

Supporting Information

Chemoproteomic study uncovers HemK2/KMT9 as a new target for NTMT1 bisubstrate inhibitors

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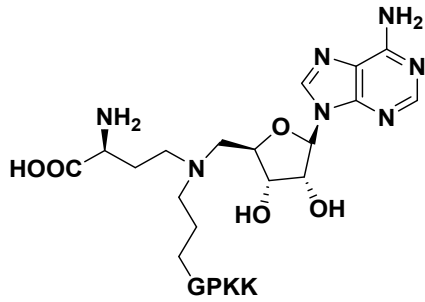
Corresponding Author * huang-r@purdue.edu

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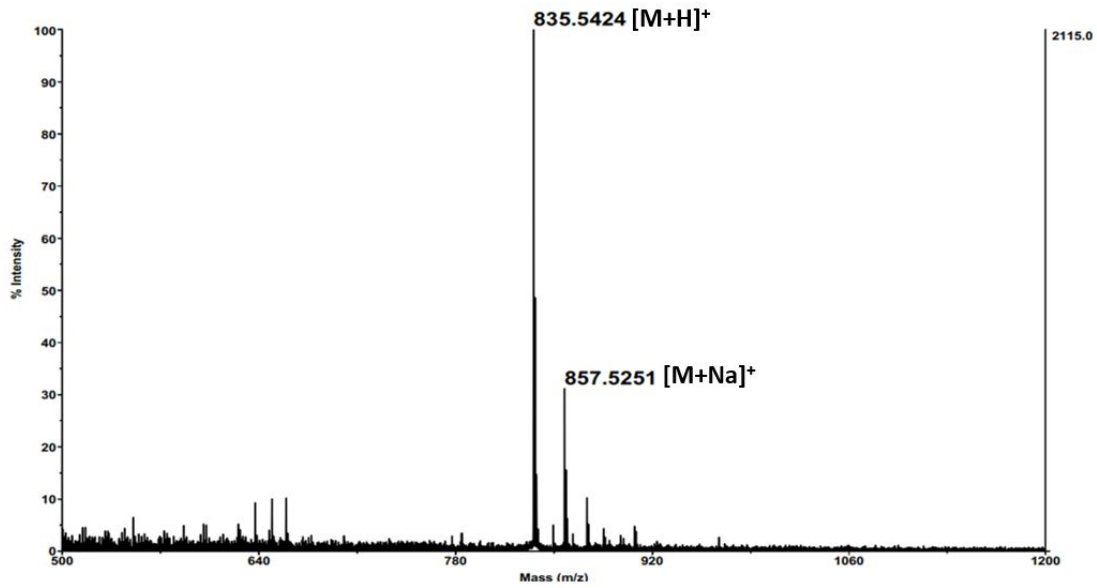
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MS and HPLC analysis of compounds 1-6

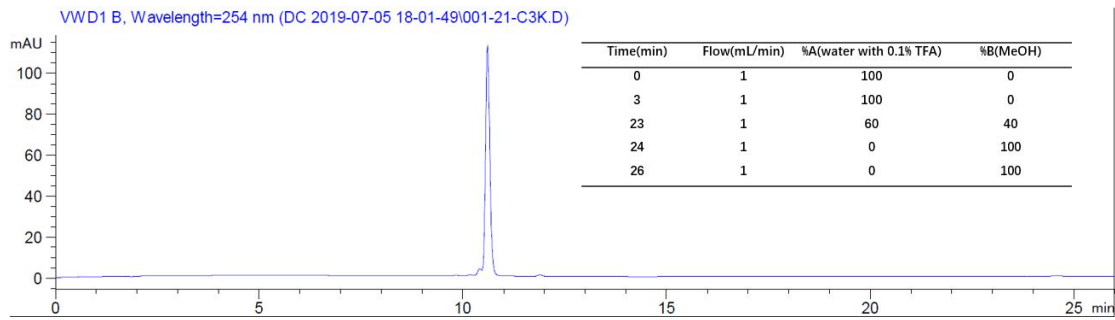
MALDI-MS and HPLC spectra of compound 1



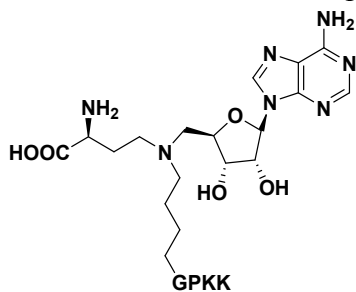
MALDI-MS spectra of compound 1



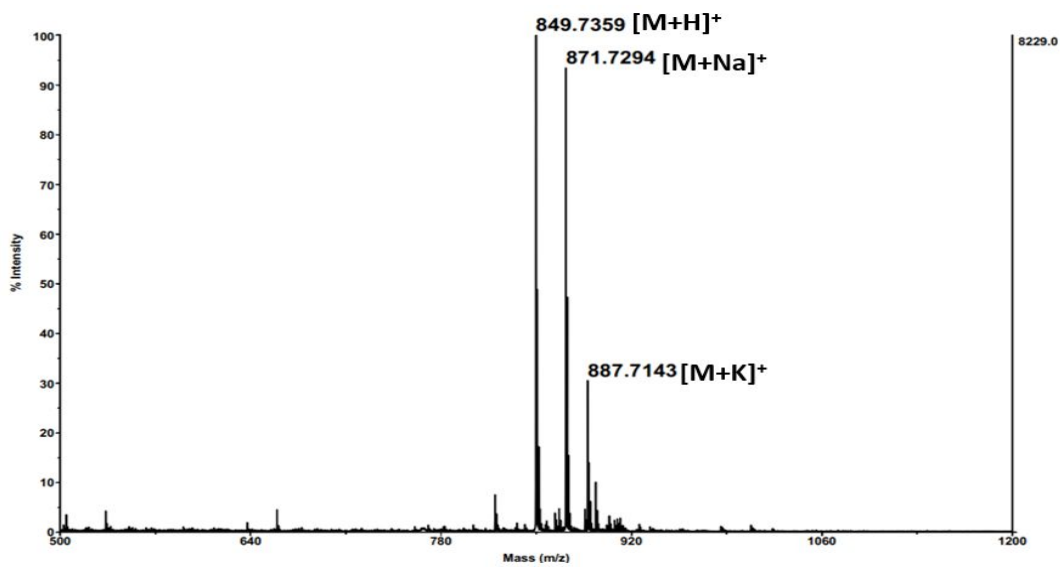
HPLC spectra of compound 1



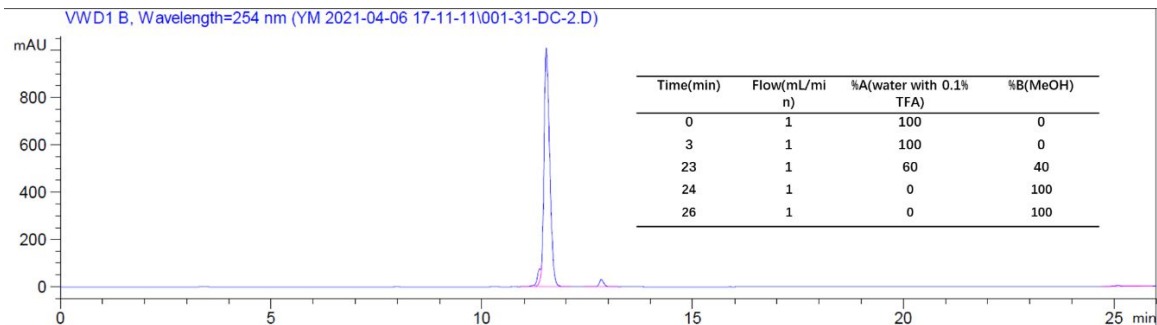
MALDI-MS and LC-MS spectra of compound **2**



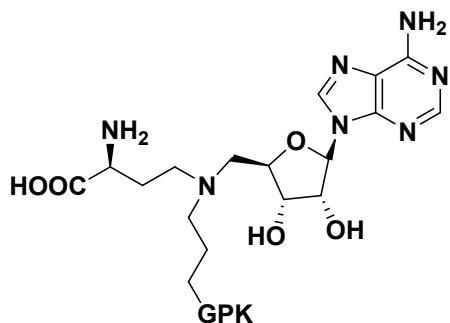
MALDI-MS spectra of compound **2**



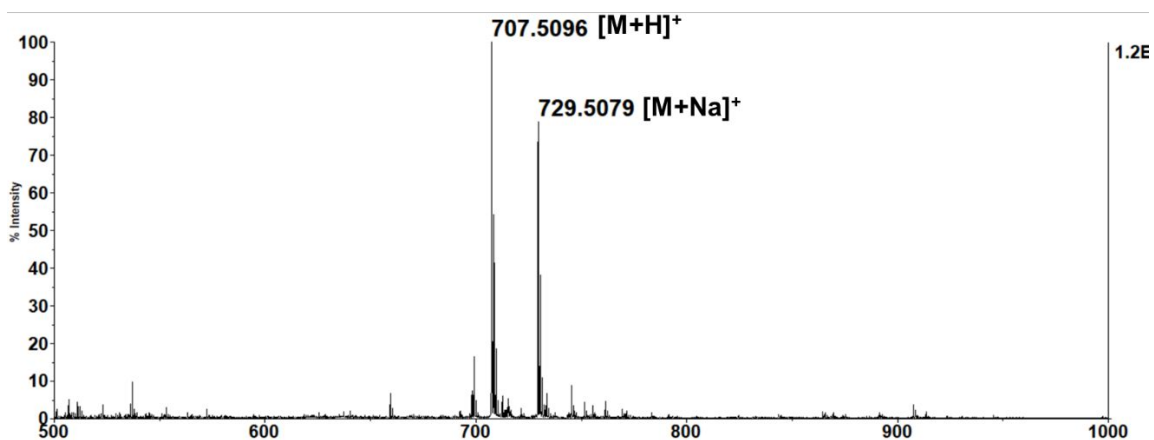
HPLC spectra of compound **2**



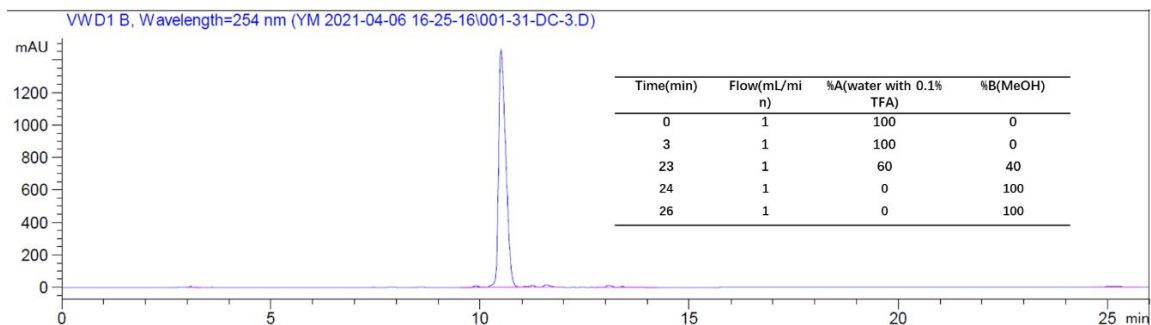
MALDI-MS and LC-MS spectra of compound **3**



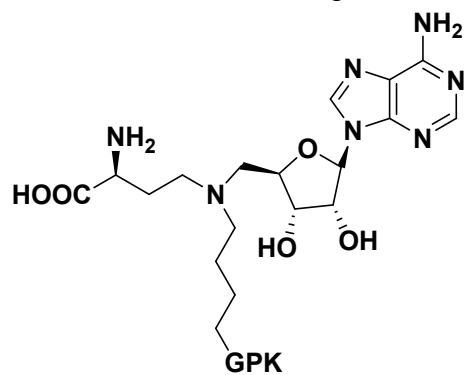
MALDI-MS spectra of compound **3**



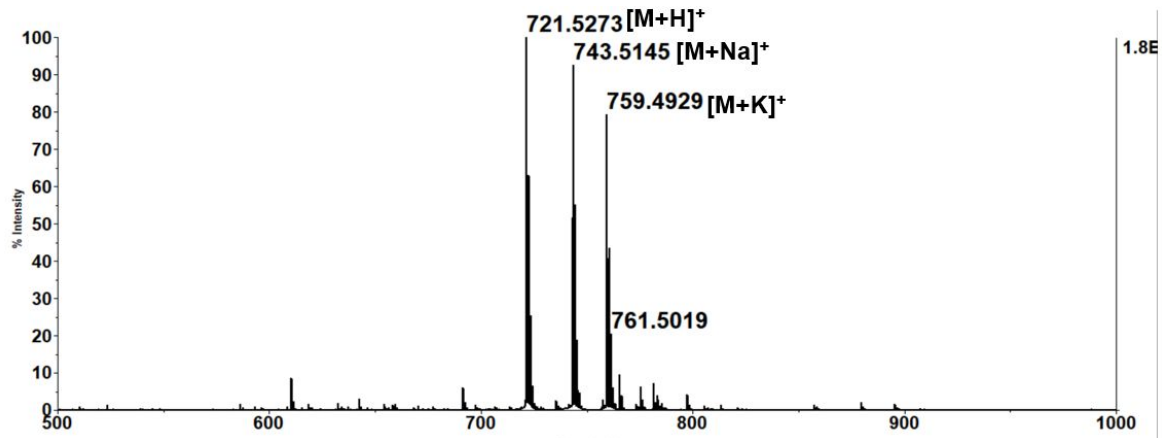
HPLC spectra of compound **3**



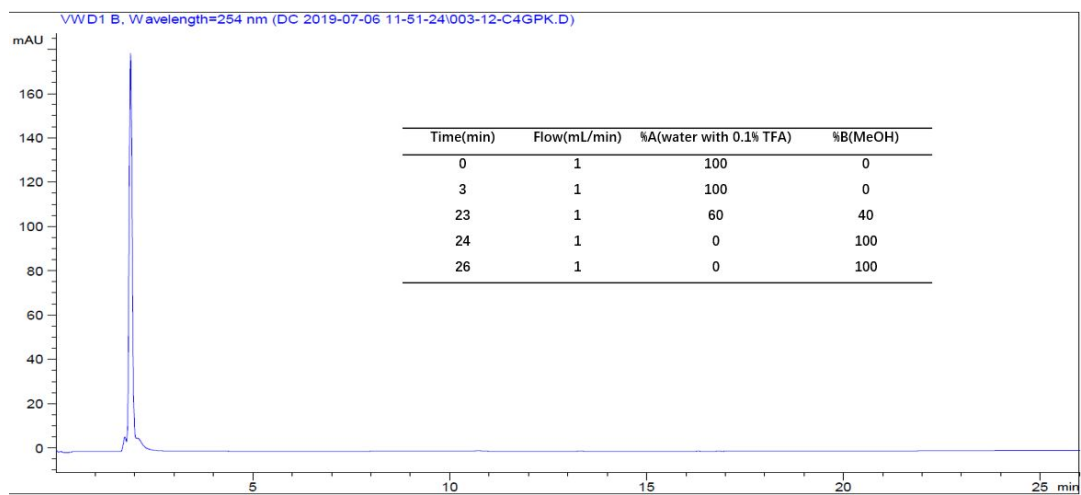
MALDI-MS and HPLC spectra of compound **4**



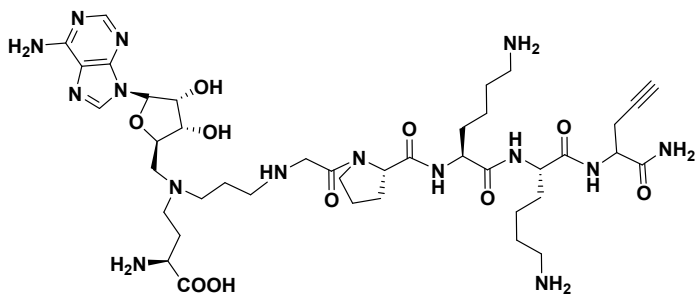
MALDI-MS spectra of compound **4**



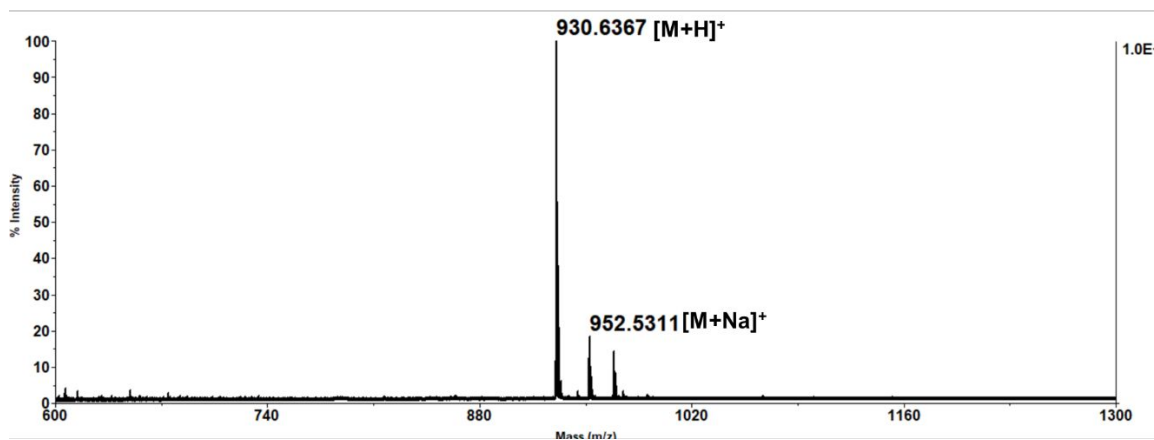
HPLC spectra of compound 4



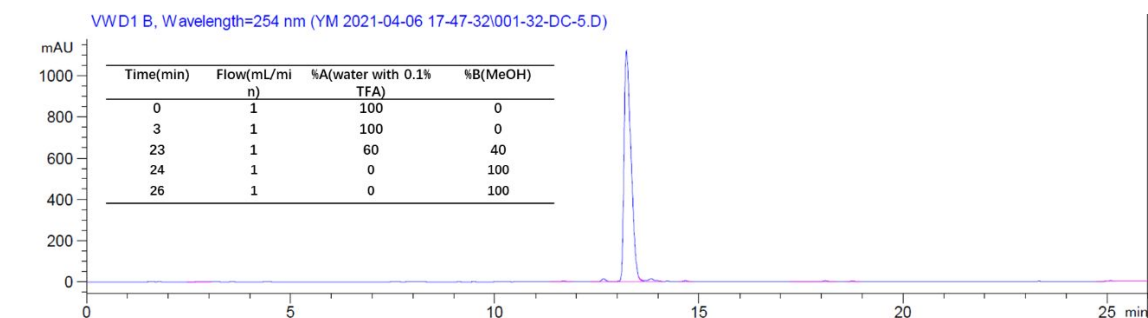
MALDI-MS and HPLC spectra of compound 5



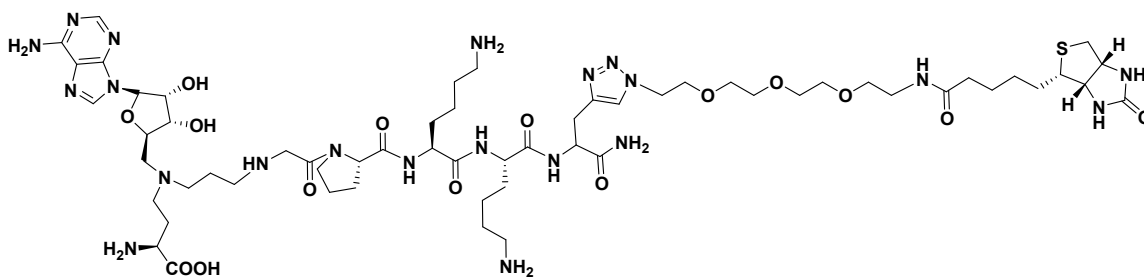
MALDI-MS spectra of compound 5



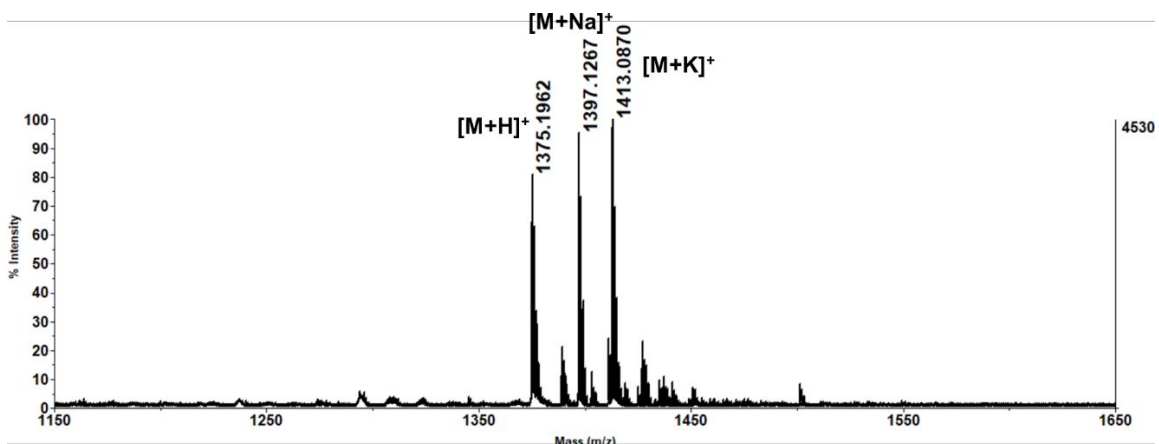
HPLC spectra of compound 5



MALDI-MS and HPLC spectra of compound 6



MALDI-MS spectra of compound 6



HPLC spectra of compound 6

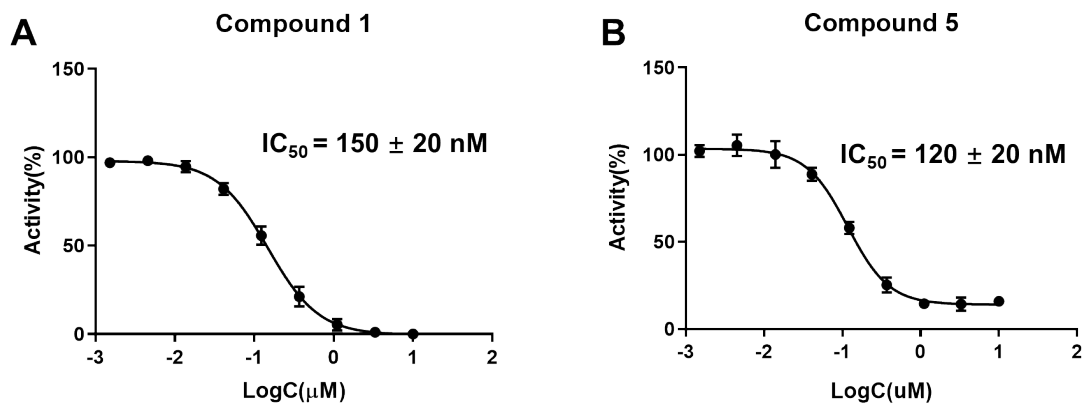
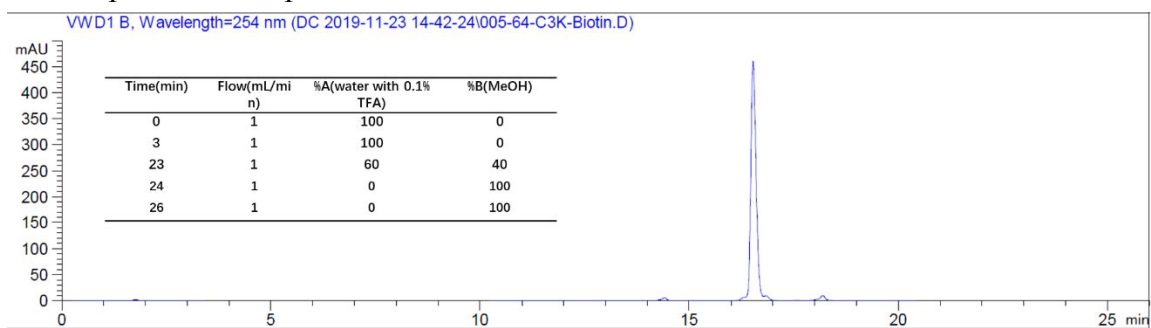


Figure S1. IC_{50} curves for compounds 1 (A) and 5 (B), respectively.

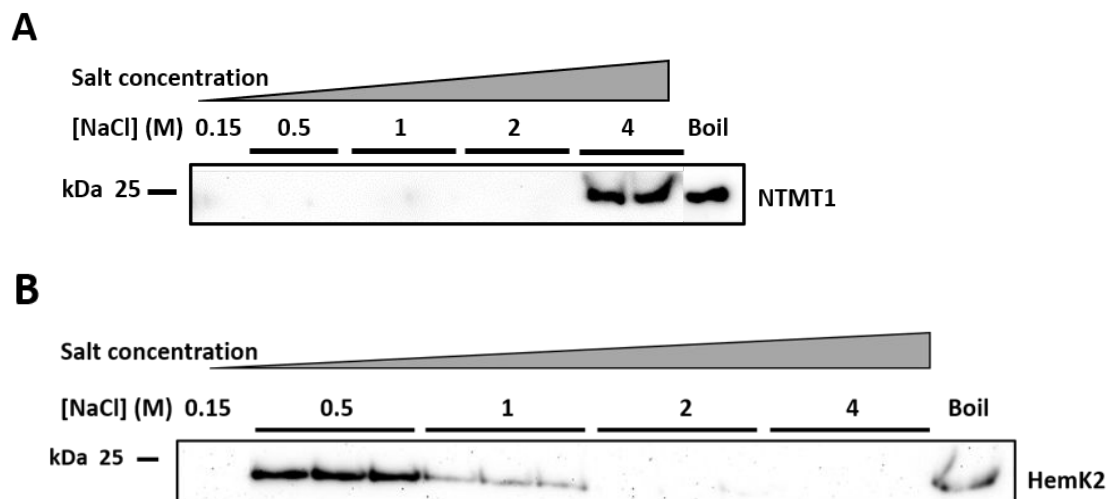


Figure S2. Pull-down studies with recombinant NTMT1 and HemK2-Trm112 complex from immobilized probe 6. (A) Probe 6 shows tight binding with NTMT1. Recombinant NTMT1 were incubated with probe 6 coupled streptavidin beads and eluted 4 M NaCl. (B) HemK2-Trm112 complex directly interacts with probe 6. HemK2 was eluted after

boiling the resin and was eluted off between 500 mM and 1M NaCl.

Table S1. Proteomic analysis of HeLa cell proteomics enriched by probe 6 through LC-MS/MS.

Accession	Protein name	Fold change = Log2(probe 6/ (inhibitor 1 + probe 6))	Confidence value = $-\log_{10}(\text{P-value})$
O14578-3	Isoform 3 of Citron Rho-interacting kinase [OS=Homo sapiens]	12.1	3.3
Q9Y5N5	HemK methyltransferase family member 2 [OS=Homo sapiens]	8.3	2.8
P51153	Ras-related protein Rab-13 [OS=Homo sapiens]	8.3	2.6
O00571	ATP-dependent RNA helicase DDX3X [OS=Homo sapiens]	7.7	2.5
Q96AG4	Leucine-rich repeat-containing protein 59 [OS=Homo sapiens]	7.6	1.6
P04843	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1 [OS=Homo sapiens]	7.6	2.5
P84085	ADP-ribosylation factor 5 [OS=Homo sapiens]	7.4	2.6
P27824-2	Isoform 2 of Calnexin [OS=Homo sapiens]	7.4	2.4

Q9BV86-1	N-terminal Xaa-Pro-Lys N-methyltransferase 1 [OS=Homo sapiens]	7.3	3.2
P38919	Eukaryotic initiation factor 4A-III [OS=Homo sapiens]	7.2	2.4
Q08211	Atp-dependent rna helicase a [OS=Homo sapiens]	6.9	2.5
Q961X5	Up-regulated during skeletal muscle growth protein 5 [OS=Homo sapiens]	6.9	2.5
P60842	Eukaryotic initiation factor 4A-I [OS=Homo sapiens]	6.8	2.4
Q9UI30	Multifunctional methyltransferase subunit TRM112-like protein [OS=Homo sapiens]	6.8	2.5
P61204	ADP-ribosylation factor 3 [OS=Homo sapiens]	6.7	2.5
P51149	ras-related protein Rab-7a [OS=Homo sapiens]	6.6	2.4
Q70UQ0-4	Isoform 4 of Inhibitor of nuclear factor kappa-B kinase-interacting protein [OS=Homo sapiens]	6.5	2.4
Q9Y3U8	60S ribosomal protein L36 [OS=Homo sapiens]	6.4	2.3
P13073	Cytochrome c oxidase subunit 4 isoform 1, mitochondrial [OS=Homo sapiens]	6.4	1.7
Q9NR30-1	Nucleolar RNA helicase 2 [OS=Homo sapiens]	6.3	2.1
P62826	GTP-binding nuclear protein RAN [OS=Homo sapiens]	6.2	2.2
P43243	Matrin-3 [OS=Homo sapiens]	6.2	2.2
O75746	Calcium-binding mitochondrial carrier protein Aralar1 [OS=Homo sapiens]	6.2	2.5
Q9UJS0-2	Isoform 2 of Calcium-binding mitochondrial carrier protein Aralar2 [OS=Homo sapiens]	6.2	2.5
P00403	Cytochrome c oxidase subunit 2 [OS=Homo sapiens]	6.2	1.9
Q6DD88	Atlastin-3 [OS=Homo sapiens]	6.1	2.3
P51148-2	Isoform 2 of Ras-related protein Rab-5C [OS=Homo sapiens]	6.0	2.3
Q96A26	Protein FAM162A [OS=Homo sapiens]	5.9	2.3

O00567	Nucleolar protein 56 [OS=Homo sapiens]	5.9	2.3
Q9NZ45	CDGSH iron-sulfur domain-containing protein 1 [OS=Homo sapiens]	5.7	2.0
P61224-1	Ras-related protein Rap-1b [OS=Homo sapiens]	5.6	2.1
Q14697-2	Isoform 2 of Neutral alpha-glucosidase AB [OS=Homo sapiens]	5.6	2.2
Q9Y277-2	Isoform 2 of Voltage-dependent anion-selective channel protein 3 [OS=Homo sapiens]	5.5	0.9
O75947-1	ATP synthase subunit d, mitochondrial [OS=Homo sapiens]	5.5	1.8
Q9BVP2	Guanine nucleotide-binding protein-like 3 [OS=Homo sapiens]	5.5	2.0
Q16790	Carbonic anhydrase 9 [OS=Homo sapiens]	5.4	1.8
O60762	Dolichol-phosphate mannosyltransferase subunit 1 [OS=Homo sapiens]	5.4	1.7
O60506	Heterogeneous nuclear ribonucleoprotein Q [OS=Homo sapiens]	5.4	0.9
O43169	Cytochrome b5 type B [OS=Homo sapiens]	5.3	1.9
Q9BWF3-1	RNA-binding protein 4 [OS=Homo sapiens]	5.2	2.1
Q9Y2X3	Nucleolar protein 58 [OS=Homo sapiens]	5.2	2.1
P36542-1	ATP synthase subunit gamma, mitochondrial [OS=Homo sapiens]	5.2	1.7
P33993-1	DNA replication licensing factor MCM7 [OS=Homo sapiens]	5.1	2.0
O43809	Cleavage and polyadenylation specificity factor subunit 5 [OS=Homo sapiens]	5.1	1.7
P12956	X-ray repair cross-complementing protein 6 [OS=Homo sapiens]	5.1	2.2
Q07065	Cytoskeleton-associated protein 4 [OS=Homo sapiens]	5.0	2.1

P01891	HLA class I histocompatibility antigen, A-68 alpha chain [OS=Homo sapiens]	5.0	1.9
P51648-2	Isoform 2 of Fatty aldehyde dehydrogenase [OS=Homo sapiens]	5.0	2.2
P22626	heterogeneous nuclear ribonucleoproteins A2/B1 [OS=Homo sapiens]	4.9	1.0
P16615	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 [OS=Homo sapiens]	4.9	0.9
Q9NVI7-2	Isoform 2 of ATPase family AAA domain-containing protein 3A [OS=Homo sapiens]	4.9	1.4
Q9Y4P3	Transducin beta-like protein 2 [OS=Homo sapiens]	4.9	2.0
P20340-1	Ras-related protein Rab-6A [OS=Homo sapiens]	4.8	1.2
P61026	ras-related protein rab-10 [OS=Homo sapiens]	4.7	1.3
P11476-1	Ras-related protein Rab-1A [OS=Homo sapiens]	4.7	1.3
P21796	voltage-dependent anion-selective channel protein 1 [OS=Homo sapiens]	4.7	1.1
P61106	Ras-related protein Rab-14 [OS=Homo sapiens]	4.7	1.3
O00264	Membrane-associated progesterone receptor component 1 [OS=Homo sapiens]	4.7	0.9
P78527	DNA-dependent protein kinase catalytic subunit [OS=Homo sapiens]	4.6	0.9
P34897-1	Serine hydroxymethyltransferase, mitochondrial [OS=Homo sapiens]	4.6	0.9
P69905	Hemoglobin subunit alpha [OS=Homo sapiens]	4.6	1.6
P63173	60s ribosomal protein l38 [OS=Homo sapiens]	4.6	1.4
P62491-1	Ras-related protein Rab-11A [OS=Homo sapiens]	4.5	1.9
P30508	HLA class I histocompatibility antigen, Cw-12 alpha chain [OS=Homo sapiens]	4.5	1.4

Q12905	Interleukin enhancer-binding factor 2 [OS=Homo sapiens]	4.5	0.9
P62273-2	Isoform 2 of 40S ribosomal protein S29 [OS=Homo sapiens]	4.4	0.8
Q8NBJ4	Golgi membrane protein 1 [OS=Homo sapiens]	4.4	1.9
Q9BVK6	Transmembrane emp24 domain-containing protein 9 [OS=Homo sapiens]	4.4	1.6
P16989-1	Y-box-binding protein 3 [OS=Homo sapiens]	4.3	1.8
P05556-1	Integrin beta-1 [OS=Homo sapiens]	4.3	0.9
P46940	Ras GTPase-activating-like protein IQGAP1 [OS=Homo sapiens]	4.2	2.3
O95292	Vesicle-associated membrane protein-associated protein B/C [OS=Homo sapiens]	4.2	1.0
P09669	Cytochrome c oxidase subunit 6C [OS=Homo sapiens]	4.2	0.9
Q9P0L0-2	Isoform 2 of Vesicle-associated membrane protein-associated protein A [OS=Homo sapiens]	4.2	1.5
O00461	Golgi integral membrane protein 4 [OS=Homo sapiens]	4.2	1.6
Q9NZ01-1	Very-long-chain enoyl-CoA reductase [OS=Homo sapiens]	4.1	0.9
P06576	ATP synthase subunit beta, mitochondrial [OS=Homo sapiens]	4.1	3.0
P61978-2	Isoform 2 of Heterogeneous nuclear ribonucleoprotein K [OS=Homo sapiens]	4.0	1.2
P22087	rRNA 2'-O-methyltransferase fibrillarin [OS=Homo sapiens]	4.0	1.3
P62910	60S ribosomal protein L32 [OS=Homo sapiens]	3.9	1.6
Q9NXW2-2	Isoform 2 of DnaJ homolog subfamily B member 12 [OS=Homo sapiens]	3.9	1.8
O43390-2	Isoform 2 of Heterogeneous nuclear ribonucleoprotein R [OS=Homo sapiens]	3.8	1.0

P27635	60S ribosomal protein L10 [OS=Homo sapiens]	3.7	1.3
Q8NE86	Calcium uniporter protein, mitochondrial [OS=Homo sapiens]	3.6	1.0
O75367-1	Core histone macro-H2A.1 [OS=Homo sapiens]	3.5	1.0
P62805	histone H4 [OS=Homo sapiens]	3.5	1.4
Q9Y5S2	Serine/threonine-protein kinase MRCK beta [OS=Homo sapiens]	3.4	1.8
P01889	HLA class I histocompatibility antigen, B-7 alpha chain [OS=Homo sapiens]	3.3	0.9
P62753	40S RIBOSOMAL PROTEIN S6 [OS=Homo sapiens]	3.3	1.2
Q14254	Flotillin-2 [OS=Homo sapiens]	3.3	1.3
P42167	Lamina-associated polypeptide 2, isoforms beta/gamma [OS=Homo sapiens]	3.3	2.0
P17301	Integrin alpha-2 [OS=Homo sapiens]	3.3	1.0
Q96CW1	AP-2 complex subunit mu [OS=Homo sapiens]	3.2	1.2
P42677	40S ribosomal protein S27 [OS=Homo sapiens]	3.2	3.5
Q96CS3	FAS-associated factor 2 [OS=Homo sapiens]	3.2	0.9
Q9HDC9	Adipocyte plasma membrane-associated protein [OS=Homo sapiens]	3.1	0.8
P49748-3	Isoform 3 of Very long-chain specific acyl-CoA dehydrogenase, mitochondrial [OS=Homo sapiens]	3.1	1.1
P50914	60S ribosomal protein L14 [OS=Homo sapiens]	3.1	2.0
P27348	14-3-3 protein theta [OS=Homo sapiens]	3.1	0.5
Q9Y265	RuvB-like 1 [OS=Homo sapiens]	3.1	1.0
P62258-1	14-3-3 protein epsilon [OS=Homo sapiens]	3.1	0.5
P17844	probable ATP-dependent RNA helicase DDX5 [OS=Homo sapiens]	3.1	2.8
P61981	14-3-3 protein gamma [OS=Homo sapiens]	3.0	0.5

P19388	DNA-directed RNA polymerases I, II, and III subunit RPABC1 [OS=Homo sapiens]	3.0	0.6
O14929	histone acetyltransferase type B catalytic subunit [OS=Homo sapiens]	3.0	0.5
P60866-2	Isoform 2 of 40S ribosomal protein S20 [OS=Homo sapiens]	3.0	1.0
Q92841	Probable ATP-dependent RNA helicase DDX17 [OS=Homo sapiens]	2.9	1.8
Q71UM5	40S ribosomal protein S27-like [OS=Homo sapiens]	2.9	2.3
P31947-1	14-3-3 protein sigma [OS=Homo sapiens]	2.9	0.4
P14625	Endoplasmic reticulum chaperone protein [OS=Homo sapiens]	2.8	3.9
P02788	Lactotransferrin [OS=Homo sapiens]	2.7	0.5
P05023	Sodium/potassium-transporting ATPase subunit alpha-1 [OS=Homo sapiens]	2.7	1.7
Q9Y5M8	signal recognition particle receptor subunit beta [OS=Homo sapiens]	2.7	1.3
P45880-1	Isoform 1 of Voltage-dependent anion-selective channel protein 2 [OS=Homo sapiens]	2.7	1.4
P53680	AP-2 complex subunit sigma [OS=Homo sapiens]	2.7	0.5
O75396	Vesicle-trafficking protein SEC22b [OS=Homo sapiens]	2.6	1.6
P48047	ATP synthase subunit O, mitochondrial [OS=Homo sapiens]	2.6	2.0
P63104-1	14-3-3 protein zeta/delta [OS=Homo sapiens]	2.6	0.5
P29401-2	Isoform 2 of Transketolase [OS=Homo sapiens]	2.6	0.9
P14868	Aspartate--tRNA ligase, cytoplasmic [OS=Homo sapiens]	2.5	1.9
O00425	Insulin-like growth factor 2 mRNA-binding protein 3 [OS=Homo sapiens]	2.5	0.6
P31946	14-3-3 protein beta/alpha [OS=Homo sapiens]	2.5	0.4

P08237-3	Isoform 3 of ATP-dependent 6-phosphofructokinase, muscle type [OS=Homo sapiens]	2.4	0.3
Q9Y6M9	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9 [OS=Homo sapiens]	2.4	0.8
P25705-1	ATP synthase subunit alpha, mitochondrial [OS=Homo sapiens]	2.4	1.7
P39023	60S ribosomal protein L3 [OS=Homo sapiens]	2.4	1.3
Q9HA64	Ketosamine-3-kinase [OS=Homo sapiens]	2.4	1.8
P32969	60S ribosomal protein L9 [OS=Homo sapiens]	2.3	2.4
Q8N1F7-1	Nuclear pore complex protein Nup93 [OS=Homo sapiens]	2.3	1.4
P62424	60S ribosomal protein L7a [OS=Homo sapiens]	2.3	1.2
Q96A08	Histone H2B type 1-A [OS=Homo sapiens]	2.3	1.0
Q16891-2	Isoform 2 of MICOS complex subunit MIC60 [OS=Homo sapiens]	2.3	1.9
Q16891-4	Isoform 4 of MICOS complex subunit MIC60 [OS=Homo sapiens]	2.3	1.9
Q96S19-4	Isoform 4 of UPF0585 protein C16orf13 [OS=Homo sapiens]	2.2	0.9
Q9Y3D9	28S ribosomal protein S23, mitochondrial [OS=Homo sapiens]	2.2	1.1
P39656	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit [OS=Homo sapiens]	2.2	0.4
Q07020	60S ribosomal protein L18 [OS=Homo sapiens]	2.2	3.0
P83731	60S ribosomal protein L24 [OS=Homo sapiens]	2.1	1.3
P40939	Trifunctional enzyme subunit alpha, mitochondrial [OS=Homo sapiens]	2.1	1.5
P52597	Heterogeneous nuclear ribonucleoprotein F [OS=Homo sapiens]	2.1	1.6

P42765	3-ketoacyl-CoA thiolase, mitochondrial [OS=Homo sapiens]	2.0	0.4
P31689-1	DnaJ homolog subfamily A member 1 [OS=Homo sapiens]	2.0	1.8
P24539	ATP synthase F(0) complex subunit B1, mitochondrial [OS=Homo sapiens]	1.9	1.5
P23396-1	40S ribosomal protein S3 [OS=Homo sapiens]	1.9	1.3
P18085	ADP-ribosylation factor 4 [OS=Homo sapiens]	1.8	1.6
Q12797	Aspartyl/Asparaginyl beta-hydroxylase [OS=Homo sapiens]	1.8	0.4
Q86UE4	protein LYRIC [OS=Homo sapiens]	1.7	0.9
P62241	40S ribosomal protein S8 [OS=Homo sapiens]	1.7	1.3
Q9Y241	HIG1 domain family member 1A, mitochondrial [OS=Homo sapiens]	1.7	0.5
P50454	Serpin H1 [OS=Homo sapiens]	1.7	0.9
P18124	60S ribosomal protein L7 [OS=Homo sapiens]	1.6	1.1
P08574	Cytochrome c1, heme protein, mitochondrial [OS=Homo sapiens]	1.6	0.4
P10809	60 kDa heat shock protein, mitochondrial [OS=Homo sapiens]	1.6	1.5
P07195	L-lactate dehydrogenase B chain [OS=Homo sapiens]	1.6	0.3
Q13492-1	Phosphatidylinositol-binding clathrin assembly protein [OS=Homo sapiens]	1.6	0.3
Q92769	Histone deacetylase 2 [OS=Homo sapiens]	1.5	0.3
P46781	40S ribosomal protein S9 [OS=Homo sapiens]	1.5	1.1
P04075	fructose-bisphosphate aldolase A [OS=Homo sapiens]	1.5	0.3
Q9Y230	RuvB-like 2 [OS=Homo sapiens]	1.5	2.0
P35268	60S ribosomal protein L22 [OS=Homo sapiens]	1.5	0.9
P08195-4	Isoform 4 of 4F2 cell-surface antigen heavy chain [OS=Homo sapiens]	1.5	0.7

P61353	60S ribosomal protein L27 [OS=Homo sapiens]	1.4	0.7
Q15233	Non-POU domain-containing octamer-binding protein [OS=Homo sapiens]	1.4	0.6
Q12931	heat shock protein 75 kDa, mitochondrial [OS=Homo sapiens]	1.4	0.2
Q15365	Poly(RC)-binding protein 1 [OS=Homo sapiens]	1.4	0.9
P62244	40S ribosomal protein S15a [OS=Homo sapiens]	1.4	1.6
P02786	Transferrin receptor protein 1 [OS=Homo sapiens]	1.3	1.5
Q7Z2W4	zinc finger CCCH-type antiviral protein 1 [OS=Homo sapiens]	1.2	0.7
Q14684	Ribosomal RNA processing protein 1 homolog B [OS=Homo sapiens]	1.2	1.0
O95782	AP-2 complex subunit alpha-1 [OS=Homo sapiens]	1.2	0.6
Q99567	Nuclear pore complex protein Nup88 [OS=Homo sapiens]	1.2	0.2
P46776	60S ribosomal protein L27a [OS=Homo sapiens]	1.2	1.0
P57721-1	Poly(rC)-binding protein 3 [OS=Homo sapiens]	1.2	1.1
Q00839	Heterogeneous nuclear ribonucleoprotein U [OS=Homo sapiens]	1.1	1.2
P31943	Heterogeneous nuclear ribonucleoprotein H [OS=Homo sapiens]	1.1	0.8
P63010-2	Isoform 2 of AP-2 complex subunit beta [OS=Homo sapiens]	1.1	0.8
P08238	Heat shock protein HSP 90-beta [OS=Homo sapiens]	1.1	2.1
P67809	Nuclease-sensitive element-binding protein 1 [OS=Homo sapiens]	1.1	0.2
P54136-1	arginine--tRNA ligase, cytoplasmic [OS=Homo sapiens]	1.1	1.3
O43175	D-3-phosphoglycerate dehydrogenase [OS=Homo sapiens]	1.1	3.1

Q9NX63	MICOS complex subunit MIC19 [OS=Homo sapiens]	1.0	1.4
P35232	Prohibitin [OS=Homo sapiens]	0.9	0.5
P62829	60S ribosomal protein L23 [OS=Homo sapiens]	0.9	0.4
Q01813	ATP-dependent 6-phosphofructokinase, platelet type [OS=Homo sapiens]	0.9	1.3
P05388	60S acidic ribosomal protein P0 [OS=Homo sapiens]	0.9	1.5
P52272	Heterogeneous nuclear ribonucleoprotein M [OS=Homo sapiens]	0.9	0.5
Q9UHX1-1	poly(U)-binding-splicing factor PUF60 [OS=Homo sapiens]	0.9	0.1
P18077	60S ribosomal protein L35a [OS=Homo sapiens]	0.9	1.7
P39019	40S ribosomal protein S19 [OS=Homo sapiens]	0.9	0.8
P28066-1	Proteasome subunit alpha type-5 [OS=Homo sapiens]	0.9	0.1
Q5QNW6-2	Isoform 2 of Histone H2B type 2-F [OS=Homo sapiens]	0.8	0.5
P62277	40S ribosomal protein S13 [OS=Homo sapiens]	0.8	0.7
P62701	40S ribosomal protein S4, X isoform [OS=Homo sapiens]	0.8	1.4
Q14980-1	nuclear mitotic apparatus protein 1 [OS=Homo sapiens]	0.8	0.4
Q09666-1	Neuroblast differentiation-associated protein AHNAK [OS=Homo sapiens]	0.8	0.9
P46783	40S ribosomal protein S10 [OS=Homo sapiens]	0.7	1.1
Q99714-1	3-hydroxyacyl-CoA dehydrogenase type-2 [OS=Homo sapiens]	0.7	0.9
P06899	Histone H2B type 1-J [OS=Homo sapiens]	0.7	0.4
P04406-1	glyceraldehyde-3-phosphate dehydrogenase [OS=Homo sapiens]	0.7	0.2
P11940-1	Polyadenylate-binding protein 1 [OS=Homo sapiens]	0.7	1.0

P46778	60S ribosomal protein L21 [OS=Homo sapiens]	0.6	0.6
P62847-4	Isoform 4 of 40S ribosomal protein S24 [OS=Homo sapiens]	0.6	0.3
P62266	40S ribosomal protein S23 [OS=Homo sapiens]	0.6	0.6
Q99623	Prohibitin-2 [OS=Homo sapiens]	0.5	0.4
P18621-3	Isoform 3 of 60S ribosomal protein L17 [OS=Homo sapiens]	0.5	0.3
P68366	Tubulin alpha-4A chain [OS=Homo sapiens]	0.5	0.3
P68104	Elongation factor 1-alpha 1 [OS=Homo sapiens]	0.5	0.4
Q96PK6-1	RNA-binding protein 14 [OS=Homo sapiens]	0.5	0.5
P35613	Basigin [OS=Homo sapiens]	0.5	0.7
Q13573	SNW domain-containing protein 1 [OS=Homo sapiens]	0.4	0.1
P26641	elongation factor 1-gamma [OS=Homo sapiens]	0.4	0.6
P84098	60S ribosomal protein L19 [OS=Homo sapiens]	0.4	0.2
P04083	annexin A1 [OS=Homo sapiens]	0.4	0.1
Q9BWM7	Sideroflexin-3 [OS=Homo sapiens]	0.4	0.1
P06493	Cyclin-dependent kinase 1 [OS=Homo sapiens]	0.3	0.3
P06733-1	alpha-enolase [OS=Homo sapiens]	0.3	0.0
P60900	Proteasome subunit alpha type-6 [OS=Homo sapiens]	0.3	0.1
Q13310-3	Isoform 3 of Polyadenylate-binding protein 4 [OS=Homo sapiens]	0.3	0.5
P62888	60S ribosomal protein L30 [OS=Homo sapiens]	0.2	0.1
P26373-1	60S ribosomal protein L13 [OS=Homo sapiens]	0.2	0.3
P07900-2	Isoform 2 of Heat shock protein HSP 90-alpha [OS=Homo sapiens]	0.2	0.4
P62913	60S ribosomal protein L11 [OS=Homo sapiens]	0.2	0.6

P62750	60S ribosomal protein L23a [OS=Homo sapiens]	0.2	0.0
Q9BUF5	Tubulin beta-6 chain [OS=Homo sapiens]	0.2	0.4
P04908	histone H2A type 1-B/E [OS=Homo sapiens]	0.2	0.1
O43795	Unconventional myosin-Ib [OS=Homo sapiens]	0.2	0.1
P27105	erythrocyte band 7 integral membrane protein [OS=Homo sapiens]	0.2	0.1
Q12965	unconventional myosin-Ie [OS=Homo sapiens]	0.1	0.1
P22695	Cytochrome b-c1 complex subunit 2, mitochondrial [OS=Homo sapiens]	0.1	0.0
P83881	60S ribosomal protein L36a [OS=Homo sapiens]	0.1	0.0
Q13509	tubulin beta-3 chain [OS=Homo sapiens]	0.1	0.1
Q92614-1	Unconventional myosin-XVIIIa [OS=Homo sapiens]	0.1	0.0
P00338-3	Isoform 3 of L-lactate dehydrogenase A chain [OS=Homo sapiens]	0.0	0.0
P07910-1	Heterogeneous nuclear ribonucleoproteins C1/C2 [OS=Homo sapiens]	0.0	0.0
P14618	Pyruvate kinase PKM [OS=Homo sapiens]	0.0	0.0
Q9UKS6	Protein kinase C and casein kinase substrate in neurons protein 3 [OS=Homo sapiens]	0.0	0.0
P68371	Tubulin beta-4B chain [OS=Homo sapiens]	0.0	0.0
P36578	60S ribosomal protein L4 [OS=Homo sapiens]	0.0	0.0
P11021	78 kDa glucose-regulated protein [OS=Homo sapiens]	0.0	0.0
P19338	Nucleolin [OS=Homo sapiens]	-0.1	0.0
P05387	60S acidic ribosomal protein P2 [OS=Homo sapiens]	-0.1	0.1
P61254	60S ribosomal protein L26 [OS=Homo sapiens]	-0.2	0.1

Q01105	Protein SET [OS=Homo sapiens]	-0.2	0.0
P21333	Filamin-A [OS=Homo sapiens]	-0.2	0.1
P07814	Bifunctional glutamate/proline--tRNA ligase [OS=Homo sapiens]	-0.2	0.1
Q02878	60S ribosomal protein L6 [OS=Homo sapiens]	-0.2	0.1
Q14244-7	Isoform 7 of Ensconsin [OS=Homo sapiens]	-0.2	0.3
P0DMV8	heat shock 70 kDa protein 1A [OS=Homo sapiens]	-0.3	0.3
P36957	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial [OS=Homo sapiens]	-0.3	0.1
P62851	40S ribosomal protein S25 [OS=Homo sapiens]	-0.3	0.2
P61513	60S ribosomal protein L37a [OS=Homo sapiens]	-0.3	0.0
P62906	60S ribosomal protein L10A [OS=Homo sapiens]	-0.3	0.5
P63096-1	Guanine nucleotide-binding protein G(i) subunit alpha-1 [OS=Homo sapiens]	-0.3	0.3
P05141	ADP/ATP translocase 2 [OS=Homo sapiens]	-0.3	0.2
P62249	40S ribosomal protein S16 [OS=Homo sapiens]	-0.3	0.3
P07437	tubulin beta chain [OS=Homo sapiens]	-0.3	0.4
Q15046	Lysine--tRNA ligase [OS=Homo sapiens]	-0.4	0.9
P38646	Stress-70 protein, mitochondrial [OS=Homo sapiens]	-0.4	0.9
P35579-1	Myosin-9 [OS=Homo sapiens]	-0.4	0.2
P49411	elongation factor Tu, mitochondrial [OS=Homo sapiens]	-0.5	0.5
Q02543	60S ribosomal protein L18a [OS=Homo sapiens]	-0.5	0.2
Q8WV41	Sorting nexin-33 [OS=Homo sapiens]	-0.5	0.1
P0C0S5	Histone H2A.Z [OS=Homo sapiens]	-0.5	0.2

Q13155	aminoacyl tRNA synthase complex-interacting multifunctional protein 2 [OS=Homo sapiens]	-0.5	0.1
Q69YQ0-1	Cytospin-A [OS=Homo sapiens]	-0.5	0.3
Q9BQE3	Tubulin alpha-1C chain [OS=Homo sapiens]	-0.6	0.5
Q4KMQ1	Taperin [OS=Homo sapiens]	-0.6	0.2
P06702	Protein S100-A9 [OS=Homo sapiens]	-0.6	0.1
Q9BVA1	Tubulin beta-2B chain [OS=Homo sapiens]	-0.6	0.7
P11142-1	Heat shock cognate 71 kDa protein [OS=Homo sapiens]	-0.6	0.7
P09651-1	Heterogeneous nuclear ribonucleoprotein A1 [OS=Homo sapiens]	-0.6	0.4
P55084	Trifunctional enzyme subunit beta, mitochondrial [OS=Homo sapiens]	-0.7	0.1
Q92522	Histone H1x [OS=Homo sapiens]	-0.7	0.1
P08754	Guanine nucleotide-binding protein G(k) subunit alpha [OS=Homo sapiens]	-0.7	0.5
Q96EY1-1	DnaJ homolog subfamily A member 3, mitochondrial [OS=Homo sapiens]	-0.7	0.2
P61247	40S ribosomal protein S3a [OS=Homo sapiens]	-0.7	0.6
P35237	serpin B6 [OS=Homo sapiens]	-0.8	0.2
P12236	ADP/ATP translocase 3 [OS=Homo sapiens]	-0.8	0.6
Q562R1	Beta-actin-like protein 2 [OS=Homo sapiens]	-0.8	0.4
P17858-1	ATP-dependent 6-phosphofructokinase, liver type [OS=Homo sapiens]	-0.8	0.7
Q81VT2	Mitotic interactor and substrate of PLK1 [OS=Homo sapiens]	-0.8	0.3
Q9HAV0	Guanine nucleotide-binding protein subunit beta-4 [OS=Homo sapiens]	-0.8	0.1
O00763	Acetyl-CoA carboxylase 2 [OS=Homo sapiens]	-0.9	1.1
P49790	Nuclear pore complex protein Nup153 [OS=Homo sapiens]	-0.9	0.2

P51571	translocon-associated protein subunit delta [OS=Homo sapiens]	-0.9	0.2
P04899-4	Isoform sGi2 of Guanine nucleotide-binding protein G(i) subunit alpha-2 [OS=Homo sapiens]	-0.9	1.1
P46777	60S ribosomal protein L5 [OS=Homo sapiens]	-1.0	0.1
P62879	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2 [OS=Homo sapiens]	-1.0	0.1
Q9Y512	sorting and assembly machinery component 50 homolog [OS=Homo sapiens]	-1.1	0.2
Q6WCQ1-2	Isoform 2 of Myosin phosphatase Rho-interacting protein [OS=Homo sapiens]	-1.1	0.2
Q9Y613-1	Isoform 2 of Epsin-1 [OS=Homo sapiens]	-1.1	1.6
P23284	peptidyl-prolyl cis-trans isomerase B [OS=Homo sapiens]	-1.1	0.5
Q5T750	Skin-specific protein 32 [OS=Homo sapiens]	-1.1	0.2
P62263	40S ribosomal protein S14 [OS=Homo sapiens]	-1.2	0.8
P05166-2	Isoform 2 of Propionyl-CoA carboxylase beta chain, mitochondrial [OS=Homo sapiens]	-1.2	0.9
Q9NZT1	Calmodulin-like protein 5 [OS=Homo sapiens]	-1.2	0.6
P05165-1	Propionyl-CoA carboxylase alpha chain, mitochondrial [OS=Homo sapiens]	-1.2	1.9
P23528	Cofilin-1 [OS=Homo sapiens]	-1.2	0.1
P02545	Prelamin-A/C [OS=Homo sapiens]	-1.2	0.2
P40429	60S ribosomal protein L13a [OS=Homo sapiens]	-1.2	0.2
P62873	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1 [OS=Homo sapiens]	-1.4	0.2
P62269	40S ribosomal protein S18 [OS=Homo sapiens]	-1.4	3.4

Q13085-1	Acetyl-CoA carboxylase 1 [OS=Homo sapiens]	-1.4	1.8
P31327-3	Isoform 3 of Carbamoyl-phosphate synthase [ammonia], mitochondrial [OS=Homo sapiens]	-1.4	1.9
P27708	CAD protein [OS=Homo sapiens]	-1.4	1.9
P62917	60S ribosomal protein L8 [OS=Homo sapiens]	-1.4	0.6
P62987	Ubiquitin-60S ribosomal protein L40 [OS=Homo sapiens]	-1.4	0.7
P62979	Ubiquitin-40S ribosomal protein S27a [OS=Homo sapiens]	-1.4	0.7
P30050-1	60S ribosomal protein L12 [OS=Homo sapiens]	-1.4	1.6
O94905-1	Erlin-2 [OS=Homo sapiens]	-1.5	0.4
Q00325-1	Phosphate carrier protein, mitochondrial [OS=Homo sapiens]	-1.5	0.8
P63000-2	Isoform B of Ras-related C3 botulinum toxin substrate 1 [OS=Homo sapiens]	-1.5	0.3
P06748	Nucleophosmin [OS=Homo sapiens]	-1.5	0.2
P62280	40S ribosomal protein S11 [OS=Homo sapiens]	-1.6	1.4
P12004	proliferating cell nuclear antigen [OS=Homo sapiens]	-1.6	1.3
Q96HS1-1	Serine/threonine-protein phosphatase Pgam5, mitochondrial [OS=Homo sapiens]	-1.7	0.9
Q06830	peroxiredoxin-1 [OS=Homo sapiens]	-1.7	0.7
Q8N3V7-1	synaptopodin [OS=Homo sapiens]	-1.9	0.4
B011T2-1	unconventional myosin-Ig [OS=Homo sapiens]	-1.9	0.5
Q8NFJ5	Retinoic acid-induced protein 3 [OS=Homo sapiens]	-1.9	1.1
P81605-2	Isoform 2 of Dermcidin [OS=Homo sapiens]	-1.9	0.5
P35658-3	Isoform 3 of Nuclear pore complex protein Nup214 [OS=Homo sapiens]	-1.9	1.0
P61626	lysozyme c [OS=Homo sapiens]	-1.9	0.8
P47756-1	F-actin-capping protein subunit beta [OS=Homo sapiens]	-1.9	0.4

P07355	Annexin A2 [OS=Homo sapiens]	-2.0	0.6
P61313-1	60S ribosomal protein L15 [OS=Homo sapiens]	-2.0	0.3
Q86V48-1	Leucine zipper protein 1 [OS=Homo sapiens]	-2.0	1.2
P29508	Serpin B3 [OS=Homo sapiens]	-2.1	0.4
O43707	Alpha-actinin-4 [OS=Homo sapiens]	-2.1	1.5
Q14978-2	Isoform Beta of Nucleolar and coiled-body phosphoprotein 1 [OS=Homo sapiens]	-2.1	1.2
Q15149-1	plectin [OS=Homo sapiens]	-2.2	0.8
Q12904-2	Isoform 2 of Aminoacyl tRNA synthase complex-interacting multifunctional protein 1 [OS=Homo sapiens]	-2.3	0.8
P51572-2	Isoform 2 of B-cell receptor-associated protein 31 [OS=Homo sapiens]	-2.3	1.4
Q13263	Transcription intermediary factor 1-beta [OS=Homo sapiens]	-2.3	1.2
O95425	Supervillin [OS=Homo sapiens]	-2.3	0.6
P09493-5	Isoform 5 of Tropomyosin alpha-1 chain [OS=Homo sapiens]	-2.4	0.4
P31153	S-adenosylmethionine synthase isoform type-2 [OS=Homo sapiens]	-2.4	0.6
O75477	erlin-1 [OS=Homo sapiens]	-2.4	0.7
Q86YZ3	Hornerin [OS=Homo sapiens]	-2.4	1.2
P25311	Zinc-alpha-2-glycoprotein [OS=Homo sapiens]	-2.5	1.1
Q9UHB6-4	Isoform 4 of LIM domain and actin-binding protein 1 [OS=Homo sapiens]	-2.5	0.8
Q9UHB6	LIM domain and actin-binding protein 1 [OS=Homo sapiens]	-2.5	0.8
P04040	catalase [OS=Homo sapiens]	-2.5	0.8
P05109	Protein S100-A8 [OS=Homo sapiens]	-2.6	0.4
P50402	Emerin [OS=Homo sapiens]	-2.6	0.7
P60660	Myosin light polypeptide 6 [OS=Homo sapiens]	-2.6	0.5
Q96P63-2	Isoform 2 of Serpin B12 [OS=Homo sapiens]	-2.7	1.3
Q08554-2	Isoform 1B of Desmocollin-1 [OS=Homo sapiens]	-2.7	0.6

P68032	Actin, alpha cardiac muscle 1 [OS=Homo sapiens]	-2.7	1.0
Q08188	Protein-glutamine gamma- glutamyltransferase E [OS=Homo sapiens]	-2.8	0.7
P60953	Cell division control protein 42 homolog [OS=Homo sapiens]	-2.8	2.7
Q13501-1	sequestosome-1 [OS=Homo sapiens]	-2.9	2.6
P48594	Serpin B4 [OS=Homo sapiens]	-2.9	0.5
O75955	Flotillin-1 [OS=Homo sapiens]	-2.9	0.9
Q96C19	EF-hand domain-containing protein D2 [OS=Homo sapiens]	-3.0	1.1
O14974	Protein phosphatase 1 regulatory subunit 12A [OS=Homo sapiens]	-3.0	1.2
Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein [OS=Homo sapiens]	-3.0	0.8
Q02218	2-oxoglutarate dehydrogenase, mitochondrial [OS=Homo sapiens]	-3.0	1.0
O14639-5	Isoform 5 of Actin-binding LIM protein 1 [OS=Homo sapiens]	-3.0	0.9
P60174	Triosephosphate isomerase [OS=Homo sapiens]	-3.1	1.2
Q8WWI1-3	Isoform 3 of LIM domain only protein 7 [OS=Homo sapiens]	-3.1	1.8
Q02413	Desmoglein-1 [OS=Homo sapiens]	-3.1	0.7
O75489	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial [OS=Homo sapiens]	-3.1	4.0
P52907	F-actin-capping protein subunit alpha-1 [OS=Homo sapiens]	-3.2	0.6
P60468	protein transport protein Sec61 subunit beta [OS=Homo sapiens]	-3.2	1.1
P32119	Peroxiredoxin-2 [OS=Homo sapiens]	-3.3	0.6
Q15517	corneodesmosin [OS=Homo sapiens]	-3.4	0.5
P11498	pyruvate carboxylase, mitochondrial [OS=Homo sapiens]	-3.5	3.3
P04792	Heat shock protein beta-1 [OS=Homo sapiens]	-3.5	1.5
Q01650	large neutral amino acids transporter small subunit 1 [OS=Homo sapiens]	-3.6	3.0

P15924-1	Desmoplakin [OS=Homo sapiens]	-3.6	0.6
P31944	Caspase-14 [OS=Homo sapiens]	-3.6	2.3
P22735	Protein-glutamine gamma-glutamyltransferase K [OS=Homo sapiens]	-3.7	1.3
Q14847-2	Isoform 2 of LIM and SH3 domain protein 1 [OS=Homo sapiens]	-3.7	4.1
Q5SRD1	Putative mitochondrial import inner membrane translocase subunit Tim23B [OS=Homo sapiens]	-3.7	0.8
P05787-2	Isoform 2 of Keratin, type II cytoskeletal 8 [OS=Homo sapiens]	-3.8	0.8
Q13813	Spectrin alpha chain, non-erythrocytic 1 [OS=Homo sapiens]	-4.0	1.8
Q13813-2	Isoform 2 of Spectrin alpha chain, non-erythrocytic 1 [OS=Homo sapiens]	-4.0	1.8
Q9ULV4-3	Isoform 3 of Coronin-1C [OS=Homo sapiens]	-4.0	0.9
P52943	Cysteine-rich protein 2 [OS=Homo sapiens]	-4.0	3.1
Q01082-3	Isoform 2 of Spectrin beta chain, non-erythrocytic 1 [OS=Homo sapiens]	-4.0	2.2
Q6NYC8	Phostensin [OS=Homo sapiens]	-4.2	2.4
P50416	Carnitine O-palmitoyltransferase 1, liver isoform [OS=Homo sapiens]	-4.3	3.9
Q01082-1	Spectrin beta chain, non-erythrocytic 1 [OS=Homo sapiens]	-4.3	2.4
O95816	BAG family molecular chaperone regulator 2 [OS=Homo sapiens]	-4.4	2.9
P16403	Histone H1.2 [OS=Homo sapiens]	-4.5	2.0
P10412	Histone H1.4 [OS=Homo sapiens]	-4.5	2.0
P49207	60S ribosomal protein L34 [OS=Homo sapiens]	-4.5	0.7
Q9NQT5	exosome complex component RRP40 [OS=Homo sapiens]	-4.5	2.6
P06753-2	Isoform 2 of Tropomyosin alpha-3 chain [OS=Homo sapiens]	-4.6	1.7
P50238	Cysteine-rich protein 1 [OS=Homo sapiens]	-4.6	3.7

Q16643-3	Isoform 3 of Drebrin [OS=Homo sapiens]	-4.7	1.3
Q9UDY2-7	Isoform 7 of Tight junction protein ZO-2 [OS=Homo sapiens]	-4.7	3.3
P14923	Junction plakoglobin [OS=Homo sapiens]	-4.7	0.7
P62081	40S ribosomal protein S7 [OS=Homo sapiens]	-4.8	1.0
P05089-2	Isoform 2 of Arginase-1 [OS=Homo sapiens]	-5.0	1.2
O14950	Myosin regulatory light chain 12B [OS=Homo sapiens]	-5.3	4.1
Q9NYL9	tropomodulin-3 [OS=Homo sapiens]	-5.4	1.4
P46779-3	Isoform 3 of 60S ribosomal protein L28 [OS=Homo sapiens]	-5.5	3.3
P68431	Histone H3.1 [OS=Homo sapiens]	-5.5	1.5
P16401	Histone H1.5 [OS=Homo sapiens]	-5.7	1.8
Q5D862	Filaggrin-2 [OS=Homo sapiens]	-5.9	1.6
O43324-1	Eukaryotic translation elongation factor 1 epsilon-1 [OS=Homo sapiens]	-6.2	3.7
P08670	Vimentin [OS=Homo sapiens]	-6.4	1.2
Q13835	Plakophilin-1 [OS=Homo sapiens]	-6.6	1.3
P62899	60S ribosomal protein L31 [OS=Homo sapiens]	-6.7	3.8
P62854	40S ribosomal protein S26 [OS=Homo sapiens]	-6.7	2.2
P08708	40S ribosomal protein S17 [OS=Homo sapiens]	-7.1	3.7
P46782	40S ribosomal protein S5 [OS=Homo sapiens]	-7.3	5.0
Q07157	Tight junction protein ZO-1 [OS=Homo sapiens]	-7.8	3.3
Q07157-2	Isoform Short of Tight junction protein ZO-1 [OS=Homo sapiens]	-7.8	3.3
P62841	40S ribosomal protein S15 [OS=Homo sapiens]	-8.2	5.7
P62633-1	Cellular nucleic acid-binding protein [OS=Homo sapiens]	-8.5	3.4
P62633-4	Isoform 4 of Cellular nucleic acid-binding protein [OS=Homo sapiens]	-8.5	3.4

Table S2. Crystallography data and refinement statistics (PDB ID: 6PVA).

Data Collection	NTMT1/1
λ (Å)	1.0332
Space group	P3 ₁ 21
a, b, c (Å)	72.95, 72.95, 82.09
α , β , γ (°)	90, 90, 120
Resolution (Å)*	30 – 1.84 (1.89 – 1.84)
Completeness (%)*	99.8 (97.8)
Redundancy*	6.5 (5.3)
R_{sym} †*	0.12 (3.3)
$I / \sigma(I)$ * †	9.9 (0.4)
CC _{1/2}	1.0 (0.14)
Refinement	
Resolution (Å)	30 – 1.84
No. reflections	22,330

R [§] /R _{free} [¶]	0.20/0.24
r.m.s. deviations	
Bonds (Å)	0.003
Angles (°)	0.728
No. Protein atoms	1858
No. Ligand atoms	59
No. Waters	170
B-factors (Å²)	
Wilson B	35.45
Protein	37.80
Ligands	34.4
Waters	42.7
Ramachandran Analysis[‡]	
Favored (%)	99.1
Allowed (%)	0.9
Outliers (%)	0
PDB code	6PVA

[†] $R_{\text{sym}} = \sum_{hkl,j} (|I_{hkl} - \langle I_{hkl} \rangle|) / \sum_{hkl,j} I_{hkl}$, where $\langle I_{hkl} \rangle$ is the average intensity for a set of j symmetry related reflections and I_{hkl} is the value of the intensity for a single reflection within a set of symmetry-related reflections.

[§] $R \text{ factor} = \sum_{hkl} (|F_o| - |F_c|) / \sum_{hkl} F_o$ where F_o is the observed structure factor amplitude and F_c is the calculated structure factor amplitude.

[¶] $R_{\text{free}} = \sum_{hkl,T} (|F_o| - |F_c|) / \sum_{hkl,T} F_o$, where a test set, T (5% of the data), is omitted from the refinement.

[‡] Performed using Molprobity within PHENIX.

* Indicates statistics for last resolution shell shown in parenthesis.