

Additional file 1. Functional annotations of 20 candidate genes from an IWGCNA of chronic fatigue syndrome data. All statistically significant genes were upregulated in the high severity group. 16 out of the 20 candidate genes were eligible for Ingenuity Pathways Analysis (IPA). (a) IPA identified four networks with a statistically significant interaction among 12 candidate genes ($p\text{-value} \approx 10^{-32}$). Hematological disease was one of the three most significant functions for this interaction (other top functions can be found in the footnotes). (b) Analysis of the 212 network eligible blue module genes identified several significant pathways that have previously been shown to be involved in CFS. (c) Using a *LEO.NB.SingleMarker* threshold of 0.3 indicates that all but three of the candidate genes are causal for the blue module gene expression (where 66 total genes were causal by this criterion).

Gene Name and Genbank Accession	Full gene name. Entrez Gene and/or GeneRIFs description. Chromosome Location	Ingenuity Pathways Gene Annotation		c) Causality	
		a) 16 out of 20 Candidate Genes	b) 212 out of 299 Module Genes	LEO score ¹³	Rank in Module
FOXN1 (NM_003593)	Forkhead box N1. Mutations result in a severely compromised immune system, T-cell immunodeficiency, skin disorder congenital alopecia. 17q11-q12	Hematological Disease ¹ Rank = 1, $p\text{-value} \approx 10^{-32}$	Cell Function ⁵ Rank = 8, $p\text{-value} \approx 10^{-16}$	0.82	6
PRDX3 (AF118073)	Peroxiredoxin 3. Antioxidant function, regulates abundance of H ₂ O ₂ , which promotes apoptosis. 10q25-q26	Hematological Disease ¹	Endocrine Disorders/ Inflammation ⁶ Rank = 6, $p\text{-value} \approx 10^{-20}$	0.77	8
SUCLA2 (AK001458)	Succinate-CoA ligase, ADP-forming, beta subunit. Defects associated with encephalomyopathy. 13q12.2-q13.3	Hematological Disease ¹	Cell Cycle ⁷ Rank = 5, $p\text{-value} \approx 10^{-22}$	0.77	9
TFB2M (AK026314)	Transcription factor B2, mitochondrial. 1q44	Hematological Disease ¹	Cell Cycle ⁷	0.69	18
MED8 (BC010019)	Mediator complex subunit 8	Hematological Disease ¹	Amino Acid Met. ⁸ Rank = 1, $p\text{-value} \approx 10^{-45}$	0.82	7
SNURF (AF101044)	SNRPN upstream reading frame. Alternative splicing/deletion leads to Angelman syndrome or Prader-Willi. 15q12	Hematological Disease ¹	Amino Acid Met. ⁸	0.53	36
DCTN2 (NM_006400)	Dynactin 2 (p50). Required in peroxisome biogenesis. 12q13.2-q13.3	Hematological Disease ¹	Amino Acid Met. ⁸	0.30	66
PGK1 (AB062432)	Phosphoglycerate kinase 1. Glycolysis. Xq13	Hematological Disease ¹	Amino Acid Met. ⁸	-0.28	132
PRKCH (BC001000)	Protein kinase C, eta. Regulates keratinocyte differentiation. 14q22-q23	Hematological Disease ¹	Connective Tissue ⁹ Rank = 2, $p\text{-value} \approx 10^{-44}$	-0.13	116

RYK (NM_002958)	RYK receptor-like tyrosine kinase. May play a role in the development of cleft lip and/or palate. 3q22	Hematological Disease ¹	Connective Tissue ⁹	-0.50	182
VAMP5 (AF077197)	Vesicle-associated membrane protein 5 (myobrevin). Associated with myogenesis. 2p11.2	Hematological Disease ¹	Connective Tissue ¹⁰ Rank = 7, p-value $\approx 10^{-18}$	0.56	32
PBLD (AK027673)	Phenazine biosynthesis-like protein domain containing. 10pter-q25.3	Hematological Disease ¹	Connective Tissue ¹⁰	0.41	50
NPAL2 (AK024017)	NIPA-like domain containing 2. 8q22.2	Digestive System ² Rank = 2, p-value $\approx 10^{-3}$	Viral Function ¹¹ Rank = 3, p-value $\approx 10^{-32}$	0.67	21
CD302 (BC020646)	C-type lectin receptor involved in cell adhesion and migration, as well as endocytosis and phagocytosis. 2q24.2	Carbohydrate Metabolism ³ Rank = 2, p-value $\approx 10^{-3}$	Viral Function ¹¹	0.38	55
PPP1R14C (AF407165)	Protein phosphatase 1, regulatory (inhibitor) subunit 14C. Enriched in brain, heart and skeletal muscle. 6q24.3-q25.3	Cancer ⁴ Rank = 2, p-value $\approx 10^{-3}$	Cell Proliferation ¹² Rank = 9, p-value $\approx 10^{-14}$	0.83	5
TMEM50A (AF081282)	Transmembrane protein 50A. May contribute to RH haplotype selection. 1p36.11	NA, Rank = 2	NA, Rank = 14	0.39	53
CRNKL1 (AF111802)	Crooked neck pre-mRNA splicing factor-like 1. 20p11.2	NA	NA	0.77	10
LTV1 (AK027815)	Protein coding. 6q24.2	NA	NA	0.65	24
AF090939	Discontinued record.	NA	NA	0.85	3
XM13557	Unmapped.	NA	NA	0.57	28

¹Cell Cycle, Cancer, Hematological Disease

²Digestive System D&F, Hepatic System D&F, Organ Dev.

³Carbohydrate Metabolism, Gene Expression, Genetic Disorder

⁴Cancer, Cellular Movement, Skeletal and Muscular Disorders

⁵Cell Fun. and Main., Small Molecule Biochem., Molecular Transport

⁶Endocrine System Disorders, Infectious Disease, Inflammatory Disease

⁷Cell Assembly and Org., Cell Cycle, DNA Replication/Recomb./Repair

⁸Post-Translational Modification, Amino Acid Metabolism, Molecular Transport

⁹Organ Morphology, Cell Morphology, Connective Tissue D&F

¹⁰Gene Expression, Cellular Development, Connective Tissue D&F

¹¹Viral Function, Cell. Assembly and Org., Cell Fun. and Maintenance

¹²Post-Translational Modification, Cancer, Cellular Growth/Proliferation

¹³LEO.NB.SingleMarker scores (converted to fold changes).

