# Aging Analysis of Mck-TSC1

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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

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	$\exp(\operatorname{coef})$	se(coef)	$\mathbf{Z}$	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	$\exp(\operatorname{coef})$	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 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 0.975 0.01258 0.9505 1.000 1 114 126 1 0.967 0.01467 0.9388 0.996 121 125 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 0.912 0.02839 244 58 1 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 0.817 0.05228 0.7206 0.926

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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 6678 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 0.0190 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 1 805 2 1 0.445 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 1935 1 0.994 0.00643 0.9810 1.000 97 139 1 0.945 0.2122 0.0449 1 935 1 0.996 0.00956 0.9678 1.000 132 127 1 0.979 0.01224 0.9549 1.000 132 127 1 0.979 0.01224 0.9549 1.000 135 124 1 0.971 0.01447 0.9428 1.000 136 124 1 0.971 0.01447 0.9428 1.000 137 124 1 0.979 0.0124 0.9549 1.000 138 124 1 0.971 0.01447 0.9428 1.000 139 124 1 0.971 0.01447 0.9428 1.000 135 124 1 0.971 0.01447 0.9428 1.000 136 124 1 0.971 0.01447 0.9428 1.000 137 127 1 0.979 0.01224 0.9549 1.000 138 127 1 0.979 0.01224 0.9549 1.000 139 129 1 0.936 0.01910 0.9213 0.996 139 1 0.335 0.10114 0.65684 1.000 139 139 6 1 0.626 0.14862 0.3932 0.997 139 6 1 0.626 0.14862 0.3932 0.997 139 6 1 0.626 0.14862 0.3932 0.997 139 6 1 0.626 0.14862 0.3932 0.997 139 6 1 0.626 0.14862 0.3932 0.997 139 6 1 0.626 0.14862 0.3932 0.997 139 6 1 0.417 0.15600 0.2007 0.868 149 4 1 0.313 0.14784 0.1241 0.790 1894 2 1 0.0104 0.09843 0.0164 0.666	316	24	1	0.783	0.06017		0.6734		0.910
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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	114	50	1				0.9420		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	452	4	1	0.735	0.2127		0.4168		1
Genotype=f1/f1; +/+           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	773	3	1	0.490	0.2452		0.1838		1
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	805	2	1	0.245	0.2122		0.0449		1
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	935	1	1	0.000	NaN		NA		NA
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									
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									
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	time		${\tt n.event}$			lower		upper	95% CI
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	50	155	1	0.994	0.00643		0.9810		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	97	139	1	0.986	0.00956		0.9678		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	132	127	1	0.979	0.01224		0.9549		1.000
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	135	124	1	0.971	0.01447		0.9428		1.000
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	218	76	1	0.958	0.01910		0.9213		0.996
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	284	51	1	0.939	0.02639		0.8889		0.992
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	596	9	1	0.835	0.10114		0.6584		1.000
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	623	8	1	0.730	0.13176		0.5129		1.000
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	718	7	1	0.626	0.14862		0.3932		0.997
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	819	6	1	0.522	0.15625		0.2901		0.938
886       3       1       0.209 0.13028       0.0614       0.709         894       2       1       0.104 0.09843       0.0164       0.663	869	5	1	0.417	0.15600		0.2007		0.868
894 2 1 0.104 0.09843 0.0164 0.663	879	4	1	0.313	0.14784		0.1241		0.790
	886	3	1	0.209	0.13028		0.0614		0.709
936 1 1 0.000 NaN NA NA	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.

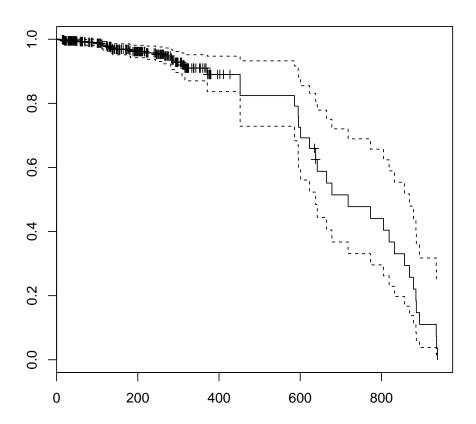


Figure 1: Survival Curve for All Muscle-TSC1 Mice

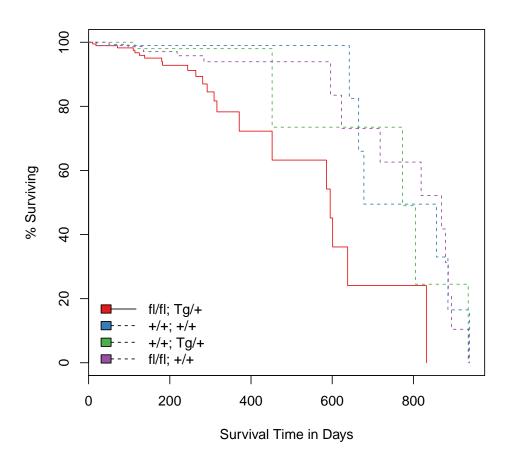


Figure 2: Survival Curve for Mck-TSC1 Mice

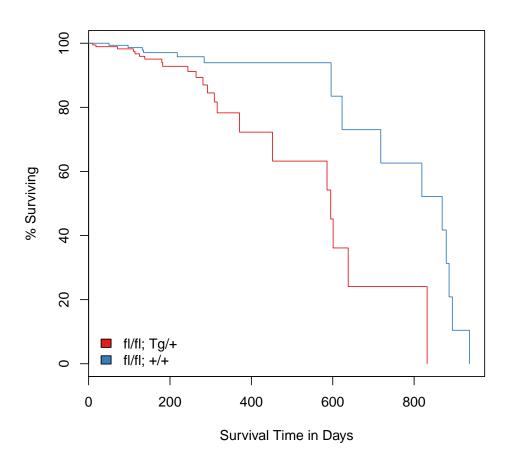


Figure 3: Survival Curve for Mck-TSC1 Mice, WT/KO Only

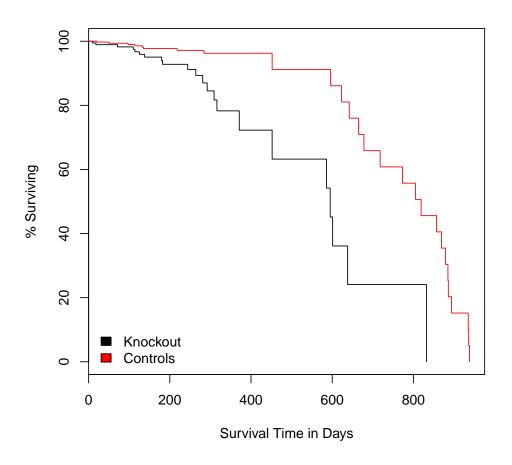


Figure 4: Survival Curve for All Muscle-TSC1 Mice, Controls Combined

	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/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, mytnorm 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	$\exp(\operatorname{coef})$	se(coef)	$\mathbf{Z}$	p
KnockoutTRUE	-1.43	0.240	0.335	-4.26	0.000020

Table 7: Muscle TSC1 Knockout Coefficients, controls combined