Electronic Supplementary Material (ESI) for Food & Function.

Supplemental materials

Table S1 Differential proteins in normal and model groups

Accession	Protein names/ Gene names	Coverage	Unique Peptides	MW [kDa]/ pI	P value	Fold change (N/M)	Expression (N/M)
P13634	Carbonic anhydrase 1 (EC 4.2.1.1) (Carbonate dehydratase I) (Carbonic anhydrase I) (CA-I)/ Ca1 Car1	6.78E+01	12	28.31/6.96	0.01292	0.70591	down
P54869	Hydroxymethylglutaryl-CoA synthase, mitochondrial (HMG-CoA synthase) (EC 2.3.3.10) (3-hydroxy-3-methylglutaryl/ Hmgcs2	46.555	22	56.79/8.41	0.00259	0.55186	down
P04117	Fatty acid-binding protein, adipocyte (3T3-L1 lipid-binding protein) (Adipocyte lipid-binding protein) (ALBP) (Adipocyte-type fatty acid-binding protein) (A-FABP) (AFABP) (Fatty acid-binding protein 4) (Myelin P2 protein homolog) (P15) (P2 adipocyte protein) (Protein 422)/ Fabp4 Ap2	51.515	8	14.64/8.40	0.00737	0.68871	down
Q91X72	Hemopexin/ Hpx Hpxn	46.52	21	51.29/7.80	0.00125	0.60439	down
Q9D816	Cytochrome P450 2C55 (EC 1.14.14.1) (CYPIIC55)/ Cyp2c55 Cyp2c-55	34.39	19	56.06/6.98	0.01866	0.69930	down
P55050	Fatty acid-binding protein, intestinal (Fatty acid-binding protein 2) (Intestinal-type fatty acid-binding protein) (I-FABP)/ Fabp2 Fabpi	44.7	8	15.12/7.24	0.0069	0.61553	down
P20065	Thymosin beta-4 (T beta 4) [Cleaved into: Hematopoietic system regulatory peptide (Seraspenide)]/ Tmsb4x Ptmb4 Tmsb4	40	3	5.67/5.06	0.00310	0.69680	down
P61226	Ras-related protein Rap-2b/ Rap2b	38.525	3	20.49/4.81	0.02265	1.40005	up
P62897	Cytochrome c, somatic/ Cycs	67.62	9	11.60/9.58	0.00429	0.69384	down
P02089	Hemoglobin subunit beta-2 (Beta-2-globin) (Hemoglobin beta-2 chain) (Hemoglobin beta-minor chain)/ Hbb-b2	72.11	3	15.87/8.05	0.02059	0.4546	down
Q91WP6	Serine protease inhibitor A3N (Serpin A3N)/ Serpina3n Spi2	21.05	3	46.69/5.82	0.03478	0.6969	down
Q3UZZ6	Sulfotransferase 1 family member D1 (ST1D1) (EC 2.8.2.-) (Amine N-sulfotransferase) (SULT-N) (Dopamine sulfotransferase Sult1d1) (Tyrosine-ester sulfotransferase)/ Sult1d1 St1d1	41.015	11	35.06/5.76	0.01123	0.6575	down
P52840	Sulfotransferase 1A1 (ST1A1) (EC 2.8.2.1) (Aryl sulfotransferase) (Phenol sulfotransferase) (Phenol/aryl sulfotransferase) (mSTp1) (ST1A4) (Sulfokinase)/ Sult1a1 St1a1 Stp Stp1	58.075	13	33.95/8.10	0.0042	0.6794	down

P31725	Protein S100-A9 (Calgranulin-B) (Leukocyte L1 complex heavy chain) (Migration inhibitory factor-related protein 14) (MRP-14) (p14) (S100 calcium-binding protein A9)/ S100a9 Cagb Mrp14	35.4	5	13.04/7.17	0.0009	0.6908	down
P16015	Carbonic anhydrase 3 (EC 4.2.1.1) (Carbonate dehydratase III) (Carbonic anhydrase III) (CA-III)/ Ca3 Car3	38.85	9	29.35/7.37	3.25E-05	0.3865	down
Q3UX10	Tubulin alpha chain-like 3/ Tubal3	10.54	2	49.96/5.58	0.0081	1.4405	up
P32261	Antithrombin-III (ATIII) (Serpin C1)/ Serpinc1 At3	26.775	14	51.97/6.46	0.0048	1.4200	up
Q61646	Haptoglobin (Zonulin) [Cleaved into: Haptoglobin alpha chain; Haptoglobin beta chain]/ Hp	37.175	13	38.73/6.29	0.0010	0.3770	down
P06344	H-2 class II histocompatibility antigen, A-U	28.71	2	30.02/8.09	0.0152	0.6994	down
P09541	Myosin light chain 4 (MLC1EMB) (Myosin light chain 1, atrial/fetal isoform) (MLC1A)/ Myl4 Mlc1a Myla	27.46	5	21.15/5.03	0.0144	0.6252	down
P28776	Indoleamine 2,3-dioxygenase 1 (IDO-1) (EC 1.13.11.52) (Indoleamine-pyrrole 2,3-dioxygenase)/ Ido1 Ido Indo	17.565	6	45.61/6.35	0.004	0.6816	down
P97816	Protein S100-G (Calbindin-D9k) (S100 calcium-binding protein G) (Vitamin D-dependent calcium-binding protein, intestinal) (CABP)/ S100g Calb3 S100d	73.42	6	8.96/4.75	0.0223	0.3770	down
Q09199	Beta-1,4 N-acetylgalactosaminyltransferase 2 (EC 2.4.1.-)/ B4galnt2 Galgt2 Ggm3	10.98	5	58.28/8.94	0.0038	0.48426	down
Q8VC49	Interferon alpha-inducible protein 27-like protein 2B (Interferon-stimulated gene 12 protein B2) (ISG12(b2))/ Ifi27l2b Isg12(b2)	19.435	5	27.76/4.70	0.02423	0.66274	down
A6X935	Inter alpha-trypsin inhibitor, heavy chain 4 (ITI heavy chain H4) (ITI-HC4) (Inter-alpha-inhibitor heavy chain 4)/ Itih4	11.04	9	104.59/6.4	0.01833	0.68984	down

P02798	Metallothionein-2 (MT-2) (Metallothionein-II) (MT-II)/ Mt2	32.79	2	6.11/7.83	9.18E-05	0.63987	down
Q3USF0	Acetylgalactosaminyl-O-glycosyl-glycoprotein beta-1,3-N-acetylglucosaminyltransferase (EC 2.4.1.147) (Core 3 synthase) (UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 6) (BGnT-6) (Beta-1,3-Gn-T6) (Beta-1,3-N-acetylglucosaminyltransferase 6) (Beta3Gn-T6)/ B3gnt6	8.95	4	43.92/8.68	0.02659	0.60090	down
Q5EBG6	Heat shock protein beta-6 (HspB6)/ Hspb6 Gm479	29.0157	4	17.51/6.00	0.00244	1.41856	up
Q8CFV9	Riboflavin kinase (EC 2.7.1.26) (ATP:riboflavin 5'-phosphotransferase) (Flavokinase) (KOI-4)/ Rfk	28.05	4	17.43/7.55	0.04759	0.67018	down
Q99JH8	ER lumen protein-retaining receptor 1 (KDEL endoplasmic reticulum protein retention receptor 1)	16.035	2	24.54/8.62	0.00317	1.44212	up

	(KDEL receptor 1)/ Kdelr1						
O88310	Intelectin-1a (Galactofuranose-binding lectin) (Intestinal lactoferrin receptor)/ Itln1 Intl Itln Itln1a Itlna	12.775	2	34.93/7.87	0.00509	0.70051	down
P12246	Serum amyloid P-component (SAP)/ Apcs Ptx2 Sap	17.86	3	26.23/6.35	0.00074	0.53263	down
Q8BK30	NADH dehydrogenase [ubiquinone] flavoprotein 3, mitochondrial (Complex I-9kD) (CI-9kD) (NADH-ubiquinone oxidoreductase 9 kDa subunit)/ Ndufv3	24.04	3	11.81/9.35	0.00875	0.69305	down
Q9R002	Interferon-activable protein 202 (Ifi-202) (Interferon-inducible protein p202) (Lupus susceptibility protein p202)/ Ifi202 Ifi202a Ifi202b	3.035	2	50.43/8.48	0.04230	0.62918	down
Q8K003	Translation machinery-associated protein 7 (Coiled-coil domain-containing protein 72)/ Tma7 Ccdc72	30.47	2	7.06/9.99	0.02013	0.67100	down
Q8BV66	Interferon-induced protein 44 (Microtubule-associated protein 44)/ Ifi44 Mtap44	3.91	2	47.82/7.03	0.03572	0.69329	down
P18608	Non-histone chromosomal protein HMG-14 (High mobility group nucleosome-binding domain-containing protein 1)/ Hmgn1 Hmg-14 Hmg14	8.855	2	10.15/9.76	0.00409	0.68234	down
P98203	Armadillo repeat protein deleted in velo-cardio-facial syndrome homolog/ Arvcf	2.075	2	105.0/6.64	0.02148	1.5285	up
Q9CQL6	39S ribosomal protein L35, mitochondrial (L35mt) (MRP-L35)/ Mrpl35	9.575	2	21.5/11.47	0.03325	1.4614	up
P11032	Granzyme A (EC 3.4.21.78) (Autocrine thymic lymphoma granzyme-like serine protease) (CTLA-3) (Fragmentin-1) (T cell-specific serine protease 1) (TSP-1)/ Gzma Ctla-3 Ctla3 Mtsp-1	16.155	4	28.58/9.36	0.00854	0.63695	down

Table S2 Differential proteins in Model and high-dose CMP33 groups

Accession	Protein names/ Gene names	Coverage	Unique Peptides	MW [kDa]/ pI	P value	Fold change (H/M)	Expression (H/M)
Q61554	Fibrillin-1/ Fbn1 Fbn-1	36.52	75	312.0/4.92	0.00039	1.5523	up
P13634	Carbonic anhydrase 1 (EC 4.2.1.1) (Carbonate dehydratase I) (Carbonic anhydrase I) (CA-I)/ Ca1 Car1	6.78E+01	12	28.31/6.96	0.01637	0.68053	down
P54869	Hydroxymethylglutaryl-CoA synthase, mitochondrial (HMG-CoA synthase) (EC 2.3.3.10) (3-hydroxy-3-methylglutaryl/ Hmgcs2	46.555	22	56.79/8.41	0.00175	0.45193	down
Q9D816	Cytochrome P450 2C55 (EC 1.14.14.1) (CYPIIC55)/ Cyp2c55 Cyp2c-55	34.39	19	56.06/6.98	0.00789	0.59701	down
P00329	Alcohol dehydrogenase 1 (EC 1.1.1.1) (ADH-A2) (Alcohol	43.6	16	39.75/8.1	0.00047	1.48350	up

	dehydrogenase A subunit)/ Adh1 Adh-1			0			
P55050	Fatty acid-binding protein, intestinal (Fatty acid-binding protein 2) (Intestinal-type fatty acid-binding protein) (I-FABP)/ Fabp2 Fabpi	44.7	8	15.12/7.24	0.00342	0.48627	down
P02089	Hemoglobin subunit beta-2 (Beta-2-globin) (Hemoglobin beta-2 chain) (Hemoglobin beta-minor chain)/ Hbb-b2	72.11	3	15.87/8.04	0.01634	0.40955	down
Q8VCT4	Carboxylesterase 1D (Carboxylesterase 3) (EC 3.1.1.1) (EC 3.1.1.67) (Fatty acid ethyl ester synthase) (FAEE synthase) (Triacylglycerol hydrolase) (TGH)/ Ces1d Ces1 Ces3	30.795	11	61.75/6.61	0.00405	0.63667	down
Q8CB12	Gasdermin-C3/Gsdmc3	42.915	6	54.15/6.58	0.00276	1.46518	up
Q8BHX1	HAUS augmin-like complex subunit 1 (Coiled-coil domain-containing protein 5)/ Haus1 Ccdc5	5.575	2	31.36/5.69	0.01264	1.41376	up
Q99J99	3-mercaptopyruvate sulfurtransferase (MST) (EC 2.8.1.2)/ Mpst	52.53	13	33.00/6.58	0.03270	0.68038	down
Q9D2Q8	Protein S100-A14 (S100 calcium-binding protein A14) (S114)/ S100a14 Gm1020 S100a15	77.885	8	11.59/5.50	0.00836	1.57511	up
Q9DD20	Methyltransferase-like protein 7B (EC 2.1.1.-)/ Mettl7b	37.295	10	28.03/8.59	0.00436	0.56568	down
Q08331	Calretinin (CR)/ Calb2	49.815	13	31.35/5.02	0.00068	0.6892	down
Q3UZZ6	Sulfotransferase 1 family member D1 (ST1D1) (EC 2.8.2.-) (Amine N-sulfotransferase) (SULT-N) (Dopamine sulfotransferase Sult1d1) (Tyrosine-ester sulfotransferase)/ Sult1d1 St1d1	41.015	11	35.06/5.76	0.01222	0.67462	down
Q8VCR2	17-beta-hydroxysteroid dehydrogenase 13 (17-beta-HSD 13) (EC 1.1.-.-) (Alcohol dehydrogenase PAN1B-like) (Short-chain dehydrogenase/reductase 9)/ Hsd17b13 Scdr9	35.53	15	61.08/8.12	0.00380	0.66287	down
P04228	H-2 class II histocompatibility antigen, A-D alpha chain/H2-Aa	29.3	2	28.22/5.00	0.03687	1.76875	up
Q5JCT0	Beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,6-N-acetylglucosaminyltransferase 3 (EC 2.4.1.102) (EC 2.4.1.150) (C2GnT-mucin type) (C2GnT-M) (Mucus-type core 2 beta-1,6-N-acetylglucosaminyltransferase)/ Gcnt3	30.89	12	50.67/8.25	0.01680	0.72141	down
O54891	Galectin-6 (Gal-6)/ Lgals6	32.39	4	34.09/8.90	0.01897	1.48636	up
P16015	Carbonic anhydrase 3 (EC 4.2.1.1) (Carbonate dehydratase III) (Carbonic anhydrase III) (CA-III)/ Ca3 Car3	38.85	9	29.35/7.37	6.41E-05	0.41894	down
Q6ZWU9	40S ribosomal protein S27/ Rps27	39.29	2	9.45/9.45	0.01843	1.58759	up
Q8R1M8	Mucosal pentraxin/Mptx1 Mptx	22.37	3	24.52/5.67	0.01022	1.47693	down
Q9Z0L8	Gamma-glutamyl hydrolase (EC 3.4.19.9) (Conjugase) (FGPH)	3.31E+01	9	35.45/7.5	0.00376	1.46759	up

	(Folylpolyglutamate hydrolase) (GH) (Gamma-Glu-x carboxypeptidase)/ Ggh			0			
Q61646	Haptoglobin (Zonulin) [Cleaved into: Haptoglobin alpha chain; Haptoglobin beta chain]/ Hp	37.175	13	38.73/6.29	0.0008	0.44172	down
P09036	Serine protease inhibitor Kazal-type 1 (P12) (Prostatic secretory glycoprotein) (Serine protease inhibitor Kazal-type 3)/ Spink1 Spink3	26.25	3	8.48/8.00	0.00102	1.46567	up
Q09199	Beta-1,4 N-acetylgalactosaminyltransferase 2 (EC 2.4.1.-)/ B4galnt2 Galgt2 Ggm3	10.98	5	58.28/8.94	0.00262	0.61541	down
P97430	Antileukoproteinase (ALP) (Secretory leukocyte protease inhibitor)/ Slpi	47.71	8	14.30/8.79	0.0035	1.53487	up
P09541	Myosin light chain 4 (MLC1EMB) (Myosin light chain 1, atrial/fetal isoform) (MLC1A)/ Myl4 Mlc1a Myla	27.46	5	21.14/5.03	0.01217	0.61157	down
P97816	Protein S100-G (Calbindin-D9k) (S100 calcium-binding protein G) (Vitamin D-dependent calcium-binding protein, intestinal) (CABP)/ S100g Calb3 S100d	73.42	6	8.96/4.75	0.02631	0.42837	down
Q8QZR5	Alanine aminotransferase 1 (ALT1) (EC 2.6.1.2) (Glutamate pyruvate transaminase 1) (GPT 1) (Glutamic--alanine transaminase 1) (Glutamic--pyruvic transaminase 1)/ Gpt Gpt1	15.225	7	55.11/6.64	0.02114	0.64268	down
Q3USF0	Acetylgalactosaminyl-O-glycosyl-glycoprotein beta-1,3-N-acetylglucosaminyltransferase (EC 2.4.1.147) (Core 3 synthase) (UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 6) (BGnT-6) (Beta-1,3-Gn-T6) (Beta-1,3-N-acetylglucosaminyltransferase 6) (Beta3Gn-T6)/ B3gnt6	8.95	4	43.92/8.68	0.0416	0.63079	down
P07091	Protein S100-A4 (Metastasin) (Metastatic cell protein) (PEL98) (Placental calcium-binding protein) (Protein 18A2) (Protein Mts1) (S100 calcium-binding protein A4)/ S100a4 Capl Mts1	25.74	4	11.71/5.31	0.0022	1.43881	up
P17717	UDP-glucuronosyltransferase 2B17 (EC 2.4.1.17) (M-1) (UDP-glucuronosyltransferase 2B5) (UDPGT 2B5)/ Ugt2b17 Ugt2b5	8.02	3	60.82/7.87	0.03670	0.56911	down
P28651	Carbonic anhydrase-related protein (CARP) (Carbonic anhydrase VIII) (CA-VIII)/ Ca8 Cals Cals1 Car8 Carp	26.115	5	33.06/4.78	0.00223	0.65100	down
P00416	Cytochrome c oxidase subunit 3 (Cytochrome c oxidase polypeptide III)/ mt-Co3 COIII Mtco3	7.66	2	29.90/7.30	0.02289	1.69243	up
P12246	Serum amyloid P-component (SAP)/ Apcs Ptx2 Sap	17.86	3	26.23/6.35	0.04406	0.61784	down
Q9QZJ6	Microfibrillar-associated protein 5 (MFAP-5) (Microfibril-associated glycoprotein 2) (MAGP-2)/ Mfap5 Magp2	24.39	4	18.53/5.93	0.00318	1.40939	up
P14432	H-2 class I histocompatibility antigen, TLA(B) alpha chain (MHC thymus leukemia antigen)/ H2-T3	8.465	2	43.45/5.29	0.02976	0.59496	down
P52927	High mobility group protein HMGI-C (High mobility group AT-hook protein 2)/ Hmga2 Hmgic	31.945	3	11.81/10.6	0.04197	0.71403	down

P70245	3-beta-hydroxysteroid-Delta(8),Delta(7)-isomerase (EC 5.3.3.5) (Cholestenol Delta-isomerase) (Delta(8)-Delta(7) sterol isomerase) (D8-D7 sterol isomerase) (Emopamil-binding protein)/ Ebp Msi	9.57	2	26.20/7.56	0.01759	1.69573	up
P43241	Homeobox protein CDX-2 (Caudal-type homeobox protein 2)/ Cdx2 Cdx-2	9.65	2	33.46/9.66	0.03109	0.5473	down
Q9EPS2	Peptide YY (PYY) (Peptide tyrosine tyrosine) [Cleaved into: Peptide YY(3-36) (PYY-II)]/ Pyy	41.325	4	11.06/5.45	0.01659	1.45185	up
Q9ESK9	RB1-inducible coiled-coil protein 1 (Coiled-coil-forming protein 1) (FAK family kinase-interacting protein of 200 kDa) (FIP200) (LaXp180)/ Rb1cc1 Cc1 Kiaa0203	2.145	3	182.2/5.49	0.00553	1.69050	up
A0JNU3	60 kDa lysophospholipase (EC 3.1.1.5) [Includes: L-asparaginase (EC 3.5.1.1) (L-asparagine amidohydrolase); Platelet-activating factor acetylhydrolase (PAF acetylhydrolase) (EC 3.1.1.47)]/ Aspg	5.67	3	60.56/5.88	0.02222	0.68260	down

Table S3 Differential proteins in Model and low-dose CMP33 groups

Accession	Protein names/ Gene names	Coverage	Unique Peptides	MW [kDa]/ pI	P value	Fold change (L/M)	Expression (L/M)
P17563	Selenium-binding protein 1 (56 kDa selenium-binding protein) (SBP56) (SP56)/ Selenbp1 Lpsb	82.1	31	52.48/6.29	0.03803	0.6515	down
Q61554	Fibrillin-1/ Fbn1 Fbn-1	36.52	75	312.0/4.92	0.00030	1.50721	up
P54869	Hydroxymethylglutaryl-CoA synthase, mitochondrial (HMG-CoA synthase) (EC 2.3.3.10) (3-hydroxy-3-methylglutaryl/ Hmgcs2	46.555	22	56.79/8.41	0.00099	0.26691	down
P13634	Carbonic anhydrase 1 (EC 4.2.1.1) (Carbonate dehydratase I) (Carbonic anhydrase I) (CA-I)/ Ca1 Car1	6.78E+01	12	28.31/6.96	0.00374	0.4497	down
O70475	UDP-glucose 6-dehydrogenase (UDP-Glc dehydrogenase) (UDP-GlcDH) (UDPGDH) (EC 1.1.1.22)/ Ugdh	70.085	28	54.80/7.56	0.00206	0.61716	down
Q91X72	Hemopexin/ Hpx Hpxn	46.52	21	51.29/7.80	0.00253	0.70858	down
Q9D816	Cytochrome P450 2C55 (EC 1.14.14.1) (CYPIIC55)/ Cyp2c55 Cyp2c-55	34.39	19	56.06/6.98	0.00311	0.35623	down
Q8VCW8	Acyl-CoA synthetase family member 2, mitochondrial (EC 6.2.1.-)/ Acsf2	46.75	24	67.91/8.18	0.00029	0.55766	down
P55050	Fatty acid-binding protein, intestinal (Fatty acid-binding protein 2) (Intestinal-type fatty acid-binding protein) (I-FABP)/ Fabp2 Fabpi	44.7	8	15.12/7.24	0.02985	0.35862	down
O88428	Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase	63.445	27	70.31/7.5	0.00027	0.62532	down

	2 (PAPS synthase 2) (PAPSS 2) (Sulfurylase kinase 2)/ Papss2 Atpsk2			8			
P24549	Retinal dehydrogenase 1 (RALDH 1) (RalDH1) (EC 1.2.1.36) (ALDH-E1) (ALHDII) (Aldehyde dehydrogenase family 1 member A1) (Aldehyde dehydrogenase, cytosolic);/ Aldh1a1 Ahd-2 Ahd2 Aldh1	42.515	12	54.43/7.80	0.00258	0.62536	down
P00329	Alcohol dehydrogenase 1 (EC 1.1.1.1) (ADH-A2) (Alcohol dehydrogenase A subunit)/ Adh1 Adh-1	43.6	16	39.75/8.10	0.00019	1.87757	up
Q8K0C5	Zymogen granule membrane protein 16 (Zymogen granule protein 16) (Secretory lectin ZG16)/ Zg16	70.06	7	18.20/9.23	0.00394	1.67572	up
Q08189	Protein-glutamine gamma-glutamyltransferase E (EC 2.3.2.13) (Transglutaminase E) (TG(E)) (TGE) (TGase E) (Transglutaminase-3) (TGase-3) [Cleaved into: Protein-glutamine gamma-glutamyltransferase E 50 kDa catalytic chain; Protein-glutamine gamma-glutamyltransferase E / Tgm3 Tgase3	46.71	24	77.26/6.81	0.01206	1.52560	up
P01901	H-2 class I histocompatibility antigen, K-B alpha chain (H-2K(B))/ H2-K1 H2-K	46.34	5	41.28/6.39	0.02957	0.63689	down
P21447	Multidrug resistance protein 1A (EC 3.6.3.44) (ATP-binding cassette sub-family B member 1A) (MDR1A) (Multidrug resistance protein 3) (P-glycoprotein 3)/ Abcb1a Abcb4 Mdr1a Mdr3 Pgy-3 Pgy3	24.61	26	140.6/8.85	0.00100	0.67526	down
Q91WG0	Acylcarnitine hydrolase (ACH M1) (EC 3.1.1.28) (Carboxylesterase 2) (CES 2) (Peroxisome proliferator-inducible acylcarnitine hydrolase)/ Ces2c Ces2	34.76	12	62.43/5.69	0.00791	0.70856	down
P31809	Carcinoembryonic antigen-related cell adhesion molecule 1 (Biliary glycoprotein 1) (BGP-1) (Biliary glycoprotein D) (MHVR1) (Murine hepatitis virus receptor) (MHV-R) (CD antigen CD66a)/ Ceacam1 Bgp Bgp1 Bgpd	14.4	5	56.98/5.58	0.01856	0.63534	down
Q9D279	Mitotic interactor and substrate of PLK1 (Mitotic spindle positioning protein)/ Misp	39.815	19	72.24/6.18	1.96E-05	0.7065	down
P02089	Hemoglobin subunit beta-2 (Beta-2-globin) (Hemoglobin beta-2 chain) (Hemoglobin beta-minor chain)/ Hbb-b2	72.11	3	15.87/8.04	0.00847	0.63468	down
Q9D7E4	UPF0449 protein C19orf25 homolog/--	26.61	2	12.10/5.24	0.01546	0.68586	down
Q8K0J2	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7 (BGnT-7) (Beta-1,3-Gn-T7) (Beta-1,3-N-acetylglucosaminyltransferase 7) (Beta3Gn-T7) (EC 2.4.1.-)/ B3gnt7	41.81	15	45.35/8.47	0.00013	1.51735	up
Q91V76	Ester hydrolase C11orf54 homolog (EC 3.1.-.-)/--	52.86	13	34.97/6.29	0.00351	0.62127	down
Q61878	Bone marrow proteoglycan (BMPG) (Proteoglycan 2) [Cleaved	30.04	7	24.24/6.2	0.03845	1.44603	up

	into: Eosinophil granule major basic protein (EMBP) (MBP)]/ Prg2 Mbp-1			0			
Q6ZWU9	40S ribosomal protein S27/ Rps27	39.29	2	9.45/9.45	0.00093	1.45145	up
Q5SF07	Insulin-like growth factor 2 mRNA-binding protein 2 (IGF2 mRNA-binding protein 2) (IMP-2) (IGF-II mRNA-binding protein 2) (VICKZ family member 2)/ Igf2bp2 Imp2 Vickz2	16.05	7	65.54/8.03	0.0023	0.69791	down
Q63886	UDP-glucuronosyltransferase 1-1 (UDPGT 1-1) (UGT1*1) (UGT1-01) (UGT1.1) (EC 2.4.1.17) (UDP-glucuronosyltransferase 1A1) (UGTBR1)/ Ugt1a1 Ugt1	25.05	3	60.01/8.62	0.00713	0.58948	down
Q8VCT4	Carboxylesterase 1D (Carboxylesterase 3) (EC 3.1.1.1) (EC 3.1.1.67) (Fatty acid ethyl ester synthase) (FAEE synthase) (Triacylglycerol hydrolase) (TGH)/ Ces1d Ces1 Ces3	30.795	11	61.75/6.61	0.00238	0.52419	down
Q8CB12	Gasdermin-C3/Gsdmc3	42.915	6	54.15/6.58	0.02085	1.49966	up
Q9D2Q8	Protein S100-A14 (S100 calcium-binding protein A14) (S114)/ S100a14 Gm1020 S100a15	77.885	8	11.59/5.50	0.01024	1.49660	up
Q9DD20	Methyltransferase-like protein 7B (EC 2.1.1.-)/ Mettl7b	37.295	10	28.03/8.59	0.00054	0.45830	down
Q08331	Calretinin (CR)/ Calb2	49.815	13	31.35/5.02	0.00013	0.60952	down
Q3UZZ6	Sulfotransferase 1 family member D1 (ST1D1) (EC 2.8.2.-) (Amine N-sulfotransferase) (SULT-N) (Dopamine sulfotransferase Sult1d1) (Tyrosine-ester sulfotransferase)/ Sult1d1 St1d1	41.015	11	35.06/5.76	0.0065	0.54946	down
P52840	Sulfotransferase 1A1 (ST1A1) (EC 2.8.2.1) (Aryl sulfotransferase) (Phenol sulfotransferase) (Phenol/aryl sulfotransferase) (mSTp1) (ST1A4) (Sulfokinase)/ Sult1a1 St1a1 Stp Stp1	58.075	13	33.95/8.10	0.00625	0.69447	down
P04228	H-2 class II histocompatibility antigen, A-D alpha chain/H2-Aa	29.3	2	28.22/5.00	0.04054	1.94148	up
P09541	Myosin light chain 4 (MLC1EMB) (Myosin light chain 1, atrial/fetal isoform) (MLC1A)/ Myl4 Mlc1a Myla	27.46	5	21.14/5.03	0.00700	0.50014	down
P28776	Indoleamine 2,3-dioxygenase 1 (IDO-1) (EC 1.13.11.52) (Indoleamine-pyrrole 2,3-dioxygenase)/ Ido1 Ido Indo	17.565	6	45.61/6.35	0.00281	0.60742	down
Q9WUZ9	Ectonucleoside triphosphate diphosphohydrolase 5 (NTPDase 5) (EC 3.6.1.6) (CD39 antigen-like 4) (ER-UDPase) (Guanosine-diphosphatase ENTPD5) (GDPase ENTPD5) (EC 3.6.1.42) (Nucleoside diphosphatase) (Uridine-diphosphatase ENTPD5) (UDPase ENTPD5)/ Entpd5 Cd39l4	34.075	9	47.07/5.29	0.02077	0.70775	down
Q99J99	3-mercaptopyruvate sulfurtransferase (MST) (EC 2.8.1.2)/ Mpst	52.53	13	33.00/6.58	0.02071	0.58966	down
Q8BK48	Pyrethroid hydrolase Ces2e (EC 3.1.1.88) (carboxylesterase	30.77	10	62.28/6.1	0.00013	0.60302	down

	2E)/ Ces2e Ces5			6			
P16015	Carbonic anhydrase 3 (EC 4.2.1.1) (Carbonate dehydratase III) (Carbonic anhydrase III) (CA-III)/ Ca3 Car3	38.85	9	29.35/7.37	8.62E-06	0.46709	down
P04228	H-2 class II histocompatibility antigen, A-D alpha chain/H2-Aa	29.3	2	28.22/5.00	0.04054	1.94148	up

Q8QZR5	Alanine aminotransferase 1 (ALT1) (EC 2.6.1.2) (Glutamate pyruvate transaminase 1) (GPT 1) (Glutamic--alanine transaminase 1) (Glutamic--pyruvic transaminase 1)/ Gpt Gpt1	15.225	7	55.11/6.64	0.00084	0.54358	down
P20060	Beta-hexosaminidase subunit beta (EC 3.2.1.52) (Beta-N-acetylhexosaminidase subunit beta) (Hexosaminidase subunit B) (N-acetyl-beta-glucosaminidase subunit beta)/ Hexb	30.785	13	33.95/8.10	0.00050	1.51796	up
Q8VCR2	17-beta-hydroxysteroid dehydrogenase 13 (17-beta-HSD 13) (EC 1.1.-.-) (Alcohol dehydrogenase PAN1B-like) (Short-chain dehydrogenase/reductase 9)/ Hsd17b13 Scdr9	35.53	15	61.08/8.12	0.00218	0.54906	down
Q8VCC2	Liver carboxylesterase 1 (EC 3.1.1.1) (Acyl-coenzyme A:cholesterol acyltransferase) (Carboxylesterase 1G) (ES-x)/ Ces1 Ces1g	25.045	10	62.64/6.00	0.00172	0.56555	down
Q9Z0L8	Gamma-glutamyl hydrolase (EC 3.4.19.9) (Conjugase) (FGPH) (Folylpolyglutamate hydrolase) (GH) (Gamma-Glu-x carboxypeptidase)/ Ggh	3.31E+01	9	35.45/7.50	0.00145	1.76685	up
Q64516	Glycerol kinase (GK) (Glycerokinase) (EC 2.7.1.30) (ATP:glycerol 3-phosphotransferase)/ Gk Gyk	25.31	13	61.19/5.87	0.00125	1.42626	up
Q61646	Haptoglobin (Zonulin) [Cleaved into: Haptoglobin alpha chain; Haptoglobin beta chain]/ Hp	37.175	13	38.73/6.29	0.00131	0.426	down
P25085	Interleukin-1 receptor antagonist protein (IL-1RN) (IL-1ra) (IRAP) (IL1 inhibitor)/ Il1rn Il-1ra	27.25	5	20.26/6.19	0.00509	1.43005	up
Q8BG07	Phospholipase D4 (PLD 4) (EC 3.1.4.4) (Choline phosphatase 4) (Phosphatidylcholine-hydrolyzing phospholipase D4)/ Pld4	10.44	5	56.12/7.31	0.00099	1.44308	up
P09036	Serine protease inhibitor Kazal-type 1 (P12) (Prostatic secretory glycoprotein) (Serine protease inhibitor Kazal-type 3)/ Spink1 Spink3	26.25	3	8.48/8.00	0.00541	1.65692	up
P06344	H-2 class II histocompatibility antigen, A-U beta chain/--	28.71	2	30.02/8.09	0.00358	1.41687	up
Q8BGT9	Polypeptide N-acetylgalactosaminyltransferase 12 (EC 2.4.1.41) (Polypeptide GalNAc transferase 12) (GalNAc-T12) (pp-GaNTase 12) (Protein-UDP acetylgalactosaminyltransferase 12) (UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 12)/ Galnt12	18.84	10	66.50/7.24	0.00126	0.66926	down
Q9D6U8	Protein FAM162A (E2-induced gene 5 protein homolog) (Growth and transformation-dependent protein) (HGTD-P)/ Fam162a E2ig5	37.42	7	17.71/9.88	0.00543	0.68534	down
P97430	Antileukoproteinase (ALP) (Secretory leukocyte protease	47.71	8	14.30/8.7	0.00133	1.84593	up

	inhibitor)/ Slpi			9			
Q9JLB0	MAGUK p55 subfamily member 6 (Dlgh4 protein) (P55T protein) (Protein associated with Lin-7 2)/ Mpp6 Dlgh4 Pals2	15.735	8	62.59/6.40	0.02377	0.69538	down
Q9QZJ6	Microfibrillar-associated protein 5 (MFAP-5) (Microfibril-associated glycoprotein 2) (MAGP-2)/ Mfap5 Magp2	24.39	4	18.53/5.93	0.00563	1.43602	up
Q9WUG6	Insulin-like peptide INSL5 (Insulin-like peptide 5) (Relaxin/insulin-like factor 2) (Relaxin/insulin-like protein) [Cleaved into: Insulin-like peptide INSL5 B chain; Insulin-like peptide INSL5 A chain]/ Insl5 Rif Rif2 Zins3	49.255	9	15.51/8.89	0.02762	1.71939	up
A6X935	Inter alpha-trypsin inhibitor, heavy chain 4 (ITI heavy chain H4) (ITI-HC4) (Inter-alpha-inhibitor heavy chain 4)/ Itih4	11.04	9	104.59/6.4	0.017807	0.70265	down
Q3USF0	Acetylgalactosaminyl-O-glycosyl-glycoprotein beta-1,3-N-acetylglucosaminyltransferase (EC 2.4.1.147) (Core 3 synthase) (UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 6) (BGnT-6) (Beta-1,3-Gn-T6) (Beta-1,3-N-acetylglucosaminyltransferase 6) (Beta3Gn-T6)/ B3gnt6	8.95	4	43.92/8.68	0.01709	0.34091	down
P07091	Protein S100-A4 (Metastasin) (Metastatic cell protein) (PEL98) (Placental calcium-binding protein) (Protein 18A2) (Protein Mts1) (S100 calcium-binding protein A4)/ S100a4 Capl Mts1	25.74	4	11.71/5.31	0.00240	1.45566	up
P01904	H-2 class II histocompatibility antigen, E-D alpha chain (H2-IE-alpha)/ H2-Ea	17.645	4	29.10/5.12	0.00845	1.49206	up
P17717	UDP-glucuronosyltransferase 2B17 (EC 2.4.1.17) (M-1) (UDP-glucuronosyltransferase 2B5) (UDPGT 2B5)/ Ugt2b17 Ugt2b5	8.02	3	60.82/7.87	0.03358	0.43664	down
P28651	Carbonic anhydrase-related protein (CARP) (Carbonic anhydrase VIII) (CA-VIII)/ Ca8 Cals Cals1 Car8 Carp	26.115	5	33.06/4.78	9.49E-05	0.54942	down
P12246	Serum amyloid P-component (SAP)/ Apcs Ptx2 Sap	17.86	3	26.23/6.35	0.002343	0.67531	down
Q8JZQ5	Amiloride-sensitive amine oxidase [copper-containing] (DAO) (Diamine oxidase) (EC 1.4.3.22) (Amiloride-binding protein 1) (Amine oxidase copper domain-containing protein 1) (Histaminase)/ Aoc1 Abp1	9.52	6	85.37/6.64	0.0049	1.40276	up
P01631	Ig kappa chain V-II region 26-10/--	19.91	3	12.26/8.88	0.02844	1.54046	up
Q3TTY5	Keratin, type II cytoskeletal 2 epidermal (Cytokeratin-2e) (CK-2e) (Epithelial keratin-2e) (Keratin-2 epidermis) (Keratin-2e) (K2e) (Type-II keratin Kb2)/ Krt2 K2e Krt2-17 Krt2a	6.22	2	70.88/8.06	0.04310	0.6776	up
Q09199	Beta-1,4 N-acetylgalactosaminyltransferase 2 (EC 2.4.1.-)/ B4galnt2 Galgt2 Ggm3	10.98	5	58.28/8.94	0.00840	0.47876	down
Q8VC49	Interferon alpha-inducible protein 27-like protein 2B (Interferon-stimulated gene 12 protein B2) (ISG12(b2))/ Ifi27l2b Isg12(b2)	19.435	5	27.76/4.70	0.01523	0.56580	down

P80560	Receptor-type tyrosine-protein phosphatase N2 (R-PTP-N2) (EC 3.1.3.48) (PTP IA-2beta) (Protein tyrosine phosphatase-NP) (PTP-NP)/ Ptprn2	4.495	4	111.4/5.95	0.03542	0.71034	down
Q5EBG6	Heat shock protein beta-6 (HspB6)/ Hspb6 Gm479	29.0157	4	17.51/6.00	0.00252	1.44682	up
P70269	Cathepsin E (EC 3.4.23.34)/ Ctse	6.045	3	42.91/4.64	0.01156	1.49459	up
P14432	H-2 class I histocompatibility antigen, TLA(B) alpha chain (MHC thymus leukemia antigen)/ H2-T3	8.465	2	43.45/5.29	0.01991	0.47438	down
P52927	High mobility group protein HMGI-C (High mobility group AT-hook protein 2)/ Hmga2 Hmgic	31.945	3	11.81/10.6	0.00295	0.64450	down
P43241	Homeobox protein CDX-2 (Caudal-type homeobox protein 2)/ Cdx2 Cdx-2	9.65	2	33.46/9.66	0.02235	0.48731	down
P62965	Cellular retinoic acid-binding protein 1 (Cellular retinoic acid-binding protein I) (CRABP-I)/ Crabp1	16.79	2	15.58/5.38	0.00546	0.69564	down
P35230	Regenerating islet-derived protein 3-beta (REG-3-beta) (Pancreatitis-associated protein 1) (Regenerating islet-derived protein III-beta) (Reg III-beta) [Cleaved into: Regenerating islet-derived protein 3-beta 16.5 kDa form; Regenerating islet-derived protein 3-beta 15 kDa form]/ Reg3b Pap Pap1	31.425	5	19.46/7.58	0.00828	0.61183	down
Q8BGS7	Choline/ethanolaminephosphotransferase 1 (mCEPT1) (EC 2.7.8.1) (EC 2.7.8.2)/ Cept1	7.695	3	46.40/8.10	0.03832	1.53822	up
Q9QXX3	Group 10 secretory phospholipase A2 (EC 3.1.1.4) (Group X secretory phospholipase A2) (GX sPLA2) (sPLA2-X) (Phosphatidylcholine 2-acylhydrolase 10)/ Pla2g10	9.605	2	16.99/6.60	0.04541	1.48692	up
A0JNU3	60 kDa lysophospholipase (EC 3.1.1.5) [Includes: L-asparaginase (EC 3.5.1.1) (L-asparagine amidohydrolase); Platelet-activating factor acetylhydrolase (PAF acetylhydrolase) (EC 3.1.1.47)]/ Aspg	5.67	3	60.56/5.88	0.01804	0.61998	down
Q3U095	NXPE family member 2 (Protein FAM55B)/ Nxpe2 Fam55b	6.99	4	63.92/9.25	0.02671	0.64652	down
Q9EPS2	Peptide YY (PYY) (Peptide tyrosine tyrosine) [Cleaved into: Peptide YY(3-36) (PYY-II)]/ Pyy	41.325	4	11.06/5.45	0.00490	1.72208	up
Q9ESK9	RB1-inducible coiled-coil protein 1 (Coiled-coil-forming protein 1) (FAK family kinase-interacting protein of 200 kDa) (FIP200) (LaXp180)/ Rb1cc1 Cc1 Kiaa0203	2.145	3	182.2/5.49	0.00873	1.87447	up
P28474	Alcohol dehydrogenase class-3 (EC 1.1.1.1) (Alcohol dehydrogenase 2) (Alcohol dehydrogenase 5) (Alcohol dehydrogenase B2) (ADH-B2) (Alcohol dehydrogenase class-III) (Glutathione-dependent formaldehyde dehydrogenase) (FALDH) (FDH) (GSH-FDH) (EC 1.1.1.-) (S-(hydroxymethyl)glutathione dehydrogenase) (EC 1.1.1.284)/	48.525	14	39.52/7.25	0.01143	0.71248	down

Adh5 Adh-2 Adh2

Table S4 Differential proteins in Model and positive drug SASP groups

Accession	Protein names/ Gene names	Coverage	Unique Peptides	MW [kDa]/ pI	P value	Fold change (SASP/M)	Expression (SASP/M)
P17563	Selenium-binding protein 1 (56 kDa selenium-binding protein) (SBP56) (SP56)/ Selenbp1 Lpsb	82.1	31	52.48/6.29	0.03749	064638	down
Q61554	Fibrillin-1/ Fbn1 Fbn-1	36.52	75	312.05/4.92	0.00718	1.56679	up
Q91V76	Ester hydrolase C11orf54 homolog (EC 3.1.-.-)	52.86	13	34.97/6.29	0.02853	0.64742	down
P13634	Carbonic anhydrase 1 (EC 4.2.1.1) (Carbonate dehydratase I) (Carbonic anhydrase I) (CA-I)/ Ca1 Car1	6.78E+01	12	28.31/6.96	0.04279	0.5021	down
P54869	Hydroxymethylglutaryl-CoA synthase, mitochondrial (HMG-CoA synthase) (EC 2.3.3.10) (3-hydroxy-3-methylglutaryl/ Hmgcs2	46.555	22	56.79/8.41	0.02162	0.32686	down
O70475	UDP-glucose 6-dehydrogenase (UDP-Glc dehydrogenase) (UDP-GlcDH) (UDPGDH) (EC 1.1.1.22)/ Ugdh	70.085	28	54.80/7.56	0.02961	0.64486	down
O88428	Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 2 (PAPS synthase 2) (PAPSS 2) (Sulfurylase kinase 2)/ Papss2 Atpsk2	63.445	27	70.31/7.58	0.01040	0.6307	down
Q9D816	Cytochrome P450 2C55 (EC 1.14.14.1) (CYPIIC55)/ Cyp2c55 Cyp2c-55	34.39	19	56.06/6.98	0.04098	0.44821	down
Q8VCW8	Acyl-CoA synthetase family member 2, mitochondrial (EC 6.2.1.-)/ Acsf2	46.75	24	67.91/8.18	0.00719	0.57314	down
P24549	Retinal dehydrogenase 1 (RALDH 1) (RalDH1) (EC 1.2.1.36) (ALDH-E1) (ALHDII) (Aldehyde dehydrogenase family 1 member A1) (Aldehyde dehydrogenase, cytosolic);/ Aldh1a1 Ahd-2 Ahd2 Aldh1	42.515	12	54.43/7.80	0.02923	0.60732	down
P00329	Alcohol dehydrogenase 1 (EC 1.1.1.1) (ADH-A2) (Alcohol dehydrogenase A subunit)/ Adh1 Adh-1	43.6	16	39.75/8.10	0.0007	1.58266	up
Q08189	Protein-glutamine gamma-glutamyltransferase E (EC 2.3.2.13) (Transglutaminase E) (TG(E)) (TGE) (TGase E) (Transglutaminase-3) (TGase-3) [Cleaved into: Protein-glutamine gamma-glutamyltransferase E 50 kDa catalytic chain; Protein-glutamine gamma-glutamyltransferase E / Tgm3 Tgase3	46.71	24	77.26/6.81	0.04585	1.74340	up
P55050	Fatty acid-binding protein, intestinal (Fatty acid-binding protein 2) (Intestinal-type fatty acid-binding protein) (I-FABP)/ Fabp2 Fabpi	44.7	8	15.12/7.24	0.03164	0.39474	down
Q8K0J2	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7 (BGnT-7) (Beta-1,3-Gn-T7)	41.81	15	45.35/8.47	0.0090	1.40394	up

	(Beta-1,3-N-acetylglucosaminyltransferase 7) (Beta3Gn-T7) (EC 2.4.1.-)/ B3gnt7						
P06801	NADP-dependent malic enzyme (NADP-ME) (EC 1.1.1.40) (Malic enzyme 1)/ Me1 Mod-1 Mod1	34.795	16	63.91/7.44	0.00469	0.70108	down
Q8BK48	Pyrethroid hydrolase Ces2e (EC 3.1.1.88) (carboxylesterase 2E)/ Ces2e Ces5	30.77	10	62.28/6.16	0.00291	0.67002	down
Q8VCT4	Carboxylesterase 1D (Carboxylesterase 3) (EC 3.1.1.1) (EC 3.1.1.67) (Fatty acid ethyl ester synthase) (FAEE synthase) (Triacylglycerol hydrolase) (TGH)/ Ces1d Ces1 Ces3	30.795	11	61.75/6.61	0.03010	0.57606	down
Q9DD20	Methyltransferase-like protein 7B (EC 2.1.1.-)/ Mettl7b	37.295	10	28.03/8.59	0.01567	0.49024	down
Q08331	Calretinin (CR)/ Calb2	49.815	13	31.35/5.02	0.00763	0.63424	down
P52840	Sulfotransferase 1A1 (ST1A1) (EC 2.8.2.1) (Aryl sulfotransferase) (Phenol sulfotransferase) (Phenol/aryl sulfotransferase) (mSTp1) (ST1A4) (Sulfokinase)/ Sult1a1 St1a1 Stp Stp1	58.075	13	33.95/8.10	0.0330	0.60614	down
Q8VCR2	17-beta-hydroxysteroid dehydrogenase 13 (17-beta-HSD 13) (EC 1.1.-.-) (Alcohol dehydrogenase PAN1B-like) (Short-chain dehydrogenase/reductase 9)/ Hsd17b13 Scdr9	35.53	15	61.08/8.12	0.03390	0.66632	down
Q5SF07	Insulin-like growth factor 2 mRNA-binding protein 2 (IGF2 mRNA-binding protein 2) (IMP-2) (IGF-II mRNA-binding protein 2) (VICKZ family member 2)/ Igf2bp2 Imp2 Vickz2	16.05	7	65.54/8.03	0.01256	0.68474	down
Q8VCC2	Liver carboxylesterase 1 (EC 3.1.1.1) (Acyl-coenzyme A:cholesterol acyltransferase) (Carboxylesterase 1G) (ES-x)/ Ces1 Ces1g	25.045	10	62.64/6.00	0.01070	0.62457	down
Q8R1M8	Mucosal pentraxin/Mptx1 Mptx	22.37	3	24.52/5.67	0.0096	2.77294	up
Q9Z0L8	Gamma-glutamyl hydrolase (EC 3.4.19.9) (Conjugase) (FGPH) (Folylpolyglutamate hydrolase) (GH) (Gamma-Glu-x carboxypeptidase)/ Ggh	3.31E+01	9	35.45/7.50	0.00402	1.55250	up
Q61646	Haptoglobin (Zonulin) [Cleaved into: Haptoglobin alpha chain; Haptoglobin beta chain]/ Hp	37.175	13	38.73/6.29	0.02130	0.51960	down
P25085	Interleukin-1 receptor antagonist protein (IL-1RN) (IL-1ra) (IRAP) (IL1 inhibitor)/ Il1rn Il-1ra	27.25	5	20.26/6.19	0.0098	1.4376	up
P09036	Serine protease inhibitor Kazal-type 1 (P12) (Prostatic secretory glycoprotein) (Serine protease inhibitor Kazal-type 3)/ Spink1 Spink3	26.25	3	8.48/8.00	0.00449	1.78329	up
Q8BGT9	Polypeptide N-acetylgalactosaminyltransferase 12 (EC 2.4.1.41) (Polypeptide GalNAc transferase 12) (GalNAc-T12) (pp-GaNTase 12) (Protein-UDP acetylgalactosaminyltransferase 12) (UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 12)/ Galnt12	18.84	10	66.50/7.24	0.01540	0.70281	down
Q9D6U8	Protein FAM162A (E2-induced gene 5 protein homolog)	37.42	7	17.71/9.88	0.00461	0.66194	down

	(Growth and transformation-dependent protein) (HGTD-P)/ Fam162a E2ig5						
P28776	Indoleamine 2,3-dioxygenase 1 (IDO-1) (EC 1.13.11.52) (Indoleamine-pyrrole 2,3-dioxygenase)/ Ido1 Ido Indo	17.565	6	45.61/6.35	0.04002	0.67855	down
Q9D8G5	Regenerating islet-derived protein 4 (REG-4)/ Reg4	35.03	6	18.39/9.64	0.00886	1.71194	up
P16015	Carbonic anhydrase 3 (EC 4.2.1.1) (Carbonate dehydratase III) (Carbonic anhydrase III) (CA-III)/ Ca3 Car3	38.85	9	29.35/7.37	0.0016	0.39925	down
Q09199	Beta-1,4 N-acetylgalactosaminyltransferase 2 (EC 2.4.1.-)/ B4galnt2 Galgt2 Ggm3	10.98	5	58.28/8.94	0.03086	0.60742	down
P27784	C-C motif chemokine 6 (Protein C10) (Small-inducible cytokine A6) [Cleaved into: CCL6(22-95); CCL6(23-95)]/ Ccl6 C10 Scya6	16.38	5	12.98/9.33	0.01524	1.51769	up
G3X9C2	F-box only protein 50 (NCC receptor protein 1) (NCCRP-1) (Non-specific cytotoxic cell receptor protein 1 homolog)/ Nccrp1 Fbxo50	13.16	2	30.39/7.12	0.01086	1.54591	up
Q3USF0	Acetylgalactosaminyl-O-glycosyl-glycoprotein beta-1,3-N-acetylglucosaminyltransferase (EC 2.4.1.147) (Core 3 synthase) (UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 6) (BGnT-6) (Beta-1,3-Gn-T6) (Beta-1,3-N-acetylglucosaminyltransferase 6) (Beta3Gn-T6)/ B3gnt6	8.95	4	43.92/8.68	0.01740	0.34995	down
P07091	Protein S100-A4 (Metastasin) (Metastatic cell protein) (PEL98) (Placental calcium-binding protein) (Protein 18A2) (Protein Mts1) (S100 calcium-binding protein A4)/ S100a4 Capl Mts1	25.74	4	11.71/5.31	0.02957	1.39772	up
P28651	Carbonic anhydrase-related protein (CARP) (Carbonic anhydrase VIII) (CA-VIII)/ Ca8 Cals Cals1 Car8 Carp	26.115	5	33.06/4.78	0.00640	0.63056	down
O89094	Caspase-14 (CASP-14) (EC 3.4.22.-) (Mini-ICE) (MICE) [Cleaved into: Caspase-14 subunit p17, mature form; Caspase-14 subunit p10, mature form; Caspase-14 subunit p20, intermediate form; Caspase-14 subunit p8, intermediate form]/ Casp14	8.95	2	29.44/4.86	0.0114	1.48795	up
P12246	Serum amyloid P-component (SAP)/ Apcs Ptx2 Sap	17.86	3	26.23/6.35	0.001407	0.64694	down
Q3TMQ6	Angiogenin-4 (EC 3.1.27.-)/ Ang4	13.19	2	16.41/8.72	0.00128	2.98337	up
Q9EPS2	Peptide YY (PYY) (Peptide tyrosine tyrosine) [Cleaved into: Peptide YY(3-36) (PYY-II)]/ Pyy	41.325	4	11.06/5.45	0.04378	1.70988	up
Q8QZR5	Alanine aminotransferase 1 (ALT1) (EC 2.6.1.2) (Glutamate pyruvate transaminase 1) (GPT 1) (Glutamic--alanine transaminase 1) (Glutamic--pyruvic transaminase 1)/ Gpt Gpt1	15.225	7	55.11/6.64	0.01877	0.59576	down
P97430	Antileukoproteinase (ALP) (Secretory leukocyte protease	47.71	8	14.30/8.79	0.02818	1.66477	up

inhibitor)/ Slpi

Table S5 Differential metabolites in normal and model groups

ID	Peak	Similarity	Mass	VIP	P value	Fold change (N/M)	Expression (N/M)
507	xylose 1	946	103	1.46444	0.046533	0.456781	down
345	beta-Alanine 2	800	174	1.0952	0.006520	2.218105	up
476	1,2,4-Benzenetriol	799	239	2.43481	0.001841	0.712714	down
400	Threitol	704	100	2.20344	0.005654	0.775444	down
815	oleic acid	676	180	1.86235	0.012592	0.403331	down
886	Purine riboside	607	259	1.53465	0.024078	0.357154	down
510	unknown	577	204	1.22786	0.046688	0.479993	down
587	azelaic acid	523	204	1.54983	0.027710	0.475854	down
655	dl-p-Hydroxyphenyllactic acid	471	179	1.72733	0.036083	0.149958	down
1054	21-hydroxypregnenolone 2	435	175	1.10893	0.025580	0.566147	down
1050	Tetrahydrocorticosterone 4	432	135	2.06118	0.024145	0.627827	down
380	oxalacetic acid	386	98	1.47429	0.026516	0.511170	down
427	Cumic Acid	367	221	1.16573	0.025113	0.419435	down
172	unknown	364	281	2.06371	0.015063	0.797646	down
64	Analyte 69	362	207	1.84702	0.047586	0.831871	down
993	Analyte 1234	356	205	2.05891	0.041797	0.386231	down
174	Analyte 203	324	75	1.55039	0.015644	4.659214	up
794	Analyte 984	308	67	1.88549	0.034430	0.615290	down
233	unknown	301	130	1.31166	0.035177	5.715434	up
146	unknown	298	100	1.72935	0.045972	0.721228	down
328	cuminic alcohol	282	373	1.92276	0.033556	0.605455	down
916	unknown	280	154	1.73009	0.027435	0.347273	down
869	Analyte 1082	271	271	2.22552	0.004616	0.666615	down
305	unknown	270	217	2.22972	0.019333	0.329821	down
989	Analyte 1230	254	196	1.89033	0.021188	0.249940	down
870	Analyte 1083	245	169	1.17485	0.012809	0.560180	down
697	N-alpha-Acetyl-L-ornithine 1	241	394	1.98477	0.033436	1.678793	up
942	Analyte 1172	229	173	1.62766	0.025190	0.285286	down
441	Analyte 535	227	263	1.48399	0.048613	0.464405	down
321	Analyte 390	218	179	1.86898	0.006838	0.335504	down
444	Analyte 538	202	447	1.60915	0.030877	0.306780	down

Table S6 Differential metabolites in model and high-dose CMP33 groups

ID	Peak	Similarity	Mass	VIP	P value	Fold change (H/M)	Expression (H/M)
647	mannose 1	931	160	1.65263	0.027153	6.73E-07	down
117	2-hydroxybutanoic acid	911	131	1.1374	0.023582	0.272445	down
619	Methyl-beta-D-galactopyranoside	874	204	2.22094	0.004549	6.465674	up
260	D-Glyceric acid	860	189	1.41016	0.003324	0.094442	down
400	Threitol	704	100	1.90677	0.003407	1.292223	up
815	oleic acid	676	180	2.39514	4.33E-05	2.49E-05	down
566	unknown	665	174	2.39409	0.049061	413465.864	up
346	unknown	591	104	1.1003	0.017899	0.245458	down
672	unknown	584	204	1.60753	0.035861	3.22E-05	down
510	unknown	577	204	2.0672	0.016919	4.725466	up
469	phenylethylamine	576	174	2.05545	0.003109	16.663492	up
637	Gluconic lactone 1	567	204	2.26437	0.003005	9.437017	up
197	4-hydroxybutyrate	546	117	1.44975	0.023105	27.544881	up
888	unknown	530	246	1.91949	0.035063	0.000189	down
937	Analyte 1167	510	205	1.42523	0.039584	2.433339	up
194	unknown	499	159	1.68376	0.027138	0.051090	down
184	Methylmalonic acid	481	281	1.47511	0.045216	1.543765	up
258	unknown	462	86	1.56735	0.005757	17.541688	up
191	Carnitine	454	117	2.00828	0.021595	9.788392	up
352	unknown	411	174	1.94925	0.012044	1.822879	up
939	Neohesperidin	410	215	2.28867	0.002430	7.916434	up
187	unknown	385	89	1.64393	0.001162	10.832687	up
624	unknown	377	231	2.10441	0.021894	13.540732	up
463	Analyte 559	373	217	1.13836	0.032848	7.387485	up
172	unknown	364	281	1.62319	0.040099	1.576885	up
64	Analyte 69	362	207	1.49763	0.011678	1.620834	up
461	Analyte 557	356	204	2.21855	0.023149	10.813429	up
1000	dihydrotestosterone	346	201	1.68311	0.040925	50.681643	up
1033	testosterone 2	346	115	2.18746	0.001022	0.020036	down
216	unknown	341	179	1.62268	0.004341	1.920555	up
73	Analyte 82	340	223	1.18074	0.001504	2.401351	up
962	androsterone 1	324	115	1.65829	0.007393	15.132319	up

894	Analyte 114	296	59	1.69011	0.023149	1.665051	up
663	erythrose 4-phosphate 1	288	211	1.2625	0.006684	0.154134	down
702	3,5-Dihydroxyphenylglycine 1	281	149	1.31385	0.005799	5.367597	up
211	unknown	271	192	2.02982	0.001219	2.40E-05	down
285	Analyte 345	266	193	1.53626	0.004258	0.300781	down
137	unknown	256	142	1.71244	0.043067	1.791557	up
819	unknown	250	183	1.69011	0.047509	1.665051	up
789	glutathione 1	245	151	1.65977	0.045804	17.317840	up
480	D-alanyl-D-alanine 2	225	174	1.63371	0.038394	3.454469	up
641	Analyte 784	214	149	1.85564	0.007323	5.030823	up
489	hexadecane	209	170	2.38935	0.001841	0.000231	down
247	unknown	199	183	1.61259	0.011837	1.925860	up

Table S7 Differential metabolites in model and low-dose CMP33 groups

ID	Peak	Similarity	Mass	VIP	P value	Fold change (L/M)	Expression (L/M)
647	mannose 1	931	160	1.74547	0.026187	4.89E-07	down
255	succinic acid	910	247	1.32196	0.047096	2.806501	up
748	N-Acetyl-beta-D-mannosamine 1	853	87	1.55693	0.045722	0.474530	down
815	oleic acid	676	180	2.53214	0.002239	0.185309	down
248	maleic acid	651	147	1.19523	0.041481	2.896996	up
559	Lyxonic acid, 1,4-lactone	575	217	1.32249	0.048508	2.059826	up
514	Analyte 627	498	205	1.96817	0.043128	1.948573	up
792	Analyte 981	489	73	1.75828	0.026974	0.236811	down
475	D-erythronolactone 2	478	217	1.4089	0.040782	3.016426	up
258	unknown	462	86	1.60388	0.041308	2.263077	up
1038	unknown	401	221	1.11695	0.039417	1.985147	up
831	Analyte 1036	399	221	1.13155	0.049731	2.127539	up
187	unknown	385	89	1.89069	0.014631	3.016673	up
104	unknown	378	149	1.13137	0.047306	2.392993	up
408	unknown	375	223	1.58961	0.042740	2.413217	up
992	Analyte 1233	353	221	1.15723	0.037856	2.209329	up
1000	dihydrotestosterone	346	201	2.55571	0.026016	5.645176	up
847	Atropine	317	82	1.19442	0.041695	2.248657	up
84	unknown	317	173	1.92706	0.031605	1.527394	up
330	1,2-Cyclohexanedione 3	254	239	1.66889	0.021613	2.757382	up

Table S8 Differential metabolites in model and SASP groups

ID	Peak	Similarity	Mass	VIP	P value	Fold change (SASP/M)	Expression (SASP/M)
647	mannose 1	931	160	1.56543	0.027153	7.39E-07	down
557	fucose 2	927	117	1.09075	0.042754	2.445961	up
152	Methyl Phosphate	884	241	1.56844	0.037733	2.208838	up
562	D-(glycerol 1-phosphate)	810	299	1.53824	0.005382	2.571632	up
430	4-aminobutyric acid 1	809	174	1.28071	0.034246	0.299131	down
808	linoleic acid	806	150	1.39428	0.025492	9.073043	up
138	3-hydroxybutyric acid	776	233	1.34375	0.04268	0.324068	down
692	D-galacturonic acid 2	756	333	1.57746	0.027098	0.000234	down
715	Saccharic acid	682	73	1.60343	0.021873	0.316204	down
815	oleic acid	676	180	2.26949	4.33E-05	2.72E-05	down
566	unknown	665	174	1.68852	0.039422	402450.598	up
982	sucrose	663	361	1.33726	0.009370	0.136772	down
771	Glucoheptonic acid 3	632	319	1.87996	0.016966	8.59E-05	down
346	unknown	591	104	1.67528	0.027659	0.322931	down
672	unknown	584	204	1.56194	0.035862	3.54E-05	down
616	unknown	552	307	1.62531	0.029414	0.335320	down
664	unknown	538	97	1.6692	0.024022	2.569348	up
888	unknown	530	246	1.8094	0.035065	0.000207	down
760	unknown	498	129	1.95546	0.002936	0.137843	down
820	linolenic acid	448	125	1.99086	0.004567	0.053969	down
969	unknown	428	317	1.32005	0.041024	0.137988	down
318	O-acetylserine 1	422	174	1.26335	0.003671	2.316098	up
352	unknown	411	174	1.70681	0.048627	1.984242	up
939	Neohesperidin	410	215	2.04635	0.018037	11.501000	up
741	Analyte 919	396	225	1.35405	0.048355	0.061326	down
585	unknown	387	163	1.19265	0.009473	0.367033	down
187	unknown	385	89	1.59057	0.033104	12.225353	up
472	3-hydroxy-3-methylglutaric acid	382	174	1.17975	0.043357	12.225356	up
725	4-Hydroxymethyl-3-methoxyphenoxyacetic acid	362	355	1.18031	0.030456	2.757885	up
731	O-Succinylhomoserine	360	281	1.32766	0.039743	2.298750	up
1000	dihydrotestosterone	346	201	2.04903	0.021155	152.5733	up

918	unknown	345	168	1.4757	0.036465	2.311600	up
397	Bis(2-hydroxypropyl)amine 2	341	174	1.37952	0.005977	1.884259	up
753	unknown	331	173	1.762	0.047140	15.567047	up
962	androsterone 1	324	115	1.63319	0.008810	41.405644	up
973	unknown	320	187	1.89944	0.001878	0.0180430	down
84	unknown	317	173	1.85098	0.020368	2.222584	up
796	Indolelactate 2	306	290	1.34643	0.026362	0.0531937	down
488	3-hydroxyphenylacetic acid	305	205	1.20701	0.039045	48.458214	up
233	unknown	301	130	1.04484	0.036576	7.167422	up
714	Guanidinosuccinic acid 3	301	273	1.57205	0.027937	0.000447	down
997	unknown	300	115	2.00425	0.020627	26.349762	up
930	Abietic Acid 1	299	81	1.04439	0.030408	9.157867	up
399	unknown	282	128	1.44156	0.014674	0.262806	down
702	3,5-Dihydroxyphenylglycine 1	281	149	1.32104	0.022931	7.825553	up
970	unknown	274	215	1.5132	0.048877	0.190742	down
211	unknown	271	192	1.88674	0.004341	2.63E-05	down
938	Analyte 1168	269	226	1.83089	0.006959	3.111095	up
61	unknown	267	86	1.50461	0.048254	0.000257	down
234	unknown	266	111	1.21246	0.035572	0.272191	down
137	unknown	256	142	1.93235	0.003460	2.249839	up
923	D-erythro-sphingosine 1	253	210	1.5301	0.028896	8.55E-06	down
929	Analyte 1157	243	221	2.24898	0.010652	0.001288	down
168	Analyte 194	231	104	2.25943	0.006276	0.000258	down
682	Analyte 835	229	213	1.14839	0.030120	33.657653	up
321	Analyte 390	218	179	1.94751	0.000319	0.125596	down
641	Analyte 784	214	149	1.81319	0.022686	6.991910	up
489	hexadecane	209	170	1.98308	0.004480	0.057417	down
247	unknown	199	183	1.77585	0.025041	2.152756	up
340	unknown	184	214	1.87703	0.020056	2.864088	up

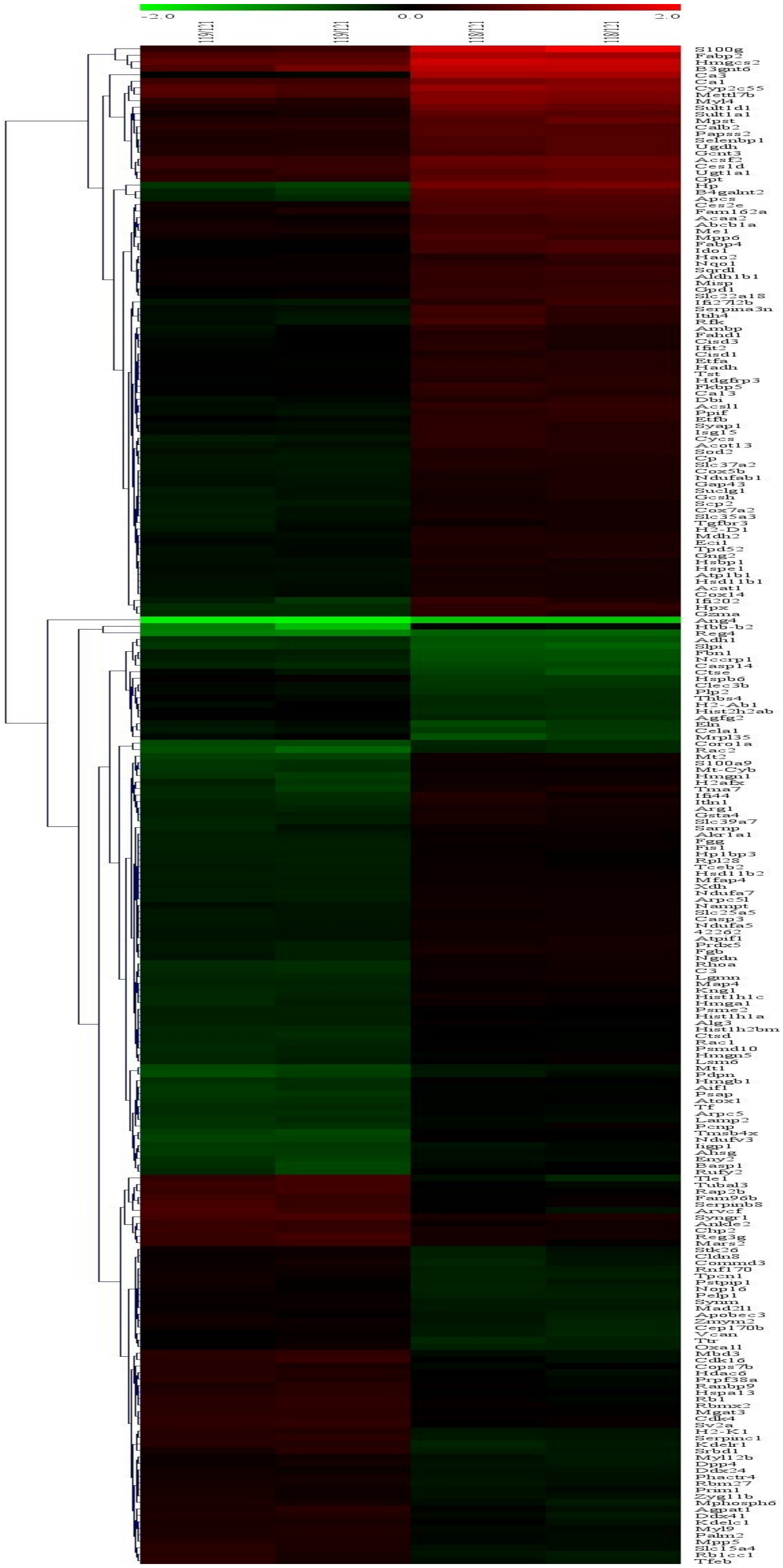

Figure S1A Clustering heatmap of differential proteins in normal and model groups

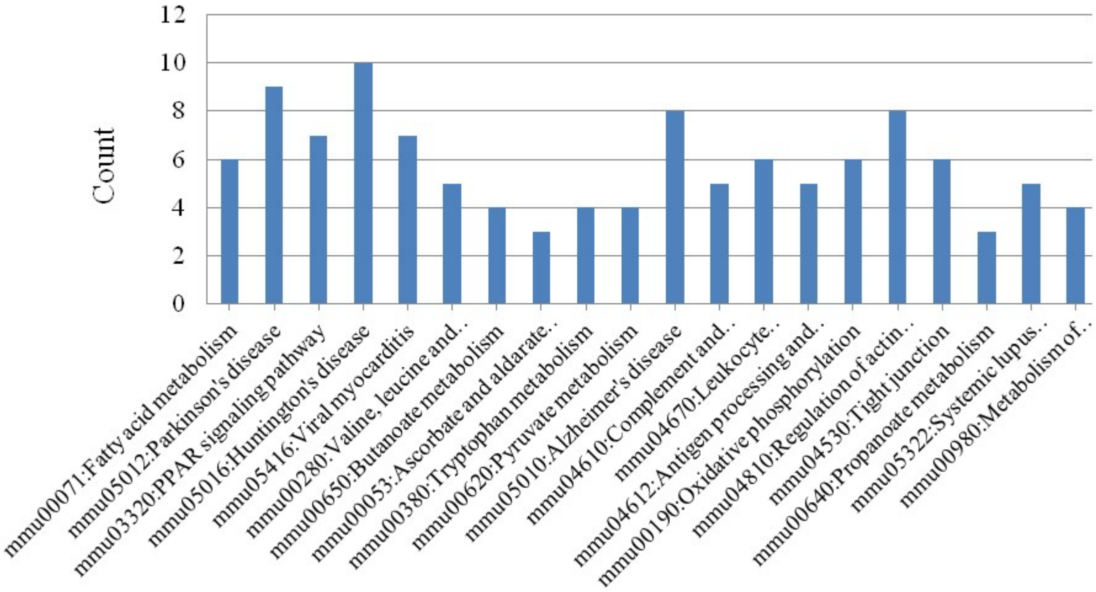

Figure S1B The KEGG metabolism pathway enrichiment anaylisis of differential proteins.

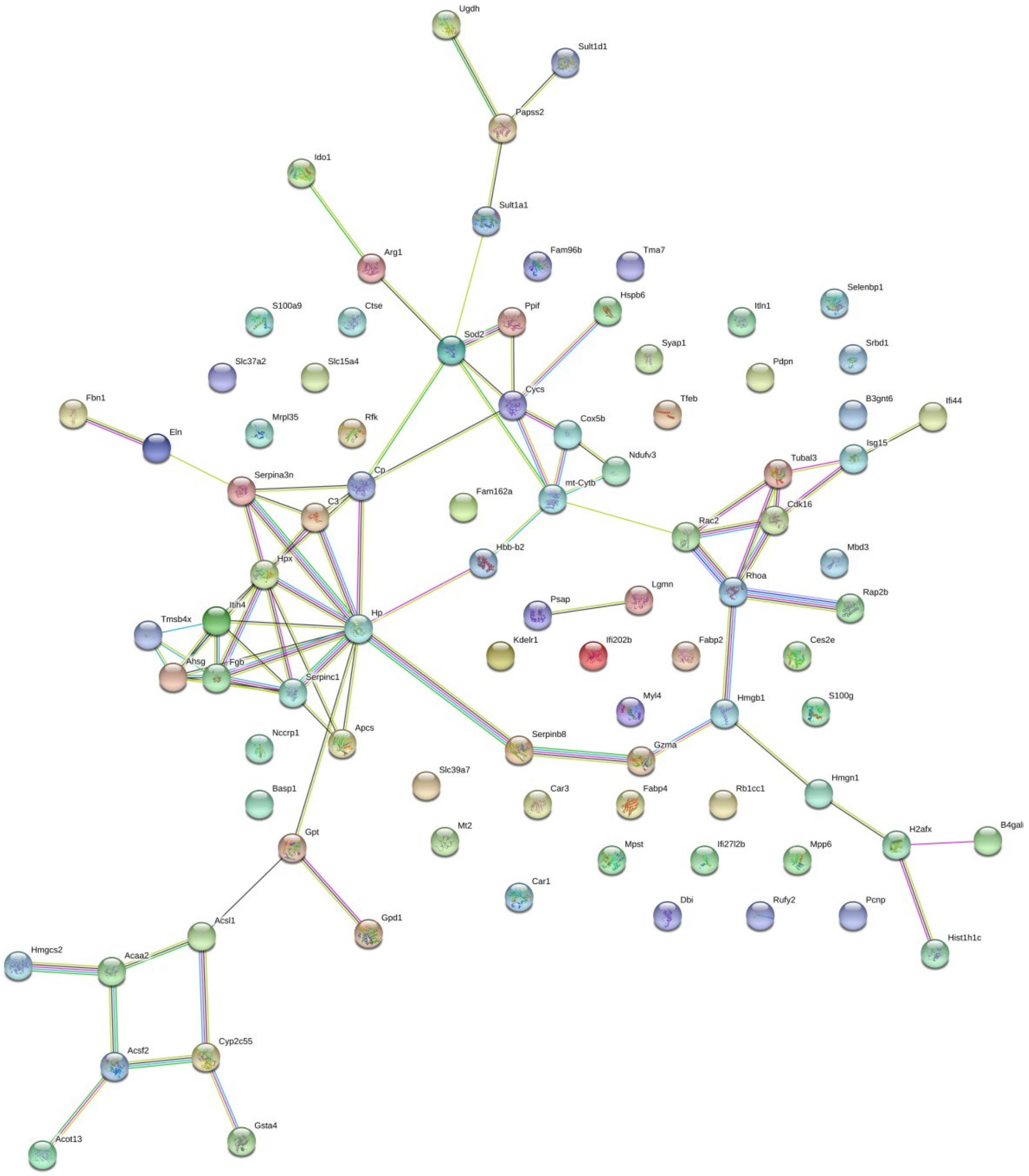

Figure S1C Interaction network for differential proteins.

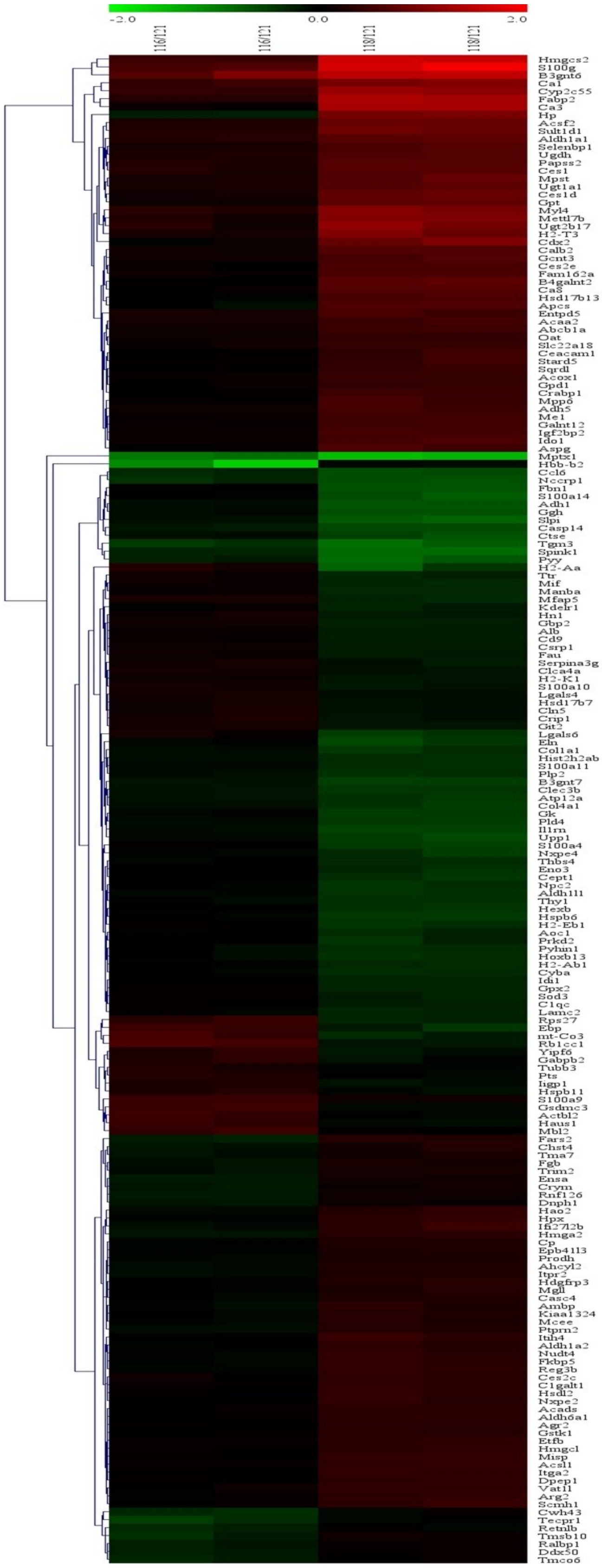

Figure S2A Clustering heatmap of differential proteins.

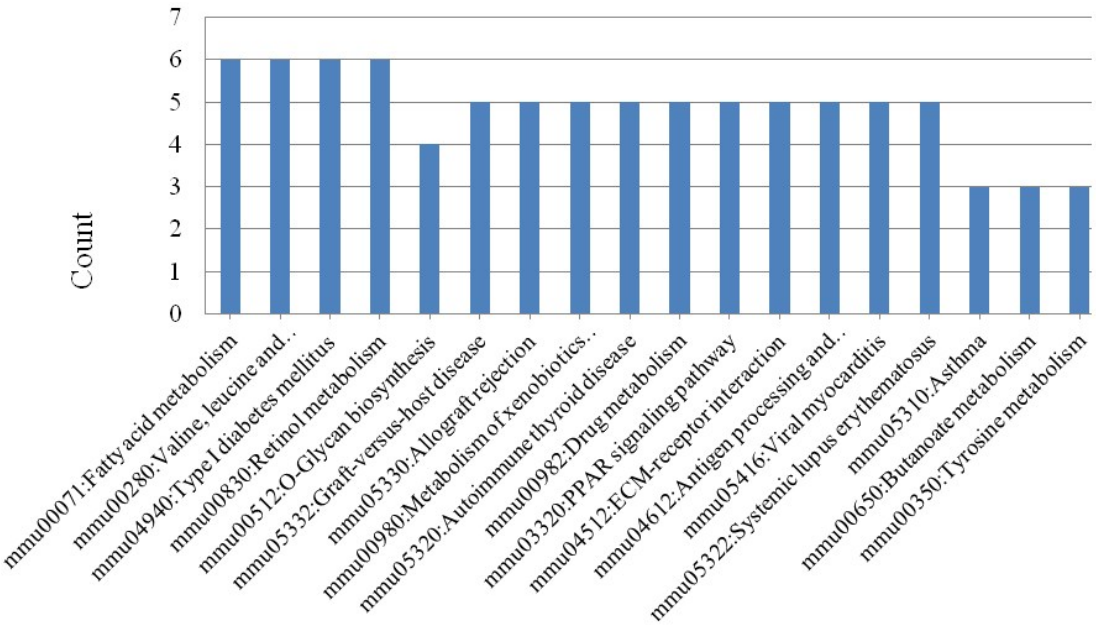

Figure S2B The KEGG metabolism pathway enrichiment anaylisis of differential proteins.

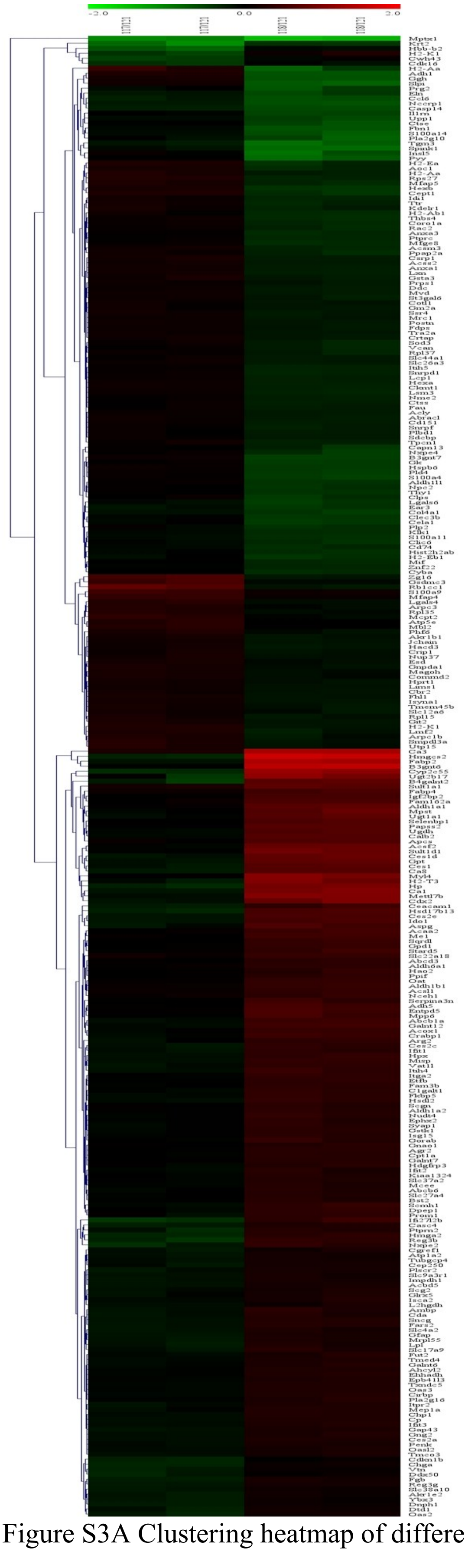

Figure S3A Clustering heatmap of differential proteins.

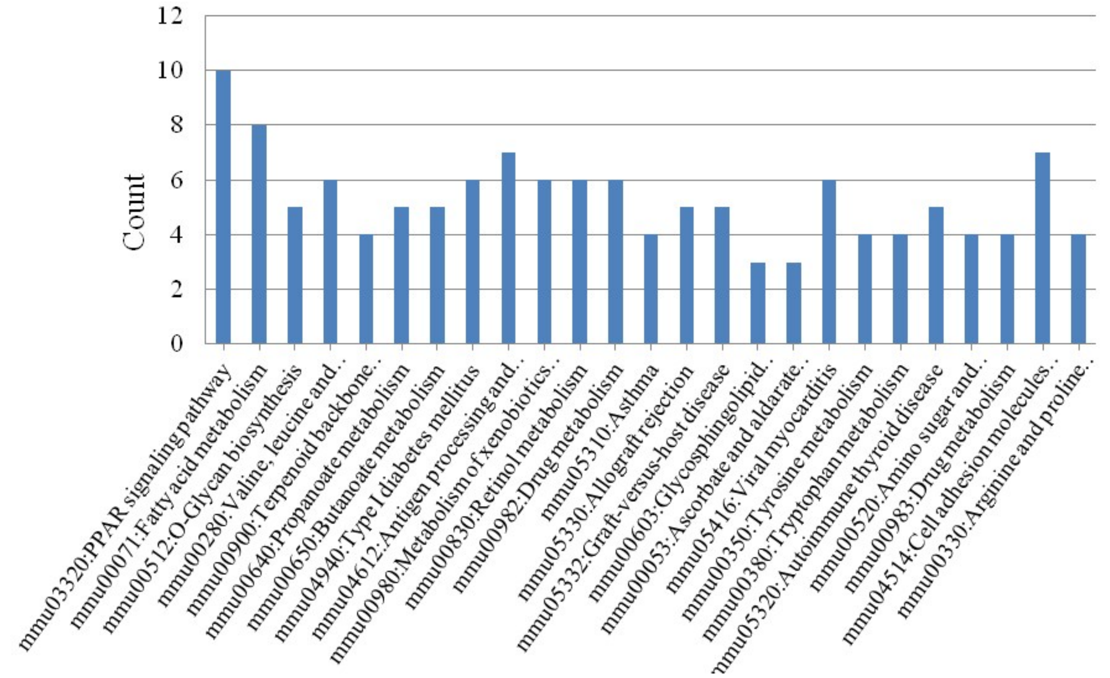

Figure S3B The KEGG metabolism pathway enrichiment anaylisis of differential proteins.

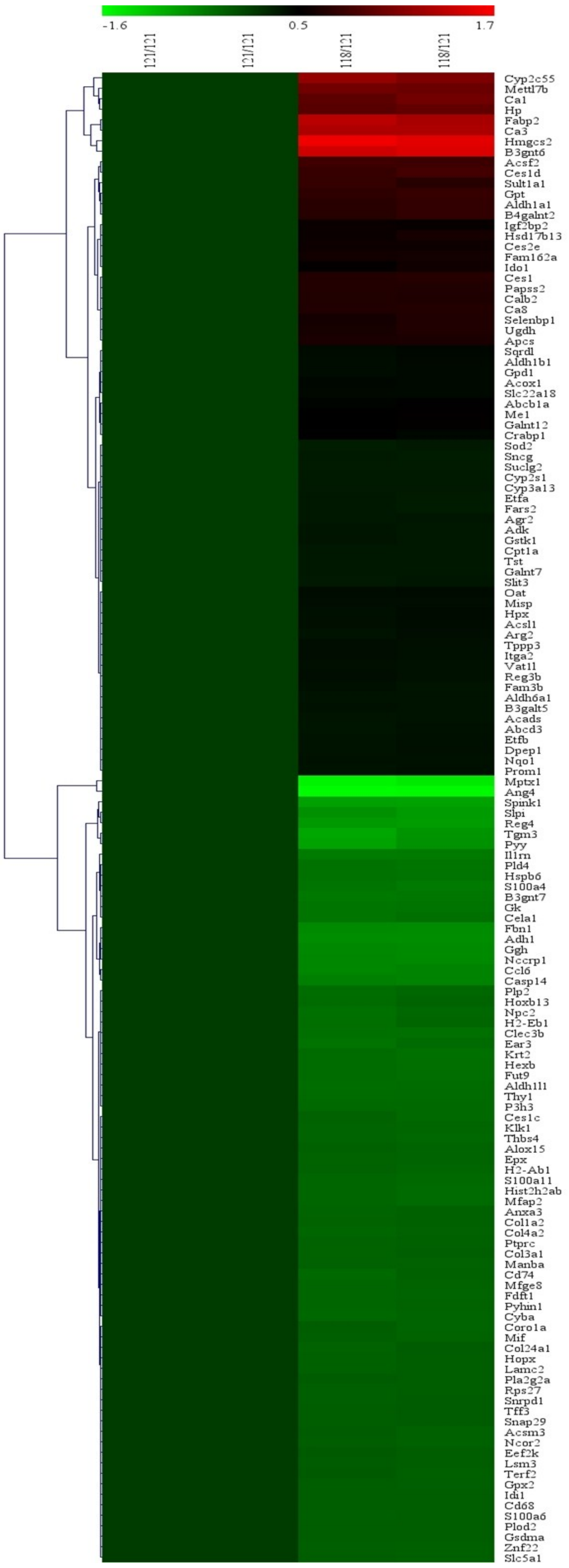

Figure S4A Clustering heatmap of differential proteins.

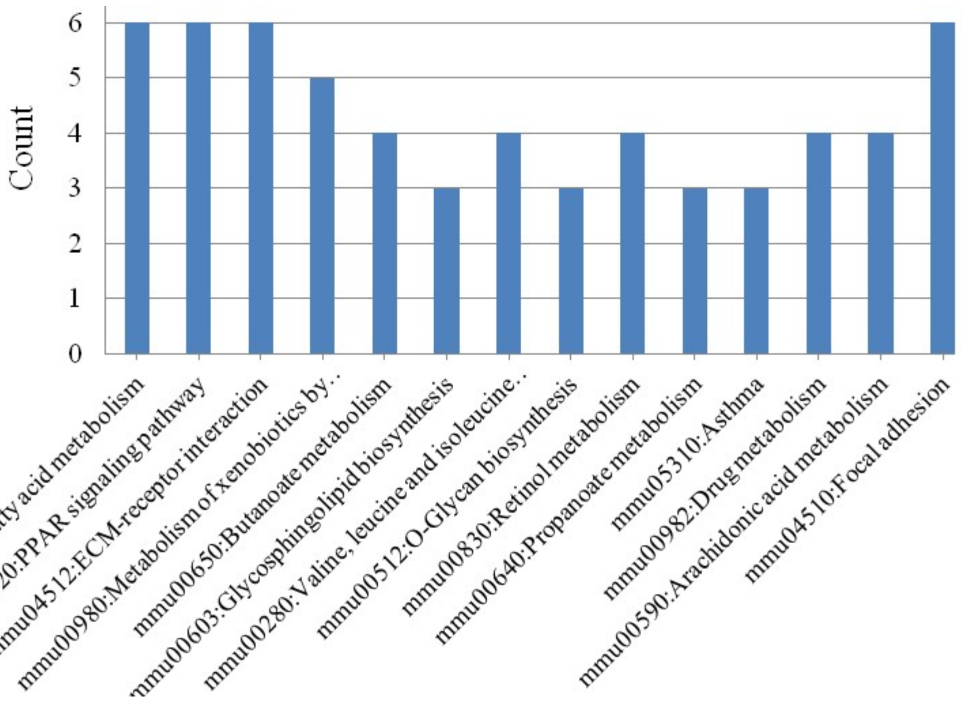

Figure S4B The KEGG metabolism pathway enrichiment anaylisis of differential proteins.