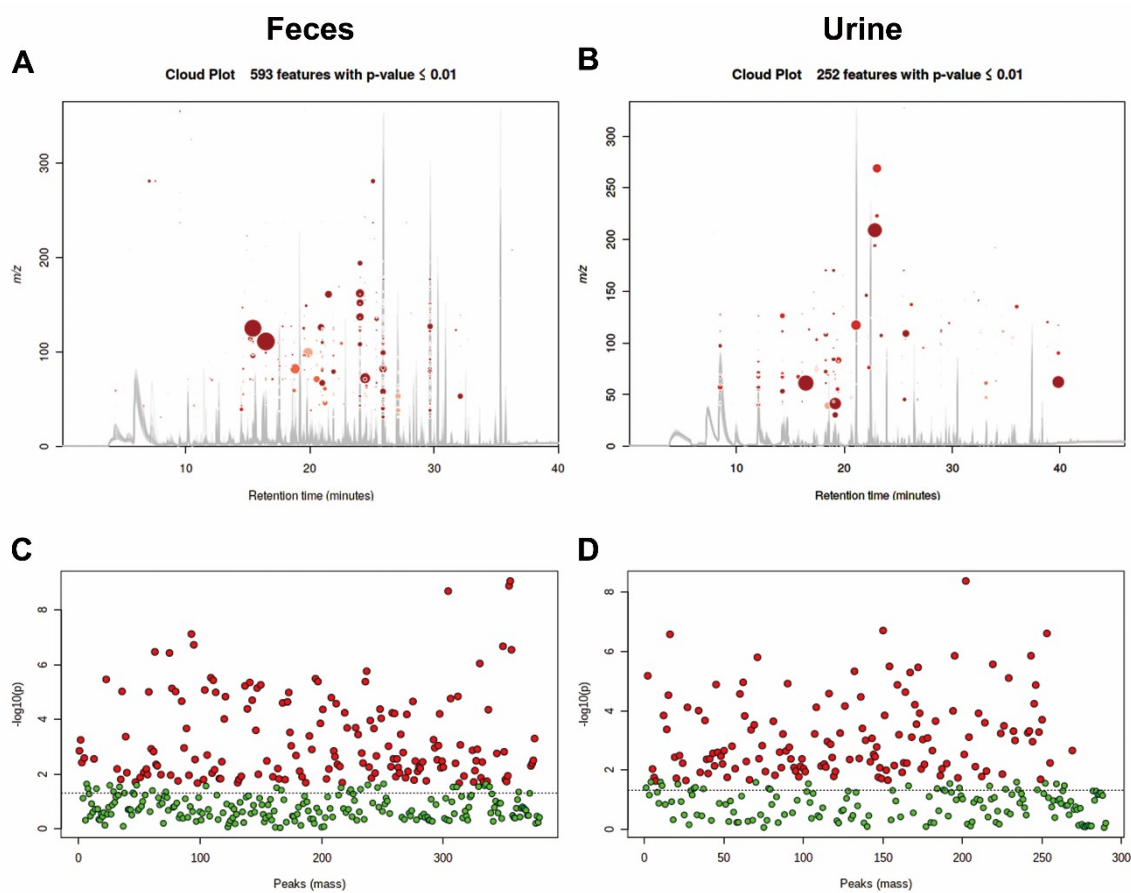


### Supplementary Figure:



**Figure S1**

Figure S1. Different treatment changed metabolites in senescence accelerated mice, significant features were shown in XCMS cloud plots of feces (A) and urine (B) with p-value ≤ 0.01. Important features of feces (C) and urine (D) selected by ANOVA plot with p-value < 0.05 by MetaboAnalyst.

## Supplementary Table:

**Table S1:**

Table S1. Body weight and organ/body weight index of mice

Group	4 month	6 month	Organ/body weight index (g/100g body weight)			
	Initial (g)	Final (g)	Heart	Liver	Spleen	Kidney
SAMR1	28.29±2.90	31.49±1.63 <sup>###</sup>	0.800±0.112	5.084±0.270	0.278±0.053	1.692±0.290
SAMP8	27.55±2.22	29.90±2.04 <sup>##</sup>	0.880±0.159	5.803±0.522 <sup>**</sup>	0.270±0.040	1.800±0.231
Donepezil	28.34±1.97	28.47±1.53	0.929±0.134	5.776±0.518 <sup>**</sup>	0.473±0.217	1.737±0.229
Metformin	27.26±2.17	30.08±2.18 <sup>##</sup>	0.893±0.249	5.594±0.399 <sup>**</sup>	0.421±0.292	1.740±0.175
Cy3Gal	28.66±1.40	30.38±1.27	0.850±0.113	5.400±0.176 <sup>*</sup>	0.367±0.167	1.701±0.265
Cy3Gal+Met	28.04±2.23	29.88±0.90 <sup>#</sup>	0.808±0.133	5.580±0.233 <sup>*</sup>	0.320±0.072	1.899±0.114

Compare with the body weight of 4 month and 6 month, #  $P < 0.05$ , ##  $P < 0.01$ , ###  $P < 0.001$

Compare with SAMR1 group, \*  $P < 0.05$ , \*\*  $P < 0.01$

**Table S2**

Table S2. Number of peak pairs of feces and urine samples from GC-MS.

Sample name	peak pair number	Sample name	peak pair number
Feces-SAMR1-1	1971	Urine-SAMR1-1	999
Feces-SAMR1-2	1713	Urine-SAMR1-2	850
Feces-SAMR1-3	1875	Urine-SAMR1-3	759
Feces-SAMR1-4	1605	Urine-SAMR1-4	776
Feces-SAMR1-5	1849	Urine-SAMR1-5	891
Feces-SAMR1-6	1768	Urine-SAMR1-6	876
Feces-SAMP8-1	1692	Urine-SAMP8-1	900
Feces-SAMP8-2	1983	Urine-SAMP8-2	927
Feces-SAMP8-3	2068	Urine-SAMP8-3	916
Feces-SAMP8-4	1754	Urine-SAMP8-4	885
Feces-SAMP8-5	2097	Urine-SAMP8-5	919
Feces-SAMP8-6	1945	Urine-SAMP8-6	1069
Feces-Donepezil-1	2012	Urine-Donepezil-1	992
Feces-Donepezil-2	1527	Urine-Donepezil-2	796
Feces-Donepezil-3	1513	Urine-Donepezil-3	888
Feces-Donepezil-4	1991	Urine-Donepezil-4	961
Feces-Donepezil-5	2027	Urine-Donepezil-5	929
Feces-Donepezil-6	1682	Urine-Donepezil-6	1056
Feces-Metformin-1	2105	Urine-Metformin-1	947
Feces-Metformin-2	1753	Urine-Metformin-2	1031
Feces-Metformin-3	1781	Urine-Metformin-3	925
Feces-Metformin-4	1604	Urine-Metformin-4	927
Feces-Metformin-5	1943	Urine-Metformin-5	981
Feces-Metformin-6	1728	Urine-Metformin-6	892
Feces-Cy3Gal-1	1837	Urine-Cy3Gal-1	822
Feces-Cy3Gal-2	2302	Urine-Cy3Gal-2	989
Feces-Cy3Gal-3	2205	Urine-Cy3Gal-3	909
Feces-Cy3Gal-4	1863	Urine-Cy3Gal-4	834
Feces-Cy3Gal-5	2192	Urine-Cy3Gal-5	909
Feces-Cy3Gal-6	2039	Urine-Cy3Gal-6	1002
Feces-Cy3Gal+Met-1	1849	Urine-Cy3Gal+Met-1	866
Feces-Cy3Gal+Met-2	1735	Urine-Cy3Gal+Met-2	972
Feces-Cy3Gal+Met-3	2090	Urine-Cy3Gal+Met-3	812
Feces-Cy3Gal+Met-4	1812	Urine-Cy3Gal+Met-4	880
Feces-Cy3Gal+Met-5	1639	Urine-Cy3Gal+Met-5	876
Feces-Cy3Gal+Met-6	2075	Urine-Cy3Gal+Met-6	886

**Table S3**

Table S3 The VIP compounds of PLS-DA model of feces samples

VIP	Feature name	RT (min)	RI <sup>a</sup>	Metabolite	Characteristic ion	ID <sup>b</sup>	CAS	Formula	Category	HMDB ID
1	M31T19	19.195	1610	Butyric acid	60, 73	A	107-92-6	C <sub>4</sub> H <sub>8</sub> O <sub>2</sub>	Carboxylic acids	HMDB0000039
2	M32T6	5.936	-	-	32	-	-	CH <sub>4</sub> O	-	-
3	M69T24	24.006	1858	6,10-dimethyl-5,9-Undecadien-2-one	43, 69	A	3796-70-1	C <sub>13</sub> H <sub>22</sub> O	Ketones	HMDB0031846
4	M60T19	15.625	1449	Acetic acid	43, 45	A	64-19-7	C <sub>2</sub> H <sub>4</sub> O <sub>2</sub>	Carboxylic acids	HMDB0000042
5	M109T25	25.356	1958	6,10-dimethyl-5,9-Undecadien-2-ol	109, 69	B	53837-34-6	C <sub>13</sub> H <sub>24</sub> O	Alcohols	-
6	M67T25	24.508	1883	3,3-dimethyl-1,5-Heptadiene	69, 41	C	67682-47-7	C <sub>9</sub> H <sub>16</sub>	Hydrocarbons	-
7	M81T26	25.871	-	-	81	-	-	-	-	-
8	M74T25	24.933	1906	Methyl isomyristate	74, 87	B	1731-88-0	C <sub>14</sub> H <sub>28</sub> O <sub>2</sub>	Esters	-
9	M117T35	35.338	2467	Indole	117, 90	A	120-72-9	C <sub>8</sub> H <sub>7</sub> N	Nitrogen-containing Carboxylic acids	HMDB0000738
10	M45T21	21.464	1725	Pentanoic acid	60, 73	A	109-52-4	C <sub>5</sub> H <sub>10</sub> O <sub>2</sub>	Carboxylic acids	-
11	M87T25	30.897	2225	Palmitic acid	74, 87	A	112-39-0	C <sub>17</sub> H <sub>34</sub> O <sub>2</sub>	Esters	HMDB0061859
12	M123T29	29.042	-	-	123	-	-	-	-	-
13	M154T26	25.841	-	-	154	-	-	-	-	-
14	M85T20	19.833	1642	Methyl pentadecanoate	57, 71	B	1921-70-6	C <sub>19</sub> H <sub>40</sub>	Hydrocarbons	HMDB0034497
15	M95T25	25.351	-	-	95	-	-	-	-	-

a Retention indices on a polyethylene glycol (PEG) column.

b Reliability of the identification proposal: A, identified, mass spectrum and RI agreed with standards; B, tentatively identified, mass spectrum agreed with the mass spectral database and RI agreed with literature data; C, tentatively identified, mass spectrum agreed with the mass spectral database.

**Table S4**

Table S4 The VIP compounds of PLS-DA model of urine samples

VIP	Feature name	RT (min)	RI <sup>a</sup>	Metabolite	Characteristic ion	ID <sup>b</sup>	CAS	Formula	Category	HMDB ID
1	M31T23	22.675	1480	2-ethyl-1-Hexanol	57, 43	A	104-76-7	C <sub>8</sub> H <sub>18</sub> O	Alcohols	HMDB0031231
2	M126T19	19.36	1338	6-methyl-5-Hepten-2-one	43, 41	B	110-93-0	C <sub>8</sub> H <sub>14</sub> O	Ketones	HMDB0035915
3	M32T7	7.334	-	-	32	-	-	CH <sub>4</sub> O	-	-
4	M41T24	23.933	1539	Linalool	71, 93	A	78-70-6	C <sub>10</sub> H <sub>18</sub> O	Alcohols	HMDB0036100
5	M57T25	24.966	1590	Hexadecane	57, 71	A	544-76-3	C <sub>16</sub> H <sub>34</sub>	Hydrocarbons	HMDB0033792
6	M97T29	28.977	-	2,3-dimethyl-Undecane	97, 71	C	17312-77-5	C <sub>13</sub> H <sub>28</sub>	Hydrocarbons	-
7	M69T26	26.46	1651	(E)- $\beta$ -Famesene	69, 41	B	18794-84-8	C <sub>15</sub> H <sub>24</sub>	Hydrocarbons	HMDB0062763
8	M111T12	12.002	1072	2-ethyl-2-Hexenal	55, 41	C	645-62-5	C <sub>8</sub> H <sub>14</sub> O	Aldehydes	HMDB0061945
9	M67T22	22.486	1471	4-methyl-2-propyl-Furan	95, 67	C	6148-37-4	C <sub>8</sub> H <sub>12</sub> O	Ethers	-
10	M191T37	37.41	2312	2,4-Di-tert-butylphenol	191, 57	A	96-76-4	C <sub>14</sub> H <sub>22</sub> O	Phenols	HMDB0013816
11	M45T27	26.794	1671	2,4,5-Trithiahexane	61, 45	B	42474-44-2	C <sub>3</sub> H <sub>8</sub> S <sub>3</sub>	Sulfur-containing	HMDB0031875
12	M111T32	31.894	1968	1-Dodecanol	55, 43	A	112-53-8	C <sub>12</sub> H <sub>26</sub> O	Alcohols	HMDB0011626
13	M96T26	25.991	-	Levomenthol	95, 71	C	2216-51-5	C <sub>10</sub> H <sub>20</sub> O	Alcohols	HMDB0003352
14	M59T22	22.195	-	N-methyl-Formamide	59, 30	C	123-39-7	C <sub>2</sub> H <sub>5</sub> NO	Diverse functional groups	HMDB0001122
15	M107T36	35.542	2193	4-ethyl-Phenol	107, 122	A	123-07-9	C <sub>8</sub> H <sub>10</sub> O	Phenols	HMDB0029306

a Retention indices on a polyethylene glycol (PEG) column.

b Reliability of the identification proposal: A, identified, mass spectrum and RI agreed with standards; B, tentatively identified, mass spectrum agreed with the mass spectral database and RI agreed with literature data; C, tentatively identified, mass spectrum agreed with the mass spectral database.