SUPPORTING INFORMATION

Effect of Copper-Catalyzed Oxidation on the Aggregation of the Islet Amyloid Polypeptide

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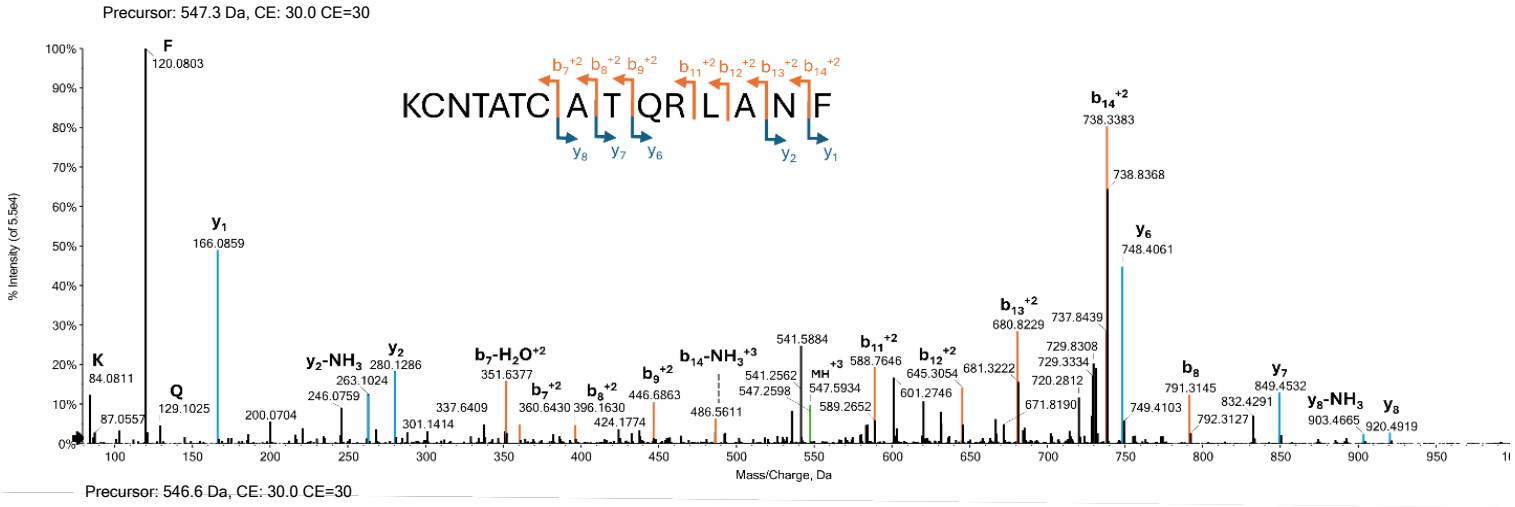
Table S1. Theoretical and experimental monoisotopic m/z values, mass accuracies, and retention times for unmodified and oxidized IAPP peptides digested with α-chymotrypsin. Detected oxidative modifications are indicated in parentheses: +16, +32, +48 and +0.98 correspond to the addition of one oxygen atom, two oxygen atoms, three oxygen atoms and deamidation, respectively.

Peptide	Charge	m/z (exact)	m/z (measured)	Error (ppm)	Retention time (min)
^{13}ANFLVHSSNNF^{23}	+2	625.3013	625.3018	0.8	8.04
^{13}ANFLVHSSNNF^{23} (+16)	+2	633.2996	633.2998	0.2	7.28
^{13}ANFLVHSSNNF^{23} (+32)	+2	641.2974	641.2953	-3.3	10.12
^{15}FLVHSSNNF^{23}	+2	532.7610	532.7620	1.8	7.20
^{15}FLVHSSNNF^{23} (+16)	+2	540.7598	540.7597	-0.1	8.88
^{16}LVHSSNNFGAIL^{27}	+3	424.5633	424.5643	2.2	9.04
^{16}LVHSSNNFGAIL^{27} (+16) / (+0.98)	+2	644.8296	644.8316	3.1	9.28
^{16}LVHSSNNFGAIL^{27} (+16)	+2	644.3383	644.3388	0.8	8.98
^{16}LVHSSNNFGAIL^{27} (+32)	+2	652.3370	652.3352	-2.8	10.81
^{16}LVHSSNNFGAIL^{27} (+48)	+2	660.3350	660.3342	-1.3	6.96
^{17}VHSSNNF^{23}	+2	402.6874	402.6868	-1.6	3.13
^{17}VHSSNNF^{23} (+16)	+2	410.6830	410.6835	1.1	4.15
^{17}VHSSNNFGAIL^{27}	+2	579.8001	579.7995	-1.1	7.20
^{17}VHSSNNFGAIL^{27} (+16)	+2	587.7965	587.7955	-1.7	8.17
^{17}VHSSNNFGAIL^{27} (+32)	+2	595.7938	595.7938	-0.1	9.94
^{17}VHSSNNFGAIL^{27} (+48)	+2	603.7909	603.7902	-1.1	6.18
^{24}GAILSSTNVGSNTY^{37} (0.98)	+2	691.8449	691.8470	-3.0	7.57
^{24}GAILSSTNVGSNTY^{37} (+32) / (+0.98)	+2	699.8465	707.8419	-2.0	7.89

A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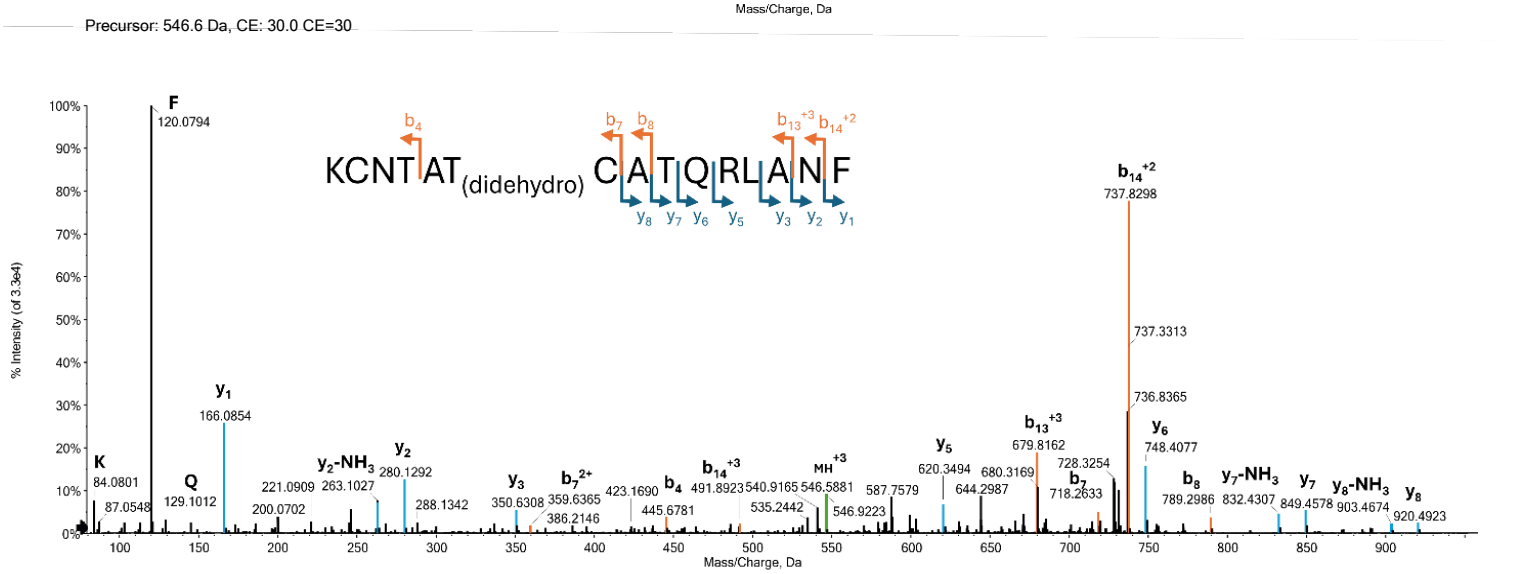
KCNTATCATQRLANF
% Intensity (of 5.5e4)
Mass/Charge, Da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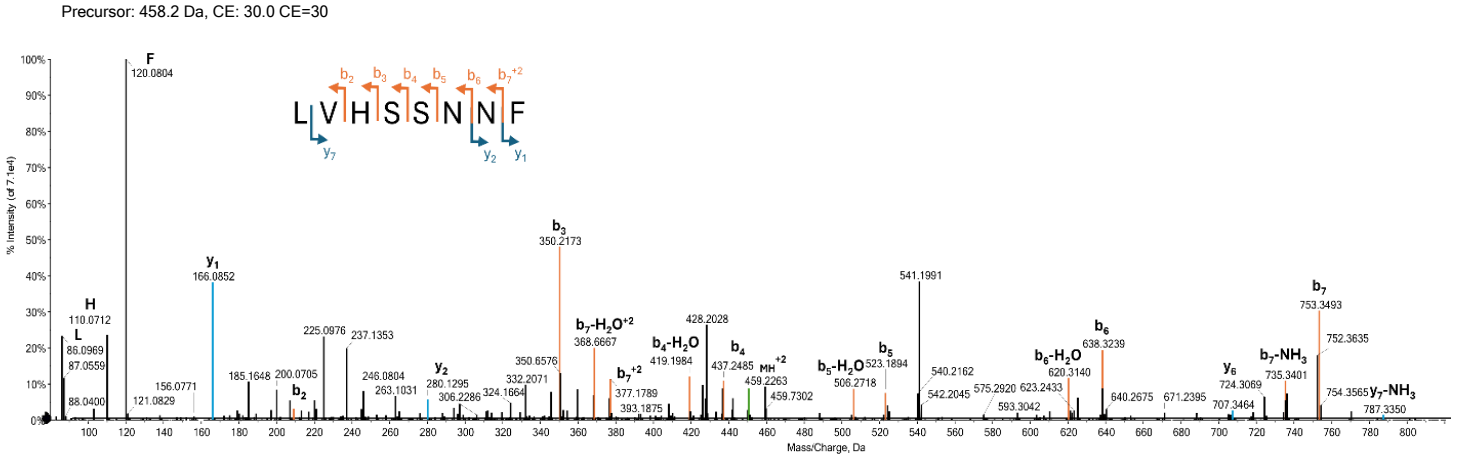
Mass/Charge, Da

B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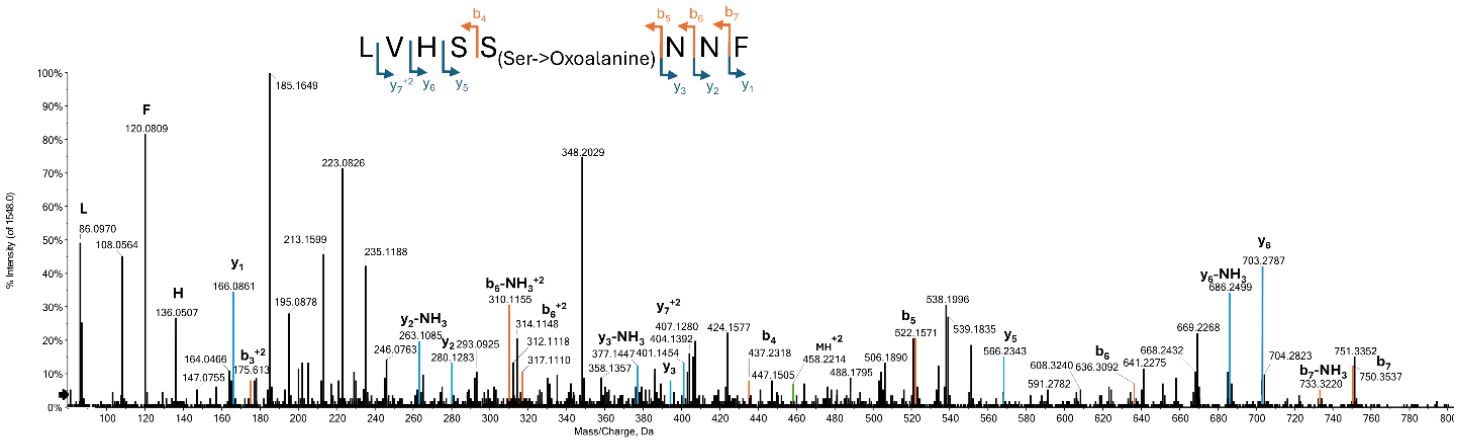
Mass/Charge, Da



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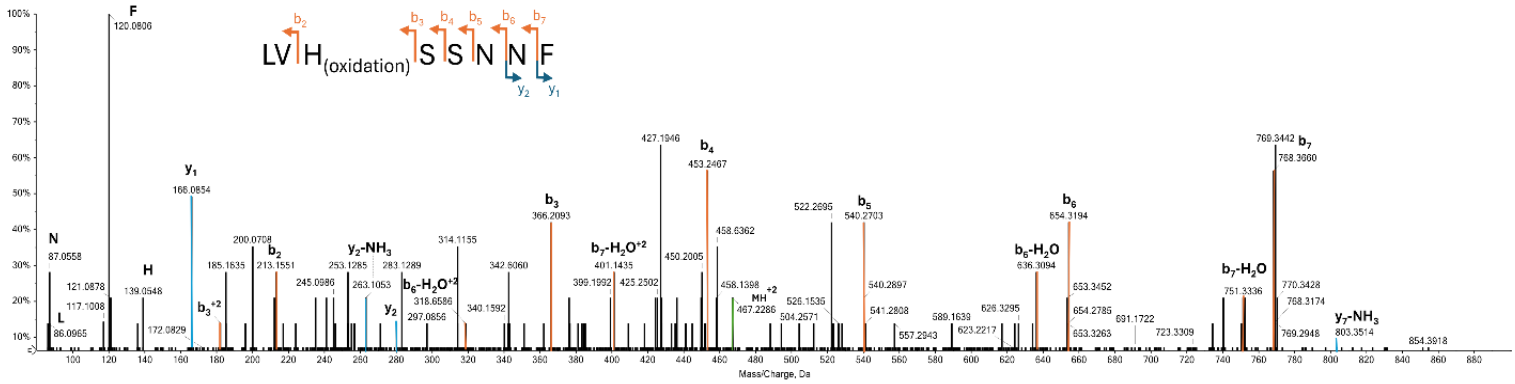

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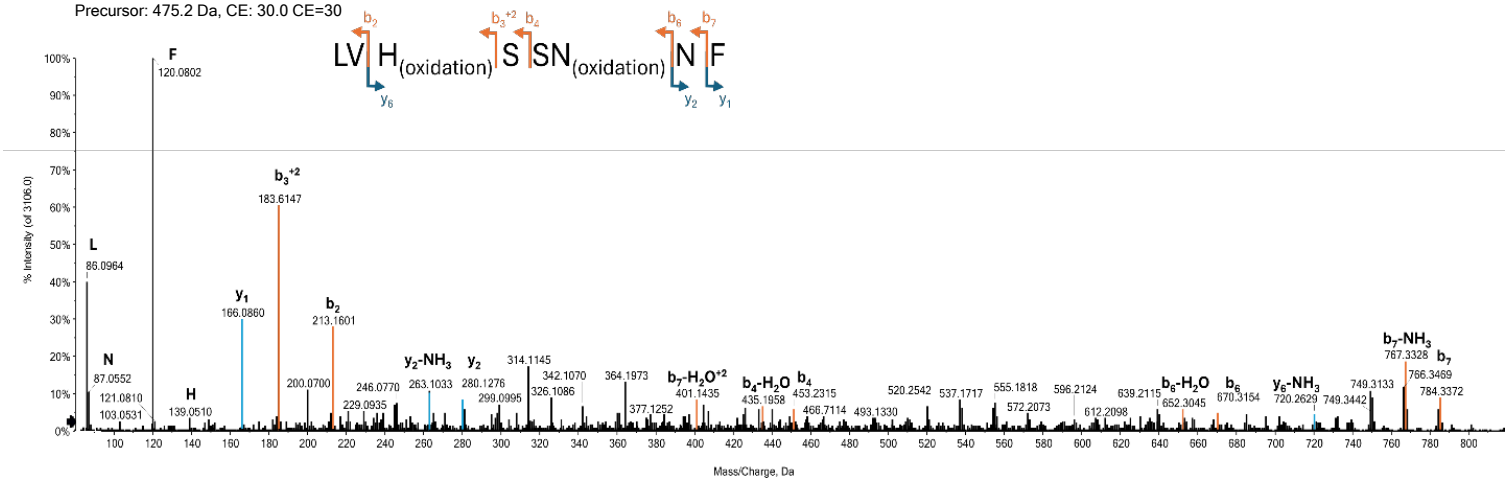

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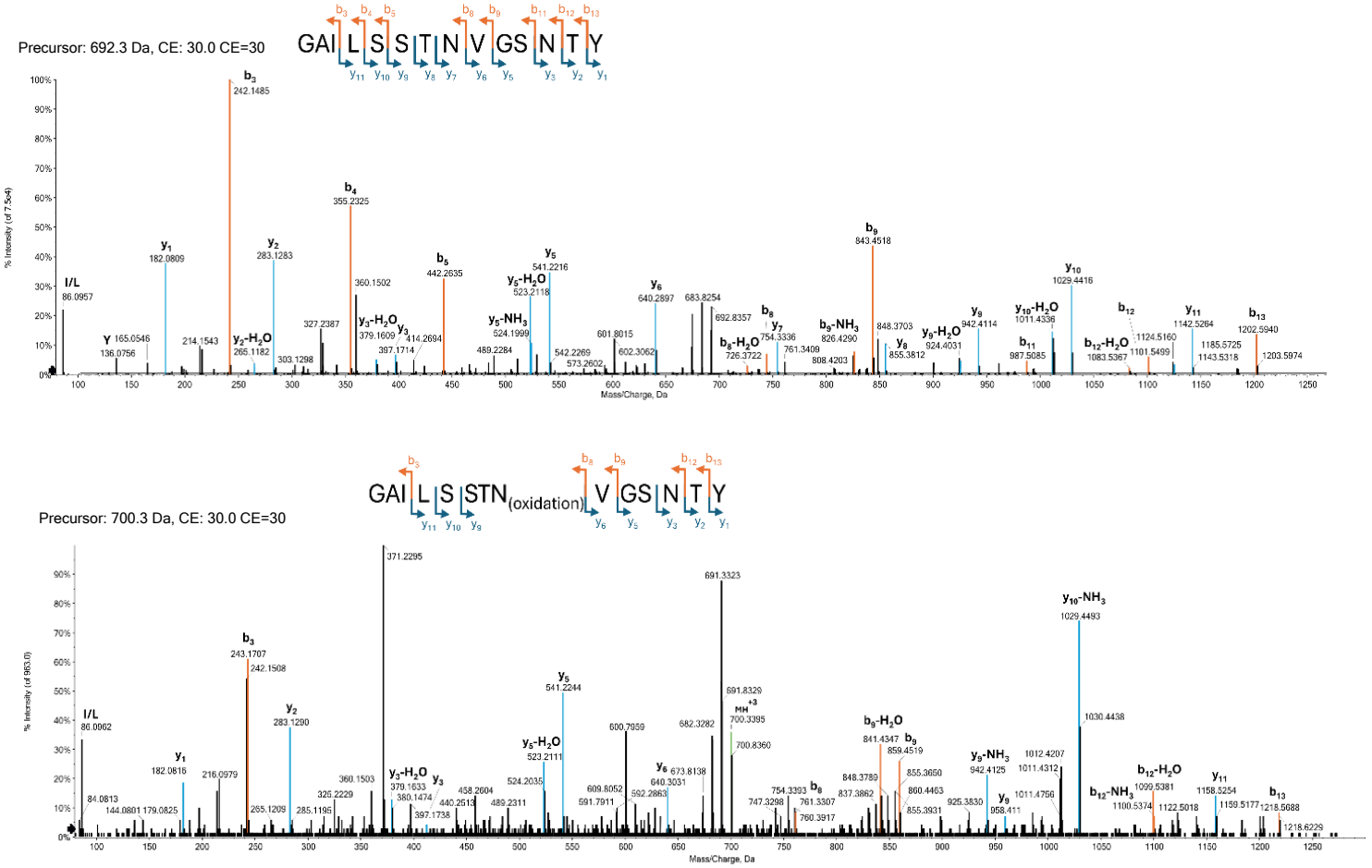


Figure S1. Identification of chymotryptic IAPP oxidation sites by LC-MS/MS. Annotated high-resolution MS/MS spectra of (**A**) ^{1}KCNTATCATQRLANF^{15}, (**B**) ^{16}LVHSSNNF^{23} and (**C**) ^{24}GAILSSTNVGSNTY^{37} peptides in their native and oxidized forms. Series of b- and y- ions are labeled in orange and blue, respectively. Precursor ions are highlighted in green and indicated above the spectra when detected. Spectra were acquired in CID mode (collision energy: 30 ± 10 V; cycle time: 1.05 s) with precursor charge states of z =+3 for IAPP$_{(1-15)}$ and z =+2 for IAPP$_{(16-23)}$ and IAPP$_{(24-37)}$. Fragment assignments were made with a mass tolerance of ± 5 ppm.

Table S2. Parameters obtained from sigmoidal fits using Boltzmann equation for fitted curves of IAPP as the means of at least four independent experiments performed in triplicates.

	Fluorescence (Y_{max})	**Half time ($t_{1/2}$)**	**Lag time (t_{lag})**
IAPP	3.27×10^6	3.561 ± 0.169	3.132
IAPP + Ascorbate	3.08×10^6	5.525 ± 0.20	3.433
IAPP + Cu^{2+}	1.24×10^6	8.104 ± 0.108	4.273
^{ox}IAPP	1.34×10^5	13.18 ± 0.2435	13.691

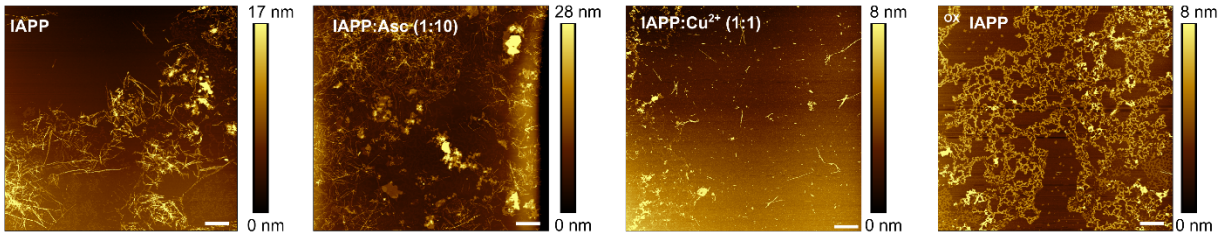
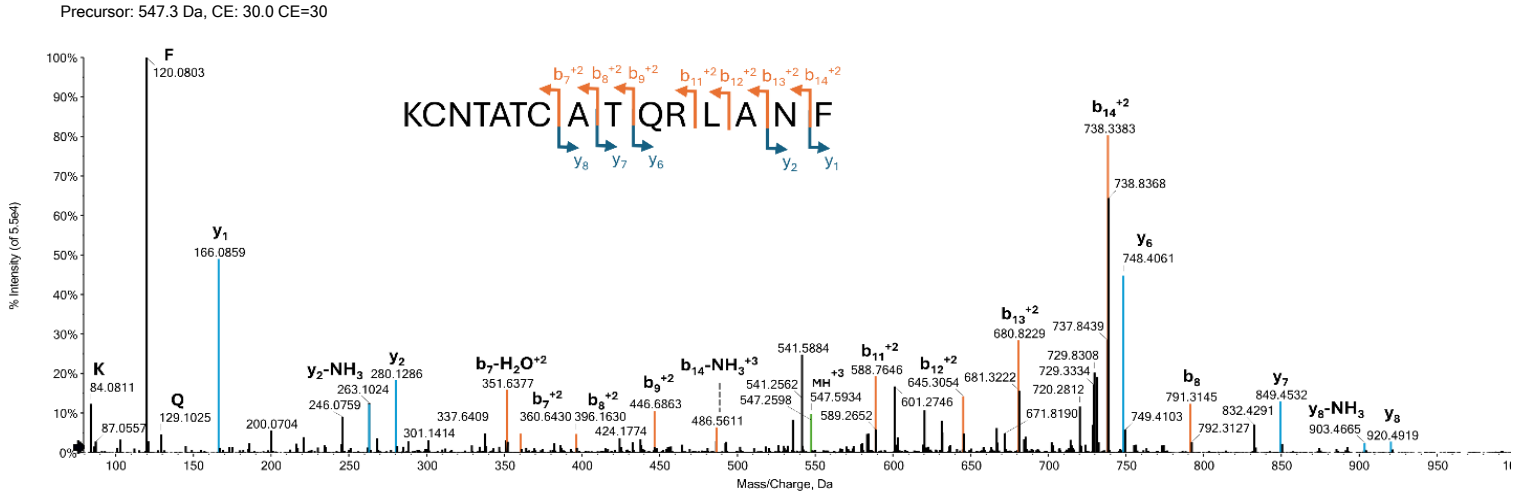


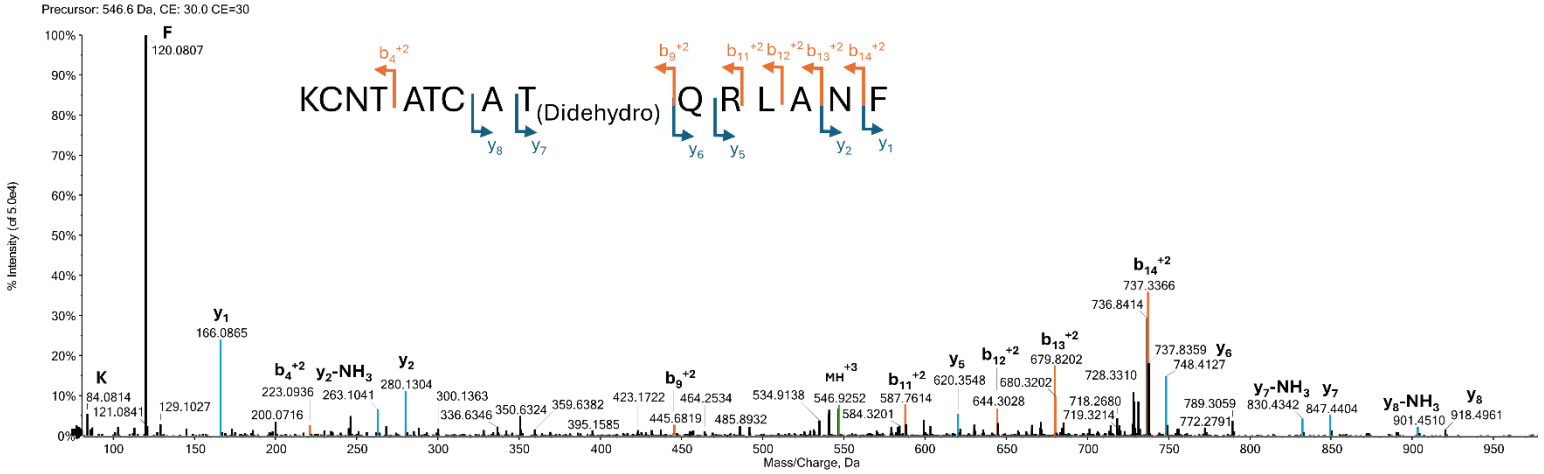
Figure S2. AFM images of IAPP (60 μM) in the presence, or absence, of copper and ascorbate, after pre-incubation under quiescent conditions for 24 h prior to analysis. Scale bar is 1 μm and scan frame is 10 μm × 10 μm.

Table S3. Theoretical and experimental monoisotopic m/z values, mass accuracies, and retention times for native [H18A]IAPP and oxidized [H18A]IAPP peptides digested with α-chymotrypsin. Detected oxidative modifications are indicated in parentheses, where –2, +16, and +32 respectively correspond to the loss of two hydrogen atoms, the addition of one oxygen atom, and the addition of two oxygen atoms.

Peptide	Charge	m/z (exact)	m/z (measured)	Error (ppm)	Retention time (min)
^{1}KCNTATCATQRLANF^{15}	+3	547.2613	547.2636	4.2	7.27
^{1}KCNTATCATQRLANF^{15} (-2)	+3	546.5895	546.5895	0	6.72
^{1}KCNTATCATQRLANF^{15} (+16)	+3	552.5930	552.5938	1.4	5.63/ 6.0/ 6.72/ 7.19
^{1}KCNTATCATQRLANF^{15} (+32)	+3	557.9246	557.9235	-1.97	6.17
^{16}LVASSNNF^{23}	+2	426.2170	426.283	3.05	6.39
^{16}LVASSNNF^{23} (-2)	+2	425.2092	425.2103	2.58	4.95/ 5.35/ 5.81
^{16}LVASSNNF^{23} (+16)	+2	434.2144	434.2138	-1.38	5.73
^{24}GAILSSTNVGSNTY^{37}	+2	692.3416	692.3427	1.58	7.98
^{24}GAILSSTNVGSNTY^{37} (-2)	+2	691.8378	691.8372	-0.86	6.59/ 6.93/ 7.03
^{24}GAILSSTNVGSNTY^{37} (+16)	+2	700.3391	700.3386	-0.71	7.58

A


Precursor: 547.3 Da, CE: 30.0 CE=30
KCNTATCATQRLANF
% Intensity (of 5.5e4)
Mass/Charge, Da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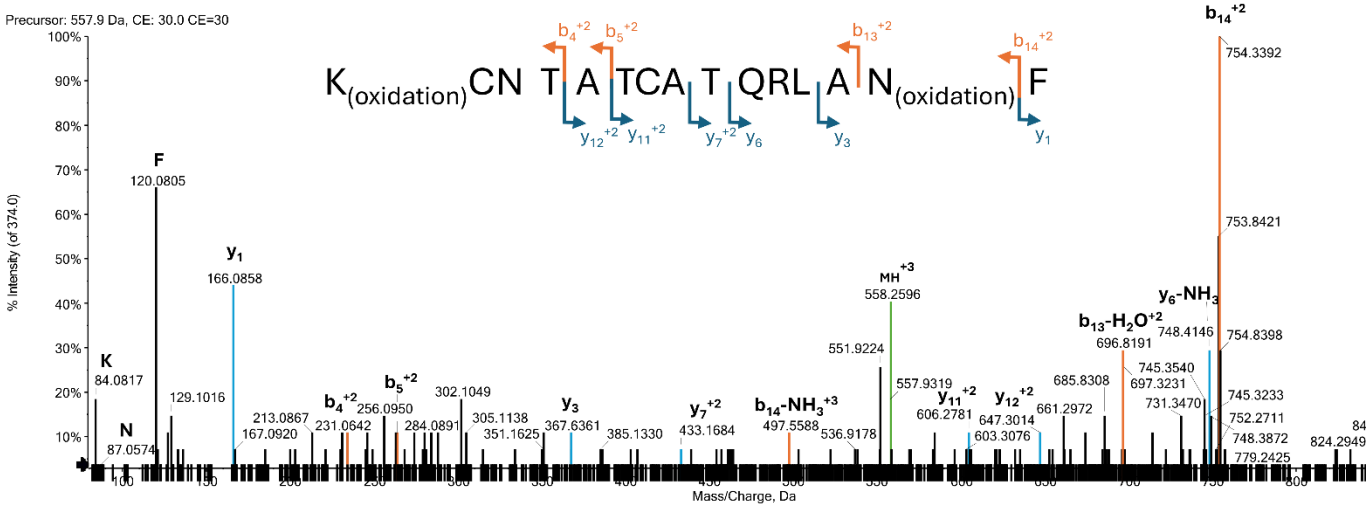
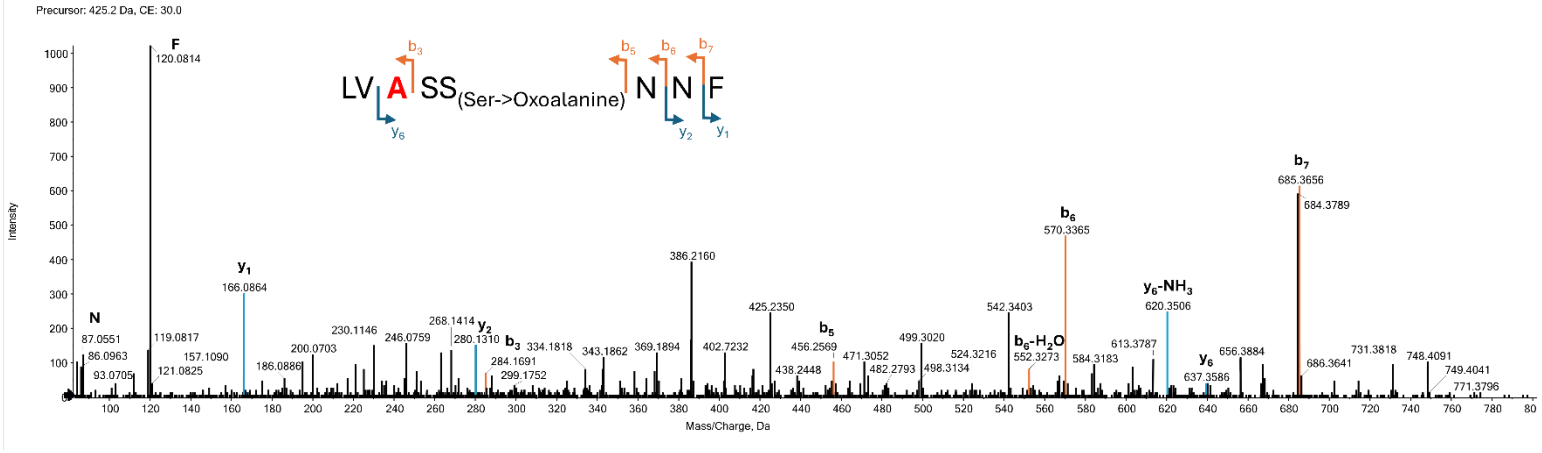
KCNTATCAT(Didehydro)QRLANF
% Intensity (of 5.0e4)
Mass/Charge, Da


Precursor: 557.9 Da, CE: 30.0 CE=30
K(oxidation)CNTATCATQRLAN(oxidation)F
% Intensity (of 374.0)
Mass/Charge, Da

B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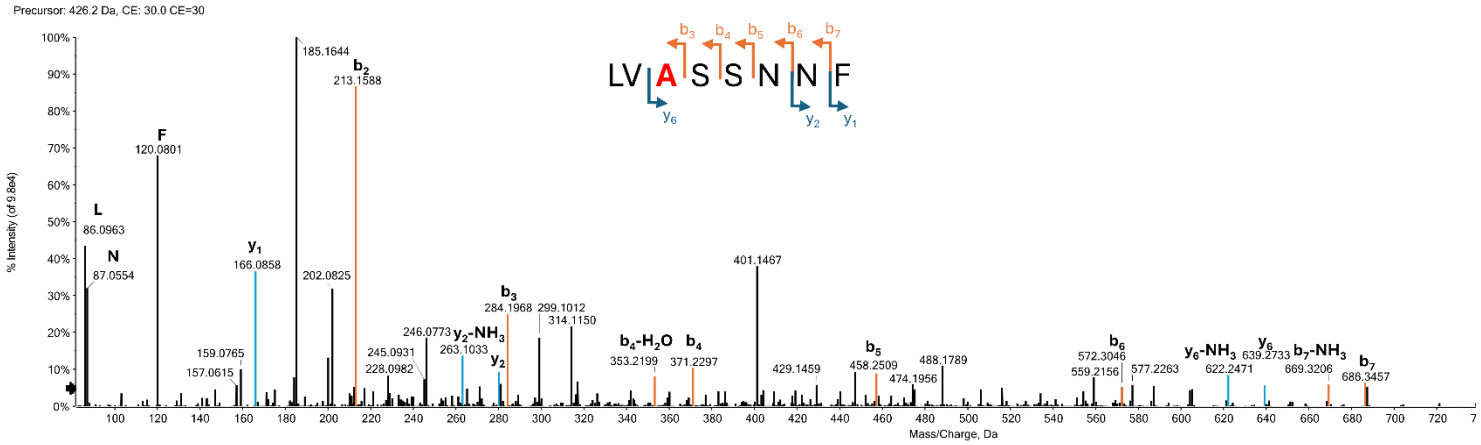
Intensity
Mass/Charge, Da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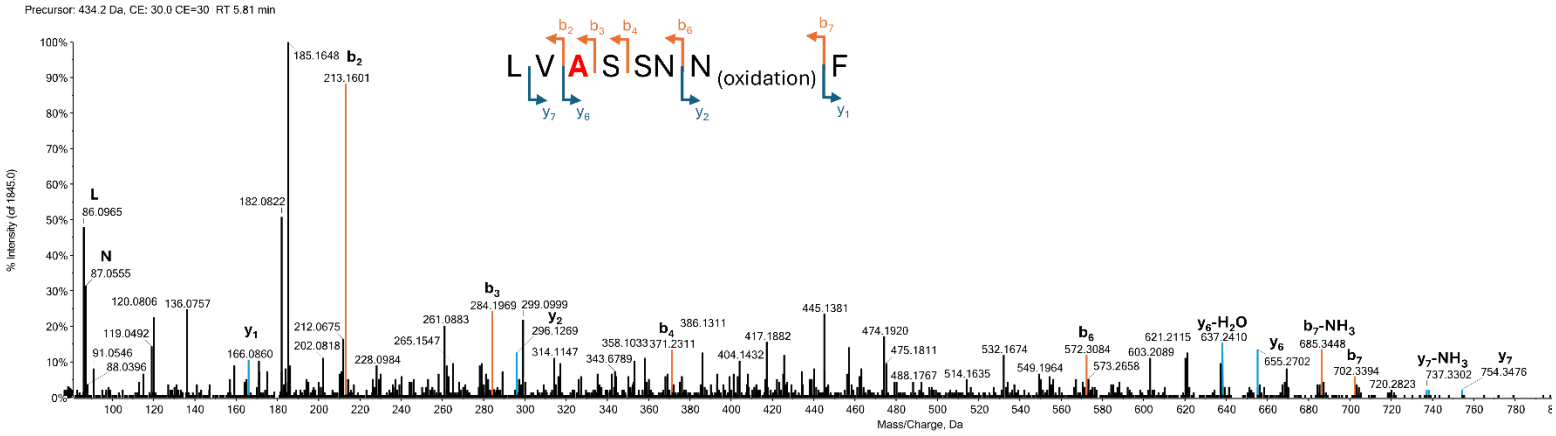
LVASSNNF
% Intensity (of 9.8e4)
Mass/Charge, Da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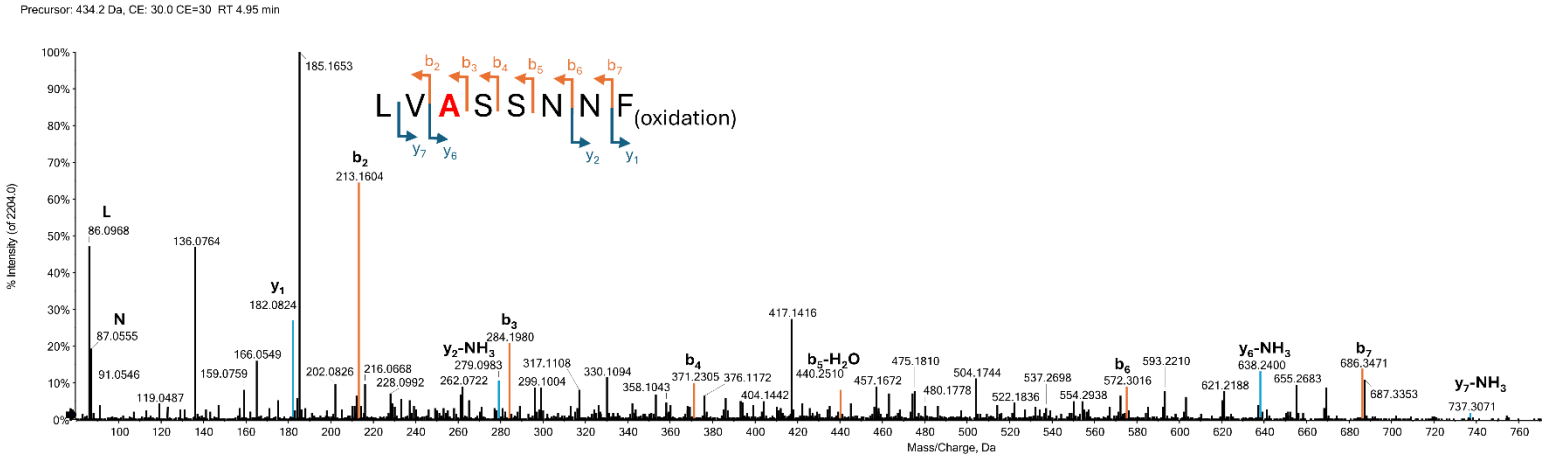
LVASSNN(oxidation)F
% Intensity (of 1845.0)
Mass/Charge, Da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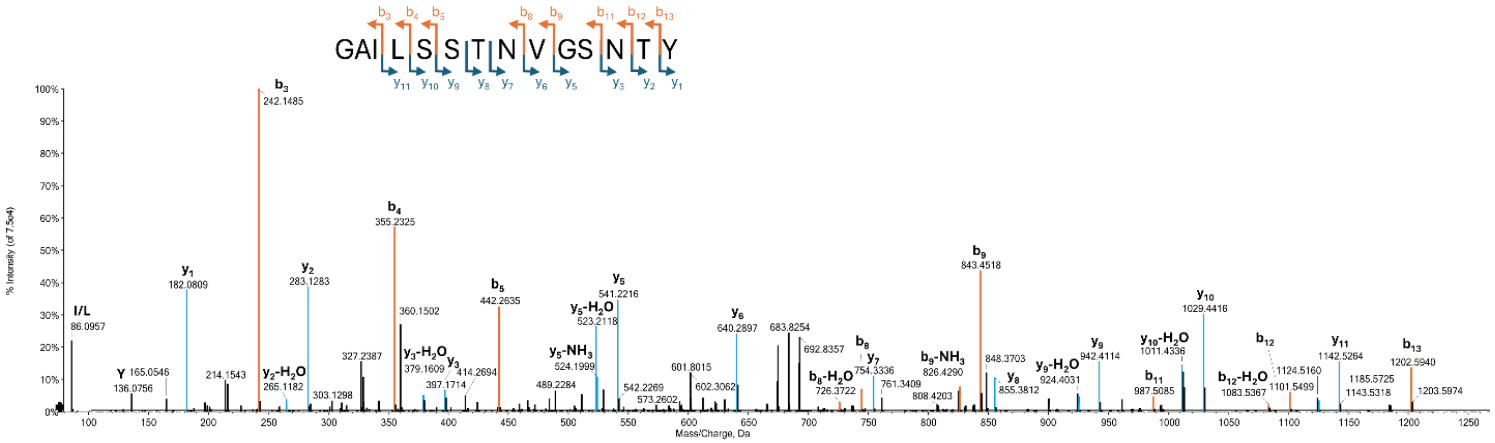
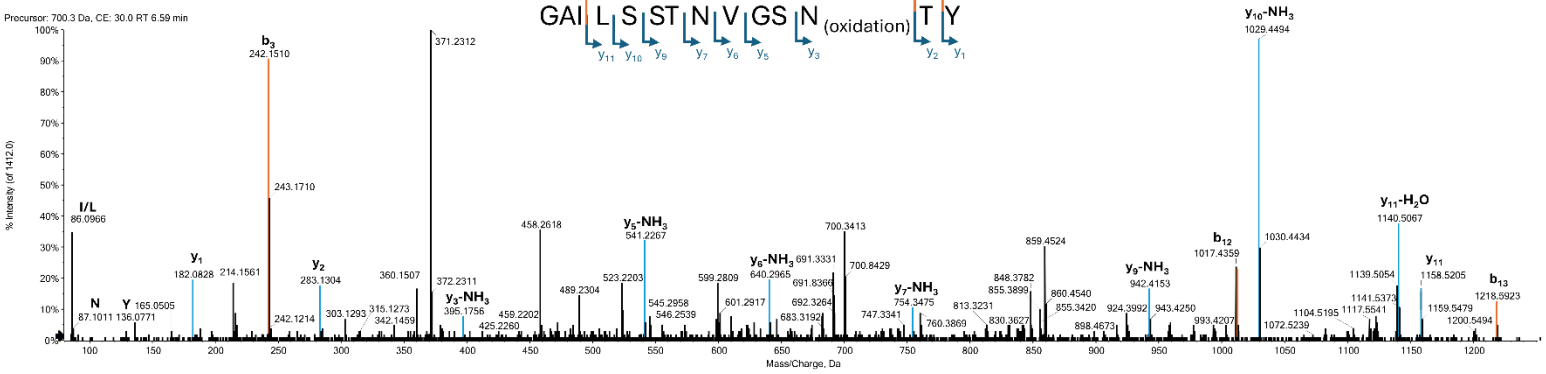
LVASSNNF(oxidation)
% Intensity (of 2204.0)
Mass/Charge, Da

C


GAILSSTNVGSNTY
% Intensity (of 7.5x4)
Mass/Charge, Da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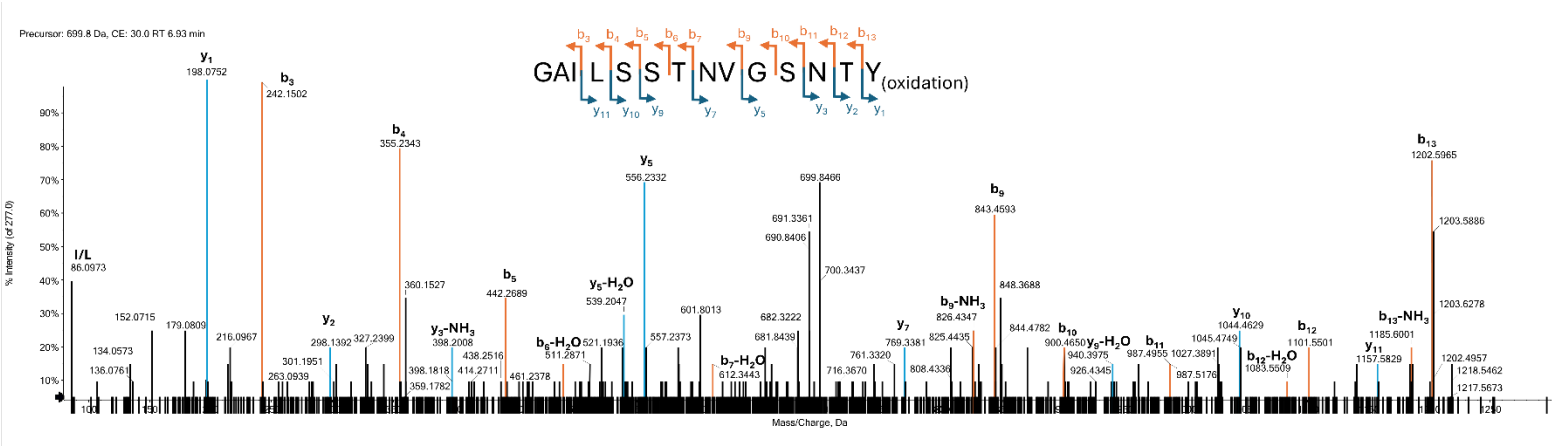
% Intensity (of 1412.0)
Mass/Charge, Da



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