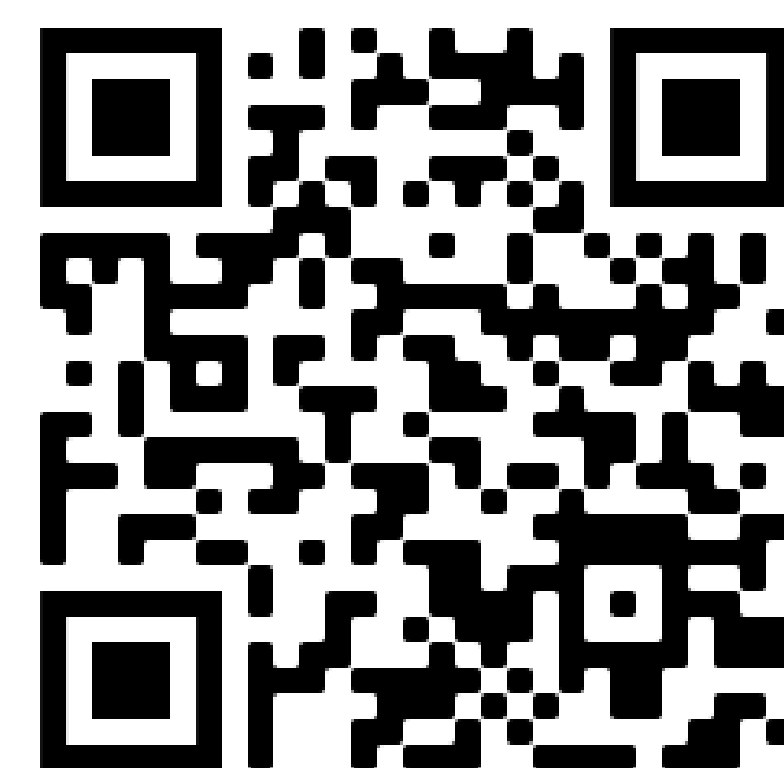
Determine how T-box transcription factors interact to control gene expression in the fly wing as a model for limb development.

Project Deliverables

- Identify changes in gene expression resulting from loss or gain of T-box gene expression.
- Characterize how expressing different combinations and levels of T-box factors affect gene expression.
- Begin to identify potential direct T-box target genes
- Begin to describe phenotypes through their gene expression profiles

Potential Impact

- First steps toward identifying pathways impacted by T-box mutant situations and ultimately explaining the observed fly wing phenotypes.
- Direct and indirect T-box target genes will be identified forming the basis for future testing by chromatin immunoprecipitation and rescue experiments.
- Unravel how multiple T-box factors interact in the same cells to affect target gene expression.
- Begin to explain the sensitivity of human development and cancers to altering the relative levels of T-box factors.



References and/or Acknowledgements

- Pflugfelder (2017). *Curr. Top. Dev. Biol.*