

Supplemental Figure 1

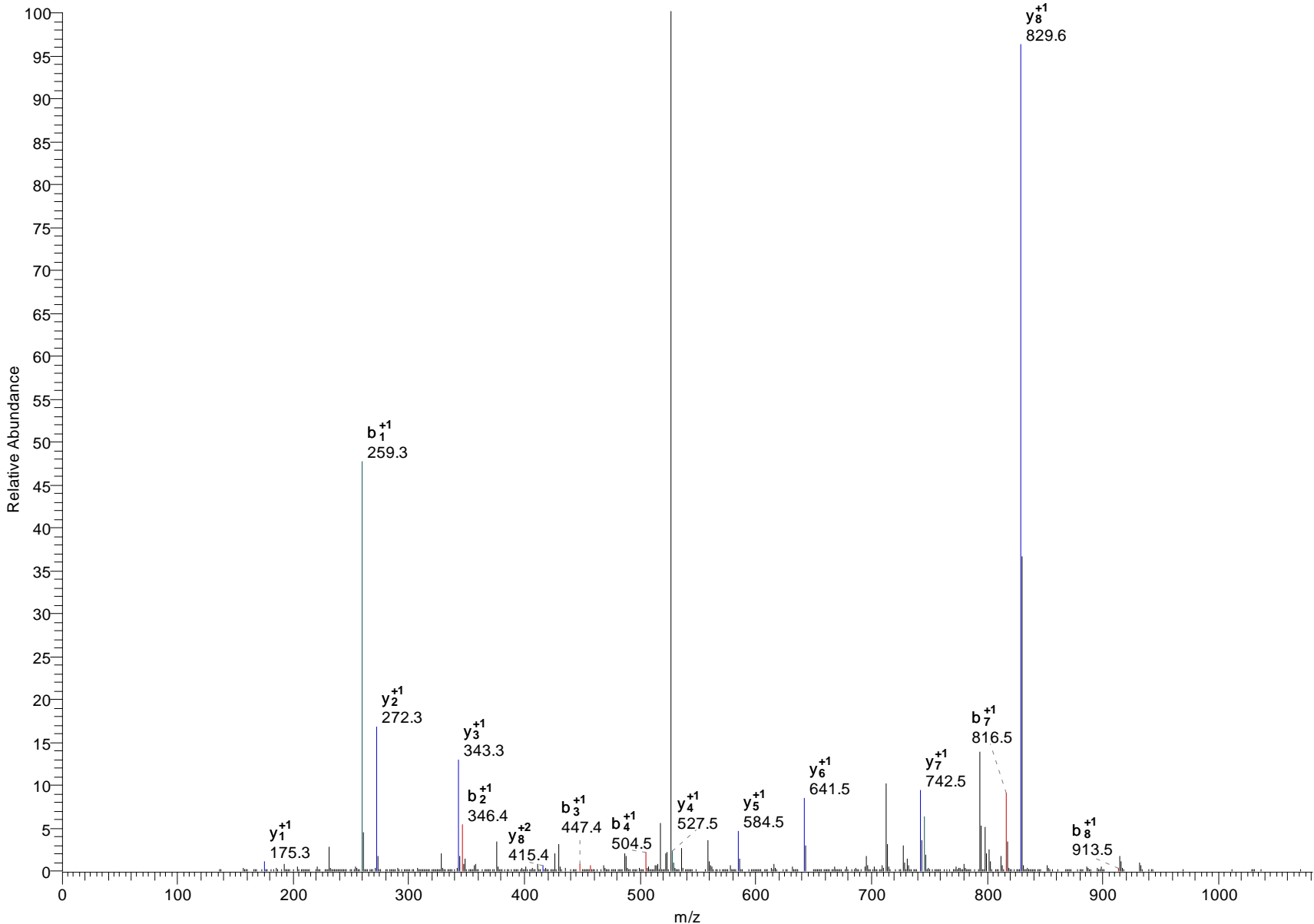
(56 MS/MS spectra)

SUPPLEMENTAL FIGURE 1. MS/MS spectra for all the peptides identified and analyzed in the study. For those peptides that cannot be resolved from the MS/MS data alone (with superscript ^b in Sup. Table 1), a representative MS/MS spectrum for one of the possible peptides is provided.

prKpr,me1:1STGAAKR

H1.4K25me1:1

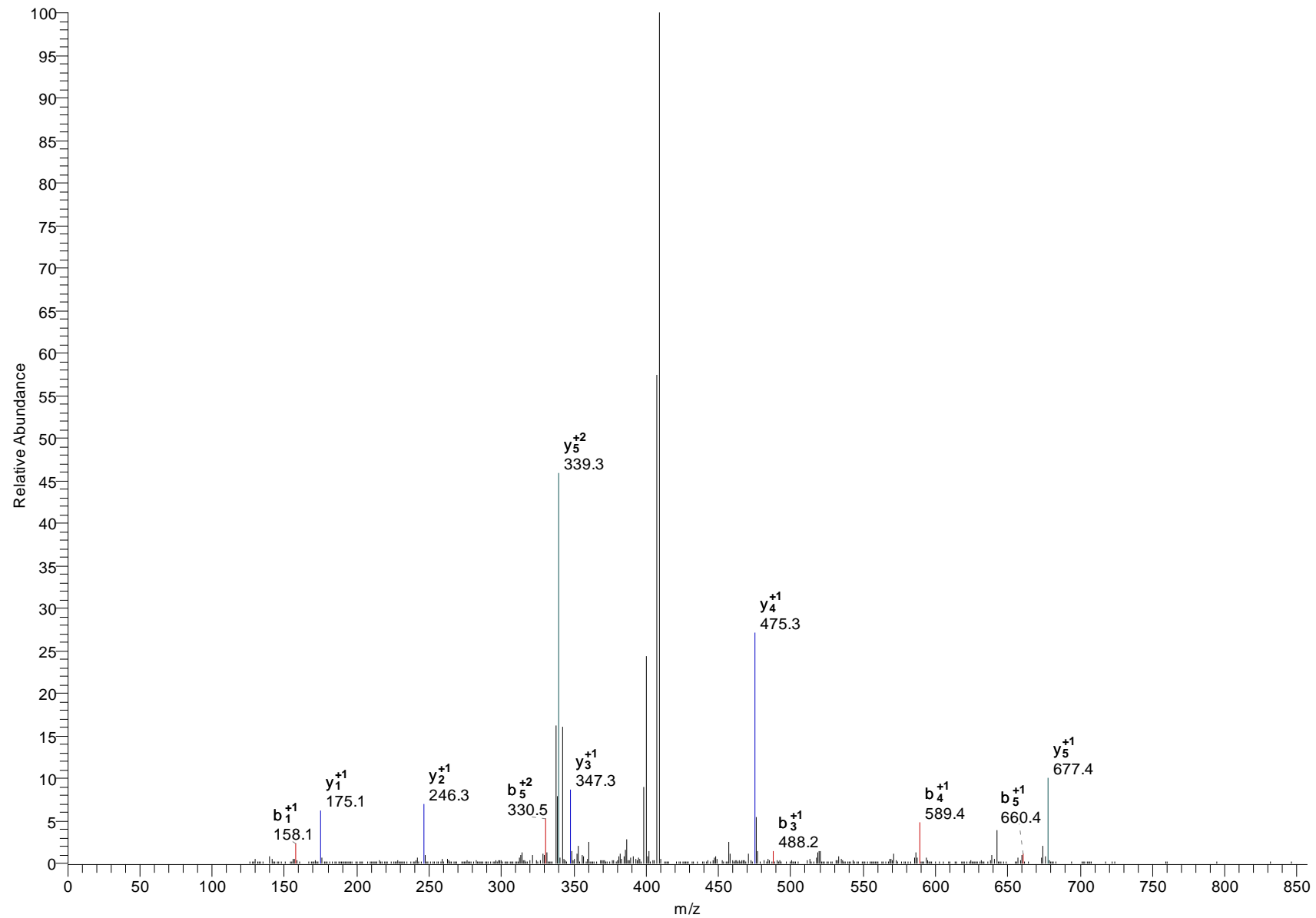
#8326-8326 RT:59.05-59.05 NL: 4.02E5



TKpr,me1:1QTAR

H3K4me1:1

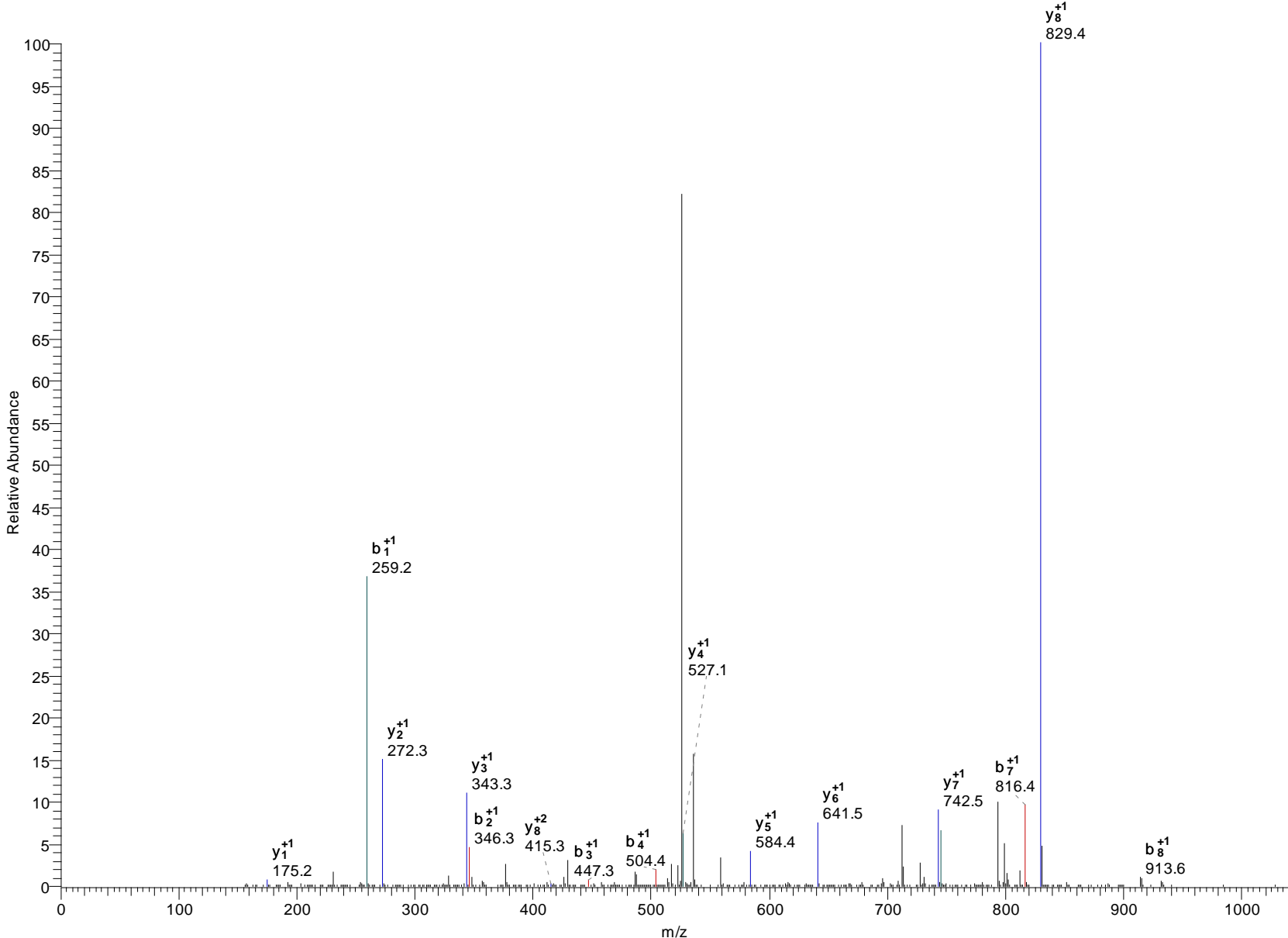
#6739-6739 RT:47.95-47.95 NL: 2.09E4



prKpr,me1:1STGGKprAPR

H3K9me1:1

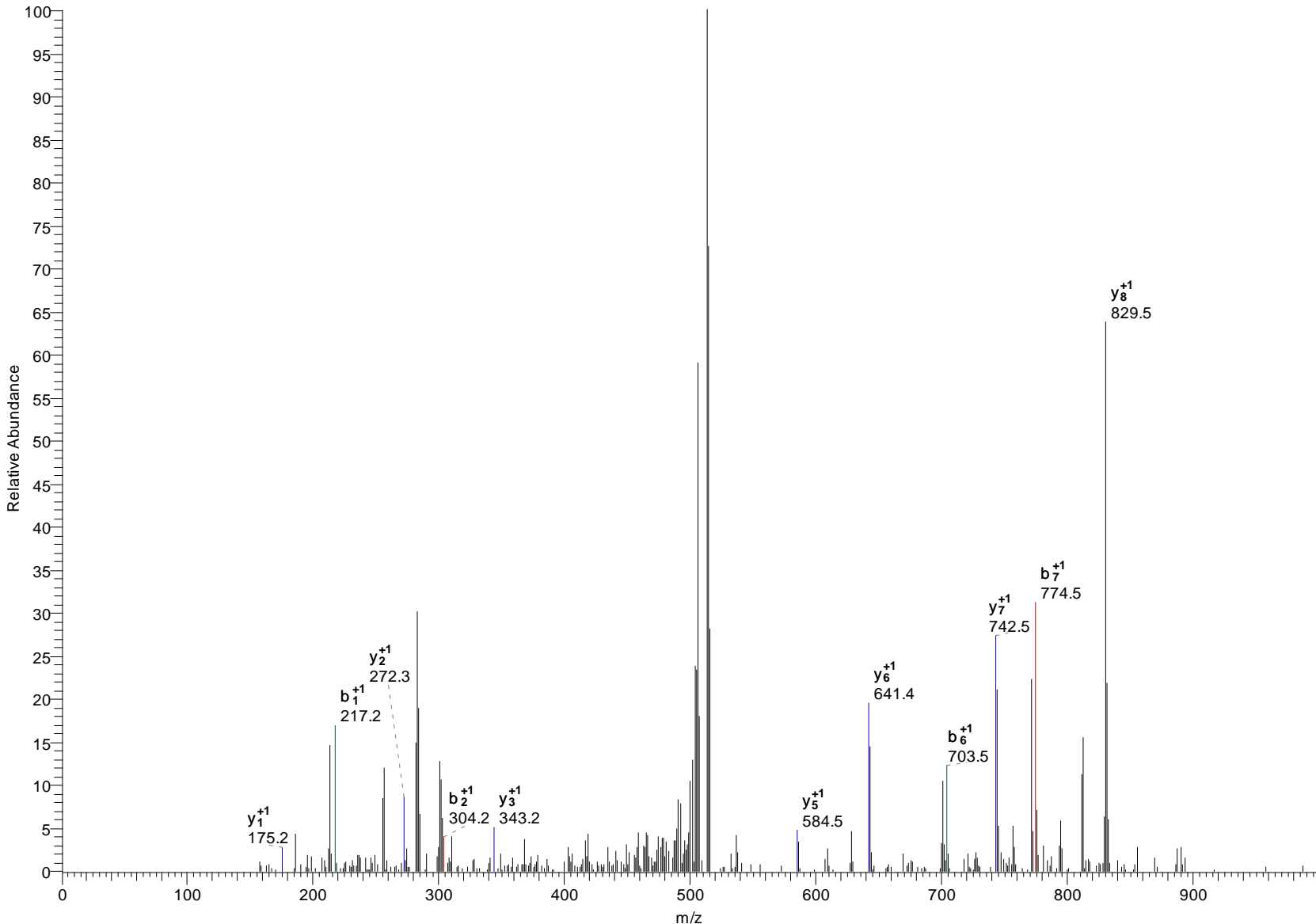
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prKme2:1STGGKprAPR

H3K9me2:1

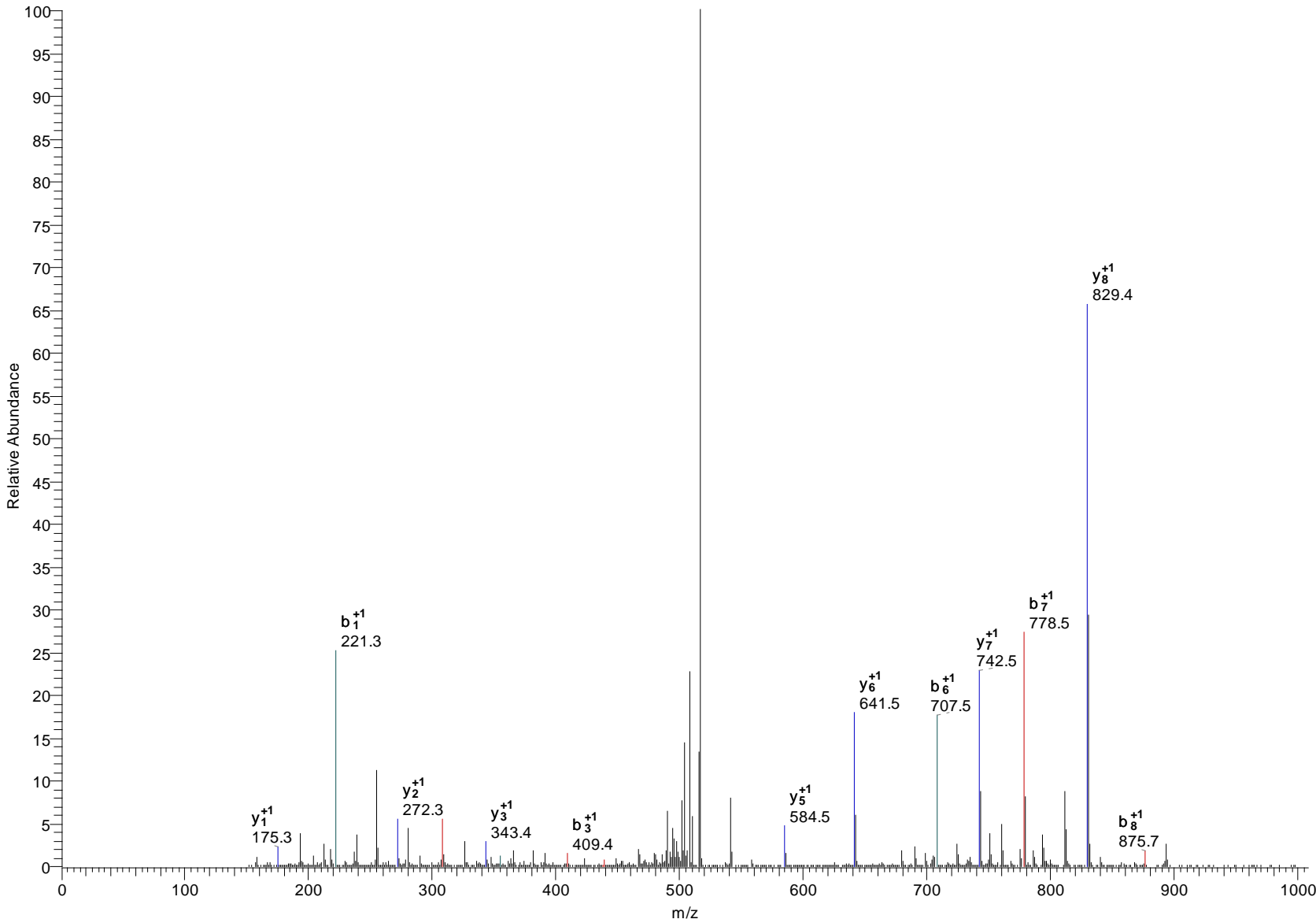
#2906-2906 RT:25.20-25.20 NL: 5.79E2



prKme2:2STGGKprAPR

H3K9me2:2

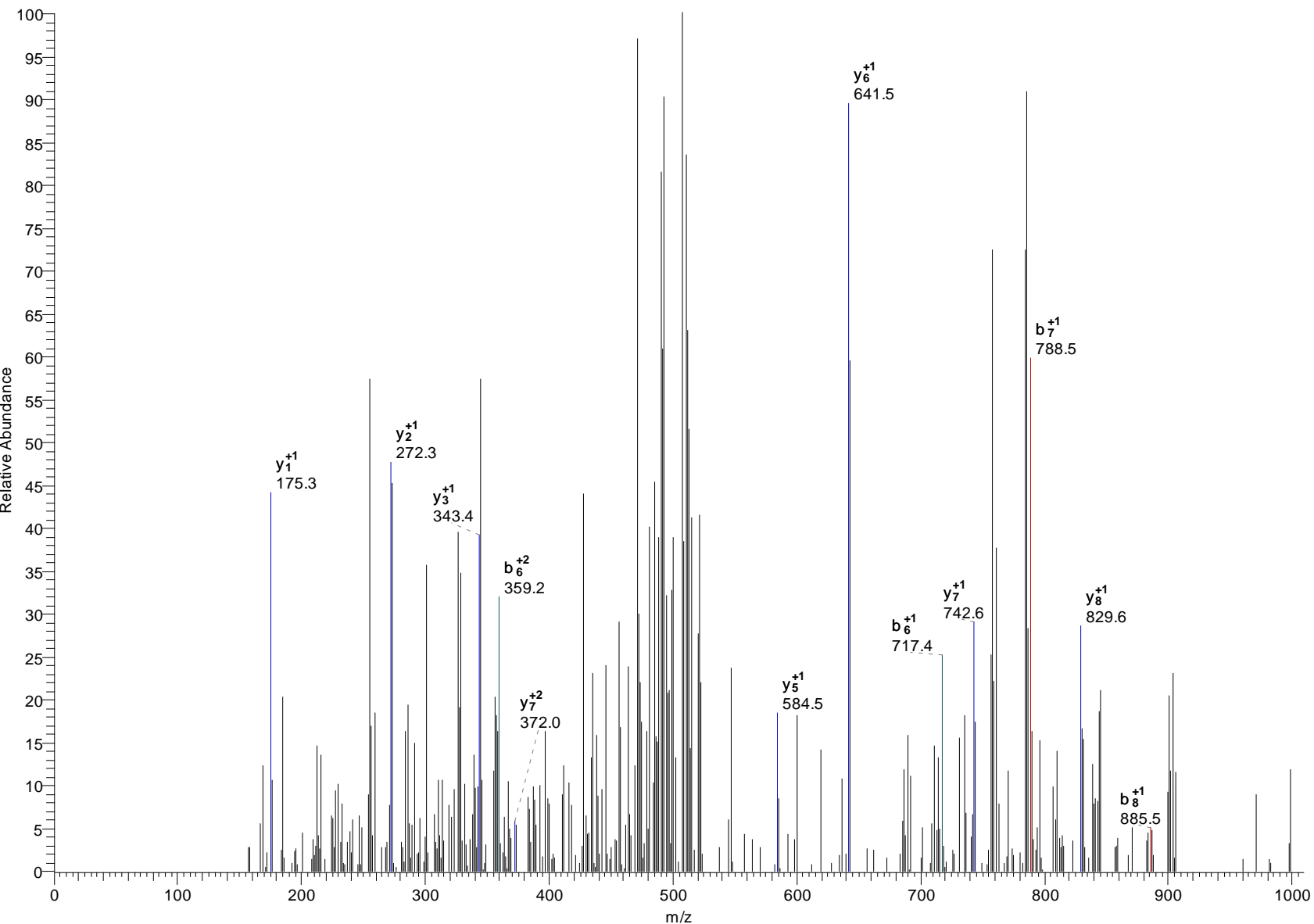
#5729-5729 RT:42.28-42.28 NL: 8.92E4



prKme3:1STGGKprAPR

H3K9me3:1

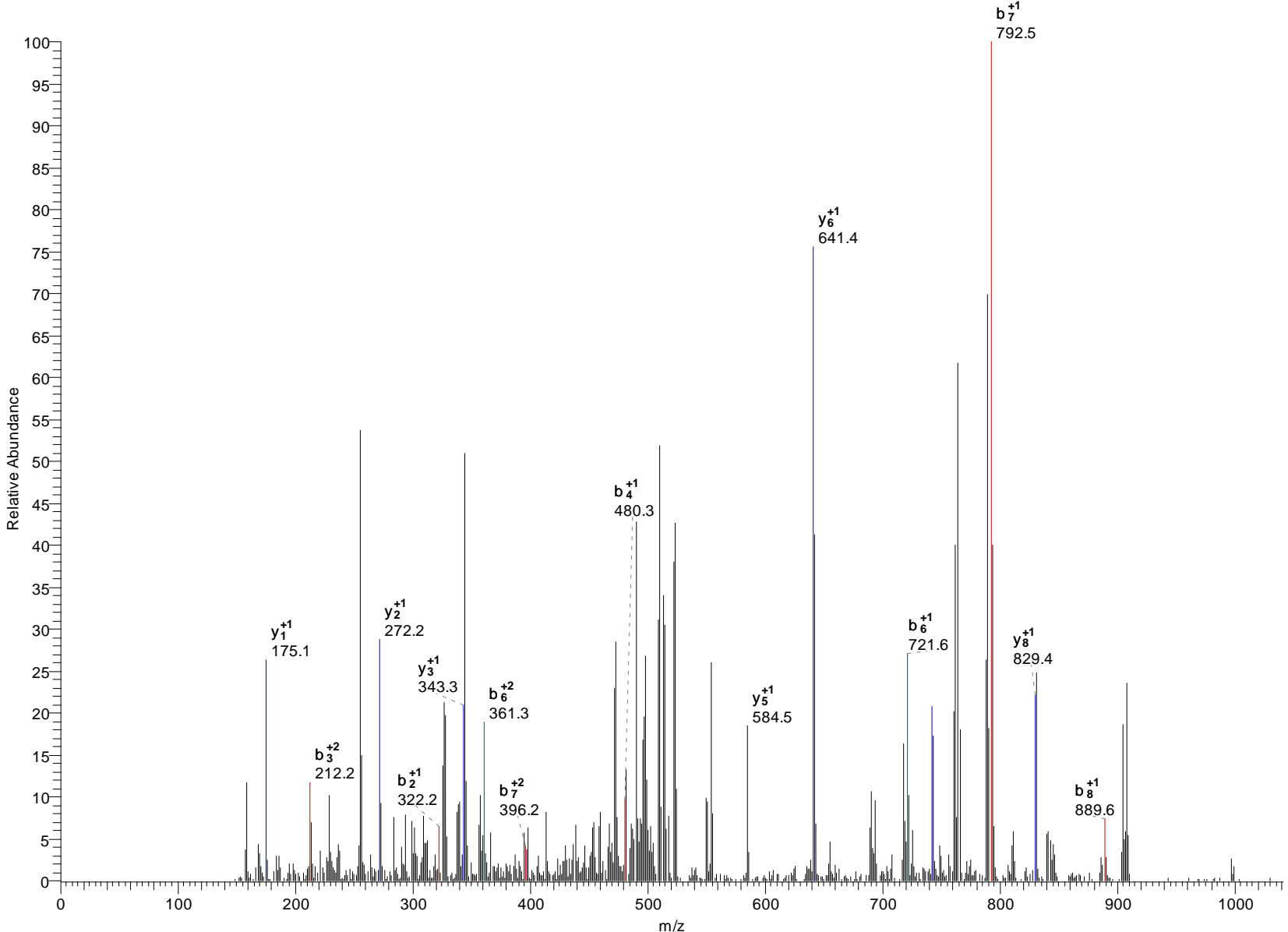
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prKme3:2STGGKprAPR

H3K9me3:2

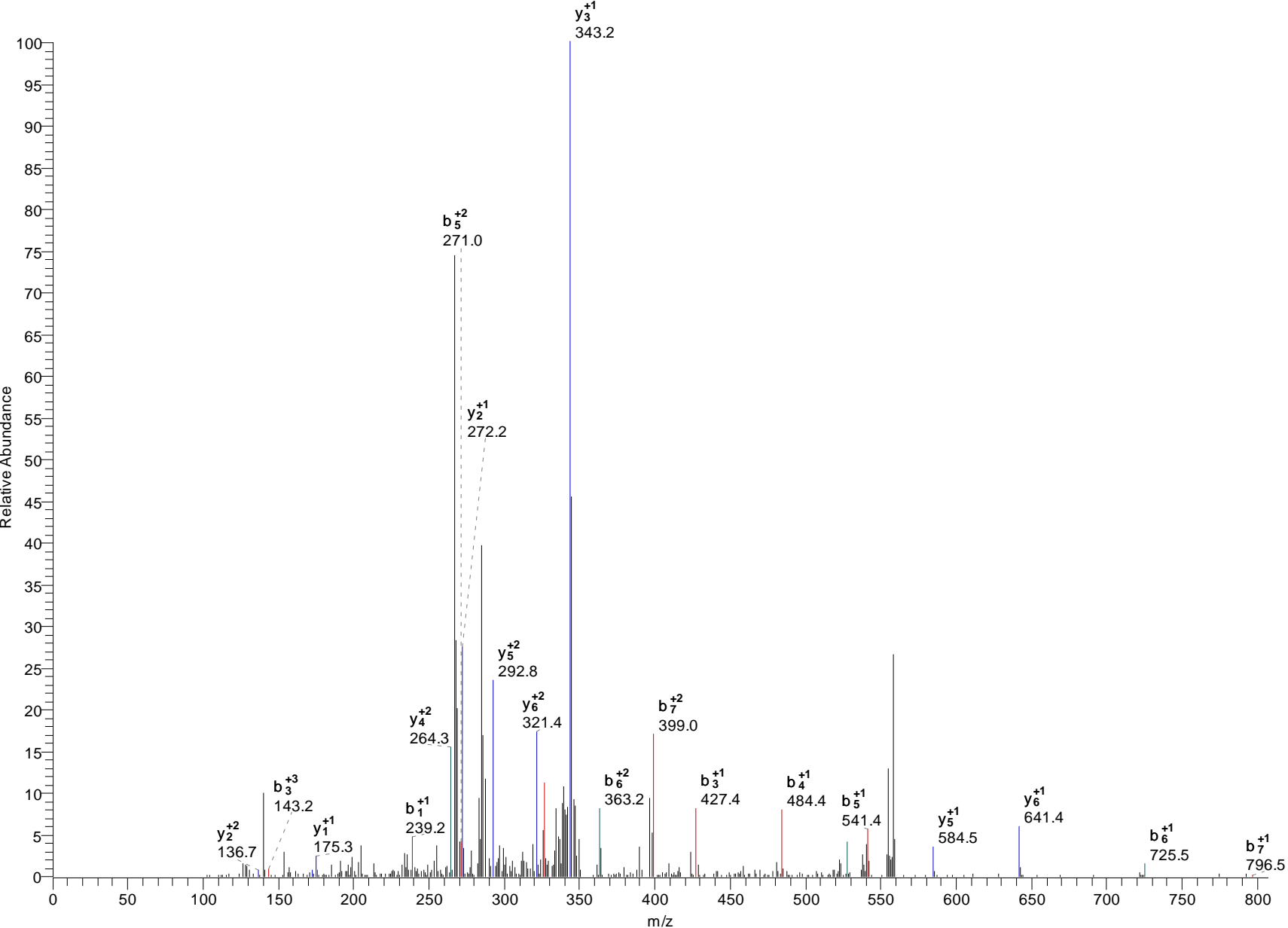
#5365-5365 RT:40.01-40.01 NL: 1.46E3



prKme3:3STGGKprAPR

H3K9me3:3

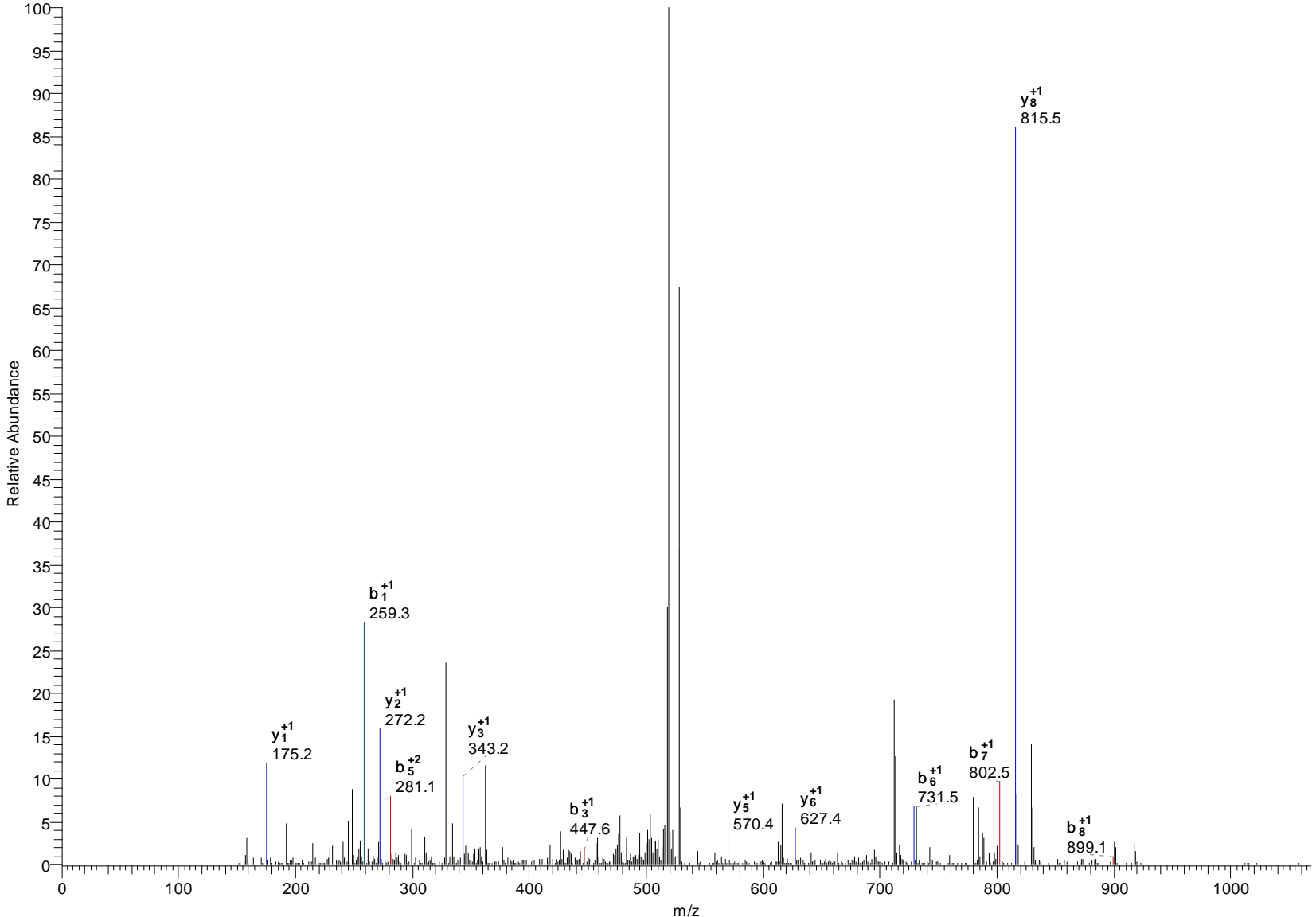
#5660-5660 RT:41.89-41.89 NL: 2.46E3



prKpr,me1:1STGGKacAPR

H3K9me1:1K14ac1

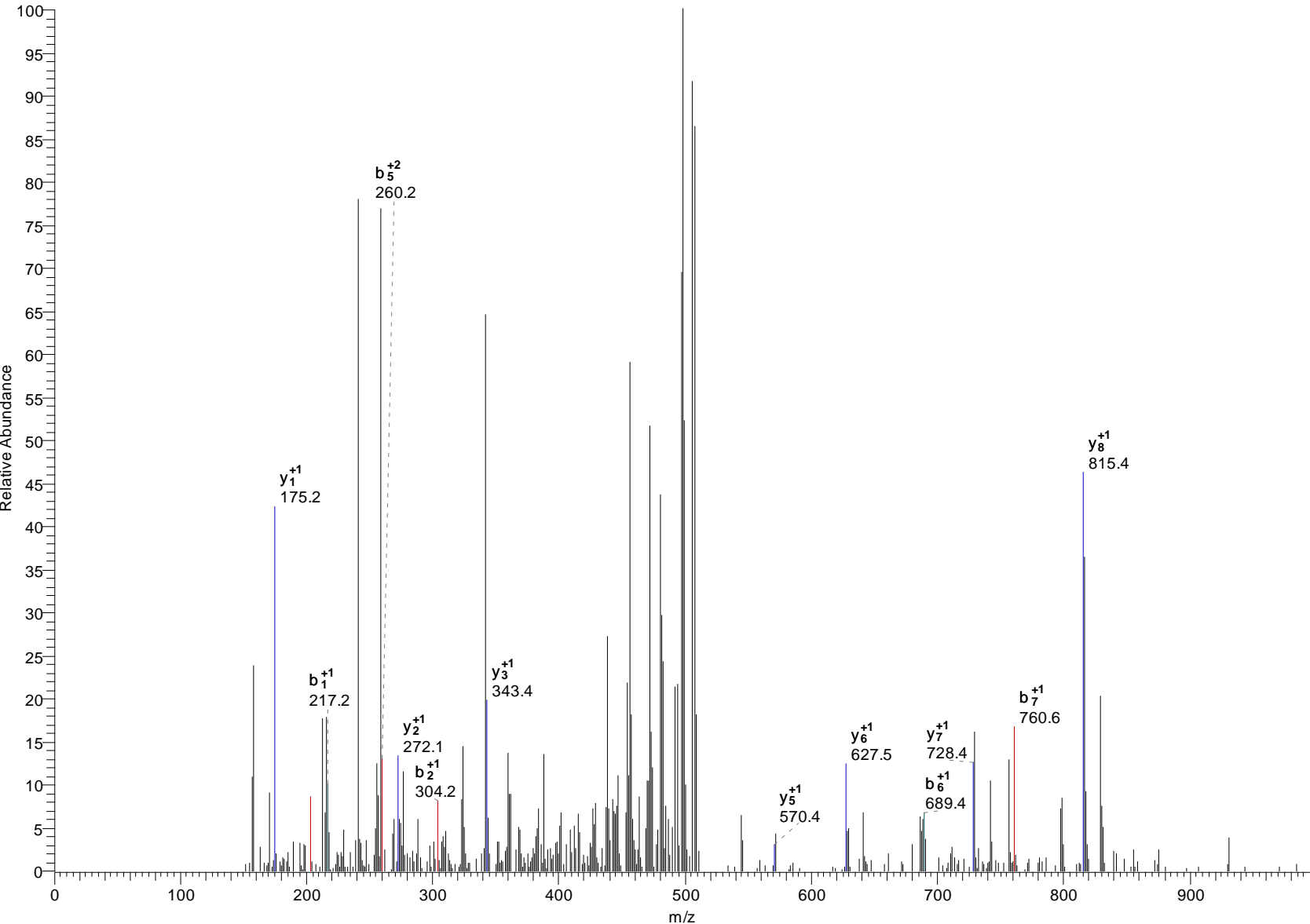
#8209-8209 RT:56.59-56.59 NL: 4.27E3



prKme2:1STGGKacAPR

H3K9me2:1K14ac1

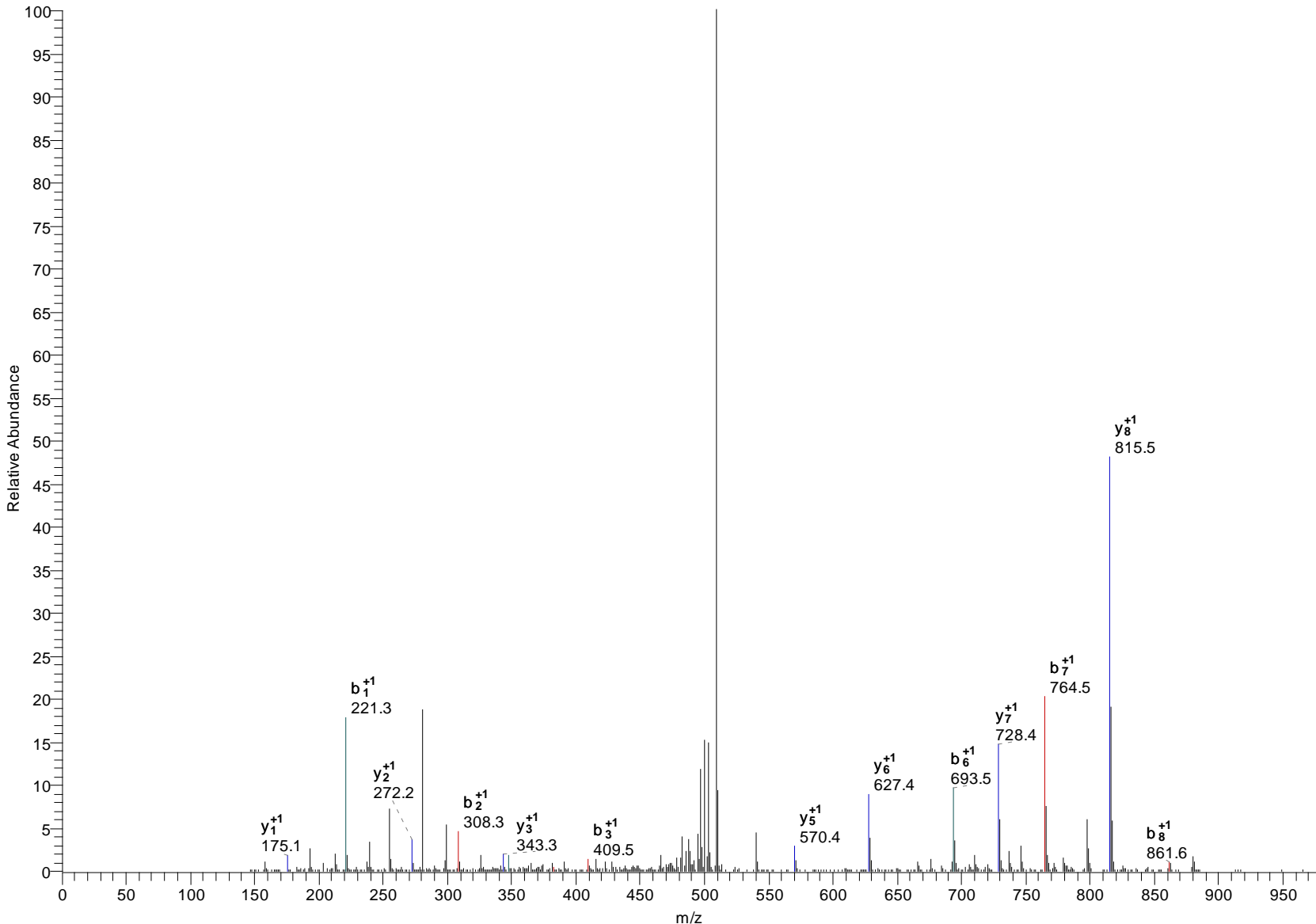
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prKme2:2STGGKacAPR

H3K9me2:2K14ac1

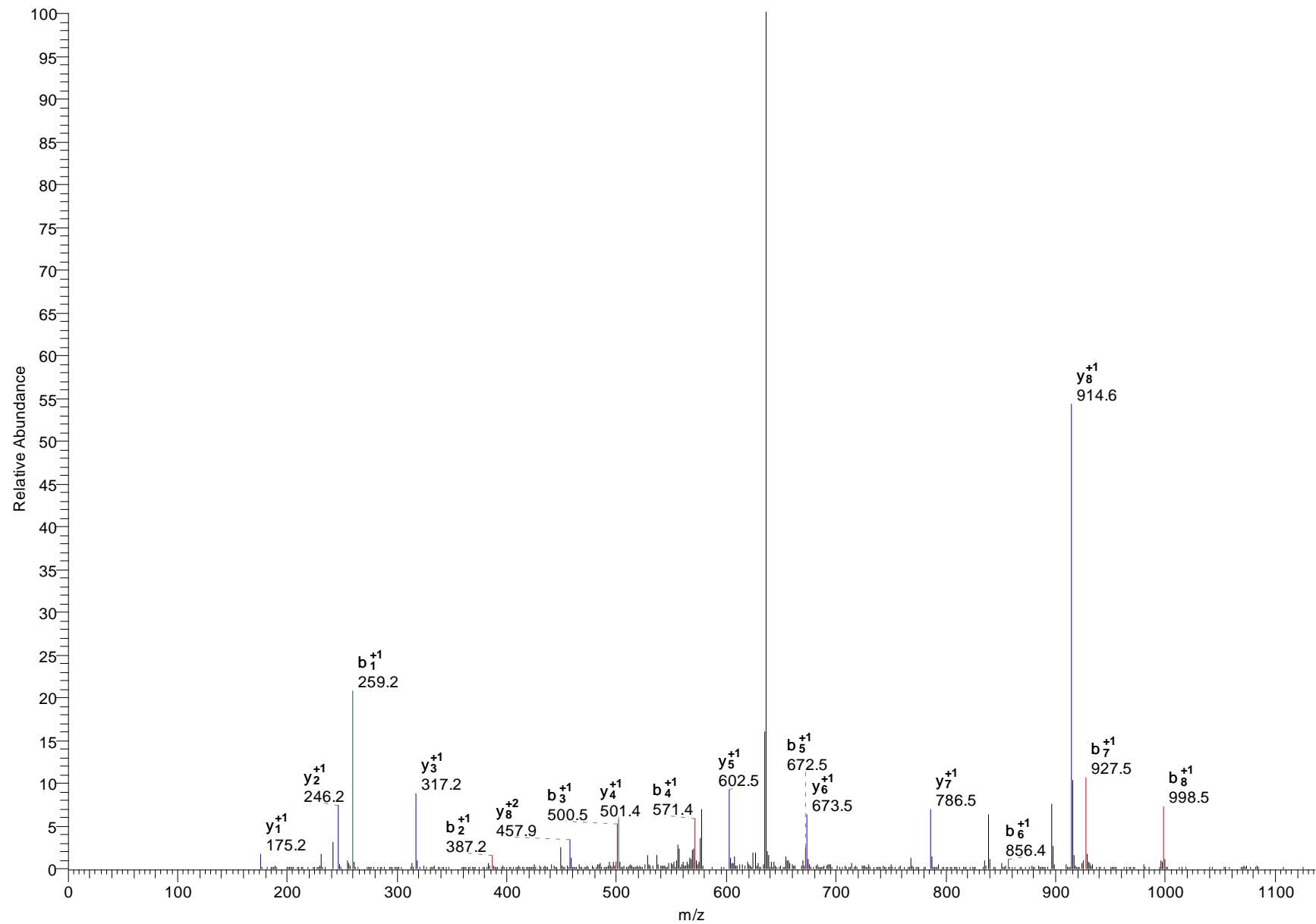
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prKpr,me1:1QLATKprAAR

H3K18me1:1

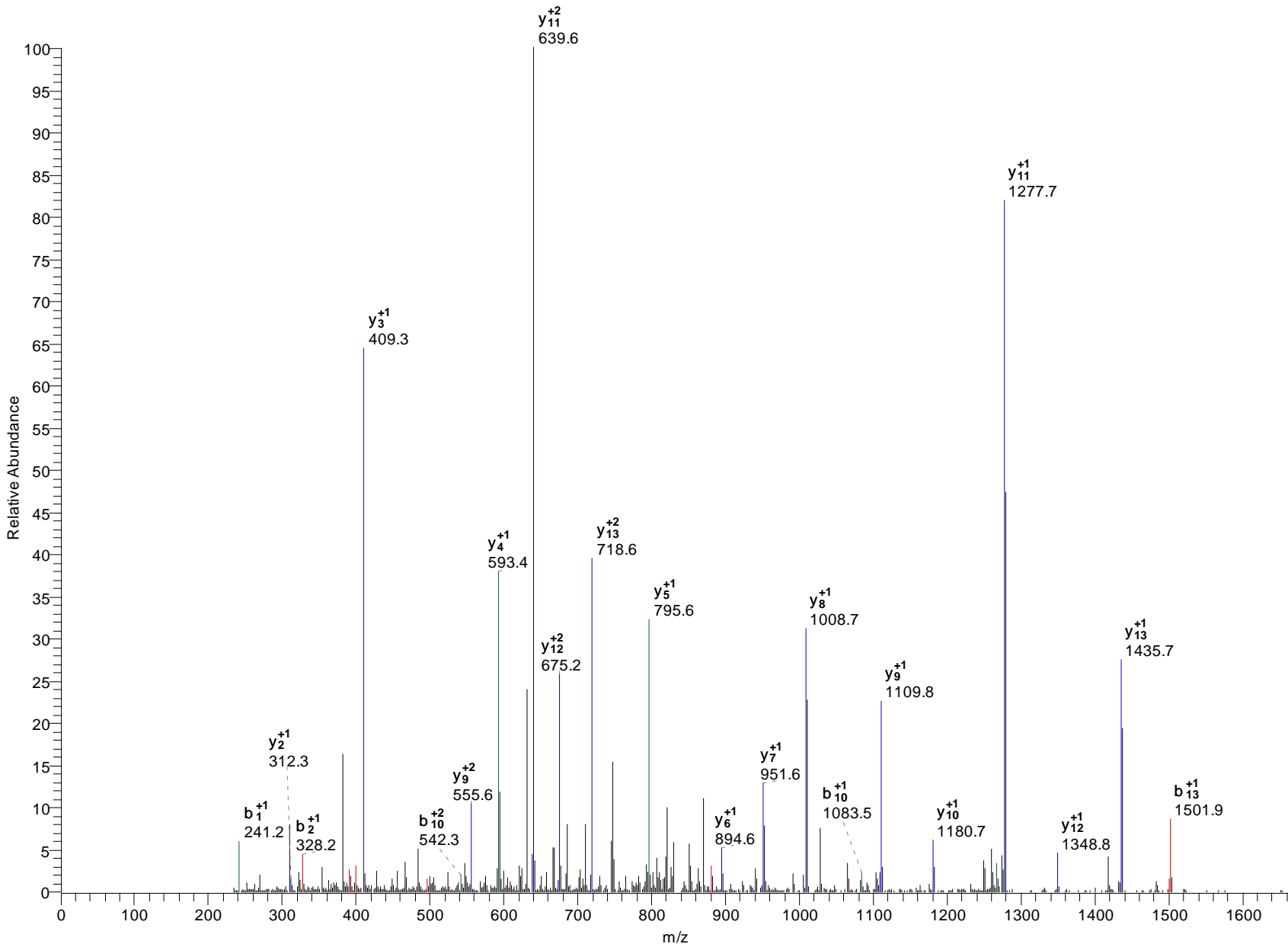
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prKprSAPATGGVKpr,me1:1KprPHR

H3K36me1:1

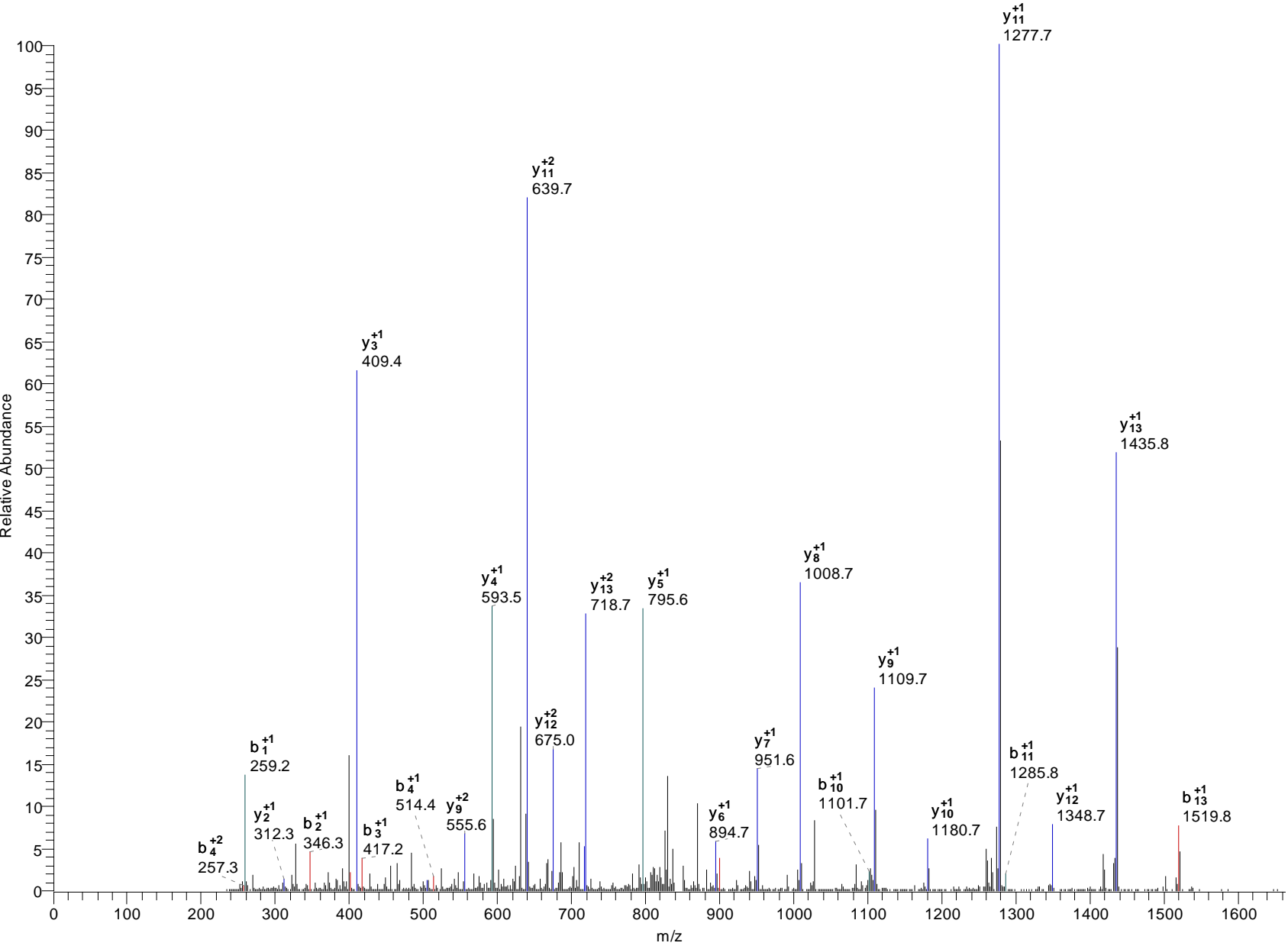
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prKpr,me1:1SAPATGGVKprKprPHR

H3K27me1:1

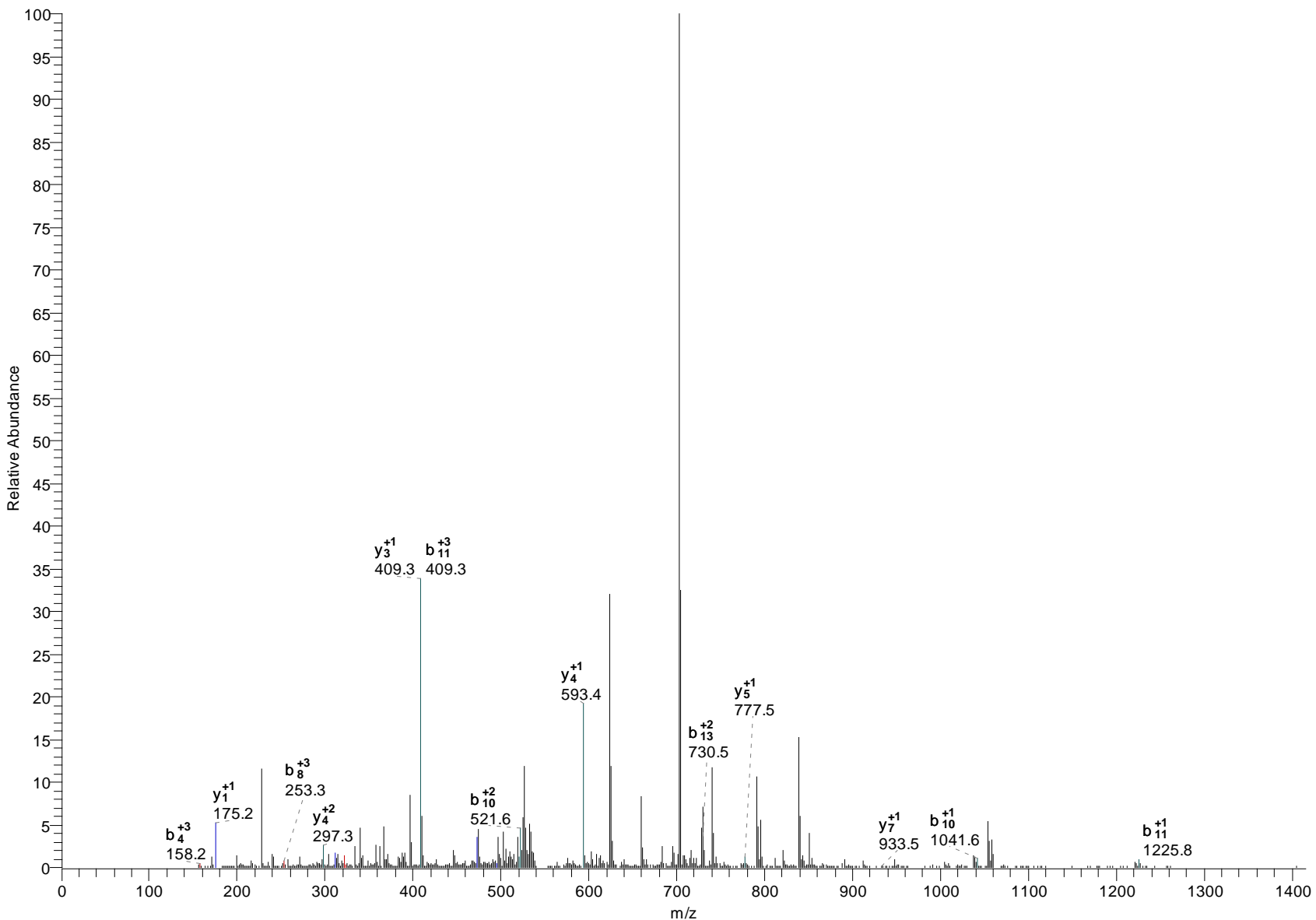
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prKme2:1SAPATGGVKprKprPHR

H3K27me2:1

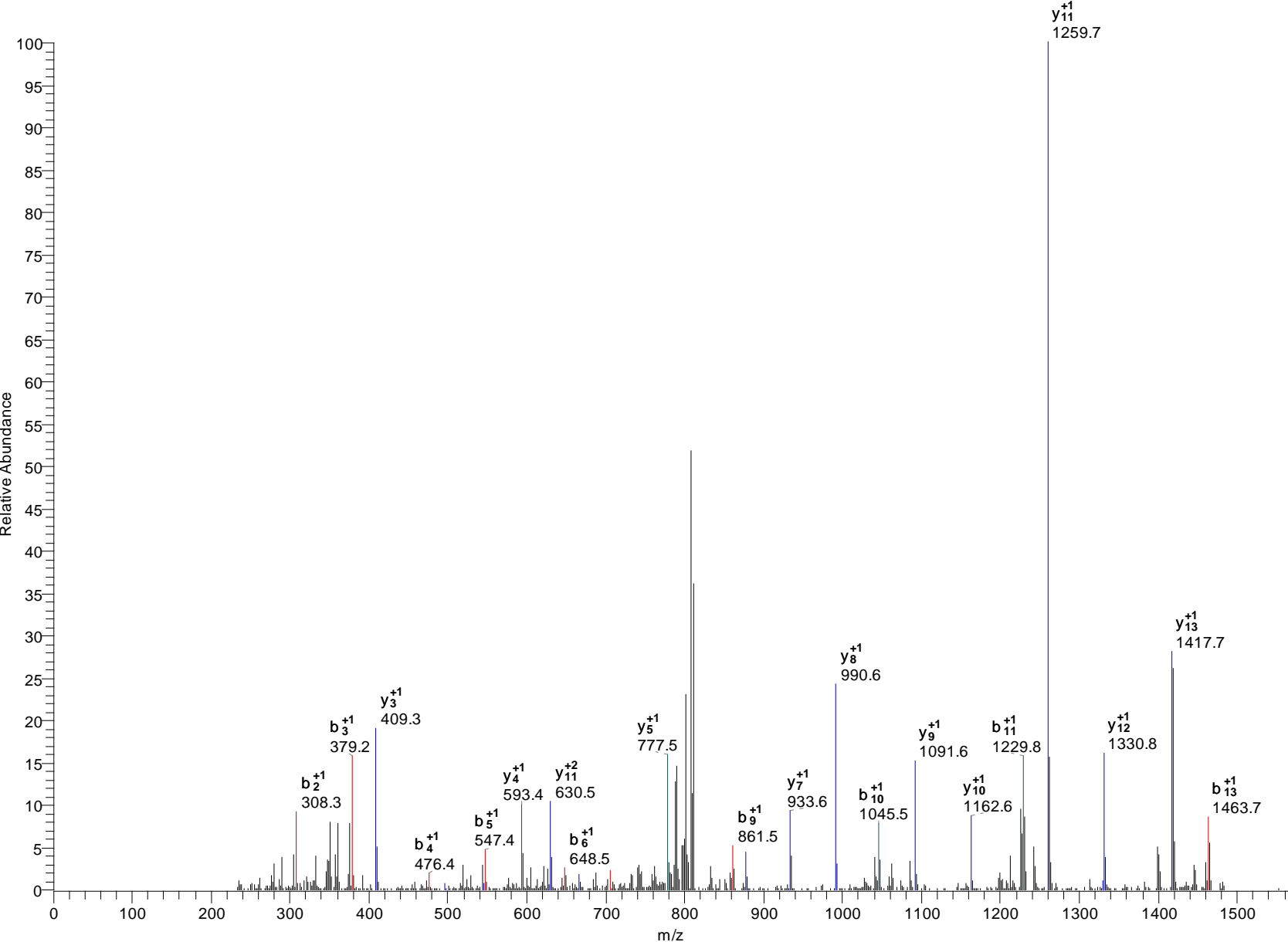
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prKme2:2SAPATGGVKprKprPHR

H3K27me2:2

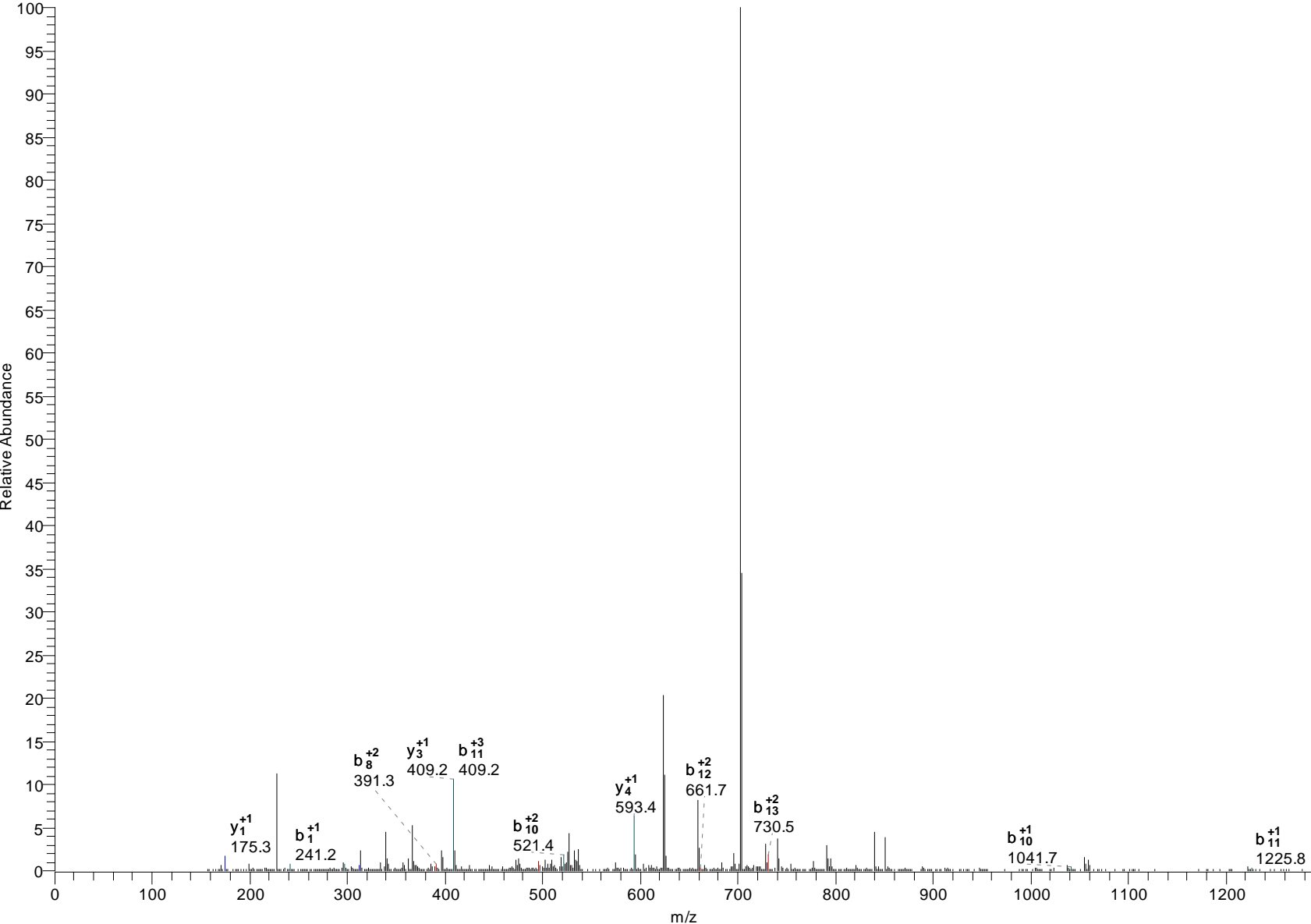
#8320-8320 RT:57.17-57.17 NL: 4.52E3



prKprSAPATGGVKme2:1KprPHR

H3K36me2:1

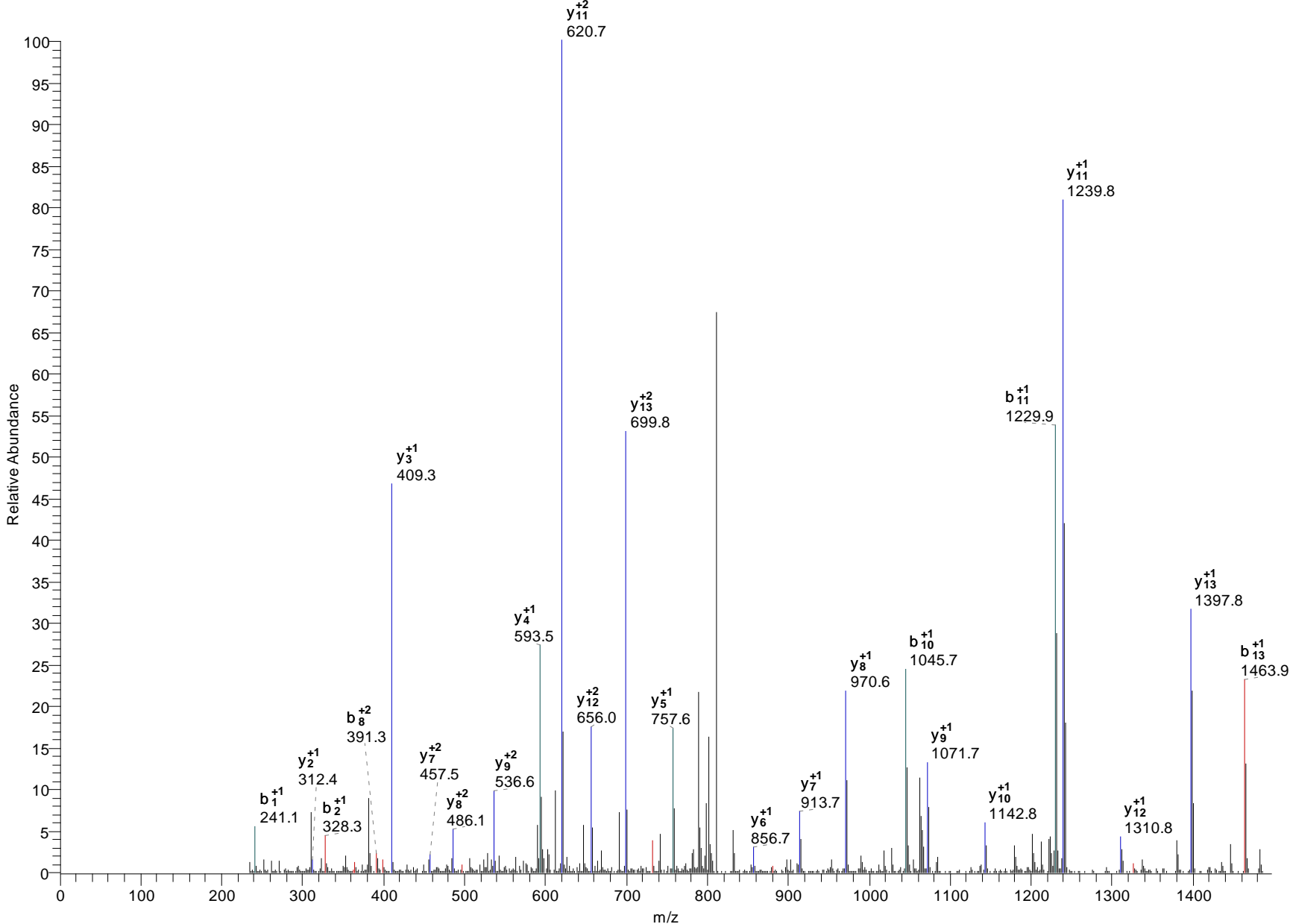
#8415-8415 RT:57.75-57.75 NL: 2.12E4



prKprSAPATGGVKme2:2KprPHR

H3K36me2:2

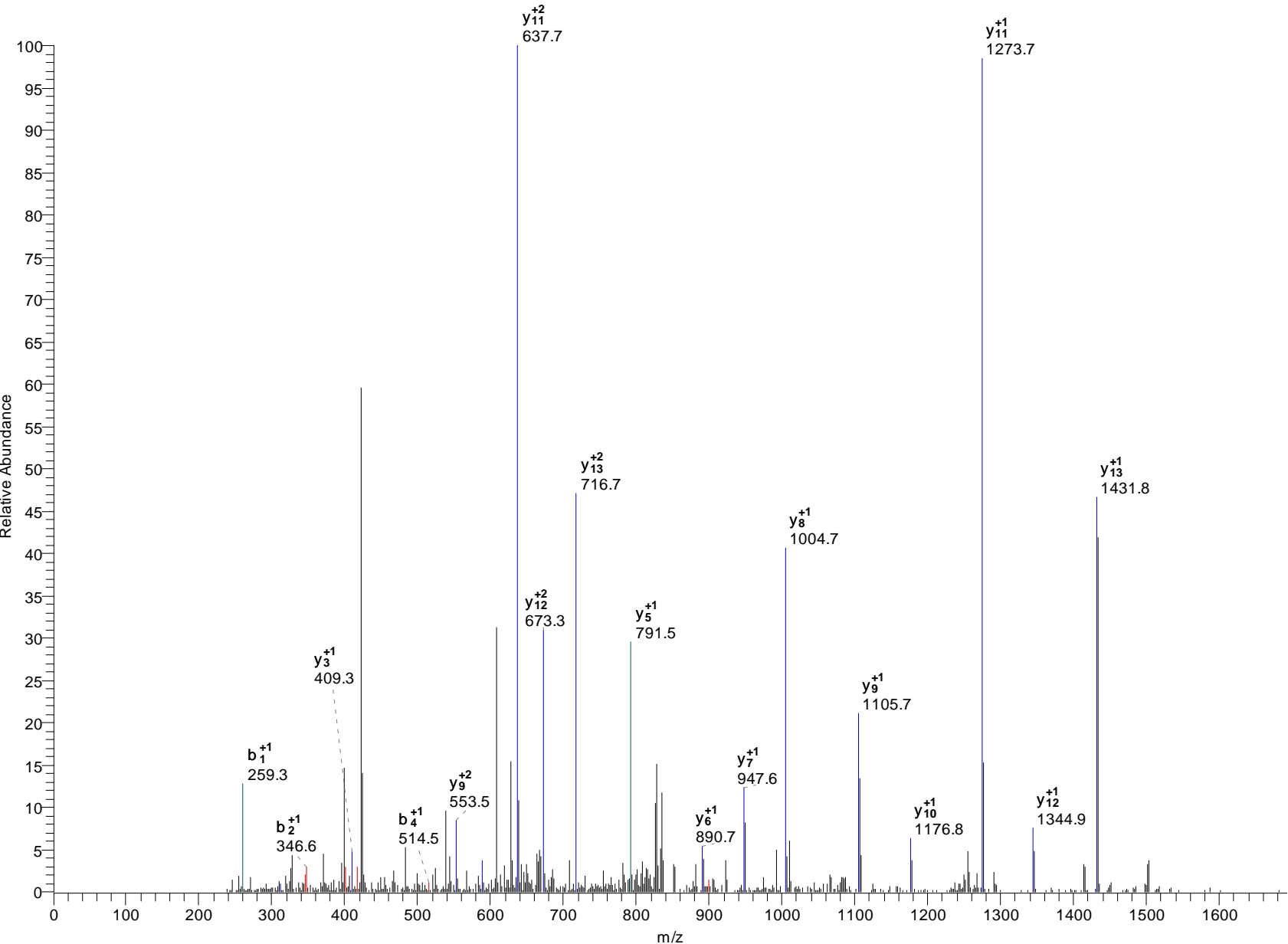
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prKpr,me1:1SAPATGGVKpr,me1:0KprPHR

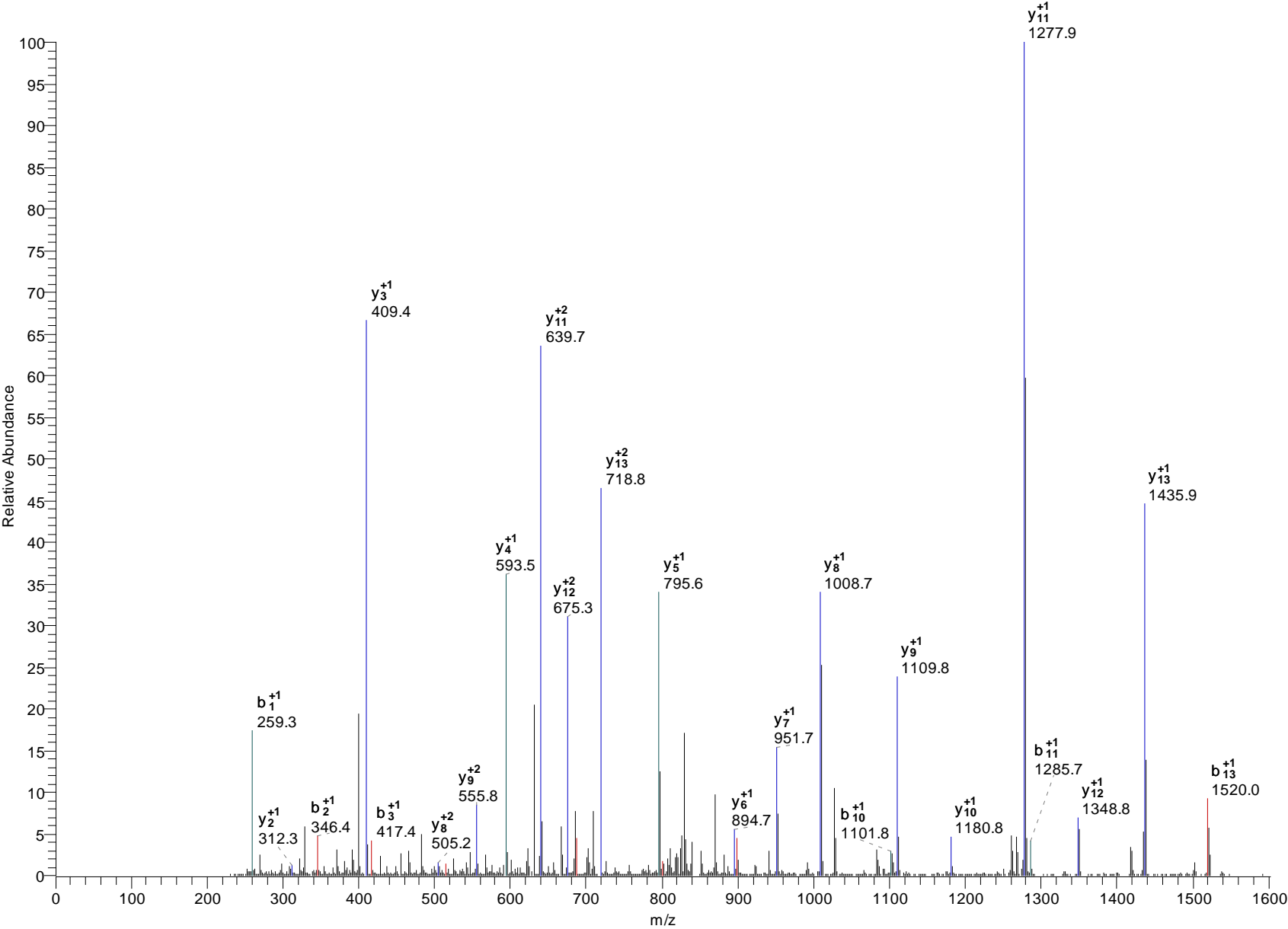
H3K27me1:1K36me1:0

#9492-9492 RT:64.14-64.14 NL: 2.61E3



prKpr,me1:1SAPATGGVKpr,me1:1KprPHR

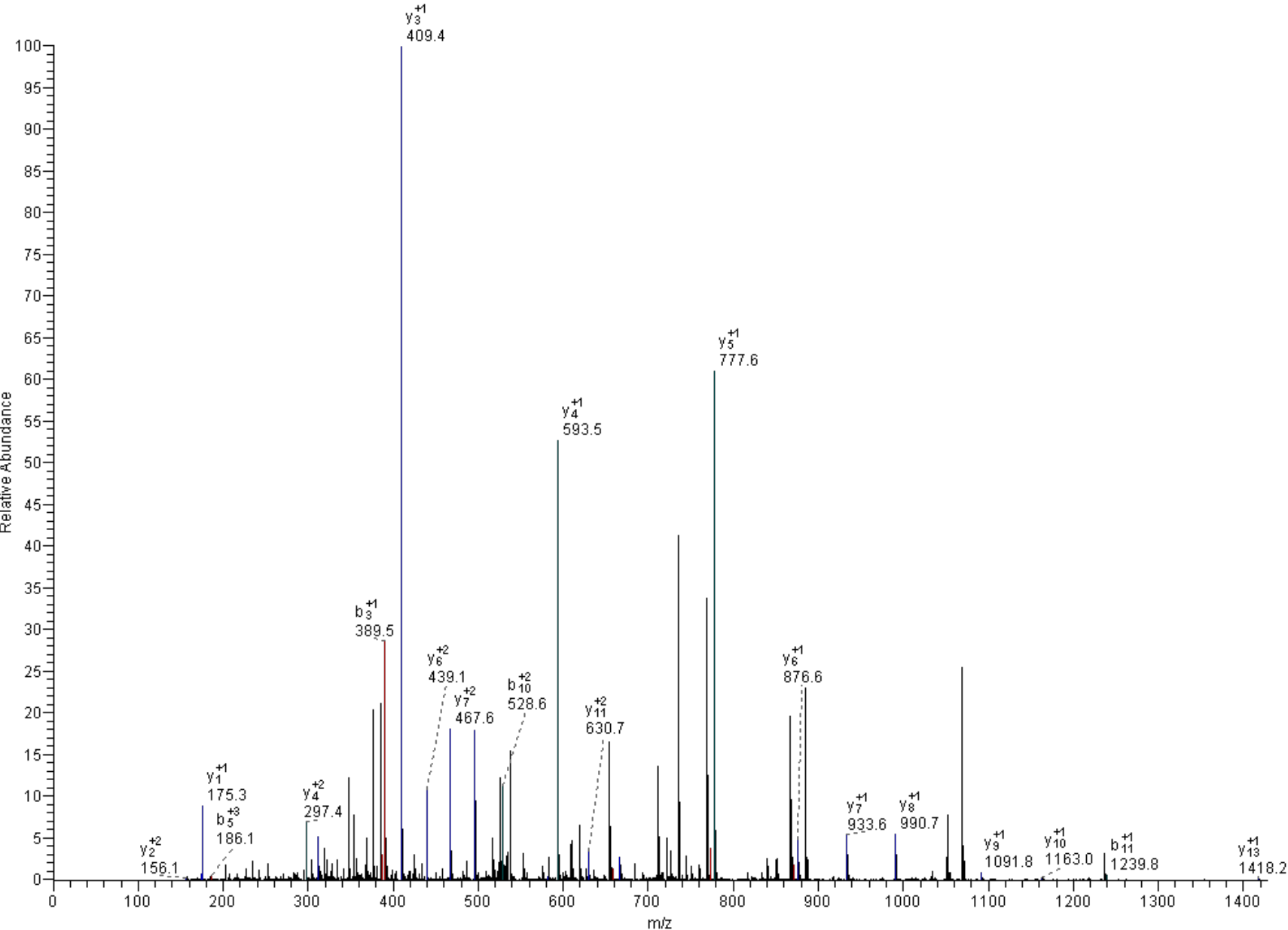
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prKme3:1SAPATGGVKprKprPHR

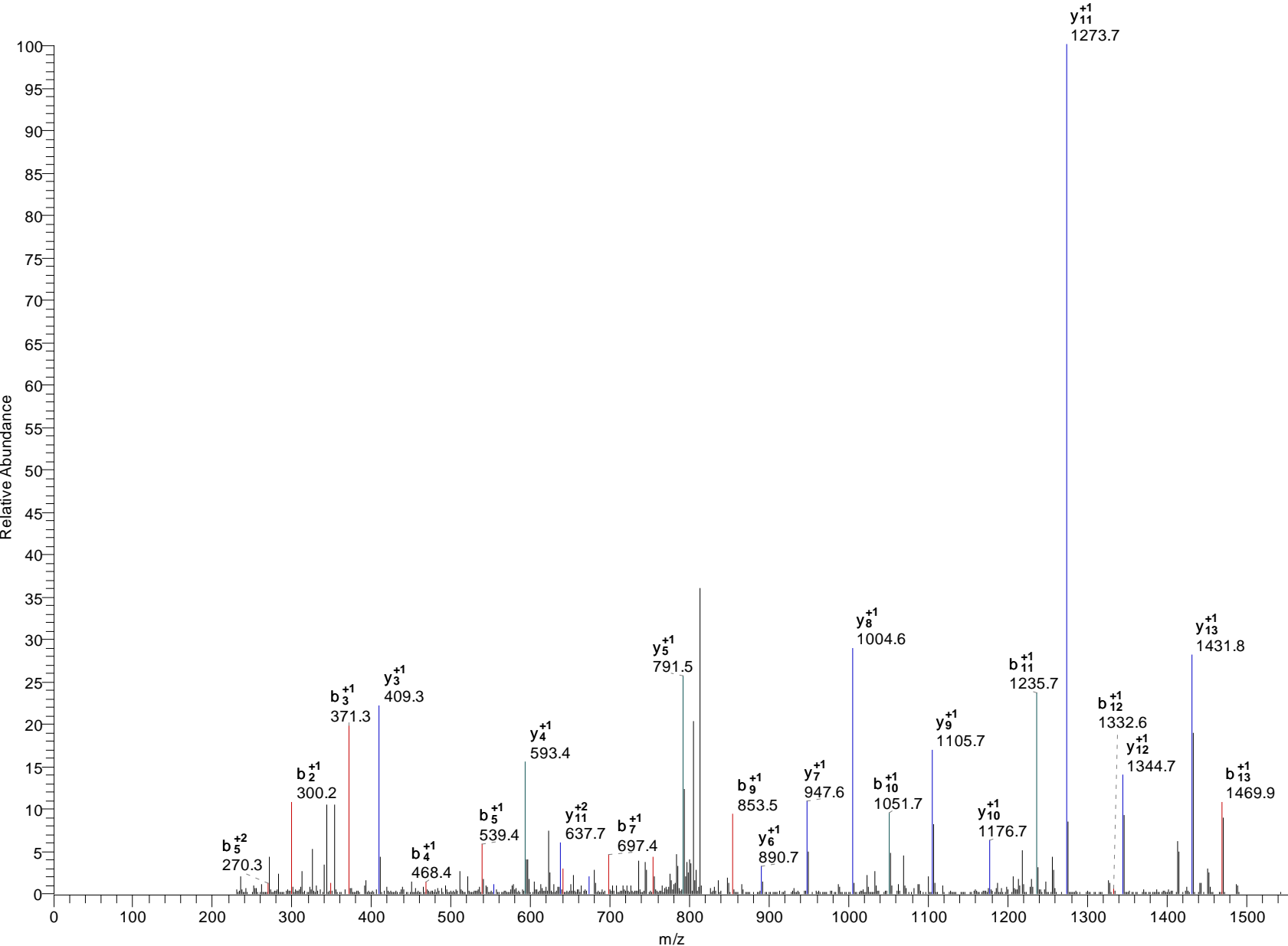
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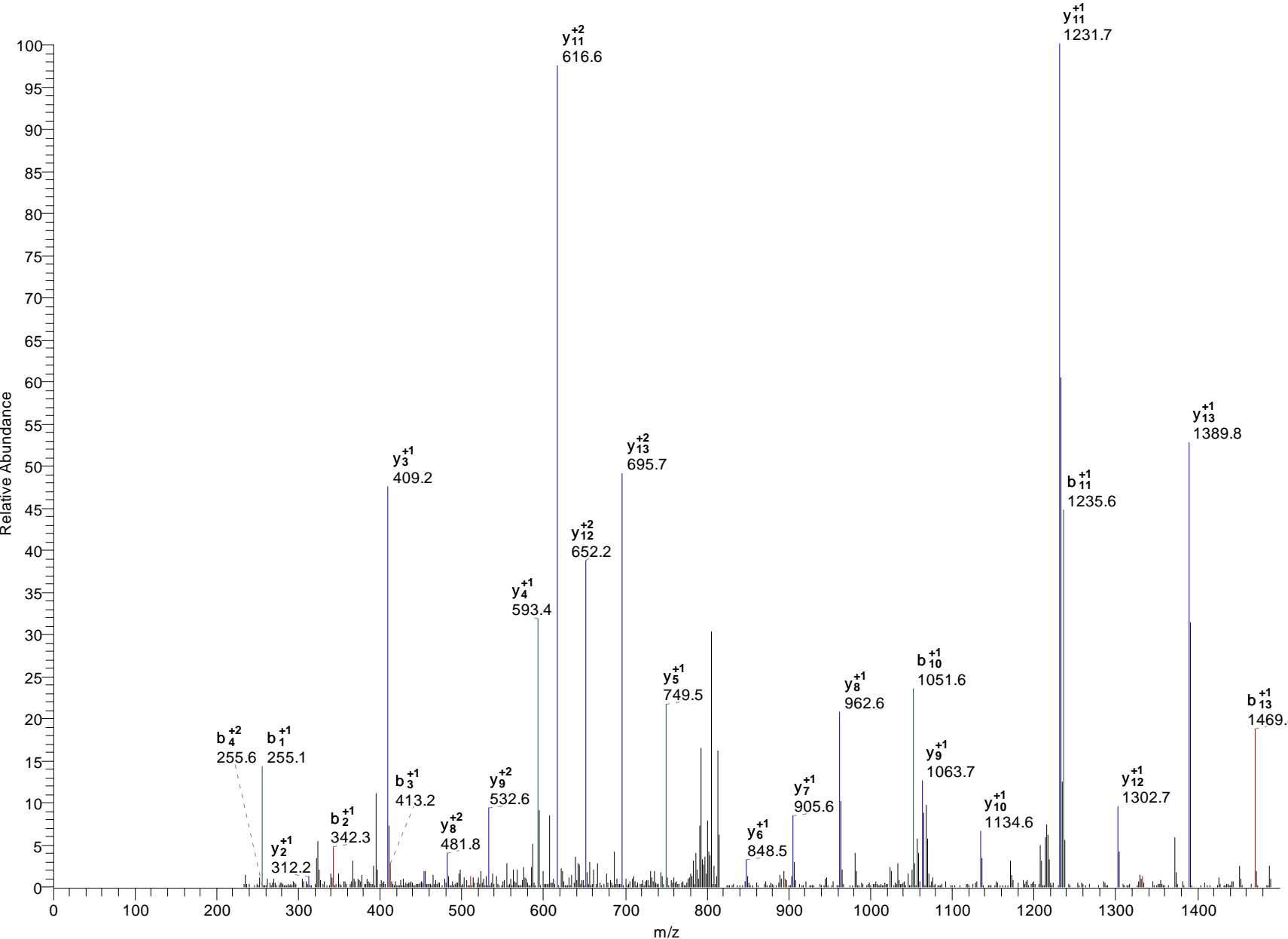
prKme2:0SAPATGGVKpr,me1:1KprPHR H3K27me2:0K36me1:1

#8620-8620 RT:58.97-58.97 NL: 6.47E3



prKpr,me1:1SAPATGGVKme2:0KprPHR H3K27me1:1K36me2:0

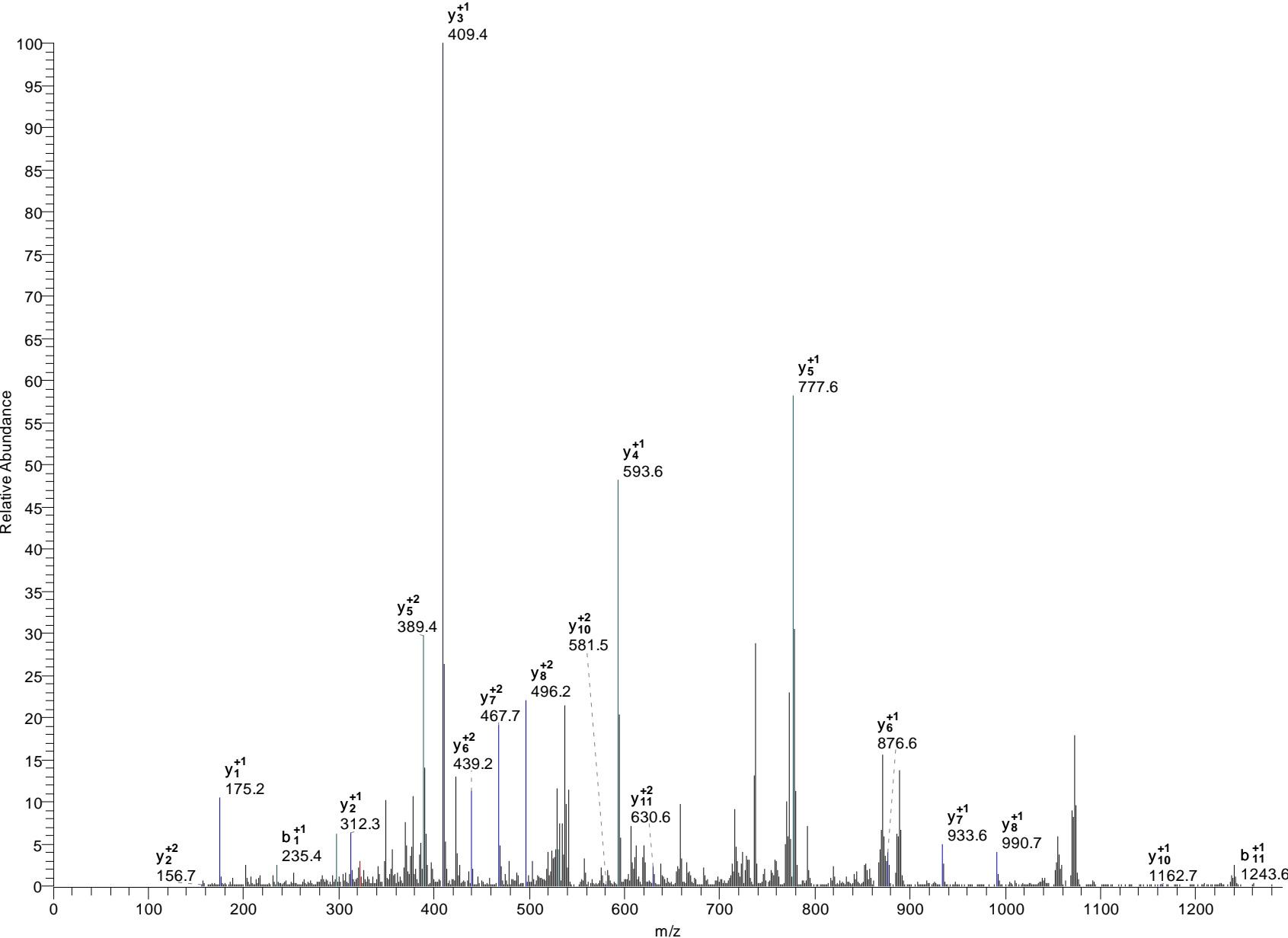
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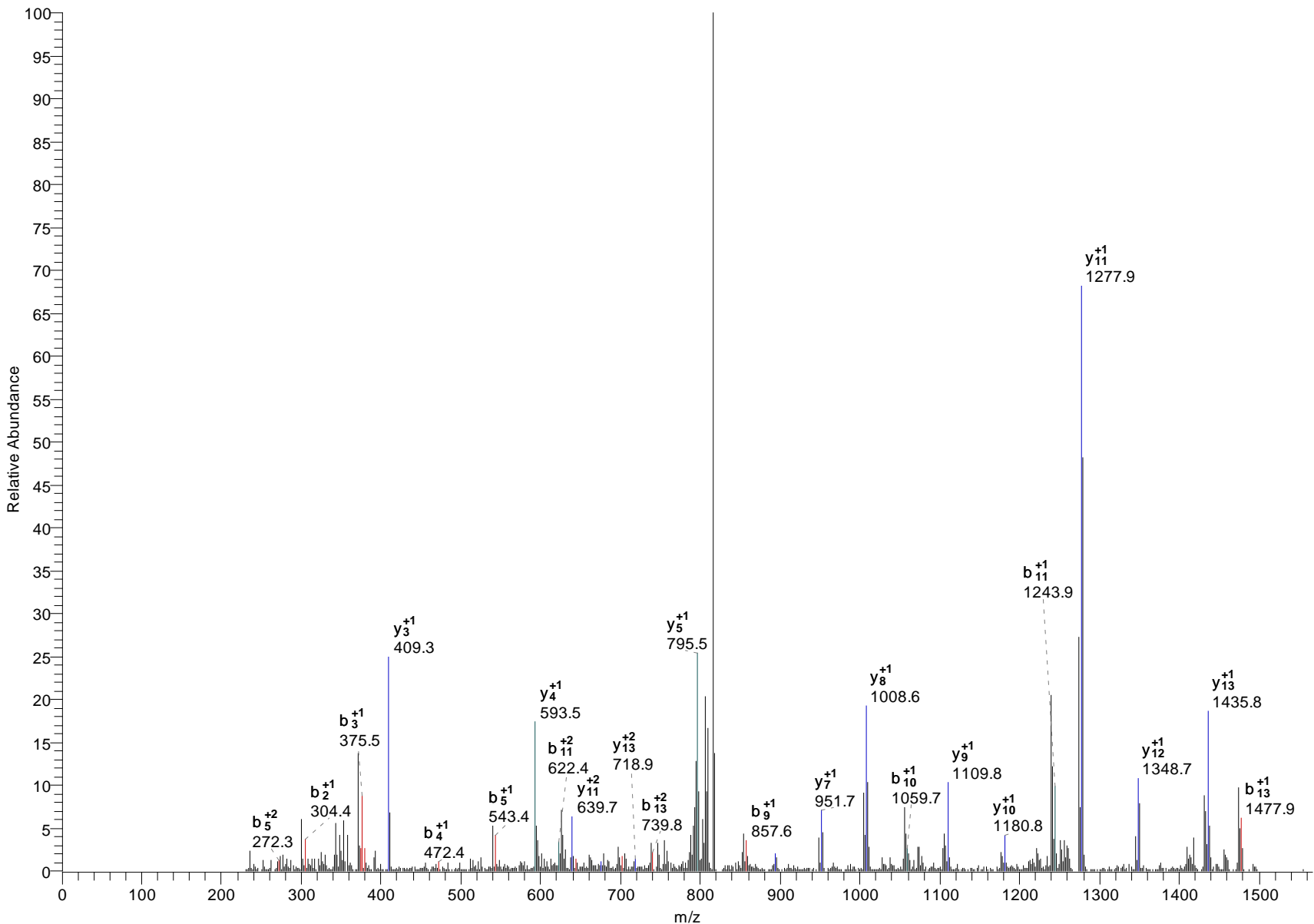
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#7502-7502 RT:52.36-52.36 NL: 4.52E4



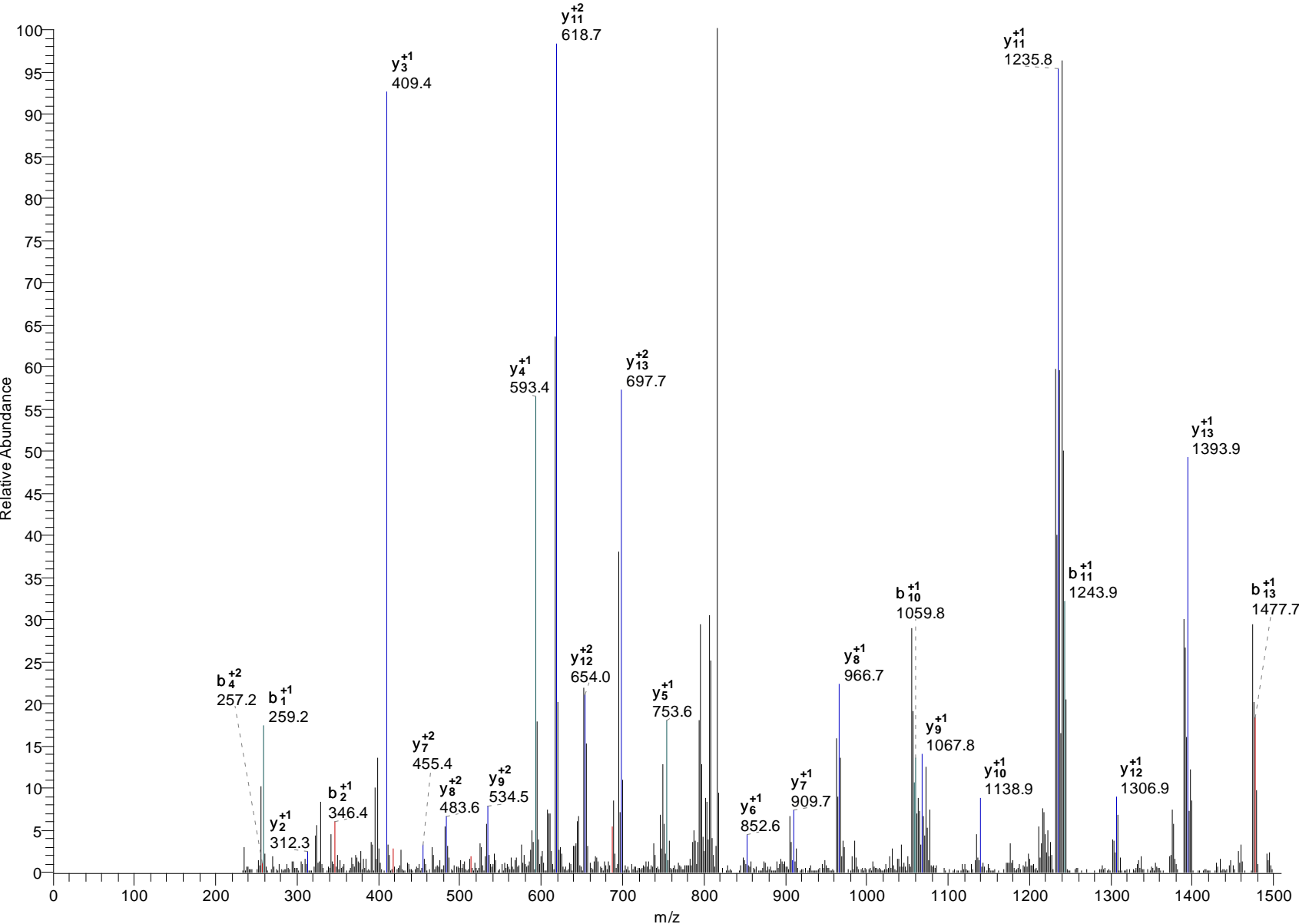
prKme2:1SAPATGGVKpr,me1:1KprPHR H3K27me2:1K36me1:1

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prKpr,me1:1SAPATGGVKme2:1KprPHR H3K27me1:1K36me2:1

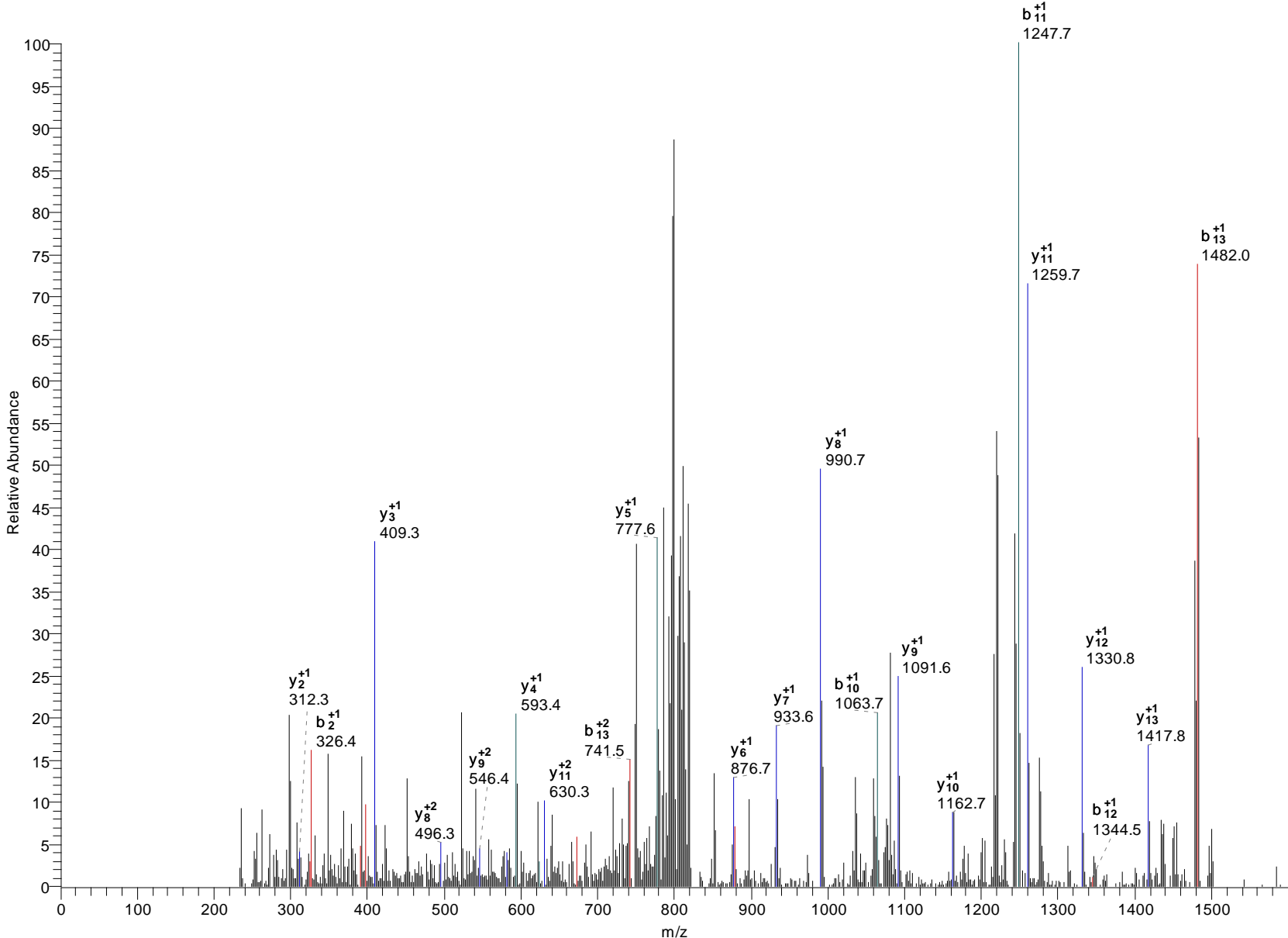
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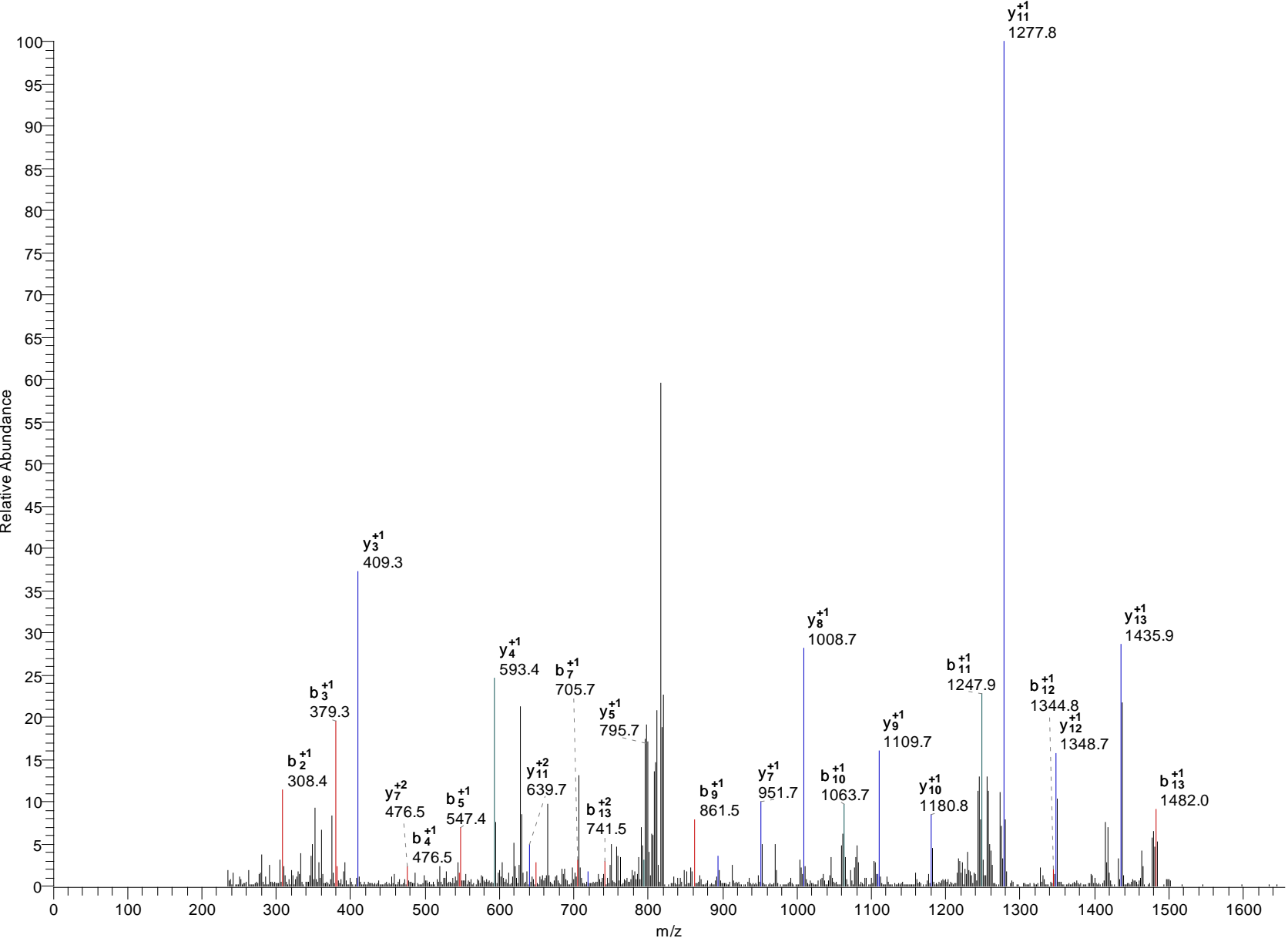
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#7547-7547 RT:52.62-52.62 NL: 1.03E3



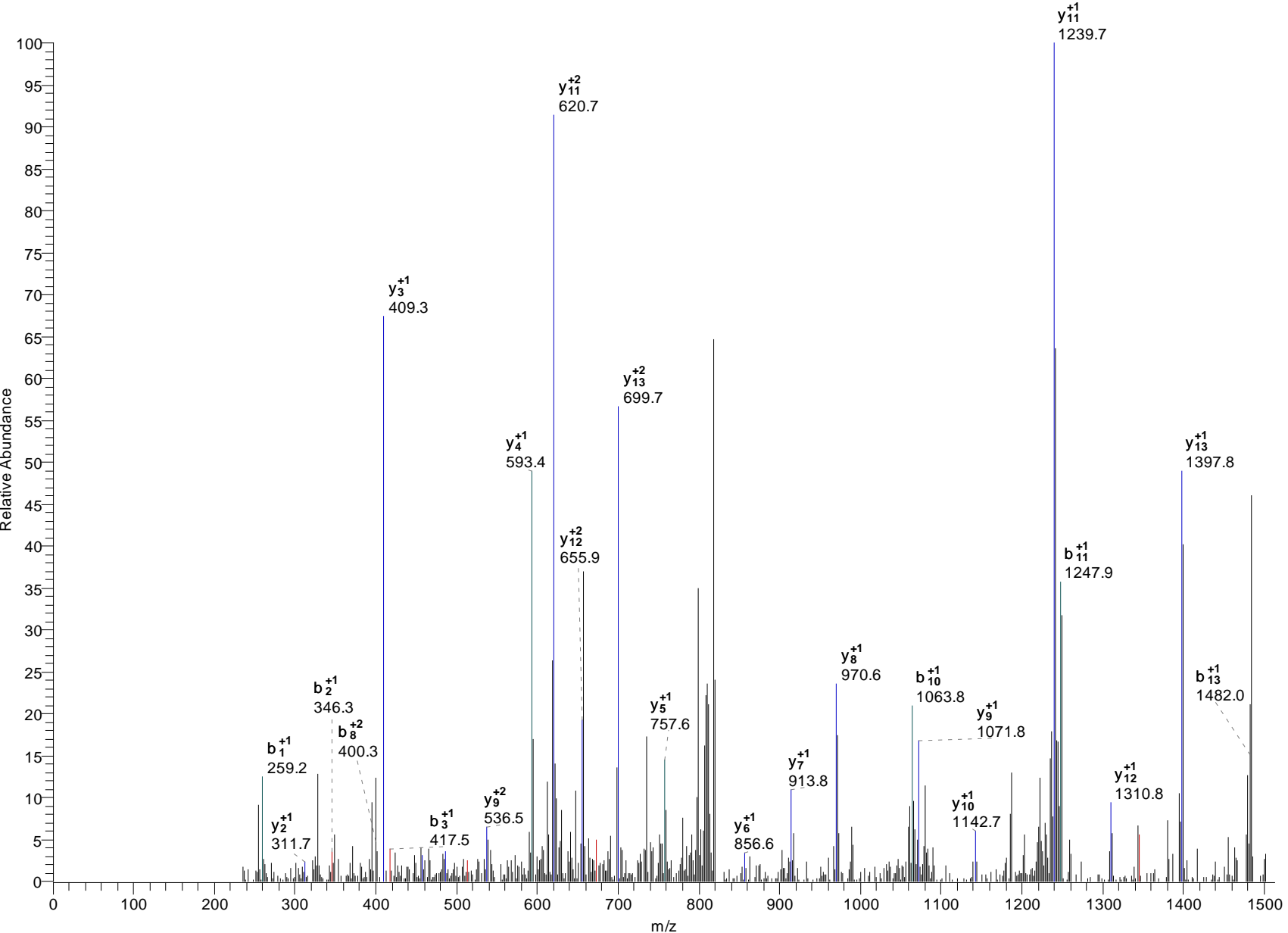
prKme2:2SAPATGGVKpr,me1:1KprPHR H3K27me2:2K36me1:1

#7964-7964 RT:55.09-55.09 NL: 7.39E3



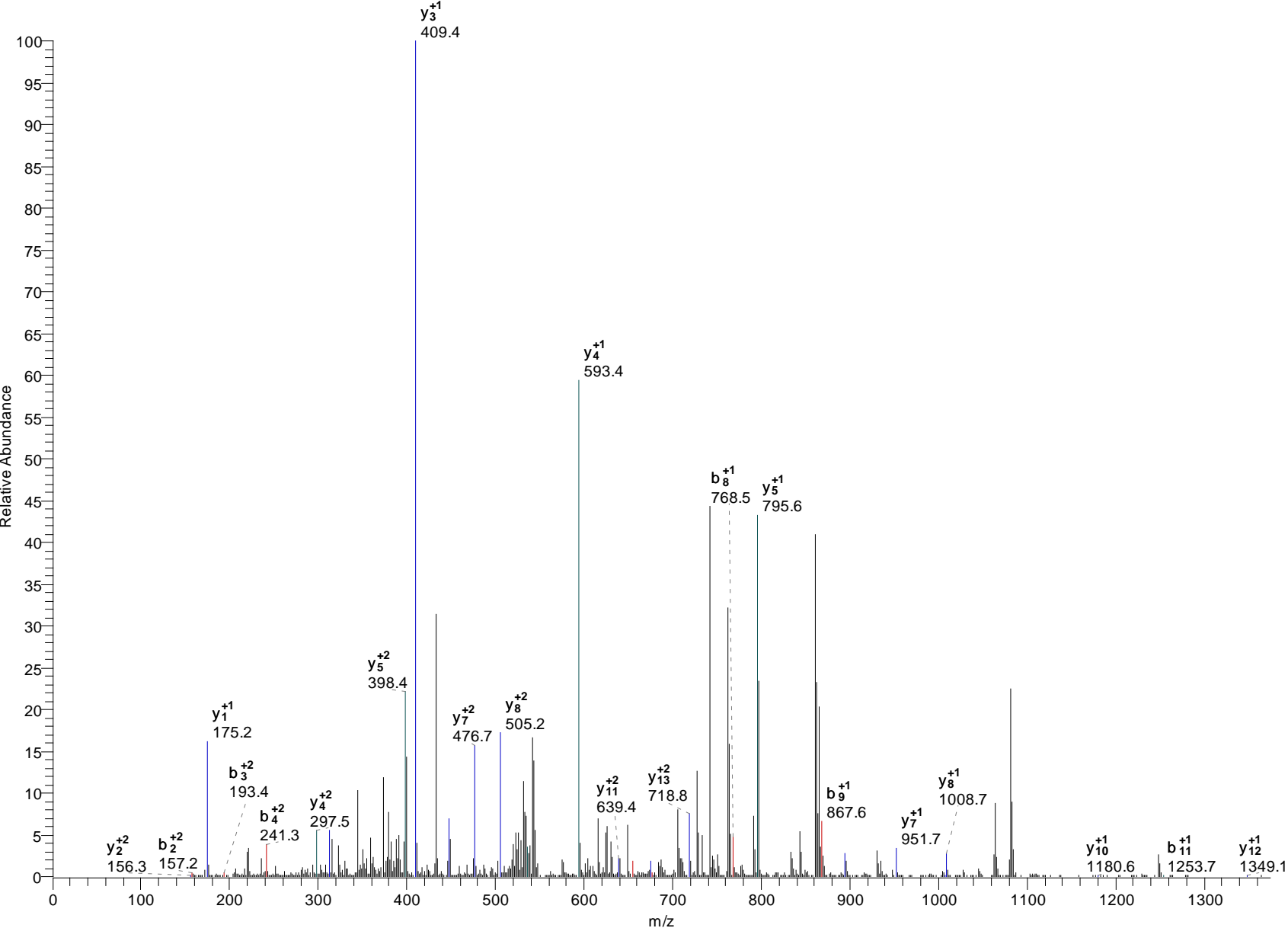
prKpr,me1:1SAPATGGVKme2:2KprPHR H3K27me1:1K36me2:2

#8614-8614 RT:58.94-58.94 NL: 9.96E2



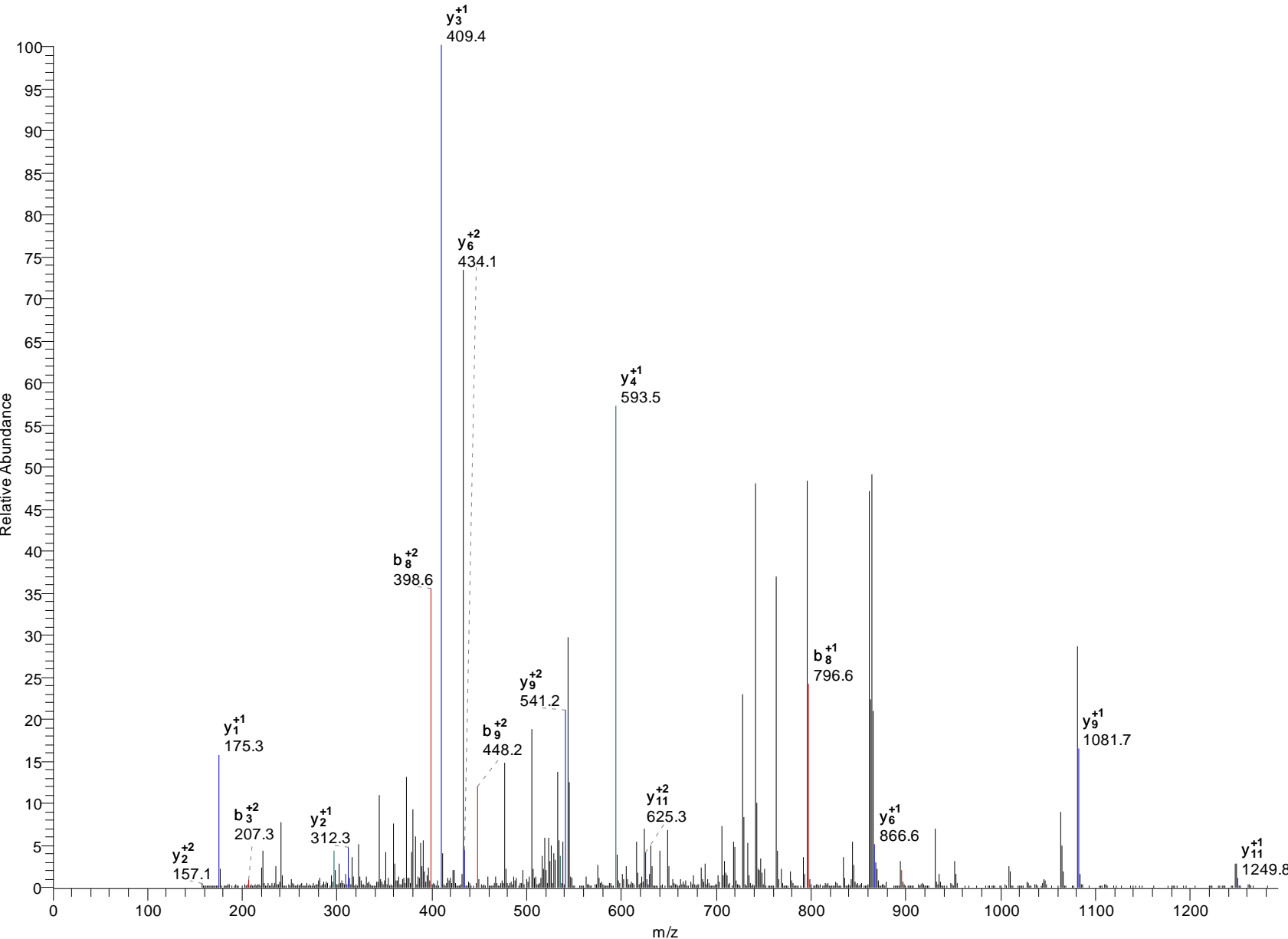
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#8140-8140 RT:56.19-56.19 NL: 4.14E5



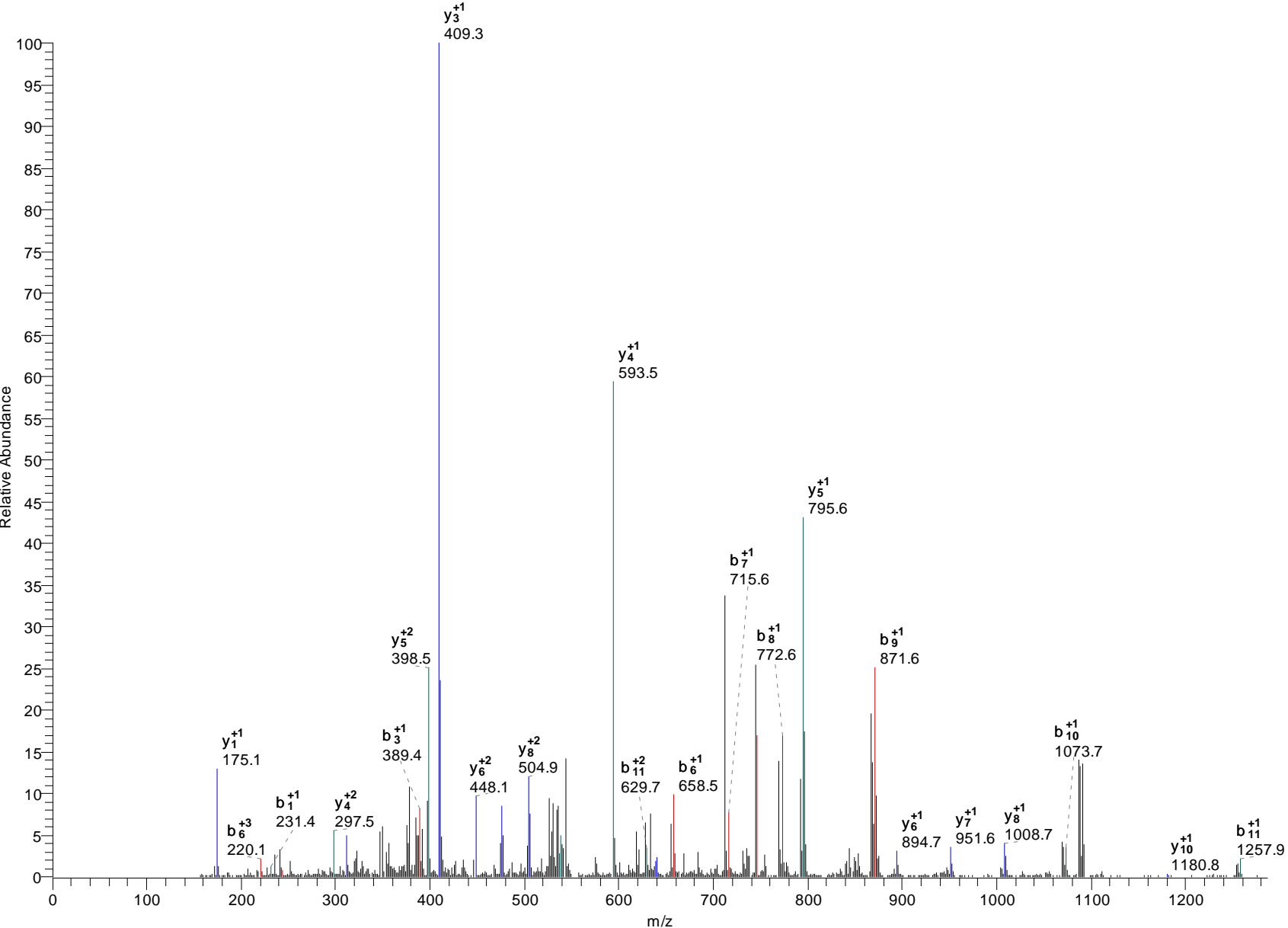
prKpr,me1:0SAPATGGVKme3:1KprPHR H3K27me1:0K36me3:1

#8495-8495 RT:58.12-58.12 NL: 4.54E5



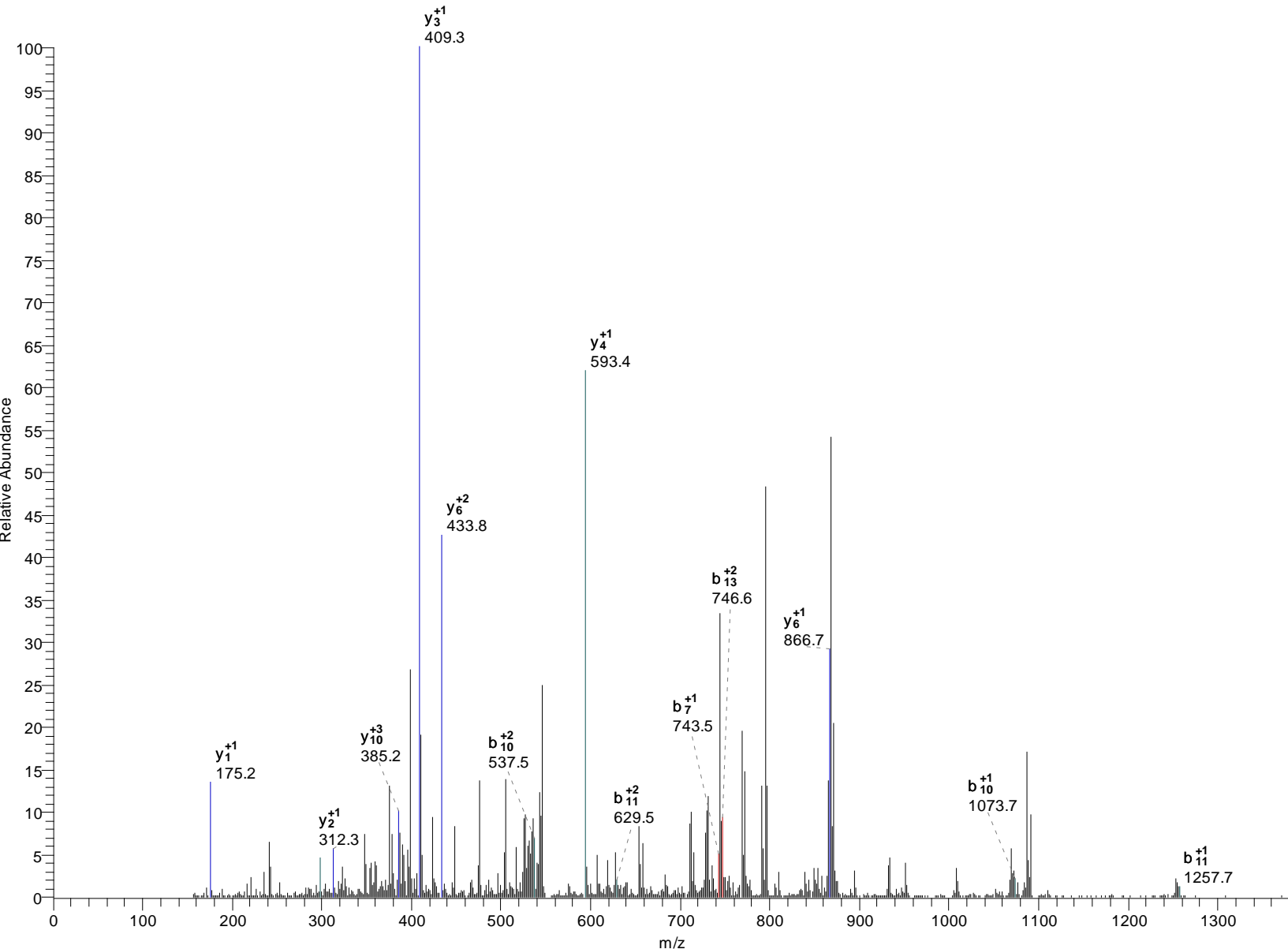
prKme3:1SAPATGGVKpr,me1:1KprPHR H3K27me3:1K36me1:1

#8141-8141 RT:56.20-56.20 NL: 6.42E4



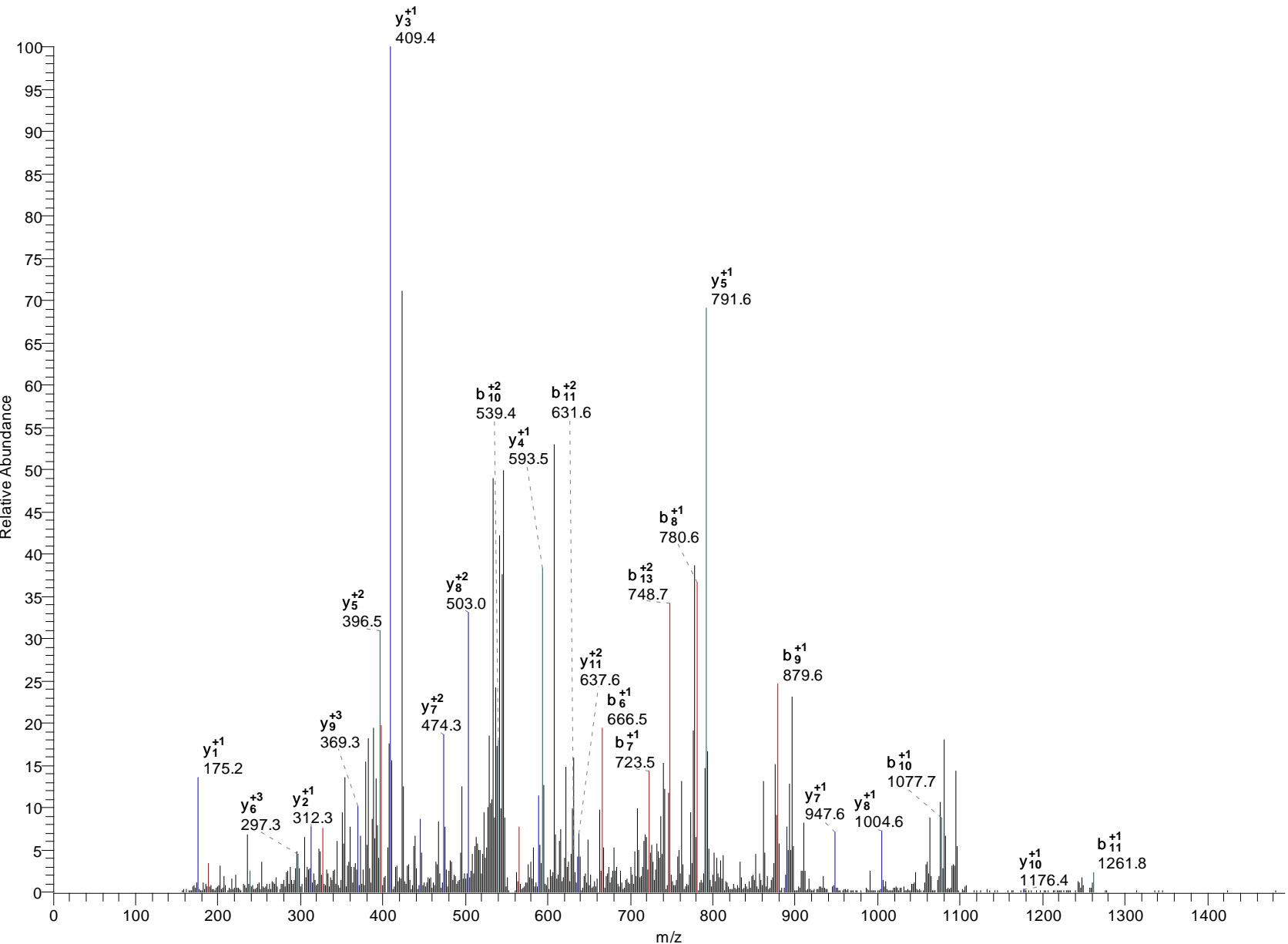
prKpr,me1:1SAPATGGVKme3:1KprPHR H3K27me1:1K36me3:1

#8475-8475 RT:58.01-58.01 NL: 3.70E4



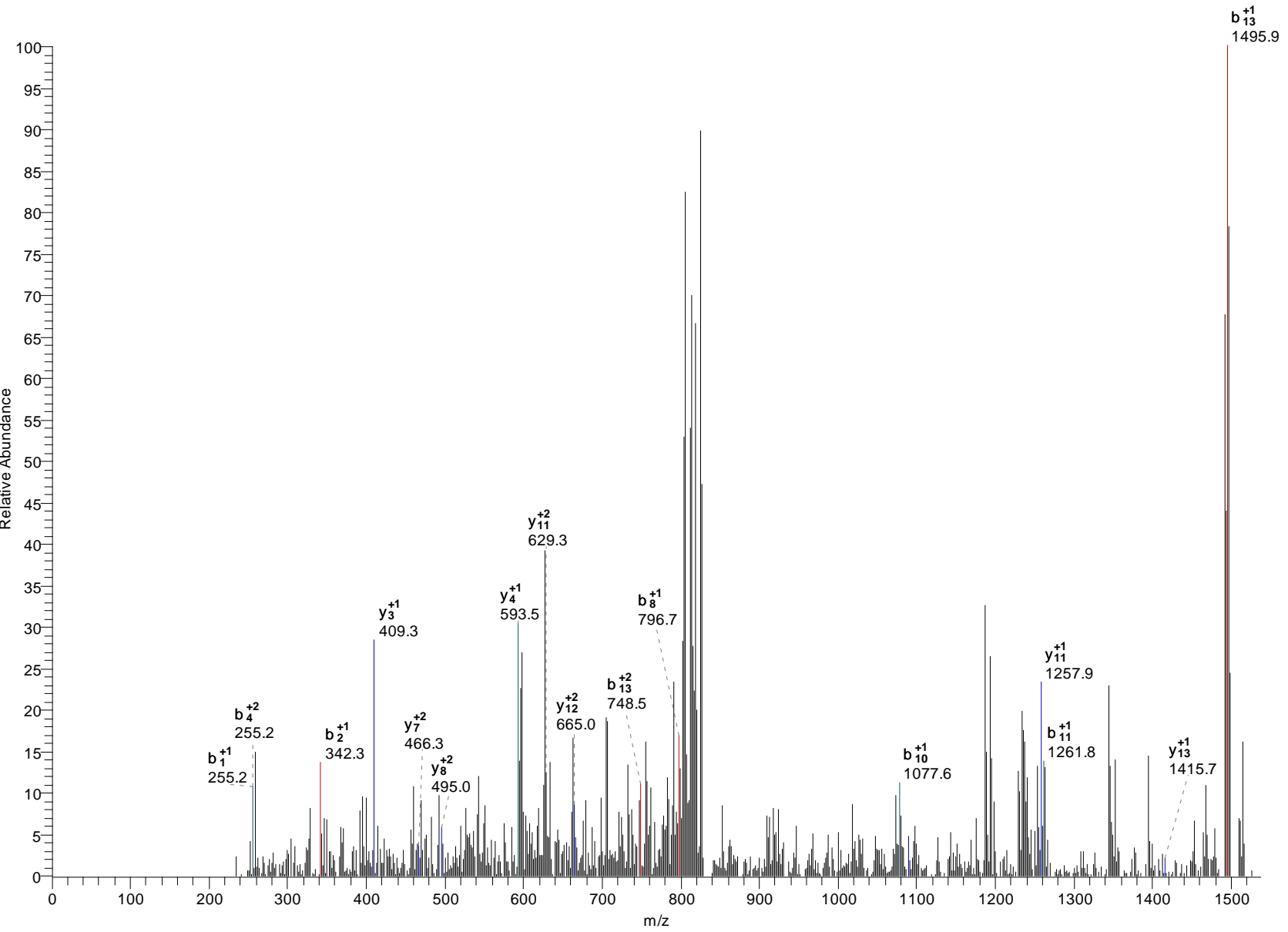
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#7849-7849 RT:56.01-56.01 NL: 4.26E3



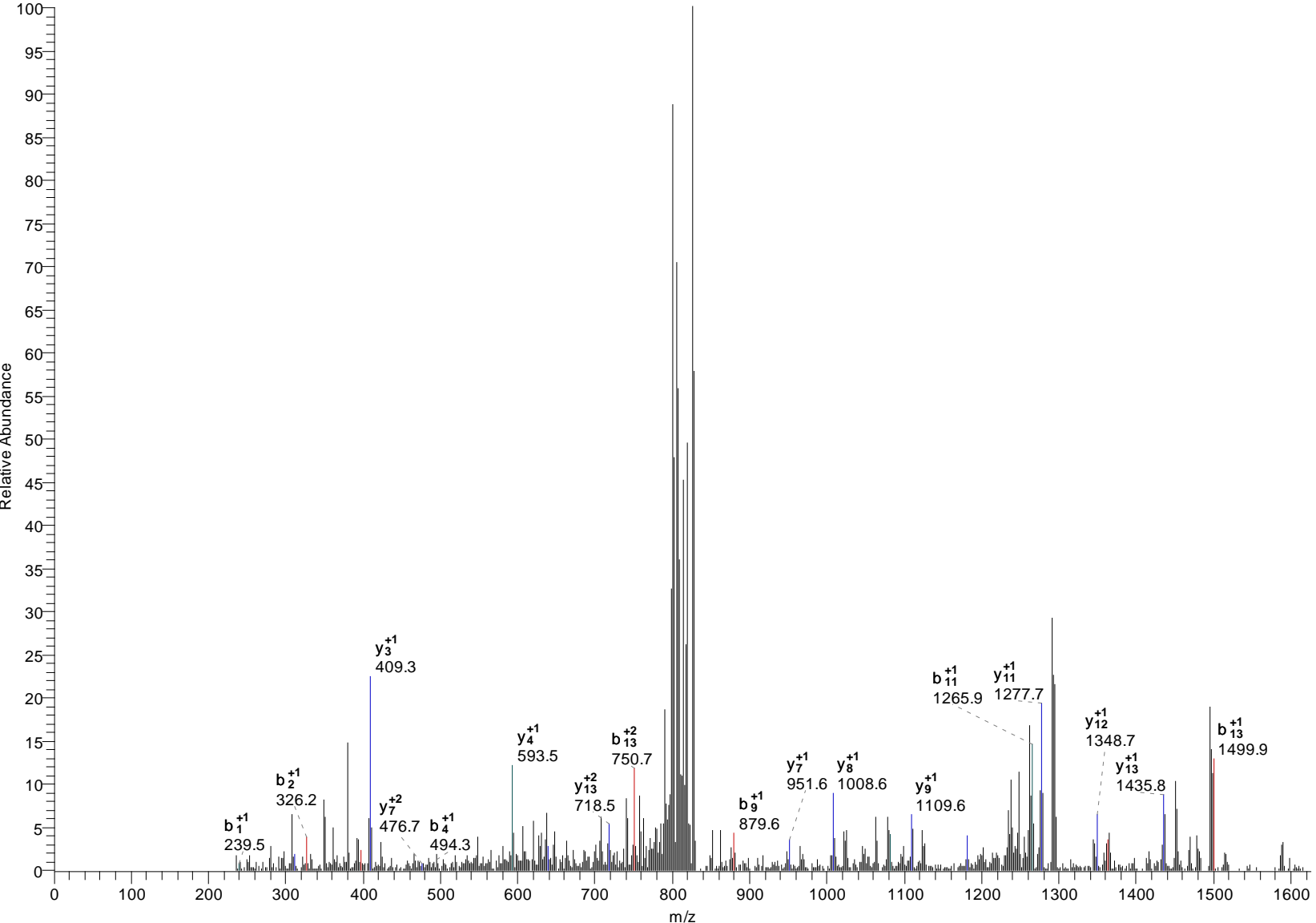
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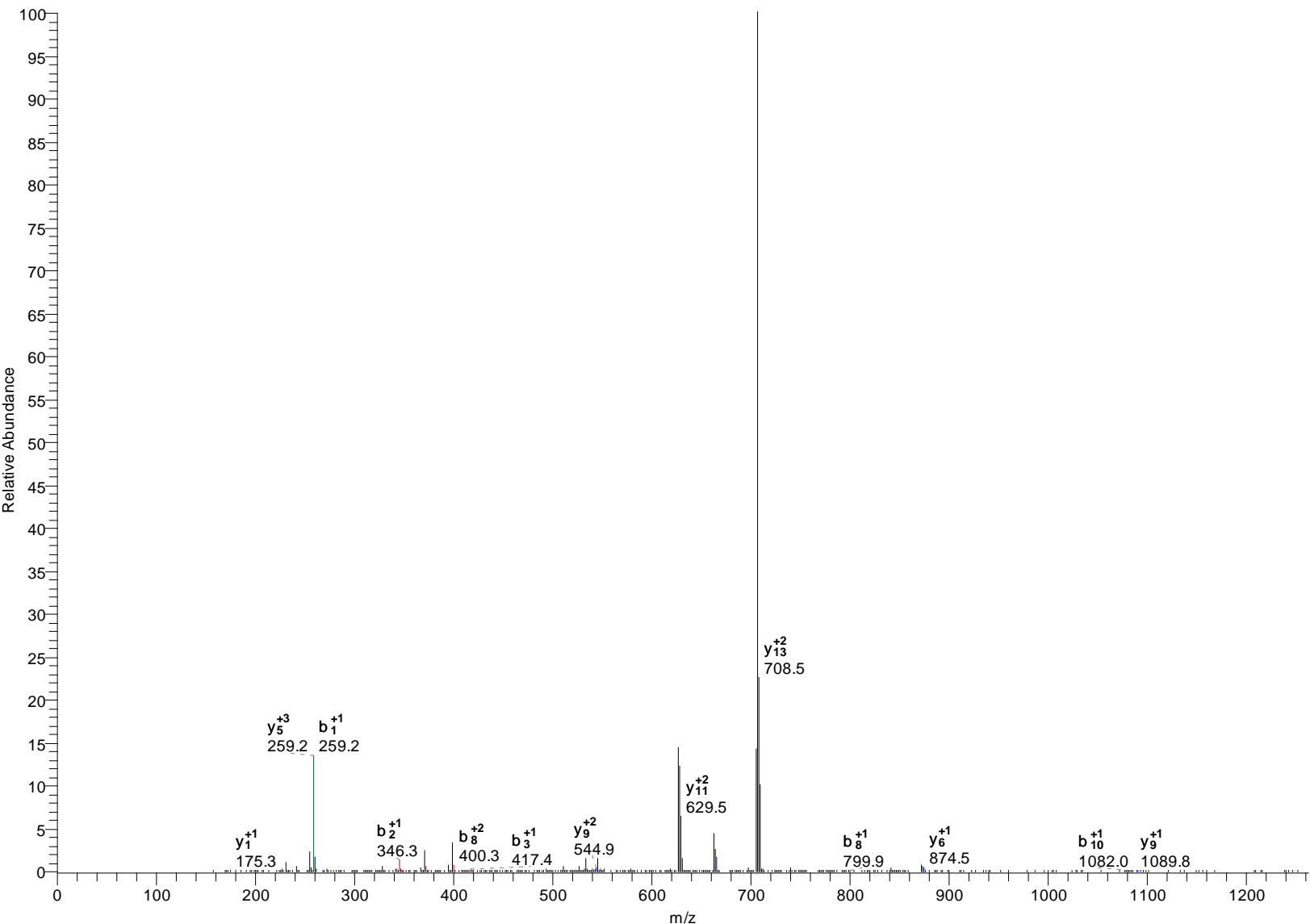
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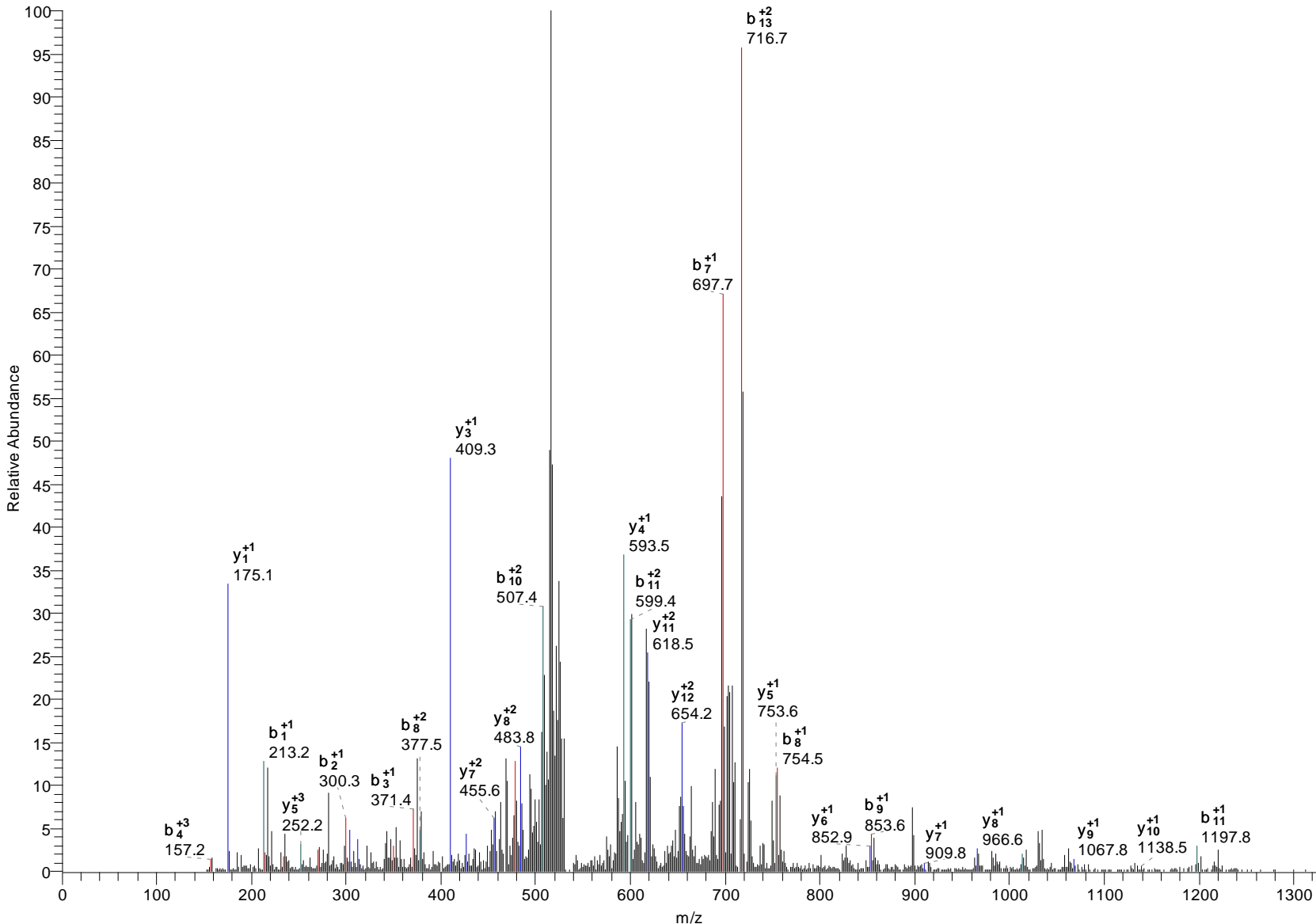
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H3K27me2:0K36me2:1

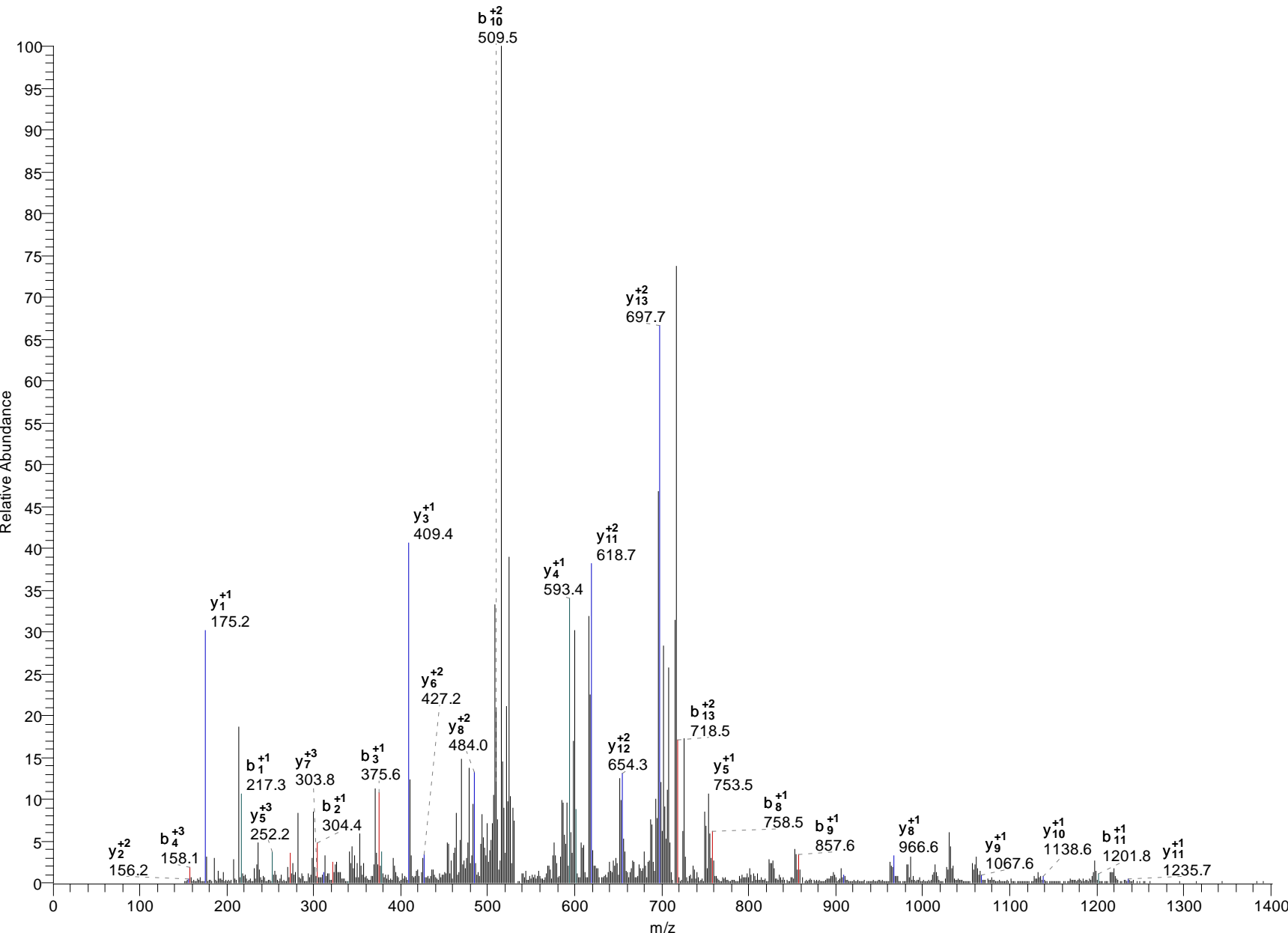
#6163-6163 RT:49.33-49.33 NL: 5.18E3



prKpr,me2:1SAPATGGVKpr,me2:1KprPHR

H3K27me2:1K36me2:1

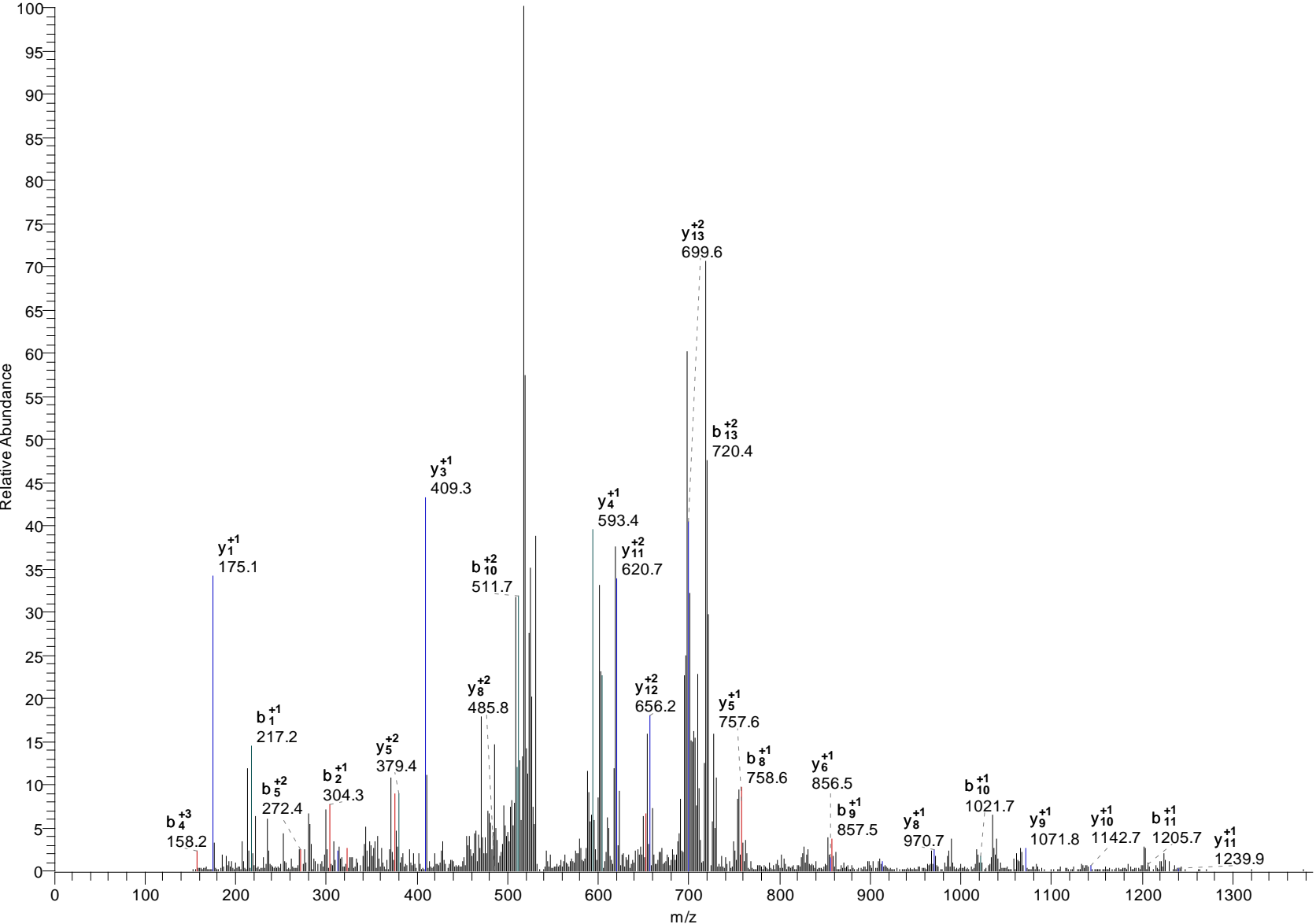
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H3K27me2:1K36me2:2

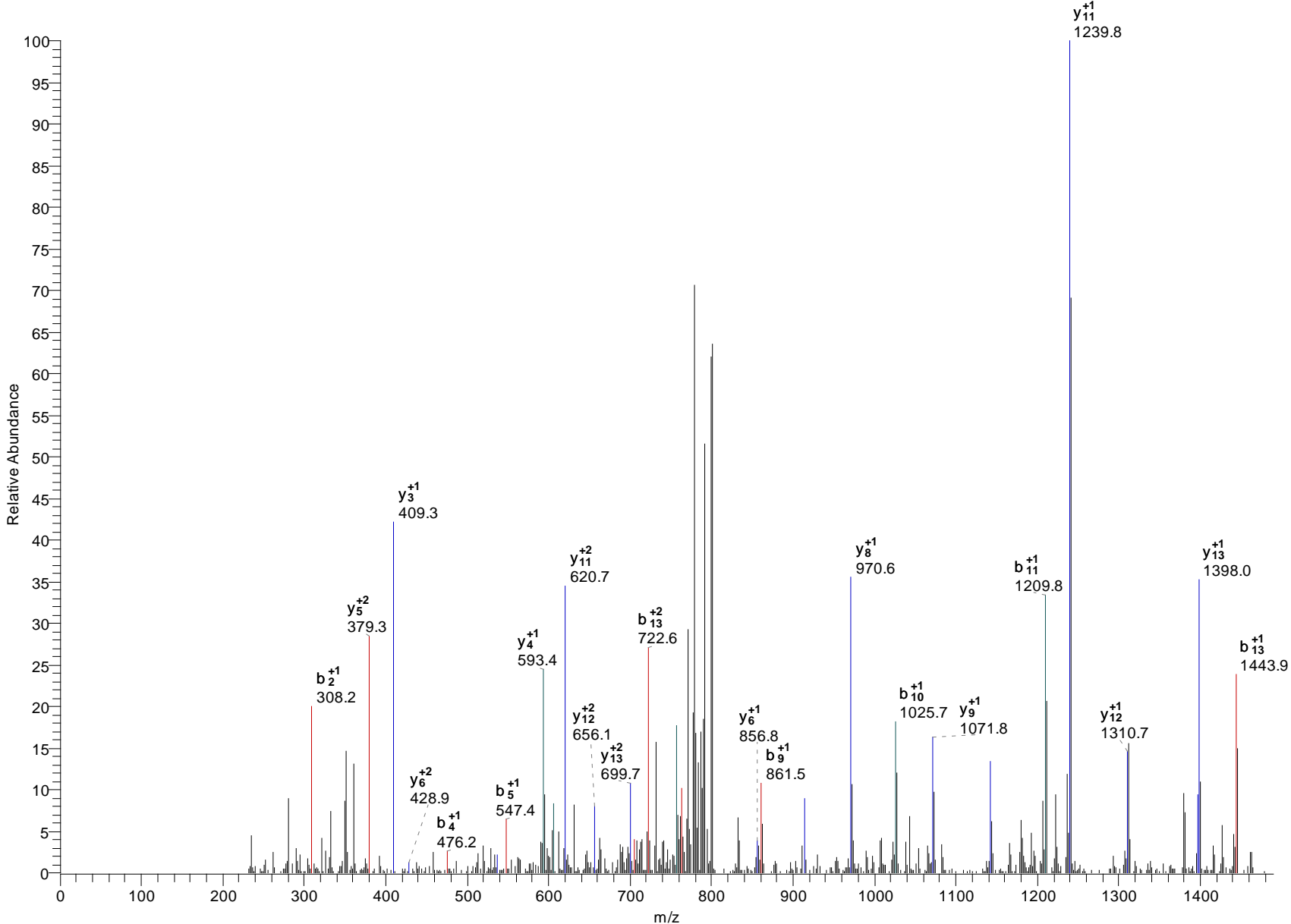
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prKpr,me2:2SAPATGGVKpr,me2:2KprPHR

H3K27me2:2K36me2:2

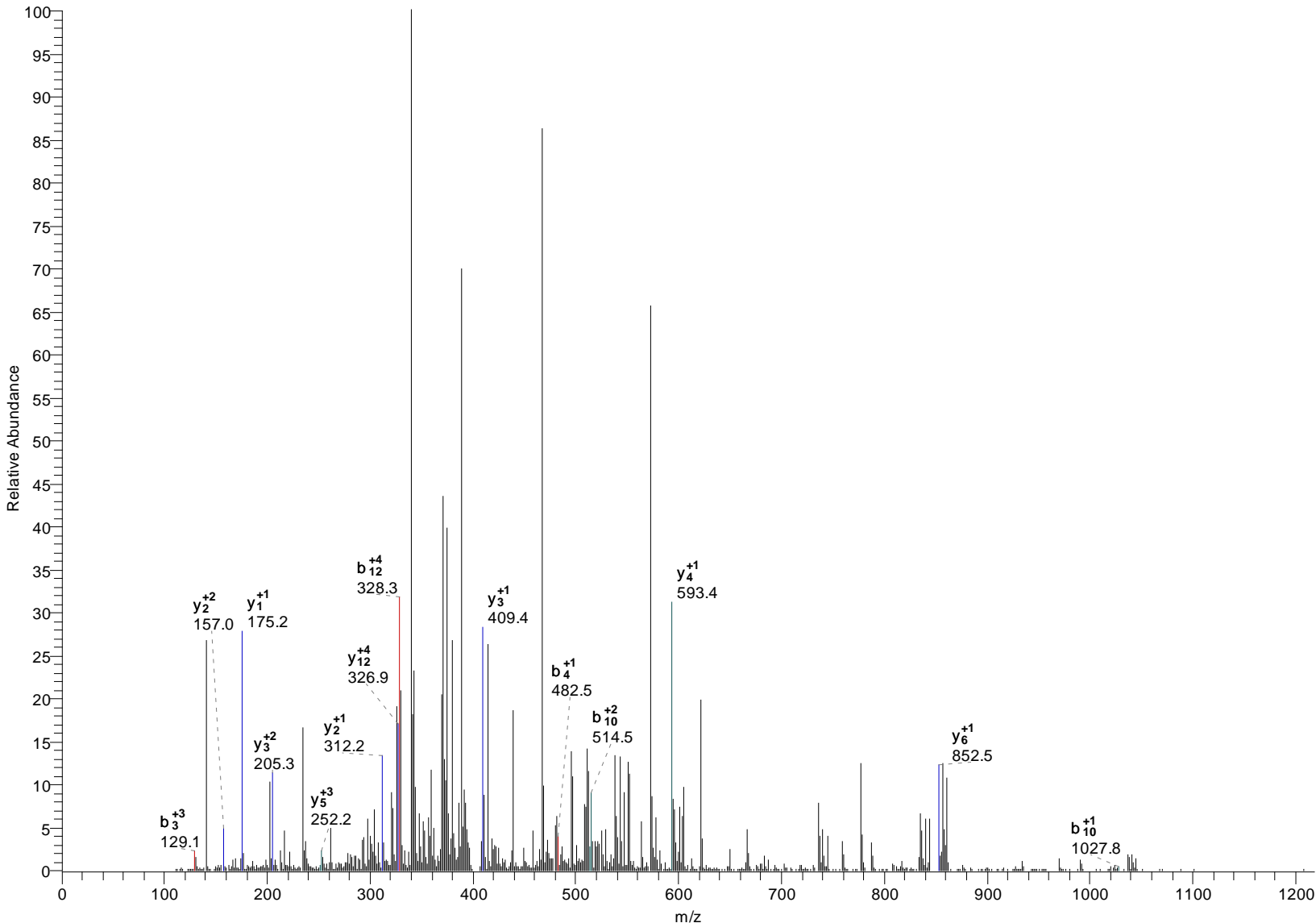
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prKme3:OSAPATGGVKme2:1KprPHR

H3K27me3:0K36me2:1

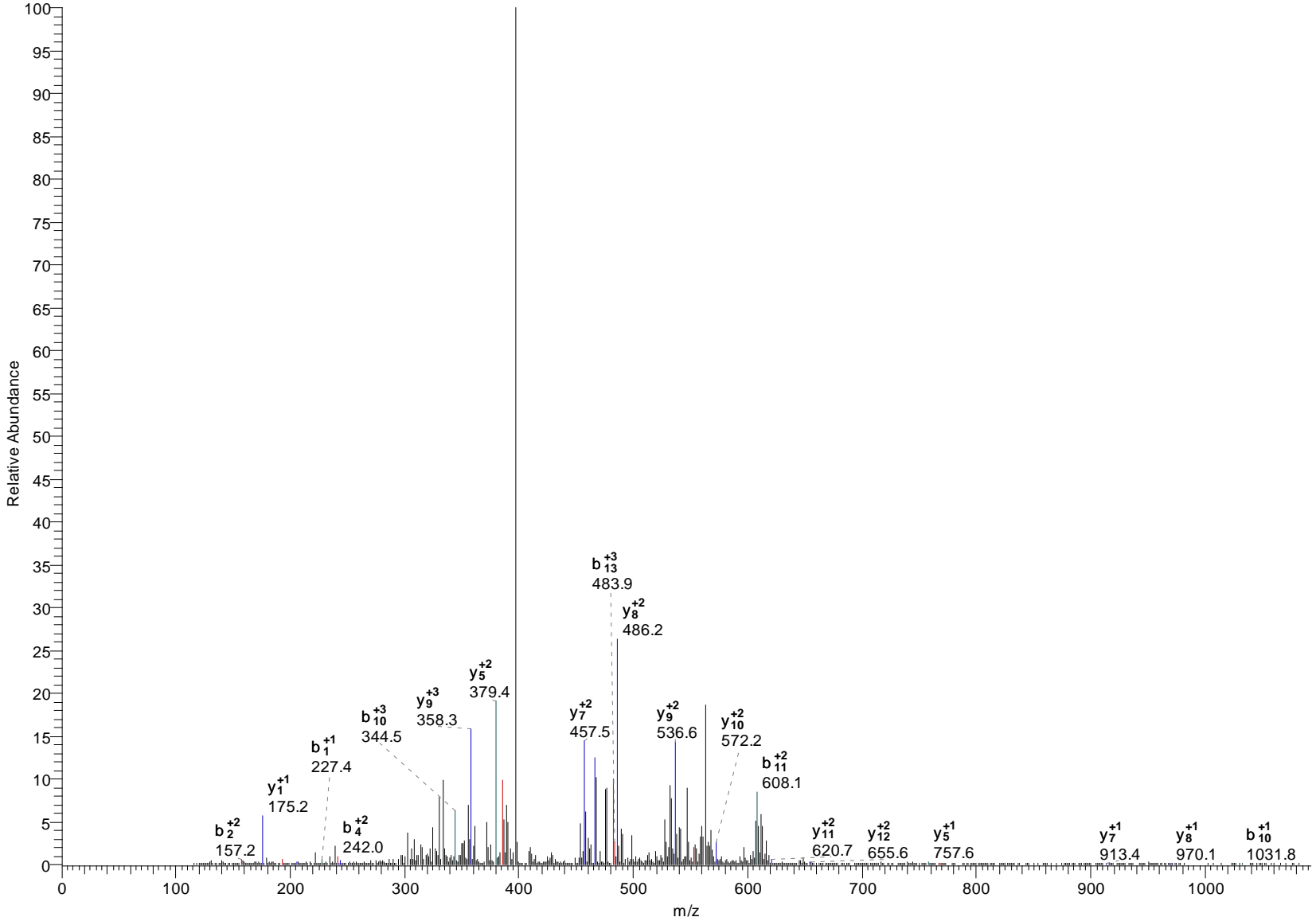
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prKme3:0SAPATGGVKme2:2KprPHR

H3K27me3:0K36me2:2

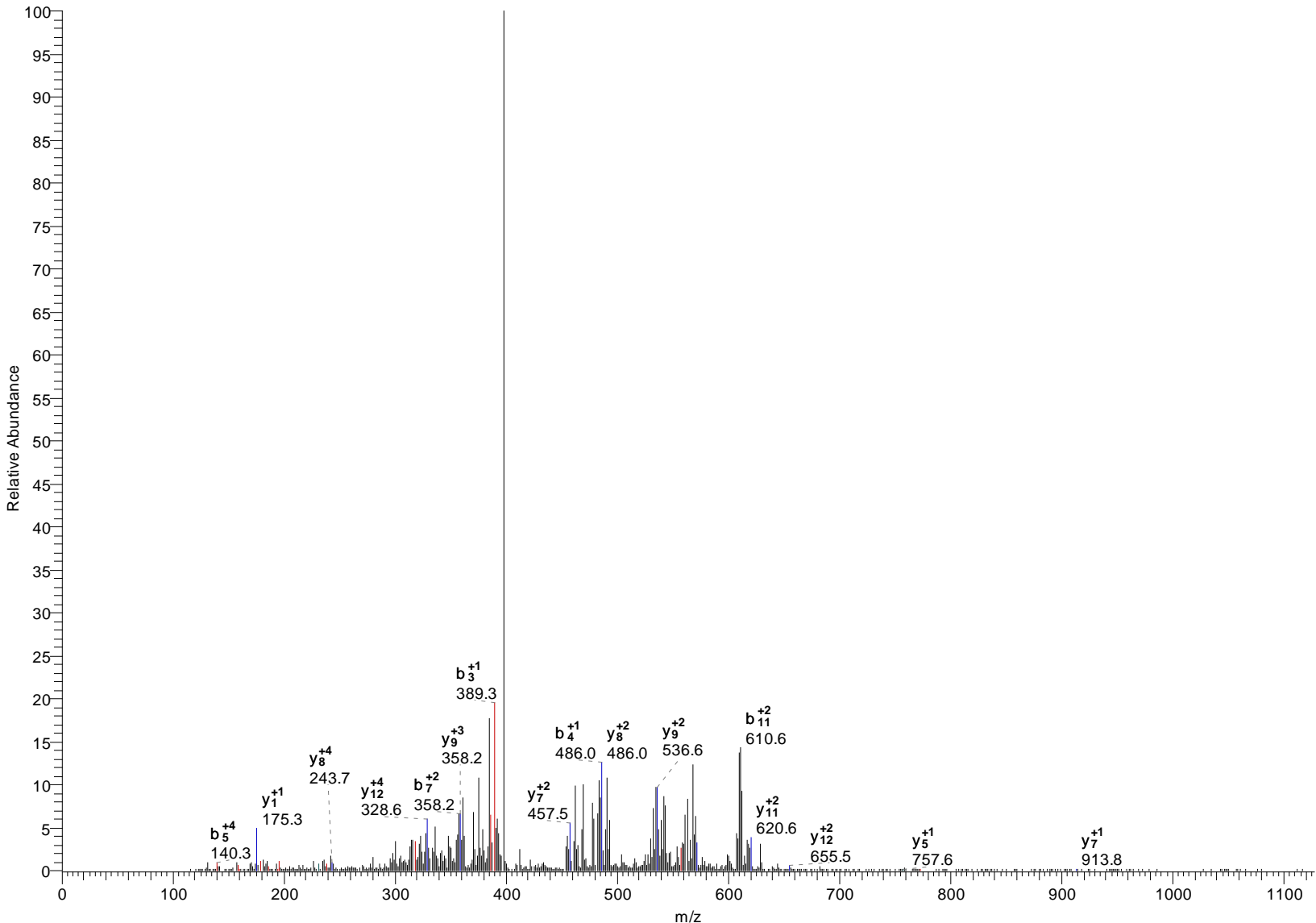
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prKme3:1SAPATGGVKme2:2KprPHR

H3K27me3:1K36me2:2

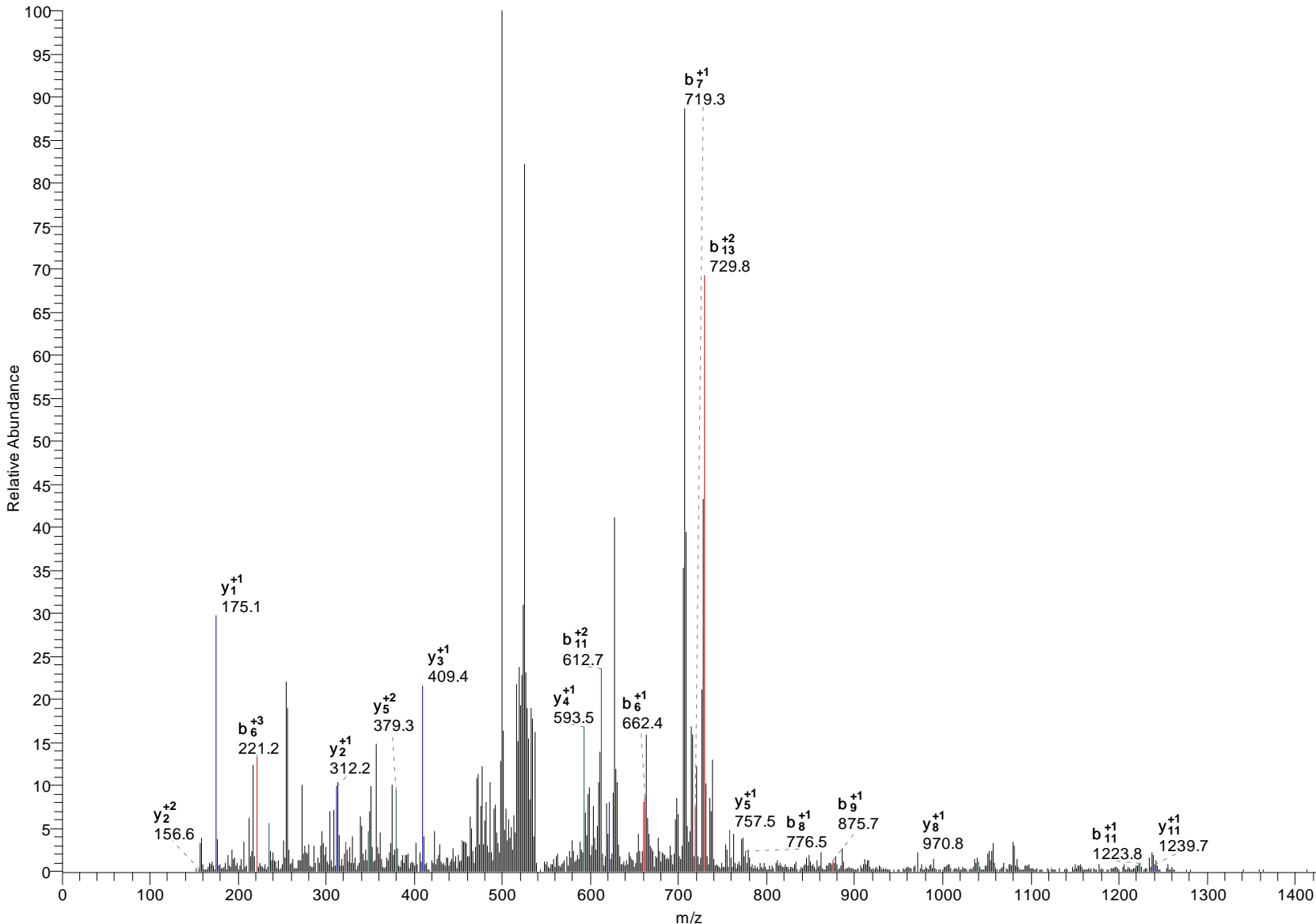
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H3K27me3:2K36me2:2

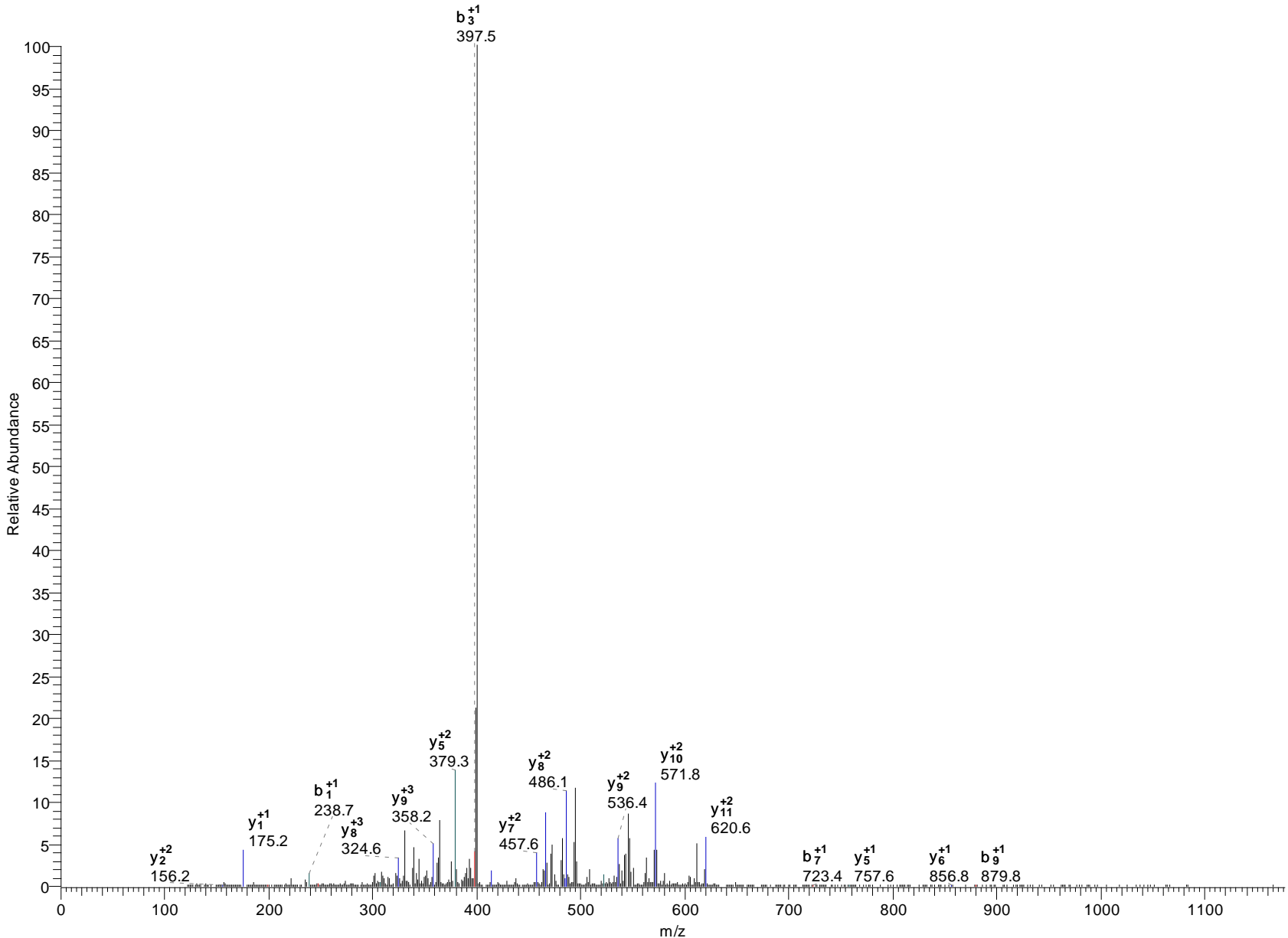
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H3K27me3:3K36me2:2

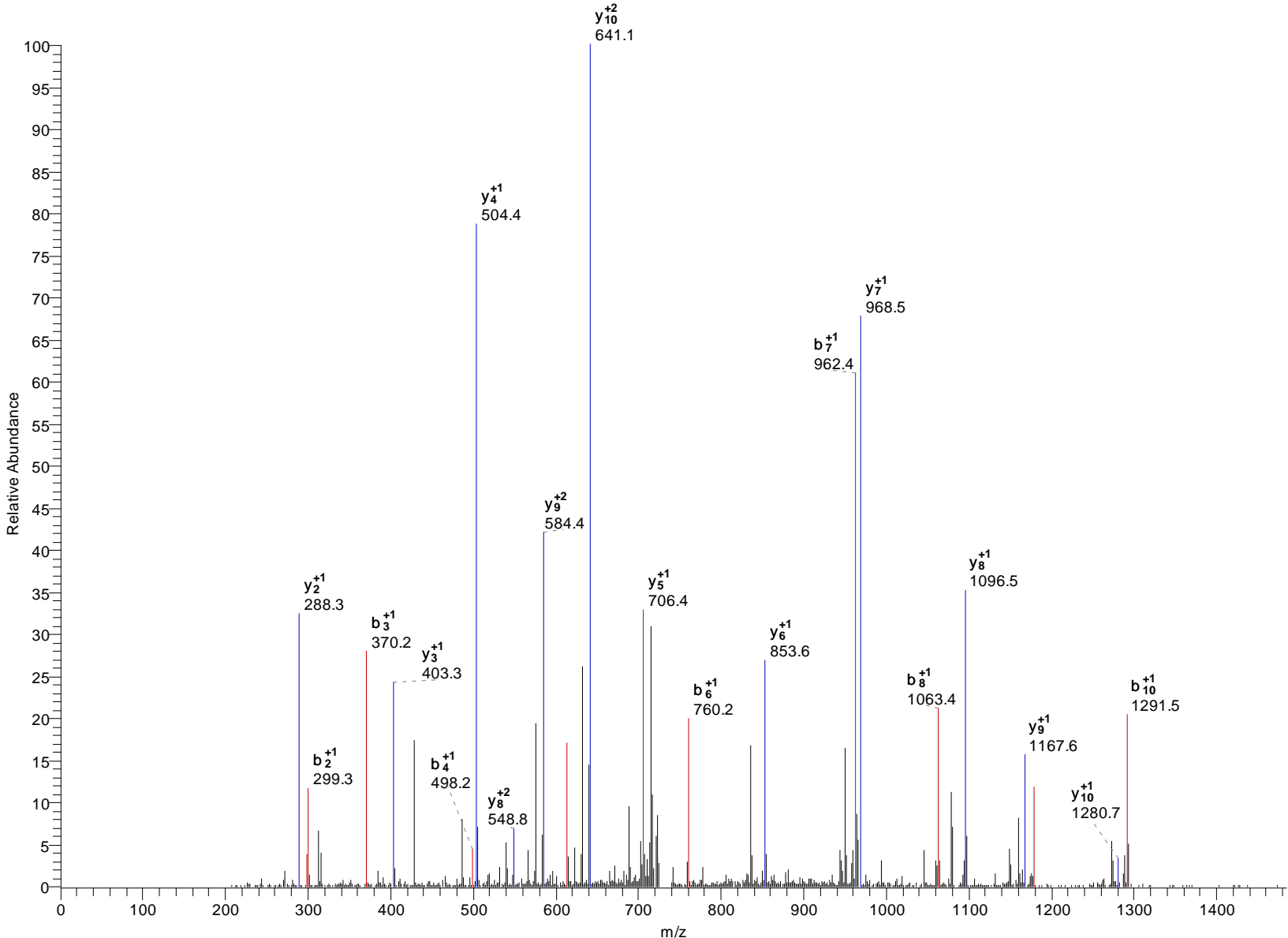
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prEIAQDFKpr,me1:1TDLR

H3K79me1:1

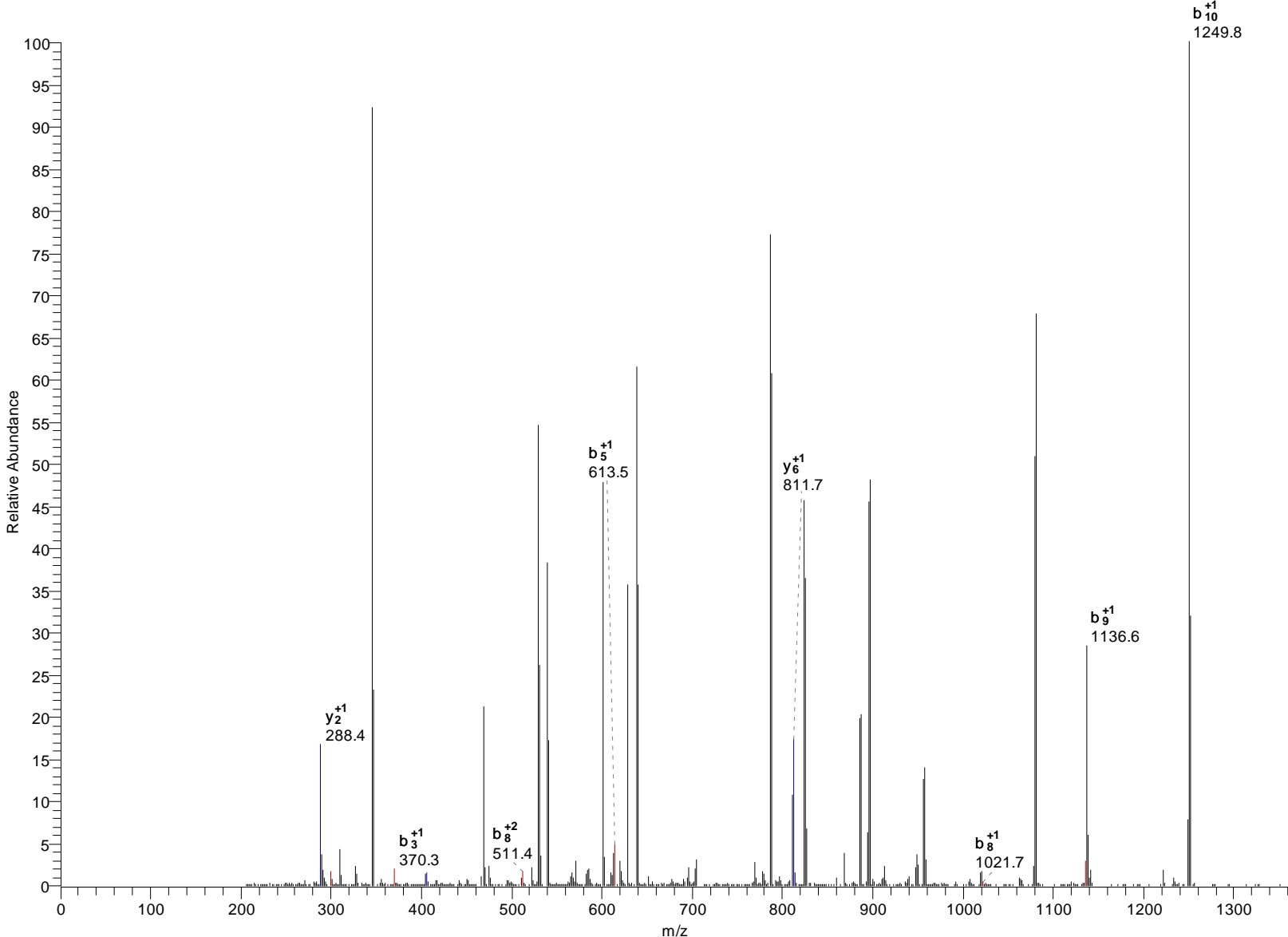
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prEIAQDFKme2:1TDLR

H3K79me2:1

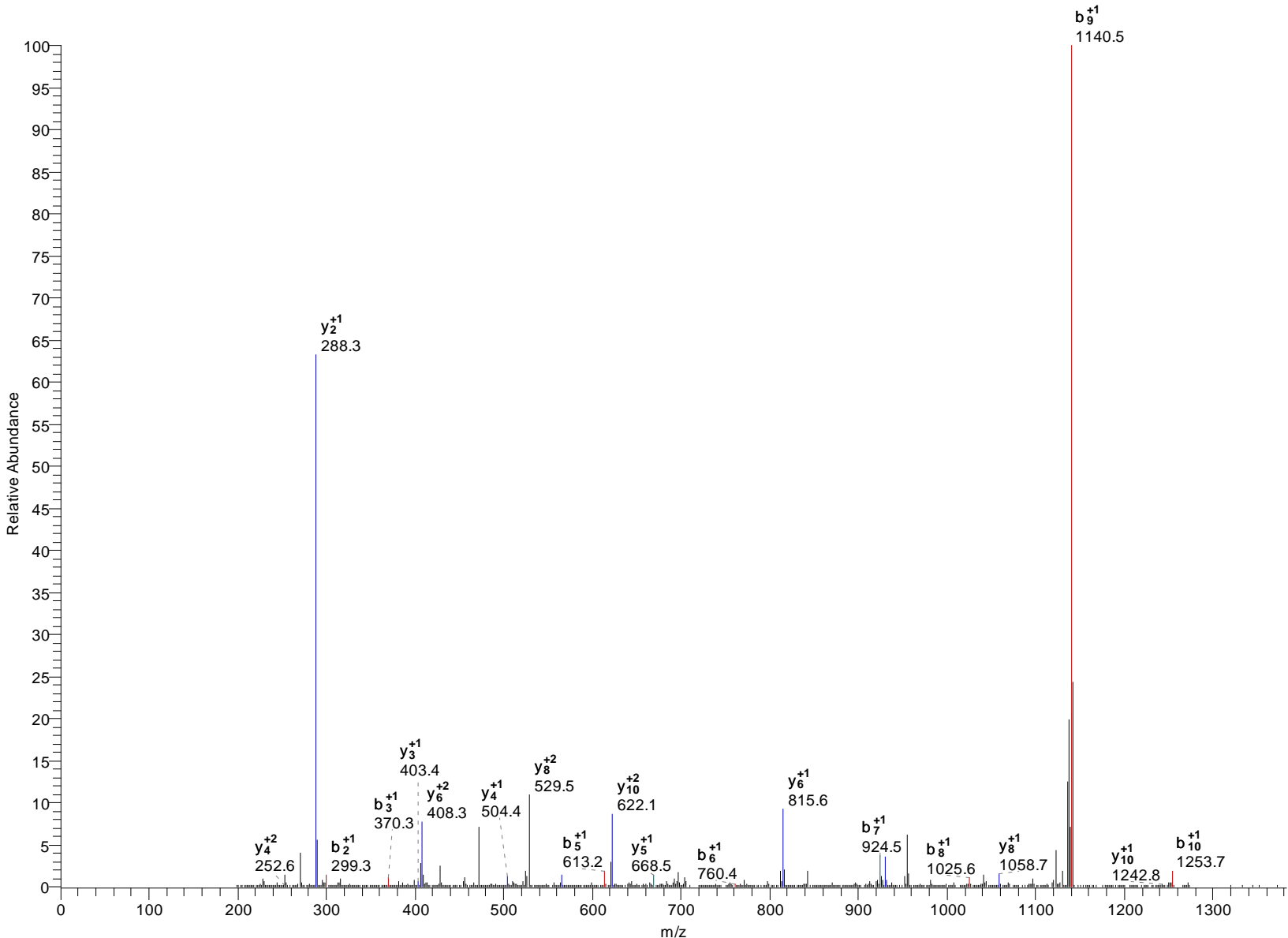
#15179-15179 RT:98.21-98.21 NL: 5.65E4



prEIAQDFKme2:2TDLR

H3K79me2:2

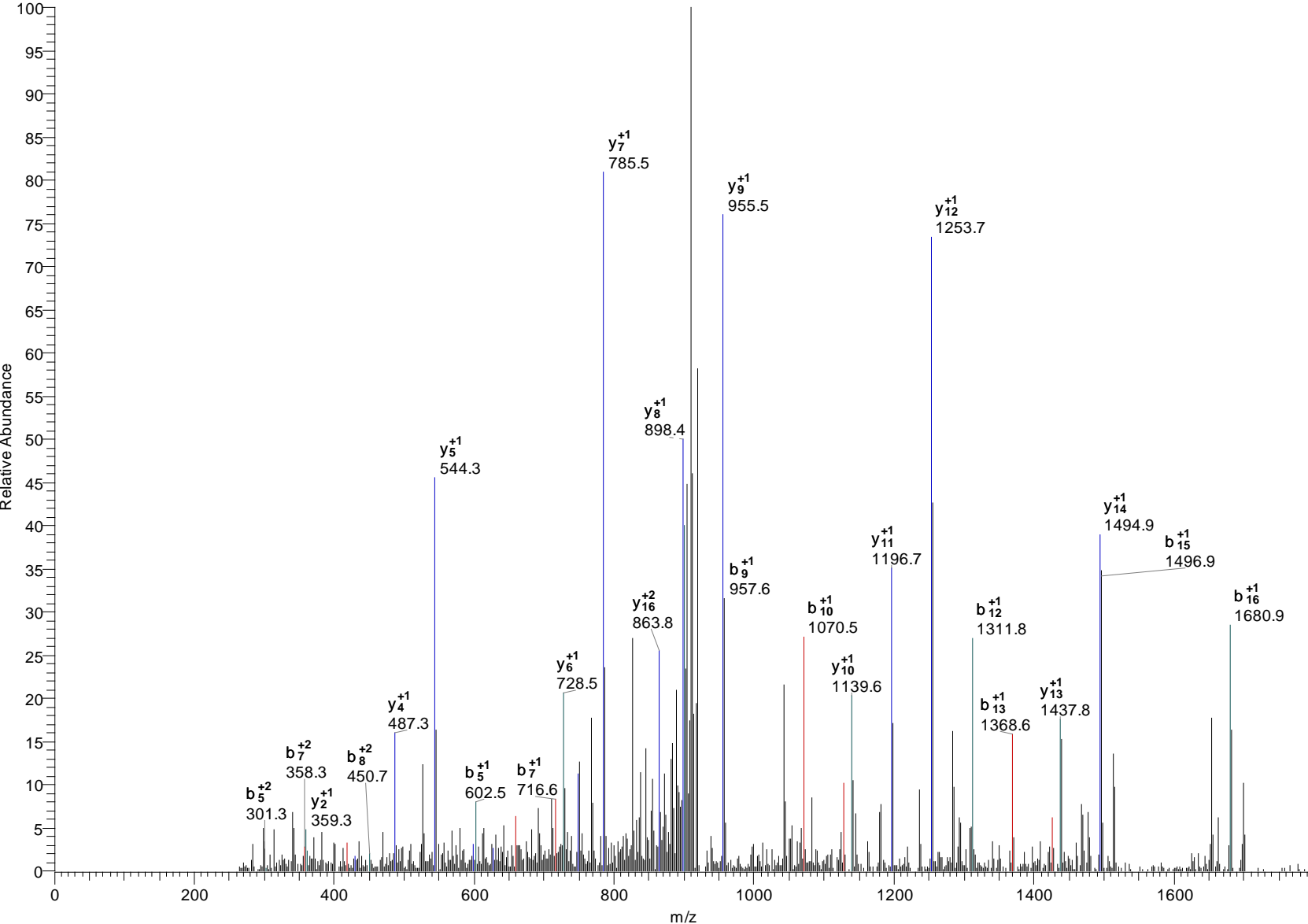
#10569-10569 RT:82.10-82.10 NL: 5.28E4



acSGRme1:1GKprGGKprGLGKprGGAKprR

H4R3me1:1

#8181-8181 RT:67.92-67.92 NL: 1.09E3

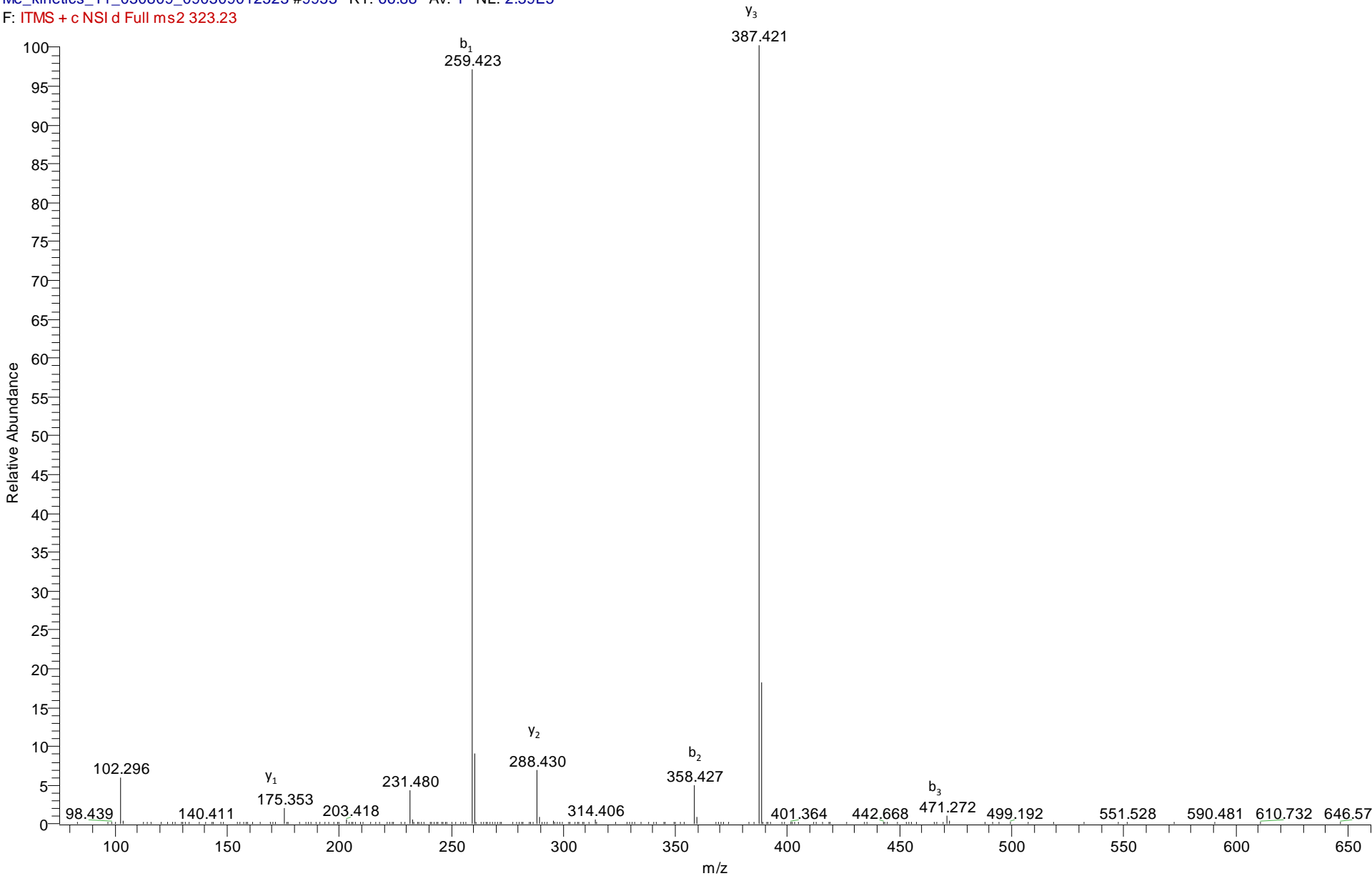


prKpr,me1:1VLR

H4K20me1:1

Me_kinetics_T1_030809_090309012523 #9953 RT: 66.88 AV: 1 NL: 2.39E5

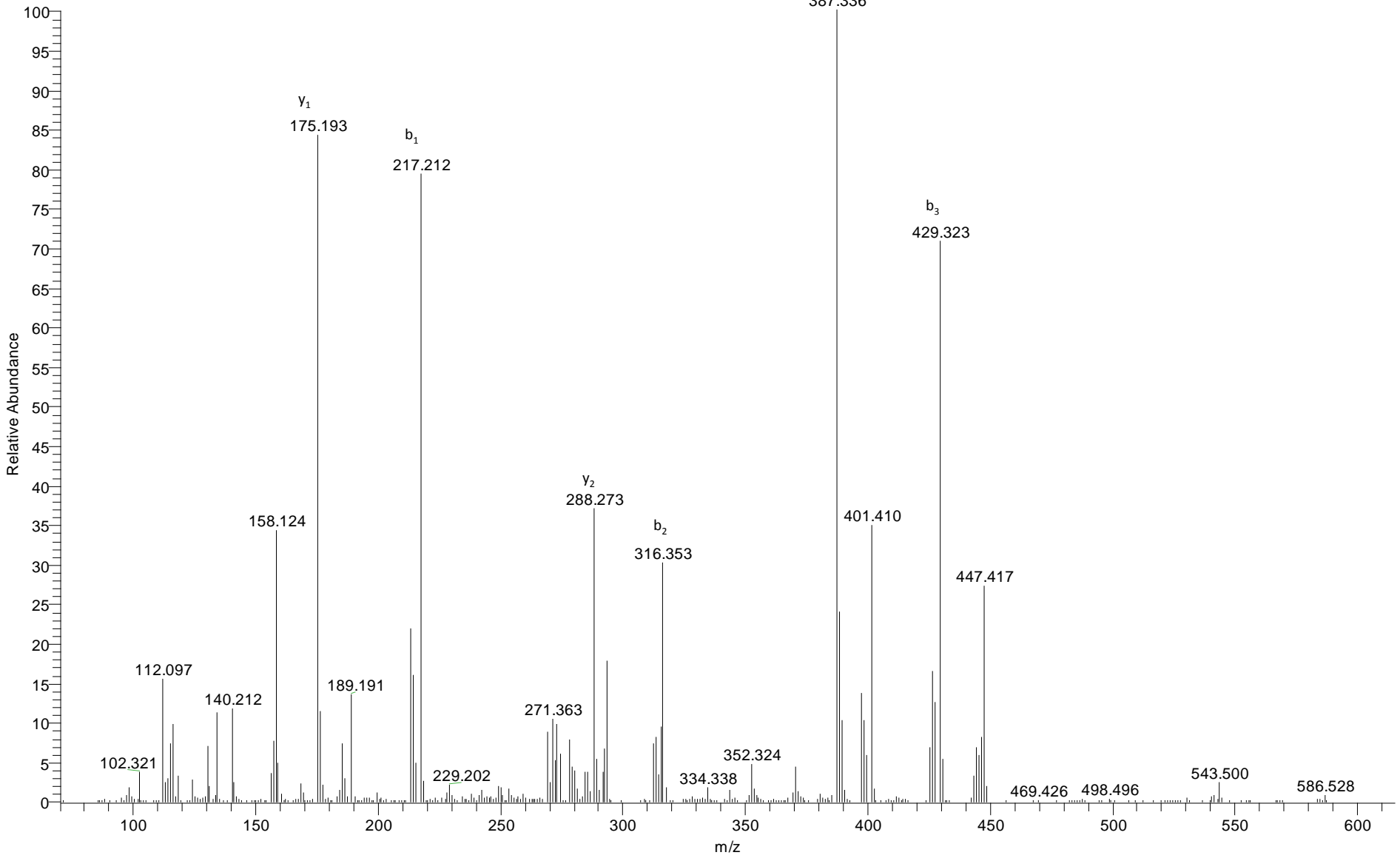
F: ITMS + c NSI d Full ms2 323.23



prKme2:1VLR

H4K20me2:1

Me_kinetics_T1_030809_090309012523 #5561 RT: 41.12 AV: 1 NL: 2.32E4
F: ITMS + c NSI d Full ms2 302.22

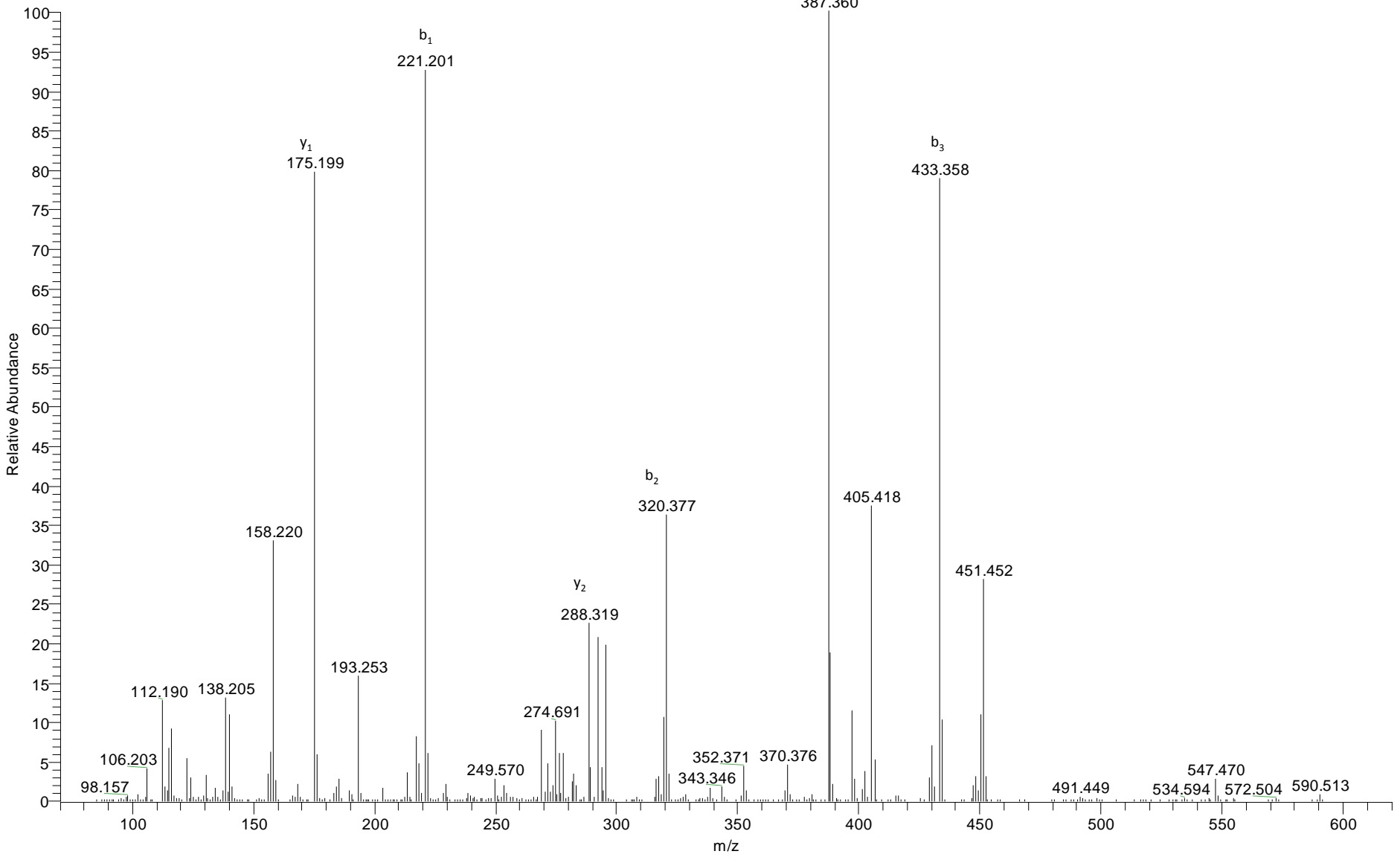


prKme2:2VLR

H4K20me2:2

Me_kinetics_T1_030809_090309012523 #5373 RT: 40.06 AV: 1 NL: 1.27E5

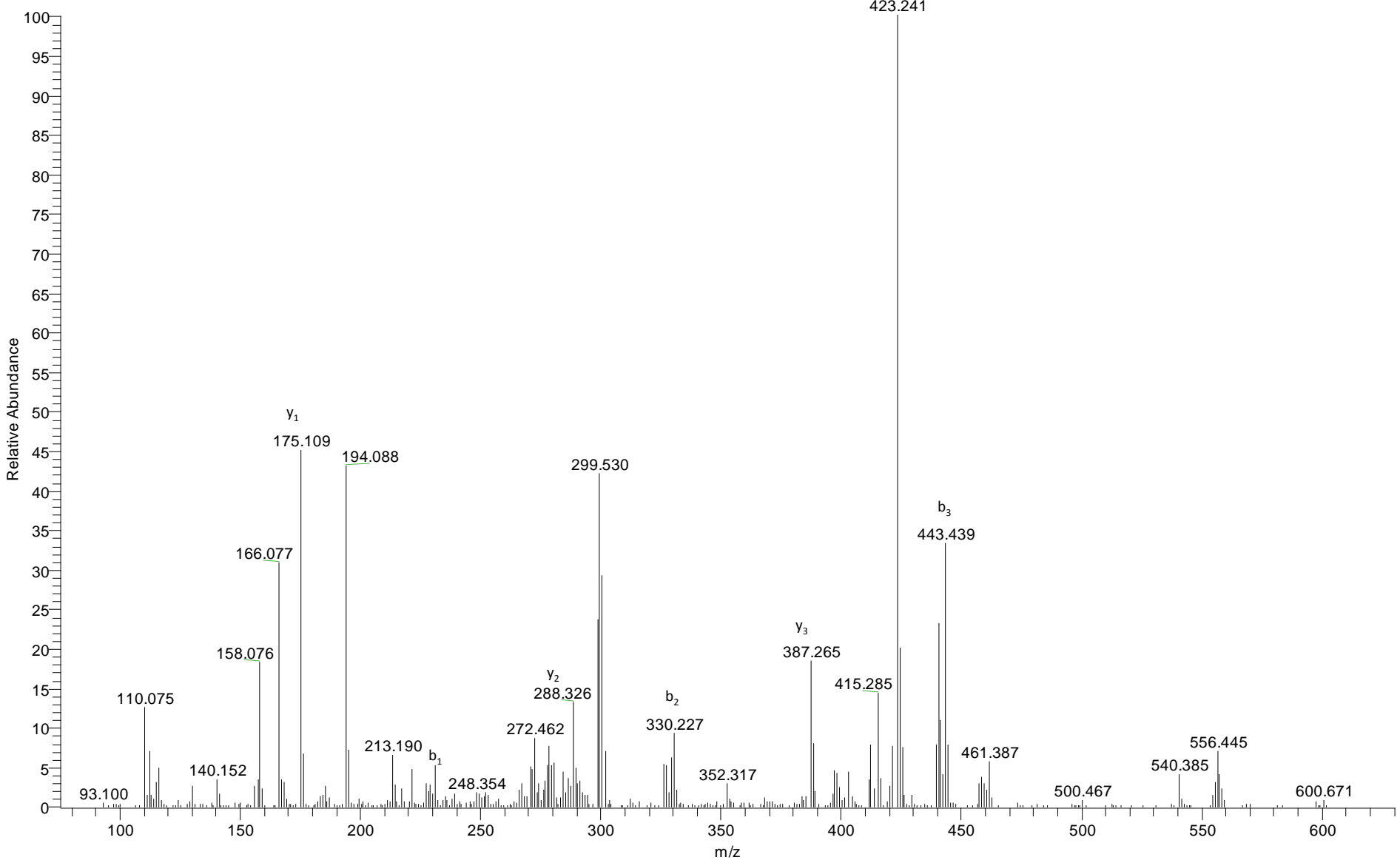
F: ITMS + c NSI d Full ms2 304.23



prKme3:1VLR

H4K20me3:1

Me_kinetics_T1_030809_090309012523 #5237 RT: 39.29 AV: 1 NL: 5.75E3
F: ITMS + c NSI d Full ms2 309.23

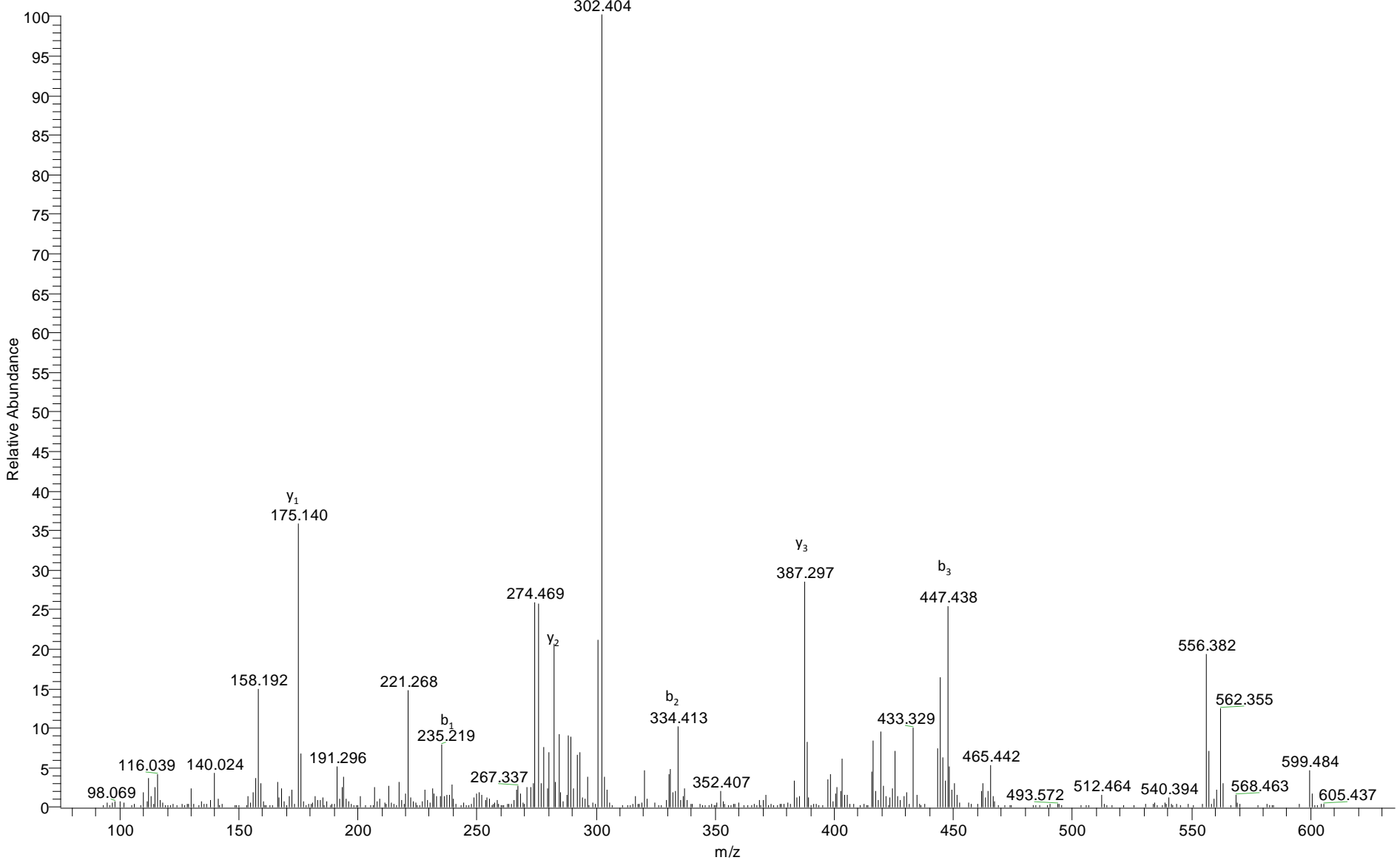


prKme3:2VLR

H4K20me3:2

Me_kinetics_T2_030809 #5184 RT: 40.79 AV: 1 NL: 5.09E3

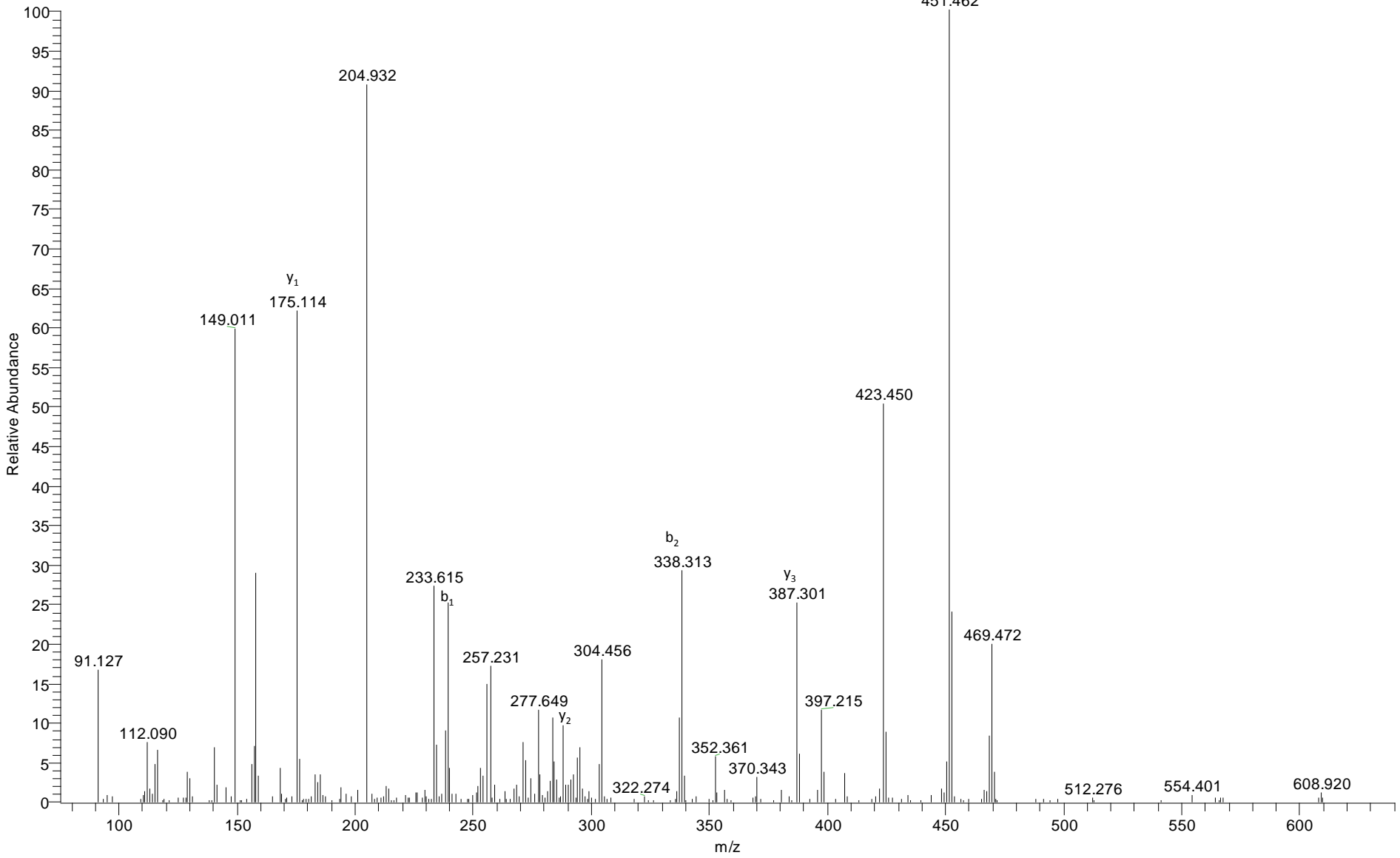
F: ITMS + c NSI d Full ms2 311.24



prKme3:3VLR

H4K20me3:3

Me_kinetics_T4_030809 #4835 RT: 36.94 AV: 1 NL: 1.90E3
F: ITMS + c NSI d Full ms2 313.25



Supplemental Figure 2

SUPPLEMENTAL FIGURE 2. Differential equations used for modeling the relative abundances of residues that can be mono-methylated (A), mono- and dimethylated (B), or mono-, di-, and trimethylated (C). In the MATLAB code (Supplemental Data), we account for dilution of the various species due to cell division in the fitting of μ . For calculating the time required for half-maximal labeling, we fit the relative levels of a fully labeled peptide species X to equation (D) at each day after introduction to labeled media. In the equation, c_1 represents the final relative level of X (more precisely, the change between the maximum relative level and the initial relative level, which is 0 for the fully labeled species), and c_2 represents the time constant. Multiplying the time constant by $\ln(2)$ yields the half-max time ($t_{1/2}$) of maximal label incorporation.

A:

$$d[0:0]/dt = \alpha - k_{0 \rightarrow 1}[0:0] - k'_{0 \rightarrow 1}[0:0] + k_{1 \rightarrow 0}[1:1] + k_{1 \rightarrow 0}[1:0] - \mu_0[0:0]$$

$$d[1:0]/dt = -k_{1 \rightarrow 0}[1:0] + k'_{0 \rightarrow 1}[0:0] - \mu_1[1:0]$$

$$d[1:1]/dt = k_{0 \rightarrow 1}[0:0] - k_{1 \rightarrow 0}[1:1] - \mu_1[1:1]$$

B:

$$d[0:0]/dt = \alpha - k_{0 \rightarrow 1}[0:0] - k'_{0 \rightarrow 1}[0:0] + k_{1 \rightarrow 0}[1:1] + k_{1 \rightarrow 0}[1:0] - \mu_0[0:0]$$

$$d[1:0]/dt = -k_{1 \rightarrow 0}[1:0] + k'_{0 \rightarrow 1}[0:0] - k_{1 \rightarrow 2}[1:0] + k_{2 \rightarrow 1}[2:1] + k_{2 \rightarrow 1}[2:0] - k'_{1 \rightarrow 2}[1:0] - \mu_1[1:0]$$

$$d[1:1]/dt = -k_{1 \rightarrow 0}[1:1] + k_{0 \rightarrow 1}[0:0] - k_{1 \rightarrow 2}[1:1] + k_{2 \rightarrow 1}[2:1] + k_{2 \rightarrow 1}[2:2] - k'_{1 \rightarrow 2}[1:1] - \mu_1[1:1]$$

$$d[2:0]/dt = -2k_{2 \rightarrow 1}[2:0] + k'_{1 \rightarrow 2}[1:0] - \mu_2[2:0]$$

$$d[2:1]/dt = -2k_{2 \rightarrow 1}[2:1] + k'_{1 \rightarrow 2}[1:1] + k_{1 \rightarrow 2}[1:0] - \mu_2[2:1]$$

$$d[2:2]/dt = -2k_{2 \rightarrow 1}[2:2] + k_{1 \rightarrow 2}[1:1] - \mu_2[2:2]$$

C:

$$d[0:0]/dt = \alpha - k_{0 \rightarrow 1}[0:0] - k'_{0 \rightarrow 1}[0:0] + k_{1 \rightarrow 0}[1:1] + k_{1 \rightarrow 0}[1:0] - \mu_0[0:0]$$

$$d[1:0]/dt = -k_{1 \rightarrow 0}[1:0] + k'_{0 \rightarrow 1}[0:0] - k_{1 \rightarrow 2}[1:0] + k_{2 \rightarrow 1}[2:1] + 2k_{2 \rightarrow 1}[2:0] - k'_{1 \rightarrow 2}[1:0] - \mu_1[1:0]$$

$$d[1:1]/dt = -k_{1 \rightarrow 0}[1:1] + k_{0 \rightarrow 1}[0:0] - k_{1 \rightarrow 2}[1:1] + k_{2 \rightarrow 1}[2:1] + 2k_{2 \rightarrow 1}[2:2] - k'_{1 \rightarrow 2}[1:1] - \mu_1[1:1]$$

$$d[2:0]/dt = -2k_{2 \rightarrow 1}[2:0] + k'_{1 \rightarrow 2}[1:0] - k'_{2 \rightarrow 3}[2:0] - k_{2 \rightarrow 3}[2:0] + 3k_{3 \rightarrow 2}[3:0] + k_{3 \rightarrow 2}[3:1] - \mu_2[2:0]$$

$$d[2:1]/dt = -2k_{2 \rightarrow 1}[2:1] + k'_{1 \rightarrow 2}[1:1] + k_{1 \rightarrow 2}[1:0] - k_{2 \rightarrow 3}[2:1] + 2k_{3 \rightarrow 2}[3:2] + k_{3 \rightarrow 2}[3:1] - k'_{2 \rightarrow 3}[2:1] - \mu_2[2:1]$$

$$d[2:2]/dt = -2k_{2 \rightarrow 1}[2:2] + k_{1 \rightarrow 2}[1:1] - k_{2 \rightarrow 3}[2:2] + 3k_{3 \rightarrow 2}[3:3] + k_{3 \rightarrow 2}[3:2] - k'_{2 \rightarrow 3}[2:2] - \mu_2[2:2]$$

$$d[3:0]/dt = -3k_{3 \rightarrow 2}[3:0] + k'_{2 \rightarrow 3}[2:0] - \mu_3[3:0]$$

$$d[3:1]/dt = k_{2 \rightarrow 3}[2:0] - 3k_{3 \rightarrow 2}[3:1] + k'_{2 \rightarrow 3}[2:1] - \mu_3[3:1]$$

$$d[3:2]/dt = k_{2 \rightarrow 3}[2:1] - 3k_{3 \rightarrow 2}[3:2] + k'_{2 \rightarrow 3}[2:2] - \mu_3[3:2]$$

$$d[3:3]/dt = k_{2 \rightarrow 3}[2:2] - 3k_{3 \rightarrow 2}[3:3] - \mu_3[3:3]$$

D:

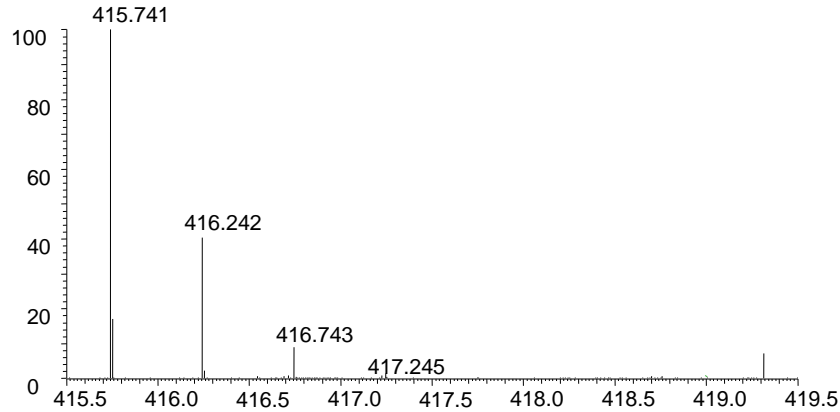
$$[X] = c_1 - c_1 \times \exp(-t/c_2)$$

Supplemental Figure 3 (14 MS spectra slides)

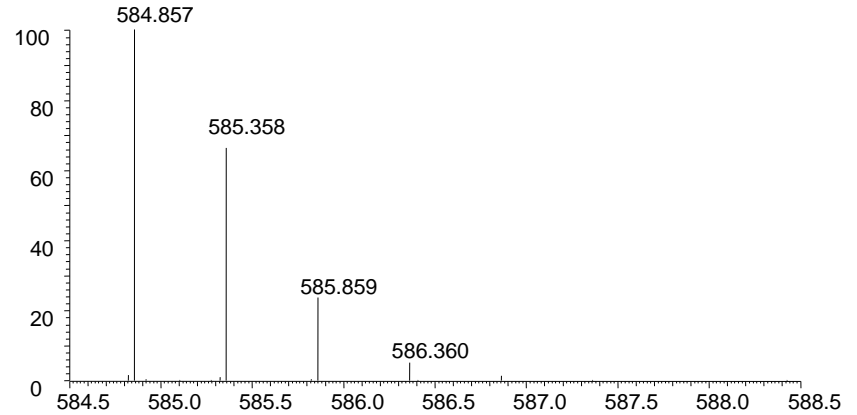
SUPPLEMENTAL FIG 3. MS spectra of the turnover for all peptides analyzed in the study, from day 0 to day 1 post introduction to labeled media. For peptides that can exist as non-oxidized or oxidized forms (labeled with “ox” in Sup. Table 1), only the non-oxidized form is provided. Furthermore, for peptides that can exist in multiple charge states, only one charge state is provided.

Day 0

H3K4me1

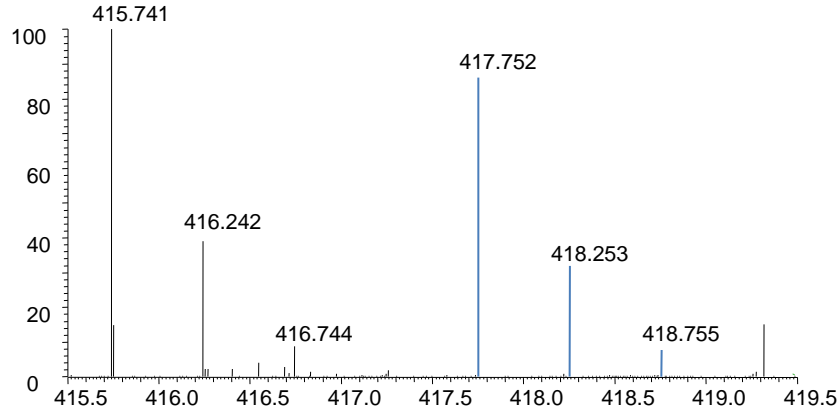


H3K18me1

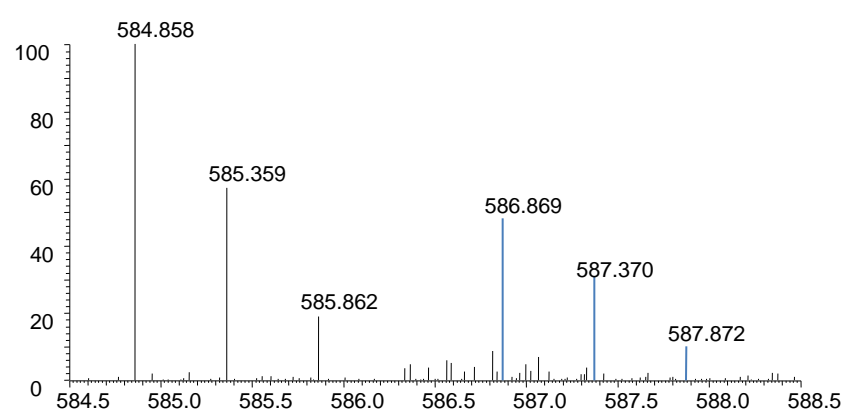


Day 1

H3K4me1



H3K18me1

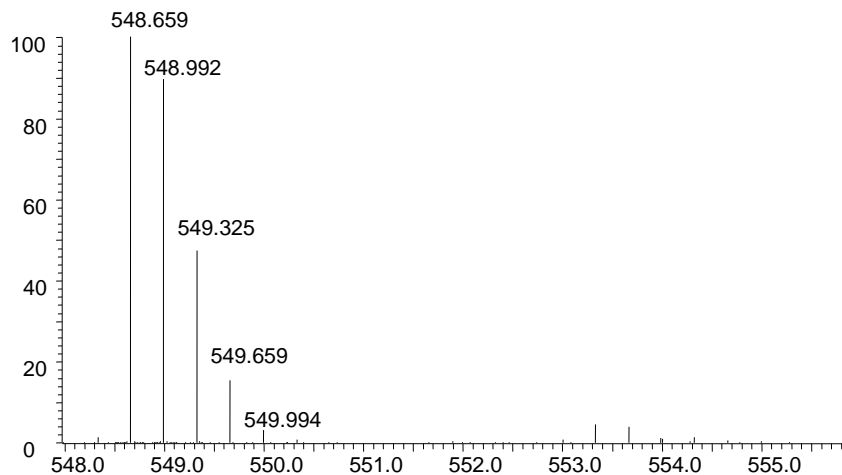
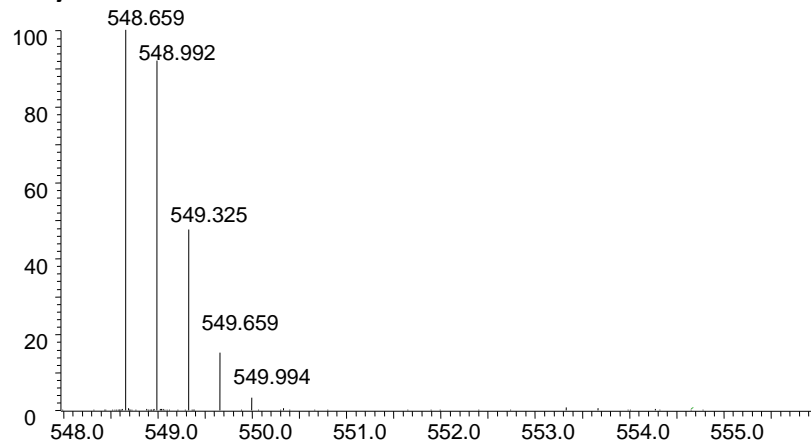


m/z

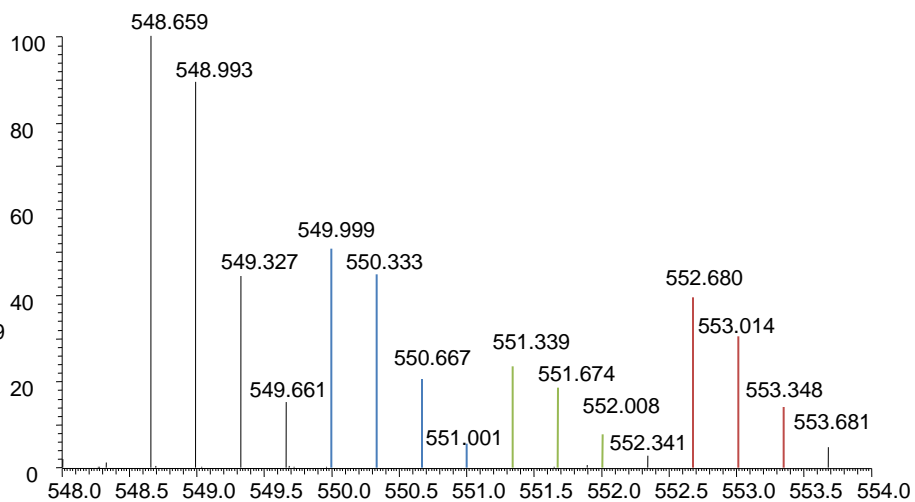
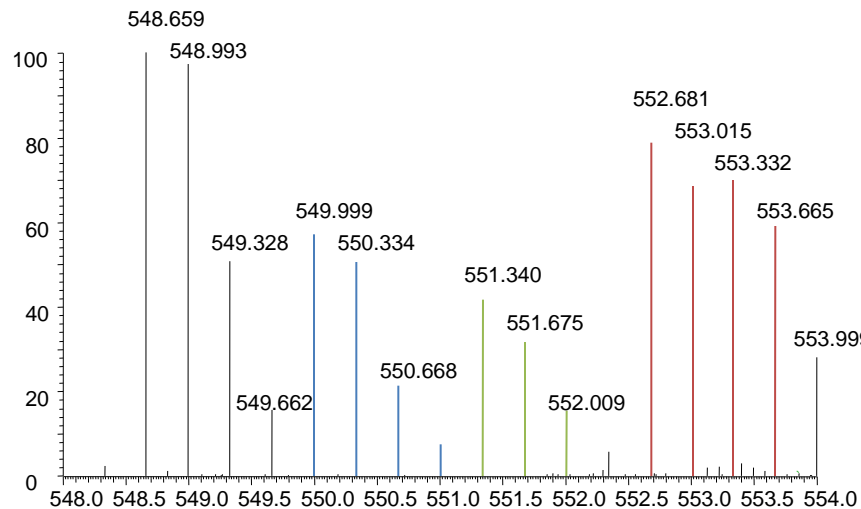
H3K27me3

H3K27me2K36me1

Day 0



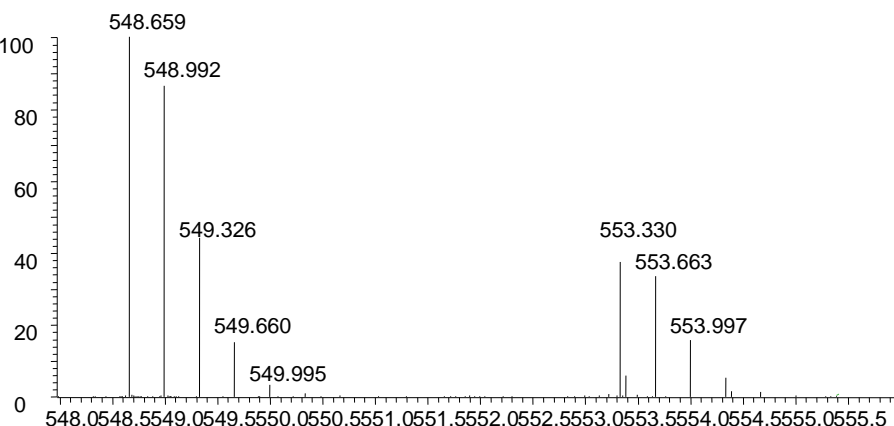
Day 1



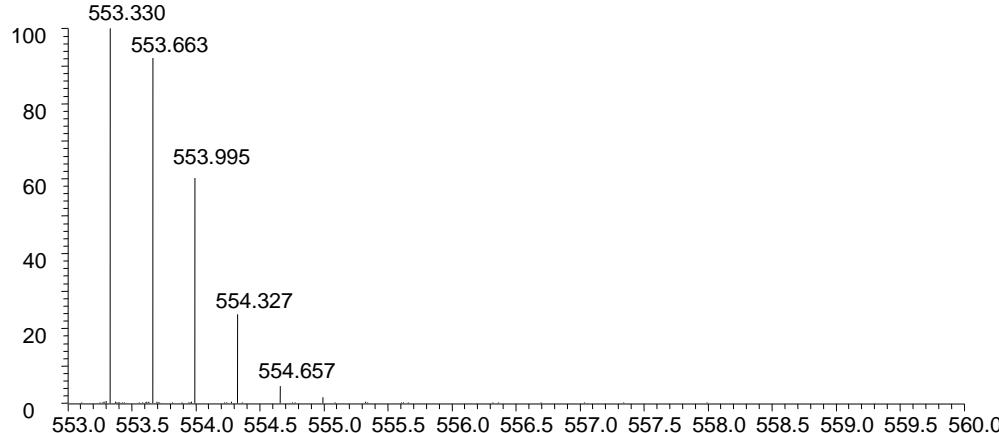
m/z

Day 0

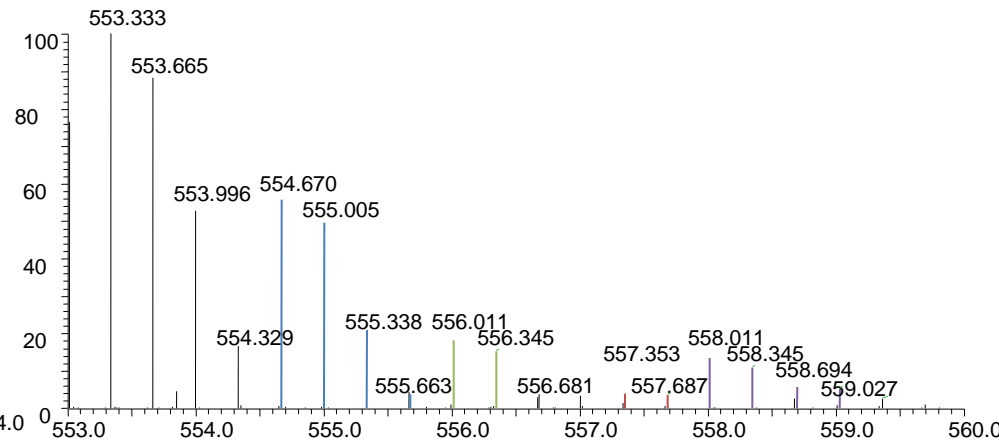
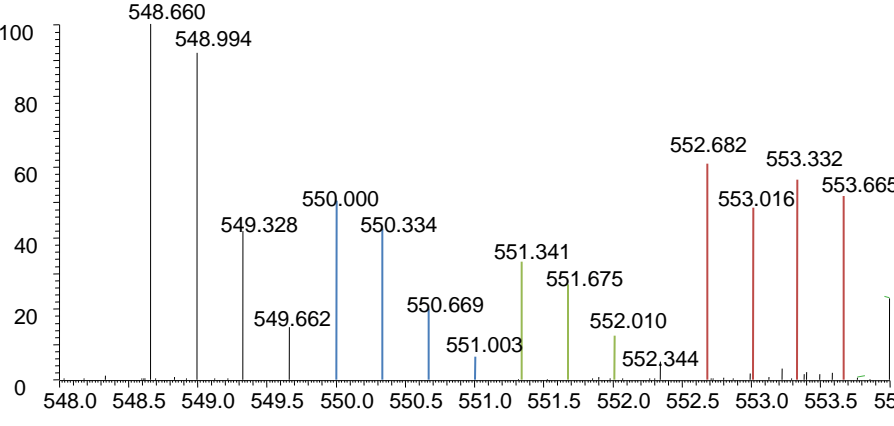
H3K27me1K36me2



H3K27me3K36me1



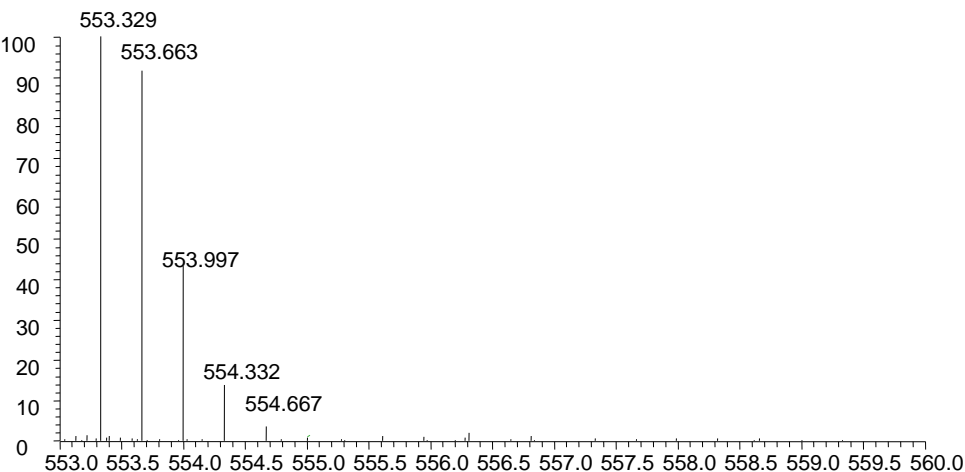
Day 1



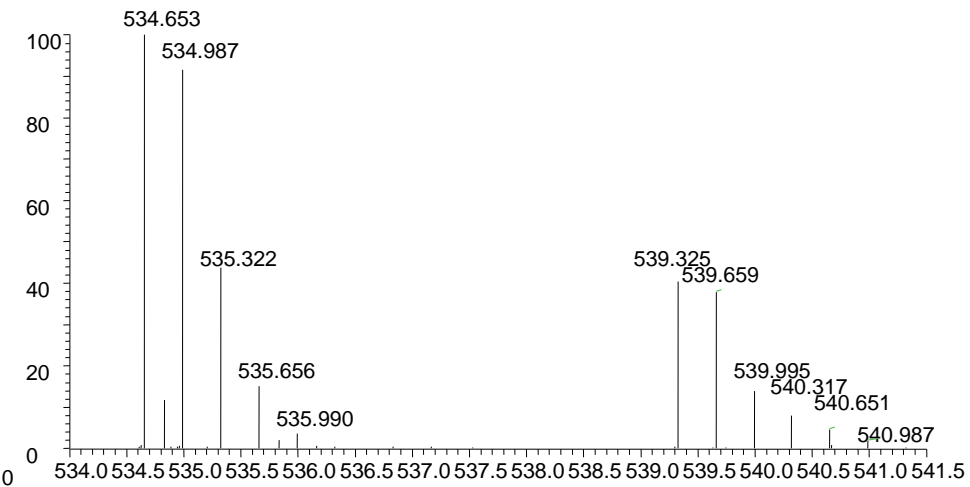
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H3K27me1K36me3

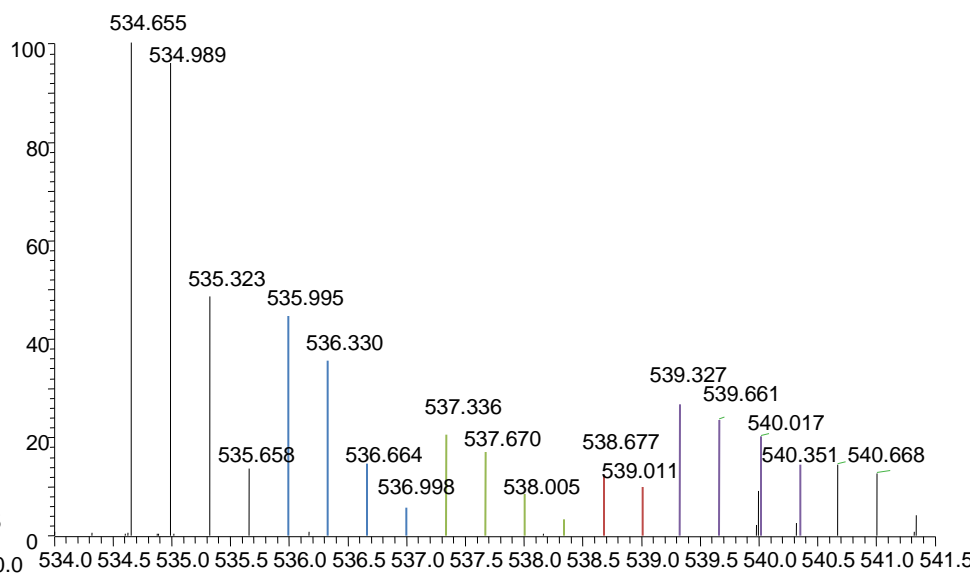
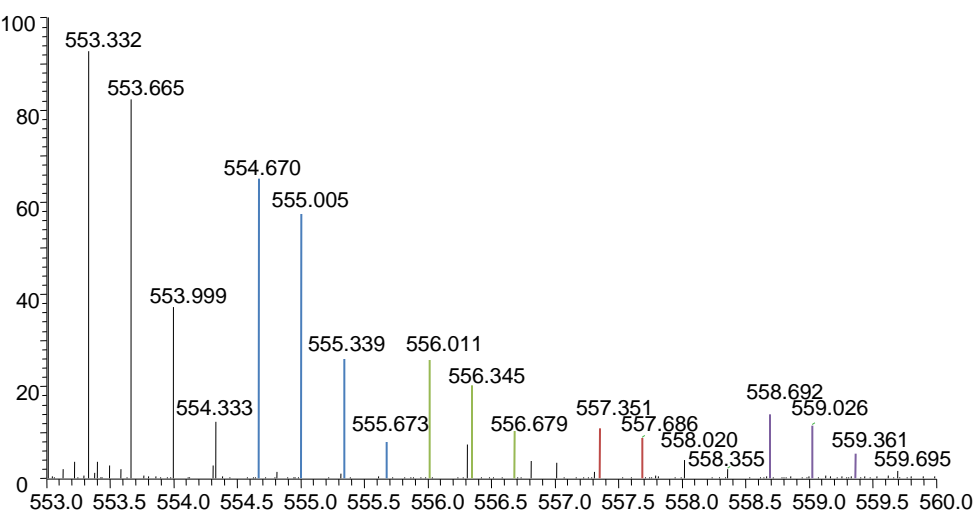
Day 0



H3K27me2K36me2



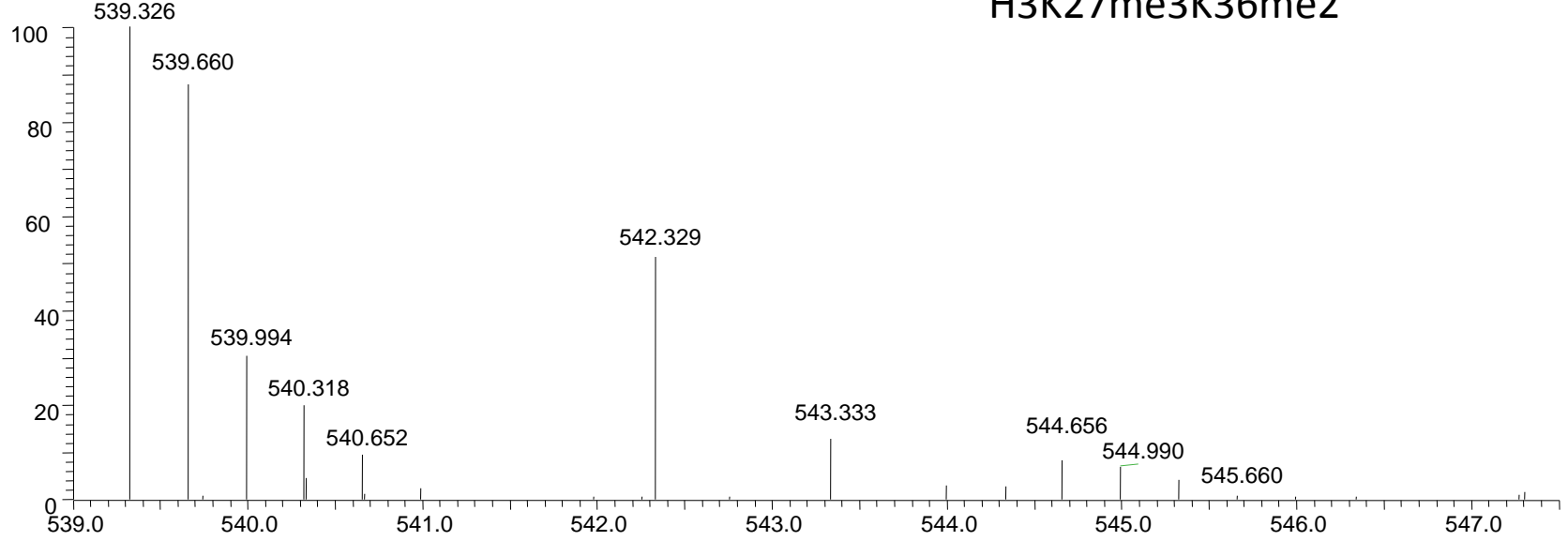
Day 1



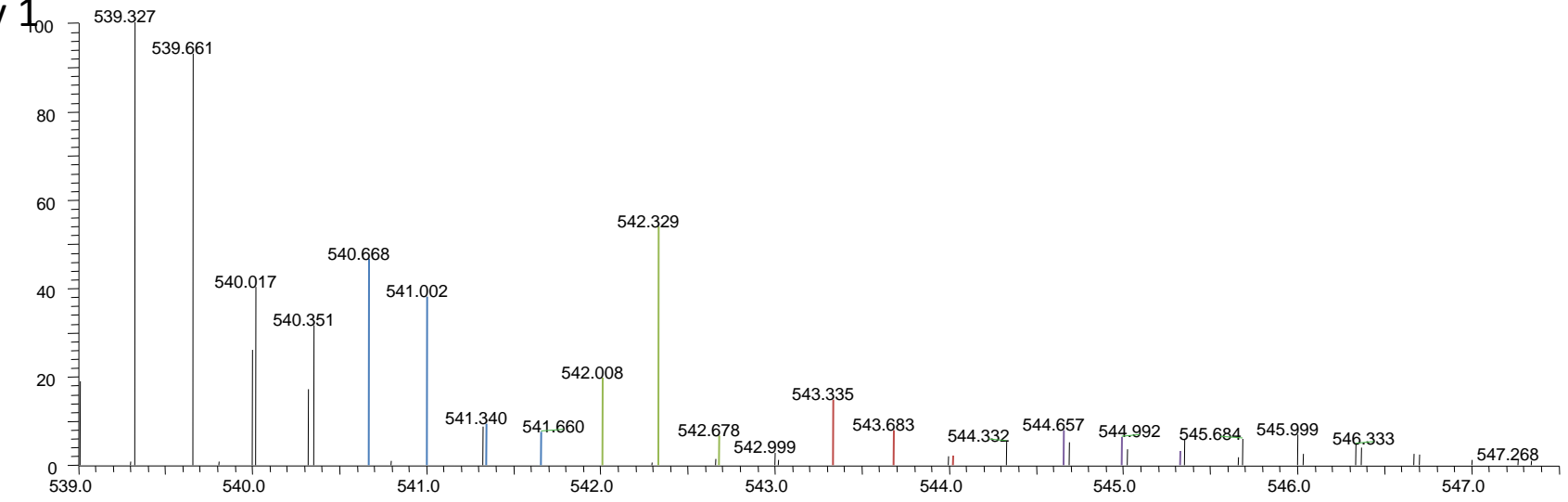
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Day 0

H3K27me3K36me2



Day 1

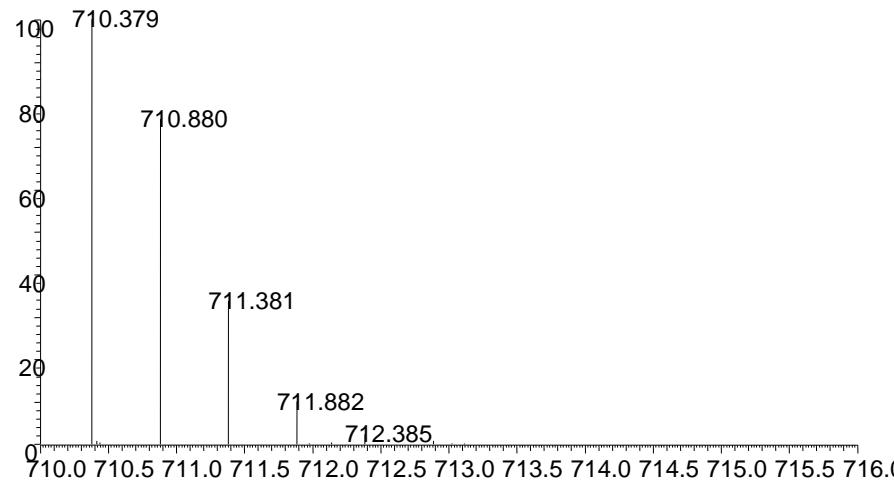
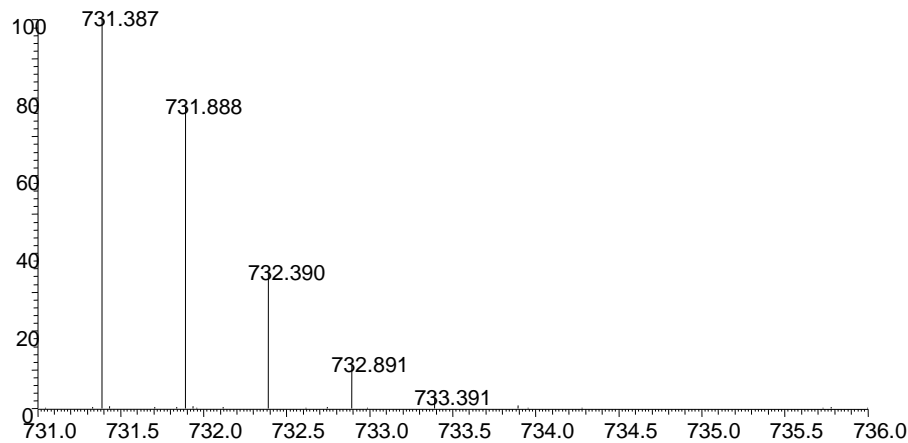


m/z

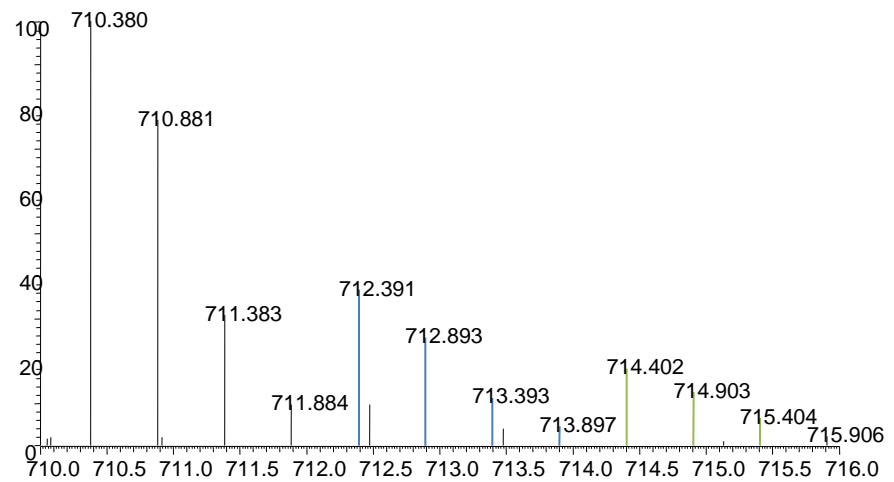
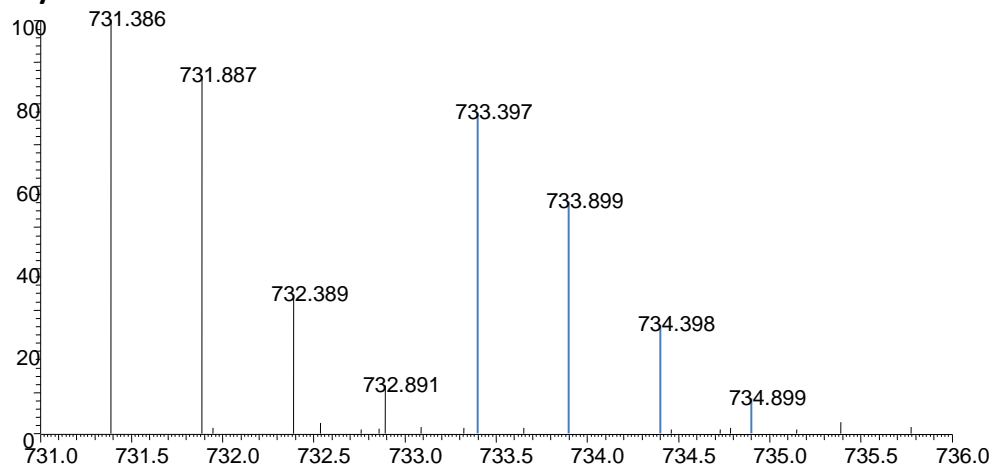
H3K79me1

H3K79me2

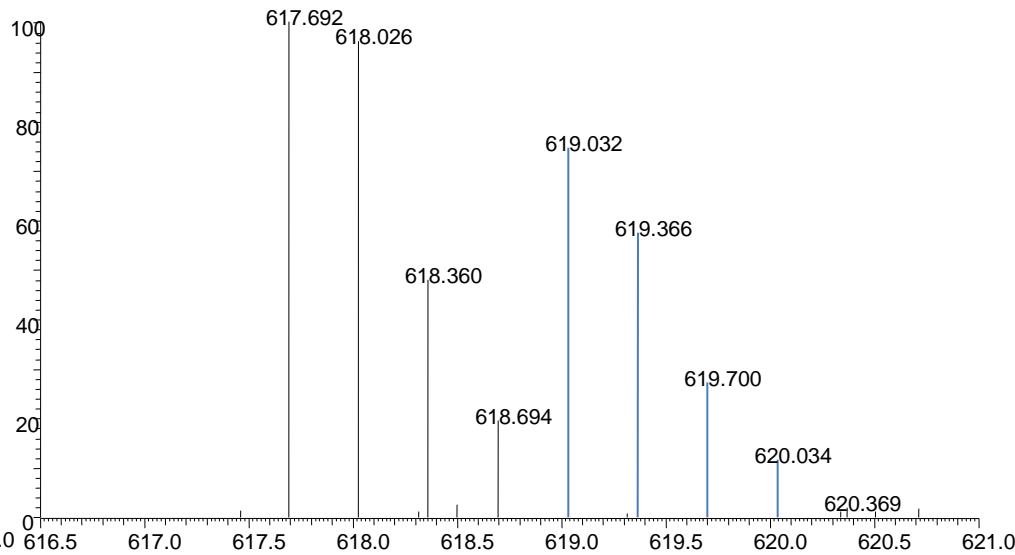
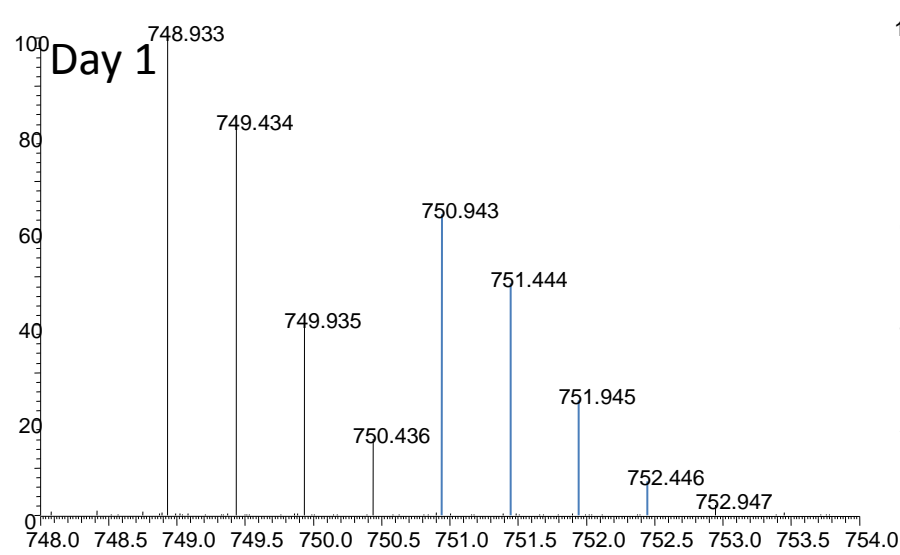
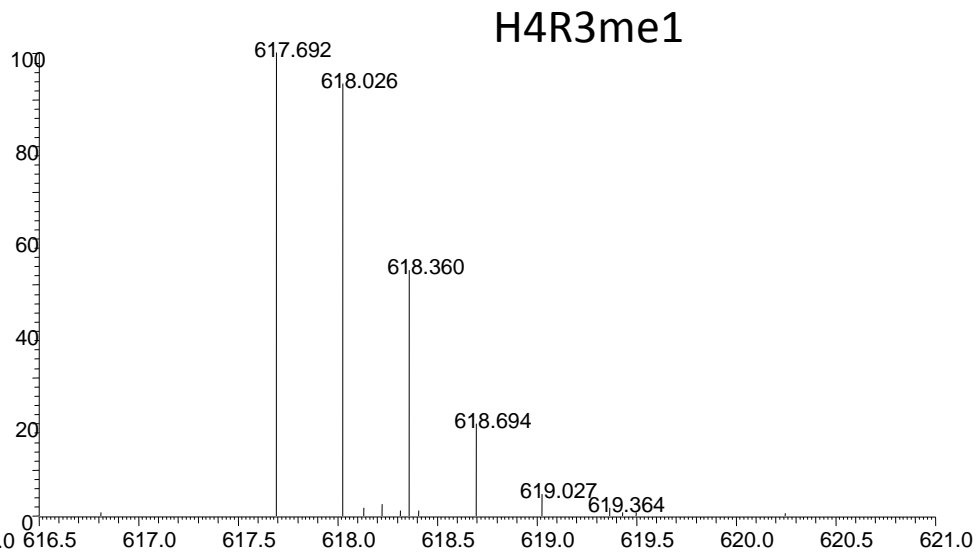
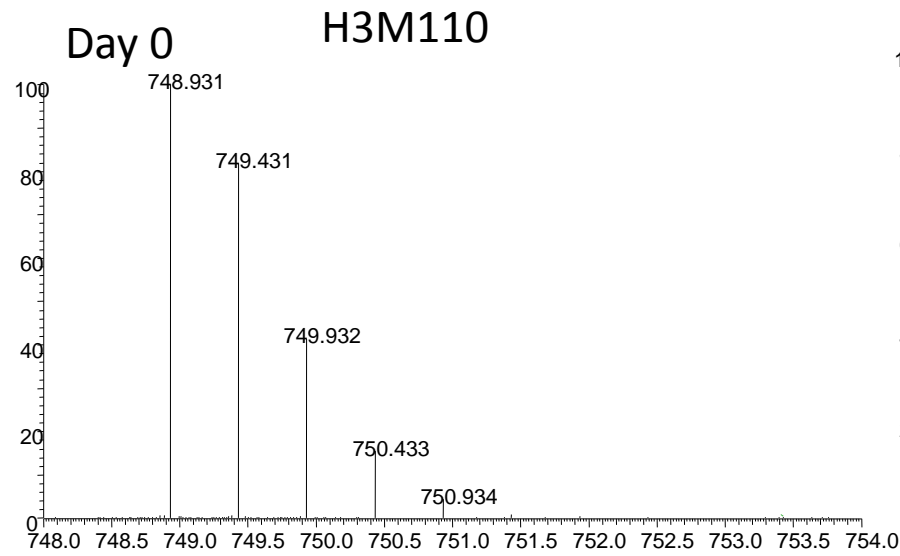
Day 0



Day 1

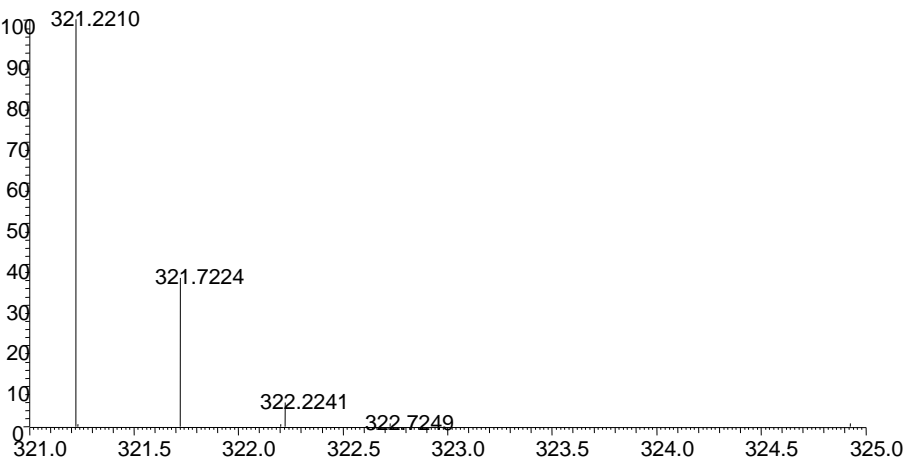


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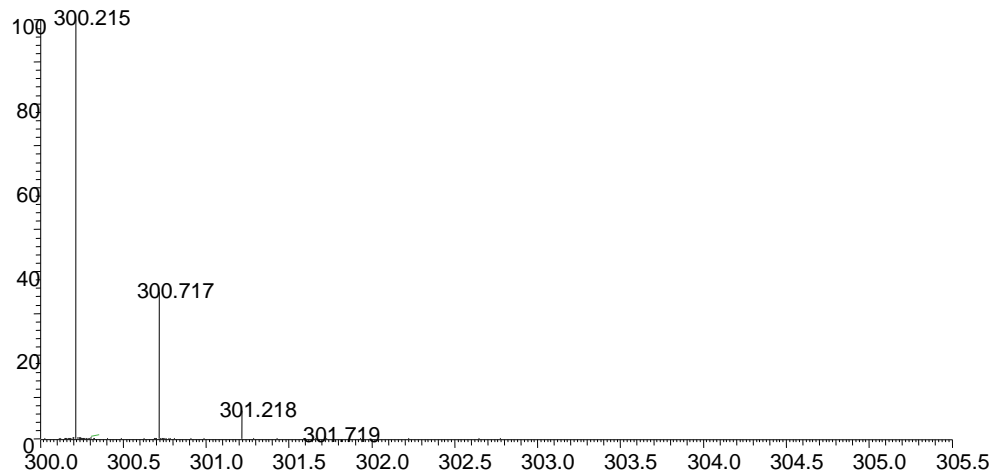


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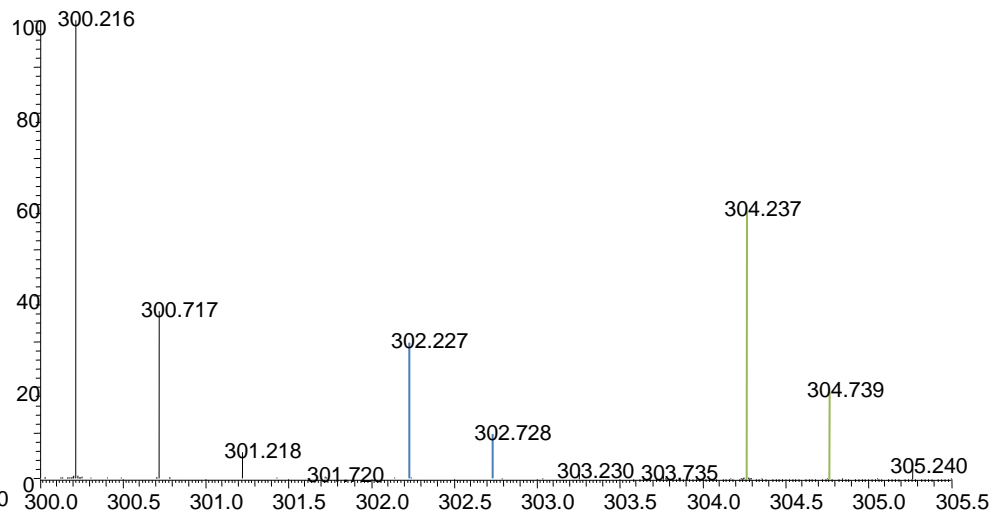
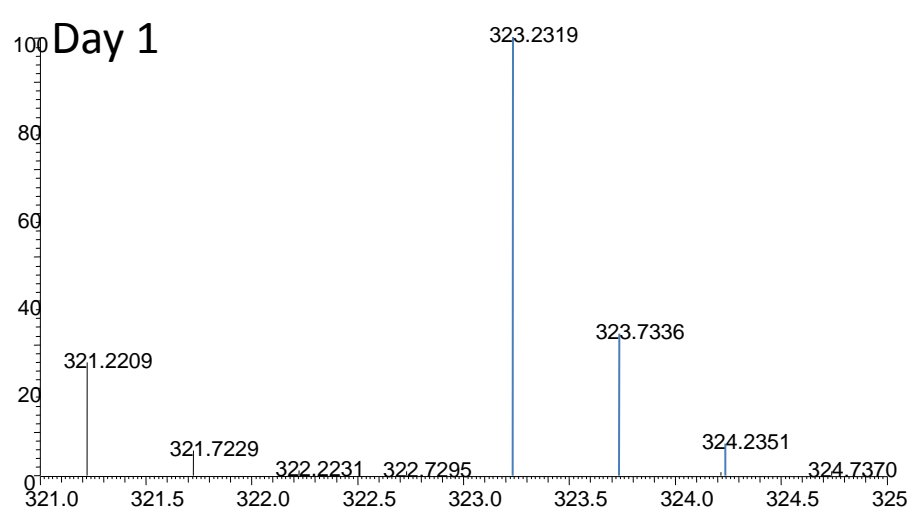
Day 0 H4K20me1



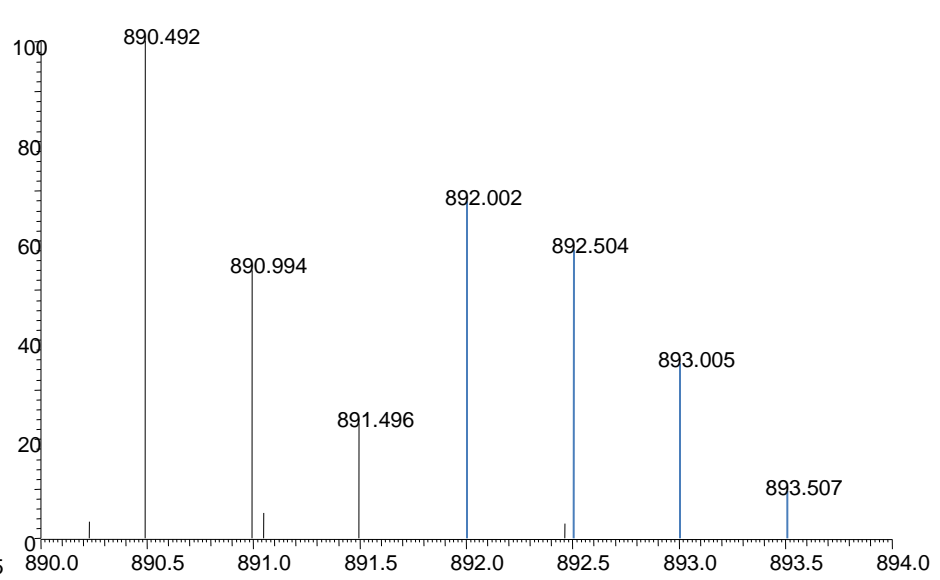
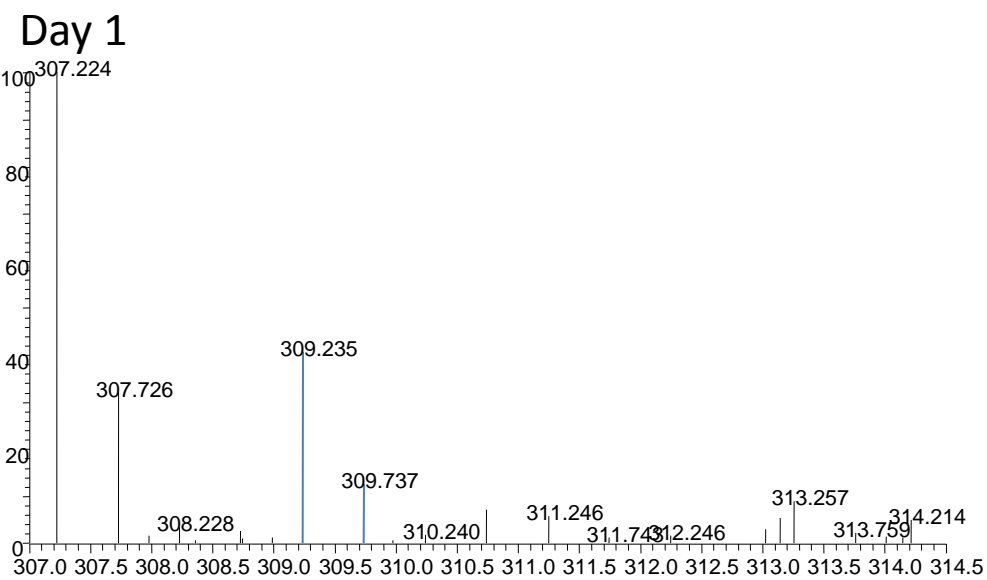
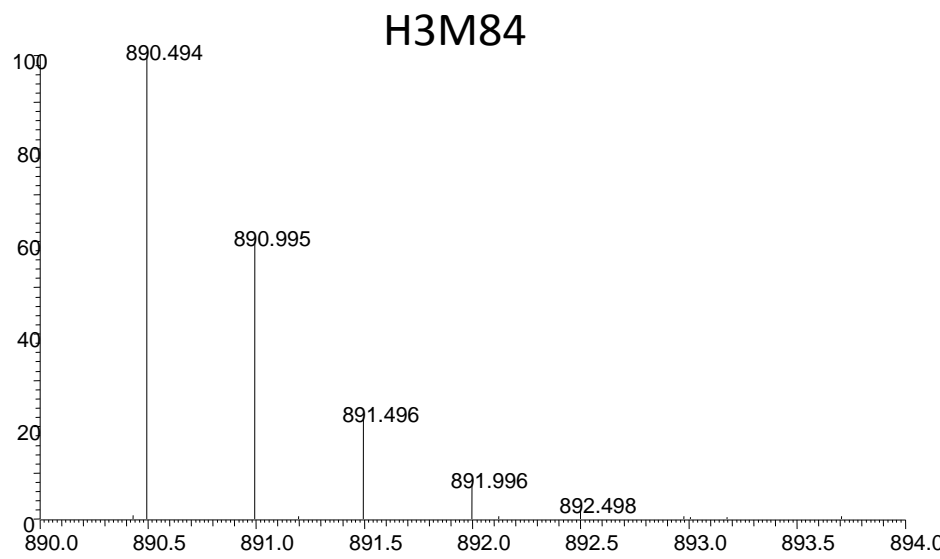
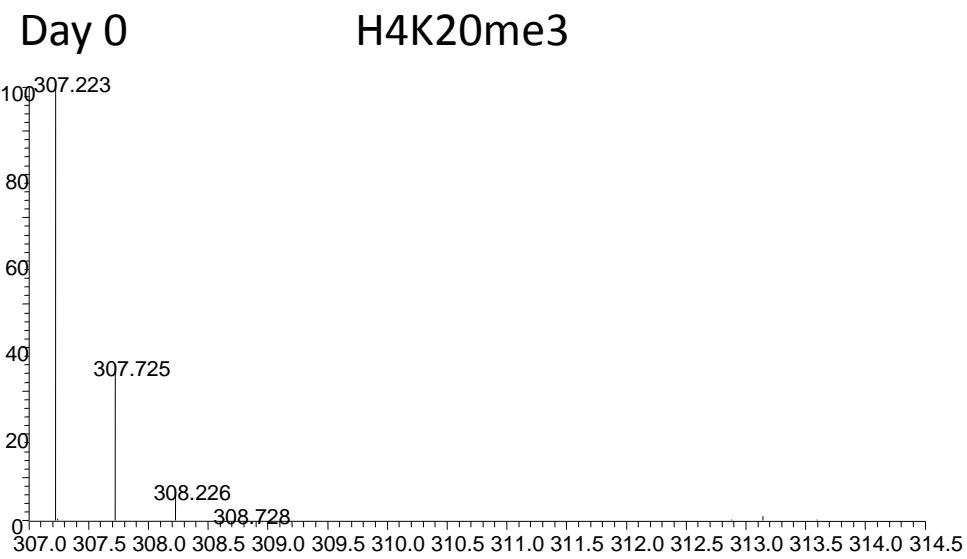
H4K20me2



Day 1



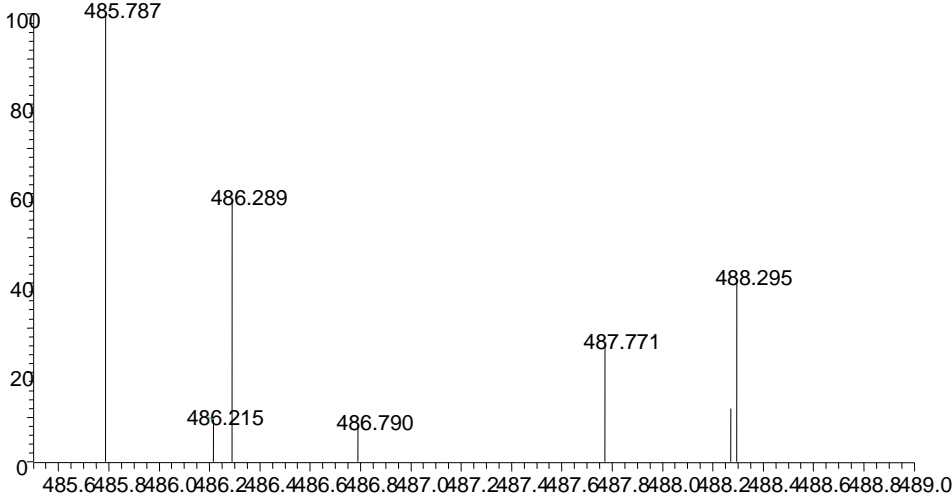
m/z



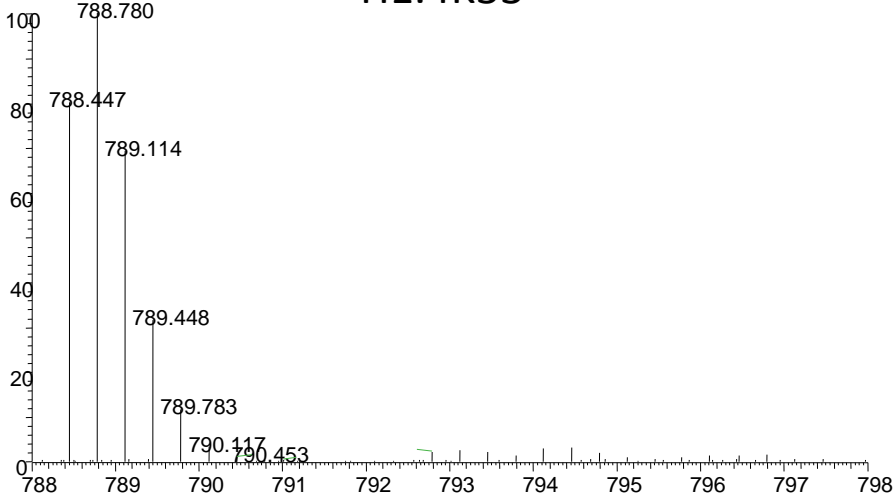
m/z

Day 0

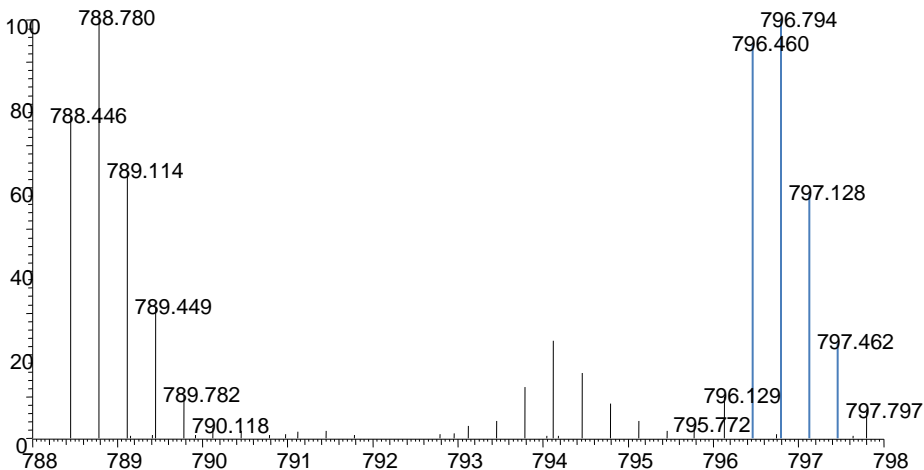
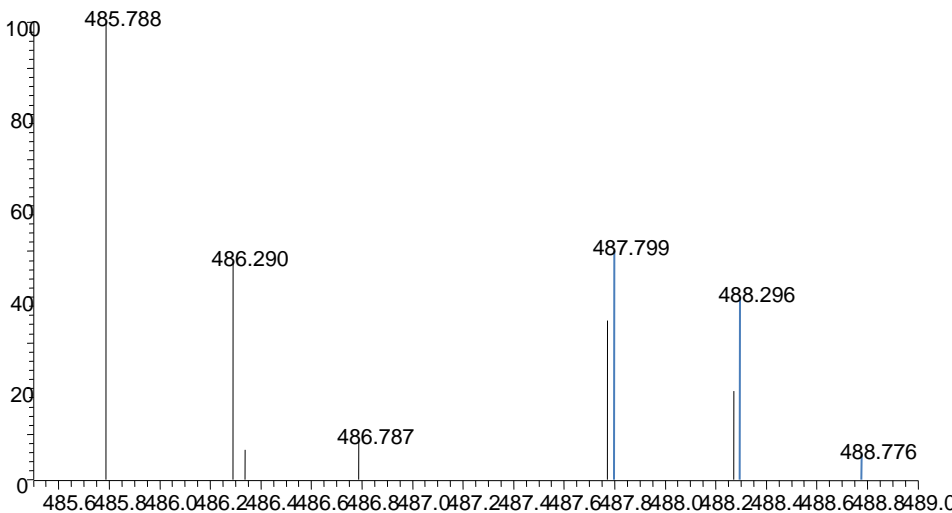
H1.4K25me1



H1.4K33

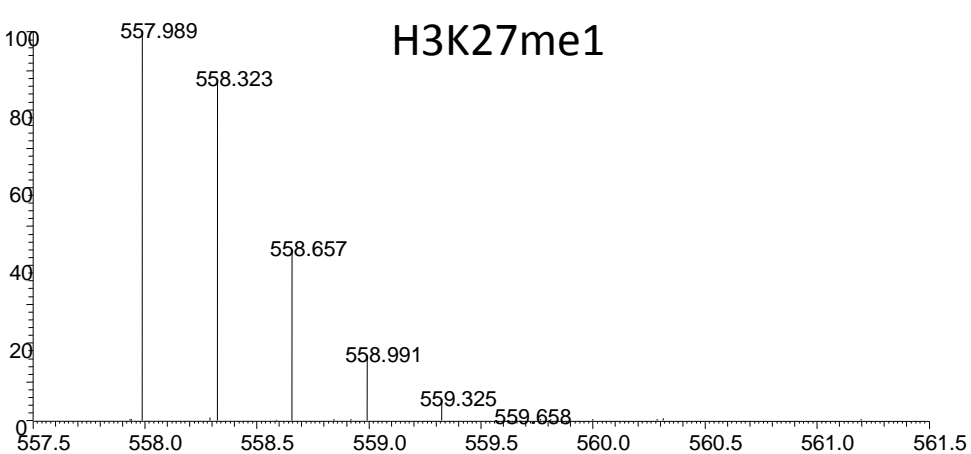
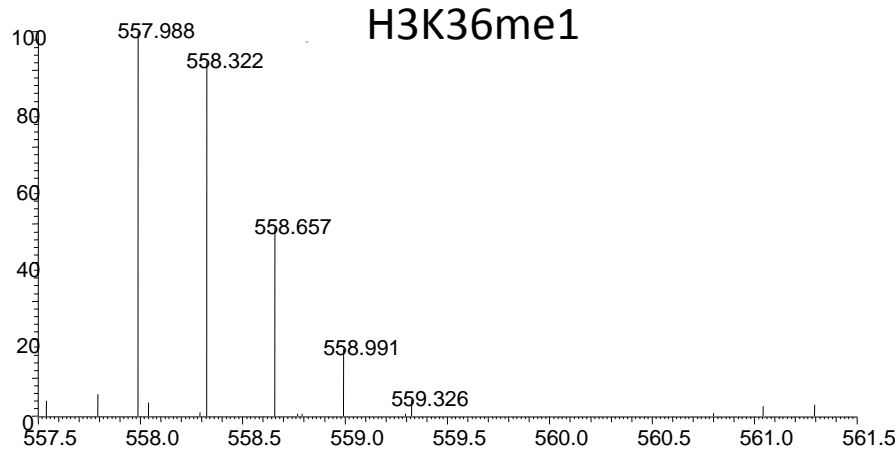


Day 1

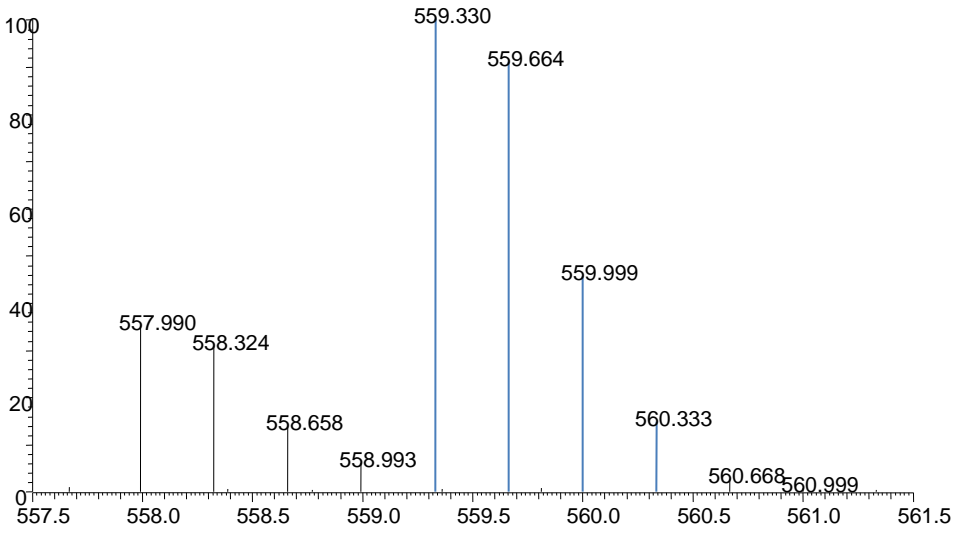
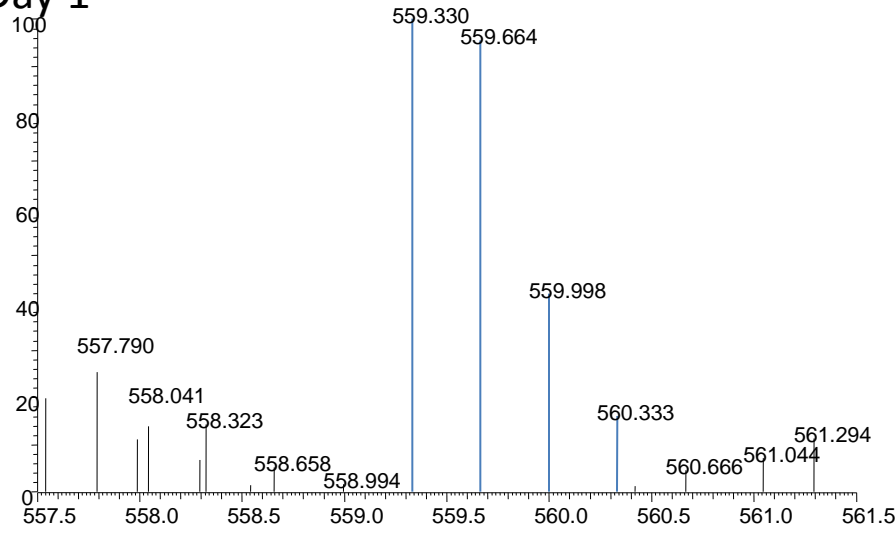


m/z

Day 0



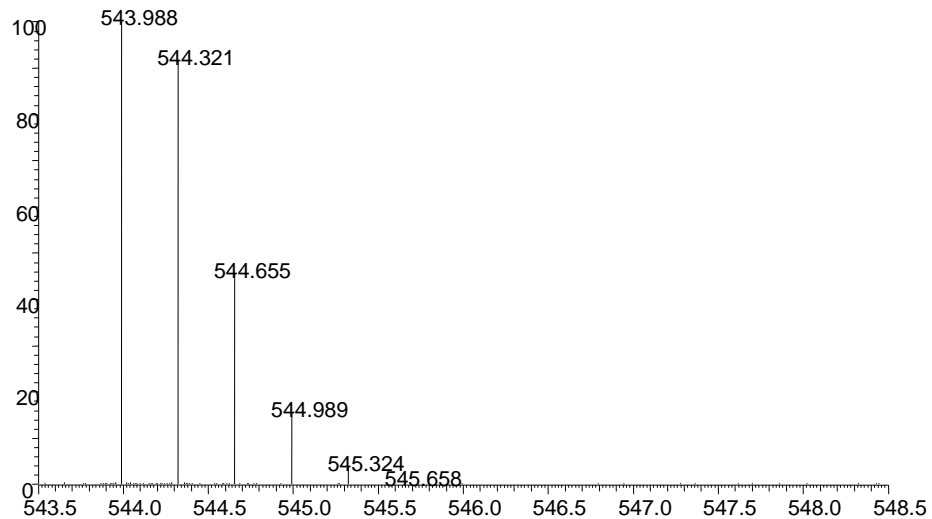
Day 1



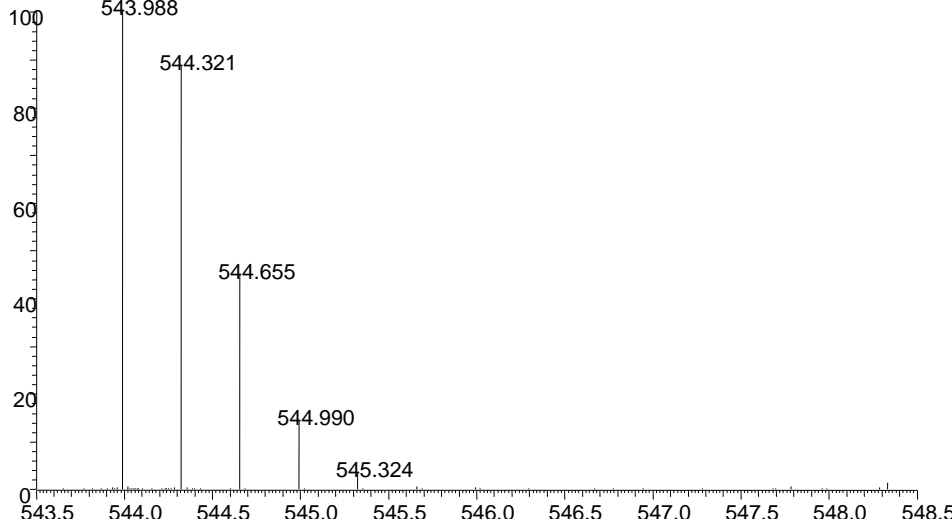
m/z

Day 0

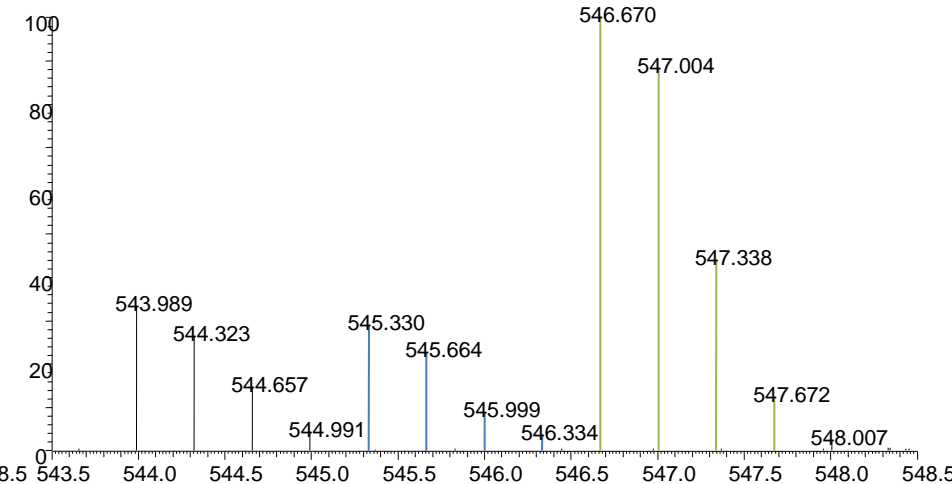
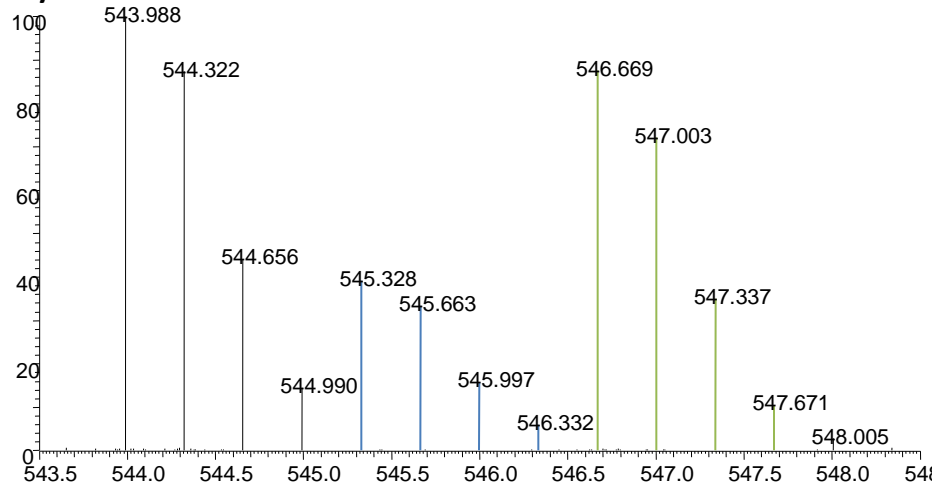
H3K27me2



H3K36me2



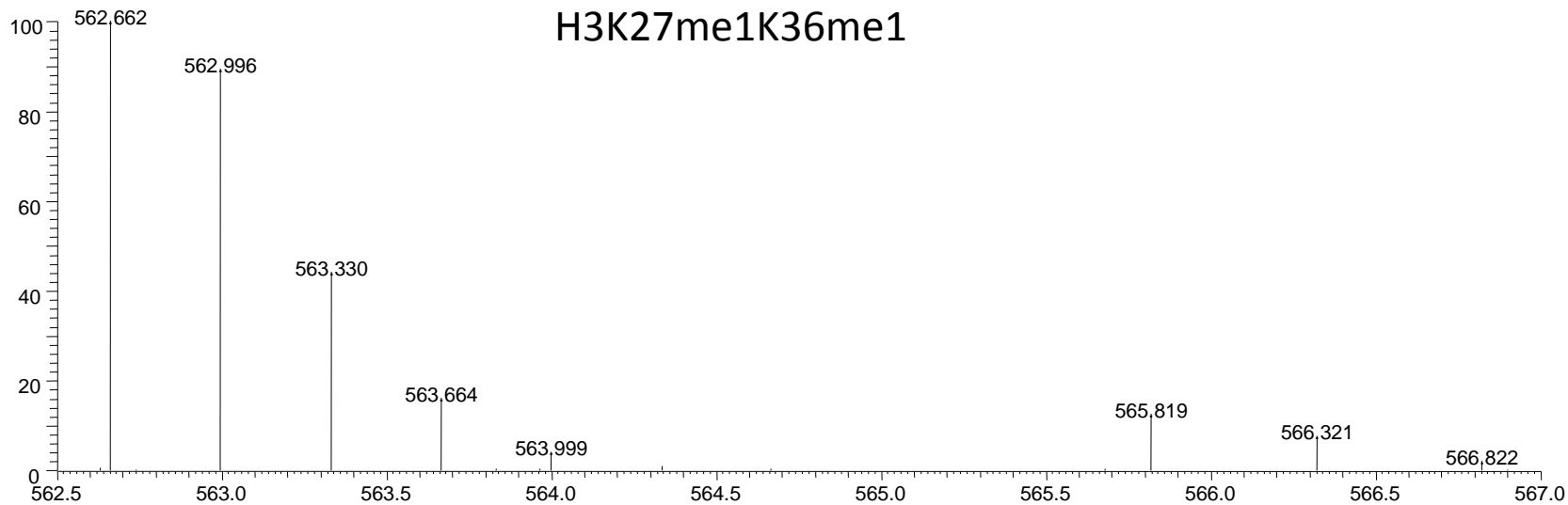
Day 1



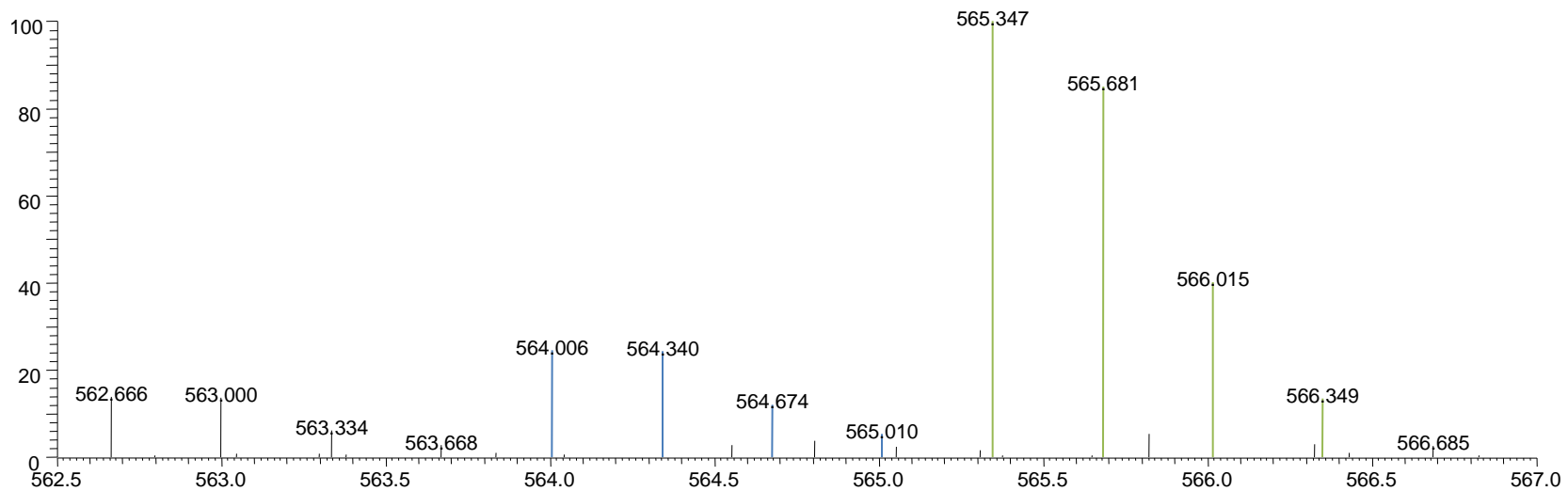
m/z

H3K27me1K36me1

Day 0



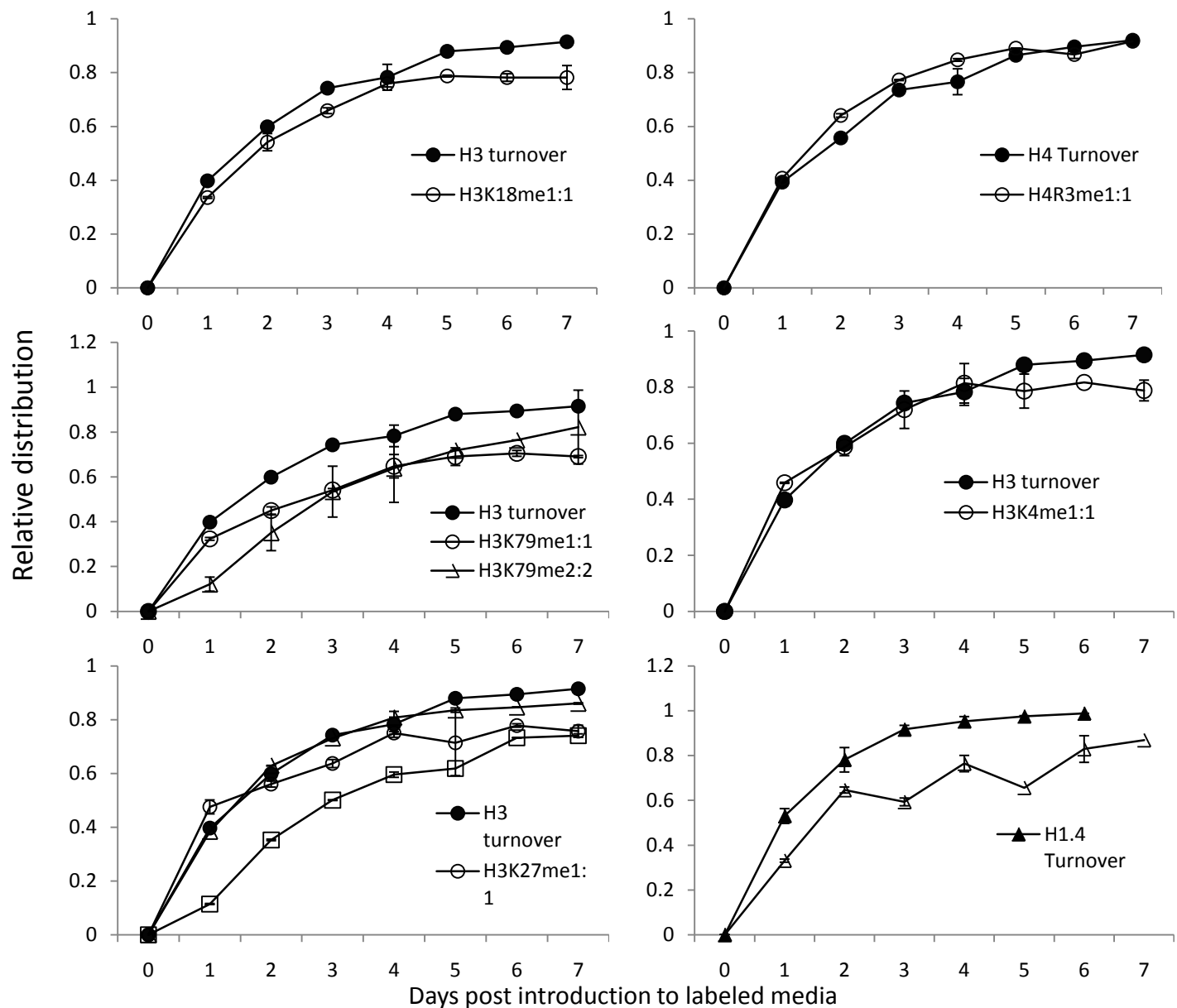
Day 1



m/z

Supplemental Fig. 4

SUPPLEMENTAL FIG 4. Relative distribution of H3K18me1, H4R3me1, H3K79me1 and me2, H3K4me1, H3K27me1, me2, and me3 and H1.4K25me1 compared to the respective overall histone turnover during the course of the pulse labeling. Markers represent averages from two technical replicates, and vertical bars denote standard error.



Supplemental Fig. 5

SUPPLEMENTAL FIGURE 5. Effect of acetylation and methylation of other residues on half-life. The average half-lives of the (A) H3K9 fully labeled peptides depending on the K14 acetylation state and of the (B) H3K27 and H3K36 fully labeled peptides depending on the methylation state of K36 and K27 respectively. Vertical bars denote standard error.

