

Table S1. Fly lines utilized in this paper.

Experimental models: Organisms/Strains			
Designation	Source of reference	Identifiers	Additional information
<i>srpHemo-Gal4</i>	PMID: 15239955	Brückner et al., 2004	<i>D. melanogaster</i>
<i>srpHemo-3xmCherry</i>	PMID: 29321168	RRID:BDSC_78358 and 78359	<i>D. melanogaster</i> (Gyoergy et al., 2018)
<i>srpHemo-H2A::3xmCherry</i>	PMID: 29321168	RRID:BDSC_78360 and 78361	<i>D. melanogaster</i> (Gyoergy et al., 2018)
<i>CG9005</i> ^{BG02278}	Bloomington <i>Drosophila</i> Stock Center (BDSC)	RRID:BDSC_12768	
<i>Df(2R)ED2222 (Df1)</i>	BDSC 8911		
<i>Df(2R)BSC259 (Df2)</i>	BDSC 23159		
<i>UAS-CG9005 RNAi 1</i>	VDRC	VDRC: v106589	
<i>UAS-CG9005 RNAi 2</i>	VDRC	VDRC: v36080	
<i>UAS-CG9005 RNAi 3</i>	BDSC	BDSC: 33362	
<i>srpHemo-HA::CG9005 (srpHemo-HA::atossa)</i>	this paper		CG9005 amplified from genome cloned into DSPL172 (PMID: 29321168)
<i>srpHemo-HA::atossa</i> ^{nls1-}	this paper		CG9005 amplified from genome cloned into DSPL172
<i>srpHemo-HA::atossa</i> ^{DUF4210-}	this paper		CG9005 amplified from genome cloned into DSPL172
<i>srpHemo-HA::atossa</i> ^{ChrSeg-}	this paper		CG9005 amplified from genome cloned into DSPL172
<i>srpHemo-HA::atossa</i> ^{DUF4210-/ChrSeg-}	this paper		CG9005 amplified from genome cloned into DSPL172
<i>srpHemo-HA::atossa</i> ^{TAD1-}	this paper		CG9005 amplified from genome cloned into DSPL172
<i>srpHemo-HA::atossa</i> ^{TAD2-}	this paper		CG9005 amplified from genome cloned into DSPL172 (PMID: 29321168)
<i>srpHemo-HA::atossa</i> ^{TAD1-/TAD2-}	this paper		CG9005 amplified from genome cloned into DSPL172
<i>srpHemo-FAM214A</i>	this paper		FAM214A amplified from dendritic cell cDNA library cloned into <i>srpHemo</i> plasmid (DSPL172)
<i>srpHemo-FAM214B</i>	this paper		FAM214B amplified from dendritic cell cDNA library

			cloned into <i>srpHemo</i> plasmid (DSPL172)
<i>UAS-HA::EGFP</i>	this paper		
<i>UAS-CG9253 RNAi</i> (<i>porthos</i>)	VDRC, RRID:	VDRC: v36589	
<i>UAS-CG9331 RNAi 1</i> (<i>GRHPR</i>)	(VDRC), RRID:	VDRC: v44653	
<i>UAS-CG9331 RNAi 2</i> (<i>GRHPR</i>)	BDSC, RRID:	BDSC: 64652	
<i>UAS-CG9331 RNAi 3</i> (<i>GRHPR</i>)	(VDRC), RRID:	VDRC: v107680	
<i>UAS-CG7144 RNAi 1</i> (<i>LKRSDH</i>)	(VDRC), RRID:	VDRC: v51346	
<i>UAS-CG7144 RNAi 2</i> (<i>LKRSDH</i>)	(VDRC), RRID:	VDRC: v109650	
<i>UAS-CG2137 RNAi 1</i> (<i>Gpo2</i>)	(VDRC), RRID:	VDRC: v1234	
<i>UAS-CG2137 RNAi 2</i> (<i>Gpo2</i>)	BDSC, RRID:	BDSC: 68145	
<i>UAS-CG11061 RNAi</i> (<i>GM130</i>)	BDSC, RRID:	BDSC: 64920	
<i>UAS-CG11061 RNAi</i> (<i>GM130</i>)	(VDRC), RRID:	VDRC: v330284	
<i>y[-] v[-];attP40- pVALIUM22-UAS-ATPsyn Subunit C (CG1746) E121Q</i>	(VDRC), RRID:	Thomas Hurd, et al., 2016	
<i>UAS-CG4769 RNAi 1 (Cyt- c1)</i>	(VDRC), RRID:	VDRC: v109809	
<i>UAS-CG4169 RNAi 2</i> (<i>UQCR-cp2</i>)	(VDRC), RRID:	VDRC: v100818	
<i>UAS-CG3731 RNAi 3</i> (<i>UQCR-cp1</i>)	(VDRC), RRID:	VDRC: v101350	
<i>UAS-CG3612 RNAi (ATP synthase F1F0)</i>	(VDRC), RRID:	VDRC: v34664	

Table S2: List of key resources used in this paper.

Antibodies			
Designation	Source of reference	Identifiers	Additional information
Chicken polyclonal anti-GFP	Aves Labs	Cat# GFP-1020, RRID:AB_10000240	
Rat monoclonal anti-HA	Roche	Roche Cat# 3F10, RRID: AB_2314622	
Mouse Lamin (lamin Dm0)	<i>Drosophila</i> Studies Hybridoma Bank (DSHB)	Cat# ADL1010	
Mouse Fibrillarlin	Rangan lab	N/A	
Mouse anti-Pyruvate Dehydrogenase E1-alpha subunit antibody (PDH E1 α) [8D10E6]	Abcam	Cat# ab110334, RRID:AB_10866116	
Rabbit antiphospho-Pyruvate Dehydrogenase E1-alpha subunit (PDH E1 α , S293)	Abcam	Cat# ab92696, RRID:AB_10711672	
Goat anti-Chicken IgY (H+L) Secondary Antibody, Alexa Fluor 488	Thermo Fisher Scientific	Cat# A-11039, RRID: AB_2534096	
Alexa Fluor 488 goat anti-rat	Thermo Fisher Scientific	Cat# A21212, RRID: AB_11180047	
Goat anti-Mouse IgG1 Secondary Antibody, Alexa Fluor 488 conjugate	Thermo Fisher Scientific	Cat# A-21121, RRID: AB_2535764	
Goat anti-Mouse IgG2b Secondary Antibody, Alexa Fluor 633 conjugate	Thermo Fisher Scientific	Cat# A-21146, RRID:AB_2535782	
Goat anti-Rabbit IgG (H+L) Secondary Antibody, Alexa Fluor 488 conjugate	Thermo Fisher Scientific	Cat# R37116, RRID: AB_2556544	
Phalloidin 488	Thermo Fisher Scientific	Cat# A12379, RRID:AB_2315147	

Phalloidin 633	Thermo Fisher Scientific	Cat# 50-6559-05, RRID:AB_2574272	
Chemicals			
Vectashield mounting medium	Vector Laboratories, RRID:SCR_000821	VectorLabs: H-1000	
Vectashield Mounting medium with DAPI	Vector Laboratories, RRID:SCR_000821	VectorLabs: H-1200	
Beckman Coulter 9/16x3.5 PA tubes		Cat. #331372	

Critical Commercial Assays			
Infusion cloning kit	Clontech's European distributor	Cat# A14606	
MEGAscript_T7 Transcription Kit	Thermo Fisher Scientific	Cat# AM1334	
MEGAscript_T3 Transcription Kit	Thermo Fisher Scientific	Cat# AM1338	
Effectene Transfection Reagent kit	Qiagen, Hilden, Germany		
DNeasy Blood & Tissue Kit	Qiagen, Hilden, Germany		
QIAGEN Rneasy Mini Kit	Qiagen, Hilden, Germany	Cat#74104	
Takyon™ No Rox SYBR MasterMix blue dTTP	Eurogentec, Liege, Belgium		
TURBO DNA-free Kit	Life Technologies	Cat# AM1907	
Agilent Seahorse XF Cell Mito Stress Test kit	Agilent Technologies, Inc., Santa Clara, CA, USA	Cat# 103015-100	
Agilent 6000 Pico kit	Agilent Technologies, Waldbronn, Germany	Cat# 5067-1513	

Table S3. The DNA plasmid constructs utilized in gene construction.

Recombinant DNA			
Designation	Source of reference	Identifiers	Additional information
<i>UAS-CG9005::FLAG::HA</i>	<i>Drosophila</i> Genomics Resource Center	DGRC: UFO03339 Flybase: FBgn0033638	<i>atossa</i>
<i>UAS-CG9253::FLAG::HA</i>	<i>Drosophila</i> Genomics Resource Center	DGRC: UFO12394 Flybase: FBgn0032919	<i>porthos</i>
<i>UAS-CG9331::FLAG::HA</i>	<i>Drosophila</i> Genomics Resource Center	DGRC: UFO02643 Flybase: FBgn0032889	Glyoxylate reductase (NADP(+)) Hydroxypyruvate reductase (GR/HPR)
<i>UAS-CG7144::FLAG::HA</i>	<i>Drosophila</i> Genomics Resource Center	DGRC: UFO05689 Flybase: FBgn0286198	Lysine ketoglutarate reductase/saccharopine dehydrogenase (LKRS DH)
<i>pAC-sgRNA-Cas9</i>	Addgene	Addgene: 49330	49330 (DSPL 232)

Table S4. Oligonucleotides utilized in gene construction.

No.	Name	Sequence
1	FP-CG9005	TAGAAGCTTCTGCAAATGATACCGACAAGCGTCACC
2	RP-CG9005	GTGCCTAGGCGCGCCCTAAATCCTGCCGGCGCT
3	FP-HACG9005	TAGAAGCTTCTGCAAATGTACCCATACGATGTTCCAGATTAC GCTGCCGCCGCCATGATACCGACAAGCGTCACC
4	RP-HACG9005	GTGCCTAGGCGCGCCAGCGTAATCTGGAACATCGTATGGGT AGGCGGGCGCAATCCTGCCGGCGCTCTC
5	infFPCG9005_NotIBluS	ACGCGGTGGCGGCCATGTACCCATACGATGTTCCAG
6	infRPCG9005_NotIBluS	CGAAGTTATGCGGCCCTAAATCCTGCCGGCGCTC
7	FP-DUF4210 [*] CG9005	TTGTGCGAGATTCGTTTGCCG
8	RP-DUF4210 [*] CG9005	AACGGACGTCCTCAAATTGAG
9	FP-ChrSeg [*] CG9005	AGTGC GCGACAGGAGAGC
10	RP- ChrSeg [*] -CG9005	AGTCGCTTCATCTGCTCGG
13	FP-FAM214A-V13	ATGAAGCCAGACCGAGATGC
14	RP-FAM214A	TCAACATCTTGGTGAAAAGTGA
15	infFP-FAM214A-V13	TAGAAGCTTCTGCAAATGAAGCCAGACCGAGATGC
16	infRP-FAM214A	GTGCCTAGGCGCGCCTCAACATCTTGGTGAAAAGTGA
17	PF-FAM214B	GGCTTCATGCGCCACGTG
18	RP-FAM214B	CGATCAGGGCAAAGGTGAATAACG
19	infFP-FAM214B	TAGAAGCTTCTGCAAGGCTTCATGCGCCACGTG
20	infRP-FAM214B	GTGCCTAGGCGCGCCCGATCAGGGCAAAGGTGA
21	Insitu-CG9005 FP1	CCTCCTGGGCTCGGCTACTGC
22	Insitu-CG9005 RP1	GATAATACGACTCACTATAGGGTTGACGTTGGGAAAATT
23	Insitu-CG9005 RP2	GATAATACGACTCACTATAGGGTTGCAAAGTTGTGCT
24	Insitu-CG9253 FP1	GGAAAGATCTCGGTCTCAATGAG
25	Insitu-CG9253 RP1	GATAATACGACTCACTATAGGGCCATCACCTCATCTCC
26	sgRNA-F1-CG9005	TTCG GCAGTCGGATGTCCGTATGCAGG
27	sgRNA-R1-CG9005	AACGCATACGGACATCCGACTGC C
28	sgRNA-F2-CG9005	TTCGCAGTTCGTAGAAGTAAGAGACGG

29	sgRNA-R2-CG9005	AACTCTTCTACTTCTACGAACTG C
30	sgRNA-F3-CG9005	TTCGCGGCGGATTCTGTCCCACCCAGG
31	sgRNA-R3-CG9005	AACGGGTGGGACAGAATCCGCCG C
32	sgRNA-F1-CG9253	TTCGGATCCAACGTGAGGCCATTCCGG
33	sgRNA-R1-CG9253	AACGAATGGCCTCACGTTGGATC C
34	sgRNA-F2-CG9253	TTCGGGCCATTCCGGTCGCCTTACAGG
35	sgRNA-R2-CG9253	AACGTAAGGCGACCGGAATGGCC C
36	sgRNA-F3-CG9253	TTCGCCCTCGTGGGGGTTAGCACGAGG
37	sgRNA-R3-CG9253	AACCGTGCTAACCCCCACGAGGG C
38	infNotI-TCHA-EGFPHA-FP	AACAGATCTGCGGCCGCATGTGTTGCCCGGGCTGCTGT
39	infNotI-TCHA-EGFP-RP	CCTCGAGCCGCGGCCGCTTAAGCGTAATCTGGCACATC
40	CG9005qPCR-FP1	TG TTCAGATTCTCGCCACCA
41	CG9005qPCR-RP1	TGAGGATTTGCCCAGCTGTT
42	CG9005qPCR-FP2	GCACGCCTTATTTGTGCGAG
43	CG9005qPCR-RP2	CCCGCATGTTCGTAGGGTATC
44	CG9005qPCR-FP3	TATGCGGCAGGGAGAAAGTT
45	CG9005qPCR-RP3	GTGGTCTCTTCTGTCCACCG
46	CG9253qPCR-FP1	GCCTTACAGGGCAAGGATGT
47	CG9253qPCR-RP1	ATGCCAATCCCGCTACCAAG
48	CG9253qPCR-FP2	TCTAGGTAGCGAGGAGGAGC
49	CG9253qPCR-RP2	TGGCCTCACGTTGGATCTTC
50	CG9253qPCR-FP3	TTCGACCACGTGCTGCTATT
51	CG9253qPCR-RP3	TTGTAGCTGCGTCTGTTCGT
52	RpL32 qPCR-FP	AGCATAACAGGCCCAAGATCG
53	RpL32 qPCR-RP	TGTTGTCGATACCCTTGGGC
54	RpS20 qPCR-FP	ACGGTGCAAAGAACCAGAACT
55	RpS20 qPCR-RP	GGAGTCTTACGGGTGGTGATG
56	pAC-sgRNA-Cas9-U6F	TTTGATTCTAAAGGAAATTTGAAAA

Table S5. List of software tools, analytical packages, and laboratory devices utilized in this paper.

Software and Algorithms		
Designation	Source of reference	Identifiers
ImageJ/FIJI		http://fiji.sc/ RRID:SCR_002285)
Imaris	Bitplane	http://www.bitplane.com/imaris/imaris , RRID:SCR_007370
Matlab	Mathworks	https://www.mathworks.com/products/matlab.html , RRID:SCR_001622
FlowJo		https://www.flowjo.com/ RRID:SCR_008520
LaVision ImSpector	LaVision BioTec	http://www.lavisionbiotec.com/ , RRID:SCR_015249
Proteome Discoverer 1.4		https://www.thermofisher.com/order/catalog/product/OPTON-30795 , RRID:SCR_014477
LightCycler 480 software (v. 1.5)	Roche Diagnostics	https://lifescience.roche.com/en_at/products/lightcycler14301-480-software-version-15.html
9 aaTAD Prediction Tool		https://www.med.muni.cz/9aaTAD/analysis.php#matches
Conserved Domain Architecture Retrieval Tool (CDART) program		https://www.ncbi.nlm.nih.gov/Structure/8exington/8exington.cgi
Conserved Domain Database (CDD)		https://www.ncbi.nlm.nih.gov/Structure/cdd/wrpsb.cgi
Prism	GraphPad	https://www.graphpad.com/scientific-software/prism/ RRID:SCR_002798
Flyrnai	sgRNA design	https://www.flyrnai.org/crispr/ http://tools.flycrispr.molbio.wisc.edu/targetFinder/
NCBI primer design tool	Primer design	https://www.ncbi.nlm.nih.gov/tools/primer-blast/
Infusion primer tool	Clontech website	http://bioinfo.clontech.com/infusion/convertPcrPrimersInit.do
HISAT2		https://ccb.jhu.edu/software/hisat2/index.shtml Kim et al., 2015
MEME Suite		http://meme-suite.org/doc/overview.html Bailey et al., 2009
Homer (v4.10.4)		http://homer.ucsd.edu/homer/

Others		
Designation	Source of reference	Identifiers
Nikon Eclipse Ti Inverted widefield Microscope	Nikon	https://www.nikoninstruments.com/en_EU/Products/Inverted-Microscopes/Eclipse-Ti-E
Zeiss LSM 800 Confocal Microscope	Zeiss	https://www.zeiss.com/microscopy/us/products/confocal-microscopes.html
LaVision 2-Photon Inverted Microscope	LaVision BioTec	http://www.lavisionbiotec.com/products/trim-scope-ii-1.html
YSI Stretch membranes	YSI	https://www.ysi.com/Accessory/id-066155/Membranes-10-Pack-Standard
LightCycler 480	Roche Diagnostics	Idaho Technology Inc., Salt Lake City, UT, USA.
FACS Aria III (BD) flow cytometer		
Leica SP8 FALCON inverted confocal	WLL, FALCON, Leica	https://www.leica-microsystems.com/products/confocal-microscopes/p/dive/
Beckman L7 ultracentrifuge	Beckman Coulter, Krefeld, Germany	