Table S1. Labeling efficiency of trypsin digested dimethylated hemoglobin peptides.

Peptide sequence	**Initial peptide (m/z)**	**Dimethylated peptides**			
		CH_2O		CD_2O	
		m/z	**Label efficiency (100%)**	**m/z**	**Label efficiency (100%)**
FFESFGDLSTPDAVMGNPK	2059.14	2115.17	98.94	2123.2	100
VLGAFSDGLAHLDNLK	1670.05	1726.09	100	1734.13	100
VGAHAGEYGAEALER	1529.89	1557.9	99.25	1561.92	99.71
EFTPPVQAAYQK	1378.83	1434.87	100	1442.92	100
VNVDEVGGEALGR	1314.8	1342.81	99.77	1346.83	100
VVAGVANALAHK	1149.7	1205.84	100	1213.88	100
MFLSFPTTK	1071.66	1127.71	99.45	1135.75	99.63
VHLTPEEK	952.6	1008.65	94.51	1016.7	95.35
VDPVNFK	818.52	874.57	100	882.62	100

Table S2. The number of identified and quantified peptides and proteins, and the mean quantification values of 1:1 mixed G-IVTAL labeled HepG2 cells in three replicated analysis.

Run	**Number of identified proteins**	**Number of identified peptides**	**Number of quantified proteins**	**Number of quantified peptides**	**quantification Mean-value (H/L)**	**Standard deviation**
1	4278	74866	3539	42078	1.022	0.721
2	4416	75161	3734	48912	1.013	0.477
3	4607	69218	3902	49120	1.02	0.496
Total	5412	31004	4426	19308		

Table S3. The number of identified and quantified peptides and proteins, and the mean quantification values of three replicate G-IVTAL analysis of dialyzed serum induced protein differential expression in HepG2.

Run	**Number of identified proteins**	**Number of identified peptides**	**Number of quantified proteins**	**Number of quantified peptides**	**quantification Mean-value (H/L)**	**Standard deviation**
1	4005	55521	3360	39899	1.039	0.459
2	4323	58000	3610	40481	1.032	0.486
3	4469	61521	3771	42950	1.038	0.473
Total	5324	37184	4288	17486		

Table S4. The 111 differential expression proteins in dialyzed serum cultivated HepG2 cells.

Uniprot	Protein Name	Averaged Ratio	Ratio (Label Induced)	Ratio (DFBS induced)	RSD %
Q9H2M3	Betaine--homocysteine S-methyltransferase 2	0.17			0.04
P13645	Keratin, type I cytoskeletal 10	0.18	0.37	0.49	0.09
P61803	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit DAD1	0.2	0.32	0.63	0.02
P46977	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3A	0.21	0.42	0.49	0.03
Q9UKY3	Putative inactive carboxylesterase 4	0.23			0.01
Q96HY6	DDRGK domain-containing protein 1	0.24	0.39	0.62	0.01
Q14165	Malectin	0.24	0.38	0.63	0.02
Q6UW68	Transmembrane protein 205	0.24	0.38	0.64	0.07
Q13087	Protein disulfide-isomerase A2	0.24			0.06
Q8N2G8	GH3 domain-containing protein	0.24			0.03
Q9P035	3-hydroxyacyl-CoA dehydratase 3	0.25	0.46	0.54	0.02
Q15005	Signal peptidase complex subunit 2	0.25	0.45	0.56	0.01
O96005	Cleft lip and palate transmembrane protein 1	0.26	0.76	0.34	0.05
Q07065	Cytoskeleton-associated protein 4	0.26	0.47	0.55	0.02
P27824	Calnexin	0.26	0.46	0.56	0.02
P43307	Translocon-associated protein subunit alpha	0.26	0.44	0.59	0.01
Q8NC56	LEM domain-containing protein 2	0.26	0.40	0.65	0.02
O14735	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	0.27	0.40	0.68	0.03
P08240	Signal recognition particle receptor subunit alpha	0.28	0.60	0.47	0.04

P16435	NADPH--cytochrome P450 reductase	0.28	0.45	0.62	0.01
P04004	Vitronectin	0.29	0.35	0.83	0.08
P42167	Lamina-associated polypeptide 2, isoforms beta/gamma	0.29	0.33	0.88	0.01
P60468	Protein transport protein Sec61 subunit beta	0.3	0.51	0.58	0.03
Q8TCT9	Minor histocompatibility antigen H13	0.3	0.46	0.65	0
O00767	Acyl-CoA desaturase	0.3	0.46	0.66	0.02
Q9HCU5	Prolactin regulatory element-binding protein	0.3	0.44	0.68	0.03
Q9Y5M8	Signal recognition particle receptor subunit beta	0.3	0.43	0.70	0.03
P33897	ATP-binding cassette sub-family D member 1	0.31	0.61	0.51	0.03
Q9UGP8	Translocation protein SEC63 homolog	0.31	0.47	0.66	0.06
O15173	Membrane-associated progesterone receptor component 2	0.31	0.45	0.69	0.04
Q99943	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha	0.31	0.35	0.89	0.12
P21549	Serine--pyruvate aminotransferase	0.31			0.09
Q9BQB6	Vitamin K epoxide reductase complex subunit 1	0.32	0.51	0.63	0.01
O14967	Calmegin	0.32	0.38	0.84	0.09
P04844	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase subunit 2	0.33	0.51	0.65	0.05
Q96AQ6	Pre-B-cell leukemia transcription factor-interacting protein 1	0.33	0.43	0.76	0.01
Q96HR9	Receptor expression-enhancing protein 6	0.33	0.41	0.81	0.09
Q92597	Protein NDRG1	0.34	1.28	0.27	0.06
Q14739	Lamin-B receptor	0.34	0.25	1.34	0.12
P19971	Thymidine phosphorylase	0.34			0.03
P09668	Pro-cathepsin H	0.34			0.11

P50416	Carnitine O-palmitoyltransferase 1, liver isoform	0.35	0.94	0.37	0.06
O15258	Protein RER1	0.35	0.60	0.58	0.06
P35610	Sterol O-acyltransferase 1	0.35	0.54	0.64	0.09
O75396	Vesicle-trafficking protein SEC22b	0.35	0.45	0.77	0.01
P04843	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	0.35	0.45	0.78	0.01
Q9P0L0	Vesicle-associated membrane protein-associated protein A	0.35	0.38	0.93	0.02
P35030	Trypsin-3	0.35			0.03
O15260	Surfeit locus protein 4	0.36	0.56	0.65	0.02
Q13724	Mannosyl-oligosaccharide glucosidase	0.36	0.44	0.82	0.02
Q9UNL2	Translocon-associated protein subunit gamma	0.36	0.40	0.91	0.03
Q9UIF9	Bromodomain adjacent to zinc finger domain protein 2A	0.36	0.38	0.94	0.09
O00264	Membrane-associated progesterone receptor component 1	0.36	0.38	0.95	0.02
P54710	Sodium/potassium-transporting ATPase subunit gamma	0.36			0.03
Q9C0E8	Protein lunapark	0.36			0.08
P00387	NADH-cytochrome b5 reductase 3	0.37	0.59	0.63	0.02
O76024	Wolframin	0.38	1.07	0.36	0.1
Q9BT22	Chitobiosyldiphosphodolichol beta-mannosyltransferase	0.38	0.63	0.60	0.07
Q9NTJ5	Phosphatidylinositide phosphatase SAC1	0.38	0.58	0.65	0.05
Q9ULC5	Long-chain-fatty-acid--CoA ligase 5	0.38			0.05
Q7Z2K6	Endoplasmic reticulum metallopeptidase 1	0.39	0.66	0.59	0.07
P49257	Protein ERGIC-53	0.39	0.65	0.60	0.01
P51572	B-cell receptor-associated protein 31	0.39	0.58	0.67	0.06
Q8TC12	Retinol dehydrogenase 11	0.39	0.48	0.82	0.08

Q15800	Methylsterol monooxygenase 1	0.39	0.47	0.83	0.05
Q9NXE4	Sphingomyelin phosphodiesterase 4	0.39	0.42	0.93	0.03
P50453	Serpin B9	0.39			0.04
Q8N2K0	Monoacylglycerol lipase ABHD12	0.4	0.78	0.51	0.01
Q86UE4	Protein LYRIC	0.4	0.57	0.70	0.04
O75844	CAAX prenyl protease 1 homolog	0.4	0.56	0.72	0.06
Q14571	Inositol 1,4,5-trisphosphate receptor type 2	0.4	0.43	0.94	0.05
O60427	Fatty acid desaturase 1	0.4			0.07
Q9NX62	Inositol monophosphatase 3	0.41	0.85	0.48	0.03
O75477	Erlin-1	0.41	0.85	0.48	0.05
Q6UWM9	UDP-glucuronosyltransferase 2A3	0.41			0.06
P09525	Annexin A4	0.42	0.84	0.50	0.01
Q53GQ0	Estradiol 17-beta-dehydrogenase 12	0.42	0.52	0.81	0.03
O95864	Fatty acid desaturase 2	0.42			0.08
Q8IWU2	Serine/threonine-protein kinase LMTK2	0.42			0.04
O95832	Claudin-1	0.43			0.04
P07099	Epoxide hydrolase 1	0.44	0.62	0.71	0.03
P04066	Tissue alpha-L-fucosidase	0.44			0.01
Q6IAN0	Dehydrogenase/reductase SDR family member 7B	0.45	0.71	0.63	0.06
Q06520	Bile salt sulfotransferase	0.45			0.02
Q9BY49	Peroxisomal trans-2-enoyl-CoA reductase	0.45			0.04
Q9UM00	Transmembrane and coiled-coil domain-containing protein 1	0.46	0.58	0.79	0.03
P10620	Microsomal glutathione S-transferase 1	0.47	0.47	1.01	0.02
P04114	Apolipoprotein B-100	0.47			0
Q9NRX5	Serine incorporator 1	2.19	0.93	2.36	0.06
Q16512	Serine/threonine-protein kinase N1	2.25	1.07	2.10	0.15
P15104	Glutamine synthetase	2.27			0.12
P08727	Keratin, type I cytoskeletal 19	2.3			0.01
Q96QD8	Sodium-coupled neutral amino acid transporter 2	2.32	0.97	2.38	0.18

P62745	Rho-related GTP-binding protein RhoB	2.39	1.16	2.06	0.26
Q9NVD7	Alpha-parvin	2.42	1.09	2.23	0.29
Q9NZJ9	Diphosphoinositol polyphosphate phosphohydrolase 2	2.54	0.95	2.68	0.11
Q9BUF5	Tubulin beta-6 chain	2.71	1.04	2.59	0.57
O14763	Tumor necrosis factor receptor superfamily member 10B	2.79	0.77	3.61	0.08
P31153	S-adenosylmethionine synthase isoform type-2	2.83	1.15	2.46	0.2
Q8NC42	E3 ubiquitin-protein ligase RNF149	2.88			0.2
P54687	Branched-chain-amino-acid aminotransferase, cytosolic	3.03	1.07	2.84	0.64
Q9Y5B0	RNA polymerase II subunit A C-terminal domain phosphatase	3.11			0.58
Q9Y287	Integral membrane protein 2B	3.16			0.47
Q9NPF0	CD320 antigen	3.25			0.43
P51654	Glypican-3	3.49			1.57
P09455	Retinol-binding protein 1	3.72			0.11
P12429	Annexin A3	3.81	1.13	3.37	0.16
Q9NV92	NEDD4 family-interacting protein 2	3.94			0.24
Q15582	Transforming growth factor-beta-induced protein ig-h3	4	0.88	4.52	0.34
Q15012	Lysosomal-associated transmembrane protein 4A	4.5			0.74
P31431	Syndecan-4	5.89			1.01

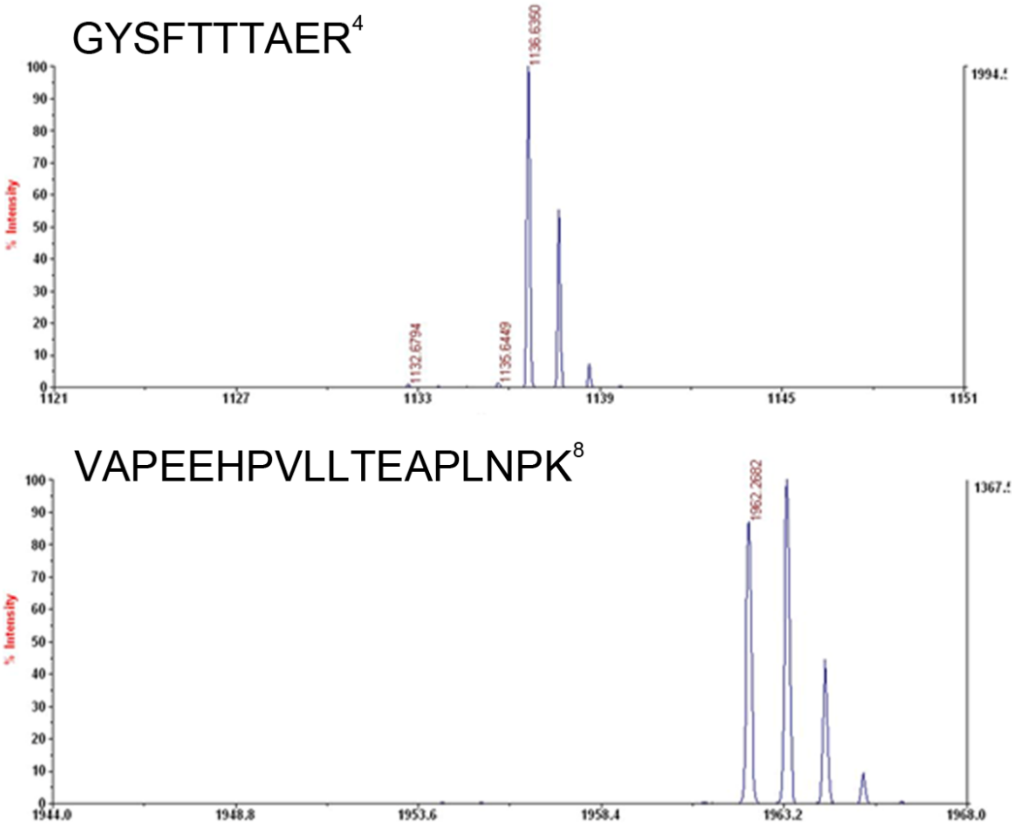

Figure S1. MS spectra of GYSFTTTAER^4 (m/z 1136.63) and VAPEEHPVLLTEAPLNPK^8（m/z 1954.24）from in-gel trypsin digested K^{8}R^4 labeled HepG2 cells.

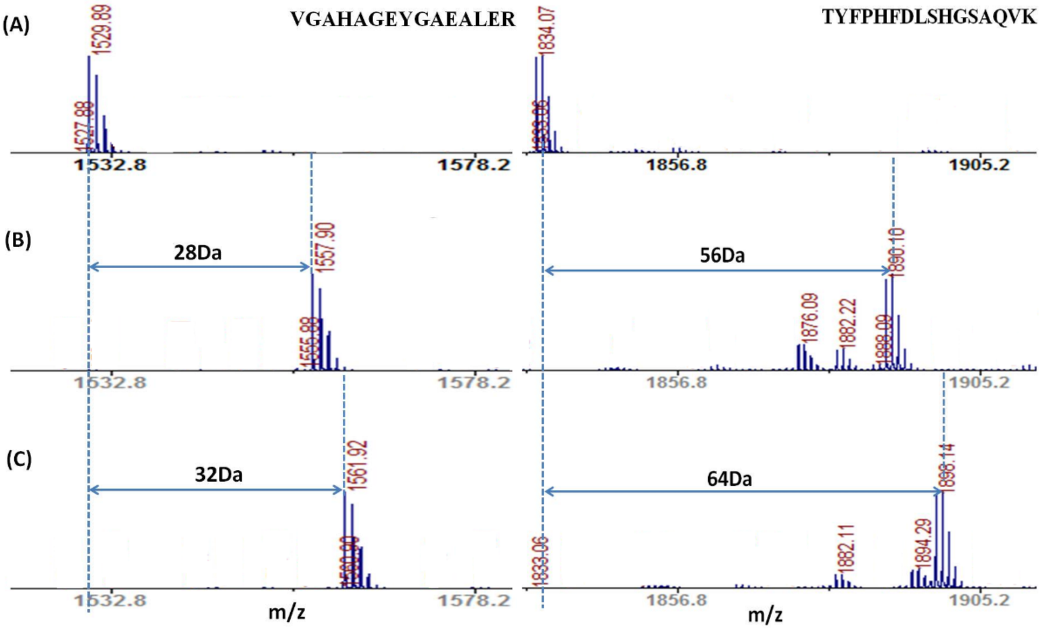

Figure S2. MS spectra of hemoglobin peptides before derivatization (A) and after CH_2O dimethylation (B) or CD_2O dimethylation (C). The left panel shows the spectra of VGAHAGEYGAEALER, right panel shows the spectra of TYFPHFDLSHGSAQVK.

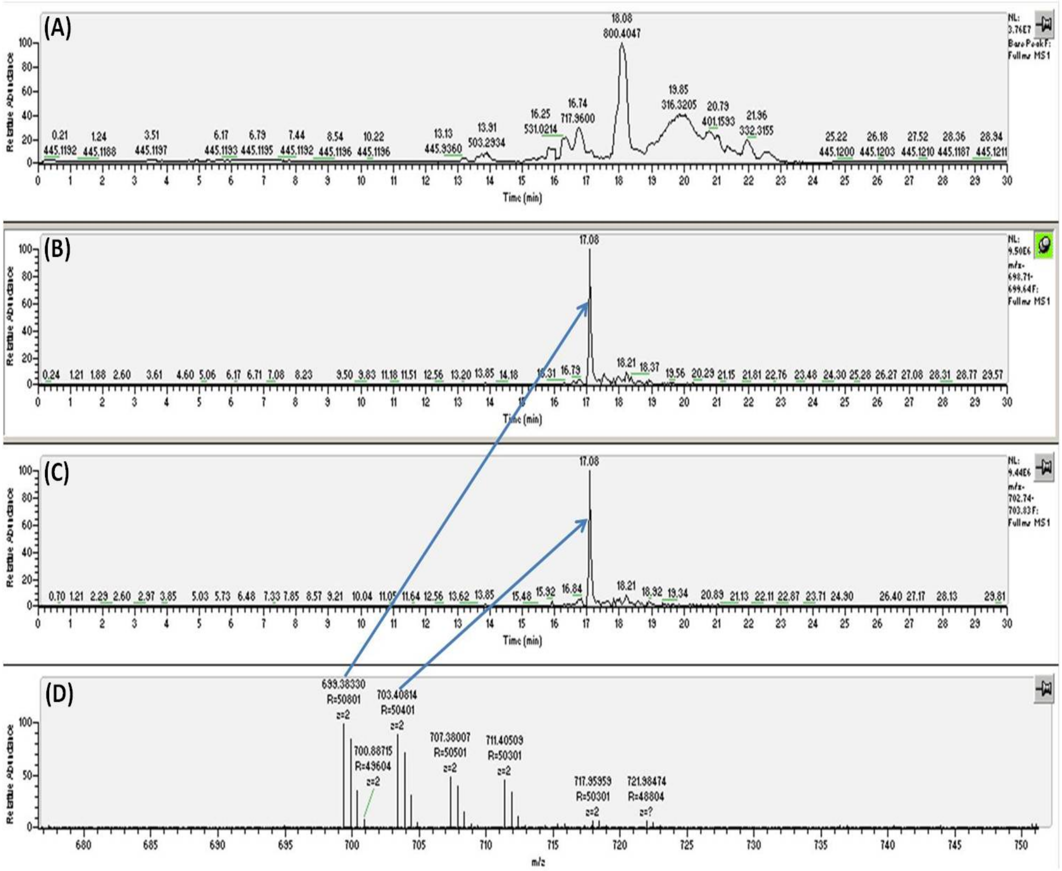

Figure S3. LC MS analysis of 1:1 mixed CH_2O and CD_2O dimethylated myoglobin peptides. Panel A shows the total ion chromatograms, and the extract ion chromatograms of $^{(+28)}$TVVLTALGGILK$^{(+28)}$ (panel B) and $^{(+32)}$TVVLTALGGILK$^{(+32)}$ (panel C) indicates identical elution time of differential isotopic dimethylated peptides. Panel D displays the corresponding MS spectrum.

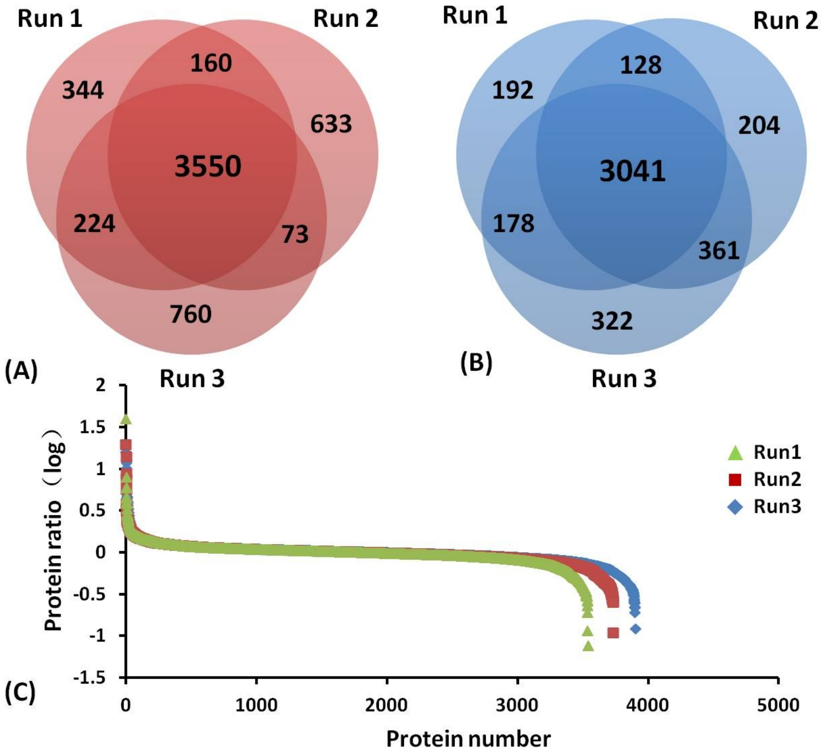

Figure S4. The number of identified or quantified proteins and their corresponding quantification values of 1:1 mixed G-IVTAL labeled HepG2 cells. The venn diagrams illustrates the overlap of identified proteins (Chart A) and quantified proteins (Chart B) among three replicated analysis. Chart C displays $\log_2$ quantification values of those proteins.