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Effects of High-Sucrose Diet in Yorkie-Induced Eye Overgrowth and Developmental Timing in *D. melanogaster*

Niranjan Nambiar
Evansville, IN
Signature School

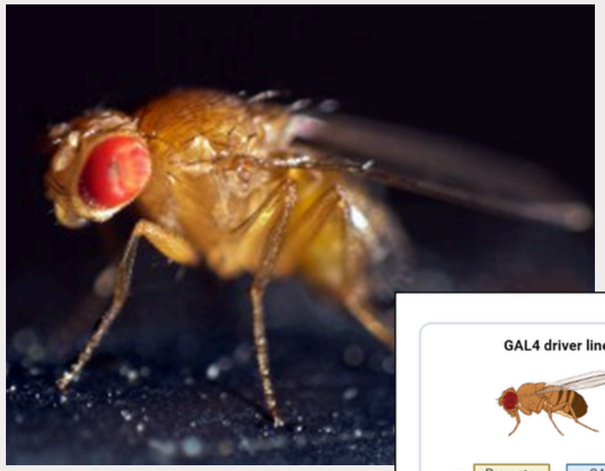
Research Question

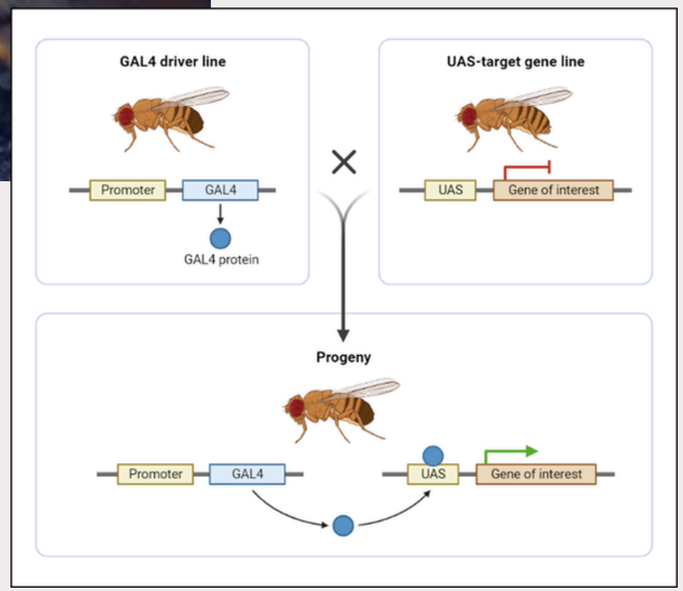
Research Question: To what extent does high-sucrose diet exposure during organismal development affect Yorkie-induced tumorigenesis and developmental timing?

Purpose: Investigating the effects of dietary sucrose on developmental timing & Yorkie activation in Drosophila imaginal tissues.

Hypothesis: Increasing concentrations of sucrose in fly media will increase Yorkie activation in developing eyes, while also slowing development.

Key Concepts

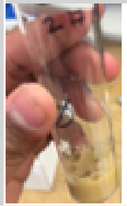


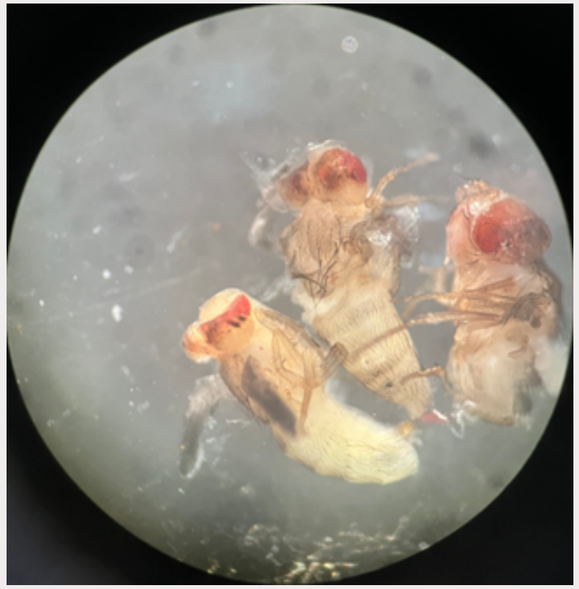


- Drosophila melanogaster is a widely used model organism, sharing ~75% of disease-related genes with humans, making it useful for studying genetic and environmental effects.
- The GAL4-UAS system enables targeted gene expression. GMR-GAL4 drives expression in eye tissue, while UAS-Yorkie activates growth pathways within the Hippo signaling pathway, causing tumor-like overgrowth.
- Yorkie (Yki), a key effector of the Hippo pathway, regulates tissue growth; when overactivated, it causes uncontrolled cell proliferation. Although normally suppressed by the Hippo pathway, this regulation is bypassed in this model.

Methodology

Genetic Crosses

Control: GMR-GAL4 (8) ♀ x OR^5 (5) ♂	A: UAS-Yki$^{[3SA]}$ (8) ♀ x GMR-GAL4 (5) ♂	B: GMR-GAL4 (8) ♀ x UAS-Yki$^{[3SA]}$ (5) ♂
 Control cross used to establish baseline developmental timing without Yorkie overexpression. Uses Oregon wild flies (OR^5)	 Cross produces offspring expressing Yorkie in developing eye tissue through the GAL4–UAS system. **MATERNAL YORKIE**	 Reciprocal cross used to control for parental origin effects in Yorkie-induced tumor phenotypes, with genotype sexes switched. **PATERNAL YORKIE**



- Raised on Semi-Defined Food
- **IV:** Sucrose concentration (0, 0.15M, 0.5M, 1M)
- **DV:** Tumor Phenotype (indicating Yki overactivation) & Developmental Time
- **Controls:** Base recipe (BDSC SDF), Temp (25°C), fly density, food volume
- **Brood Transfer:** Adults are transferred to new vials every 24 hours for 4 days to generate 4 synced broods for more data.
- **Dissection:** Pupae were dissected from pupal cases for examination.
- **Pupae Count**: Pupae counted daily to measure developmental rates.

Data Analysis

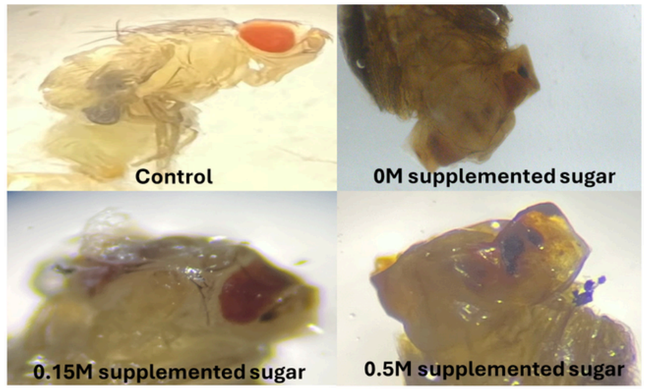
Development Rates

- Plotted percentages of pupae that have developed in each experimental group (averaged out all vials in each group)
- Standard Deviations accounted for

Tumor Severity

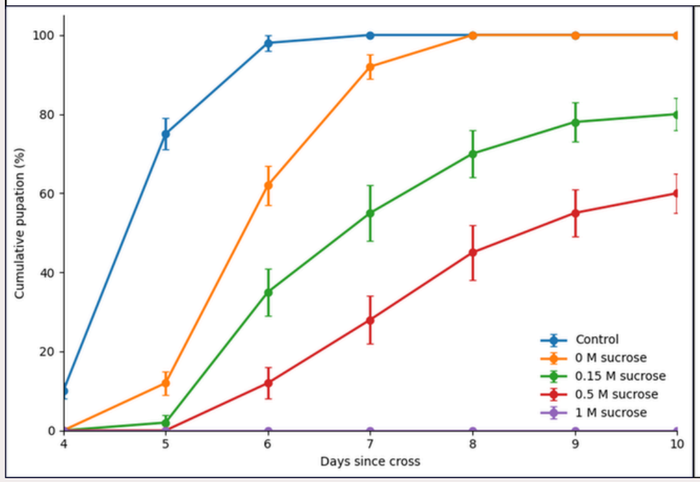
- Scored flies on a phenotypic tumor scale (0-3)
- Averaged out all vials, and created distribution graphs and bar charts w/ standard deviations

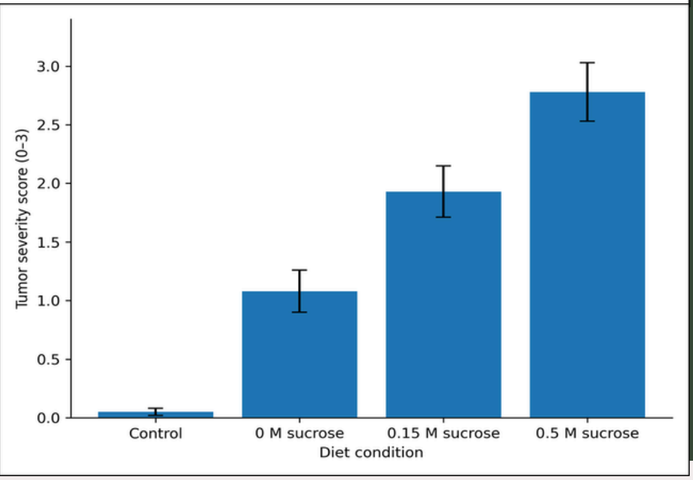
Fig 1. Representative Eye Tumor Phenotypes and Scoring Criteria



Tumor Severity Scoring Criteria
Eye phenotypes were categorized using a 4pt severity scale based on the degree of tissue overgrowth and distortion observed in dissected heads.

Score 0: Normal morphology
Smooth eye surface with no visible tissue expansion.
Score 1: Mild overgrowth
Slight enlargement of eye tissue with minor distortion of normal eye.
Score 2: Moderate overgrowth
Clear expansion of eye tissue and disruption of normal morphology.
Score 3: Severe tumor phenotype
Extensive tissue overgrowth with major deformation





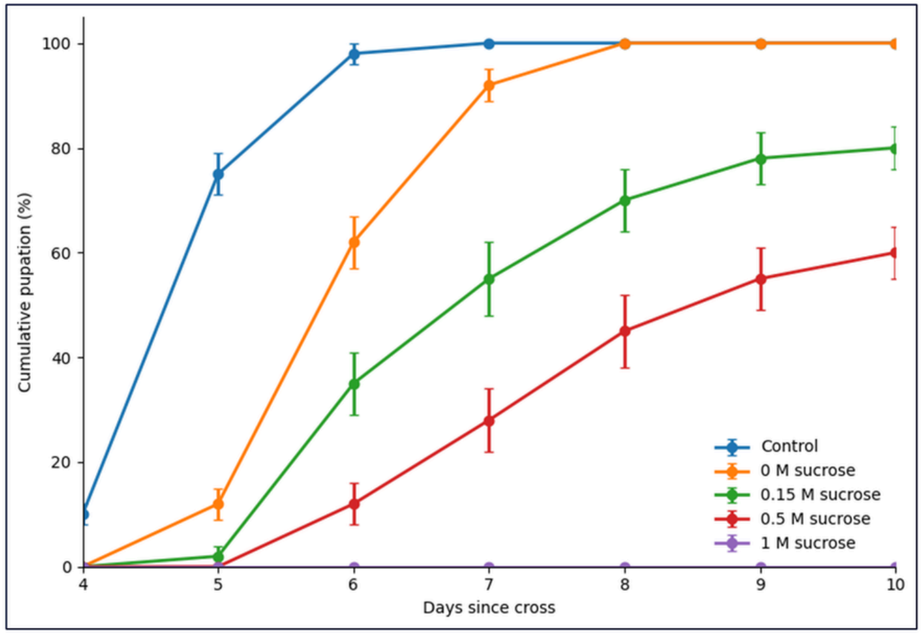
Diet condition	Final pupation (%)	Day of 50% pupation	Mean tumor score ± SD	Dominant phenotype
Control	100	~5	0.05 ± 0.03	Score 0 (Normal)
0 M sucrose	100	~6	1.08 ± 0.18	Score 1 (Mild)
0.15 M sucrose	80	~7	1.93 ± 0.22	Score 2 (Moderate)
0.5 M sucrose	60	~8–9	2.78 ± 0.25	Score 3 (Severe)
1 M sucrose	0	—	—	No pupation observed

Results

01 Slower Developmental Timing

- Increased sucrose concentrations lead to slower rates of pupation
- Large sucrose concentrations are reaching pupation percentages slower than those with less sugar
- 1M sucrose concentration (extreme end) with the Yorkie combination was so lethal that it yielded ZERO PUPAE in all vials!
    - Shows extreme correlation between Yorkie overactivation and sucrose concentration increase

Fig 2. HSD Development Timing



Graph depicts percentages of offspring that have pupated *X days* after the initial parental cross (see genetic crosses in methodology). 1M sucrose yielded zero pupae, proving the GMR-GAL4; UAS-Yki$^{[3SA]}$ with +1M sucrose lethal.

Results

02 Increased Tumorigenesis

- As the sucrose concentration increases, more and more flies start to exhibit more severe tumor phenotypes
  - In the distribution graph, the dominant color turns warmer (more red), indicating increasing tumor severity
  - Bar Graph clearly exhibits an increasing tumor severity mean, indicating direct correlation between increasing sucrose concentrations and tumor severity.

Fig 3. Distribution of Tumor Severity

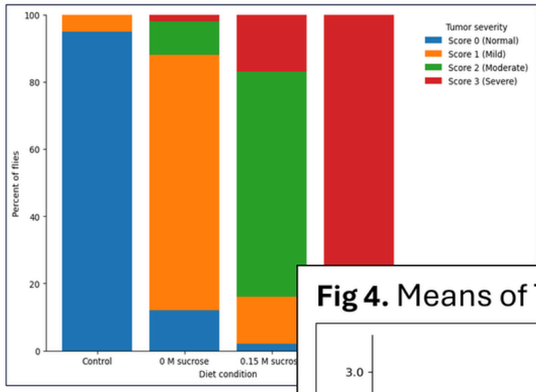
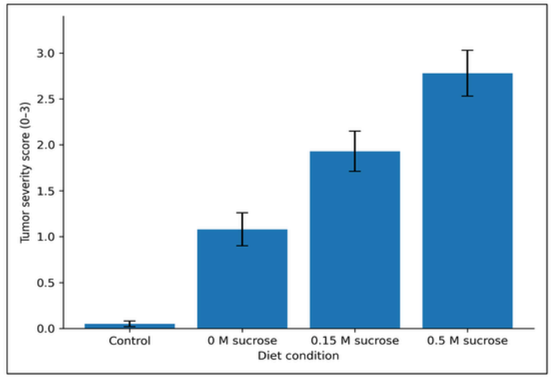


Chart depicts bars for each expe
divides each bar into colored se
percentages of flies that scored

Fig 4. Means of Tumor Scoring



Bar graph depicts bar averages of the tumor scoring between each experimental cross and includes standard deviations for each group. General trend shows that increased sucrose leads to higher tumor scoring.

Conclusions & Implications

Conclusions

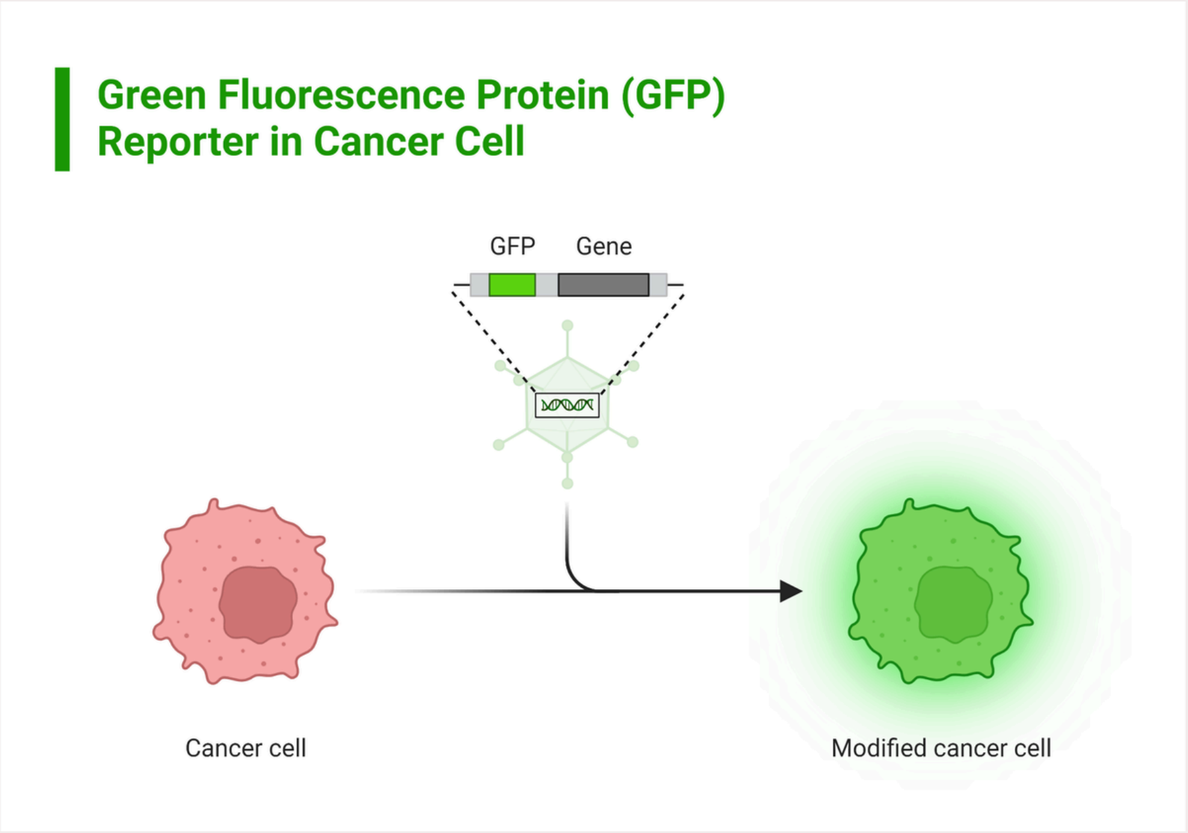
- Pupation rate significantly increased in response to increase of sucrose levels in SDGF base.
- Increased dietary sucrose of 1M with GMR-GAL4; UAS-Yki[3SA] significantly increases mortality, prevents organismal development, and pupation, making it unable to use for experimentation
- Dietary sucrose levels increase Yki tumor severity

Implications:

- Increased dietary sucrose delayed development and exacerbated Yorkie-driven tumor phenotypes in Drosophila, suggesting that metabolic environment can influence conserved growth-regulation pathways such as YAP/TAZ that are implicated in human cancers.

Future Work

Future Work: Using GFP-based reporters to quantify Yorkie pathway activity and establish a direct mechanistic link between dietary sucrose levels and oncogene-driven tumor progression.



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