

SUPPLEMENTAL DIGITAL CONTENT 7: NGS-ANALYSES AND GENE INFORMATION ABOUT DIFFERENTIALLY EXPRESSED GENES IN LIPEDEMA

TABLE: DOWNREGULATED GENES IN LIPEDEMA STAGE I

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000177875	CCDC184	Coiled-Coil Domain- Containing Protein 184	-1,86	0,00000117	Protein Coding gene of unknown function	

TABLE: UPREGULATED GENES IN LIPEDEMA STAGE II

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG0000064886	CHI3L2	Chitinase 3 Like 2	2,233	0,000084404	Involved in regulation of cobalamin deficiency in adipocytes	(Ogunkolade, Adaikalakoteswari et al. 2022)
ENSG0000077585	GPR137B	G Protein-Coupled Receptor 137B	1,008	0,000089576	Involved in cellular response to cell growth and energy	(Gan, Seki et al. 2019)
ENSG00000173372	C1QA	Complement C1q A Chain	1,416	0,000000771	Factor of the complement system, regulator of inflammation of adipose tissue	(Lei, Seldin et al. 2017)
ENSG00000289692		Novel Protein	1,561	0,000000499	Unknown function	
ENSG00000159189	C1QC	Complement C1q C Chain	1,464	0,000002735	Factor of the complement system, regulator of inflammation of adipose tissue	(Lei, Seldin et al. 2017)

ENSG00000173369	C1QB	Complement C1q B Chain	1,811	0,000000036	component of complement system. Might be involved in metabolic processes in obesity	(Das, Ma et al. 2015)
ENSG00000066294	CD84	CD84 Molecule	1,423	0,000000000	Modulates the recruitment and differentiation of immune cells. regulates immunoglobulin epsilon receptor signaling in mast cells.	(Alvarez-Errico, Oliver-Vila et al. 2011)
ENSG00000291141	M12793	unknown	2,964	0,000061208	Similar to embigin pseudogene 1	
ENSG00000284180	MIR3606	MicroRNA 3606	0,857	0,000057437	unknown	
ENSG00000244122	UGT1A7	UDP Glucuronosyltransferase Family 1 Member A7	5,128	0,000092879	Known to be involved in the regulation of adipose tissue formation of lipedema	(Ishaq, Bandara et al. 2022)

ENSG00000136689	IL1RN	Interleukin 1 Receptor Antagonist	2,729	0,000108648	Anti-inflammatory antagonist of interleukin-1 family important to inhibit immune dysregulation and uncontrolled inflammation.	(Lopez-Ortega, Moreno-Corona et al. 2022)
ENSG00000145107	TM4SF19	Transmembrane 4 L Six Family Member 19	3,546	0,000016314	Might be involved in various cellular processes including cell proliferation, motility, and adhesion; might be involved in inflammation of adipose tissue.	(Ding, Li et al. 2020);
ENSG00000182578	CSF1R	Colony Stimulating Factor 1 Receptor	1,104	0,000002175	cell-surface receptor for CSF1 and IL34 regulating cell survival, proliferation and differentiation Activates signaling pathways like the MAP/ ERK and the JNK pathway as well as the STAT3 and STAT5. Might be involved in inflammatory processes in obesity. Soluble CSF1 is increased in blood samples of patients with lipedema.	(Wei, Nandi et al. 2010); (Guo, Bertola et al. 2019); (Nandipati, Subramanian et al. 2017); (Nankam, Cornely et al. 2022)
ENSG00000196743	GM2A	Ganglioside GM2 Activator	0,892	0,000119171	Known to be a marker of adipose tissue	(Lee, Norheim et al. 2016)

ENSG00000095970	TREM2	Triggering Receptor Expressed On Myeloid Cells 2	3,241	0,000091596	Binds to lipoproteins and phospholipids; activator of the immune response in macrophages; involved in the regulation of osteoclast differentiation and inflammation in adipocytes.	(Sudom, Talreja et al. 2018); (Bouchon, Dietrich et al. 2000); (Paloneva, Mandelin et al. 2003); (Chavakis, Alexaki et al. 2023)
ENSG00000124491	F13A1	Coagulation Factor XIII A Chain	1,413	0,000004902	Factor of the blood coagulation cascade. Might be associated with adipocyte metabolism and inflammation.	(Kaartinen, Arora et al. 2020)
ENSG00000244255		novel complement component 2 (C2) and complement factor B (CFB) protein	1,636	0,000127859	unknown.	
ENSG00000166278	C2	Complement C2	1,674	0,000016485	Factor of the classical pathway of the complement system, regulator of inflammation of adipose tissue	(Kaye, Lokki et al. 2017)
ENSG00000236120	lncRNA LINC03070	Long Intergenic Non-Protein Coding RNA 3070	1,943	0,000000248	unknown	

ENSG00000155659	VSIG4	V-Set And Immunoglobulin Domain Containing 4	1,743	0,000000397	Modulator of immune response	
ENSG00000038945	MSR1	Macrophage Scavenger Receptor 1	1,769	0,000050673	Might be a regulator of osteoporosis and obesity. Involved in Inflammation.	(Kogelman, Cirera et al. 2014)
ENSG00000166927	MS4A7	Membrane Spanning 4-Domains A7	1,356	0,000000330	Marker of adipose tissue macrophages	(Capel, Klimcakova et al. 2009)
ENSG00000134955	SLC37A2	Solute Carrier Family 37 Member 2	2,086	0,000009390	cytoplasmic glucose transporter, might be involved in the immune response of macrophages in inflammation processes of adipocytes	(Kim, Tillison et al. 2007)
ENSG00000110079	MS4A4A	Membrane Spanning 4-Domains A4A	1,322	0,000010101	Might be involved in inflammation of adipose tissue	(Capel, Klimcakova et al. 2009)

ENSG00000110077	MS4A6A	Membrane Spanning 4-Domains A6A	1,101	0,000008332	Might be involved in inflammation of adipose tissue	(Capel, Klimcakova et al. 2009)
ENSG00000137491	SLCO2B1	Solute Carrier Organic Anion Transporter Family Member 2B1	1,462	0,000007802	Marker of preadipocytes and adipocytes	(Karakus, Schmid et al. 2022)
ENSG00000165457	FOLR2	Folate Receptor Beta	1,208	0,000003954	Might bind to folic acid. Folate might be involved in metabolism of adipocytes	(Chan, Chan et al. 2022)
ENSG00000110324	IL10RA	Interleukin 10 Receptor Subunit Alpha	1,236	0,000000007	Cell surface receptor with anti-inflammatory function	(Yoon, Logsdon et al. 2006)
ENSG00000260314	MRC1	Mannose Receptor C-Type 1	1,222	0,000012811	The MRC1/CD68 Ratio is correlating with adiponectin level.	(Moreno-Navarrete, Ortega et al. 2013)

ENSG00000187164	SHTN1	Shootin 1	0,923	0,000079118	Might be involved in neuronal function of nociceptors	(Zeidler, Kummer et al. 2021)
ENSG00000060982	BCAT1	Branched Chain Amino Acid Transaminase 1	1,623	0,000000063	Involved in catabolism of amino acids, associated with inflammation	(Papathanassiou, Ko et al. 2017)
ENSG00000256482	lncRNA	Novel Transcript, Antisense To BCAT1	2,715	0,000002258	unknown	
ENSG00000010610	CD4	CD4 Molecule	1,005	0,000018921	Membrane protein regulating immune response	
ENSG00000177575	CD163	CD163 Molecule	1,795	0,000012761	Membrane protein regulating immune response	

ENSG00000100600	LGMN	Legumain	0,957	0,000083476	Might be involved in osteoblasts and adipocytes differentiation	(Jafari, Qanie et al. 2017)
ENSG00000276168	RN7SL1	RNA Component Of Signal Recognition Particle 7SL1	1,212	0,000080161	unknown	
ENSG00000129226	CD68	CD68 Molecule	1,333	0,000053934	Membrane protein regulating immune response. The MRC1/CD68 Ratio is correlating with adiponectin level.	(Moreno-Navarrete, Ortega et al. 2013)
ENSG00000204103	MAFB	MAF BZIP Transcription Factor B	0,852	0,000021651	Regulator of lipid accumulation, adipocyte differentiation and inflammation	(Pettersson, Acosta et al. 2015)
ENSG00000090659	CD209	CD209 Molecule	1,660	0,000000026	Membrane protein regulating immune response	

ENSG00000288669	Novel Protein, Readthrough CD209 - CLEC4G	Uncharacterized Protein	1,662	0,000001818	unknown	
ENSG00000186818	LILRB4	Leukocyte Immunoglobulin Like Receptor B4	2,215	0,000000583	Inhibitory receptor of immune response, Receptor for lipoproteins	(Yang, Qian et al. 2022); (Deng, Gui et al. 2018)
ENSG00000102575	ACP5	Acid Phosphatase 5, Tartrate Resistant	2,016	0,000005519	Involved in bone development, adipogenesis and proliferation of adipocytes	(Lang, Patlaka et al. 2021)
ENSG00000093072	ADA2	Adenosine Deaminase 2	0,895	0,000016730	Might be involved in the Regulation of metabolism	(Miller, Clark et al. 2019)

TABLE: DOWNREGULATED GENES IN LIPEDEMA STAGE II

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000163017	ACTG2	Actin Gamma 2, Smooth Muscle	-4,62410488	0,000018	Might be involved in regulation of adipose tissue in a hormonal dependent manner	(Corton, Botella-Carretero et al. 2007)
ENSG00000136546	SCN7A	Sodium Voltage-Gated Channel Alpha Subunit 7	-3,76155132	0,000050	Might be involved in the regulation of pain	(Ke, He et al. 2012)
ENSG00000151967	SCHIP1	Schwannomin Interacting Protein 1	-0,93438102	0,000026	Neuronal signalling	
ENSG00000283154	IQCJ-SCHIP1	IQCJ-SCHIP1 Readthrough Transcript Protein	-1,00171241	0,000001	interacts with the Neurofibromatosis type 2 (NF2) protein	(Kwasnicka-Crawford, Carson et al. 2006)
ENSG00000064651	SLC12A2	Solute Carrier Family 12 Member 2	-1,99905012	0,000097	Might be involved in neuropathic pain	(Delpire, Wolfe et al. 2016); (Laird, Garcia-Nicas et al. 2004)

ENSG00000120729	MYOT	Myotilin	-1,79337528	0,000131	Involved in muscle cell stability	
ENSG00000164764	SBSPON	Somatomedin B And Thrombospondin Type 1 Domain Containing	-3,54005673	0,000048	Regulating protein of metabolism	
ENSG00000137872	SEMA6D	Semaphorin 6D	-1,13486186	0,000133	Might be regulating PPARG and could be involved in inflammation	(Kang, Nakanishi et al. 2018)
ENSG00000140538	NTRK3	Neurotrophic Receptor Tyrosine Kinase 3	-1,44531483	0,000075	Might be involved in regulation of adipocytes hypertrophy	(Bove, Monto et al. 2021)
ENSG00000263335		Novel Transcript, Antisense to MYH11, lncRNA	-3,56426668	0,000051	unknown	

ENSG00000133392	MYH11	Myosin Heavy Chain 11	-3,550069	0,000085	Motor protein	
ENSG00000276564	lncRNA Lnc-ERCC4-3	Novel Transcript, lncRNA	-2,1701041	0,000016	unknown	
ENSG00000130176	CNN1	Calponin 1	-4,10671	0,000032	Secreted factor of pre-adipocytes involved in angiogenesis	(Yang, Li et al. 2023)
ENSG00000288827	lncRNA Sense Intronic to DHX34	Novel Transcript, Sense Intronic to DHX34, lncRNA	-2,0141476	0,000121	unknown	

TABLE: UPREGULATED GENES IN LIPEDEMA STAGE III

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000172260	NEGR1	Neuronal Growth Regulator 1	0,772	0,0000483222	<p>Predicted to be involved in feeding behavior and locomotory behavior.</p> <p>NEGR1 regulates cellular fat content and lipid trafficking in white adipose tissue,</p> <p>Is involved in catabolism with sex specific alterations</p>	<p>(Boender, van Gestel et al. 2014),</p> <p>(Yoo, Joo et al. 2022),</p> <p>(Kaare, Mikheim et al. 2021)</p>
ENSG00000116774	OLFML3	Olfactomedin Like 3	0,941	0,0000416149	<p>Involved in dorsoventral patterning during early development and matrix-related function.</p> <p>Regulator of angiogenesis, lymphangiogenesis, pericyte coverage in cancer and tumor-associated macrophage recruitment.</p>	(Stalin, Imhof et al. 2021)
ENSG00000228536	lncRNA	LYPLAL1 Antisense RNA 1	1,479	0,0000544394	Regulates adipogenic differentiation of human mesenchymal stem cells	(Yang, Fan et al. 2021)
ENSG00000158869	FCER1G	Fc epsilon receptor Ig	1,465	0,0000106411	<p>Might be involved in Inflammation</p> <p>Involved in adipocyte metabolism and lipogenesis</p>	(Palming, Gabriellsson et al. 2006)

ENSG00000072694	FCGR2B	Fc Gamma Receptor IIb	1,051	0,0000043087	Receptor for the Fc region involved in phagocytosis and modulation of antibody production by B-cells. Involved in adipocyte metabolism	(Palming, Gabriellsson et al. 2006)
ENSG00000173369	C1QB	Complement C1q B Chain	1,262	0,0000906077	component of complement system. Mediator of the Interaction of C1q with the Fc regions of IgG or IgM antibody. Might be involved in metabolic processes in obesity	(Das, Ma et al. 2015)
ENSG00000066294	CD84	CD84 Molecule	1,636	0,0000000004	Modulates the recruitment and differentiation of immune cells. regulates immunoglobulin epsilon receptor signaling in mast cells.	(Alvarez-Errico, Oliver-Vila et al. 2011)
ENSG00000081985	IL12RB2	Interleukin 12 Receptor Subunit Beta 2	1,667	0,0000110795	Receptor for interleukin-12. Involved in JAK2/STAT4 pathway. Regulates proliferation of immune cells. Might be involved in adipose tissue inflammation.	(Kawai, Autieri et al. 2021)
ENSG00000136689	IL1RN	Interleukin 1 Receptor Antagonist	2,205	0,0000581751	Anti-inflammatory antagonist of interleukin-1 family important to inhibit immune dysregulation and uncontrolled inflammation.	(Lopez-Ortega, Moreno-Corona et al. 2022)
ENSG00000235897	lncRNA	TM4SF19 Antisense RNA 1	3,410	0,0001305345	Might be involved in cancer pathogenesis and cell proliferation	(Yu, Wang et al. 2022)

ENSG00000163751	CPA3	Carboxypeptidase A3	1,568	0,0001089757	Might be involved in regulation of Inflammation of adipocytes.	(Koh, Choi et al. 2020)
ENSG00000144959	NCEH1	Neutral Cholesterol Ester Hydrolase 1	1,599	0,0000243316	Might be involved in ether lipid metabolic process and in SMAD protein signal transduction	(Chiang, Niessen et al. 2006);
ENSG00000145107	TM4SF19	Transmembrane 4 L Six Family Member 19	4,248	0,0000049059	Might be involved in various cellular processes including cell proliferation, motility, and adhesion; might be involved in inflammation of adipose tissue	(Ding, Li et al. 2020)
ENSG00000240661	BTNL12P	Butyrophilin Like 12, Pseudogene	0,764	0,0000905021	unknown	
ENSG00000138669	PRKG2	Protein Kinase CGMP-Dependent 2	2,277	0,0000781957	regulator of intestinal secretion and bone growth, as well as activator of the kinases of the MAPK/ERK pathway in osteoblasts regulating adipogenesis and osteoblastogenesis from mesenchymal stem cells	(Diaz-Gonzalez, Wadhwa et al. 2022); (Yi, Wu et al. 2021)
ENSG00000145685	LHFPL2	LHFPL Tetraspan Subfamily Member 2	0,758	0,0000915985	member of the lipoma HMGIC fusion partner (LHFP) gene family of unknown function	(Zhao, Zhou et al. 2016)
ENSG00000164611	PTTG1	PTTG1 Regulator Of Sister Chromatid Separation, Securin	2,686	0,0000010748	Regulator of chromosome stability and apoptosis. Might be involved in adipocyte differentiation.	(Espina, Mendez-Vidal et al. 2009)
ENSG00000182578	CSF1R	Colony Stimulating Factor 1 Receptor	1,203	0,0000012736	cell-surface receptor for CSF1 and IL34 regulating cell survival, proliferation and differentiation macrophages and monocytes, plays an important role in immunity and inflammation, involved	(Wei, Nandi et al. 2010); (Guo, Bertola et al. 2019); (Nandipati, Subramanian et al. 2017);

					in bone development. Activates signaling pathways like the MAP/ ERK and the JNK pathway as well as the STAT3 and STAT5. Might be involved in inflammatory processes in obesity. CSF1 is increased in blood samples of patients with lipedema	(Nankam, Cornely et al. 2022)
ENSG00000170458	CD14	CD14 Molecule	1,116	0,0000010656	Mediator of immune response, involved in differentiation, inflammation and lipid metabolism of adipocytes.	(Estruch, Bancells et al. 2013); (Fernandez-Real, Perez del Pulgar et al. 2011)
ENSG00000145569	OTULINL	OTU Deubiquitinase With Linear Linkage Specificity Like	0,934	0,0000228417	Might be involved in autoinflammatory diseases	(Aksentijevich and Zhou 2017)
ENSG00000095970	TREM2	Triggering Receptor Expressed On Myeloid Cells 2	3,428	0,0000396164	Binds to lipoproteins and phospholipids; activator of the immune response in macrophages; involved in the regulation of osteoclast differentiation and inflammation in adipocytes.	(Sudom, Talreja et al. 2018); (Bouchon, Dietrich et al. 2000); (Paloneva, Mandelin et al. 2003); (Chavakis, Alexaki et al. 2023)
ENSG00000124491	F13A1	Coagulation Factor XIII A Chain	1,447	0,0000002665	Factor of the blood coagulation cascade involved in fibrin, stabilizing fibrin clots. Might be associated with adipocyte metabolism and inflammation.	(Kartinen, Arora et al. 2020)

ENSG00000146070	PLA2G7	Phospholipase A2 Group VII	3,009	0,0000044060	involved in lipid catabolism and inflammation. Might be a mediator in obesity.	(Tjoelker, Wilder et al. 1995); (Cao and Lee 2022)
ENSG00000244255		novel complement component 2 (C2) and complement factor B (CFB) protein	1,427	0,0000015496	unknown.	
ENSG00000243649	CFB	Complement Factor B	1,241	0,0001051277	Factor of the alternative complement system, involved in proliferation and differentiation of immune cells, might be involved in adipocyte maturation	(Matsunaga, Iwashita et al. 2018)
ENSG00000166278	C2	Complement C2	1,500	0,0000126342	Factor of the classical pathway of the complement system, regulator of inflammation of adipose tissue	(Kaye, Lokki et al. 2017)
ENSG00000106066	CPVL	Carboxypeptidase Vitellogenic Like	1,087	0,0000004500	Might be involved lysosomal degradation and inflammation of adipose tissue.	(Kartinen, Arora et al. 2020)
ENSG00000136235	GPNMB	Glycoprotein Nmb	1,334	0,0000053534	unknown	
ENSG00000236120	lncRNA LINC03070	Long Intergenic Non-Protein Coding RNA 3070	2,408	0,0000034569	unknown	
ENSG00000155659	VSIG4	V-Set And Immunoglobulin Domain Containing 4	1,632	0,0000040008	Modulator of immune response	
ENSG00000165168	CYBB	Cytochrome B-245 Beta Chain	1,120	0,0000036905	component of a respiratory chain.	
ENSG00000189233	NUGGC	Nuclear GTPase, Germinal Center Associated	2,604	0,0000161425	Might be involved in cellular processes of apoptosis and cell cycle.	
ENSG00000134028	ADAMDEC1	ADAM Like Decysin 1	4,183	0,0001069346	belonging to the disintegrin	(Jasso, Jaiswal et al. 2022)

					metalloproteinase family. Might be involved in ECM remodelling	
ENSG00000069482	GAL	Galanin And GMAP Prepropeptide	5,583	0,0001358686	Endocrine hormone of the central and peripheral nervous systems regulating growth hormone and insulin release and adrenal secretion.	(Zhang, Fang et al. 2017)
ENSG00000197629	MPEG1	Macrophage Expressed 1	0,888	0,0000111580	Involved in immune response:	(McCormack, de Armas et al. 2015)
ENSG00000134955	SLC37A2	Solute Carrier Family 37 Member 2	1,706	0,0000000816	cytoplasmic glucose transporter, might be involved in the immune response of macrophages in inflammation processes of adipocytes	(Kim, Tillison et al. 2007)
ENSG00000254979	Novel Protein	Solute Carrier Family 43 Member	0,869	0,0000131522	unknown	
ENSG00000134802	SLC43A3	Solute Carrier Family 43, Member 3	0,783	0,0000284415	Nucleobase transporter, Might be regulate fatty acid transport in adipocytes	(Hasbargen, Shen et al. 2020)
ENSG00000110079	MS4A4A	Membrane Spanning 4-Domains A4A	1,243	0,0000410402	Might be involved in inflammation of adipose tissue	(Capel, Klimcakova et al. 2009)
ENSG00000177363	LRRN4CL	LRRN4 C-Terminal Like	0,940	0,0000536505	unknown	
ENSG00000110077	MS4A6A	Membrane Spanning 4-Domains A6A	1,023	0,0000212315	Might be involved in inflammation of adipose tissue	(Capel, Klimcakova et al. 2009)
ENSG00000165457	FOLR2	Folate Receptor Beta	1,236	0,0000428971	Might bind to folic acid. Folate might be involved in metabolism of adipocytes	(Chan, Chan et al. 2022)

ENSG00000110324	IL10RA	Interleukin 10 Receptor Subunit Alpha	1,215	0,0000000048	Cell surface receptor with anti-inflammatory function	(Yoon, Logsdon et al. 2006)
ENSG00000149534	MS4A2	Membrane Spanning 4-Domains A2	1,367	0,0000346694	Might be involved in Inflammation	(Cruse, Kaur et al. 2010)
ENSG00000122870	BICC1	BicC Family RNA Binding Protein 1	1,050	0,0000266395	regulator of Wnt signaling pathway	(Kraus, Clauin et al. 2012)
ENSG00000198246	SLC29A3	Solute Carrier Family 29 Member 3	1,311	0,0000518546	Nucleosid transporter across lysosomal and mitochondrial membranes	(Baldwin, Yao et al. 2005)
ENSG00000060982	BCAT1	Branched Chain Amino Acid Transaminase 1	1,648	0,0000000005	Involved in catabolism of amino acids, associated with inflammation	(Papathanassiou, Ko et al. 2017)
ENSG00000256482	lncRNA	Novel Transcript, Antisense To BCAT1	2,613	0,0001184082	unknown	
ENSG00000159403	C1R	Complement C1r	0,917	0,0001325241	Factor of the classical pathway of the complement system.	
ENSG00000139329	LUM	Lumican	1,487	0,0000042820	Proteoglycan that binds to collagen fibrils and glycosaminoglycans. Might be involved in ECM remodelling in adipose tissue	(Wolff, Taranko et al. 2019) (Guzman-Ruiz, Tercero-Alcazar et al. 2020)
ENSG00000010610	CD4	CD4 Molecule	1,134	0,0000000520	Membrane protein regulating immune response	
ENSG00000177575	CD163	CD163 Molecule	1,645	0,0000001228	Membrane protein regulating immune response	
ENSG00000171860	C3AR1	Complement C3a Receptor 1	1,456	0,0000009417	Receptor for complement factor	
ENSG00000182326	C1S	Complement C1s	0,993	0,0000163763	Complement factor of the classical pathway	

ENSG00000102802	MEDAG	Mesenteric Estrogen Dependent Adipogenesis	1,032	0,0001758196	Involved in processes that promote adipocyte differentiation, lipid accumulation, and glucose uptake in mature adipocytes	(Zhang, Chen et al. 2012)
ENSG00000169508	GPR183	G Protein-Coupled Receptor 183	1,230	0,0001400237	Receptor regulating immune response, related to cholesterol metabolism and bone development.	(Hannedouche, Zhang et al. 2011); (Bened-Jensen, Smethurst et al. 2011)
ENSG00000137804	NUSAP1	Nucleolar And Spindle Associated Protein 1	2,112	0,0000000013	Microtubule-associated protein	
ENSG00000166147	FBN1	Fibrillin 1	1,263	0,0000400748	extracellular matrix component, related to adipogenesis	(Davis, Arner et al. 2016)
ENSG00000102962	CCL22	C-C Motif Chemokine Ligand 22	3,194	0,0000019038	May play a role in immune response	
ENSG00000140931	CMTM3	CKLF Like MARVEL Transmembrane Domain Containing 3	0,772	0,0000931464	chemokine-like factor	
ENSG00000129226	CD68	CD68 Molecule	1,370	0,0000121498	Membrane protein regulating immune response	
ENSG00000271605	MILR1	Mast Cell Immunoglobulin Like Receptor 1	1,874	0,0000040404	Immunoglobulin-like receptor involved in mast cells response	
ENSG00000230113	lncRNA	Novel Transcript	1,270	0,0001493932	unknown	
ENSG00000161921	CXCL16	C-X-C Motif Chemokine Ligand 16	0,977	0,0000599116	May play a role in immune response	
ENSG00000132205	EMILIN2	Elastin Microfibril Interfacer 2	1,245	0,0000029998	Involved the formation of the elastic fiber, ECM remodelling and mesenchymal stem cell differentiation.	(Da Ros, Persano et al. 2022);

						(Schiavinato, Keene et al. 2016)
ENSG00000090659	CD209	CD209 Molecule	1,572	0,0000022585	Membrane protein regulating immune response	
ENSG00000288669	Novel Protein, Readthrough CD209 - CLEC4G	Uncharacterized Protein	1,528	0,0000537204	unknown	
ENSG00000186818	LILRB4	Leukocyte Immunoglobulin Like Receptor B4	1,984	0,0000000629	Inhibitory receptor of immune response, Receptor for lipoproteins	(Yang, Qian et al. 2022); (Deng, Gui et al. 2018)
ENSG00000102575	ACP5	Acid Phosphatase 5, Tartrate Resistant	2,102	0,0000004423	Involved in bone development, adipogenesis and proliferation of adipocytes	(Lang, Patlaka et al. 2021)
ENSG00000275395	FCGBP	Fc Gamma Binding Protein	2,459	0,0000084735	May be involved in the mucosal homeostasis	

TABLE: DOWNREGULATED GENES IN LIPEDEMA STAGE III

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000177133	LncRNA PRDM16-DT	PRDM16 Divergent Transcript	-1,9814	0,0000159	Might be a regulator of brown adipogenesis	(Ding, Lim et al. 2018)
ENSG00000152642	GPD1L	Glycerol-3- Phosphate Dehydrogenase 1 Like	-0,8709	0,0000377	Involved in cellular energy production, GPD1L is upregulated during weight loss and downregulated during weight gain.	(He, Sun et al. 2017)
ENSG00000183837	PNMA3	PNMA Family Member 3	-1,5514	0,0000245	Neuronal protein associated with paraneoplastic development.	(Schuller, Jenne et al. 2005)
ENSG00000180785	OR51E1	Olfactory Receptor Family 51 Subfamily E Member 1	-2,0924	0,0000060	Odorant receptor, may play a role as metabolic regulator	(Jovancevic, Dendorfer et al. 2017)
ENSG00000177875	CCDC184	Coiled-Coil Domain Containing 184	-1,8538	0,0001733	Might be a neuronal protein	(Pensold and Zimmer 2018)

ENSG00000290912	HERC2 Pseudogene7	unknown	-1,7645	0,0000465	
ENSG00000270885	RASL10B	RAS Like Family 10 Member B	-2,1481	0,0000760	Predicted to be involved in positive regulation of peptide hormone secretio, might have tumor suppressor potential. (Zou, Hu et al. 2006)
ENSG00000166582	CENPV	Centromere Protein V	-0,9364	0,0001042	Involved in the organization of chromosomes
ENSG00000183963	SMTN	Smoothelin	-1,3777	0,0001102	Structural protein of the cytoskeleton

TABLE: UPREGULATED GENES: BMI-CORRECTED SUBGROUP ANALYSIS IN LIPEDEMA ST. II

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000173369	C1QB	Complement C1q B Chain	1.60753988015826	0,000003	Component of complement system. Mediator of the Interaction of C1q with the Fc regions of IgG or IgM antibody. Might be involved in metabolic processes in obesity	(Das, Ma et al. 2015)
ENSG00000287763	lncRNA Lnc-PLGLB1-6/-9	Novel Transcript lncRNA	4.1402539463962	0,000005	unknown	
ENSG00000130226	DPP6	Dipeptidyl Peptidase Like 6	4.73230218430268	0,000001	Regulates the expression of potassium channels	(Seikel and Trimmer 2009)
ENSG00000177575	CD163	CD163 Molecule	1.53318226851322	0,000002	Membrane protein regulating immune response	

TABLE: DOWNREGULATED GENES: BMI-CORRECTED SUBGROUP ANALYSIS IN LIPEDEMA ST. III

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000178568	ERBB4	Erb-B2 Receptor Tyrosine Kinase 4	-2,42	0,0000007	Might be involved in adipocyte differentiation. Might be downregulated in obesity. Pro-angiogenic factor.	(Wang, Zhang et al. 2022); (Nugroho, Ikeda et al. 2018)
ENSG00000284931	Novel Protein	Globin Family Profile Domain-Containing Protein	-5.83	0,0000008	unknown	
ENSG00000196565	HBG2	Hemoglobin Subunit Gamma 2	-4,97	0,000004	Part of neonatal Hemoglobin	

TABLE: UPREGULATED GENES: BMI-CORRECTED SUBGROUP ANALYSIS IN LIPEDEMA ST. III

GENE CODE	Gene	Name	log FC	p-value	Function	Citation
ENSG00000066294	CD84	CD84 Molecule	1,36	0,000005	Modulates the recruitment and differentiation of immune cells. regulates immunoglobulin epsilon receptor signaling in mast cells.	(Alvarez-Errico, Oliver-Vila et al. 2011)
ENSG00000060982	BCAT1	Branched Chain Amino Acid Transaminase 1	1,74	0,000002	Involved in catabolism of amino acids, associated with inflammation	(Papathanassiou, Ko et al. 2017)
ENSG00000139329	LUM	Lumican	1,52	0,000005	Proteoglycan that binds to collagen fibrils and glycosaminoglycans. Might be involved in ECM remodelling in adipose tissue	(Wolff, Taranko et al. 2019) (Guzman-Ruiz, Tercero-Alcazar et al. 2020)
ENSG00000177575	CD163	CD163 Molecule	1,71	0,000000002	Membrane protein regulating immune response	
ENSG00000090659	CD209	CD209 Molecule	1,43	0,000004	Membrane protein regulating immune response	

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