SUPPLEMENTARY FIGURES

Α

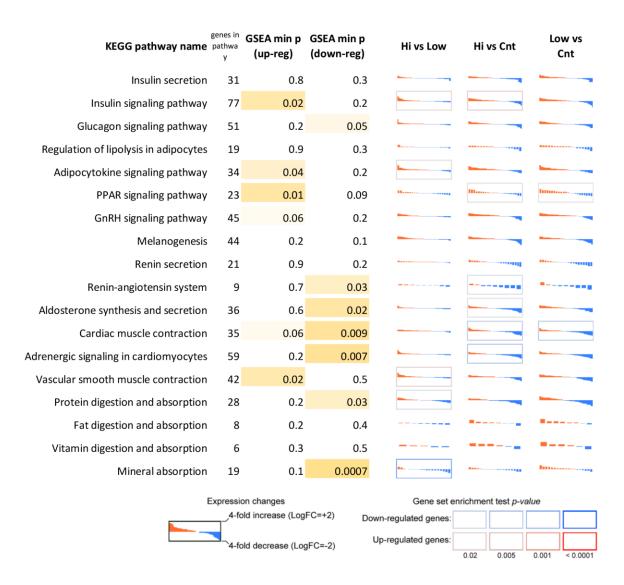
KEGG pathway name	genes in pathwa Y		GSEA min p (down-reg)	Hi vs Low	Hi vs Cnt	Low vs Cnt
Carbon metabolism	78	0.04	0.004			
2-Oxocarboxylic acid metabolism	14	0.2	0.003		•••••	
Fatty acid metabolism	36	0.2	0.0002			
Biosynthesis of amino acids	49	0.0006	8.0603E-05			
Amino sugar and nucleotide sugar metabolism	30	0.04	0.03			
Inositol phosphate metabolism	39	0.02	0.4			
Oxidative phosphorylation	109	0.003	1.972E-06			
Fatty acid elongation	21	0.5	0.0003			·····
Biosynthesis of unsaturated fatty acids	18	0.3	0.0002		••	!
Pyrimidine metabolism	34	0.02	0.2			
Glycine, serine and threonine metabolism	18	0.06	0.02		h	
Cysteine and methionine metabolism	29	0.1	0.1			
Valine, leucine and isoleucine degradation	32	0.1	0.1			
Valine, leucine and isoleucine biosynthesis	2	1.0	1.0			
Lysine degradation	43	0.04	0.05			
Arginine biosynthesis	9	0.6	0.2			
Arginine and proline metabolism	29	0.03	0.005			
N-Glycan biosynthesis	33	0.5	0.02			
Mucin type O-glycan biosynthesis	11	0.4	0.07			
Other types of O-glycan biosynthesis	15	0.03	0.07	••	II	
Glycosaminoglycan biosynthesis - chondroitin	13	0.002	0.006	••	•	************
Glycosaminoglycan biosynthesis - heparan	11	0.03	0.2			
Folate biosynthesis	12	0.3	0.04			
Expression changes Gene se					enrichment test p-v	alue
		4-fold increase (LogFC=+2) 4-fold decrease (LogFC=-2)		own-regulated genes:		
	4-fc			Up-regulated genes:	0.02 0.005	0.001 < 0.0001

KEGG pathway name	genes in pathwa y	GSEA min p (up-reg)	GSEA min p (down-reg)	Hi vs Low	Hiv	s Cnt	Low vs Cnt
RNA polymerase	28	0.003	0.09		-		
Basal transcription factors	30	0.002	0.0010			_	
Spliceosome	110	1.4076E-05	8.6847E-05				
Ribosome	130	9.8511E-11	0.06				
Aminoacyl-tRNA biosynthesis	37	0.5	0.02				
RNA transport	125	0.0005	3.9509E-07				
mRNA surveillance pathway	66	0.001	0.02				
Ribosome biogenesis in eukaryotes	64	0.1	0.006				
Protein export	21	0.03	1.7607E-05		*****		•
Protein processing in endoplasmic reticulum	122	0.03	0.004				
SNARE interactions in vesicular transport	24	0.003	0.4		III		111111111111111111111111111111111111111
Ubiquitin mediated proteolysis	93	0.002	0.0008				
Proteasome	39	0.10	0.002				
RNA degradation	59	0.002	0.006				
DNA replication	32	0.004	3.6776E-05				
Base excision repair	28	0.10	0.01			-	
Nucleotide excision repair	37	0.008	5.9647E-05				
Mismatch repair	19	0.006	0.0002		•••••		•••••
Homologous recombination	28	0.001	0.009				
Non-homologous end-joining	8	0.06	0.07				
Fanconi anemia pathway	34	0.01	0.2				
ABC transporters	11	0.3	0.06				
Expression changes Gene set er 4-fold increase (LogFC=+2) Up-regulated genes: Up-regulated genes:					enrichmer 0.02	0.005	0.001 < 0.0001

KEGG pathway name	genes in pathwa y	GSEA min p (up-reg)	GSEA min p (down-reg)	Hi vs Low	Hi vs Cnt	Low vs Cnt
Ras signaling pathway	91	0.08	0.2			
Rap1 signaling pathway	85	0.1	0.3			
MAPK signaling pathway	136	0.06	0.1			
ErbB signaling pathway	48	0.01	0.09			
Wnt signaling pathway	74	0.2	0.3			
Notch signaling pathway	29	0.04	0.03			
Hedgehog signaling pathway	22	0.2	0.5			
TGF-beta signaling pathway	43	0.3	0.09			
Hippo signaling pathway	81	0.007	0.03			
Hippo signaling pathway - multiple species	16	0.04	0.5			terror and the same of the sam
VEGF signaling pathway	30	0.005	0.1			
JAK-STAT signaling pathway	53	0.2	0.8			
NF-kappa B signaling pathway	40	0.04	0.2			
TNF signaling pathway	55	0.007	0.04			
HIF-1 signaling pathway	59	0.1	0.01			
FoxO signaling pathway	69	0.009	0.5			
Calcium signaling pathway	56	0.6	0.2			
Phosphatidylinositol signaling system	53	0.0008	0.2			
Phospholipase D signaling pathway	64	0.3	0.1			
Sphingolipid signaling pathway	63	0.003	0.1			
cAMP signaling pathway	71	0.3	0.1			
cGMP-PKG signaling pathway	66	0.2	0.2			
PI3K-Akt signaling pathway	144	0.4	0.1			
AMPK signaling pathway	67	0.2	0.002			
mTOR signaling pathway	85	0.04	0.07			
Neuroactive ligand-receptor interaction	23	1.0	0.9			lo
Ex	4-fold	changes increase (LogFC decrease (LogFC	. Down	Gene set enrich		ue

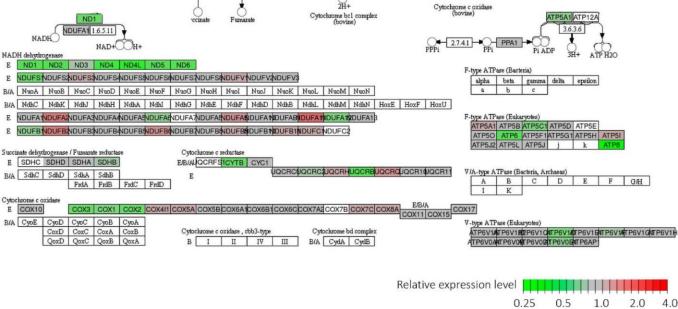
KEGG pathway name	genes in pathwa y	GSEA min p (up-reg)	GSEA min p (down-reg)	Hi vs Low	Hi vs Cnt	Low vs Cnt
Cytokine-cytokine receptor interaction	35	0.8	0.9			
ECM-receptor interaction	28	0.07	0.003			
Cell adhesion molecules (CAMs)	35	0.3	0.8			
Endocytosis	166	0.0009	7.4532E-05			
Phagosome	65	0.2	0.5			
Lysosome	85	8.9928E-05	0.008			
Peroxisome	45	0.1	0.07			
Autophagy - animal	82	0.1	0.02			
Regulation of actin cytoskeleton	109	0.002	0.2			
Cell cycle	97	0.0001	2.7889E-05			
Oocyte meiosis	70	0.04	0.01			
Apoptosis	81	0.008	0.1			
Apoptosis - multiple species	18	0.06	0.6			
p53 signaling pathway	44	0.01	0.1			
Focal adhesion	100	0.02	0.0005			
Adherens junction	49	9.9419E-05	0.007			
Tight junction	85	0.2	0.08			
Gap junction	40	0.10	0.3			
ling pathways regulating pluripotency of stem cells	56	0.008	0.04			
RIG-I-like receptor signaling pathway	34	0.04	0.2			
Cytosolic DNA-sensing pathway	34	0.003	0.2			
Natural killer cell mediated cytotoxicity	40	0.2	0.6			
Antigen processing and presentation	30	0.8	0.02			
T cell receptor signaling pathway	46	0.003	0.2			
B cell receptor signaling pathway	34	0.001	0.08			
Fc epsilon RI signaling pathway	28	0.08	0.05			
Fc gamma R-mediated phagocytosis	51	0.01	0.2			
Leukocyte transendothelial migration	47	0.006	0.3			
Intestinal immune network for IgA production	4	0.9	1.0			
Chemokine signaling pathway	68	0.08	0.1			
	4-fc	on changes old increase (LogF old decrease (Log	, ,	Gene set e own-regulated genes: Up-regulated genes:	enrichment test p-va	0.001 < 0.0001

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Supplementary Figure 1. Differential expression profiles of genes participating KEGG pathways according to the RNA-Seq data for MRC5-SV40 cell line treated with Abisil. On the figure, each cell demonstrates the sorted expression level log fold changes after Abisil treatment (red – upregulation, blue – downregulation) for genes participating a current KEGG pathway (vertical axis range is from 4-fold downregulation to 4-fold upregulation). Cell borders indicate whether a pathway is enriched with up- (red border) or downregulated (blue border) genes. *GSEA min p (up/down-reg)* – minimal p-value in a gene set enrichment analyses (GSEA; Fisher's exact test) for the pathway. *Hi vs Low* – comparison of cells treated with 50 and 5 μg/ml; *Hi vs Cnt* – comparison of cells treated with Abisil 50 μg/ml and non-treated cells; *Low vs Cnt* – comparison of cells treated with Abisil 5 μg/ml and non-treated cells. (A) Cell metabolism. (B) Main cellular processes. (C) Cell signaling pathways. (D) Immune response pathways, cell cycle, apoptosis, autophagy. (E) Miscellaneous pathways.

A Abisil 5 μg/ml compared to non-treated cells Complex IV Complex V 2×2H+ NADH dehydrogenase (Thermus themophilus VIb Membrane domain (Hydrophobic arm Sdh SdhD -BU Flunit 1/202 2H+ H₂O 2H+ Cytochrome c oxidas (bovine) Cytochrome bc1 complex (bovine) ND1 NDUFA1 1.6.5.11 NADH 2.7.4.1 PPA1 NADH dehydrogenas E ND1 ND2 ND3 ND4 ND4L ND5 ND6 F-type ATPase (Bacteria) E NDUFS NDUFS NDUFS NDUFS NDUFS NDUFS NDUFS NDUFS NDUFV NDUFV NDUFV NDUFV alpha beta gamma delta epsilon B/A NuoA NuoB NuoC NuoD NuoE NuoF NuoG NuoH NuoI NuoJ NuoK NuoL NuoM NuoN B/A NdhC NdhK NdhJ NdhH NdhA NdhI NdhG NdhE NdhF NdhA NdhK HoxE HoxF HoxU E NDUFA NDUF ATP5A1 ATP5B ATP5C1 ATP5D ATP5E ATP5O ATP6 ATP5F1ATP5G1 ATP5H ATP5I E NOUFB NOUFF NOUF E SDHC SDHD SDHA SDHB E/B/AUQCRFSICYTB CYC1 BUQCRQUQCR10UQCR11 B/A SdhC SdhD SdhA SdhB V/A-type ATPase (Ba G/H FrdA FrdB FrdC FrdD Cytochrome c or E COX10 COX3 COX1 COX2 COX411 COX5A COX5B COX6A COX6B COX6C COX7A2 COX7B COX7C COX8A COX11 COX15 COX17 B/A CyoE CyoD CyoC CyoB CyoA V-type ATPase (Eukaryotes) me c oxidase, cbb3-type CoxA Cytochrome bd cor ATP6V1ATP6V1EEP6V1CHTP6V1ATP6V1EHTP6V1ATP6V1CHTP6V1H B I II IV III B/A CydA CydB OoxD OoxC OoxB OoxA ATP6VOATP6VORTP6VORTP6AP **B** Abisil 50 μg/ml compared to non-treated cells 2H+ Cytochrome c oxidase (bovine) ome bc1 complex (bovine) PPA1 O 2.7.4.1 → PPPi NAD+OOH+ F-type ATPase (Bacteria) E NOUFS NOUF alpha beta gamma delta epsilon B/A NuoA NuoB NuoC NuoD NuoE NuoF NuoG NuoH NuoI NuoJ NuoK NuoL NuoM NuoN B/A NdhC NdhK NdhJ NdhH NdhA NdhI NdhG NdhE NdhE NdhF NdhB NdhB NdhL NdhM NdhN HoxE HoxF HoxU E NOUFA NOUF

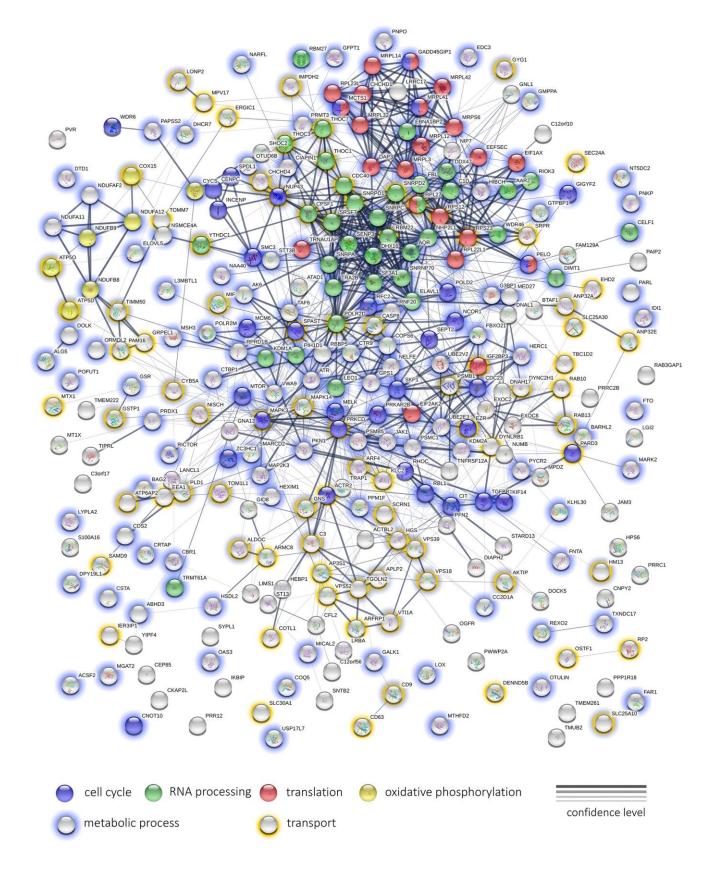


Supplementary Figure 2. Diagram illustrating expression changes of genes participating oxidative phosphorylation pathway (KEGG) introduced by Abisil treatment (MRC5-SV40 cell line): $5 \mu g/ml$ (A) and $50 \mu g/ml$ (B). Green – downregulation, red – upregulation.

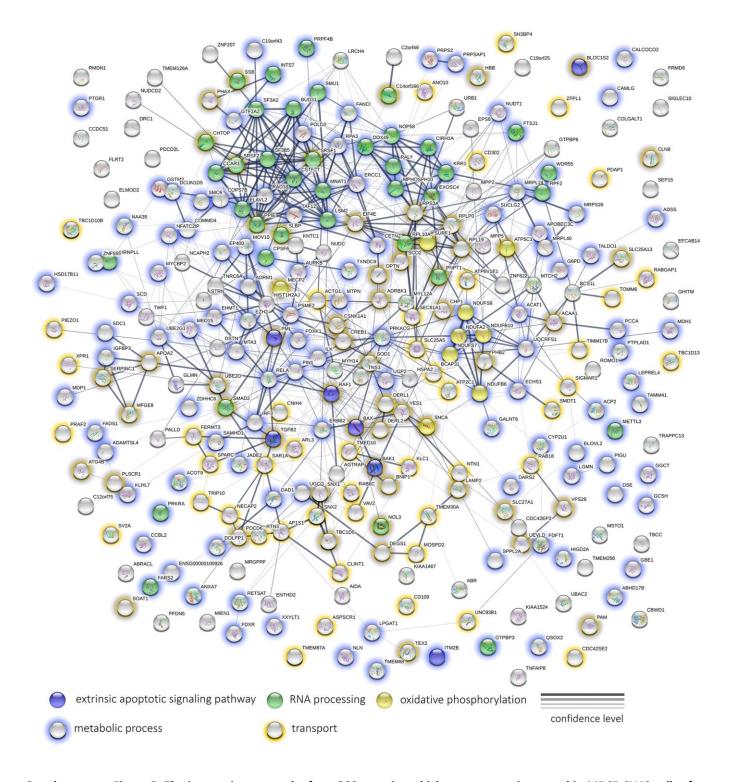
Relative expression level (normalized to the average value for each gene) 4.0 2.0 1.0 0.5 0.25 5 μg/ml control $50 \, \mu g/ml$ Spearman's r p-value (QLF test) 10-6 10-3 10-1

Top 5000 differentialy expressed genes (control- 5 μg/ml- 50 μg/ml)

Supplementary Figure 3. Heatmap demonstrating expression level profiles of top 5000 genes (MRC5-SV40 cell line), expression of which gradually increases/decreases with the increase of Abisyl concentration (0 μ g/ml - 5 μ g/ml - 50 μ g/ml).



Supplementary Figure 4. The interaction network of top 300 proteins which content was decreased (or not detected) in MRC5-SV40 cells after Abisil treatment (50 μ g/ml). The width of the connecting lines indicates the confidence level of protein interaction (best – mentions in curated databases, experimental data for human; worst – found interacting putative homologs in other organisms).



Supplementary Figure 5. The interaction network of top 300 proteins which content was increased in MRC5-SV40 cells after Abisil treatment (or detected only in treated cells). The width of the connecting lines indicates the confidence level of protein interaction (best – mentions in curated databases, experimental data for human; worst – found interacting putative homologs in other organisms).