Supplementary Information for

A Mesh-Duox pathway regulates homeostasis in the insect gut

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# These authors contributed equally to this work.

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Supplementary Figures 1-21

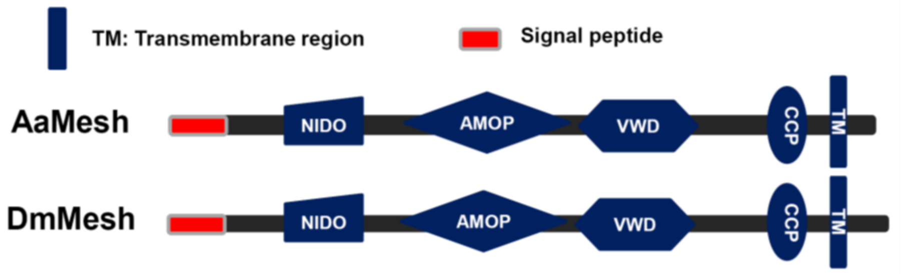
Supplementary Tables 1-6

Supplementary Materials:

a

Name	Gene Number	Length(aa)	Identity to DmMesh
AaMesh	AAEL005432	1405	63%
DmMesh	CG31004	1454	/

b

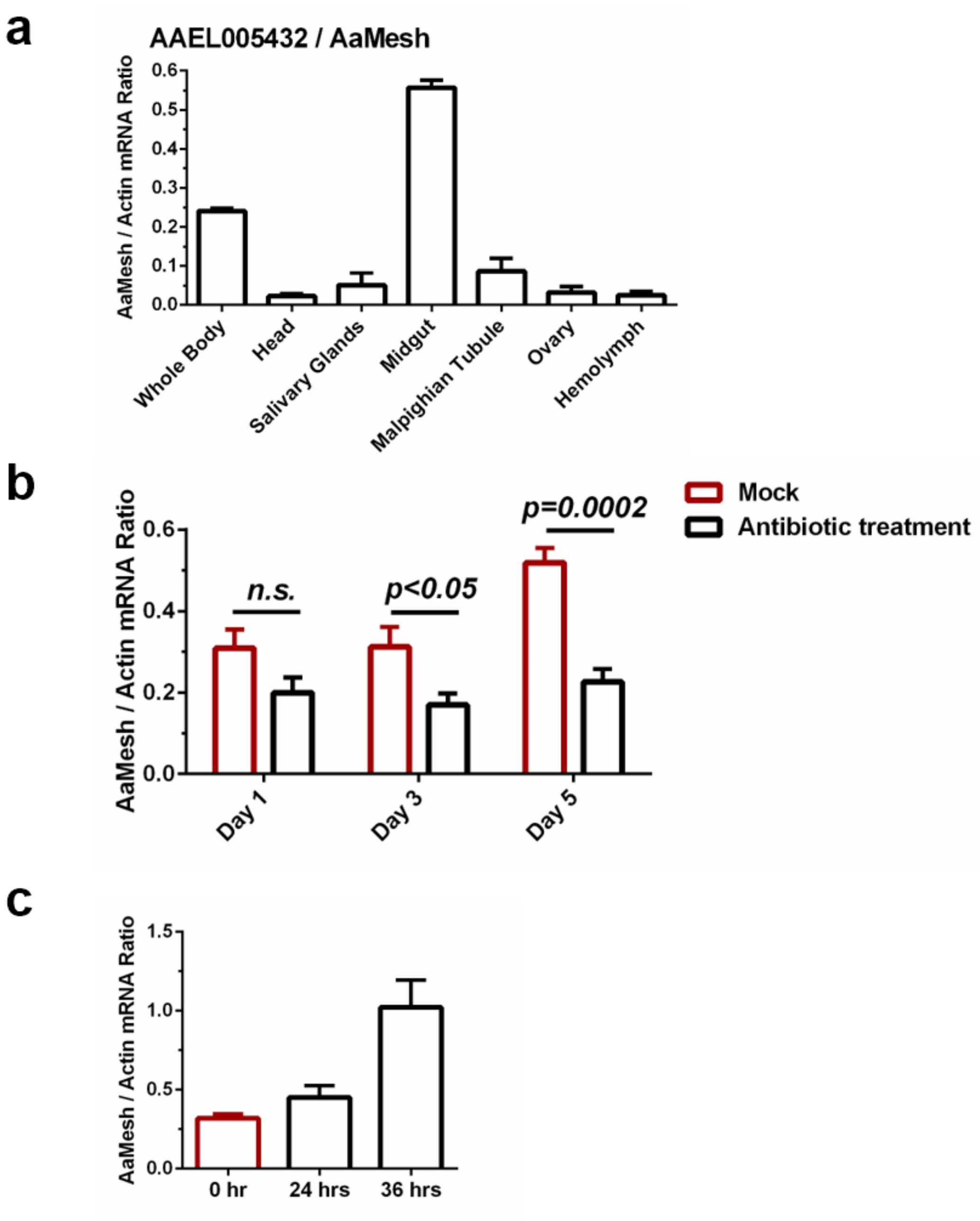


Supplementary Figure 1

Bioinformatic comparison and functional module analysis of Mesh in mosquitoes and *Drosophila*

(a) Percentage of amino acid identity between *A. aegypti* (AaMesh) and *D. melanogaster* Mesh (DmMesh).

(b) Schematic representation of AaMesh and DmMesh. The functional modules were predicted using the SMART (http://smart.embl-heidelberg.de/smart/set_mode.cgi?GENOMIC=1) and Pfam (http://pfam.sanger.ac.uk/) websites.



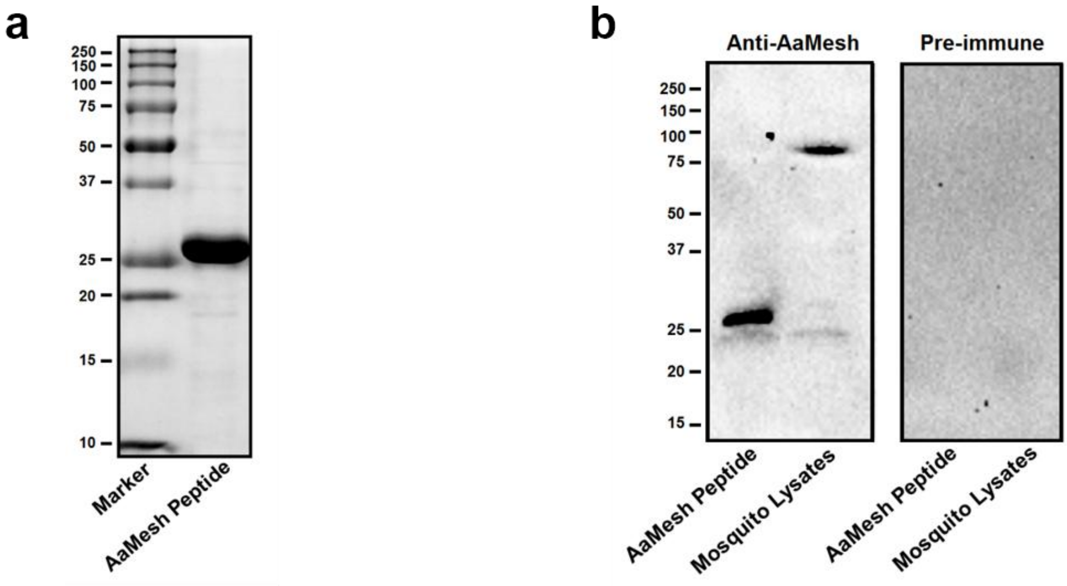
Supplementary Figure 2

Regulation of the *AaMesh* gene by the burden of the symbiotic microbiome in the mosquito guts

(a) Tissue distribution of *AaMesh* in *A. aegypti*.

(b) Oral introduction of antibiotics reduced the *AaMesh* expression in the mosquito guts. The midguts from the antibiotic-treated mosquitoes were isolated over a time course for *AaMesh* detection.

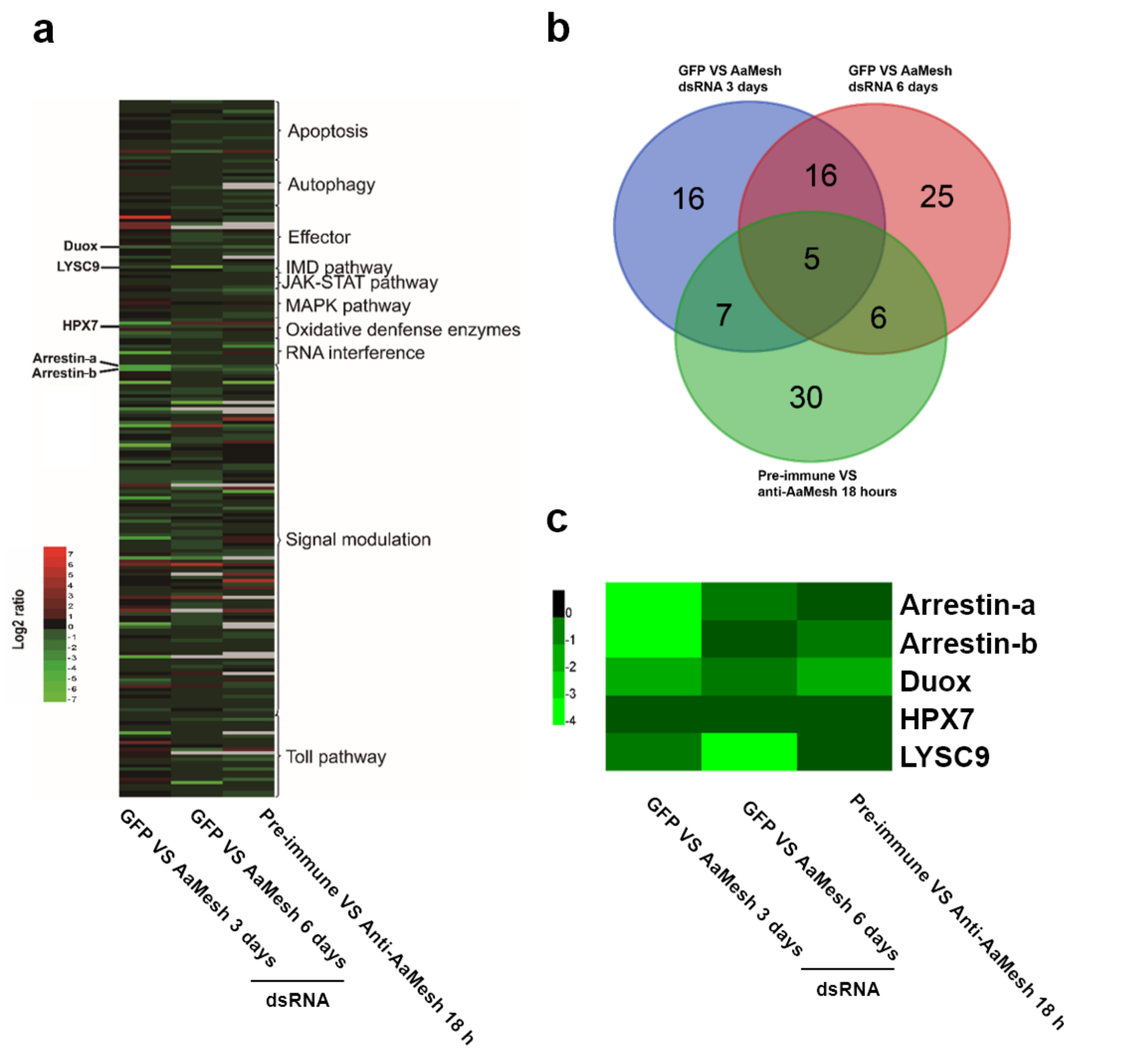
(c) Responses of *AaMesh* after a blood meal in the mosquito midguts. The midguts from the blood-fed mosquitoes were isolated over a time course to measure the *AaMesh* abundance. (a-c) The total RNA was isolated from mosquito tissues to determine *AaMesh* expression by SYBR Green qPCR. The *AaMesh* abundance was normalized by *A. aegypti actin*. The qPCR primers are described in Supplementary Table 6. The data were represented as the mean ±S.E.M. The data were analyzed using the non-parametric *Mann-Whitney* test. All results were reproduced by at least 3 independent experiments.



Supplementary Figure 3

Generation of a murine AaMesh antibody

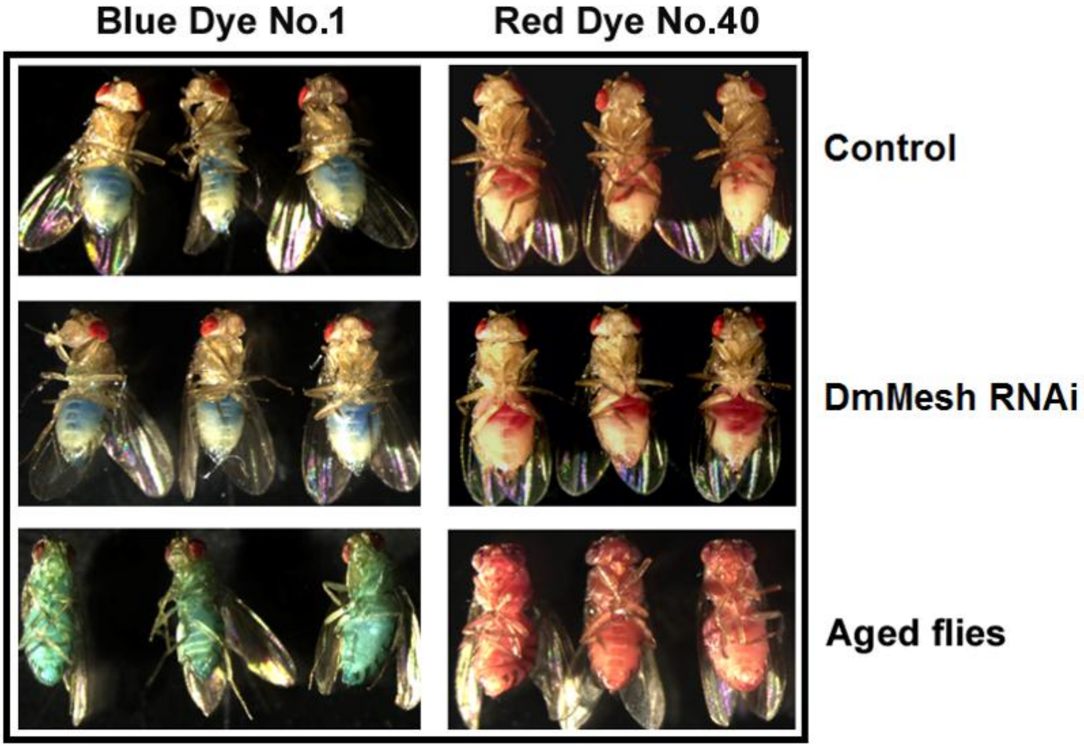
Generation of a murine AaMesh antibody. (a) Purification of the AaMesh peptide expressed *by E. coli*. The peptide purification was verified by SDS-PAGE with Coomassie blue staining. (b) Validation of the AaMesh polyclonal antibody. A mouse-derived AaMesh polyclonal antibody, generated by a recombinant peptide from *E. coli* (a), was used to detect the recombinant AaMesh peptide expressed by *E. coil* or the native AaMesh in mosquito lysates (Left panel). The same samples probed by murine pre-immune serum served as a negative control (Right panel).



Supplementary Figure 4

Regulation of immune-related genes in the midguts of *AaMesh*-suppressed mosquitoes

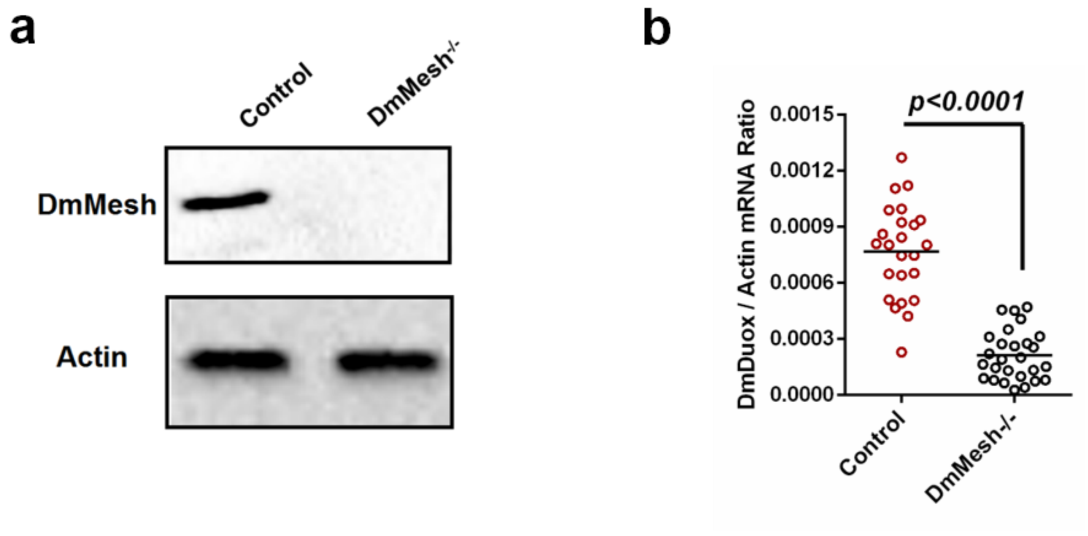
AaMesh was silenced by dsRNA thoracic inoculation in *A. aegypti*, and the mosquito midguts were subsequently dissected at 3 days and 6 days post gene suppression. Meanwhile, the midguts of AaMesh antiserum-fed mosquitoes (1:100 dilution) were collected at 18 hours after a blood meal. The midguts from the *GFP* dsRNA-treated and pre-immune antiserum-fed mosquitoes served as negative controls. Gene regulation in the midguts was measured by RNA-Seq. (a) Analysis of immune-related immune signaling components, enzymes and effectors. Immune-related genes were clustered according to immune pathways and factors. (b) Overlap of down-regulated immune genes in these 3 different experimental conditions. Immune genes with log_2 ratio (read number in *AaMesh*-suppressed midgut / read number in control midgut) ≤ -0.4 were selected for further analysis. (C) Five immune genes were consistently suppressed in the 3 different experimental conditions. The original RNA-Seq data is available in Supplementary Table 1.



Supplementary Figure 5

Measurement of the gut integrity of the *DmMesh* RNAi flies

The *DmMesh* RNAi flies were fed by regular food with 2.5% (wt/vol) Red dye no.40 or Blue dye no.1, respectively. The aged flies (30 days old) were fed by the same materials as a positive control (Aged flies). The *GFP* RNAi flies served as negative controls (Control). The experiment was reproduced by 3 times.

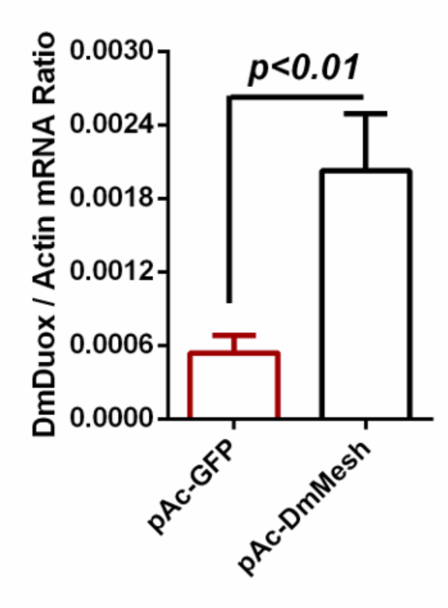


Supplementary Figure 6

Regulation of DmDuox in homozygous *DmMesh*$^{-/-}$ *Drosophila* larvae.

(a) Detection of DmMesh in the whole homozygous *DmMesh*$^{-/-}$ larvae. The DmMesh was measured in the larvae lysates by western blotting with a murine AaMesh antibody.

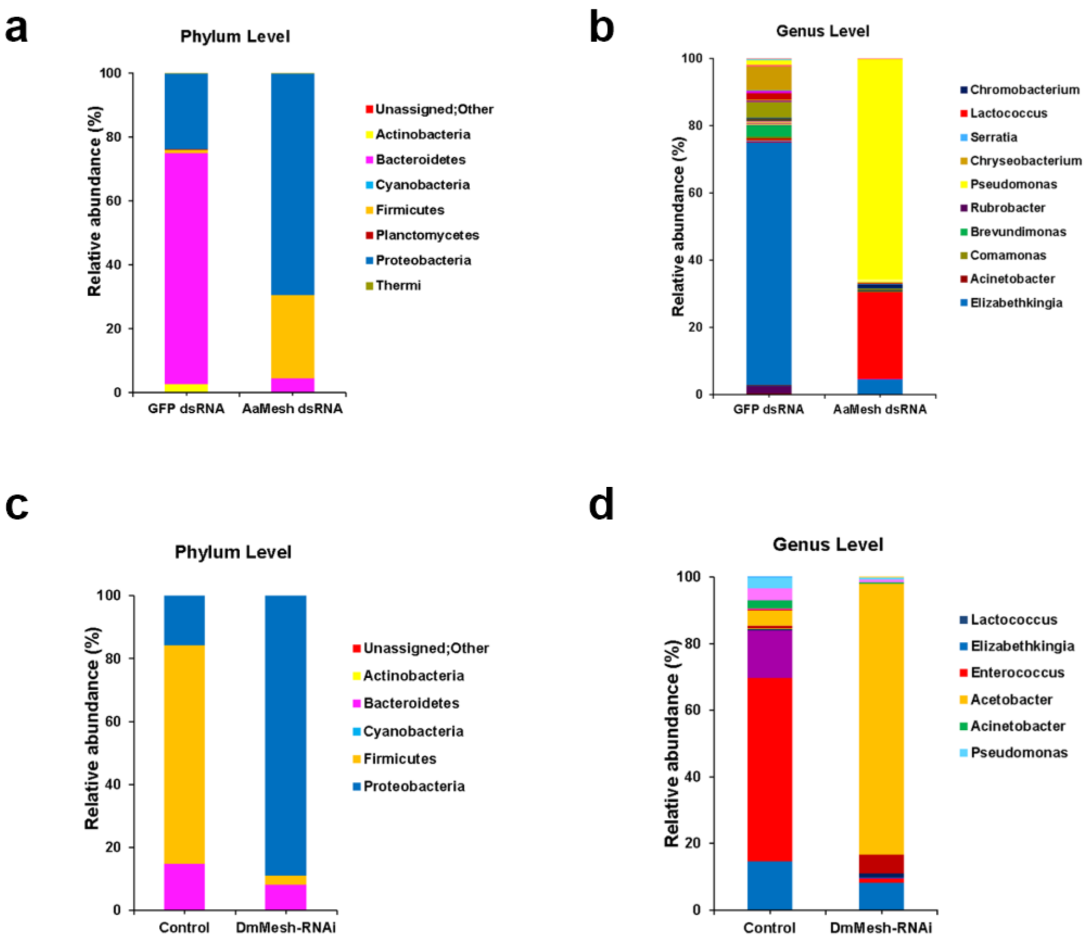
(b) Regulation of *DmDuox* in homozygous *DmMesh*$^{-/-}$ larvae. Total RNA was isolated from the wild-type or the *DmMesh*$^{-/-}$ larvae to detect the *DmDuox* abundance using SYBR Green qPCR. One dot represents one fly gut. The horizontal line represents the mean value of the results. The data were analyzed using the non-parametric *Mann-Whitney* test.



Supplementary Figure 7

Ectopic expression of *DmMesh* in *Drosophila* S2 cells enhanced *Duox* expression.

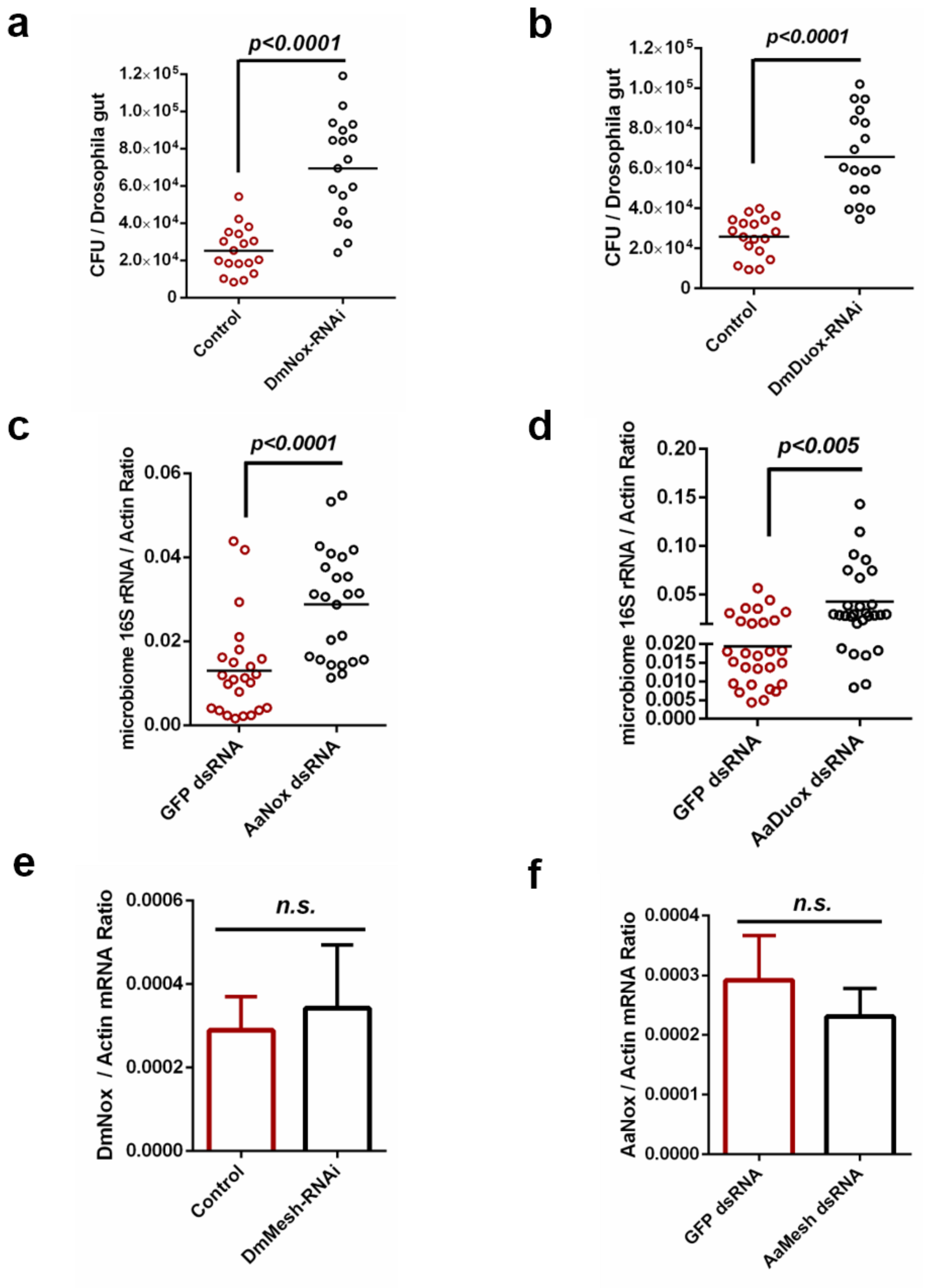
The recombinant plasmid pAc-*DmMesh* was transfected into S2 cells. Transfection of a control plasmid pAc-*GFP* served as a negative control. *Duox* expression was determined by SYBR Green qPCR at 36 hours post transfection and normalized against *Drosophila actin* (*CG12051*). The qPCR primers are described in Supplementary Table 6. The data are presented as the mean ±S.E.M. The data were analyzed using the non-parametric *Mann*-*Whitney* test. The results were repeated by 3 independent experiments.



Supplementary Figure 8

Regulation of gut bacterial composition in *Mesh*-silencing mosquito and *Drosophila*

The guts of *AaMesh*-silenced mosquito (a-b) and *DmMesh* RNAi *Drosophila* (c-d) were exploited for a 16S rDNA sequencing. The midguts of *AaMesh*-silenced mosquito were isolated at 6 days post dsRNA thoracic microinjection. The *GF*P dsRNA-microinjected mosquitoes and *GFP* RNAi flies were used as mock controls. The gut bacterial composition was analyzed by *QIIME*.



Supplementary Figure 9

Mesh regulates *Duox*, but not *Nox* expression, for regulation of gut microbiome in *A. aegypti* and *Drosophila*

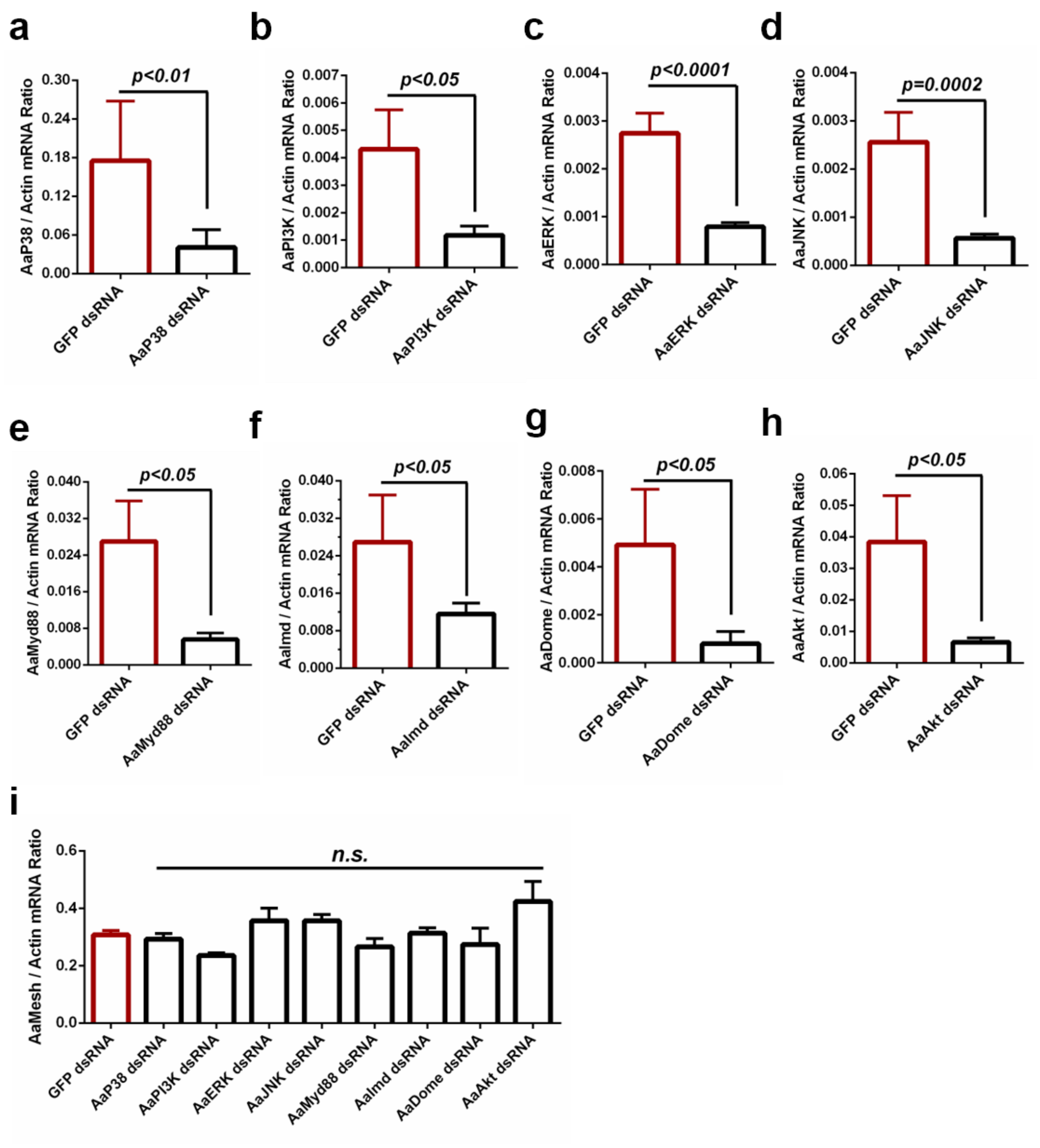
(a-b) Regulation of the gut commensal bacteria in the *DmNox* (a) and *DmDuox* (b) RNAi

Drosophila. Both *DmNox* RNAi and *DmDuox* RNAi GAL4 *Drosophila* lines were driven by a midgut-specific *NP3084* promoter. *GFP* RNAi flies were used as negative controls. The burden of gut microbes was determined by a CFU assay.

(c-d) Knockdown of either *AaNox* (c) or *AaDuox* (d) enhanced the burden of gut microbiome in *A. aegypti*. The genes were silenced via thoracic microinjection of dsRNA. The *GFP* dsRNA-treated mosquitoes served as mock controls. The 16S rRNA was measured by SYBR Green qPCR and normalized against *A. aegypti actin* (*AAEL011197*). The qPCR primers are described in Supplementary Table 6. One dot represents one gut. The horizontal line represents the mean value of the results.

(e-f) Silencing *Mesh* does not regulate the *Nox* expression in *Drosophila* (e) and mosquito (f). The *Nox* genes was measured by SYBR Green qPCR. The qPCR primers are described in Supplementary Table 6.

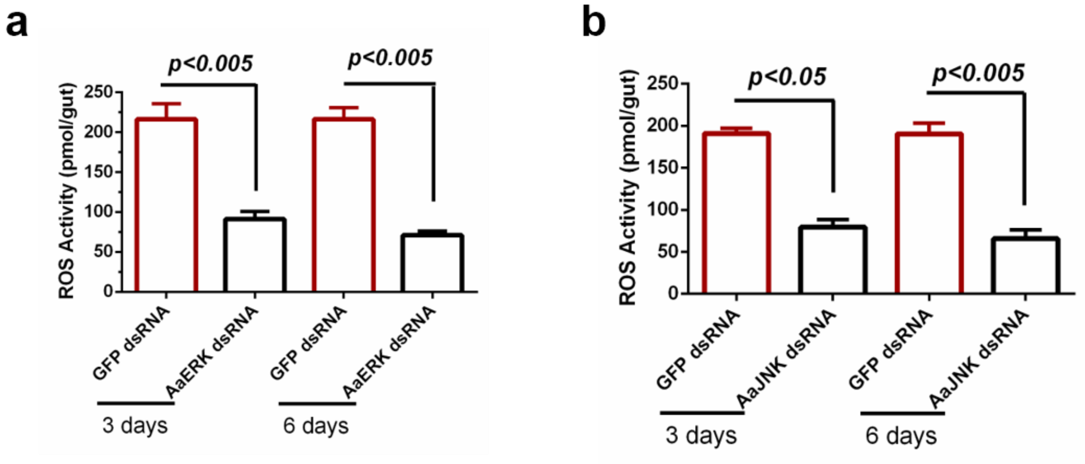
(a-b, e-f) The data are presented as the mean ± S.E.M. (a-f) The data were analyzed using the non-parametric *Mann-Whitney* test. All results were repeated by 3 independent experiments.



Supplementary Figure 10

Regulation of the *AaMesh* mRNA abundance in the midguts of the immune components-silenced mosquitoes

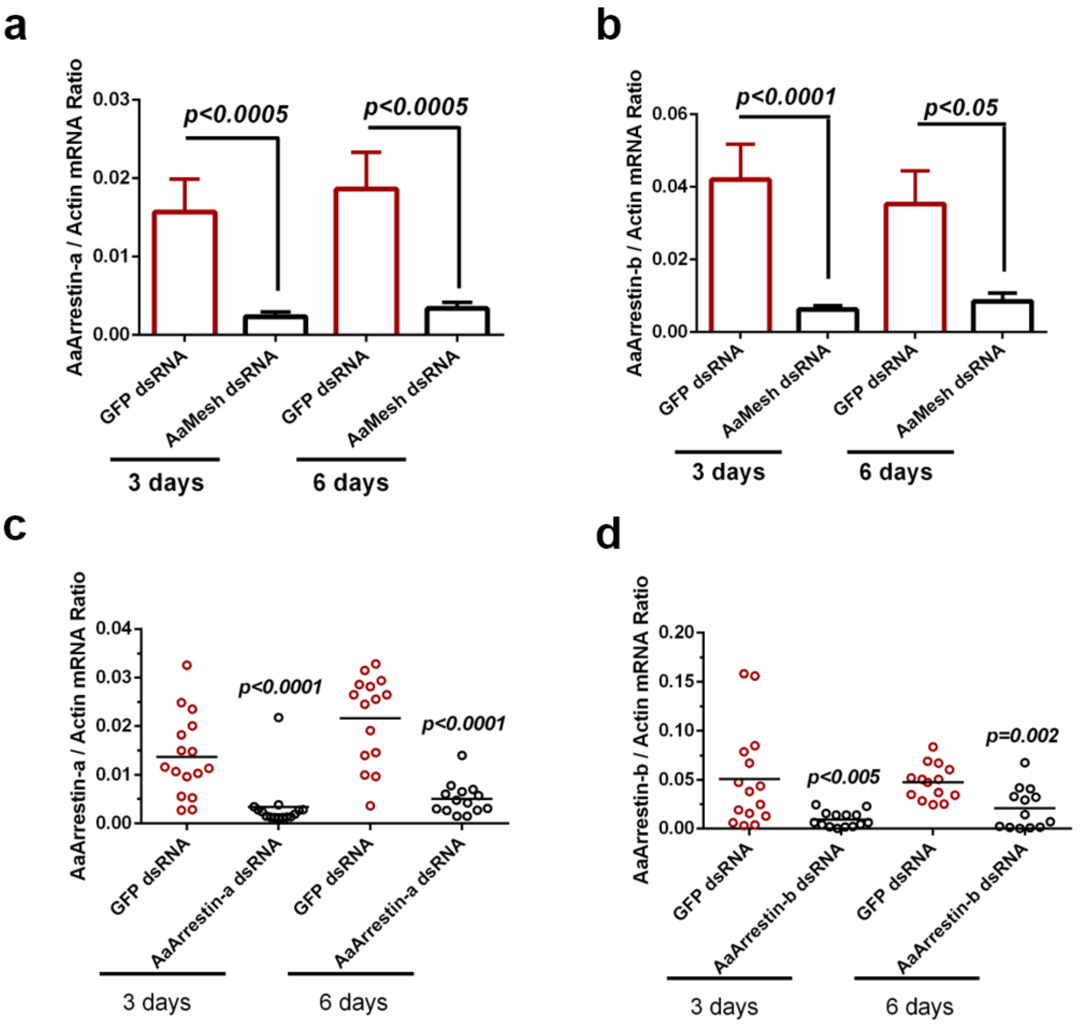
The dsRNA of these immune component genes were inoculated into mosquitoes. *GFP* dsRNA served as a mock control. The midguts of the treated mosquitoes were dissected 6 days after dsRNA inoculation. The expression levels of both immune component genes (a-h) and *AaMesh* (i) were determined by SYBR Green qPCR and normalized by *A. aegypti actin*. The qPCR primers are described in Supplementary Table 6. The data were represented as the mean ± S.E.M. The data were analyzed using the non-parametric *Mann-Whitney* test.



Supplementary Figure 11

Regulation of ROS activity in the guts of *AaERK*- and *AaJNK*-silenced mosquitoes.

Regulation of ROS activity in the guts of *AaERK*- and *AaJNK*-silenced mosquitoes. The ROS activity was detected using a H_2O_2 assay. *GFP* dsRNA-treated mosquitoes served as mock controls. The data were presented as the mean ± S.E.M. The data were analyzed using the non-parametric *Mann*-*Whitney* test. The results were combined from 3 independent experiments.



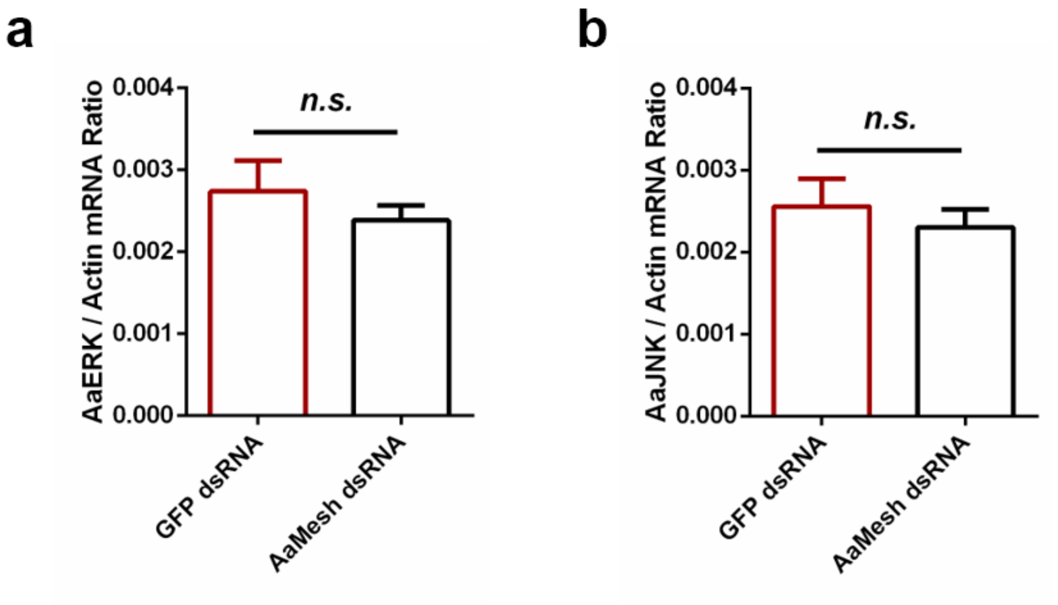
Supplementary Figure 12

Regulation of *AaArrestin* genes in the midguts of *AaMesh* silencing mosquitoes, and knockdown efficiency of *AaArrestins* in the mosquito midguts

(a-b) The *AaMesh* gene was silenced via thoracic dsRNA microinjection. *GFP* dsRNA-inoculated mosquitoes served as mock controls. Both *AaArrestin-a* (a) and *AaArrestin-b* (b) mRNA abundance in the midguts of *AaMesh* silencing mosquitoes was assessed by SYBR Green qPCR. The data were presented as the mean ± S.E.M.

(c-d) Two *AaArrestins* dsRNAs were inoculated into mosquitoes. *GFP* dsRNA served as a mock control. The midguts of the treated mosquitoes were dissected after dsRNA inoculation. The expression levels of *AaArrestin-a* (c) and *AaArrestin-b* (d) were determined using SYBR Green qPCR and normalized by *A. aegypti actin*. One dot represents one mosquito gut. The horizontal line represents the mean value of the results.

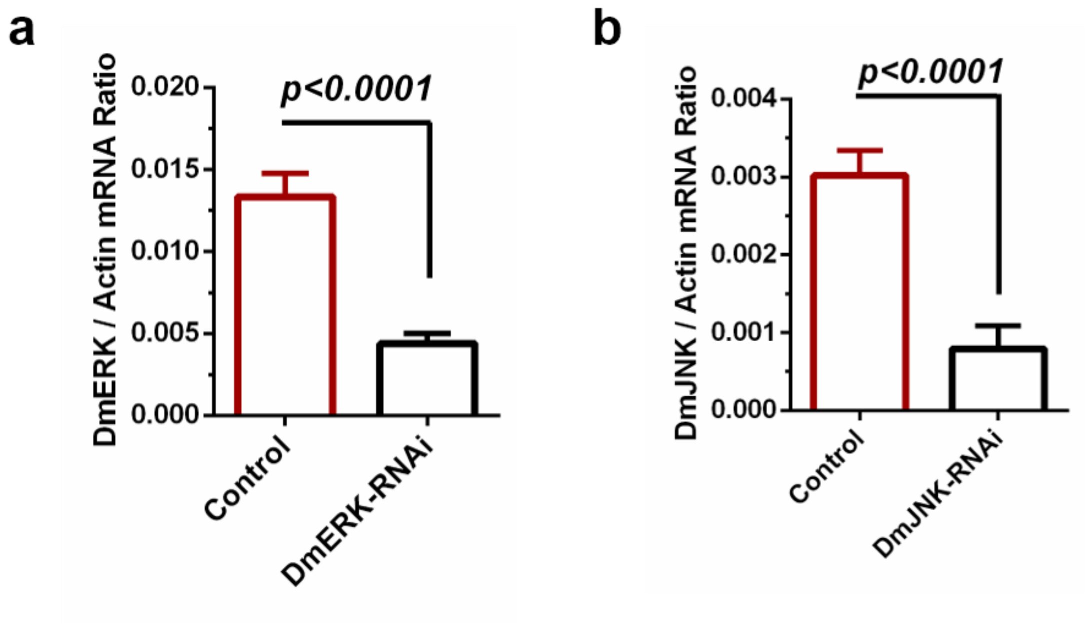
(a-d) The qPCR primers are described in Supplementary Table 6. The data were analyzed using the non-parametric *Mann-Whitney* test.



Supplementary Figure 13

Regulation of *AaERK* and *AaJNK* in the midguts of *AaMesh* silencing mosquitoes

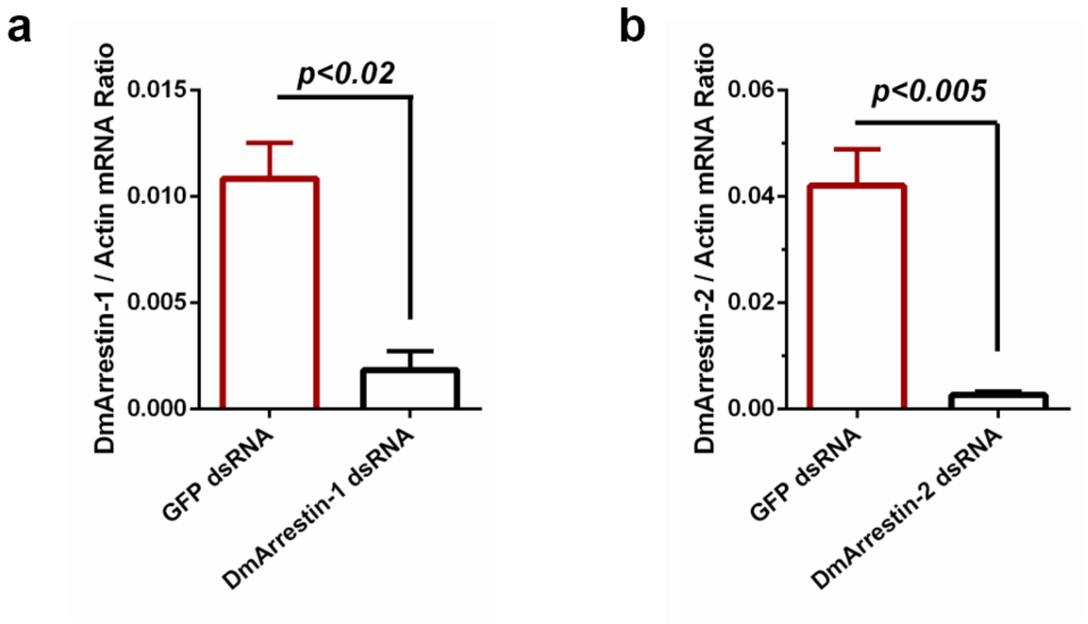
Both *AaERK* (a) and *AaJNK* (b) mRNA were assessed by SYBR Green qPCR in the midguts of *AaMesh* silencing mosquitoes. *GFP* dsRNA-inoculated mosquitoes served as mock controls. The qPCR primers are described in Supplementary Table 6. The data were represented as the mean ± S.E.M. The data were analyzed using the non-parametric *Mann-Whitney* test.



Supplementary Figure 14

Knockdown efficiency in *DmERK* and *DmJNK* RNAi *Drosophila*

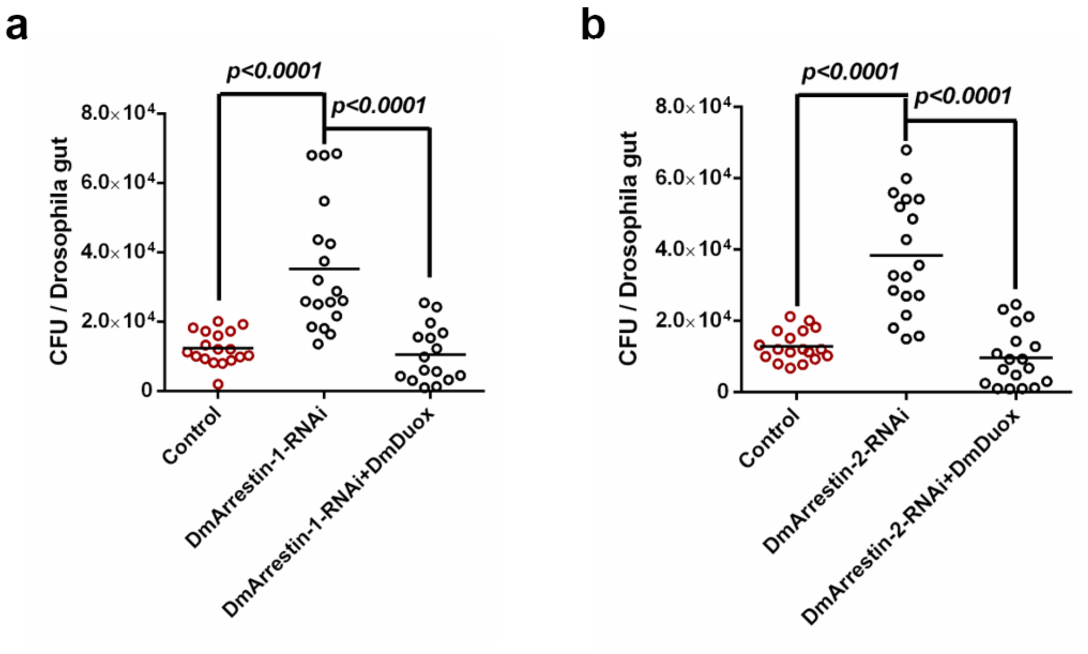
Knockdown efficiency in *DmERK* (a) and Dm*JNK* (b) RNAi *Drosophila*. The *DmERK* and *DmJNK* RNAi *Drosophila* strains were generated by a GAL4 line driven by *NP3084* promoter. The *NP3084 / GFP-RNAi* flies served as a negative control. The mRNA abundance in the midguts of *DmERK* and *DmJNK* RNAi flies was assessed by SYBR Green qPCR. The qPCR primers are described in Supplementary Table 6. The data were presented as the mean ± S.E.M.



Supplementary Figure 15

Knockdown efficiency of *DmArresin-1* and *DmArresin-2* in S2 cells

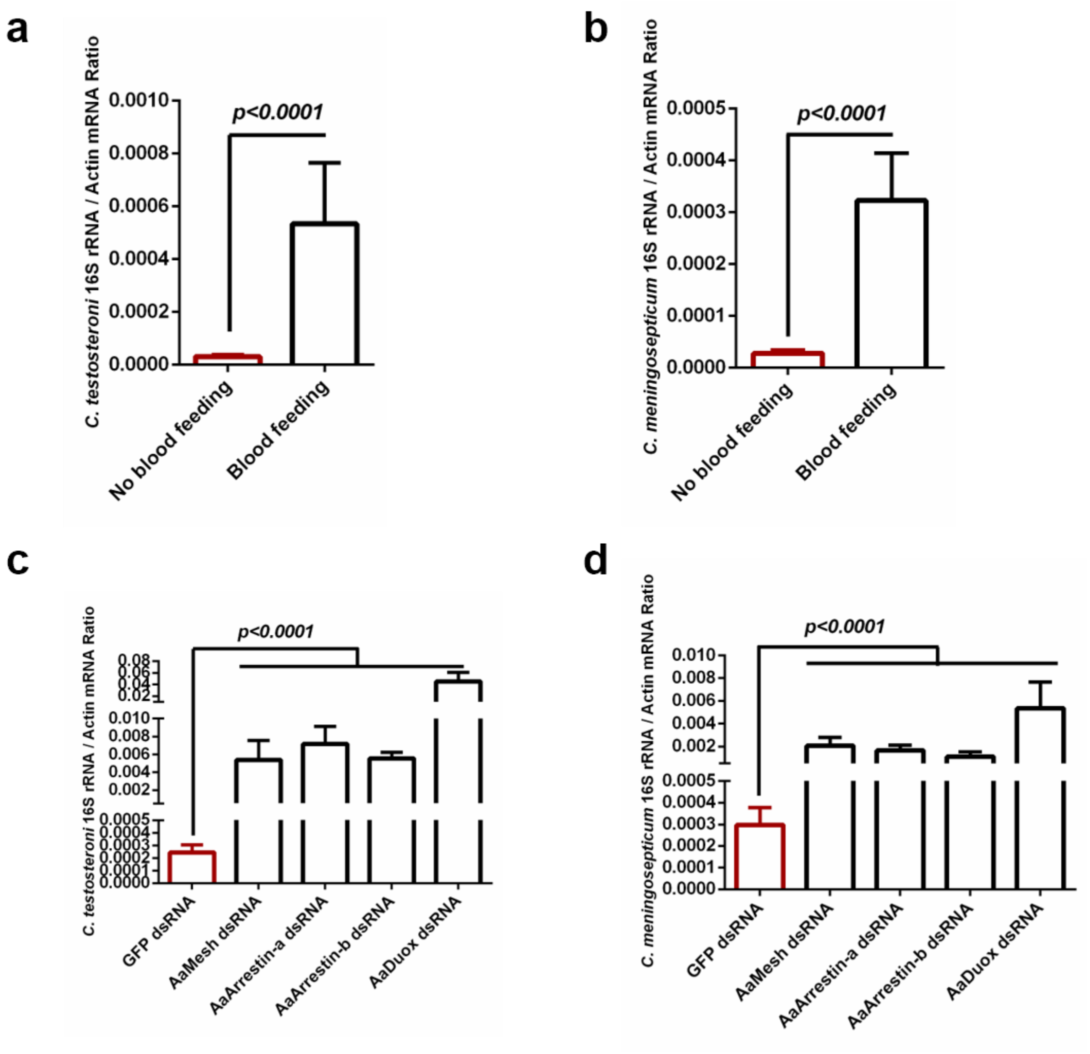
Both *DmArrestin-1* (a) and *DmArrestin-2* (b) were silenced by dsRNA transfection in the *Drosophila* S2 cells. The abundance of the *DmArrestins* gene was determined by SYBR Green qPCR and normalized by *Drosophila actin* (*CG12051*). The qPCR primers are described in Supplementary Table 6. The data were represented as the mean ± S.E.M. The data were analyzed using the non-parametric *Mann-Whitney* test.



Supplementary Figure 16

Reduction of burden of gut microbiome by rescuing *DmDuox* into the *DmArrestin*-RNAi flies.

(a-b) Ectopic expression of *DmDuox* into the *DmArrestin-1* (a) and *DmArrestin-2* (b) RNAi flies reduced the burden of gut microbiome, respectively. The burden of the gut microbiome was determined by a CFU assay. *GFP* RNAi flies served as mock controls. One dot represents a *drosophila* gut. The horizontal line represents the mean value of the results. The data were analyzed using the non-parametric *Mann-Whitney* test. All results were repeated by 3 independent experiments.



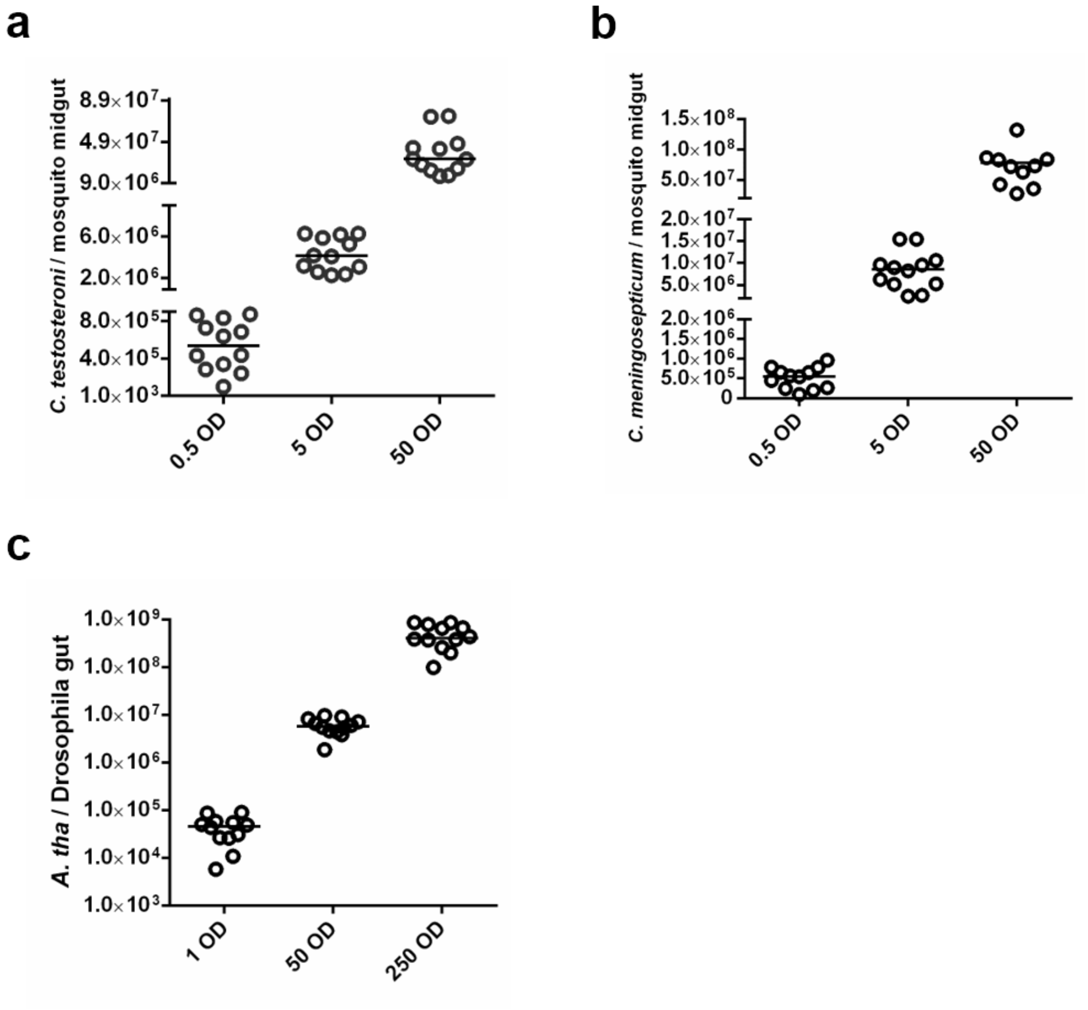
Supplementary Figure 17

Regulation of gut commensal bacteria in either the blood feeding mosquitoes or the AaMesh signaling-interrupted mosquitoes

(a-b) Regulation of burdens of gut commensal bacteria in blood feeding. Both *C. testosteroni* and *C. meningosepticum* have been routinely identified as cultivable gut commensals in *Aedes* mosquitoes. The mosquito midguts, isolated at 12 hours post blood feeding, were collected for detection of *C. testosteroni* (a) and *C. meningosepticum* (b) burden by qPCR. The midguts of mosquito fed with sugar served as a negative control.

(c-d) Genetic interruption of Mesh-mediated signaling components enhanced the burden of these gut bacteria. *AaMesh*, *AaArrestin-a*, *AaArrestin-b* and *AaDuox* were silenced by dsRNA thoracic inoculation in *A. aegypti*, respectively. Mosquitoes inoculated by *GFP* dsRNA were used as negative controls. The mosquito midguts, isolated at 12 hours post blood feeding, were collected for detection of *C. testosteroni* (c) and *C. meningosepticum* (d) burden by qPCR.

(a-d) The bacterial 16S rRNA was determined by SYBR Green qPCR and normalized against *A. aegypti actin*. The qPCR primers are described in Supplementary Table 6. The data were represented as the mean ± S.E.M. The data were analyzed using the non-parametric *Mann-Whitney* test. All results were repeated by 3 independent experiments.



Supplementary Figure 18

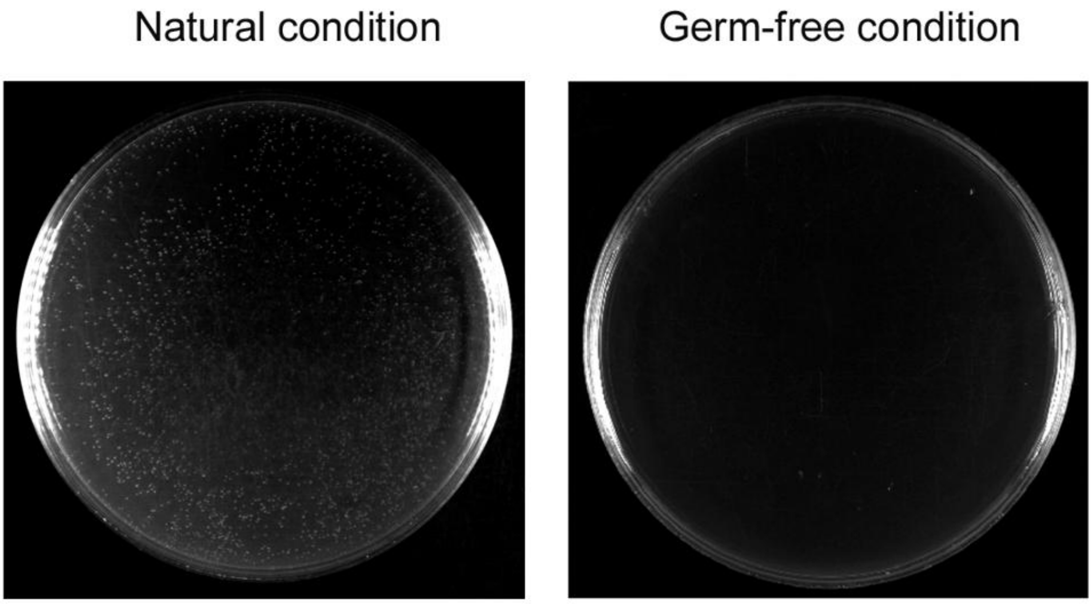
Counting the number of acquired bacteria in the midgut of individual *Drosophila* and mosquito.

(a) Counting the number of acquired *C. testosteroni* in the midgut of individual mosquito. A serial of *C. testosteroni* (0.5 OD, 5 OD and 50 OD) with fresh blood was exploited to feed the antibiotic-treated mosquitoes.

(b) Measurement of the number of acquired *C. meningosepticum* in the midgut of individual mosquito. A serial of *C. meningosepticum* (0.5 OD, 5 OD and 50 OD) with fresh blood was fed into the antibiotic-treated mosquitoes.

(c) Determining the number of acquired *A. thailandicus* in the midgut of individual *Drosophlia.* A serial of *A. thailandicus* (1 OD, 50 OD and 250 OD), mixed with the standard *Drosophila* food respectively, was exploited to feed the germ-free flies. The germ-free flies were hatched and reared in an aseptic condition.

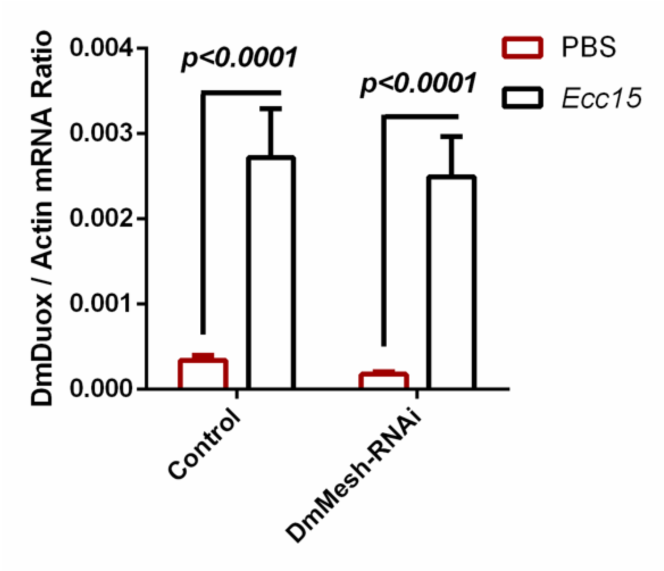
(a-c) Twelve insects in each group were randomly selected for the gut isolation, and subsequently the bacterial number was counted by a CFU assay. One dot represents an insect gut. The horizontal line represents the mean value of the results.



Supplementary Figure 19

Validation of aseptic condition in the midgut of germ-free flies

The midguts of untreated flies and germ-free flies were ground in PBS buffer. Bacterial number was assessed by a CFU assay on LB plates.



Supplementary Figure 20

The role of Mesh-mediated signaling pathway in response to pathogen infection of *Drosophila*

A *Drosophila* pathogen, *Erwinia carotovora carotovora 15* (*Ecc15*), was used to feed both *DmMesh-RNAi* and control flies, with the standard *Drosophila* food. The flies fed by the standard *Drosophila* food with PBS buffer acted as mock controls. The *DmDuox* expression in the *Drosophila* midgut was determined by qPCR and normalized against *Drosophila actin*. The qPCR primers are described in Supplementary Table 6. The data were represented as the mean ± S.E.M. The data were analyzed using the non-parametric *Mann-Whitney* test. The experiment was repeated 3 times with the similar results.

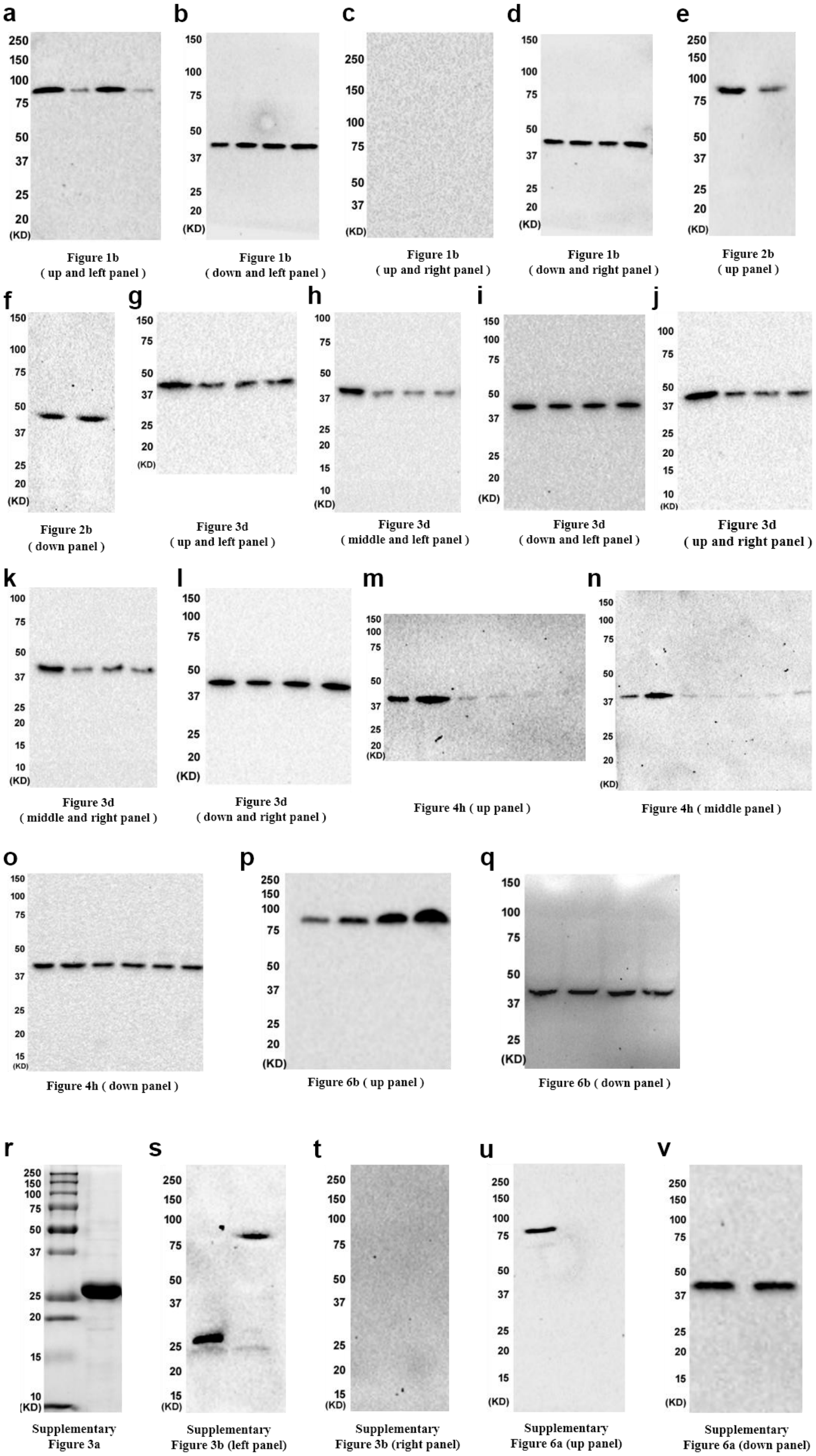

a
Figure 1b (up and left panel)
b
Figure 1b (down and left panel)
c
Figure 1b (up and right panel)
d
Figure 1b (down and right panel)
e
Figure 2b (up panel)
f
Figure 2b (down panel)
g
Figure 3d (up and left panel)
h
Figure 3d (middle and left panel)
i
Figure 3d (down and left panel)
j
Figure 3d (up and right panel)
k
Figure 3d (middle and right panel)
l
Figure 3d (down and right panel)
m
Figure 4h (up panel)
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Figure 4h (middle panel)
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Figure 4h (down panel)
p
Figure 6b (up panel)
q
Figure 6b (down panel)
r
Supplementary Figure 3a
s
Supplementary Figure 3b (left panel)
t
Supplementary Figure 3b (right panel)
u
Supplementary Figure 6a (up panel)
v
Supplementary Figure 6a (down panel)

Supplementary Figure 21

Full-length blots from Figures 1, 2, 3, 4, 6 and Supplementary Figure 3 and 6

a-d, Validation of an AaMesh antibody in the guts of *AaMesh*-silenced mosquitoes. **e-f,** The knockdown efficiency in the guts of *DmMesh* RNAi flies. **g-l,** Genetic suppression of *AaMesh* and *AaArrestins* impaired the phosphorylation of AaERK and AaJNK in the mosquito guts. **m-o,** Both *DmArrestin-1* and *DmArrestin-2* knockdown suppressed the phosphorylation of DmERK (p-ERK) and DmJNK (p-JNK) in the pAc-DmMesh-trnasfected *Drosophila* S2 cells. **p-q,** Oral introduction of *A. thailandicus* (*A. tha*) induced the DmMesh expression. **r,** Purification of the AaMesh peptide expressed *by E. coli*. **s-t,** Validation of the AaMesh polyclonal antibody. **u-v,** Detection of DmMesh in the whole homozygous *DmMesh*$^{-/-}$ larvae.

Supplementary Table 1. Regulation of immune genes in the AaMesh-impaired midguts

Function Group	Gene Name	Gene Number	Log$_2$ Ratio		
			AaMesh/*GFP* dsRNA 3 days	*AaMesh*/*GFP* dsRNA 6 days	AaMesh antibody/Pre-immune
Apoptosis	CASPL1	AAEL014148	0.866733469	-0.573991383	0.371968777
Apoptosis	CASPL2	AAEL011562	0.188337039	0.145523658	0.195819326
Apoptosis	CASPS1	AAEL014658	-0.161785657	-0.177313602	0.262449253
Apoptosis	CASPS15	AAEL005963	0.72177919	1.696470816	-1.883186335
Apoptosis	CASPS16	AAEL005956	1.427785992	0.101492988	-0.301040728
Apoptosis	CASPS17	AAEL005955	0.76650987	0.267933205	0.914752713
Apoptosis	CASPS18	AAEL003439	1.145098894	-0.380170847	-0.643306487
Apoptosis	CASPS19	AAEL003444	1.304355465	-0.087132592	-0.079246751
Apoptosis	CASPS21	AAEL017498	1.345387068	0.189342455	-0.227561524
Apoptosis	CASPS7	AAEL012143	0.476237656	0.232947603	0.122702992
Apoptosis	CASPS8	AAEL014348	1.299022184	-0.215344126	0.110451451
Apoptosis	CED-6	AAEL012967	0.962788921	-0.288244969	-1.114783447
Apoptosis	CED-6	AAEL012821	0.835428233	-0.523323435	0.102447269
Apoptosis	IAP1	AAEL009074	0.435079065	0.045968739	-0.029902063
Apoptosis	IAP2	AAEL006633	0.573374526	0.41289414	-0.092331881
Apoptosis	IAP5	AAEL014251	5.247927513	-2.150559677	5.169925001
Apoptosis	IAP6	AAEL012446	0.86270769	0.259828739	0.339269992
Apoptosis	IAP9	AAEL012512	-0.91195904	0.519002697	0.338305301
Autophagy	Autophagy related gene	AAEL016987	2.455511249	0.678071905	-1.482663925
Autophagy	Autophagy related gene	AAEL013995	0.710280486	0.620599545	0.337625029
Autophagy	Autophagy related gene	AAEL003799	1.093841754	0.382333334	0.027593369
Autophagy	Autophagy related gene	AAEL013815	0.473069621	-0.023458973	-0.887525271
Autophagy	Autophagy related gene	AAEL013063	4.061111514	-0.271708739	1.566346823

Autophagy	Autophagy related gene	AAEL002286	0.344959064	-0.157227375	-0.44170545
Autophagy	Autophagy related gene	AAEL010641	0.157744731	0.054290156	0.24687739
Autophagy	Autophagy related gene	AAEL010516	0.486514013	-0.064011758	NA
Autophagy	Autophagy related gene	AAEL010427	0.234929068	-0.36882907	NA
Autophagy	Autophagy related gene	AAEL009105	0.384945434	0.154520308	0.140106884
Autophagy	Autophagy related gene	AAEL009089	1.003260329	-0.221916363	-1.31802364
Autophagy	Autophagy related gene	AAEL007228	0.719892081	-0.031478231	0.121745272
Autophagy	Autophagy related gene	AAEL007162	1.452032718	0.230617753	-0.68475139
Autophagy	Autophagy related gene	AAEL000955	0.258286795	0.178078885	-0.019628807
Effector	CECA	AAEL000627	0.403064858	-0.628199595	0.39550533
Effector	CECB	AAEL004223	1.33451934	0.332097641	-0.375600475
Effector	CECE	AAEL000611	1.789015331	0.690415267	1.588998014
Effector	CECG	AAEL015515	10.56605404	0.424256029	-1.486792082
Effector	CECH	AAEL017211	1.647160134	0.955422372	-0.353677149
Effector	CECI	AAEL000775	6.044394119	-1.988684687	NA
Effector	CECJ	AAEL000777	6.781359714	NA	NA
Effector	CECN	AAEL000621	1.881499958	-0.07028694	2.584962501
Effector	DEFA	AAEL003841	2.392947558	-0.601941822	-0.305986551
Effector	DEFC	AAEL003832	0.088103992	-0.850118517	-1.116592129
Effector	DEFD	AAEL003857	1.243905394	-0.352015925	0.713658221
Effector	DEFE	AAEL003849	2.795943715	0.199267951	-0.192854544
Effector	DUOX	AAEL007563	-2.1069153	-1.2251198	-2.3923174
Effector	LYSC11	AAEL003723	1.241286834	-0.051640464	0.268458078
Effector	LYSC4	AAEL017132	1.139189408	-0.013838907	-1.413691074
Effector	LYSC6	AAEL005988	-0.514573173	0.319459839	NA
Effector	LYSC7A	AAEL010100	1.378792194	0.362832734	0.924259485

Effector	LYSC7B	AAEL015404	0.724276503	0.058686624	-0.005810818
Effector	LYSC9	AAEL009670	-1.128104826	-6.491853096	-0.415037499
Imd	IMD	AAEL010083	1.025068034	1.49810411	-0.416555327
Imd	REL2	AAEL007624	0.542460733	-0.062510979	0.106041637
JAK-STAT	DOME	AAEL012471	0.934972433	0.034716205	0.130396637
JAK-STAT	HOP	AAEL012553	0.732402506	0.357223986	-0.300062526
JAK-STAT	STAT1	AAEL009692	0.242360838	0.004907131	0.097447145
MAPK	Erk1/2	AAEL013939	2.328948523	0.811487537	-0.707819249
MAPK	Erk1/2	AAEL007958	2	-0.662268227	-1.584962501
Imd	IKK1	AAEL003245	0.267365898	0.065517411	-0.437835628
Imd	IKK2	AAEL012510	0.506347946	-0.052626931	-0.0222559
MAPK	JNK	AAEL008634	2.75996742	-0.138552375	-0.153912683
MAPK	JNK	AAEL008622	3.30580843	0.911190733	3.169925001
MAPK	MAPKK	AAEL003359	2.251178048	0.398031074	-0.042228235
MAPK	MAPKK	AAEL001622	0.548533714	-0.157791246	0.268551411
MAPK	MAPKK4	AAEL003013	1.371808564	0.17954942	-0.37378585
MAPK	P38MAPK	AAEL008379	0.956572235	0.028083784	-0.371429065
Oxidative defense enzymes	HPX2	AAEL013171	0.528694281	-0.623271858	0
Oxidative defense enzymes	HPX6	AAEL012481	-4.807354922	5.392317423	4.807354922
Oxidative defense enzymes	HPX7	AAEL004401	-0.421137699	-0.832722068	-0.459431619
Oxidative defense enzymes	HPX8A	AAEL004388	4.087462841	-0.061029433	3
Oxidative defense	HPX8B	AAEL004390	-1.988684687	-0.579047487	0.292180751

enzymes					
Oxidative defense enzymes	PERC	AAEL004386	-0.584962501	-0.620887782	0.763932642
RNA interference	Dicer-1	AAEL006794	1.282132927	0.165222382	-0.237797114
RNA interference	Dicer-1	AAEL001612	1.666262603	0.725140159	-0.61667136
RNA interference	PIWI	AAEL008076	-0.584962501	0.045596866	-3.906890596
RNA interference	PIWI	AAEL007823	0.456664595	-0.31000571	-0.251626734
RNA interference	PIWI3	AAEL013692	-5.209453366	-0.663204524	4.247927513
RNA interference	PIWI4	AAEL007698	0.151248052	-0.138914779	-0.0726278
RNA interference	PIWI5	AAEL013233	0.325416027	0.07854711	0.043990014
RNA interference	PIWI6	AAEL013227	0.392317423	0.071181565	0.236687535
Signal Modulation	Arrestin a	AAEL013535	-4.11401626	-1.9541963	-0.551045006
Signal Modulation	Arrestin b	AAEL003116	-4.282692932	-0.403064858	-1.9995094
Signal Modulation	beta-arrestin 1	AAEL013704	2.512907564	0.408962985	-0.333423734
Signal Modulation	beta-arrestin 1	AAEL012004	2.122228259	0.214563048	0.176453044
Signal Modulation	CLIP	AAEL014005	1.224630894	-0.169618859	0.905003486
Signal Modulation	CLIP	AAEL014004	-7.562242424	0.326500825	-6.523561956
Signal Modulation	CLIP	AAEL003279	0.675377796	0.010397847	0.257332046
Signal Modulation	CLIP	AAEL009726	0.307572802	-0.648903322	0.393663848
Signal Modulation	CLIP	AAEL009722	-1.227640499	-0.397849567	2.060120992
Signal Modulation	CLIP	AAEL001098	1.67474218	-0.246179186	0
Signal Modulation	CLIP	AAEL006576	-1.19962753	-0.719844592	0.721344614
Signal Modulation	CLIP	AAEL014724	-0.263034406	-6.584962501	NA
Signal Modulation	CLIPA1	AAEL002601	1.345644164	0.402437462	0
Signal Modulation	CLIPA15	AAEL002126	-2.807354922	NA	NA
Signal Modulation	CLIPA16	AAEL008404	-0.94753258	-2.478047297	NA

Signal Modulation	CLIPA17	AAEL007006	0.08246216	-0.309684499	0.584962501
Signal Modulation	CLIPB	AAEL017555	1.66862043	0.232734366	7.238404739
Signal Modulation	CLIPB1	AAEL000074	-2.492598483	-0.646762329	1.495810123
Signal Modulation	CLIPB13B	AAEL003253	-5.672425342	7.14974712	-1.974004791
Signal Modulation	CLIPB15	AAEL014349	0.635977787	0.289096702	-0.41686717
Signal Modulation	CLIPB19	AAEL000059	-0.936806174	0.012600037	0
Signal Modulation	CLIPB21	AAEL001084	1.986579484	-0.144816553	-0.584962501
Signal Modulation	CLIPB22	AAEL008668	1.829269698	-0.40053793	-0.591360272
Signal Modulation	CLIPB23	AAEL012785	-0.807354922	-0.956056652	5.321928095
Signal Modulation	CLIPB24	AAEL014140	-6.375039431	-0.109624491	1.021695071
Signal Modulation	CLIPB25	AAEL014137	-0.94753258	1	1.054447784
Signal Modulation	CLIPB27	AAEL007993	0.998783049	-0.264216216	1.307281319
Signal Modulation	CLIPB28	AAEL013245	1.064130337	0.025535092	1
Signal Modulation	CLIPB29	AAEL006674	-0.002729793	-0.413580477	1.345208919
Signal Modulation	CLIPB30	AAEL000760	-2.256339753	1.708233876	1.041820176
Signal Modulation	CLIPB31	AAEL006161	1.763437806	0.673556424	-1
Signal Modulation	CLIPB33	AAEL000099	0.084064265	0.090480746	-1.457472766
Signal Modulation	CLIPB34	AAEL000028	-0.694865495	-0.49413258	0.645211611
Signal Modulation	CLIPB35	AAEL000037	-1.335603032	-0.675761333	1.261585189
Signal Modulation	CLIPB36	AAEL017325	-1.079727192	-0.379530956	0.537797393
Signal Modulation	CLIPB37	AAEL005431	-0.402546555	-1.755515991	1
Signal Modulation	CLIPB39	AAEL003632	5.087462841	NA	NA
Signal Modulation	CLIPB40	AAEL003614	-0.321928095	-1.598078001	4.906890596
Signal Modulation	CLIPB41	AAEL003631	-0.906890596	0.275634443	-5.491853096
Signal Modulation	CLIPB42	AAEL006168	0.08246216	-0.986325063	0
Signal Modulation	CLIPB43	AAEL014354	-5.044394119	-0.448862377	0.956931278

Signal Modulation	CLIPB45	AAEL001077	0.446800062	-0.005427072	-0.233097122
Signal Modulation	CLIPB46	AAEL005093	1.758637386	-0.51603216	-0.13439594
Signal Modulation	CLIPB5	AAEL005064	0.331621491	0.059297184	-2.14543044
Signal Modulation	CLIPB6	AAEL000038	0.673349495	-0.277533976	0.523051899
Signal Modulation	CLIPB8	AAEL003625	-1.286579833	-0.645867849	1.361280923
Signal Modulation	CLIPB9	AAEL003610	-0.137503524	1.95419631	-0.125530882
Signal Modulation	CLIPC1	AAEL011991	-1.652076697	-0.11042399	1.584962501
Signal Modulation	CLIPC12	AAEL012711	0.074000581	-0.700439718	0.672425342
Signal Modulation	CLIPC13	AAEL012712	-0.316857105	-0.054861935	0.846194664
Signal Modulation	CLIPC2	AAEL007593	-0.328084955	-0.402933013	0.244611046
Signal Modulation	CLIPC3	AAEL007597	-0.841302254	-0.463400521	1.823677227
Signal Modulation	CLIPC5A	AAEL004518	-4	0.731183242	4
Signal Modulation	CLIPC5B	AAEL004524	0.087462841	-1.086711633	4
Signal Modulation	CLIPC6	AAEL004540	-0.234465254	-0.4896763	1
Signal Modulation	CLIPD1	AAEL007796	0.256339753	-0.877794068	0.156725504
Signal Modulation	CLIPD6	AAEL002124	0.086877451	-0.24954217	-0.358793389
Signal Modulation	CLIPD7	AAEL015439	3.097412502	-0.571415969	-0.480625841
Signal Modulation	CLIPE11	AAEL005800	-4.754887502	-3.807354922	NA
Signal Modulation	CLIPE8	AAEL005792	5.209453366	0.231815675	-0.598637438
Signal Modulation	CTL14	AAEL011453	6.442943496	8.21916852	5.357552005
Signal Modulation	CTL16	AAEL000533	0.50389089	0	1.579085934
Signal Modulation	CTL18	AAEL005482	2.133814289	-0.005697405	-0.78956873
Signal Modulation	CTL20	AAEL011407	0.10433666	NA	6.918863237
Signal Modulation	CTL24	AAEL002524	1.732220592	-0.836501268	-0.263034406
Signal Modulation	CTL25	AAEL000556	1.035502985	1	8.703903573
Signal Modulation	CTL6	AAEL003119	1.770605736	-0.076466536	-0.400735066

Signal Modulation	CTLGA1	AAEL011078	0.827163403	1.330916878	4.95419631
Signal Modulation	CTLGA2_b	AAEL013853	0.503110747	0.39818443	0.108059746
Signal Modulation	CTLGA3	AAEL011070	0.672835257	-0.512554005	-0.2410081
Signal Modulation	CTLGA4	AAEL017484	5.584962501	7.118941073	NA
Signal Modulation	CTLGA5	AAEL005641	1.870108873	-0.139463898	-0.026685658
Signal Modulation	CTLGA7	AAEL017265	1.464551454	-0.377988054	0.223350704
Signal Modulation	CTLGA8	AAEL011610	3.997265032	-0.533914895	0.547487795
Signal Modulation	CTLGA9_a	AAEL014385	5.857980995	NA	5.781359714
Signal Modulation	CTLMA11	AAEL000543	-0.501880759	-0.662965013	0.486698484
Signal Modulation	CTLMA12	AAEL011455	1.664815808	-1.104469267	1
Signal Modulation	CTLMA14	AAEL014382	1.98112199	-0.382222702	-0.207276218
Signal Modulation	CTLMA15	AAEL000563	-5.459431619	-0.415037499	NA
Signal Modulation	CTLSE1	AAEL008929	-2	0.604071324	NA
Signal Modulation	GALE1	AAEL003541	0.51315313	0.10059437	-0.303392143
Signal Modulation	GALE12	AAEL009842	0.826334772	0.067326978	-0.526880194
Signal Modulation	GALE13	AAEL009845	1.018279736	-0.256503408	-0.97340579
Signal Modulation	GALE14	AAEL009850	0.280745856	-0.353252511	0.362398626
Signal Modulation	GALE2	AAEL012135	0.513822824	0.021151264	0.185140494
Signal Modulation	GALE3	AAEL004196	0.4680812	-0.162127311	0.183748677
Signal Modulation	GALE5	AAEL003844	-0.136146086	0.018925425	0.503649674
Signal Modulation	GALE6A	AAEL005294	2.412939033	-0.181656367	NA
Signal Modulation	GALE6B	AAEL012003	-5.426264755	NA	NA
Signal Modulation	GALE8B_a	AAEL005293	0.623091446	-0.305711536	0.241603882
Signal Modulation	SCRAL1	AAEL015308	0.247251409	0.182653306	-0.398435532
Signal Modulation	SCRASP1	AAEL009192	0.735311127	-0.617511195	-0.110747066
Signal Modulation	SCRB10	AAEL007748	-0.177787119	0.017382078	1.544320516

Signal Modulation	SCRB16	AAEL005981	1.662965013	3.584962501	NA
Signal Modulation	SCRB17	AAEL008370	0.416580214	0	0.120784711
Signal Modulation	SCRB3	AAEL005979	-2.268488836	-0.321928095	4.392317423
Signal Modulation	SCRB5	AAEL011222	-0.593679718	0.6983443	-1.070389328
Signal Modulation	SCRB6	AAEL002741	4.584962501	3.584962501	-1
Signal Modulation	SCRB7	AAEL000234	1.408968663	0.027032959	-0.151655414
Signal Modulation	SCRB8	AAEL000227	0.444943984	0.479587815	-0.170352403
Signal Modulation	SCRB9	AAEL000256	2.102361718	-0.107640723	-1
Signal Modulation	SCRBQ1	AAEL009420	0.075981918	0.313284	0.368067633
Signal Modulation	SCRBQ2	AAEL009423	0.630664714	0.077006645	-0.151086078
Signal Modulation	SCRBQ3	AAEL009432	0.147906057	0.206959451	0.219424409
Signal Modulation	SCRC1	AAEL006355	-0.898120386	1.070389328	-1
Signal Modulation	SCRC2	AAEL006361	0.115477217	-0.310340121	0
Toll	CACT	AAEL000709	-0.191724952	0.119652203	0.095476315
Imd	FADD	AAEL001932	-0.051428239	-0.980100443	-1.802963153
Toll	MYD	AAEL007768	1.724513853	0.266633375	-0.128254491
Toll	PELLE	AAEL006571	-0.173610048	0.628452324	0.137858911
Toll	REL1A	AAEL007696	0.028827406	0.1616709	0.068456979
Toll	SPZ1C	AAEL013433	-6.22881869	0	NA
Toll	SPZ3A	AAEL008596	0.719892081	0.225292312	-0.364764293
Toll	SPZ3B	AAEL014950	1.104829973	-0.248048226	0.44625623
Toll	SPZ4	AAEL007897	6.794415866	-0.185031894	0
Toll	SPZ5	AAEL001929	1.509861045	2.017073513	0
Toll	SPZ6	AAEL012164	4	-1.584962501	4.95419631
Toll	TOLL	AAEL001771	2.321928095	NA	NA
Toll	TOLL	AAEL015018	2.184337659	0.352406511	-0.922757001

Toll	TOLL10	AAEL004000	0.321928095	-1	-2
Toll	TOLL11	AAEL009551	0.884522783	0.440572591	0
Toll	TOLL1A	AAEL007613	1.851677253	0.247092862	0.142352923
Toll	TOLL4	AAEL017523	-0.925999419	0.135883428	-1.963474124
Toll	TOLL5A	AAEL007619	1.393914208	-0.283031314	-0.30218416
Toll	TOLL5B	AAEL000057	1.437155905	0.169925001	0.127111918
Toll	TOLL6	AAEL000671	3.700439718	0	-2
Toll	TOLL7	AAEL002583	2.321928095	-5.247927513	0.716207034
Toll	TOLL9A	AAEL013441	0.65732382	0.298210834	0.10269495
Toll	TOLL9B	AAEL011734	0.47714903	0.51908019	0.035436045
Toll	Toll-like receptor	AAEL006212	1.595669007	0.196320736	-1.115477217
Toll	TUBE	AAEL007642	0.9510904	-0.051715037	-1.344334508

Supplementary Table 2. Relative abundance of bacteria phylum in mosquito midgut (%)

Taxa	GFP dsRNA	AaMesh dsRNA
Unassigned;Other	0.026585563	0.018609894
k__Bacteria;p__Actinobacteria	2.670253945	0.179186694
k__Bacteria;p__Bacteroidetes	72.33346803	4.392998426
k__Bacteria;p__Cyanobacteria	4.25E-03	0
k__Bacteria;p__Firmicutes	1.150623166	26.0575737
k__Bacteria;p__Planctomycetes	0.020736739	5.85E-03
k__Bacteria;p__Proteobacteria	23.77759581	69.34365562
k__Bacteria;p__[Thermi]	0.016483049	2.13E-03

k: Kingdom; p: Phylum.

Supplementary Table 3. Relative abundance of bacteria genus in mosquito midgut (%)

Taxa	GFP dsRNA	AaMesh dsRNA
Unassigned;Other;Other;Other;Other;Other	0.026585563	0.018609894
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Brevibacteriaceae;g__Brevibacterium	0.022863584	0.001063423
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Corynebacteriaceae;g__Corynebacterium	0.001063423	0.001595134
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Micrococcaceae;g__Kocuria	0.052107703	0.001063423
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Micrococcaceae;g__Micrococcus	0.162703645	0.00425369
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Nocardioidaceae;g__	0.00850738	0
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Nocardioidaceae;g__Nocardioides	0.022331873	0.000531711
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Propionibacteriaceae;g__Propionibacterium	0.057956527	0.002126845
k__Bacteria;p__Actinobacteria;c__Rubrobacteria;o__Rubrobacterales;f__Rubrobacteraceae;g__Rubrobacter	2.342719809	0.168552469
k__Bacteria;p__Bacteroidetes;c__Cytophagia;o__Cytophagales;f__Cytophagaceae;g__	0.009039091	0
k__Bacteria;p__Bacteroidetes;c__Cytophagia;o__Cytophagales;f__Cytophagaceae;g__Spirosoma	0.014356204	0.009039091
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__Flavobacteriaceae;g__	0.005317113	0.004785401
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__Flavobacteriaceae;g__Flavobacterium	0.094644604	0.012229359
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Moraxellaceae;g__Acinetobacter	0.199391722	0.005317113
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__[Weeksellaceae];g__Elizabethkingia	71.99848994	4.357905483
k__Bacteria;p__Bacteroidetes;c__Sphingobacteriia;o__Sphingobacteriales;f__Sphingobacteriaceae;g__Sphingobacterium	0.012229359	0.003721979
k__Bacteria;p__Cyanobacteria;c__Chloroplast;o__Chlorophyta;f__Trebouxiophyceae;g__	0.00425369	0
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__Bacillaceae;g__Anoxybacillus	0.090390914	0.003190268
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__Bacillaceae;g__Bacillus	0.092517759	0.001063423
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__Planococcaceae;g__Planococcus	0.036156366	0.000531711
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__Staphylococcaceae;g__Staphylococcus	0.155791399	0.048385725
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Aerococcaceae;g__	0.108469097	0
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Aerococcaceae;g__Aerococcus	0.182908673	0
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Enterococcaceae;Other	0.001063423	0.081883534
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus	0.044663746	0
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Lactococcus	0.360500234	25.92198732
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus	0.039346633	0
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Catonella	0.007443958	0
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Veillonellaceae;g__Veillonella	0.023395295	0
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__[Tissierellaceae];g__Anaerococcus	0.007975669	0.000531711
k__Bacteria;p__Planctomycetes;c__Planctomycetia;o__Planctomycetales;f__Planctomycetaceae;g__Planctomyces	0.020736739	0.005848824
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Caulobacterales;f__Caulobacteraceae;g__	0.597643456	0.065400485
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Caulobacterales;f__Caulobacteraceae;g__Brevundimonas	3.323195372	0.017546472

Taxa	GFP dsRNA	AaMesh dsRNA
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Caulobacterales;f__Caulobacteraceae;g__Mycoplana	0.168552469	0.027117274
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__;g__	0.020205028	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Beijerinckiaceae;g__	0.007975669	0.000531711
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Bradyrhizobiaceae;g__	0.002126845	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Brucellaceae;g__Ochrobactrum	0.09730316	0.018078183
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Hyphomicrobiaceae;g__Devosia	0.002126845	0.000531711
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Hyphomicrobiaceae;g__Hyphomicrobium	0.085605513	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Methylobacteriaceae;g__	0.018609894	0.026053852
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Methylobacteriaceae;g__Methylobacterium	0.007975669	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Phyllobacteriaceae;Other	0.01701476	0.006912246
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Rhizobiaceae;g__Agrobacterium	0.044663746	0.004785401
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhizobiales;f__Xanthobacteraceae;g__Xanthobacter	0.096771449	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodobacterales;f__Hyphomonadaceae;g__	0.06752733	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodobacterales;f__Rhodobacteraceae;g__Anaerospora	0.173337871	0.026053852
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodobacterales;f__Rhodobacteraceae;g__Paracoccus	0.023395295	0.006912246
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodobacterales;f__Rhodobacteraceae;g__Rhodobacter	0.006912246	0.000531711
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodobacterales;f__Rhodobacteraceae;g__Rubellimicrobium	0.051044281	0.002658556
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodospirillales;f__Acetobacteraceae;g__	0.107937386	0.035624654
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodospirillales;f__Acetobacteraceae;g__Acetobacter	0	0.081883534
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodospirillales;f__Rhodospirillaceae;g__	0.004785401	0.003190268
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Sphingomonadales;f__Sphingomonadaceae;g__	0.00850738	0.010102514
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Sphingomonadales;f__Sphingomonadaceae;g__Sphingobium	0.037219788	0
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Sphingomonadales;f__Sphingomonadaceae;g__Sphingomonas	0.193542898	0.028712408
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Sphingomonadales;f__Sphingomonadaceae;g__Sphingopyxis	0.061678506	0.001595134
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__;g__	0.01701476	0
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Alcaligenaceae;g__Achromobacter	0.922519035	0.222787018
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Comamonadaceae;g__	0.05901995	0.000531711
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Comamonadaceae;g__Acidovorax	0.045195457	0
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Comamonadaceae;g__Comamonas	4.730635076	0.449296014
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Comamonadaceae;g__Delftia	0.309987664	0.001063423
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Oxalobacteraceae;Other	0.049980858	0
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Oxalobacteraceae;g__	0.048385725	0.000531711
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Oxalobacteraceae;g__Ralstonia	0.040410056	0.020205028
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Methylophilales;f__Methylophilaceae;g__	0.006912246	0

Taxa	GFP dsRNA	AaMesh dsRNA
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Neisseriales;f__Neisseriaceae;g__Chromobacterium	0.00850738	1.206452848
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Rhodocyclales;f__Rhodocyclaceae;g__Zoogloea	0.001063423	0
k__Bacteria;p__Proteobacteria;c__Deltaproteobacteria;o__Myxococcales;f__Haliangiaceae;g__	0	0.006380535
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Aeromonadales;f__Aeromonadaceae;g__	0.125483857	0.027117274
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Alteromonadales;f__Alteromonadaceae;g__Cellvibrio	0.02126845	0.003721979
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__	1.864179676	0.153132843
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Enterobacter	0.058488239	0.000531711
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Morganella	0.784805819	0.040410056
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Serratia	0.026053852	0
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__[Weeksellaceae];g__Chryseobacterium	7.137691948	0.37166617
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Moraxellaceae;g__Enhydrobacter	0.02126845	0.04625888
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Pseudomonadaceae;Other	0.451422859	0.018078183
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Pseudomonadaceae;g__	0.003721979	0.74705432
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Pseudomonadaceae;g__Pseudomonas	1.429239866	65.61795483
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Xanthomonadales;f__Xanthomonadaceae;g__	0.280743545	0.04200519
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Xanthomonadales;f__Xanthomonadaceae;g__Pseudoxanthomor	0.00850738	0.000531711
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Xanthomonadales;f__Xanthomonadaceae;g__Stenotrophomona:	0.099430006	0.003721979
k__Bacteria;p__[Thermi];c__Deinococci;o__Thermales;f__Thermaceae;g__Thermus	0.016483049	0.002126845

k: Kingdom; p: Phylum; c: Class; o: Order; f: Family; g: Genus.

Supplementary Table 4. Relative abundance of bacteria phylum in *Drosophila* gut (%)

#OTU ID	Control	DmMesh RNAi
Unassigned;Other	0.021002554	0.032236479
k__Bacteria;p__Actinobacteria	0.108431793	0.018071965
k__Bacteria;p__Bacteroidetes	14.74428169	8.235931952
k__Bacteria;p__Cyanobacteria	0	8.30E-03
k__Bacteria;p__Firmicutes	69.58195148	2.859766432
k__Bacteria;p__Proteobacteria	15.54433249	88.84568984

k: Kingdom; p: Phylum.

Supplementary Table 5. Relative abundance of bacteria genus in *Drosophila* gut (%)

#OTU ID	Control	DmMesh RNAi
Unassigned;Other;Other;Other;Other;Other	0.021002554	0.032236479
k__Bacteria;p__Actinobacteria;c__Rubrobacteria;o__Rubrobacterales;f__Rubrobacteraceae;g__Rubrobacter	0.108431793	0.018071965
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__Flavobacteriaceae;g__Flavobacterium	0.004395883	0.000488431
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__[Weeksellaceae];g__Chryseobacterium	0.012699219	0.009280198
k__Bacteria;p__Bacteroidetes;c__Flavobacteriia;o__Flavobacteriales;f__[Weeksellaceae];g__Elizabethkingia	14.72718659	8.226163322
k__Bacteria;p__Cyanobacteria;c__Chloroplast;o__Streptophyta;f__;g__	0	0.008303335
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Aerococcaceae;g__Aerococcus	0.00341902	0.004395883
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Enterococcaceae;g__Enterococcus	54.92607589	1.236708558
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__	14.15718703	0.320899495
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus	0.00341902	0.067891978
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Leuconostocaceae;g__Leuconostoc	0	0.001465294
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Lactococcus	0.49185052	1.228405222
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Caulobacterales;f__Caulobacteraceae;g__	0.023444712	0.004884315
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Caulobacterales;f__Caulobacteraceae;g__Brevundimonas	0.185115538	0.014164513
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodobacterales;f__Rhodobacteraceae;g__Anaerospora	0.003907452	0.001953726
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodospirillales;f__Acetobacteraceae;Other	0.721413325	5.507553593
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodospirillales;f__Acetobacteraceae;g__	0.356066563	0.01318765
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rhodospirillales;f__Acetobacteraceae;g__Acetobacter	4.425189389	81.3790375
k__Bacteria;p__Proteobacteria;c__Alphaproteobacteria;o__Rickettsiales;f__Rickettsiaceae;g__Wolbachia	0.050308444	0.001465294
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Alcaligenaceae;g__Achromobacter	0.049820013	0.017583534
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Comamonadaceae;g__Comamonas	0.201722209	0.072776293
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Comamonadaceae;g__Delftia	0.002442157	0.001953726
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Neisseriales;f__Neisseriaceae;g__Chromobacterium	0.038586088	0.009280198
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__	0.06838041	0.020025691
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Morganella	0.017095102	0.004395883
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Moraxellaceae;g__Acinetobacter	2.493442807	0.250076928
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Pseudomonadaceae;g__	3.663724681	0.91190161
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Pseudomonadaceae;g__Pseudomonas	3.226090057	0.629099772
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Xanthomonadales;f__Xanthomonadaceae;g__	0.016606671	0.006349609
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Xanthomonadales;f__Xanthomonadaceae;g__Stenotrophomona	0.000976863	0

k: Kingdom; p: Phylum; c: Class; o: Order; f: Family; g: Genus.

Supplementary Table 6. Primers for qPCR, dsRNA synthesis and genes cloning

Primers for cloning into pAc5.1/V5-His/A	**Upper primer**	**Lower primer**
DmMesh (V5 tag in the C-terminal)	GGGGTACCATGCGTTTCAAACTGTTTGTG	CCGCTCGAGGACCTCCGTGGACTTCTG
The primers for genes cloning(pET28)	**Upper primer**	**Lower primer**
AaMesh(994-1174 aa)	CCGGAATTCGTGATAGCACCAAATTTGAACA	GGACTCGAGCACAGCGCGTAGACATTCGG
The primers for RT-QPCR	**Upper primer**	**Lower primer**
AaMesh	GGCGTGGGGAAAGCGTTATT	TTCGGGGGTAAGAATTGTGACG
AaJNK	GATCCGGGGAGGAGTGCTG	CATGAACGAGGGCGACGG
AaERK	GTGACAAAGACAAAGGTTGCCATC	TCGTGTTTGAACCGGGTG
AaP38	AATGCTGGAACTAGACGC	ATACAGCGAAGACGTTGG
AaPI3K	GGCACCAAGGATGGGTTTATG	CAAATCTTCCGCATAGGTCCAC
AaMyd88	CGTGATTGGCGAGGGTTGTTTC	ATCCGCTCCAATGCTCGTTTCC
AaImd	TCGTCAAACTCGGTTTTCCT	TGGCGGAGTTGAAGGTAAAG
AaAkt	TATCGGCACTCGGCTATCTACA	GTCTTCGTTGTGCGTCCGTAG
AaDome	AAACGGTGGCAAAATGAACT	CATACAGCCGGCTTTCTTCT
AaArrestin-a	GGTGTCGATGTGGTGCTCTTCC	AGCCTGGTTGAATCGGACATCC
AaArrestin-b	AGCAAGCATATCGCCTCACTGG	GGCGGTCCTTGTTGCTGGAA
AaDuox	ATGCTGAGCCCAGAGAGATT	TTTCCTCATCAGTCCAATCG
AaNox	TCCACAATACGGTTTCGCTA	GCCGTCCAACAGAAATTGTA
AaActin	GAACACCCAGTCCTGCTGACA	TGCGTCATCTTCTCACGGTTAG
Bacterium Universal 16s rRNA	TCCTACGGGAGGCAGCAGT	GGACTACCAGGGTATCTAATCCTGTT
C. testosteroni 16s rRNA	CGAAAAGCCTGGGGCTAATAT	CCATCTCTGGTAAGTTCCTGC
C. meningosepticum 16s rRNA	ACATGGTCACCACTTCGTGAGA	GTCGCATCCGTTGTTGTCACTT
DmMesh	CTTCTACGGCTTCCGATTCAACTAC	GTCCTACACGGCACTTGCTGAA
DmActin	CCCAAGGCCAACCGTGAGAA	CGGAGGCGTACAGCGAGAGC
DmERK	ATTTGCGACTTTGGATTGGCTC	TCTAAAGCCAACGCATCAGCAT
DmJNK	CAGCACCAACACTACACCGTCG	CATTTGGATGACCTGGCAGAGAT
DmDuox	CATTCCCCTGGACTCGCAC	TCGTGCGATTGGGTGGAC
DmNox	GCCGCAAACTGATTTCCTG	GTCTTCTTGATGCTGCGTATGC
DmArrestin-1	GCATCGCCGTTGAGGGTGATAT	CCTCGCATCCTGACTGGCAATA
DmArrestin-1	CGCCAATCTCACCAAGACCTTC	TCGTCCTTCAAGTGACCATCCA
The primers for double-strand RNA synthesis	**Upper primer**	**Lower primer**
GFP	TAATACGACTCACTATAGGGGTGAGCAAGGGCGAGGAG	TAATACGACTCACTATAGGGCATGATATAGACGTTGTGGCTGTT
AAEL004725	TAATACGACTCACTATAGGGCCACGGGGCCTCACAAACAG	TAATACGACTCACTATAGGGCTTACAGAACGGCGGAGGATGG
AAEL005432 (AaMesh)	TAATACGACTCACTATAGGGTTGGCCCCGACGAAATGAC	TAATACGACTCACTATAGGGACTCCGGCGCAAACACCAG
AAEL005982	TAATACGACTCACTATAGGGTTTTGAAGGAGGCCATAAGTGC	TAATACGACTCACTATAGGGTACGCCCAAGCTCAAAACCTAC
AAEL006355	TAATACGACTCACTATAGGGTGCGCTAGCCGGTCATTTCAT	TAATACGACTCACTATAGGGCGGCATAGTCGGGGCAACAT
AAEL006361	TAATACGACTCACTATAGGGCGGCGCGTTTCATTTCTCC	TAATACGACTCACTATAGGGGCGGCAGTCGACTCATCAGG
AAEL008069	TAATACGACTCACTATAGGGGCTACGGGCCGTGAAGAGTGTA	TAATACGACTCACTATAGGGTGGCTCCGATAGGCATAAGTCG
AAEL008929	TAATACGACTCACTATAGGGGGGGCAAAGATCAACCGAACAA	TAATACGACTCACTATAGGGAAGGCCGCACGACAGGACAG
AAEL009266	TAATACGACTCACTATAGGGGTGGGCCTCCGGGTAAGATTC	TAATACGACTCACTATAGGGTTCCCGGGTAAACGATGAGC
AAEL012452	TAATACGACTCACTATAGGGGTGCGCCCCATCATTCAACC	TAATACGACTCACTATAGGGCTCGCATCGGCTTCCCTCAA
AAEL014356	TAATACGACTCACTATAGGGCTGTGGCGTCGGCATAGAAGC	TAATACGACTCACTATAGGGAGGGCGCGTCCAACCATTT
AaArrestin-a	TAATACGACTCACTATAGGGGGCCTCCGAACAGATCTATCCA	TAATACGACTCACTATAGGGGCCTTGACTTTCTTCACCACCT
AaArrestin-b	TAATACGACTCACTATAGGGCTCCAAGGAGTTGGTCCTGTGC	TAATACGACTCACTATAGGGCGGTCTTGCGTGAGTTGTTCGT
AaJNK	TAATACGACTCACTATAGGGATTTGAGGTCCCTTCGCGGTACA	TAATACGACTCACTATAGGGAGATGACCTGGCACAGATT
AaERK	TAATACGACTCACTATAGGGAAGATGGTACCGAGCGCCG	TAATACGACTCACTATAGGGAGCGCCAGGGCTTCCTCGA
AaP38	TAATACGACTCACTATAGGGATCTGTTCTGCAACGGACA	TAATACGACTCACTATAGGGACCCGTAGAATCTGATAGA
AaPI3K	TAATACGACTCACTATAGGGCTCATCAACAACATCACCAATCTG	TAATACGACTCACTATAGGGTACTGGAAGTTGATAATCGGGTG
AaMyd88	TAATACGACTCACTATAGGGGGCGATTGGTGGTTGTTATT	TAATACGACTCACTATAGGGTTGAGCGCATTGCTAACATC
AaImd	TAATACGACTCACTATAGGGAAGGCCTTCTACCAATGTAA	TAATACGACTCACTATAGGGGCACAGTGTTTTAGACTTTC
AaAkt	TAATACGACTCACTATAGGGACCGTACGAGGCTGCCAG	TAATACGACTCACTATAGGGGTACGCGATTCTCGGCCA
AaDome	TAATACGACTCACTATAGGGCCATCTCCACCACGAAACTT	TAATACGACTCACTATAGGGCCGGTGGTTGCCATATAATC
DmArrestin-1	TAATACGACTCACTATAGGGGAGATGATCGGTCTGCGGTTCC	TAATACGACTCACTATAGGGTCTTCTCGCCGTGATGGTACAG
DmArrestin-2	TAATACGACTCACTATAGGGGGAGATGACACCGATGCAGGAG	TAATACGACTCACTATAGGGTGCTCTTCACGGACTTCTTGGA
AaNox	TAATACGACTCACTATAGGGGCTCAGCACGCCATTCTCATTG	TAATACGACTCACTATAGGGACACGGTCACTTTGCCCTTCTT
AaDuox	TAATACGACTCACTATAGGGAGCCCGGAGAGTTGTAGTAG	TAATACGACTCACTATAGGGGTTGAGCGCTCCCAGATC
The primers for generate *DmMesh-/-* Flies		
DmMesh-gRNA-1	TAATACGACTCACTATAGGTCTTTCCGATCAAGGACGTTTTAGAGCTAGAAATAGC	
DmMesh-gRNA-2	TAATACGACTCACTATAGGACGCCCGGTGTTTACTTCGTTTTAGAGCTAGAAATAGC	
DmMesh-gRNA-check	ATCCAACAATCTCCTCCTCTTACAGC	AAATGCCACGAGAAACAAGGG