

Supporting Information
for
Isotope Labelling - Paired Homologous Double Neutral Loss
Scan - Mass Spectrometry for Profiling of Metabolites with
Carboxyl Group

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Table S1. Linear regression parameters of DMBA/d⁴-DMBA labelled JA, GA3 and 12-C fatty acid. The d⁴-DMBA labelled analytes were fixed at a concentration of 50.0 ng/mL, and the concentrations of DMBA labelled analytes varied from 5.00 ng/mL to 500 ng/mL. The data were based on triplicate measurements.

Analytes	Linear range (light / heavy)	Regression line		R ²	LOD (ng / mL)
		Slope	Intercept		
JA	0.1-10	1.003	0.0207	0.9992	0.120
GA3	0.1-10	0.988	0.0656	0.9995	0.252
12-C fatty acid	0.1-10	1.004	0.0081	0.9994	0.0812

Table S2. The list of metabolites detected by IL-HPLC-PHDNL-MS method. The metabolites with peak area ratio (wounded group / control group) higher than 1.50 or lower than 0.667 are indicated by shadow.

Forward labelling ^a						Reverse labelling ^b					
m/z	Peak Area	m/z	Peak Area	RT /	W/N ^e	m/z	Peak Area	m/z	Peak Area	RT /	W/N
(NL45) ^c	(RSD%)	(NL49) ^d	(RSD%)	min	(RSD%)	(NL49)	(RSD%)	(NL45)	(RSD%)	min	(RSD%)
207-208	2.86E+04(14)	211-212	3.11E+04(13)	2.5	0.92(7.8)	211-212	3.02E+04(14)	207-208	3.64E+04(15)	2.5	0.84(6.6)
208-209	6.59E+05(20)	212-213	6.14E+05(19)	2.8	1.05(3.8)	212-213	7.03E+05(15)	208-209	6.90E+05(13)	2.9	1.06(4.9)
209-210	8.02E+04(17)	213-214	8.52E+04(15)	3.4	0.92(6.2)	213-214	8.53E+04(18)	209-210	8.99E+04(19)	3.5	0.93(7.9)
210-211	1.29E+04(19)	214-215	1.17E+04(21)	4.4	1.10(5.5)	214-215	1.37E+04(11)	210-211	1.38E+04(12)	4.5	0.97(8.2)
211-212	6.31E+04(22)	215-216	6.56E+04(22)	5.6	0.98(4.2)	215-216	7.14E+04(18)	211-212	7.32E+04(19)	5.7	1.00(6.0)
211-212	2.86E+04(14)	215-216	2.54E+04(14)	6.0	1.12(3.2)	215-216	3.12E+04(15)	211-212	2.83E+04(17)	6.1	1.13(4.6)
214-215	4.40E+04(19)	218-219	5.58E+04(20)	10.1	0.76(7.4)	218-219	5.13E+04(13)	214-215	5.98E+04(12)	10.1	0.82(7.9)
215-216	1.33E+06(15)	219-220	1.55E+06(14)	10.1	0.90(1.6)	219-220	1.46E+06(17)	215-216	1.61E+06(17)	10.3	0.91(7.5)
216-217	1.41E+05(17)	220-221	1.53E+05(17)	11.6	0.94(5.6)	220-221	1.67E+05(10)	216-217	1.70E+05(9)	11.7	1.01(6.4)
217-218	1.79E+04(20)	221-222		2.6		221-222	1.95E+04(11)	217-218		2.7	
217-218	1.68E+04(14)	221-222	1.76E+04(13)	10.4	0.94(6.5)	221-222	1.90E+04(17)	217-218	1.94E+04(17)	10.5	0.93(5.2)
218-219	2.99E+04(17)	222-223	3.34E+04(18)	2.0	0.92(3.5)	222-223	3.46E+04(17)	218-219	3.93E+04(15)	2.1	0.84(3.4)
218-219	3.16E+04(14)	222-223	2.80E+04(14)	11.1	1.12(5.9)	222-223	3.48E+04(15)	218-219	2.95E+04(17)	11.4	1.20(5.5)
219-220	6.04E+04(16)	223-224	6.96E+04(16)	1.9	0.87(5.5)	223-224	7.12E+04(16)	219-220	7.31E+04(16)	2.0	0.97(9.0)
219-220	6.32E+04(14)	223-224	5.48E+04(13)	11.2	1.15(5.9)	223-224	7.18E+04(16)	219-220	6.48E+04(18)	11.4	1.09(7.7)
221-222	4.65E+04(15)	225-226	4.06E+04(16)	8.1	1.18(6.7)	225-226	5.02E+04(18)	221-222	4.69E+04(16)	8.2	1.11(5.4)
222-223	1.14E+04(18)	226-227	1.23E+04(19)	1.9	0.94(7.7)	226-227	1.27E+04(14)	222-223	1.40E+04(14)	2.0	0.90(6.1)
222-223	1.23E+04(18)	226-227	1.29E+04(17)	8.1	0.98(3.4)	226-227	1.26E+04(11)	222-223	1.34E+04(13)	8.1	0.94(5.7)
223-224	2.81E+04(21)	227-228	2.77E+04(22)	3.7	0.99(3.4)	227-228	3.15E+04(19)	223-224	3.06E+04(21)	3.8	1.00(4.6)
225-226	1.43E+04(20)	229-230	1.39E+04(22)	9.0	1.01(3.7)	229-230	1.73E+04(14)	225-226	1.51E+04(16)	9.0	1.12(6.3)
225-226	1.48E+04(21)	229-230	1.38E+04(19)	9.9	1.03(3.9)	229-230	1.71E+04(10)	225-226	1.52E+04(9)	10.0	1.16(3.7)
229-230	3.22E+04(22)	233-234	4.05E+04(23)	3.1	0.81(6.0)	233-234	3.96E+04(12)	229-230	4.29E+04(11)	3.1	0.94(3.7)
229-230	2.09E+04(17)	233-234	1.82E+04(18)	12.7	1.18(4.1)	233-234	2.20E+04(17)	229-230	2.16E+04(15)	12.8	1.06(6.9)
233-234	1.02E+05(15)	237-238	6.36E+04(14)	2.5	1.57(5.8)	237-238	1.08E+05(16)	233-234	7.24E+04(14)	2.6	1.40(3.2)
234-235	3.78E+04(19)	238-239	3.88E+04(18)	8.5	0.99(6.2)	238-239	4.12E+04(17)	234-235	4.23E+04(17)	8.6	0.96(2.9)
235-236	5.39E+05(22)	239-240	4.83E+05(22)	11.2	1.11(6.1)	239-240	5.65E+05(10)	235-236	5.59E+05(10)	11.2	0.98(5.5)
236-237	7.51E+04(22)	240-241	7.28E+04(20)	3.2	1.01(3.3)	240-241	8.25E+04(19)	236-237	7.62E+04(18)	3.3	1.02(4.8)
243-244	3.05E+04(16)	247-248	2.95E+04(15)	14.2	1.03(4.6)	247-248	3.26E+04(16)	243-244	3.42E+04(17)	14.2	0.98(5.8)
244-245	1.18E+04(21)	248-249	1.05E+04(21)	4.3	1.07(3.4)	248-249	1.33E+04(16)	244-245	1.09E+04(17)	4.4	1.21(5.8)
244-245	1.10E+04(21)	248-249	1.05E+04(22)	14.2	1.04(6.9)	248-249	1.24E+04(11)	244-245	1.12E+04(10)	14.3	1.08(6.2)
246-247	6.27E+03(13)	250-251	7.31E+03(13)	2.0	0.86(7.5)	250-251	6.87E+03(18)	246-247	7.74E+03(17)	2.1	0.86(6.2)
246-247	6.46E+03(20)	250-251	5.87E+03(22)	16.3	1.11(6.2)	250-251	6.89E+03(10)	246-247	6.65E+03(11)	16.5	0.99(3.0)
247-248	5.85E+04(22)	251-252	6.45E+04(21)	1.9	0.91(6.6)	251-252	6.60E+04(16)	247-248	7.52E+04(18)	2.0	0.89(6.5)
247-248	2.80E+04(15)	251-252	3.34E+04(16)	11.2	0.86(7.8)	251-252	3.08E+04(13)	247-248	3.55E+04(12)	11.3	0.87(6.0)
247-248	5.86E+04(16)	251-252	5.61E+04(18)	16.3	1.02(6.0)	251-252	6.86E+04(14)	247-248	5.95E+04(16)	16.5	1.15(4.6)
249-250	2.01E+04(19)	253-254	1.87E+04(18)	8.1	1.12(6.5)	253-254	2.14E+04(19)	249-250	2.21E+04(18)	8.2	0.98(6.0)
249-250	1.20E+04(20)	253-254	4.22E+03(20)	13.6	2.85(6.2)	253-254	1.33E+04(10)	249-250	4.62E+03(11)	13.8	2.79(6.3)

253-254	1.19E+04(15)	257-258	1.33E+04(16)	3.5	0.91(6.5)	257-258	1.39E+04(17)	253-254	1.58E+04(19)	3.6	0.92(4.5)
253-254	1.26E+04(19)	257-258	1.38E+04(19)	3.6	0.90(6.7)	257-258	1.33E+04(19)	253-254	1.54E+04(18)	3.7	0.88(7.2)
254-255	1.47E+05(13)	258-259	7.08E+04(13)	4.7	2.05(4.6)	258-259	1.70E+05(13)	254-255	7.56E+04(14)	4.8	2.14(8.0)
255-256	2.56E+04(13)	259-260	2.18E+04(12)	16.7	1.16(4.2)	259-260	2.73E+04(11)	255-256	2.51E+04(10)	16.7	1.09(7.2)
255-256	2.59E+04(17)	259-260	2.17E+04(15)	17.1	1.22(5.1)	259-260	2.68E+04(16)	255-256	2.49E+04(15)	17.1	1.08(2.3)
257-258	7.74E+04(19)	261-262	6.36E+04(18)	18.3	1.17(5.7)	261-262	8.77E+04(10)	257-258	7.50E+04(9)	18.3	1.22(6.2)
258-259	1.30E+04(17)	262-263	1.58E+04(18)	16.1	0.82(5.9)	262-263	1.36E+04(10)	258-259	1.76E+04(11)	16.3	0.75(4.5)
261-262	1.79E+04(18)	265-266	1.62E+04(19)	12.8	1.16(2.9)	265-266	2.06E+04(12)	261-262	1.86E+04(13)	12.9	1.14(5.1)
269-270	2.31E+04(16)	273-274	2.49E+04(17)	8.4	0.94(7.6)	273-274	2.47E+04(13)	269-270	2.90E+04(14)	8.5	0.85(5.5)
270-271	2.01E+05(14)	274-275	1.99E+05(14)	8.4	0.99(6.7)	274-275	2.20E+05(18)	270-271	2.05E+05(21)	8.5	1.11(7.8)
271-272	3.85E+04(18)	275-276	9.94E+03(18)	18.7	3.91(7.0)	275-276	4.60E+04(15)	271-272	1.11E+04(14)	18.9	4.18(5.0)
271-272	6.19E+04(21)	275-276	5.86E+04(21)	20.1	1.03(5.4)	275-276	6.56E+04(12)	271-272	6.92E+04(13)	20.1	0.97(5.4)
272-273	2.00E+04(17)	276-277	2.08E+04(17)	4.1	0.98(6.0)	276-277	2.13E+04(13)	272-273	2.23E+04(15)	4.2	0.96(5.5)
272-273	1.90E+04(19)	276-277	2.13E+04(21)	8.3	0.92(5.9)	276-277	2.26E+04(15)	272-273	2.41E+04(16)	8.4	0.99(3.2)
274-275	4.18E+04(15)	278-279	4.49E+04(16)	1.9	0.92(6.2)	278-279	4.47E+04(12)	274-275	4.68E+04(12)	1.9	0.94(7.8)
274-275	4.02E+04(14)	278-279	3.58E+04(14)	19.3	1.15(3.6)	278-279	4.39E+04(14)	274-275	3.94E+04(12)	19.5	1.07(4.9)
275-276	1.64E+05(20)	279-280	1.76E+05(19)	4.0	0.98(4.5)	279-280	1.88E+05(12)	275-276	2.04E+05(14)	4.1	0.94(6.3)
275-276	1.65E+05(21)	279-280	1.44E+05(22)	19.5	1.17(2.3)	279-280	1.80E+05(13)	275-276	1.65E+05(12)	19.7	1.10(5.9)
276-277	2.53E+04(21)	280-281	2.82E+04(22)	1.9	0.90(5.9)	280-281	2.98E+04(14)	276-277	3.04E+04(16)	2.0	0.97(6.6)
276-277	2.61E+04(17)	280-281	2.30E+04(17)	20.1	1.10(4.0)	280-281	2.84E+04(15)	276-277	2.52E+04(15)	20.2	1.14(6.3)
277-278	4.15E+03(18)	281-282	4.30E+03(17)	1.7	0.99(5.3)	281-282	4.40E+03(13)	277-278	4.75E+03(14)	1.8	0.93(7.6)
277-278	3.93E+03(20)	281-282	3.54E+03(20)	3.7	1.12(6.5)	281-282	4.53E+03(19)	277-278	4.12E+03(18)	3.8	1.07(7.7)
277-278	9.78E+03(20)	281-282	1.05E+04(19)	16.1	0.91(5.9)	281-282	1.01E+04(11)	277-278	1.16E+04(12)	16.2	0.90(5.7)
279-280	2.21E+04(13)	283-284		6.6		283-284	2.43E+04(14)	279-280		6.7	
279-280	2.20E+04(21)	283-284	2.57E+04(22)	12.2	0.88(3.6)	283-284	2.59E+04(12)	279-280	2.58E+04(12)	12.3	1.02(7.3)
285-286	7.35E+04(16)	289-290	8.33E+04(15)	2.2	0.91(5.6)	289-290	7.97E+04(18)	285-286	9.19E+04(19)	2.3	0.87(6.1)
285-286	1.26E+04(22)	289-290	1.47E+04(24)	15.1	0.89(5.9)	289-290	1.38E+04(18)	285-286	1.54E+04(21)	15.2	0.94(3.4)
285-286	7.64E+04(20)	289-290	6.87E+04(19)	19.4	1.07(6.3)	289-290	8.12E+04(19)	285-286	7.34E+04(21)	19.3	1.09(3.9)
285-286	1.29E+04(21)	289-290	1.46E+04(20)	20.2	0.86(4.2)	289-290	1.43E+04(10)	285-286	1.54E+04(10)	20.4	0.94(6.2)
286-287	1.21E+04(20)	290-291	1.21E+04(21)	20.7	1.01(5.2)	290-291	1.27E+04(14)	286-287	1.28E+04(13)	20.8	0.98(7.5)
288-289	4.36E+04(13)	292-293	4.01E+04(12)	9.3	1.10(4.2)	292-293	4.78E+04(11)	288-289	4.48E+04(11)	9.4	1.04(5.8)
288-289	4.13E+04(17)	292-293	4.04E+04(17)	24.7	1.02(5.2)	292-293	4.69E+04(11)	288-289	4.70E+04(12)	24.8	1.01(7.9)
289-290	2.76E+04(21)	293-294	2.20E+04(23)	5.3	1.22(5.9)	293-294	2.92E+04(14)	289-290	2.48E+04(13)	5.4	1.23(5.7)
290-291	1.55E+04(15)	294-295	1.63E+04(15)	2.0	0.96(5.9)	294-295	1.70E+04(14)	290-291	1.76E+04(15)	2.1	0.96(5.6)
290-291	1.45E+04(13)	294-295	1.32E+04(14)	4.7	1.08(5.4)	294-295	1.66E+04(12)	290-291	1.52E+04(13)	4.8	1.07(5.7)
297-298	1.53E+04(18)	301-302	1.80E+04(16)	21.2	0.87(7.8)	301-302	1.59E+04(18)	297-298	2.05E+04(21)	21.4	0.78(4.7)
298-299	3.84E+04(22)	302-303	4.63E+04(20)	13.2	0.83(6.3)	302-303	4.11E+04(11)	298-299	5.13E+04(12)	13.2	0.82(6.7)
298-299	1.71E+04(16)	302-303	1.75E+04(17)	22.3	1.00(5.5)	302-303	1.91E+04(19)	298-299	2.05E+04(18)	22.3	0.90(5.0)
299-300	3.06E+05(20)	303-304	3.07E+05(19)	23.1	1.04(5.0)	303-304	3.34E+05(10)	299-300	3.39E+05(10)	23.3	0.99(6.6)
300-301	5.87E+04(20)	304-305	5.55E+04(22)	20.2	1.05(5.7)	304-305	6.48E+04(13)	300-301	6.35E+04(15)	20.3	1.03(5.5)
302-303	1.33E+04(15)	306-307	1.60E+04(16)	28.1	0.83(8.8)	306-307	1.59E+04(11)	302-303	1.62E+04(12)	28.3	1.00(3.3)
302-303	1.35E+04(21)	306-307	1.24E+04(21)	29.2	1.11(2.8)	306-307	1.59E+04(15)	302-303	1.35E+04(17)	29.4	1.19(3.9)
303-304	6.29E+04(14)	307-308	7.14E+04(14)	3.3	0.85(5.8)	307-308	6.70E+04(11)	303-304	7.59E+04(9)	3.4	0.89(6.6)

303-304	7.82E+03(22)	307-308	8.95E+03(21)	13.1	0.91(4.4)	307-308	8.62E+03(16)	303-304	1.02E+04(16)	13.4	0.84(3.6)
303-304	6.23E+04(20)	307-308	5.62E+04(19)	23.6	1.10(7.1)	307-308	7.25E+04(11)	303-304	6.15E+04(11)	23.7	1.20(6.5)
304-305	1.26E+04(17)	308-309	1.29E+04(18)	3.3	0.99(5.8)	308-309	1.36E+04(19)	304-305	1.51E+04(17)	3.4	0.90(6.6)
304-305	1.17E+04(21)	308-309	1.14E+04(21)	23.7	0.98(5.7)	308-309	1.37E+04(18)	304-305	1.18E+04(21)	23.8	1.10(8.0)
307-308	1.31E+04(17)	311-312	1.21E+04(17)	6.7	1.04(5.9)	311-312	1.46E+04(16)	307-308	1.36E+04(15)	6.7	1.05(4.0)
307-308	1.33E+04(22)	311-312	1.16E+04(23)	12.2	1.13(6.5)	311-312	1.42E+04(11)	307-308	1.38E+04(10)	12.3	1.06(6.4)
313-314	3.47E+04(21)	317-318	3.88E+04(22)	7.8	0.90(4.5)	317-318	3.85E+04(13)	313-314	4.18E+04(14)	7.8	0.88(6.9)
313-314	3.64E+04(20)	317-318	3.04E+04(18)	23.7	1.20(5.9)	317-318	3.92E+04(13)	313-314	3.53E+04(13)	23.7	1.09(5.1)
314-315	8.27E+03(17)	318-319	8.12E+03(18)	40.6	1.04(4.9)	318-319	8.89E+03(16)	314-315	8.59E+03(19)	40.7	1.06(5.6)
319-320	5.83E+03(20)	323-324	6.46E+03(18)	2.1	0.90(5.6)	323-324	6.86E+03(10)	319-320	7.03E+03(11)	2.2	0.99(7.4)
319-320	5.88E+03(18)	323-324	5.24E+03(20)	20.4	1.10(6.7)	323-324	6.70E+03(14)	319-320	6.21E+03(14)	20.5	1.13(6.7)
324-325	1.44E+04(19)	328-329	1.67E+04(20)	6.8	0.83(6.2)	328-329	1.61E+04(12)	324-325	1.84E+04(13)	6.9	0.89(5.6)
324-325	1.40E+04(14)	328-329	1.25E+04(13)	15.3	1.11(6.2)	328-329	1.54E+04(15)	324-325	1.47E+04(15)	15.4	1.04(6.8)
383-384	2.43E+04(13)	387-388	2.59E+04(14)	9.9	0.92(6.3)	387-388	2.87E+04(12)	383-384	2.92E+04(12)	10.0	1.01(5.0)
383-384	2.61E+04(15)	387-388	2.65E+04(16)	17.3	0.99(5.5)	387-388	2.83E+04(13)	383-384	2.97E+04(11)	17.4	0.93(5.6)
387-388	3.38E+04(19)	391-392	3.62E+04(19)	10.7	0.95(7.2)	391-392	3.84E+04(16)	387-388	3.66E+04(18)	10.8	1.06(6.7)
387-388	3.56E+04(16)	391-392	3.54E+04(16)	17.3	1.02(6.7)	391-392	4.00E+04(15)	387-388	3.91E+04(13)	17.4	1.07(4.4)
388-389	1.26E+04(20)	392-393	1.43E+04(19)	3.3	0.90(6.5)	392-393	1.40E+04(15)	388-389	1.58E+04(15)	3.4	0.89(5.9)
388-389	1.24E+04(14)	392-393	1.41E+04(14)	17.4	0.86(8.6)	392-393	1.41E+04(19)	388-389	1.60E+04(19)	17.3	0.94(2.0)
402-403	8.07E+04(17)	406-407	8.17E+04(17)	5.5	0.98(4.0)	406-407	8.82E+04(10)	402-403	9.03E+04(9)	5.6	0.99(7.3)
403-404	5.83E+03(20)	407-408	6.68E+03(20)	3.3	0.89(3.9)	407-408	6.85E+03(12)	403-404	7.34E+03(12)	3.4	0.94(3.6)
403-404	6.16E+03(20)	407-408	5.26E+03(21)	6.4	1.19(7.1)	407-408	7.00E+03(10)	403-404	5.95E+03(9)	6.5	1.19(5.1)
404-405	1.92E+04(22)	408-409	1.75E+04(24)	3.3	1.07(5.8)	408-409	2.17E+04(14)	404-405	1.90E+04(14)	3.3	1.14(8.1)

^a Forward labelling, tomato leaves from wounded group and control group were pretreated and labelled with DMAB and d⁴-DMBA, respectively.

^b Reverse labelling, tomato leaves from wounded group and control group were pretreated and labelled with d⁴-DMBA and DMAB, respectively.

^c Ion chromatogram extracted from total ion chromatogram by neutral loss scan (NL 45 Da).

^d Ion chromatogram extracted from total ion chromatogram by neutral loss scan (NL 49 Da).

^e The peak area ratios of wounded samples over control samples.

Table S3. One sample t-test of peak area ratios of each metabolite from six independently biological experiments (3 forward labelling experiments and 3 reverse labelling experiments). The fold changes (both up- and down-regulated) larger than 1.50 and the *p*-values less than 0.01 were considered statistically significant difference. Rows of metabolites which meet our arbitrary criteria are indicating by shading. Peak area ratios can not be obtained for the two metabolites only detected in the wounded samples, therefore their statistics for the t-test are not shown.

One-sample t Test						
Test Value = 1						
m/z ^a (RT/min)	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
207-208(2.5)	-4.078	5	.010	-.14672	-.2392	-.0542
208-209(2.8)	1.943	5	.110	.04846	-.0156	.1126
209-210(3.4)	-1.795	5	.133	-.02785	-.0677	.0120
210-211(4.4)	.156	5	.882	.00334	-.0519	.0586
211-212(5.6)	-4.044	5	.010	-.06787	-.1110	-.0247
211-212(6)	4.219	5	.008	.06787	.0265	.1092
214-215(10.1)	-4.657	5	.006	-.17871	-.2774	-.0801
215-216(10.1)	-8.001	5	.000	-.15365	-.2030	-.1043
216-217(11.6)	-2.918	5	.033	-.07892	-.1485	-.0094
217-218(2.6)						
217-218(10.4)	-.834	5	.442	-.02599	-.1061	.0541
218-219(2)	-4.124	5	.009	-.12019	-.1951	-.0453
218-219(11.1)	6.410	5	.001	.16268	.0974	.2279
219-220(1.9)	-3.844	5	.012	-.10603	-.1769	-.0351
219-220(11.2)	6.081	5	.002	.13711	.0791	.1951
221-222(8.1)	2.919	5	.033	.07642	.0091	.1437
222-223(1.9)	-3.114	5	.026	-.08150	-.1488	-.0142
222-223(8.1)	-7.452	5	.001	-.08186	-.1101	-.0536
223-224(3.7)	-1.187	5	.289	-.03017	-.0955	.0352
225-226(9)	1.754	5	.140	.08125	-.0378	.2003
225-226(9.9)	4.688	5	.005	.10815	.0488	.1674
229-230(3.1)	-5.276	5	.003	-.14316	-.2129	-.0734
229-230(12.7)	1.898	5	.116	.08357	-.0296	.1967
233-234(2.5)	13.162	5	.000	.51681	.4159	.6177
234-235(8.5)	-1.594	5	.172	-.04473	-.1169	.0274
235-236(11.2)	1.396	5	.222	.04030	-.0339	.1145
236-237(3.2)	2.231	5	.076	.06941	-.0106	.1494
243-244(14.2)	-.215	5	.838	-.00384	-.0498	.0421
244-245(4.3)	6.842	5	.001	.15789	.0986	.2172
244-245(14.2)	1.049	5	.342	.03150	-.0457	.1087
246-247(2)	-7.828	5	.001	-.13552	-.1800	-.0910
246-247(16.3)	2.965	5	.031	.06508	.0087	.1215

247-248(1.9)	-4.681	5	.005	-.10919	-.1692	-.0492
247-248(11.2)	-7.358	5	.001	-.13864	-.1871	-.0902
247-248(16.3)	2.163	5	.083	.10126	-.0191	.2216
249-250(8.1)	-.546	5	.609	-.01532	-.0875	.0568
249-250(13.6)	26.434	5	.000	1.82598	1.6484	2.0035
253-254(3.5)	-7.389	5	.001	-.11336	-.1528	-.0739
253-254(3.6)	-5.192	5	.003	-.09598	-.1435	-.0485
254-255(4.7)	16.188	5	.000	1.12647	.9476	1.3054
255-256(16.7)	6.491	5	.001	.11769	.0711	.1643
255-256(17.1)	3.940	5	.011	.13416	.0466	.2217
257-258(18.3)	15.862	5	.000	.20092	.1684	.2335
258-259(16.1)	-12.583	5	.000	-.22579	-.2719	-.1797
261-262(12.8)	2.290	5	.071	.08314	-.0102	.1765
269-270(8.4)	-2.447	5	.058	-.11151	-.2286	.0056
270-271(8.4)	.113	5	.914	.00284	-.0615	.0671
271-272(18.7)	18.446	5	.000	2.85734	2.4592	3.2555
271-272(20.1)	1.867	5	.121	.03401	-.0128	.0809
272-273(4.1)	-1.778	5	.136	-.04361	-.1067	.0194
272-273(8.3)	-10.216	5	.000	-.10739	-.1344	-.0804
274-275(1.9)	-4.588	5	.006	-.06995	-.1091	-.0308
274-275(19.3)	2.837	5	.036	.08773	.0082	.1672
275-276(4)	-4.043	5	.010	-.08910	-.1458	-.0324
275-276(19.5)	2.617	5	.047	.08862	.0016	.1757
276-277(1.9)	-2.996	5	.030	-.10142	-.1884	-.0144
276-277(20.1)	16.644	5	.000	.19213	.1625	.2218
277-278(1.7)	-3.535	5	.017	-.06047	-.1044	-.0165
277-278(3.7)	4.292	5	.008	.09255	.0371	.1480
277-278(16.1)	-5.697	5	.002	-.12190	-.1769	-.0669
279-280(6.6)						
279-280(12.2)	-1.829	5	.127	-.08642	-.2079	.0350
285-286(2.2)	-5.294	5	.003	-.13053	-.1939	-.0672
285-286(15.1)	-6.151	5	.002	-.13355	-.1894	-.0777
285-286(19.4)	5.610	5	.002	.15514	.0840	.2262
285-286(20.2)	-2.747	5	.040	-.09984	-.1933	-.0064
286-287(20.7)	-.339	5	.748	-.01020	-.0875	.0671
288-289(9.3)	1.969	5	.106	.04732	-.0145	.1091
288-289(24.7)	-.230	5	.827	-.00549	-.0669	.0559
289-290(5.3)	6.148	5	.002	.19658	.1144	.2788
290-291(2)	-3.364	5	.020	-.06227	-.1099	-.0147
290-291(4.7)	3.822	5	.012	.09961	.0326	.1666
297-298(21.2)	-8.506	5	.000	-.17599	-.2292	-.1228
298-299(13.2)	-9.013	5	.000	-.17162	-.2206	-.1227
298-299(22.3)	-1.382	5	.226	-.03465	-.0991	.0298
299-300(23.1)	.542	5	.611	.01149	-.0429	.0659

300-301(20.2)	1.617	5	.167	.05323	-.0314	.1379
302-303(28.1)	-1.680	5	.154	-.08289	-.2097	.0439
302-303(29.2)	3.385	5	.020	.14350	.0345	.2525
303-304(3.3)	-3.066	5	.028	-.08316	-.1529	-.0134
303-304(13.1)	-5.852	5	.002	-.12019	-.1730	-.0674
303-304(23.6)	3.899	5	.011	.14707	.0501	.2440
304-305(3.3)	-3.074	5	.028	-.07071	-.1298	-.0116
304-305(23.7)	2.444	5	.058	.09024	-.0047	.1852
307-308(6.7)	5.587	5	.003	.10056	.0543	.1468
307-308(12.2)	2.440	5	.059	.08590	-.0046	.1764
313-314(7.8)	-4.804	5	.005	-.09813	-.1506	-.0456
313-314(23.7)	3.315	5	.021	.10514	.0236	.1867
314-315(40.6)	-.721	5	.503	-.01341	-.0612	.0344
319-320(2.1)	-1.152	5	.301	-.03301	-.1066	.0406
319-320(20.4)	4.899	5	.004	.09043	.0430	.1379
324-325(6.8)	-10.204	5	.000	-.15336	-.1920	-.1147
324-325(15.3)	3.320	5	.021	.10198	.0230	.1809
383-384(9.9)	-.748	5	.488	-.01338	-.0593	.0326
383-384(17.3)	-3.131	5	.026	-.06136	-.1117	-.0110
387-388(10.7)	-.404	5	.703	-.01376	-.1014	.0739
387-388(17.3)	.056	5	.958	.00124	-.0562	.0587
388-389(3.3)	-8.039	5	.000	-.09318	-.1230	-.0634
388-389(17.4)	-4.310	5	.008	-.09724	-.1552	-.0392
402-403(5.5)	.135	5	.898	.00344	-.0619	.0688
403-404(3.3)	-2.812	5	.037	-.09352	-.1790	-.0080
403-404(6.4)	7.070	5	.001	.21496	.1368	.2931
404-405(3.3)	4.406	5	.007	.15706	.0654	.2487

^a m/z values of metabolites labelled with DMBA.

Figure S1. The pathway for synthesis of DMBA and d⁴-DMBA.

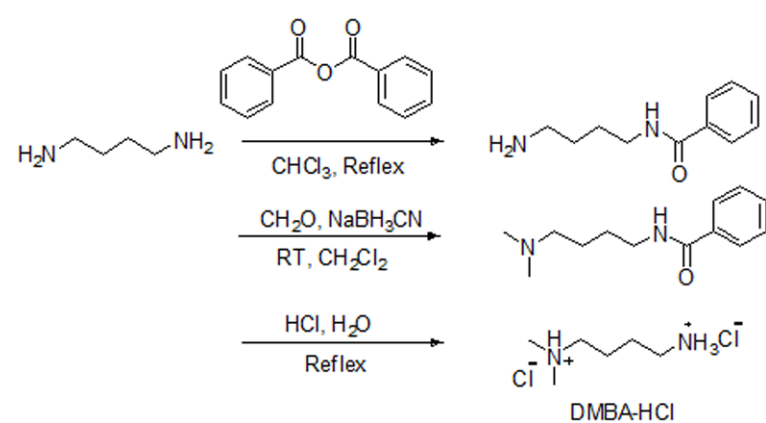


Figure S2. The reactions of DMBA and d⁴-DMBA with carboxylic acid metabolites.

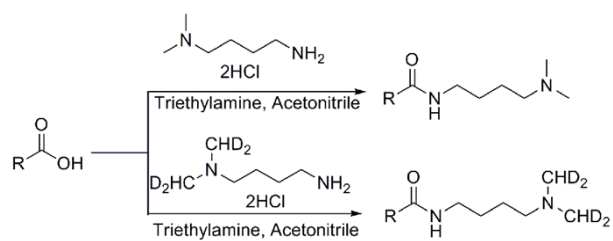


Figure S3. Product ion mass spectra of the metabolite at m/z 233 eluted at 2.53 min (m/z 233-2.53 min) after labelling. The collision energies increase from the top spectrum to the down spectrum (20 V, 35 V and 50 V, respectively).

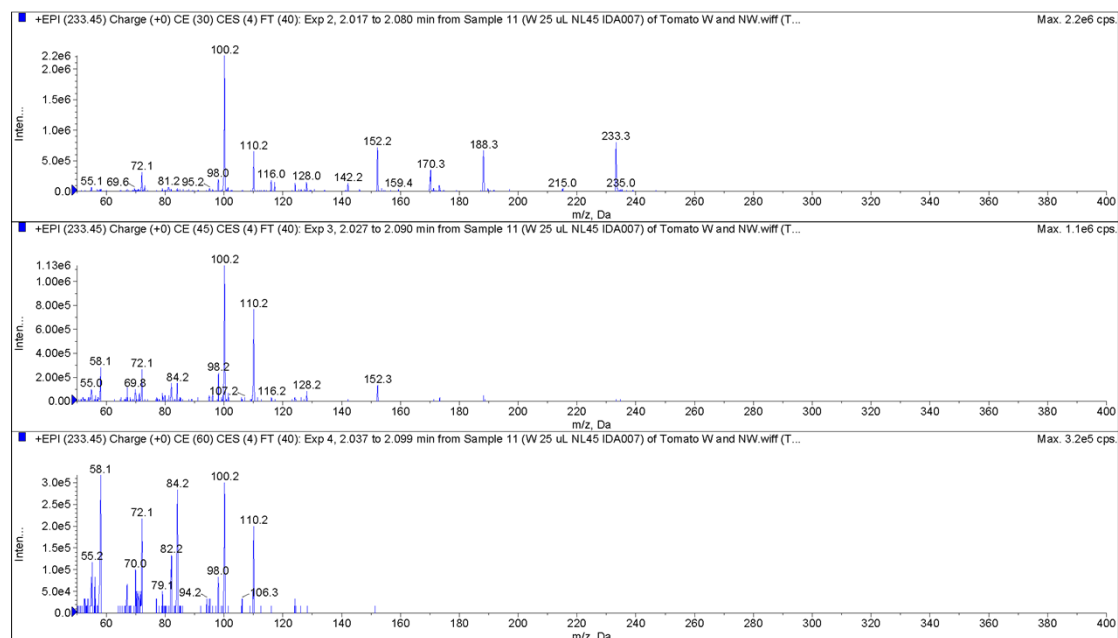


Figure S4. The proposed fragmentation pathway of the potential biomarker (m/z 233-2.53 min) after labelling.

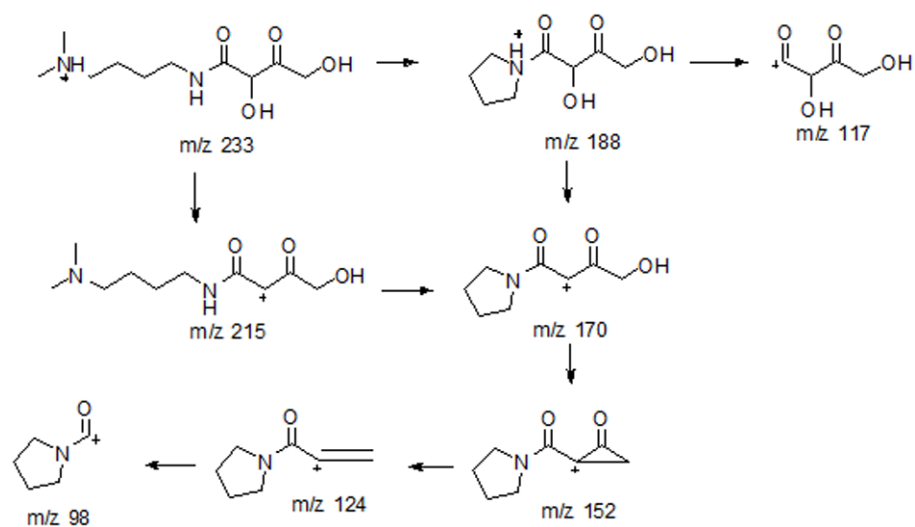


Figure S5. Product ion mass spectra of the potential biomarker at m/z 217 eluted at 2.61 min (m/z 217-2.61 min) after labelling. The collision energies increase from the top spectrum to the down spectrum (20 V, 35 V and 50 V, respectively).

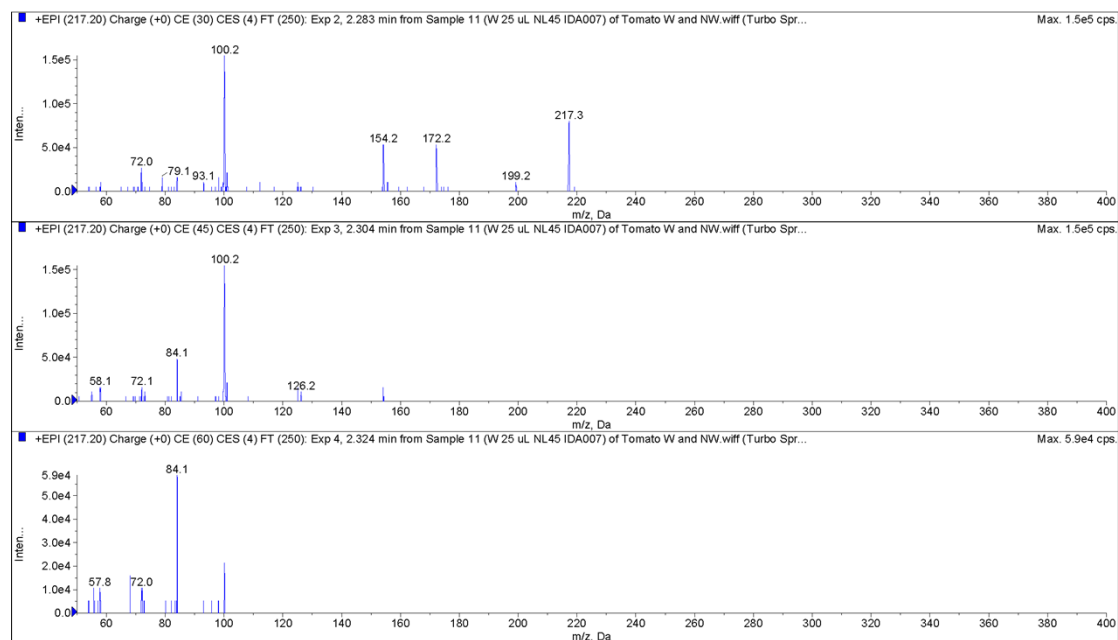


Figure S6. The proposed fragmentation pathway of the potential biomarker (m/z 217-2.61 min) after labelling.

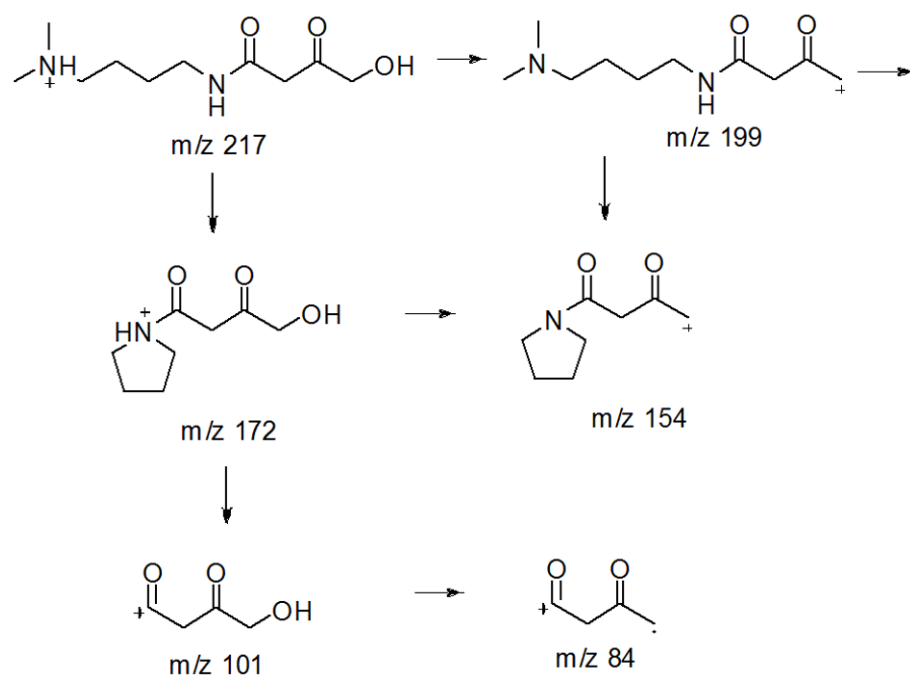


Figure S7. Product ion mass spectra of the potential biomarker at m/z 254 eluted at 4.75 min (m/z 254-4.75 min) after labelling. The collision energies increase from the top spectrum to the down spectrum (20 V, 35 V and 50 V, respectively).

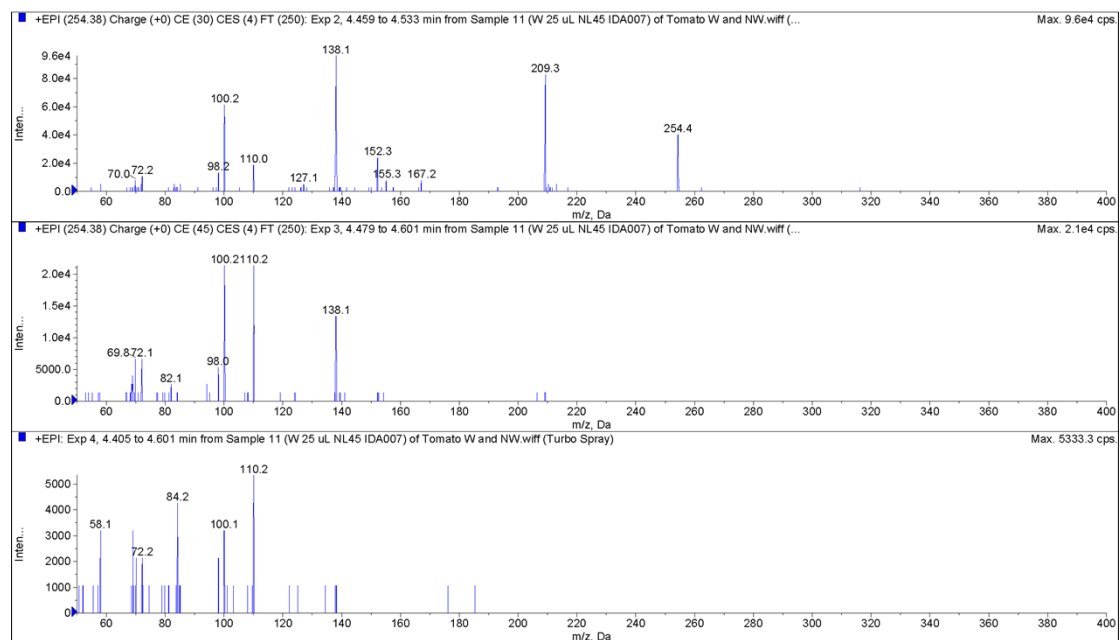


Figure S8. The proposed fragmentation pathway of the potential biomarker (m/z 254-4.75 min) after labelling.

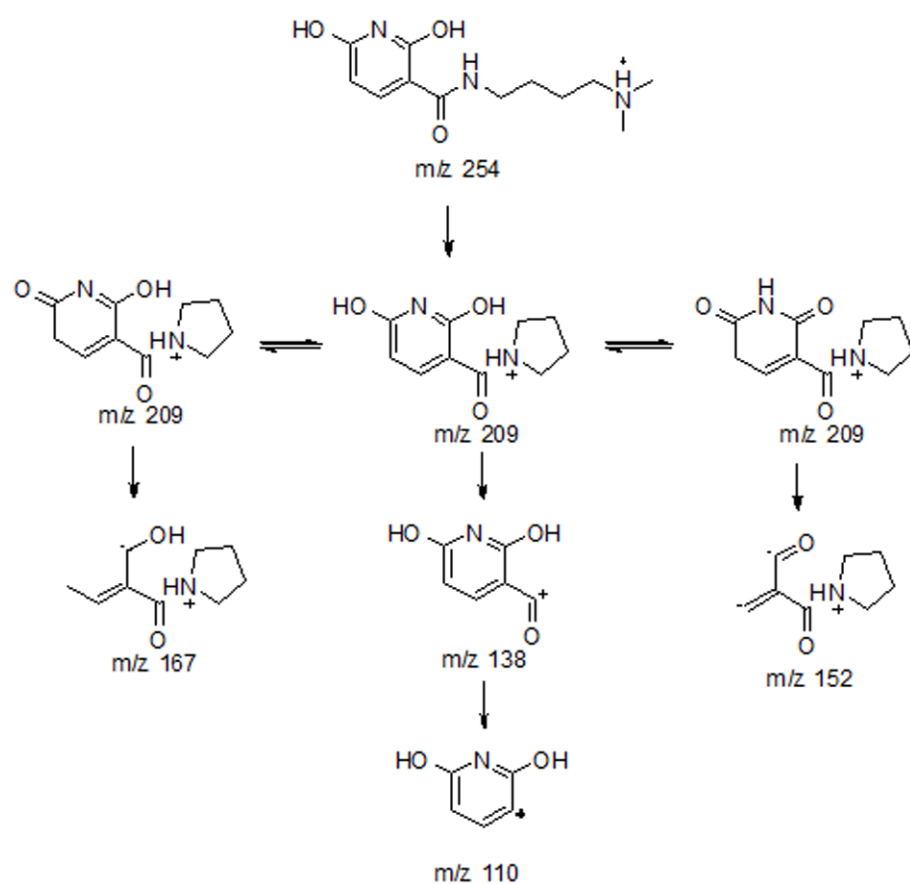


Figure S9. Product ion mass spectra of the potential biomarker at m/z 279 eluted at 6.69 min (m/z 279-6.69 min) after labelling. The collision energies increase from the top spectrum to the down spectrum (20 V, 35 V and 50 V, respectively).

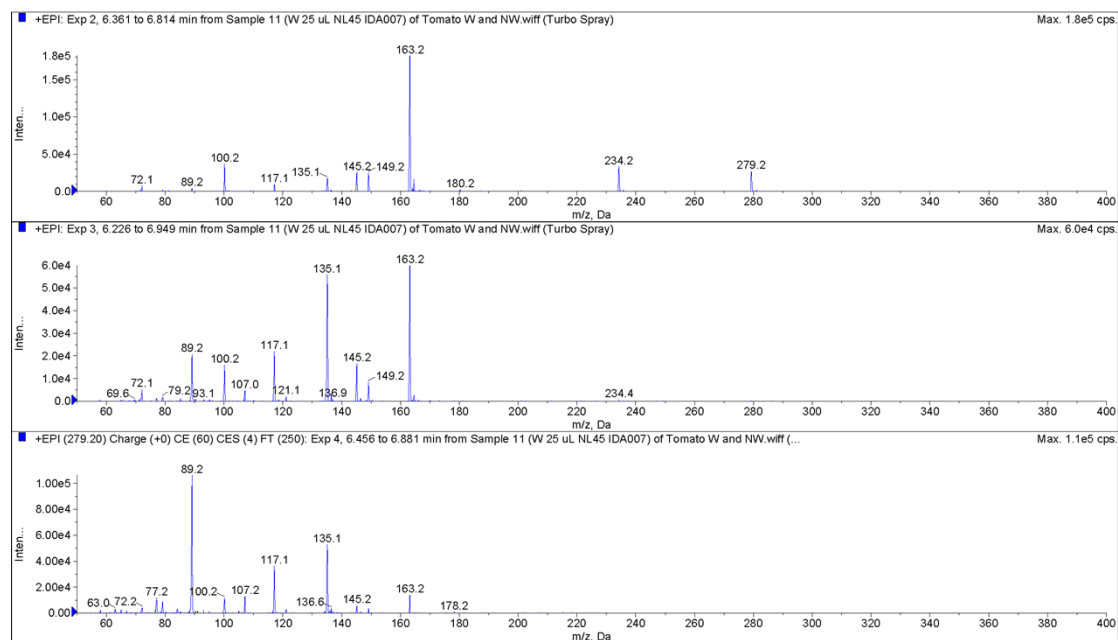


Figure S10. The proposed fragmentation pathway of the potential biomarker (m/z 279-6.69 min) after labelling.

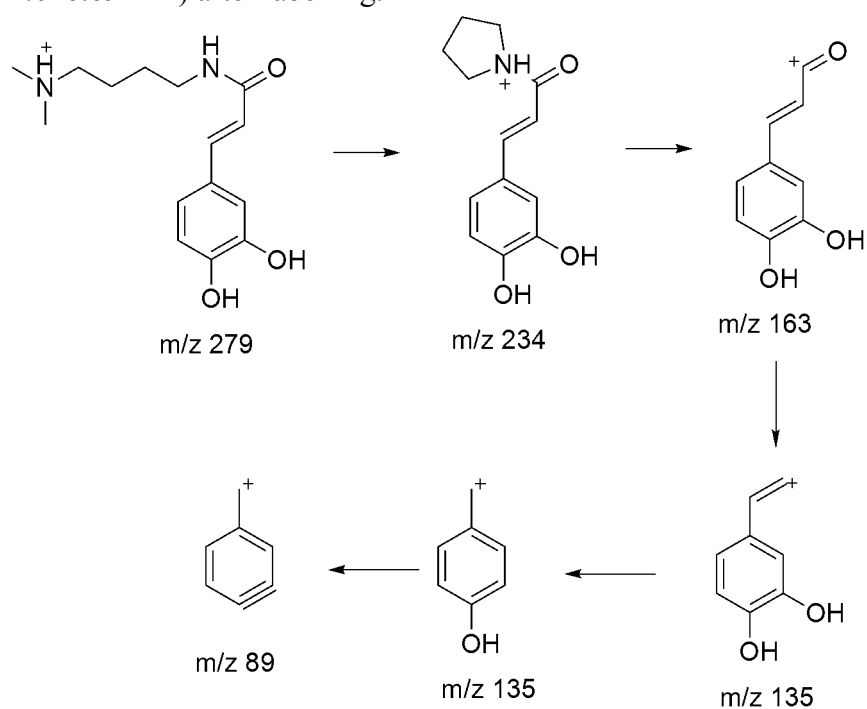


Figure S11. Product ion mass spectra of the potential biomarker at m/z 249 eluted at 13.6 min (m/z 249-13.6 min) after labelling. The collision energies increase from the top spectrum to the down spectrum (20 V, 35 V and 50 V, respectively).

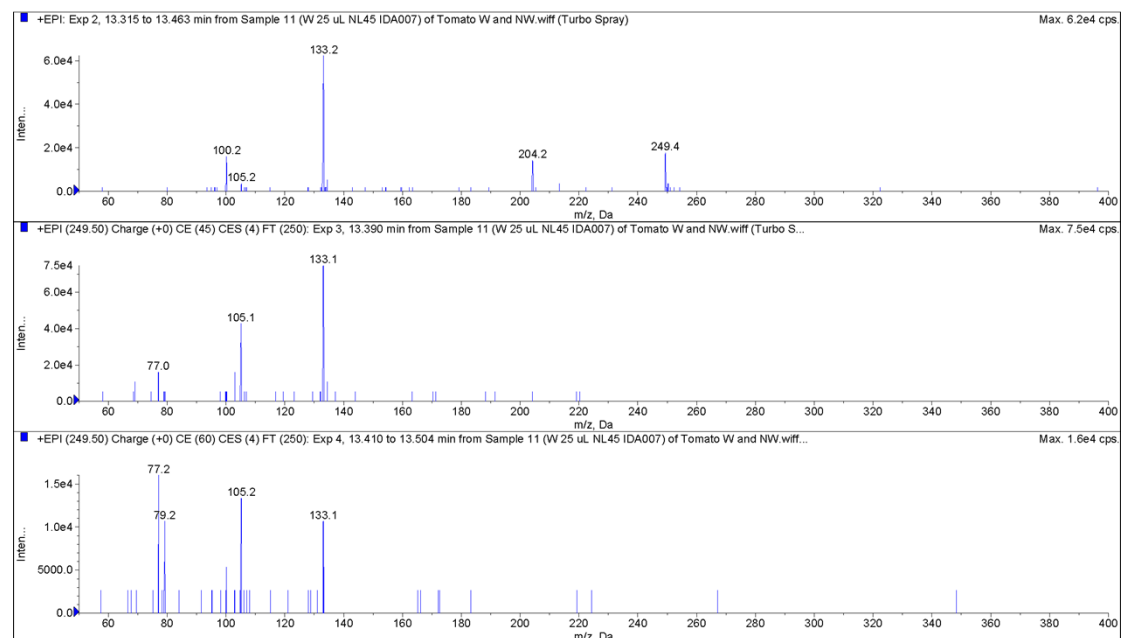


Figure S12. The proposed fragmentation pathway of the potential biomarker (m/z 249-13.6 min) after labelling.

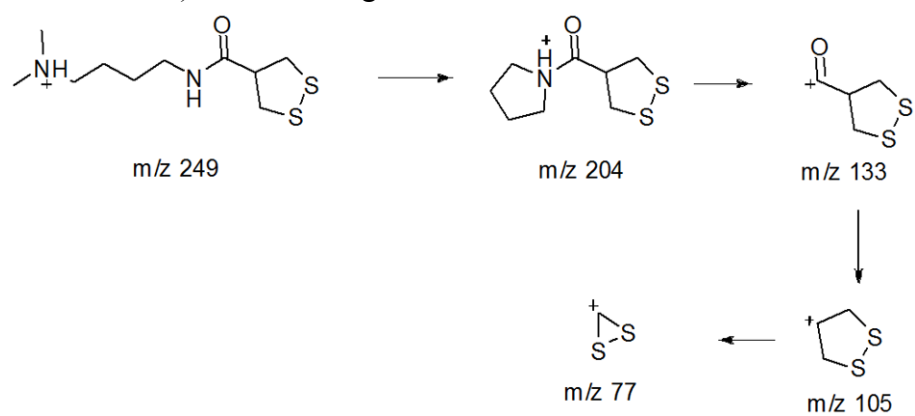


Figure S13. Product ion mass spectra of the potential biomarker at m/z 271 eluted at 18.9 min (m/z 271-18.9 min) after labelling. The collision energies increase from the top spectrum to the down spectrum (20 V, 35 V and 50 V, respectively).

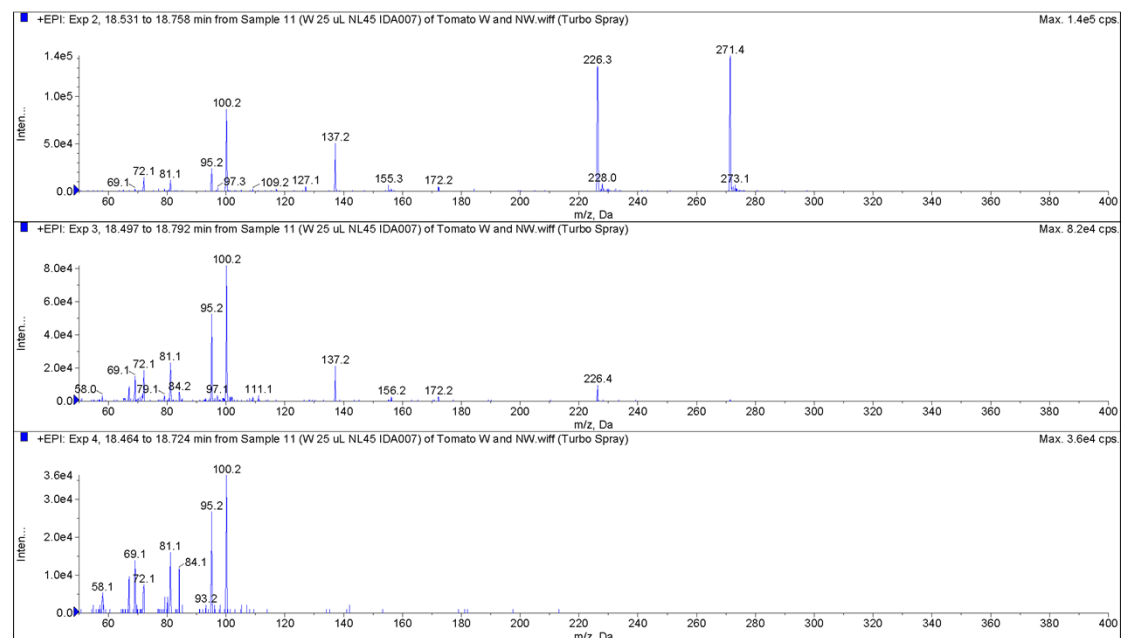


Figure S14. The proposed fragmentation pathway of the potential biomarker (m/z 271-18.9 min) after labelling.

