A genetic screen for mechanisms that counter extra centrosomes

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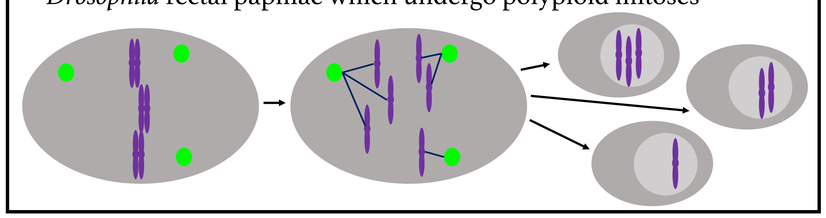
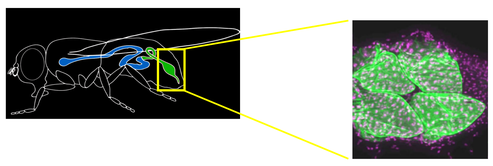
Significance and background

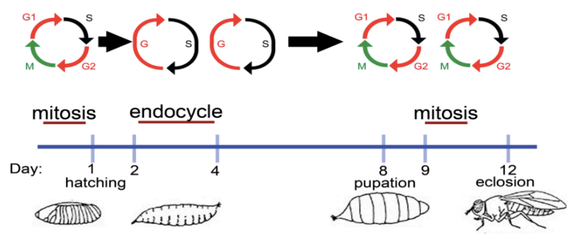
- Cells tightly regulate centrosome number → for the majority of cells, more than two centrosomes per cell results in adverse phenotypes including aneuploidy and defects in cell motility
- We are studying mechanisms that counter extra centrosomes in the *Drosophila* rectal papillae which undergo polyploid mitoses



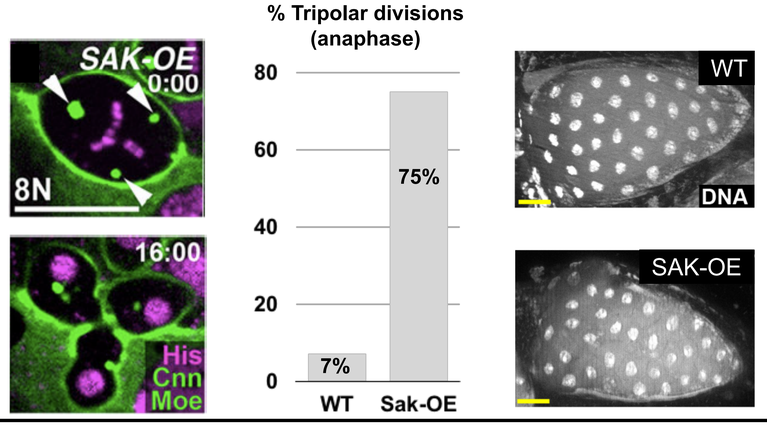
Drosophila rectal papillae are necessary for proper water and salt balance



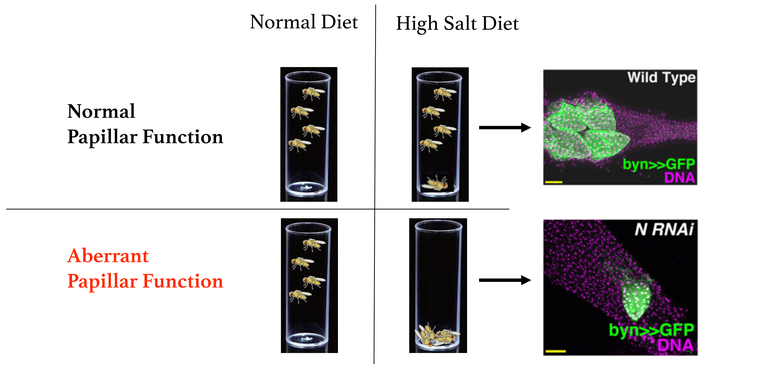
Papillar cells undergo endocycles and then reenter the cell cycle to complete two rounds of mitosis!

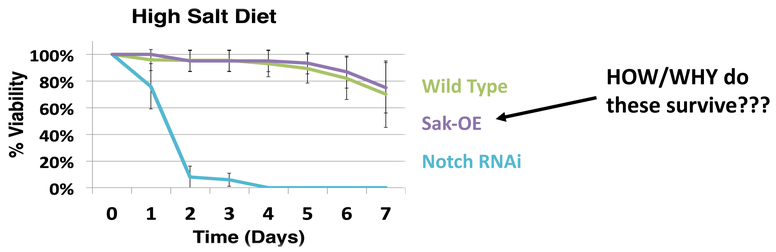


Papillae develop and function normally despite extra centrosomes and multipolar divisions[1]

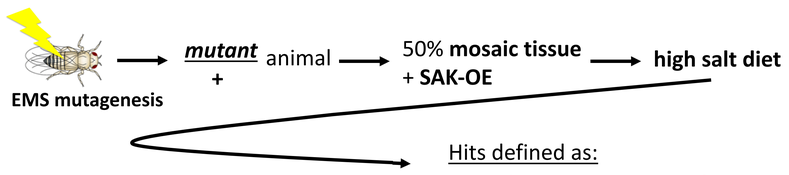


Feeding on a high salt diet is a simple screening assay for aberrant papillar function[1]

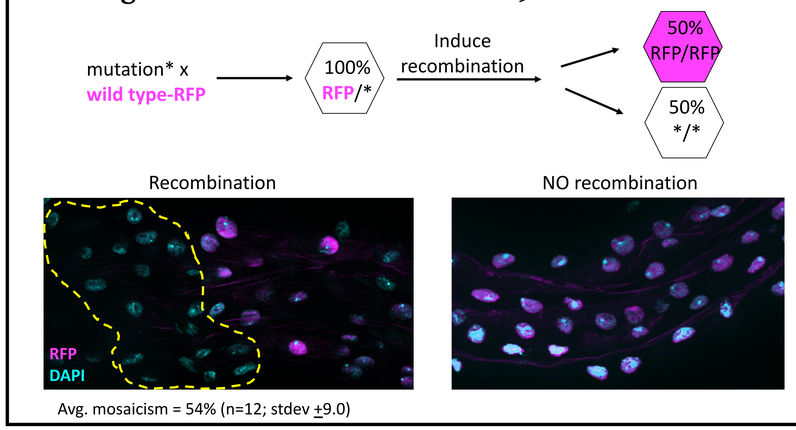




We are conducting a forward genetics screen to uncover genes involved in tolerance to extra centrosomes[2]

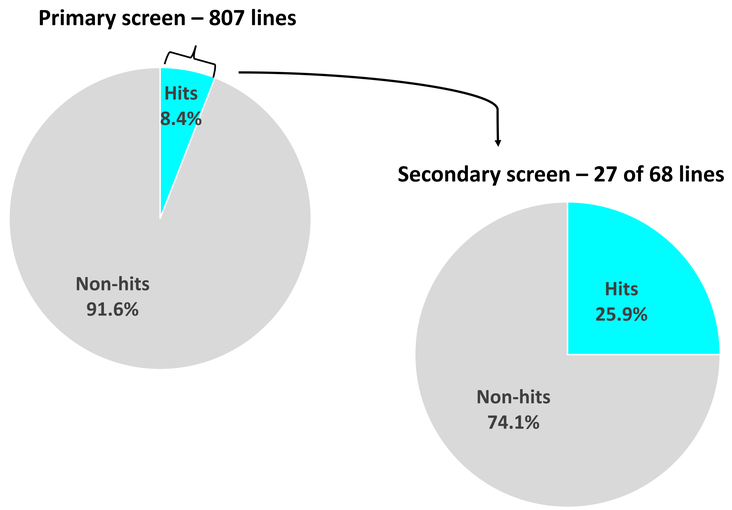


We can generate rectal tissue that is 50% mosaic



Avg. mosaicism = 54% (n=12; stdev ±9.0)

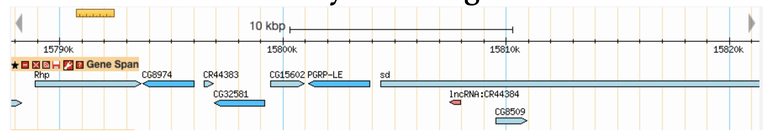
To date we have generated ~1100 recessive mutations on the X chromosome and have screened 807 with the high salt diet assay



Hits are confirmed through follow up analyses to confirm if:

- extra centrosomes are necessary for phenotype
- the mutation is recessive
- the phenotype is salt specific
- mutant cells have aberrant morphology in SAK-OE background

Using duplication stocks we have genetically mapped our first hit to a relatively small region



→ we will further map using available deletion stocks
→ we will confirm using miseq genomic sequencing

Acknowledgements and Funding

PEW
National Institutes of Health
Translational Research Institute for Space Health
Fox Lab Members

Works Cited

1. Schoenfelder, KP et al. *Development* (2014). **141**, 3551 – 3560.
2. Haelterman, NA et al. *Genome Research* (2014). **24**, 1707-1718.