

Heterogeneity of Aging

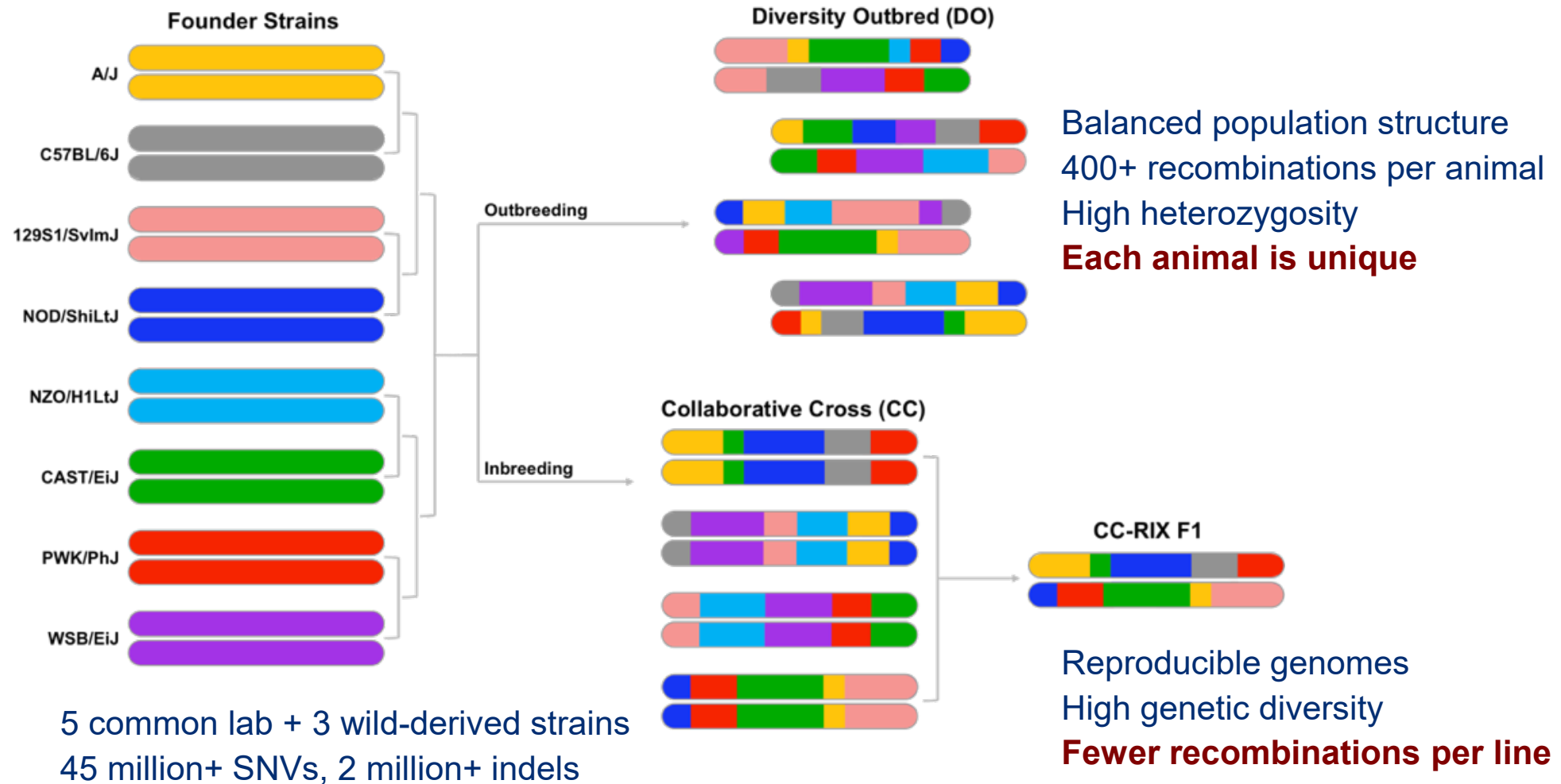
Genetics, Environment, GxE, or Noise?





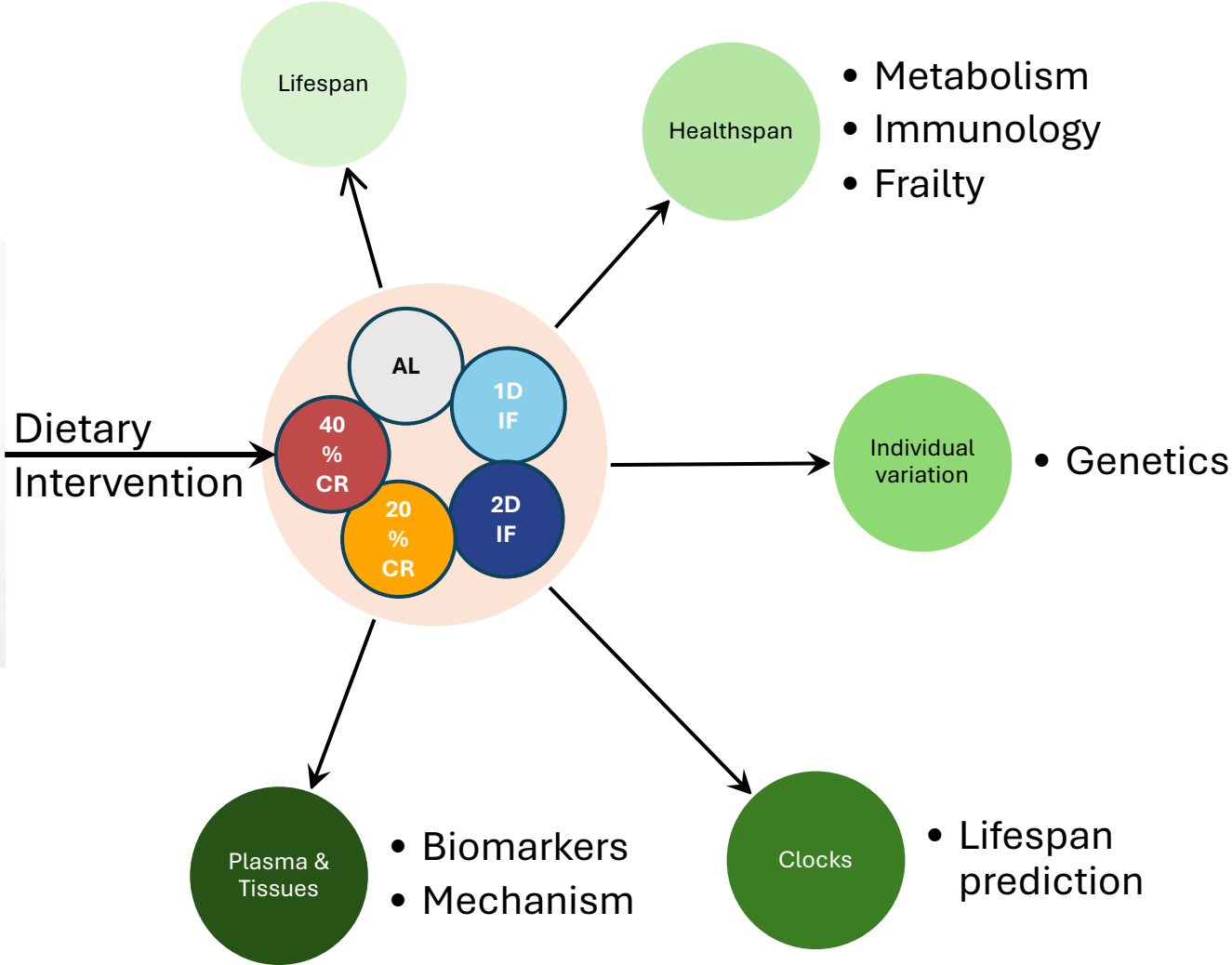


Diversity Outbred and Collaborative Cross



Aging Studies with Outbred Mice

Caloric restriction and intermittent fasting in Diversity Outbred Mice



Dietary Interventions

Ad libitum



AL

3.43
g/day

Mo Tu We Th Fr Sa Sn

Unlimited amount of food

Caloric restriction



20% CR

2.75
g/day

Mo Tu We Th Fr Sa Sn

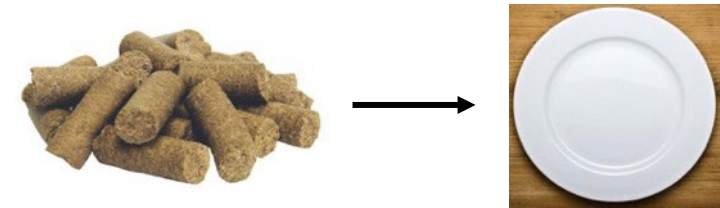
40% CR

2.06
g/day

3x meal

*Fed daily at 2pm

Intermittent fasting

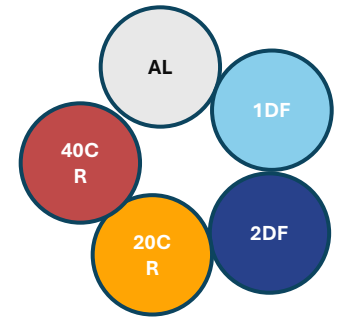


No food for 24 (1D IF) or
48 (2D IF) consecutive
hours per week

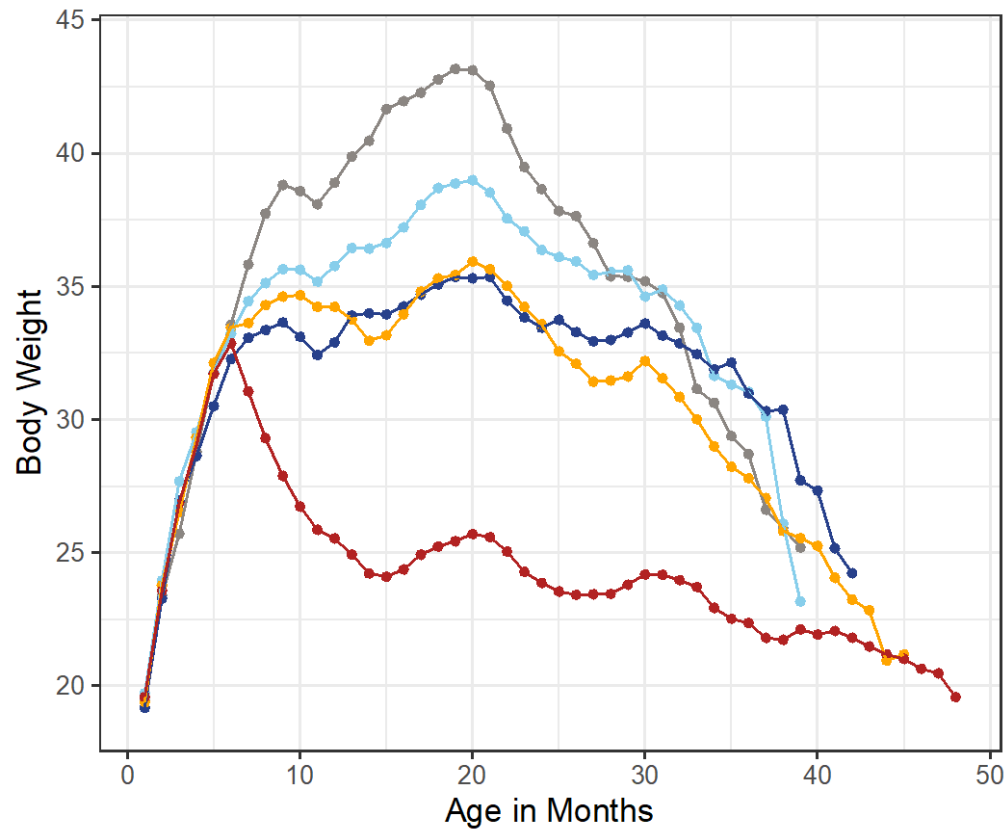
1DF Mo Tu We Th Fr Sa Sn
2DF Mo Tu We Th Fr Sa Sn

*Food added or removed at 2pm

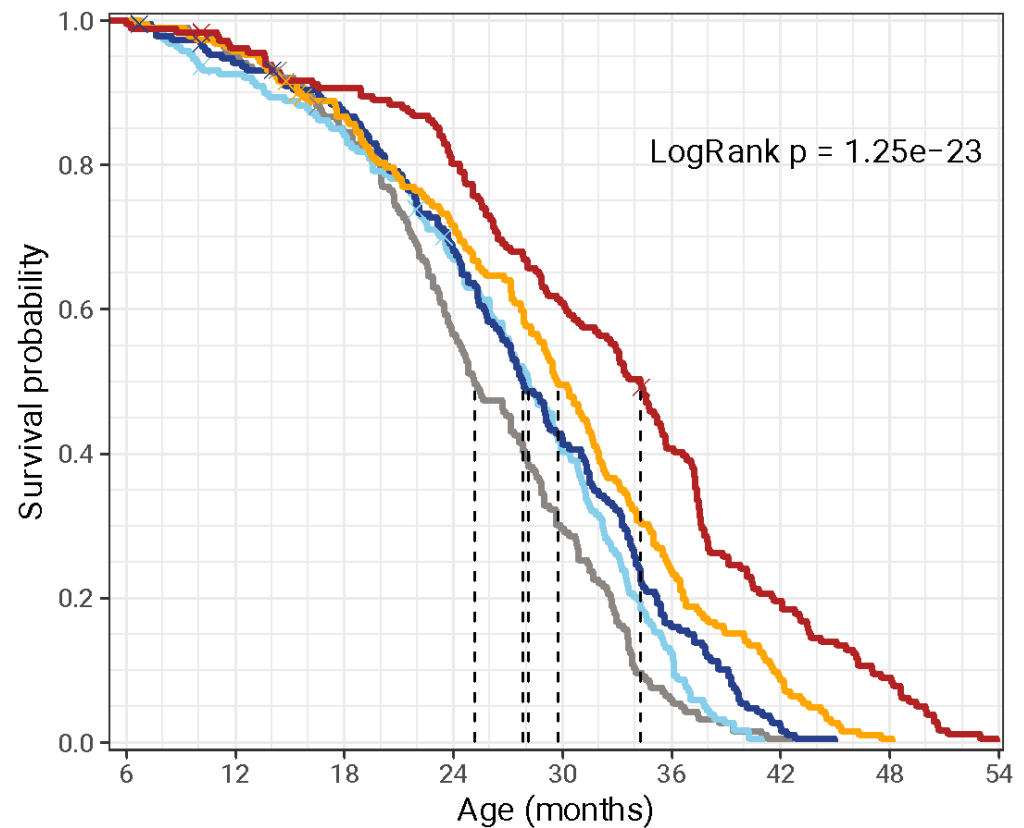
DR Reduced Body Weight and Extended Lifespan



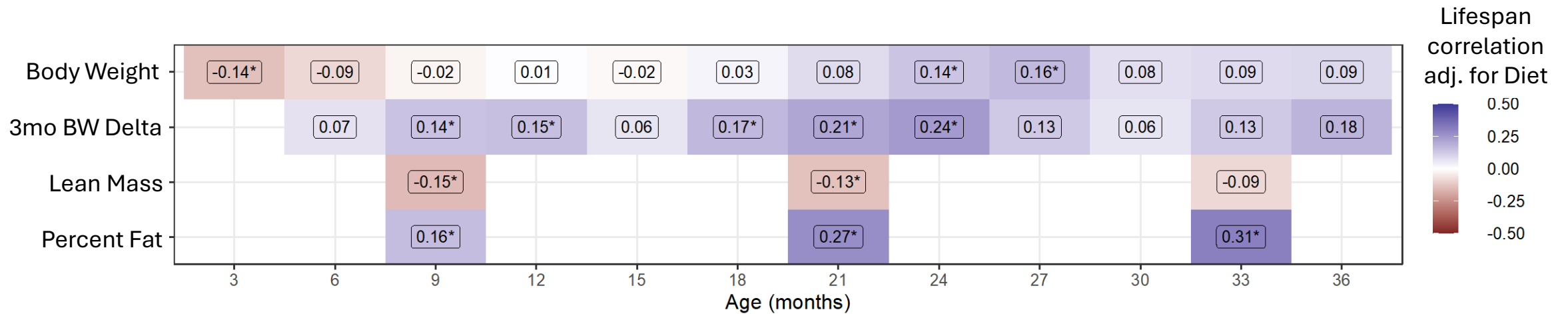
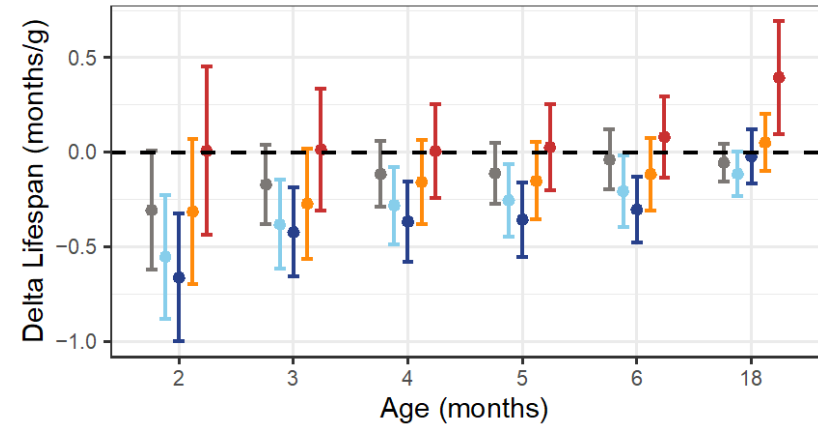
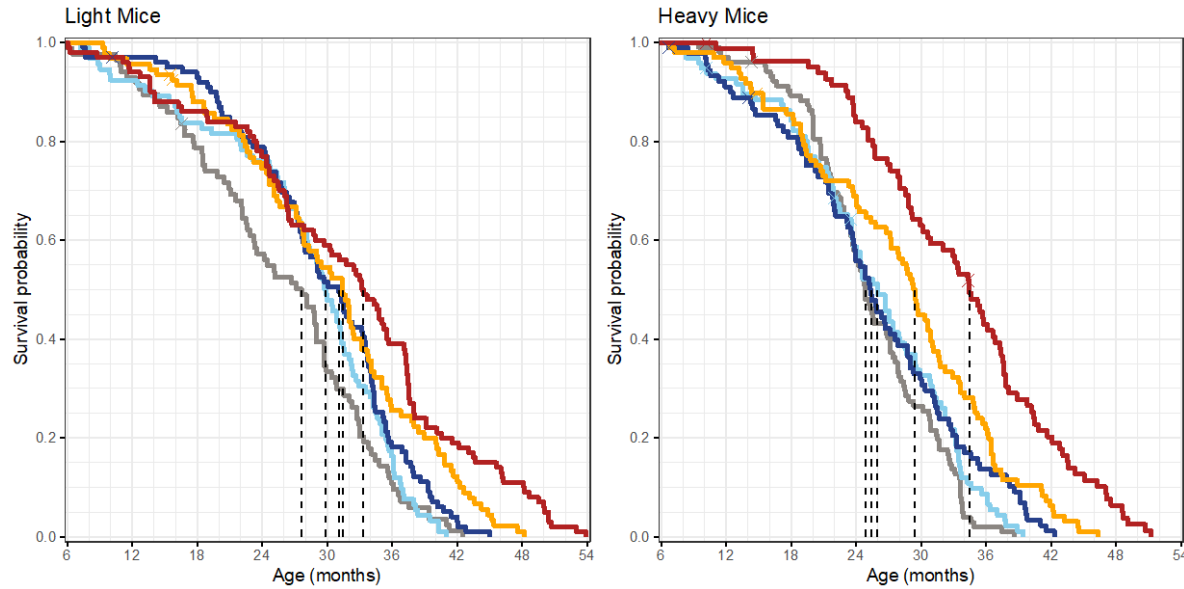
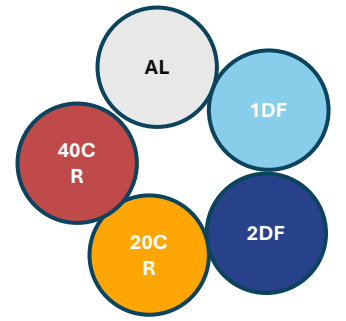
Body Weight



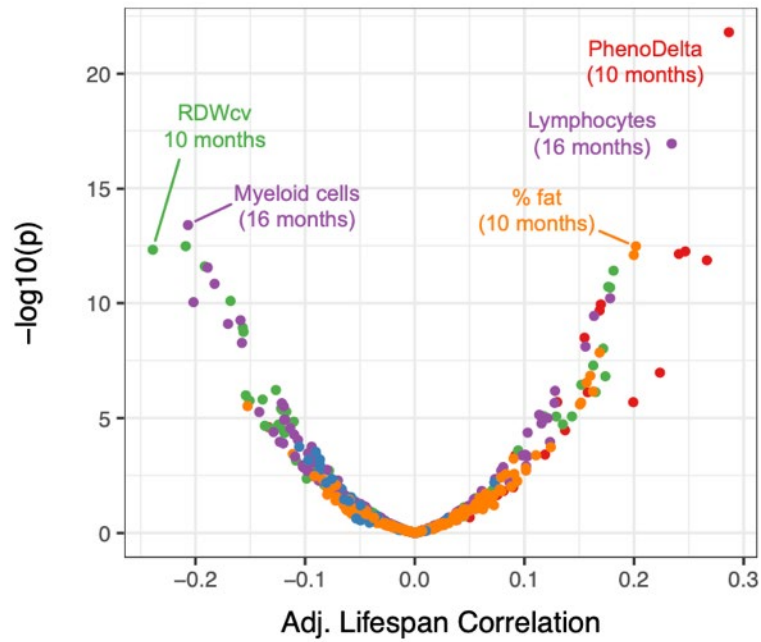
Lifespan



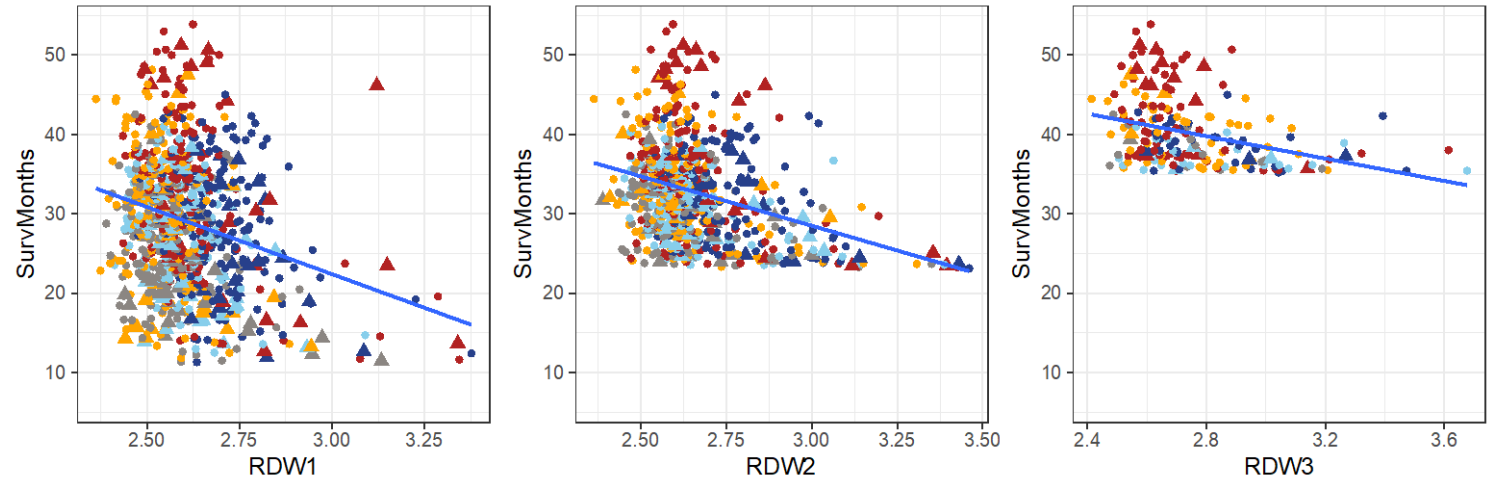
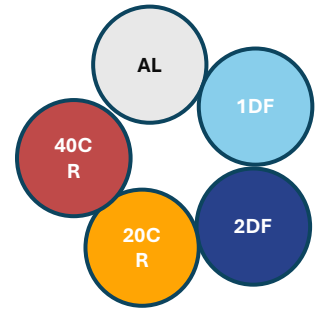
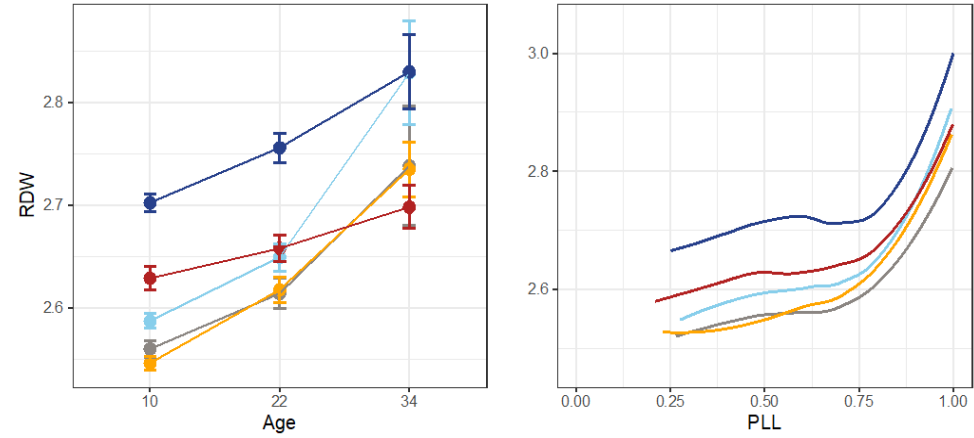
Early Bodyweight Alters Diet Response



Traits that predict lifespan

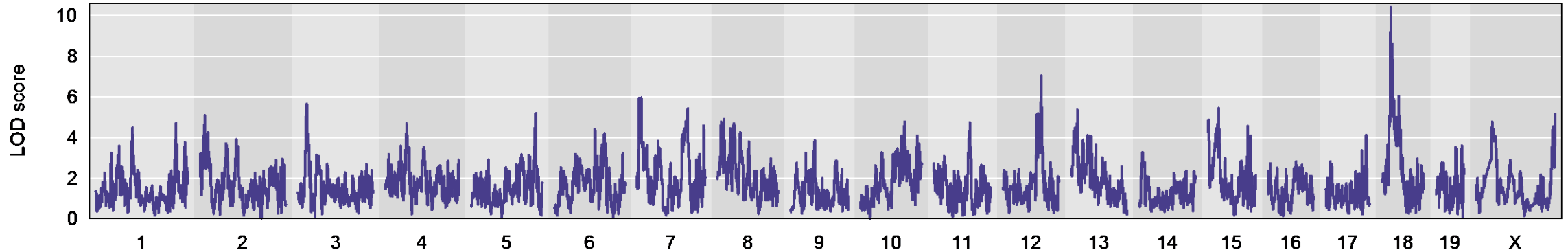


RDW – red cell distribution width



Genetic Mapping of Lifespan

Lifespan QTL on Chr 18

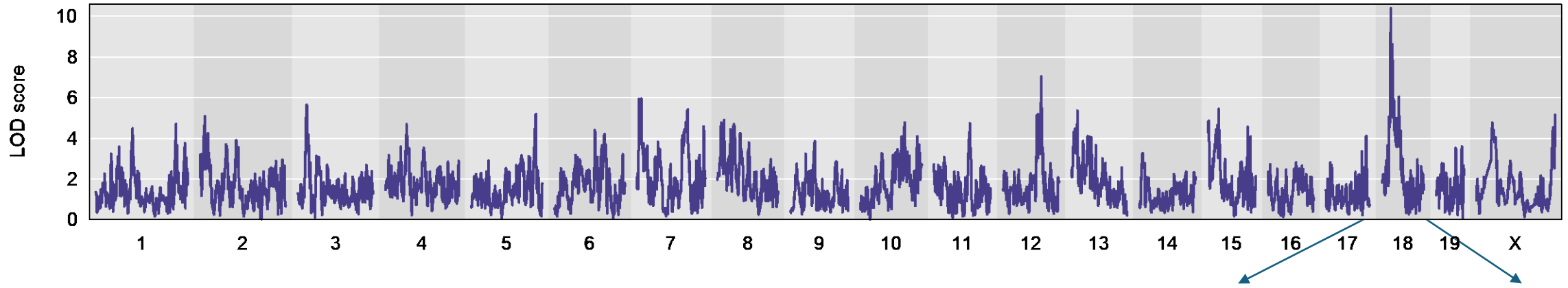


Variance Explained

Diet	6.6%
BW_6	1.0%
Chr 18	4.5%
Genetics (adj)	15.7%

Genetic Mapping of Lifespan

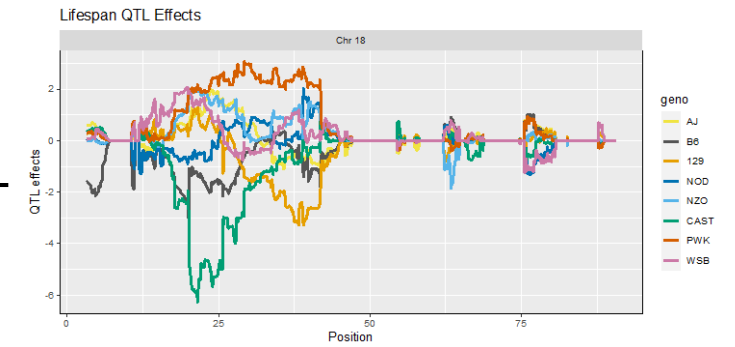
Lifespan QTL on Chr 18



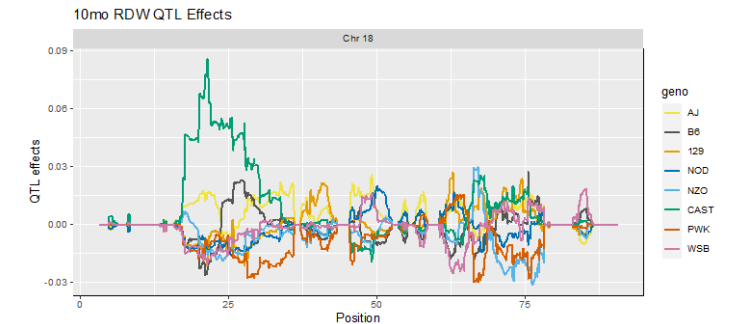
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Lifespan QTL

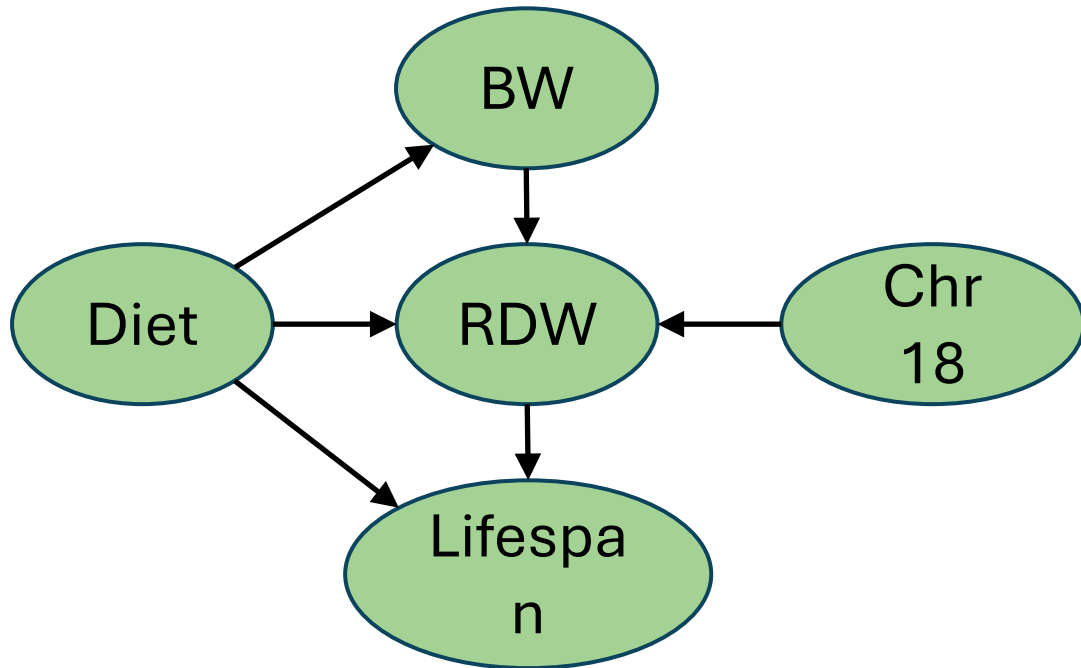
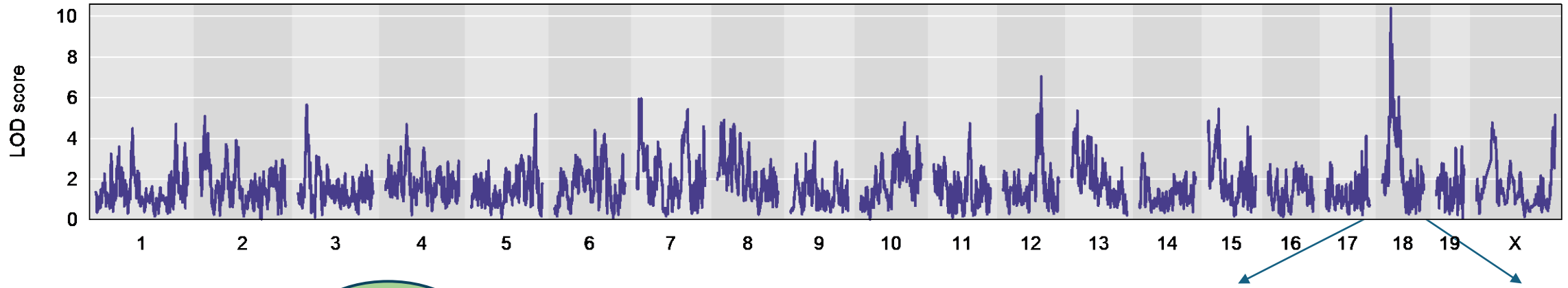


RDW QTL

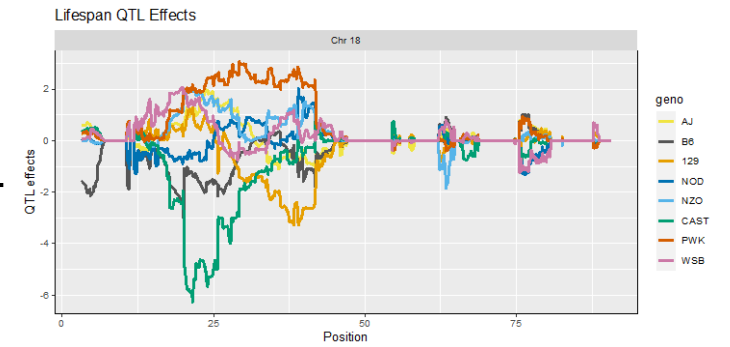


Genetic Mapping of Lifespan

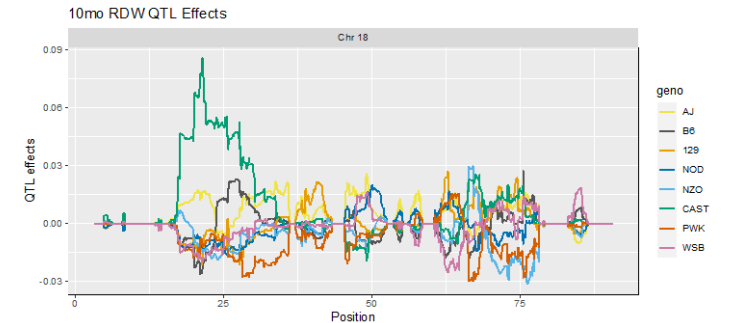
Lifespan QTL on Chr 18



Lifespan QTL

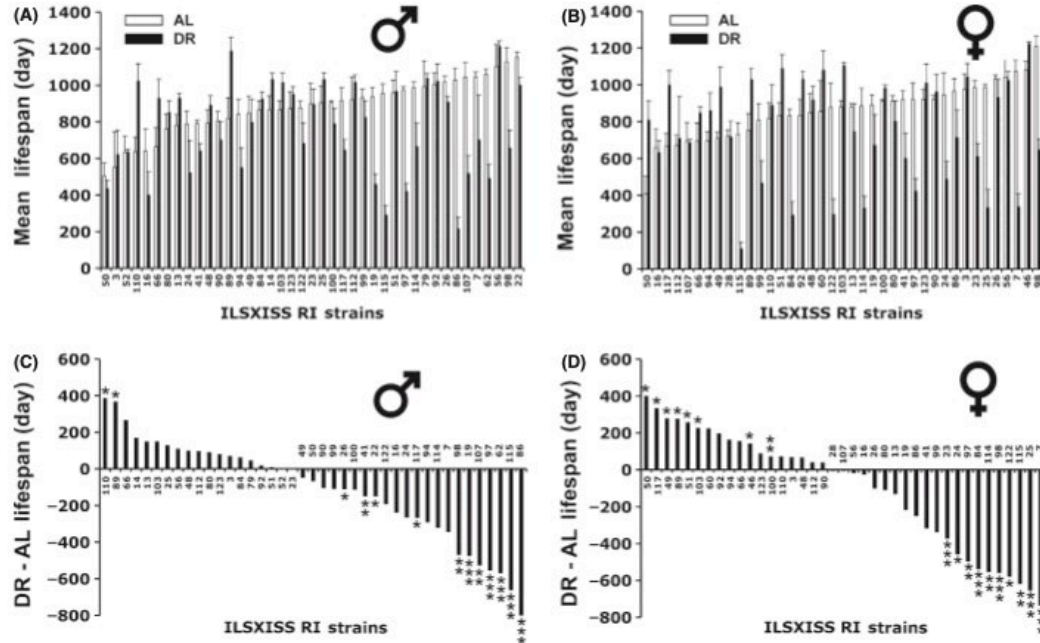


RDW QTL

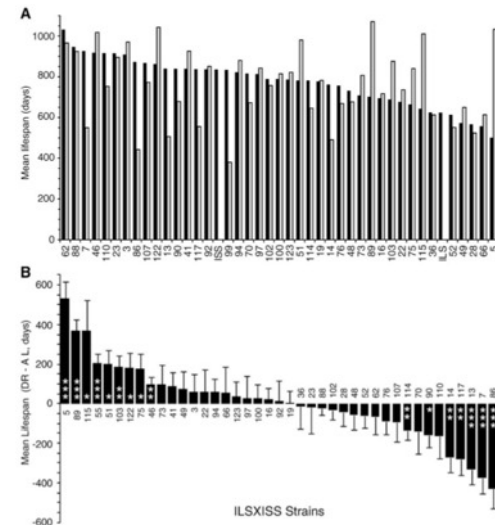


Aging Studies with Inbred Mice

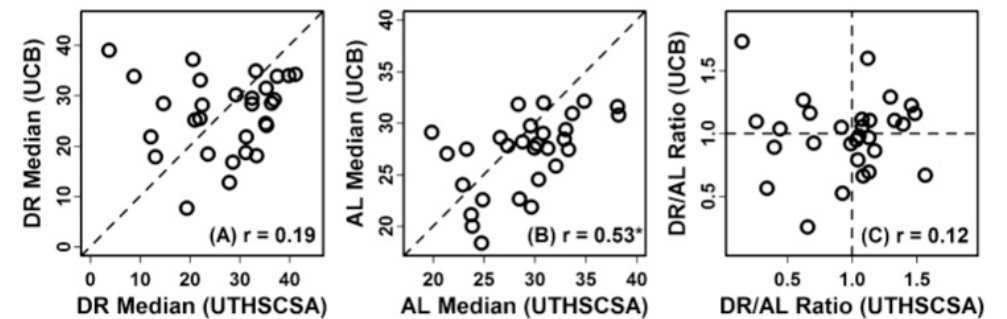
Power and Reproducibility in GxE Lifespan Studies



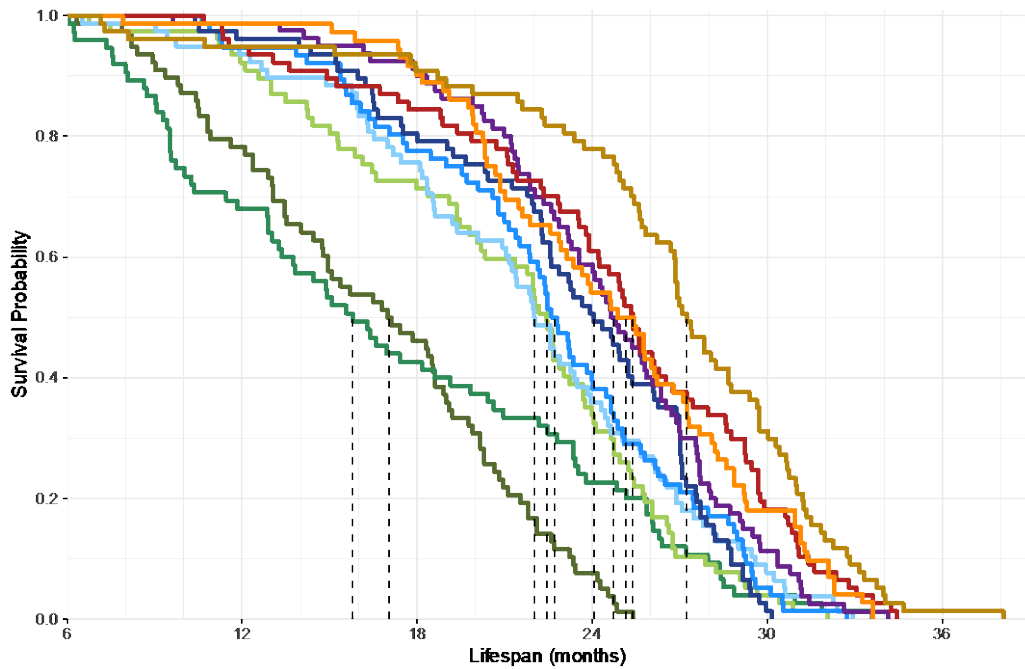
Liao et al, 2010



Rikke et al, 2010

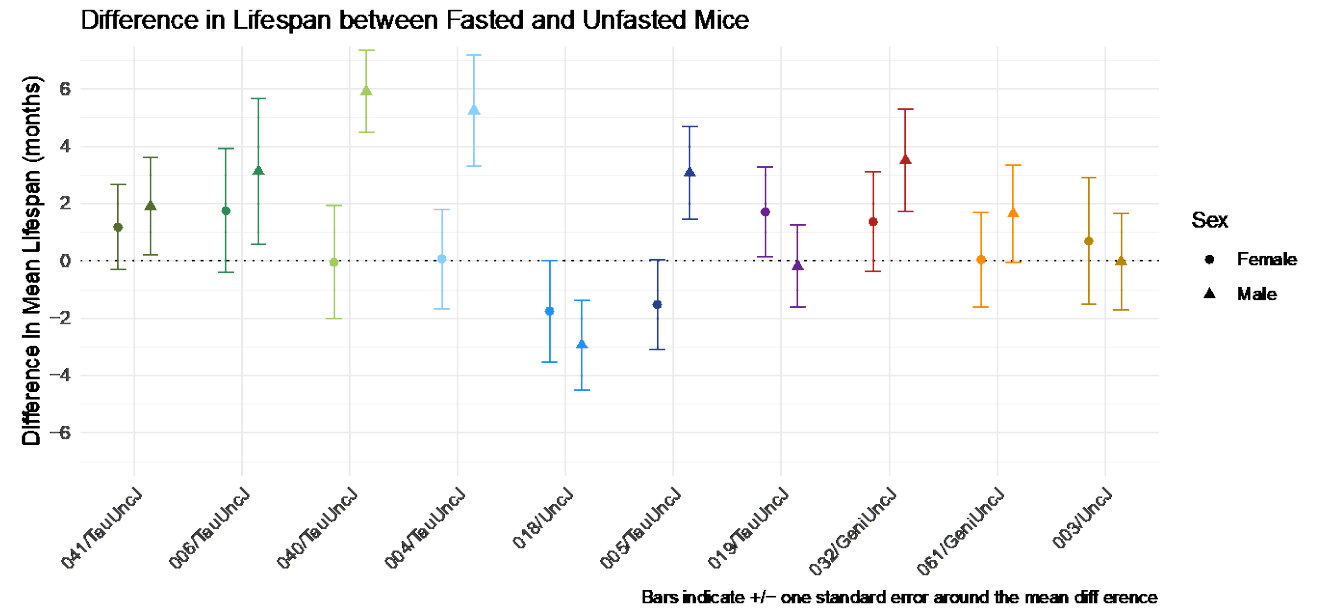


Effect of Strain, Sex and Diet on lifespan of CC strains



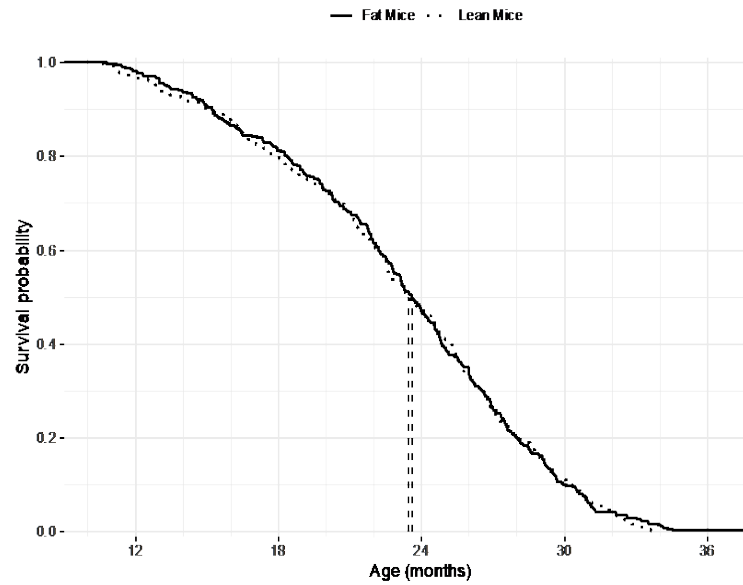
Strain:

041/TauUncJ	040/TauUncJ	018/UncJ	019/TauUncJ	061/GeniUncJ
006/TauUncJ	004/TauUncJ	005/TauUncJ	032/GeniUncJ	003/UncJ

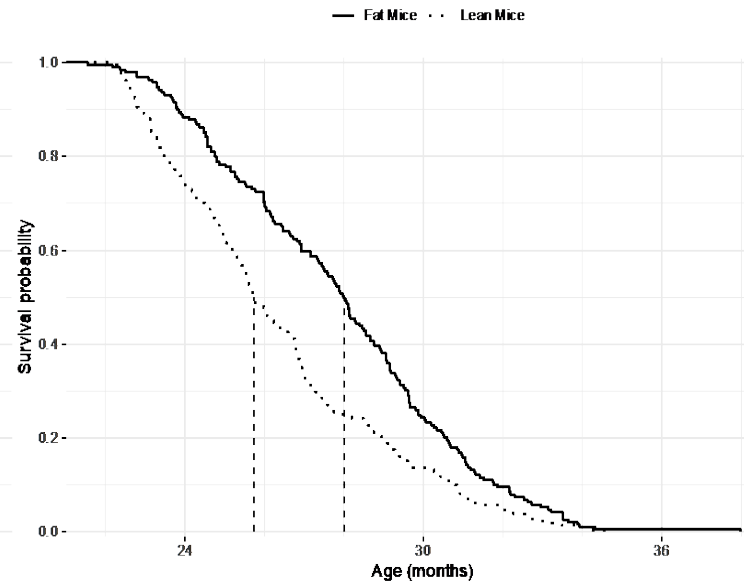


CC Lifespan by Adiposity

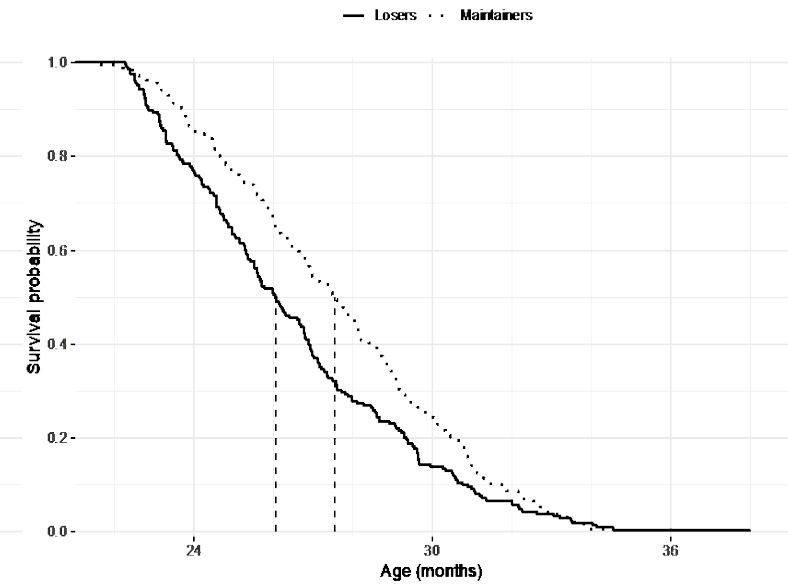
10 Month Fat



22 Month Fat

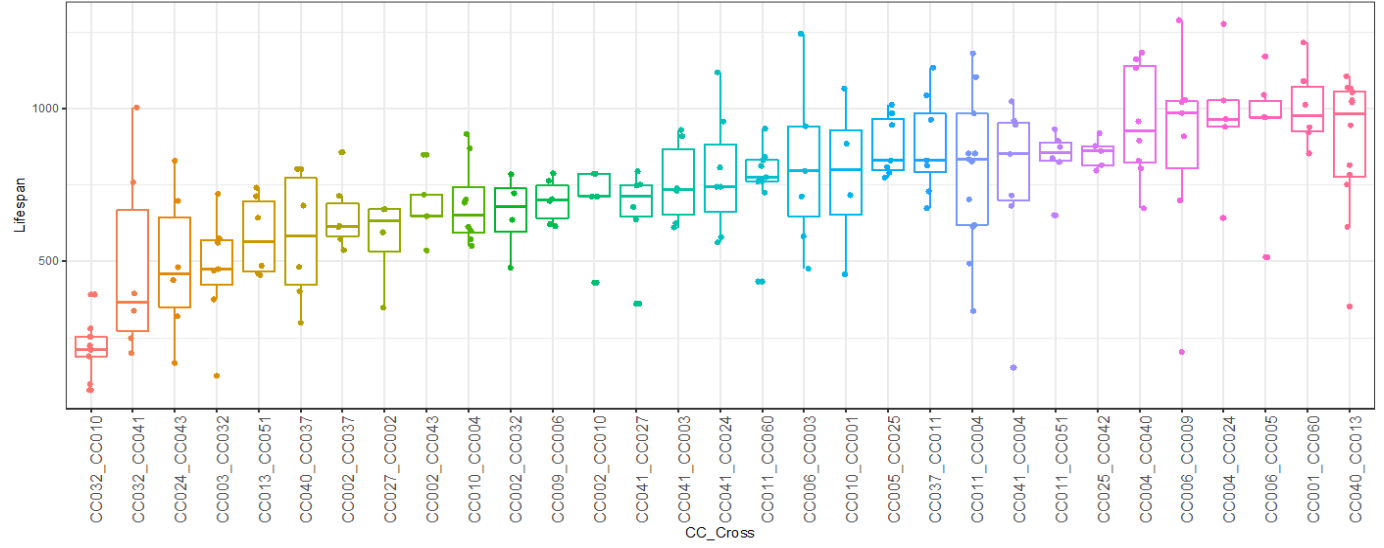
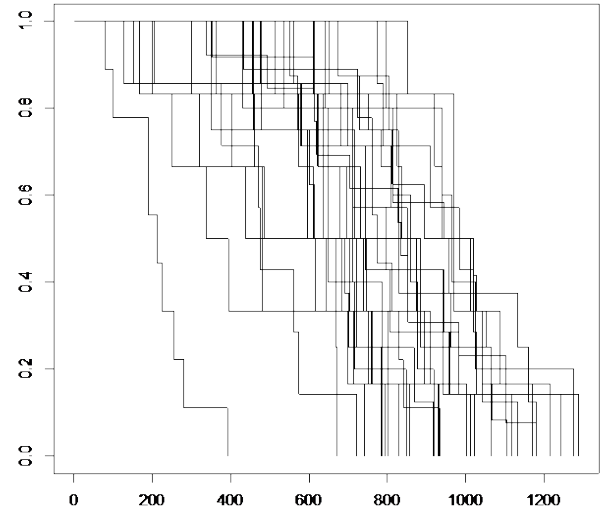
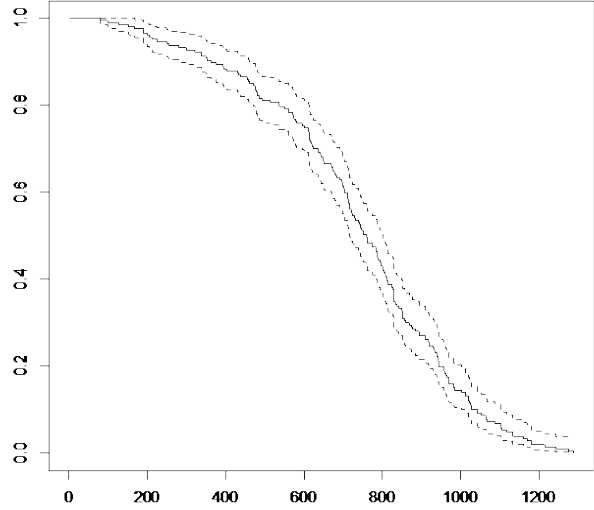
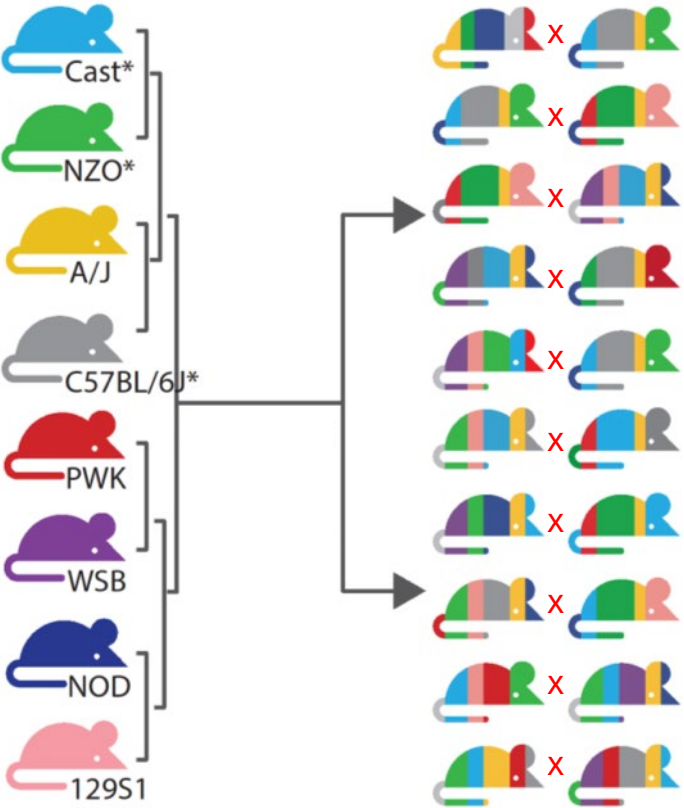


Delta Fat



Aging Studies with Hybrid Mice

CC-RIX Lifespan (JAX NSC)



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Adam Freund
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NIA Nathan Shock Center
Calico Life Sciences LLC



A Nathan Shock Center of Excellence
in the Basic Biology of Aging



Is Aging Programmed in our Genes?

