Supplementary Material

Supplementary Experimental Procedures

Extraction of Low-Mass Serum Fraction

The low mass serum protein component was extracted from samples using modified standard protocol:[1] In-solution membrane electrophoresis was performed using a ProteomeSep electrophoresis instrument (NuSep, Sydney, Australia). Pooled serum samples were created by combining 30µL aliquots of individual patient samples based on CD behavioral phenotype: ICD (*n* = 16), SCD (*n* = 9), FCD (*n* = 9). Protease inhibitor (Roche, Basel, Switzerland) was added to pooled serum samples according to manufacturer recommendations and treated serums were then diluted with 150µL of 180mM Tris/20mM EACA/4M urea buffer, pH 10.2; in a 1:1 ratio. The ProteomeSep electrophoresis instrument was set up with a 5-chamber cartridge assembly using 5, 25, 45, 65 and 125 kDa polyacrylamide membranes (NuSep) and a 1 kDa regenerated cellulose membrane (Millipore, MA, USA). Cartridge assemblies were loaded into the separation unit of the instrument with 100mL of 90mM Tris/10mM EACA/2M urea buffer, pH 10.2 circulating around the electrodes for 10 minutes prior to sample loading. Serum samples (150µL) were then loaded into the cathode high mass chambers and 150µL of 90mM Tris/10mM EACA/2M urea buffer, pH 10.2, was loaded into the remaining mass restricted chambers. Fractionation was performed at 50V for 30mins followed by 250V for 2h30mins at 15°C. After separation, 1-25, 25-45, 45-65, 65-125 and >125kDa fractions were collected. Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) was performed on the 1-25kDa (low-mass) fraction.

Immunoblot Assay

For dot blots of serum proteins: Desmoglein-1 (DSG1), Desmoplakin (DSK), and Fatty Acid Binding Protein 5 (FABP5), 5µL of individual serums were dotted onto PVDF membranes and dried overnight.

Membranes were blocked in milk blotto (10% milk, 10mM 1M tris/HCl pH 7.5, 0.9% NaCl) for 24h before incubation in primary antibody (1mg/mL) for 3h (DSG1: diluted to 1:500 in blotto, DSK: 1:1000, FABP5: 1:200) and secondary antibody (Anti-Rabbit IgG) for 1h (1mg/mL antibody diluted to 1:1000 in blotto). Membranes were washed in chemiluminescence buffer (10mM 1M tris/HCl pH 8.5, 0.9% NaCl, 0.05% Tween 20), incubated in enhanced chemiluminescent substrate (SuperSignal West Femto, Thermo Scientific, USA), and developed. Quantitation of blots was performed in triplicate and measured by integrated density at a 300 ppi scale using ImageJ1.48v (NIH) with the Bob Dougherty microarray plugin (OptiNav, Inc). Primary rabbit polyclonal antibodies (1mg/mL) for DSG1 (cat no. ab103473), DSK (cat no. ab71690), and FABP5 (cat no. ab37267) were purchased from Abcam (Cambridge, UK).

Multiple Reaction Monitoring (MRM) Assay

To develop the tier 2 MRM serological assay (NCI-Clinical Proteomic Tumor Analysis Consortium (CPTAC))[4] for FABP5, LC-MS/MS sequenced FABP5 peptides (*N*=3) were searched against the National Center for Biotechnology Information (NCBI) Protein BLAST database for uniqueness, and a transition list was developed for a proteotypic peptide in Skyline SRM environment v1.4 (MacCoss Lab, UW) using MS/MS information from the SRMAtlas human library (Institute for Systems Biology, WA, USA). The 5 daughter ion transition list was tested in human serum samples using iterative experimentation using Tier 3 MRM assays (NCI-CPTAC)[4] and validated by retention time and MRM matching with synthetic light and heavy stable isotope internal standards for final Tier 2 requirements. For the final tier 2 assay, 2µl of serum (equating to 57µg ± 7% of protein) were trypsin digested at an approximate 1:100 enzyme-to-protein ratio, desalted with C18 stagetip columns, spiked with a stable $C^{13}N^{15}$-labelled isotope internal standard and analyzed on a 4000QTrap (ABSCIEX, MA, USA) mass spectrometer coupled to a Dionex Ultimate 3000 liquid chromatograph (Thermo Fisher Scientific, MA, USA). Quantitation was performed using a Reverse-Polynomial Dilution (RPD) calibration curve (stable heavy isotope ($C^{13}N^{15}$)

dilution).[5] The back-calculated error margin of the MRM assay was calculated as [(observed concentration)/(expected concentration)] x 100 (%); and precision by % coefficient of variation (CV%).[6, 7] $C^{13}N^{15}$-labelled peptides were custom-developed and purchased from Sigma-Alrich (Missouri, MO). Samples were run in triplicate and mean values were used for statistical analyses. Representative sample triplicates were run inter-day to evaluate analytical %CV. Pertinent Tier 2 assay information have been reported in compliance with National Cancer Institute-Clinical Proteomic Tumor Analysis Consortium (NCI-CPTAC) and the National Heart, Lung and Blood Institute's (NHLBI) Proteomics Centers recommendations (Supplementary Table 1; Supplementary Figure 1).[4]

LC-MS/MS data has been deposited at the PRIDE proteomics data repository (European Bioinformatics Institute, Cambridge, UK) with the dataset identifier PXD001821 at (http://www.ebi.ac.uk/pride/archive/) and the MRM dataset has been deposited at PeptideAtlas (Institute for Systems Biology, WA, USA) with the identifier PASS00661 (http://www.peptideatlas.org/PASS/PASS00661).

Statistical Analyses & Development of Serum Epithelial Components (SEC) Score

Discriminant function analysis was used to determine the ability of DSG1, DSK and FABP5 to classify complication in CD and to measure the standardized canonical discrimination function coefficients of each protein in the model ($Protein_{DF}$). The coefficient of each protein in discriminating CCD vs ICD was then used for weighting the protein's contribution to the SEC score. SEC score was hence calculated as:

$SEC = DSG1_{DF}(DSG1\ value) + DSK_{DF}(DSK\ value) + FABP5_{DF}(FABP5\ value)$

A multiple regression was not used to evaluate association between clinical parameters, biomarker values and SEC score due to multicollinearity between several independent variables: Ileal disease was significantly correlated with resection(s) ($P<0.0001$), ESR ($P = 0.004$) and duration of disease ($P = 0.040$). Resection(s) was additionally correlated with ESR ($P = .004$) and duration of disease ($P = 0.004$). Gender

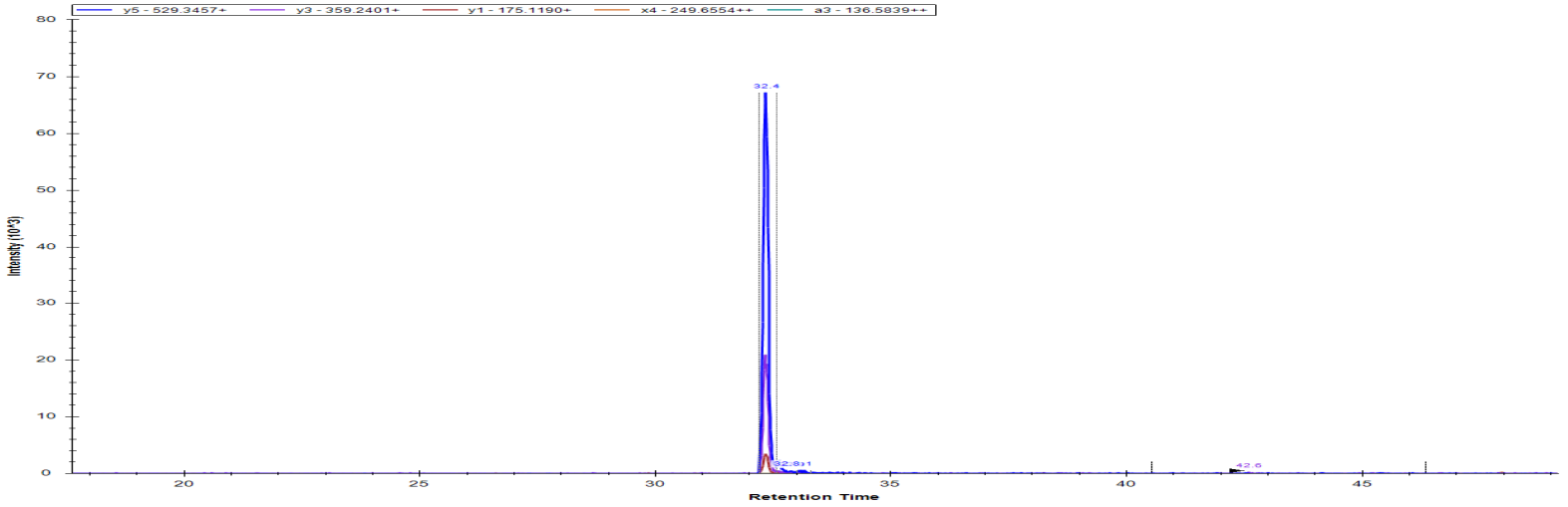
was correlated with age (P = .005) and age at diagnosis (P<0.001) in this cohort, and age was correlated with age at diagnosis (P<0.001). Steroidal therapy was correlated with mesalazines (P = 0.044). Categorization of disease location into ileal and non-ileal for comparisons was made based on known ileal association with complicated disease.[8, 9]

Supplementary Table 1. Tier-2 level Multiple Reaction Monitoring Assay Parameters. **Bold** font denotes the $C^{13}N^{15}$ stable-isotope labeled residue of the peptide's corresponding analog. Q1 and Q3 refer to the mass/charge ratios selected at the first and third quadrupoles, respectively. Interference assessment was performed manually (please refer to Supplementary figure 1A-B) and by One-Way ANOVA comparisons of retention time (RT)[1], Full Width Half Maximum (FWHM)[2] and Full Width at Base (FWB)[3] values between the analyte and stable-isotope analog for 10 full technical replicate samples (all $P>0.05$). For the quantitative performance parameters of this assay please refer to the Results section of the manuscript and Figure 6B.

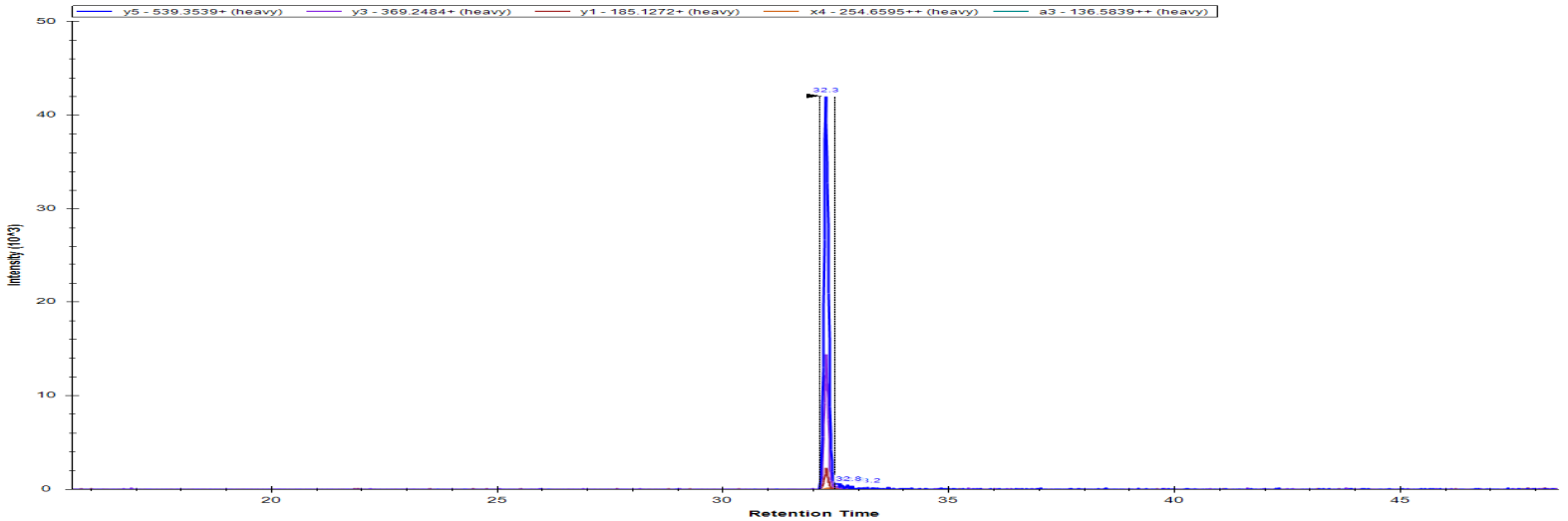
Instrument: AB Sciex 4000 QTrap											
Mode: Positive Ion											
Cycle time (seconds): 0.2501											
Dwell time (milliseconds): 20.0											
Pause time (milliseconds): 5.007											
Data depository: SRMAtlas dataset identifier: PASS00661 **URL:** http://www.peptideatlas.org/PASS/PASS00661											
Sample Medium: Human blood serum											
Analyte Details			**Acquisition Parameters**						**Interference Assessment**		
Protein	**Uniprot Accession**	**Peptide**	**Declustering Potential (V)**	**Collision Energy (V)**	**MRM Transitions (m/z)**				**Observed RT[1]**	**Peak shape**	
					Q1	**Q3**				**FWHM[2]**	**FWB[3]**
Fatty Acid Binding Protein, epidermal (FABP5)	Q01469	ELGVGIAL**R**	65	22.2	464.28++	529.35+	359.24+	175.12+	32.19 ± 0.08	0.17 ± 0.02	0.52 ± 0.03
					469.29++	539.35+	369.25+	185.13+	32.17 ± 0.09	0.12 ± 0.04	0.44 ± 0.03

Supplementary Figure 1. Interference Assessment of ELVGIAR peptide. (*A*) 100fmol/µL peptide and (*B*) 100fmol/µL C13N15-labeled stable isotope analog in 0.1% formic acid. (*C*) 100fmol/µL peptide and (*D*) 100fmol/µL C13N15-labeled stable isotope analog in unfractionated human blood serum.

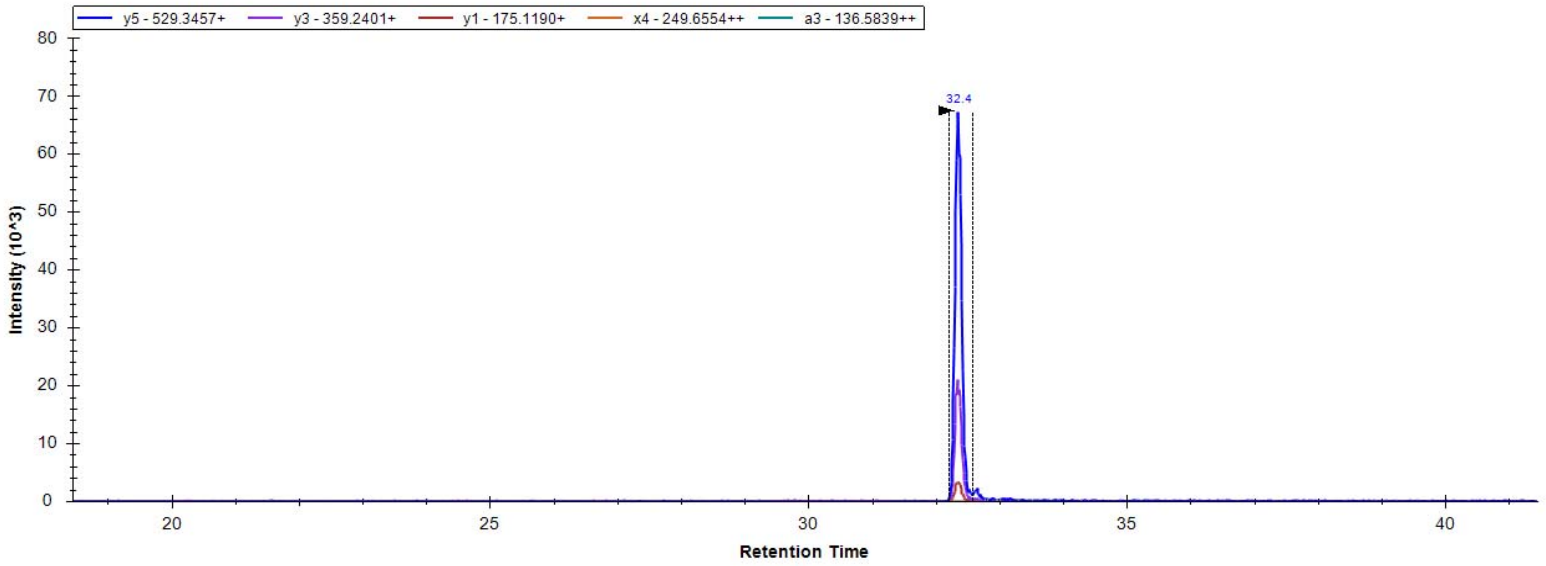
A



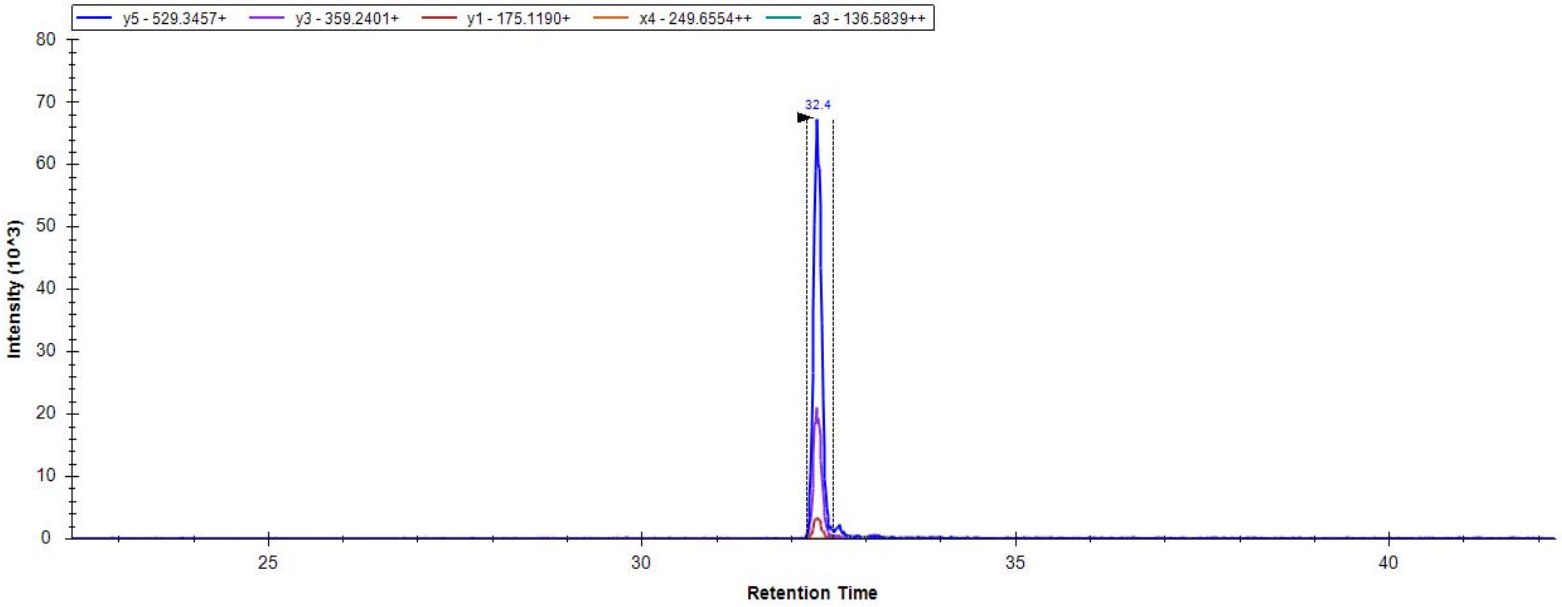
B



C

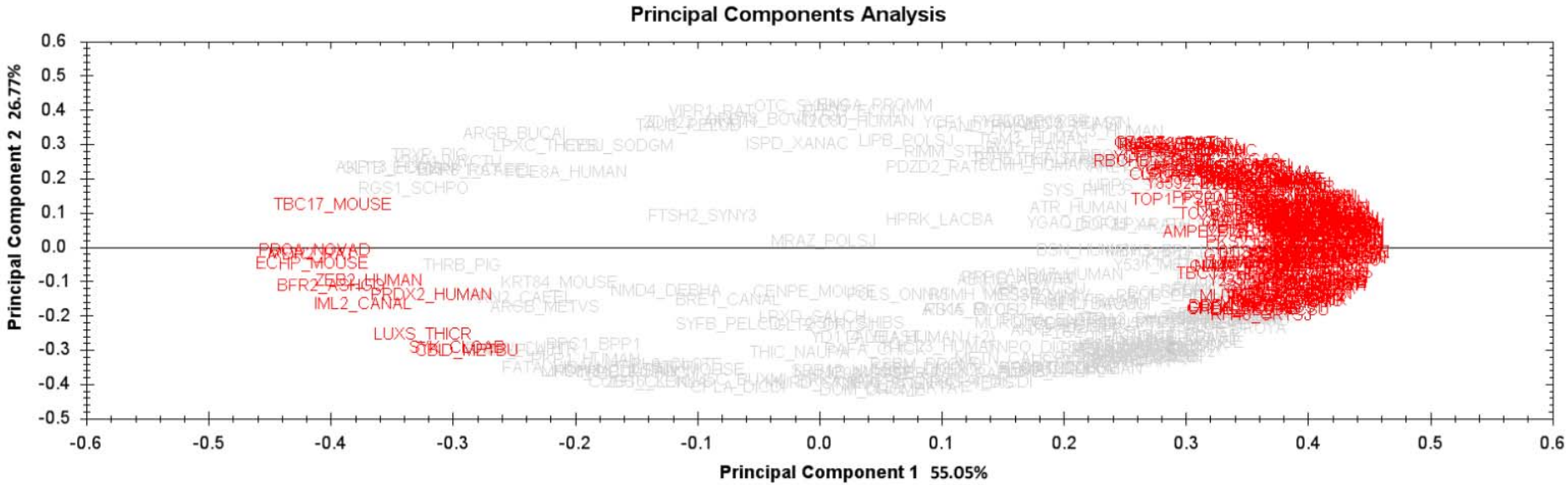

y5 - 529.3457+
y3 - 359.2401+
y1 - 175.1190+
x4 - 249.6554++
a3 - 136.5839++
32.4
Intensity (10^3)
Retention Time

D


y5 - 529.3457+
y3 - 359.2401+
y1 - 175.1190+
x4 - 249.6554++
a3 - 136.5839++
32.4
Intensity (10^3)
Retention Time

Supplementary Results

Supplementary Figure 2. Principal components scatterplot of low-mass serum proteins sequenced by LC-MS/MS. Proteins are identified by uniprot accession number (*N*=496). The red accession numbers indicate the significantly changing proteins (*P*<0.05, *q*<0.01, power>80%). The proteins on the left were upregulated in ICD (*N*=11) and the proteins on the right upregulated in CCD (*N*=161).



Supplementary Table 2. High-confidence modulating low-mass serum proteins between Complicated (stricturing & fistulizing) Crohn's Disease (CCD) and uncomplicated Inflammatory Crohn's Disease (ICD) by label-free quantitative LC-MS/MS. Proteins with a fold change greater than 1 are upregulated in CCD while those with a fold change less than 1 are downregulated. The *p*-value is calculated by One-way ANOVA and the *q*-value is the probability of a false positive after multiple testing correction. [†]Indicates annotation to enriched functional clusters by DAVID analysis. [‡]Indicates downregulated proteins that did not annotate to any enriched clusters by DAVID.

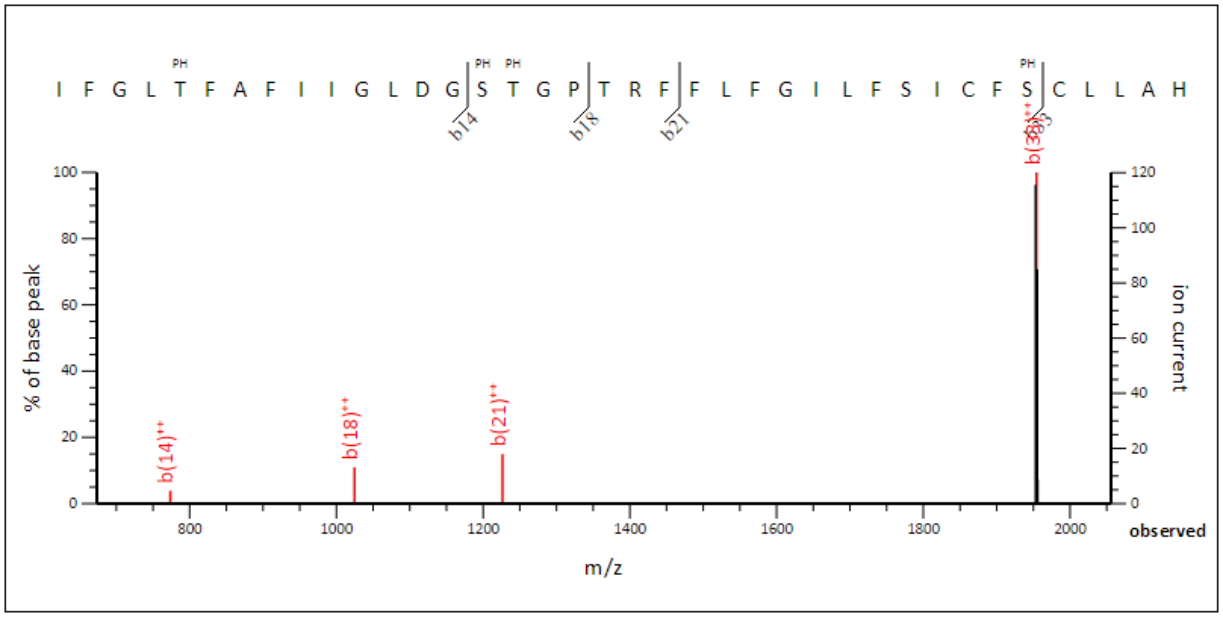
Uniprot. Acc	No. Peptides	Mascot Confidence Score	% Coverage of Protein	Protein	Fold change	*P*-value	*q*-value	Power
K1C9_HUMAN[†]	126	7906.5	90	Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3	2.91E+01	2.00E-09	4.11E-08	1
K2C1_HUMAN[†]	111	6218.55	77	Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6	2.27E+01	5.95E-08	3.59E-07	1
HORN_HUMAN[†]	59	2747.61	23	Hornerin OS=Homo sapiens GN=HRNR PE=1 SV=2	2.51E+01	1.31E-08	1.20E-07	1
DESP_HUMAN[†]	58	2674.43	24	Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3	4.80E+00	3.41E-06	7.19E-06	1
K1C14_HUMAN[†]	53	2647.45	76	Keratin, type I cytoskeletal 14 OS=Homo sapiens GN=KRT14 PE=1 SV=4	2.02E+01	3.29E-09	4.52E-08	1
K1C10_HUMAN[†]	53	3094.16	67	Keratin, type I cytoskeletal 10 OS=Homo sapiens GN=KRT10 PE=1 SV=6	6.78E+00	3.74E-06	7.70E-06	1
K1C16_HUMAN[†]	48	2462.82	72	Keratin, type I cytoskeletal 16 OS=Homo sapiens GN=KRT16 PE=1 SV=4	2.66E+01	1.37E-07	6.24E-07	1
K2C5_PANTR	48	2258.08	61	Keratin, type II cytoskeletal 5 OS=Pan troglodytes GN=KRT5 PE=2 SV=1	1.01E+01	1.22E-04	1.33E-04	1
K2C1_CANFA	43	2322.3	36	Keratin, type II cytoskeletal 1 OS=Canisfamiliaris GN=KRT1 PE=2 SV=1	4.70E+03	2.15E-04	2.19E-04	1
K2C6C_HUMAN[†]	42	2020.19	64	Keratin, type II cytoskeletal 6C OS=Homo sapiens GN=KRT6C PE=1 SV=3	3.65E+00	9.57E-04	7.57E-04	1
K2C6A_HUMAN[†]	40	1901.77	64	Keratin, type II cytoskeletal 6A OS=Homo sapiens GN=KRT6A PE=1 SV=3	7.80E+00	4.48E-04	3.87E-04	1
K2C6B_HUMAN[†]	38	1761.68	63	Keratin, type II cytoskeletal 6B OS=Homo sapiens GN=KRT6B PE=1 SV=5	2.71E+01	1.28E-09	3.50E-08	1
K22E_HUMAN[†]	38	2493.34	70	Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens GN=KRT2 PE=1 SV=2	8.62E+00	1.36E-06	3.50E-06	1
PLAK_HUMAN[†]	25	1231.78	37	Junction plakoglobin OS=Homo sapiens GN=JUP PE=1 SV=3	4.56E+00	8.83E-06	1.48E-05	1
K22E_RAT	17	797.49	25	Keratin, type II cytoskeletal 2 epidermal OS=Rattusnorvegicus GN=Krt2 PE=2 SV=1	5.27E+02	2.74E-04	2.71E-04	1

DSG1_HUMAN[†]	16	717.24	28	Desmoglein-1 OS=Homo sapiens GN=DSG1 PE=1 SV=2	2.03E+00	1.10E-03	8.23E-04	1
K2C73_RAT	12	535.51	15	Keratin, type II cytoskeletal 73 OS=Rattusnorvegicus GN=Krt73 PE=1 SV=1	5.74E+01	1.06E-02	5.23E-03	0.88
K2C78_HUMAN[†]	12	525.01	35	Keratin, type II cytoskeletal 78 OS=Homo sapiens GN=KRT78 PE=1 SV=2	3.50E+00	3.24E-03	2.08E-03	0.98
POF1B_HUMAN[†]	7	250.03	21	Protein POF1B OS=Homo sapiens GN=POF1B PE=1 SV=2	3.24E+00	3.71E-04	3.42E-04	1
DSC1_HUMAN[†]	6	266.84	10	Desmocollin-1 OS=Homo sapiens GN=DSC1 PE=1 SV=2	7.31E+01	2.78E-08	2.29E-07	1
HSPB1_HUMAN[†]	5	147.73	33	Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2	1.90E+01	8.24E-07	2.26E-06	1
[†] **CATA_HUMAN**[†]	5	178.36	15	Catalase OS=Homo sapiens GN=CAT PE=1 SV=3	9.93E+00	5.31E-08	3.59E-07	1
PRDX1_HUMAN[†]	5	171.65	18	Peroxiredoxin-1 OS=Homo sapiens GN=PRDX1 PE=1 SV=1	6.13E+00	2.06E-03	1.41E-03	0.99
FILA2_HUMAN[†]	5	192.18	7	Filaggrin-2 OS=Homo sapiens GN=FLG2 PE=1 SV=1	5.52E+00	6.17E-03	3.53E-03	0.94
KPYM_PONAB	4	187.84	11	Pyruvate kinase isozyme M1 OS=Pongoabelii GN=PKM2 PE=2 SV=3	2.29E+01	3.14E-06	6.80E-06	1
FILA_HUMAN[†]	4	116.74	3	Filaggrin OS=Homo sapiens GN=FLG PE=1 SV=3	2.19E+01	1.10E-04	1.25E-04	1
ANXA2_BOVIN	4	194.8	18	Annexin A2 OS=Bostaurus GN=ANXA2 PE=1 SV=2	6.71E+00	4.10E-04	3.66E-04	1
CALL5_HUMAN[†]	3	159.87	21	Calmodulin-like protein 5 OS=Homo sapiens GN=CALML5 PE=1 SV=2	1.97E+05	5.62E-06	1.01E-05	1
FABP5_HUMAN[†]	3	130.92	13	Fatty acid-binding protein, epidermal OS=Homo sapiens GN=FABP5 PE=1 SV=3	2.42E+02	3.63E-07	1.30E-06	1
SBSN_HUMAN[†]	3	115.32	19	Suprabasin OS=Homo sapiens GN=SBSN PE=2 SV=1	2.28E+02	4.30E-04	3.76E-04	1
CDSN_HUMAN[†]	3	98.26	19	Corneodesmosin OS=Homo sapiens GN=CDSN PE=1 SV=3	1.33E+02	8.12E-04	6.55E-04	1
OVAL_CHICK	3	117.27	26	Ovalbumin OS=Gallus gallus GN=SERPINB14 PE=1 SV=2	5.61E+01	6.10E-08	3.59E-07	1
ENOA_MESAU	3	108.62	32	Alpha-enolase (Fragments) OS=Mesocricetusauratus GN=ENO1 PE=1 SV=1	2.46E+01	1.77E-07	7.66E-07	1
K1C9_MOUSE	3	76.66	12	Keratin, type I cytoskeletal 9 OS=Musmusculus GN=Krt9 PE=1 SV=2	1.23E+01	3.15E-10	1.29E-08	1
G3P_HUMAN	3	130.08	14	Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3	1.20E+01	4.70E-03	2.83E-03	0.96
LEUC_NITHX	3	78.4	4	3-isopropylmalate dehydratase large subunit OS=Nitrobacterhamburgensis (strain X14 / DSM 10229) GN=leuC PE=3 SV=1	4.75E+00	3.29E-04	3.15E-04	1
BCSA4_ACEXY	2	47.32	1	Putative cellulose synthase 2 OS=Acetobacterxylinus GN=bcsABII-A PE=3 SV=1	3.37E+06	7.24E-11	5.96E-09	1
ARAB_BACSU	2	44.5	2	Ribulokinase OS=Bacillus subtilis GN=araB PE=2 SV=1	2.09E+05	1.00E-02	4.99E-03	0.89
SAMP_ANALU	2	29.09	50	Serum amyloid P-component (Fragment) OS=Anarhichas lupus PE=1 SV=1	1.88E+05	6.86E-07	2.07E-06	1

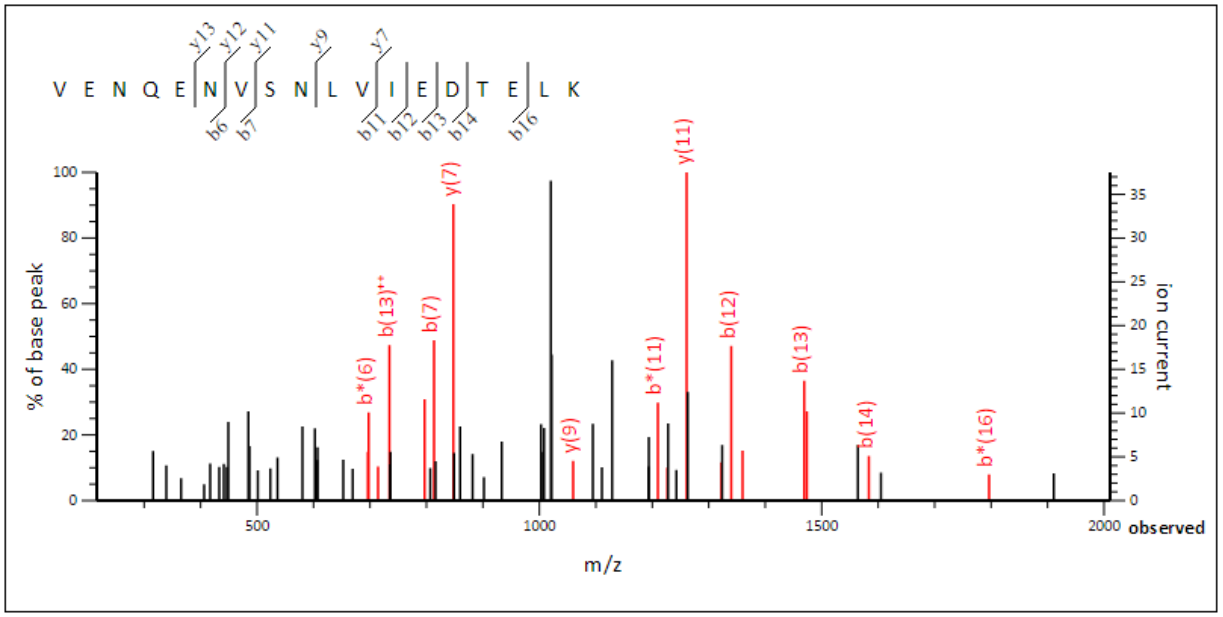
Y538_CORU7	2	41.54	2	UPF0371 protein cu0538 OS=Corynebacteriumurealyticum (strain ATCC 43042 / DSM 7109) GN=cu0538 PE=3 SV=1	3.43E+04	7.70E-04	6.27E-04	1
CPT1A_MOUSE	2	44.2	6	Carnitine O-palmitoyltransferase 1, liver isoform OS=Musmusculus GN=Cpt1a PE=2 SV=4	2.58E+04	1.19E-03	8.77E-04	1
S12A9_MOUSE	2	45.06	3	Solute carrier family 12 member 9 OS=Musmusculus GN=Slc12a9 PE=1 SV=1	1.37E+04	2.33E-06	5.26E-06	1
DEOD_CLOB8	2	56.63	10	Purine nucleoside phosphorylasedeoD-type OS=Clostridium beijerinckii (strain ATCC 51743 / NCIMB 8052) GN=deoD PE=3 SV=1	8.52E+03	4.86E-03	2.90E-03	0.96
UACA_HUMAN†	2	46.77	2	Uvealautoantigen with coiled-coil domains and ankyrin repeats OS=Homo sapiens GN=UACA PE=1 SV=2	9.98E+02	4.67E-06	9.15E-06	1
KPRP_HUMAN†	2	41.65	3	Keratinocyte proline-rich protein OS=Homo sapiens GN=KPRP PE=1 SV=1	1.29E+02	1.03E-03	7.78E-04	1
BST1_CANGA	2	53.32	4	GPI inositol-deacylase OS=Candida glabrata GN=BST1 PE=3 SV=1	1.23E+02	1.37E-03	9.77E-04	1
GPI10_ASPFU	2	45.78	2	GPI mannosyltransferase 3 OS=Aspergillusfumigatus GN=gpi10 PE=3 SV=1	6.90E+01	2.37E-06	5.26E-06	1
ACTB_BOSMU	2	101.21	20	Actin, cytoplasmic 1 OS=Bosmutusgrunniens GN=ACTB PE=2 SV=1	6.10E+01	7.79E-07	2.21E-06	1
SPB3_HUMAN†	2	67.42	7	Serpin B3 OS=Homo sapiens GN=SERPINB3 PE=1 SV=2	5.29E+01	2.85E-07	1.06E-06	1
IF2P_MOUSE	2	43.01	1	Eukaryotic translation initiation factor 5B OS=Musmusculus GN=Eif5b PE=1 SV=2	3.71E+01	4.04E-05	5.19E-05	1
PP220_ASFM2	2	46.32	3	Polyprotein pp220 OS=African swine fever virus (isolate Tick/Malawi/Lil 20-1/1983) GN=Mal-100 PE=2 SV=1	2.91E+01	4.25E-03	2.59E-03	0.96
THIO_PONAB	2	125.72	22	Thioredoxin OS=Pongoabelii GN=TXN PE=3 SV=3	2.63E+01	1.44E-04	1.54E-04	1
YCF24_CYAPA	2	58.91	2	UPF0051 protein ycf24 OS=Cyanophoraparadoxa GN=ycf24 PE=3 SV=1	1.98E+01	9.19E-03	4.64E-03	0.9
UB403_WSSVS	2	50.78	1	RING finger containing E3 ubiquitin-protein ligase WSV403 OS=White spot syndrome virus (isolate Shrimp/China/Tongan/1996) GN=WSV403 PE=4 SV=1	1.35E+01	1.27E-04	1.37E-04	1
HSLO_ACHLI	2	33.54	4	33 kDachaperonin OS=Acholeplasmalaidlawii (strain PG-8A) GN=hslO PE=3 SV=1	1.06E+01	2.03E-05	3.09E-05	1
DSC3_HUMAN†	2	41.3	5	Desmocollin-3 OS=Homo sapiens GN=DSC3 PE=1 SV=3	9.59E+00	3.49E-04	3.30E-04	1
RPOC1_PROMA	2	56.01	2	DNA-directed RNA polymerase subunit gamma OS=Prochlorococcusmarinus GN=rpoC1 PE=3 SV=2	8.82E+00	4.52E-04	3.87E-04	1
SVEP1_RAT	2	47.14	2	Sushi, von Willebrand factor type A, EGF and pentraxin domain-containing protein 1 OS=Rattusnorvegicus GN=Svep1 PE=1 SV=1	4.05E+00	8.97E-04	7.17E-04	1
FBX50_HUMAN	4	149	13	F-box only protein 50 OS=Homo sapiens GN=NCCRP1 PE=1 SV=1	2.78E+00	7.51E-03	4.00E-03	0.92

PRDX2_HUMAN[±]	2	63.46	9	Peroxiredoxin-2 OS=Homo sapiens GN=PRDX2 PE=1 SV=5	3.93E-01	7.53E-03	4.00E-03	0.92
TBC17_MOUSE[±]	2	55.35	2	TBC1 domain family member 17 OS=Musmusculus GN=Tbc1d17 PE=2 SV=1	2.10E-01	1.32E-03	9.50E-04	1
MDR2_RAT[±]	2	42.33	2	Multidrug resistance protein 2 OS=Rattusnorvegicus GN=Abcb4 PE=1 SV=1	2.03E-01	5.66E-07	1.79E-06	1
RAI3_HUMAN[†]	1	27.3	10	Retinoic acid-induced protein 3 OS=Homo sapiens GN=GPRC5A PE=1 SV=2	4.81E+04	6.51E-03	3.67E-03	0.93
CAP1_HUMAN[†]	1	26.35	7	Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5	1.64E+04	3.11E-09	4.52E-08	1
MYH9_HUMAN[†]	1	32.48	2	Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	3.11E+03	7.27E-03	3.92E-03	0.92
CASPE_HUMAN[†]	1	28.37	4	Caspase-14 OS=Homo sapiens GN=CASP14 PE=1 SV=2	7.26E+01	1.15E-03	8.55E-04	1
KLHL3_HUMAN[†]	1	27.9	1	Kelch-like protein 3 OS=Homo sapiens GN=KLHL3 PE=1 SV=2	5.64E+01	2.34E-05	3.44E-05	1
TJAP1_HUMAN[†]	1	32.92	1	Tight junction-associated protein 1 OS=Homo sapiens GN=TJAP1 PE=1 SV=1	8.39E+00	9.78E-04	7.62E-04	1
LUXS_THICR[±]	1	24.45	14	S-ribosylhomocysteinelyase OS=Thiomicrospiracrunogena (strain XCL-2) GN=luxS PE=3 SV=1	3.02E-01	2.27E-03	1.53E-03	0.99
ZEB2_HUMAN[±]	1	24.85	1	Zinc finger E-box-binding homeobox 2 OS=Homo sapiens GN=ZEB2 PE=1 SV=1	1.67E-01	9.82E-04	7.62E-04	1
SYK_CLOAB[±]	1	24.84	7	Lysyl-tRNAsynthetase OS=Clostridium acetobutylicum GN=lysS PE=3 SV=1	9.53E-02	7.29E-03	3.92E-03	0.92
IML2_CANAL[±]	1	28.79	1	Mitochondrial outer membrane protein IML2 OS=Candida albicans GN=IML2 PE=3 SV=1	1.65E-02	8.10E-05	9.66E-05	1
CBID_METBU[±]	1	23.36	2	Putative cobalt-precorrin-6A synthase [deacetylating] OS=Methanococcoidesburtonii (strain DSM 6242) GN=cbiD PE=3 SV=1	1.02E-02	9.14E-03	4.64E-03	0.9
BFR2_ASHGO[±]	1	38.09	1	Protein BFR2 OS=Ashbyagossypii GN=BFR2 PE=3 SV=1	9.48E-03	4.75E-07	1.57E-06	1
PROA_NOVAD[±]	1	34.67	2	Gamma-glutamyl phosphate reductase OS=Novosphingobiumaromaticivorans (strain DSM 12444) GN=proA PE=3 SV=1	2.83E-03	4.45E-06	8.94E-06	1
ECHP_MOUSE[±]	1	26.83	1	Peroxisomalbifunctional enzyme OS=Musmusculus GN=Ehhadh PE=1 SV=3	1.81E-03	1.17E-07	5.65E-07	1

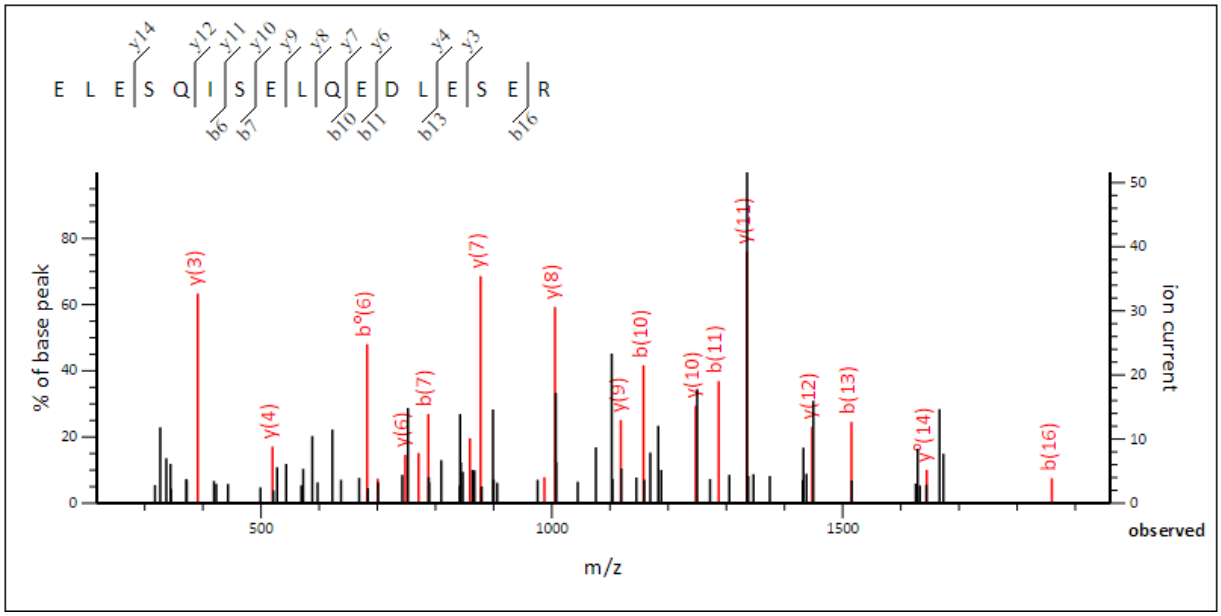
Supplementary Figure 3. Annotated spectrum for RAI3_HUMAN



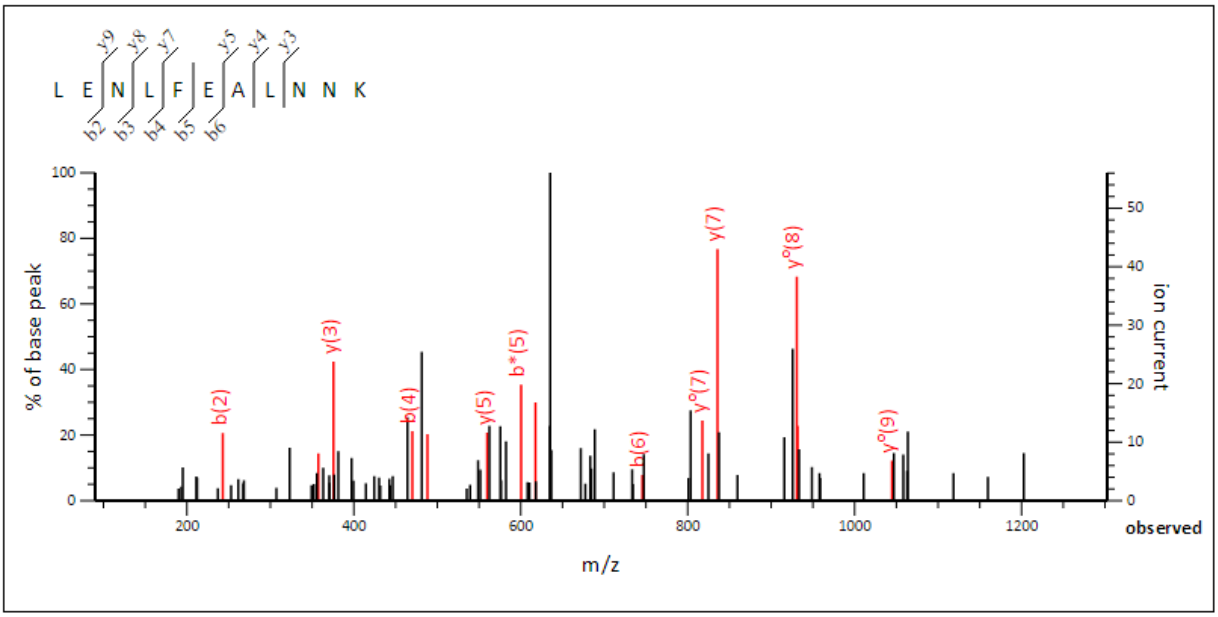
Supplementary Figure 4. Annotated spectrum for CAP1_HUMAN



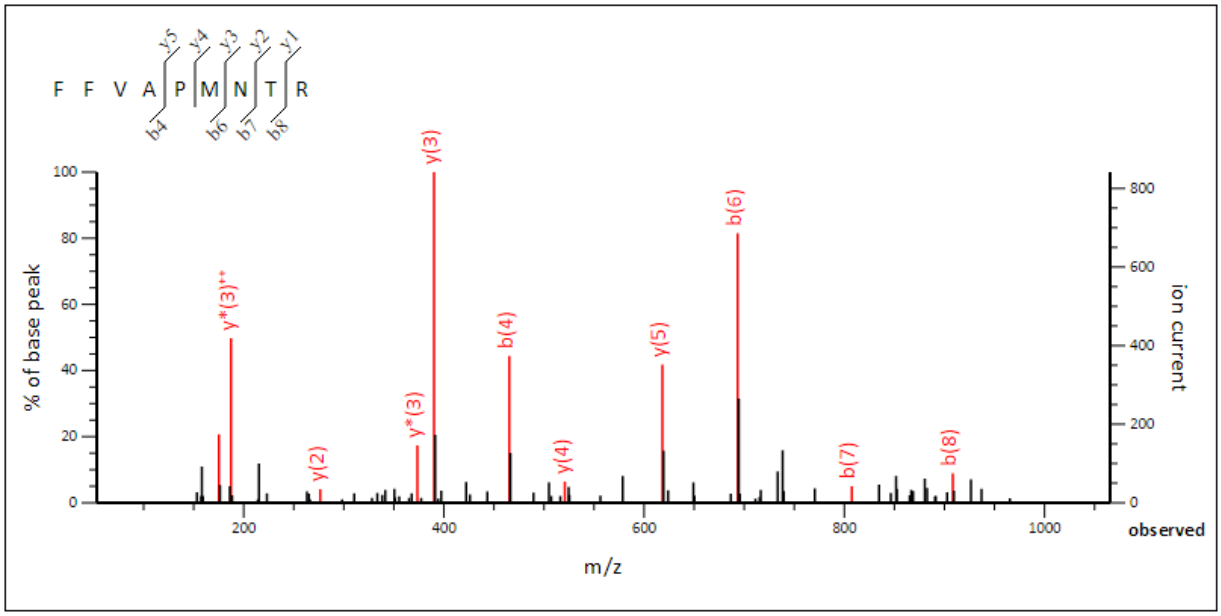
Supplementary Figure 5. Annotated spectrum for MYH9_HUMAN



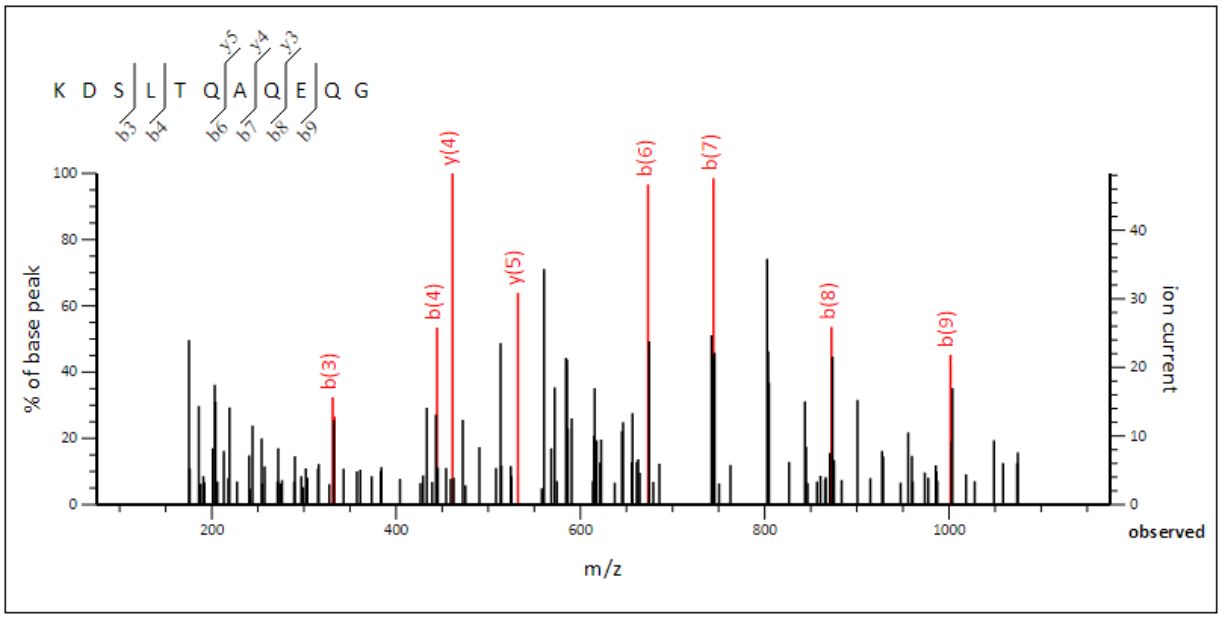
Supplementary Figure 6. Annotated spectrum for CASPE_HUMAN



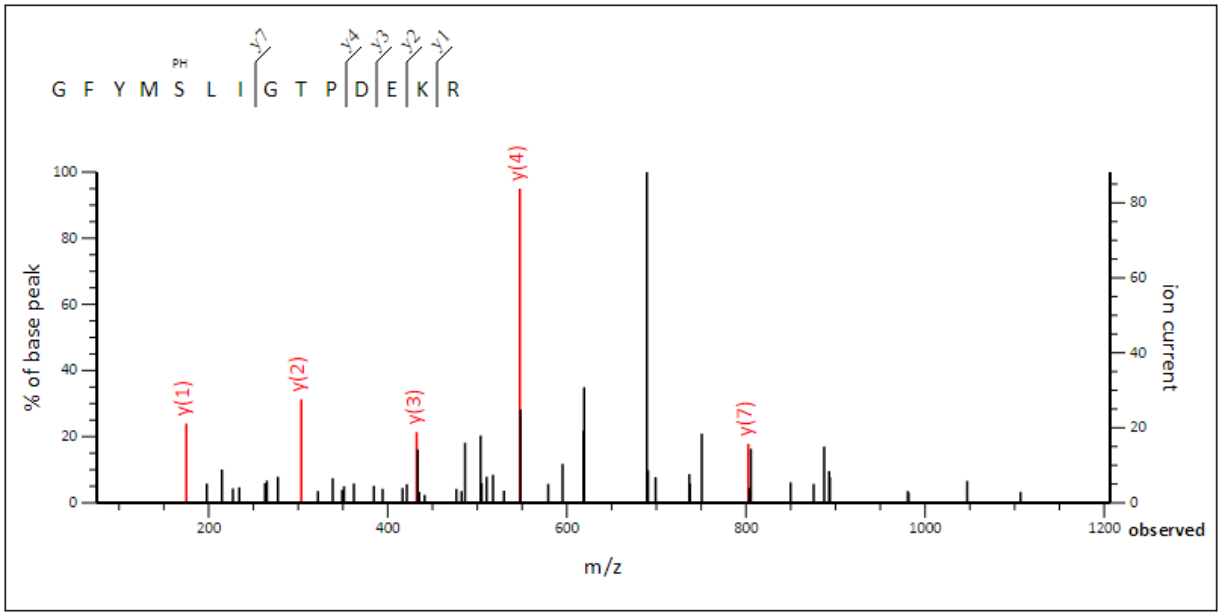
Supplementary Figure 7. Annotated spectrum for KLHL3_HUMAN



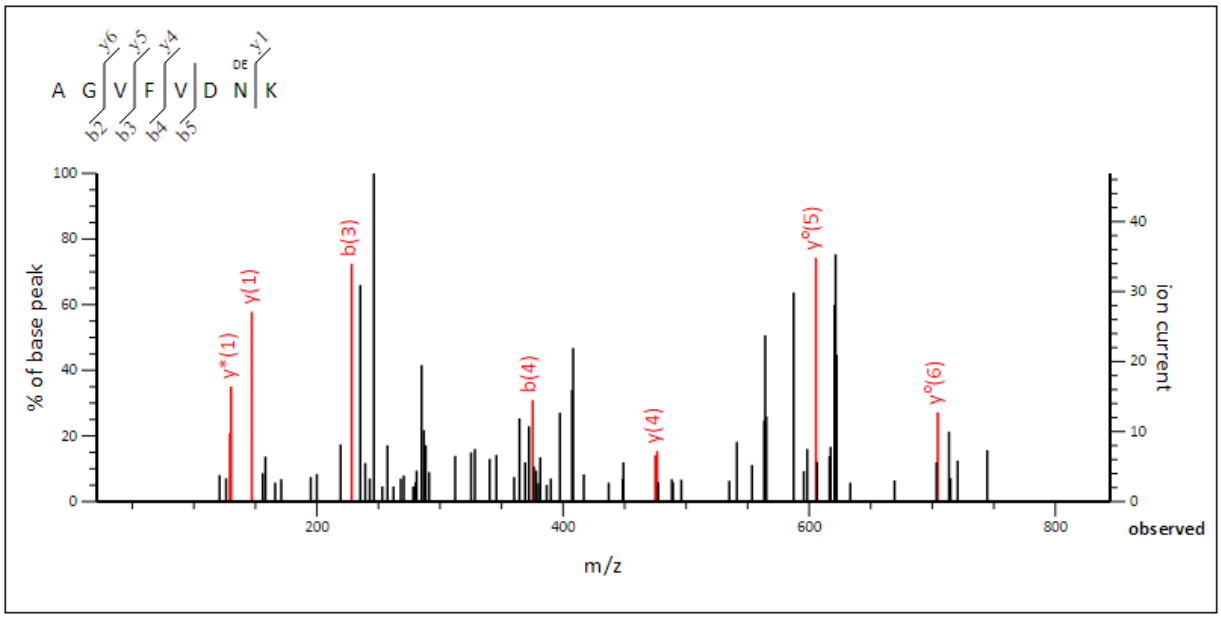
Supplementary Figure 8. Annotated spectrum for TJAP1_HUMAN



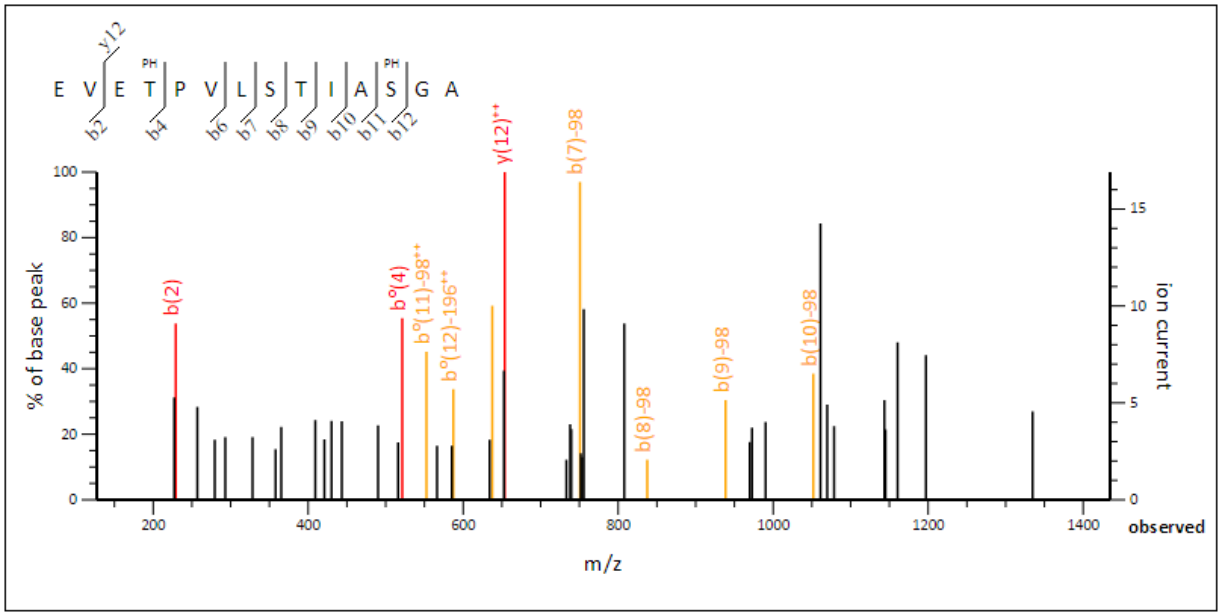
Supplementary Figure 9. Annotated spectrum for LUXS_THICR



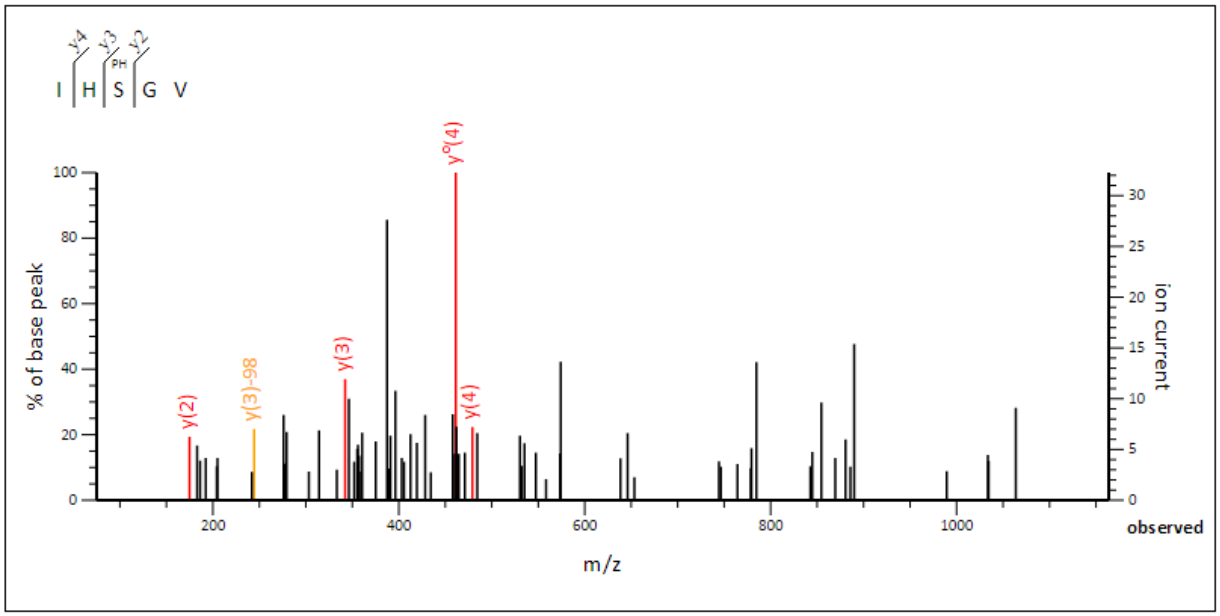
Supplementary Figure 10. Annotated spectrum for ZEB2_HUMAN



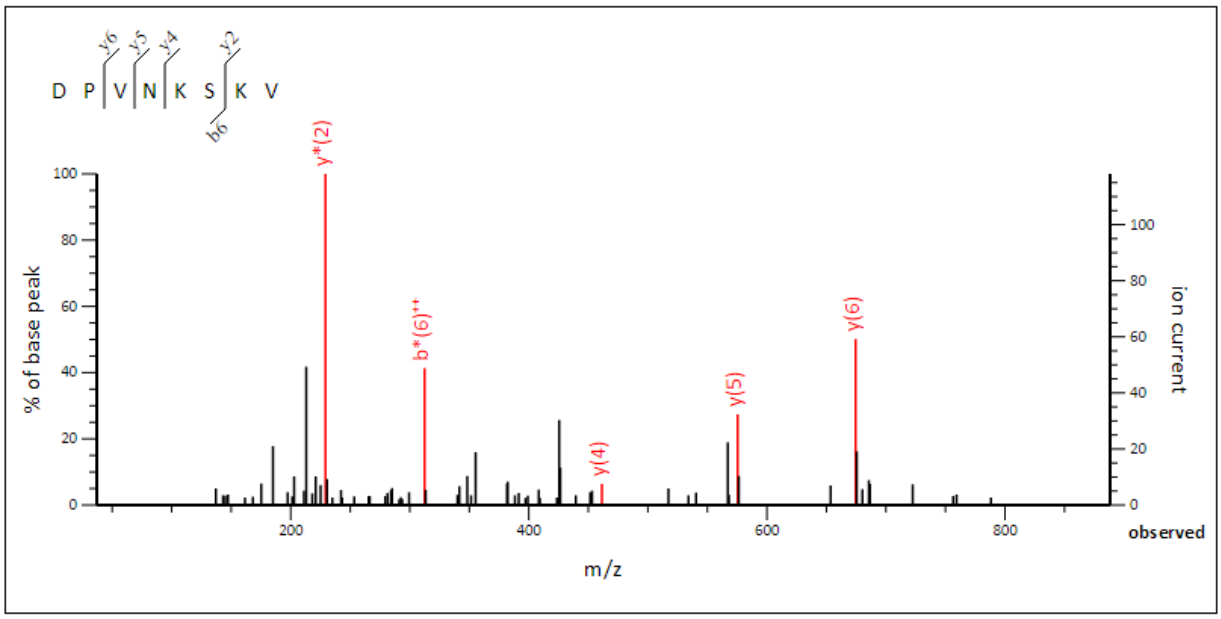
Supplementary Figure 11. Annotated spectrum for SYK_CLOAB



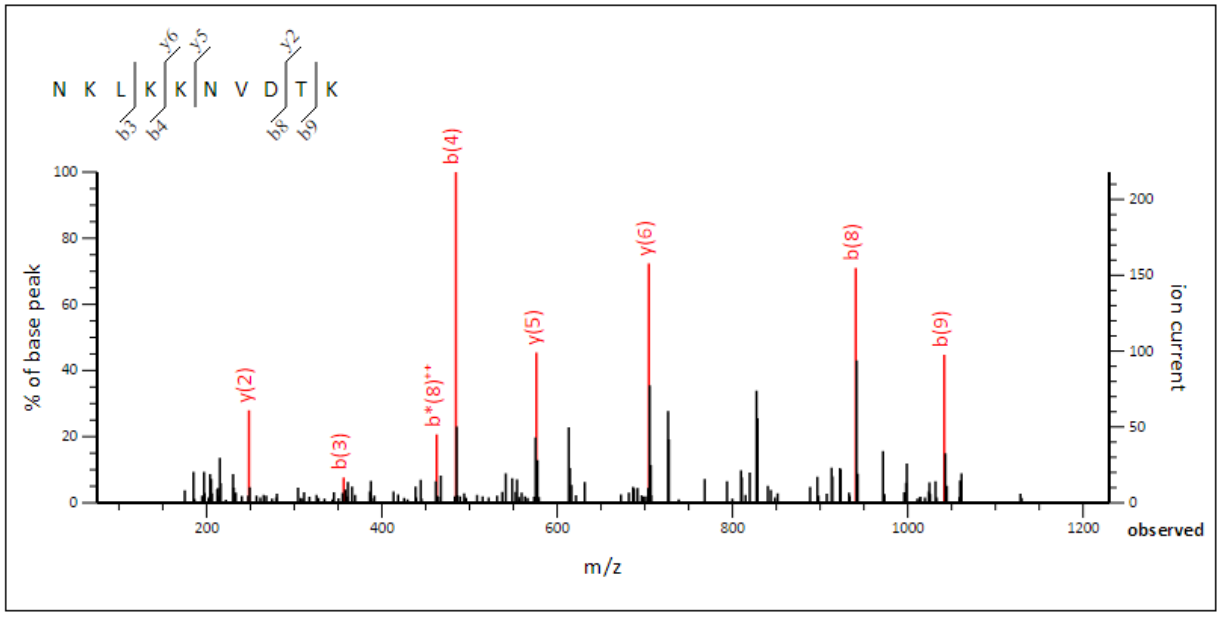
Supplementary Figure 12. Annotated spectrum for IML2_CLOAB



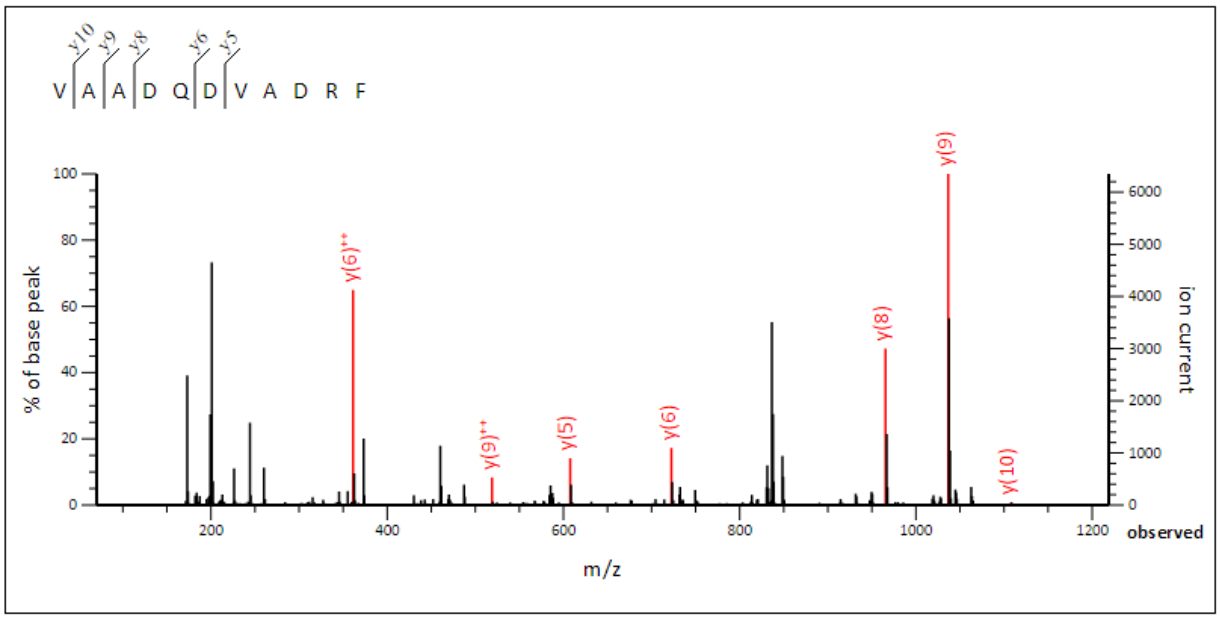
Supplementary Figure 13. Annotated spectrum for CBID_METBU



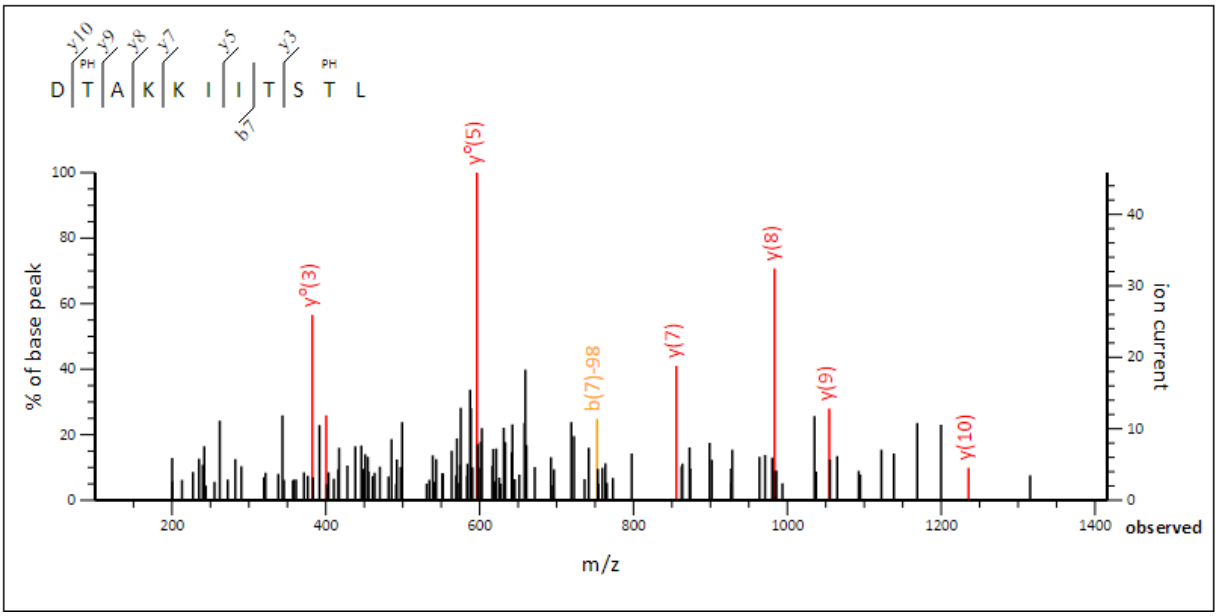
Supplementary Figure 14. Annotated spectrum for CBID_METBU



Supplementary Figure 15. Annotated spectrum for PROA_NOVAD



Supplementary Figure 16. Annotated spectrum for ECHP_MOUSE



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