

Supplementary Material

Figures:

Suppl. Figure 1: Network analysis organs without serum.

In a GeneMANIA[®] network analysis each circle represents a gene. The input proteins/genes are depicted as striped circles of the same size, while the monochromatic circles, whose size is proportional to the number of interactions according to the software, can be considered as “relevant” related genes found by GeneMANIA[®] searching in many large, publicly available biological datasets (including protein-protein, protein-DNA and genetic interactions, pathways, reactions, gene and protein expression data, protein domains and phenotypic screening profiles). Lines linking different circles can be distinguished from their colour, mainly: violent represents co-expression (when expression levels are similar across conditions in a gene expression study); light orange represents predicted functional relationships between genes; light blue represents co-localization (when genes are expressed in the same tissue, or proteins found in the same location); light yellow represents shared protein domains (when two gene products have the same protein domain).



Tables:

Suppl. Table 1: Fifty-one functions filtered by absolute number (cut-off ≥ 7) from the original 159 deriving from GeneMania[®] network analysis of the whole dataset without the serum proteins. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
generation of precursor metabolites and energy	17	196	8'67%	cps1, gnmt, ogdh, dlst, aco2, aldoa, gapdh, suclg2, eno1, fbp1, gpd1, aldh5a1, acadm , mdh , ndufs1 , mif , aldob
coenzyme metabolic process	14	161	8'70%	Gnmt, ogdh, dlst, fasn, suclg2, g6pd, acss1, gpd1, mdh2 , mdh1 , dlat , acaa2 , taldo1 , adob
cofactor metabolic process	14	196	7'14%	gnmt, aldoa, akr1a1, gapdh, eno1, g6pd, fbp1, gpd1, aldh5a1, acadm , taldo1 , mif , aldob , pc
monosaccharide metabolic process	14	199	7'04%	Gnmt, ogdh, dlst, fasn, suclg2, g6pd, acss1, gpd1, mdh2 , mdh1 , dlat , acaa2 , taldo1 , adob
glucose metabolic process	13	171	7'60%	gnmt, aldoa, gapdh, eno1, g6pd, fbp1, gpd1, aldh5a1, acadm , taldo1 , mif , aldob , pc
hexose metabolic process	13	186	6'99%	gnmt, aldoa, gapdh, eno1, g6pd, fbp1, gpd1, aldh5a1, acadm , taldo1 , mif , aldob , pc
cellular amino acid metabolic process	12	257	4'67%	gnmt, got1, glul, ckb, g6pd, ddah1, aldh5a1, ckmt1b, cps1, ivd, uroc1, ckm
mitochondrial inner membrane	12	269	4'46%	cps1, hspd1, cox5b, pc , acat1 , acaa2 , ndufs1 , atp5b , uqcrfs1 , cyc1 , mdh2 , atp5a1
organelle inner membrane	12	285	4'21%	cps1, hspd1, cox5b, pc , acat1 , acaa2 , ndufs1 , atp5b , uqcrfs1 , cyc1 , mdh2 , atp5a1
single-organism carbohydrate catabolic process	11	90	12'22%	cps1, aldoa, akr1a1, gapdh, eno1, c6pd, fbp1, gpd1, taldo1 , mif , aldob
carbohydrate catabolic process	11	95	11'58%	cps1, aldoa, akr1a1, gapdh, eno1, c6pd, fbp1, gpd1, taldo1 , mif , aldob
energy derivation by oxidation of organic compounds	11	137	8'03%	cps1, gnmt, ogdh, aco2, suclg2, gpd1, aldh5a1, dlst, ndufs1 , mdh2 , acadm
monosaccharide catabolic process	10	63	15'87%	aldoa, akr1a1, gapdh, eno1, g6pd, fbp1, gpd1, taldo1 , mif , aldob
dicarboxylic acid metabolic process	10	76	13'16%	gnmt, ogdh, glul, suclg2, aldh5a1, got1, dlst, mdh1 , mdh2 , pc
mitochondrial matrix	10	132	7'58%	cps1, acadl, ivd, suclg2, acss1, acadm , acaa2 , atp5b , acat1 , mdh2
cofactor binding	10	148	6'76%	acadl, fasn, pitpna, g6pd, alb, gpd1, aldh5a1, acat1 , acadm , mdh1
small molecule catabolic process	10	173	5'78%	aldh5a1, acadl, got1, oxct1, akr1a1, ivd, acadm , cpt2 , acaa2
protein homooligomerization	10	198	5'05%	gnmt, glul, aldoa, fbp1, aldh5a1, ivd, acadl, mif , acat1 , acadm
carboxylic acid biosynthetic process	10	200	5'00%	acss1, ckmt1b, acadl, got1, glul, fasn, akr1a1, acadm , ckm , mif

organic acid biosynthetic process	10	200	5'00%	acss1, ckmt1b, acadl, got1, glul, fasn, akr1a1, acadm, ckm, mif
adenyl ribonucleotide binding	10	289	3'46%	cps1, myh7, myh6, pebp1, fbp1, map2k1, pc, atp5a1, atp5b
adenyl nucleotide binding	10	293	3'41%	cps1, myh7, myh6, pebp1, fbp1, map2k1, pc, atp5a1, atp5b
glucose catabolic process	9	57	15'79%	fbp1, gpd1, aldoa, gapdh, eno1, g6pd, taldo1, mif, aldob
hexose catabolic process	9	61	14'75%	fbp1, gpd1, aldoa, gapdh, eno1, g6pd, taldo1, mif, aldob
coenzyme binding	9	110	8'18%	acadl, fasn, pitpna, g6pd, gpd1, aldh5a1, acat1, acadm, mdh1
carbohydrate biosynthetic process	9	121	7'44%	gnmt, got1, akr1a1, gapdh, g6pd, fbp1, gpd1, pc, acadm
carboxylic acid catabolic process	9	132	6'82%	uroc1, acadl, got1, akr1a1, aldh5a1, ivd, acadm, cpt2, acaa2
organic acid catabolic process	9	132	6'82%	uroc1, acadl, got1, akr1a1, aldh5a1, ivd, acadm, cpt2, acaa2
carboxylic acid binding	9	175	5'14%	cps1, gnmt, got1, glul, pitpna, ddah1, alb, aldh5a1, pc
organic acid binding	9	176	5'11%	cps1, gnmt, got1, glul, pitpna, ddah1, alb, aldh5a1, pc
fatty acid metabolic process	9	235	3'83%	acss1, aldh5a1, acadl, fasn, ivd, acadm, cpt2, acaa2, mif
ATP binding	9	261	3'45%	cps1, myh7, myh6, pebp1, fbp1, map2k1, glul, pc, atp5a1, atp5b
nicotinamide nucleotide metabolic process	8	43	18'60%	gpd1, dlst, ogdh, g6pd, mdh2, mdh1, taldo1, aldob
pyridine nucleotide metabolic process	8	43	18'60%	gpd1, dlst, ogdh, g6pd, mdh2, mdh1, taldo1, aldob
pyridine-containing compound metabolic process	8	51	15'69%	gpd1, dlst, ogdh, g6pd, mdh2, mdh1, taldo1, aldob
monosaccharide biosynthetic process	8	51	15'69%	gnmt, akr1a1, gapdh, g6pd, fbp1, gpd1, pc, acadm
oxidoreduction coenzyme metabolic process	8	51	15'69%	gpd1, dlst, ogdh, g6pd, mdh2, mdh1, taldo1, aldob
cellular respiration	8	69	11'59%	aldh5a1, ogdh, aco2, suclg2, gpd1, dlst, ndufs1, mdh2
cellular modified amino acid metabolic process	8	145	5'52%	cps1, gnmt, ckb, ddah1, ckmt1b, g6pd, aldh5a1, ckm
alpha-amino acid metabolic process	8	154	5'19%	cps1, gnmt, got1, glul, ddah1, aldh5a1, ivd, uroc1
purine ribonucleoside monophosphate metabolic process	8	199	4'02%	adk, myh7, myh6, nsf, aldoa, atp5a1, atp5b, ndufs1
purine nucleoside monophosphate metabolic process	8	200	4'00%	adk, myh7, myh6, nsf, aldoa, atp5a1, atp5b, ndufs1
ribonucleoside monophosphate metabolic process	8	203	3'94%	adk, myh7, myh6, nsf, aldoa, atp5a1, atp5b, ndufs1
nucleoside monophosphate metabolic process	8	214	3'74%	adk, myh7, myh6, nsf, aldoa, atp5a1, atp5b, ndufs1
glycolysis	7	46	15'22%	fbp1, gpd1, aldoa, gapdh, eno1, mif, aldob
monocarboxylic acid catabolic process	7	76	9'21%	acadl, akr1a1, aldh5a1, ivd, acadm, cpt2, acaa2
ATP metabolic process	7	179	3'91%	aldoa, myh7, myh6, nsf, atp5a1, atp5b, ndufs1
cellular carbohydrate metabolic process	7	191	3'66%	cps1, gnmt, got1, fbp1, gpd1, acadm, mif

response to glucocorticoid	7	218	3'21%	cps1, got1, pebp1, map2k1, acadm, mif, aldob
response to corticosteroid	7	232	3'02%	cps1, got1, pebp1, map2k1, acadm, mif, aldob
monovalent inorganic cation transport	7	283	2'47%	atp6v1b1, cox5b, nsf, uqcrfs1, atp5a1, atp5b, mif

Suppl. Table 2: Network analysis serum functions absolute number. Thirty-three functions filtered by absolute number (cut-off ≥ 6) from the original 166 deriving from GeneMania[®] network analysis of the serum-protein dataset. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
blood microparticle	22	97	22'68%	apcs, hp, c3, tf, apoa1, cfb, apoe, serping1, fga, alb, itih4, gc, ahsg, c9, hpx, fgb, pon1, ambp, apoa2, f2, c4bpa, fgg
glycerolipid metabolic process	9	211	4'27%	c3, apoa1, apoe, apoa5, apoh, pon1, cps1, apoa2, apoc3
phospholipid binding	9	222	4'05%	apoe, apoa1, apoa5, apoh, fabp1, pon1, cps1, apoa2, apoc3
negative regulation of hydrolase activity	9	264	3'41%	fetub, kng2, apoa1, serping1, serpina1, fabp1, ambp, apoa2, apoc3
lipid transport	8	174	4'60%	apoe, apoa1, apoa5, apoh, fabp1, pon1, apoa2, apoc3
regeneration	8	184	4'35%	fga, hp, apoa1, apoe, apoa5, ahsg, apoa2, apoh
enzyme inhibitor activity	8	197	4'06%	fetub, apoa1, serping1, serpina1, ahsg, ambp, apoa2, apoc3
wound healing	8	287	2'79%	fga, c3, apoe, apoa5, c9, fgb, f2, apoh
high-density lipoprotein particle	7	15	46'67%	apoe, apoa1, apoa5, apoh, pon1, apoa2, apoc3
plasma lipoprotein particle	7	19	36'84%	apoe, apoa1, apoa5, apoh, pon1, apoa2, apoc3
protein-lipid complex	7	20	35'00%	apoe, apoa1, apoa5, apoh, pon1, apoa2, apoc3
acylglycerol metabolic process	7	75	9'33%	c3, apoe, apoa5, apoh, apoc3, apoa2, cps1
neutral lipid metabolic process	7	77	9'09%	c3, apoe, apoa5, apoh, apoc3, apoa2, cps1
acute inflammatory response	7	96	7'29%	hp, c3, tf, itih4, serping1, ahsg, apoa2
lipid localization	7	136	5'15%	apoe, apoa1, apoa5, apoh, fabp1, apoa2, apoc3
regulation of lipid metabolic process	7	229	3'06%	c3, apoa1, apoe, apoa5, fabp1, apoa2, apoc3
regulation of body fluid levels	7	246	2'85%	c3, apoe, gc, fga, c9, f2, apoh
extracellular matrix	7	262	2'67%	apcs, alb, tf, rbp3, f2, apoh, ahsg
triglyceride-rich lipoprotein particle	6	14	42'86%	apoe, apoa1, apoa5, apoh, apoc3, apoa2
very-low-density lipoprotein particle	6	14	42'86%	apoe, apoa1, apoa5, apoh, apoc3, apoa2
triglyceride metabolic process	6	67	8'96%	c3, apoe, apoa5, apoh, apoc3, cps1
organ regeneration	6	92	6'52%	hp, apoa1, apoa5, ahsg, apoa2, apoh
blood coagulation	6	110	5'45%	c3, apoe, fga, c9, f2, apoh
hemostasis	6	112	5'36%	c3, apoe, fga, c9, f2, apoh
coagulation	6	115	5'22%	c3, apoe, fga, c9, f2, apoh
negative regulation of endopeptidase activity	6	156	3'85%	fetub, kng2, serping1, serpina1, fabp1, ambp

Function	Genes in network	Genes in genome	Ratio	Names
lipid catabolic process	6	157	3'82%	apoe, apoa5, fabp1, cps1, apoa2, apoc3
negative regulation of peptidase activity	6	159	3'77%	fetub, kng2, serping1, serpina1, fabp1, ambp
steroid metabolic process	6	200	3'00%	gc, apoa1, apoe, apoc3, pon1, apoa2
alcohol metabolic process	6	211	2'84%	gc, apoa1, apoe, apoc3, pon1, apoa2
regulation of endopeptidase activity	6	276	2'17%	fetub, kng2, serping1, serpina1, fabp1, ambp
organic anion transport	6	279	2'15%	dpysl2, apoa1, apoe, apoc3, fabp1, apoa2
regulation of peptidase activity	6	288	2'08%	fetub, kng2, serping1, serpina1, fabp1, ambp

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Suppl. Table 3: Subcluster 2 (gpd1, eno1, ald5a1, coro1a, atp6v1b2, ckb, alb, fasn, acy1, fbp1, fscn1, ald7a1, cct3, gpd1, ogdh, oxct1, ca1). Seventeen functions filtered by prevalence (cut-off $\geq 10\%$) from the original 51 deriving from GeneMania[®] network analysis of the whole dataset without the serum proteins. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
NADH metabolic process	3	12	25'00%	gpd1, ogdh, aldob
ribonucleoside diphosphate biosynthetic process	2	10	20'00%	atp5a1, atp5b
carbohydrate phosphatase activity	2	10	20'00%	fbp1, fbp2
ADP metabolic process	2	11	18'18%	atp5a1, atp5b
MHC class I protein binding	2	11	18'18%	atp5a1, atp5b
sterol esterification	2	12	16'67%	apoa2, scd
cholesterol esterification	2	12	16'67%	apoa2, scd
steroid esterification	2	12	16'67%	apoa2, scd
acetyl-CoA biosynthetic process	2	13	15'38%	acly, pdhb
nucleoside diphosphate biosynthetic process	2	13	15'38%	atp5a1, atp5b
oxidoreductase activity, acting on the aldehyde or oxo group of donors	4	31	12'90%	ald7a1, ald5a1, ogdh, pdhb
NAD metabolic process	3	24	12'50%	gpd1, ogdh, aldob
oxidoreductase activity, acting on the aldehyde or oxo group of donors, NAD or NADP as acceptor	3	25	12'00%	ald7a1, ald5a1, ogdh
acetyl-CoA metabolic process	3	26	11'54%	fasn, acly, pdhb
gluconeogenesis	5	44	11'36%	fbp1, gpd1, pgk1, fbp2, rbp4
hexose biosynthetic process	5	46	10'87%	fbp1, gpd1, pgk1, fbp2, rbp4
glycolysis	5	46	10'87%	fbp1, eno1, gpd1, pgk1, aldob

Suppl. Table 4: Subcluster 2 (gpd1, eno1, aldh5a1, coro1a, atp6v1b2, ckb, alb, fasn, acy1, fbp1, fscn1, aldh7a1, cct3, gpd1, ogdh, oxct1, ca1). Nineteen functions filtered by absolute number (cut-off ≥ 5) from the original 51 deriving from GeneMania[®] network analysis of the whole dataset without the serum proteins. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
glucose metabolic process	8	171	4'68%	fbp1, aldh5a1, gpd1, eno1, pgk1, fbp2, aldob, rbp4
hexose metabolic process	8	186	4'30%	fbp1, aldh5a1, gpd1, eno1, pgk1, fbp2, aldob, rbp4
generation of precursor metabolites and energy	8	196	4'08%	fbp1, aldh5a1, gpd1, eno1, ogdh, pgk1, pdhb, aldob
monosaccharide metabolic process	8	199	4'02%	fbp1, aldh5a1, gpd1, eno1, pgk1, fbp2, aldob, rbp4
coenzyme metabolic process	7	161	4'35%	gpd1, fasn, ogdh, acly, pdhb, acot2, aldob
cofactor metabolic process	7	196	3'57%	gpd1, fasn, ogdh, acly, pdhb, acot2, aldob
fatty acid metabolic process	6	235	2'55%	aldh5a1, fasn, acly, acot2, scd, fabp1
gluconeogenesis	5	44	11'36%	fbp1, gpd1, pgk1, fbp2, rbp4
hexose biosynthetic process	5	46	10'87%	fbp1, gpd1, pgk1, fbp2, rbp4
glycolysis	5	46	10'87%	fbp1, eno1, gpd1, pgk1, aldob
monosaccharide biosynthetic process	5	51	9'80%	fbp1, gpd1, pgk1, fbp2, rbp4
acyl-CoA metabolic process	5	53	9'43%	fasn, ogdh, acot2, pdhb, acly
thioester metabolic process	5	53	9'43%	fasn, ogdh, acot2, pdhb, acly
glucose catabolic process	5	57	8'77%	fbp1, eno1, gpd1, pgk1, aldob
hexose catabolic process	5	61	8'20%	fbp1, eno1, gpd1, pgk1, aldob
monosaccharide catabolic process	5	63	7'94%	fbp1, eno1, gpd1, pgk1, aldob
single-organism carbohydrate catabolic process	5	90	5'56%	fbp1, eno1, gpd1, pgk1, aldob
carbohydrate catabolic process	5	95	5'26%	fbp1, eno1, gpd1, pgk1, aldob
carbohydrate biosynthetic process	5	121	4'13%	fbp1, gpd1, pgk1, fbp2, rbp4

Suppl. Table 5: Subcluster 3 (gapdh, cps1, aldoa, glul, myh6, myh7, oplah, got1, acss1). Twenty functions filtered by prevalence (cut-off $\geq 10\%$) from the original 90 deriving from GeneMania[®] network analysis of the whole dataset without the serum proteins. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
striated muscle thin filament	4	13	30'77%	tnni1, tnnt3, tnnc2, acta1
myofilament	4	15	26'67%	tnni1, tnnt3, tnnc2, acta1
actin-dependent ATPase activity	2	13	15'38%	myh6, myh7
structural constituent of muscle	3	20	15'00%	myh6, myh7, mylplf
ATP biosynthetic process	3	20	15'00%	aldoa, atp5b, pkm
microfilament motor activity	2	14	14'29%	myh6, myh7
glutamate binding	2	14	14'29%	glul, cps1
myosin II complex	2	14	14'29%	myh6, myh7
purine ribonucleoside triphosphate biosynthetic process	3	22	13'64%	aldoa, atp5b, pkm
purine nucleoside triphosphate biosynthetic process	3	23	13'04%	aldoa, atp5b, pkm
ribonucleoside triphosphate biosynthetic process	3	24	12'50%	aldoa, atp5b, pkm
adult heart development	2	16	12'50%	myh6, myh7
transferase activity, transferring nitrogenous groups	2	17	11'76%	got1, gapdh
regulation of the force of heart contraction	3	26	11'54%	myh6, atp2a2, myl3
myosin complex	3	26	11'54%	myh6, myh7, myl3
glycogen catabolic process	2	18	11'11%	cps1, pygm
cellular polysaccharide catabolic process	2	18	11'11%	cps1, pygm
glucan catabolic process	2	18	11'11%	cps1, pygm
polysaccharide catabolic process	2	18	11'11%	cps1, pygm
glutamate metabolic process	2	20	10'00%	got1, glul

Suppl. Table 6: Subcluster 3 (gapdh, cps1, aldoa, glul, myh6, myh7, oplah, got1, acss1). Twenty-seven functions filtered by absolute number (cut-off ≥ 5) from the original 90 deriving from GeneMania[®] network analysis of the whole dataset without the serum proteins. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
muscle system process	13	242	5'37%	myh6, myh7, aldoa, tnnt3 , actn2 , atp2a2 , tnni1 , myl3 , mybpc2 , tnnc2 , mylpf , acta1 , mybpc1
muscle contraction	12	198	6'06%	myh6, myh7, aldoa, tnnt3 , actn2 , atp2a2 , tnni1 , myl3 , mybpc2 , tnnc2 , mylpf , mybpc1
sarcomere	8	140	5'71%	myh6, myh7, tnnt3 , tnnc2 , actn2 , acta1 , tnni1 , myl3
contractile fiber part	8	153	5'23%	myh6, myh7, tnnt3 , tnnc2 , actn2 , acta1 , tnni1 , myl3
myofibril	8	167	4'79%	myh6, myh7, tnnt3 , tnnc2 , actn2 , acta1 , tnni1 , myl3
contractile fiber	8	176	4'55%	myh6, myh7, tnnt3 , tnnc2 , actn2 , acta1 , tnni1 , myl3
adenyl ribonucleotide binding	8	289	2'77%	myh6, myh7, glul, cps1, pkm , pygm , atp5b , atp2a2
adenyl nucleotide binding	8	293	2'73%	myh6, myh7, glul, cps1, pkm , pygm , atp5b , atp2a2
ATP metabolic process	7	179	3'91%	myh6, myh7, aldoa, pkm , atp2a2 , atp5b , tnnt3
purine ribonucleoside monophosphate metabolic process	7	199	3'52%	myh6, myh7, aldoa, pkm , atp2a2 , atp5b , tnnt3
purine nucleoside monophosphate metabolic process	7	200	3'50%	myh6, myh7, aldoa, pkm , atp2a2 , atp5b , tnnt3
ribonucleoside monophosphate metabolic process	7	203	3'45%	myh6, myh7, aldoa, pkm , atp2a2 , atp5b , tnnt3
nucleoside monophosphate metabolic process	7	214	3'27%	myh6, myh7, aldoa, pkm , atp2a2 , atp5b , tnnt3
ATP binding	6	261	2'30%	myh6, myh7, glul, cps1, atp5b , atp2a2
single-organism carbohydrate catabolic process	5	90	5'56%	gapdh, aldoa, cps1, pkm , pygm
carbohydrate catabolic process	5	95	5'26%	gapdh, aldoa, cps1, pkm , pygm
striated muscle contraction	5	97	5'15%	myh6, aldoa, tnnt3 , tnnc2 , myl3
ATPase activity, coupled	5	133	3'76%	myh6, myh7, tnnt3 , atp5b , atp2a2
ATP catabolic process	5	152	3'29%	myh6, myh7, tnnt3 , atp5b , atp2a2
purine ribonucleoside monophosphate catabolic process	5	156	3'21%	myh6, myh7, tnnt3 , atp5b , atp2a2

Function	Genes in network	Genes in genome	Ratio	Names
ribonucleoside monophosphate catabolic process	5	156	3'21%	myh6, myh7, tnnt3 , atp5b , atp2a2
purine nucleoside monophosphate catabolic process	5	157	3'18%	myh6, myh7, tnnt3 , atp5b , atp2a2
nucleoside monophosphate catabolic process	5	159	3'14%	myh6, myh7, tnnt3 , atp5b , atp2a2
ATPase activity	5	186	2'69%	myh6, myh7, tnnt3 , atp5b , atp2a2
generation of precursor metabolites and energy	5	196	2'55%	gapdh, cps1, aldoa, pkm , pygm
carboxylic acid biosynthetic process	5	200	2'50%	acss1, glul, got1, ckm , pkm
organic acid biosynthetic process	5	200	2'50%	acss1, glul, got1, ckm , pkm

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Suppl. Table 7: Subcluster of similarly up-regulated proteins from the serum-protein dataset (c3, kng2, dpysl2, igh-6, apoa1, hp, alb, tf, gc, apoe, cfb). Forty-four functions filtered by prevalence (cut-off $\geq 15\%$) from the original 190 deriving from GeneMania[®] network analysis of this subcluster dataset. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software

Function	Genes in network	Genes in genome	Ratio	Names
triglyceride-rich lipoprotein particle	7	14	50'00%	apoA1, apoe, apoA4, apoh, apoc3, apoc1, apoA5
very-low-density lipoprotein particle	7	14	50'00%	apoA1, apoe, apoA4, apoh, apoc3, apoc1, apoA5
high-density lipoprotein particle	7	15	46'67%	apoA1, apoe, apoA4, apoh, apoc3, apoc1, apoA5
phospholipid efflux	5	11	45'45%	apoA1, apoe, apoA4, apoc3, apoc1
plasma lipoprotein particle	7	19	36'84%	apoA1, apoe, apoA4, apoh, apoc3, apoc1, apoA5
protein-lipid complex	7	20	35'00%	apoA1, apoe, apoA4, apoh, apoc3, apoc1, apoA5
plasma lipoprotein particle remodeling	6	18	33'33%	apoA1, apoe, apoA4, apoc3, apoc1, apoA5
protein-lipid complex remodeling	6	18	33'33%	apoA1, apoe, apoA4, apoc3, apoc1, apoA5
macromolecular complex remodeling	6	18	33'33%	apoA1, apoe, apoA4, apoc3, apoc1, apoA5
lipase inhibitor activity	3	10	30'00%	apoA1, apoc1, apoc3
sterol transporter activity	3	10	30'00%	apoA1, apoe, apoA4
cholesterol transporter activity	3	10	30'00%	apoA1, apoe, apoA4
reverse cholesterol transport	3	11	27'27%	apoA1, apoe, apoA4
peripheral nervous system axon regeneration	3	12	25'00%	apoA1, apoe, apoA4
steroid esterification	3	12	25'00%	apoA1, apoe, apoA4
sterol esterification	3	12	25'00%	apoA1, apoe, apoA4
cholesterol esterification	3	12	25'00%	apoA1, apoe, apoA4
negative regulation of lipase activity	3	13	23'08%	apoA1, apoc1, apoc3
plasma lipoprotein particle organization	6	27	22'22%	apoA1, apoe, apoA4, apoc3, apoc1, apoA5
protein-lipid complex subunit organization	6	29	20'69%	apoA1, apoe, apoA4, apoc3, apoc1, apoA5
lipoprotein particle receptor binding	4	20	20'00%	apoA1, apoe, apoc3, apoA5
triglyceride catabolic process	3	15	20'00%	apoc3, apoA5, apoA4
negative regulation of fatty acid biosynthetic process	2	10	20'00%	apoc3, apoc1
lipase activator activity	2	10	20'00%	apoh, apoA5
negative regulation of cholesterol transport	2	10	20'00%	apoc3, apoc1
negative regulation of sterol transport	2	10	20'00%	apoc3, apoc1
high-density lipoprotein particle remodeling	2	10	20'00%	apoe, apoc3
regulation of Cdc42 protein signal transduction	3	16	18'75%	apoA1, apoe, apoc3
mucosal immune response	2	11	18'18%	ltf, apoA4

Function	Genes in network	Genes in genome	Ratio	Names
protein-lipid complex assembly	3	17	17'65%	apoa1, apoe, apoa4
regulation of sterol transport	5	29	17'24%	apoa1, apoe, apoa4, apoc3, apoc1
regulation of cholesterol transport	5	29	17'24%	apoa1, apoe, apoa4, apoc3, apoc1
phospholipid transport	6	36	16'67%	apoa1, apoe, apoa4, fabp1, apoc3, apoc1
regulation of lipoprotein particle clearance	2	12	16'67%	apoc3, apoc1
organ or tissue specific immune response	2	12	16'67%	ltf, apoa4
regulation of triglyceride metabolic process	4	25	16'00%	c3, apoa5, apoa4, apoc3
regulation of fatty acid biosynthetic process	4	25	16'00%	apoc3, apoc1, apoa5, apoa4
regulation of plasma lipoprotein particle levels	6	38	15'79%	apoa1, apoe, apoa4, apoc3, apoc1, apoa5
intestinal absorption	3	19	15'79%	apoa1, apoa4, fabp1
positive regulation of lipid catabolic process	3	19	15'79%	fabp1, apoa5, apoa4
positive regulation of fatty acid biosynthetic process	2	13	15'38%	apoa5, apoa4
regulation of lipoprotein lipase activity	5	33	15'15%	apoh, apoc3, apoc1, apoa5, apoa4
neutral lipid catabolic process	3	20	15'00%	apoc3, apoa5, apoa4
acylglycerol catabolic process	3	20	15'00%	apoc3, apoa5, apoa4

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Suppl. Table 8: Subcluster of similarly up-regulated proteins from the serum-protein dataset (c3, kng2, dpysl2, igh-6, apoa1, hp, alb, tf, gc, apoe, cfb). Fifty-nine functions filtered by absolute number (cut-off ≥ 5) from the original 190 deriving from GeneMania[®] network analysis of this subcluster dataset. Column 1 shows the functions names. Columns 2 and 3 show respectively the number of annotated genes in the displayed network and the number of genes with that annotation in the genome. In column 5: names in bold letters represent the genes predicted by the software.

Function	Genes in network	Genes in genome	Ratio	Names
blood microparticle	13	97	13'40%	tf, hp, c3, apoa1, apoe, gc, cfb, alb, ambp, itih4, ahsg, apoa4, atm
lipid localization	9	136	6'62%	apoa1, apoe, apo4, rbp4, apoh, fabp1, apoc3, apoc1, apo5
lipid transport	9	174	5'17%	apoa1, apoe, apo4, rbp4, apoh, fabp1, apoc3, apoc1, apo5
regeneration	8	184	4'35%	hp, apoa1, apoe, apo4, apoh, afp, apo5, ahsg
glycerolipid metabolic process	8	211	3'79%	c3, apoa1, apoe, apo4, apoh, apoc3, apoc1, apo5
regulation of lipid metabolic process	8	229	3'49%	c3, apoa1, apoe, apo4, fabp1, apoc3, apoc1, apo5
triglyceride-rich lipoprotein particle	7	14	50'00%	apoa1, apoe, apo4, apoh, apoc3, apoc1, apo5
very-low-density lipoprotein particle	7	14	50'00%	apoa1, apoe, apo4, apoh, apoc3, apoc1, apo5
high-density lipoprotein particle	7	15	46'67%	apoa1, apoe, apo4, apoh, apoc3, apoc1, apo5
plasma lipoprotein particle	7	19	36'84%	apoa1, apoe, apo4, apoh, apoc3, apoc1, apo5
protein-lipid complex	7	20	35'00%	apoa1, apoe, apo4, apoh, apoc3, apoc1, apo5
triglyceride metabolic process	7	67	10'45%	c3, apoe, apo4, apoh, apoc3, apoc1, apo5
acylglycerol metabolic process	7	75	9'33%	c3, apoe, apo4, apoh, apoc3, apoc1, apo5
neutral lipid metabolic process	7	77	9'09%	c3, apoe, apo4, apoh, apoc3, apoc1, apo5
steroid metabolic process	7	200	3'50%	gc, apoa1, apoe, apo4, afp, apoc3, apoc1
phospholipid binding	7	222	3'15%	apoa1, apoe, apo4, apoh, fabp1, apoc3, apo5
negative regulation of hydrolase activity	7	264	2'65%	apoa1, kng2, fabp1, ambp, serpina1, apoc3, apoc1
organic anion transport	7	279	2'51%	dpysl2, apoa1, apoe, apo4, fabp1, apoc3, apoc1
plasma lipoprotein particle remodeling	6	18	33'33%	apoa1, apoe, apo4, apoc3, apoc1, apo5
protein-lipid complex remodeling	6	18	33'33%	apoa1, apoe, apo4, apoc3, apoc1, apo5
macromolecular complex remodeling	6	18	33'33%	apoa1, apoe, apo4, apoc3, apoc1, apo5
plasma lipoprotein particle organization	6	27	22'22%	apoa1, apoe, apo4, apoc3, apoc1, apo5
protein-lipid complex subunit organization	6	29	20'69%	apoa1, apoe, apo4, apoc3, apoc1, apo5
phospholipid transport	6	36	16'67%	apoa1, apoe, apo4, fabp1, apoc3, apoc1

Function	Genes in network	Genes in genome	Ratio	Names
regulation of plasma lipoprotein particle levels	6	38	15'79%	apoa1, apoe, apoa4 , apoc3 , apoc1 , apoa5
organophosphate ester transport	6	53	11'32%	apoa1, apoe, apoa4 , fabp1 , apoc3 , apoc1
lipid transporter activity	6	55	10'91%	apoa1, apoe, apoa4 , rbp4 , fabp1 , apoc3
regulation of lipase activity	6	74	8'11%	apoa1, apoc1 , apoa5 , apoa4 , apoh , apoc3
organ regeneration	6	92	6'52%	hp, apoa1, apoa5 , ahsg , apoh , afp
regulation of lipid biosynthetic process	6	118	5'08%	c3, apoe, apoa4 , apoc3 , apoc1 , apoa5
cellular ketone metabolic process	6	145	4'14%	afp , apoc3 , apoc1 , apoa5 , apoa4 , fabp1
lipid catabolic process	6	157	3'82%	apoe, apoa4 , fabp1 , apoc3 , apoc1 , apoa5
enzyme inhibitor activity	6	197	3'05%	apoa1, apoc1 , ahsg , ambp , serpina1 , apoc3
alcohol metabolic process	6	211	2'84%	gc, apoa1, apoe, apoa4 , apoc3 , apoc1
enzyme activator activity	6	225	2'67%	apoa1, apoe, apoa4 , apoh , ltf , apoa5
phospholipid efflux	5	11	45'45%	apoa1, apoe, apoa4 , apoc3 , apoc1
regulation of sterol transport	5	29	17'24%	apoa1, apoe, apoa4 , apoc3 , apoc1
regulation of cholesterol transport	5	29	17'24%	apoa1, apoe, apoa4 , apoc3 , apoc1
regulation of lipoprotein lipase activity	5	33	15'15%	apoh , apoc3 , apoc1 , apoa5 , apoa4
cholesterol efflux	5	36	13'89%	apoa1, apoe, apoa4 , apoc3 , apoc1
regulation of lipid catabolic process	5	42	11'90%	fabp1 , apoc3 , apoc1 , apoa5 , apoa4
cholesterol transport	5	55	9'09%	apoa1, apoe, apoa4 , apoc3 , apoc1
sterol transport	5	55	9'09%	apoa1, apoe, apoa4 , apoc3 , apoc1
cholesterol homeostasis	5	57	8'77%	apoa1, apoe, apoa4 , apoc3 , apoa5
sterol homeostasis	5	58	8'62%	apoa1, apoe, apoa4 , apoc3 , apoa5
regulation of fatty acid metabolic process	5	59	8'47%	fabp1 , apoc3 , apoc1 , apoa5 , apoa4
regulation of lipid transport	5	75	6'67%	apoa1, apoe, apoa4 , apoc3 , apoc1
cholesterol metabolic process	5	80	6'25%	apoa1, apoe, apoa4 , apoc3 , apoc1
sterol metabolic process	5	81	6'17%	apoa1, apoe, apoa4 , apoc3 , apoc1
lipid homeostasis	5	87	5'75%	apoa1, apoe, apoa4 , apoc3 , apoa5
acute inflammatory response	5	96	5'21%	tf, hp, c3, itih4 , ahsg
regulation of cellular ketone metabolic process	5	102	4'90%	fabp1 , apoc3 , apoc1 , apoa5 , apoa4
positive regulation of lipid metabolic process	5	106	4'72%	apoa1, apoe, apoa4 , fabp1 , apoa5
cellular lipid catabolic process	5	123	4'07%	fabp1 , apoc3 , apoc1 , apoa5 , apoa4
organic hydroxy compound transport	5	140	3'57%	apoa1, apoe, apoa4 , apoc3 , apoc1
tissue homeostasis	5	170	2'94%	tf, alb, ahsg , rbp4 , ltf
anatomical structure homeostasis	5	224	2'23%	tf, alb, ahsg , rbp4 , ltf
fatty acid metabolic process	5	235	2'13%	fabp1 , apoc3 , apoc1 , apoa5 , apoa4
transition metal ion binding	5	239	2'09%	tf, alb, apoa4 , meltf , ltf