Nagaprashantha LD et al Supplementary Fig 1

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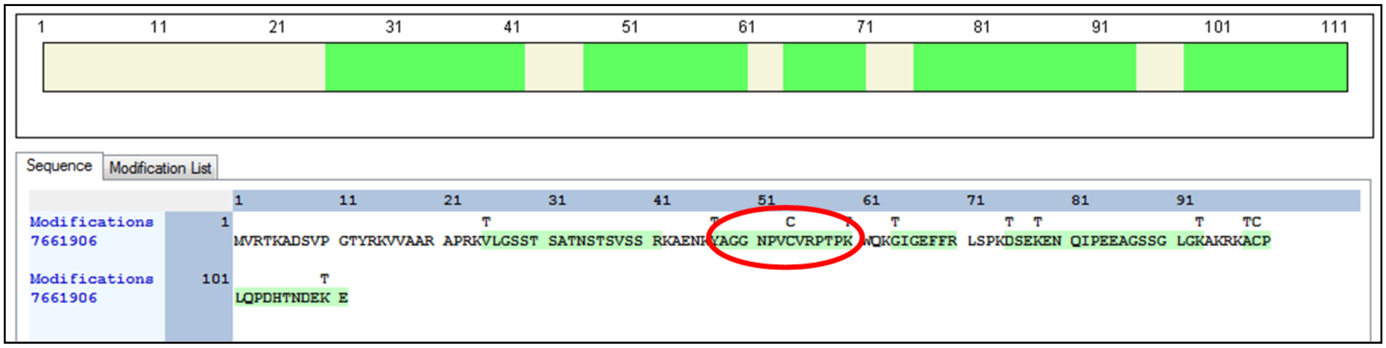

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            1          11         21         31         41         51         61         71         81         91
Modifications     1                         T                        T        C    T    T              T  T                T    TC
7661906           MVRTKADSVP GTYRKVVAAR APRKVLGSST SATNSTSVSS RKAENKYAGG NPVCVRPTPK WQKGIGEFFR LSPKDSEKEN QIPEEAGSSG LGKAKRKACP

Modifications   101       T
7661906           LQPDHTNDEK E
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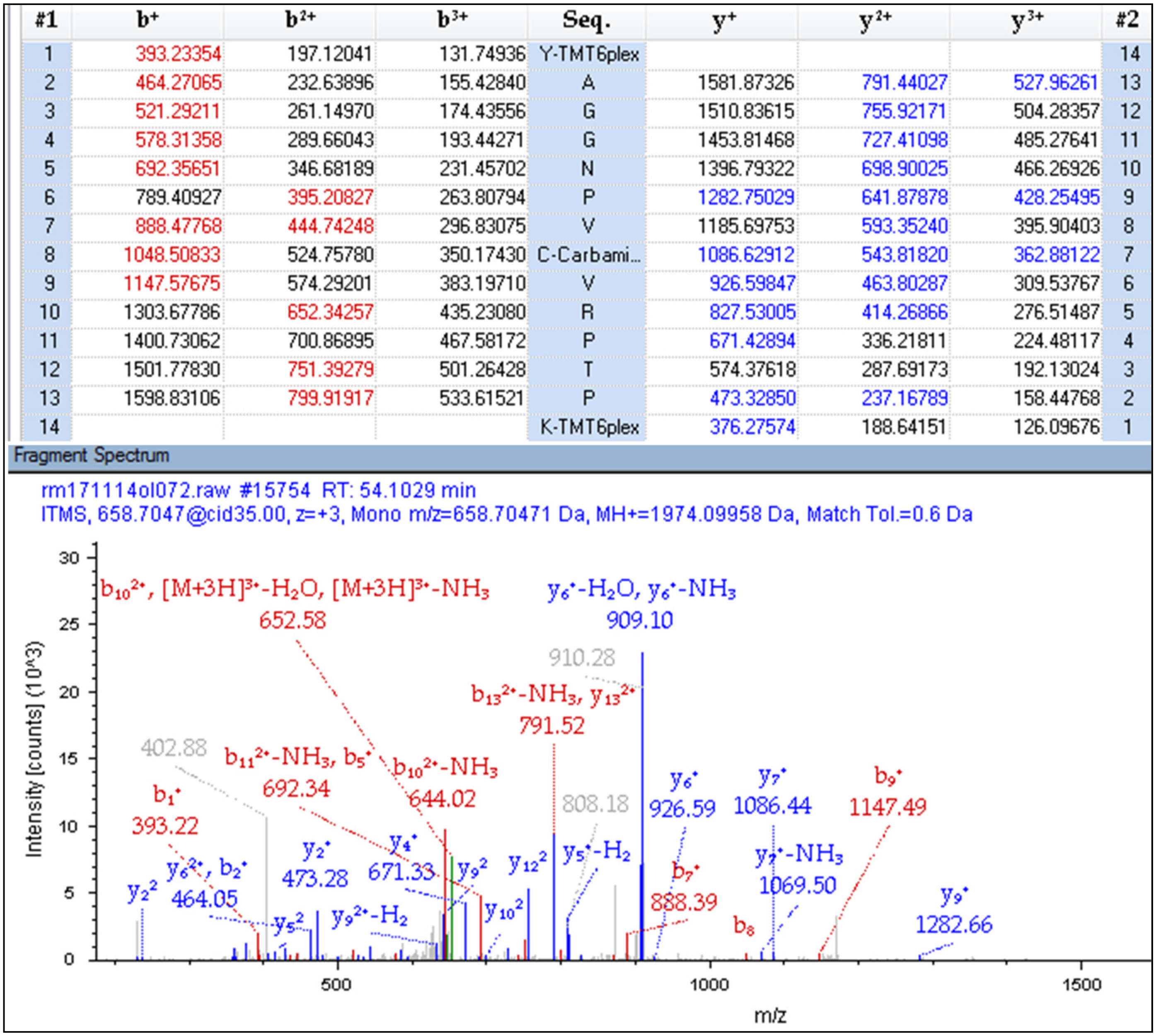
B



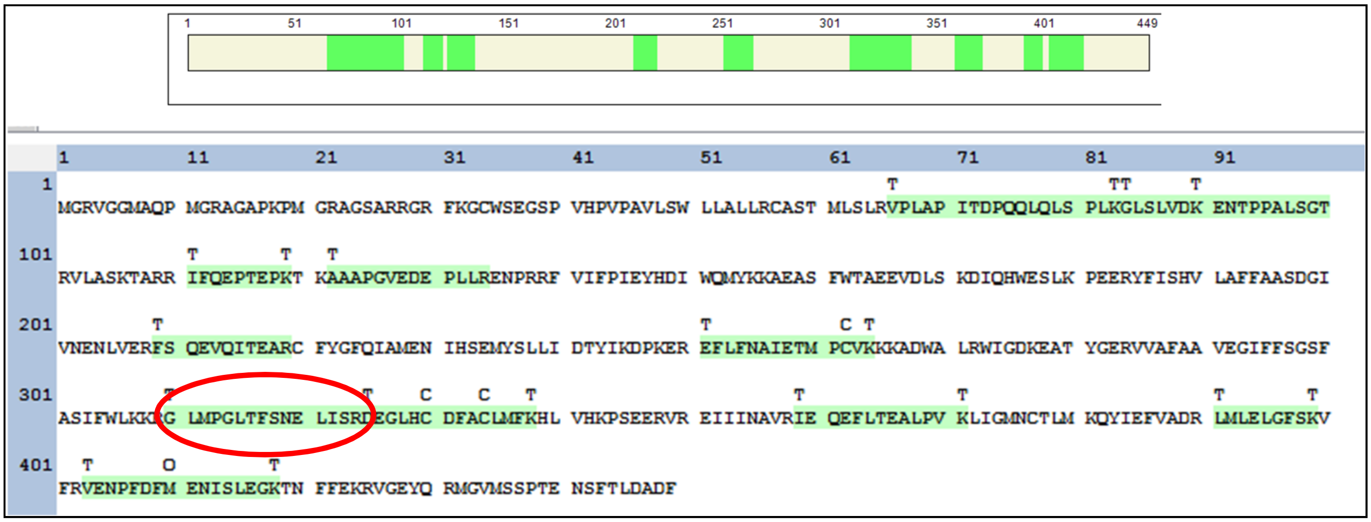
#1	b⁺	b²⁺	b³⁺	Seq.	y⁺	y²⁺	y³⁺	#2
1	393.23354	197.12041	131.74936	Y-TMT6plex				14
2	464.27065	232.63896	155.42840	A	1581.87326	791.44027	527.96261	13
3	521.29211	261.14970	174.43556	G	1510.83615	755.92171	504.28357	12
4	578.31358	289.66043	193.44271	G	1453.81468	727.41098	485.27641	11
5	692.35651	346.68189	231.45702	N	1396.79322	698.90025	466.26926	10
6	789.40927	395.20827	263.80794	P	1282.75029	641.87878	428.25495	9
7	888.47768	444.74248	296.83075	V	1185.69753	593.35240	395.90403	8
8	1048.50833	524.75780	350.17430	C-Carbami...	1086.62912	543.81820	362.88122	7
9	1147.57675	574.29201	383.19710	V	926.59847	463.80287	309.53767	6
10	1303.67786	652.34257	435.23080	R	827.53005	414.26866	276.51487	5
11	1400.73062	700.86895	467.58172	P	671.42894	336.21811	224.48117	4
12	1501.77830	751.39279	501.26428	T	574.37618	287.69173	192.13024	3
13	1598.83106	799.91917	533.61521	P	473.32850	237.16789	158.44768	2
14				K-TMT6plex	376.27574	188.64151	126.09676	1

Fragment Spectrum

rm171114ol072.raw #15754 RT: 54.1029 min
ITMS, 658.7047@cid35.00, z=+3, Mono m/z=658.70471 Da, MH+=1974.09958 Da, Match Tol.=0.6 Da

Nagaprashantha LD et al Supplementary Fig 2

A



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      1          11         21         31         41         51         61         71         81         91
    1                                                                        T                  TT    T
      MGRVGGMAQP MGRAGAPKPM GRAGSARRGR FKGCWSEGSP VHPVPAVLSW LLALLRCAST MLSLRVPLAP ITDPQQLQLS PLKGLSLVDK ENTPPALSGT
  101            T      T    T
      RVLASKTARR IFQEPTEPKT KAAAPGVEDE PLLRENPRRF VIFPIEYHDI WQMYKKAEAS FWTAEEVDLS KDIQHWESLK PEERYFISHV LAFFAASDGI
  201         T                                              T           C T
      VNENLVERFS QEVQITEARC FYGFQIAMEN IHSEMYSLLI DTYIKDPKER EFLFNAIETM PCVKKKADWA LRWIGDKEAT YGERVVAFAA VEGIFFSGSF
  301          T                T    C    C   T                                 T  T                     T       T
      ASIFWLKKRG LMPGLTFSNE LISRDEGLHC DFACLMFKHL VHKPSEERVR EIIINAVRIE QEFLTEALPV KLIGMNCTLM KQYIEFVADR LMLELGFSKV
  401   T      O        T
      FRVENPFDFM ENISLEGKTN FFEKRVGEYQ RMGVMSSPTE NSFTLDADF
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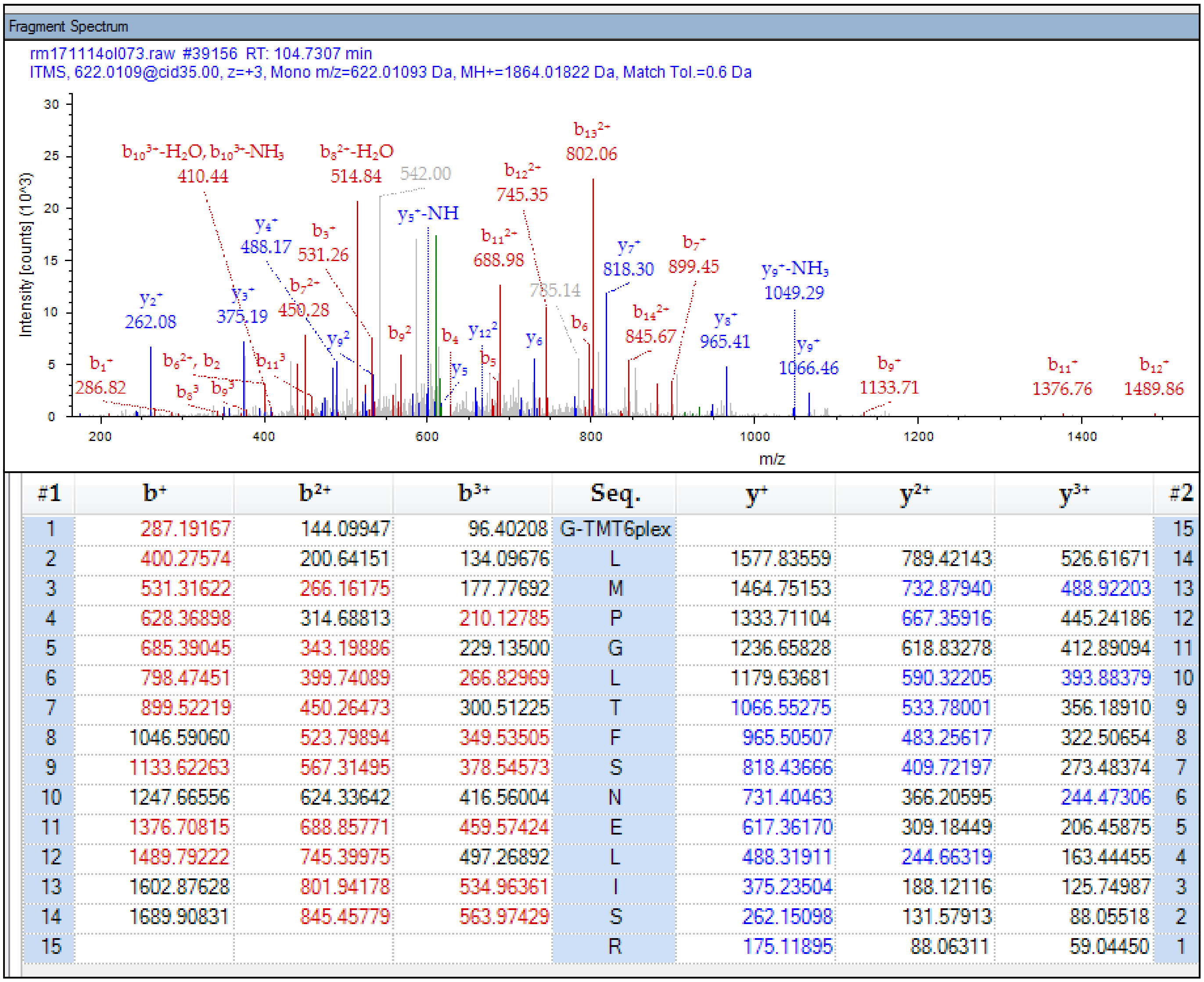
B



Fragment Spectrum

rm171114ol073.raw #39156 RT: 104.7307 min

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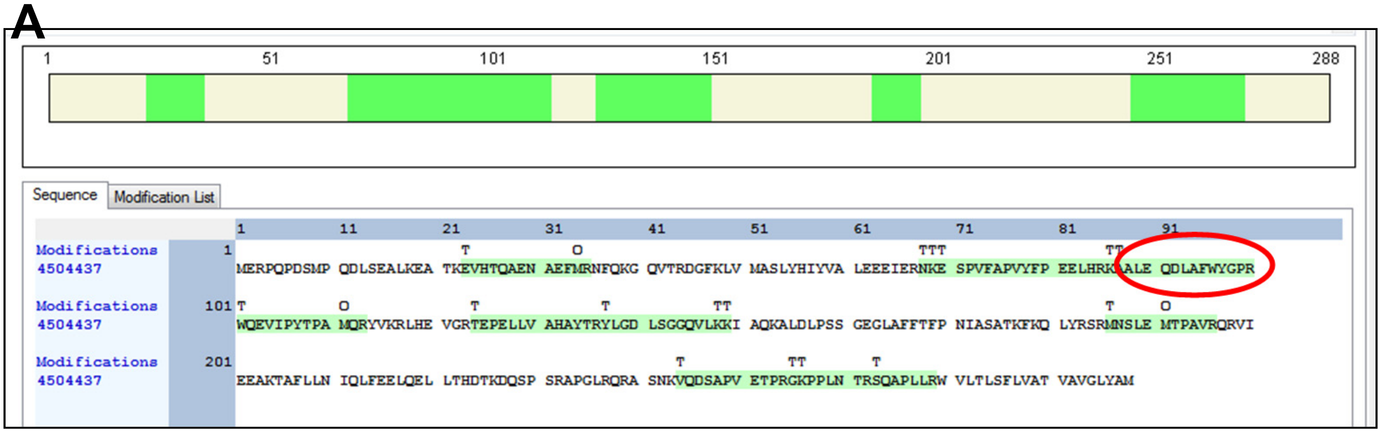
#1	b⁺	b²⁺	b³⁺	Seq.	y⁺	y²⁺	y³⁺	#2
1	287.19167	144.09947	96.40208	G-TMT6plex				15
2	400.27574	200.64151	134.09676	L	1577.83559	789.42143	526.61671	14
3	531.31622	266.16175	177.77692	M	1464.75153	732.87940	488.92203	13
4	628.36898	314.68813	210.12785	P	1333.71104	667.35916	445.24186	12
5	685.39045	343.19886	229.13500	G	1236.65828	618.83278	412.89094	11
6	798.47451	399.74089	266.82969	L	1179.63681	590.32205	393.88379	10
7	899.52219	450.26473	300.51225	T	1066.55275	533.78001	356.18910	9
8	1046.59060	523.79894	349.53505	F	965.50507	483.25617	322.50654	8
9	1133.62263	567.31495	378.54573	S	818.43666	409.72197	273.48374	7
10	1247.66556	624.33642	416.56004	N	731.40463	366.20595	244.47306	6
11	1376.70815	688.85771	459.57424	E	617.36170	309.18449	206.45875	5
12	1489.79222	745.39975	497.26892	L	488.31911	244.66319	163.44455	4
13	1602.87628	801.94178	534.96361	I	375.23504	188.12116	125.74987	3
14	1689.90831	845.45779	563.97429	S	262.15098	131.57913	88.05518	2
15				R	175.11895	88.06311	59.04450	1

Nagaprashantha LD et al Supplementary Fig 3

A



```
                       1         11        21        31        41        51        61        71        81        91
Modifications     1                        T          O                                                TTT                TT
4504437             MERPQPDSMP QDLSEALKEA TKEVHTQAEN AEFMRNFQKG QVTRDGFKLV MASLYHIYVA LEEEIERNKE SPVFAPVYFP EELHRKQALE QDLAFWYGPR

Modifications   101 T          O           T            T           TT                                             T     O
4504437             WQEVIPYTPA MQRYVKRLHE VGRTEPELLV AHAYTRYLGD LSGGQVLKKI AQKALDLPSS GEGLAFFTFP NIASATKFKQ LYRSRMNSLE MTPAVRQRVI

Modifications   201                                                     T           TT        T
4504437             EEAKTAFLLN IQLFEELQEL LTHDTKDQSP SRAPGLRQRA SNKVQDSAPV ETPRGKPPLN TRSQAPLLRW VLTLSFLVAT VAVGLYAM
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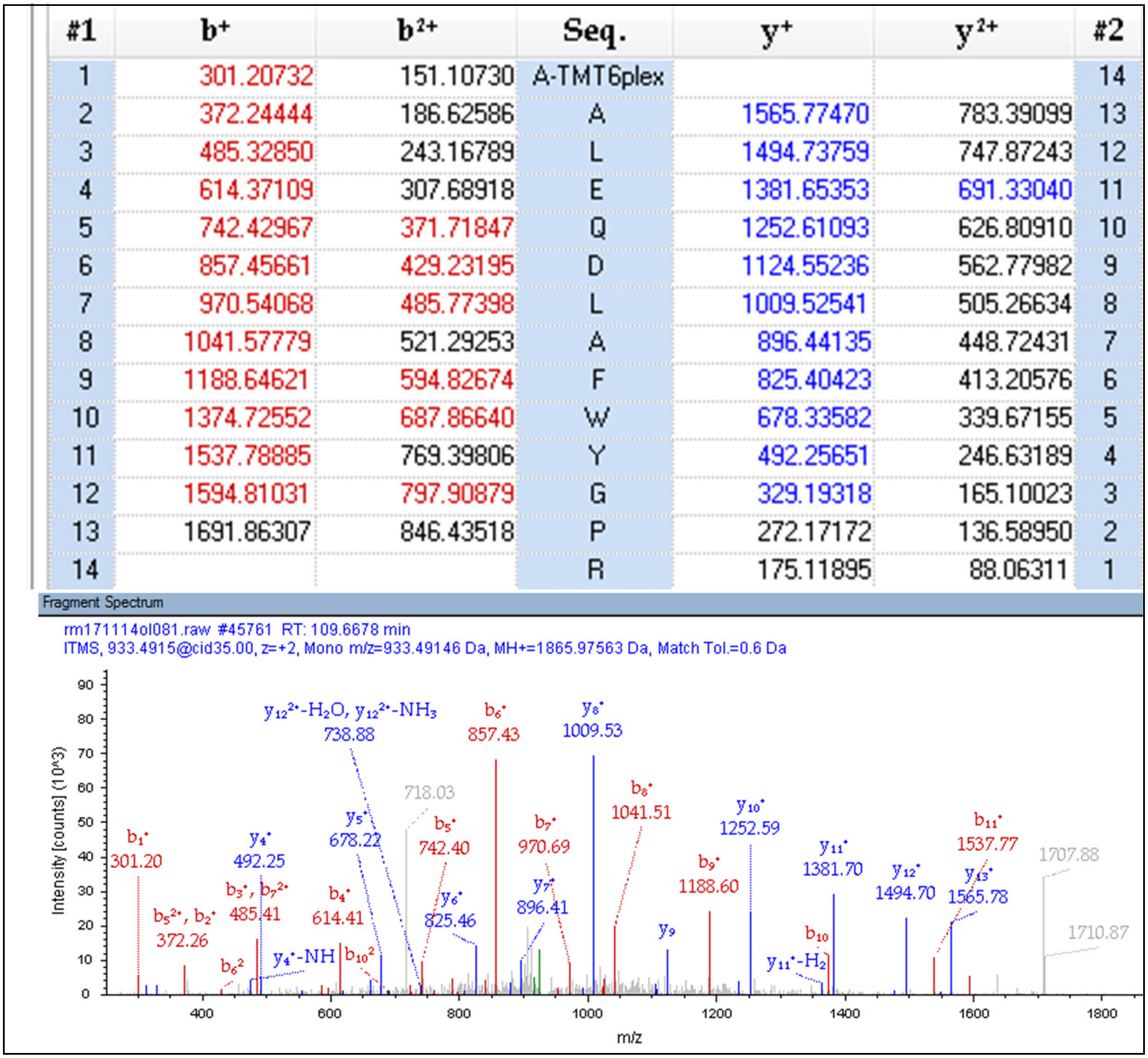
B



#1	b⁺	b²⁺	Seq.	y⁺	y²⁺	#2
1	301.20732	151.10730	A-TMT6plex			14
2	372.24444	186.62586	A	1565.77470	783.39099	13
3	485.32850	243.16789	L	1494.73759	747.87243	12
4	614.37109	307.68918	E	1381.65353	691.33040	11
5	742.42967	371.71847	Q	1252.61093	626.80910	10
6	857.45661	429.23195	D	1124.55236	562.77982	9
7	970.54068	485.77398	L	1009.52541	505.26634	8
8	1041.57779	521.29253	A	896.44135	448.72431	7
9	1188.64621	594.82674	F	825.40423	413.20576	6
10	1374.72552	687.86640	W	678.33582	339.67155	5
11	1537.78885	769.39806	Y	492.25651	246.63189	4
12	1594.81031	797.90879	G	329.19318	165.10023	3
13	1691.86307	846.43518	P	272.17172	136.58950	2
14			R	175.11895	88.06311	1

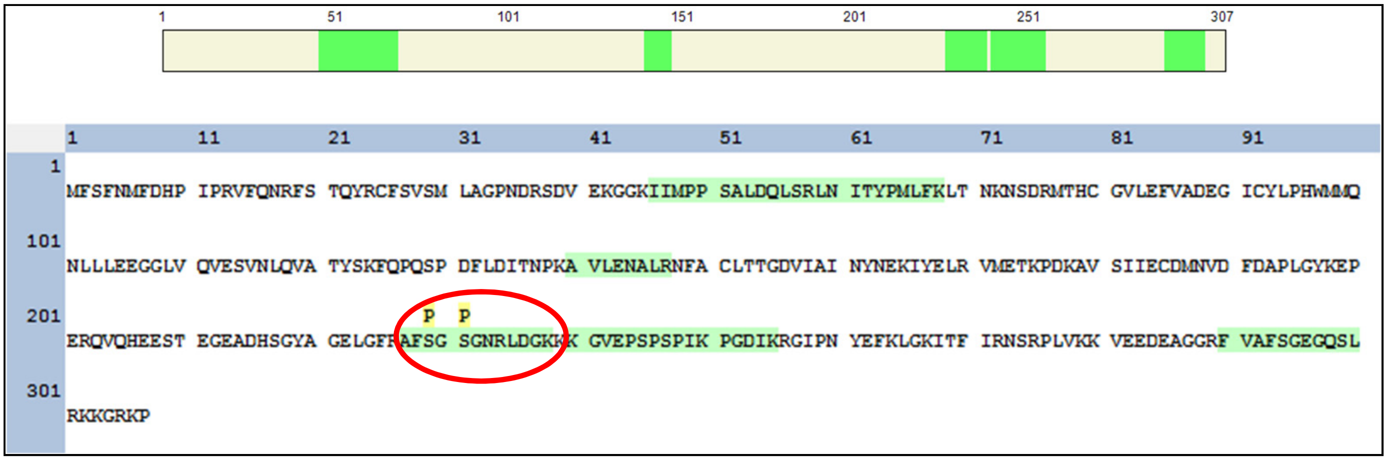
Fragment Spectrum

rm171114ol081.raw #45761 RT: 109.6678 min

ITMS, 933.4915@cid35.00, z=+2, Mono m/z=933.49146 Da, MH+=1865.97563 Da, Match Tol.=0.6 Da

Nagaprashantha LD et al Supplementary Fig 4

A



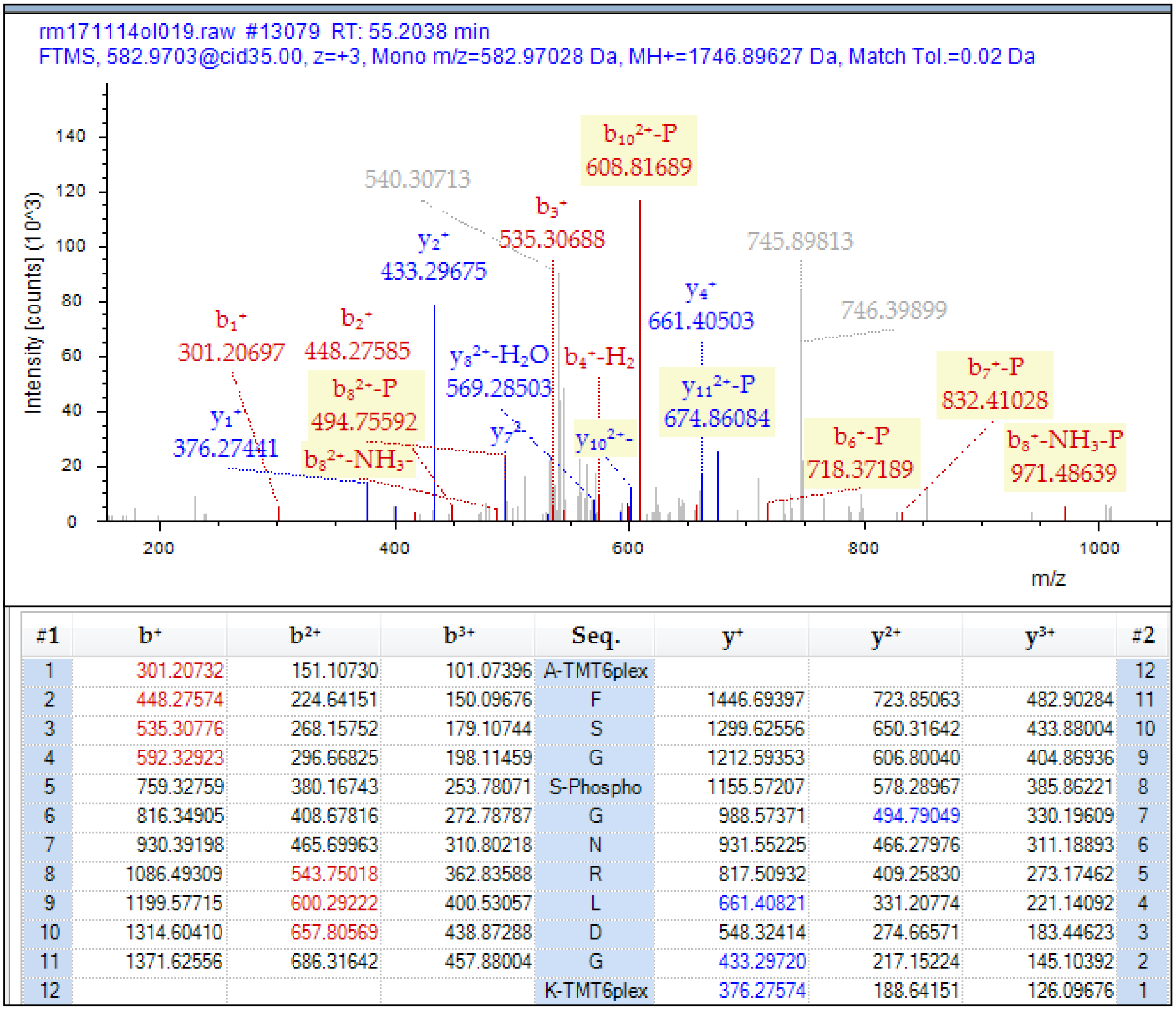
1
MFSFNMFDHP IPRVFQNRFS TQYRCFSVSM LAGPNDRSDV EKGGKIIMPP SALDQLSRLN ITYPMLFKLT NKNSDRMTHC GVLEFVADEG ICYLPHWMMQ

101
NLLLEEGGLV QVESVNLQVA TYSKFQPQSP DFLDITNPKA VLENALRNFA CLTTGDVIAI NYNEKIYELR VMETKPDKAV SIIECDMNVD FDAPLGYKEP

201
ERQVQHEEST EGEADHSGYA GELGFRAFSG SGNRLDGKKK GVEPSPSPIK PGDIKRGIPN YEFKLGKITF IRNSRPLVKK VEEDEAGGRF VAFSGEGQSL

301
RKKGRKP

B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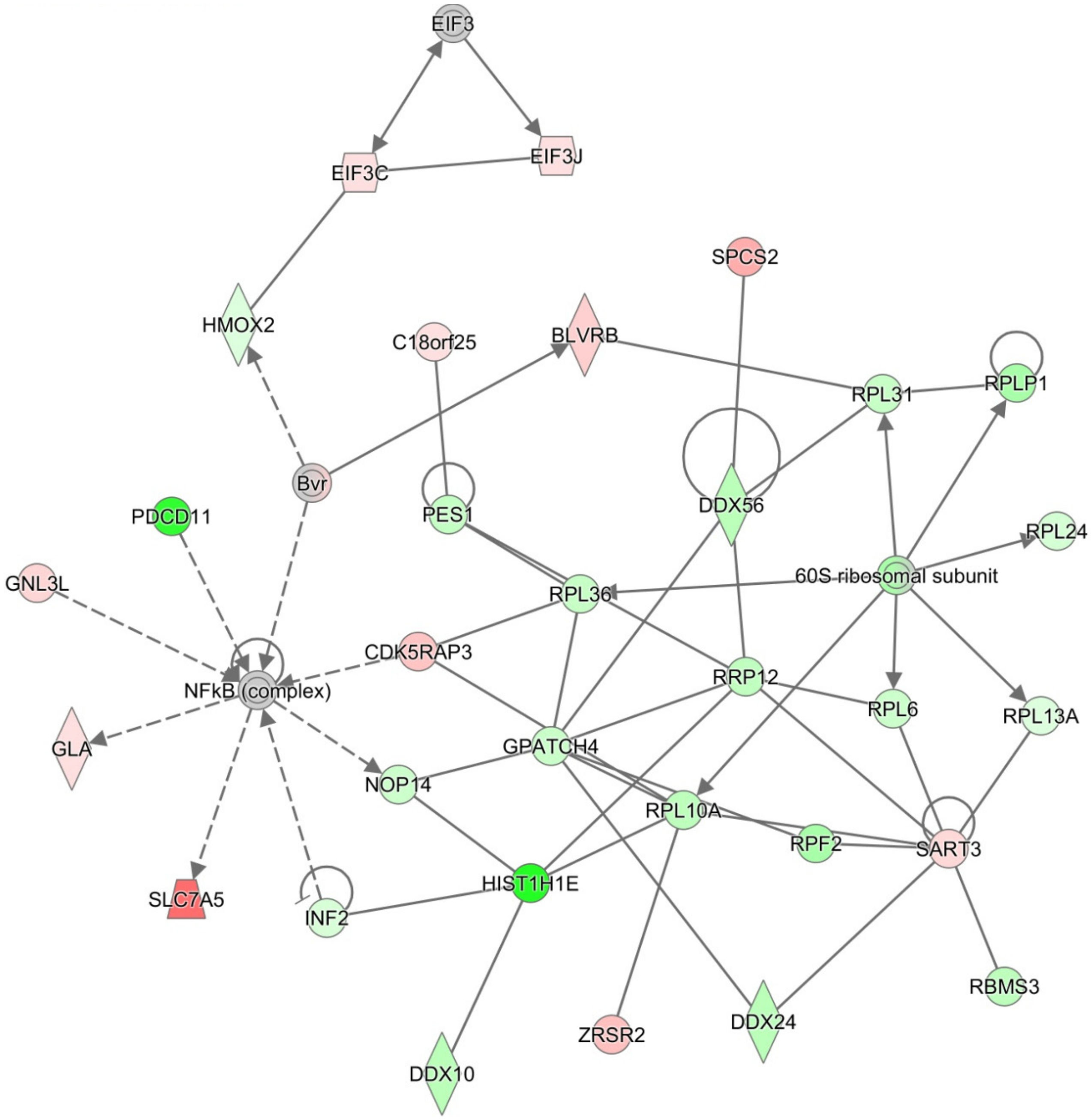
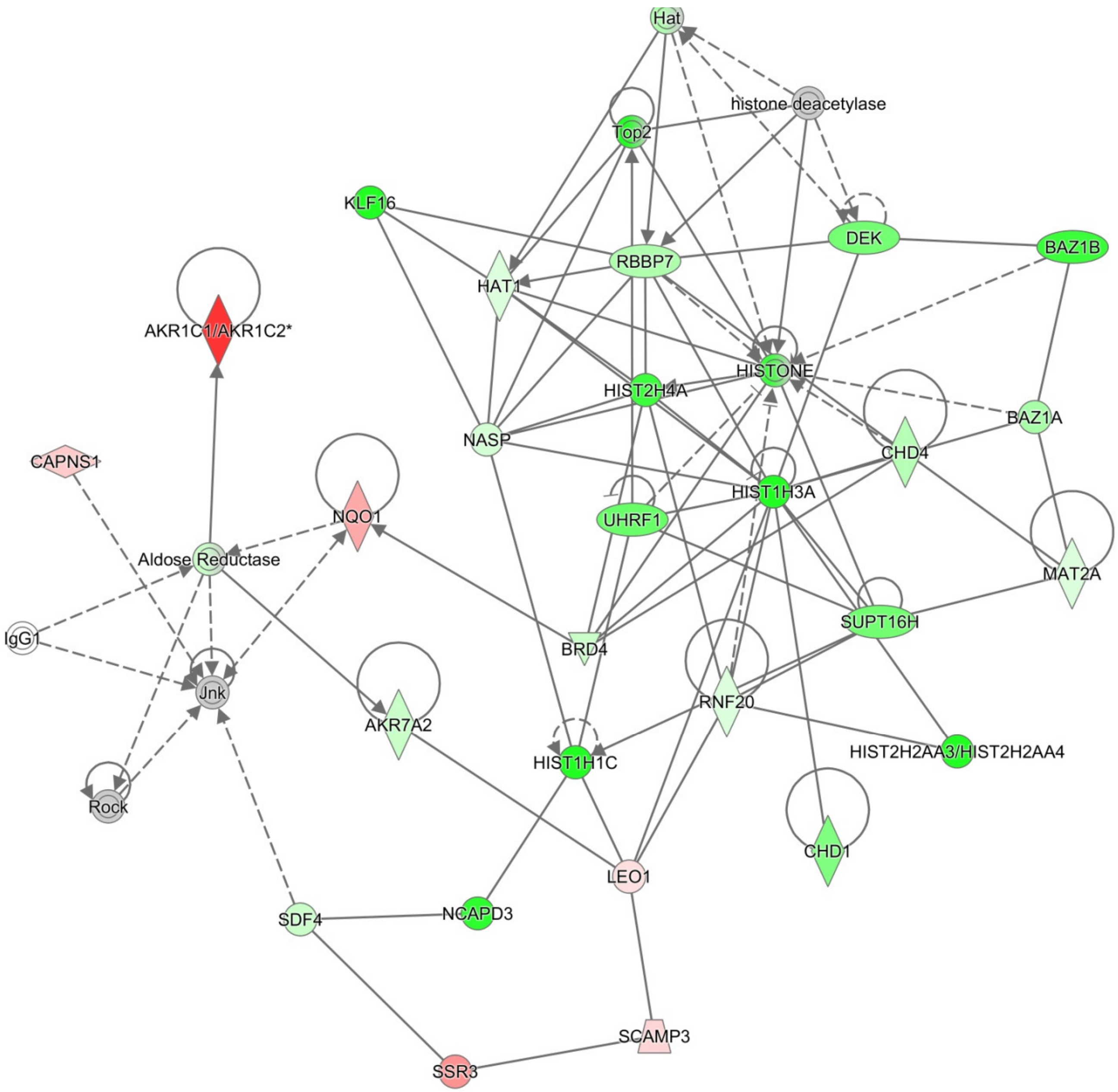
#1	b^+	b^{2+}	b^{3+}	Seq.	y^+	y^{2+}	y^{3+}	#2
1	301.20732	151.10730	101.07396	A-TMT6plex				12
2	448.27574	224.64151	150.09676	F	1446.69397	723.85063	482.90284	11
3	535.30776	268.15752	179.10744	S	1299.62556	650.31642	433.88004	10
4	592.32923	296.66825	198.11459	G	1212.59353	606.80040	404.86936	9
5	759.32759	380.16743	253.78071	S-Phospho	1155.57207	578.28967	385.86221	8
6	816.34905	408.67816	272.78787	G	988.57371	494.79049	330.19609	7
7	930.39198	465.69963	310.80218	N	931.55225	466.27976	311.18893	6
8	1086.49309	543.75018	362.83588	R	817.50932	409.25830	273.17462	5
9	1199.57715	600.29222	400.53057	L	661.40821	331.20774	221.14092	4
10	1314.60410	657.80569	438.87288	D	548.32414	274.66571	183.44623	3
11	1371.62556	686.31642	457.88004	G	433.29720	217.15224	145.10392	2
12				K-TMT6plex	376.27574	188.64151	126.09676	1

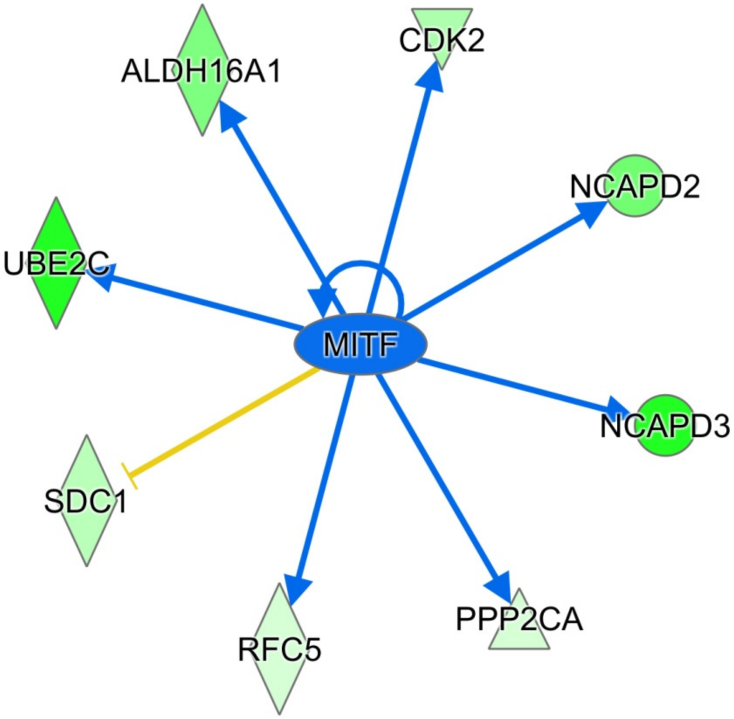
Nagaprashantha LD et al Supplementary Fig 5



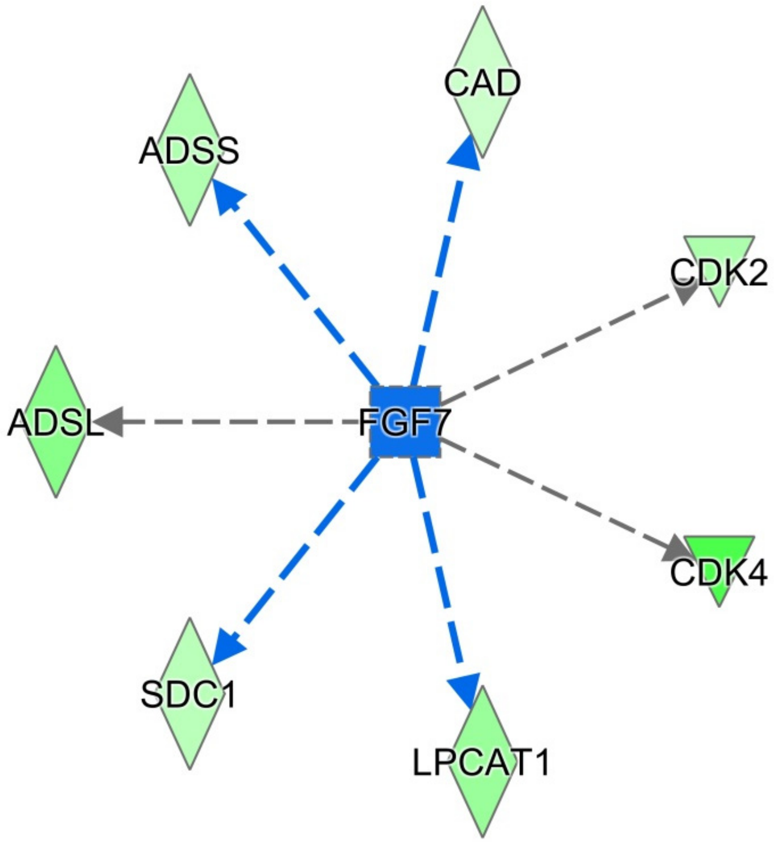
Nagaprashantha LD et al Supplementary Fig 6



Nagaprashantha LD et al Supplementary Fig 7



Nagaprashantha LD et al Supplementary Fig 8



Supplemental Figure Legends:

Supplemental Figure S1: Identification of the non-phosphorylated protein PCNA associated isoform 1 (PAF1) peptide YAGGNPVCVRPTTPK: ***A*,** The PAF1 protein showing the sequence coverage following TMT 10plex MS/MS analyses in breast cancer cells. ***B*,** The MS/MS spectrum obtained by Proteome Discoverer 2.2 software corresponding to PAF1 peptide YAGGNPVCVRPTTPK. The MS/MS spectra were extracted and searched using Thermo Proteome Discoverer 2.2/Sequest HT against the NCBI Homo Sapiens Reference Sequences database.

Supplemental Figure S2: Identification of the non-phosphorylated protein ribonucleotide reductase M2 subunit (RRM2) peptide GLMPGLTFSNELISR: ***A*,** The RRM2 protein showing the sequence coverage following TMT 10plex MS/MS analyses in breast cancer cells. ***B*,** The MS/MS spectrum obtained by Proteome Discoverer 2.2 software corresponding to RRM2 peptide GLMPGLTFSNELISRAKR. The MS/MS spectra were extracted and searched using Thermo Proteome Discoverer 2.2/Sequest HT against the NCBI Homo Sapiens Reference Sequences database.

Supplemental Figure S3: Identification of the non-phosphorylated protein Heme Oxygenase 1 (HO1) peptide AALEQDLAFWYGPR: ***A*,** The HO1 protein showing the sequence coverage following TMT 10plex MS/MS analyses in BC cells. ***B*,** The MS/MS spectrum obtained by Proteome Discoverer 2.2 software corresponding to HO1 peptide AALEQDLAFWYGPR. The MS/MS spectra were extracted and searched using Thermo Proteome Discoverer 2.2/Sequest HT against the NCBI Homo Sapiens Reference Sequences database.

Supplemental Figure S4: Identification of the phosphoprotein ubiquitin fusion degradation protein 1 (UFD1) peptide AFSGp-SGNRLDGK: ***A*,** The UFD1 protein showing the sequence coverage following TMT 10plex MS/MS analyses in BC cells. ***B*,** The MS/MS spectrum obtained by Proteome Discoverer 2.2 software corresponding to UFD1 phosphopeptide AFSGp-SGNRLDGK. The MS/MS spectra were extracted and searched using Thermo Proteome Discoverer 2.2/Sequest HT against the NCBI Homo Sapiens Reference Sequences database.

Supplemental Figure S5: Effect of 2HF on Small Molecule Biochemistry Network in MCF7 cells. Ingenuity Pathway Analyses (IPA) revealing the regulation of small molecule biochemistry network and associated proteins including 60S ribosomal subunit, DDX56, RPL10A, HIST1H1E, PDCD11 and HMOX2 in MCF7 breast cancer cells.

Supplemental Figure S6: Effect of 2HF on Cell Cycle Network in MCF7 cells. Ingenuity Pathway Analyses (IPA) revealing the regulation of cell cycle and associated proteins including HIST1HC, Top2, DEK, KLF16 and NCAPD3 in MCF7 breast cancer cells.

Supplemental Figure S7: Effect of 2HF on MITF Network in MDA-MB231 cells. Ingenuity Pathway Analyses (IPA) revealing the regulation of MITF network and associated proteins including CDK2, UBE2C, NCAPD3 and SDC1 in MDA-MB231 breast cancer cells.

Supplemental Figure S8: Effect of 2HF on FGF7 Network in MDA-MB231 cells. Ingenuity Pathway Analyses (IPA) revealing the regulation of FGF7 network and associated proteins including CDK4, CDK2, CAD and LPCAT1 in MDA-MB231 breast cancer cells.