

Table S1. Read statistics of 16s rRNA and metagenome sequencing.

Library	Sample name	Sample	Raw data	QIIME2
			Reads	Sequence variants
16s rRNA library	A16-16s	Aging (Week1)	759,054	192,011
	A17-16s		1,150,359	443,170
	A6-16s	Aging (Week4)	1,265,379	347,357
	A7-16s		656,935	113,601
	A8-16s		1,261,683	355,781
	A9-16s		790,104	214,215
	A1-16s	Aging (Week20)	339,830	80,670
	A2-16s		552,334	132,833
	A3-16s		1,234,048	266,863
	A4-16s		935,997	225,855
	A5-16s	Aging (Week50)	824,221	210,852
	A11-16s		400,141	85,757
	A12-16s		249,593	54,339
	A13-16s		258,439	21,617
	A14-16s		366,322	104,475
	A15-16s		183,029	45,305
	A24-16s	Aging (Week100)	453,212	115,669
	A25-16s		413,167	101,028
	A26-16s		369,154	83,746
	A27-16s		1,014,126	227,604
	A28-16s	Co-housing Co-Young	1,049,964	250,802
	C1-16s		136,575	26,169
	C2-16s		144,087	26,419
	C3-16s		161,722	35,917
	C4-16s		146,017	25,060
	C5-16s		136,247	35,962
	C6-16s		234,192	29,918
	C7-16s		151,688	35,025
	C8-16s	Co-housing Co-Aged	117,396	25,623
	C9-16s		61,853	15,597
	C10-16s		141,078	29,533
	C20-16s		124,279	28,113
	C30-16s		155,716	31,855

C40-16s		125,790	29,724
C50-16s		175,343	32,948
C60-16s		178,033	33,371
C70-16s		109,923	28,203
C80-16s		149,736	33,780
C90-16s		161,162	36,264
OY-Y1-16s	Parabiosis Hetero-Young	708,001	56,441
OY-Y2-16s		803,928	60,012
OY-Y3-16s		647,779	54,537
OY-Y4-16s		384,013	89,848
OY-Y5-16s		572,869	127,315
OY-O1-16s	Parabiosis Hetero-Aged	241,320	11,187
OY-O2-16s		848,270	68,856
OY-O3-16s		595,260	73,032
OY-O4-16s		936,483	109,548
YY1-16s	Parabiosis Iso-Young	244,059	42,432
YY2-16s		936,833	77,717
YY3-16s		357,921	77,464
YY4-16s		321,752	87,203
YY5-16s		423,085	131,791
YY6-16s		1,002,458	231,947
YY7-16s		843,748	251,719
YY8-16s		472,525	117,938
OO1-16s	Parabiosis Iso-Aged	346,107	24,283
OO2-16s		257,536	60,415
OO3-16s		614,589	117,453
OO4-16s		804,066	124,271
Serum-8iv-8-01	Serum-injection Young to Aged (iv8)	52,511	10,782
Serum-8iv-8-02		52,548	12,154
Serum-8iv-8-03		60,348	10,731
Serum-8iv-8-12		82,408	13,931
Serum-16iv-8-04		168,148	26,764
Serum-16iv-8-05		113,574	21,447
Serum-16iv-8-14		129,719	26,435
Serum-16iv-8-15		79,199	20,087
Serum-16iv-8-16		124,788	29,158
Serum-16iv-16-04		105,379	20,383

Serum-16iv-16-05	Serum-injection	130,625	23,848
Serum-16iv-16-14	Young to Aged (iv16)	138,906	32,002
Serum-16iv-16-15		103,904	24,414
Serum-16iv-16-16		133,815	30,396
YtoY8-11-16s	Serum-injection	35,055	3,844
YtoY8-1-16s	Young to Young (iv8)	34,296	4,650
YtoY8-2-16s		149,244	24,322
YtoY8-3-16s		35,811	5,061
YtoY8-4-16s		37,931	3,728
YtoY8-5-16s		67,985	2,877
YtoY8-6-16s		1,203,921	180,696
YtoY8-7-16s		67,991	14,843
YtoY8-8-16s		266,256	41,533
YtoY8-9-16s		32,111	4,712
YtoY16-6-16s	Serum-injection	75,277	14,950
YtoY16-7-16s	Young to Young (iv16)	93,962	14,791
YtoY16-8-16s		67,436	10,956
YtoY16-9-16s		280,909	39,441
OldAK10-16s	AK administration	77,667	12,796
OldAK11-16s		43,708	8,163
OldAK12-16s		84,655	12,802
OldAK13-16s		88,393	11,038
OldAK14-16s		94,523	11,737
OldAK15-16s		71,244	9,169
OldAK6-16s		74,236	8,232
OldAK8-16s		93,143	14,511
OldV1-16s		84,869	10,111
OldV1-2-16s		75,909	9,203
OldV2-16s	Vehicle only	78,558	7,642
OldV3-16s		1,392,223	140,351
OldV3-2-16s		86,657	13,307
OldV4-16s		99,173	13,187
OldV4-2-16s		91,077	13,251
OldV5-16s		60,100	7,125
OldV6-16s		64,499	8,814
OldV7-16s		84,257	10,306
OldV8-16s		79,722	9,094

Library	Sample name	Sample	Raw data		Quality control (MG-RAST)		Gene prediction		
			Reads	Length (bp)	QC failed	QC passed	Ribosomal RNA gene	Reads with known functions	Reads with unknown functions
Metagenome library	A16	Aging (Week1)	3,560,386	343	509,738	3,050,648	28,649 (1%)	1,421,743 (49.00%)	1,451,378 (50.02%)
	A17		2,139,136	336	217,117	1,922,019	14,543 (1%)	822,163 (45.41%)	973,808 (53.79%)
	A6	Aging (Week4)	3,410,794	352	271,348	3,139,446	21,691 (1%)	2,358,242 (75.12%)	759,513 (24.19%)
	A7		4,121,549	340	1,719,921	2,401,628	19,479 (1%)	2,142,346 (89.20%)	239,803 (9.99%)
	A8	Aging (Week20)	3,257,130	349	292,267	2,964,863	19,520 (1%)	2,504,308 (84.47%)	441,035 (14.88%)
	A9		3,494,225	344	359,280	3,134,945	22,700 (1%)	2,326,423 (74.21%)	785,822 (25.07%)
	A1		2,530,032	332	208,669	2,321,363	15,230 (1%)	1,953,110 (84.14%)	353,023 (15.21%)
	A2		2,129,405	323	203,776	1,925,629	11,907 (1%)	1,657,137 (86.06%)	256,585 (13.32%)
	A3		3,571,464	337	446,637	3,124,827	22,161 (1%)	2,732,726 (87.45%)	369,940 (11.84%)
	A4	Aging (Week50)	2,237,355	339	204,965	2,032,390	12,980 (1%)	1,734,577 (85.35%)	284,833 (14.01%)
	A5		6,104,820	339	997,235	5,107,585	39,944 (1%)	4,026,606 (78.84%)	1,041,035 (20.38%)
	A11		2,851,025	344	305,916	2,545,109	16,459 (1%)	2,065,831 (81.17%)	462,819 (18.18%)
	A12		3,004,109	331	362,321	2,641,788	30,009 (1%)	1810062 (68.52%)	801717 (31.48%)
	A13		2,717,098	342	317,153	2,399,945	20,116 (1%)	2,068,043 (86.17%)	311,786 (12.99%)
	A14	Aging (Week100)	3,255,758	340	366,123	2,889,635	22,518 (1%)	2,413,720 (83.53%)	453,397 (15.69%)
	A15		3,402,356	337	322,593	3,079,763	23,683 (1%)	2,632,194 (85.47%)	423,886 (13.76%)
	A24		2,639,380	342	196,877	2,442,503	22,404 (1%)	1,943,896 (79.59%)	476,203 (19.50%)
	A25		3,199,177	347	322,089	2,877,088	25,079 (1%)	2,416,682 (84.00%)	435,327 (15.13%)
	A26		2,701,511	346	18,205	2,683,306	27,196 (1%)	1,826,371 (68.06%)	829,739 (30.92%)
	A27	Co-housing Co-Young	3,204,270	345	378,430	2,825,840	26,685 (1%)	2,314,911 (81.92%)	484,244 (17.14%)
	A28		2,706,741	335	162,859	2,543,882	16,260 (1%)	2,043,088 (80.31%)	484,534 (19.05%)
	C3-1		5,304,841	349	22,864	5,281,977	44,904 (1%)	3,789,442 (71.74%)	1,447,631 (27.41%)
	C3-2		6,434,506	350	1,145,390	5,289,116	35,780 (1%)	4,364,857 (82.53%)	888,479 (16.80%)
	C3-3		4,995,904	349	665,744	4,330,160	28,582 (1%)	3,434,243 (79.31%)	867,335 (20.03%)
	C3-4	Co-Young	4,110,449	345	585,607	3,524,842	29,042 (1%)	3,079,448 (87.36%)	416,352 (11.81%)
	C3-5		3,783,779	355	264,617	3,519,162	23,702 (1%)	2,869,856 (81.55%)	625,604 (17.78%)
	C3-6		3,919,226	353	26,310	3,892,916	37,793 (1%)	2,844,970 (73.08%)	1,010,153 (25.95%)
	C6-4		4,887,579	354	635,065	4,252,514	30,725 (1%)	3,527,593 (82.95%)	694,196 (16.32%)
	C6-5		3,636,200	344	444,662	3,191,538	21,751 (1%)	2,532,198 (79.34%)	637,589 (19.98%)
	C6-6	C3-10	4,590,490	356	634,756	3,955,734	28,782 (1%)	3,383,726 (85.54%)	543,226 (13.73%)
	C3-10		3,879,336	343	563,100	3,316,236	22,988 (1%)	2,712,880 (81.81%)	580,368 (17.50%)

C3-20	Co-housing Co-Aged	4,019,805	349	450,110	3,569,695	24,463 (1%)	2,833,704 (79.38%)	711,528 (19.93%)
C3-30		4,293,989	342	355,692	3,938,297	26,848 (1%)	2,638,170 (66.99%)	1,273,279 (32.33%)
C3-40		5,207,190	356	715,748	4,491,442	32,847 (1%)	3,797,531 (84.55%)	661,064 (14.72%)
C3-50		3,371,812	339	495,800	2,876,012	23,001 (1%)	2,469,250 (85.86%)	383,761 (13.34%)
C3-60		4,117,093	355	672,978	3,444,115	27,561 (1%)	2,929,993 (85.07%)	486,561 (14.13%)
C6-40		4,769,955	355	564,531	4,205,424	28,499 (1%)	3,291,838 (78.28%)	885,087 (21.05%)
C6-50		4,753,125	354	791,629	3,961,496	28,559 (1%)	3,368,725 (85.04%)	564,212 (14.24%)
C6-60		3,582,024	350	366,398	3,215,626	21,477 (1%)	2,600,575 (80.87%)	593,574 (18.46%)
OY-Y1	Parabiosis	2,180,580	340	472,234	1,708,346	16,239 (1%)	1,061,871 (62.2%)	630,236 (36.9%)
OY-Y2	Hetero- Young	2,917,992	332	271,454	2,646,538	15,703 (1%)	2,215,383 (83.71%)	415,452 (15.70%)
OY-Y3		3,058,229	353	170,662	2,887,567	10,957 (0%)	2,299,215 (79.62%)	577,395 (20.00%)
OY-Y4		3,729,589	355	424,488	3,305,101	18,008 (1%)	2,586,649 (78.26%)	700,444 (21.19%)
OY-O1	Parabiosis	3,097,182	352	249,950	2,847,232	13,719 (0%)	2,326,082 (81.70%)	507,431 (17.82%)
OY-O2	Hetero- Aged	3,123,240	358	245,255	2,877,985	14,391 (1%)	2,312,513 (80.35%)	551,081 (19.15%)
OY-O3		3,679,412	337	454,741	3,224,671	21,110 (1%)	2,664,721 (82.64%)	538,840 (16.71%)
OY-O4		3,051,665	344	562,028	2,489,637	14,982 (1%)	2,169,167 (87.13%)	305,488 (12.27%)
YY1	Parabiosis	3,551,312	331	420,458	3,130,854	17,855 (1%)	2,592,275 (82.80%)	520,724 (16.63%)
YY2	Iso- Young	4,122,268	339	590,168	3,532,100	22,458 (1%)	2,788,258 (78.94%)	721,384 (20.42%)
YY3		3,464,376	354	441,214	3,023,162	13,557 (0%)	2,540,286 (84.03%)	469,319 (15.52%)
YY4		2,867,284	346	426,913	2,440,371	15,759 (1%)	1,777,407 (72.83%)	647,205 (26.52%)
YY5		3,411,914	337	685,459	2,726,455	18,614 (1%)	2,435,826 (89.34%)	272,015 (9.98%)
YY6		2,583,837	341	396,743	2,187,094	12,199 (1%)	1,702,211 (77.83%)	472,684 (21.61%)
YY7		3,243,403	335	376,260	2,867,143	19,629 (1%)	2,400,790 (83.73%)	446,724 (15.58%)
YY8		2,869,815	346	200,834	2,668,981	17,195 (1%)	2,185,405 (81.88%)	466,381 (17.47%)
OO1	Parabiosis	2,860,930	348	214,156	2,646,774	16,565 (1%)	2,084,371 (78.75%)	545,838 (20.62%)
OO2	Iso-Aged	3,427,569	347	303,219	3,124,350	17,744 (1%)	2,501,399 (80.06%)	605,207 (19.37%)
OO3		4,701,302	348	433,376	4,267,926	36,411 (1%)	2,742,438 (64.26%)	1,489,077 (34.89%)
OO4		3,142,834	343	796,861	2,345,973	14,313 (1%)	1,955,698 (83.36%)	375,962 (16.03%)
8iv 8 1	Serum- injection Young to Aged (iv8)	1,912,853	345	130,366	1,782,487	14,557 (1%)	1,477,597 (82.90%)	290,333 (16.29%)
8iv 8 2		2,472,280	354	174,082	2,298,198	18,245 (1%)	1,918,185 (83.46%)	361,768 (15.74%)
8iv 8 3		2,418,510	356	265,359	2,153,151	21,081 (1%)	1,870,437 (86.87%)	261,633 (12.15%)
16iv 8 4		2,340,729	359	372,729	1,968,000	14,624 (1%)	1,749,409 (88.89%)	203,967 (10.36%)
16iv 8 5		2,099,592	359	132,992	1,966,600	14,097 (1%)	1,576,877 (80.18%)	375,626 (19.10%)
8iv 8 12		2,672,682	360	321,469	2,351,213	22,648 (1%)	2,058,772 (87.56%)	269,793 (11.47%)
8iv 8 13		2,365,721	368	144,808	2,220,913	15,747 (1%)	1,837,940 (82.76%)	367,226 (16.53%)
16iv 8 14		2,436,675	366	231,289	2,205,386	15,633 (1%)	1,837,062 (83.30%)	352,691 (15.99%)
16iv 8 15		2,877,990	363	194,542	2,683,448	17,605 (1%)	2,232,463 (83.19%)	433,380 (16.15%)

16iv 8 16		2,271,201	374	153,746	2,117,455	14,798 (1%)	1,746,809 (82.50%)	355,848 (16.81%)
16iv 16 4	Serum-injection	2,166,725	360	538,625	1,628,100	13,273 (1%)	1,333,534 (81.91%)	281,293 (17.28%)
16iv 16 5		2,421,420	358	162,291	2,259,129	15,935 (1%)	1,850,447 (81.91%)	392,747 (17.38%)
16iv 16 14	Young to Aged (iv16)	2,236,312	355	147,466	2,088,846	12,486 (1%)	1,725,304 (82.60%)	351,056 (16.81%)
16iv 16 15		1,921,825	353	170,866	1,750,959	13,151 (1%)	1,472,887 (84.12%)	264,921 (15.13%)
16iv 16 16		1,892,504	371	93,668	1,798,836	11,033 (1%)	1,513,903 (84.16%)	273,900 (15.23%)
Y-to-Y-8-1	Serum-injection	2,066,695	349	307,783	1,758,912	11,421 (1%)	1,492,265 (84.84%)	255,226 (14.51%)
Y-to-Y-8-2		2,179,868	353	191,875	1,987,993	14,337 (1%)	1,681,811 (84.60%)	291,845 (14.68%)
Y-to-Y-8-3	Young to Young (iv8)	1,870,502	355	146,946	1,723,556	11,627 (1%)	1,384,635 (80.34%)	327,294 (18.99%)
Y-to-Y-8-4		1,895,983	352	184,783	1,711,200	10,563 (1%)	1,437,355 (84.00%)	263,282 (15.39%)
Y-to-Y-8-5		1,644,941	346	120,756	1,524,185	12,343 (1%)	1,240,560 (81.39%)	271,282 (17.80%)
Y-to-Y-8-6		1,946,742	346	218,461	1,728,281	13,029 (1%)	1,449,903 (83.89%)	265,349 (15.35%)
Y-to-Y-8-7		1,728,684	348	193,256	1,535,428	12,232 (1%)	1,321,475 (86.07%)	201,721 (13.14%)
Y-to-Y-8-8		1,532,361	347	95,417	1,436,944	10,725 (1%)	1,143,377 (79.57%)	282,842 (19.68%)
Y-to-Y-8-9		2,174,361	355	185,794	1,988,567	17,134 (1%)	1,663,136 (83.63%)	308,297 (15.50%)
Y-to-Y-8-11		2,156,026	357	143,179	2,012,847	13,179 (1%)	1,679,420 (83.44%)	320,248 (15.91%)
Y-to-Y-16-6	Serum-injection	1,722,630	356	110,209	1,612,421	14,114 (1%)	1,227,640 (76.14%)	370,667 (22.99%)
Y-to-Y-16-7	Young to Young (iv16)	1,990,069	354	129,461	1,860,608	14,265 (1%)	1,547,912 (83.19%)	298,431 (16.04%)
Y-to-Y-16-8		1,811,045	349	101,826	1,709,219	12,348 (1%)	1,316,342 (77.01%)	380,529 (22.26%)
Y-to-Y-16-9		1,918,704	355	123,092	1,795,612	12,770 (1%)	1,405,767 (78.29%)	377,075 (21.00%)
22w-ak5	AK administration	2,183,447	353	138,544	2,044,903	15,219 (1%)	1,640,051 (80.20%)	389,633 (19.05%)
22w-ak6		1,514,569	350	69,671	1,444,898	9,783 (1%)	1,153,210 (79.81%)	281,905 (19.51%)
22w-ak8		1,669,728	347	74,075	1,595,653	9,434 (1%)	1,225,607 (76.81%)	360,612 (22.60%)
22w-ak9		1,702,860	351	89,830	1,613,030	9,527 (1%)	1,275,397 (79.07%)	328,106 (20.34%)
22w-ak10		1,323,462	354	66,282	1,257,180	8,074 (1%)	983,720 (78.25%)	265,386 (21.11%)
22w-ak11		1,602,441	352	68,439	1,534,002	11,785 (1%)	1,242,965 (81.03%)	279,252 (18.20%)
22w-ak12		1,597,264	351	98,369	1,498,895	10,684 (1%)	1,160,267 (77.41%)	327,944 (21.88%)
22w-ak13		1,538,080	354	81,352	1,456,728	9,733 (1%)	1,188,712 (81.60%)	258,283 (17.73%)
22w-ak14		1,478,840	348	96,728	1,382,112	9,211 (1%)	1,150,819 (83.27%)	222,082 (16.07%)
22w-ak15		1,853,018	360	105,009	1,748,009	13,007 (1%)	1,407,528 (80.52%)	327,474 (18.73%)
22w-v1-2	Vehicle only	1,810,233	343	93,578	1,716,655	12,916 (1%)	1,337,694 (77.92%)	366,045 (21.32%)
22w-v1		1,885,415	356	95,510	1,789,905	11,029 (1%)	1,415,062 (79.06%)	363,814 (20.33%)

22w-v2	2,029,327	353	135,408	1,893,919	15,546 (1%)	1,383,610 (73.06%)	494,763 (26.12%)
22w-v3-2	1,400,108	346	82,932	1,317,176	10,451 (1%)	1,047,458 (79.52%)	259,267 (19.68%)
22w-v3	1,951,734	333	137,928	1,813,806	9,242 (1%)	1,365,775 (75.30%)	438,789 (24.19%)
22w-v4-2	2,028,839	347	109,633	1,919,206	13,861 (1%)	1,546,140 (80.56%)	359,205 (18.72%)
22w-v4	1,369,663	351	80,941	1,288,722	8,110 (1%)	987,545 (76.63%)	293,067 (22.74%)
22w-v5	1,319,988	347	70,657	1,249,331	10,217 (1%)	1,014,900 (81.24%)	224,214 (17.95%)
22w-v6	1,621,916	348	107,813	1,514,103	10,766 (1%)	1,206,625 (79.69%)	296,712 (19.60%)
22w-v7	1,733,476	346	82,226	1,651,250	11,178 (1%)	1,298,632 (78.65%)	341,440 (20.68%)
22w-v8	1,454,574	347	81,121	1,373,453	9,221 (1%)	1,075,752 (78.32%)	288,480 (21.00%)