Electronic Supplementary Material (ESI) for Molecular BioSystems.

Table S1 Statistical Parameters and Chemical identifiers of key early-response metabolites for radiation exposure at different time points after irradiation.

Name	HMDB	KEGG	p value			FDR		
			5h	24h	48h	5h	24h	48h
Guaiacol	HMDB01398	C01502	3.53E-08	4.97E-05	8.59E-04	5.27E-07	7.78E-04	9.62E-09
Fumaric acid	HMDB00134	C00122	4.39E-01	8.45E-12	2.71E-09	4.87E-01	1.05E-09	4.46E-08
Pelargonic acid	HMDB00847	C01601	5.45E-01	2.64E-10	1.68E-06	5.83E-01	2.17E-08	1.17E-05
Hydroxyphenyllactic acid	HMDB00755	C03672	5.44E-05	4.30E-04	3.57E-08	3.70E-04	5.44E-03	4.69E-07
Malic acid	HMDB00744	C00711	1.98E-01	1.50E-09	6.15E-05	2.62E-01	8.21E-08	2.13E-04
Pyroglutamic acid	HMDB00267	C01879	8.01E-06	3.67E-04	3.13E-01	6.94E-05	4.83E-03	3.71E-01
Succinic acid	HMDB00254	C00042	2.49E-01	6.18E-04	1.80E-03	3.06E-01	6.77E-03	4.10E-03
Pimelic acid	HMDB00857	C02656	3.46E-02	3.67E-03	6.24E-06	7.02E-02	2.32E-02	3.50E-05
Adipic acid	HMDB00448	C06104	5.10E-02	1.83E-03	3.11E-05	9.18E-02	1.33E-02	1.22E-04
3-(3-Hydroxyphenyl)propanoic acid	HMDB00375	C11457	5.51E-05	1.96E-05	6.26E-05	3.70E-04	3.30E-04	2.15E-04
Myristic acid	HMDB00806	C06424	5.00E-01	1.94E-09	3.14E-07	5.43E-01	9.10E-08	1.22E-04
Palmitic acid	HMDB00220	C00249	5.61E-01	3.47E-07	1.41E-05	5.97E-01	9.65E-06	2.15E-04
Daidzein	HMDB03312	C10208	4.14E-05	8.23E-03	7.34E-04	3.03E-04	3.98E-02	1.82E-03
L-Histidine	HMDB00177	C00135	9.22E-05	2.10E-03	2.31E-03	5.51E-04	1.47E-02	5.07E-03
Phenylalanine	HMDB00159	C00079	1.47E-06	2.01E-05	1.01E-01	1.52E-05	3.30E-04	1.33E-01
L-Threonine	HMDB00167	C00188	2.43E-04	7.96E-03	2.12E-01	1.25E-03	3.97E-02	2.41E-01
L-Leucine	HMDB00687	C00123	3.42E-03	1.30E-02	8.58E-05	1.09E-02	3.62E-02	2.82E-04
L-Isoleucine	HMDB00172	C00407	1.83E-03	8.15E-03	4.05E-04	6.83E-03	3.98E-02	1.09E-03

L-Glycine	HMDB00123	C00037	6.61E-03	4.11E-03	3.61E-01	1.81E-02	2.50E-02	3.93E-01
L-Lysine	HMDB00182	C00047	8.14E-05	1.90E-04	9.79E-05	4.96E-04	2.72E-03	3.19E-04
Oxalic acid	HMDB02329	C00209	4.87E-02	1.75E-03	8.59E-04	8.78E-02	1.33E-02	2.10E-03
Phosphoric acid	HMDB02142	C00009	3.52E-02	1.44E-03	9.21E-06	6.97E-02	1.16E-02	4.81E-05
Citric acid	HMDB00094	C00158	2.62E-03	5.42E-02	1.75E-02	8.99E-03	1.46E-01	3.07E-02
Oxoglutaric acid	HMDB00208	C00026	>0.05	1.97E-05	5.00E-08	>0.05	3.30E-04	6.08E-07
Hippuric acid	HMDB00714	C01586	1.96E-11	4.65E-03	8.62E-12	6.44E-10	2.68E-02	5.67E-10
Trehalose	HMDB00975	C01083	2.31E-02	1.86E-02	1.19E-03	4.94E-02	7.46E-02	2.81E-03
L-Aspartic acid	HMDB00191	C00049	2.52E-04	1.07E-03	2.11E-06	1.28E-03	9.22E-03	1.41E-05
Citrulline	HMDB00904	C00327	7.86E-13	9.55E-12	2.26E-23	4.79E-11	1.05E-09	7.44E-21

Table S2 The key metabolite pathway analysis for radiation exposure ranked by p value ($p \leq 0.1$).

Metabolic Pathway	Total	Expected	Hits	Raw p	Holm adjust	FDR	Impact
Aminoacyl-tRNA biosynthesis	75	0.93477	8	2.06E-06	0.000164	0.000164	0.11268
Citrate cycle (TCA cycle)	20	0.24927	4	8.28E-05	0.006543	0.003313	0.18034
Alanine, aspartate and glutamate metabolism	24	0.29913	4	0.000175	0.013683	0.003663	0.26781
Phenylalanine metabolism	45	0.56086	5	0.000183	0.014103	0.003663	0.15717
Nitrogen metabolism	39	0.48608	4	0.001192	0.090594	0.019072	0.00067
Glyoxylate and dicarboxylate metabolism	50	0.62318	4	0.003034	0.22753	0.040449	0.1322
Valine, leucine and isoleucine biosynthesis	27	0.33652	3	0.004178	0.30919	0.047752	0.0265

Note. “total” is the number of metabolites in the set, “Hit” is the number of user entered metabolites which match metabolites in set, “Raw p” is the raw p-value, “Holm adjust” is the p-value after Bonferroni corrected, “FDR” is false-discovery rate.

Table S3 The changes of urinary excretion level of metabolites after normalization at 5h post-irradiation

Metabolites	Control (n=10)	2Gy (n=10)	4Gy (n=10)	6Gy (n=10)	8Gy (n=10)
Oxalic acid	-0.6+0.57	-0.61+1.68	0.43+1.35	-0.42+2.03	1.29+2.02※#§
Guaiacol	0.64+0.44	0.12+0.48※	-0.35+0.3※#	-0.34+0.45※#	-0.55+0.08※#
Phosphoric acid	-5.74+2.9	4.19+13.73※	4.55+5.54※	3.9+7.68※	2.52+6.68※
Fumaric acid	0.61+0.46	0.32+0.78	0.76+0.59	0.32+1	0.23+0.66
Pelargonic acid	-0.14+0.23	0.17+0.55	0.05+0.41	0.42+1.27	0.12+0.67
Hydroxyphenyllac-tic acid	0.28+0.32	0.13+0.45	-0.26+0.15※#	-0.25+0.47※#	-0.44+0.09※#
Malic acid	0.56+0.49	0.08+0.95	0.83+0.65	0.14+1.09&	0.68+0.84
Pyroglutamic acid	0.06+1.02	-2.25+1.49※	-2.17+0.75※	-2.48+1.48※	-2.78+0.71※
Succinic acid	0.49+0.51	-0.13+0.86	0.45+0.7	-0.02+0.91	0.08+0.69
Oxoglutaric acid	2.42+2.35	-0.5+2.83※	1.35+1.27	0.99+3.35	0.57+2.51
Pimelic acid	0.12+0.1	0.16+0.37	0.09+0.22	-0.03+0.27	-0.15+0.16※#&
Adipic acid	0.28+0.28	-0.16+0.41※	0.12+0.17	-0.02+0.49	-0.11+0.31※
3-(3-Hydroxyphenyl)propanoic acid	0.27+0.38	0.14+1.11	-0.69+0.23※#	-0.62+0.48※#	-0.87+0.11※#
Citric acid	2.14+3.92	-2.56+5.94※	3.31+6.08	-0.38+8.05	8.87+6.59※#&§
Hippuric acid	4.34+2.59	-0.4+4.03※	-3.91+2.66※#	-4.83+2.09※#	-6.61+0.79※#&§
Myristic acid	-0.63+2.04	0.9+4.67	0.96+3.94	-1.73+3.13	0.31+5
Palmitic acid	-0.31+1.13	0.43+2.72	0.43+2.28	-1.09+2	0.13+3.06
Trehalose	-2.94+5.77	-5.39+6.11	-2.33+5.98	-1.9+7.54	4.55+7.31※#&§
Daidzein	0.3+0.33	-0.17+0.25※	-0.19+0.3※	-0.24+0.34※	-0.36+0.09※
L-Histidine	0.53+0.21	-0.01+0.42※	-0.26+0.37※	-0.03+0.46※&	-0.23+0.29※
L-Phenylalanine	0.62+0.25	-0.21+0.17※	-0.45+0.47※	-0.22+0.56※	0.27+0.42※#&
L-Threonine	-0.21+0.38	-0.07+0.24	-0.05+0.27	-0.12+0.38	0.45+0.29※#&§
L-Leucine	0.59+0.27	0.03+0.16※	-0.21+0.25※#	-0.54+1.3※	0.12+0.19※&
L-Isoleucine	0.56+0.22	0.06+0.18※	-0.18+0.28※#	-0.55+1.2※	0.12+0.2※&
L-Aspartic acid	-0.96+0.66	-0.17+0.64※	0.22+0.84※	0.31+0.72※	0.59+0.8※#
Glycine	0.4+0.53	-0.36+0.37※	-0.23+0.2※	0.24+0.85#&	-0.05+0.26※
L-Lysine	0.56+0.45	0.26+0.46	-0.19+0.56※#	-0.11+0.59※	-0.53+0.26※#§
Citrulline	0.82+0.25	0+0.37※	-0.18+0.23※	-0.01+0.34※	-0.64+0.24※#&§

Note. Compared with control, ※ $p < 0.05$; Compared with 2 Gy, # $p < 0.05$; Compared with 4 Gy, & $p < 0.05$; Compared with 6 Gy, § $p < 0.05$

Normalization procedure: (1) The sample normalization (row-wise)utilized total area of components that are common to all samples (i.e. the area of each component was normalized to total integrated area of components); (2) Data scaling adopted Pareto

scaling method, the formula is $\overset{\circ}{x}_{ij} = \frac{x_{ij} - \overline{x_i}}{\sqrt{s_i}}$

Table S4 The changes of urinary excretion level of metabolites after normalization at 24h post-irradiation

Metabolites	Control (n=10)	2Gy (n=10)	4Gy (n=10)	6Gy (n=9)	8Gy (n=10)
Oxalic acid	-0.6+0.57	-1.13+0.67	0.16+1.45#	0.08+1.19#	1+1.44※#
Guaiacol	0.64+0.44	0.5+0.79	-0.18+0.38※#	-0.34+0.45※#	-0.37+0.32※#
Phosphoric acid	-5.74+2.9	-5.29+2.93	-0.6+4.69※	0.19+6.18※#	3.5+8.2※#
Fumaric acid	0.61+0.46	-0.49+0.3※	-0.53+0.26※	-0.66+0.32※	-0.73+0.23※
Pelargonic acid	-0.14+0.23	-0.56+0.03※	-0.53+0.1※	-0.52+0.06※	-0.54+0.04※
Hydroxyphenyllact-ic acid	0.28+0.32	0.55+0.57	-0.03+0.39#	-0.06+0.29#	-0.22+0.28※#
Malic acid	0.56+0.49	-0.6+0.34※	-0.53+0.41※	-0.77+0.33※&	-0.73+0.33※
Pyroglutamic acid	0.06+1.02	3.96+3.52※	2.31+2.2※	3.59+2.45※	0.08+1.53#&§
Succinic acid	0.49+0.51	-0.32+0.51※	-0.19+0.51※	-0.45+0.52※	-0.43+0.44※
Oxoglutaric acid	2.42+2.35	-1.52+1.4※	-0.67+1.68※	-1.37+2.21※	-1.75+1.14※
Pimelic acid	0.12+0.1	0.02+0.13	0.04+0.17	-0.04+0.12※	-0.11+0.1※#&
Adipic acid	0.28+0.28	-0.17+0.21※	0.03+0.28※	-0.11+0.35※	-0.18+0.21※
3-(3-Hydroxyphenyl)propanoic acid	0.27+0.38	1.96+1.47※	0.08+0.88#	0.04+0.68#	-0.27+0.86#
Citric acid	2.14+3.92	-3.61+5.03※	0.24+6.64	-3.82+3.7※	-0.4+5.27
Hippuric acid	4.34+2.59	6.48+5.8	0.31+4.6#	1.16+4.34#	-1.48+6.04※#
Myristic acid	-0.63+2.04	-3.55+0※	-3.55+0.01※	-3.55+0※	-3.55+0※
Palmitic acid	-0.31+1.13	-1.91+0.27※	-1.95+0.49※	-1.82+0.4※	-1.84+0.32※
Trehalose	-2.94+5.77	-6.27+7.86	2.17+9.59	0.1+14.11	10.61+15.35※#§
Daidzein	0.3+0.33	0.56+0.52	-0.08+0.31※#	0.03+0.32#	0.04+0.5#
L-Histidine	0.53+0.21	0+0.99	-0.22+1.07※	-0.15+1.01※	-0.65+0.66#
L-Phenylalanine	0.62+0.25	-0.49+0.46※	-0.58+0.95※	-0.51+1.06※	0.45+0.78#&
L-Threonine	-0.21+0.38	-0.01+0.47	-0.45+1.5	-0.25+0.8	0.97+0.59※#&§
L-Leucine	0.59+0.27	0.06+0.39※	-0.19+0.55※	-0.79+1.94※	0.09+0.27※
L-Isoleucine	0.56+0.22	0.08+0.37※	-0.17+0.49※	-0.84+1.94※	0.08+0.33
L-Aspartic acid	-0.96+0.66	0.08+0.91※	-0.24+0.96	0.39+0.79※&	0.74+0.85※&
Glycine	0.4+0.53	-0.62+0.69※	-0.53+0.39※	0.42+1.55&	0.03+0.47&
L-Lysine	0.56+0.45	0.4+0.74	-0.02+1.03	-0.23+0.98	-0.99+0.53※&
Citrulline	0.82+0.25	0.1+0.68※	-0.26+0.45※	-0.13+0.68※	-1.15+0.47※#&§

Note. Compared with control, ※ $p < 0.05$; Compared with 2 Gy, # $p < 0.05$; Compared with 4 Gy, & $p < 0.05$; Compared with 6 Gy, § $p < 0.05$

Normalization procedure: (1) The sample normalization (row-wise)utilized total

area of components that are common to all samples (i.e. the area of each component was normalized to total integrated area of components); (2) Data scaling adopted Pareto scaling method, the formula is $\overset{\circ}{x}_{ij} = \frac{x_{ij} - \overline{x_i}}{\sqrt{s_i}}$

Table S5 The changes of urinary excretion level of metabolites after normalization at 48h post-irradiation

Metabolites	Control (n=10)	2Gy (n=10)	4Gy (n=10)	6Gy (n=9)	8Gy (n=9)
Oxalic acid	-0.6+0.57	-0.92+0.8	0.64+0.71※#	0.88+1.6※#	0.57+1.33※#
Guaiacol	0.64+0.44	0.45+0.47	-0.26+0.22※#	-0.49+0.16※#	-0.49+0.32※#
Phosphoric acid	-5.74+2.9	-7.02+3.6	3.76+5.44※#	2.86+7.08※#	5.5+8.36※#
Fumaric acid	0.61+0.46	0.31+0.43	-0.36+0.35※#	-0.65+0.26※#&	-0.55+0.4※#
Pelargonic acid	-0.14+0.23	0.46+0.17※	0.33+0.16※	0.44+0.32※	0.65+0.4※&
Hydroxyphenyllact-ic acid	0.28+0.32	0.48+0.46	-0.1+0.19※#	-0.31+0.14※#	-0.39+0.19※#&
Malic acid	0.56+0.49	0.21+0.52	-0.15+0.54※	-0.59+0.36※#	-0.43+0.6※#
Pyroglutamic acid	0.06+1.02	0.48+2.01	0.36+1.27	-0.12+1.74	-0.91+1.31
Succinic acid	0.49+0.51	0.36+0.7	-0.21+0.48※	-0.42+0.42※#	-0.3+0.65※
Oxoglutaric acid	2.42+2.35	1.15+1.99	-2.06+1.12※#	-2.29+1.09※#	-1.71+1.4※#
Pimelic acid	0.12+0.1	0.02+0.16	-0.04+0.15※#	-0.16+0.1※#&	-0.21+0.13※#&
Adipic acid	0.28+0.28	0.26+0.31	-0.15+0.2※#	-0.24+0.21※#	-0.14+0.29※#
3-(3-Hydroxyphenyl)propanoic acid	0.27+0.38	0.24+0.43	0.01+0.49	-0.39+0.28※#&	-0.54+0.37※#&
Citric acid	2.14+3.92	-3.45+2.56※	-0.34+4.25	-3.2+3.39※	-1.97+5.23
Hippuric acid	4.34+2.59	5.64+2.87	-1.8+2.68※#	-3.95+1.81※#&	-4.36+3.29※#&
Myristic acid	-0.63+2.04	3.5+1.06※	3.2+0.96※	3.97+2.41※	5.57+2.69※#&
Palmitic acid	-0.31+1.13	2.2+1※	1.48+0.59※	1.99+1.64※	3.21+1.88※&
Trehalose	-2.94+5.77	-6.71+4.09	2.31+4.45#	5.17+9.86※#	7.82+12.39※#
Daidzein	0.3+0.33	0.07+0.35	-0.19+0.24※#	-0.19+0.09※	-0.21+0.33※#
L-Histidine	0.53+0.21	0.07+0.42※	0.02+0.51※	0.12+0.29※	-0.49+0.44※#&§
L-Phenylalanine	0.62+0.25	-0.13+0.39※	-0.06+0.6※	-0.1+0.56※	-0.09+0.27※
L-Threonine	-0.21+0.38	-0.01+0.35	0.01+0.27	-0.12+0.31	0.23+0.38
L-Leucine	0.59+0.27	-0.12+0.36※	-0.14+0.68※	-0.12+0.32※	-0.32+0.27※
L-Isoleucine	0.56+0.22	-0.21+0.39※	-0.26+0.88※	-0.1+0.29※	-0.13+0.25※
L-Aspartic acid	-0.96+0.66	0.42+0.52※	0.39+0.75※	-0.22+0.71※	0.56+0.55※§
Glycine	0.4+0.53	0.16+0.33	-0.04+0.43	-0.23+0.42※	0.13+0.37
L-Lysine	0.56+0.45	-0.28+0.47※	0.06+0.43※	0.12+0.34	-0.47+0.42※&§
Citrulline	0.82+0.25	0.58+0.23※	-0.05+0.26※#	-0.54+0.24※#&	-1.14+0.24※#&§

Note. Compared with control, ※$p < 0.05$; Compared with 2 Gy, #$p< 0.05$; Compared with 4 Gy, &$p< 0.05$; Compared with 6 Gy, §$p < 0.05$

Normalization procedure: (1) The sample normalization (row-wise)utilized total area of components that are common to all samples (i.e. the area of each component was normalized to total integrated area of components); (2) Data scaling adopted Pareto scaling method, the formula is $\overset{\circ}{x}_{ij} = \frac{x_{ij} - \overline{x_i}}{\sqrt{s_i}}$

Table S6 The comparison of urinary excretion patterns of specific amino acids from different radiation doses between the current study and one past study at 5h post-irradiation

Metabolites	Control		2Gy		4Gy		6Gy		8Gy	
	U(n=10)	U^a(n=13)	U (n=10)	U^a(n=10)	U(n=10)	U^a(n=11)	U(n=10)	U^a(n=10)	U(n=10)	U^a(n=10)
L-Histidine	0.53+0.21	*14.62±5.29*	-0.01+0.42※	*14.49±1.85*	-0.26+0.37※	*11.87±2.5*	-0.03+0.46※&	*14.87±3.3*	-0.23+0.29※	*11.2±3.24*
L-Phenylalanine	0.62+0.25	*2.5±0.88*	-0.21+0.17※	*3.49±1.71*	-0.45+0.47※	*2.49±0.47*	-0.22+0.56※	*3.21±1.49*	0.27+0.42※#&	*2.5±1.1*
L-Leucine	0.59+0.27	*3.06±0.76*	0.03+0.16※	4.36±2.63	-0.21+0.25※#	*3.32±0.87*	-0.54+1.3※	3.46±1.04	0.12+0.19※&	3.1±1.09
L-Isoleucine	0.56+0.22	*2.24±0.51*	0.06+0.18※	*3.23±1.08*※	-0.18+0.28※#	*2.32±0.63*	-0.55+1.2※	2.65±0.93	0.12+0.2※&	2.11±0.69#
L-Aspartic acid	-0.96+0.66	*1.67±0.97*	-0.17+0.64※	*0.44±0.14*※※	0.22+0.84※	*0.73±0.5*※	0.31+0.72※	*0.45±0.26*※※	0.59+0.8※#	*0.52±0.52*※
Glycine	0.4+0.53	*30.42±7.5*	-0.36+0.37※	*38.48±5.91*	-0.23+0.2※	*29.87±7.51*	0.24+0.85#&	*34.93±8.97*	-0.05+0.26※	*33.37±15.7*
L-Lysine	0.56+0.45	*95.64±58.94*	0.26+0.46	*12.28±3.21*	-0.19+0.56※#	*6.86±2.47*	-0.11+0.59※	*10.53±4.35*	-0.53+0.26※#§	*7.75±3.54*
Citrulline	0.82+0.25	*1.9±0.63*	0+0.37※	*1.52±0.58*	-0.18+0.23※	*1.75±1.05*	-0.01+0.34※	*1.71±0.42*	-0.64+0.24※#&§	*1.35±0.42*

Note. Compared with control, ※ $p < 0.05$; Compared with 2 Gy, # $p < 0.05$; Compared with 4 Gy, & $p < 0.05$; Compared with 6 Gy, § $p < 0.05$; U represents urine samples in this study with normalization by sum, U^a represents urine samples in a past work with normalization by creatinine (reference 21).

Table S7 The comparison of urinary excretion patterns of specific amino acids from different radiation doses between the current study and one past study at 24h post-irradiation

Metabolites	Control		2Gy		4Gy		6Gy		8Gy	
	U(n=10)	U^a(n=13)	U (n=10)	U^a(n=8)	U(n=10)	U^a(n=10)	U(n=9)	U^a(n=8)	U(n=10)	U^a(n=10)
L-Histidine	0.53+0.21	*14.62±5.29*	0+0.99	*11.74±1.47*	-0.22+1.07※	*10.27±2.5*	-0.15+1.01※	*13.85±3.89*	-0.65+0.66#	*8.73±3.22*※
L-Phenylalanine	0.62+0.25	*2.5±0.88*	-0.49+0.46※	*2.01±0.38*	-0.58+0.95※	*2.13±0.88*	-0.51+1.06※	*2.37±0.74*	0.45+0.78#&	*1.77±0.33*
L-Leucine	0.59+0.27	*3.06±0.76*	0.06+0.39※	*2.36±0.38*	-0.19+0.55※	*2.88±1.99*	-0.79+1.94※	*2.46±0.7*	0.09+0.27※	*2.05±0.37*
L-Isoleucine	0.56+0.22	*2.24±0.51*	0.08+0.37※	*1.65±0.22*※	-0.17+0.49※	*2.02±1.26*	-0.84+1.94※	*1.69±0.54*	0.08+0.33	*1.45±0.27*※※
L-Aspartic acid	-0.96+0.66	*1.67±0.97*	0.08+0.91※	*1.72±0.43*	-0.24+0.96	*1.77±1*	0.39+0.79※&	*1.45±1.1*	0.74+0.85※&	*1.27±0.6*
Glycine	0.4+0.53	*30.42±7.5*	-0.62+0.69※	*25.53±2.66*	-0.53+0.39※	*25.55±8.16*	0.42+1.55&	*27.35±6.1*	0.03+0.47&	*23.64±4.37*
L-Lysine	0.56+0.45	*95.64±58.94*	0.4+0.74	*9.08±2.3*※※	-0.02+1.03	*7.4±1.97*※※	-0.23+0.98	*10.44±2.5*※※	-0.99+0.53※&	*6.54±2.19*※※§
Citrulline	0.82+0.25	*1.9±0.63*	0.1+0.68※	*1.34±0.33*	-0.26+0.45※	*1.54±0.91*	-0.13+0.68※	*1.28±0.35*	-1.15+0.47※#& §	*1.05±0.25*※※

Note. Compared with control, ※ $p < 0.05$; Compared with 2 Gy, # $p < 0.05$; Compared with 4 Gy, & $p < 0.05$; Compared with 6 Gy, § $p < 0.05$; U represents urine samples in this study with normalization by sum, U^a represents urine samples in a past work with normalization by creatinine (reference 21).

Table S8 The comparison of urinary excretion patterns of specific amino acids from different radiation doses between the current study and one past study at 48h post-irradiation

Metabolites	Control		2Gy		4Gy		6Gy		8Gy	
	U(n=10)	U^a(n=13)	U (n=10)	U^a(n=10)	U(n=10)	U^a(n=10)	U(n=9)	U^a(n=10)	U(n=9)	U^a(n=10)
L-Histidine	0.53+0.21	*14.62±5.29*	0.07+0.42※	*12.52±2.34*	0.02+0.51※	*9.75±2.08*※	0.12+0.29※	*13.18±2.36*	-0.49+0.44※#&§	*9.55±4.35*※
L-Phenylalanine	0.62+0.25	*2.5±0.88*	-0.13+0.39※	*2.16±0.46*	-0.06+0.6※	*2.35±0.71*	-0.1+0.56※	*2.82±0.62*	-0.09+0.27※	*1.97±1.01*
L-Leucine	0.59+0.27	*3.06±0.76*	-0.12+0.36※	*2.51±0.53*	-0.14+0.68※	*2.67±0.9*	-0.12+0.32※	*2.93±0.67*	-0.32+0.27※	*2.34±0.85*
L-Isoleucine	0.56+0.22	*2.24±0.51*	-0.21+0.39※	*1.84±1.09*	-0.26+0.88※	*2.2±1.34*	-0.1+0.29※	*2.12±0.49*	-0.13+0.25※	*1.61±0.53*
L-Aspartic acid	-0.96+0.66	*1.67±0.97*	0.42+0.52※	*1.68±0.99*	0.39+0.75※	*3.11±1.99*	-0.22+0.71※	*2.39±1.25*	0.56+0.55※§	*2.21±1.28*
Glycine	0.4+0.53	*30.42±7.5*	0.16+0.33	*30.46±8.29*	-0.04+0.43	*35.87±14.52*	-0.23+0.42※	*44.66±8.47*※	0.13+0.37	*34.31±14.13*
L-Lysine	0.56+0.45	*95.64±58.94*	-0.28+0.47※	*10.54±3.12*※※	0.06+0.43※	*8.23±4.63*※※	0.12+0.34	*9.86±2.78*※※	-0.47+0.42※&§	*6.59±4.23*※※
Citrulline	0.82+0.25	*1.9±0.63*	0.58+0.23※	*1.21±0.7*	-0.05+0.26※#	*1.28±0.87*	-0.54+0.24※#&	*0.85±0.21*※※	-1.14+0.24※#&§	*0.51±0.17*※※

Note. Compared with control, ※ $p < 0.05$; Compared with 2 Gy, # $p < 0.05$; Compared with 4 Gy, & $p < 0.05$; Compared with 6 Gy, § $p < 0.05$; U represents urine samples in this study with normalization by sum, U^a represents urine samples in a past work with normalization by creatinine (reference 21).

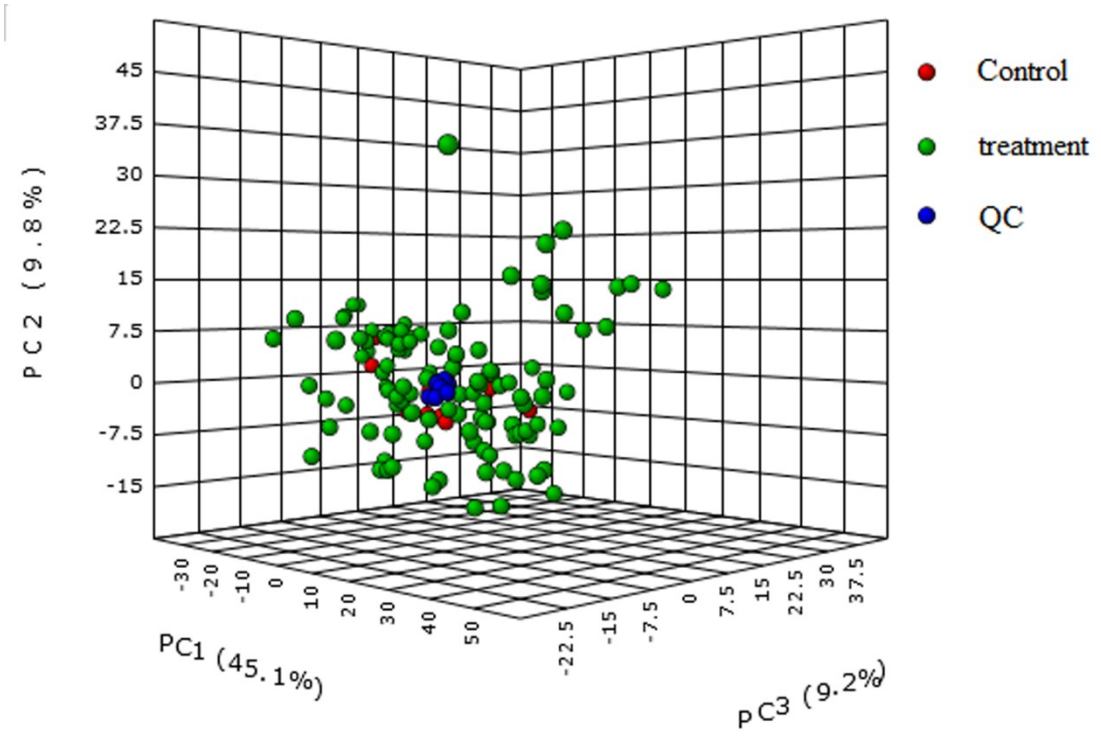
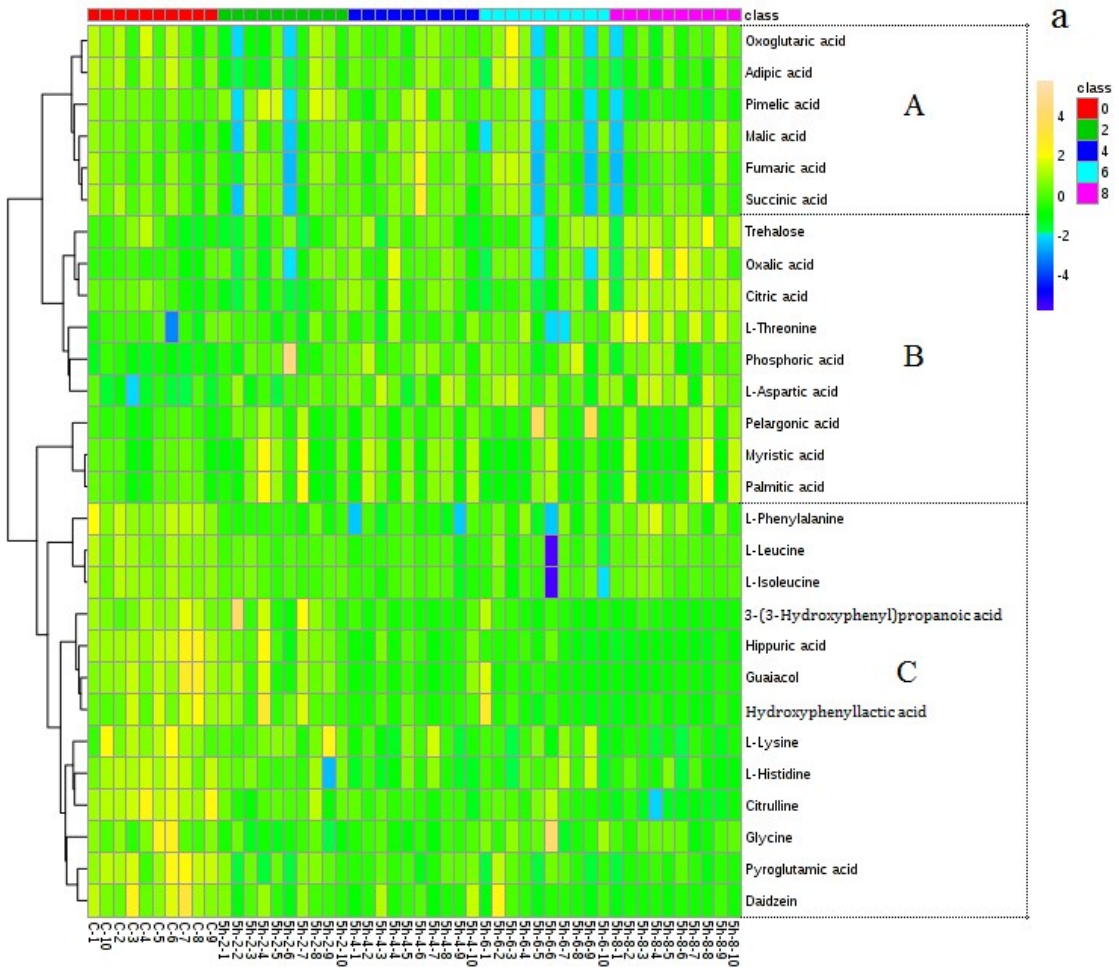


Fig.S1 PCA score plot based on the data generated from GC-MS reflects the sample distributions. The QC samples aggregate tightly together, indicating small technique variation compared to the biological variation.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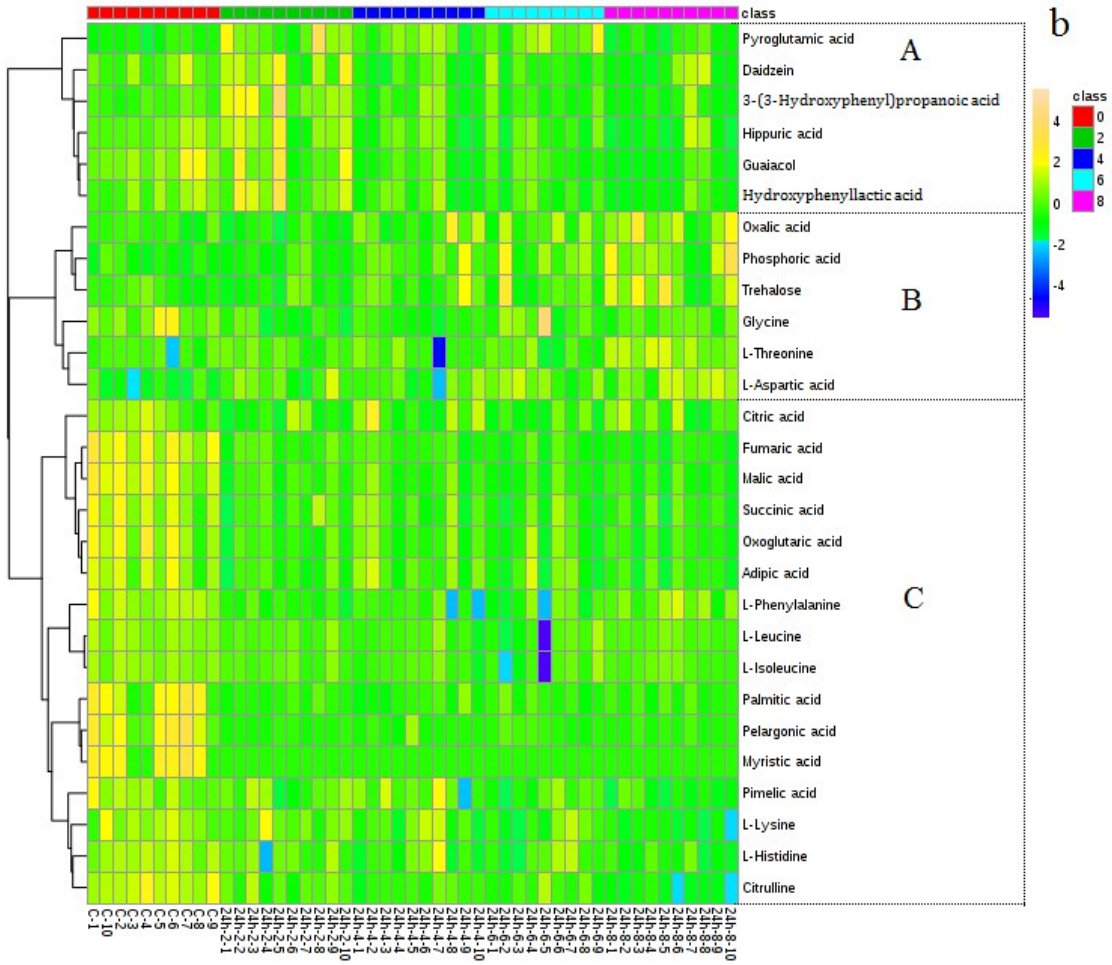
Adipic acid
Pimelic acid
Malic acid
Fumaric acid
Succinic acid
Trehalose
Oxalic acid
Citric acid
L-Threonine
Phosphoric acid
L-Aspartic acid
Pelargonic acid
Myristic acid
Palmitic acid
L-Phenylalanine
L-Leucine
L-Isoleucine
3-(3-Hydroxyphenyl)propanoic acid
Hippuric acid
Guaiacol
Hydroxyphenyllactic acid
L-Lysine
L-Histidine
Citrulline
Glycine
Pyroglutamic acid
Daidzein
A
B
C
4
2
0
-2
-4
class
0
2
4
6
8


b
class
Pyroglutamic acid
Daidzein
3-(3-Hydroxyphenyl)propanoic acid
Hippuric acid
Guaiacol
Hydroxyphenyllactic acid
Oxalic acid
Phosphoric acid
Trehalose
Glycine
L-Threonine
L-Aspartic acid
Citric acid
Fumaric acid
Malic acid
Succinic acid
Oxoglutaric acid
Adipic acid
L-Phenylalanine
L-Leucine
L-Isoleucine
Palmitic acid
Pelargonic acid
Myristic acid
Pimelic acid
L-Lysine
L-Histidine
Citrulline
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B
C
4
2
0
-2
-4
class
0
2
4
6
8

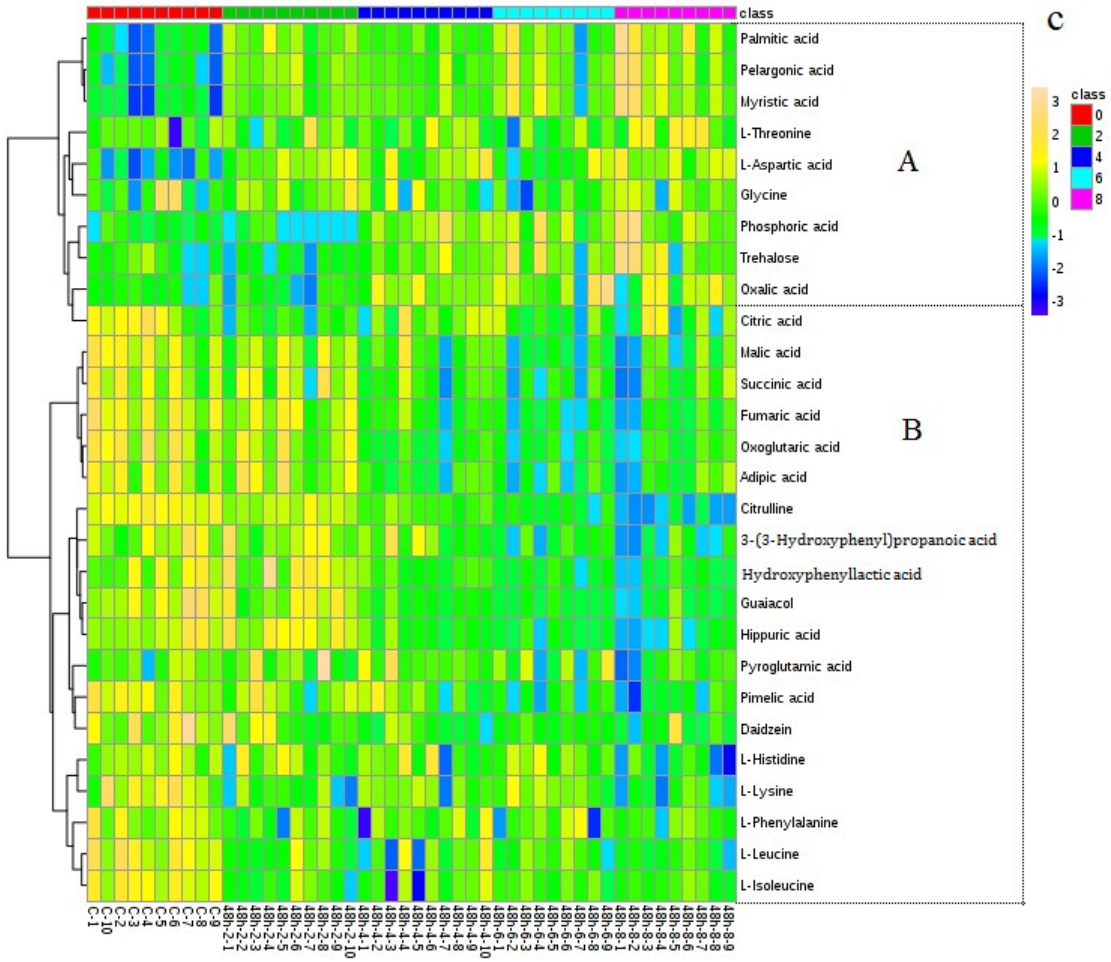

Fig.S2 Heat maps of 28 differential metabolites in urine samples listed in Table S1 at (a) 5h, (b) 24h, (c) 48h post-exposure.

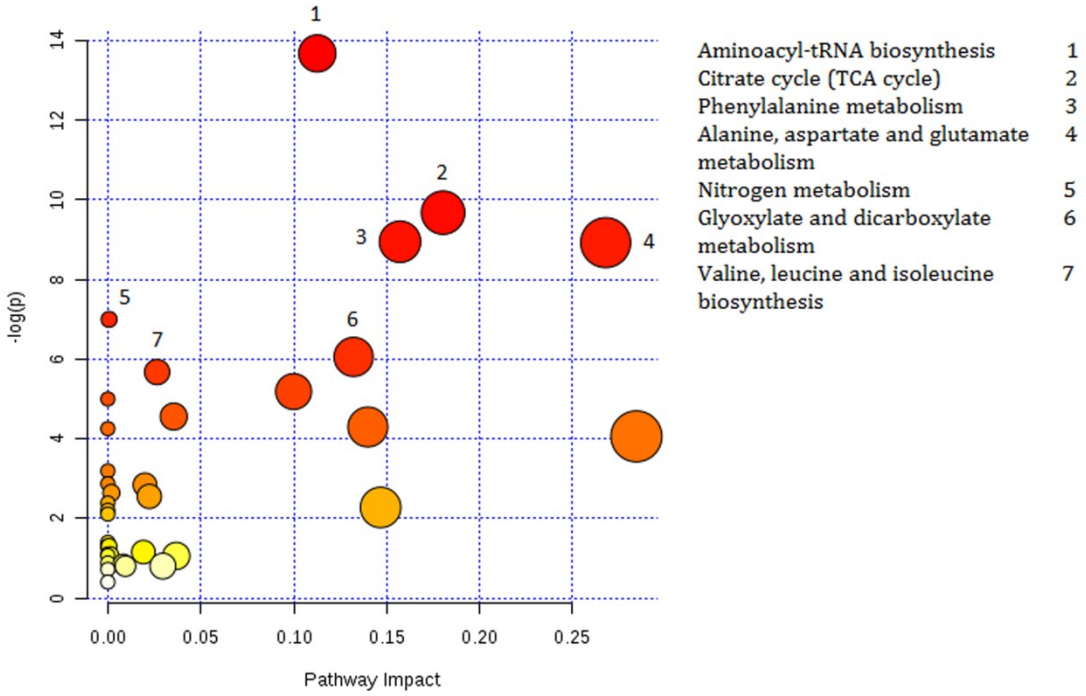

Fig.S3 Pathway analysis of urinary samples from un-irradiated control and irradiated groups based on 28 pathway-matched metabolites.

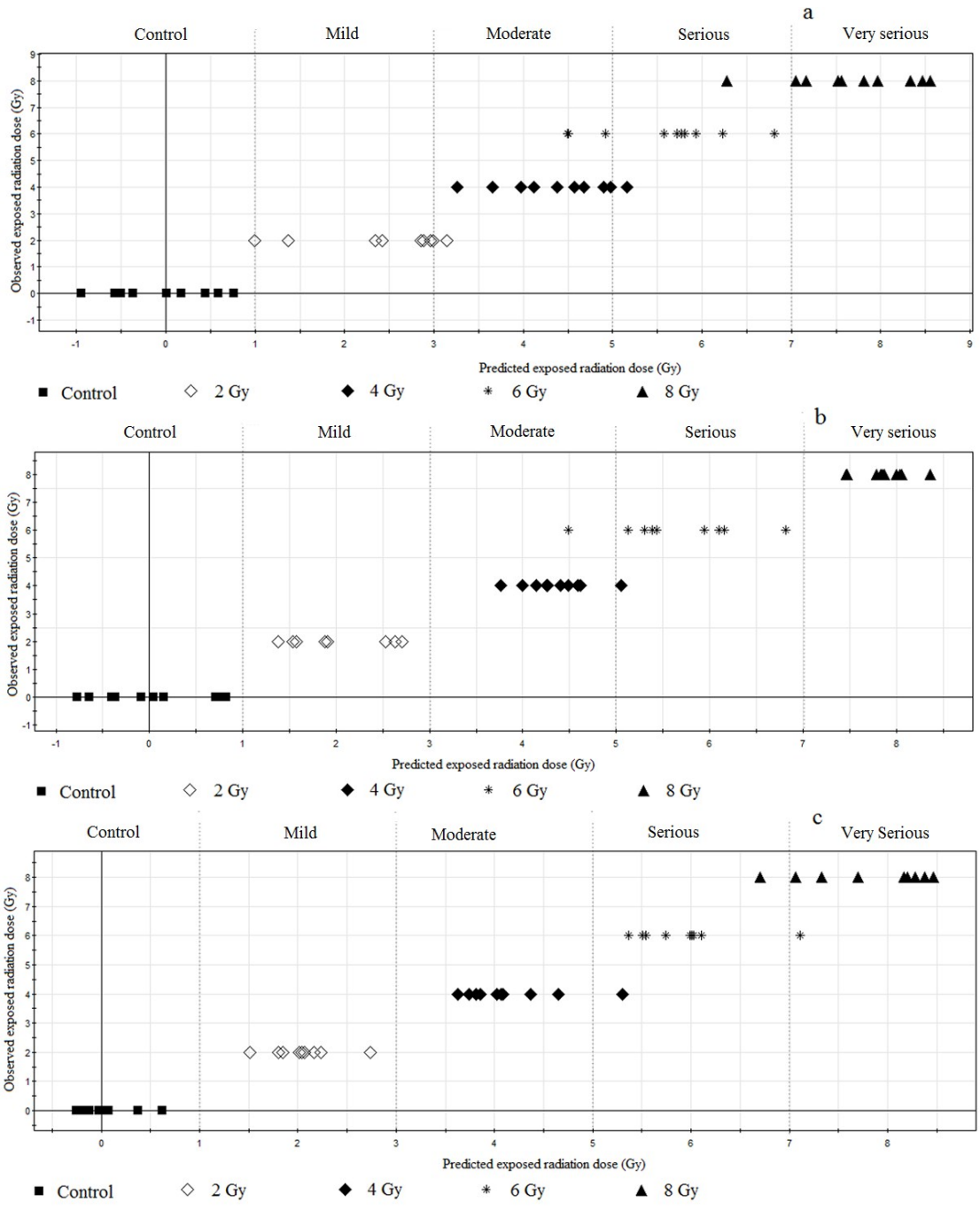

Fig.S4 Comparison between the predicted radiation doses at 5h post radiation exposure and observed values based on the panel of potential biomarkers.