

SUPPLEMENTARY DATA

Hypochlorite-modification of sphingomyelin generates chlorinated lipid species that induce apoptosis and proteome alterations in dopaminergic PC12 neurons *in vitro*

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Table I – Assignment of molecular ions produced by modification of SM(d18:1/16:0) by HOCl (added as reagent or generated enzymatically)

m/z	SM species
703.6	SM(d18:1/16:0)
705.6	SM(d18:0/16:0) (impurity)
719.6	SM(d18:1/16:0)epoxide
725.6	SM(d18:1/16:0)Na ⁺
727.6	SM(d18:0/16:0)Na ⁺
737.6	(SM(d18:1/16:0)chloride) or: SM(d18:1/16:0)chloramide
755.6	SM(d18:1/16:0)chlorohydrin
759.6	SM(d18:1/16:0)chlorohydrin-H ₂ O+Na ⁺
771.6	SM(d18:1/16:0)chlorohydrin chloramide-H ₂ O
777.6	SM(d18:1/16:0)chlorohydrin+Na ⁺
789.6	SM(d18:1/16:0)chlorohydrin chloramide

Tables II and III - Information on accession numbers, protein name, spot number in the corresponding gel, number of acquired spectra, number of distinct peptides, MS score, % amino acid coverage, theoretical Mw and pI, experimental Mw and pI, and fold-regulation. Protein identifications are based on multiple peptide sequences with a minimum number of three distinct peptides and protein identification in at least two out of the three gels.

TABLE IIA: Upregulated proteins in response to SM

Protein name	RefSeq/UniProt accession number	Spot	Spectra	Distinct peptides	Distinct summed MS/MS search score	% AA coverage	MW theor. (Da)	MW exper. (Da)	pI theor.	pI exper.	Regulation control - SM (Cy2/Cy3)	Gel				
												Gel 1	Gel 2	Gel 3		
leucine aminopeptidase 3	NP_001011910 Q68FS4	859	41	10	148,65	23	56150,4	63956	6,78	6,95	3,08					
		1035	108	18	341,73	44	56150,4	58930	6,78	6,75	2,3					
		997	134	18	334,9	44	56150,4	58020	6,78	6,9	2,41					
PREDICTED: similar to Fascin, isoform 2	NP_001094276 B5DE1	859	17	9	114,02	17	54550,3	63956	6,44	6,95	3,08					
		710	12	6	92,13	15	54550,3	71581	6,44	6,75	2,04					
		1035	88	17	304,05	40	54550,3	58930	6,44	6,75	2,3					
		997	131	23	395,38	52	54550,3	58020	6,44	6,9	2,41					
		aldehyde dehydrogenase family 3, member A1	NP_114178 P11883	859	14	6	74,2	13	50338,9	63956	6,33	6,95	3,08			
				1035	107	15	270,5	29	50338,9	58930	6,33	6,75	2,3			
944	58			13	210,95	38	50338,9	60793	6,33	6,9	2					
		997	24	7	115,62	13	50338,9	58020	6,33	6,9	2,41					
		proteasome (prosome, macropain) subunit, alpha type 1	NP_058974 P18420	1873	17	6	77,37	24	29517,7	36654	6,14	6,7	3,79			
				1983	178	14	231,29	57	29517,7	32124	6,14	6,55	2,38			
1996	89			14	220,22	58	29517,7	31383	6,14	6,75	2,29					
superoxide dismutase 2	NP_058747 P07895	2309	39	5	84,93	29	24683,2	25859	8,96	8,7	4,78					
		2324	11	5	81,41	22	24683,2	25859	8,96	7,95	2,21					
		2324	87	7	122,4	32	24683,2	22813	8,96	8,6	3,73					
		2307	62	7	110,97	23	24683,2	23534	8,96	8,65	4,83					
		peroxiredoxin 1	NP_476455 Q63716	2324	57	9	145,33	45	22109,5	25859	8,27	7,95	2,21			
				2324	32	10	156,35	49	22109,5	22813	8,27	8,6	3,73			
2307	4			4	55,49	19	22109,5	23534	8,27	8,65	4,83					
PREDICTED: similar to aldehyde dehydrogenase family 7, member A1	NP_695212 Q64057	859	10	6	73,19	13	58749	63956	7,99	6,95	3,08					
		1035	12	6	100,17	15	58749	58930	7,99	6,75	2,3					
Glutathione transferase omega-1 (GSTO 1-1)	NP_001007603 Q9Z339	1873	15	6	79,17	23	27669,1	36654	6,25	6,7	3,79					
		1983	50	9	137,4	40	27669,1	32124	6,25	6,55	2,38					
acidic ribosomal phosphoprotein P0	NP_071797 P19945	1497	16	7	104,94	30	34215,7	45457	5,91	5,95	2,02					
		1682	14	4	72,25	13	34215,7	40884	5,91	5,35	3,2					
dihydrofolate reductase	NP_569084 Q920D2	2339	44	8	128,14	45	21638,2	24733	6,77	7,45	2,4					
		2354	34	8	123	42	21638,2	22636	6,77	7,55	2,04					
lectin, galactose binding, soluble 1	NP_063969 P11762	2695	91	8	139,31	58	14856,9	13258	5,14	4,8	3,25					
		2805	127	9	151,26	58	14856,9	11505	5,14	4,7	2,6					
phosphoglycerate Kinase 1	NP_445743 P16617	1211	15	6	77,82	15	44538,7	53124	8,02	8,4	2,93					
		1215	33	9	146,5	26	44538,7	53124	8,02	8,25	2,9					
		1217	54	13	182,16	41	44538,7	53124	8,02	8,5	2,7					
		1218	14	7	86,5	20	44538,7	53520	8,02	8,65	2,61					
		1219	181	20	329,08	80	44538,7	53520	8,02	8,7	2,86					
		1232	66	12	174,64	33	44538,7	53520	8,02	8,9	2,38					
		1497	69	15	252,11	52	44538,7	45457	8,02	5,95	2,02					
		1646	95	17	299,66	39	44538,7	40567	8,02	5,8	2,07					
		septin 6	NP_001100678 B3GNI4	974	14	5	75,88	13	49782	62085	6,24	7,2	2,36			
1041	79			15	257,93	43	49782	55807	6,24	7,05	3,66					
eukaryotic translation initiation factor 4A1, isoform CRA_a	NP_955404 Q6P3V8	1146	16	8	132,63	22	44607,4	55807	5,61	5,15	2,45					
		1283	38	13	215,35	35	44607,4	50439	5,61	5,3	2,89					
Cathepsin D precursor	NP_599161 P24268	1369	47	9	159,52	28	44681	48139	6,66	5,55	2,4					
		1376	35	5	80,59	14	44681	48139	6,66	5,75	2,94					
		1438	47	9	157,51	29	44681	45588	6,66	5,85	2,26					
MYG1 protein	NP_001005545 Q641W2	1376	19	6	105,97	15	42889	48139	6,02	5,75	2,94					
		1438	41	12	228,53	38	42889	45588	6,02	5,85	2,26					
PREDICTED: similar to transcriptional activator protein Pur-alpha	NP_001017503 Q68A21	1376	6	3	41,95	9	33018	48139	6,2	5,75	2,94					
		1438	7	4	56,79	11	33018	45588	6,2	5,85	2,26					
heterogeneous nuclear ribonucleoprotein C	NP_001020804 Q4V8K6	1821	6	3	49,77	12	32857,2	36952	4,86	4,55	5,47					

		1902	20	6	98,68	22	32857,2	33658	4,86	4,6	2,85
phosphatidylethanolamine binding protein	NP_058932 P31044	2285	61	7	123,81	39	20801,5	23717	5,47	7,15	4,7
		2366	82	10	169,74	53	20801,5	22286	5,47	5,3	3,04
voltage dependent anion channel (Vdac1)	NP_112643 Q9Z2L0	1851	64	12	216,24	61	31966	35820	8,35	9,7	2,1
		1827	57	11	197,03	50	31966	36381	8,35	9,55	2,02
		1833	26	7	126,51	35	31966	36381	8,35	9,6	2,19
tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein	NP_113791 P62260	1953	322	18	349,5	80	29121,9	33658	4,55	4,25	3,73
		2016	152	18	309,97	69	29121,9	30185	4,55	4,2	3,43
Peroxiredoxin 2	NP_058865 P35704	2285	7	4	61,95	19	21797,8	23717	5,34	5,15	4,7
		2366	5	3	46,92	17	21797,8	22286	5,34	5,3	3,04

TABLE IIB: Downregulated proteins in response to SM

Protein name	RefSeq/UniProt accession number	Spot	Spectra	Distinct peptides	Distinct summed MS/MS search score	% AA coverage	Gel			Regulation control - SM (Cy2/Cy3)	
							Gel 1	Gel 2	Gel 3		
						MW theor. (Da)	MW exper. (Da)	pl theor.	pl exper.		
gamma-butyrobetaine,2-oxoglutarate dioxygenase	NP_742059 P54001	657	31	14	183,32	30	60924,5	71488	5,7	5,9	-3.31
		819	5	4	55,57	8	60924,5	65711	5,7	5,7	-2.18
		770	84	15	259,52	28	60924,5	66741	5,7	5,8	-2.99
PREDICTED: similar to Alpha-enolase (NNE (Enolase 1))	NP_036686 P04764	1025	7	4	51,11	7	53924	58505	5,81	6,3	-2
		1067	93	14	226,25	38	53924	56794	5,81	6,8	-2.2
		1237	19	6	83,13	18	53924	52731	5,81	6,25	-2.08
		1105	351	22	402,48	53	53924	57571	5,81	6,25	-2.31
		1108	222	22	395,45	49	53924	56243	5,81	6,05	-2.89
		1113	113	19	333,56	46	53924	56243	5,81	6,65	-2.21
		1115	51	11	180,93	20	53924	56243	5,81	6,5	-2.06
		1122	310	20	361,67	45	53924	56243	5,81	6,15	-2.83
		1182	216	22	388,9	53	53924	54520	5,81	6,6	-2.86
		1197	320	23	425,03	53	53924	54520	5,81	6,25	-3.17
		1118	191	20	340,08	46	53924	54946	5,81	6,8	-2.59
		1149	134	19	332,31	49	53924	54097	5,81	6,6	-2.61
		1151	258	20	361,38	52	53924	53262	5,81	6,5	-2.8
		1153	211	21	379,23	53	53924	53262	5,81	6,25	-2.52
		1156	139	17	317,71	39	53924	53262	5,81	6,15	-2.75
1222	104	21	362,86	55	53924	50439	5,81	6,5	-2.47		
calreticulin	NP_071794 P18418	1042	12	5	72,94	14	47995,7	58506	4,33	3,8	-5.22
		1110	6	3	41,75	7	47995,7	56682	4,33	4	-2.01
		1133	11	3	43,09	7	47995,7	55807	4,33	3,9	-3.08
1198	15	3	52,09	8	47995,7	52034	4,33	3,8	-6.29		
calumenin isoform a	NP_071980 Q3MID6	1126	45	13	180,61	39	37063,9	55133	4,49	3,95	-3
		1059	26	8	135,37	19	37063,9	58930	4,49	3,95	-3.28
		1110	85	14	236,23	42	37063,9	56682	4,49	4	-2.01
		1133	199	19	345,44	48	37063,9	55807	4,49	3,9	-3.08
		1183	144	18	345,34	52	37063,9	52849	4,49	3,95	-3.75
1216	116	18	335,94	55	37063,9	51630	4,49	3,9	-3.22		
1238	50	11	200,77	36	37063,9	50049	4,49	4	-3.31		
aldolase C	NP_036629 P09117	1382	6	4	50,99	14	39284	50061	6,67	7,25	-2.22
		1500	8	4	62,08	12	39284	46303	6,67	7,5	-3.12
		1425	82	13	241,73	40	39284	46664	6,67	7,6	-2.45
heterogeneous nuclear ribonucleoprotein A2/B1	NP_001098083 A7VCJ2	1668-2	40	12	163,06	36	37477,9	41583	8,97	9,3	-3.02
		1785	15	5	80,97	14	37477,9	37824	8,97	8,85	-4.86
		1795	3	3	51,36	11	37477,9	37824	8,97	8,6	-4.17
		1799	62	11	199,38	39	37477,9	37824	8,97	9	-2.95
1701	62	15	229,19	46	37477,9	39020	8,97	9,5	-2.61		
triosephosphate isomerase 1	NP_075211 P48500	2112	71	12	216,83	58	31011,7	30901	5,56	7,35	-2.28
		2115	31	8	144,38	38	31011,7	30446	5,56	7,15	-2.95
		2120	107	12	209,32	58	31011,7	29997	5,56	7,55	-7.45
		2170	406	16	313,3	70	31011,7	26653	5,56	7,55	-4
		2153	193	13	248,7	55	31011,7	27282	5,56	7,7	-5.67
2167	109	10	195,53	41	31011,7	27071	5,56	7,3	-2.32		
Protein disulfide-isomerase precursor (Prolyl 4-hydroxylase subunit beta)	NP_037130 P04785	895	46	11	156,95	22	56951,6	63013	4,82	4,6	-2.36
		885	26	10	170,99	20	56951,6	64195	4,82	4,4	-3.93
dipeptidylpeptidase 7	NP_114179 Q9EPB1	895	6	3	45,61	6	55114,6	63013	4,86	4,6	-2.36
		885	15	5	90,99	10	55114,6	64195	4,86	4,4	-3.93
TAR DNA binding protein	NP_001011979 -	1169	4	3	42,43	9	44518	53919	6,26	6,05	-2.85
		1260	14	5	59,04	11	44518	53124	6,26	6,7	-2.15
		1380	56	10	182,71	24	44518	48139	6,26	6	-2.24
ERO1-like	NP_612537 Q8R4A1	657	10	4	60,9	10	54115,8	71488	6,1	5,9	-3.31
		819	50	13	222,51	29	54115,8	65711	6,1	5,7	-2.18
vimentin	NP_112402 P31000	814	49	17	231,54	38	53733	65883	5,06	5	-2.49
		895	51	13	201,59	28	53733	63013	5,06	4,6	-2.36
		885	6	3	50,07	6	53733	64195	5,06	4,4	-3.93
lactate dehydrogenase A	NP_058721 P04642	1668	27	8	107,02	28	36450,7	41583	8,45	9,3	-3.02
		1785	351	20	356,85	65	36450,7	37824	8,45	8,85	-4.86
		1795	162	13	223,53	40	36450,7	37824	8,45	8,6	-4.17
		1799	128	16	276,72	51	36450,7	37824	8,45	9	-2.95
far upstream element (FUSE) binding protein 1	NP_001032742 Q32PX7	529	31	10	147,43	20	67197,4	78730	7,18	7,45	-2.04
		559	24	7	101,19	13	67197,4	76996	7,18	7,8	-2.27
		624	102	17	306,64	30	67197,4	74420	7,18	7,4	-2.05
636	152	20	348,21	36	67197,4	74420	7,18	7,7	-2.01		

PREDICTED: similar to pyruvate kinase 3	NP_445749 P11980	762	10	4	50,77	7	57877,3	68883	7,57	8,05	-3,17
		750	77	14	235,25	35	57877,3	68883	7,57	7,7	-3,67
		863	39	11	171,98	25	57877,3	64912	7,57	7,35	-2,47
		861	12	6	75,1	13	57877,3	64912	7,57	7,2	-2,72
		811	46	15	251,36	32	57877,3	65201	7,57	7,65	-2,52
		815	39	11	167,5	24	57877,3	65201	7,57	7,75	-2,56
		817	110	19	351,75	41	57877,3	65201	7,57	7,85	-2,93
calumenin isoform b	NP_001029070 Q3MID6	1042	22	8	119,4	27	37148	58506	4,43	3,8	-5,22
		1198	120	15	285,82	46	37148	52034	4,43	3,8	-6,29
tropomyosin 3, gamma isoform 2	NP_001029242 Q63607	1889	33	8	112,93	28	33280,8	36382	4,73	4,4	-2,04
		1984	4	3	33,93	10	33280,8	31383	4,73	4,25	-2,32
glutathione S-transferase, mu 2	NP_803175 P08010	2173	53	11	141,97	48	25702,8	29120	6,91	8,1	-2,34
		2180	152	20	364,39	78	25702,8	26653	6,91	8,1	-2,44
Adenosine kinase (Adenosine 5'-phosphotransferase)	NP_037027 Q64640	1169	19	9	137,53	32	40133,9	53919	5,72	6,05	-2,85
		1303	7	4	61,2	14	40133,9	48894	5,72	6,1	-2,36
ErbB3-binding protein 1	NP_001004206 Q6AYD3	1169	7	3	43,29	8	43657	53919	6,41	6,05	-2,85
		1172	93	16	284,02	42	43657	52440	6,41	6,8	-2,48
		1222	10	4	72,83	10	43657	50439	6,41	6,5	-2,47
		1303	13	5	81,45	12	43657	48894	6,41	6,1	-2,36
similar to Poi(yrC)-binding protein 1 (predicted)	NP_001013241 Q6AYU5	1382	41	7	100,06	29	35512,7	50061	7,03	7,25	-2,22
		1425	15	5	80,5	20	35512,7	46664	7,03	7,6	-2,45
malate dehydrogenase, mitochondrial	NP_112413 P04636	1668,2	3	3	36,24	10	35683,8	41583	8,93	9,3	-3,02
		1701	3	3	39,88	10	35683,8	39020	8,93	9,5	-2,61
tumor protein D52	NP_001099891 -	2151	19	7	101,04	34	24268,9	29555	4,68	4,6	-5,28
		2213	46	9	162,31	37	24268,9	25636	4,68	4,05	-5,39
procollagen-proline, 2-oxoglutarate 4-dioxygenase, alpha II polypeptide	NP_001101745 -	819	33	8	141,83	16	60867,4	65711	5,69	5,7	-2,18
		770	7	3	48,61	6	60867,4	66741	5,69	5,8	-2,99
M2 pyruvate kinase	NP_445749 P11980	843	196	26	503,44	55	57781,2	64696	7,15	7,4	-2,2
		860	115	15	261,82	27	57781,2	64696	7,15	7,3	-2,86
		862	134	23	426	52	57781,2	64696	7,15	7,85	-3,47
		863	197	24	456,1	49	57781,2	64696	7,15	7,45	-2,91
		864	228	25	479,42	51	57781,2	64696	7,15	7,7	-2,43
		865	185	22	423,66	45	57781,2	64696	7,15	7,75	-2,61
		803	48	13	198,16	31	57781,2	65201	7,15	7,6	-2,96
		810	47	16	284,42	37	57781,2	65201	7,15	7,45	-3,25
		958	84	18	327,71	41	57781,2	60332	7,15	7,15	-2,34
		1090	67	18	312,3	45	57781,2	55375	7,15	5,7	-2,86
		catalase	NP_036652 P04762	843	19	11	172,15	27	59757,5	64696	7,07
860	86			16	285,82	35	59757,5	64696	7,07	7,3	-2,86
863	27			11	182,63	25	59757,5	64696	7,07	7,45	-2,91
864	41			13	220,61	29	59757,5	64696	7,07	7,7	-2,43
803	12			7	104,2	18	59757,5	65201	7,07	7,6	-2,96
		810	7	3	57,59	7	59757,5	65201	7,07	7,45	-3,25
		811	19	7	116,07	16	59757,5	65201	7,07	7,65	-2,52
actin, alpha 1, skeletal muscle, isoform CRA_a	NP_062085 P68136	1182	17	3	53,58	8	51496,2	54520	5,91	6,6	-2,86
		1153	5	3	45,18	8	51496,2	53262	5,91	6,25	-2,52
heterogeneous nuclear ribonucleo-protein; type A/B hnRNP p40AIF-C1	NP_112620 Q9QX81	1463	48	7	132,84	23	36233	46664	6,48	6,7	-2,02
		1453	91	9	161,55	25	36233	45588	6,48	6,9	-2,81
poly(rC) binding protein 2	NP_001013241 Q6AYU5	1463	18	4	71,02	13	38580,3	46664	6,33	6,7	-2,02
		1554	10	3	53,7	9	38580,3	43509	6,33	6,6	-2,15
		1453	22	5	88,31	17	38580,3	45588	6,33	6,9	-2,81
calponin 3, acidic	NP_062232 P37397	1508	25	8	138,73	29	36434,9	45588	5,47	5,25	-3,12
		1535	11	5	93,24	17	36434,9	42506	5,47	5,4	-3,39
Aspartate aminotransferase, cytoplasmic (Transaminase A)	NP_036703 P13221	1500	36	11	168,02	29	46429	46303	6,73	7,5	-3,12
		1425	56	14	239,8	40	46429	46664	6,73	7,6	-2,45
cathepsin B preproprotein	NP_072119 Q6IN22	1508	14	5	83,28	15	37544,4	45588	5,47	5,25	-3,12
		1563	5	3	49,89	11	37544,4	42506	5,47	5,5	-2,07
replication factor C (activator 1) 4	NP_001099339 B4F778	1554	52	13	222,79	38	39957,2	43509	6,21	6,6	-2,15
		1564	17	6	91,77	18	39957,2	41203	6,21	6,9	-2,02
annexin A1	NP_037036 P07150	1588	503	25	434,78	71	38829,7	42506	6,96	7,1	-2,1
		1625	62	15	252,26	44	38829,7	41849	6,96	6,3	-3,43
		1543	262	26	443,52	72	38829,7	42506	6,96	7,25	-2,09
		1564	42	11	178,16	34	38829,7	41203	6,96	6,9	-2,02
		1642	21	7	114,46	22	38829,7	40567	6,96	6,15	-2,81

PREDICTED: similar to methionine adenosyltransferase II, beta	NP_001037747 Q5U2R0	1588	19	6	109,42	24	37374,9	42506	6,46	7,1	-2,1
		1543	5	3	56,68	14	37374,9	42506	6,46	7,25	-2,09
lactate dehydrogenase B	NP_036727 P42123	1640	8	3	54,87	12	36612,6	41203	5,7	5,8	-2,05
		1728	10	4	57,09	9	36612,6	38120	5,7	5,6	-2,73
pyrroline-5-carboxylate reductase 1	NP_001099327 B2RYR3	1906	42	8	143,32	27	32226,5	34186	6,36	6,8	-2,14
		1892	82	15	281,6	54	32226,5	34186	6,36	7,05	-2,72
galectin 3	NP_114020 P08699	2031	25	4	71,88	16	27229,7	30659	8,92	9,4	-2,09
		2002	23	8	128,67	35	27229,7	31383	8,92	9,3	-2,02
phosphoglycerate mutase type B subunit	NP_445742 P25113	2116	95	13	243,66	63	28846,2	27926	7,07	7,15	-2,96
		2119	207	15	295,67	65	28846,2	27926	7,07	7,05	-2,61
		2102	41	7	126,74	37	28846,2	28809	7,07	7,3	-2,72
		2106	179	12	231,21	52	28846,2	28364	7,07	7,25	-2,36
phosphomannomutase 2	NP_001100443 B5DF46	2116	84	9	153,72	39	27708,9	27926	6,9	7,15	-2,96
		2102	37	10	165,77	44	27708,9	28809	6,9	7,3	-2,72
enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	NP_511178 P14604	2116	6	3	53,88	16	31516,6	27926	8,4	7,15	-2,96
		2119	57	8	144,85	34	31516,6	27926	8,4	7,05	-2,61
		2106	83	10	176,71	38	31516,6	28364	8,4	7,25	-2,36
Ppib protein	NP_071981 P24368	2487	57	11	190,42	46	23802,7	17375	9,5	8,75	-2,17
		2485	32	9	154,3	43	23802,7	18635	9,5	8,8	-2,23
transaldolase	NP_113999 Q9EQS0	1583	56	11	202,91	31	37476,3	42838	6,57	6	-3,07
		1625	66	14	255,69	37	37476,3	41849	6,57	6,3	-3,43
		1640	30	7	116,78	21	37476,3	41203	6,57	5,8	-2,05
		1642	36	12	201,57	32	37476,3	40567	6,57	6,15	-2,81
cofilin 1	NP_058843 P45592	2487	11	2	39,75	15	18532,6	17375	8,22	8,75	-2,17
		2485	11	3	58,15	27	18532,6	18635	8,22	8,8	-2,23

TABLE IIIA: Upregulated proteins in response to HOCl-SM

Protein name	RefSeq/UniProt accession number	Spot	Spectra	Distinct peptides	Distinct summed MS/MS search score	% AA coverage	MW theor. (Da)	MW exper. (Da)	pI theor.	pI exper.	Regulation control - HOCl-SM (Cy2/Cy5)	Gel		
												Gel 1	Gel 2	Gel 3
voltage dependent anion channel (Vdac1)	Q9Z2L0 NP_112643	1829	25	9	120,82	38	31966	37479	8,35	9,45	2,54			
		1835	81	11	178,52	51	31966	37479	8,35	9,6	2,61			
		1851	64	12	216,24	61	31966	35820	8,35	9,7	2,97			
		1855	83	12	209,38	54	31966	35820	8,35	9,55	2,59			
		1822	21	6	101,37	24	31966	36381	8,35	9,15	2,91			
		1827	57	11	197,03	50	31966	36381	8,35	9,55	2,67			
		1833	26	7	126,51	35	31966	36381	8,35	9,6	2,85			
calcylin binding protein	Q6AYK6 NP_001004208	2043	19	5	60,1	20	26541,3	32070	7,64	7,9	2,96			
		2095	113	13	224,51	41	26541,3	28586	7,64	7,8	3,93			
		2065	5	3	32,28	8	26541,3	29489	7,64	6,95	3,7			
adenylate kinase 2 isoform a	NP_112248 P29410	2043	29	7	101,9	29	26392,7	32070	7,01	7,9	2,96			
		2095	72	9	151	43	26392,7	28586	7,01	7,8	3,93			
proteasome (prosome, macropain) subunit, alpha type 4	NP_058977 P21670	2031	9	3	39,44	13	29498	31832	7,58	8,1	3,74			
		2039	17	5	66,87	18	29498	29719	7,58	8,1	3,65			
expressed in non-metastatic cells 1, protein (NM23A)	NP_612557 Q05982	2566	48	10	164,21	67	17192,8	17320	5,96	5,95	7			
		2605	16	6	90,61	46	17192,8	15223	5,96	6	6,12			
heterogeneous nuclear ribonucleoprotein C	NP_001020804 Q4V8K6	1821	6	3	49,77	12	32857,2	36952	4,86	4,55	2,44			
		1902	20	6	98,68	22	32857,2	33658	4,86	4,6	2,11			
L-3-hydroxyacyl-Coenzyme A dehydrogenase	NP_476534 Q9WVK7	1855	12	5	82,59	14	34448	35820	8,83	9,55	2,59			
		1822	13	4	63,01	11	34448	36381	8,83	9,15	2,91			
		1827	31	6	106,46	14	34448	36381	8,83	9,55	2,67			
PREDICTED: similar to calmodulin 1	NP_114175 P62161	2443	12	2	32,16	20	14440,4	19678	4,36	3,15	5,07			
		2475	11	2	36,79	20	14440,4	18781	4,36	3,4	6,22			
		2502	13	2	35,83	20	14440,4	17241	4,36	3,4	2,24			
		2535	14	3	52,49	21	14440,4	17241	4,36	3,15	4,73			
Heat shock protein beta-1 (HSP 27)	NP_114176 P42930	2151	363	13	220,57	57	22892,8	27282	6,12	5,75	2,37			
		2193	85	11	188,31	51	22892,8	26038	6,12	5,3	2,11			
		2264	17	4	50,16	17	22892,8	24277	6,12	5,5	2,05			

TABLE IIIB: Downregulated proteins in response to HOCl-SM

Protein name	RefSeq/UniProt accession number	Spot	Spectra	Distinct peptides	Distinct summed MS/MS search score	% AA coverage	MW theor. (Da)	MW exper. (Da)	Gel 1		Gel 2		Regulation control - HOCl-SM (Cy2/Cy5)
									pl theor.	pl exper.	pl theor.	pl exper.	
lactate dehydrogenase A	NP_058721 P04642	1682	61	14	198,24	51	36450,7	41583	8,45	9,05			-2.29
		1785	351	20	356,85	65	36450,7	37824	8,45	8,85			-3.6
		1786	160	18	321,47	63	36450,7	37824	8,45	9,15			-3.72
		1794	167	19	333,91	65	36450,7	37824	8,45	9,3			-3.05
		1795	162	13	223,53	40	36450,7	37824	8,45	8,6			-3.59
		1799	128	16	276,72	51	36450,7	37824	8,45	9			-2.46
		1714	98	18	278,12	63	36450,7	39020	8,45	8,95			-3.51
cofilin 1	NP_058843 P45592	2504	4	3	39,6	17	18532,6	18933	8,22	8,9			-2.52
		2487	11	2	39,75	15	18532,6	17375	8,22	8,75			-2.76
		2485	11	3	58,15	27	18532,6	18635	8,22	8,8			-2.7
cofilin 1	NP_058843 P45592	2538	42	7	123,05	42	18532,6	18108	8,22	8,95			-2.36
		2519	69	10	188,49	51	18532,6	16454	8,22	8,9			-2.78
proteasome (prosome, macropain) subunit, beta type, 9	NP_036840 Q6MGA6	2447	15	3	54,04	14	23343,6	21321	4,89	4,3			-2.48
		2438	14	3	50,07	16	23343,6	19832	4,89	4,3			-2.12
ornithine aminotransferase	NP_071966 P04182	1255	63	12	195,86	28	48332,9	51630	6,53	6,25			-2.79
		1304	72	15	261,81	43	48332,9	48894	6,53	6,5			-2.23
non-catalytic region of tyrosine kinase adaptor protein 1	NP_001100321 B2RZ33	1255	37	11	176,31	29	42876,7	51630	6,07	6,25			-2.79
		1304	9	5	80,29	14	42876,7	48894	6,07	6,5			-2.23
adenylosuccinate synthetase, non muscle	NP_001099445 -	1255	10	6	96,11	14	50085,4	51630	5,98	6,25			-2.79
		1304	4	4	57,85	12	50085,4	48894	5,98	6,5			-2.23
Aspartate aminotransferase, cytoplasmic (Transaminase A)	NP_036703 P13221	1500	36	11	168,02	29	46429	46303	6,73	7,5			-3.65
		1425	56	14	239,8	40	46429	46664	6,73	7,6			-2.15
voltage dependent anion channel (Vdac1)	NP_112643 Q9Z2L0	1922	12	4	71,46	15	32577,8	33921	8,3	8			-3.57
		1866	9	4	59,53	17	32577,8	34722	8,3	8,05			-3.07
voltage-dependent anion channel 2	NP_112644 P81155	1922	7	4	54,95	14	31746	33921	7,44	8			-3.57
		1925	12	5	76,83	21	31746	33921	7,44	8,1			-2.62
		1753	18	6	105,27	24	31746	38120	7,44	7,6			-2.16
hypertrophic agonist responsive protein B64, isoform CRA_c	NP_001094010 Q711G3	2028	49	10	158,99	48	28004,4	31139	5,64	5,25			-2.65
		2089	15	5	68,97	18	28004,4	28586	5,64	5,7			-2.84
phosphoglycerate mutase type B subunit	NP_445742 P25113	2116	95	13	243,66	63	28846,2	27926	7,07	7,15			-3.51
		2119	207	15	295,67	65	28846,2	27926	7,07	7,05			-3.24
		2102	41	7	126,74	37	28846,2	28809	7,07	7,3			-2.98
		2106	179	12	231,21	52	28846,2	28364	7,07	7,25			-2.73
phosphomannomutase 2	NP_001100443 B5DF46	2116	84	9	153,72	39	27708,9	27926	6,9	7,15			-3.51
		2102	37	10	165,77	44	27708,9	28809	6,9	7,3			-2.98
enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	NP_511178 P14604	2116	6	3	53,88	16	31516,6	27926	8,4	7,15			-3.51
		2119	57	8	144,85	34	31516,6	27926	8,4	7,05			-3.24
		2106	83	10	176,71	38	31516,6	28364	8,4	7,25			-2.73
pyrroline-5-carboxylate reductase-like	NP_001011993 Q5PQJ6	2178	22	6	108,36	22	28878,7	26653	6,59	7,45			-2.44
		2142	35	5	89,21	18	28878,7	27495	6,59	7,6			-2.18
Ppib protein	NP_071981 P24368	2487	57	11	190,42	46	23802,7	17375	9,5	8,75			-2.76
		2485	32	9	154,3	43	23802,7	18635	9,5	8,8			-2.7
phosphoglycerate kinase 1	NP_445743 P16617	1364	89	19	341,2	57	44538,7	49276	8,02	7,25			-2.35
		1366	75	16	281,76	44	44538,7	49276	8,02	7,9			-3.38
		1379	21	6	111,69	14	44538,7	48515	8,02	8,05			-3.26
		1389	211	23	398,37	58	44538,7	48894	8,02	8,5			-4.47
		1390	201	22	361,81	48	44538,7	48894	8,02	8,6			-4.27
		1399	93	20	325,27	43	44538,7	48894	8,02	8,75			-5.66
		1400	106	20	344,16	52	44538,7	48894	8,02	8,9			-6.31
		1406	71	15	298,54	45	44538,7	48894	8,02	9,2			-3.26
		1409	119	22	400,43	61	44538,7	48894	8,02	9,05			-3.16
		1573	40	12	213,36	32	44538,7	43172	8,02	5,7			-3.05
		1285	370	29	522,86	76	44538,7	49661	8,02	8,5			-2.48
		1286	330	30	532,92	79	44538,7	49661	8,02	8,6			-2.75
		1290	26	10	146,36	23	44538,7	49661	8,02	8,7			-2.76
aldolase A, isoform CRA_e	NP_036627	1474	76	14	239,73	38	45086,5	47396	8,03	9,7			-3.97

P05065	1480	63	9	158,5	20	45086,5	47396	8,03	9,5	-4,54	
	1482	102	15	278,53	41	45086,5	47396	8,03	8,75	-3,34	
	1483	140	17	310,68	50	45086,5	47396	8,03	9,1	-2,77	
	1484	103	12	222,09	36	45086,5	47396	8,03	9,4	-4,43	
	1489	112	13	238,66	38	45086,5	47396	8,03	8,6	-3,97	
	1490	35	12	213,56	34	45086,5	47396	8,03	8,9	-4,57	
	1286	52	11	196,58	32	45086,5	49661	8,03	8,6	-2,75	
	1390	66	10	172	26	45086,5	47396	8,03	8,8	-2,05	
similar to Pol(yrC)-binding protein 1 (predicted)	NP_001013241 Q6AYU5	1447	10	5	77,88	22	35512,7	47396	7,03	7,1	-3,03
		1425	15	5	80,5	20	35512,7	46664	7,03	7,6	-2,15
aldolase C	NP_036629 P09117	1500	8	4	62,08	12	39284	46303	6,67	7,5	-3,65
		1425	82	13	241,73	40	39284	46664	6,67	7,6	-2,15
Malate dehydrogenase 1, NAD (soluble)	NP_150238 O88989	1761	85	10	169,62	28	36484,3	38717	5,92	6,15	-2,41
		1771	44	10	139,48	30	36484,3	36952	5,92	6,35	-2,64
		1806	54	6	101,41	17	36484,3	35820	5,92	6,4	-4,06
guanine nucleotide binding protein, beta polypeptide 2-like 1	NP_570090 P63245	1921	66	12	204,85	41	35095	34186	7,6	7,9	-2,97
		1922	104	14	241,83	51	35095	33921	7,6	8	-3,57
		1925	84	13	221,74	43	35095	33921	7,6	8,1	-2,62
		1866	81	13	233,8	48	35095	34722	7,6	8,05	-3,07
		1870	82	12	206,44	45	35095	34722	7,6	8	-3,29
triosephosphate isomerase 1	NP_075211 P48500	2178	80	11	213,97	50	31011,7	26653	5,56	7,45	-2,44
		2142	70	13	239,12	55	31011,7	27495	5,56	7,6	-2,18
protease (prosome, macropain) 28 subunit, alpha	NP_058960 Q6P9V7	2028	31	9	144,51	37	28635,1	31139	5,63	5,25	-2,65
		2089	14	5	62,13	20	28635,1	28586	5,63	5,7	-2,84

Fig. II: IPA analysis

Networks of interacting proteins were generated through Ingenuity Pathway analysis. Proteins identified (displayed as abbreviated gene names) were connected with interaction partners known from the literature and information stored in the Ingenuity Pathways Knowledge Base. Upregulated proteins are shown in red, downregulated in green. Solid lines represent direct interaction and dashed lines indirect interaction. Two networks generated from protein regulation in response to SM (**A**, **B**) and one network generated in response to HOCl-SM (**C**) are shown.

A. Network A contained 15 identified proteins (out of 34 molecules present in the network) identified proteins and involved top functions in Energy Production, Molecular Transport, and Nucleic Acid Metabolism (score = 44)

ADK, Adenosine kinase; ALDOC, Fructose-bisphosphate aldolase C (brain-type aldolase); APP, Amyloid beta A4 protein; CALU, Calumenin; CBS, Cystathionine beta-synthase; CNN3, Calponin-3; CTSD, Cathepsin D; DHFR, Dihydrofolate reductase; DPP7, Dipeptidyl-peptidase 2; ECHS1, Enoyl-CoA hydratase, mitochondrial; EIF4A1, Eukaryotic initiation factor 4A-I; ENO1, Alpha-enolase; ERBB2, Receptor tyrosine-protein kinase erbB-2; HNRNPA2B1, Heterogeneous nuclear ribonucleoproteins A2/B1; LAMP2, Lysosome-associated membrane glycoprotein 2; LAP3, Cytosol aminopeptidase; MDH1, Malate dehydrogenase, cytoplasmic; MDH2, Malate dehydrogenase, mitochondrial; MYC, N-myc proto-oncogene protein; P4HA1, Prolyl 4-hydroxylase subunit alpha-1; PCBP2, PCBP2 protein; PGAM1, Phosphoglycerate mutase 1; PRDX2, Peroxiredoxin-2; PURB, Transcriptional activator protein Pur-beta; RPL27, 60S ribosomal protein L27; SLC2A4, Solute carrier family 2, facilitated glucose transporter member 4 (Glucose transporter type 4, insulin-responsive); SP3, Transcription factor Sp3; TALDO1, Transaldolase; TNF, Tumor necrosis factor; TPD52, Tumor protein D52; TPD52L1, Tumor protein D53 (Tumor protein D52-like 1)

B. Network B contained 16 identified proteins (out of 35 molecules present in the network) and involved top functions in Small Molecule Biochemistry, Molecular Transport, and Free Radical Scavenging (score = 26)

ABCC9, ATP-binding cassette transporter sub-family C member 9 (Sulfonylurea receptor 2); ACP, Acid phosphatases; ALDH7A1, Alpha-aminoacidic semialdehyde dehydrogenase; Akt, RAC-alpha serine/threonine-protein kinase (AKT, protein kinase B); FSH, Follicle-stimulating hormone; GMFB, GMFB protein (Glia maturation factor, beta); GOT1, Aspartate aminotransferase, cytoplasmic; GST, Glutathione S-transferase; GSTA5, Glutathione S-transferase A5; GSTM1, Glutathione S-transferase Mu 1; GSTM2, Glutathione S-transferase Mu 2; GSTM3, Glutathione S-transferase Mu 3; GSTO1, Glutathione S-transferase omega-1; HYOU1, Hypoxia up-regulated protein 1; KCNJ11, ATP-sensitive inward rectifier potassium channel 11; LDHA, L-lactate dehydrogenase A chain; LDHB, L-lactate dehydrogenase B

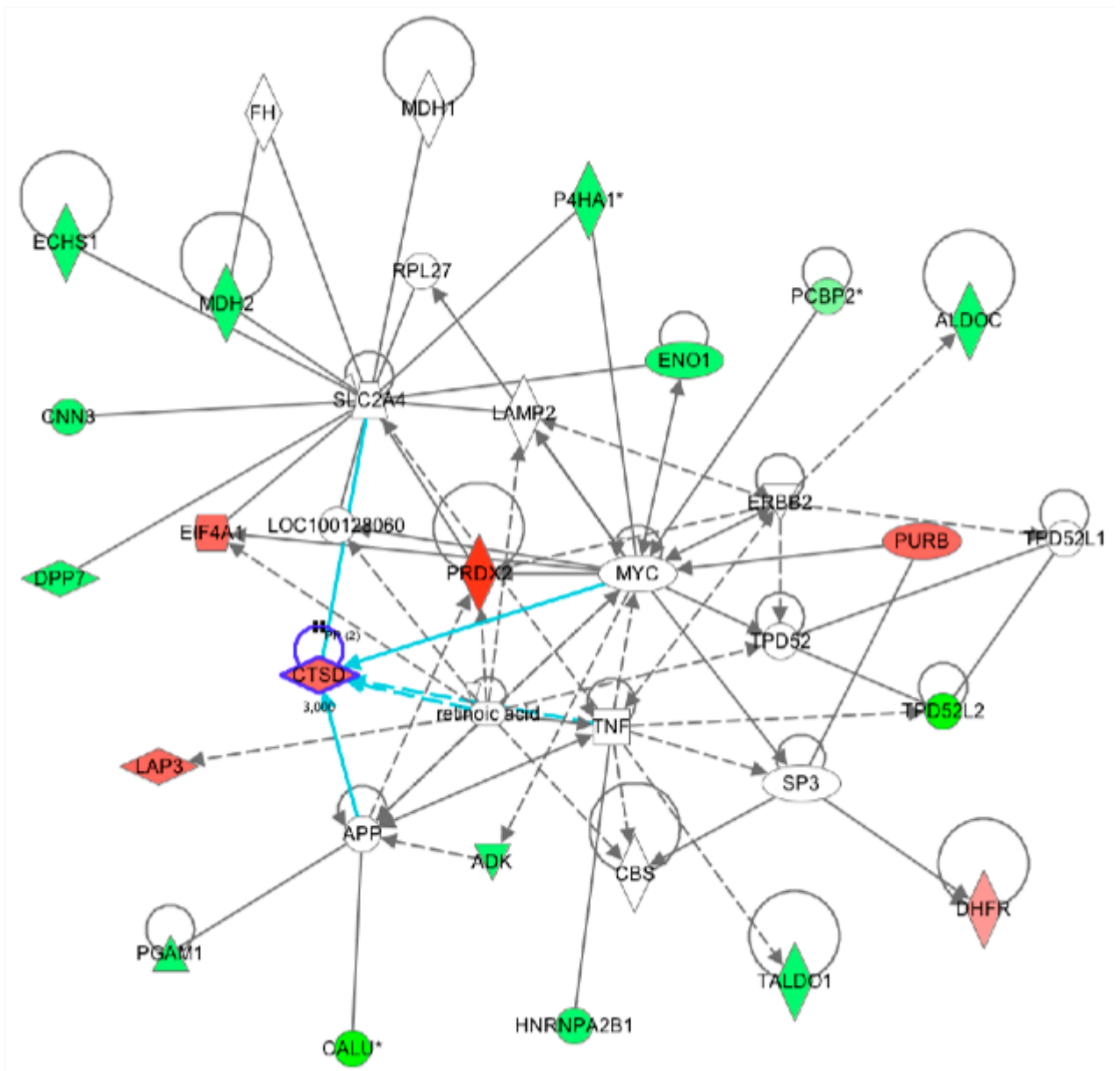
chain; MGST1, Microsomal glutathione S-transferase 1; Ncoa-Nr112-Rxra, Nuclear receptor coactivator-Retinoic acid receptor RXR-alpha
 NFkB, Nuclear factor NF-kappa-B complex; PA2G4, Proliferation-associated protein 2G4;
 PGK2, Phosphoglycerate kinase 2; PKM2, Pyruvate kinase isozymes M1/M2; PRDX1, Peroxiredoxin-1
 PRDX2, Peroxiredoxin-2; PRDX4, Peroxiredoxin-4; RPLP0, 60S acidic ribosomal protein P0;
 RPLP2, 60S acidic ribosomal protein P2; SRXN1, Sulfiredoxin-1

C. Network C contained 21 identified proteins (out of 35 molecules present in the network)

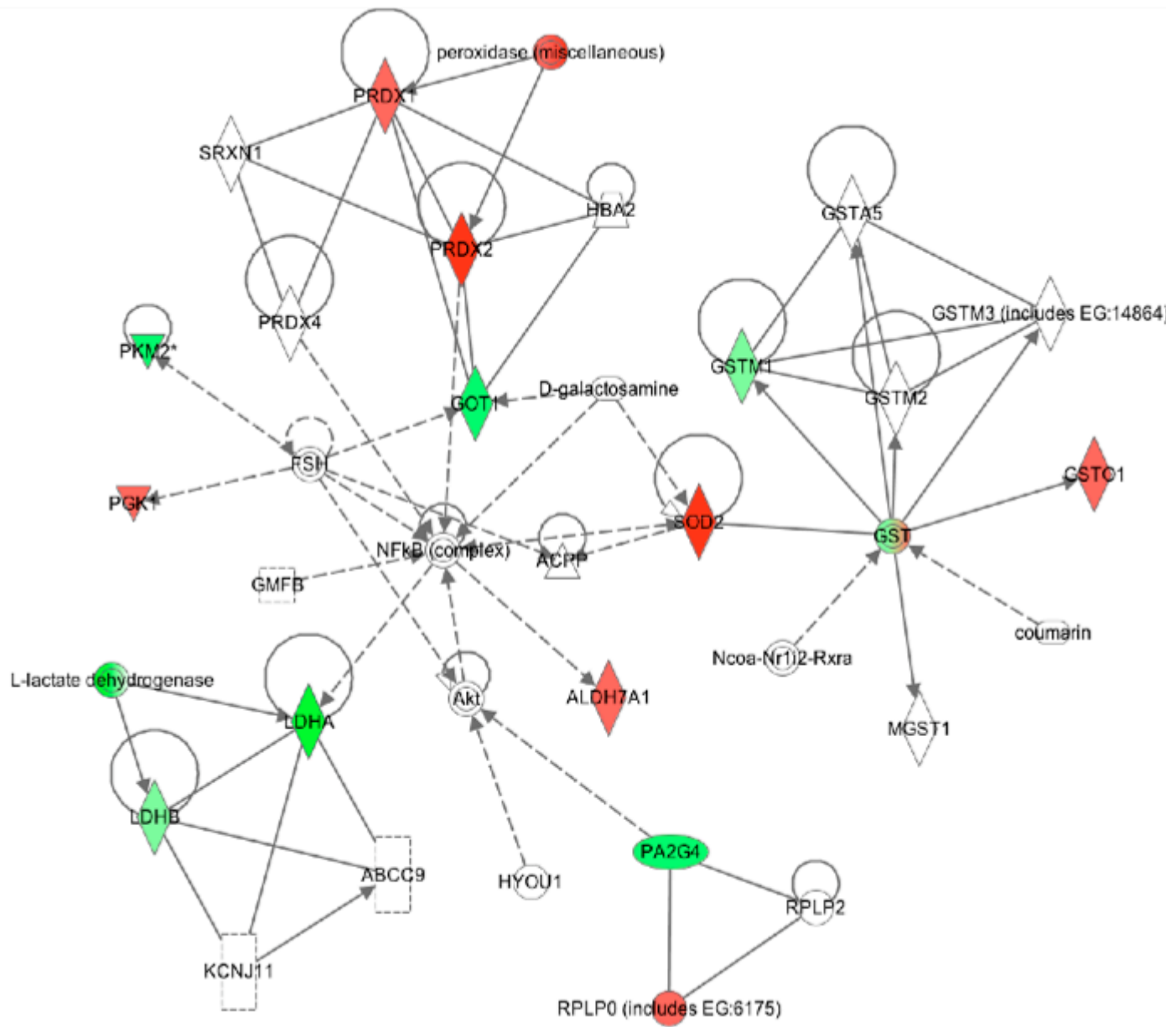
and involved top functions in Carbohydrate Metabolism, Energy Production, and Molecular Transport (score = 48)

AK2, Adenylate kinase 2, mitochondrial; AK3, GTP:AMP phosphotransferase mitochondrial;
 ALDOA, Fructose-bisphosphate aldolase A; ALDOC, Fructose-bisphosphate aldolase C;
 ARF6, ADP-ribosylation factor 6; ATP6V1E1, V-type proton ATPase subunit E 1; CACYBP, Calcyclin-binding protein;
 CFL1, Cofilin-1; DHRS2, Dehydrogenase/reductase member 2;
 ECHS1, Enoyl-CoA hydratase, mitochondrial; GOT1, Aspartate aminotransferase, cytoplasmic;
 GPD2, Glycerol-3-phosphate dehydrogenase, mitochondrial; HADH, 3-hydroxyacyl-CoA dehydrogenase type-2;
 HGF, Hepatocyte growth factor; HK1, Hexokinase-1; HNRNPC, Heterogeneous nuclear ribonucleoproteins C1/C2; Ldh, L-lactate dehydrogenase;
 LDHA, L-lactate dehydrogenase A chain
 LDHB, L-lactate dehydrogenase B chain; LOC729708, PREDICTED: similar to Triosephosphate isomerase (TIM) (Triose-phosphate isomerase) isoform 1; MDH1, Malate dehydrogenase 1, mitochondrial;
 NME3, Nucleoside diphosphate kinase 3; NME1, Nucleoside diphosphate kinase A
 OAT, Ornithine aminotransferase; PGAM1, Phosphoglycerate mutase 1; PGK1, Phosphoglycerate kinase 1;
 RPS25, 40S ribosomal protein S25; SF3A1, Splicing factor 3 subunit 1; SLC2A4, Solute carrier family 2, facilitated glucose transporter member 4 (Glucose transporter type 4, insulin-responsive);
 TNF, Tumor necrosis factor; TOMM20, Mitochondrial import receptor subunit TOM20 homolog; VDAC1, Voltage-dependent anion-selective channel protein 1;
 VDAC2, Voltage-dependent anion-selective channel protein 2

—: Binding; →: Acts on; —: Direct interaction; - - -: Indirect interaction; ▽: Kinase; ◁: Peptidase; ◇: Enzyme; □: Cytokine;
 ▲: Transporter; ○: Transcriptional regulator; ⬡: Translational regulator; ●: Other



Suppl. Fig. IIA



Suppl. Fig. IIB

