

**Supplemental figure 1:** Cloning strategy.

A) The complete nucleotide sequence of  $\alpha 1$ ACT, with its endogenous start and stop codons, was subcloned from the C-terminal portion of human  $\alpha 1$ A cDNA into pWalium10(moe) (red portion of the vector). Also shown are the annealing sites for primers used to confirm that pWalium landed into attP2 in the correct orientation.

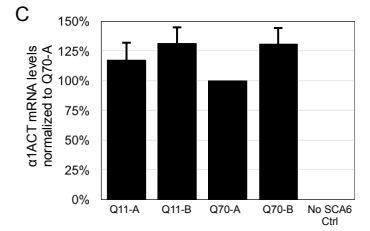
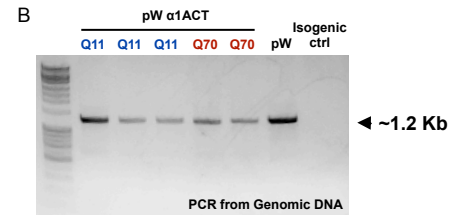
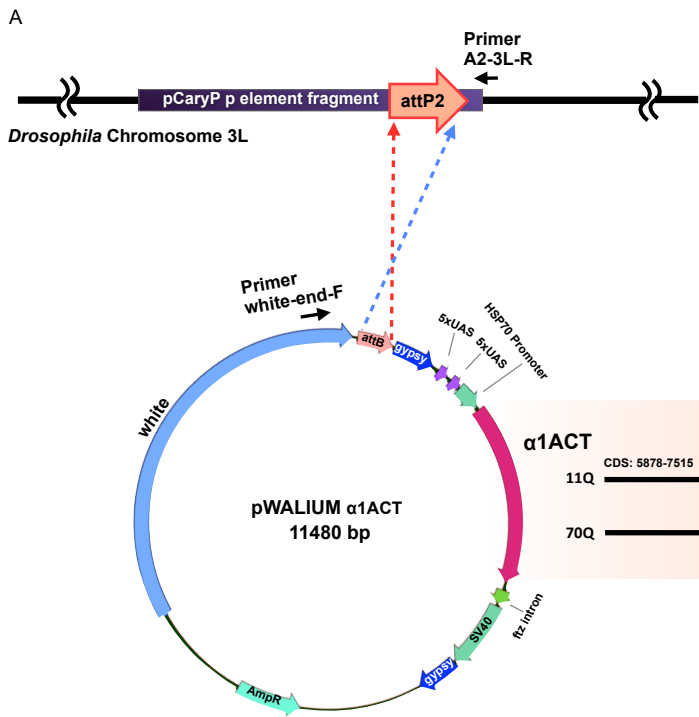
B) PCR from genomic DNA showing that the transgene landed into attP2 in the correct orientation. Isogenic ctrl: this is the line into which the transgenes were injected.

C) qRT-PCR of  $\alpha 1$ ACT message in pupae, driven by sqh-Gal4. N=3.

**Supplemental figure 2:** (A-C) summary of toxicity from  $\alpha 1$ ACT(Q70) when it is expressed throughout the fly by itself or alongside potential modifiers.

**Supplemental table 1:** Comprehensive list of fly stocks used.

Supplemental figure 1



## Supplemental figure 2

A

<b>Sqh-Gal4 driving <math>\alpha</math>1ACT(Q70)</b>	
<b>Without <math>\alpha</math>1ACT(Q11)</b>	<b>With <math>\alpha</math>1ACT(Q11)</b>
Pharate adult lethality & adult death during eclosion	Pharate adult lethality & adult death during eclosion

B

<b>Sqh-Gal4 driving <math>\alpha</math>1ACT(Q70)</b>	
<b>Without UAS-DnaJ-1</b>	<b>With UAS-DnaJ-1</b>
Pharate adult lethality & adult death during eclosion	Adults eclose successfully and survive two-three weeks

C

<b>Sqh-Gal4 driving <math>\alpha</math>1ACT(Q70)</b>	
<b>Wild Type Kap-<math>\alpha</math>3</b>	<b>Heterozygous Kap-<math>\alpha</math>3[D93]</b>
Pharate adult lethality & adult death during eclosion	Pharate adult lethality & adult death during eclosion

## Supplemental table 1

Genotype	Source	FlyBase ID	Stock Number	Associated alleles	Description	Shown in the figures
y[1] sc[*] v[1]; P{y[+7.7]}=UAS-Ctrl}attP2	Todi Lab			pWaiium10-moe-empty vector	Isogenic host strain for the 1aCT line	Yes
y[1] sc[*] v[1]; P{y[+7.7]}=UAS-1aCT-11Q}attP2.15-7	Todi Lab			CACNA1A	UAS-1aCT-11Q	Yes
y[1] sc[*] v[1]; P{y[+7.7]}=UAS-1aCT-11Q}attP2.15-8	Todi Lab			CACNA1A	UAS-1aCT-11Q	Yes
y[1] sc[*] v[1]; P{y[+7.7]}=UAS-1aCT-70Q}attP2.1A	Todi Lab			CACNA1A	UAS-1aCT-70Q	Yes
y[1] sc[*] v[1]; P{y[+7.7]}=UAS-1aCT-70Q}attP2.7-2	Todi Lab			CACNA1A	UAS-1aCT-70Q	Yes
w[*]; +; P{w[+mC]}=longGMR-GAL4}3	Bloomington	FBst0008121	8121		gmr-Gal4	Yes
w[*]; P{w[+mC]}=longGMR-GAL4}2; +	Bloomington	FBst0009146	9146		gmr-Gal4	Yes
w[*]; P{w[+mC]}=sqh-GAL4}2; +	Kiehart Lab	FBti0074562			sqh-Gal4	Yes
P{w[+mW.hs]}=GawB}elav[C155]	Bloomington	FBst0000458	458		elav-Gal4	Yes
y[1] w[*]; P{w[+mC]}=GAL4-Mef2.R}3	Bloomington	FBst0027390	27390		mef2-Gal4	Yes
w[1118]; P{w[+m*]}=GAL4}repo/TM3, Sb[1]	Bloomington	FBst0007415	7415		repo-Gal4	Yes
y[1] w[*]; P{w[+mC]}=UAS-mCD8::GFP.L}LL5	Bloomington	FBst0005137	5137		UAS-CD8:GFP	Yes
w[*]; P{w[+mC]}=UAS-DnaJ-1.K}3	Bloomington	FBst0030553	30553	CG10578	UAS-DnaJ-1	Yes
w[*]; P{w[+mC]}=UAS-ataxin-3-WT}E6.2; +	Todi Lab			Ataxin-3	UAS-Ataxin-3-WT	Yes
w[*]; Kap-alpha3[D93]/TM6B, Tb[1]	Bloomington	FBst0025397	25397	CG9423	Kap-α3 loss of function allele	Yes
y[1] v[1]; P{y[+7.7]}v[+t1.8]}=TRIP.JF02686}attP2	Bloomington	FBst0027535	27535	CG9423	Kap-α3 RNAi	Yes
w[1118]; P{GD11489}v21978	VDRC	FBst0454348	v21978	CG4968	CG4968 RNAi	Yes
w[1118]; P{GD14218}v24030	VDRC	FBst0455268	v24030	CG9448	trbd RNAi	Yes
w[1118]; +; +	VDRC		VDRC60000		Isogenic line for VDRC	Yes
y[1] v[1]; P{y[+7.7]}=CaryP}attP2	Bloomington	FBst0036303	36303		Isogenic host strain for attP2	Yes