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Genes Affecting Intestinal Stem Cell Development Influence Longevity in Female Drosophila on a High Sugar Diet

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Genetic Influence on Intestinal Stem Cells Within Female *Drosophila* Fed a High Sugar Diet

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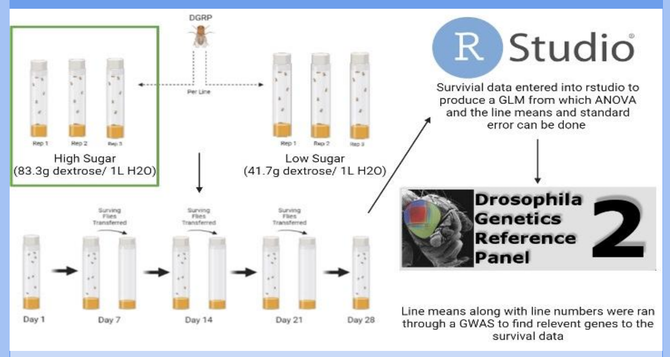
Background

- Approximately 20% of the American adult population is clincially obese and approximately 7% have diabetes.[1] Obesity and diabetes are influenced by genetic factors and high sugar diets.
- Understanding which genes are involved can help identify potential treatment targets.
- Interestingly, genes affecting many diseases are known to vary between males and females and thus the sexes should be studied separately.
- *Drosophila melanogaster* shares many analogous metabolic processes with humans, can serve as a model for sugar metabolism and allows us to easily study the genetic basis to complex traits in an individual sex.

Research Questions

1. ***Is there a genetic basis for difference in survival between female Drosophila melanogaster fed a high sugar diet* (HSD)*?***
2. ***What genes are responsible for observed differences in survival?***

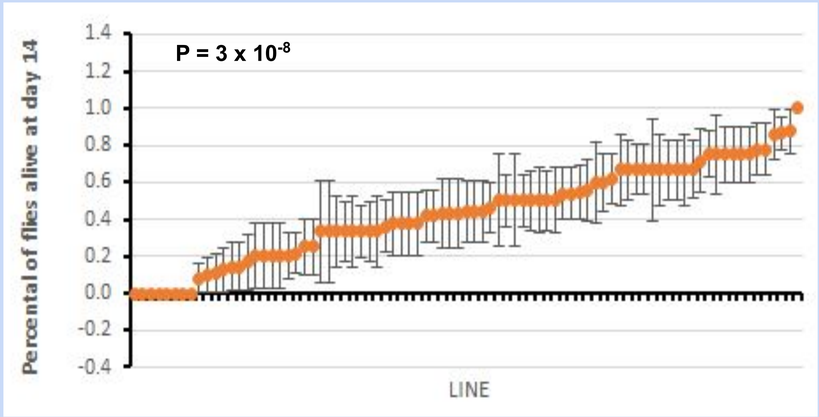
Methods



- The number of surviving flies was measured weekly in 3 replicates from 86 DGRP lines
- DGRP lines are fully sequenced inbred lines allowing for genotype-phenotype mapping.
- Differences in longevity between females from different lines reared on the high sugar diet were tested using a generalized linear model at day 14
- Genes affecting longevity were identified through a genome wide association study (GWAS, DGRP2 website) using the line means from the glm model

Results

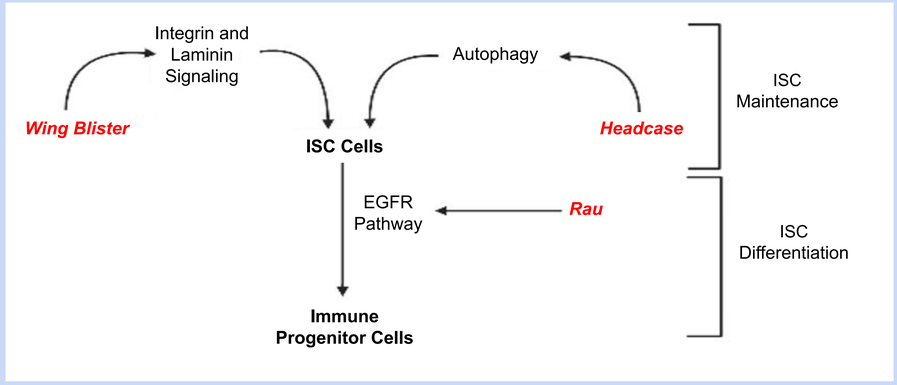
Mean Longevity Differs Significantly Between Inbred Lines Indicating Genetic Differences Affecting Survival



9 Unique Genes Associated With Significant Differences in Means Longevity

Gene Name	Function	Gene Name	Function
FBgn0031745	RTK Signaling	*FBgn0039075*	No Data
FBgn0261563	Laminin Molecules	*FBgn0003165*	mRNA Translation
FBgn0010113	Trachea Function	*FBgn0040843*	Reproduction
FBgn0262593	K+ Channel Moderation	*FBgn00480843*	No Data
FBgn0003138	No Data		

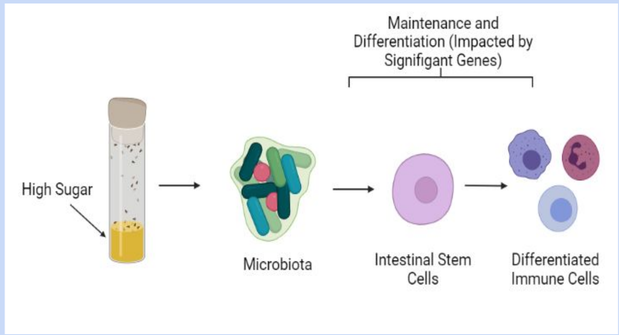
Multiple Associated Genes Affect Intestinal Stem Cell Maintenance and Differentiation



Discussion

Genes affecting intestinal Stem Cell (ISC) maintenance and differentiation are related to immune function and differential longevity within *Drosophila*, (*headcase*, *wing blister* and *rau*)

- High sugar diets are known to affect the *Drosophila* microbiome which in turn is known to influence the production and differentiation of ISCs.[2,3]
- ISCs differentiate into immune progenitor cells that are essential for a healthy immune response.[4]
- The effect that the HSD may be having on the *Drosophila* microbiome and the consequent effects on ISCs potentially explains the significant variation in the longevity of various DGRP lines.



Future Research

- Knocking out expression (via CRISPR/cas9), or knocking down (via RNAi) could verify our associations and ISC and immune cell abundance could be quantified using transgenic markers to test for a relationship with ISC function.
- We hypothesize that the *Drosophila* immune response, as well as longevity, will decrease in response to the decreased expression of associated genes and we propose testing longevity of these lines after an immune challenge.

References

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