Supplementary Information

Comparative profiling of analog targets: a case study on resveratrol for mouse melanoma metastasis suppression

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Supplementary Figures

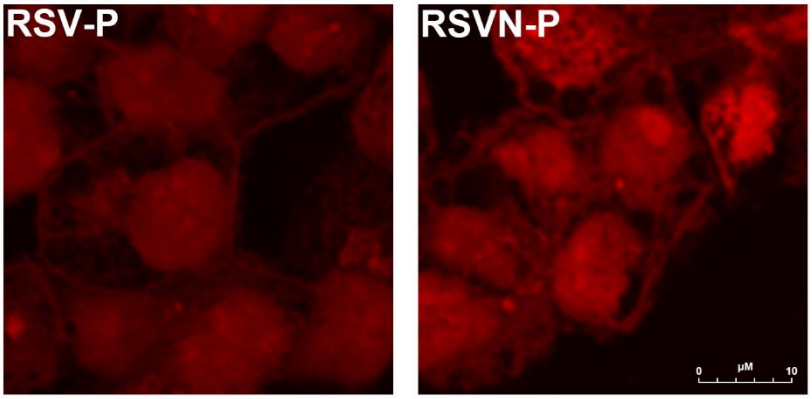


Figure S1. Distribution of targets of RSV and RSVN in B16F10 cells

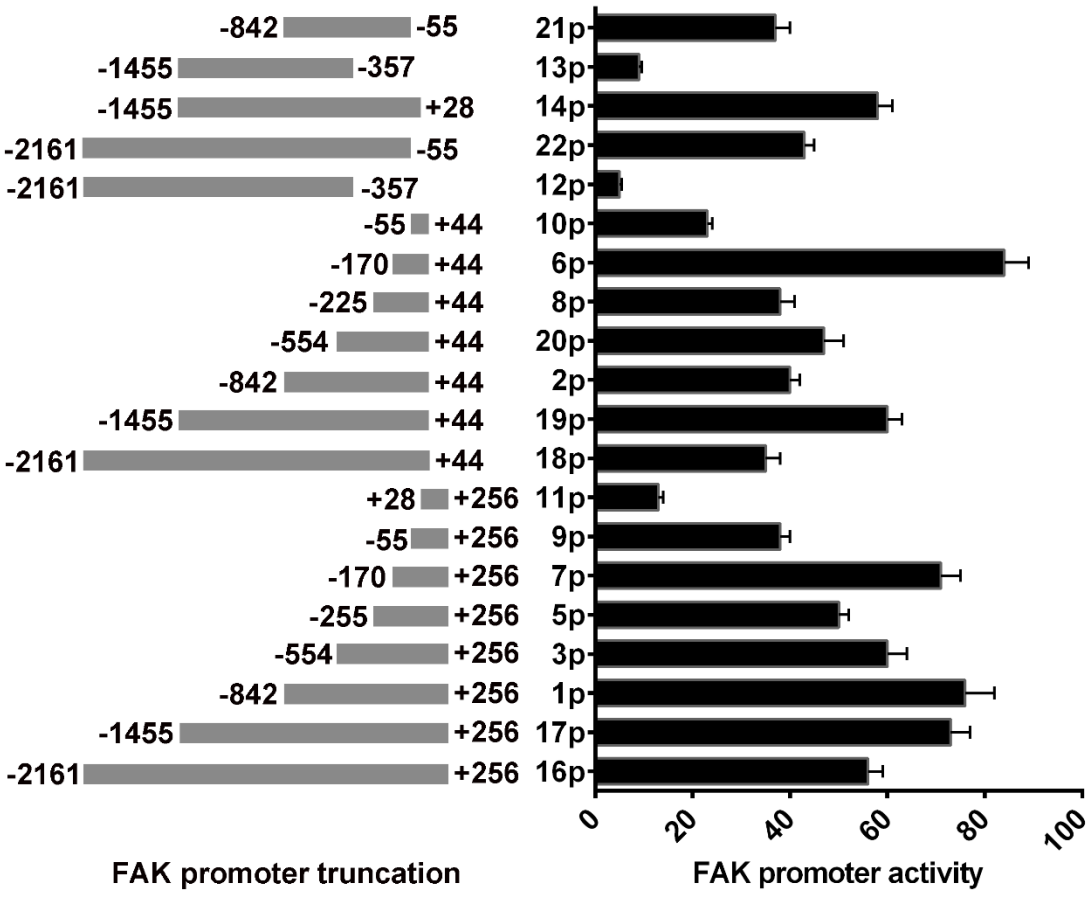


Figure S2. Transcription activity of FAK promoter truncations

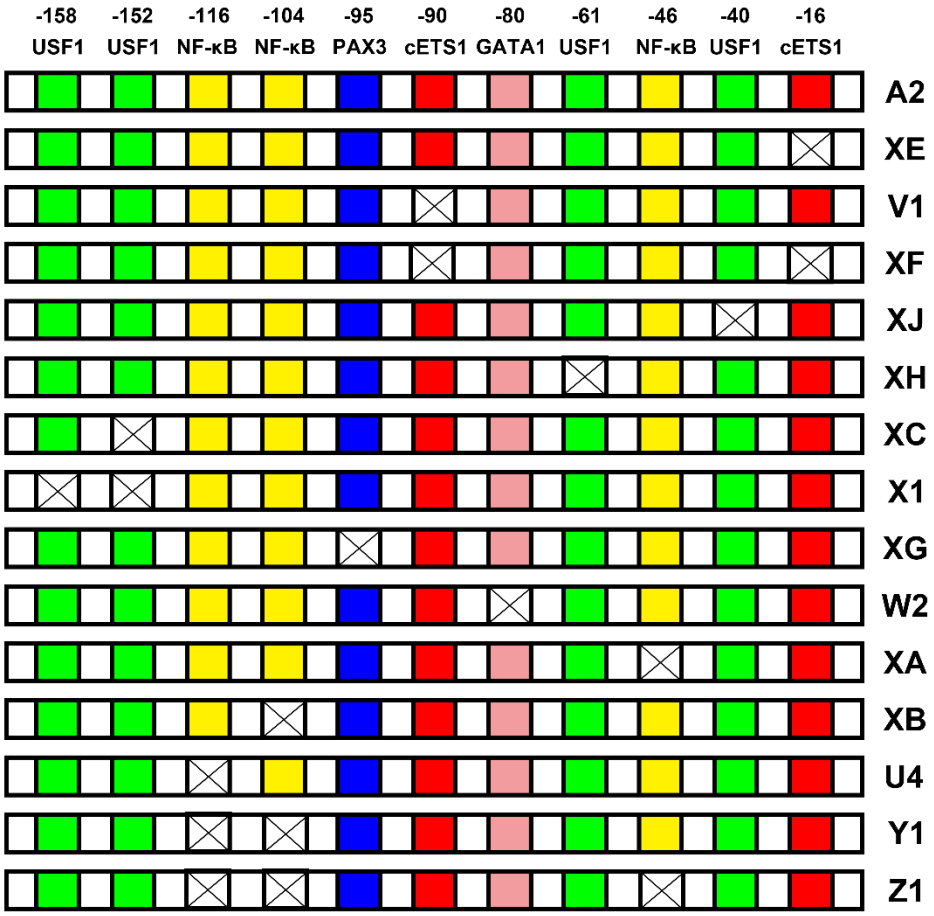


Figure S3. Transcription factor binding sites analysis of FAK promoter using P-Match software and the gene reporter plamids used in the study.

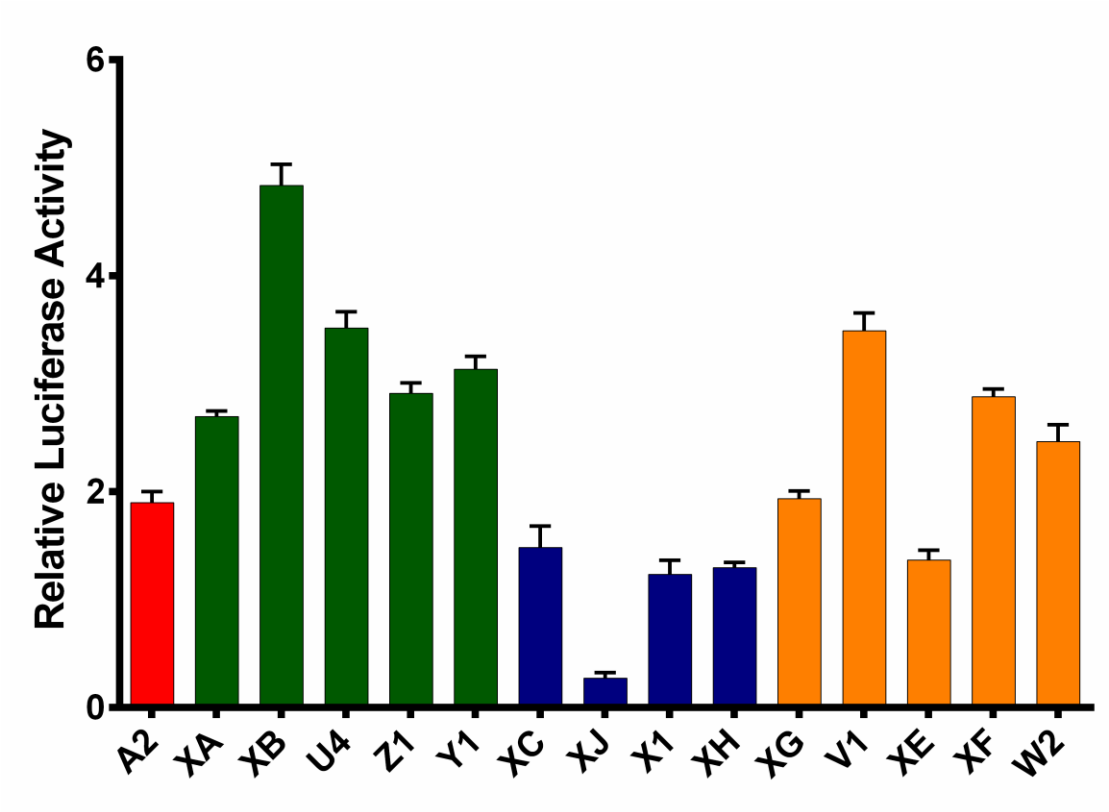


Figure S4. Transcription activity of the mutations of FAK promoter from dual-luciferase assay.

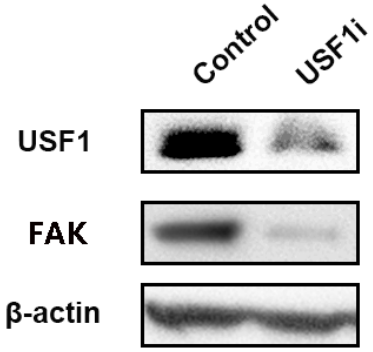
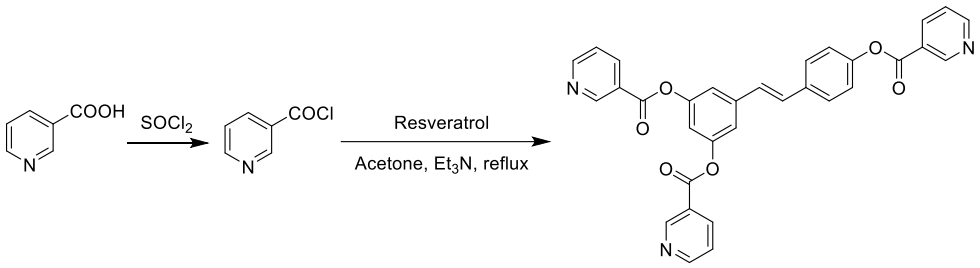


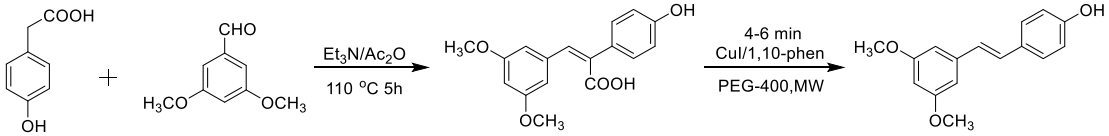
Figure S5. Expression level of USF1 and FAK in B16F10 cells with or without the treatment of USF1's siRNA.

Supplementary Methods

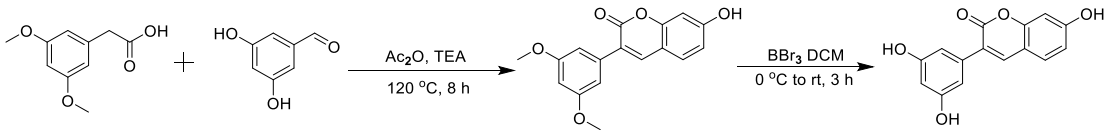
Synthesis of RSVT



Synthesis of PTER



Synthesis of RSVN



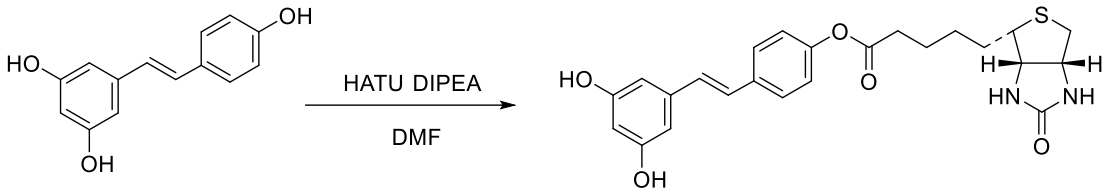
3-(3,5-Dimethoxyphenyl)-7-hydroxy-2H-chromen-2-one

RSVN

3-(3,5-Dimethoxyphenyl)-7-hydroxy-2H-chromen-2-one Triethylamine (8 ml) was added to a solution of 2-(3,5-dimethoxyphenyl)acetic acid (4 g, 20 mmol) and 3,5-dihydroxybenzaldehyde (2.8 g, 20 mmol) in acetic anhydride (20 mL) The mixture was heated to 120 ℃ and stirred for 8 h. After cooling, it was poured into ice water, stirred, and stored for 4 h. The precipitated yellowish solid was filtered, washed with water, dried, and recrystallized from ethyl acetate. The title compound 4.5 g (75%) was obtained as a light yellow solid. LC-MS show M+1 (299).

To a solution of 3-(3,5-Dimethoxyphenyl)-7-hydroxy-2H-chromen-2-one (2 g, 6.7 mmol) in DCM (50 mL) was drop wise added BBr_3 (5 g, 20.1 mmol) at 0 ℃. The mixture was stirred at room temperature for 3 h under Ar atmosphere. Then quenching by H_2O at – 10 ℃, adjusted pH=8 by $NaHCO_3$ (aq), extracted with EA for three times, the organic phase was dried and concentrated, the residue was purified by column chromatography with PE:EA=1:1 to give the title compound as a light yellow solid (1.2 g, 65%). LC-MS show M+1 (271).

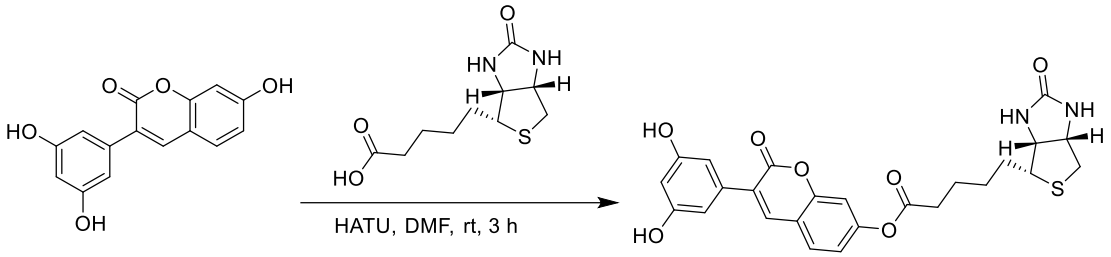
Synthesis of RSV-P



Resveratrol RSV-P

To a solution of biotin (50 mg, 2.05 mmol) in DMF (20 mL) was added HATU (800 mg, 2.1 mmol) at 0 ℃. Then resveratrol (502 mg, 2.2 mmol) and DIPEA (323 mg, 2.5 mmol) were added under Ar atmosphere. The mixture was stirred for 3 h at room temperature. The mixture was concentrated in vacuo, the residue was purified by column chromatography with DCM : CH_3OH = 4 : 1 to give the title compound as a white solid (110 mg, 11%). LC-MS show M+1 (454.8).

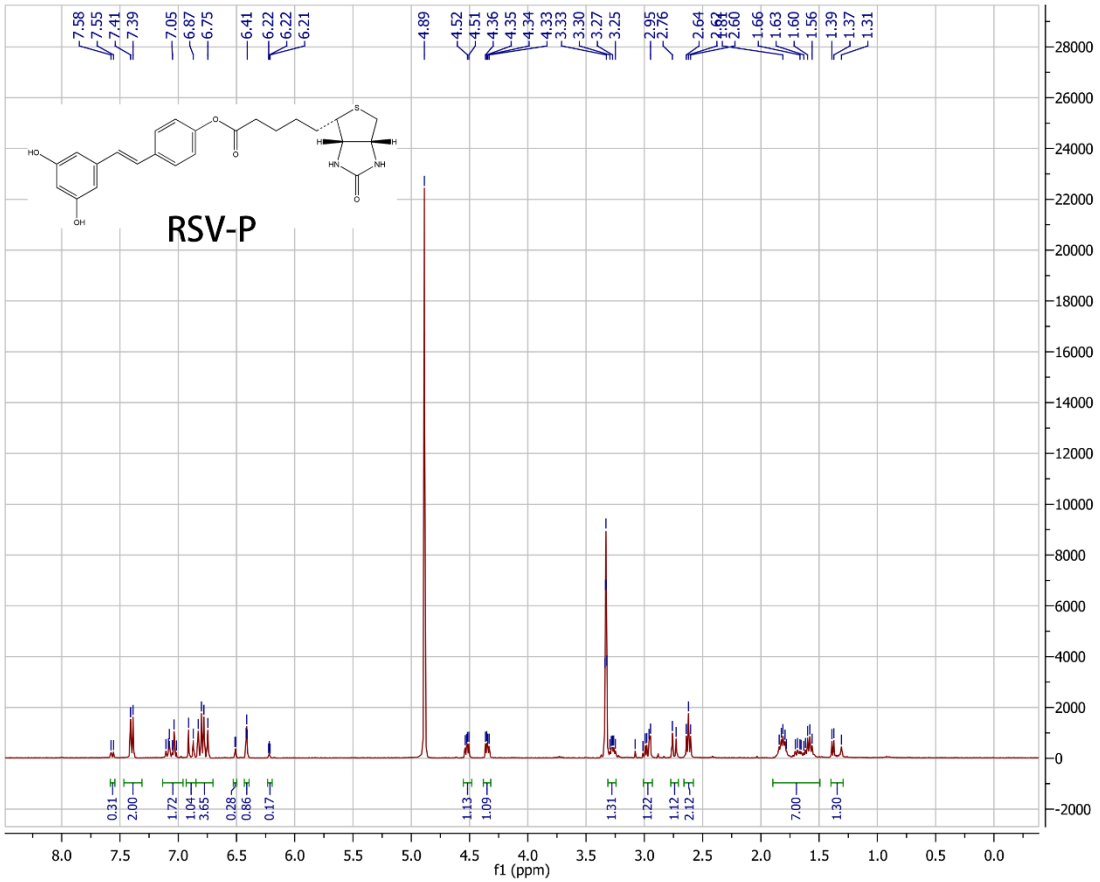
Synthesis of RSVN-P

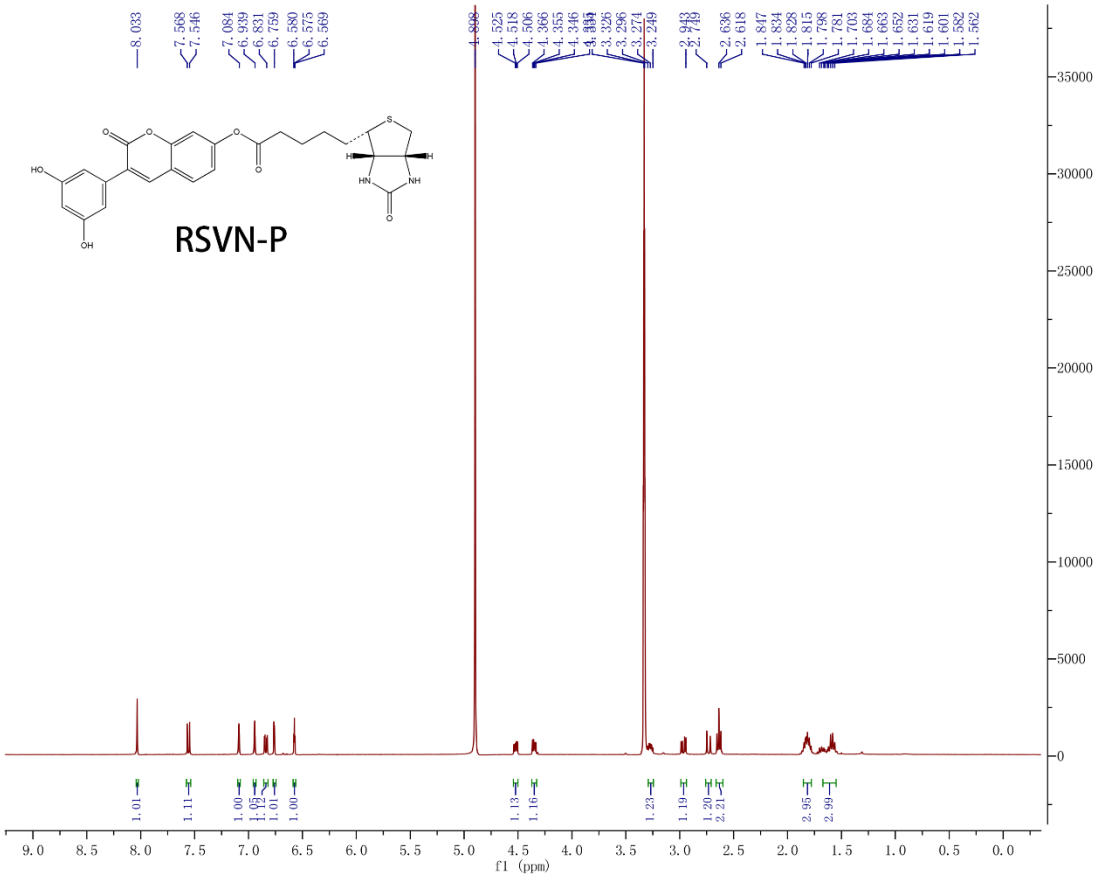


RSVN RSVN-P

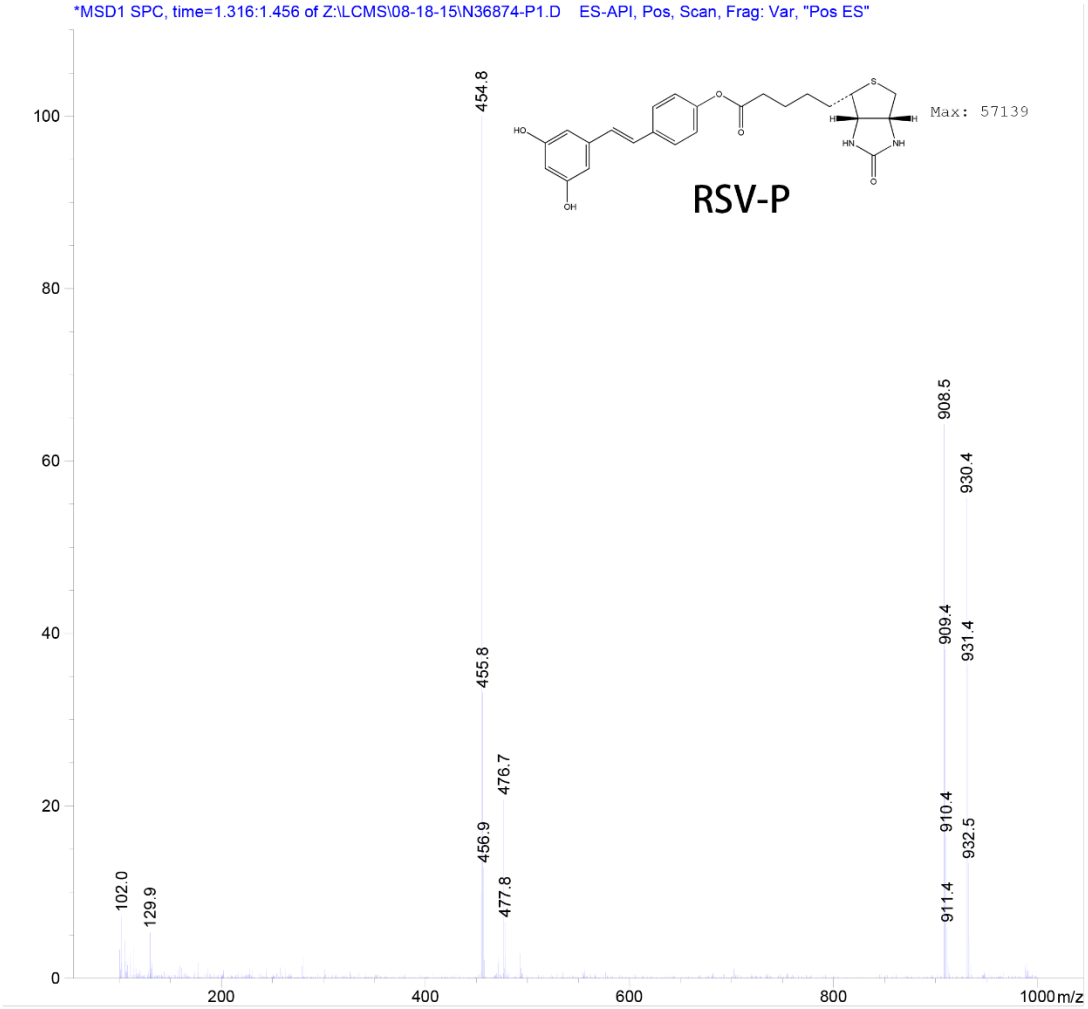
To a solution of biotin (50 mg, 2.05 mmol) in DMF (20 mL) was added HATU (800 mg, 2.1 mmol) at 0 ℃. Then NJ-2-4 (600 mg, 2.2 mmol) and DIPEA (323 mg, 2.5 mmol) were added under Ar atmosphere. The mixture was stirred for 3 h at room temperature. The mixture was concentrated in vacuo, the residue was purified by column chromatography with DCM: CH_3OH = 5:1 to give the title compound as a white solid (110 mg, 11%). LC-MS show M+1 (496.9).

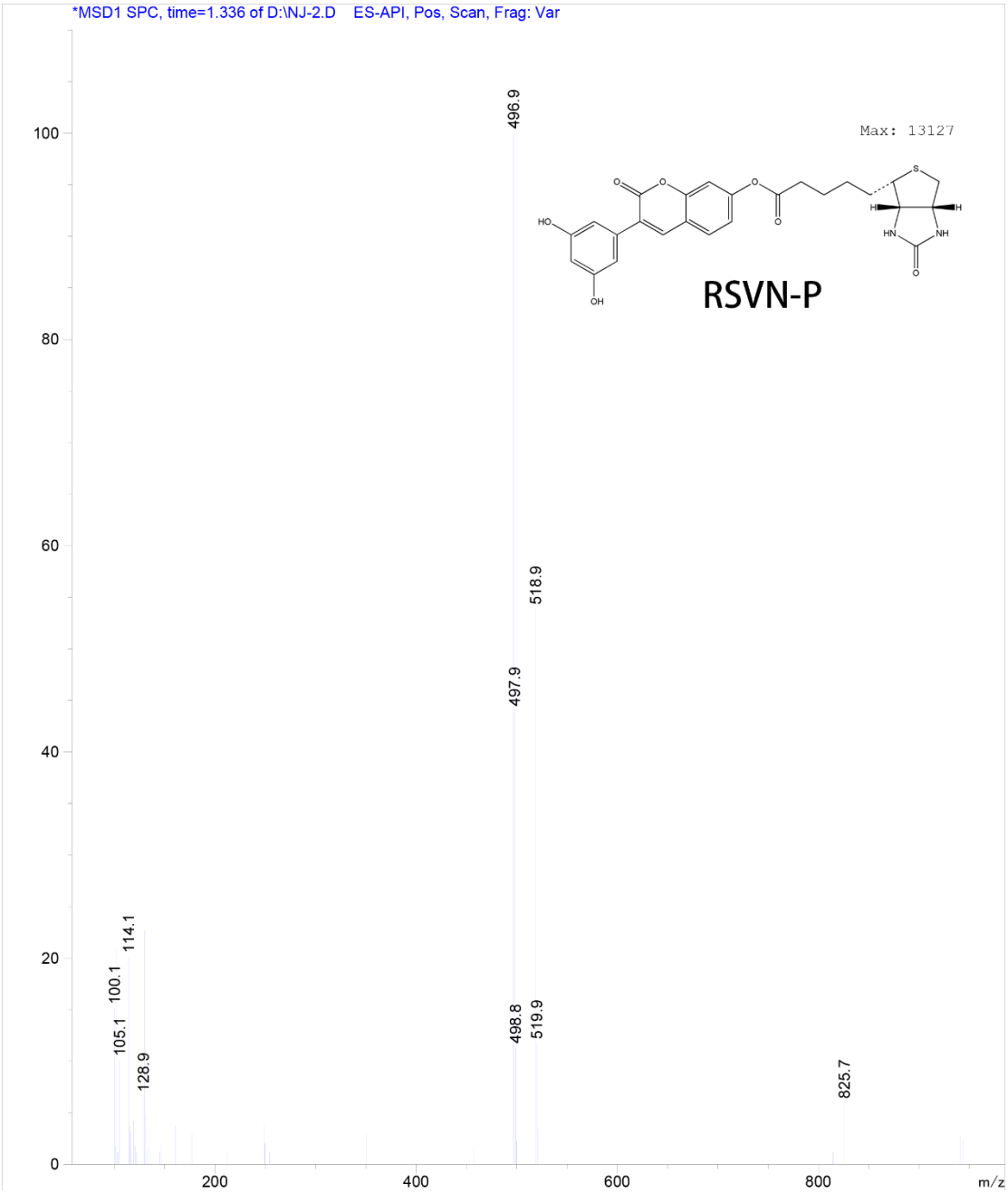
NMR spectra




RSVN-P
8.033
7.568
7.546
7.084
6.939
6.831
6.759
6.580
6.575
6.569
4.809
4.525
4.518
4.506
4.366
4.355
4.346
3.326
3.296
3.274
3.249
2.943
2.749
2.636
2.618
1.847
1.834
1.828
1.815
1.798
1.781
1.703
1.684
1.663
1.652
1.631
1.619
1.601
1.582
1.562
1.01
1.11
1.00
1.02
1.01
1.00
1.13
1.16
1.23
1.19
1.20
2.21
2.95
2.99
f1 (ppm)

Mass spectrum




*MSD1 SPC, time=1.336 of D:\NJ-2.D ES-API, Pos, Scan, Frag: Var
Max: 13127
RSVN-P
496.9
518.9
497.9
114.1
100.1
105.1
128.9
498.8
519.9
825.7
100
80
60
40
20
0
200
400
600
800
m/z