Supplementary Tables and Figures

Supplementary Table 1. Selected differentially expressed genes between control and GMH treatment at three time points

	Day 10				Day 30				Day 50		
name	function	logFC [1]	FDR [2]	name	function	logFC	FDR	name	function	logFC	FDR
Swim	WG signaling	-0.5066	0.01496	CecA1	AMP [3]	2.732	1.81E-05	CecC	AMP	1.2539	1.02E-06
Socs36E	JAK/STAT & EGFR	-0.59	0.03549	LManVI	MMP [4]	1.1272	8.68E-38	CecA1	AMP	0.9497	0.00013
Ets21c	EGFR/ MAPK	-0.7393	0.0015	LManV	MMP	0.992	7.84E-19	AttC	AMP	0.7401	0.02805
Mkp3	EGFR/ MAPK	-0.9869	4.24E-10	LManIII	MMP	0.7395	7.90E-17	DptA	AMP	0.6725	0.02259
				Socs36E	JAK/STAT & EGFR	-0.6497	4.60E-09	PGRP-SB1	IMD signaling	0.7451	0.03088
				Ets21c	EGFR/ MAPK	-0.7395	3.41E-05	Socs36E	JAK/STAT & EGFR	-0.6141	0.01164
				AttD	AMP	-0.8592	0.00672	Swim	WG signaling	-0.6583	0.00048
				Upd3	JAK/STAT	-1.0442	0.00019	Upd3	JAK/STAT	-0.9782	3.65E-05
								Upd2	JAK/STAT	-1.5398	0.00108

Note. 1. logFC, log fold change; 2. FDR, false discovery rate; 3. AMP, antimicrobial peptide; 4. MMP, mannose metabolic process

Supplementary Table 2. GO enrichment categories on Day 50

| Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
☐	GOTERM_BP_DIRECT	antibacterial humoral response	RT		4	8.0	1.4E-4	2.2E-2
☐	GOTERM_BP_DIRECT	innate immune response	RT		5	10.0	7.7E-4	5.9E-2
☐	GOTERM_BP_DIRECT	humoral immune response	RT		3	6.0	3.5E-3	1.7E-1
☐	GOTERM_BP_DIRECT	response to bacterium	RT		3	6.0	1.1E-2	3.5E-1
☐	GOTERM_BP_DIRECT	intestinal epithelial structure maintenance	RT		2	4.0	1.5E-2	3.7E-1
☐	GOTERM_BP_DIRECT	defense response to bacterium	RT		3	6.0	1.6E-2	3.4E-1
☐	GOTERM_BP_DIRECT	defense response to Gram-positive bacterium	RT		3	6.0	1.7E-2	3.1E-1
☐	GOTERM_BP_DIRECT	immune response	RT		3	6.0	2.2E-2	3.6E-1
☐	GOTERM_BP_DIRECT	paracrine signaling	RT		2	4.0	2.9E-2	4.1E-1
☐	GOTERM_BP_DIRECT	JAK-STAT cascade	RT		2	4.0	4.8E-2	5.4E-1
☐	GOTERM_BP_DIRECT	defense response to Gram-negative bacterium	RT		3	6.0	7.4E-2	6.7E-1
☐	GOTERM_BP_DIRECT	regulation of JAK-STAT cascade	RT		2	4.0	7.6E-2	6.5E-1
☐	GOTERM_BP_DIRECT	positive regulation of JAK-STAT cascade	RT		2	4.0	9.0E-2	6.8E-1
☐	KEGG_PATHWAY	Hippo signaling pathway - fly	RT		2	4.0	9.7E-2	4.0E-1

Supplementary Figure 1. GMH extends lifespan in virgin female flies in strain of B18. (A) In replicate 1, the mean lifespan in control group is 58.76 days, and 74.91 days in GMH group, representing a significant increase by 27.48% (p= 0.0e+00). (B) In replicate 2, the mean lifespans are 59.92 and 70.37 days respectively in control and GMH groups, representing a significant increase by 17.44% (p= 1.9e-08).

(A) Replicate 1
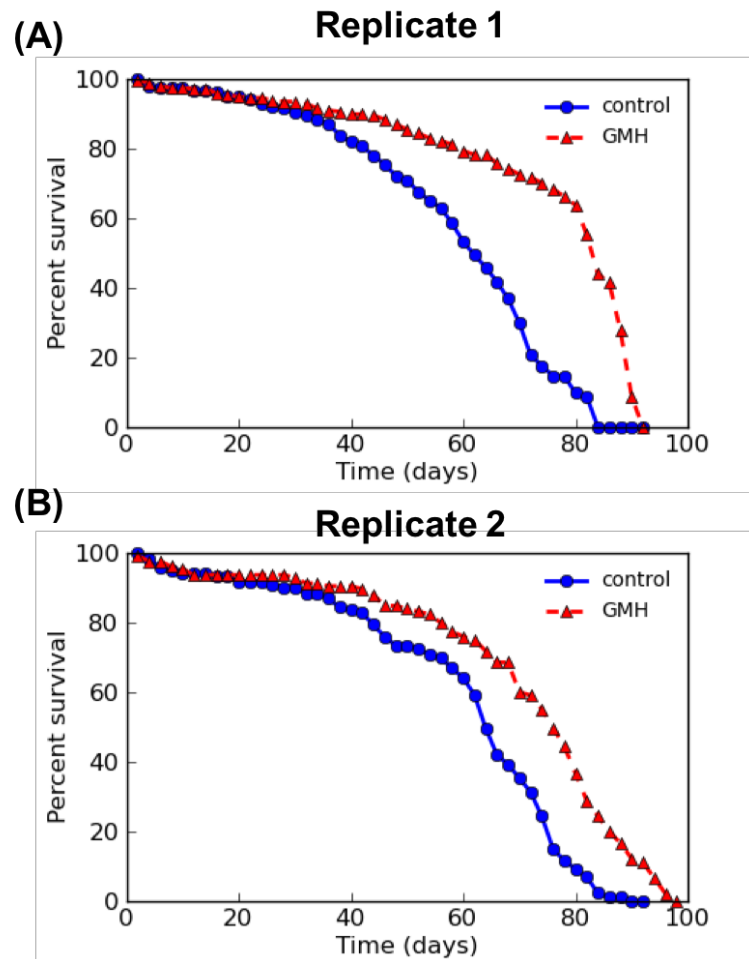
(B) Replicate 2

Supplementary Figure 2. The relative amount of food intake when flies are fed on control or GMH food. Flies used are mated females of stain B18. There are three biological replicates with 20 individual flies per replicate. Error bars represent standard errors. Please note that the food intake estimates here are only relative amounts.
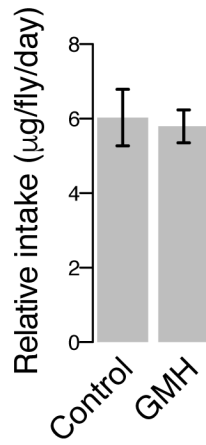
Supplementary Figure 3. The relative abundance of *Lactobacillus* and *Acetobacter* as measured in our 16S rRNA sequencing experiment. (A) There is no difference in the relative abundance of *Lactobacillus* between control and GMH groups from day 10 to day 30. On day 40, the relative abundance of *Lactobacillus* is significantly lower in GMH groups (FDR = 0.0049); (B) The relative abundance of *Acetobacter* increases along the process of aging in both control and GMH diets. At day 40, there is a trend that the relative abundance of *Acetobacter* in GMH group is higher than control group, but not significant.

(A)

(B)
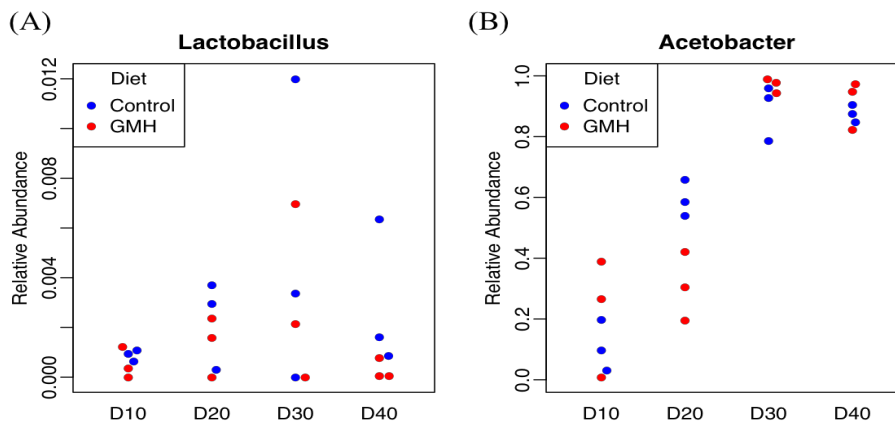
Supplementary Figure 4. The effect of age on gene expression

(A)Principle component analysis of the RNA-seq data had a clear separation of age; MA plot showed significant differentially expressed genes (B) between day 10 and day 30; and (C) day 30 and day 50.
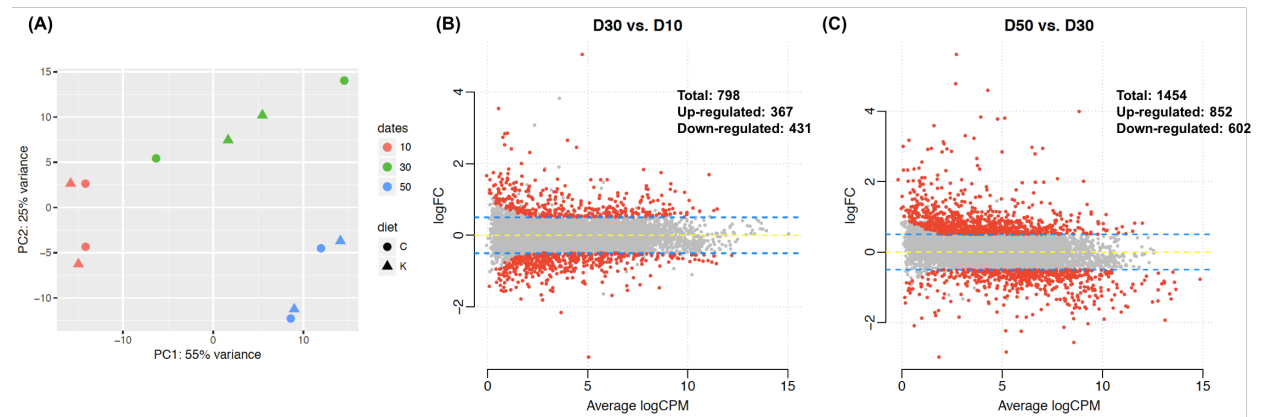
Supplementary Figure 5. Differentially expressed genes at day 10 and day 50

MA plot show significantly differentially expressed genes at (A) day 10 and (B) day 50
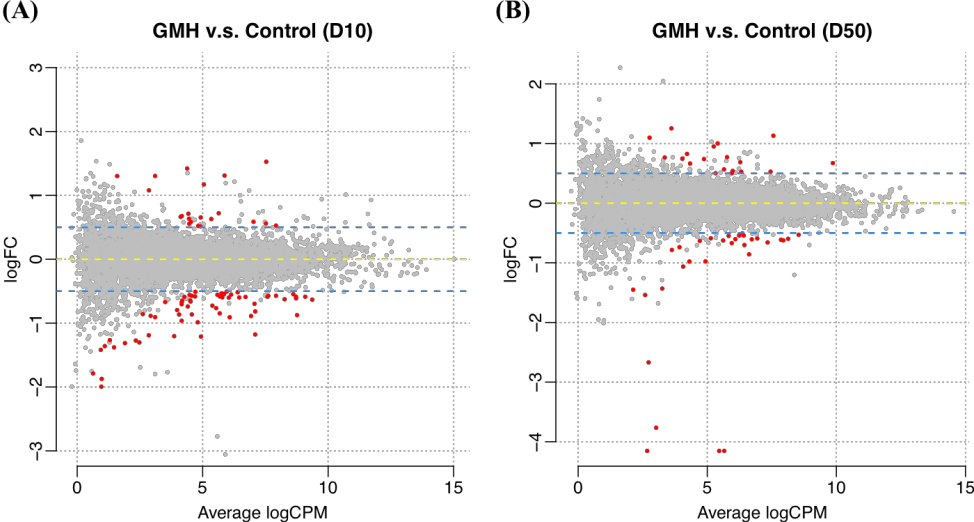
Supplementary Figure 6. Significantly up- and down-regulated pathways at different ages in GMH-treated groups in comparison to control groups

(A) The up-regulated pathways and (B) down-regulated pathways at day 30 comparing with day 10; (C) The up-regulated pathways and (D) down-regulated pathways at day 50 comparing with day 30.