

**Supplementary Figure 1.** (a-e) Relative expression levels of TNF- $\alpha$ , IL-6, IL-10, IL-12, and IL-1 $\beta$  in colon tissues. (f, g) Serum concentrations of TNF- $\alpha$  and IL-6.

**Supplementary Figure 2.** (a) KEGG pathway enrichment bubble plot of the gut microbiota. (b) Volcano plot of differentially abundant metabolites in the Old vs. Young comparison, identifying 235 significantly altered compounds (116 upregulated, 119 downregulated). (c, d) Heatmaps displaying the top 30 differentially abundant metabolites in the (c) Old vs. Young and (d) PSPA vs. Old comparisons. (e) KEGG pathway enrichment bubble plot of differential metabolites in the Old vs. Young comparison (screened by VIP > 1.0 and p < 0.05). (f) Correlation heatmap illustrating the associations between differential microbial taxa and differential metabolites.

**Supplementary Figure 3.** Both naturally aged colonic organoids and those treated in the continuous presence of 0.5 mM AAPH were co-treated with varying concentrations of PSPAs for 72 h. (a) Relative mRNA levels of Atg5, Atg10, Atg12, and Atg101. (b) Relative mRNA levels of Atg5, Atg10, Atg12, and Atg101.

**Supplementary Figure 4.** (a) Volcano plot of differentially expressed genes between Young and Old groups. (b) Heatmap of differentially expressed genes between Young and Old groups. (c) Venn diagram of differential genes among different comparisons. (d) Clustered heatmap of correlations between differential genes and differential metabolites.

**Table S1.** Nutritional composition table

	gm%	kcal%
Protein	14	15.2
Fat	4	9.7
Carbohydrate	67.9	75.1
Total	-	100
kcal/gm	3.81	-

**Table S2.** Feed formula

Ingredient	gm	kcal
Casein, 30 Mesh	140	560
L-Cystine	1.8	7.2
Corn Starch	465.7	1862.82
Maltodextrin	155	620
Sucrose	100	400
Soybean Oil	40	360
Cellulose	50	0
Mineral Mix (AIN-93M-MX)	35	0
Vitamin Mix (AIN-93-VX)	10	40
Choline Bitartrate	2.5	0
Tert-Butylhydroquinone	0.008	0
Total	1000.008	3850.02

**Table S3.** Primers names and sequences.

Primer	Sequence(5'→3')
TNF- $\alpha$	F: CACCATGAGCACAGAAAGCA R: TAGACAGAAGAGCGTGGTGG
Gapdh	F: GCATGGCCTTCCGTGTTCCCTA R: GATGCCTGCTTCACCACCTTCT
Zo-1	F: GGAGATGTTTATGCGGACGG R: CCATTGCTGTGCTCTTAGCG
Occludin	F: TTGAAAGTCCACCTCCTTACAGA R: CCGGATAAAAAGAGTACGCTGG
Claudin-3	F: GTACAAGACGAGACGGCCAA R: CGTACAACCCAGCTCCCATC
Muc2	F: CTGACCAAGAGCGAACACAA R: CATGACTGGAAGCAACTGGA
Lgr5	F: GAGTCAACCCAAGCCTTAGTATCC R: CATGGGACAAATGCAACTGAAG
Ki67	F: CAGTACTCGGAATGCAGCAA R: CAGTCTTCAGGGGCTCTGTC
ChgA	F: CGATCCAGAAAGATGATGGTC R: CGGAAGCCTCTGTCTTTCC
Ccnd1	F: AGGCGGATGAGAACAAGCAGAC R: TGGAGGGTGGGTGGAAATGAAC
Cdk4	F: AGGACCTGAGGACATACCTGGAC R: GCCGCTTAGAACTGACGCATTAG
Cdkn1a	F: CGAGAACGGTGGAACCTTGACTTC R: CGGGACCCAGGGCTCAGG
Axin2	F: GCAGGCTGGCAGAGGTGTC R: CTTGGGTTGGCGAAGGGTGAG
Atoh1	F: CTTGCCGACTCGCTTCTCAG R: TCTGTGCCATCATCGCTGTTAGG
Atg5	F: AAAGATGTGCTTCGAGATGTGT R: CACTTTGTCAGTTACCAACGTCA
Atg10	F: CATCTCACCAGATCTCAAGAAGGA R: CGACATGCGTAAGCAACGTT
Atg12	F: CTGCTGGCGACACCAAGAAA R: CGTGTTGCTCTACTGCCC
Atg101	F: GGAGGTGTGGACTGTCAAGG R: ACACGTTGTCCACCTCTGAC
p16	F: CGGTATCTACTCTCCTCCGC R: GTTGCCAGAAGTGAAGCCAA
P21	F: TCCACAGCGATATCCAGACA R: GGACATCACCAGATTGGAC

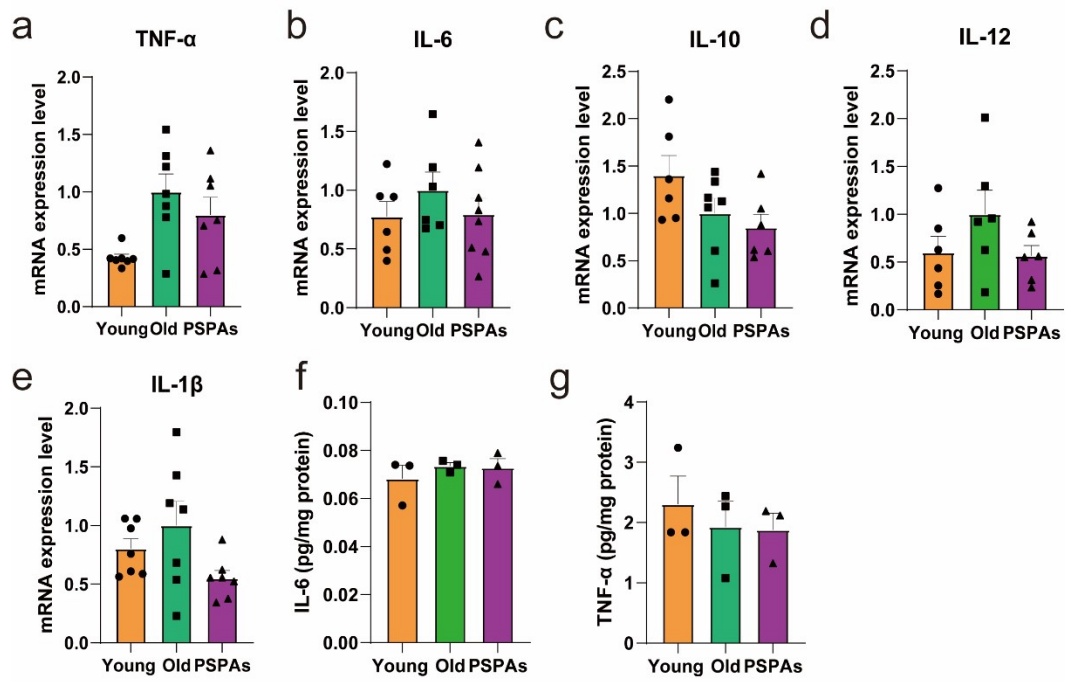
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IL-6	F: TACCACTCCCAACAGACCTG R: GGTACTCCAGAAACCAGAGG
IL-10	F: GAAGACCCTCAGGATGCG R: CCAAGGAGTTGTTTCCGTTA
IL-12	F: AGTGACATGTGGAATGGCGT R: CAGTTCAATGGGCAGGGTCT
IL-1 $\beta$	F: ACTCATTGTGGCTGTGGAGA R: TTGTTTCATCTCGGAGCCTGT

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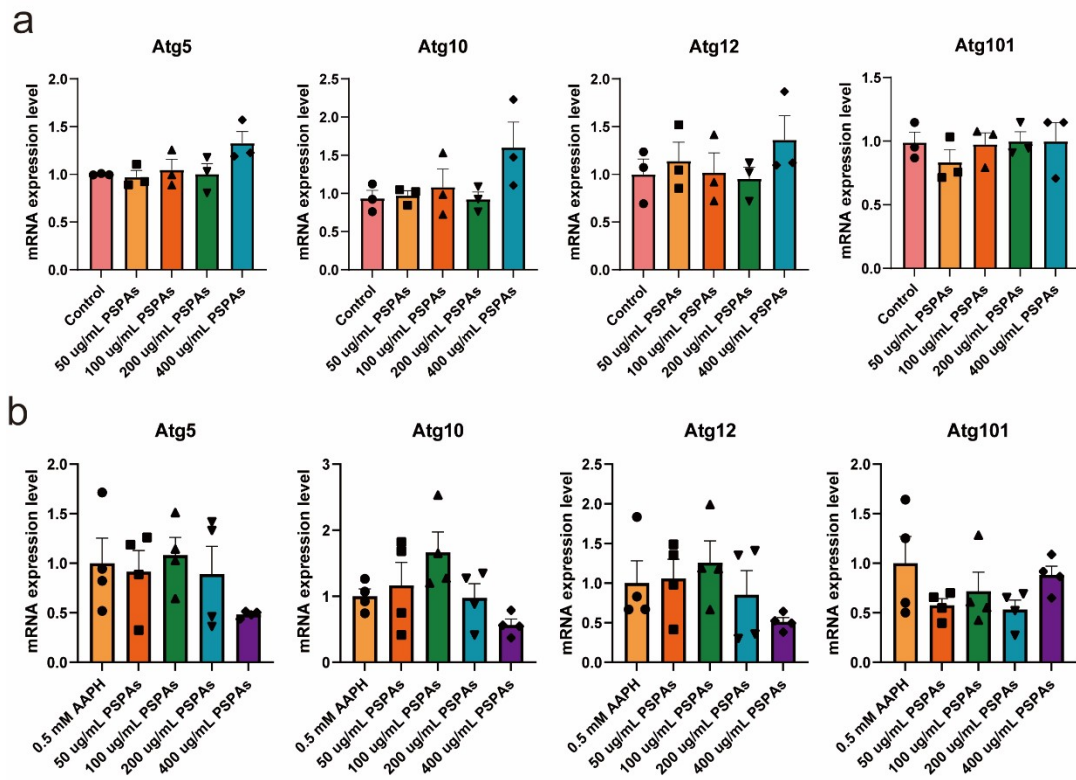
**Table S3.** Primers names and sequences (continued Table).

Supplementary Figure 1.



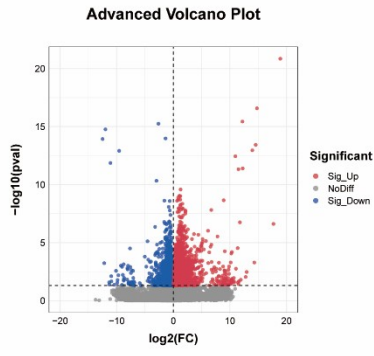


Supplementary Figure 3.

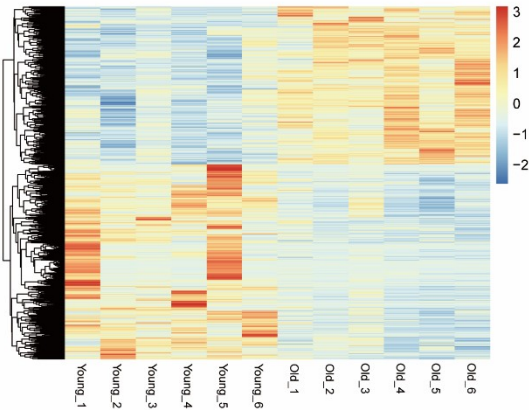


# Supplementary Figure 4.

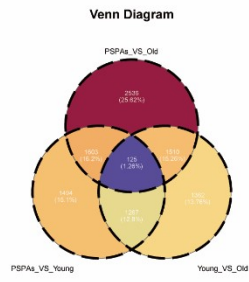
a



b



c



d

