Role of Germline-Intrinsic Meiotic Genes in Influencing Somatic Aging

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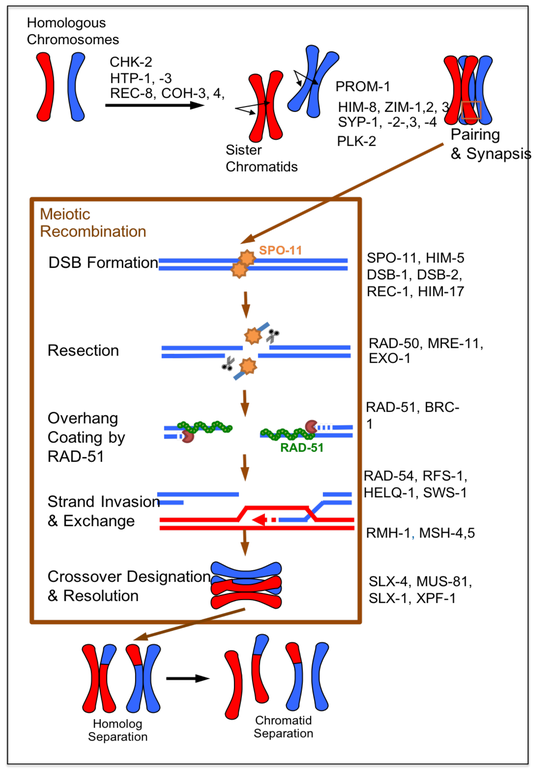
Background

There is a clear link between increased maternal age, meiotic defects and fertility. Human studies have indicated correlative evidence for germline fidelity impacting health. However the causative role of meiotic integrity on organismal aging has not been studied in any species.

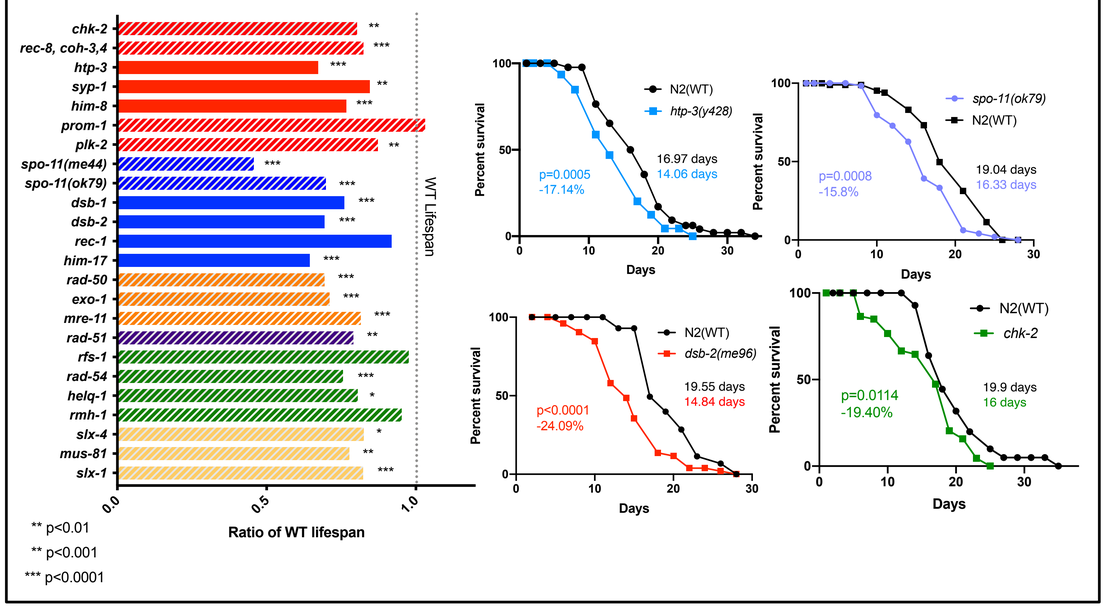


C. elegans provides a model to study this question because the somatic cells are post mitotic, therefore uncoupling germline functions from DNA damage. Our preliminary results suggest that mutations in all aspects of meiosis effect lifespan. This led us to propose the hypothesis <u>hypothesis that genes that govern meiotic fidelity in the germline influence the rate of aging of the whole organism</u>

Specific aims

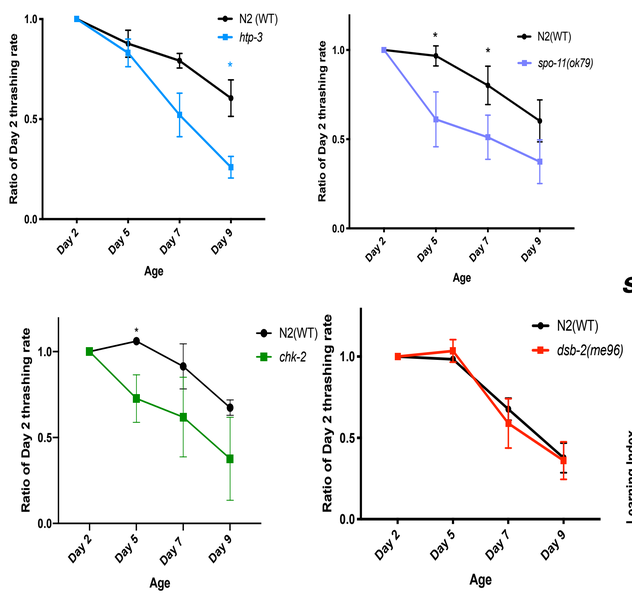
1. Do meiotic gene mutations affect the rate of aging of the animal?
2. How are signals about meiosis integrity transmitted from the germline to the somatic tissues?
3. What somatic mechanisms underlie the accelerated aging induced by meiosis disruption?

Mutations in all stages of meiosis reduce lifespan

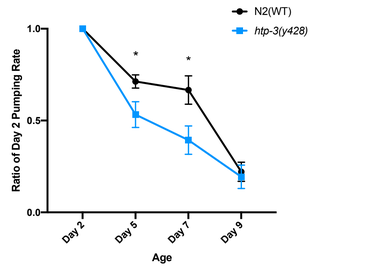


Mutations in meiotic genes cause decline in healthspan features

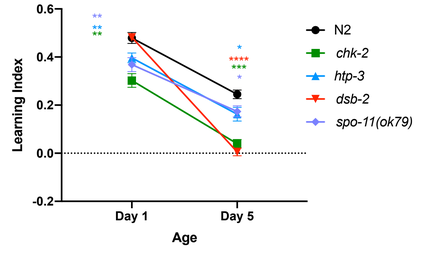
spo-11, htp-3, and *chk-2* mutants demonstrate premature decline in mobility



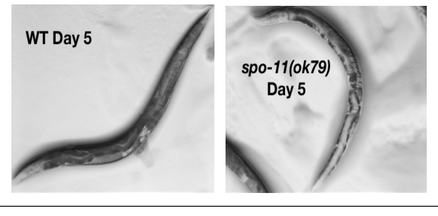
htp-3 mutants demonstrate premature decline of pumping



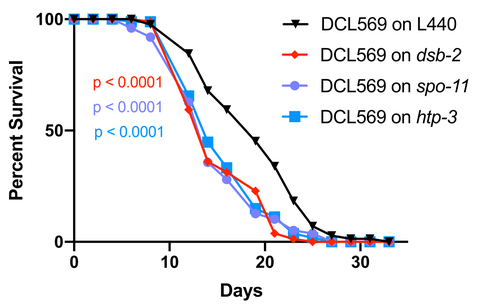
spo-11, htp-3, dsb-2, and chk-2 mutants exhibit decline in neurological function



spo-11 mutants demonstrate early decline in tissue integrity



Meiotic genes reduce lifespan when knocked down in the germline



Conclusions and future directions

Overall mutations in meiosis impact somatic aging. Disrupting meiotic genes while impacting lifespan does not have a uniform impact on different aspects of healthspan. However we found that mutations in some of the meiosis genes we tested resulted in decline in certain aspects of healthspan.

We will continue to investigate this relationship between germline integrity and somatic aging by exploring the mechanism and signaling pathways involved.

Acknowledgements

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