Table S1. Decrease in Dystroglycan mRNA level in *Dg^{RNAi}:tub-Gal4* mutant

Genotype	Dg Average C_T	RpL32 Average C_T	ΔC_T Dg-RpL32[1]	$\Delta\Delta C_T$ ΔC_T-$\Delta C_{T,control}$[2]	Average Dg relative to control[3]	Dg mRNA fold reduction relative to control[4]
tub-Gal4/+	23.33±0.07	18.35±0.20	4.98±0.21	0.00±0.30	1.00±0.21	1.00±0.21
Dg^{RNAi}:tub-Gal4/+	25.94±0.13	18.37±0.11	7.57±0.18	2.59±0.28	0.17±0.03	6.02±1.16

Table S2. Decrease in Dystrophin mRNA level in *$Dys^{N\text{-}RNAi}$:act-Gal4* mutant

Genotype	Dys Average C_T	RpL32 Average C_T	ΔC_T Dys-RpL32[1]	$\Delta\Delta C_T$ ΔC_T-$\Delta C_{T,\ control}$[2]	Average Dys relative to control[3]	Dys mRNA fold reduction relative to control[4]
act-Gal4/+	21.25±0.11	15.60±0.03	5.65±0.11	0.00±0.16	1.00±0.11	1.00±0.11
$Dys^{N\text{-}RNAi}$:act-Gal4/+	23.47±0.06	16.49±0.03	6.96±0.07	1.33±0.13	0.40±0.04	2.51±0.23

[1] the ΔC_T value is determined by subtracting the average RpL32 C_T value from the average Dg (Dys) C_T value. The standard deviation of the difference is calculated from the standard deviations of the Dg (Dys) and RpL32 values using the following formula" $s=\sqrt{s_1^2 + s_2^2}$, where s=std dev;

[2] the calculation of the $\Delta\Delta C_T$ involves subtraction by the ΔC_T calibrator value. This standard deviation is determined the same as in 'a';

[3] the range given for Dg (Dys) relative to Control is determined by evaluating the expression: $2^{-\Delta\Delta CT}$ where the error is determined using regressional analysis;

[4] the fold reduction given for Dg (Dys) relative to Control is determined by evaluating the expression: $2^{\Delta\Delta CT}$ where the error is determined using regressional analysis.

Table S3. Frequency of muscle degeneration caused by reduction by one copy of screened genes in *Dys* and *Dg* mutant background

Gene name	Allele	Loss-of-function mutants									RNAi mutants						Control		
		DysDf x			*Dg^{O86}* x			*Dg^{323}* x			*$Dys^{N\text{-}RNAi}$:act-Gal4* x			*Dg^{RNAi}:tub-Gal4* x			*w^{1118}* x		
		degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value
w	*[1118]*	3.3±3.3	n=227	-	1.0±1.0	n=90	-	5.0	n=112	-	19.2±4.5	n=292	-	9.7±2.2	n=129	-	4.2±2.0	n=98	-
βv-Integrin	*[BG01037]*	27.2	n=258	17.19**	62.6	n=179	57.74**	NA	-	-	NA	-	-	NA	-	-	4.0	n=198	0.07
Cam	*[n339]*	21.8	n=55	12.20 **	6.7	n=75	2.86	0.0	n=20	3.20	74.3	n=35	31.30**	20.2	n=104	3.06	3.7	n=27	0.03
capt	*[E593]*	31.4	n=35	21.16**	0.0	n=60	0.50	0.0	n=22	3.20	45.3	n=137	9.76**	7.5	n=67	0.08	14.5	n=69	4.62*
	[E636]	44.0	n=50	33.32**	5.1	n=78	1.57	13.2	n=106	2.84	63.5	n=107	22.67**	21.9	n=96	3.90	0.0	n=7	2.40
CG34400	*[c03838]*	15.2	n=33	6.42*	32.1	n=28	27.37**	41.7	n=12	27.29**	37.5	n=16	5.27*	73.9	n=23	47.78**	9.1	n=11	0.14
CG7845	*[EMS-Mod4]* [1]	25.0	n=36	15.14**	37.0	n=54	32.24**	31.4	n=51	17.72**	16.7	n=12	0.06	28.6	n=35	8.36**	4.8	n=147	0.02
chif	*[BG02820]* [2]	41.9	n=105	31.27**	9.2	n=54	5.08*	18.5	n=91	6.64**	16.3	n=92	0.10	12.4	n=265	0.13	7.6	n=131	0.49
	[EY05746]	26.2	n=42	16.25**	8.8	n=114	4.71*	11.4	n=70	1.78	10.9	n=78	1.77	40.3	n=134	17.52**	10.9	n=82	2.15
	[A507], CyO	21.4	n=42	11.83**	NA	-	-	NA	-	-	NA	-	-	19.5	n=87	2.65	0.0	n=31	2.43
del	*[3]*	NA	-	-	NA	-	-	14.0	n=50	3.36	12.8	n=47	0.91	2.5	n=39	3.15	NA	-	-
	[KG10262]	0.0	n=50	2.72	2.6	n=38	0.10	5.9	n=17	0.001	16.8	n=113	0.05	6.0	n=17	0.46	NA	-	-
Dmn	*[k16109]* [2]	3.0	n=33	0.07	NA	-	-	3.0	n=33	0.12	20.0	n=20	0.001	6.5	n=123	0.29	NA	-	-
Fhos	*[EY09842]*	17.5	n=57	8.37**	9.0	n=155	4.90*	5.2	n=116	0.06	31.1	n=122	2.36	28.6	n=14	8.36*	0.0	n=36	2.43
	[A055]	32.0	n=25	21.73**	15.5	n=71	11.04**	21.3	n=47	8.90**	12.8	n=47	0.91	24.0	n=154	5.24*	2.3	n=44	0.12
Fkbp13	*[P962]*	2.9	n=34	1.60	16.6	n=28	12.20**	30.5	n=74	16.9**	15.4	n=13	0.22	5.9	n=41	0.50	3.4	n=29	0.01
gcm	*[KG01117]* [2]	13.3	n=160	4.87*	0.0	n=116	0.50	4.3	n=70	0.01	15.7	n=184	0.18	19.0	n=84	2.40	NA	-	-
	[rA87]	0.0	n=85	1.60	NA	-	-	12.2	n=41	2.23	13.1	n=61	0.80	8.0	n=26	0.03	NA	-	-
Grh	*[IM]*	0.0	n=21	1.60	2.8	n=72	0.17	3.4	n=58	0.04	8.7	n=52	3.22	5.4	n=56	0.72	7.5	n=53	0.45
Lis-1	*[k13209]* [2]	19.8	n=111	10.40**	9.0	n=109	4.90*	12.2	n=24	2.24	26.5	n=68	0.87	14.8	n=195	0.68	13	n=117	3.53
	[k11702]	31.8	n=22	21.54**	12.1	n=58	7.78**	0.0	n=41	3.20	9.6	n=48	2.56	14.5	n=62	0.59	8.7	n=103	0.94
	[G10.14]	37.5	n=16	27.01**	0.0	n=24	0.50	NA	-	-	19.1	n=68	0.02	9.9	n=81	0.03	0.0	n=72	2.43
mbl	*[E27]*	23.8	n=42	14.03**	12.0	n=25	7.69**	28.3	n=60	14.93**	40.0	n=70	6.63**	22.8	n=149	4.50*	1.0	n=98	0.93
nAcRa-30D	*[EY13897]* [2]	29.4	n=68	19.26**	4.5	n=176	1.13	6.5	n=93	0.02	8.9	n=146	3.07	8.8	n=90	0.001	NA	-	-
	[KG05852]	9.4	n=53	2.05	7.5	n=187	3.33	1.5	n=67	0.96	14.3	n=91	0.45	5.5	n=72	0.67	NA	-	-
Nrk	*[k14301]* [2]	37.5	n=48	27.02**	19.9	n=58	15.33**	47.0	n=34	32.33**	15.0	n=40	0.29	16.9	n=230	1.44	7.0	n=185	0.29
Pgk	*[KG07478]*	10.1	n=99	2.51	30.0	n=80	25.29**	NA	-	-	NA	-	-	NA	-	-	9.5	n=105	1.34
POSH	*[k15815]* [2]	1.1	n=90	0.32	0.0	n=82	0.50	0.0	n=75	3.20	10.8	n=37	1.82	18.2	n=33	2.02	6.6	n=61	0.18
Rack1	*[EY00128]* [2]	18.1	n=83	8.89**	5.6	n=107	1.96	33.3	n=15	19.45**	11.6	n=112	1.41	11.3	n=133	0.02	3.8	n=105	0.05
	[1.8]	11.1	n=27	3.21	10.3	n=68	6.09*	8.9	n=45	0.60	9.5	n=42	2.63	12.3	n=122	0.12	0.0	n=127	2.44
	[EE]	13.8	n=36	5.27*	19.7	n=132	15.13**	7.4	n=27	0.16	76.9	n=39	33.45**	19.0	n=216	2.40	7.3	n=82	0.38
robo	*[2]*	0.0	n=27	1.60	0.9	n=110	0.42	0.0	n=20	3.20	4.4	n=45	8.06**	0.9	n=107	5.73*	3.6	n=84	0.02
SP1070	*[UifE(br)155]* [3]	5.4	n=74	0.13	16.4	n=91	11.41**	4.0	n=20	0.05	30.7	n=88	2.20	13.8	n=94	0.41	18.1	n=105	7.46**
	[Uif2B7] [3]	14.1	n=142	5.52*	12.3	n=81	7.97**	4.4	n=91	0.02	37.6	n=117	5.33*	44.4	n=9	20.99*	21.1	n=90	9.99**
SP2353	*[MB00605]*	0.0	n=59	1.60	12.0	n=52	7.69**	18.5	n=40	6.64**	11.1	n=27	1.66	16.5	n=121	1.28	1.6	n=62	0.44
vimar	*[k16722]* [2]	4.3	n=46	0.06	4.6	n=55	1.20	54.8	n=73	39.82**	12.7	n=71	0.94	33.8	n=65	12.27**	11.2	n=89	2.33
	[09]	0.0	n=84	1.60	9.4	n=32	5.26*	16.4	n=110	5.05*	12.9	n=70	0.87	32.7	n=49	11.41**	0.7	n=142	0.93

All mutant alleles obtained from BDSC, except [1] – described previously (Kucherenko et al., 2008), [2] – obtained from DGRC, [3] – described previously (Zhang and Ward, 2009)

NA – not analyzed

The results were statistically compared using χ^2 test with one degree of freedom and Yates`s correction, *p≤0.05; **p≤0.01

Table S4. Other tested genes that did not show genetic interaction with DGC in muscles

Gene name	Allele	Loss-of-function mutants								
		DysDf x			Dg^{O86} x			w^{1118} x		
		degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value	degenerated muscles, %	n, analyzed muscles	χ^2-value
w	*[1118]*	3.3±3.3	n=227	-	1.0±1.0	n=90	-	4.2±2.0	n=98	-
argos	*[Delta7]*	4.6	n=131	0.01	2.9	n=173	0.21	10.1	n=158	1.69
Dl	*[RevF10]*	12.3	n=112	4.10*	5.0	n=159	1.50	12.0	n=125	2.85
dpp	*[KG08191]*	1.8	n=111	0.05	3.7	n=54	0.61	0.0	n=126	2.43
fra	*[3]*	10.7	n=178	2.90	7.7	n=52	3.73	11.6	n=69	2.59
hipk	*[BG00855]*	1.6	n=127	0.10	2.7	n=73	0.13	6.3	n=176	0.11
kek1	*[k07332]*	10.5	n=143	2.80	6.7	n=84	2.86	8.7	n=92	0.95
kis	*[BG01657]*	3.9	n=204	0.02	5.4	n=56	1.80	4.6	n=109	0.04
msk	*[5]*	NA	-	-	3.6	n=139	0.55	10.4	n=134	1.88
Sdc	*[10608]*	2.1	n=143	0.01	6.4	n=110	2.61	7.6	n=159	0.47
Sema-1a	*[k13702]*	10.7	n=56	2.93	3.5	n=116	0.50	12.1	n=99	2.93
Sema-2a	*[k11240]*	1.2	n=168	0.27	5.4	n=112	1.80	2.4	n=166	0.09
slit	*[1118]*	14.4	n=167	5.76*	8.9	n=112	4.80*	15.6	n=186	5.46*
stan	*[19alpha]*	0.8	n=122	0.52	7.7	n=91	3.73	1.6	n=63	0.44
wg	*[Sp-1]*	0.0	n=147	1.60	4.7	n=146	1.28	10.5	n=76	1.92

all mutant alleles obtained from BDSC;

NA – not analyzed;

the results were statistically compared using χ^2 test with one degree of freedom and Yates`s correction, *p≤0.05

Table S5. Muscle degeneration in wild type and dystrophic animals in response to stress

[§]TMD - total muscle degeneration, EMD - extreme muscle degeneration,
[Ø]Statistics were calculated with one-way ANOVA and post Dannett's tests; the mean difference is significant at the 0.05 level,

	Experimental conditions	Genotype	Analyzed muscles, n	% of TMD (EMD)[§], Mean±SE	Statistical analysis[Ø], *p*			
					Within "experimental conditions"		Within "experimental group"	
					TMD	EMD	TMD	EMD
Experimental group 1	25°C, normal food, 13-15d old	*OregonR*	743	6.03±1.58 (0)	control		control[◊]	
		w^{1118}	461	6.01±0.34 (0)	*p*=1.000	-		
	18°C, normal food, 13-15d old (10d)*	*OregonR*	1091	2.65±0.78 (0)	control		*p*=0.843	-
		w^{1118}	426	3.28±2.03 (0)	*p*=1.000	-		
	33°C, normal food, 13-15d old (10d)*	*OregonR*	510	21.00±6.80 (1.50)	control		***p*=2x10^{-6}**	*p*=0.450
		w^{1118}	955	19.17±2.50 (1.02)	*p*=1.000	*p*=1.000		
	25°C, normal food, 25 d old	*OregonR*	1213	4.10±2.29 (0)	control		*p*=0.832	-
		w^{1118}	395	2.50±1.51 (0)	*p*=0.716	-		
	25°C, Paraquat, 13-15d old (10d)*	*OregonR*	633	14.79±6.26 (10.95)	control		***p*=0.01**	***p*=0.008**
		w^{1118}	75	11.92±6.26 (10.07)	*p*=1.000	*p*=1.000		
	25°C, sugar-free food, 13-15d old (10d)*	*OregonR*	279	4.80±1.10 (0)	control		*p*=0.656	*p*=1.000
		w^{1118}	685	6.17±1.07 (0)	*p*=0.999	*p*=0.978		
Experimental group 2	25°C, normal food, 8-10d old	*OregonR*	518	0.90±0.20 (0)	control		control for *OregonR*	
		DysDf	244	6.90±1.30 (0)	***p*=0.036**	-	control for *DysDf*	
		$Dg^{O86/O55}$	101	4.50±1.10 (0)	*p*=0.129	-	control for $Dg^{O86/O55}$	
	18°C, normal food, 8-10d old	*OregonR*	303	1.90±1.90 (0)	control		*p*=0.524	-
		DysDf	852	10.30±0.70 (4.63)	***p*=0.004**	*p*=0.166	*p*=0.348	***p*=0.050**
		$Dg^{O86/O55}$	256	7.90±2.20 (5.60)	***p*=0.049**	*p*=0.172	*p*=0.179	*p*=0.076
	33°C, normal food, 8-10d old (7d)*	*OregonR*	1309	4.10±0.70 (1.20)	control		*p*=0.127	*p*=0.232
		DysDf	711	13.80±1.50 (2.70)	***p*=1x10^{-4}**	*p*=0.762	*p*=0.125	*p*=0.310
		$Dg^{O86/O55}$	421	7.50±1.90 (2.50)	*p*=0.211	*p*=0.726	*p*=0.225	*p*=0.322
	25°C, Paraquat, 8-10d old (7d)*	*OregonR*	201	5.70±1.90 (0)	control		*p*=0.093	-
		DysDf	218	13.00±4.40 (0)	*p*=0.163	-	*p*=0.162	-
		$Dg^{O86/O55}$	186	10.50±1.60 (0)	*p*=0.485	-	*p*=0.051	-
Experimental group 3	25°C, normal food, 5d old	*OregonR*	166	1.00±1.00 (0)	control		control for *OregonR*	
		DysDf	174	4.80±2.50 (0)	*p*=0.087	-	control for *DysDf*	
		$Dg^{O86/O55}$	82	3.70±1.70 (0)	*p*=0.314	-	control for $Dg^{O86/O55}$	
	25°C, sugar-free food, 5d old (4d)*	*OregonR*	501	0.50±0.50 (0)	control		*p*=0.466	-
		DysDf	173	8.10±6.30 (0)	*p*=0.167	-	*p*=0.393	-
		$Dg^{O86/O55}$	541	10.80±4.40 (5.60)	***p*=0.050**	***p*=0.011**	***p*=0.044**	***p*=0.032**
	25°C, normal food 20d old	*OregonR*	98	3.00±3.00 (0)	control		*p*=0.881	-
		DysDf	131	21.00±2.60 (1.70)	***p*=0.004**	*p*=0.433	***p*=0.024**	*p*=0.317
		$Dg^{O86/O55}$	214	7.20±1.40 (3.65)	*p*=0.224	*p*=0.258	*p*=0.209	*p*=0.200

[◊]since there is no a statistically significant difference between the two control lines (*OregonR* and w^{1118}) within "experimental conditions" groups these two genotypes were treated as one data set in further analysis,
*in parenthesis is shown the time flies were kept at the experimental conditions

Table S6. Metabolic rate of DGC mutants and *OregonR* line under the normal and sugar-free food conditions

Genotype	CO_2 production under the normal food conditions[1] ($\mu lCO_2 \times hr^{-1} \times fly^{-1}$)	Number of measure-ments	CO_2 production under the sugar-free food conditions[1] ($\mu lCO_2 \times hr^{-1} \times fly^{-1}$)	Number of measure-ments	Fold decrease in metabolic rate on sugar-free food[1,2]
OregonR	2.20±0.15	n=10	0.43±0.14	n=3	5.12±0.46
DysDf	2.41±0.09	n=13	1.03±0.09	n=7	2.34±0.13
$Dg^{O86/O55}$	2.36±0.18	n=6	1.46±0.19	n=7	1.60±0.12

[1]Mean±SE

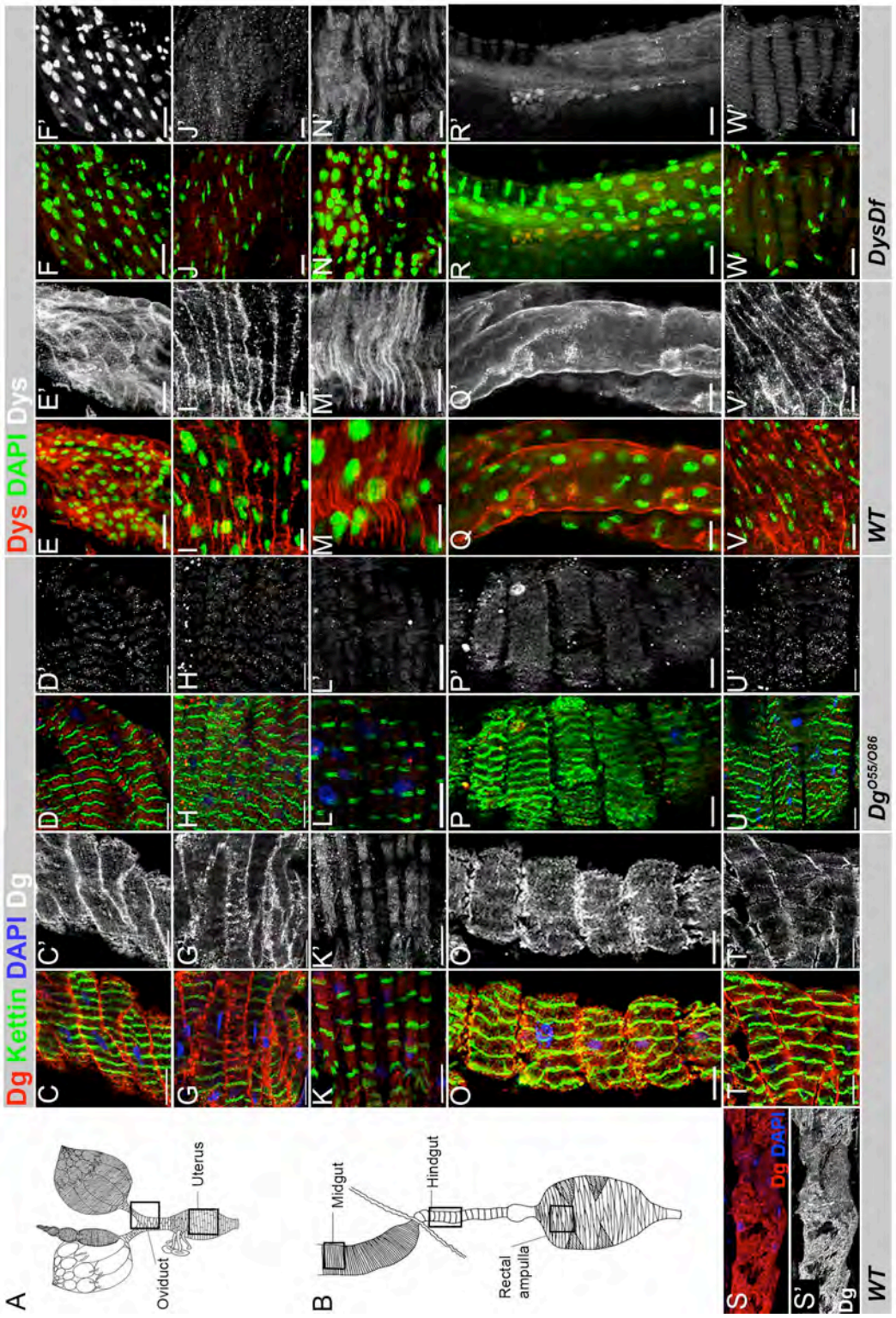
[2]to determine the fold reduction in CO_2 production the amount of CO_2 generated under normal food conditions was divided by the amount of CO_2 generated under sugar-free food conditions for each genotype tested.

Supplementary Figure Legends

Supplementary Fig. 1. DGC is localized in the sarcolemma of different *Drosophila* muscle types. Schematic view of *Drosophila* reproductive system (A) and intestinal tract morphology (B). Squares show part of the organ analyzed for presence of DGC in muscle tissue. (C-R, T-W) Detection of Dg and Dys (red in C-R, T-W and white in C'-R', T'-W') in oviduct (C-F), uterus (G-J), midgut (K-N), hindgut (O-R) and rectal ampulla (T-W) muscles. Both Dg and Dys are localized to the sarcolemma. Dystroglycan can also be seen to a lesser extent in regions correlated with Z-discs as indicated by Kettin (green in C-D, G-H, K-l, O-P and T-U) localization in uterus muscles. Neither Dg nor Dys staining is detected in Dg^{O86}/Dg^{O55} (D, H, L, P, U) or *DysDf* (F, J, N, R, W) loss-of-function mutants. (S, S') The Dystroglycan antibody localization was seen in heart muscles. Nuclei are visualized with DAPI.

Supplementary Fig. 2. DGC mutants have age-dependant muscle degeneration and climbing defects. (A-J) H&E-stained transverse (A-F, J) and longitudinal (G-I) IFM sections from 10 day old (A-C) and 20 day old (G-J) *DysDf*, Dg^{O86}/Dg^{O55} and $DysDf/Dg^{O86}$ mutants and wild type flies. Ten day old mutant flies exhibit mild changes in muscle tissue morphology, while 20 day old flies have more deteriorated muscles (arrows) and exhibit cases with severe loss of muscle tissue (arrowheads). Muscle degeneration is seen more often from the muscle termini (H); on transverse sections degenerated muscles are pale and form vacuoles indicating necrosis (I). Dystrophin homozygous viable (*DysDf*) flies and Dystroglycan semi-lethal transheterozygotes Dg^{O86}/Dg^{O55} show reduced ability to climb (K). Statistics were done using Student's t-test, **p≤0.01, *** p≤0.001. Oil red O-stained IFMs of *WT* (L) and *DysDf* (M) flies. Intramuscular lipid droplets are indicated with arrows. In addition, the different behavior in *Dys* and *Dg* mutants was noticed: while *Dys* deficient flies were shaking and not able to climb, the *Dg* mutant animals performed uncoordinated movements and jumped randomly.

Supplementary Figure 1



Supplementary Figure 2