Aging Analysis of Mck-TSC1

Dave Bridges, Kaleigh Fisher and Binbin Lu

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Data Entry

These data are accumulated from the database. The analysis includes all alive animals, animals which were sacrificed and animals which died of natural causes (denoted in the database as "Unknown"). Animals which died with an estimated death date are excluded from the analysis. We are testing the effects of age on death by natural causes.

Mck-TSC1 Mice

Analysis

The data is saved in `/Users/davebridges/Documents/Source/DrosophilaMuscleFunction/Lifespan` with the data saved as ../Data/Mouse Log.csv and analysed using R [1]. The data was analysed using the survival package [2, 3]. Log rank tests were performed using the coin package [4, 5]. This plot analyses all of the natural deaths (marked in the database as unknown) This analysis contains a total of **625** animals, from which we have detected **49** natural deaths. See Table 5 for a summary of natural deaths and see Figure 1 for the combined death curves with errors.

Comparing all Four Genotypes

This analysis looks at all four genotypes for Mck-TSC1.

```
        Asymptotic K-Sample Logrank Test

data:  survobj.mck by
         Genotype (fl/fl; Tg/+, +/+; +/+, +/+; Tg/+, fl/fl; +/+)
chi-squared = 15.987, df = 3, p-value = 0.001141
```

The chi-squared test for comparing all four genotypes is significant, with a p-value of 8.7e-05. The results of these tests are in Table 1. The effects of each genotype, relative to the knockout strains are in Table 2. These data are visualised in Figure 2. This means that the knockout mice are 3.67 to 5.35 times more likely to die at any given time, depending on the strain.

	test	df	pvalue
Likelihood ratio test	18.6538	3	0.000322
Wald test	18.5000	3	0.000348
Score (logrank) test	21.3806	3	0.000088

Table 1: Muscle TSC1 Knockout Tests

	coef	exp(coef)	se(coef)	z	p
Genotype+/+; +/+	-1.68	0.187	0.496	-3.38	0.000719
Genotype+/+; Tg/+	-1.46	0.232	0.520	-2.81	0.004996
Genotypefl/fl; +/+	-1.30	0.273	0.377	-3.45	0.000565

Table 2: Muscle TSC1 Knockout Coefficients, relative to Knockout

Comparing Floxed to Knockout

This section only compares fl/fl;+/+ to fl/fl;Tg/+.

The chi-squared test for comparing the two genotypes is significant, with a p-value of 0.001515. The results of these tests are in Table 3. The effects of each genotype, relative to the knockout strains are in Table 4. These results are presented graphically in Figure 2. This means that the knockout mice are 3.28 times more likely to die at any given time.

	test	df	pvalue
Likelihood ratio test	10.0349	1	0.001536
Wald test	9.0900	1	0.002569
Score (logrank) test	10.0598	1	0.001515

Table 3: Muscle TSC1 Knockout Tests (WT vs KO)

	coef	exp(coef)	se(coef)	z	p
Genotypefl/fl; +/+	-1.19	0.305	0.394	-3.02	0.002569

Table 4: Muscle TSC1 Knockout Coefficients, relative to Knockout (WT vs KO)

Death Logs

This table shows the age, and at risk individuals for each natural death, along with the % survival and the confidence intervals.

```
Call: survfit(formula = survobj.mck ~ Genotype, data = data.known.mck)

                Genotype=fl/fl; Tg/+
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
   10    188       1    0.995 0.00530       0.9843        1.000
   18    184       1    0.989 0.00754       0.9746        1.000
   71    145       1    0.982 0.01012       0.9628        1.000
  110    129       1    0.975 0.01258       0.9505        1.000
  114    126       1    0.967 0.01467       0.9388        0.996
  125    121       1    0.959 0.01658       0.9271        0.992
  138    112       1    0.951 0.01851       0.9149        0.988
  180     86       1    0.939 0.02135       0.8986        0.982
  182     82       1    0.928 0.02396       0.8822        0.976
  244     58       1    0.912 0.02839       0.8580        0.969
  264     49       1    0.893 0.03336       0.8304        0.961
  281     38       1    0.870 0.03992       0.7951        0.952
  292     35       1    0.845 0.04587       0.7598        0.940
  309     30       1    0.817 0.05228       0.7206        0.926
```

```
 316     24       1    0.783 0.06017       0.6734        0.910
 371     13       1    0.723 0.08020       0.5814        0.898
 452      8       1    0.632 0.10984       0.4498        0.889
 586      7       1    0.542 0.12592       0.3437        0.855
 595      6       1    0.452 0.13346       0.2531        0.806
 601      5       1    0.361 0.13389       0.1748        0.747
 638      3       1    0.241 0.13281       0.0817        0.710
 832      1       1    0.000     NaN           NA           NA

               Genotype=+/+; +/+
time n.risk n.event survival std.err lower 95% CI upper 95% CI
  20     98       1    0.990  0.0102       0.9701        1.000
 642      6       1    0.825  0.1508       0.5764        1.000
 665      5       1    0.660  0.1906       0.3746        1.000
 678      4       1    0.495  0.2021       0.2223        1.000
 857      3       1    0.330  0.1905       0.1064        1.000
 885      2       1    0.165  0.1506       0.0276        0.987
 938      1       1    0.000     NaN           NA           NA

               Genotype=+/+; Tg/+
time n.risk n.event survival std.err lower 95% CI upper 95% CI
 114     50       1    0.980  0.0198       0.9420            1
 452      4       1    0.735  0.2127       0.4168            1
 773      3       1    0.490  0.2452       0.1838            1
 805      2       1    0.245  0.2122       0.0449            1
 935      1       1    0.000     NaN           NA           NA

               Genotype=fl/fl; +/+
time n.risk n.event survival std.err lower 95% CI upper 95% CI
  50    155       1    0.994 0.00643       0.9810        1.000
  97    139       1    0.986 0.00956       0.9678        1.000
 132    127       1    0.979 0.01224       0.9549        1.000
 135    124       1    0.971 0.01447       0.9428        1.000
 218     76       1    0.958 0.01910       0.9213        0.996
 284     51       1    0.939 0.02639       0.8889        0.992
 596      9       1    0.835 0.10114       0.6584        1.000
 623      8       1    0.730 0.13176       0.5129        1.000
 718      7       1    0.626 0.14862       0.3932        0.997
 819      6       1    0.522 0.15625       0.2901        0.938
 869      5       1    0.417 0.15600       0.2007        0.868
 879      4       1    0.313 0.14784       0.1241        0.790
 886      3       1    0.209 0.13028       0.0614        0.709
 894      2       1    0.104 0.09843       0.0164        0.663
 936      1       1    0.000     NaN           NA           NA
```

Combining the Control Mice

The chi-squared test for comparing the two genotypes is significant, with a p-value of 4.7e-06. The results of these tests are in Table 6. The effects of each genotype, relative to the knockout strains are in Table 7. These results are presented graphically in Figure 4. This means that the knockout mice are 4.17 times more likely to die at any given time.

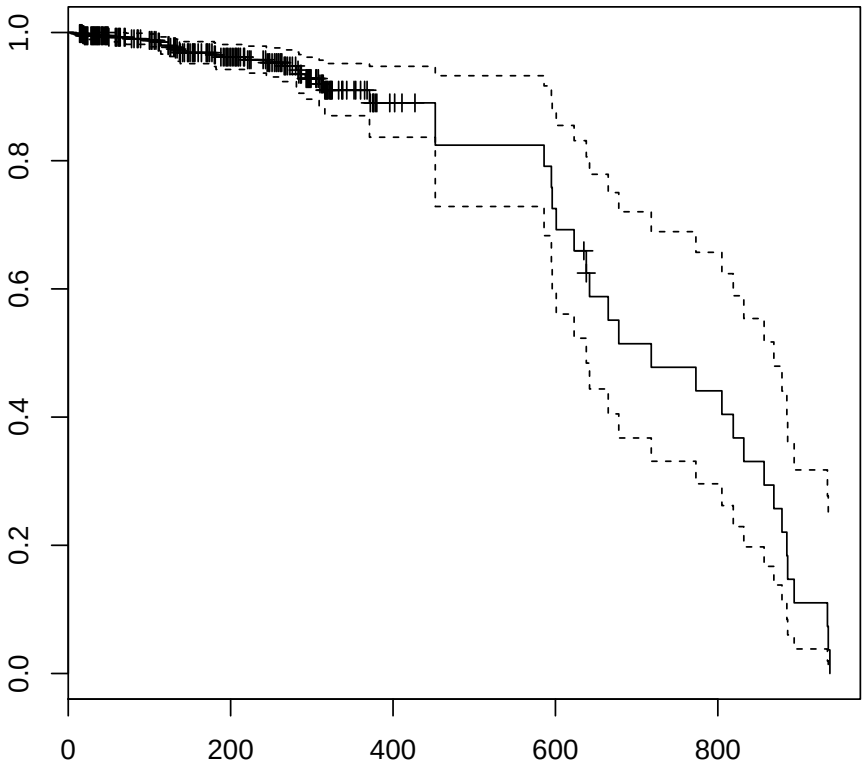

Figure 1: Survival Curve for All Muscle-TSC1 Mice

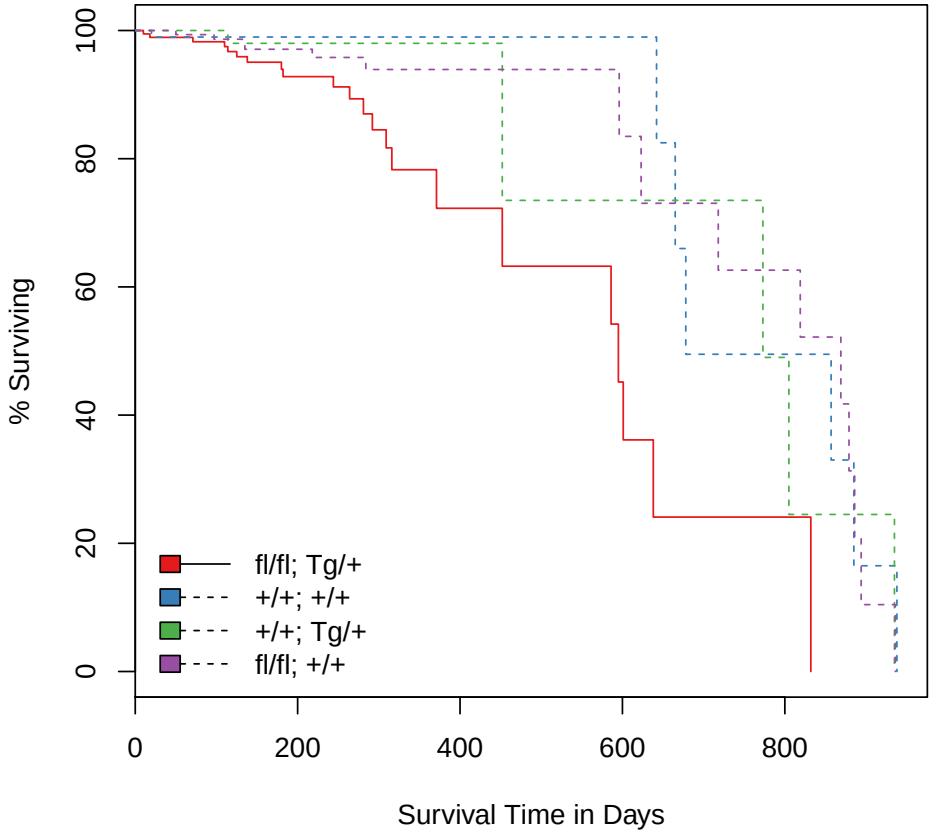

Figure 2: Survival Curve for Mck-TSC1 Mice

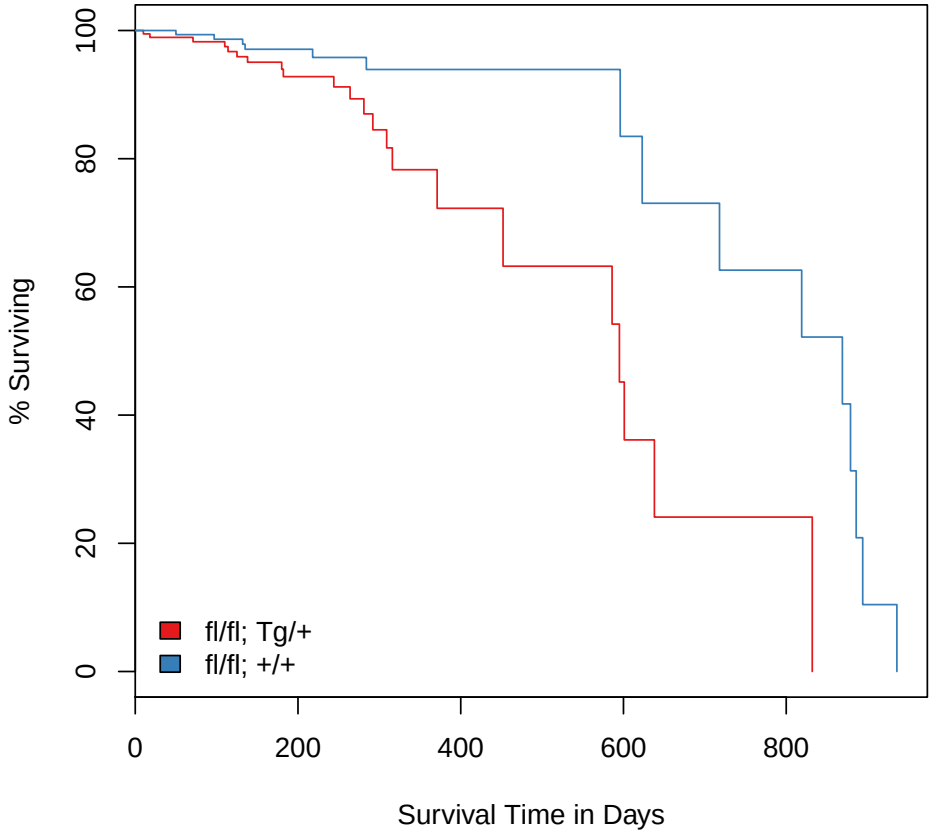

Figure 3: Survival Curve for Mck-TSC1 Mice, WT/KO Only

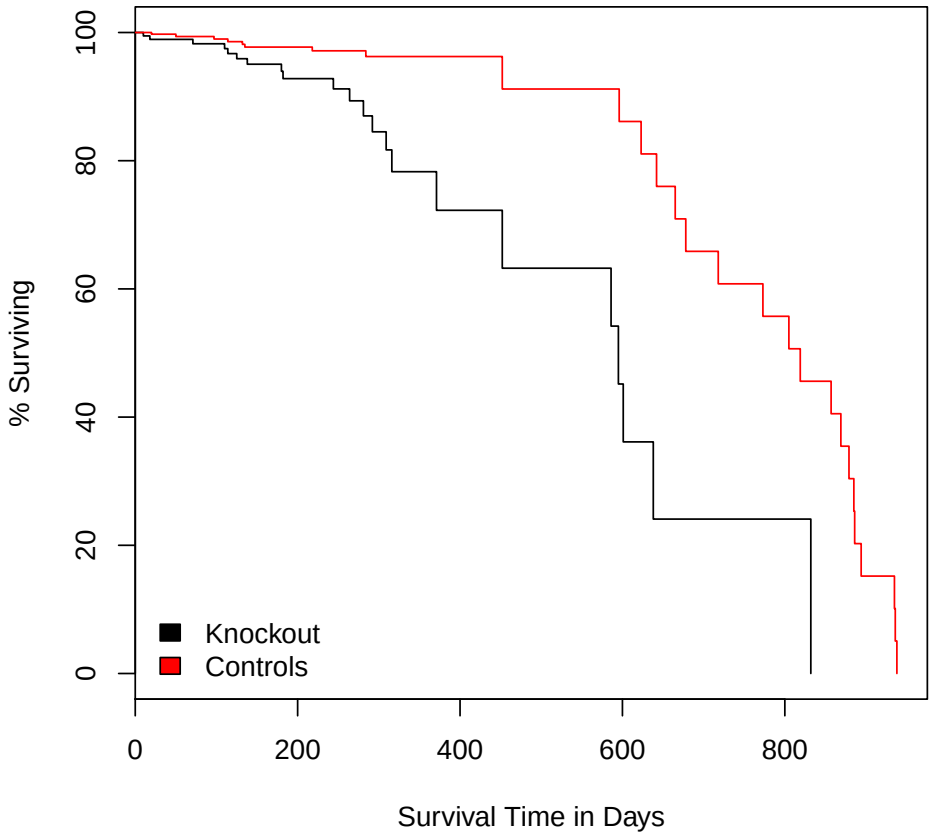

Figure 4: Survival Curve for All Muscle-TSC1 Mice, Controls Combined

	Total Animals	Natural Deaths
Genotype=fl/fl; Tg/+	188	22
Genotype=+/+; +/+	125	7
Genotype=+/+; Tg/+	104	5
Genotype=fl/fl; +/+	208	15

Table 5: Muscle TSC1 Knockout Summary

	test	df	pvalue
Likelihood ratio test	18.0155	1	0.000022
Wald test	18.1700	1	0.000020
Score (logrank) test	20.9417	1	0.000005

Table 6: Muscle TSC1 Knockout Tests controls combined

References

[1] R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria, 2015.

[2] Terry M Therneau. *A Package for Survival Analysis in S*, 2015. version 2.38.

[3] Terry M. Therneau and Patricia M. Grambsch. *Modeling Survival Data: Extending the Cox Model*. Springer, New York, 2000.

[4] Torsten Hothorn, Kurt Hornik, Mark A. van de Wiel, and Achim Zeileis. A lego system for conditional inference. *The American Statistician*, 60(3):257–263, 2006.

[5] Torsten Hothorn, Kurt Hornik, Mark A. van de Wiel, and Achim Zeileis. Implementing a class of permutation tests: The coin package. *Journal of Statistical Software*, 28(8):1–23, 2008.

Session Information

- R version 3.2.2 (2015-08-14), `x86_64-apple-darwin13.4.0`
- Locale: `en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8`
- Base packages: base, datasets, graphics, grDevices, methods, stats, utils
- Other packages: bibtex 0.4.0, coin 1.1-2, RColorBrewer 1.1-2, survival 2.38-3, xtable 1.8-0
- Loaded via a namespace (and not attached): codetools 0.2-14, grid 3.2.2, lattice 0.20-33, modeltools 0.2-21, multcomp 1.4-1, mvtnorm 1.0-3, sandwich 2.3-4, splines 3.2.2, stats4 3.2.2, TH.data 1.0-6, tools 3.2.2, zoo 1.7-12

	coef	exp(coef)	se(coef)	z	p
KnockoutTRUE	-1.43	0.240	0.335	-4.26	0.000020

Table 7: Muscle TSC1 Knockout Coefficients, controls combined