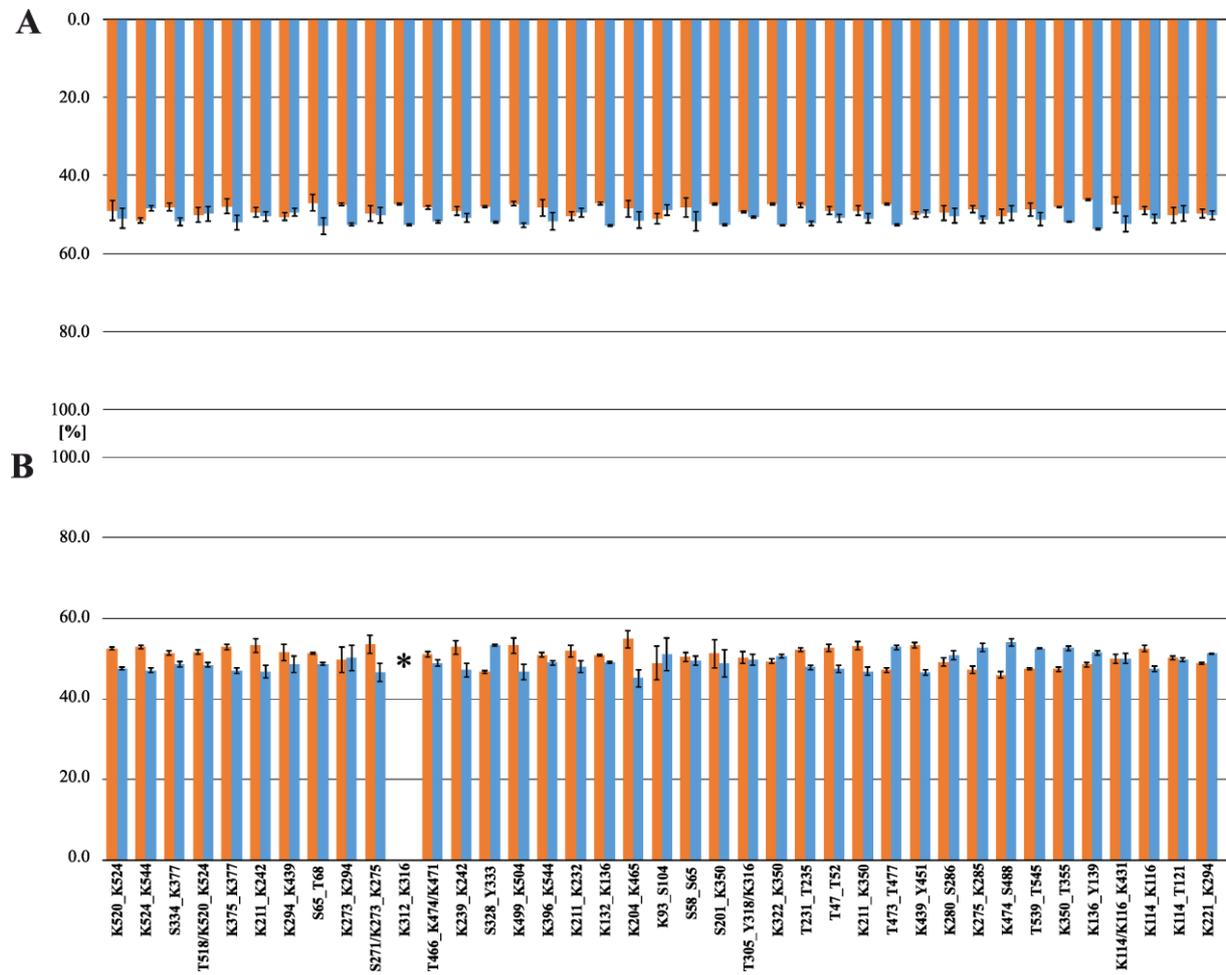
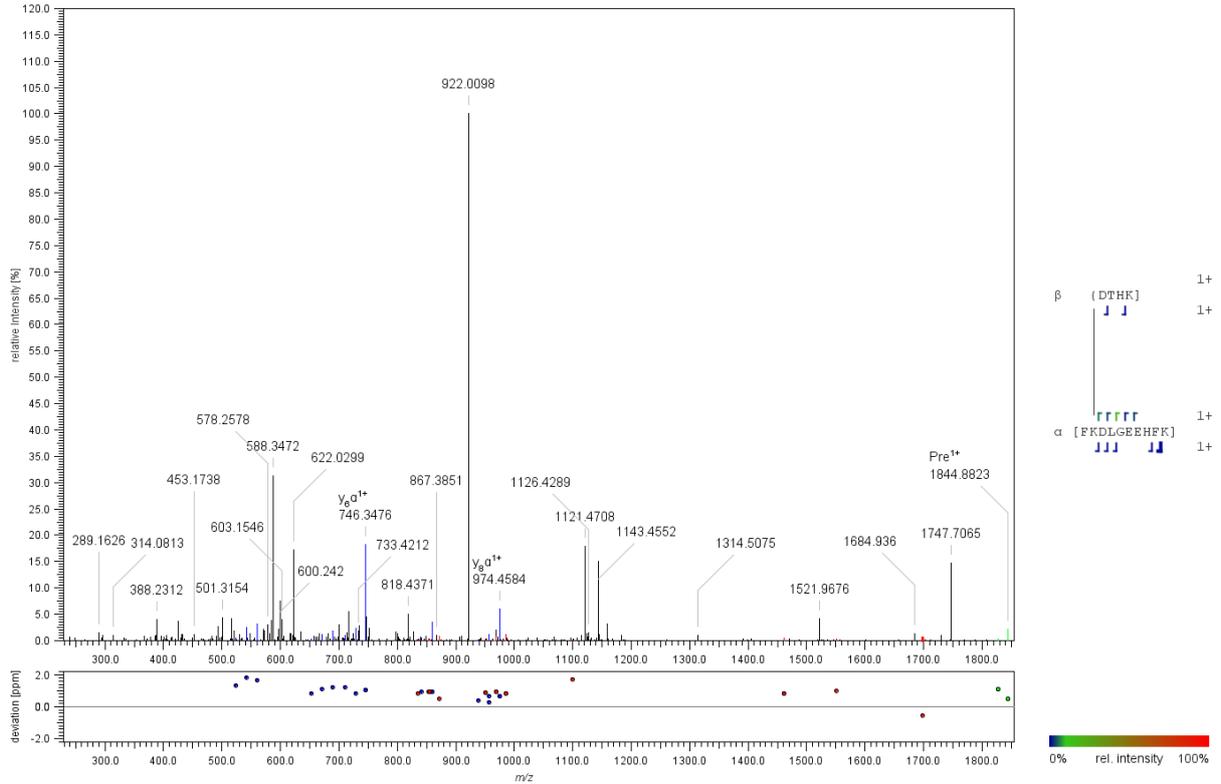


**Figure S1:** Relative quantification of light (orange) and heavy (blue) cross-linked peptides for two control samples. Figure A represent sample labeled with DSG/d4-DSG while figure B showed BSA cross-links using equimolar mixture of BS2G/d4-BS2G. As it is shown, ratios of light/heavy form for all cross-links are close to expected 50:50 value. In case of K312–K316 (\*), the signal intensities for polar BS2G/d4-BS2G were insufficient for quantification which correspond to preference of non-polar DSG cross-linker presented in main article.

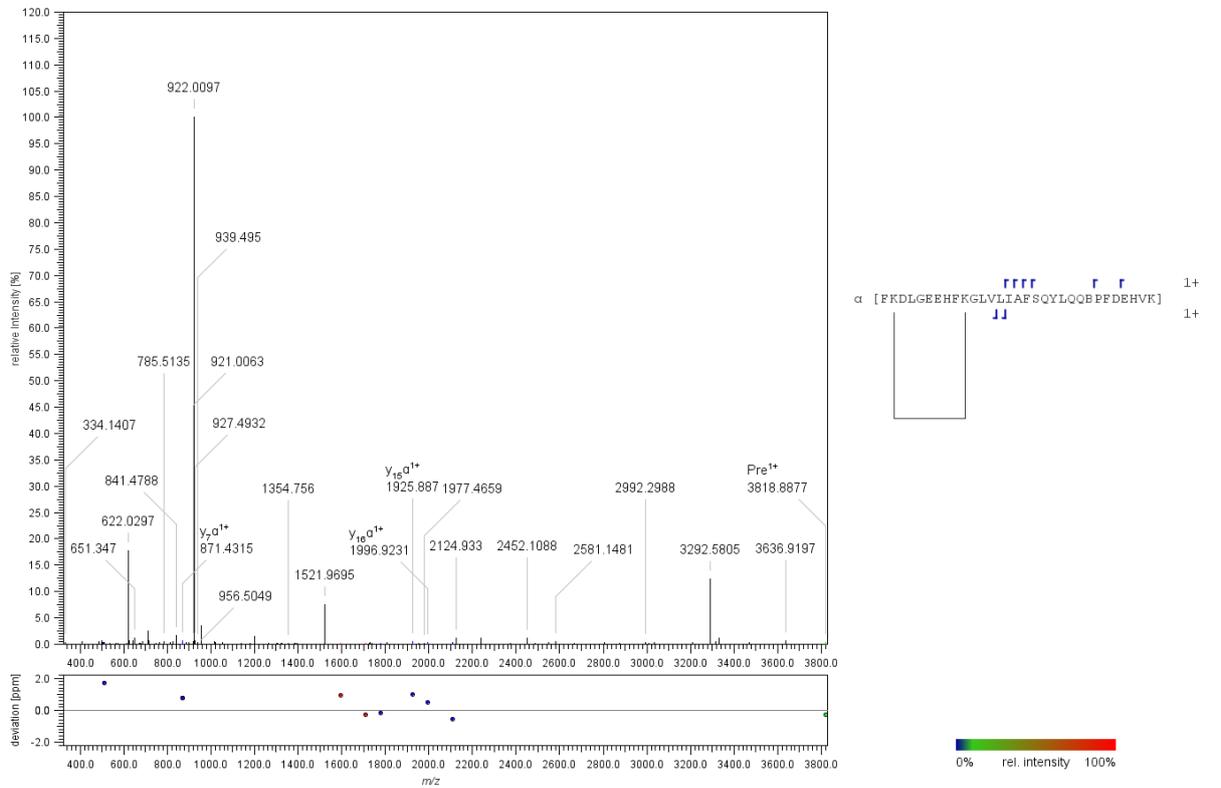


**Figure S2:** StavroX identification of 67 common cross-links.

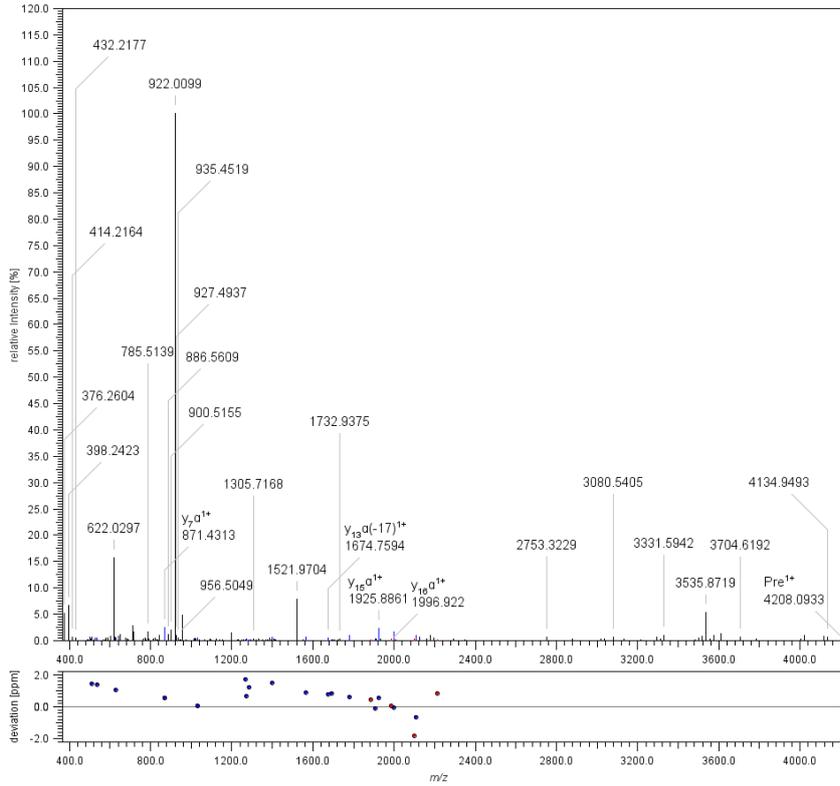
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [DTHK] (0) Score (77)  
 Scan: 186 (-BSA from 0 to 4) identified signals (0.0)  
 theor. Mass (M + H+): 1844.8814 Peptide  $\alpha$ : [FKDLGEEHFK] (K2) intense signals (0.036)  
 meas. Mass (M + H+): 1844.8811 (-BSA from 11 to 20) ion series (0.024)  
 Deviation: -3.14 ppm Crosslinker: DSGnond Intensity Ratio (0.028)  
 m/z: 1844.88110386534 hits/possible ions (0.003)  
 Charge: +1



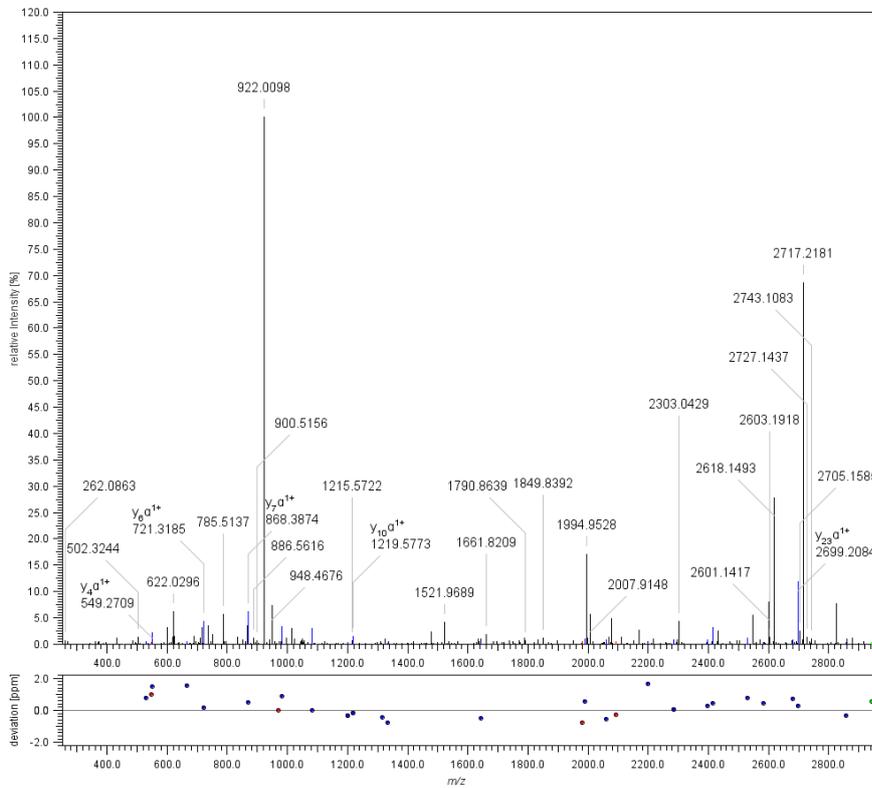
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [FKDLGEEHFKGLVLIAFSQYLQBPFDHVK] (K2) Score (25)  
 Scan: 776 (-BSA from 11 to 41) identified signals (0.009)  
 theor. Mass (M + H+): 3818.8887 Peptide -1 (K10) intense signals (0.091)  
 meas. Mass (M + H+): 3818.8888 (intrapep. from 0 to 0) ion series (0.036)  
 Deviation: 0.02 ppm Crosslinker: DSGnond Intensity Ratio (0.09)  
 m/z: 3818.888771099 hits/possible ions (0.052)  
 Charge: +1



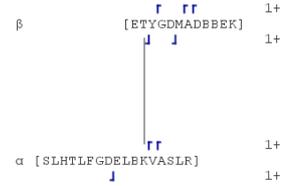
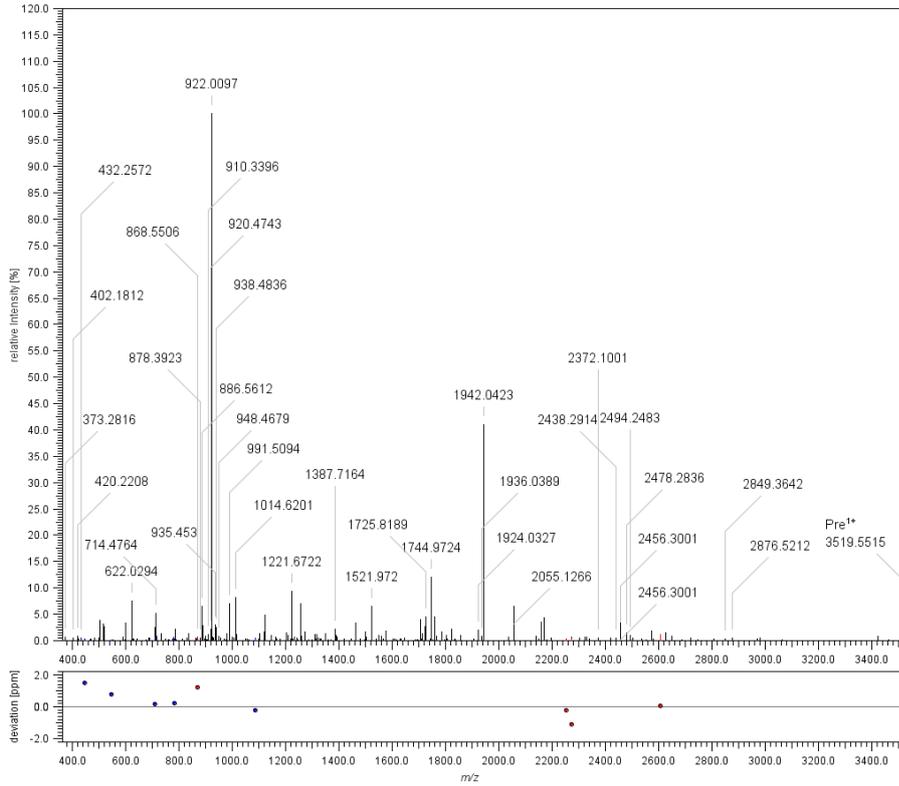
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [KFWGK] (K1) Score (59)  
 Scan: 710 (-BSA from 132 to 136) identified signals (0.0)  
 theor. Mass (M + H+): 4208.095 Peptide  $\alpha$ : [DLGEEHFKGLVLIASFQYLQOBPFDEHVK] (K2) intense signals (0.091)  
 meas. Mass (M + H+): 4208.0957 (-BSA from 13 to 41) ion series (0.024)  
 Deviation: 0.16 ppm Crosslinker: DSGnond Intensity Ratio (0.045)  
 m/z: 4208.09568230795 hits/possible ions (0.033)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [TBVADESHAGBEKSLHTLFGDELBK] (K13) Score (126)  
 Scan: 404 (-BSA from 52 to 76) identified signals (0.0)  
 theor. Mass (M + H+): 2960.2859 Peptide -1 (S14) intense signals (0.014)  
 meas. Mass (M + H+): 2960.2838 (intrap. from 0 to 0) ion series (0.0)  
 Deviation: -0.72 ppm Crosslinker: DSGnond Intensity Ratio (0.032)  
 m/z: 2960.28379284584 hits/possible ions (0.015)  
 Charge: +1

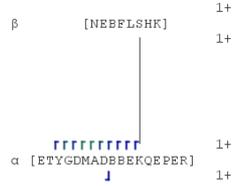
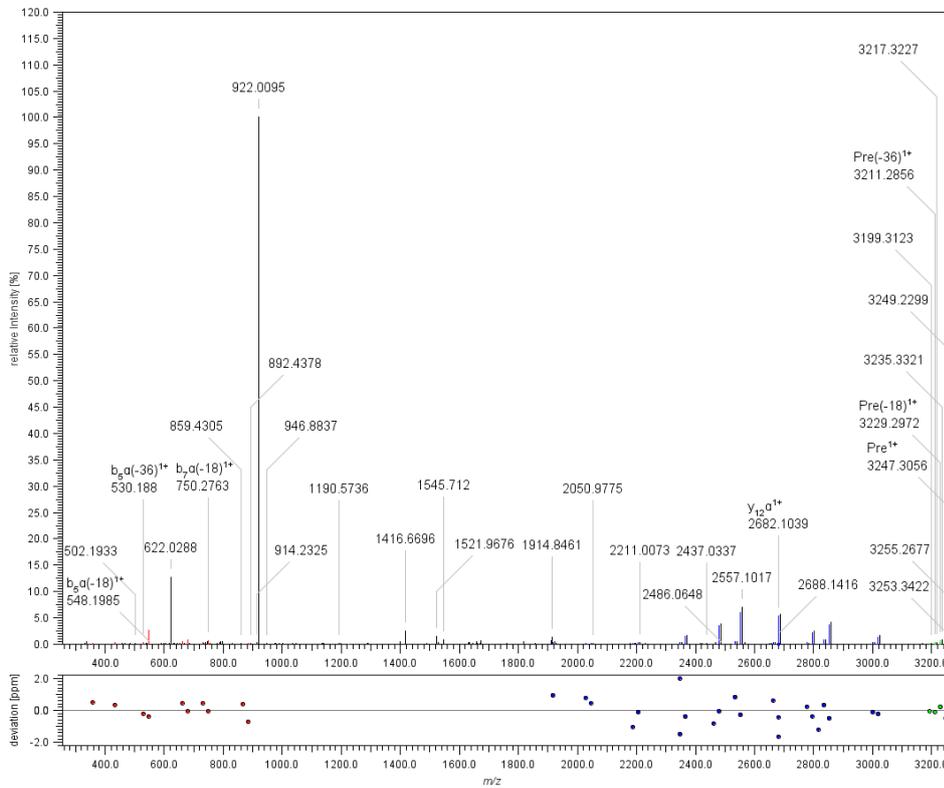


File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [ETYGDMADBBEK] (T2) Score (15)  
 Scan: 588 (-BSA from 82 to 93) identified signals (0.019)  
 theor. Mass (M + H+): 3519.5535 Peptide  $\alpha$ : [SLHTLFGDELBRKVASLR] (K12) intense signals (0.091)  
 meas. Mass (M + H+): 3519.5526 (-BSA from 65 to 81) ion series (0.066)  
 Deviation: -0.25 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 3519.55261572028 hits/possible ions (0.054)  
 Charge: +1



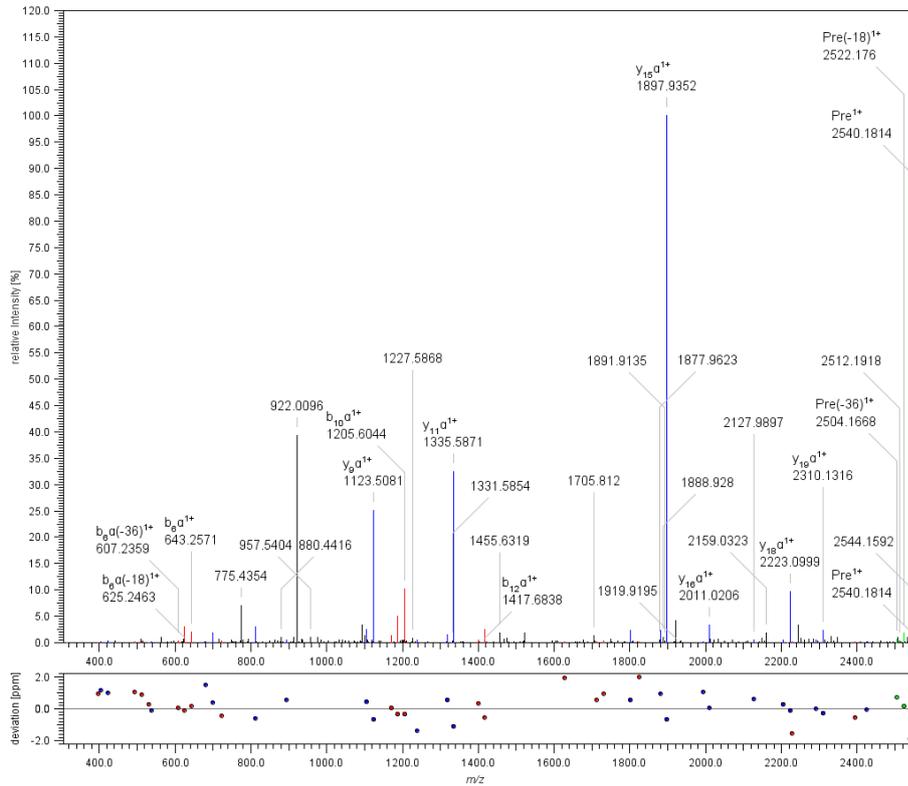
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File: D:\DATA\... 2018\BSA\_B1\_11123.zhrs Peptide  $\beta$ : [NEBFLSHK] (S6) Score (64)  
 Scan: 262 (-BSA from 99 to 106) identified signals (0.0)  
 theor. Mass (M + H+): 3247.3071 Peptide  $\alpha$ : [ETYGDMADBBEKQEPER] (K12) intense signals (0.091)  
 meas. Mass (M + H+): 3247.3067 (-BSA from 92 to 99) ion series (0.034)  
 Deviation: -0.13 ppm Crosslinker: DSGnond Intensity Ratio (0.05)  
 m/z: 3247.30671229574 hits/possible ions (0.011)  
 Charge: +1

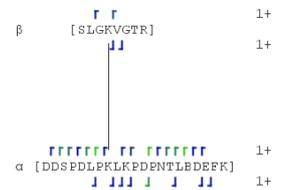
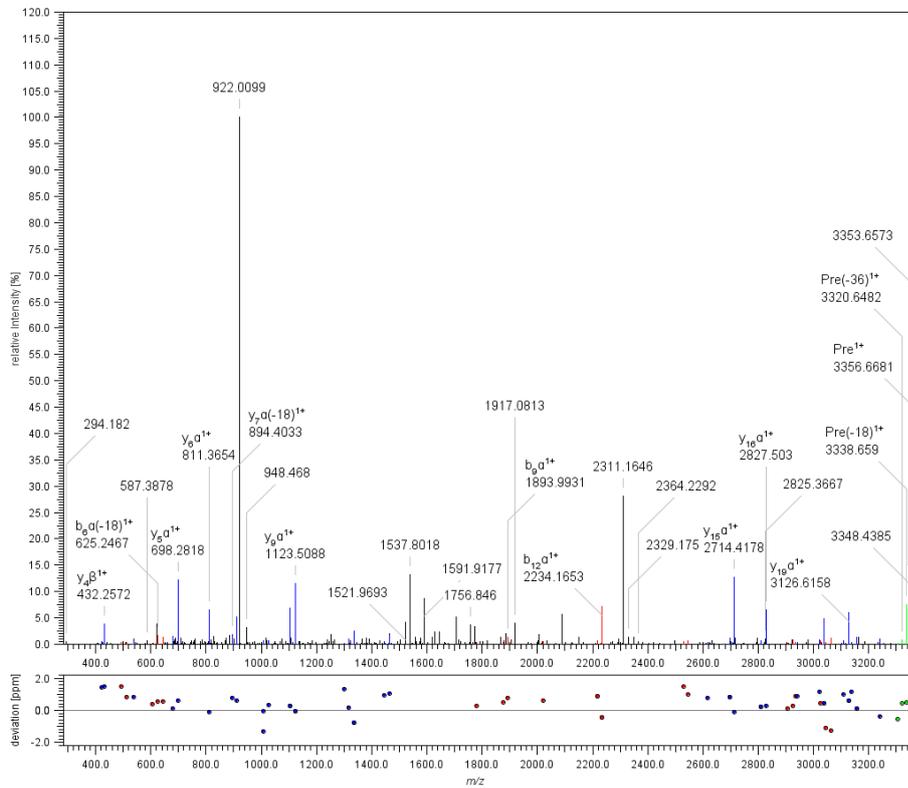


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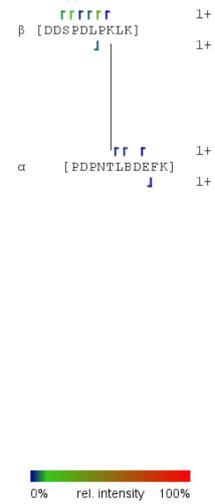
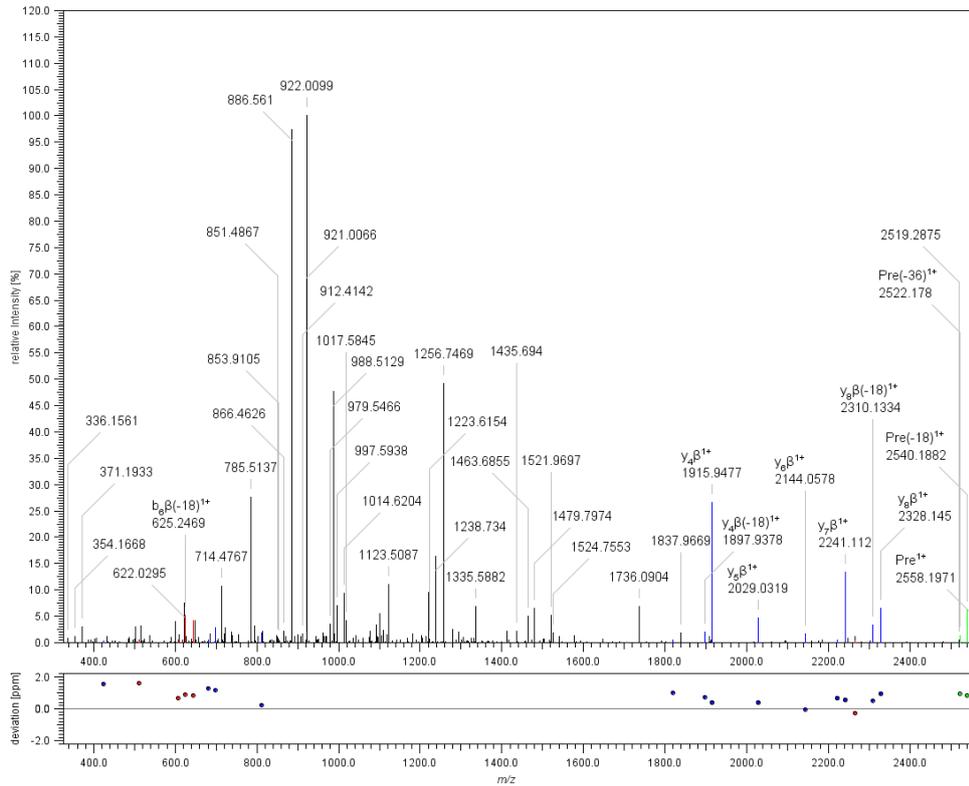
File: D:\DATA1... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [DDSPDLPLKLPDPNTLBDEFK] (K8) Score (214)  
 Scan: 498 (-BSA from 107 to 127) identified signals (0.0)  
 theor. Mass (M + H+): 2540.1861 Peptide -1 (K10) intense signals (0.0)  
 meas. Mass (M + H+): 2540.1855 (intrap. from 0 to 0) ion series (0.0)  
 Deviation: -0.22 ppm Crosslinker: DSGnond Intensity Ratio (0.0)  
 m/z: 2540.1855936491 hits/possible ions (0.003)  
 Charge: +1



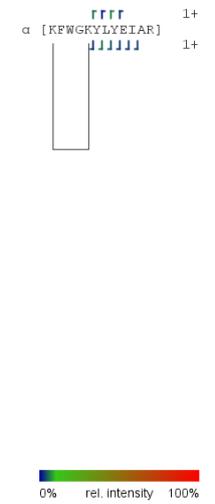
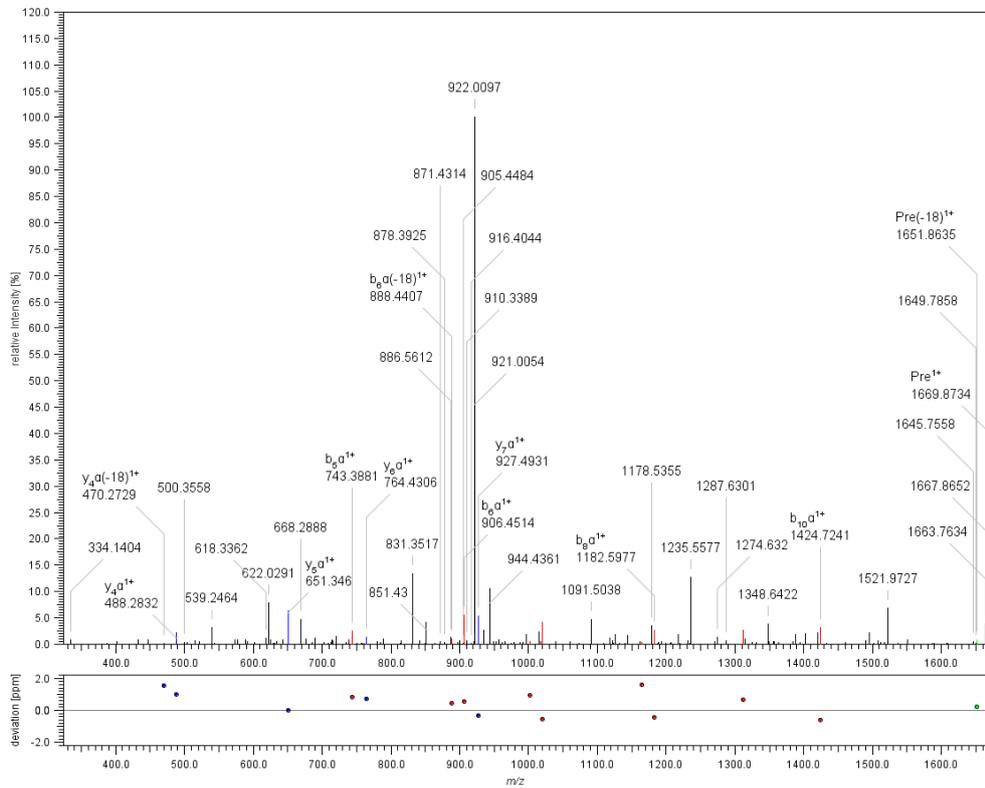
File: D:\DATA1... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [SLGKVGTR] (K4) Score (131)  
 Scan: 412 (-BSA from 428 to 435) identified signals (0.0)  
 theor. Mass (M + H+): 3356.6679 Peptide  $\alpha$ : [DDSPDLPLKLPDPNTLBDEFK] (K8) intense signals (0.002)  
 meas. Mass (M + H+): 3356.6667 (-BSA from 107 to 127) ion series (0.004)  
 Deviation: 0.26 ppm Crosslinker: DSGnond Intensity Ratio (0.008)  
 m/z: 3356.66874068139 hits/possible ions (0.005)  
 Charge: +1



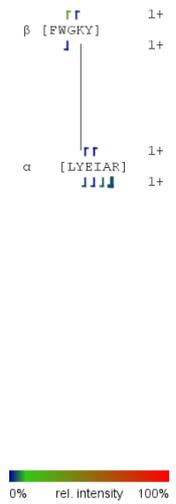
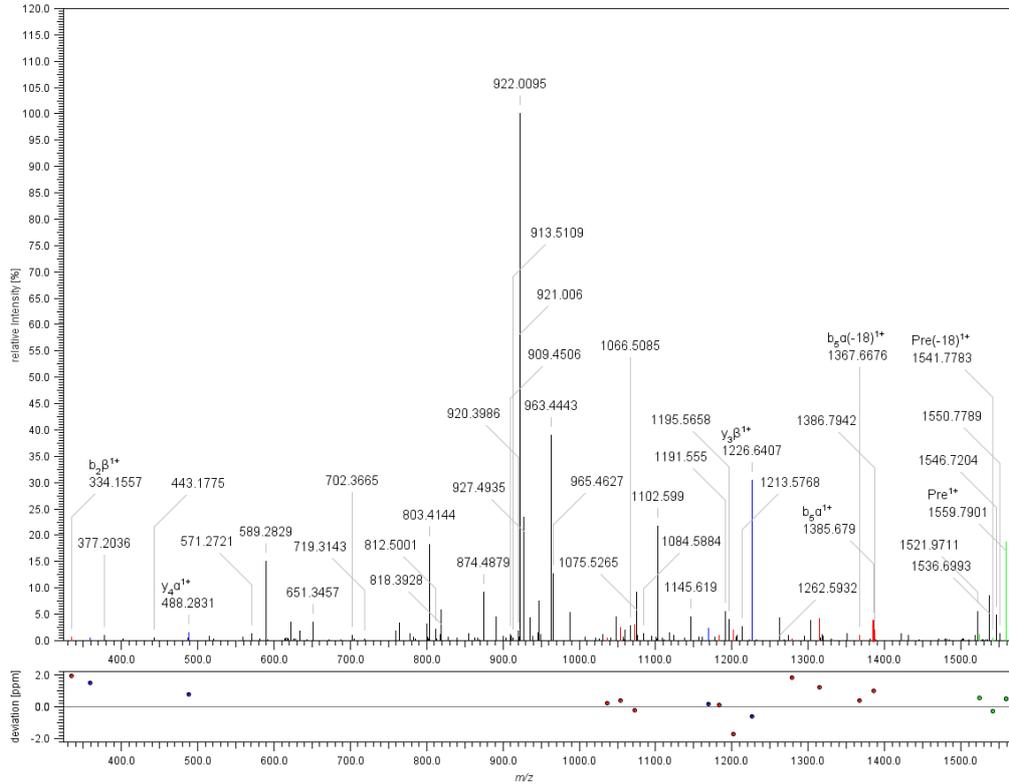
File: D:\DATA... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [DDSPDLKLIK] (K8) Score (72)  
 Scan: 440 (-BSA from 107 to 116) identified signals (0.002)  
 theor. Mass (M + H+): 2558.1967 Peptide  $\alpha$ : [PDNLTLEDFK] (T5) intense signals (0.005)  
 meas. Mass (M + H+): 2558.1973 (-BSA from 117 to 127) ion series (0.007)  
 Deviation 0.24 ppm Crosslinker: DSGnond Intensity Ratio (0.054)  
 m/z: 2558.19729739035 hits/possible ions (0.022)  
 Charge: +1



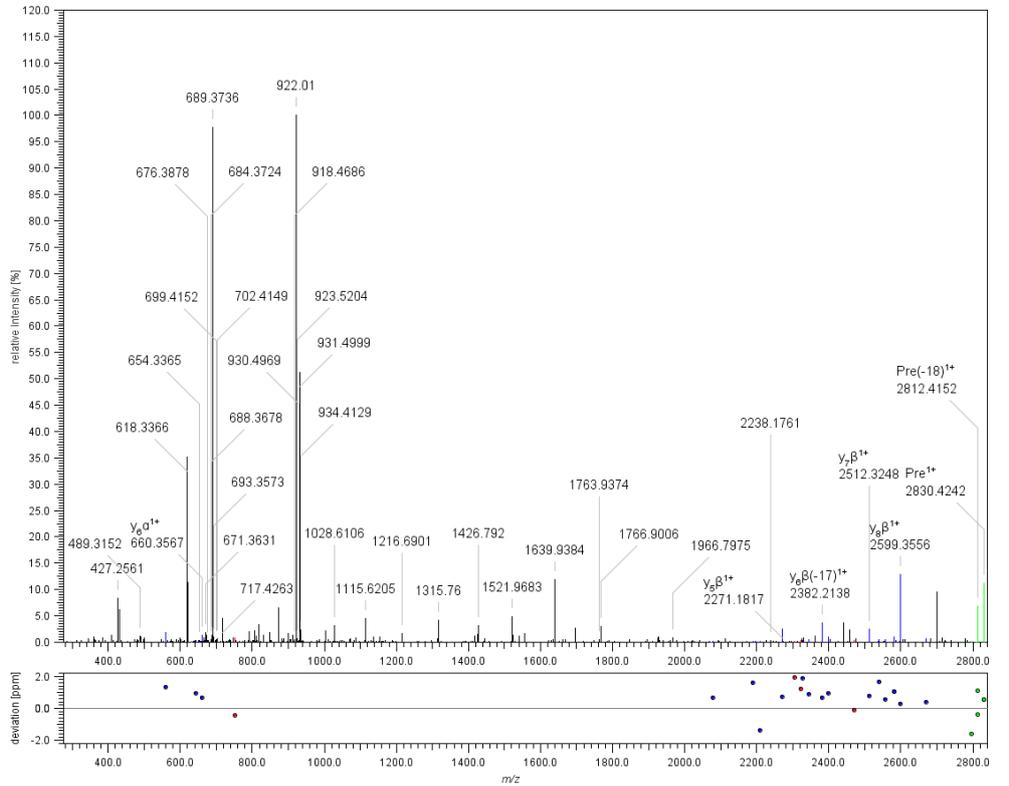
File: D:\DATA... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [KFWGKYLEIAR] (K1) Score (107)  
 Scan: 610 (-BSA from 132 to 143) identified signals (0.001)  
 theor. Mass (M + H+): 1669.8737 Peptide -1 (K5) intense signals (0.091)  
 meas. Mass (M + H+): 1669.8743 (intrapep. from 0 to 0) ion series (0.0)  
 Deviation 0.37 ppm Crosslinker: DSGnond Intensity Ratio (0.061)  
 m/z: 1669.87430903699 hits/possible ions (0.006)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [FWGKY] (K4) Score (70)  
 Scan: 546 (-BSA from 133 to 137) identified signals (0.001)  
 theor. Mass (M + H+): 1559.7893 Peptide  $\alpha$ : [LVEIAR] (Y2) intense signals (0.058)  
 meas. Mass (M + H+): 1559.7908 (-BSA from 138 to 143) ion series (0.002)  
 Deviation 0.84 ppm Crosslinker: DSGnond Intensity Ratio (0.068)  
 m/z: 1559.79075843476 hits/possible ions (0.01)  
 Charge: +1

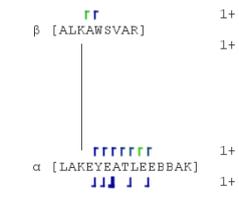
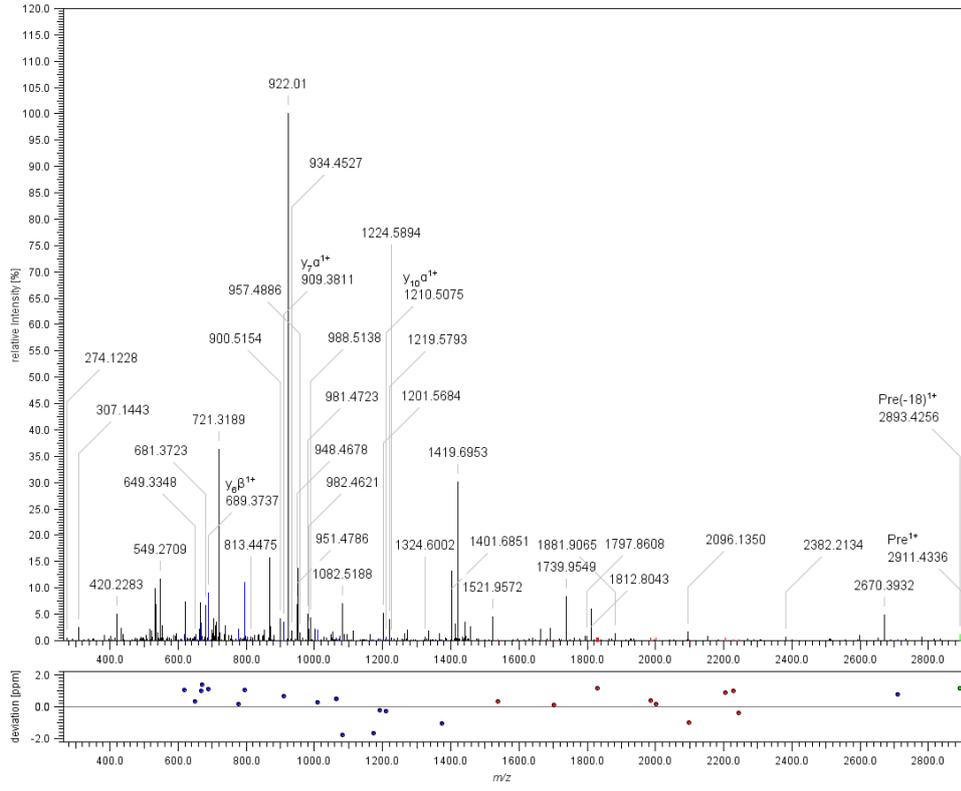


File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [BASIQKFGER] (K6) Score (83)  
 Scan: 302 (-BSA from 199 to 208) identified signals (0.002)  
 theor. Mass (M + H+): 2830.4226 Peptide  $\alpha$ : [LVLHEKTPVSEK] (K7) intense signals (0.048)  
 meas. Mass (M + H+): 2830.4226 (-BSA from 459 to 471) ion series (0.0)  
 Deviation 0.01 ppm Crosslinker: DSGnond Intensity Ratio (0.084)  
 m/z: 2830.42263538881 hits/possible ions (0.02)  
 Charge: +1

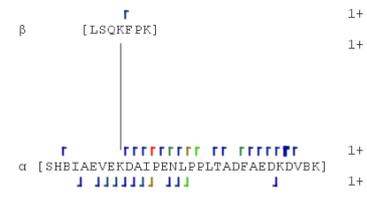
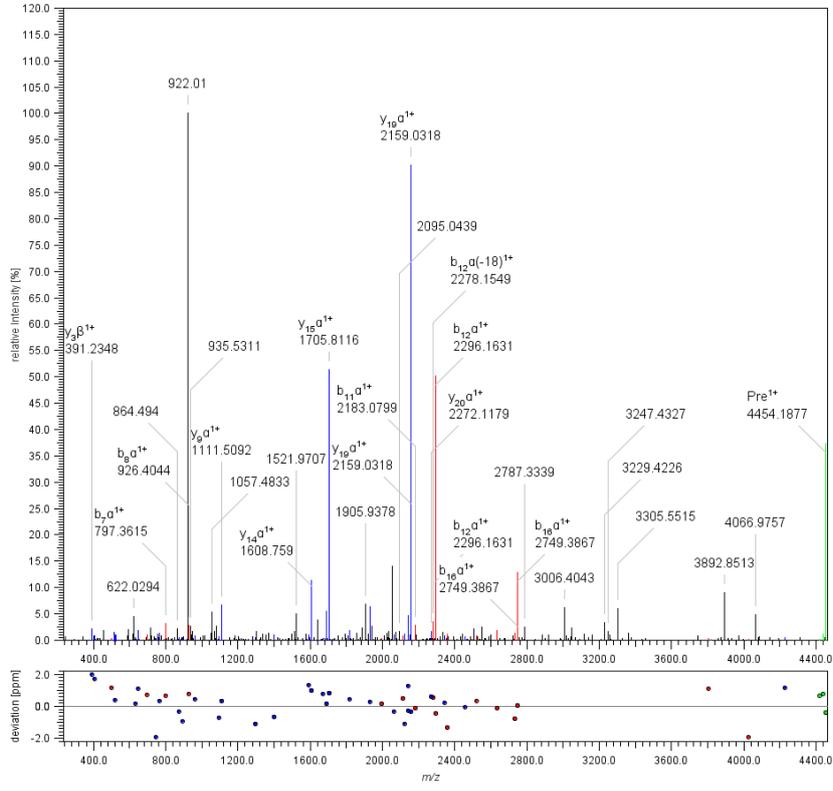




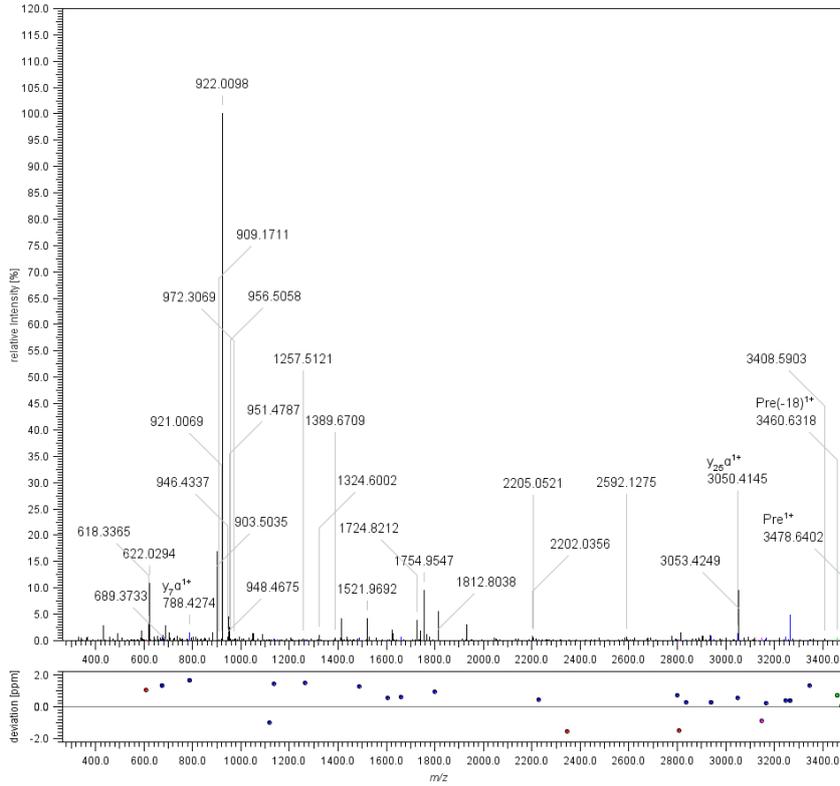
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [ALKAWSVAR] (K3) Score (72)  
 Scan: 360 (-BSA from 209 to 217) identified signals (0.001)  
 theor. Mass (M + H+): 2911.4328 Peptide  $\alpha$ : [LAKEYEATLEEBBAK] (K3) intense signals (0.058)  
 meas. Mass (M + H+): 2911.4319 (-BSA from 346 to 362) ion series (0.001)  
 Deviation: -0.28 ppm Crosslinker: DSGnond Intensity Ratio (0.078)  
 m/z: 2911.43203194563 hits/possible ions (0.015)  
 Charge: +1



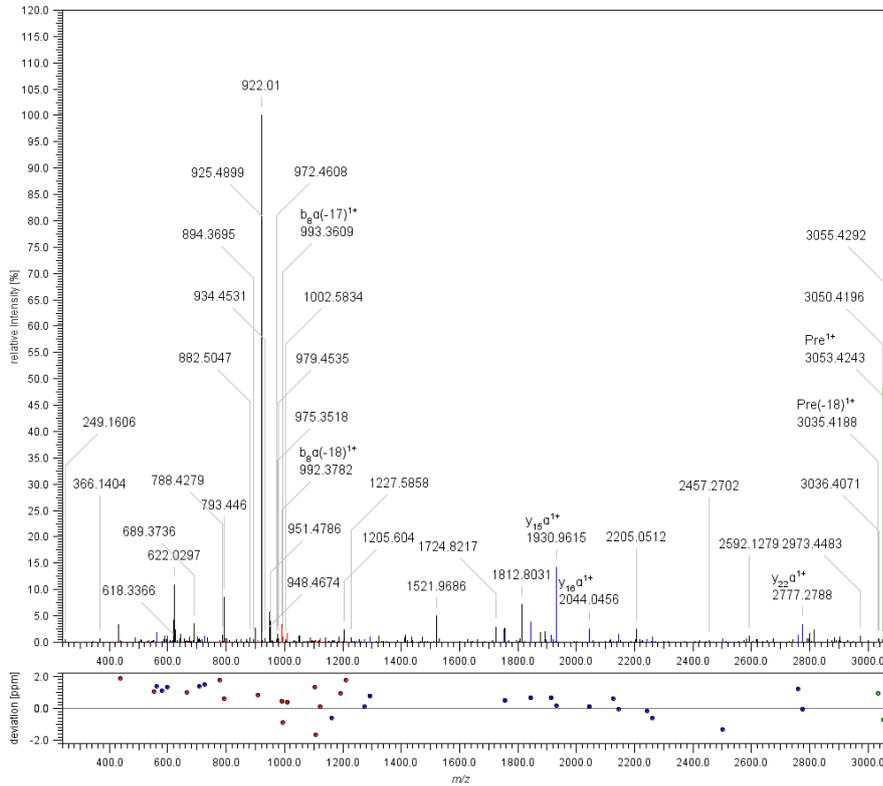
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [LSQKFPK] (K4) Score (154)  
 Scan: 472 (-BSA from 218 to 224) identified signals (0.0)  
 theor. Mass (M + H+): 4454.1894 Peptide  $\alpha$ : [SHBIAEVEKDAIPENLPPLTADFAEDKDVBK] (K3) intense signals (0.0)  
 meas. Mass (M + H+): 4454.1866 (-BSA from 286 to 316) ion series (0.029)  
 Deviation: -0.2 ppm Crosslinker: DSGnond Intensity Ratio (0.0)  
 m/z: 4454.18655204467 hits/possible ions (0.013)  
 Charge: +1



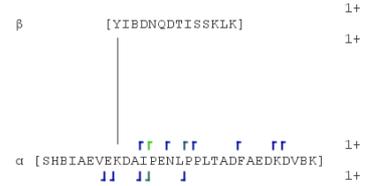
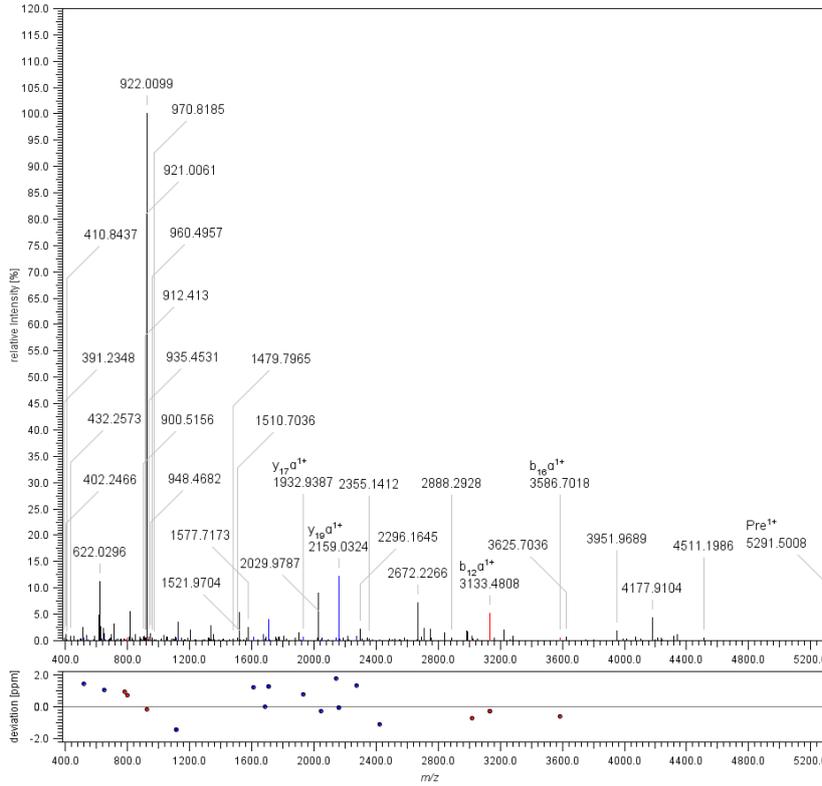
File: D:\DATA... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ [LVTDLTKVHK]EBBHGDLLEBADDRADLAK (K) (77)  
 Scan: 374 (-BSA from 233 to 261) identified signals (0.001)  
 theor. Mass (M + H+): 3478.6399 Peptide -1 (K10) intense signals (0.091)  
 meas. Mass (M + H+): 3478.6399 (intrap. from 0 to 0) ion series (0.0)  
 Deviation: -0.03 ppm Crosslinker: DSGnond Intensity Ratio (0.082)  
 m/z: 3478.63985624369 hits/possible ions (0.022)  
 Charge: +1



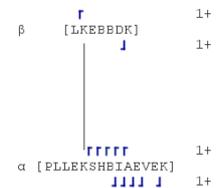
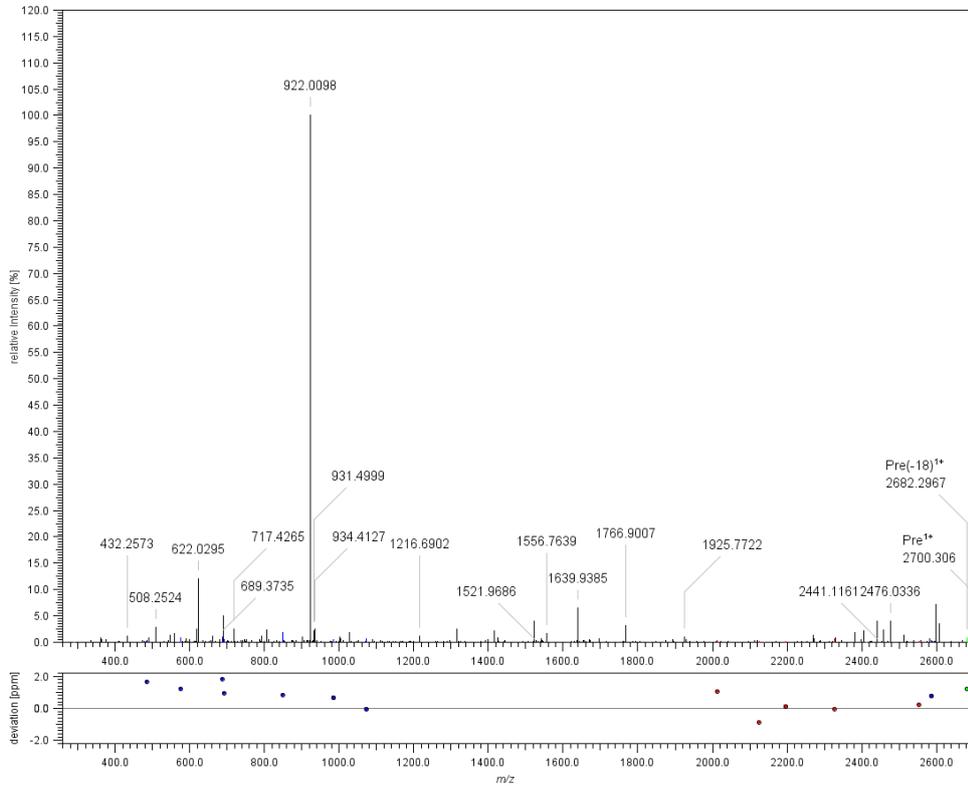
File: D:\DATA... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ [YIBDNQDTISSK]LKEBBDKPLLEK (K12) Score (138)  
 Scan: 374 (-BSA from 262 to 285) identified signals (0.0)  
 theor. Mass (M + H+): 3053.4264 Peptide -1 (K14) intense signals (0.007)  
 meas. Mass (M + H+): 3053.4249 (intrap. from 0 to 0) ion series (0.0)  
 Deviation: -0.51 ppm Crosslinker: DSGnond Intensity Ratio (0.068)  
 m/z: 3053.42488940512 hits/possible ions (0.008)  
 Charge: +1



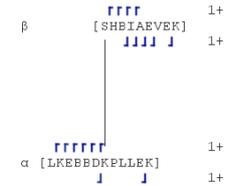
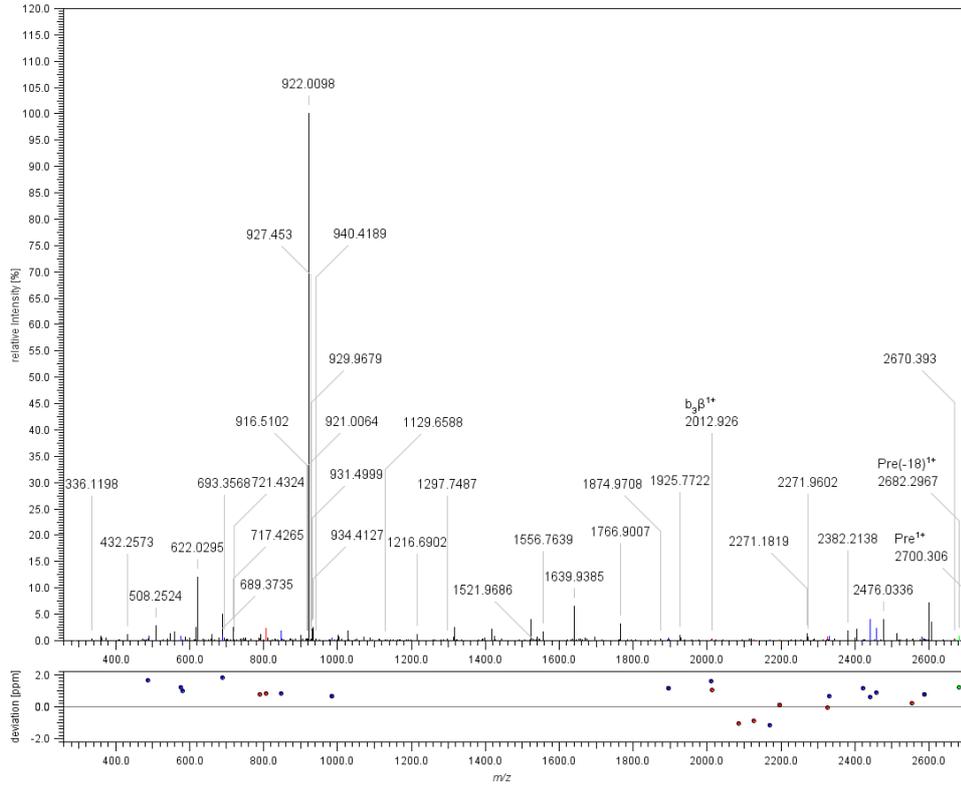
File: D:\DATA1... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [YIBDNQDTISSK]K (Y1) Score (73)  
 Scan: 490 (-BSA from 262 to 275) identified signals (0.001)  
 theor. Mass (M + H+): 5291.5069 Peptide  $\alpha$ : [SHBIAEVEKDAIPENLPPLTADFAEDK]DVBK (K5) intense signals (0.002)  
 meas. Mass (M + H+): 5291.5047 (-BSA from 286 to 316) ion series (0.047)  
 Deviation: -0.41 ppm Crosslinker: DSGnond Intensity Ratio (0.011)  
 m/z: 5291.5047158703 hits/possible ions (0.048)  
 Charge: +1



File: D:\DATA1... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [LKEBBDK]K (K2) Score (31)  
 Scan: 300 (-BSA from 274 to 280) identified signals (0.006)  
 theor. Mass (M + H+): 2700.3041 Peptide  $\alpha$ : [P]LLEK[SHBIAEVEK]K (K5) intense signals (0.091)  
 meas. Mass (M + H+): 2700.3042 (-BSA from 281 to 294) ion series (0.034)  
 Deviation: 0.03 ppm Crosslinker: DSGnond Intensity Ratio (0.09)  
 m/z: 2700.30420517758 hits/possible ions (0.03)  
 Charge: +1

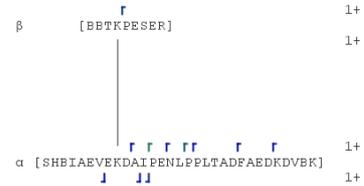
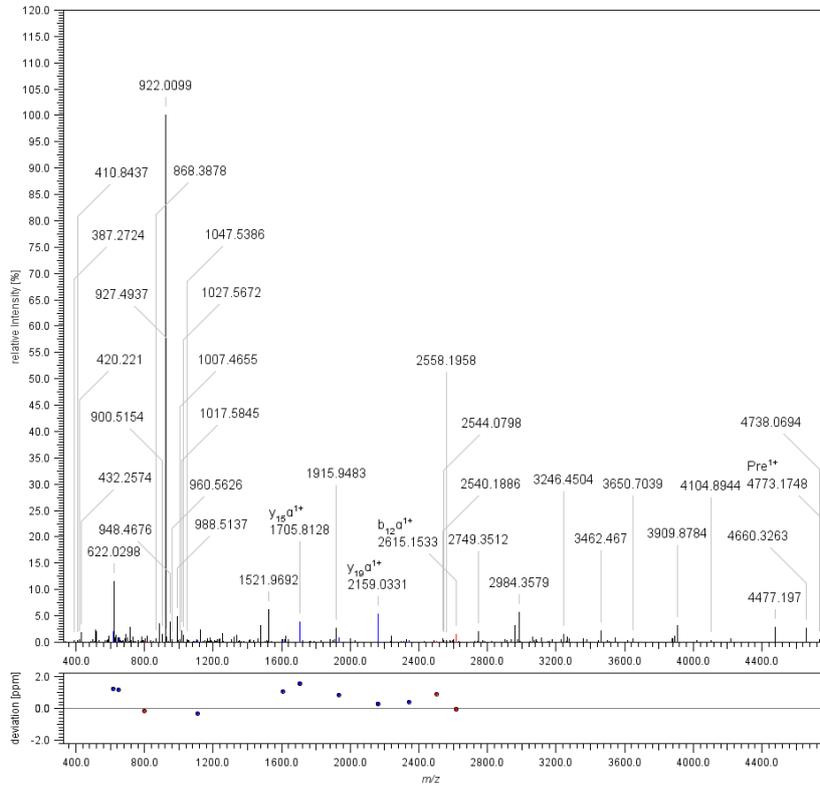


File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [SHBIAEVEK] (S1) Score (99)  
 Scan: 300 (-BSA from 286 to 294) identified signals (0.001)  
 theor. Mass (M + H+): 2700.3041 Peptide  $\alpha$ : [LKEBBDKPLEEK] (K7) intense signals (0.091)  
 meas. Mass (M + H+): 2700.3042 (-BSA from 274 to 285) ion series (0.0)  
 Deviation 0.03 ppm Crosslinker: DSGnond Intensity Ratio (0.085)  
 m/z: 2700.30420517758 hits/possible ions (0.015)  
 Charge: +1



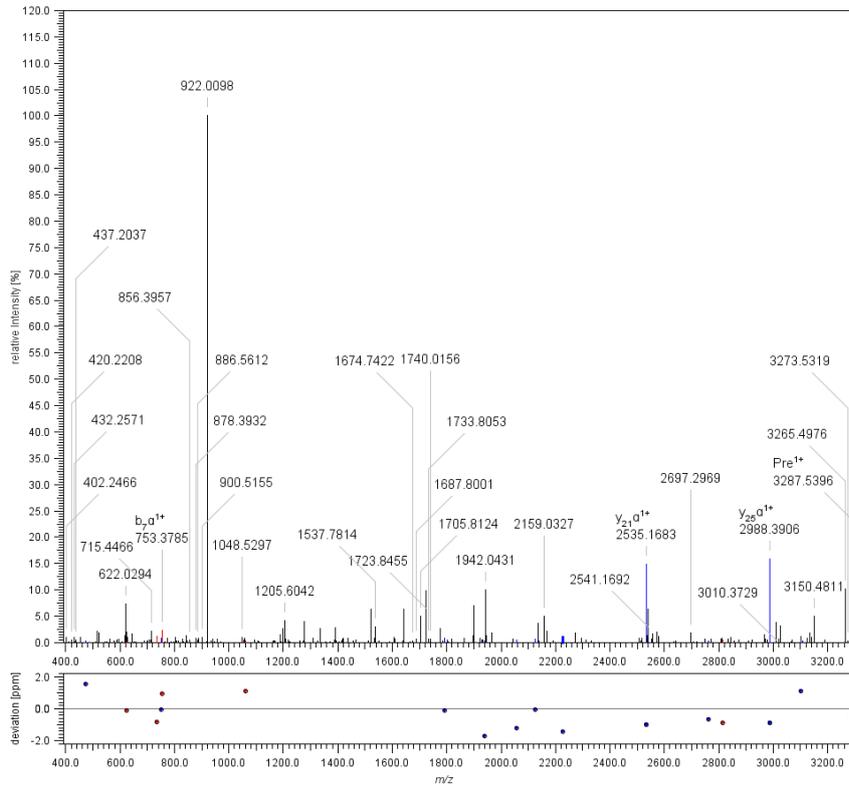
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File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [BBTKPESER] (K4) Score (25)  
 Scan: 444 (-BSA from 436 to 444) identified signals (0.012)  
 theor. Mass (M + H+): 4773.1787 Peptide  $\alpha$ : [SHBIAEVEKDAIPENLPPLTADFAEDKDVBR] (K8) intense signals (0.091)  
 meas. Mass (M + H+): 4773.1787 (-BSA from 286 to 316) ion series (0.042)  
 Deviation 0.0 ppm Crosslinker: DSGnond Intensity Ratio (0.047)  
 m/z: 4773.17867638061 hits/possible ions (0.06)  
 Charge: +1



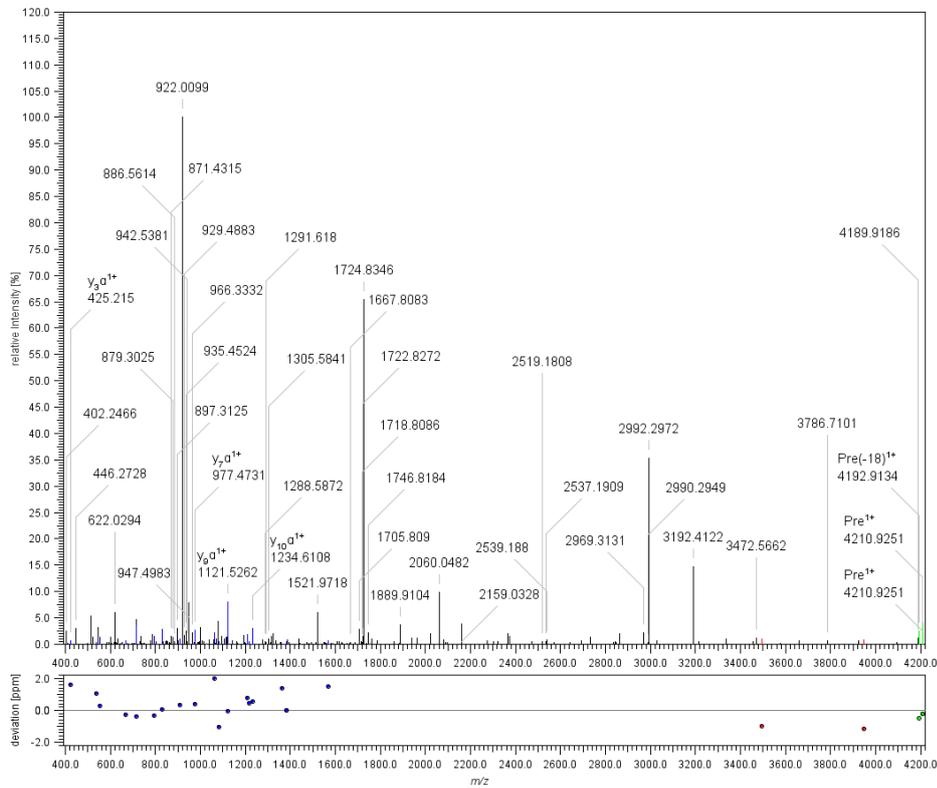
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File: D:\DATA\... 2018BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [DAIPENLEPLTADFAEDKDVBNKYQEA] (K) (38)re (92)  
 Scan: 520 (-BSA from 295 to 322) identified signals (0.002)  
 theor. Mass (M + H+): 3287.5413 Peptide -1 (K22) intense signals (0.001)  
 meas. Mass (M + H+): 3287.5395 (intrap. from 0 to 0) ion series (0.003)  
 Deviation: -0.53 ppm Crosslinker: DSGnond Intensity Ratio (0.027)  
 m/z: 3287.53953418087 hits/possible ions (0.033)  
 Charge: +1



$\alpha$  [DAIPENLEPLTADFAEDKDVBNKYQEA] 1+  
 1+

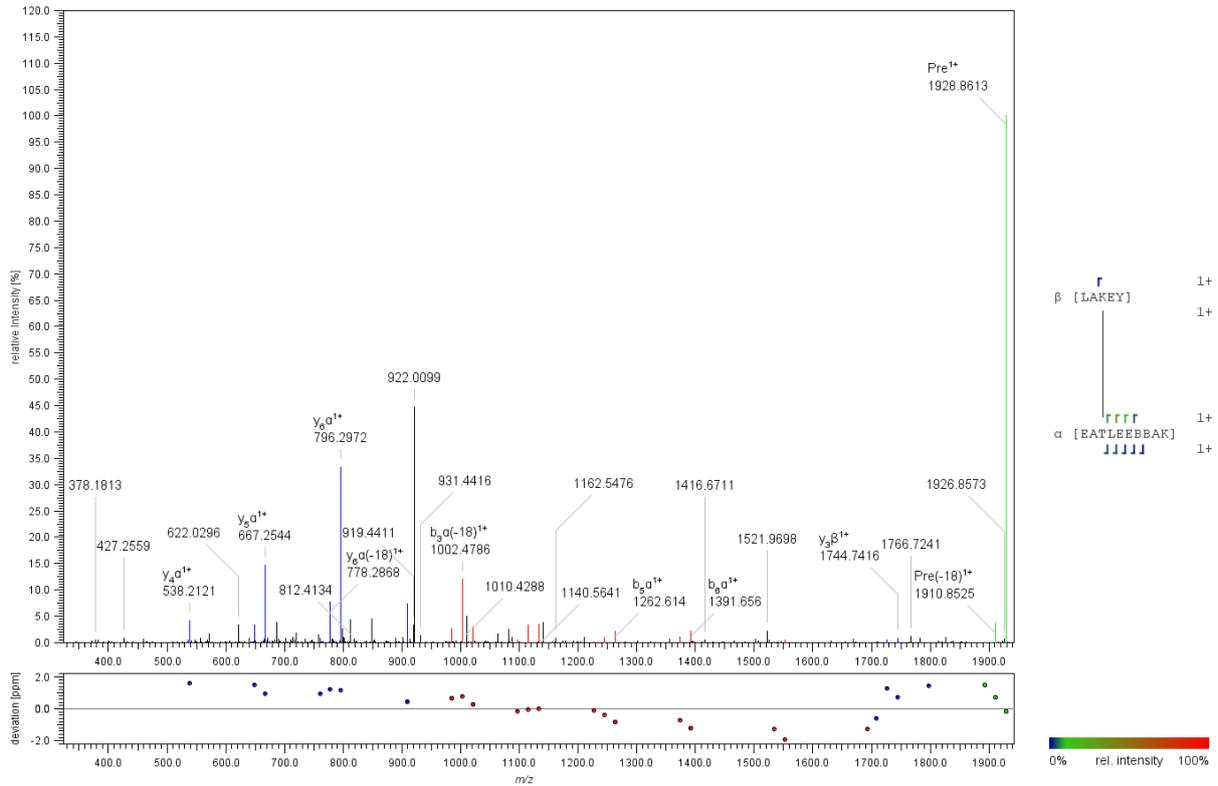
File: D:\DATA\... 2018BSA\_X3\_11134.zhrs Peptide  $\beta$ : [LAKEYEATLEEBBAK] (K)3 (80)  
 Scan: 566 (-BSA from 348 to 362) identified signals (0.001)  
 theor. Mass (M + H+): 4210.926 Peptide  $\alpha$ : [NYQEAQDAFLGSLFLEYYSR] (Y)2 (0.091)  
 meas. Mass (M + H+): 4210.9237 (-BSA from 317 to 335) ion series (0.0)  
 Deviation: -0.53 ppm Crosslinker: DSGnond Intensity Ratio (0.068)  
 m/z: 4210.92378758087 hits/possible ions (0.034)  
 Charge: +1



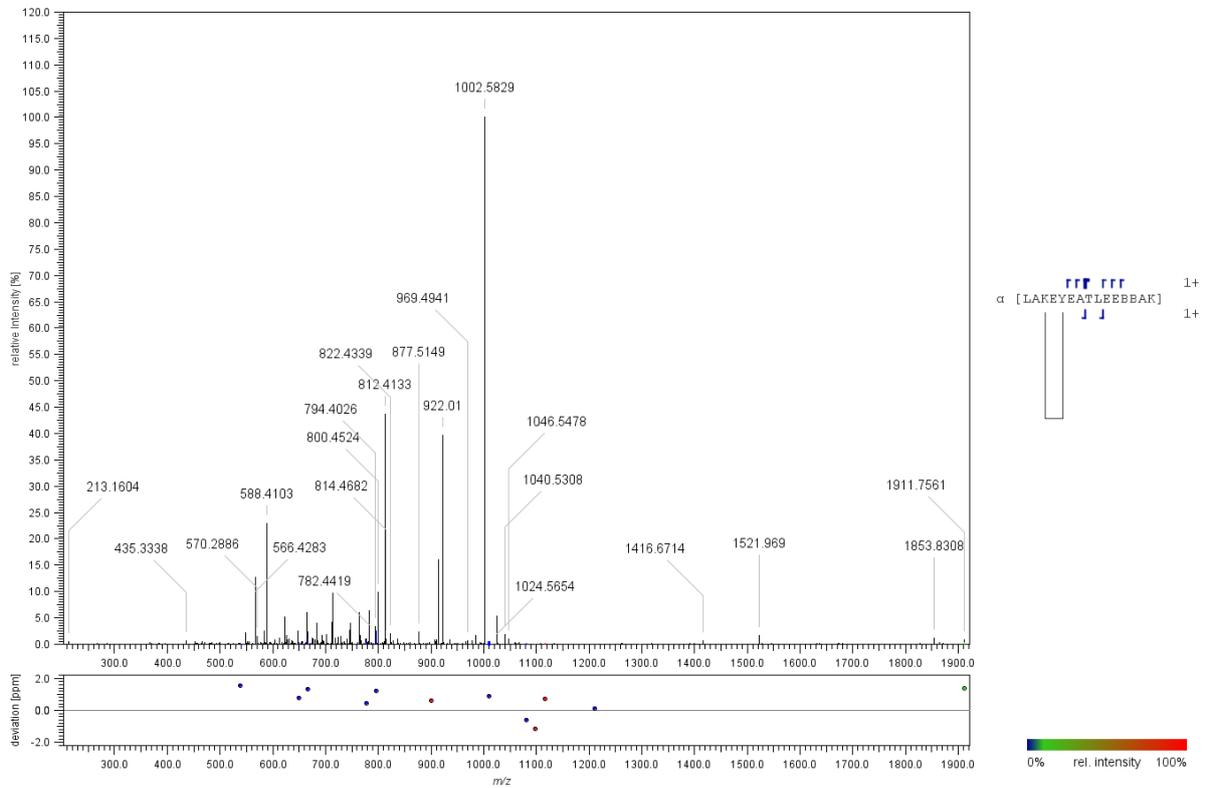
$\beta$  [LAKEYEATLEEBBAK] 1+  
 1+

$\alpha$  [NYQEAQDAFLGSLFLEYYSR] 1+  
 1+

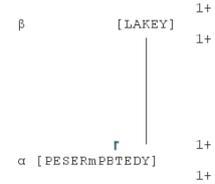
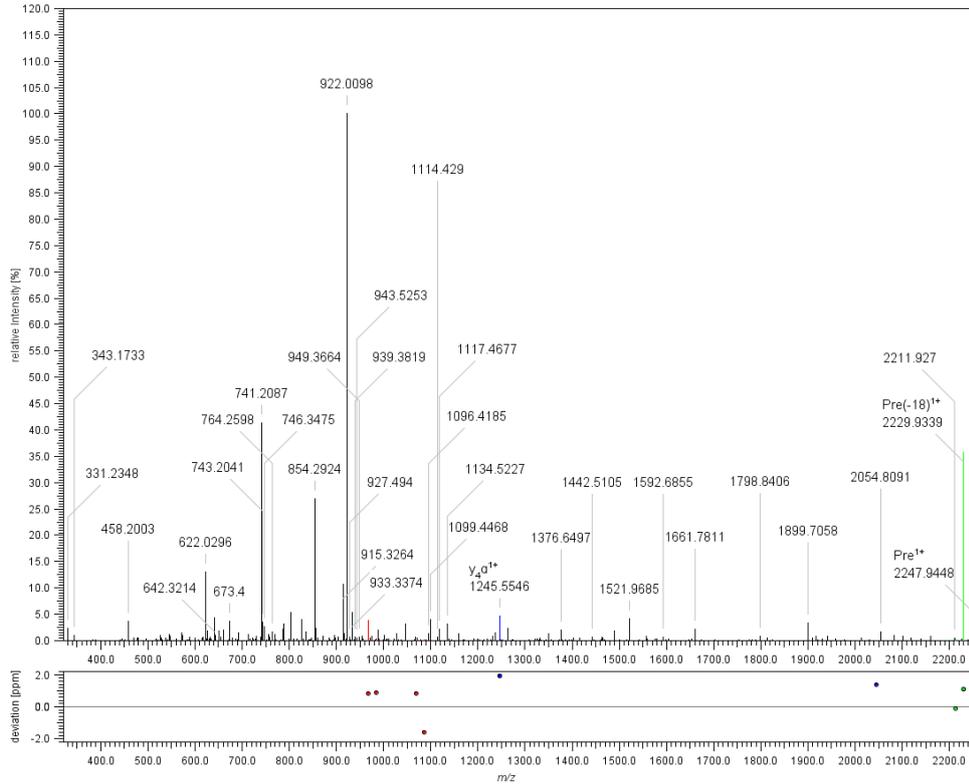
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ [LAKEY] (K3) Score (125)  
 Scan: 274 (-BSA from 348 to 352) identified signals (0.001)  
 theor. Mass (M + H+): 1928.8616 Peptide  $\alpha$ [EATLEEBBAK] (T3) intense signals (0.001)  
 meas. Mass (M + H+): 1928.8614 (-BSA from 353 to 362) ion series (0.001)  
 Deviation: -3.08 ppm Crosslinker: DSGnond Intensity Ratio (0.007)  
 m/z: 1928.86144641879 hits/possible ions (0.005)  
 Charge: +1



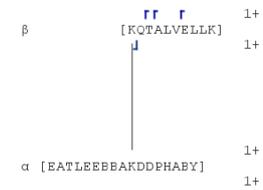
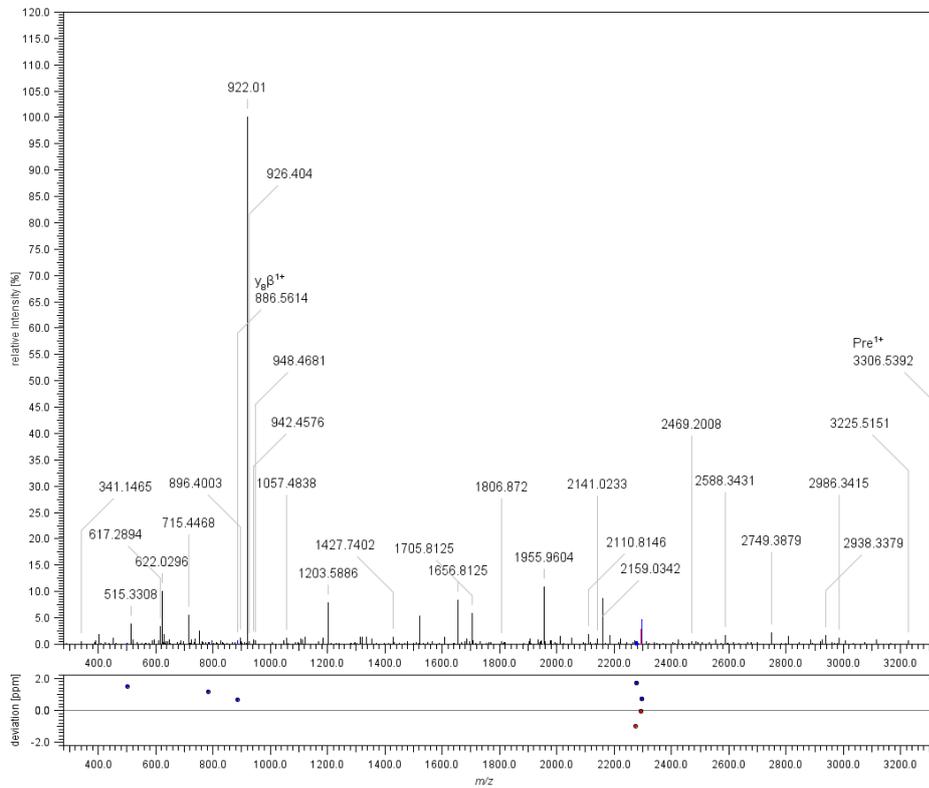
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ [LAKEYEATLEEBBAK] (K3) Score (36)  
 Scan: 278 (-BSA from 348 to 362) identified signals (0.045)  
 theor. Mass (M + H+): 1910.851 Peptide -1 (Y5) intense signals (0.091)  
 meas. Mass (M + H+): 1910.8521 (intrapep. from 0 to 0) ion series (0.002)  
 Deviation: 0.56 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 1910.85211676209 hits/possible ions (0.026)  
 Charge: +1



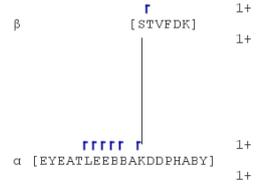
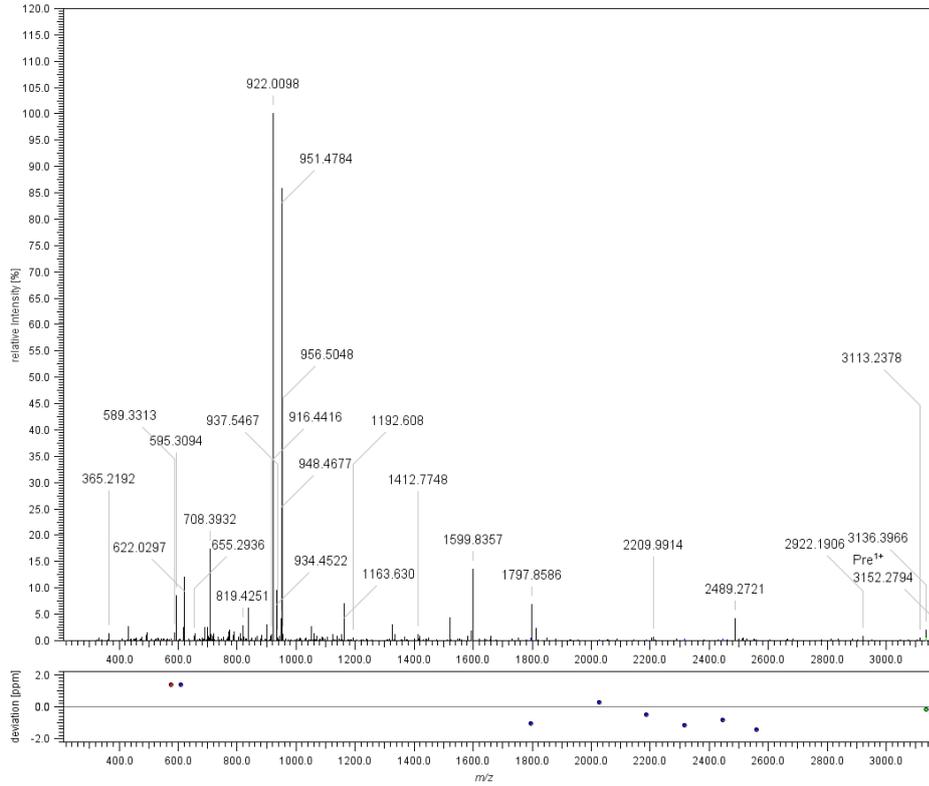
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [LAKEY] (K3) Score (12)  
 Scan: 246 (-BSA from 348 to 352) identified signals (0.068)  
 theor. Mass (M + H+): 2247.942 Peptide  $\alpha$ : [PESERmPBTEdY] (Y12) intense signals (0.091)  
 meas. Mass (M + H+): 2247.9399 (-BSA from 440 to 451) ion series (0.033)  
 Deviation: -0.94 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 2247.93992081038 hits/possible ions (0.05)  
 Charge: +1



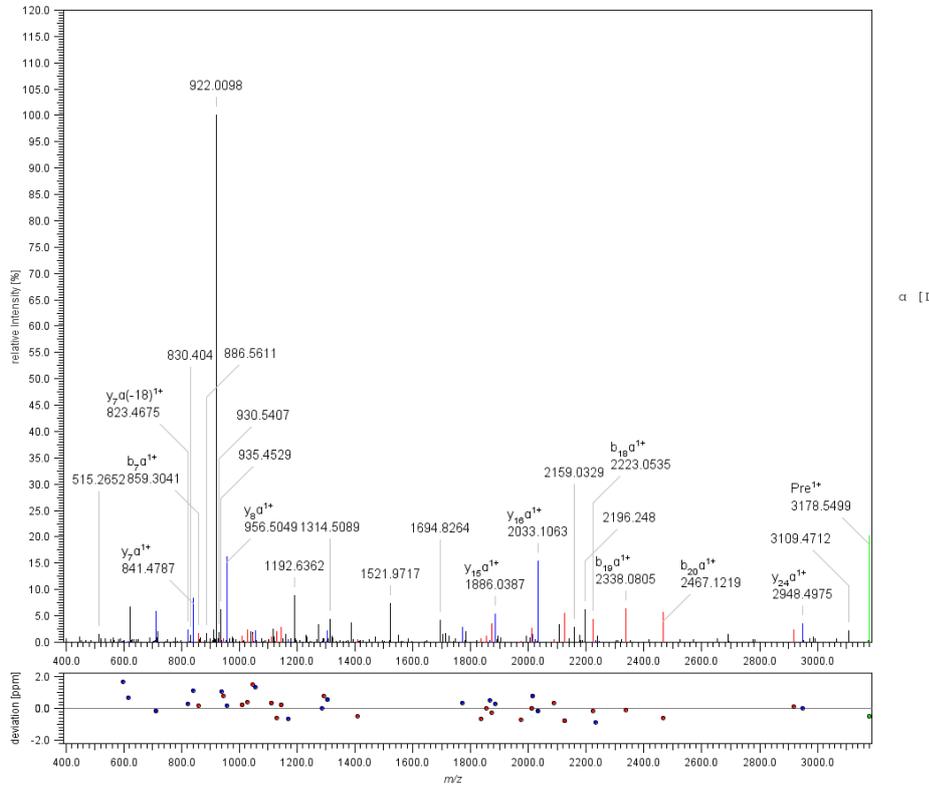
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [KOTALVELLQ] (K1) Score (8)  
 Scan: 476 (-BSA from 524 to 533) identified signals (0.047)  
 theor. Mass (M + H+): 3306.5327 Peptide  $\alpha$ : [EATLEEBBAKDDPHABY] (K10) intense signals (0.091)  
 meas. Mass (M + H+): 3306.5358 (-BSA from 353 to 369) ion series (0.067)  
 Deviation: 0.94 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 3306.53579618722 hits/possible ions (0.059)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [STVFDK] (S1) Score (5)  
 Scan: 348 (-BSA from 370 to 375) identified signals (0.063)  
 theo. Mass (M + H+): 3152.2806 Peptide  $\alpha$ : [YEATLEEBBAK/DDPHABY] (K12) intense signals (0.091)  
 meas. Mass (M + H+): 3152.2792 (-BSA from 361 to 369) ion series (0.091)  
 Deviation: -0.43 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 3152.2791962696 hits/possible ions (0.056)  
 Charge: +1



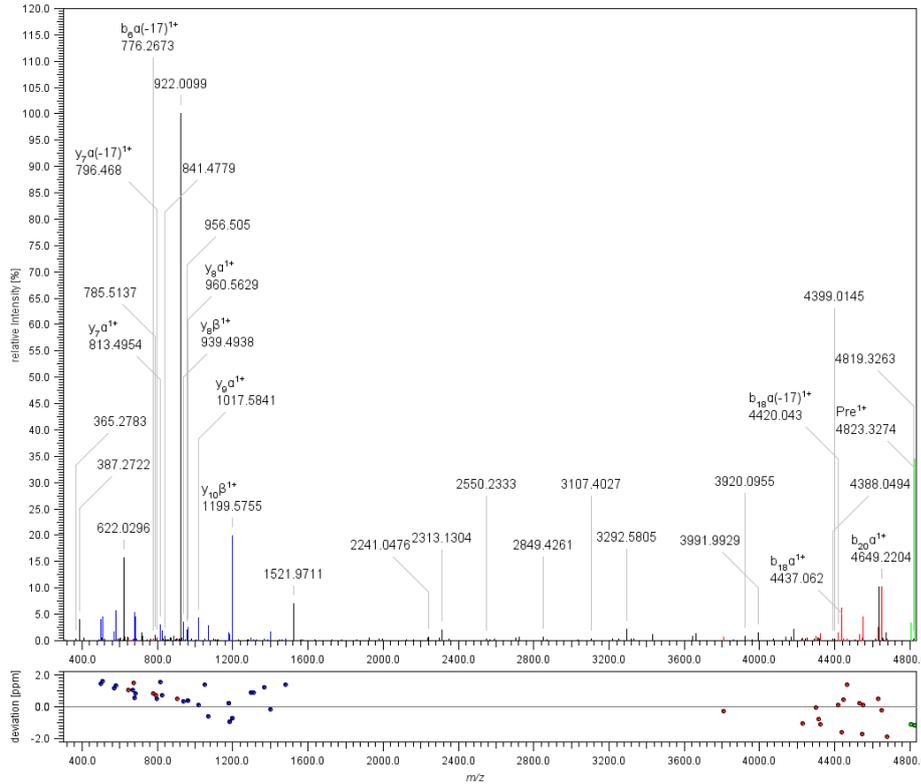
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [DDPHABYSTVFDK] (K13)core (190) Score (190)  
 Scan: 602 (-BSA from 363 to 388) identified signals (0.0) intense signals (0.001)  
 theo. Mass (M + H+): 3178.5514 Peptide -1 (K15) ion series (0.0)  
 meas. Mass (M + H+): 3178.5524 (intrapep. from 0 to 0) Intensity Ratio (0.001)  
 Deviation: 0.34 ppm Crosslinker: DSGnond hits/possible ions (0.007)  
 m/z: 3178.55245604588  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Scan: 756  
 theor. Mass (M + H+): 4823.3331 meas. Mass (M + H+): 4823.3263  
 Deviation: -0.99 ppm m/z: 4823.32634609907  
 Charge: +1

Peptide  $\beta$ : [ATEEQIKVTVMENFVAFVDK] (K7) (-BSA from 538 to 556)  
 Peptide  $\alpha$ : [QNBDQFEKLGEGYGFQNALIVR] (K8) (-BSA from 389 to 409)  
 Crosslinker: DSGnond

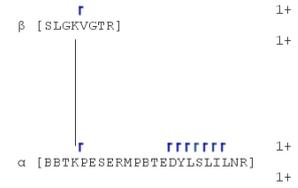
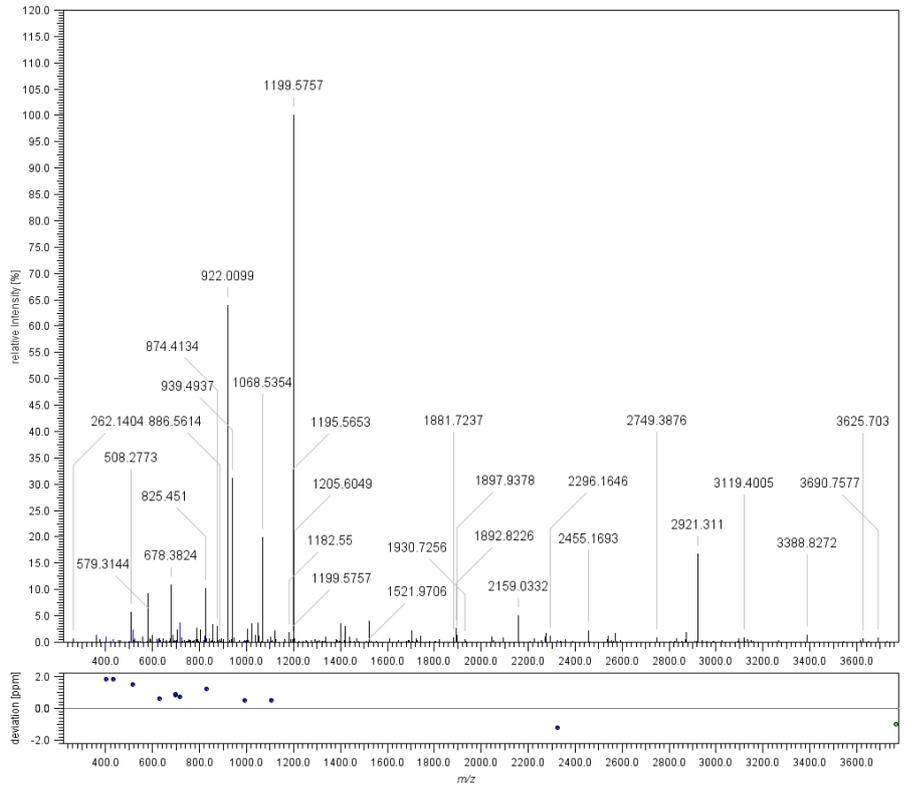
Score (175)  
 identified signals (0.0)  
 intense signals (0.002)  
 ion series (0.0)  
 Intensity Ratio (0.002)  
 hits/possible ions (0.016)



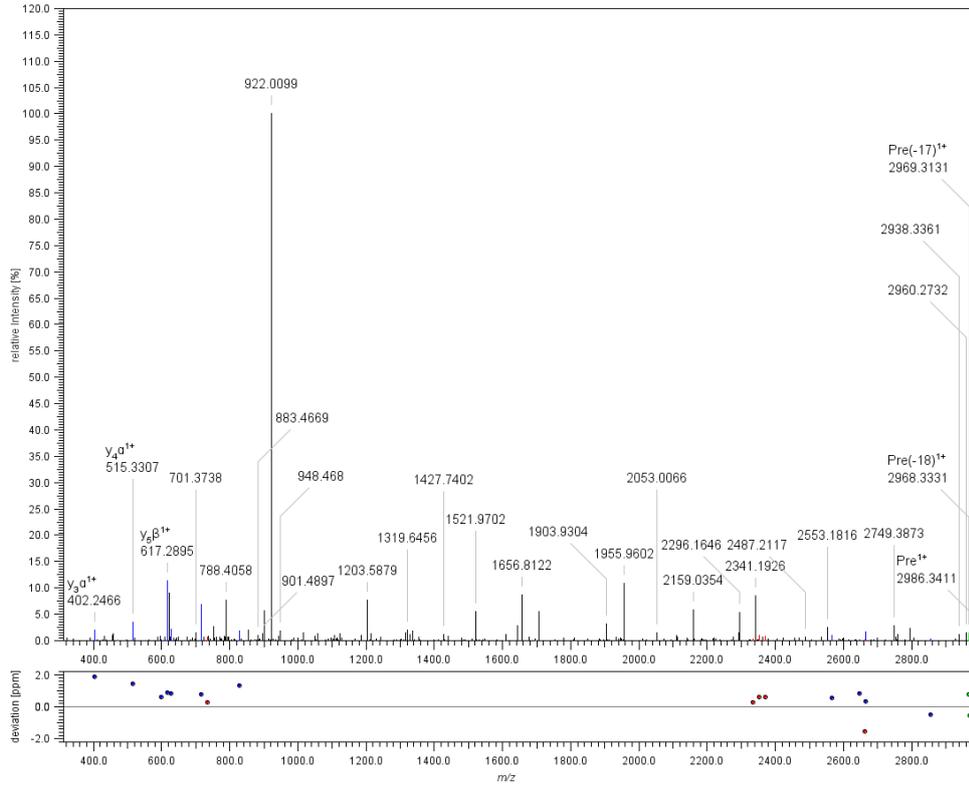
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Scan: 516  
 theor. Mass (M + H+): 3784.8125 meas. Mass (M + H+): 3784.8125  
 Deviation: -0.01 ppm m/z: 3784.81246335752  
 Charge: +1

Peptide  $\beta$ : [SLGKVGTR] (K4) (-BSA from 428 to 435)  
 Peptide  $\alpha$ : [BETKPESEKRPBTEDYLSLILNLR] (K4) (-BSA from 436 to 456)  
 Crosslinker: DSGnond

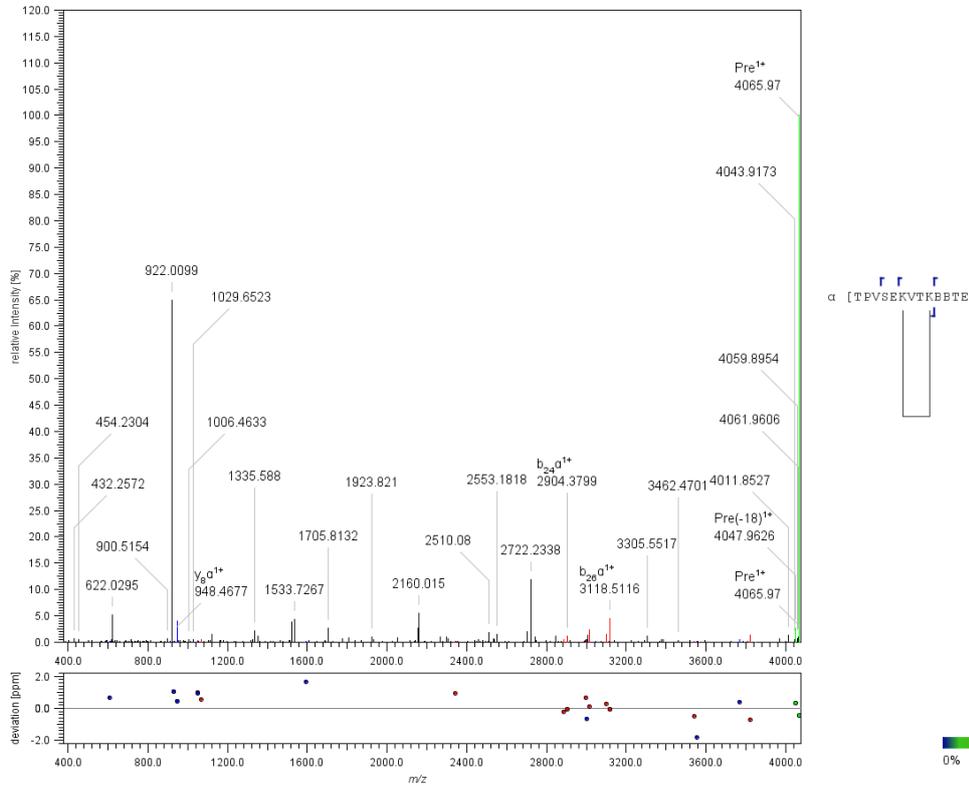
Score (22)  
 identified signals (0.015)  
 intense signals (0.091)  
 ion series (0.034)  
 Intensity Ratio (0.091)  
 hits/possible ions (0.051)



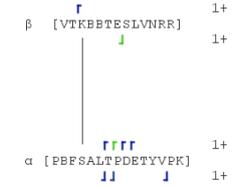
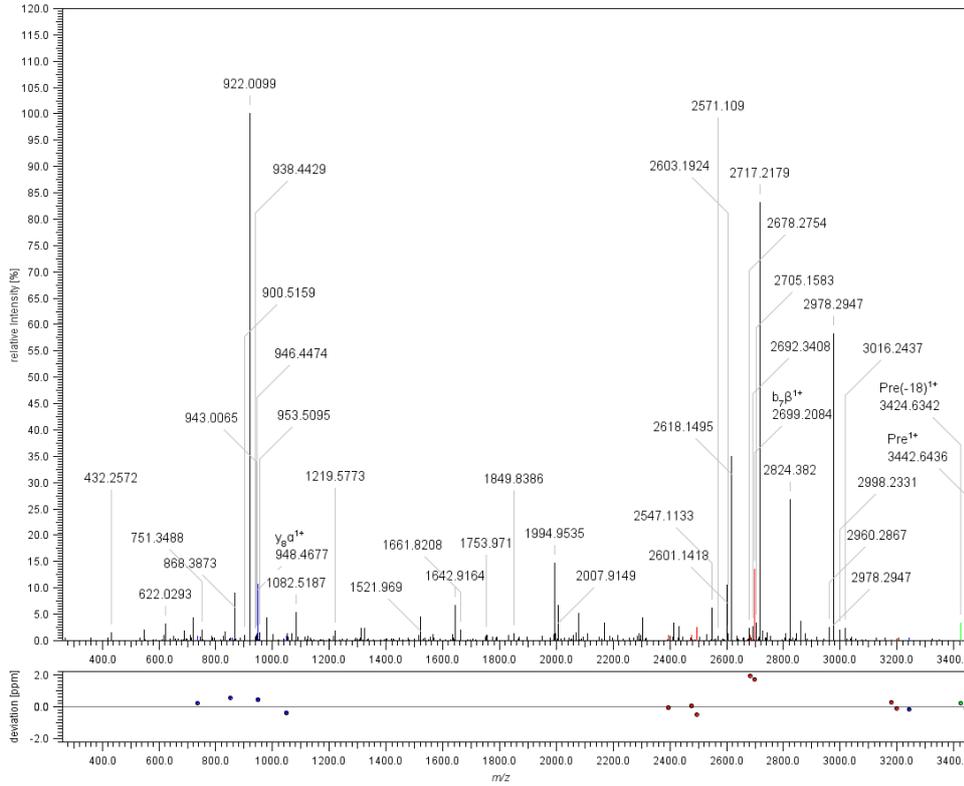
File: D:\DATA\... 2018BSA\_X3\_11134.zhrs Peptide  $\beta$ : [BBTKPESEK] (K4) Score (84)  
 Scan: 478 (-BSA from 436 to 444) identified signals (0.003)  
 theor. Mass (M + H+): 2986.3413 Peptide  $\alpha$ : [MPBTEDYLSLILNR] (Y7) intense signals (0.002)  
 meas. Mass (M + H+): 2986.3397 (-BSA from 445 to 456) ion series (0.002)  
 Deviation: -0.55 ppm Crosslinker: DSGnond Intensity Ratio (0.046)  
 m/z: 2986.33968151684 hits/possible ions (0.029)  
 Charge: +1



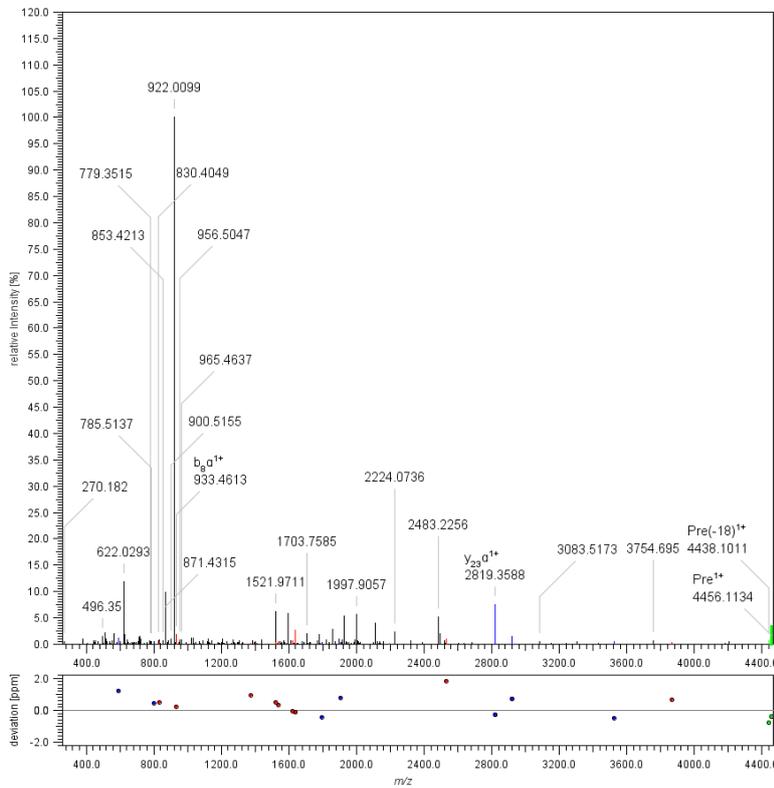
File: D:\DATA\... 2018BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [TPVSEKVTKBETESLVNRRPBFSAITPDETIVPK] (K6) Score (55)  
 Scan: 466 (-BSA from 466 to 499) identified signals (0.001)  
 theor. Mass (M + H+): 4065.9718 Peptide -1 (K9) intense signals (0.091)  
 meas. Mass (M + H+): 4065.9699 (intrapep. from 0 to 0) ion series (0.005)  
 Deviation: -0.47 ppm Crosslinker: DSGnond Intensity Ratio (0.068)  
 m/z: 4065.9694433917 hits/possible ions (0.034)  
 Charge: +1



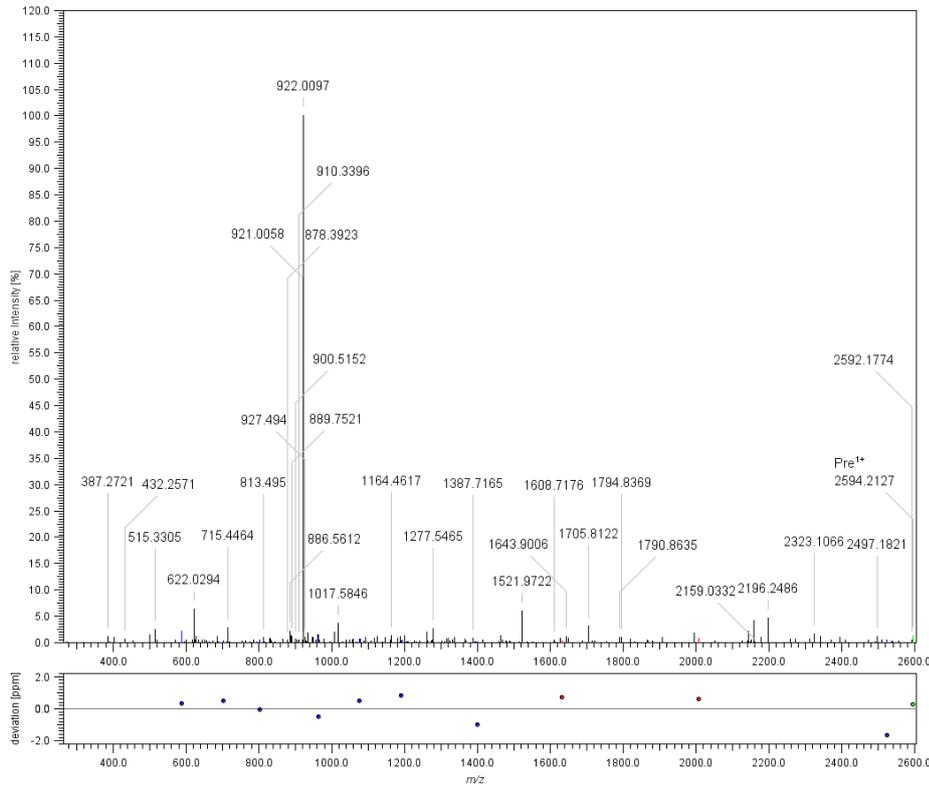
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [VTKBBTESLVNRR] (K3) Score (29)  
 Scan: 406 (-BSA from 472 to 484) identified signals (0.026)  
 theor. Mass (M + H+): 3442.644 Peptide  $\alpha$ : [PBFSAITPDETYVPK] (S4) intense signals (0.01)  
 meas. Mass (M + H+): 3442.6446 (-BSA from 485 to 499) ion series (0.058)  
 Deviation 0.18 ppm Crosslinker: DSGnond Intensity Ratio (0.086)  
 m/z: 3442.64459450295 hits/possible ions (0.049)  
 Charge: +1



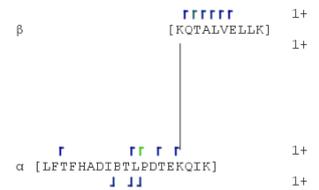
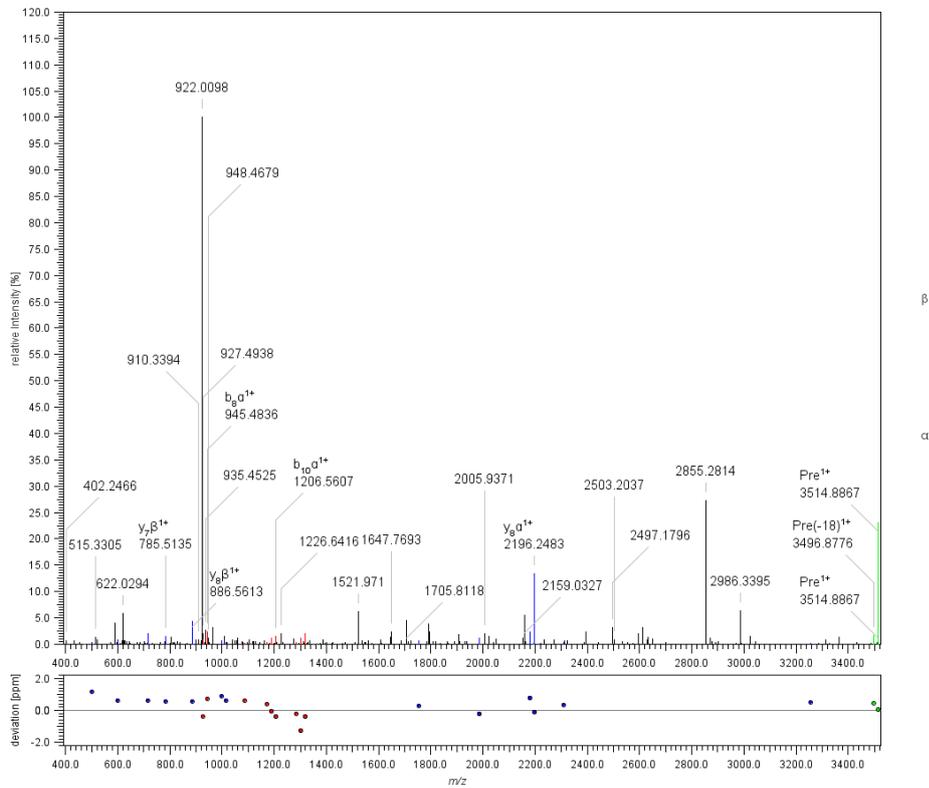
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [RPBFSALTPDETYVPKAFDEKLFTHADIBTLPDTEK] (K16) (52) identified signals (0.001)  
 Scan: 664 (-BSA from 484 to 520) intense signals (0.091)  
 theor. Mass (M + H+): 4456.1152 Peptide -1 (K21) ion series (0.007)  
 meas. Mass (M + H+): 4456.1121 (intrapep. from 0 to 0) Intensity Ratio (0.058)  
 Deviation -0.7 ppm Crosslinker: DSGnond hits/possible ions (0.041)  
 m/z: 4456.11207926735  
 Charge: +1



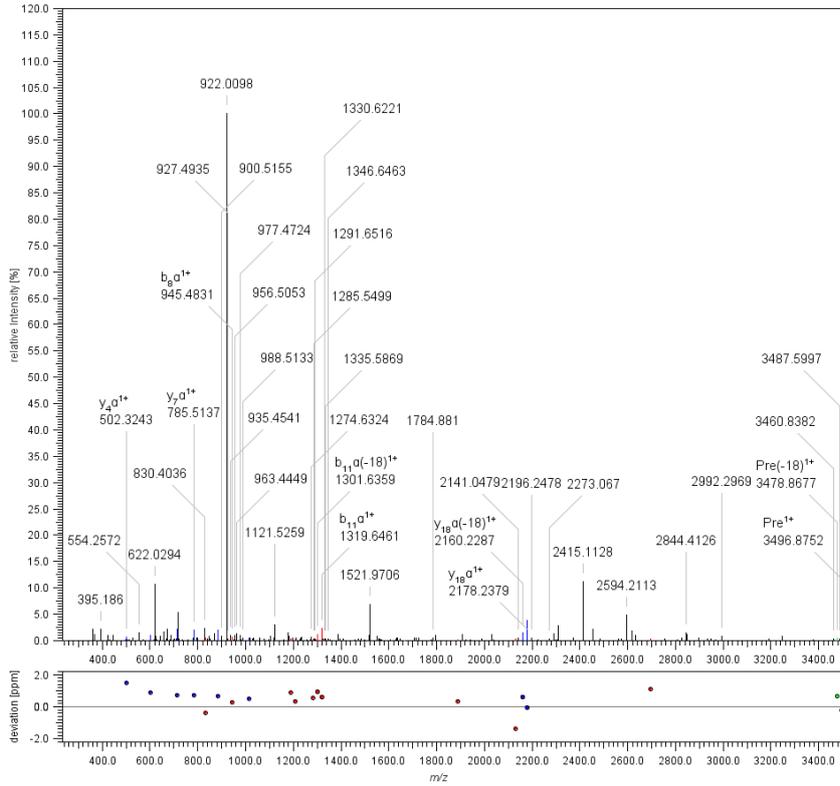
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [AFDEKLFTHADIBLPDTEK] (K5) Score (51)  
 Scan: 548 (-BSA from 500 to 520) identified signals (0.012)  
 theo. Mass (M + H+): 2594.2118 Peptide -1 (T8) intense signals (0.091)  
 meas. Mass (M + H+): 2594.2129 (intrap. from 0 to 0) ion series (0.001)  
 Deviation 0.36 ppm Crosslinker: DSGnond Intensity Ratio (0.087)  
 m/z: 2594.21286784952 hits/possible ions (0.04)  
 Charge: +1



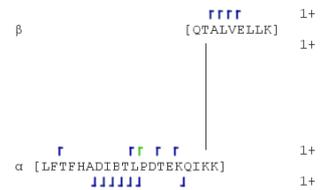
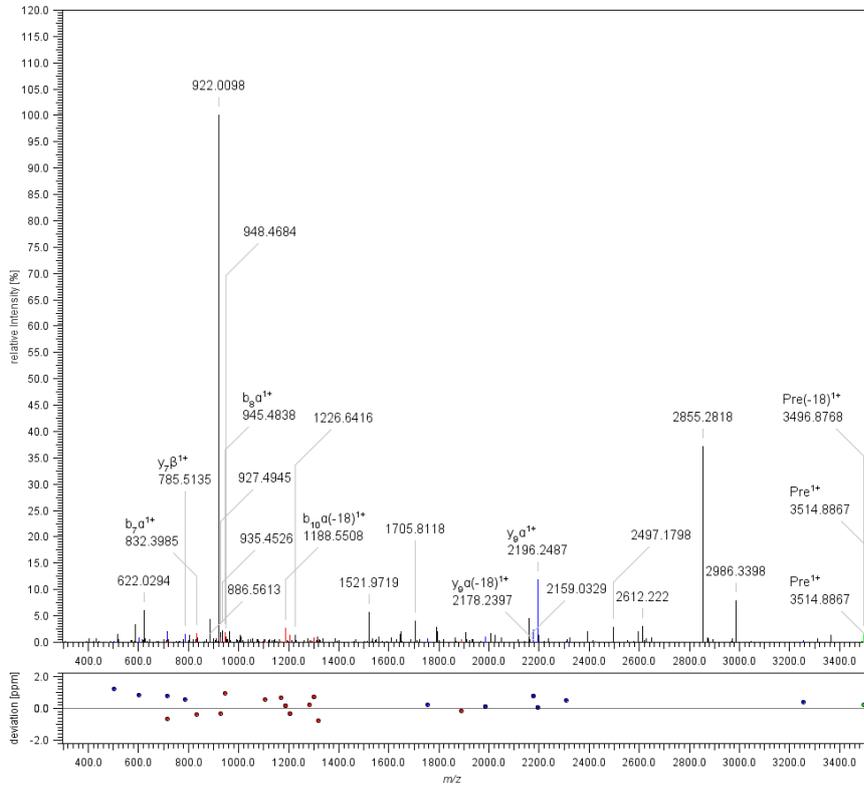
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [KOTALVELLK] (K1) Score (110)  
 Scan: 550 (-BSA from 524 to 533) identified signals (0.0)  
 theo. Mass (M + H+): 3514.8866 Peptide  $\alpha$ : [LFTFHADIBLPDTEKQIK] (K16) intense signals (0.007)  
 meas. Mass (M + H+): 3514.8873 (-BSA from 505 to 523) ion series (0.0)  
 Deviation 0.22 ppm Crosslinker: DSGnond Intensity Ratio (0.024)  
 m/z: 3514.88733585748 hits/possible ions (0.026)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [LFTFHADIBTLDPTEKQIKKOTALVELLK] (K19)pre (74)  
 Scan: 642 (-BSA from 505 to 533) identified signals (0.001)  
 theor. Mass (M + H+): 3496.876 Peptide -1 (K20) intense signals (0.091)  
 meas. Mass (M + H+): 3496.8765 (intrap. from 0 to 0) ion series (0.001)  
 Deviation 0.13 ppm Crosslinker: DSGnond Intensity Ratio (0.055)  
 m/z: 3496.87646684352 hits/possible ions (0.034)  
 Charge: +1

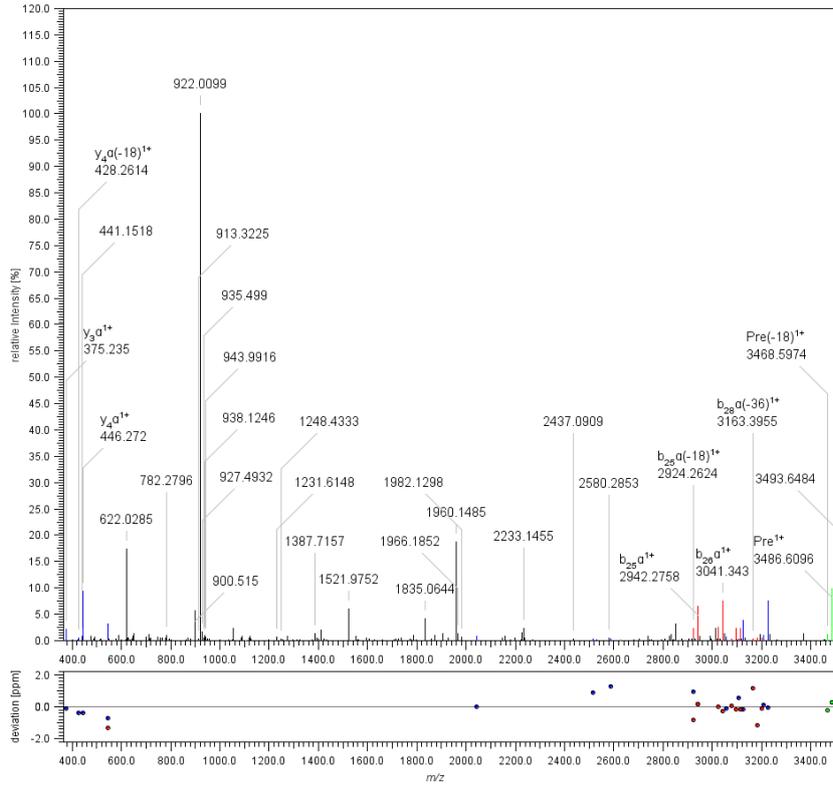


File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [OTALVELLK] (T2) Score (104)  
 Scan: 546 (-BSA from 525 to 533) identified signals (0.0)  
 theor. Mass (M + H+): 3514.8866 Peptide  $\alpha$ : [LFTFHADIBTLDPTEKQIKK] (K19) intense signals (0.007)  
 meas. Mass (M + H+): 3514.8871 (-BSA from 505 to 524) ion series (0.0)  
 Deviation 0.16 ppm Crosslinker: DSGnond Intensity Ratio (0.04)  
 m/z: 3514.88713308024 hits/possible ions (0.026)  
 Charge: +1

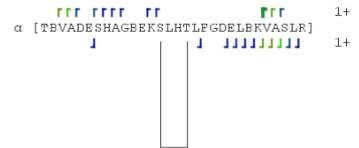
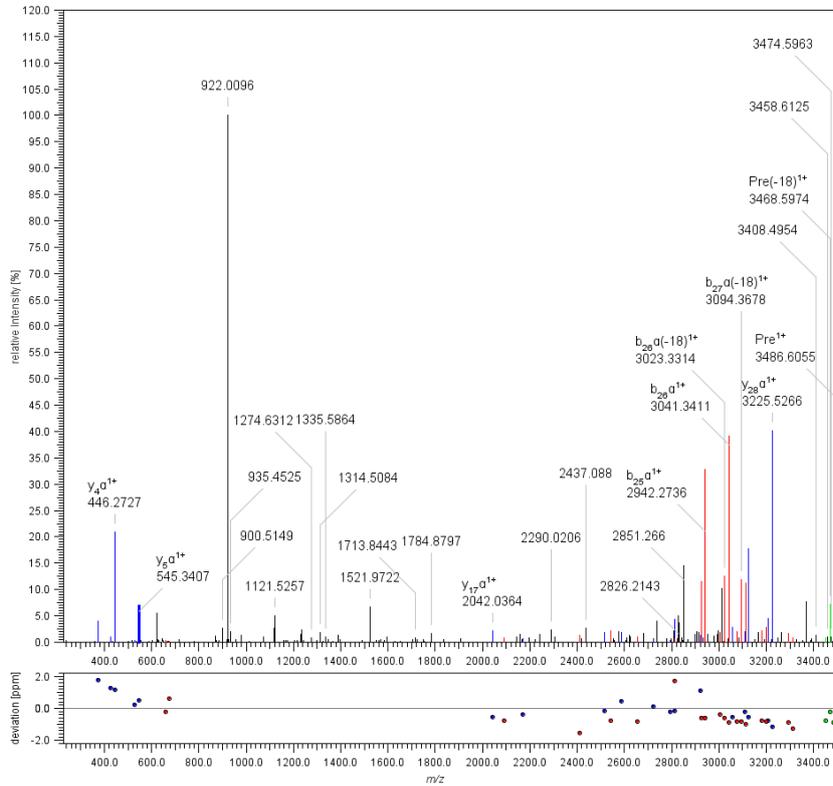




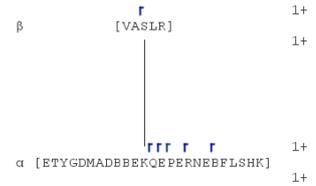
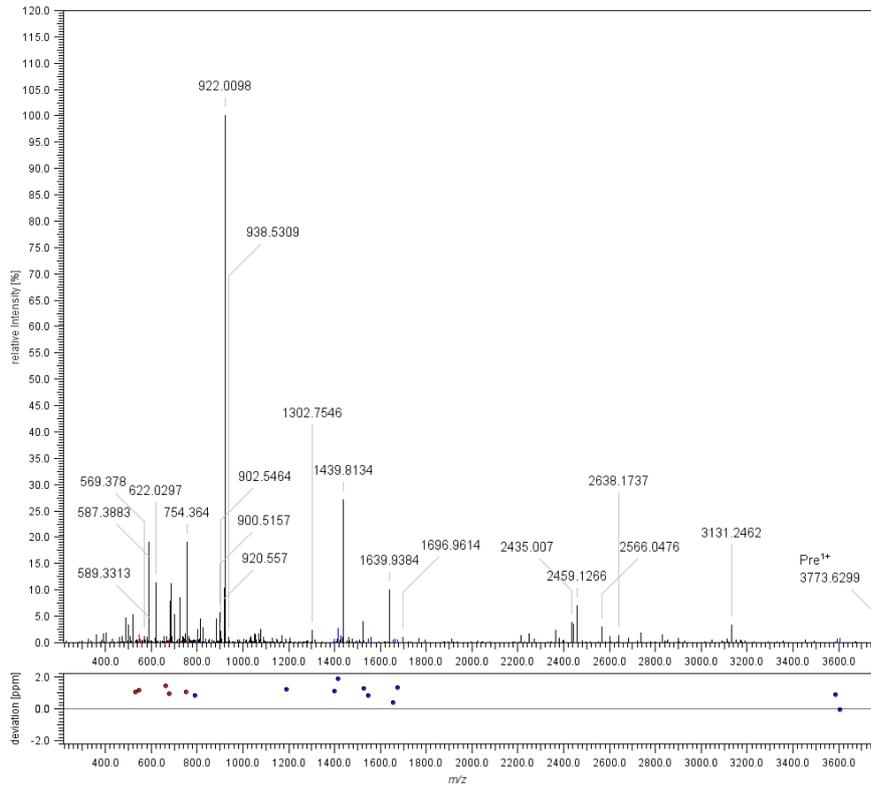
File: D:\DATA\... 2018\BSA\_A1\_11104.zhrs Peptide  $\alpha$ : [TBVADESHAGBEKSLHTLFGDELBKVASLR]~~(88)~~ (113)  
 Scan: 616 (-BSA from 52 to 81) identified signals (0.0)  
 theor. Mass (M + H+): 3486.6086 Peptide -1 (K25) intense signals (0.091)  
 meas. Mass (M + H+): 3486.6062 (intrap. from 0 to 0) ion series (0.0)  
 Deviation: -0.14 ppm Crosslinker: DSGnond Intensity Ratio (0.003)  
 m/z: 3486.60816515732 hits/possible ions (0.012)  
 Charge: +1



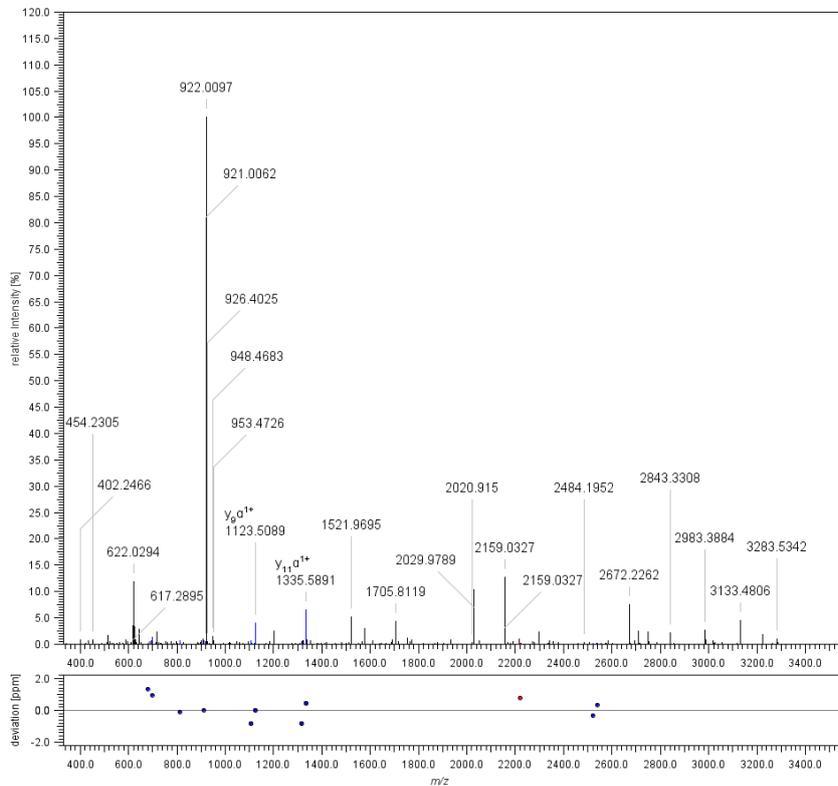
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [TBVADESHAGBEKSLHTLFGDELBKVASLR]~~(88)~~ (206)  
 Scan: 634 (-BSA from 52 to 81) identified signals (0.0)  
 theor. Mass (M + H+): 3486.6086 Peptide -1 (T17) intense signals (0.0)  
 meas. Mass (M + H+): 3486.6064 (intrap. from 0 to 0) ion series (0.0)  
 Deviation: -0.07 ppm Crosslinker: DSGnond Intensity Ratio (0.0)  
 m/z: 3486.6083961222 hits/possible ions (0.01)  
 Charge: +1



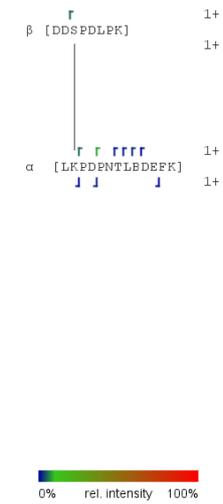
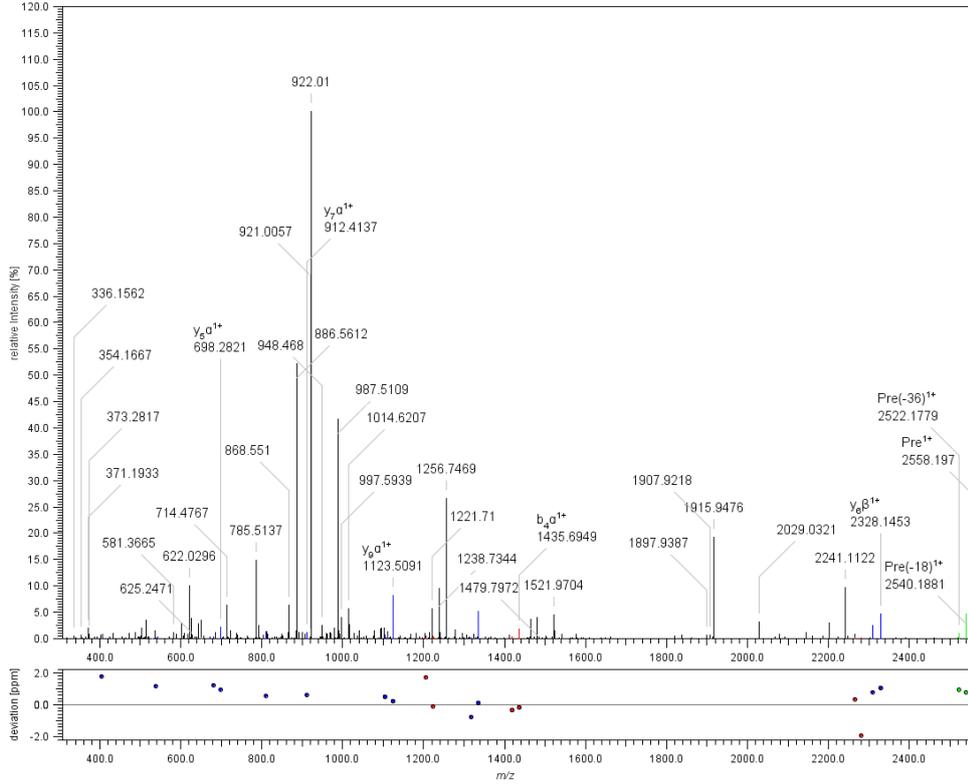
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [VASLR] (S3) Score (25)  
 Scan: 314 (-BSA from 77 to 81) identified signals (0.014)  
 theor. Mass (M + H+): 3773.6299 Peptide  $\alpha$ : [ETYGDMADBBEKQEPERNEBFLSHK] (K17) intense signals (0.091)  
 meas. Mass (M + H+): 3773.6261 (-BSA from 82 to 106) ion series (0.027)  
 Deviation: -3.46 ppm Crosslinker: DSGnond Intensity Ratio (0.09)  
 m/z: 3773.62813005655 hits/possible ions (0.04)  
 Charge: +1



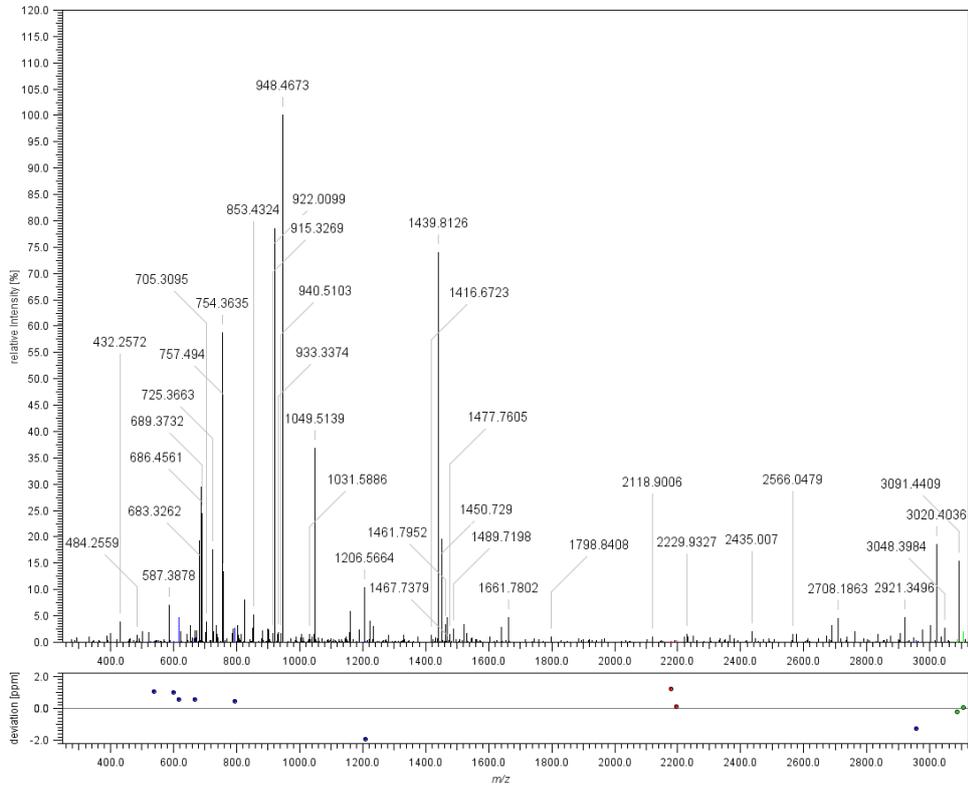
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [NEBFLSHKDDSPDLKPKDPNTLBDEFK] (S21) Score (34)  
 Scan: 490 (-BSA from 99 to 127) identified signals (0.006)  
 theor. Mass (M + H+): 3555.6407 Peptide  $\beta$ : [K16] intense signals (0.091)  
 meas. Mass (M + H+): 3555.6424 (intrapep. from 0 to 0) ion series (0.02)  
 Deviation: 0.49 ppm Crosslinker: DSGnond Intensity Ratio (0.065)  
 m/z: 3555.64241255199 hits/possible ions (0.044)  
 Charge: +1



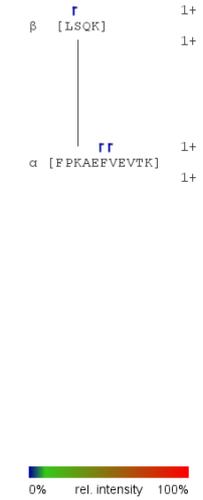
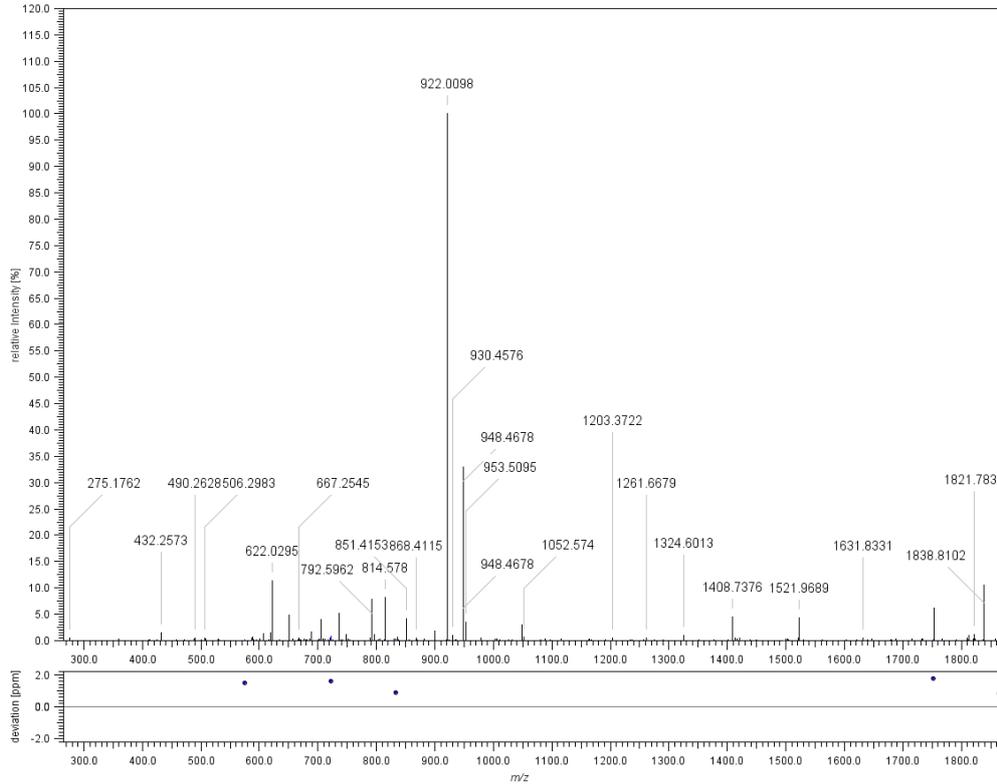
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [DDSPDLPK] (S3) Score (38)  
 Scan: 438 (-BSA from 107 to 114) identified signals (0.002)  
 theor. Mass (M + H+): 2558.1967 Peptide  $\alpha$ : [LKPDPNTLBLEDFK] (K2) intense signals (0.091)  
 meas. Mass (M + H+): 2558.1973 (-BSA from 115 to 127) ion series (0.039)  
 Deviation 0.24 ppm Crosslinker: DSGnond Intensity Ratio (0.081)  
 m/z: 2558.19728720129 hits/possible ions (0.023)  
 Charge: +1



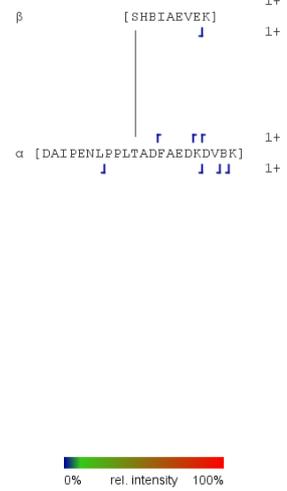
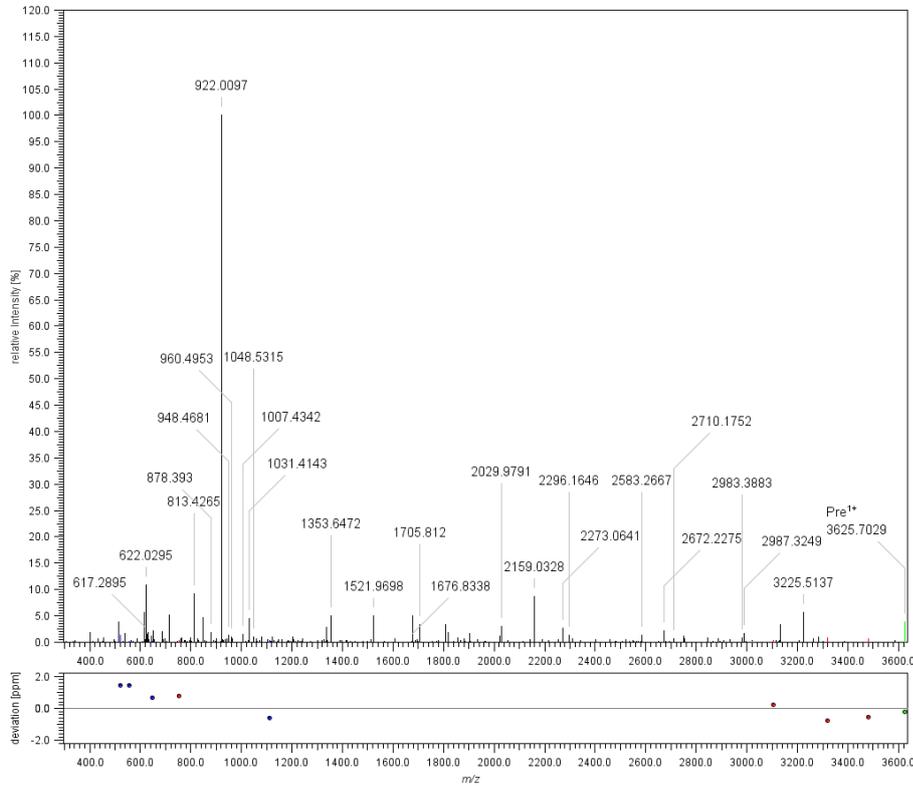
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [BASIQKFGER] (S3) Score (9)  
 Scan: 324 (-BSA from 199 to 208) identified signals (0.077)  
 theor. Mass (M + H+): 3105.4326 Peptide  $\alpha$ : [LAKEYEATLEEBBAK] (K3) intense signals (0.091)  
 meas. Mass (M + H+): 3105.4299 (-BSA from 346 to 362) ion series (0.046)  
 Deviation -0.87 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 3105.42987684733 hits/possible ions (0.053)  
 Charge: +1



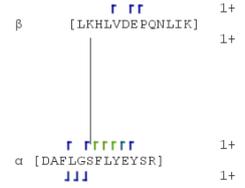
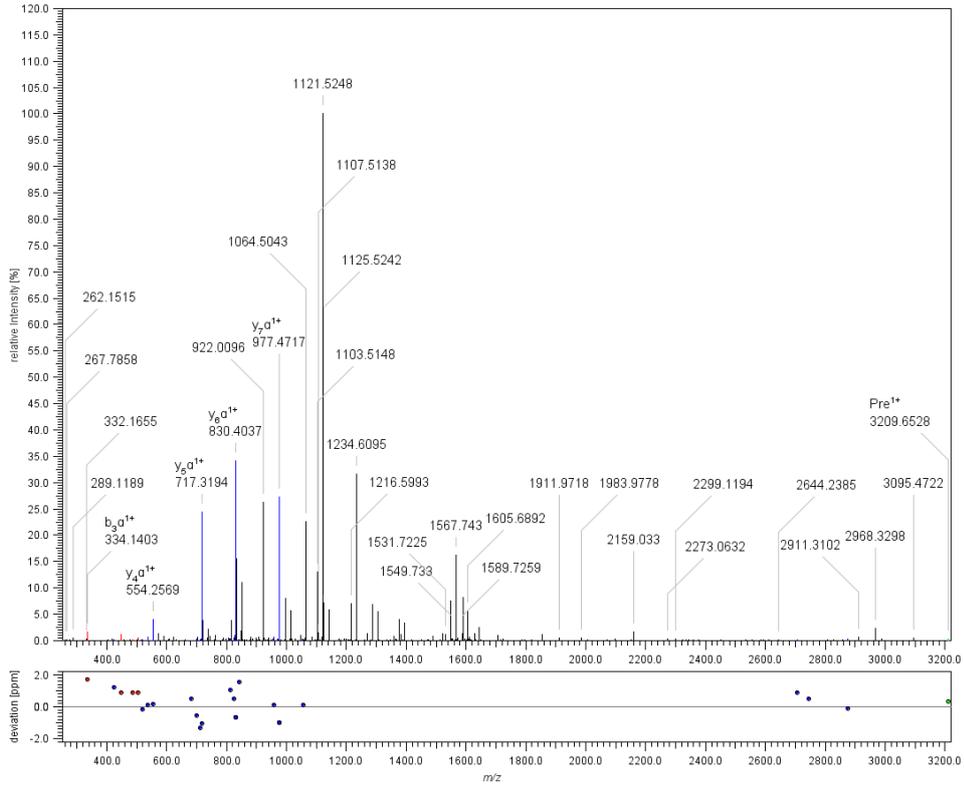
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [LSQK] (S2) Score (10)  
 Scan: 394 (-BSA from 218 to 221) identified signals (0.076)  
 theor. Mass (M + H+): 1865.0055 Peptide  $\alpha$ : [FPKAEFVEVTK] (K3) intense signals (0.091)  
 meas. Mass (M + H+): 1865.0054 (-BSA from 222 to 232) ion series (0.035)  
 Deviation: -0.06 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 1865.00537447638 hits/possible ions (0.058)  
 Charge: +1



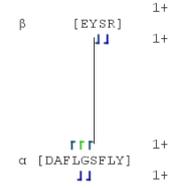
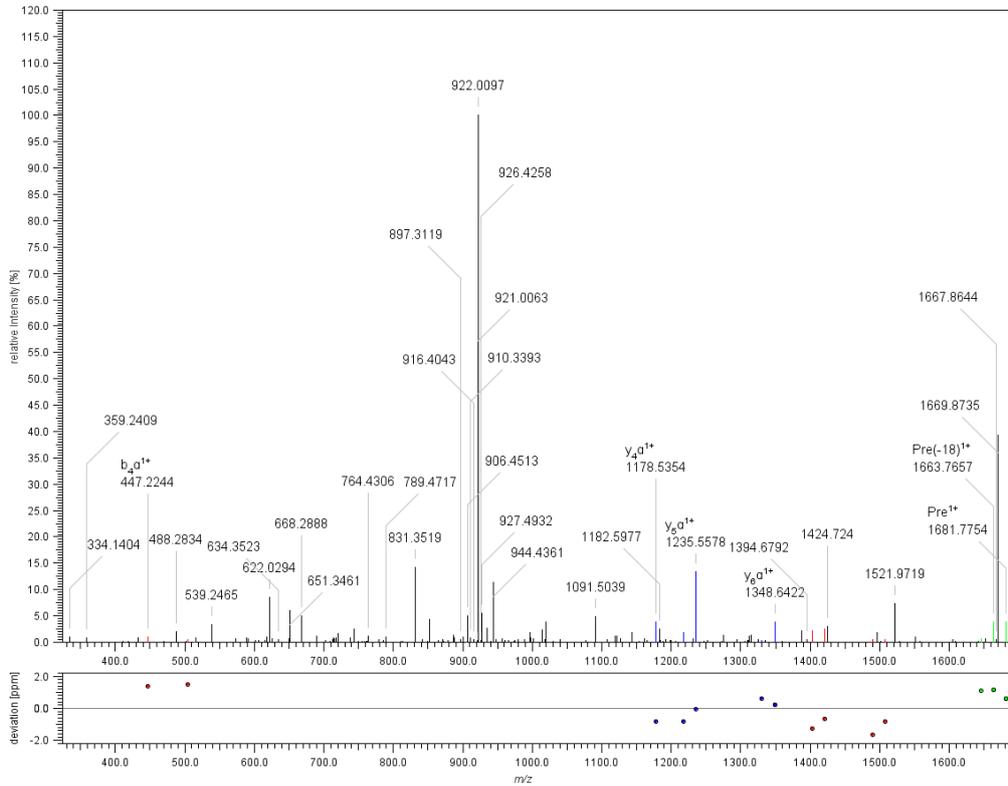
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [SHBIAEVEK] (S1) Score (18)  
 Scan: 492 (-BSA from 286 to 294) identified signals (0.02)  
 theor. Mass (M + H+): 3625.7037 Peptide  $\alpha$ : [DAIPENLPLTADFAEDKDVBK] (T11) intense signals (0.091)  
 meas. Mass (M + H+): 3625.7035 (-BSA from 295 to 316) ion series (0.042)  
 Deviation: -0.03 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 3625.70353258908 hits/possible ions (0.056)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Scan: 554  
 theor. Mass (M + H+): 3209.6517 meas. Mass (M + H+): 3209.6536 Deviation 0.57 ppm m/z: 3209.6535945901 Charge: +1  
 Peptide  $\beta$ : [LKHLVDEPQNLIK] (K2) (-BSA from 376 to 388)  
 Peptide  $\alpha$ : [DAFLGSEFLYEYSR] (S6) (-BSA from 323 to 335)  
 Crosslinker: DSGnond  
 Score: (76)  
 identified signals: (0.001)  
 intense signals: (0.005)  
 ion series: (0.009)  
 Intensity Ratio: (0.034)  
 hits/possible ions: (0.022)

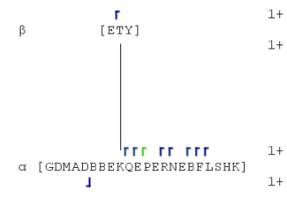
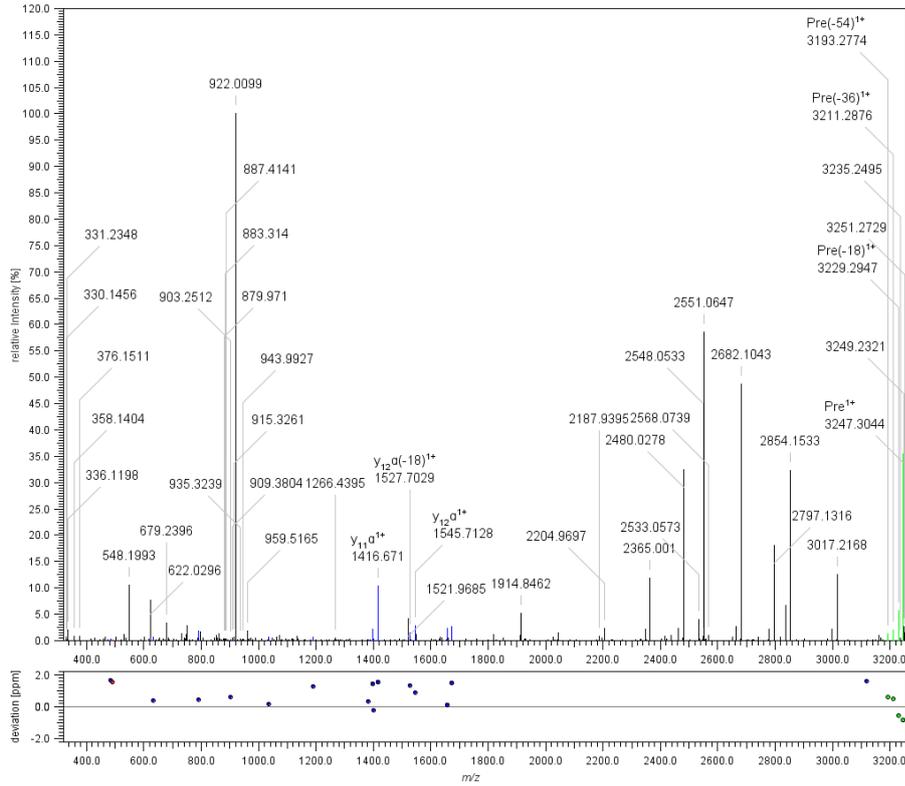


File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Scan: 616  
 theor. Mass (M + H+): 1681.7744 meas. Mass (M + H+): 1681.7753 Deviation 0.5 ppm m/z: 1681.77526785219 Charge: +1  
 Peptide  $\beta$ : [EYSR] (Y2) (-BSA from 332 to 335)  
 Peptide  $\alpha$ : [DAFLGSEFLY] (S6) (-BSA from 323 to 331)  
 Crosslinker: DSGnond  
 Score: (70)  
 identified signals: (0.004)  
 intense signals: (0.014)  
 ion series: (0.001)  
 Intensity Ratio: (0.085)  
 hits/possible ions: (0.022)

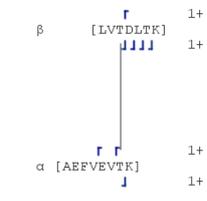
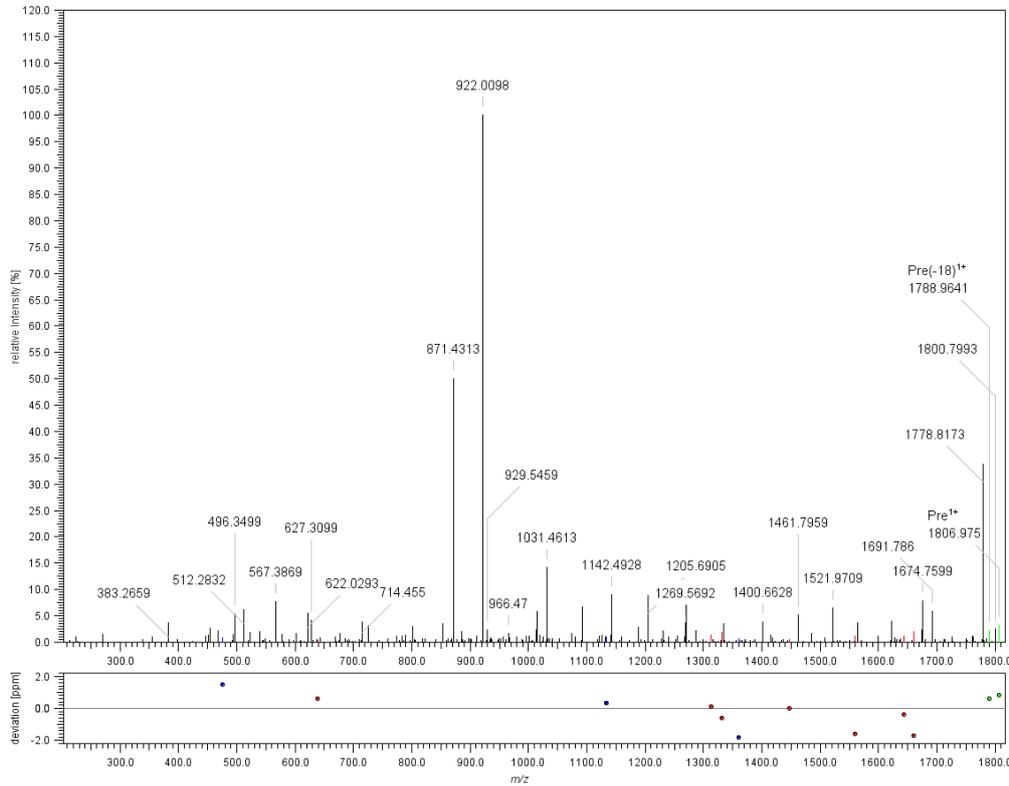




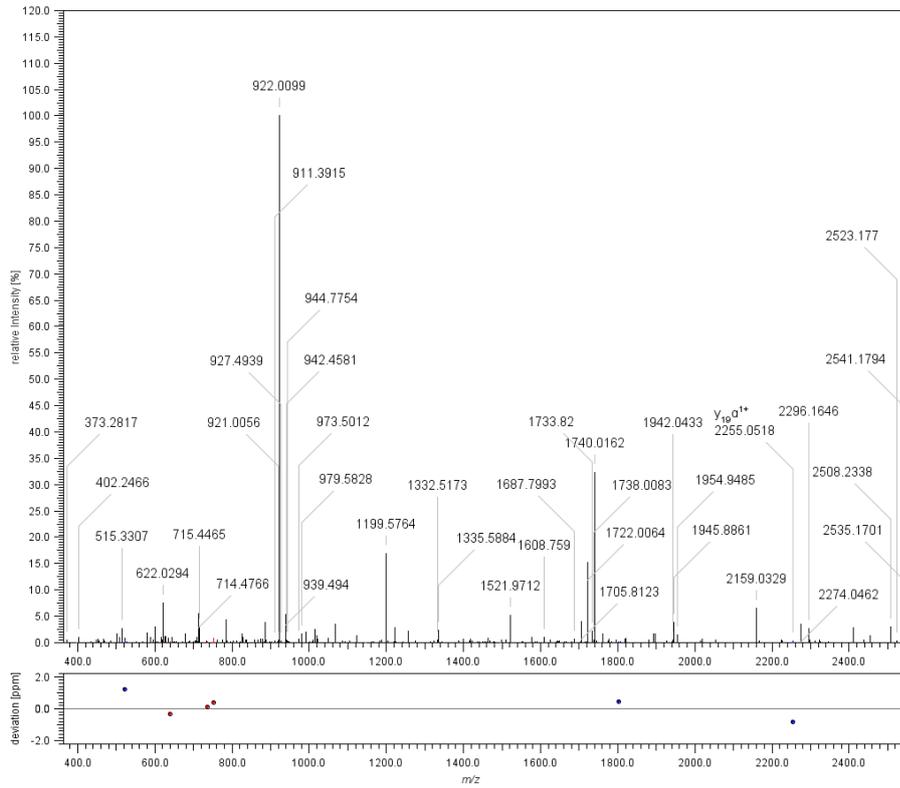
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [ETV] (T2) Score (39)  
 Scan: 266 (-BSA from 82 to 84) identified signals (0.004)  
 theor. Mass (M + H+): 3247.3071 Peptide  $\alpha$ : [GDMADBBEKQEPERNEBFLSHK] (K9) intense signals (0.072)  
 meas. Mass (M + H+): 3247.3076 (-BSA from 85 to 106) ion series (0.02)  
 Deviation 0.15 ppm Crosslinker: DSGnond Intensity Ratio (0.075)  
 m/z: 3247.3076176841 hits/possible ions (0.033)  
 Charge: +1



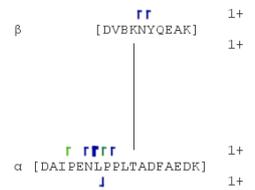
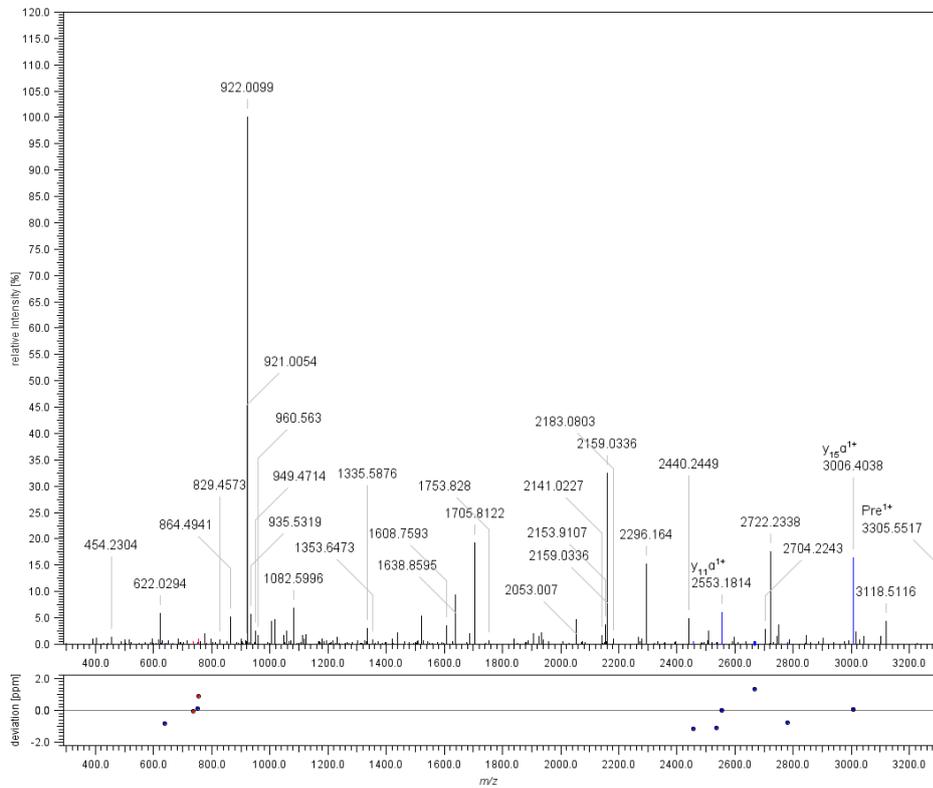
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [LVTDLTK] (T3) Score (29)  
 Scan: 654 (-BSA from 233 to 239) identified signals (0.008)  
 theor. Mass (M + H+): 1806.9735 Peptide  $\alpha$ : [AEFVEVTK] (T7) intense signals (0.091)  
 meas. Mass (M + H+): 1806.974 (-BSA from 225 to 232) ion series (0.044)  
 Deviation 0.24 ppm Crosslinker: DSGnond Intensity Ratio (0.091)  
 m/z: 1806.97395921773 hits/possible ions (0.024)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [DAIPENLPLLTADFAEDK] (T11) Score (12)  
 Scan: 516 (-BSA from 295 to 316) identified signals (0.067)  
 theor. Mass (M + H+): 2554.2018 Peptide -1 (K18) intense signals (0.091)  
 meas. Mass (M + H+): 2554.201 (intrapep. from 0 to 0) ion series (0.03)  
 Deviation: -0.28 ppm Crosslinker: DSGnond Intensity Ratio (0.081)  
 m/z: 2554.20101597664 hits/possible ions (0.052)  
 Charge: +1



File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [DVBKNIYQEA] (K4) Score (34)  
 Scan: 468 (-BSA from 313 to 322) identified signals (0.019)  
 theor. Mass (M + H+): 3305.5518 Peptide  $\alpha$ : [DAIPENLPLLTADFAEDK] (T11) intense signals (0.048)  
 meas. Mass (M + H+): 3305.5512 (-BSA from 295 to 312) ion series (0.01)  
 Deviation: -0.17 ppm Crosslinker: DSGnond Intensity Ratio (0.068)  
 m/z: 3305.551246672 hits/possible ions (0.05)  
 Charge: +1

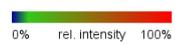
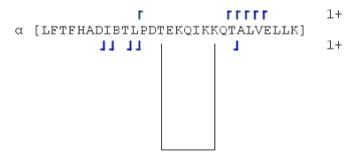
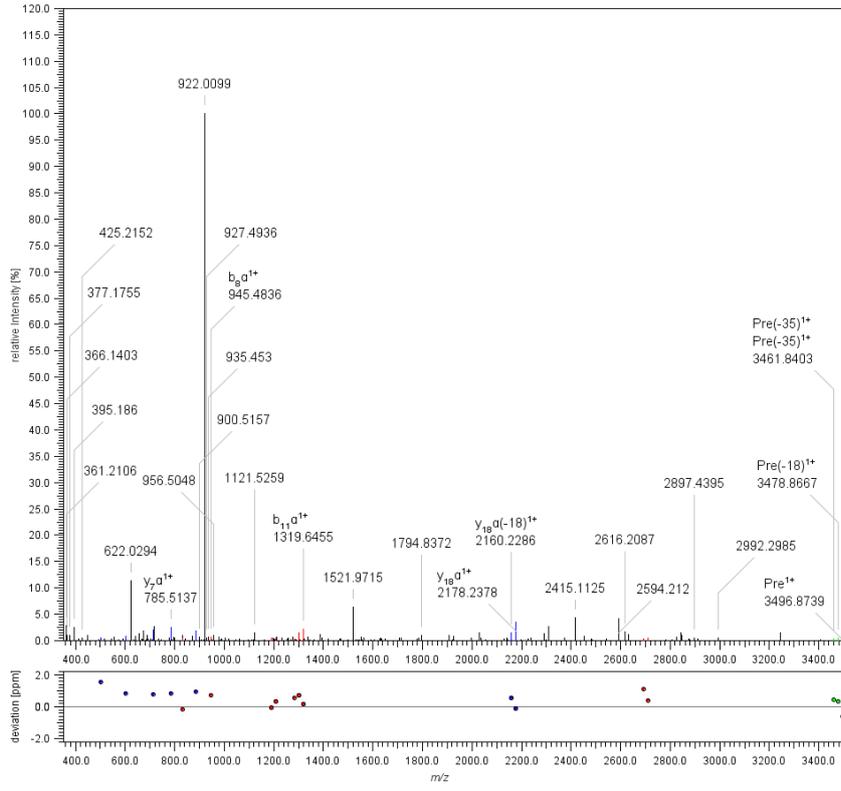




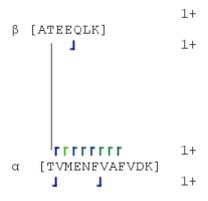
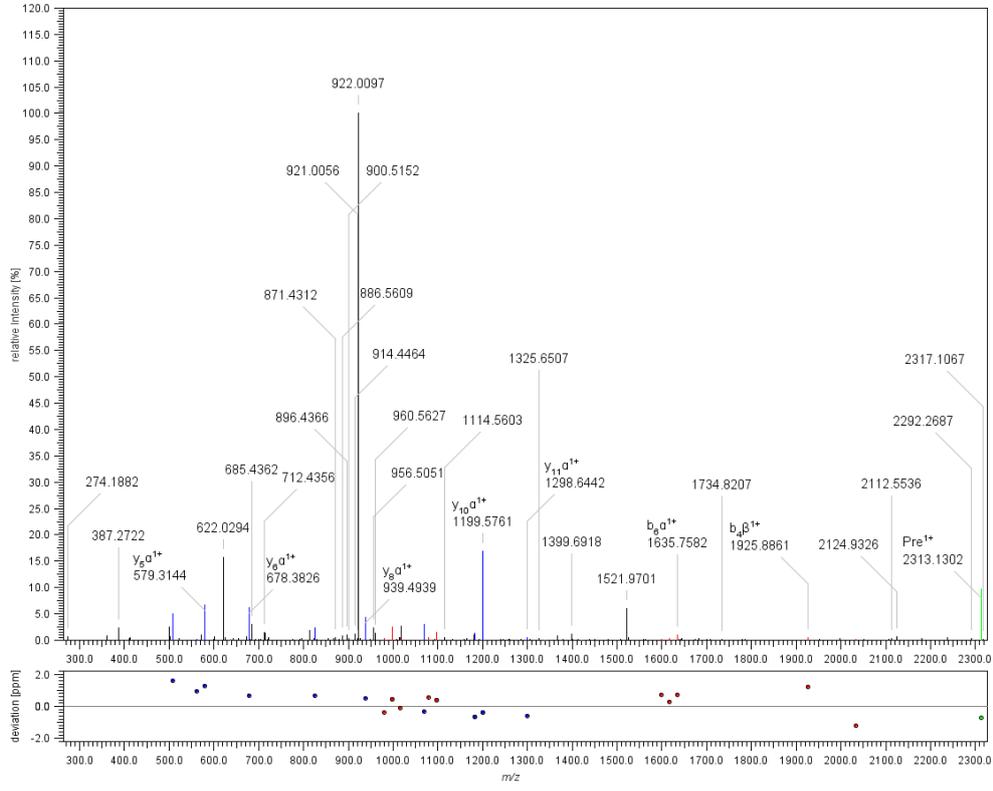




File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\alpha$ : [LFTFHADIBTLPDTEKQIKKOTALVELLK] (T2) Score (67)  
 Scan: 642 (-BSA from 505 to 533) identified signals (0.001)  
 theor. Mass (M + H+): 3496.876 Peptide -1 (K20) intense signals (0.091)  
 meas. Mass (M + H+): 3496.8764 (intrap. from 0 to 0) ion series (0.002)  
 Deviation 0.12 ppm Crosslinker: DSGnond Intensity Ratio (0.049)  
 m/z: 3496.87641311003 hits/possible ions (0.03)  
 Charge: +1



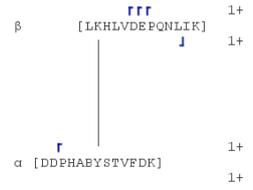
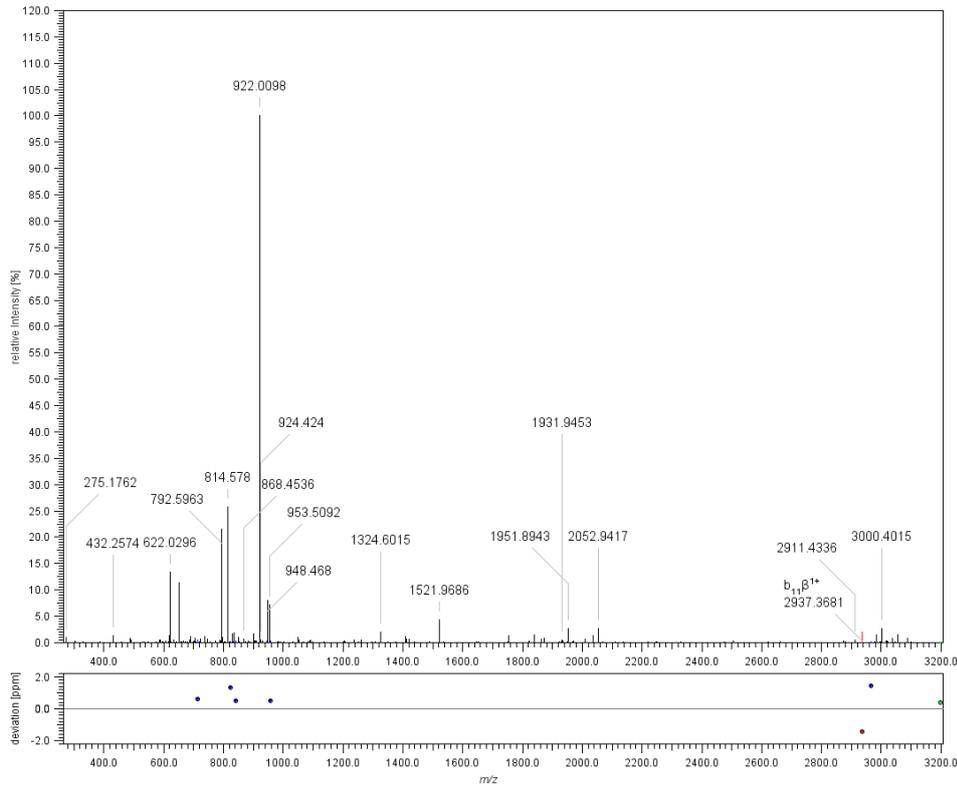
File: D:\DATA\... 2018\BSA\_X3\_11134.zhrs Peptide  $\beta$ : [ATEEQLK] (T2) Score (98)  
 Scan: 756 (-BSA from 538 to 544) identified signals (0.0)  
 theor. Mass (M + H+): 2313.1319 Peptide  $\alpha$ : [TVMENFVAFVDRK] (T1) intense signals (0.002)  
 meas. Mass (M + H+): 2313.1296 (-BSA from 545 to 556) ion series (0.034)  
 Deviation -0.99 ppm Crosslinker: DSGnond Intensity Ratio (0.006)  
 m/z: 2313.12960766344 hits/possible ions (0.016)  
 Charge: +1



File: D:\DATA... 2018BSA\_X3\_11134.zhrs  
 Scan: 386  
 theor. Mass (M + H+): 3196.5619  
 meas. Mass (M + H+): 3196.5647  
 Deviation 0.87 ppm  
 m/z: 3196.56470745254  
 Charge: +1

Peptide  $\beta$ : [LKHLVDEPQNLIK] (K2)  
 (-BSA from 376 to 388)  
 Peptide  $\alpha$ : [DDPHABYSTVFQK] (Y7)  
 (-BSA from 363 to 375)  
 Crosslinker: DSGnond

Score (8)  
 identified signals (0.061)  
 intense signals (0.091)  
 ion series (0.054)  
 intensity Ratio (0.091)  
 hits/possible ions (0.065)



**Table S1:** StavroX identification of BSA cross-linked peptides prepared with cross-linking mixture of DSG/d6-BS2G and d6-DSG/BS2G. All listed cross-links were common for both sample triplicates. However, only 39 of them were quantified by mMass software due to the insufficient intensity of {0–K12 cross-link.

Entry	XL a.a.	XL a.a.	Ca-Ca Distance (Å)
1	{0	K12	19.543
2	K114	T121	16.189
3	K114	K116	6.097
4	K114/K116	K431	19.903/21.274
5	K132	K136	6.039
6	K136	Y139	5.112
7	K204	K465	13.237
8	K211	K242	9.735
9	K211	K350	13.537
10	K211	K232	11.021
11	K221	K294	4.292
12	K239	K242	5.084
13	K273	K294	7.675
14	K273	K275	5.738
15	K275	K285	10.23
16	K280	S286	8.745
17	K294	K439	18.376
18	K312	K316	8.686
19	K322	K350	11.985
20	K350	T355	8.745
21	K375	K377	5.637
22	K396	K544	14.584
23	K439	Y451	13.919
24	K474	S488	13.166
25	K499	K504	13.393
26	K520	K524	6.418
27	K524	K544	14.335
28	K93	S104	14.008
29	S201	K350	14.465
30	S328	Y333	8.495
31	S58	S65	14.243
32	S65	T68	5.318
33	T231	T235	6.34
34	T305	K316	16.501
35	T466	K471/K474	13.722/14.415
36	T47	T52	8.778
37	T473	T477	6.059
38	T518/K520	K524	10.142/6.418
39	T539	T545	9.774
40	Y333/S334	K377	11.918/14.025

**Table S2:** StavroX identification of BSA cross-linked peptides prepared with non-labeled DSG (A), BS2G (B) and equimolar mixture of DSG/BS2G (C) cross-linker. All listed cross-links were common for each cross-linked sample triplicate.

**A) DSG**

<b>Entry</b>	<b>XL a.a.</b>	<b>XL a.a.</b>	<b>Ca-Ca Distance (Å)</b>
1	{0	K12	19.543
2	K114	T121	16.189
3	K114	K116	6.097
4	K114/K116	K431	19.903/21.274
5	K132	K136	6.039
6	K136	Y139	5.112
7	K204	K465	13.237
8	K204	K350	16.426
9	K211	K242	9.735
10	K211	K239	8.958
11	K211	K350	13.537
12	K211	K232	11.021
13	K221	K294	4.292
14	K239	K242	5.084
15	K273	K275	5.738
16	K275	K285	10.23
17	K275	K280	9.923
18	K280	S286	8.745
19	K312	K316	8.686
20	K350	T355	8.745
21	K350	Y352	5.308
22	K375	K377	5.637
23	K396	K544	14.584
24	K413	S418	12.72
25	K413	K535/K537	13.277/11.363
26	K439	Y451	13.919
27	K474	S488	13.166
28	K499	K504	13.393
29	K504	T507	5.397
30	K523	K524	3.772
31	K524	K544	14.335
32	K93	S104	14.008
33	S109	K116	18.685
34	S201	K204	5.526
35	S328	Y333/S334	8.495/9.854
36	S334	K377	14.025
37	S469	K471	5.238
38	S58	S65	14.243
39	S65	T68	5.318
40	T231	T235	6.34
41	T305	K316	16.501
42	T305	K312	11.794
43	T438	K439	3.809
44	T466	K471/K474	13.722/14.415
45	T473	T477	6.059
46	T539	T545	9.774

47	T83	K93	19.03
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**B) BS2G**

<b>Entry</b>	<b>XL a.a.</b>	<b>XL a.a.</b>	<b>Ca-Ca Distance (Å)</b>
1	{0	K12	19.543
2	K114	T121	16.189
3	K114	K116	6.097
4	K114/K116	K431	19.903/21.274
5	K12	K20	12.094
6	K131	K136	8.856
7	K132	K136	6.039
8	K136	Y139	5.112
9	K204	K465	13.237
10	K211	K350	13.537
11	K211	K242	9.735
12	K221	K294	4.292
13	K273	K275	5.738
14	K275	K285	10.23
15	K275	K280	9.923
16	K280	S286	8.745
17	K322	K350	11.985
18	K350	T355	8.745
19	K350	Y352	5.308
20	K375	K377	5.637
21	K377	K388	19.879
22	K396	K544	14.584
23	K413	K535/K537	13.277/11.363
24	K439	Y451	13.919
25	K474	S488	13.166
26	K499	K504	13.393
27	K523	T526	5.406
28	K524	K544	14.335
29	S109	K116	18.685
30	S109	K114	12.882
31	S201	K204	5.526
32	S328	K377	18.538
33	S328	Y333/S334	8.495/9.854
34	S370	K377	13.43
35	S58	S65	14.243
36	T231	T235	6.34
37	T238	K239	3.837
38	T466	K471/K474	13.722/14.415
39	T47	T52	8.778
40	T473	T477	6.059
41	T495	K499	12.579
42	T518	K523	8.731
43	T518/K520	K524	10.142/6.418
44	T539	T545	9.774
45	Y318	K322	4.796
46	Y333/S334	K377	11.918/14.025

C) DSG/BS2G

Entry	XL a.a.	XL a.a.	Ca-Ca Distance (Å)
1	{0	K12	19.543
2	K114	T121	16.189
3	K114	K116	6.097
4	K114/K116	K431	19.903/21.274
5	K12	K20	12.094
6	K132	K136	6.039
7	K136	Y139	5.112
8	K20	K132	11.506
9	K204	K465	13.237
10	K211	K242	9.735
11	K211	K350	13.537
12	K211	K232	11.021
13	K221	K294	4.292
14	K239	K242	5.084
15	K273	K275	5.738
16	K273	K294	7.675
17	K275	K285	10.23
18	K280	S286	8.745
19	K294	K439	18.376
20	K312	K316	8.686
21	K322	K350	11.985
22	K350	T355	8.745
23	K350	Y451	20.017
24	K350	Y352	5.308
25	K362	K524	57.688
26	K362	S370	13.06
27	K375	K377	5.637
28	K396	K544	14.584
29	K431	K439	13.513
30	K439	Y451	13.919
31	K471	K474	5.409
32	K474	S488	13.166
33	K499	K504	13.393
34	K504	T507	5.397
35	K520	K524	6.418
36	K523	K524	3.772
37	K523	T526	5.406
38	K524	K544	14.335
39	K64	S65	3.814
40	K76	T83	13.206
41	K93	S104	14.008
42	S109	K116	18.685
43	S109	K114	12.882
44	S201	K350	14.465
45	S219	K224	8.066
46	S286	T305	35.81
47	S328	K377	18.538
48	S328	Y333	8.495
49	S58	S65	14.243
50	S65	T68	5.318

51	S79	K93	18.069
52	T231	T235	6.34
53	T305	K316	16.501
54	T305	K312	11.794
55	T438	K439	3.809
56	T466	K471/K474	13.722/14.415
57	T47	T52	8.778
58	T473	T477	6.059
59	T477	S488	15.629
60	T495	K499	12.579
61	T518	K523	8.731
62	T518/K520	K524	10.142/6.418
63	T52	K76	20.575
64	T539	T545	9.774
65	T83	K93	19.03
66	Y333/S334	K377	11.918/14.025
67	Y369/S370	K377	13.857/13.430