Supplementary material

Supplementary table 1: PBMC genes from obese boys repressed or overexpressed in the LR group compared with the HR group at baseline **(A)** and the genes downregulated or upregulated in the HR group after the moderate calorie-restriction **(B)**.

A)

Gene symbol	Accesion code	Description	Biological process	p-value	FDR	FC
IGKC	BC073772	Immunoglobulin kappa constant	Immune response	0.007	0.363	-1.753
IGKC	AF113887	Immunoglobulin kappa constant	Immune response	0.026	0.513	-1.641
HLA-DRB3	NM_022555	Major histocompatibility complex, class II, DR beta 3	Antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	0.017	0.463	-1.590
LOC652493	ENST00000390249	NA	Biological process unclassified	0.035	0.544	-1.545
APOBEC3B	NM_004900	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide	Biological process unclassified	0.022	0.499	-1.542
IGKC	ENST00000390273	Immunoglobulin kappa constant	Immune response	0.013	0.437	-1.525
LOC100291056	ENST00000390631	NA	Biological process unclassified	0.019	0.471	-1.518
ELOVL7	NM_024930	ELOVL family member 7, elongation of long chain fatty acids	Fatty acid biosynthetic process	0.022	0.504	1.500
PCSK6	NM_002570	Proprotein convertase subtilisin	Glycoprotein metabolic process	0.003	0.286	1.501
LEPR	NM_002303	Leptin receptor	Angiogenesis	0.004	0.304	1.502
CTDSPL	NM_001008392	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A	Biological process unclassified	0.006	0.363	1.504
ME1	NM_002395	Malic enzyme 1, NADP(+)-dependent, cytosolic	Carbohydrate metabolic process	0.009	0.406	1.511
EGF	NM_001963	Epidermal growth factor	Activation of MAPKK activity	0.017	0.463	1.518
ITGB5	NM_002213	Integrin, beta 5	Muscle contraction	0.000	0.152	1.518
EPB49	NM_001978	Erythrocyte membrane protein band 4.9 (dematin)	Cytoskeleton organization	0.000	0.161	1.521
PBX1	NM_002585	Pre-B-cell leukemia homeobox 1	Urogenital system development	0.008	0.379	1.521
GPR34	NM_001097579	G protein-coupled receptor 34	Intracellular protein transport	0.013	0.437	1.523
WASF3	NM_006646	WAS protein family, member 3	Protein complex assembly	0.019	0.471	1.530
PDZK1IP1	NM_005764	PDZK1 interacting protein 1	Biological process unclassified	0.045	0.568	1.530
MARCH2	NM_016496	Membrane-associated ring finger (C3HC4) 2	Endocytosis	0.001	0.176	1.535
VIL1	NM_007127	Villin 1	Protein complex assembly	0.001	0.217	1.536
CD8B	NM_172099	CD8b molecule	Immune response	0.010	0.420	1.541
SLC6A4	NM_001045	Solute carrier family 6 (neurotransmitter transporter, serotonin), member 4	Neurotransmitter uptake	0.007	0.368	1.545
MFSD1	NM_022736	Major facilitator superfamily domain containing 1	Transmembrane transport	0.002	0.220	1.551
ASAP2	NM_003887	ArfGAP with SH3 domain, ankyrin repeat and PH domain 2	Regulation of ARFGTPase activity	0.000	0.081	1.565
LIPH	NM_139248	Lipase, member H	Lipid catabolic process	0.014	0.447	1.572
ALOX12	NM_000697	Arachidonate 12-lipoxygenase	Oxygen and reactive oxygen species metabolic process	0.015	0.451	1.585
ITGB3	NM_000212	Integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61	Cell-substrate junction assembly	0.001	0.161	1.594
MPL	NM_005373	Myeloproliferative leukemia virus oncogene	Cell surface receptor linked signaling pathway	0.007	0.367	1.595
SH3BGRL2	NM_031469	SH3 domain binding glutamic acid-rich protein like 2	Biological process unclassified	0.003	0.263	1.597

ENKUR	NM_145010	Enkurin, TRPC channel interacting protein	Biological process unclassified	0.005	0.324	1.617
THBS1	NM_003246	Thrombospondin 1	Activation of MAPK activity	0.013	0.437	1.622
GUCY1B3	NM_000857	Guanylate cyclase 1, soluble, beta 3	cGMP biosynthetic process	0.002	0.222	1.626
DNM3	NM_015569	Dynamin 3	Endocytosis	0.000	0.161	1.630
CALD1	NM_033138	Caldesmon 1	Cellular component movement	0.006	0.352	1.634
GP1BA	NM_000173	Glycoprotein Ib (platelet), alpha polypeptide	Cell adhesion	0.000	0.137	1.647
PDE3A	NM_000921	Phosphodiesterase 3A, cGMP-inhibited	Oocyte maturation	0.003	0.267	1.652
FSTL1	NM_007085	Follistatin-like 1	BMP signaling pathway	0.014	0.450	1.665
ENDOD1	NM_015036	Endonuclease domain containing 1	Biological process unclassified	0.002	0.217	1.666
CTTN	NM_005231	Cortactin	Biological process unclassified	0.008	0.379	1.688
LTBP1	NM_206943	Latent transforming growth factor beta binding protein 1	Biological process unclassified	0.001	0.161	1.693
CLEC1B	NM_016509	C-type lectin domain family 1, member B	Defense response	0.009	0.392	1.699
ITGA2B	NM_000419	Integrin, alpha 2b (platelet glycoprotein IIb of IIb/IIIa, antigen CD41)	Cell adhesion	0.003	0.274	1.705
PRKAR2B	NM_002736	Protein kinase, cAMP-dependent, regulatory, type II, beta	Regulation of protein amino acid phosphorylation	0.001	0.161	1.718
SNORA30	NR_002966	Small nucleolar RNA, H/ACA box 30	Biological process unclassified	0.000	0.137	1.749
PVALB	NM_002854	Parvalbumin	Biological process unclassified	0.017	0.463	1.780
SELP	NM_003005	Selectin P (granule membrane protein 140kDa, antigen CD62)	Regulation of cellular extravasation	0.001	0.161	1.817
TFPI	NM_006287	Tissue factor pathway inhibitor	Blood coagulation	0.000	0.152	1.817
MMRN1	NM_007351	Multimerin 1	Cell adhesion	0.000	0.137	1.835
PKHD1L1	NM_177531	Polycystic kidney and hepatic disease 1 (autosomal recessive)-like 1	Biological process unclassified	0.000	0.081	1.871
GSTM4	NM_000850	Glutathione S-transferase mu 4	Metabolic process	0.036	0.544	1.911
JAM3	NM_032801	Junctional adhesion molecule 3	Biological process unclassified	0.004	0.307	2.091
LGALS2	NM_006498	Lectin, galactoside-binding, soluble, 2	Biological process unclassified	0.012	0.434	2.378
HLA-DPB1	NM_002121	Major histocompatibility complex, class II, DP beta 1	Antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	0.041	0.548	2.441
SIRPB1	NM_006065	Signal-regulatory protein beta 1	Signal transduction	0.000	0.001	4.087

Transcript with ±1.5-FC and p-value<0.05 were considered significant. FDR: false discovery rate; FC: fold-change; NA: not available. The genes selected for validation with QPCR appear with their gene symbol in bold and their rows highlighted in grey.

B)

Gene symbol	Accesion code	Description	Biological process	p-value	FDR	FC
AREG	NM_001657	Amphiregulin	Epidermal growth factor receptor signaling pathway	0.002	0.286	-3.215
HBEGF	NM_001945	Heparin-binding EGF-like growth factor	Signal transduction	0.005	0.336	-2.544
NR4A2	NM_006186	Nuclear receptor subfamily 4, group A, member 2	Response to hypoxia	0.001	0.255	-2.490
NR4A3	NM_006981	Nuclear receptor subfamily 4, group A, member 3	Mesoderm formation	0.004	0.301	-2.468
CSNK1D	NM_001893	Casein kinase 1, delta	DNA repair	0.019	0.371	-2.415
RGS1	NM_002922	Regulator of G-protein signaling 1	Immune response	0.001	0.255	-2.216
TNFAIP3	NM_006290	Tumor necrosis factor, alpha-induced protein 3	Apoptosis	0.002	0.286	-2.135
GRASP	NM_181711	GRP1 (general receptor for phosphoinositides 1)-associated	Signal transduction	0.003	0.299	-2.050
MOP-1	AB014771	NA	Biological process unclassified	0.022	0.371	-2.021
SIK1	NM_173354	Salt-inducible kinase 1	Negative regulation of transcription from RNA polymerase II	0.003	0.299	-1.984
RASGEF1B	NM_152545	RasGEF domain family, member 1B	Regulation of small GTPase mediated signal transduction	0.034	0.386	-1.946
MIR221	NR_029635	MicroRNA 221	Biological process unclassified	0.020	0.371	-1.898
NR4A1	NM_002135	Nuclear receptor subfamily 4, group A, member 1	Regulation of transcription, DNA-dependent	0.004	0.333	-1.865
CD83	NM_004233	CD83 molecule	Defense response	0.026	0.375	-1.859
CD69	NM_001781	CD69 molecule	Biological process unclassified	0.013	0.371	-1.859
EREG	NM_001432	Epiregulin	Angiogenesis	0.000	0.232	-1.753
PER1	NM_002616	Period homolog 1 (Drosophila)	Regulation of transcription, DNA-dependent	0.002	0.286	-1.740
CCL3L1	NM_021006	Chemokine (C-C motif) ligand 3-like 1	Chemotaxis	0.028	0.376	-1.693
DUSP2	NM_004418	Dual specificity phosphatase 2	Inactivation of MAPK activity	0.028	0.375	-1.691
PPP1R15A	NM_014330	Protein phosphatase 1, regulatory (inhibitor) subunit 1	Regulation of translation	0.032	0.383	-1.665
NFKBIA	NM_020529	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	Protein import into nucleus, translocation	0.011	0.371	-1.665
JUN	NM_002228	Jun oncogene	Angiogenesis	0.016	0.371	-1.664
ZC3H12A	NM_025079	Zinc finger CCCH-type containing 12A	Angiogenesis	0.016	0.371	-1.637
FOSL1	NM_005438	FOS-like antigen 1	Regulation of transcription from RNA polymerase II promoter	0.043	0.393	-1.620
FLJ14107	NR_027715	Hypothetical LOC80094	Biological process unclassified	0.030	0.379	-1.610
NFKBID	NM_139239	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, delta	Inflammatory response	0.020	0.371	-1.600
PFKFB3	NM_004566	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	Fructose 2,6-bisphosphate metabolic process	0.024	0.371	-1.575
LRRFIP1	NM_001137550	Leucine rich repeat (in FLII) interacting protein 1	Regulation of transcription from RNA polymerase II	0.048	0.399	-1.550
DDIT4	NM_019058	DNA-damage-inducible transcript 4	Response to hypoxia	0.008	0.368	-1.541
FAM46C	NM_017709	Family with sequence similarity 46, member C	Biological process unclassified	0.005	0.346	-1.526
DUSP8	NM_004420	Dual specificity phosphatase 8	Inactivation of MAPK activity	0.048	0.399	-1.522
OSM	NM_020530	Oncostatin M	Positive regulation of acute inflammatory response	0.030	0.381	-1.520

PLK3	NM_004073	Polo-like kinase 3 (Drosophila)	Protein amino acid phosphorylation	0.044	0.393	-1.516
BTLA	NM_181780	B and T lymphocyte associated	Immune response-regulating cell surface receptor signalling pathway	0.017	0.371	1.510
BBS10	NM_024685	Bardet-Biedl syndrome 10	Retina homeostasis	0.009	0.371	1.523
LOC100128751	AY194294	NA	Biological process unclassified	0.044	0.393	1.532
CD180	NM_005582	CD180 molecule	Inflammatory response	0.007	0.348	1.555
FANCF	NM_022725	Fanconi anemia, complementation group F	DNA repair	0.013	0.371	1.557
GIMAP4	NM_018326	GTPase, IMAP family member 4	Biological process unclassified	0.047	0.399	1.586
C8orf44	NM_019607	Chromosome 8 open reading frame 44	Protein amino acid phosphorylation	0.010	0.371	1.589
GIMAP8	NM_175571	GTPase, IMAP family member 8	Biological process unclassified	0.006	0.348	1.670
ZNF780B	NM_001005851	Zinc finger protein 780B	Regulation of transcription, DNA-dependent	0.010	0.371	1.789

Transcript with ±1.5-FC and $p\text{-value}<0.05$ were considered significant. FDR: false discovery rate; FC: fold-change; NA: not available.

Supplementary table 2: Gene analysis as classified by Gene Ontology (GO), biological processes, that were significantly different between high and low responders at baseline. FE: Fold Enrichment.

GO Categories	Number of Genes	p-value	(FE)
Platelet activation	8	1.60E-04	6.6
JAK-STAT cascade	7	3.30E-03	4.7
Unsaturated fatty acid biosynthetic process	5	3.90E-02	3.9
Blood coagulation	14	1.30E-04	3.6
Regulation of blood coagulation	5	4.70E-02	3.6
Haemostasis	14	2.30E-04	3.4
Fatty acid biosynthetic process	9	1.00E-02	3.0
Regulation of body fluid levels	14	2.80E-03	2.6
Regulation of homeostatic process	11	1.20E-02	2.5
Regulation of I-kappaB kinase/NF-kappaB cascade	10	2.10E-02	2.5
Homeostasis of number of cells	9	3.70E-02	2.4
Chromatin assembly	8	4.80E-02	2.4
Positive regulation of cell differentiation	19	2.90E-03	2.2
Negative regulation of programmed cell death	28	6.00E-04	2.0
Regulation of cell motion	15	1.60E-02	2.0
Intracellular transport	41	2.30E-03	1.6
Intracellular signalling cascade	68	2.80E-03	1.4
Regulation of cell death	44	1.80E-02	1.4
Response to wounding	29	4.80E-02	1.4

Supplementary table 3: Gene analysis as classified by Gene Ontology (GO), biological processes, that were significantly change by the nutritional intervention in high and low responder groups. FE: Fold Enrichment.

GO Categories	High responders			Low responders		
	Number of Genes	p-value	FE	Number of Genes	p-value	FE
Angiogenesis				14	4.00E-02	1.8
Cellular response to stress	42	1.30E-02	1.5	41	2.20E-02	1.4
Cytoplasmic sequestering of NF-kappa				3	2.40E-02	11.6
Defence response				42	4.50E-02	1.3
ER-nuclear signalling pathway	6	3.20E-02	3.3			
Glycerophospholipid biosynthetic process	9	2.20E-02	2.6			
I-kappaB kinase/NF-kappaB cascade				9	1.50E-02	2.8
Immune response				65	3.90E-07	1.9
IMP metabolic process	3	3.40E-02	9.7			
Inflammatory response				28	8.70E-03	1.7
Leukocyte homeostasis				6	3.60E-02	3.2
Lymphocyte differentiation	11	3.80E-02	2.1			
Lymphocyte homeostasis	6	1.30E-02	4.2	6	1.30E-02	4.1
Macromolecule catabolic process	59	2.13E-03	1.5	55	1.30E-02	1.4
Negative regulation of NF-kappaB import into nucleus	3	4.60E-02	8.3	4	4.10E-03	11.1
Negative regulation of transcription factor import into nucleus				5	4.60E-03	6.9
Positive regulation of chemokine production				3	4.70E-02	8.3
Positive regulation of defence response to virus by host				3	2.40E-02	11.6
Positive regulation of epithelial to mesenchymal transition	3	4.60E-02	8.3			
Positive regulation of gene expression				41	3.60E-02	1.4
Positive regulation of innate immune response	7	2.90E-02	3.0			
Positive regulation of lymphocyte activation				13	4.10E-03	2.6
Positive regulation of nitrogen compound metabolic process				47	1.40E-02	1.4
Regulation of cytokine production	18	1.20E-02	1.9			
Regulation of I-kappaB kinase/NF-kappaB cascade				11	4.90E-02	2.0
Regulation of lymphocyte activation				17	3.80E-03	2.2
Regulation of NF-kappaB import into nucleus				5	1.20E-02	5.4
Regulation of nitric oxide biosynthetic process				5	4.80E-02	3.6
Response to corticosterone stimulus	4	4.60E-02	4.9			
Response to protein stimulus				12	2.20E-02	2.2
Response to unfolded protein				9	2.90E-02	2.5
Response to virus				12	2.30E-02	2.2