Electronic Supplementary Material (ESI) for Analyst.

Table S1. Transitions Used for MRM Analysis

Q1	Q3	name	DP	CE
426.750527	694.424636	SASLHLPK.+2y6.light	62.2	20.2
426.750527	494.308544	SASLHLPK.+2y4.light	62.2	24.2
426.750527	357.249632	SASLHLPK.+2y3.light	62.2	25.2
426.750527	496.251423	SASLHLPK.+2b5.light	62.2	24.2
426.750527	609.335487	SASLHLPK.+2b6.light	62.2	21.2
601.991497	827.462144	LQHLENELTHDIITK.+3y7.light	75	31.3
601.991497	726.414465	LQHLENELTHDIITK.+3y6.light	75	31.3
601.991497	589.355553	LQHLENELTHDIITK.+3y5.light	75	35.3
601.991497	379.208829	LQHLENELTHDIITK.+3b3.light	75	34.3
601.991497	864.421007	LQHLENELTHDIITK.+3b7.light	75	30.3
796.899376	1134.590198	ELSEALGQIFDSQR.+2y10.light	89.2	41.5
796.899376	1063.553084	ELSEALGQIFDSQR.+2y9.light	89.2	42.5
796.899376	950.46902	ELSEALGQIFDSQR.+2y8.light	89.2	39.5
796.899376	765.388979	ELSEALGQIFDSQR.+2y6.light	89.2	38.5
796.899376	652.304915	ELSEALGQIFDSQR.+2y5.light	89.2	33.5
442.889379	674.371932	ASHEEVEGLVEK.+3y6.light	63.4	19.7
442.889379	545.329339	ASHEEVEGLVEK.+3y5.light	63.4	19.7
442.889379	488.307875	ASHEEVEGLVEK.+3y4.light	63.4	20.7
442.889379	554.220516	ASHEEVEGLVEK.+3b5.light	63.4	22.7
442.889379	653.28893	ASHEEVEGLVEK.+3b6.light	63.4	19.7
410.719227	721.362764	VGFAEAAR.+2y7.light	61.1	20.6
410.719227	664.3413	VGFAEAAR.+2y6.light	61.1	19.6
410.719227	517.272886	VGFAEAAR.+2y5.light	61.1	21.6
410.719227	446.235772	VGFAEAAR.+2y4.light	61.1	22.6
410.719227	504.245275	VGFAEAAR.+2b5.light	61.1	18.6

Table S2. The RSDs of the calibration mixtures for quantification

	100:1	**10:1**	**5:1**	**2:1**	**1:1**	**1:2**	**1:5**	**1:10**
$\mathbf{P_{A1AT\text{-}1}}$	—	4.0%	1.6%	1.6%	0.8%	0.2%	3.2%	2.4%
$\mathbf{P_{A1AT\text{-}2}}$	11.8%	4.2%	2.1%	7.4%	4.0%	0.5%	4.7%	10.9%
$\mathbf{P_{LG3BP\text{-}1}}$	—	10.0%	6.5%	1.3%	2.6%	6.4%	5.7%	8.8%
$\mathbf{P_{LG3BP\text{-}2}}$	4.4%	3.2%	4.4%	13.8%	1.7%	5.2%	2.7%	9.5%
$\mathbf{P_{CTSD}}$	25.5%	8.6%	22.1%	1.3%	8.0%	3.6%	6.6%	3.3%

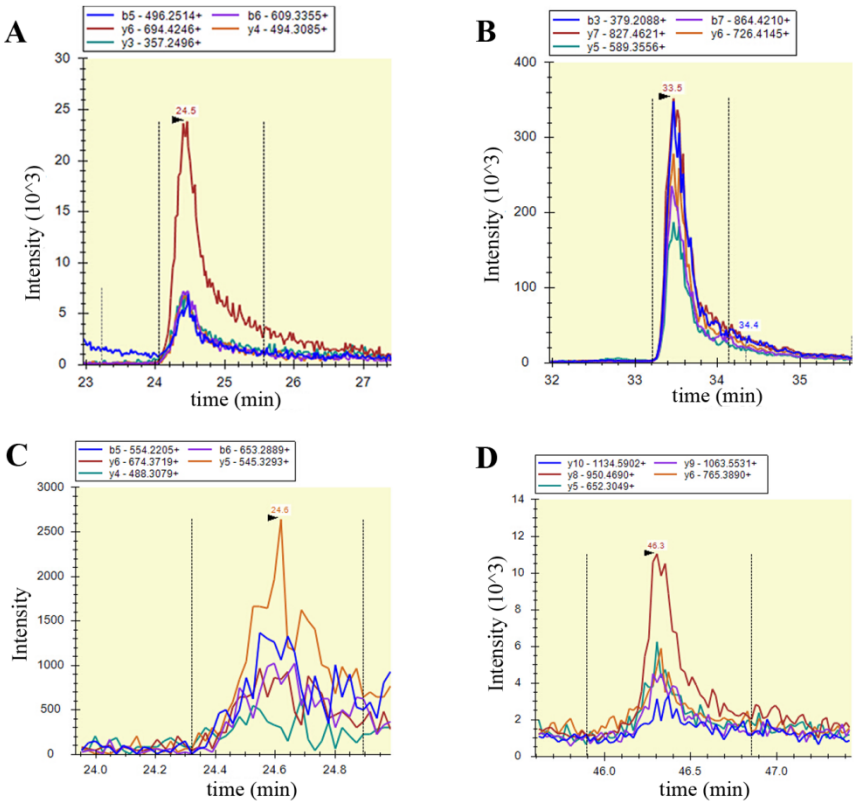

Figure S1. The MRM traces of target peptides of A1AT and LG3BP. A: SASLHLPK, B: LQHLENELTHDIITK, C: ASHEEVEGLVEK, D: ELSEALGQIFDSQR.

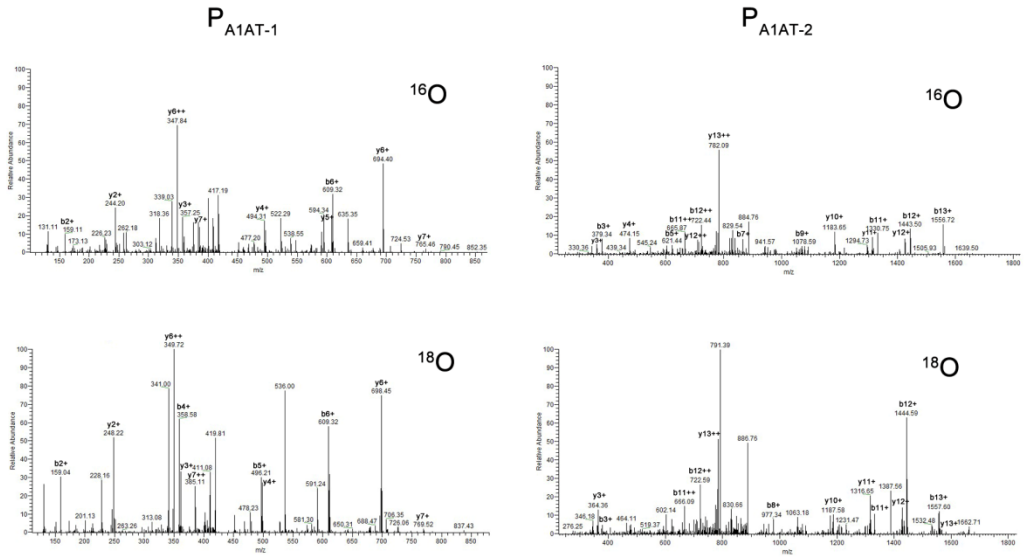

Figure S2. The MS/MS spectra of ^{16}O-labeled and ^{18}O-labeled peptides of A1AT. The MS/MS spectra of both ^{16}O-labeled and ^{18}O-labeled peptides showed high quality and could be successfully matched to theoretical spectra in database search.

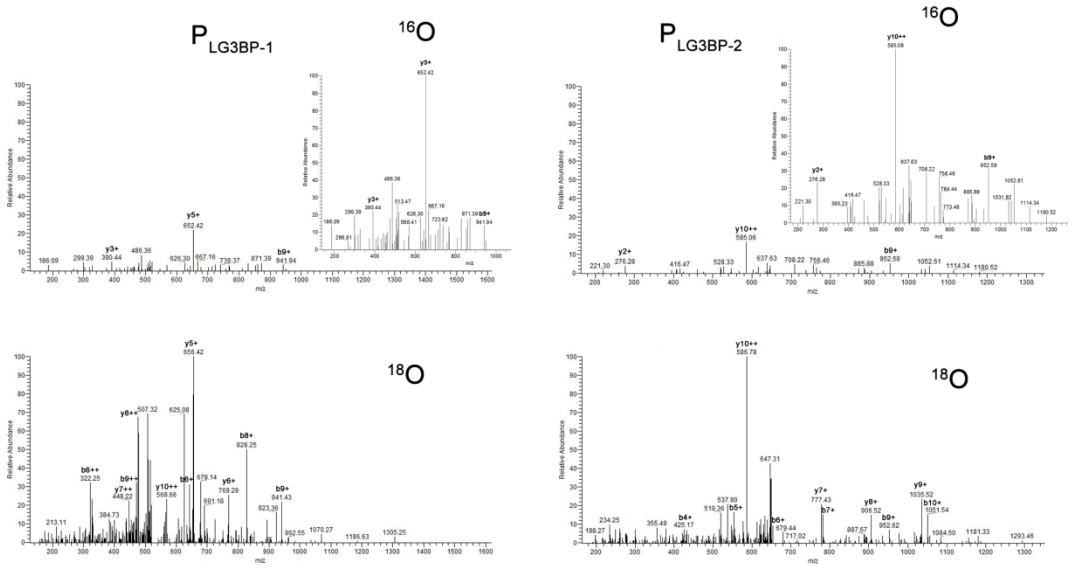

Figure S3. The MS/MS spectra of ^{16}O-labeled and ^{18}O-labeled peptides of LG3BP. Only the MS/MS spectra of ^{18}O-labeled peptides could be successfully matched to theoretical spectra in database search. The MS/MS spectra of ^{16}O-labeled peptides could not pass the threshold of database search. For comparison, MS/MS spectra of ^{16}O-labeled were modified using the same absolute intensity with ^{18}O-labeled, and their original spectra was shown in top right corner.

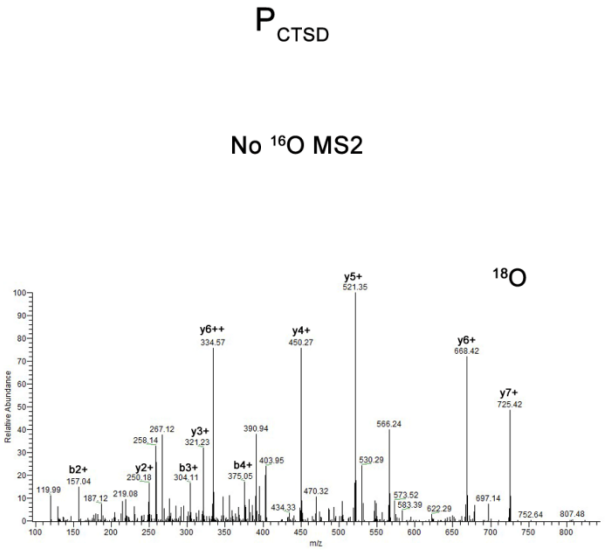

Figure S4. The MS/MS spectrum of ^{18}O-labeled peptide of CTSD. Only the MS/MS spectrum of ^{18}O-labeled peptide could be obtained and successfully matched to theoretical spectra in database search. The intensity of ^{16}O-labeled peak in MS was too low, which could not be selected for CID. Therefore, no MS/MS spectrum of ^{16}O-labeled peptide was obtained.

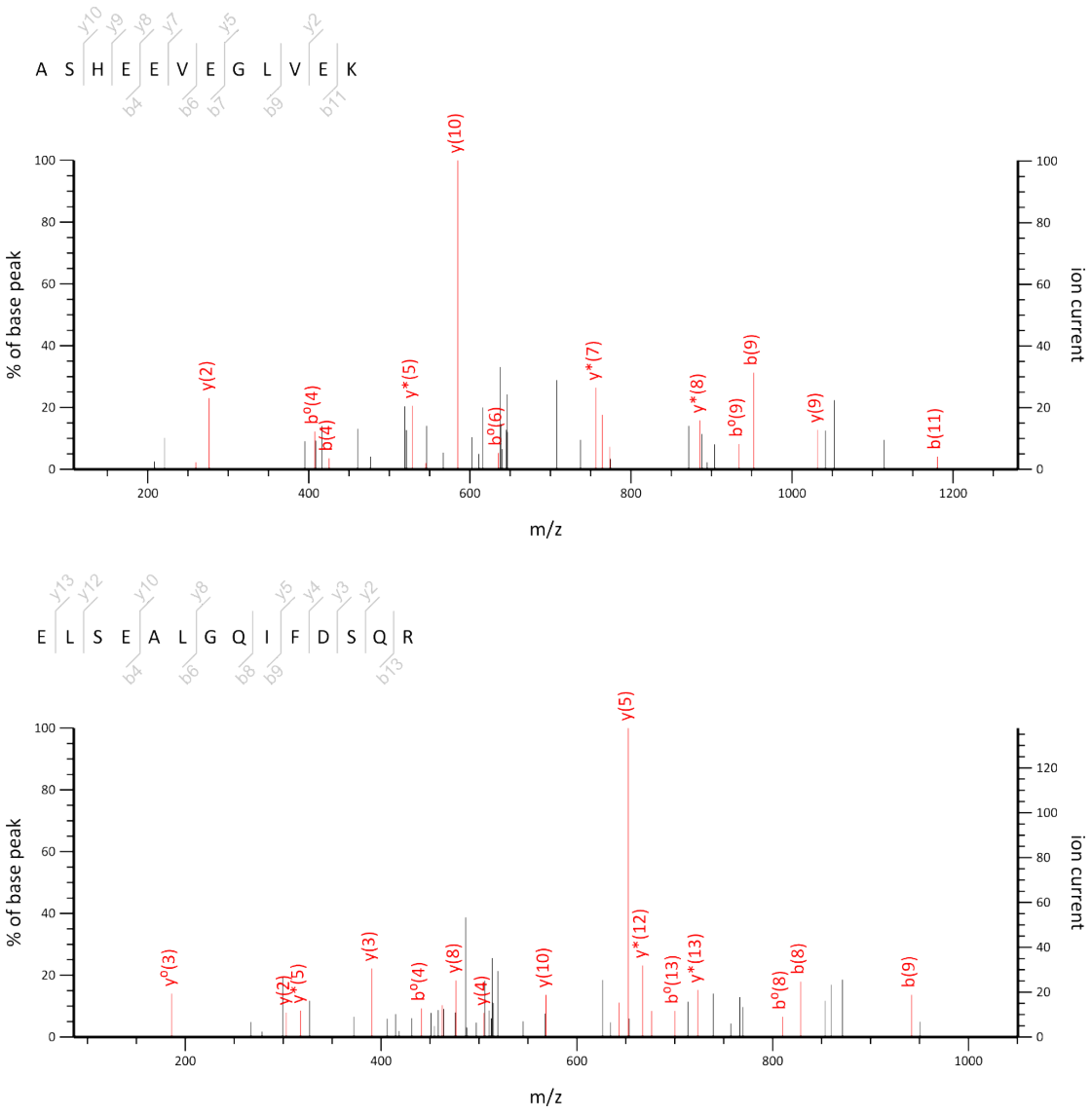

Figure S5. The assigned spectra including $-H_2O$, $-NH_3$ and +2H Peaks

^{16}O-labeled and ^{18}O-labeled of LG3BP peptides. The top-ranking peptides of the two unidentified spectra were assigned to corresponding ^{16}O peptides of LG3BP, However, Peptide Prophet probability was less than 0.90.

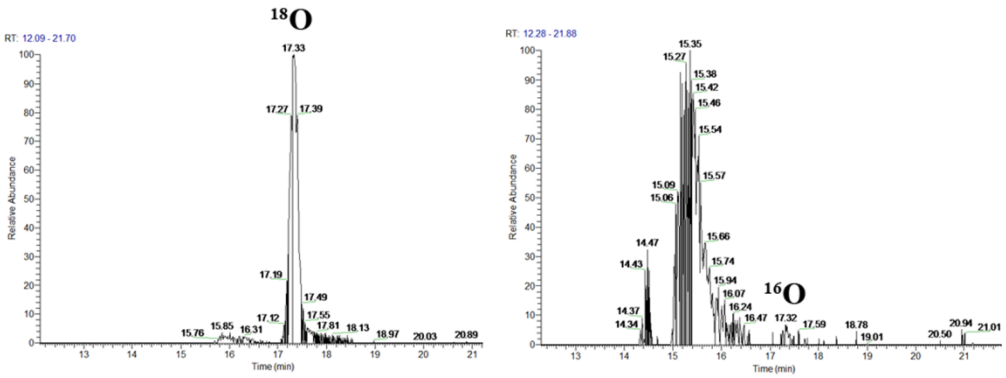

Figure S6. The extract ion chromatographs of ^{18}O-labeled and native (^{16}O-labeled) peptides of CTSD.

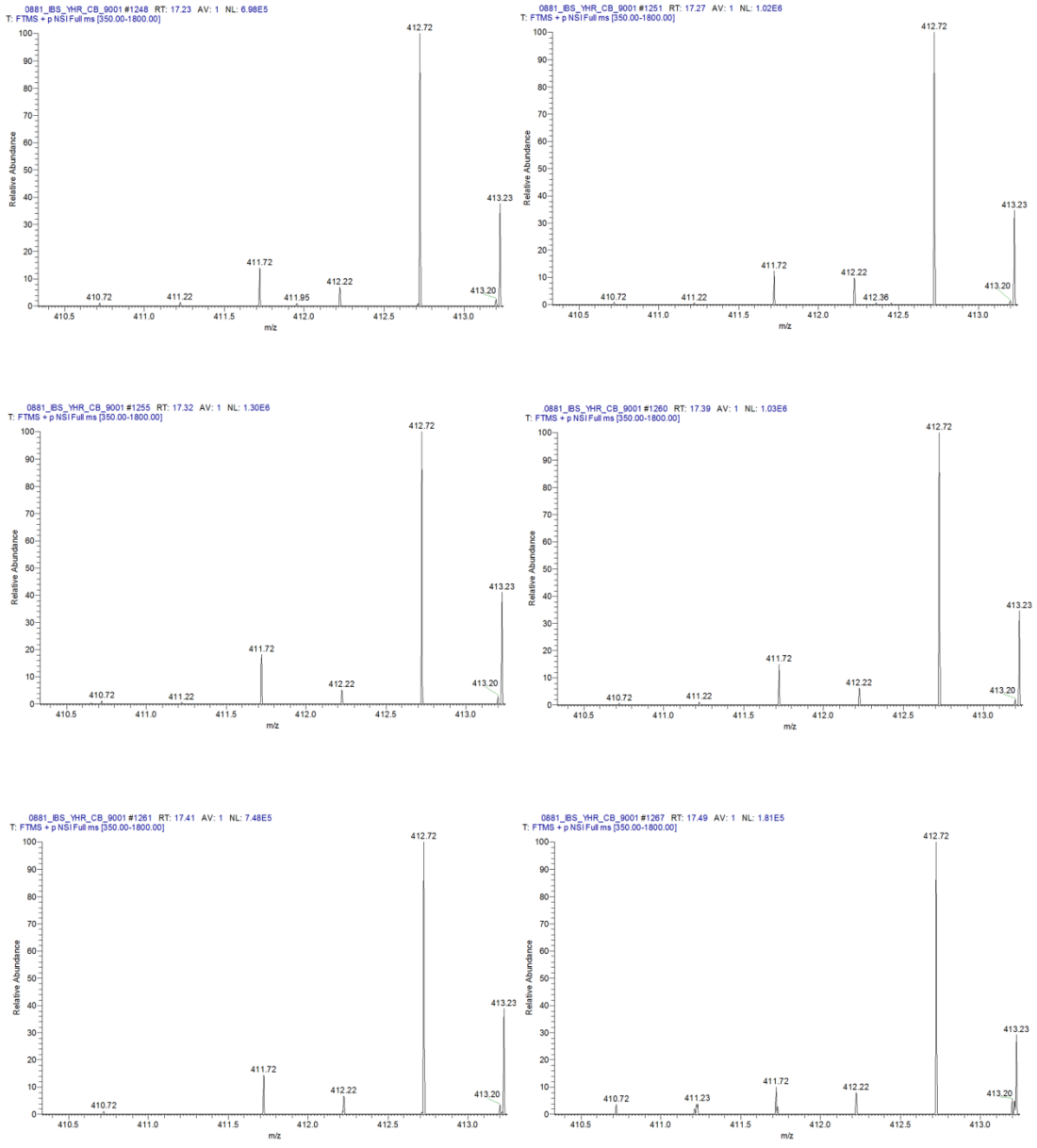

Figure S7. The MS1 scans of $P_{CTSD.}$ During the elution time, multiple consecutive MS1 scans were present.