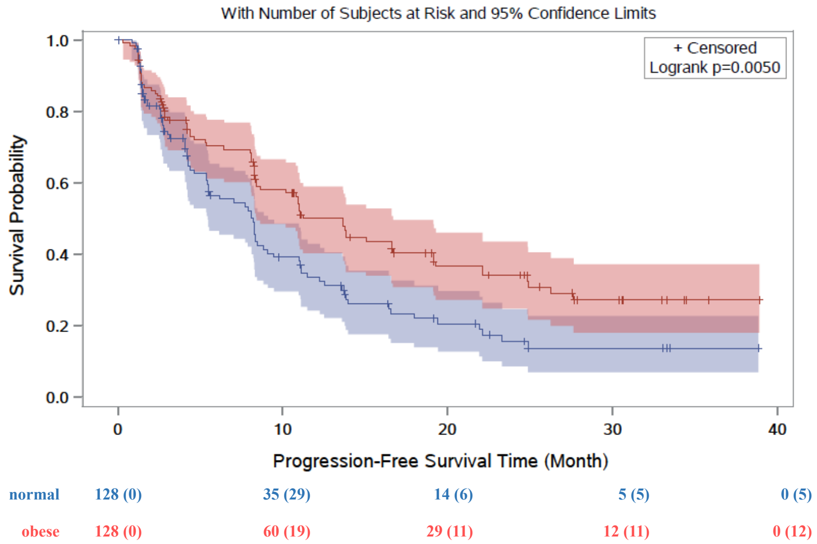
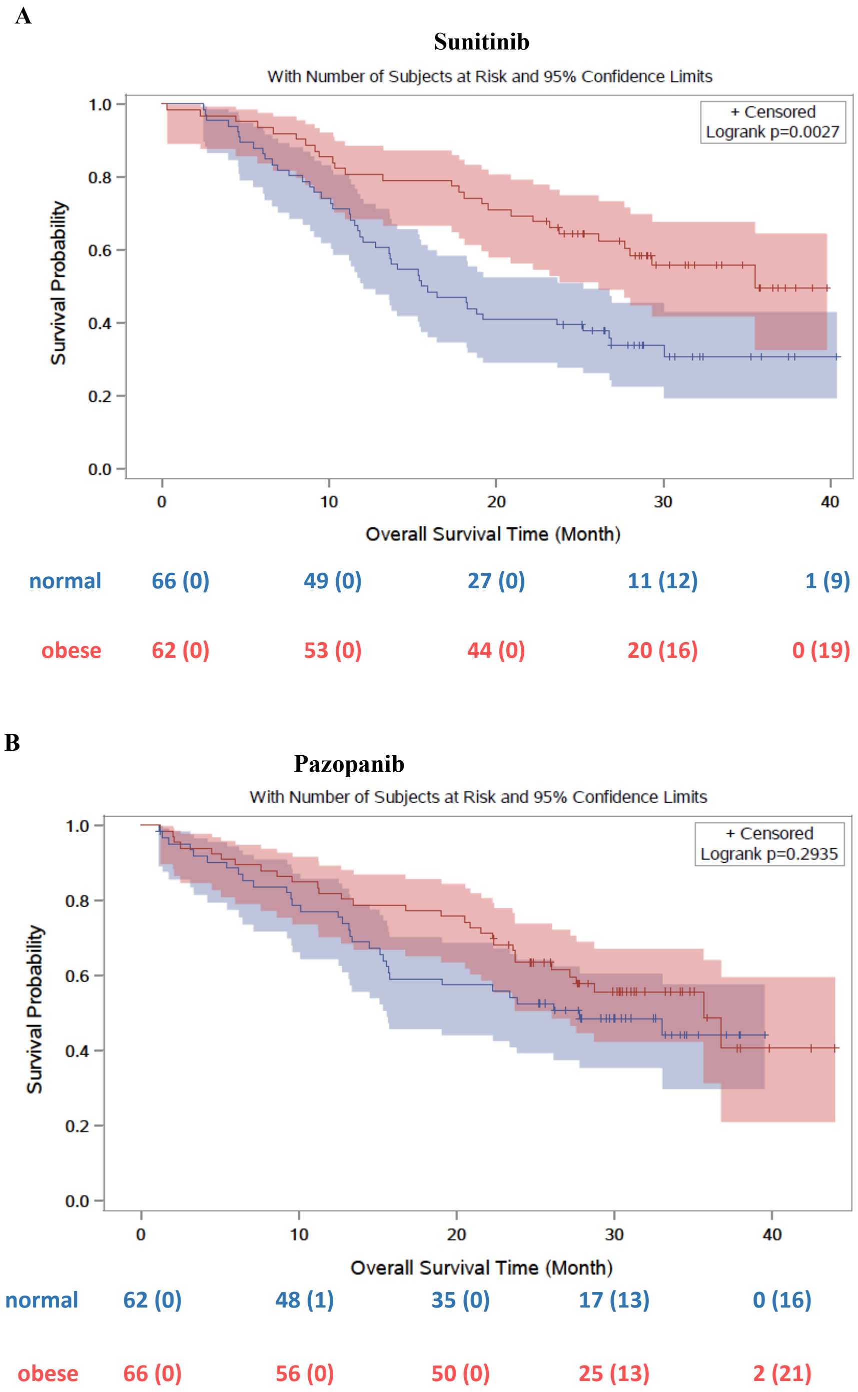
***Supplementary figure 1*: Obese patients in the COMPARZ cohort have improved PFS compared to normal weight patients.** Kaplan-Meier curve suggesting differences in PFS between obese and normal weight patients in the COMPARZ clinical trial. PFS=progression-free survival.



***Supplementary figure 2 (A-B):* COMPARZ analysis of overall survival by BMI stratified by treatment arm.**
Kaplan-Meier curves demonstrating differences in OS between obese vs. normal weight patients in the COMPARZ clinical trial treated with (A) sunitinib and (B) pazopanib. OS=overall survival. BMI=body mass index. The survival advantage of obese is more pronounced in the Sunitinib arm than the Pazopanib arm.



***Supplementary Figure 3 (A-C):* Obesity is associated with improved survival outcomes in the TCGA, COMPARZ, and MSK immunotherapy (IO) cohorts by three BMI categories**

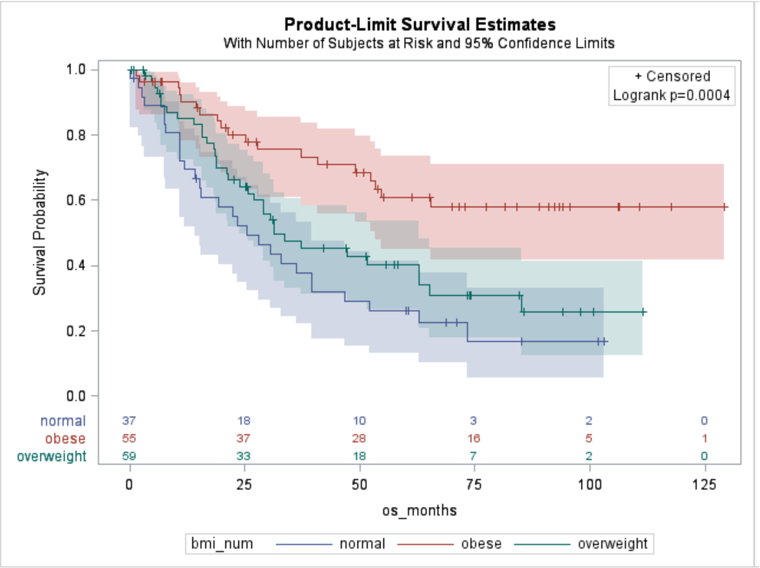
Unadjusted Kaplan-Meier curves demonstrating differences in OS between normal and obese patients in the (A) TCGA, (B) COMPARZ, and (C) MSK immunotherapy (IO) cohorts. HR=hazard ratio. aHR = adjusted HR. CI=confidence interval. OS=overall survival. TCGA=The Cancer Genome Atlas clear cell kidney cancer. MSK=Memorial Sloan Kettering. NR=not reached.

*TCGA cohort was adjusted for stage and grade. COMPARZ and MSK IO cohorts adjusted for IMDC alone.

^The association of BMI with overall survival in the MSK IO cohort was no longer statistically significant after adjustment for IMDC.

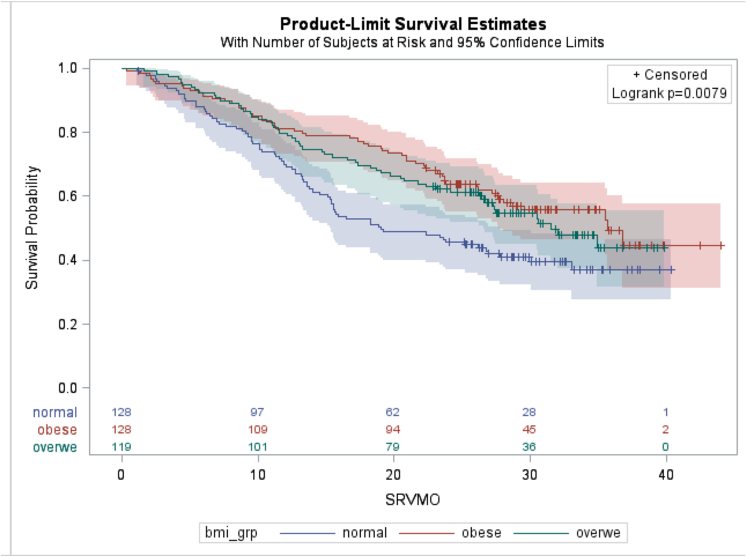
A

TCGA

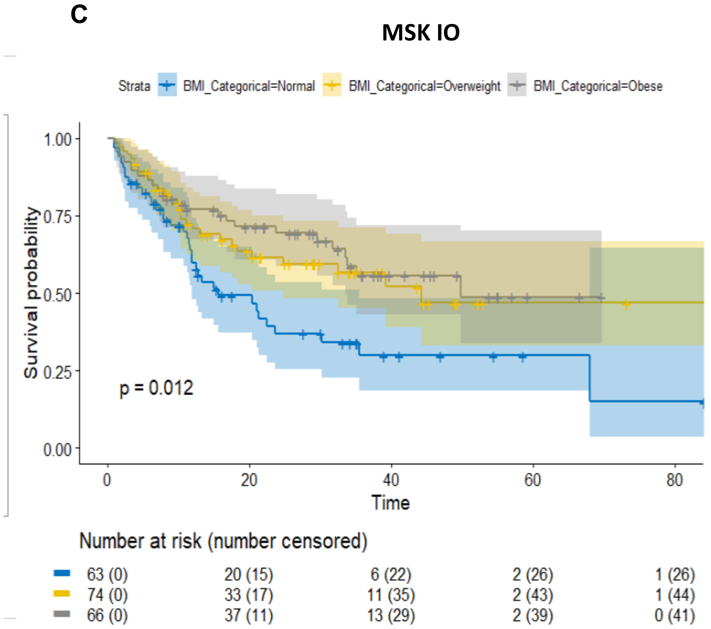


B

COMPARZ



C

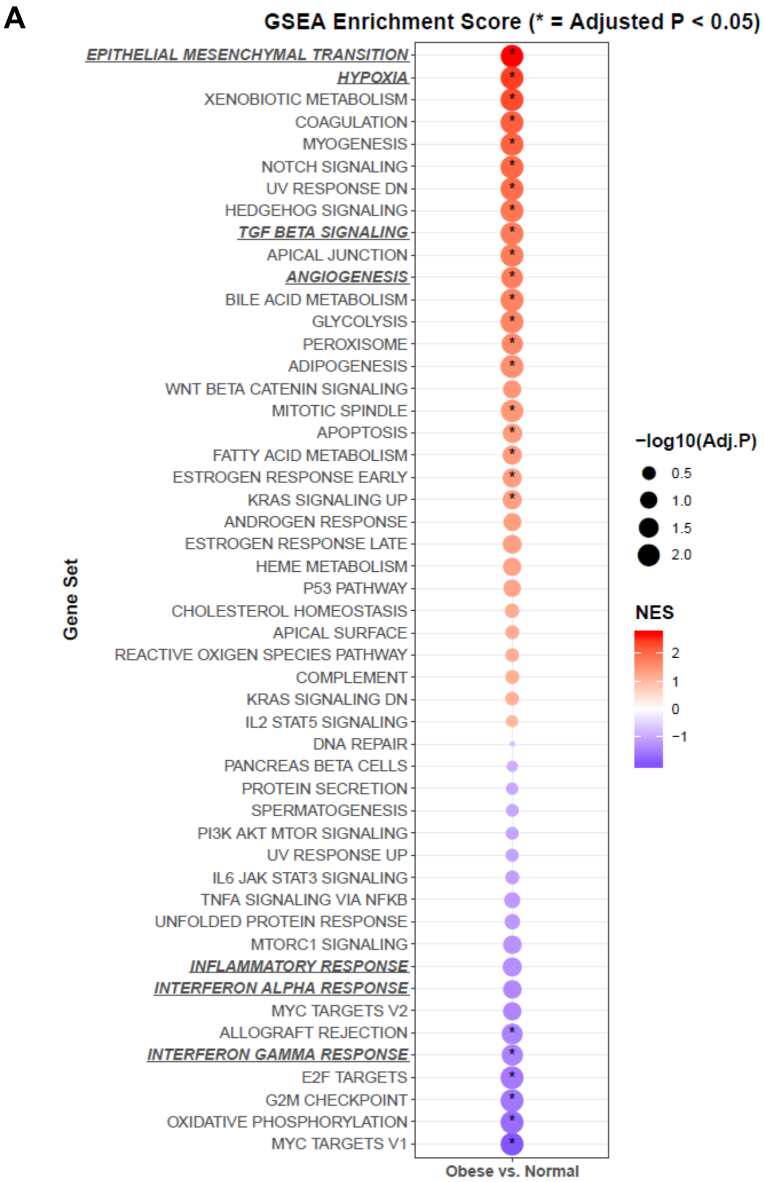


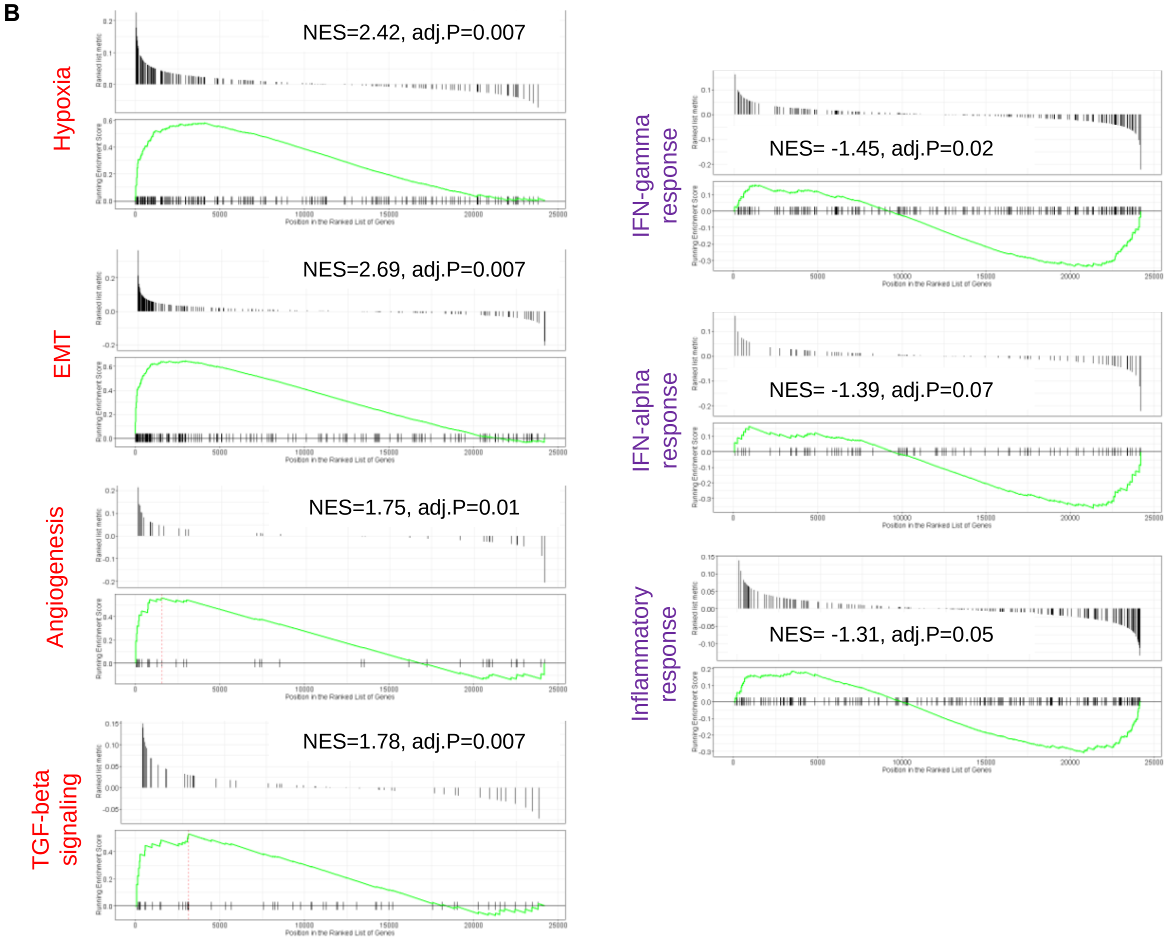
MSK IO

Number at risk (number censored)

🟦	63 (0)	20 (15)	6 (22)	2 (26)	1 (26)
🟨	74 (0)	33 (17)	11 (35)	2 (43)	1 (44)
⬛	66 (0)	37 (11)	13 (29)	2 (39)	0 (41)

Supplementary Figure 4 (A-B): **ccRCC tumors among obese patients in the COMPARZ cohort harbor significantly different transcriptomic gene signatures compared to normal weight patients**
(A) GSEA analysis of Hallmark gene sets comparing differences between obese versus normal weight patients. Specific pathways of interest are italicized and underlined in the legend (B) Enrichment plots for gene expression pathways highlighted in (A). Enrichment scores are ranked and colored based on the NES and sized by the -log10 transformed value of the adjusted p-value. Colors signify the directionality and strength of enrichment, red=up and purple=down. GSEA=gene set enrichment analysis. NES=normalized enrichment score. TGF=transcription factor. EMT=epithelial mesenchymal transition. IFN=interferon.

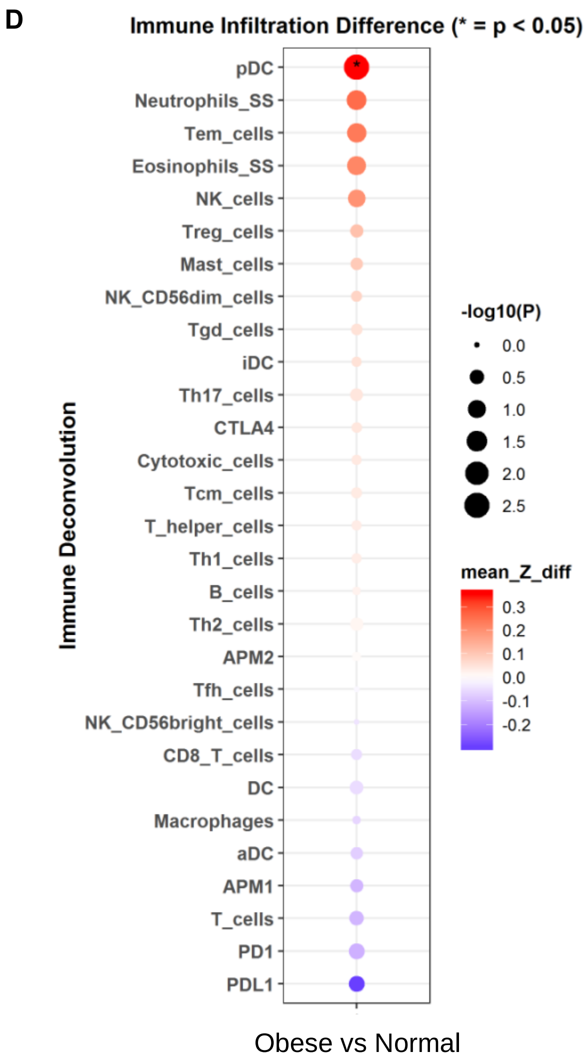



B
Hypoxia
NES=2.42, adj.P=0.007
EMT
NES=2.69, adj.P=0.007
Angiogenesis
NES=1.75, adj.P=0.01
TGF-beta signaling
NES=1.78, adj.P=0.007
IFN-gamma response
NES= -1.45, adj.P=0.02
IFN-alpha response
NES= -1.39, adj.P=0.07
Inflammatory response
NES= -1.31, adj.P=0.05
Ranked list metric
Running Enrichment Score
Position in the Ranked List of Genes
0
5000
10000
15000
20000
25000

,

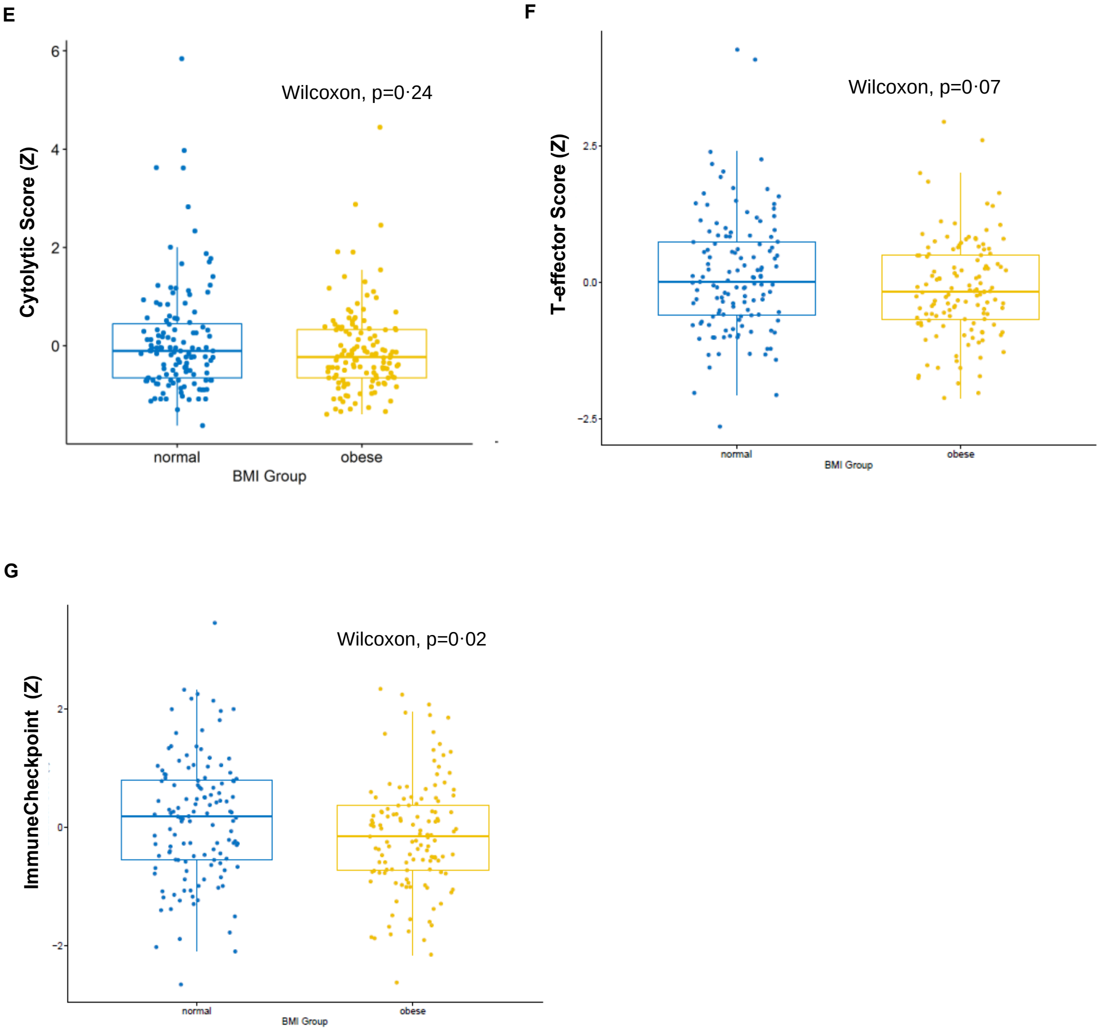
Supplementary Figure 4 (D): **Obese patients in the COMPARZ cohort harbor minimal differences in the tumor immune microenvironment compared to normal weight patients**

(D) Demonstrates ssGSEA immune deconvolution utilized to test the differences in specific immune cell populations and immune check-point molecules between obese and normal weight patients in the COMPARZ cohort. mean_Z_diff=mean z-score difference. Colors signify the directionality of infiltration changes, red=up and purple=down. The size of the circle corresponds to the negative value of log10(P). P=Wilcoxon–Mann–Whitney test p value. Immune deconvolution terms are defined in supplementary table 2.



Supplementary Figure 4 (E-G): **Obese patients in the COMPARZ cohort harbor minimal differences in the tumor immune microenvironment compared to normal weight patients**

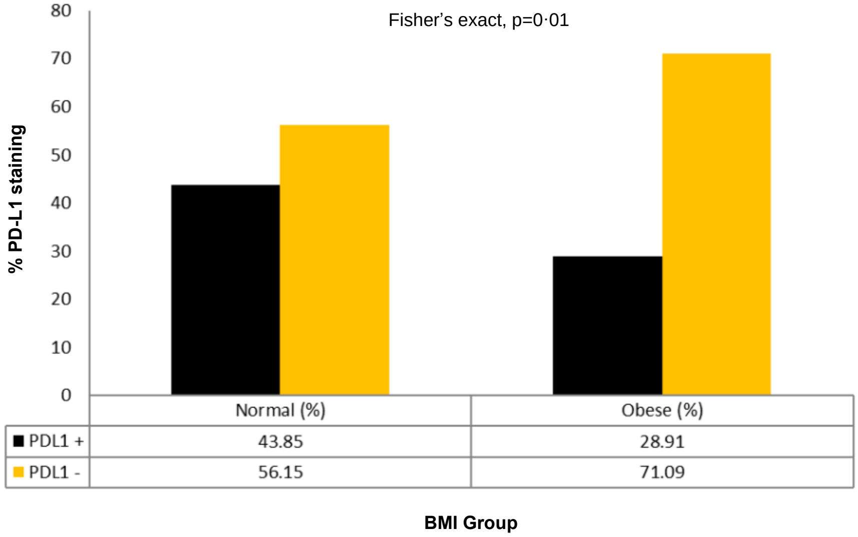
Box plots demonstrating insignificant differences in (E) cytolytic score, (F) T-effector score, and significant differences in (G) immune checkpoint score between obese (n=128) and normal weight (n=128) patients in the COMPARZ cohort. Z=z-score. Wilcoxon=Wilcoxon–Mann–Whitney test. Z=z-score.



***Supplementary Figure 4 (H):* Obese patients in the COMPARZ cohort harbor minimal differences in the tumor immune microenvironment compared to normal weight patients**

(H) Demonstrates differences in tumoral PD-L1 expression by immunohistochemistry staining between obese (n=128) and normal weight (n=130) patients in the COMPARZ cohort

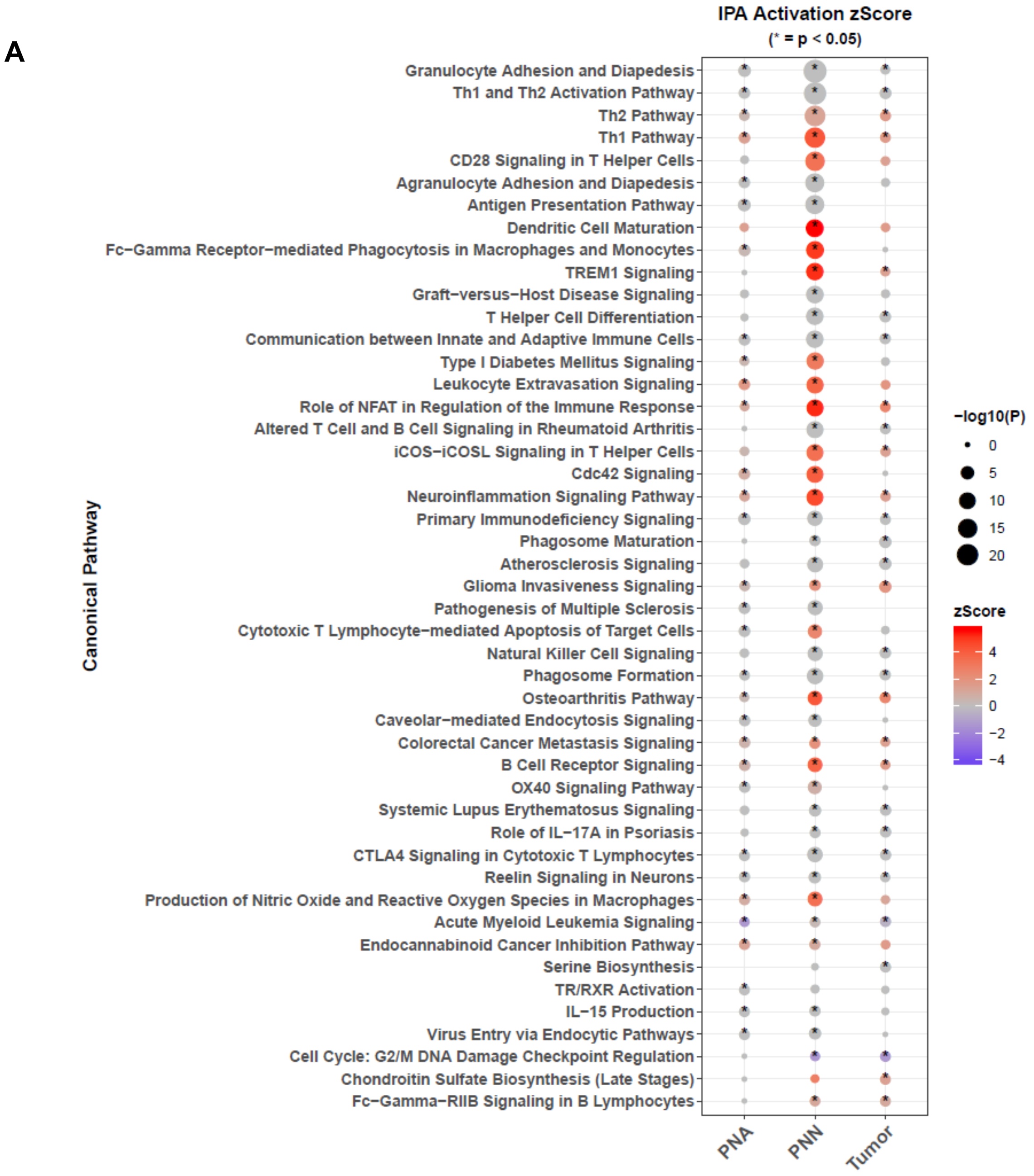
H



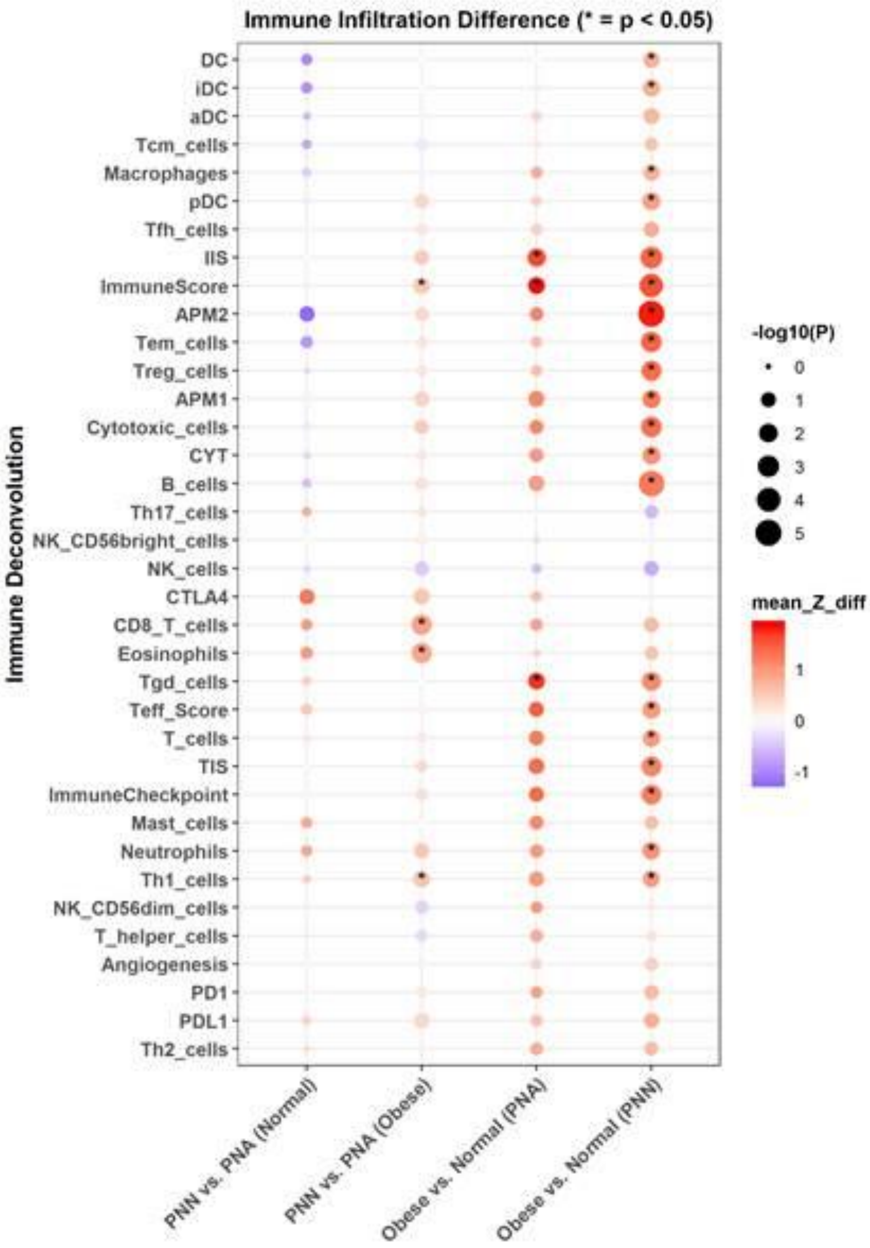
	Normal (%)	Obese (%)
■ PDL1 +	43.85	28.91
🟨 PDL1 -	56.15	71.09

Supplementary Figure 5 (A-B): **Perinephric fat of obese patients demonstrates increased inflammation and hypoxia compared to normal weight patients**

In the MSK prospective cohort of non-metastatic ccRCC patients we performed (A) merged 20 most significantly enriched IPA Canonical Pathways from each comparison between obese and normal weight in perinephric fat and tumor. Positive and negative z-score indicate activated and inactivated signaling of the pathway respectively. (B) immune infiltration (ssGSEA score) comparisons between PNN and PNA samples in obese and normal weight as well as between obese and normal weight in perinephric fat samples. PNA=perinephric fat away. PNN=perinephric fat near. IPA=Ingenuity Pathway Analysis. zScore=IPA predicted pathway activation score. Mean Z diff=mean z score difference. P=nominal p value. The size of the circle corresponds to the negative value of log10(P). Colors signify the directionality and strength of enrichment, red=up and purple=down. CYT=cytolytic score. Immune deconvolution terms are defined in supplementary table 2.

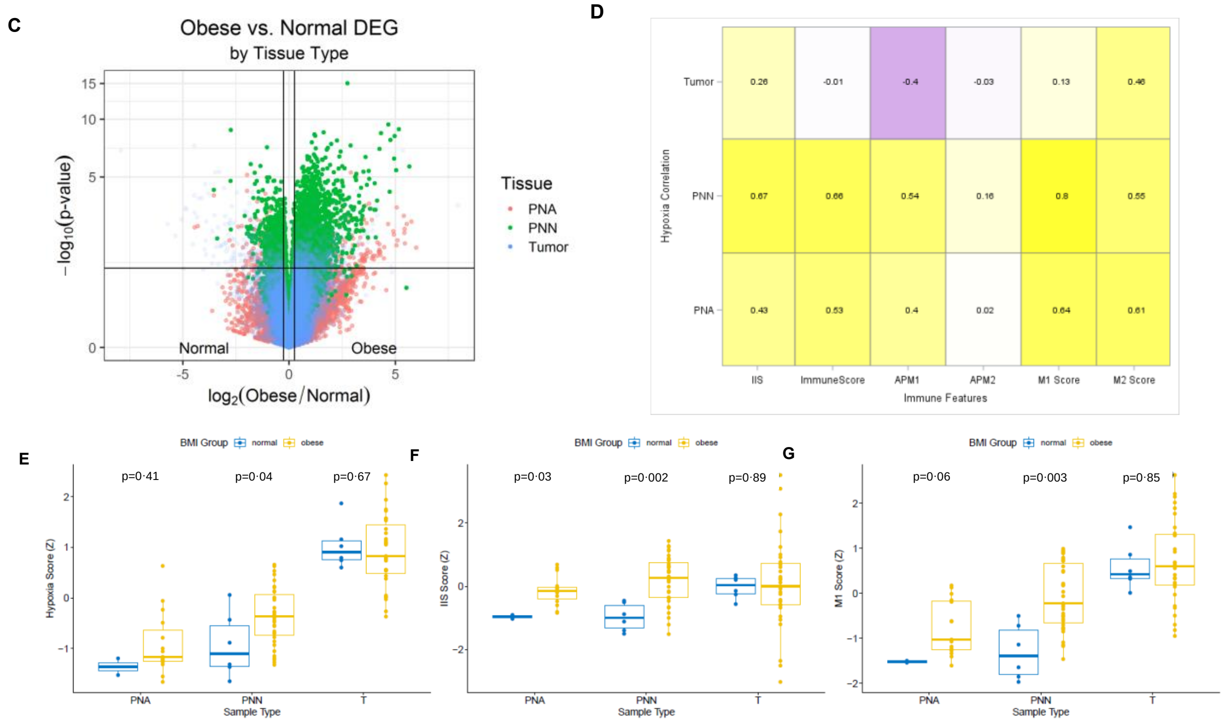


B

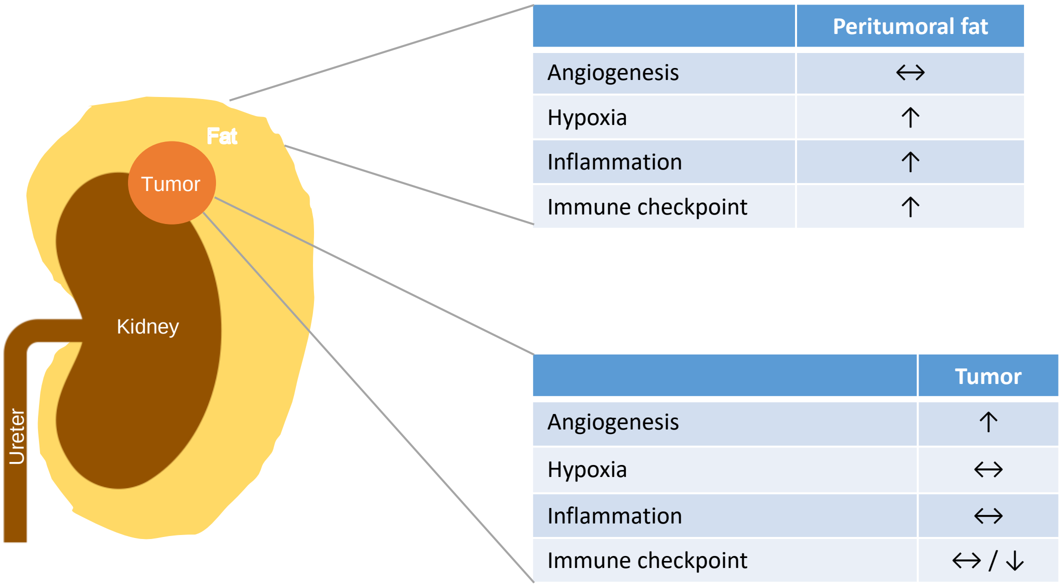

Immune Infiltration Difference (* = p < 0.05)
Immune Deconvolution
DC
iDC
aDC
Tcm_cells
Macrophages
pDC
Tfh_cells
IIS
ImmuneScore
APM2
Tem_cells
Treg_cells
APM1
Cytotoxic_cells
CYT
B_cells
Th17_cells
NK_CD56bright_cells
NK_cells
CTLA4
CD8_T_cells
Eosinophils
Tgd_cells
Teff_Score
T_cells
TIS
ImmuneCheckpoint
Mast_cells
Neutrophils
Th1_cells
NK_CD56dim_cells
T_helper_cells
Angiogenesis
PD1
PDL1
Th2_cells
PNN vs. PNA (Normal)
PNN vs. PNA (Obese)
Obese vs. Normal (PNA)
Obese vs. Normal (PNN)
-log10(P)
0
1
2
3
4
5
mean_Z_diff
1
0
-1

Supplementary Figure 5 (C-G): **Perinephric fat of obese patients demonstrates increased inflammation and hypoxia compared to normal weight patients**

In the MSK prospective cohort of non-metastatic ccRCC patients, (C) Volcano plot demonstrating gene expression differences between obese and normal weight patients in tumor and perinephric fat. (D) Spearman correlation between the deconvolved hypoxia score and immune feature scores. Box plots demonstrating differences in (E) hypoxia, (F) IIS, and (G) M1 scores between obese and normal weight in PNA, PNN, and tumor. PNA=perinephric fat away. PNN=perinephric fat near. T=tumor. IIS=immune infiltration score. APM1=antigen presenting machinery 1. APM2=antigen presenting machinery 2. M1 score=type 1 macrophage. M2 score=type 2 macrophage. Z=z-score.



***Supplementary Figure 5 (H):* Summary of findings in the tumor and peritumoral fat of obese compared to normal weight patients**
In the MSK prospective cohort of non-metastatic ccRCC patients, (H) Summary of gene expression findings.



	Peritumoral fat
Angiogenesis	↔
Hypoxia	↑
Inflammation	↑
Immune checkpoint	↑

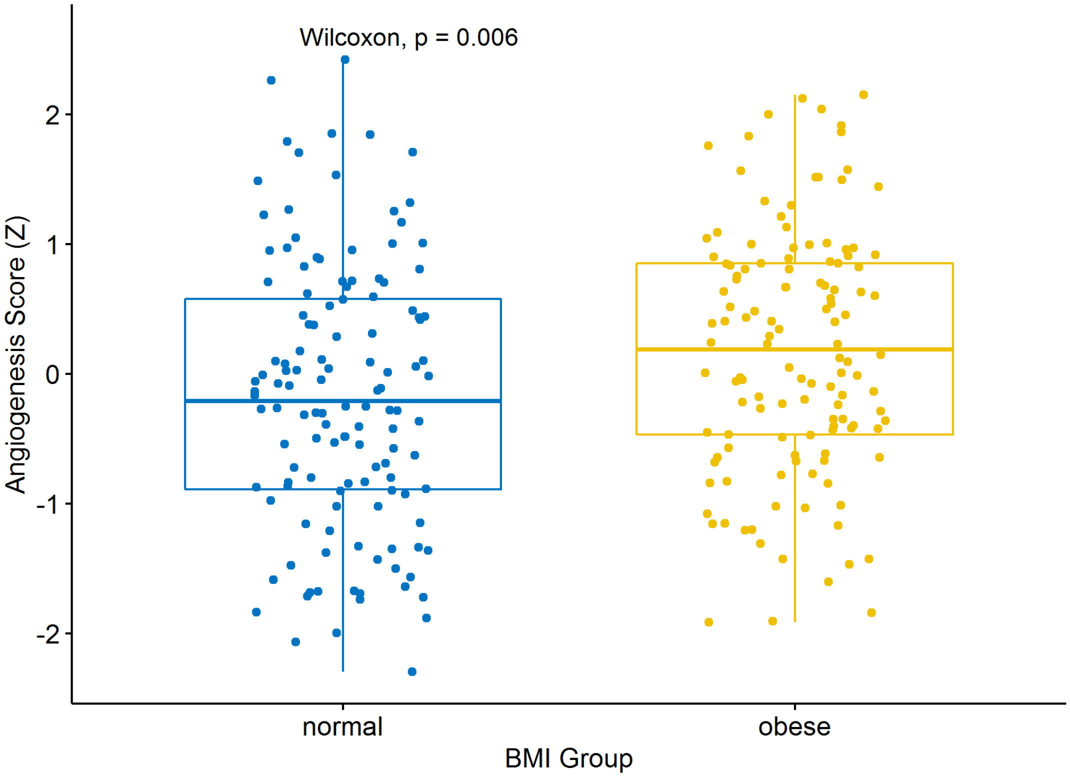
	Tumor
Angiogenesis	↑
Hypoxia	↔
Inflammation	↔
Immune checkpoint	↔ / ↓

Supplementary figure 6(A-B): **Obese patients have higher tumor angiogenesis scores compared to normal weight patients (p=0.006)**
(A) Angiogenesis gene signatures and corresponding genes within each signature (B) Box plot suggesting differences in tumor angiogenesis scores between obese (n=128) vs normal weight (n=128) patients in the COMPARZ clinical cohort using the McDermott, et al. (Nat Med, 2018) angiogenesis signature.

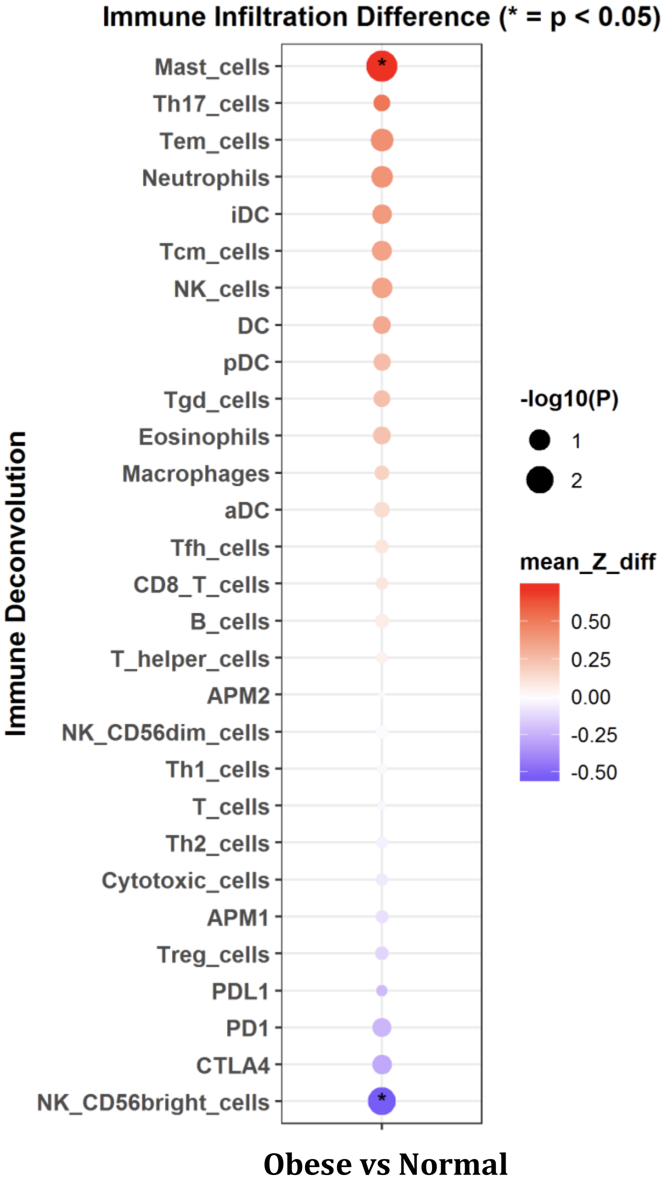
A

Signature	**Genes**
MSigDB Angiogenesis signature	*APOH, APP, CCND2, COL3A1, COL5A2, CXCL6, FGFR1, FSTL1, ITGAV, JAG1, JAG2, KCNJ8, LPL, LRPAP1, LUM, MSX1, NRP1, OLR1, PDGFA, PF4, PGLYRP1, POSTN, PRG2, PTK2, S100A4, SERPINA5, SLCO2A1, SPP1. STC1, THBD, TIMP1, TNFRSF21, VAV2, VCAN, VEGFA, VTN*
Masiero et. al angiogenesis signature	*A2M,ACVRL1,APLNR,CDH5,COL15A1,EDNRB,EBF1,S1PR1,ENG,GNG11,LRRC32,ITGA9,KDR,PECAM1,PTPRB,ZNF423,CNRIP1,ADGRA2,TEK,LDB2,TIE1,CLEC3B,SPARCL1,RGS5,CALCRL,VWF,JAM2,PLVAP,ADGRL4,MYCT1,PDGFD,EMCN,RHOJ,ROBO4,ADGRF5,GIMAP8,CLEC14A,TM4SF18,ADCY4,ESAM,ECSCR*
McDermott, et al. angiogenesis signature	*VEGFA, KDR, ESM1, PECAM1, ANGPLTL4, CD34*

B



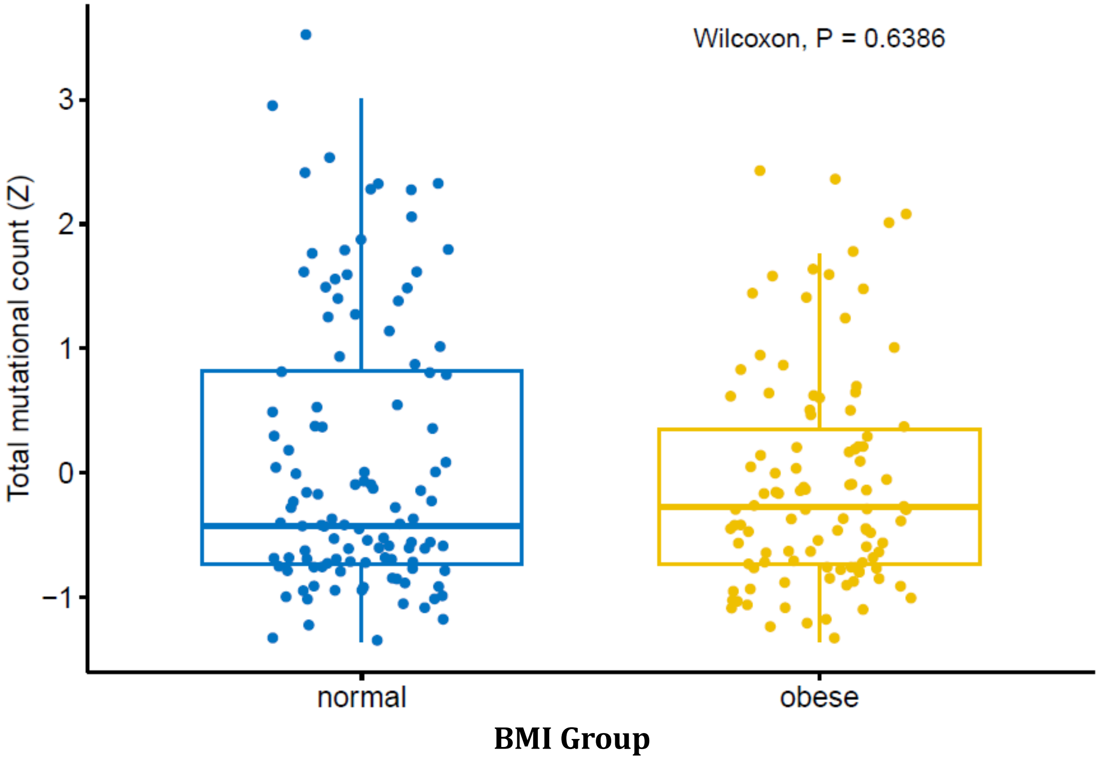
Supplementary figure 7: **Tumor immune deconvolution in TCGA AJCC stage III/IV cohort**
TCGA=The Cancer Genome Atlas clear cell kidney cancer. Mean_Z_diff=mean z-score difference. P=Wilcoxon–Mann–Whitney test p value. IIS=immune infiltration score. TIS=T-cell infiltration score. Immune deconvolution terms are defined in supplementary table 2. The size of the circle corresponds to the negative value of log10(P). Colors signify the directionality of immune infiltration differences of obese compared to normal weight where red=up and purple=down.



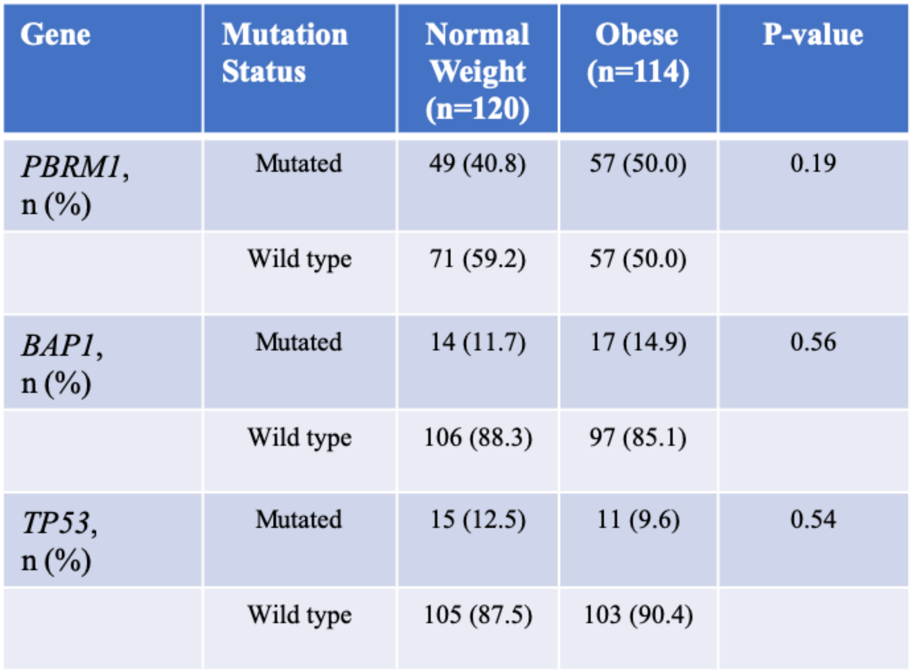
***Supplementary figure 8 (A-B)*: There are no differences in tumor mutational burden or in common gene mutations by BMI in the COMPARZ clinical trial**

(A) Box plot suggests no significant differences by BMI in tumor mutational burden (p=0.64). (B) Similarly, there were no significant differences in commonly mutated ccRCC genes PBRM1, BAP1 and TP53 by BMI category (all p-values>0.05). P-values derived using the Fisher's exact test. BMI=body mass index.

A



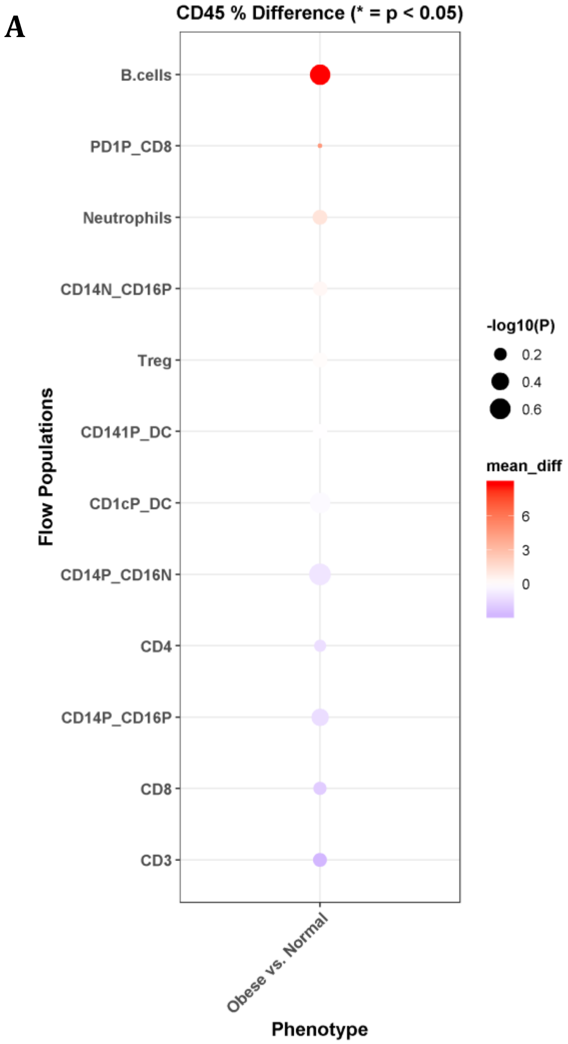
B



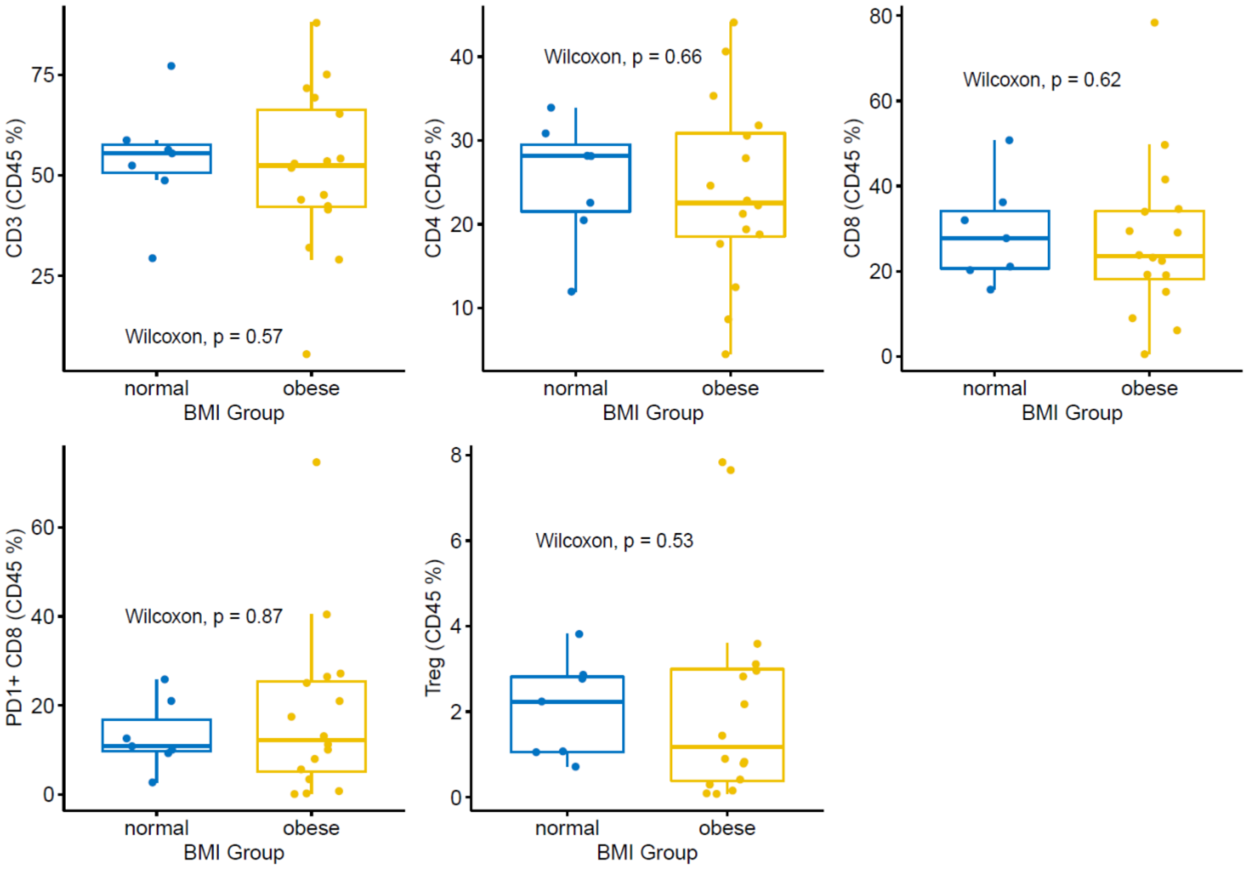
Gene	Mutation Status	Normal Weight (n=120)	Obese (n=114)	P-value
PBRM1, n (%)	Mutated	49 (40.8)	57 (50.0)	0.19
	Wild type	71 (59.2)	57 (50.0)	
BAP1, n (%)	Mutated	14 (11.7)	17 (14.9)	0.56
	Wild type	106 (88.3)	97 (85.1)	
TP53, n (%)	Mutated	15 (12.5)	11 (9.6)	0.54
	Wild type	105 (87.5)	103 (90.4)	

***Supplementary figure 9 (A-F):* No significant differences in immune cell populations in normal weight vs obese patient tumors analyzed by flow cytometry.**

Major immune populations within primary tumors from a cohort of normal weight (n=7) and obese (n=16) patients were evaluated by flow cytometry. (A) Shows overall differences in indicated immune populations between obese versus normal patients where the size of the circle corresponds to the negative value of log10(P). Colors signify the directionality of immune infiltration differences of obese compared to normal weight where red=up and purple=down. (B) specifically shows infiltration levels of T cell populations in obese and normal weight patients. All cell populations are expressed as a percentage of CD45$_{+}$ cells and further defined as follows: B-cells (CD19+), CD3 (T-cells; SSC$_{lo}$, CD3+), CD8 (CD8 T cells; SSC$_{lo}$, CD3+, CD8+), PD1P_CD8 (PD-1+ CD8 T cells), CD4 (CD4 T cells; SSC$_{lo}$, CD3+ CD4+ FoxP3-), Treg (Regulatory T cells; CD4 T cells; SSC$_{lo}$, CD3+ CD4+ FoxP3+), neutrophils (CD3-CD19-CD15+, SSC$_{hi}$), monocytes/macrophages (CD3-CD19-HLA-DR+ cells that are CD14+CD16-, CD14+CD16+ or CD14-CD16+; designated CD14P_CD16N, CD14P_CD16P or CD14N_CD16P respectively), conventional dendritic cell subsets 1 or 2 (CD3-CD19-CD14-CD16-HLA-DR+ cells that are CD141+ or CD1a+ respectively).



B



CD3 (CD45 %)
75
50
25
Wilcoxon, p = 0.57
normal
obese
BMI Group
CD4 (CD45 %)
40
30
20
10
Wilcoxon, p = 0.66
normal
obese
BMI Group
CD8 (CD45 %)
80
60
40
20
0
Wilcoxon, p = 0.62
normal
obese
BMI Group
PD1+ CD8 (CD45 %)
60
40
20
0
Wilcoxon, p = 0.87
normal
obese
BMI Group
Treg (CD45 %)
8
6
4
2
0
Wilcoxon, p = 0.53
normal
obese
BMI Group

***Supplementary table 1*: Clinicopathologic characteristics of prospective perinephric fat study**

	N=62
Age, median (SD)	58·9 (17·1)
Male, n (%)	48 (77·4)
BMI, median (SD)	31·3 (7·5)
BMI category, n (%)	
Normal	6 (9·7)
Overweight	20 (32·2)
Obese	36 (58·1)
AJCC Stage, n (%)	
I	38 (61·3)
II	1 (1·6)
III	23 (37·1)

BMI=body mass index. SD=standard deviation.

Supplementary table 2: **Immune deconvolution legend.**

Th17	Th17 helper T cells
NK_cells	Natural killer cells
Teff_score	T effector score
Th1	Th1 helper T cells
T_helper_cells	All T-helper cells
CYT	Cytolytic score
IIS	Immune infiltration score
TIS	T-cell infiltration score
APM1	Antigen presenting machinery 1
APM2	Antigen presenting machinery 2
Tem	T effector memory
Tcm	T central memory
iDC	Immature dendritic cells
aDC	Activated dendritic cell
NK_CD56_bright_cells	Innate lymphoid cells
Tfh	T follicular helper cells
pDC	plasmacytoid dendritic cells
NK_CD56_dim_cells	Conventional natural killer cells
Tgd	T gamma-delta cells

Supplementary table 3. Assessment of body mass index as a continuous variable and impact on overall survival across cohorts

Cohort	Hazard Ratio	95% Confidence Intervals	
COMPARZ	0.97	0.95	1.00
TCGA	0.92	0.88	0.97
MSK IO	0.94	0.90	0.98

Supplementary table 4. Assessment of the association of BMI with overall survival in the MSK IO cohort after adjustment for IMDC risk criteria and sex. BMI reference=normal. IMDC reference=good. Sex reference=male.

Analysis of Maximum Likelihood Estimates

Parameter		DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits		Label
BMI_Categorical	**Obese**	1	-0.50598	0.29897	2.8644	0.0906	0.603	0.336	1.083	BMI Category Obese
IMDC_Risk	**2**	1	0.41722	0.42582	0.9600	0.3272	1.518	0.659	3.497	IMDC_Risk 2
IMDC_Risk	**3**	1	1.06000	0.49599	4.5674	0.0326	2.886	1.092	7.630	IMDC_Risk 3
Sex		1	-0.28566	0.30062	0.9029	0.3420	0.752	0.417	1.355	Sex

Supplementary table 5. Raw data for COMPARZ GSEA analysis (appendix p 9-10).

Description	Set Size	Enrichment Ecore	NES	p-value	p-adjust	Core Enrichment
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	197	0.644	2.686	0.002	0.007	THY1/TAGLN/SPARC/COL4A1/BGN/COL1A2/COL4A2/MGP/COL3A1/ACTA2/VEGFA/COL1A1/FN1/TIMP3/RHOB/LRP1/PDGFRB/ANPEP/MYL9/TGFBI/CTGF/COL6A3/PMEPA1/CDH6/HTRA1/COL6A2/GJA1/TGFB1/VIM/CXCL12/SLIT3/CALD1/COL5A2/LGALS1/FLNA/FBLN5/COL5A1/ABI3BP/ITGB5/TPM2/NID2/MMP2/ITGA5/ITGB1/DKK1/FMOD/SNAI2/FSTL1/IGFBP4/VCAM1/TIMP1/TPM1/SGCB/NNMT/SDC1/CDH2/QSOX1/TGFBR3/ECM1/BMP1/PCOLCE2/SNTB1/COL5A3/IGFBP3/THBS1/CDH11/LAMC1/NT5E/EDIL3/FBN1/PLOD1/DPYSL3/ELN/GEM/ITGAV/CTHRC1/DST/COL16A1/SPOCK1/CYR61/DAB2/EFEMP2/LAMA2/SERPINH1/SERPINE1/JUN
HALLMARK_GLYCOLYSIS	198	0.394	1.645	0.002	0.007	ANGPTL4/PHKA2/VEGFA/AK4/TGFBI/LDHA/CYB5A/EGLN3/DDIT4/COL5A1/CXCR4/ALDOB/P4HA1/STC1/MXI1/MPI/SDC1/PFKP/ANG/QSOX1/SLC37A4/SOD1/GYS2/IGFBP3/IRS2/CACNA1H/ENO1/PYGL/PPFIA4/G6PD/NT5E/MIF/PLOD1/PAM/HDLBP/AGRN/PC/GYS1/PDK3/RPE/ALDH9A1/GOT1/SDC2/CITED2/GPR87/GNE/TPBG/FAM162A/GLRX/ANKZF1/CHST1/SAP30/ABCB6/PGK1/NOL3/ALDH7A1/TFF3
HALLMARK_XENOBIOTIC_METABOLISM	198	0.554	2.308	0.002	0.007	PDK4/CRP/ENPEP/CES1/HRG/ABCC2/CYB5A/CYP2J2/ABCC3/CAT/UPB1/AQP9/FABP1/CYP2E1/EPHX1/SERPINA6/HNF4A/MBL2/SHMT2/CNDP2/NDRG2/PINK1/AKR1C3/TAT/FMO3/HMOX1/CYP4F2/AOX1/IGFBP4/ENTPD5/ITIH1/CFB/ARG1/ITIH4/AKR1C2/VTN/RBP4/TMBIM6/ECH1/XDH/SLC35D1/ATOH8/GCKR/PMM1/CYP1A2/ADH1C/DHPS/LEAP2/SLC22A1/PLG/BLVRB/PTGR1/ARG2/FETUB/TTPA/JUP/ACO2/HSD17B2/LCAT/PC/HSD11B1/ANGPTL3/REG1A/ACOX2/PDLIM5/ACOX1/ADH5/PTGDS/ETFDH/SERPINE1/ALDH9A1/TDO2/ETS2/F10/ID2/ACP1
HALLMARK_APICAL_JUNCTION	196	0.424	1.768	0.002	0.007	THY1/VWF/PECAM1/MYH9/MYL9/TGFBI/CD34/CDH6/CD99/ACTN1/MSN/NFASC/CX3CL1/ACTN4/MMP2/ITGB1/VCAM1/ICAM2/IKBKG/SHC1/ITGA9/JAM3/MMP9/PCDH1/CLDN18/BMP1/TSPAN4/CALB2/CDH1/CDH11/VCL/CTNND1
HALLMARK_HYPOXIA	196	0.580	2.417	0.002	0.007	BGN/ANGPTL4/PGF/VEGFA/MYH9/PLIN2/ALDOC/ERRFI1/AK4/TGFBI/CTGF/EFNA1/NDRG1/PCK1/LDHA/CCNG2/FOXO3/DDIT4/CA12/PTRF/PFKL/COL5A1/FOS/CXCR4/ALDOB/CDKN1B/NEDD4L/SLC2A5/P4HA1/HMOX1/STC1/MXI1/PKLR/ZFP36/RORA/PFKP/ETS1/EDN2/GPI/SLC37A4/TMEM45A/KLF7/SCARB1/TIPARP/IGFBP3/IRS2/DUSP1/PDK1/ENO1/TGFB3/PPFIA4/MIF/BNIP3L/SELENBP1/PAM/HDLBP/KLF6/ADM/BRS3/PPP1R3C/BTG1/BCL2/CP/GYS1/PDK3/CYR61/SERPINE1/JUN/PDGFB/PHKG1/SDC2/CITED2/SIAH2/LALBA/PFKFB3/TPBG/FAM162A/KDM3A/GLRX/ANKZF1/GRHPR/WSB1/SAP30/AKAP12/PGK1

HALLMARK_MYOGENESIS	199	0.498	2.071	0.002	0.007	TAGLN/SPARC/COL4A2/COL3A1/MYH11/COL1A1/MYH9/IGFBP7/COL6A3/ERBB3/APP/COL6A2/TGFB1/FXYD1/RIT1/AEBP1/CLU/ITGB5/TPM2/CDH13/ITGB1/DES/DMD/APLNR/SORBS1/PLXNB2/ABLIM1/FHL1/MEF2D/NOTCH1/FDPS/IGFBP3/GJA5/CACNA1H/COX6A2/HRC/PPFIA4/MB/SVIL/SMTN/COL15A1/AGRN/PC/PPP1R3C
HALLMARK_ADIPOGENESIS	193	0.370	1.536	0.002	0.007	SPARCL1/COL4A1/ANGPTL4/ENPP2/ORM1/PLIN2/ACAA2/LAMA4/CAT/CCNG2/ACLY/PTRF/PFKL/ITSN1/ADCY6/CMBL/MGLL/SORBS1/CD151/FZD4/BCL6/SCARB1/STOM/SOD1/PHLDB1/ECH1/ACADM/BCKDHA/DHCR7/MGST3/ACADL/COL15A1/ACO2/BAZ2A/LIFR/ETFB/ECHS1
HALLMARK_TGF_BETA_SIGNALING	54	0.531	1.775	0.002	0.007	SPTBN1/ENG/PMEPA1/ID3/LTBP2/TGFB1/PPM1A/SMAD6/ID1/CDH1/THBS1/CTNNB1/SKI/SERPINE1/SMAD7/JUNB/FURIN/ID2
HALLMARK_BILE_ACID_METABOLISM	112	0.446	1.700	0.002	0.007	GC/CAT/AQP9/TTR/SERPINA6/RBP1/AR/SLC27A2/APOA1/SLC23A2/ABCA2/SOD1/ALDH8A1/NR1H4/NR1I2/ALDH1A1/FADS2/CYP7B1/DIO1/EFHC1/AGXT/ALDH9A1/PEX6/HAO1/PECR/RXRA/DHCR24/ABCG8/SCP2/GNMT/CYP39A1
HALLMARK_HEDGEHOG_SIGNALING	35	0.595	1.844	0.002	0.007	THY1/VEGFA/MYH9/NRP1/DPYSL2/LDB1/PTCH1/PLG
HALLMARK_COAGULATION	136	0.539	2.108	0.002	0.007	SPARC/VWF/A2M/PECAM1/FN1/TIMP3/LRP1/TF/HRG/SERPINC1/HTRA1/CPB2/SERPING1/C9/HNF4A/MBL2/CLU/FGA/C8B/HMGCS2/F9/MMP2/HPN/RGN/TIMP1/ITIH1/CRIP2/CFI/CFB/ANG/APOA1/PRSS23/KLF7/MMP9/C8A/APOC3/BMP1/F13B/THBS1/CSRP1/THBD/PLG/FBN1/SERPINA1/CTSO/CASP9/P2RY1/MST1/F2/ACOX2/CFH/PEF1/GSN/SERPINE1/CPN1/KLKB1/FURIN/PDGFB/F10/SERPINB2/MMP8/MMP1
HALLMARK_UV_RESPONSE_DN	141	0.499	1.957	0.002	0.007	COL1A2/COL3A1/COL1A1/PDGFRB/IGFBP5/NRP1/ANXA4/GJA1/COL5A2/FBLN5/CDKN1B/LTBP1/TFPI/SNAI2/NFIB/PTPRM/GRK5/ATP2B4/TGFBR2/MGLL/ID1/TGFBR3/SYNE1/APBB2/DUSP1/LAMC1/FZD2/CDC42BPA/EFEMP1/CDON/PDLIM5/CYR61/DAB2/SERPINE1/SMAD7/RXRA/SDC2/CITED2/PIAS3/LDLR
HALLMARK_NOTCH_SIGNALING	31	0.656	2.008	0.002	0.007	NOTCH3/JAG1/CCND1/HEYL/NOTCH1/KAT2A/TCF7L2/MAML2/ARRB1/DLL1/FZD5/SAP30/FZD1/ST3GAL6/NOTCH2/PSEN2/LFNG
HALLMARK_E2F_TARGETS	198	-0.364	-1.554	0.002	0.007	PRPS1/RAD21/NME1/CDKN1A/MCM7/TRIP13/RFC3/HMMR/CENPM/CDC20/RRM2/PRIM2/MCM2/MKI67/RNASEH2A/KIF18B/NUP107/DUT/CSE1L/SYNCRIP/TIMELESS/NUP205/MLH1/TCF19/SPC25/ATAD2/CHEK2/CDK1/CCNB2/RBBP7/MAD2L1/PCNA/PAICS/RQCD1/SMC4/TMPO/NBN/DCK/ANP32E/POLD2/USP1/TIPIN/MCM4/CDKN2C/CHEK1/TBRG4/SMC6/NCAPD2/TUBG1/DCLRE1B/POLD1/PA2G4/UBE2T/LMNB1/PHF5A/GINS3/MTHFD2/RPA3/DEK/PMS2/NUP153/CKS1B/TOP2A/PRKDC/SRSF2/HUS1/GINS1/NAA38/PLK1/TUBB/UBE2S/BIRC5/HN1/NUDT21/NAP1L1/H2AFX/SLBP/CDK4/TK1/TFRC/IPO7/RAN/HMGA1/KPNA2/GSPT1/CKS2/HMGB3

HALLMARK_G2M_CHECKPOINT	198	-0.370	-1.581	0.002	0.007	LMNB1/CDC45/KIF11/DKC1/H2AFV/BUB1/PTTG3P/CUL4A/CKS1B/EGF/TOP2A/HSPA8/DBF4/E2F3/SRSF2/PRC1/HUS1/PLK1/BCL3/CDC27/UBE2S/MT2A/BIRC5/EFNA5/KPNB1/HN1/UBE2C/TOP1/ODC1/G3BP1/H2AFX/KIF5B/CENPA/SLC7A1/CDK4/SLC38A1/HMGA1/KPNA2/GSPT1/HIF1A/CKS2/HMGB3/SLC7A5
HALLMARK_MYC_TARGETS_V1	197	-0.463	-1.974	0.002	0.007	SMARCC1/USP1/UBE2L3/RNPS1/VDAC3/PSMA2/MCM4/TUFM/UBE2E1/TYMS/SNRPD1/SSB/ERH/NPM1/PSMC6/PABPC4/PA2G4/EIF4E/HNRNPC/HDAC2/PHB/RPS10/CDC45/HSPD1/PHB2/PCBP1/HSP90AB1/SNRPA1/DEK/NCBP2/HNRNPA3/C1QBP/PSMB3/CCT3/PSMA1/SRSF2/PRDX3/YWHAQ/KARS/SRPK1/SLC25A3/IARS/EIF4A1/GOT2/PPM1G/POLE3/EXOSC7/CCT4/ILF2/PSMD14/PSMD1/KPNB1/SRM/RPL22/SNRPB2/XPOT/AIMP2/NAP1L1/NDUFAB1/ODC1/PSMA7/PSMD7/G3BP1/PPIA/PSMA4/PTGES3/EIF1AX/CDK4/ETF1/EIF2S2/CBX3/CCT2/RPS2/RPL14/DDX21/RAN/GLO1/KPNA2/GSPT1/COX5A/SET
HALLMARK_OXIDATIVE_PHOSPHORYLATION	197	-0.402	-1.713	0.002	0.007	NDUFS8/IMMT/ATP6V0B/ATP5D/NDUFA7/COX10/NDUFS3/MRPL35/NDUFA2/ATP6V1E1/SUPV3L1/SDHD/BAX/PDHA1/PRDX3/NDUFB5/NDUFA4/SLC25A3/IDH3A/AIFM1/OPA1/PDP1/PDHB/ATP5B/SDHC/NDUFA9/HCCS/ATP5L/ATP6V0E1/GOT2/UQCRC2/LRPPRC/VDAC2/ATP5G1/UQCRFS1/ATP5C1/COX6A1/ATP5J2/ATP6V1C1/ATP6V1H/DLD/ATP6AP1/NDUFAB1/CS/ATP5E/SUCLG1/ATP5H/NDUFB1/ATP5I/NDUFA3/UQCR11/ATP6V1F/ATP6V1D/NDUFB3/NDUFA1/COX6C/NNT/ATP5G3/CYCS/COX7B/COX5A/ATP6V0C/LDHB/SLC25A5
HALLMARK_MITOTIC_SPINDLE	198	0.344	1.434	0.004	0.010	MYH9/SPTBN1/SORBS2/EZR/SYNPO/FLNA/NET1/ITSN1/ACTN4/NUMA1/ARHGEF12/WASF2/EPB41/PLEKHG2/ARAP3/NEDD9/TUBGCP6/PCNT/NCK2/CAPZB/VCL/HDAC6/CDC42BPA/CENPE/PREX1/CDK5RAP2/KLC1/CTTN/TAOK2/CYTH2/MYO9B/DST/CLIP2/SUN2/PDLIM5/PKD2/MAP3K11/GSN
HALLMARK_ANGIOGENESIS	36	0.559	1.754	0.006	0.015	COL3A1/VEGFA/JAG1/APOH/APP/NRP1/COL5A2/FSTL1/SLCO2A1/STC1/TIMP1/VTN/THBD
HALLMARK_INTERFERON_GAMMA_RESPONSE	196	-0.340	-1.445	0.007	0.017	MTHFD2/IL18BP/CIITA/ICAM1/UBE2L6/PSMB9/PARP12/IL10RA/HLA-B/PSMA3/SRI/IRF5/LAP3/PIM1/HLA-A/MT2A/CXCL11/HLA-DMA/LGALS3BP/IFIH1/SECTM1/CD274/CD38/TNFAIP2/PLSCR1/PSME2/CXCL9/FCGR1A/SLAMF7/CD86/PTPN1/EIF2AK2/HLA-G/CXCL10/SAMHD1/SOCS3/NAMPT/TAP1/RIPK2/UPP1/GZMA/WARS/CCL5/HIF1A/STAT1/IFI27/IFI30
HALLMARK_PEROXISOME	103	0.434	1.634	0.007	0.018	ALB/CAT/DHRS3/TTR/SERPINA6/SLC27A2/EHHADH/SLC23A2/HAO2/SOD1/CEL/FDPS/ECH1/ECI2/NR1I2/ALDH1A1/HSD11B2/PEX5/CNBP/UGT2B17/MSH2/DIO1/ABCB4/ACOX1/ALDH9A1/PEX6/DHCR24/SCP2/FABP6/SOD2

HALLMARK_ALLOGRAFT_REJECTION	200	-0.333	-1.428	0.009	0.021	IRF4/IL6/GBP2/AARS/EIF3A/CCND2/IL12RB1/NLRP3/LYN/IL12B/GALNT1/F2R/CXCR3/ICAM1/ELANE/CCL13/ACHE/EREG/HLA-DMB/PTPRC/CD8B/UBE2D1/FYB/IL2RG/CD3G/BCL3/CCR5/CD47/CD7/CAPG/HLA-A/CSF1/HLA-DMA/IL18/CXCL9/RARS/CTSS/FCGR2B/CD86/IL2RA/CD2/HLA-G/HLA-DOA/SRGN/TAP1/RIPK2/TAP2/CD8A/GZMA/WARS/CXCL13/GPR65/GCNT1/CCR1/CCL5/HIF1A/STAT1/CCL4
HALLMARK_APOPTOSIS	159	0.349	1.401	0.021	0.045	BGN/TXNIP/TIMP3/RHOB/PDGFRB/CCND1/ERBB3/APP/CLU/CDKN1B/MMP2/CASP8/TIMP2/HMOX1/TIMP1/BTG2/NEDD9/TGFBR3/SOD1/HGF/GSTM1/BNIP3L/MADD/CASP9/ADD1/F2/CTNNB1/CREBBP/GSN/JUN/SMAD7/PSEN1/TNF/RARA/SPTAN1/CFLAR/FEZ1/IFITM3/SOD2/TNFSF10
HALLMARK_ESTROGEN_RESPONSE_EARLY	199	0.327	1.360	0.025	0.050	CCND1/GJA1/INHBB/PDZK1/CXCL12/DHRS3/CA12/RAB17/MAST4/FOS/SLC7A2/AR/IGFBP4/MAPT/KRT19/SLC27A2/ABLIM1/PRSS23/AQP3/SCARB1/TIPARP/SLC1A1/KDM4B/SEC14L2/SLC9A3R1/PODXL/MED13L/CALB2/DEPTOR/MYOF/SYBU/DHCR7/BLVRB/SVIL/BCL2/SYNGR1/ESRP2/SYT12/SIAH2/ZNF185/RARA/NPY1R/TPBG/KRT15/IL6ST/FKBP5/IL17RB/FLNB/GAB2/RHOBTB3/FRK/TFF3/NBL1/DLC1/ELOVL2/ANXA9
HALLMARK_KRAS_SIGNALING_UP	193	0.326	1.351	0.025	0.050	PLVAP/SPARCL1/ANGPTL4/PECAM1/ENG/ANO1/NRP1/CFHR2/CXCR4/PPBP/TFPI/TRIB2/CFB/TOR1AIP2/FLT4/ETS1/ARG1/MMP9/RBP4/GPRC5B/IGFBP3/MAP7/SLPI/NR1H4/USH1C/GUCY1A3/IL33/JUP/HSD11B1/HIST1H2BB/BTBD3
HALLMARK_FATTY_ACID_METABOLISM	156	0.347	1.390	0.026	0.050	CYP4A11/LDHA/ACAA2/ALDH3A2/AOC3/ACADVL/S100A10/CYP4A22/FABP1/LGALS1/EPHX1/HMGCS2/SERINC1/CPT1A/MGLL/EHHADH/HAO2/APEX1/GPD1/UROD/CEL/ECH1/ACADM/ECI2/ADH1C/MIF/CRYZ/CA6/ALDH1A1/ACADL/PPARA/ACO2/ECHS1/ACAT2/ACOX1/ETFDH/SDHA/ALDH9A1/TDO2/DHCR24
HALLMARK_INFLAMMATORY_RESPONSE	197	-0.307	-1.306	0.028	0.051	NLRP3/MET/PTPRE/CD48/TNFSF9/LYN/IL12B/ICAM1/NPFFR2/PVR/RASGRP1/EBI3/EREG/IL10RA/SRI/SPHK1/AHR/CXCL6/CSF1/CXCL11/IL18/MEP1A/CSF3/ADORA2B/GPC3/CD14/CXCL9/C3AR1/RHOG/EIF2AK2/CXCL10/SLC7A1/C5AR1/PTGER4/NAMPT/RIPK2/CYBB/ITGB8/PLAUR/OPRK1/OLR1/MSR1/RGS1/CCL5/HIF1A/NOD2
HALLMARK_ESTROGEN_RESPONSE_LATE	199	0.319	1.326	0.032	0.058	CCND1/S100A9/ALDH3A2/PDZK1/CXCL12/CA12/FOS/CYP4F11/ASS1/HMGCS2/EMP2/IGFBP4/MAPT/KRT19/ATP2B4/SLC27A2/ZFP36/TPSAB1/CXCL14/PRSS23/SCARB1/SLC9A3R1/CDH1/UNC13B/MYOF/DHCR7/BLVRB/SERPINA1/SORD/DLG5/ETFB/SGK1/BCL2/ACOX2/IMPA2/SERPINA5/ID2/SIAH2/NPY1R/TPBG/IL6ST/FKBP5/CPE/CA2/IL17RB/FLNB/METTL3/PLAC1/FRK/TFF3/NBL1/CHST8/PRLR/ANXA9/TST

HALLMARK_MTORC1_SIGNALING	198	-0.297	-1.267	0.039	0.065	HSPA9/TUBG1/PSMG1/PSMC6/SQLE/PSAT1/STIP1/GSK3B/ITGB2/GLA/HSPD1/MAP2K3/NFIL3/RAB1A/ACACA/TCEA1/SLC1A5/ASNS/MTHFD2/IMMT/ELOVL5/BUB1/ABCF2/RPN1/MLLT11/SEC11A/TES/TUBA4A/PSPH/VLDLR/ACSL3/PSMA3/PLK1/HSPA5/PSMD14/ATP5G1/PDAP1/CYB5B/PPA1/GMPS/GGA2/M6PR/PPIA/PSMA4/ACTR3/CCT6A/SKAP2/YKT6/BHLHE40/ETF1/EIF2S2/TFRC/PSMC2/NAMPT/ATP6V1D/HSPA4/WARS/LGMN/CTSC/SLC7A5/IFI30
HALLMARK_INTERFERON_ALPHA_RESPONSE	93	-0.362	-1.386	0.039	0.065	PSMB9/PARP12/PSMA3/LAP3/CD47/GMPR/CSF1/CXCL11/LGALS3BP/IFIH1/PLSCR1/PSME2/EIF2AK2/CXCL10/HLA-C/TAP1/RIPK2/WARS/IFI27/IFI30
HALLMARK_MYC_TARGETS_V2	57	-0.399	-1.411	0.043	0.069	NOC4L/MCM4/TBRG4/NPM1/PA2G4/PHB/HSPD1/PPRC1/SUPV3L1/PLK1/WDR43/SRM/AIMP2/DUSP2/NIP7/CDK4/CBX3
HALLMARK_HEME_METABOLISM	196	0.309	1.288	0.048	0.075	HBB/TNS1/CAT/FOXO3/ARHGEF12/EPB41/MXI1/SIDT2/BTG2/HBD/FECH/AQP3/ALAS2/UROD/SEC14L1/EZH1/RBM5/CCDC28A/MGST3/BNIP3L/BLVRB/SELENBP1/HIST1H4C/KHNYN/HBBP1/PC/CROCCP2/ADD1/GYPE/SLC25A37/GLRX5/TNRC6B/RIOK3/TAL1/DCAF11/LMO2/NFE2L1/BSG/SLC10A3/ALDH1L1/CA2/FTCD/ADD2/ABCB6/RNF19A
HALLMARK_WNT_BETA_CATENIN_SIGNALING	42	0.453	1.450	0.050	0.075	JAG1/NOTCH4/DKK1/NOTCH1/PTCH1/KAT2A/TCF7/CSNK1E/CTNNB1/JAG2/HDAC5/DLL1/HEY1/MAML1/NUMB
HALLMARK_ANDROGEN_RESPONSE	100	0.355	1.333	0.056	0.082	CCND1/NDRG1/PMEPA1/ACTN1/AZGP1/HMGCR/SLC38A2/KRT19/LMAN1/SEPP1/ARID5B/MAP7/GUCY1A3/TSC22D1/SORD/LIFR/SGK1/ITGAV/PDLIM5/STEAP4/DHCR24/MAK/HERC3/KLK3/FKBP5/CAMKK2/AKAP12/PTPN21/B2M/IQGAP2/HMGCS1
HALLMARK_P53_PATHWAY	198	0.302	1.259	0.072	0.103	TXNIP/NDRG1/ZBTB16/APP/PITPNC1/TGFB1/INHBB/FOXO3/DDIT4/S100A10/EPHX1/FOS/SP1/RPL18/CDH13/HMOX1/PLXNB2/SDC1/BTG2/DDB2/GPX2/LRMP/STOM/FGF13/NOTCH1/HEXIM1/PHLDA3/SLC35D1/PMM1/TSC22D1/ERCC5/CCNK/BTG1/CD81/MXD4/TSPYL2/RAB40C/JAG2/JUN/PRMT2/CTSF/RXRA
HALLMARK_TNFA_SIGNALING_VIA_NFKB	198	-0.275	-1.175	0.124	0.172	REL/PLEK/FOSL1/SLC2A6/ATF3/IL6/TUBB2A/MAP2K3/NFIL3/PTPRE/NR4A2/TNFSF9/BIRC3/IL12B/SLC16A6/BMP2/CLCF1/ICAM1/YRDC/BTG3/NINJ1/DUSP4/TRIB1/RELB/SPHK1/BCL3/NFE2L2/TNFAIP8/CXCL6/NFAT5/CSF1/CXCL11/IFIH1/IL18/NR4A3/DRAM1/TNFAIP2/DUSP5/ZC3H12A/B4GALT5/DUSP2/CXCL10/KLF10/SAT1/BHLHE40/LITAF/PLAU/SOCS3/PTGER4/NAMPT/TAP1/RIPK2/TNC/PLAUR/OLR1/CCL5/G0S2/PHLDA2/CCL4
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	110	-0.299	-1.179	0.148	0.200	HSPA9/ATF6/NPM1/LSM1/PSAT1/ARFGAP1/EIF4E/KDELR3/ATF3/TUBB2A/EXOSC1/DKC1/ASNS/MTHFD2/HYOU1/CKS1B/DCP1A/SEC11A/DCP2/EIF4G1/SPCS1/IARS/EIF4A1/HSPA5/CHAC1/XPOT/H2AFX/PARN/GEMIN4/KIF5B/PAIP1/DNAJC3/ATP6V0D1/KHSRP/SLC7A5
HALLMARK_CHOLESTEROL_HOMEOSTASIS	73	0.329	1.167	0.212	0.279	ALDOC/JAG1/ERRFI1/CLU/HMGCR/ADH4/CYP51A1/ABCA2/FDPS/ECH1/LSS/DHCR7/PMVK/FADS2/ACAT2/CTNNB1/PDK3

HALLMARK_IL6_JAK_STAT3_SIGNALING	87	-0.292	-1.109	0.248	0.316	STAM2/CXCL1/PF4/IL13RA1/TNFRSF1B/SOCS1/IL17RA/PLA2G2A/IL6/IL9R/IL12RB1/PTPN2/EBI3/BAK1/IL2RG/GRB2/TNFRSF21/PIM1/CSF1/CXCL11/CD38/PTPN11/CD14/CXCL9/TNFRSF12A/PTPN1/IL2RA/CXCL10/SOCS3/CXCL13/CCR1/STAT1
HALLMARK_COMPLEMENT	194	0.264	1.099	0.254	0.316	COL4A2/FN1/LRP1/NOTCH4/SERPINC1/S100A9/SPOCK2/SERPING1/C9/HNF4A/CLU/CDH13/DOCK9/TIMP2/TIMP1/ITIH1/CFB/ANG/S100A12/HSPA1A/CSRP1/PLG/FCN1/SERPINA1/CASP10/BRPF3/CTSO/CASP9/F2/CP/CFH/SERPINE1/KLKB1/ZEB1/PDGFB/F10/PSEN1/SERPINB2/MMP8
HALLMARK_APICAL_SURFACE	44	0.351	1.129	0.259	0.316	THY1/APP/CX3CL1
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	46	0.344	1.116	0.277	0.330	MGST1/CAT/PFKP/PDLIM1/SOD1/G6PD/GLRX2/MPO/JUNB/GLRX/SOD2/STK25/PRDX4/ATOX1/NQO1/EGLN2/MSRA
HALLMARK_KRAS_SIGNALING_DN	194	0.259	1.077	0.295	0.343	SLC6A3/AKR1B10/ZBTB16/SYNPO/FGF16/CPB1/KRT5/CLPS/ITIH3/CAMK1D/BTG2/C5/EDN2/SEPP1/EDN1/THNSL2/PLAG1/HSD11B2/KCNE2/KRT1/ABCB11/NRIP2/SGK1/UGT2B17/TGM1/SLC38A3/CLSTN3/TCF7L1/SERPINB2/CD40LG/ADCK3/SERPINA10/CYP39A1/KRT15/KCNMB1
HALLMARK_UV_RESPONSE_UP	155	-0.255	-1.054	0.354	0.402	IL6/MSX1/RAB27A/CHKA/ASNS/MAPK8IP2/LYN/GAL/GRINA/BMP2/RPN1/ICAM1/FEN1/RASGRP1/AP2S1/TUBA4A/BTG3/SLC6A12/BAK1/PTPRD/CLTB/PPP1R2/EPCAM/POLE3/PDAP1/ATP6V1C1/DNAJA1/CYB5B/HSPA2/H2AFX/GPX3/YKT6/EIF2S3/GLS/TFRC/RRAD/TAP1/ATP6V1F/DDX21
HALLMARK_PI3K_AKT_MTOR_SIGNALING	105	-0.267	-1.043	0.362	0.403	PFN1/CDK1/TBK1/TRAF2/PIN1/IRAK4/PPP1CA/E2F1/HRAS/DAPP1/SMAD2/YWHAB/CFL1/DDIT3/PRKAR2A/NCK1/ITPR2/MKNK1/PITX2/MAPK10/EIF4E/GSK3B/CLTC/FGF22/MAP2K3/ACACA/ARHGDIA/THEM4/IL2RG/PRKAG1/GRB2/SFN/RAC1/PTPN11/ACTR3/CDK4/ARPC3/DUSP3
HALLMARK_SPERMATOGENESIS	134	-0.250	-1.020	0.404	0.439	TLE4/GPR182/TALDO1/STAM2/PRKAR2A/VDAC3/TTK/TOPBP1/PSMG1/ART3/DNAJB8/IDE/CRISP2/PGS1/TNNI3/MLF1/BUB1/ZNRF4/CSNK2A2/MEP1B/CHFR/DBF4/ADCYAP1/DMRT1/ODF1/GSG1/HSPA2/AGFG1/TNP1/CFTR/NF2/GSTM3/PCSK1N
HALLMARK_PROTEIN_SECRETION	96	-0.263	-1.014	0.434	0.462	CLCN3/SEC22B/ARFGEF2/COPB2/AP2B1/SNAP23/ARFGEF1/VAMP7/CLTC/TSPAN8/RAB5A/GLA/RAB14/AP2S1/SNX2/DNM1L/VAMP3/GOLGA4/ATP6V1H/SCRN1/M6PR/YKT6/ADAM10/CLTA/CTSC
HALLMARK_IL2_STAT5_SIGNALING	196	0.239	0.997	0.463	0.482	PLIN2/RHOB/NDRG1/SERPINC1/NRP1/ANXA4/DHRS3/SELL/SPRY4/P4HA1/SMPDL3A/COL6A1/RORA/IL3RA/ECM1/LTB/PTCH1/NT5E/KLF6/SH3BGRL2/ITGAV/CD81/BCL2/SYT11/MYO1C/FURIN/GUCY1B3/SHE/SERPINB6/APLP1/DENND5A/GPR83/IFITM3/CA2/TNFSF10/CD79B
HALLMARK_PANCREAS_BETA_CELLS	40	-0.283	-0.932	0.586	0.598	SRP14/PAX6/INSM1/NEUROG3/DPP4/MAFB/ELP4/SEC11A/SPCS1/PCSK2/NKX2-2/CHGA/PAK3

HALLMARK_DNA_REPAIR	141	-0.159	-0.656	0.998	0.998	POLR1D/MRPL40/GTF2A2/NME1/CLP1/NUDT9/RFC3/CSTF3/ERCC2/RALA/DUT/POLR2D/RAD52/SNAPC5/PNP/GTF2H3/CDA/PCNA/POLR3C/TK2/ITPA/ZNRD1/RNMT/RAD51/AK1/BOLA2/POLB/TSG101/TYMS/ADRM1/POLR2K/ERCC4/POLD1/COX17/POM121/RPA3/NCBP2/ZNF707/ARL6IP1/FEN1/MPG/DGUOK/NUDT21/NME3/TAF13/EIF1B/SDCBP

Supplementary table 6. Raw data for COMPARZ ssGSEA analysis (appendix p 11).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
pDC	0.355	0.003	0.091	2.505
Neutrophils_SS	0.260	0.051	0.474	1.295
Tem_cells	0.238	0.060	0.474	1.224
Eosinophils_SS	0.218	0.065	0.474	1.185
NK_cells	0.199	0.115	0.667	0.939
Treg_cells	0.115	0.445	0.897	0.352
Mast_cells	0.099	0.520	0.897	0.284
NK_CD56dim_cells	0.080	0.638	0.897	0.195
Tgd_cells	0.055	0.616	0.897	0.211
iDC	0.054	0.729	0.897	0.137
Th17_cells	0.047	0.473	0.897	0.326
CTLA4	0.045	0.702	0.897	0.154
Cytotoxic_cells	0.041	0.743	0.897	0.129
Tcm_cells	0.038	0.654	0.897	0.184
T_helper_cells	0.035	0.738	0.897	0.132
Th1_cells	0.033	0.729	0.897	0.137
B_cells	0.023	0.896	0.962	0.048
Th2_cells	0.018	0.435	0.897	0.362
APM2	0.008	0.809	0.938	0.092
Tfh_cells	-0.012	0.995	1.000	0.002
NK_CD56bright_cells	-0.041	1.000	1.000	0.000
CD8_T_cells	-0.051	0.663	0.897	0.179
DC	-0.053	0.364	0.897	0.439
Macrophages	-0.063	0.881	0.962	0.055
aDC	-0.074	0.516	0.897	0.287
APM1	-0.112	0.437	0.897	0.360
T_cells	-0.113	0.313	0.897	0.504
PD1	-0.121	0.210	0.869	0.678
PDL1	-0.293	0.201	0.869	0.698

Supplementary table 7. Raw data for TCGA ssGSEA analysis (appendix p 19).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
Mast_cells	0.717	0.002	0.047	2.792
Th17_cells	0.516	0.334	0.693	0.476
Tem_cells	0.429	0.065	0.624	1.190
Neutrophils	0.415	0.094	0.667	1.028
iDC	0.388	0.168	0.667	0.775
Tcm_cells	0.360	0.139	0.667	0.858
NK_cells	0.355	0.121	0.667	0.918
DC	0.333	0.272	0.693	0.565
pDC	0.255	0.319	0.693	0.496
Tgd_cells	0.246	0.323	0.693	0.491
Eosinophils	0.237	0.252	0.693	0.598
Macrophages	0.173	0.519	0.903	0.285
aDC	0.132	0.405	0.783	0.392
Tfh_cells	0.099	0.620	0.903	0.208
CD8_T_cells	0.098	0.716	0.903	0.145
B_cells	0.066	0.571	0.903	0.243
T_helper_cells	0.052	0.781	0.906	0.107
APM2	0.031	0.997	0.997	0.001
NK_CD56dim_cells	-0.014	0.682	0.903	0.166
Th1_cells	-0.022	0.854	0.918	0.068
T_cells	-0.027	0.947	0.981	0.024
Th2_cells	-0.048	0.758	0.906	0.121
Cytotoxic_cells	-0.070	0.716	0.903	0.145
APM1	-0.099	0.687	0.903	0.163
Treg_cells	-0.134	0.614	0.903	0.212
PDL1	-0.221	0.818	0.912	0.087
PD1	-0.233	0.207	0.667	0.684
CTLA4	-0.279	0.185	0.667	0.732
NK_CD56bright_cells	-0.532	0.009	0.130	2.049

Supplementary table 8. Raw data for PNN IPA analysis in peritumoral fat cohort (appendix p 14).

Ingenuity Canonical Pathways	-log10(p-value)	z-score	Ratio	Molecules
Granulocyte Adhesion and Diapedesis	23.5		0.397	C5,C5AR1,CCL16,CCL19,CCL2,CCL22,CCL23,CCL26,CCL28,CCL3,CCL4,CCL4L1/CCL4L2,CCL5,CCL8,CLDN10,CLDN2,CLDN4,CLDN9,CSF3,CSF3R,CX3CL1,CXCL1,CXCL10,CXCL11,CXCL13,CXCL14,CXCL16,CXCL3,CXCL8,CXCL9,CXCR2,CXCR4,FPR1,FPR2,FPR3,GNAI2,HRH2,ICAM1,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,ITGA2,ITGA4,ITGA5,ITGAL,ITGB2,MMP25,MMP9,MSN,NGFR,PECAM1,PF4,PPBP,SDC1,SDC2,SDC3,SELE,SELL,SELP,SELPLG,THY1,TNF,TNFRSF11B,TNFRSF1B,XCL1,XCL2
Th1 and Th2 Activation Pathway	21.5		0.374	ACVR2B,BHLHE41,CCR1,CCR4,CCR5,CD247,CD274,CD28,CD3D,CD3E,CD4,CD86,CD8A,CXCR4,CXCR6,DLL4,FLT3,GATA3,GFI1,HAVCR2,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,ICAM1,ICOS,IKZF1,IL10RA,IL12RB1,IL18,IL18R1,IL1RL1,IL2RG,IL33,IL4R,IL6,IRF1,IRS1,IRS2,ITGB2,JAK3,JUN,KLB,KLRC1,KLRD1,LGALS9,mir-21,mir-29,NFATC2,NOTCH2,PIK3R3,PIK3R5,PRKCQ,RUNX3,S1PR1,SOCS3,SPI1,TGFB1,TGFBR2,VAV1
Th2 Pathway	17.7	1.218543592	0.375	ACVR2B,BHLHE41,CCR1,CCR4,CCR5,CD247,CD28,CD3D,CD3E,CD4,CD86,CXCR4,CXCR6,FLT3,GATA3,GFI1,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,ICAM1,ICOS,IKZF1,IL12RB1,IL1RL1,IL2RG,IL33,IL4R,IRS1,IRS2,ITGB2,JAK3,JUN,KLB,mir-21,NFATC2,NOTCH2,PIK3R3,PIK3R5,PRKCQ,RUNX3,S1PR1,SOCS3,SPI1,TGFB1,TGFBR2,VAV1
Th1 Pathway	17.2	4.217756949	0.387	CCR5,CD247,CD274,CD28,CD3D,CD3E,CD4,CD86,CD8A,DLL4,FLT3,GATA3,HAVCR2,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,ICAM1,ICOS,IL10RA,IL12RB1,IL18,IL18R1,IL6,IRF1,IRS1,IRS2,ITGB2,JAK3,KLB,KLRC1,KLRD1,LGALS9,mir-21,mir-29,NFATC2,NOTCH2,PIK3R3,PIK3R5,PRKCQ,RUNX3,SOCS3,VAV1
CD28 Signaling in T Helper Cells	14.8	3.307475463	0.366	ACTR3,AKT2,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CARD11,CD247,CD28,CD3D,CD3E,CD4,CD86,CHP1,FCER1G,FLT3,GRAP2,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IKBKE,IRS1,IRS2,ITK,ITPR2,JUN,KLB,LCK,LCP2,MAPK10,NFATC2,NFKBIE,PIK3R3,PIK3R5,PRKCQ,PTPN6,PTPRC,SYK,VAV1,WAS
Agranulocyte Adhesion and Diapedesis	13.7		0.307	ACTB,ACTG1,C5,C5AR1,CCL16,CCL19,CCL2,CCL22,CCL23,CCL26,CCL28,CCL3,CCL4,CCL4L1/CCL4L2,CCL5,CCL8,CLDN10,CLDN2,CLDN4,CLDN9,CX3CL1,CXCL1,CXCL10,CXCL11,CXCL13,CXCL14,CXCL16,CXCL3,CXCL8,CXCL9,CXCR1,CXCR2,CXCR4,GNAI2,ICAM1,IL18,IL1B,IL1R1,IL1RN,IL33,ITGA2,ITGA4,ITGA5,ITGB2,MMP25,MMP9,MSN,MYH7B,MYL4,PECAM1,PF4,PPBP,SELE,SELL,SELP,SELPLG,TNF,XCL1,XCL2
Antigen Presentation Pathway	13.7		0.615	B2M,CD74,CIITA,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,MR1,PSMB8,PSMB9,TAP1,TAP2
Dendritic Cell Maturation	12.1	5.631783122	0.291	AKT2,B2M,CCR7,CD1C,CD1D,CD86,COL10A1,FCER1G,FCGR1A,FCGR1B,FCGR2A,FCGR3A/FCGR3B,FLT3,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,ICAM1,IKBKE,IL15,IL18,IL1B,IL1RN,IL32,IL33,IL6,IRF8,IRS1,IRS2,KLB,LEP,LTB,LY75,MAPK10,MYD88,NFKBIE,NGFR,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,RELB,TLR2,TNF,TNFRSF11B,TNFRSF1B,TREM2,TYROBP
Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes	11.7	5	0.383	ACTB,ACTG1,ACTR3,AKT2,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,FCGR1A,FCGR2A,FCGR3A/FCGR3B,FGR,FYB1,HCK,INPP5D,LCP2,LYN,MYO5A,NCF1,PIK3R3,PLD1,PLD2,PLD4,PLD6,PRKCB,PRKCQ,PTK2B,RAC2,SYK,VASP,VAV1,VAV2,VAV3,WAS

TREM1 Signaling	11.2	5.208553759	0.413	AKT2,CASP1,CASP5,CCL2,CCL3,CD86,CIITA,CXCL3,CXCL8,ICAM1,IL18,IL1B,IL1RL1,IL6,ITGA5,ITGAX,LAT2,MYD88,NLRC4,NLRP12,NLRP2,NLRP3,NLRP6,NOD2,PLCG2,TLR10,TLR2,TLR8,TNF,TREM1,TYROBP
Graft-versus-Host Disease Signaling	11		0.5	CD28,CD86,FASLG,FCER1G,GZMB,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,IL18,IL1B,IL1RN,IL33,IL6,PRF1,TNF
T Helper Cell Differentiation	10.8		0.411	CD28,CD86,FCER1G,FOXP3,GATA3,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,ICOS,IL10RA,IL12RB1,IL18,IL18R1,IL2RG,IL4R,IL6,NGFR,RORC,TGFB1,TGFBR2,TNF,TNFRSF11B,TNFRSF1B
Communication between Innate and Adaptive Immune Cells	10.7		0.365	B2M,CCL3,CCL4,CCL5,CCR7,CD28,CD4,CD79A,CD79B,CD86,CD8A,CD8B,CXCL10,CXCL8,FCER1G,HLA-A,HLA-B,HLA-C,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,IGHD,IGHM,IL15,IL18,IL1B,IL1RN,IL33,IL6,TLR10,TLR2,TLR8,TNF,TNFSF13B
Type I Diabetes Mellitus Signaling	10.6	2.984810029	0.342	BID,CASP3,CASP9,CD247,CD28,CD3D,CD3E,CD86,FASLG,FCER1G,GZMB,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,ICA1,IKBKE,IL1B,IL1R1,IRF1,MAP3K5,MAPK10,MYD88,NFKBIE,NGFR,PRF1,SOCS3,TNF,TNFRSF11B,TNFRSF1B
Leukocyte Extravasation Signaling	10.5	3.75277675	0.268	ACTB,ACTG1,ACTN2,ARHGAP6,ARHGAP9,BMX,BTK,CD44,CLDN10,CLDN2,CLDN4,CLDN9,CTNNA2,CXCR4,EDIL3,FLT3,GNAI2,ICAM1,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGAL,ITGB2,ITK,JAM2,KLB,MAPK10,MMP25,MMP9,MSN,NCF1,NCF2,NCF4,PECAM1,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,PTK2B,RAC2,RAP1GAP,RASGRP1,RASSF5,RHOH,SELPLG,SPN,THY1,TIMP1,VASP,VAV1,VAV2,VAV3,WAS,WIPF1
Role of NFAT in Regulation of the Immune Response	10.5	5.285714286	0.276	AKT2,BLNK,BTK,CD247,CD28,CD3D,CD3E,CD4,CD79A,CD79B,CD86,CHP1,FCER1A,FCER1G,FCGR1A,FCGR1B,FCGR2A,FCGR3A/FCGR3B,FLT3,GNA15,GNAI2,GNB4,GNG2,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IKBKE,IRS1,IRS2,ITK,ITPR2,JUN,KLB,LCK,LCP2,LYN,MEF2C,NFATC2,NFKBIE,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCG2,PRKCQ,RCAN1,SYK
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	10.2		0.367	CD28,CD79A,CD79B,CD86,CXCL13,FASLG,FCER1G,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IL15,IL18,IL1B,IL1RN,IL33,IL6,LTB,RELB,SLAMF1,SPP1,TGFB1,TLR10,TLR2,TLR8,TNF,TNFSF13B
iCOS-iCOSL Signaling in T Helper Cells	10.1	3.412500739	0.32	AKT2,CD247,CD28,CD3D,CD3E,CD4,CD86,CHP1,FCER1G,FLT3,GRAP2,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,ICOS,IKBKE,IL2RG,INPP5D,IRS1,IRS2,ITK,ITPR2,KLB,LCK,LCP2,NFATC2,NFKBIE,PIK3R3,PIK3R5,PRKCQ,PTPRC,TRAT1,VAV1
Cdc42 Signaling	10.1	4.016632088	0.287	ACTR3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,B2M,CD247,CD3D,CD3E,CDC42SE1,CFL1,DIAPH1,DIAPH3,EXOC6,FCER1G,FGD3,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,IQGAP3,ITGA2,ITGA4,ITGA5,ITK,JUN,MAPK10,MYL12A,MYL4,MYLK,VAV1,VAV2,WAS,WIPF1
Neuroinflammation Signaling Pathway	10.1	4.608176876	0.233	ACVR2B,AKT2,B2M,BACE2,BDNF,BIRC3,BIRC5,CASP1,CASP3,CCL2,CCL3,CCL5,CD86,CHP1,CX3CL1,CXCL10,CXCL8,FASLG,FLT3,GABRA2,GABRE,GRIN3A,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,ICAM1,IKBKE,IL18,IL1B,IL1R1,IL34,IL6,IRAK2,IRS1,IRS2,JAK3,JUN,KLB,MAPK10,MMP9,MYD88,NCF2,NFATC2,NLRP3,NOX4,P2RX7,PIK3R3,PIK3R5,PLA2G2A,PLA2G2D,PLCG2,PYCARD,S100B,SNCA,SYK,TGFB1,TGFBR2,TICAM2,TIRAP,TLR10,TLR2,TLR8,TNF,TREM2,TYROBP
T Cell Exhaustion Signaling Pathway	9.52	2.400980192	0.268	ACVR2B,AKT2,BATF,BTLA,CD274,CD28,CD86,EOMES,FCER1G,FLT3,GZMB,HAVCR2,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,IL10RA,IL12RB1,IL6,IRS1,IRS2,JAK3,JUN,KLB,LAG3,LGALS9,MAPK10,NFATC2,PIK3R3,PIK3R5,PLCG2,PPM1J,PPP2R5A,PRDM1,PRKCQ,PTPN6,TCF7,TGFB1,TGFBR2
B Cell Development	9.35		0.528	CD19,CD79A,CD79B,CD86,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IGHD,IGHM,IL7R,PTPRC,SPN

Phagosome Formation	9.01		0.293	C3AR1,C5AR1,CLEC7A,CR1,CR2,FCAR,FCER1A,FCER1G,FCGR1A,FCGR1B,FCGR2A,FCGR3A/FCGR3B,FLT3,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGAX,ITGB2,KLB,MSR1,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,SYK,TLR10,TLR2,TLR8,VTN
Crosstalk between Dendritic Cells and Natural Killer Cells	9		0.348	ACTB,ACTG1,CCR7,CD226,CD28,CD69,CD86,CSF2RB,FASLG,HLA-A,HLA-B,HLA-C,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,IL15,IL18,IL2RG,IL3RA,IL6,ITGAL,KLRD1,LTB,MICB,NCR3,PRF1,TNF,TNFRSF1B,TREM2,TYROBP
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	8.44		0.217	ADAMTS4,AKT2,C5,C5AR1,CCL2,CCL5,CCND1,CEBPA,CHP1,CXCL8,F2RL1,FCGR1A,FCGR3A/FCGR3B,FLT3,FRZB,FZD7,FZD9,ICAM1,IKBKE,IL15,IL18,IL18R1,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL32,IL33,IL6,IRAK2,IRS1,IRS2,JUN,KLB,LEF1,LTB,MYC,MYD88,NFATC2,NFKBIE,NGFR,OSM,PDGFA,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,ROR2,SELE,SFRP2,SFRP4,SOCS3,TCF7,TGFB1,TLR10,TLR2,TLR8,TNF,TNFRSF11B,TNFRSF1B,TNFSF13B,TRAF4,VEGFC,WNT2B,WNT3
LXR/RXR Activation	8.2	-3.053290134	0.298	ABCG1,ALB,APOC1,APOL1,CCL2,CD14,CLU,FDFT1,HADH,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IL6,LBP,LY96,LYZ,MLXIPL,MMP9,MSR1,MYLIP,NGFR,PLTP,PON3,S100A8,SAA1,SERPINA1,TF,TNF,TNFRSF11B,TNFRSF1B,VTN
Inflammasome pathway	8.08	3.605551275	0.65	AIM2,CASP1,CASP5,CTSB,IL18,IL1B,MYD88,NLRC4,NLRP1,NLRP3,NOD2,P2RX7,PYCARD
Atherosclerosis Signaling	8.03		0.289	ALB,ALOX15B,ALOX5,APOC1,APOL1,CCL2,CCR2,CLU,COL10A1,CXCL8,CXCR4,ICAM1,IL18,IL1B,IL1RN,IL33,IL6,ITGA4,ITGB2,LYZ,MMP9,MSR1,PAFAH1B3,PDGFA,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,RARRES3,S100A8,SELE,SELP,SELPLG,SERPINA1,TGFB1,TNF
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	7.87	2.449489743	0.26	C1QA,C1QB,C3AR1,C5,C5AR1,CASP1,CCL5,CLCF1,CLEC7A,CXCL8,FASLG,FLT3,IL15,IL18,IL1B,IL33,IL6,IRS1,IRS2,KLB,LEP,LTB,MAPK10,MAVS,MYD88,NLRC4,NLRP3,NOD2,OAS2,OSM,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,PTX3,SYK,TGFB1,TLR2,TLR8,TNF,TNFSF13B,TNFSF15,TNFSF8
CTLA4 Signaling in Cytotoxic T Lymphocytes	7.5		0.307	AKT2,AP1M2,AP1S2,AP2S1,B2M,CD247,CD28,CD3D,CD3E,CD86,CD8A,CD8B,FCER1G,FLT3,GRAP2,HLA-A,HLA-B,HLA-C,IRS1,IRS2,KLB,LCK,LCP2,PIK3R3,PIK3R5,PPM1J,PPP2R5A,PTPN22,PTPN6,SYK,TRAT1
Tec Kinase Signaling	7.46	4.666666667	0.25	ACTB,ACTG1,BLK,BMX,BTK,FASLG,FCER1A,FCER1G,FGR,FLT3,GNA15,GNAI2,GNB4,GNG2,HCK,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITK,JAK3,KLB,LCK,LYN,MAPK10,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,PTK2B,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,TNF,TNFRSF10A,TNFRSF10B,VAV1,VAV2,VAV3,WAS
Primary Immunodeficiency Signaling	7.19		0.4	BLNK,BTK,CD19,CD3D,CD3E,CD4,CD79A,CD8A,CIITA,ICOS,IGHD,IGHM,IGLL1/IGLL5,IL2RG,IL7R,JAK3,LCK,PTPRC,TAP1,TAP2
Natural Killer Cell Signaling	7.03		0.271	AKT2,CD244,CD247,CD300A,FCER1G,FCGR2A,FCGR3A/FCGR3B,FLT3,HCST,INPP5D,INPP5J,IRS1,IRS2,KLB,KLRB1,KLRC1,KLRD1,LCK,LCP2,LILRB1,NCR3,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,PTPN6,RAC2,SH2D1A,SIGLEC7,SYK,SYNJ2,TYROBP,VAV1,VAV2,VAV3
Hepatic Fibrosis / Hepatic Stellate Cell Activation	7		0.242	A2M,BAX,CCL2,CCL5,CCR5,CCR7,CD14,COL10A1,COL11A1,COL24A1,COL6A6,CTGF,CXCL3,CXCL8,CXCL9,FASLG,HGF,ICAM1,IGFBP4,IL10RA,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL4R,IL6,KLF6,LBP,LEP,LY96,MMP9,MYH7B,MYL4,NGFR,PDGFA,SERPINE1,TGFA,TGFB1,TGFBR2,TIMP1,TNF,TNFRSF11B,TNFRSF1B,VEGFC
Pathogenesis of Multiple Sclerosis	6.87		0.889	CCL3,CCL4,CCL5,CCR1,CCR5,CXCL10,CXCL11,CXCL9
PKCθ Signaling in T Lymphocytes	6.85	4.64371646	0.247	CACNA2D3,CACNG8,CARD11,CD247,CD28,CD3D,CD3E,CD4,CD86,CHP1,FCER1G,FLT3,GRAP2,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IKBKE,IRS1,IRS2,JUN,KLB,LCK,LCP2,MAP3K5,MAP3K8,NFATC2,NFKBIE,PIK3R3,PIK3R5,PLCG2,PRKCQ,RAC2,VAV1,VAV2,VAV3
Hepatic Cholestasis	6.71		0.239	ABCB1,ABCC3,ADCY6,ATP8B1,CD14,CLCF1,CXCL8,FASLG,IKBKE,IL15,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IL6,INSR,IRAK2,JUN,LBP,LEP,LTB,LY96,MAPK10,MYD88,NFKBIE,NGFR,OSM,PPARA,P

				RKCB,PRKCQ,SLCO3A1,TGFB1,TIRAP,TJP2,TNF,TNFRSF11B,TNFRSF1B,TNFSF13B,TNFSF15,TNFSF8
B Cell Receptor Signaling	6.66	3.794733192	0.234	AKT2,BCL2A1,BLNK,BTK,CD19,CD22,CD79A,CD79B,CFL1,DAPP1,FCGR2A,FLT3,IGHD,IGHM,IKBKE,INPP5D,INPP5J,IRS1,IRS2,JUN,KLB,LYN,MAP3K5,MAP3K8,MEF2C,NFATC2,NFKBIE,PAG1,PAX5,PIK3AP1,PIK3R3,PIK3R5,PLCG2,POU2F2,PRKCB,PRKCQ,PTK2B,PTPN6,PTPRC,RAC2,RASSF5,SYK,SYNJ2,VAV1,VAV2,VAV3
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	6.6	3.394673699	0.23	AKT2,ALB,APOC1,APOL1,CAT,CLU,FLT3,IKBKE,IRF1,IRF8,IRS1,IRS2,JAK3,JUN,KLB,LYZ,MAP3K5,MAP3K8,MAPK10,NCF1,NCF2,NCF4,NFKBIE,NGFR,PIK3R3,PIK3R5,PLCG2,PPARA,PPM1J,PPP1R14B,PPP2R5A,PRKCB,PRKCQ,PTPN6,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,S100A8,SERPINA1,SPI1,TLR2,TNF,TNFRSF11B,TNFRSF1B
Osteoarthritis Pathway	6.49	4.216691571	0.226	ADAMTS4,ADIPOQ,ALPL,BMP2,CASP1,CASP3,CASP4,CASP5,CASP9,COL10A1,CTNNA2,CXCL8,CXCR2,FRZB,FZD7,FZD9,GLI3,GLIS1,HIF1A,HTRA1,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,ITGA2,ITGA4,ITGA5,LEF1,LEP,MEF2C,MMP9,NAMPT,P2RX7,PTCH1,RUNX2,S100A8,S100A9,SMAD6,SPHK1,SPP1,TCF7,TGFB1,TGFBR2,TLR2,TNF,TNFRSF1B,VEGFC
IL-10 Signaling	6.45		0.333	BLVRA,CCR1,CCR5,CD14,FCGR2A,IKBKE,IL10RA,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IL4R,IL6,JUN,LBP,MAP4K4,NFKBIE,SOCS3,TNF
IL-8 Signaling	6.3	3.618136135	0.223	AKT2,ANGPT2,ARRB2,BAX,CCND1,CR2,CXCL1,CXCL8,CXCR1,CXCR2,EIF4EBP1,FLT3,GNAI2,GNB4,GNG2,HBEGF,ICAM1,IKBKE,IRAK2,IRS1,IRS2,ITGAX,ITGB2,JUN,KLB,MAP4K4,MAPK10,MMP9,NCF2,NOX4,PIK3R3,PIK3R5,PLCB2,PLD1,PLD2,PLD4,PLD6,PRKCB,PRKCQ,PTK2B,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,VASP,VEGFC
Autoimmune Thyroid Disease Signaling	5.88		0.367	CD28,CD86,FASLG,FCER1G,GZMB,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,PRF1
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	5.82		0.212	ADAMTS4,AKT2,ALPL,BIRC3,BMP2,BMP3,CASP9,CHP1,FLT3,FRZB,FZD7,FZD9,IKBKE,IL18,IL18R1,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IL6,IRS1,IRS2,ITGA2,ITGA5,JUN,KLB,LEF1,MAP3K5,MAPK10,NFATC2,NFKBIE,NGFR,PIK3R3,PIK3R5,PTK2B,RUNX2,SFRP2,SFRP4,SMAD6,SPP1,TCF7,TGFB1,TNF,TNFRSF11B,TNFRSF1B,WNT2B,WNT3
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	5.77	2.529822128	0.438	B2M,BID,CASP3,CASP9,CD247,CD3D,CD3E,FASLG,FCER1G,GZMB,HLA-A,HLA-B,HLA-C,PRF1
T Cell Receptor Signaling	5.67		0.258	BMX,BTK,CARD11,CD247,CD28,CD3D,CD3E,CD4,CD8A,CD8B,FLT3,GRAP2,IKBKE,IRS1,IRS2,ITK,JUN,KLB,LCK,LCP2,NFATC2,PAG1,PIK3R3,PIK3R5,PRKCQ,PTPN7,PTPRC,RASGRP1,VAV1,VAV2,VAV3
Cardiac Hypertrophy Signaling (Enhanced)	5.63	3.849741916	0.175	ACVR2B,ADCY6,AKAP13,AKT2,CHP1,CLCF1,CSF2RB,CTF1,CXCL8,CXCR1,CXCR2,DIAPH1,DIAPH3,EIF4EBP1,FASLG,FGF10,FGF11,FGF7,FGFRL1,FLT3,FZD7,FZD9,GNA15,GNAI2,GNG2,IFNLR1,IKBKE,IL10RA,IL12RB1,IL15,IL18,IL18R1,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL20RA,IL20RB,IL2RG,IL33,IL3RA,IL4R,IL6,IL7R,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITPR2,JUN,KLB,LEP,LTB,MAP3K5,MAP3K8,MAPK10,MEF2C,MYC,NFATC2,NGFR,NPR1,OSM,PDE11A,PDE1B,PDE3A,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PLD6,PRKCB,PRKCQ,RCAN1,TGFB1,TGFBR2,TNF,TNFRSF11B,TNFRSF1B,TNFSF13B,TNFSF15,TNFSF8,WNT2B,WNT3
Calcium-induced T Lymphocyte Apoptosis	5.58	4.024922359	0.318	CD247,CD3D,CD3E,CD4,CHP1,FCER1G,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,ITPR2,LCK,NFATC2,PRKCB,PRKCQ
NF-κB Signaling	5.48	2.967301476	0.221	AKT2,BMP2,CARD11,CSNK2A2,FCER1G,FLT3,IL18,IL1B,IL1R1,IL1R2,IL1RN,IL33,INSR,IRS1,IRS2,KLB,LCK,MAP3K8,MAP4K4,MYD88,NFKBIE,NGFR,NTRK1,NTRK3,PELI1,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,RELB,TGFA,TGFBR2,TIRAP,TLR10,TLR2,TLR8,TNF,TNFAIP3,TNFRSF11B,TNFRSF1B,TNFSF13B
STAT3 Pathway	5.42	1.147078669	0.244	CDKN1A,CISH,CSF2RB,CXCR1,CXCR2,HGF,IFNLR1,IL10RA,IL12RB1,IL18R1,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL20RA,IL20RB,IL2RG,IL3RA,IL4R,IL7R,INSR,MAPK10,MYC,NGFR,NTRK1,NTRK3,PIM1,PTPN6,SOCS3,TGFA,TGFB1,TGFBR2

Signaling by Rho Family GTPases	5.3	3.618136135	0.201	ACTB,ACTG1,ACTR3,ARHGEF19,ARHGEF2,ARHGEF3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CDC42EP3,CDH23,CDH24,CDH3,CFL1,CIT,DES,DIAPH3,FLT3,GNA15,GNAI2,GNB4,GNG2,IRS1,IRS2,ITGA2,ITGA4,ITGA5,JUN,KLB,MAPK10,MSN,MYL12A,MYL4,MYLK,NCF2,NOX4,PIK3R3,PIK3R5,PLD1,PTK2B,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,STMN1,WAS,WIPF1
OX40 Signaling Pathway	5.3	0.707106781	0.278	B2M,CD247,CD3D,CD3E,CD4,FCER1G,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,JUN,MAPK10,NFKBIE
Axonal Guidance Signaling	5.26		0.172	ABLIM2,ACTR3,ADAM11,ADAM23,ADAM28,ADAM32,ADAMTS1,ADAMTS10,ADAMTS4,AFG3L2,AKT2,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,BDNF,BMP2,BMP3,CFL1,CHP1,CXCR4,ECE2,ECEL1,ENPEP,EPHA4,EPHA7,FLT3,FZD7,FZD9,GLI3,GLIS1,GNA15,GNAI2,GNB4,GNG2,IRS1,IRS2,ITGA2,ITGA4,ITGA5,KLB,MICAL1,MME,MMP25,MMP9,MYL12A,MYL4,NFATC2,NGFR,NTRK1,NTRK3,PDGFA,PFN1,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,PTCH1,RAC2,RASSF5,RND1,ROBO1,SDC2,SEMA4A,SEMA4D,SEMA4F,SEMA4G,SEMA6B,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3,VASP,VEGFC,WAS,WIPF1,WNT2B,WNT3
HMGB1 Signaling	5.25	2.886751346	0.221	AKT2,CCL2,CLCF1,CXCL8,FASLG,FLT3,ICAM1,IL15,IL18,IL1B,IL1R1,IL33,IL6,IRS1,IRS2,JUN,KLB,LEP,LTB,MAPK10,NGFR,OSM,PIK3R3,PIK3R5,PLAT,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,SELE,SERPINE1,TGFB1,TNF,TNFRSF11B,TNFRSF1B,TNFSF13B,TNFSF15,TNFSF8
PI3K Signaling in B Lymphocytes	5.2	3.528211425	0.239	AKT2,ATF3,ATF7,BLK,BLNK,BTK,CD19,CD79A,CD79B,CHP1,CR2,DAPP1,IKBKE,IL4R,INPP5D,IRS1,IRS2,ITPR2,JUN,LYN,NFATC2,NFKBIE,PIK3AP1,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PTPRC,SYK,VAV1,VAV2,VAV3
Actin Cytoskeleton Signaling	5.2	3.781176708	0.205	ACTB,ACTG1,ACTN2,ACTR3,ARHGAP24,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CD14,CFL1,CYFIP2,DIAPH1,DIAPH3,F2R,FGD3,FGF10,FGF11,FGF7,FLT3,IQGAP3,IRS1,IRS2,ITGA2,ITGA4,ITGA5,KLB,LBP,MATK,MSN,MYH7B,MYL12A,MYL4,MYLK,NCKAP1L,PDGFA,PFN1,PIK3R3,PIK3R5,RAC2,TIAM1,TMSB10/TMSB4X,VAV1,VAV2,VAV3,WAS
Nur77 Signaling in T Lymphocytes	5.19		0.322	CASP3,CASP9,CD247,CD28,CD3D,CD3E,CD86,CHP1,FCER1G,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5
Allograft Rejection Signaling	5.15		0.279	B2M,CD28,CD86,FASLG,FCER1G,GZMB,HLA-A,HLA-B,HLA-C,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DPA1,HLA-DPB1,HLA-DQA1,HLA-DQA2,HLA-DQB1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,PRF1,TNF
IL-6 Signaling	5.13	3.286335345	0.237	A2M,ABCB1,AKT2,CD14,CSNK2A2,CXCL8,FLT3,IKBKE,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IL6,IRS1,IRS2,JUN,KLB,LBP,MAP4K4,MAPK10,MCL1,NFKBIE,NGFR,PIK3R3,PIK3R5,SOCS3,TNF,TNFRSF11B,TNFRSF1B
Integrin Signaling	5.12	3.703280399	0.205	ACTB,ACTG1,ACTN2,ACTR3,AKT2,ARF4,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,ASAP1,CAPN6,CAPN8,CAPN9,FLT3,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGA8,ITGAD,ITGAL,ITGAX,ITGB2,ITGB4,KLB,MYL12A,MYLK,NEDD9,PFN1,PIK3R3,PIK3R5,PLCG2,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,TSPAN1,TSPAN7,VASP,WAS,WIPF1
LPS/IL-1 Mediated Inhibition of RXR Function	5.03	2.293658555	0.205	ABCB1,ABCC3,ABCC4,ABCG1,ACSL1,ALDH1A2,ALDH2,ALDH6A1,ALDH7A1,ALDH9A1,APOC1,CAT,CD14,CHST11,CYP2C8,FABP4,FABP5,FMO2,GSTM1,GSTM5,HMGCS2,HS3ST2,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IL4I1,JUN,LBP,LY96,MYD88,NGFR,PAPSS2,PLTP,PPARA,PPARGC1B,SULT1A1,SULT1A2,SULT1B1,TNF,TNFRSF11B,TNFRSF1B
Tumoricidal Function of Hepatic Natural Killer Cells	4.88	1.666666667	0.458	BAX,BID,CASP3,CASP9,FASLG,GZMB,ICAM1,ITGAL,PRF1,SERPINB9,SRGN
fMLP Signaling in Neutrophils	4.76	3.137858162	0.235	ACTR3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CHP1,FLT3,FPR1,FPR2,FPR3,GNAI2,GNB4,GNG2,IRS1,IRS2,ITPR2,KLB,NCF1,NCF2,NFATC2,NFKBIE,NOX4,PIK3R3,PIK3R5,PLCB2,PLCB4,PRKCB,PRKCQ,WAS
Role of Hypercytokinemia/hyperchemokinemia in the	4.69		0.349	CCL2,CCL3,CCL4,CCL5,CCR1,CCR5,CXCL10,CXCL8,IL15,IL18,IL1B,IL1RN,IL33,IL6,TNF

Pathogenesis of Influenza				
Remodeling of Epithelial Adherens Junctions	4.66	2.828427125	0.29	ACTB,ACTG1,ACTN2,ACTR3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CTNNA2,DNM3,HGF,MAPRE1,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3
RhoGDI Signaling	4.55	-3.771711343	0.211	ACTB,ACTG1,ACTR3,ARHGAP6,ARHGAP9,ARHGDIB,ARHGEF19,ARHGEF2,ARHGEF3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CD44,CDH23,CDH24,CDH3,CFL1,ESR2,GNA15,GNAI2,GNB4,GNG2,GRIP1,ITGA2,ITGA4,ITGA5,MSN,MYL12A,MYL4,RAC2,RHOC,RHOG,RHOH,RHOU,RND1
Antioxidant Action of Vitamin C	4.52	-2.236067977	0.243	CSF2RB,GLRX,IKBKE,MAPK10,NFKBIE,NXN,PAFAH1B3,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,PLCB2,PLCB4,PLCD4,PLCG2,PLD1,PLD2,PLD4,PLD6,RARRES3,SLC2A3,SLC2A4,SLC2A5,TNF,TXN,TXNRD1
Toll-like Receptor Signaling	4.52	1.5	0.276	CD14,IL18,IL1B,IL1RL1,IL1RN,IL33,IRAK2,JUN,LBP,LY96,MAP4K4,MYD88,PPARA,TICAM2,TIRAP,TLR10,TLR2,TLR8,TNF,TNFAIP3,TRAF4
IL-4 Signaling	4.52		0.253	AKT2,FLT3,HLA-A,HLA-B,HLA-DMA,HLA-DMB,HLA-DOA,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IL2RG,IL4R,INPP5D,INPP5J,IRS1,IRS2,JAK3,KLB,NFATC2,PIK3R3,PIK3R5,PTPN6,SYNJ2
Clathrin-mediated Endocytosis Signaling	4.47		0.202	ACTB,ACTG1,ACTR3,ALB,AP1M2,AP1S2,AP2S1,APOC1,APOL1,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,ARRB2,CHP1,CLU,CSNK2A2,DAB2,DNM3,F2R,FGF10,FGF11,FGF7,FLT3,IRS1,IRS2,ITGA5,ITGB2,ITGB4,KLB,LYZ,MYO1E,PDGFA,PIK3R3,PIK3R5,S100A8,SERPINA1,TF,TFRC,VEGFC
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	4.46		0.5	CCL2,CCL3,CCL4,CCL5,CSF3,CXCL1,IL1B,IL6,TNF
Caveolar-mediated Endocytosis Signaling	4.46		0.282	ACTB,ACTG1,ALB,B2M,CD48,COPG2,FLOT1,HLA-A,HLA-B,HLA-C,INSR,ITGA2,ITGA4,ITGA5,ITGA8,ITGAD,ITGAL,ITGAX,ITGB2,ITGB4
Regulation of Actin-based Motility by Rho	4.45	4.264014327	0.255	ACTB,ACTR3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CFL1,ITGA2,ITGA4,ITGA5,MYL12A,MYL4,MYLK,PFN1,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,WAS,WIPF1
Superpathway of Inositol Phosphate Compounds	4.24	3.202469977	0.192	ALPL,CA3,CD19,CD28,CD86,CDC25B,DUSP2,DUSP5,EYA4,FLT3,HACD2,ICOS,INPP5D,INPP5J,IRS1,IRS2,ITPKC,KLB,LCK,MTMR8,PHOSPHO1,PIK3AP1,PIK3R3,PIK3R5,PIP4K2A,PLCB2,PLCB4,PLCD4,PLCG2,PLD4,PPFIA3,PPP1R14B,PPP1R1B,PPP2R5A,PTPN22,PTPN6,PTPN7,PTPRC,PTPRF,PTPRJ,RAC2,RHOG,SOCS3,SYNJ2,TRAT1,VAV1
Phospholipase C Signaling	4.1	5.239956379	0.187	ADCY6,ARHGEF19,ARHGEF2,ARHGEF3,BLNK,BTK,CD247,CD3D,CD3E,CD79A,CD79B,CHP1,FCER1G,FCGR2A,GNB4,GNG2,GRAP2,ITGA2,ITGA4,ITGA5,ITK,ITPR2,LCK,LCP2,LYN,MEF2C,MYL12A,MYL4,NFATC2,PLA2G2A,PLA2G2D,PLCB2,PLCB4,PLCD4,PLCG2,PLD1,PLD2,PLD4,PLD6,PRKCB,PRKCQ,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,SYK
Pancreatic Adenocarcinoma Signaling	4.04	1.279204298	0.226	AKT2,BIRC5,BRCA2,CASP9,CCND1,CDK2,CDKN1A,CDKN2A,E2F3,FLT3,HBEGF,IRS1,IRS2,JAK3,KLB,MAPK10,MMP9,PIK3R3,PIK3R5,PLD1,PLD2,PLD4,PLD6,RAD51,TGFA,TGFB1,TGFBR2,VEGFC
Gαq Signaling	3.85	1.825741858	0.202	AKT2,BTK,CHP1,FLT3,GNA15,GNB4,GNG2,IKBKE,IRS1,IRS2,ITPR2,KLB,NFATC2,NFKBIE,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCG2,PLD1,PLD2,PLD4,PLD6,PRKCB,PRKCQ,PTK2B,RAC2,RGS16,RGS18,RGS2,RHOC,RHOG,RHOH,RHOU,RND1
Actin Nucleation by ARP-WASP Complex	3.85	4	0.264	ACTR3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,ITGA2,ITGA4,ITGA5,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,VASP,WAS,WIPF1
Sphingosine-1-phosphate Signaling	3.82	1.568929081	0.216	ADCY6,AKT2,CASP1,CASP3,CASP4,CASP5,CASP9,FLT3,GNAI2,IRS1,IRS2,KLB,PDGFA,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PTK2B,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,S1PR1,S1PR5,SPHK1

Role of Tissue Factor in Cancer	3.76		0.215	AKT2,ARRB2,BLK,CASP3,CCN1,CFL1,CTGF,CXCL1,CXCL8,F2RL1,FGR,FLT3,GNA15,HBEGF,HCK,IL1B,IRS1,IRS2,KLB,LCK,LYN,PDIA2,PIK3R3,PIK3R5,PLAUR,PTK2B,RPS6KA1,RPS6KA6,VEGFC
Fc Epsilon RI Signaling	3.67	2.2	0.215	AKT2,BTK,FCER1A,FCER1G,FLT3,GRAP2,INPP5D,INPP5J,IRS1,IRS2,KLB,LCP2,LYN,MAPK10,PIK3R3,PIK3R5,PLA2G2A,PLA2G2D,PLCG2,PRKCB,PRKCQ,RAC2,SYK,SYNJ2,TNF,VAV1,VAV2,VAV3
ILK Signaling	3.62	2.263009527	0.19	ACTB,ACTG1,ACTN2,AKT2,BMP2,CASP3,CCND1,CFL1,FBLIM1,FERMT2,FLT3,HIF1A,IRS1,IRS2,ITGB2,ITGB4,JUN,KLB,LEF1,MAPK10,MMP9,MYC,MYH7B,MYL4,PIK3R3,PIK3R5,PPM1J,PPP1R14B,PPP2R5A,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,SNAI1,TMSB10/TMSB4X,TNF,VEGFC
Reelin Signaling in Neurons	3.54		0.234	ARHGEF2,ARHGEF3,BLK,DAB1,FGR,FLT3,HCK,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGAL,ITGB2,KLB,LCK,LYN,MAP4K1,MAPK10,PAFAH1B3,PIK3R3,PIK3R5
Complement System	3.52	-0.377964473	0.324	C1QA,C1QB,C3AR1,C5,C5AR1,CD59,CFI,CR1,CR2,ITGAX,ITGB2,MASP2
Epithelial Adherens Junction Signaling	3.49		0.203	ACTB,ACTG1,ACTN2,ACTR3,ACVR2B,AKT2,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CTNNA2,HGF,LEF1,MAGI2,MYH7B,MYL4,NECTIN3,NOTCH2,SNAI1,TCF7,TGFBR2,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3,VAV2,WAS
Phospholipases	3.46	2.182820625	0.262	LIPG,PAFAH1B3,PLA1A,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,PLCB2,PLCB4,PLCD4,PLCG2,PLD1,PLD2,PLD4,PLD6,RARRES3
Virus Entry via Endocytic Pathways	3.43		0.215	ACTB,ACTG1,AP1M2,AP1S2,AP2S1,B2M,FLT3,HLA-A,HLA-B,HLA-C,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGAL,ITGB2,ITGB4,KLB,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,RAC2,TFRC
Systemic Lupus Erythematosus Signaling	3.38		0.18	AKT2,C5,CD22,CD247,CD28,CD3D,CD3E,CD72,CD79A,CD79B,CD86,CREM,FCER1G,FCGR1A,FCGR1B,FCGR2A,FCGR3A/FCGR3B,FLT3,HLA-A,HLA-B,HLA-C,HLA-E,IGHM,IL18,IL1B,IL1RN,IL33,IL6,INPP5D,IRS1,IRS2,JUN,KLB,LCK,LYN,NFATC2,PIK3R3,PIK3R5,PLCG2,PTPN6,PTPRC,TNF,TNFSF13B
Salvage Pathways of Pyrimidine Deoxyribonucleotides	3.24	2.236067977	0.625	APOBEC3A,APOBEC3B,APOBEC3G,CDA,TK1
Eicosanoid Signaling	3.21	2.529822128	0.25	ALOX15B,ALOX5,ALOX5AP,CYSLTR1,DPEP2,FPR2,HPGDS,PAFAH1B3,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,PTGFR,PTGIR,RARRES3,TBXAS1
Molecular Mechanisms of Cancer	3.16		0.159	ADCY6,AKT2,ARHGEF19,ARHGEF2,ARHGEF3,BAX,BID,BIRC3,BMP2,BMP3,CASP3,CASP9,CCND1,CCNE2,CDC25B,CDK1,CDK2,CDK20,CDKN1A,CDKN2A,CDKN2C,CTNNA2,E2F3,FANCD2,FASLG,FLT3,FZD7,FZD9,GNA15,GNAI2,HIF1A,IRS1,IRS2,ITGA2,ITGA4,ITGA5,JAK3,JUN,KLB,LEF1,MAP3K5,MAPK10,MYC,NFKBIE,PIK3R3,PIK3R5,PLCB2,PLCB4,PMAIP1,PRKCB,PRKCQ,PTCH1,RAC2,RASGRP1,RHOC,RHOG,RHOH,RHOU,RND1,SMAD6,TGFB1,TGFBR2,WNT2B,WNT3
Ethanol Degradation IV	3.14	-1.666666667	0.36	ACSL1,ACSS2,ACSS3,ALDH1A2,ALDH2,ALDH7A1,ALDH9A1,CAT,GPX7
Coagulation System	3.14	0.301511345	0.314	A2M,F13A1,F2R,F5,PLAT,PLAUR,PROS1,SERPINA1,SERPINE1,THBD,VWF
CCR5 Signaling in Macrophages	3.12	2.110579412	0.223	CACNA2D3,CACNG8,CCL3,CCL4,CCL5,CCR5,CD247,CD3D,CD3E,CD4,FASLG,FCER1G,GNAI2,GNB4,GNG2,JUN,MAPK10,PLCG2,PRKCB,PRKCQ,PTK2B
Rac Signaling	3.1	3.4	0.205	ACTR3,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CD44,CFL1,CYFIP2,FLT3,IQGAP3,IRS1,IRS2,ITGA2,ITGA4,ITGA5,JUN,KLB,NCF2,NOX4,PIK3R3,PIK3R5,PLD1,PTK2B,TIAM1
IL-12 Signaling and Production in Macrophages	3.06		0.196	AKT2,ALB,APOC1,APOL1,CLU,FLT3,IKBKE,IL12RB1,IL18,IRF1,IRF8,IRS1,IRS2,JUN,KLB,LYZ,MAP3K8,MAPK10,MYD88,PIK3R3,PIK3R5,PRKCB,PRKCQ,S100A8,SERPINA1,SPI1,TGFB1,TLR2,TNF
p70S6K Signaling	2.97	2.353393622	0.196	AKT2,BTK,CD19,CD79A,CD79B,F2R,F2RL1,FLT3,GNAI2,IL2RG,IL4R,IRS1,IRS2,KLB,LYN,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PLD1,PPM1J,PPP2R5A,PRKCB,PRKCQ,SYK,YWHAH
Acute Phase Response Signaling	2.92	3.271651525	0.184	A2M,AKT2,ALB,C5,CP,CRABP1,FTL,IKBKE,IL18,IL1B,IL1R1,IL1RN,IL33,IL6,JUN,LBP,MAP3K5,MYD88,NFKBIE,NGFR,OSM,OSMR,PIK3R3,RBP5,SAA1,SERPINA1,SERPINE1,SOCS3,TF,TNF,TNFRSF11B,TNFRSF1B,VWF

Death Receptor Signaling	2.91	2.236067977	0.22	ACTB,ACTG1,ARHGDIB,BID,BIRC3,CASP3,CASP9,FASLG,IKBKE,MAP3K5,MAP4K4,NFKBIE,PARP12,PARP14,PARP16,TNF,TNFRSF10A,TNFRSF10B,TNFRSF1B,TNFSF15
IL-23 Signaling Pathway	2.9	0	0.25	AKT2,FLT3,FOXP3,HIF1A,IL12RB1,IL1B,IRS1,IRS2,KLB,PIK3R3,PIK3R5,RORC,RUNX1,SOCS3,TNF
Induction of Apoptosis by HIV1	2.82	1.290994449	0.246	BAX,BID,BIRC3,CASP3,CASP9,CXCR4,FASLG,IKBKE,MAP3K5,MAPK10,NFKBIE,NGFR,TNF,TNFRSF11B,TNFRSF1B
Apoptosis Signaling	2.81	-0.447213595	0.212	BAX,BCL2A1,BID,BIRC3,CAPN6,CAPN8,CAPN9,CASP3,CASP9,CDK1,FASLG,IKBKE,MAP3K5,MAP4K4,MCL1,NFKBIE,PLCG2,PRKCQ,RPS6KA1,TNF,TNFRSF1B
Endothelin-1 Signaling	2.78	2.743977362	0.176	ADCY6,CASP1,CASP3,CASP4,CASP5,CASP9,ECE2,FLT3,GNA15,GNAI2,IRS1,IRS2,ITPR2,JUN,KLB,MAPK10,MYC,PAFAH1B3,PIK3R3,PIK3R5,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,PLCB2,PLCB4,PLCD4,PLCG2,PLD1,PLD2,PLD4,PLD6,PRKCB,PRKCQ,RARRES3
Human Embryonic Stem Cell Pluripotency	2.78		0.19	AKT2,BDNF,BMP2,BMP3,FGFRL1,FLT3,FZD7,FZD9,IRS1,IRS2,KLB,LEF1,NODAL,NTRK1,NTRK3,PDGFA,PIK3R3,PIK3R5,POU5F1,S1PR1,S1PR5,SMAD6,SPHK1,TCF7,TGFB1,TGFBR2,WNT2B,WNT3
IL-7 Signaling Pathway	2.78	1.605910137	0.215	AKT2,BAX,CCND1,CDK2,FLT3,HGF,IGHM,IL2RG,IL7R,IRS1,IRS2,JAK3,JUN,KLB,LYN,MCL1,MYC,PAX5,PIK3R3,PIK3R5
3-phosphoinositide Biosynthesis	2.74	2.611164839	0.176	ALPL,CA3,CD19,CD28,CD86,CDC25B,DUSP2,DUSP5,EYA4,FLT3,HACD2,ICOS,IRS1,IRS2,KLB,LCK,MTMR8,PHOSPHO1,PIK3AP1,PIK3R3,PIK3R5,PPFIA3,PPP1R14B,PPP1R1B,PPP2R5A,PTPN22,PTPN6,PTPN7,PTPRC,PTPRF,PTPRJ,RAC2,RHOG,SOCS3,TRAT1,VAV1
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	2.73		0.348	CCL2,CCL3,CCL4,CCL5,CSF3,CXCL1,IL1B,TNF
14-3-3-mediated Signaling	2.69	0.688247202	0.19	AKT2,BAX,FLT3,IRS1,IRS2,JUN,KLB,MAP3K5,MAPK10,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,RPS6KA1,SNCA,TNF,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3,YWHAH
Inhibition of Angiogenesis by TSP1	2.66	0.707106781	0.294	AKT2,CASP3,JUN,MAPK10,MMP9,SDC1,SDC2,TGFB1,TGFBR2,THBS1
Glioma Invasiveness Signaling	2.58	2	0.211	CD44,F2R,FLT3,HMMR,IRS1,IRS2,KLB,MMP9,PIK3R3,PIK3R5,PLAUR,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,TIMP1,VTN
HGF Signaling	2.56	1.279204298	0.194	AKT2,CCND1,CDK2,CDKN1A,CDKN2A,ETS2,FLT3,HGF,IL6,IRS1,IRS2,ITGA2,ITGA4,ITGA5,JUN,KLB,MAP3K5,MAP3K8,MAPK10,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ
p38 MAPK Signaling	2.52	3.577708764	0.195	CDC25B,FASLG,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,IRAK2,MAP3K5,MAP4K1,MEF2C,MYC,PLA2G2A,PLA2G2D,RPS6KA1,RPS6KA6,TGFB1,TGFBR2,TNF,TNFRSF1B
NF-κB Activation by Viruses	2.5	2.357022604	0.204	AKT2,CCR5,CD4,CR2,FLT3,IKBKE,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGAL,ITGB2,KLB,LCK,NFKBIE,PIK3R3,PIK3R5,PRKCB,PRKCQ
PTEN Signaling	2.47	-0.208514414	0.19	AKT2,CASP3,CASP9,CCND1,CDKN1A,CSNK2A2,FASLG,IKBKE,INPP5D,INPP5J,INSR,ITGA2,ITGA4,ITGA5,MAGI2,NGFR,NTRK1,NTRK3,PIK3R3,PIK3R5,RAC2,SYNJ2,TGFBR2,YWHAH
IL-17A Signaling in Gastric Cells	2.47	1.341640786	0.32	CCL5,CXCL1,CXCL10,CXCL11,CXCL8,JUN,MAPK10,TNF
p53 Signaling	2.43	1.414213562	0.195	AKT2,BAX,BIRC5,CCND1,CDK2,CDKN1A,CDKN2A,DRAM1,FLT3,HIF1A,IRS1,IRS2,JUN,KLB,PIK3R3,PIK3R5,PLAGL1,PMAIP1,SERPINE2,THBS1,TNFRSF10A,TNFRSF10B
Phagosome Maturation	2.43		0.182	ATP6V0B,ATP6V0D1,ATP6V1B2,ATP6V1C2,B2M,CTSB,CTSS,CTSV,CTSW,CTSZ,DYNC1I1,DYNC2H1,HLA-A,HLA-B,HLA-C,HLA-DRA,HLA-DRB1,HLA-DRB5,NCF2,NOX4,TAP1,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3
Docosahexaenoic Acid	2.43		0.241	AKT2,BAX,BCL2A1,BID,CASP3,CASP9,FLT3,IL1B,IRS1,IRS2,KLB,PIK3R3,PIK3R5

(DHA) Signaling				
IL-15 Production	2.38		0.19	ALK,BLK,BMX,BTK,EPHA4,FGR,HCK,IL15,IL6,INSR,IRF1,ITK,JAK3,LCK,LYN,MATK,MERTK,NTRK1,NTRK3,PTK2B,ROR2,STYK1,SYK
Estrogen-mediated S-phase Entry	2.36	1.414213562	0.308	CCND1,CCNE2,CDK1,CDK2,CDKN1A,E2F3,ESR2,MYC
Hematopoiesis from Pluripotent Stem Cells	2.35		0.245	CD247,CD3D,CD3E,CD4,CD8A,CD8B,CSF3,CXCL8,FCER1G,IGHD,IGHM,IL6
Acetate Conversion to Acetyl-CoA	2.35		0.75	ACSL1,ACSS2,ACSS3
Aryl Hydrocarbon Receptor Signaling	2.34	0.727606875	0.182	AHR,ALDH1A2,ALDH2,ALDH6A1,ALDH7A1,ALDH9A1,BAX,CCND1,CCNE2,CDK2,CDKN1A,CDKN2A,CYP1B1,ESR2,FASLG,GSTM1,GSTM5,IL1B,IL6,JUN,MYC,NFIC,NFIX,NQO1,TGFB1,TNF
Granzyme B Signaling	2.34	1.341640786	0.375	BID,CASP3,CASP9,GZMB,LMNB1,PRF1
Parkinson's Signaling	2.34		0.375	CASP3,CASP9,GPR37,SNCA,SNCAIP,UCHL1
Vitamin-C Transport	2.34		0.375	GLRX,NXN,SLC2A3,SLC2A4,TXN,TXNRD1
Oxidative Ethanol Degradation III	2.33	-1.889822365	0.333	ACSL1,ACSS2,ACSS3,ALDH1A2,ALDH2,ALDH7A1,ALDH9A1
Apelin Cardiomyocyte Signaling Pathway	2.33	0.688247202	0.191	AKT2,CAT,FLT3,GNAI2,HIF1A,IRS1,IRS2,KLB,MAPK10,MYL12A,MYL4,MYLK,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,SLC8A1,TGFB1
RhoA Signaling	2.29	2.984810029	0.187	ACTB,ACTG1,ACTR3,ANLN,ARHGAP6,ARHGAP9,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CDC42EP3,CFL1,CIT,LPAR2,MSN,MYL12A,MYL4,MYLK,PFN1,PLD1,PTK2B
Germ Cell-Sertoli Cell Junction Signaling	2.29		0.17	A2M,ACTB,ACTG1,ACTN2,CFL1,CTNNA2,FLT3,IRS1,IRS2,ITGA2,KLB,MAP3K5,MAP3K8,MAPK10,NECTIN3,PIK3R3,PIK3R5,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,TGFB1,TGFBR2,TNF,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3
Endocannabinoid Cancer Inhibition Pathway	2.28	1	0.176	ADCY6,AKT2,ATF3,CASP1,CASP3,CASP4,CASP5,CASP9,CCND1,CCNE2,CDKN1A,FLT3,GNAI2,GPR55,HIF1A,IRS1,IRS2,KLB,LEF1,MYC,PIK3R3,PIK3R5,SPTLC2,TCF7,TRPV1,TWIST1,TWIST2,VEGFC
Gα12/13 Signaling	2.22	1.632993162	0.178	AKT2,BTK,CDH23,CDH24,CDH3,F2R,F2RL1,FLT3,IKBKE,IRS1,IRS2,JUN,KLB,LPAR2,MAP3K5,MAPK10,MEF2C,MYL12A,MYL4,NFKBIE,PIK3R3,PIK3R5,PTK2B,VAV1,VAV2,VAV3
CXCR4 Signaling	2.21	3	0.169	ADCY6,AKT2,CD4,CXCR4,ELMO1,FLT3,GNA15,GNAI2,GNB4,GNG2,IRS1,IRS2,ITPR2,JUN,KLB,LYN,MAPK10,MYL12A,MYL4,PIK3R3,PIK3R5,PLCB2,PLCB4,PRKCB,PRKCQ,RAC2,RHOC,RHOG,RHOH,RHOU,RND1
Apelin Cardiac Fibroblast Signaling Pathway	2.21	-2.645751311	0.318	AKT2,ANGPT2,CTGF,IL6,SERPINE1,SPHK1,TGFB1
PPAR Signaling	2.2	-4.024922359	0.192	CITED2,IKBKE,IL18,IL18RAP,IL1B,IL1R1,IL1R2,IL1RL1,IL1RN,IL33,INSR,JUN,MAP4K4,NFKBIE,NGFR,PDGFA,PPARA,TNF,TNFRSF11B,TNFRSF1B
Airway Pathology in Chronic Obstructive Pulmonary Disease	2.2		0.5	CXCL3,CXCL8,MMP9,TNF
Colorectal Cancer Metastasis Signaling	2.19	2.057983022	0.157	ADCY6,AKT2,BAX,BIRC5,CASP3,CASP9,CCND1,FLT3,FZD7,FZD9,GNB4,GNG2,GRK3,IL6,IRS1,IRS2,JAK3,JUN,KLB,LEF1,MAPK10,MMP25,MMP9,MYC,PIK3R3,PIK3R5,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,TCF7,TGFB1,TGFBR2,TLR10,TLR2,TLR8,TNF,VEGFC,WNT2B,WNT3
Cholecystokinin/Gastrin-	2.15	4.024922359	0.185	CREM,EPHA4,IL18,IL1B,IL1RN,IL33,ITPR2,JUN,MAPK10,MEF2C,PLCB2,PLCB4,PRKCB,PRKCQ,PTK2B,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,TNF

mediated Signaling				
FAT10 Cancer Signaling Pathway	2.11	2.110579412	0.239	ACVR2B,AKT2,CXCR4,IKBKE,IL6,NGFR,TGFB1,TGFBR2,TNF,TNFRSF11B,TNFRSF1B
Ethanol Degradation II	2.11	-2.333333333	0.265	ACSL1,ACSS2,ACSS3,ADH1B,ADHFE1,ALDH1A2,ALDH2,ALDH7A1,ALDH9A1
Sertoli Cell-Sertoli Cell Junction Signaling	2.1		0.167	A2M,ACTB,ACTG1,ACTN2,AKT2,CLDN10,CLDN2,CLDN4,CLDN9,CTNNA2,ITGA2,ITGA4,ITGA5,JAM2,JUN,MAGI2,MAP3K5,MAP3K8,MAPK10,NECTIN3,SPTA1,SPTB,TJP2,TNF,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3,WAS
Sperm Motility	2.07	2.182820625	0.16	ALK,BLK,BMX,BTK,EPHA4,FGR,HCK,INSR,ITK,ITPR2,JAK3,LCK,LYN,MATK,MERTK,NPR1,NTRK1,NTRK3,PAFAH1B3,PDE1B,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,PTK2B,RARRES3,ROR2,STYK1,SYK
Role of IL-17A in Psoriasis	2.07		0.385	CXCL1,CXCL3,CXCL8,S100A8,S100A9
Factors Promoting Cardiogenesis in Vertebrates	2.06		0.194	ACVR2B,BMP2,BMP3,CCNE2,CDC6,CDK2,FZD7,FZD9,LEF1,MEF2C,NODAL,NOX4,PRKCB,PRKCQ,TCF7,TGFB1,TGFBR2,WNT3
Valine Degradation I	2.06	-0.816496581	0.333	ABAT,ALDH6A1,BCAT1,BCAT2,DBT,SDS
Glioblastoma Multiforme Signaling	2.05	1.176696811	0.167	AKT2,CCND1,CDK2,CDKN1A,CDKN2A,E2F3,FLT3,FZD7,FZD9,IRS1,IRS2,ITPR2,KLB,LEF1,MYC,PDGFA,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,WNT2B,WNT3
Wnt/β-catenin Signaling	2.04	-0.816496581	0.168	ACVR2B,AKT2,AXIN2,BCL9,CCND1,CD44,CDH3,CDKN2A,CSNK2A2,FRZB,FZD7,FZD9,JUN,LEF1,MAP4K1,MYC,POU5F1,PPM1J,PPP2R5A,SFRP2,SFRP4,SOX4,SOX6,TCF7,TGFB1,TGFBR2,TLE4,WNT2B,WNT3
IL-9 Signaling	2.04	0.333333333	0.234	CISH,FLT3,IL2RG,IRS1,IRS2,JAK3,KLB,PIK3R3,PIK3R5,SOCS3,TNF
Myc Mediated Apoptosis Signaling	2.02		0.2	AKT2,BAX,BID,CASP3,CASP9,CDKN2A,FASLG,FLT3,IRS1,IRS2,KLB,MAPK10,MYC,PIK3R3,PIK3R5,YWHAH
Lysine Degradation V	1.99		0.6	AADAT,ALDH7A1,PIPOX
Tetrahydrofolate Salvage from 5,10-methenyltetrahydrofolate	1.99		0.6	MTHFD1,MTHFD1L,MTHFD2
MSP-RON Signaling Pathway	1.98		0.203	ACTB,ACTG1,CCL2,CCR2,CSF2RB,FLT3,IL3RA,IRS1,IRS2,ITGB2,KLB,PIK3R3,PIK3R5,TLR2,TNF
Alanine Biosynthesis II	1.95		1	GPT,GPT2
Alanine Degradation III	1.95		1	GPT,GPT2
Cysteine Biosynthesis/ Homocysteine Degradation	1.95		1	CBS/CBSL,CTH
Guanine and Guanosine Salvage I	1.95		1	HPRT1,PNP
Sulfate Activation for Sulfonation	1.95		1	PAPSS1,PAPSS2
β-alanine Degradation I	1.95		1	ABAT,ALDH6A1
Tight Junction Signaling	1.95		0.167	ACTB,ACTG1,AKT2,ARHGEF2,CEBPA,CLDN10,CLDN2,CLDN4,CLDN9,JAM2,JUN,MAGI2,MYH7B,MYL4,MYLK,NECTIN3,NGFR,PPM1J,PPP2R5A,RAB13,TGFB1,TGFBR2,TIAM1,TJP2,TNF,TNFRSF11B,TNFRSF1B,VASP

DNA damage-induced 14-3-3σ Signaling	1.94		0.316	AKT2,CCNB1,CCNB2,CCNE2,CDK1,CDK2
GADD45 Signaling	1.94		0.316	CCNB1,CCND1,CCNE2,CDK1,CDK2,CDKN1A
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	1.92		0.191	CARD11,CD247,CD28,CD3D,CD3E,CHP1,IKBKE,JUN,MAPK10,NFATC2,NFKBIE,PLCG2,TGFB1,TGFBR2,VAV1,VAV2,VAV3
Role of MAPK Signaling in the Pathogenesis of Influenza	1.92		0.195	AKT2,BAX,CASP3,CCL2,CCL5,CXCL10,MAP3K5,MAPK10,PAFAH1B3,PLA2G16,PLA2G2A,PLA2G2D,PLA2G7,PLB1,RARRES3,TNF
Acute Myeloid Leukemia Signaling	1.92	0.277350098	0.184	AKT2,CCND1,CEBPA,CSF2RB,CSF3R,EIF4EBP1,FLT3,IDH1,IRS1,IRS2,KLB,LEF1,MYC,PIK3R3,PIK3R5,PIM1,RUNX1,SPI1,TCF7
Ephrin A Signaling	1.9		0.21	CFL1,EPHA4,EPHA7,FLT3,IRS1,IRS2,KLB,NGFR,PIK3R3,PIK3R5,VAV1,VAV2,VAV3
Lymphotoxin β Receptor Signaling	1.89	0.577350269	0.203	AKT2,CASP3,CASP9,CXCL1,FLT3,IKBKE,IRS1,IRS2,KLB,LTB,PIK3R3,PIK3R5,RELB,TRAF4
FcγRIIB Signaling in B Lymphocytes	1.87	1.069044968	0.189	BLNK,BTK,CACNA2D3,CACNG8,CD79A,CD79B,FLT3,INPP5D,IRS1,IRS2,KLB,LYN,MAPK10,PIK3R3,PIK3R5,PLCG2,SYK
G Protein Signaling Mediated by Tubby	1.86		0.258	GNB4,GNG2,INSR,LCK,PLCB2,PLCB4,PLCG2,TUB
Th17 Activation Pathway	1.83	2.5	0.187	AHR,BATF,CCR6,FCER1G,FOXP3,HIF1A,IL12RB1,IL1B,IL1R1,IL6,IRAK2,JAK3,MYD88,NFATC2,RORC,RUNX1,SOCS3
Adrenomedullin signaling pathway	1.83	1.889822365	0.157	ADCY6,AKT2,BAX,CASP3,CTH,FLT3,GNA15,GPR37,HIF1A,IL18,IL1B,IL1RN,IL33,IRS1,IRS2,ITPR2,KCNH2,KCNQ3,KLB,MAPK10,MATK,MYLK,NPR1,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PTK2B,RAMP3,SMARCC2,TNF
Role of IL-17A in Arthritis	1.83		0.2	CCL2,CCL5,CXCL1,CXCL3,CXCL8,FLT3,IRS1,IRS2,KLB,MAPK10,NFKBIE,PIK3R3,PIK3R5,RPS6KA1
GM-CSF Signaling	1.82	1.290994449	0.19	AKT2,BCL2A1,CCND1,CISH,CSF2RB,FLT3,HCK,IRS1,IRS2,KLB,LYN,PIK3R3,PIK3R5,PIM1,PRKCB,RUNX1
GP6 Signaling Pathway	1.8	1.963961012	0.17	AKT2,BTK,COL10A1,COL11A1,COL24A1,COL6A6,FCER1G,FLT3,GRAP2,IRS1,IRS2,KLB,LAMA3,LAMC2,LCP2,LYN,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,RHOG,SYK
VDR/RXR Activation	1.78	1.154700538	0.192	CCL5,CD14,CDKN1A,CEBPA,CXCL10,IL1RL1,MXD1,PDGFA,PRKCB,PRKCQ,RUNX2,SERPINB1,SPP1,THBD,VDR
Choline Biosynthesis III	1.78	-0.447213595	0.333	CEPT1,PLD1,PLD2,PLD4,PLD6
iNOS Signaling	1.74	2.121320344	0.222	CD14,IKBKE,IRAK2,IRF1,JAK3,JUN,LBP,LY96,MYD88,NFKBIE
Growth Hormone Signaling	1.73	0	0.186	A2M,CEBPA,FLT3,IRS1,IRS2,KLB,PIK3R3,PIK3R5,PLCG2,PRKCB,PRKCQ,PTPN6,RPS6KA1,RPS6KA6,SLC2A4,SOCS3
Chondroitin and Dermatan Biosynthesis	1.72		0.5	CHSY1,CHSY3,CSGALNACT1
Urea Cycle	1.72		0.5	ARG1,ASS1,CPS1
Glucocorticoid Receptor Signaling	1.71		0.143	A2M,ACTB,AKT2,ANXA1,AR,CCL2,CCL3,CCL5,CD163,CD247,CD3D,CD3E,CDKN1A,CDKN1C,CEBPA,CHP1,CXCL3,CXCL8,FCGR1A,FLT3,HSPA1L,HSPA6,ICAM1,IKBKE,IL1B,IL1R2,IL1RN,IL6,IRS1,IRS2,JAK3,JUN,KLB,MAPK10,NFATC2,NFKBIE,PBX1,PCK1,PIK3R3,PIK3R5,POU2F2,SELE,SERPINE1,SGK1,SMARCC2,TAF13,TGFB1,TGFBR2,TNF,YWHAH
IL-15 Signaling	1.69		0.184	AKT2,CXCL8,FASLG,FLT3,IL15,IL2RG,IL6,IRS1,IRS2,JAK3,KLB,LCK,PIK3R3,PIK3R5,SYK,TNF

Small Cell Lung Cancer Signaling	1.69	0.577350269	0.184	AKT2,BID,CASP9,CCND1,CCNE2,CDK2,FLT3,IKBKE,IRS1,IRS2,KLB,MYC,NFKBIE,PIK3R3,PIK3R5,TRAF4
Breast Cancer Regulation by Stathmin1	1.69		0.153	ADCY6,ARHGEF19,ARHGEF2,ARHGEF3,CCNE2,CDK1,CDK2,CDKN1A,E2F3,FLT3,GNAI2,GNB4,GNG2,IRS1,IRS2,ITPR2,KLB,PIK3R3,PIK3R5,PLCB2,PLCB4,PPM1J,PPP1R14B,PPP2R5A,PRKCB,PRKCQ,STMN1,TUBA1B,TUBA1C,TUBA3C/TUBA3D,TUBA4A,TUBA8,TUBB3
Synaptogenesis Signaling Pathway	1.68	3.354894804	0.144	ACTR3,ADCY6,AKT2,AP2S1,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,BDNF,CADM1,CDH23,CDH24,CDH3,CFL1,CHN1,DAB1,DLG4,EIF4EBP1,EIF4EBP2,EPHA4,EPHA7,FGR,FLT3,GRIN3A,HCK,IRS1,IRS2,KLB,LCK,LYN,NECTIN3,PIK3R3,PIK3R5,PLCG2,RASGRP1,SNCA,SNCG,STXBP1,STXBP2,SYT12,SYT15,SYT17,THBS1,TIAM1,WAS
D-myo-inositol-5-phosphate Metabolism	1.66	2.353393622	0.16	ALPL,CA3,CDC25B,DUSP2,DUSP5,EYA4,HACD2,MTMR8,PHOSPHO1,PIP4K2A,PLCB2,PLCB4,PLCD4,PLCG2,PLD4,PPFIA3,PPP1R14B,PPP1R1B,PPP2R5A,PTPN22,PTPN6,PTPN7,PTPRC,PTPRF,PTPRJ,SOCS3
PI3K/AKT Signaling	1.65	1.605910137	0.167	AKT2,CCND1,CDKN1A,EIF4EBP1,GDF15,IKBKE,INPP5D,INPP5J,ITGA2,ITGA4,ITGA5,JAK3,MAP3K5,MAP3K8,MCL1,NFKBIE,PIK3R3,PPM1J,PPP2R5A,SYNJ2,THEM4,YWHAH
FAK Signaling	1.64		0.173	ACTB,ACTG1,AKT2,ASAP1,CAPN6,CAPN8,CAPN9,FLT3,HMMR,IRS1,IRS2,ITGA2,ITGA4,ITGA5,KLB,PIK3R3,PIK3R5,PLCG2,WAS
Role of JAK1 and JAK3 in γc Cytokine Signaling	1.64		0.185	BLNK,FLT3,IL15,IL2RG,IL4R,IL7R,IRS1,IRS2,JAK3,KLB,PIK3R3,PIK3R5,PTK2B,SOCS3,SYK
Retinoic acid Mediated Apoptosis Signaling	1.64	2.110579412	0.2	BID,CASP3,CASP9,CRABP1,IRF1,PARP12,PARP14,PARP16,TNFRSF10A,TNFRSF10B,TNFRSF10C,TNFRSF10D
FXR/RXR Activation	1.6		0.167	AKT2,ALB,APOC1,APOL1,CLU,FBP1,IL18,IL1B,IL1RN,IL33,MAPK10,MLXIPL,PLTP,PON3,PPARA,SAA1,SDC1,SERPINA1,TF,TNF,VTN
Role of Cytokines in Mediating Communication between Immune Cells	1.6		0.204	CSF3,CXCL8,IL15,IL18,IL1B,IL1RN,IL32,IL33,IL6,TGFB1,TNF
IL-2 Signaling	1.59	0.904534034	0.187	AKT2,CSNK2A2,FLT3,IL2RG,IRS1,IRS2,JAK3,JUN,KLB,LCK,PIK3R3,PIK3R5,PTK2B,SYK
Salvage Pathways of Pyrimidine Ribonucleotides	1.57	3.152963125	0.175	AK7,AKT2,APOBEC3A,APOBEC3B,APOBEC3G,CDA,CDK1,CDK2,MAP3K8,PCK1,PIM1,PRKCQ,PRKX,SGK1,TTK,UCK2,UPP1
NRF2-mediated Oxidative Stress Response	1.52	1.697749375	0.15	ABCC4,ACTB,ACTG1,BACH1,CAT,DNAJB11,DNAJB5,FLT3,FOSL1,FTH1,FTL,GCLC,GCLM,GSR,GSTM1,GSTM5,HERPUD1,HSPB8,IRS1,IRS2,JUN,KLB,MAFF,MAP3K5,NQO1,PIK3R3,PIK3R5,PRKCB,PRKCQ,TXN,TXNRD1
Thioredoxin Pathway	1.52		0.429	NXN,TXN,TXNRD1
4-aminobutyrate Degradation I	1.5		0.667	ABAT,SUCLG2
Glutathione Biosynthesis	1.5		0.667	GCLC,GCLM
L-carnitine Biosynthesis	1.5		0.667	ALDH9A1,TMLHE
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	1.5	-1.414213562	0.204	CCNB1,CCNB2,CDC25B,CDK1,CDKN1A,CDKN2A,CKS2,RPS6KA1,TOP2A,YWHAH
UVA-Induced MAPK Signaling	1.49	0.301511345	0.167	CASP3,CASP9,FLT3,IRS1,IRS2,JUN,KLB,MAPK10,PARP12,PARP14,PARP16,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,RPS6KA1,RPS6KA6
HER-2 Signaling in Breast Cancer	1.49		0.172	AKT2,AREG,CASP9,CCND1,CCNE2,CDKN1A,FLT3,IRS1,IRS2,ITGB2,ITGB4,KLB,MAP3K5,PIK3R3,PIK3R5,PRKCB,PRKCQ

Iron homeostasis signaling pathway	1.48		0.161	ATP6V0B,ATP6V0D1,ATP6V1B2,ATP6V1C2,BMP2,BMP3,CD163,CP,FTH1,FTL,GDF15,HEPH,HIF1A,IL6,JAK3,PDGFA,SLC11A1,SLC25A37,SLC39A14,SLC46A1,TF,TFRC
Interferon Signaling	1.48	2.828427125	0.222	BAX,IFI35,IFITM1,IFITM2,IFITM3,IRF1,PSMB8,TAP1
SPINK1 General Cancer Pathway	1.47	-1.603567451	0.176	AKT2,FLT3,GZMA,IL6,IRS1,IRS2,JAK3,KLB,MT1A,MT1F,MT1G,MT1M,MT2A,PIK3R3,PIK3R5
TNFR2 Signaling	1.46	1.341640786	0.233	BIRC3,IKBKE,JUN,NFKBIE,TNF,TNFAIP3,TNFRSF1B
Regulation of the Epithelial-Mesenchymal Transition Pathway	1.44		0.149	AKT2,BCL9,ESRP2,FGF10,FGF11,FGF7,FGFRL1,FLT3,FZD7,FZD9,HGF,HIF1A,ID2,IRS1,IRS2,JAK3,KLB,LEF1,MMP9,NOTCH2,PIK3R3,PIK3R5,SNAI1,TCF7,TGFB1,TGFBR2,TWIST1,TWIST2,WNT2B,WNT3
Dopamine Degradation	1.42	0.707106781	0.216	ALDH1A2,ALDH2,ALDH7A1,ALDH9A1,IL4I1,SULT1A1,SULT1A2,SULT1B1
PDGF Signaling	1.42	1.5	0.168	CSNK2A2,FLT3,INPP5D,INPP5J,IRS1,IRS2,JAK3,JUN,KLB,MYC,PDGFA,PIK3R3,PIK3R5,PLCG2,PRKCB,SPHK1,SYNJ2
Type II Diabetes Mellitus Signaling	1.41	1.885618083	0.155	ACSL1,ADIPOQ,AKT2,CACNA2D3,CACNG8,FLT3,IKBKE,INSR,IRS1,IRS2,KLB,MAP3K5,MAPK10,NFKBIE,NGFR,PIK3R3,PIK3R5,PRKCB,PRKCQ,SLC2A4,SOCS3,TNF,TNFRSF11B,TNFRSF1B
Paxillin Signaling	1.41	0.832050294	0.161	ACTB,ACTG1,ACTN2,FLT3,IRS1,IRS2,ITGA2,ITGA4,ITGA5,ITGA8,ITGAD,ITGAL,ITGAX,ITGB2,ITGB4,KLB,MAPK10,PIK3R3,PIK3R5,PTK2B
Protein Kinase A Signaling	1.39	-0.6172134	0.135	ADCY6,ADD2,AKAP13,AKAP6,CDC25B,CDKN3,CHP1,CREM,DUSP2,DUSP4,DUSP5,EYA1,GLI3,GNAI2,GNB4,GNG2,ITPR2,KDELR3,LEF1,LIPE,MYL12A,MYL4,MYLK,NFATC2,NFKBIE,NGFR,PDE11A,PDE1B,PDE3A,PLCB2,PLCB4,PLCD4,PLCG2,PLD6,PPP1R14B,PPP1R1B,PRKCB,PRKCQ,PTCH1,PTK2B,PTPN22,PTPN3,PTPN6,PTPN7,PTPRC,PTPRE,PTPRF,PTPRJ,TCF7,TGFB1,TGFBR2,UBASH3B,VASP,YWHAH
Neuropathic Pain Signaling In Dorsal Horn Neurons	1.39	1.414213562	0.162	BDNF,FLT3,GPR37,GRIN3A,IRS1,IRS2,ITPR2,KCNH2,KCNQ3,KLB,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,PRKCB,PRKCQ,TACR1
Ephrin Receptor Signaling	1.37	3.837612894	0.15	ACTR3,AKT2,ARPC1B,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CFL1,CXCR4,EPHA4,EPHA7,GNA15,GNAI2,GNB4,GNG2,GRIN3A,ITGA2,ITGA4,ITGA5,MAP4K4,PDGFA,RAC2,SDC2,VEGFC,WAS,WIPF1
IL-17A Signaling in Airway Cells	1.37	0	0.175	AKT2,CXCL1,CXCL3,FLT3,IKBKE,IL6,IRS1,IRS2,JAK3,KLB,MAPK10,NFKBIE,PIK3R3,PIK3R5
Role of IL-17F in Allergic Inflammatory Airway Diseases	1.35	2.121320344	0.2	CCL2,CCL4,CXCL1,CXCL10,CXCL8,IL1B,IL6,RPS6KA1,RPS6KA6
Adenine and Adenosine Salvage III	1.35		0.375	ADA2,HPRT1,PNP
Histidine Degradation III	1.35		0.375	MTHFD1,MTHFD1L,MTHFD2
Superoxide Radicals Degradation	1.35		0.375	CAT,GPX7,NQO1
G-Protein Coupled Receptor Signaling	1.35		0.14	ADCY6,ADORA1,ADORA3,AKT2,CCR4,CXCR2,DUSP4,FLT3,FPR1,FPR2,GNA15,GNAI2,HRH2,HTR7,IKBKE,IRS1,IRS2,KLB,MAP3K8,NFKBIE,P2RY13,PDE11A,PDE1B,PDE3A,PIK3R3,PIK3R5,PLCB2,PLCB4,PLD6,PRKCB,PTGIR,PTK2B,RAP1GAP,RASGRP1,RGS10,RGS16,RGS18,RGS2,RPS6KA1,S1PR1
Leptin Signaling in Obesity	1.35	-1	0.17	ADCY6,AKT2,FLT3,IRS1,IRS2,KLB,LEP,PDE3A,PIK3R3,PIK3R5,PLCB2,PLCB4,PLCD4,PLCG2,SOCS3
Sumoylation Pathway	1.35	-1.154700538	0.165	AR,ARHGDIB,CEBPA,FASLG,ISG20,JUN,MAP3K5,MAPK10,RAC2,RHOC,RHOG,RHOH,RHOU,RND1,SNCA,UBA2,ZNF217

Mitotic Roles of Polo-Like Kinase	1.35	1	0.182	CCNB1,CCNB2,CDC20,CDC25B,CDC7,CDK1,ESPL1,PLK3,PPM1J,PPP2R5A,PTTG1,TGFB1
Xenobiotic Metabolism Signaling	1.34		0.139	ABCB1,ABCC3,AHR,ALDH1A2,ALDH2,ALDH6A1,ALDH7A1,ALDH9A1,ANKRA2,CAT,CES1,CHST11,CITED2,CYP1B1,CYP2C8,FLT3,FMO2,FTL,GCLC,GRIP1,GSTM1,GSTM5,HS3ST2,IL1B,IL4I1,IL6,IRS1,IRS2,KLB,MAP3K5,MAP3K8,NQO1,PIK3R3,PIK3R5,PPM1J,PPP2R5A,PRKCB,PRKCQ,SULT1A1,SULT1A2,SULT1B1,TNF
IL-17 Signaling	1.33		0.167	AKT2,CCL2,CXCL1,CXCL10,CXCL11,CXCL8,FLT3,IL6,IRS1,IRS2,JUN,KLB,MAPK10,PIK3R3,PIK3R5,TIMP1
Neuregulin Signaling	1.33	1.941450687	0.167	AKT2,AREG,BTC,DLG4,EREG,HBEGF,ITGA2,ITGA4,ITGA5,MATK,MYC,PIK3R3,PLCG2,PRKCB,PRKCQ,TGFA
Ceramide Signaling	1.32	2.5	0.163	AKT2,FLT3,IRS1,IRS2,JUN,KLB,NGFR,PIK3R3,PIK3R5,PPM1J,PPP2R5A,S1PR1,S1PR5,SPHK1,TNF,TNFRSF11B,TNFRSF1B
RANK Signaling in Osteoclasts	1.32	0	0.163	AKT2,BIRC3,CHP1,FLT3,IKBKE,IRS1,IRS2,JUN,KLB,MAP3K5,MAP3K8,MAPK10,NFATC2,NFKBIE,PIK3R3,PIK3R5,PTK2B
3-phosphoinositide Degradation	1.32	2.041241452	0.152	ALPL,CA3,CDC25B,DUSP2,DUSP5,EYA4,HACD2,INPP4B,INPP5D,INPP5J,MTMR8,PHOSPHO1,PPFIA3,PPP1R14B,PPP1R1B,PPP2R5A,PTPN22,PTPN6,PTPN7,PTPRC,PTPRF,PTPRJ,SOCS3,SYNJ2

Supplementary table 9. Raw data for PNA IPA analysis in peritumoral fat cohort (appendix p 14).

Ingenuity Canonical Pathways	-log10(p-value)	z-score	Ratio	Molecules
Antigen Presentation Pathway	4.04		0.179	B2M,HLA-C,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,PSMB8
Granulocyte Adhesion and Diapedesis	3.8		0.0838	CCL19,CCL4,CCL5,CSF3,CXCL10,FPR1,FPR2,ITGA4,ITGAL,MMP14,MMP28,SELE,SELL,THY1,XCL2
Primary Immunodeficiency Signaling	3.35		0.14	CD3E,CD8A,IGHD,IGHM,IGLL1/IGLL5,IL2RG,PTPRC
Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes	2.9	0.333333333	0.0957	FCGR3A/FCGR3B,FYB1,GAB2,LCP2,PLD6,PTK2B,RAB11B,RAC2,SRC
Communication between Innate and Adaptive Immune Cells	2.84		0.0938	B2M,CCL4,CCL5,CD8A,CXCL10,HLA-C,HLA-DRA,IGHD,IGHM
Th1 Pathway	2.79	1.341640786	0.0803	CD3E,CD8A,FGFR4,GAB2,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,KLRD1,RUNX3,STAT1
Pathogenesis of Multiple Sclerosis	2.79		0.333	CCL4,CCL5,CXCL10
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	2.74		0.156	B2M,CASP9,CD3E,GZMB,HLA-C
Th1 and Th2 Activation Pathway	2.63		0.0695	CD3E,CD8A,FGFR4,GAB2,GFI1,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,IL2RG,KLRD1,RUNX3,STAT1
Cdc42 Signaling	2.58	0.816496581	0.0719	B2M,CD3E,CDC42EP2,DIAPH3,HLA-C,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,ITGA4,MYL4,SRC
Leukocyte Extravasation Signaling	2.56	1.732050808	0.0657	CD44,FGFR4,GAB2,ITGA4,ITGAL,MMP14,MMP28,PTK2B,RAC2,RASGRP1,RASSF5,RHOH,SRC,THY1
Agranulocyte Adhesion and Diapedesis	2.53		0.0677	CCL19,CCL4,CCL5,CXCL10,ITGA4,ITGB7,MMP14,MMP28,MYH7B,MYL4,SELE,SELL,XCL2
Caveolar-mediated Endocytosis Signaling	2.44		0.0986	B2M,CD48,HLA-C,ITGA4,ITGAL,ITGB7,SRC
Colorectal Cancer Metastasis Signaling	2.44	0.577350269	0.0599	AXIN1,BIRC5,CASP9,FGFR4,GAB2,LEF1,MMP14,MMP28,MSH2,RAC2,RHOD,RHOH,SMAD3,SRC,STAT1,TCF7L1
B Cell Receptor Signaling	2.43	0.632455532	0.066	CD22,CREBBP,EGR1,FGFR4,GAB2,IGHD,IGHM,INPPL1,MAP2K7,PTK2B,PTPRC,RAC2,RASSF5

OX40 Signaling Pathway	2.43		0.0889	B2M,CD3E,HLA-C,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,TRAF3
Reelin Signaling in Neurons	2.32		0.0851	ARHGEF4,CDK5,FGFR4,GAB2,ITGA4,ITGAL,MAP2K7,SRC
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	2.3	0.904534034	0.0637	CLU,CREBBP,FGFR4,GAB2,MAP2K7,PPP1R14A,PPP2R3B,RAC2,RHOD,RHOH,S100A8,SERPINA1,STAT1
Endocannabinoid Cancer Inhibition Pathway	2.29	1.264911064	0.0692	CASP1,CASP9,CREBBP,FGFR4,GAB2,LEF1,MAP2K7,SRC,TCF7L1,TWIST2,VIM
TR/RXR Activation	2.16		0.08	AKR1C3,FGFR4,GAB2,NCOR2,RCAN2,RXRA,SREBF2,THRA
IL-15 Production	2.16		0.0744	ALK,CSF2RA,ERBB4,FGFR4,MAP2K7,MST1R,PTK2B,SRC,STAT1
Virus Entry via Endocytic Pathways	2.16		0.0744	B2M,FGFR4,GAB2,HLA-C,ITGA4,ITGAL,ITGB7,RAC2,SRC
CTLA4 Signaling in Cytotoxic T Lymphocytes	2.13		0.0792	B2M,CD3E,CD8A,FGFR4,GAB2,HLA-C,LCP2,PPP2R3B
Superpathway of Inositol Phosphate Compounds	2.11	-1.732050808	0.0583	ERBB4,EYA4,FGFR4,GAB2,INPPL1,NT5C,NUDT3,PIP4K2A,PPFIBP2,PPP1R14A,PTPN23,PTPRC,RAC2,SRC
Activation of IRF by Cytosolic Pattern Recognition Receptors	2.09	0	0.0952	CREBBP,DHX58,IFIH1,STAT1,TRAF3,ZBP1
Sumoylation Pathway	2.08	0.377964473	0.0777	ARHGDIB,CREBBP,PIAS4,RAC2,RCC1,RFC4,RHOD,RHOH
Allograft Rejection Signaling	1.99		0.0814	B2M,GZMB,HLA-C,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA
Th2 Pathway	1.98	0.447213595	0.0658	CD3E,FGFR4,GAB2,GFI1,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,IL2RG,RUNX3
Regulation of the Epithelial-Mesenchymal Transition Pathway	1.95		0.0597	AXIN1,EGR1,ESRP2,FGF10,FGF13,FGFR4,GAB2,LEF1,MAP2K7,SMAD3,TCF7L1,TWIST2
Hematopoiesis from Pluripotent Stem Cells	1.94		0.102	CD3E,CD8A,CSF3,IGHD,IGHM
RhoGDI Signaling	1.9	0	0.0611	ARHGDIB,ARHGEF4,CD44,CDH23,CREBBP,ITGA4,MYL4,RAC2,RHOD,RHOH,SRC
Glioma Invasiveness Signaling	1.89	0.447213595	0.0778	CD44,F2R,FGFR4,GAB2,RAC2,RHOD,RHOH
Differential Regulation of Cytokine	1.89		0.167	CCL4,CCL5,CSF3

Production in Macrophages and T Helper Cells by IL-17A and IL-17F				
3-phosphoinositide Biosynthesis	1.89	-1.897366596	0.0585	ERBB4,EYA4,FGFR4,GAB2,NT5C,NUDT3,PPFIBP2,PPP1R14A,PTPN23,PTPRC,RAC2,SRC
ILK Signaling	1.89	0.333333333	0.0585	CREBBP,FGFR4,GAB2,ITGB7,LEF1,MYH7B,MYL4,PPP2R3B,RAC2,RHOD,RHOH,VIM
Signaling by Rho Family GTPases	1.84	-0.577350269	0.0541	ARHGEF4,CDC42EP2,CDH23,DIAPH3,FGFR4,GAB2,ITGA4,MAP2K7,MYL4,PTK2B,RAC2,RHOD,RHOH,VIM
Clathrin-mediated Endocytosis Signaling	1.84		0.0577	CLU,F2R,FGF10,FGF13,FGFR4,GAB2,HIP1,ITGB7,RAB11B,S100A8,SERPINA1,SRC
Actin Cytoskeleton Signaling	1.83	1	0.0556	ARHGEF4,CYFIP2,DIAPH3,F2R,FGF10,FGF13,FGFR4,GAB2,GSN,ITGA4,MYH7B,MYL4,RAC2
Neuroinflammation Signaling Pathway	1.81	1.069044968	0.0511	B2M,BIRC3,BIRC5,CASP1,CCL5,CREBBP,CXCL10,FGFR4,GAB2,HLA-C,HLA-DRA,PLA2G2D,SLC6A1,STAT1,TICAM2,TRAF3
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	1.8		0.0551	AXIN1,BIRC3,CASP9,FGFR4,GAB2,GSN,LEF1,MAP2K7,MMP14,PTK2B,RUNX2,SRC,TCF7L1
Phagosome Formation	1.77		0.0643	FCER1A,FCGR1B,FCGR3A/FCGR3B,FGFR4,GAB2,ITGA4,RAC2,RHOD,RHOH
B Cell Development	1.76		0.111	HLA-DRA,IGHD,IGHM,PTPRC
T Cell Exhaustion Signaling Pathway	1.74	0	0.0579	FGFR4,GAB2,GZMB,HLA-C,HLA-DPA1,HLA-DPB1,HLA-DQB2,HLA-DRA,PPP2R3B,SMAD3,STAT1
LXR/RXR Activation	1.69	0	0.0661	CLU,LY96,NCOR2,RXRA,S100A8,SAA2,SCD,SERPINA1
Wnt/β-catenin Signaling	1.62	0.632455532	0.0578	AXIN1,AXIN2,CD44,CREBBP,CSNK1E,LEF1,PPP2R3B,SOX12,SRC,TCF7L1
Citrulline Biosynthesis	1.61		0.222	ARG1,LOC102724788/PRODH
Folate Transformations I	1.61		0.222	MTHFD1L,MTHFS
Acute Myeloid Leukemia Signaling	1.6	-1.341640786	0.068	CSF2RA,FGFR4,GAB2,LEF1,MAP2K7,PIM2,TCF7L1
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-	1.6		0.13	CCL4,CCL5,CSF3

17A and IL-17F				
RANK Signaling in Osteoclasts	1.58	-0.816496581	0.0673	BIRC3,FGFR4,GAB2,GSN,MAP2K7,PTK2B,SRC
Integrin Signaling	1.56	0.632455532	0.0524	CAPN10,CAPN9,FGFR4,GAB2,GSN,ITGA4,ITGAL,ITGB7,RAC2,RHOD,RHOH,SRC
Tumoricidal Function of Hepatic Natural Killer Cells	1.55		0.125	CASP9,GZMB,ITGAL
Histamine Biosynthesis	1.55		1	HDC
Lanosterol Biosynthesis	1.55		1	LSS
Sorbitol Degradation I	1.55		1	SORD
Thiamin Salvage III	1.55		1	TPK1
Phospholipase C Signaling	1.54	0	0.0506	ARHGEF4,CD3E,CREBBP,ITGA4,LCP2,MYL4,PLA2G2D,PLD6,PPP1R14A,RAC2,RHOD,RHOH,SRC
Fc Epsilon RI Signaling	1.53	1.133893419	0.0615	FCER1A,FGFR4,GAB2,INPPL1,LCP2,MAP2K7,PLA2G2D,RAC2
Tec Kinase Signaling	1.52	0.707106781	0.0556	FCER1A,FGFR4,GAB2,ITGA4,PTK2B,RAC2,RHOD,RHOH,SRC,STAT1
HIPPO signaling	1.5		0.0706	CD44,CSNK1E,DLG5,PPP1R14A,PPP2R3B,SMAD3
ERK/MAPK Signaling	1.49	1.264911064	0.0529	CREBBP,FGFR4,GAB2,ITGA4,PLA2G2D,PPP1R14A,PPP2R3B,PTK2B,RAC2,SRC,STAT1
Role of RIG1-like Receptors in Antiviral Innate Immunity	1.47		0.0909	CREBBP,DHX58,IFIH1,TRAF3
PXR/RXR Activation	1.46		0.0769	ABCC3,CYP3A4,GSTM1,RXRA,SCD
Sphingosine-1-phosphate Signaling	1.46	0	0.0597	CASP1,CASP9,FGFR4,GAB2,PTK2B,RAC2,RHOD,RHOH
Molecular Mechanisms of Cancer	1.46		0.0448	ARHGEF4,AXIN1,BIRC3,CASP9,CDK1,CDK5,CREBBP,FGFR4,GAB2,ITGA4,LEF1,PTCH1,RAC2,RASGRP1,RHOD,RHOH,SMAD3,SRC
Role of Tissue Factor in Cancer	1.45		0.0593	CTGF,CYR61,EGR1,FGFR4,GAB2,PDIA2,PTK2B,SRC
Hepatic Fibrosis / Hepatic Stellate Cell Activation	1.44		0.0538	A2M,CCL5,COL9A1,COL9A3,CTGF,LY96,MYH7B,MYL4,SMAD3,STAT1
Osteoarthritis Pathway	1.44	0.333333333	0.0519	CASP1,CASP9,CREBBP,GLI3,ITGA4,LEF1,PTCH1,RUNX2,S100A8,SMAD3,TCF7L1
Type I Diabetes Mellitus Signaling	1.44	0.447213595	0.0631	CASP9,CD3E,GZMB,HLA-C,HLA-DRA,MAP2K7,STAT1
Regulation of Cellular Mechanics by Calpain Protease	1.43	-0.447213595	0.0758	CAPN10,CAPN9,CDK1,ITGA4,SRC

Crosstalk between Dendritic Cells and Natural Killer Cells	1.42		0.0674	CD69,HLA-C,HLA-DRA,IL2RG,ITGAL,KLRD1
Amyotrophic Lateral Sclerosis Signaling	1.41	-0.816496581	0.0619	BIRC3,CAPN10,CAPN9,CASP1,CASP9,FGFR4,GAB2
Germ Cell-Sertoli Cell Junction Signaling	1.41		0.0532	A2M,AXIN1,FGFR4,GAB2,GSN,MAP2K7,RAC2,RHOD,RHOH,SRC
IL-9 Signaling	1.38		0.0851	FGFR4,GAB2,IL2RG,STAT1
Lymphotoxin β Receptor Signaling	1.36		0.0725	CASP9,CREBBP,FGFR4,GAB2,TRAF3
EGF Signaling	1.34	-1	0.0714	FGFR4,GAB2,MAP2K7,SRC,STAT1
Regulation of Actin-based Motility by Rho	1.32	1.341640786	0.0638	GSN,ITGA4,MYL4,RAC2,RHOD,RHOH
Bile Acid Biosynthesis, Neutral Pathway	1.31		0.154	AKR1C3,CYP3A4
Urate Biosynthesis/Inosine 5'-phosphate Degradation	1.31		0.154	IMPDH1,NT5C
Role of NFAT in Regulation of the Immune Response	1.31	1	0.051	CD3E,CSNK1E,FCER1A,FCGR1B,FCGR3A/FCGR3B,FGFR4,GAB2,HLA-DRA,LCP2,RCAN2

Supplementary table 10. Raw data for TUMOR IPA analysis in peritumoral fat cohort (appendix p 14).

Ingenuity Canonical Pathways	-log10(p-value)	zScore	Ratio	Molecules
Phagosome Maturation	3.34		0.0811	ATP6V0A4,ATP6V1B1,ATP6V1C2,CTSF,CTSS,CTSZ,NOS1,SNAP25,TUBA3C/TUBA3D,TUBB3,TUBB4B,VPS37B
Atherosclerosis Signaling	3.32		0.0859	ALOX15B,APOC1,APOE,CXCR4,MMP1,MMP9,PLA2G2D,PLA2G7,PLBD1,S100A8,SELPLG
Glioma Invasiveness Signaling	3.29	1.889822365	0.1	CD44,FGFR3,FLT3,HMMR,MMP9,PIK3R6,PLAUR,RHOBTB2,RHOQ
Th1 and Th2 Activation Pathway	2.94		0.0695	CD4,CD80,CD86,CXCR4,FGFR3,FLT3,HAVCR1,IL10RA,IL18R1,IL2RA,KLRD1,PIK3R6,TIMD4
Natural Killer Cell Signaling	2.63		0.0752	CD300A,FCER1G,FCGR2A,FGFR3,FLT3,INPP5J,KLRB1,KLRD1,PIK3R6,SIGLEC7
T Helper Cell Differentiation	2.57		0.0959	CD80,CD86,CXCR5,FCER1G,IL10RA,IL18R1,IL2RA
Phagosome Formation	2.47		0.0714	CR1,FCER1G,FCGR2A,FCGR2B,FGFR3,FLT3,PIK3R6,RHOBTB2,RHOQ,TLR5
Communication between Innate and Adaptive Immune Cells	2.47		0.0833	CD4,CD79A,CD80,CD86,FCER1G,IGHM,TLR5,TNFSF13B
Osteoarthritis Pathway	2.46	2.529822128	0.0613	CASP5,CASP8,DKK1,FGFR3,MMP1,MMP9,PTH1R,PTHLH,S100A8,S100A9,SMAD6,SOX9,TCF7
Systemic Lupus Erythematosus Signaling	2.42		0.0586	CD22,CD79A,CD80,CD86,FCER1G,FCGR2A,FCGR2B,FGFR3,FLT3,IGHM,KNG1,PIK3R6,PIM2,TNFSF13B
Role of IL-17A in Psoriasis	2.4		0.231	CCL20,S100A8,S100A9
CTLA4 Signaling in Cytotoxic T Lymphocytes	2.34		0.0792	AP1S3,CD80,CD86,FCER1G,FGFR3,FLT3,PIK3R6,PPP2R2C
Acute Myeloid Leukemia Signaling	2.29	-0.447213595	0.0777	CCND1,CSF2RA,FGFR3,FLT3,IDH1,PIK3R6,PIM2,TCF7
Th2 Pathway	2.21	1.632993162	0.0658	CD4,CD80,CD86,CXCR4,FGFR3,FLT3,HAVCR1,IL2RA,PIK3R6,TIMD4
Serine Biosynthesis	2.2		0.4	PSAT1,PSPH
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.08	-1.341640786	0.102	AURKA,CCNB2,CDC25C,GADD45A,TOP2A
Chondroitin Sulfate Biosynthesis (Late Stages)	2.08	1.341640786	0.102	CHST11,CHST9,HS3ST2,HS6ST1,SULT1A1
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	2.07		0.0778	CD79A,CD80,CD86,FCER1G,SLAMF1,TLR5,TNFSF13B
FcγRIIB Signaling in B Lymphocytes	2.07	1	0.0778	BTK,CACNB4,CD79A,FCGR2B,FGFR3,FLT3,PIK3R6
Th1 Pathway	2.04	1.632993162	0.0657	CD4,CD80,CD86,FGFR3,FLT3,IL10RA,IL18R1,KLRD1,PIK3R6
Primary Immunodeficiency Signaling	2.04		0.1	BTK,CD4,CD79A,IGHM,IGLL1/IGLL5
Coagulation System	1.92	2	0.114	F13A1,KNG1,PLAUR,PROC
Role of NFAT in Regulation of the Immune Response	1.89	2.529822128	0.0561	BTK,CD4,CD79A,CD80,CD86,FCER1G,FCGR2A,FCGR2B,FGFR3,FLT3,PIK3R6
Superpathway of Serine and Glycine Biosynthesis I	1.89		0.286	PSAT1,PSPH
Opioid Signaling Pathway	1.88	-2.309401077	0.052	CACNB4,FOSB,GRK3,NOS1,PNOC,RGS1,RGS10,RGS17,RGS18,RGS20,RGS7,RYR2,SRF
LXR/RXR Activation	1.88	0	0.0661	APOC1,APOE,APOH,GC,KNG1,MMP9,RXRA,S100A8
B Cell Development	1.87		0.111	CD79A,CD80,CD86,IGHM
Inflammasome pathway	1.85		0.15	CASP5,CASP8,NLRP3
VDR/RXR Activation	1.82		0.0769	GADD45A,IGFBP1,IGFBP6,KLF4,RXRA,TRPV6

Chondroitin Sulfate Biosynthesis	1.81	1.341640786	0.0877	CHST11,CHST9,HS3ST2,HS6ST1,SULT1A1
iCOS-iCOSL Signaling in T Helper Cells	1.8	1.341640786	0.064	CD4,CD80,CD86,FCER1G,FGFR3,FLT3,IL2RA,PIK3R6
Neuroinflammation Signaling Pathway	1.79	1.386750491	0.0479	CALB2,CASP8,CD80,CD86,FGFR3,FLT3,GAD1,MMP9,NLRP3,PIK3R6,PLA2G2D,S100B,SNCA,TLR5,TREM2
Airway Pathology in Chronic Obstructive Pulmonary Disease	1.78		0.25	MMP1,MMP9
Inhibition of Matrix Metalloproteases	1.76	-1	0.103	ADAM12,MMP1,MMP9,TFPI2
Ephrin A Signaling	1.67		0.0806	EFNA5,EPHA6,FGFR3,FLT3,PIK3R6
GM-CSF Signaling	1.67	0	0.0714	CCND1,CISH,CSF2RA,FGFR3,FLT3,PIK3R6
GP6 Signaling Pathway	1.62	1.133893419	0.0593	BTK,COL11A1,COL24A1,FCER1G,FGFR3,FLT3,LAMB2,PIK3R6
Small Cell Lung Cancer Signaling	1.61	-1	0.069	CCND1,FGFR3,FLT3,NOS1,PIK3R6,RXRA
Mitotic Roles of Polo-Like Kinase	1.56		0.0758	CCNB2,CDC16,CDC25C,PPP2R2C,PRC1
Dermatan Sulfate Biosynthesis (Late Stages)	1.52	1	0.087	CHST11,HS3ST2,HS6ST1,SULT1A1
Eicosanoid Signaling	1.51		0.0735	ALOX15B,PLA2G2D,PLA2G7,PLBD1,TBXAS1
B Cell Receptor Signaling	1.5	1.632993162	0.0508	BTK,CD22,CD79A,FCGR2A,FCGR2B,FGFR3,FLT3,IGHM,INPP5J,PIK3R6
IL-9 Signaling	1.49		0.0851	CISH,FGFR3,FLT3,PIK3R6
IL-7 Signaling Pathway	1.48	0	0.0645	CCND1,CXCR5,FGFR3,FLT3,IGHM,PIK3R6
Role of IL-17A in Arthritis	1.47		0.0714	CCL20,FGFR3,FLT3,MMP1,PIK3R6
Reelin Signaling in Neurons	1.46		0.0638	APBB1,APOE,ARHGEF4,FGFR3,FLT3,PIK3R6
Wnt/β-catenin Signaling	1.45	1.414213562	0.052	CCND1,CD44,DKK1,PPP2R2C,SFRP1,SOX15,SOX9,TCF7,WNT5A
eNOS Signaling	1.44	0	0.0517	AQP2,AQP3,AQP4,AQP6,CASP8,FGFR3,FLT3,KNG1,PIK3R6
Guanosine Nucleotides Degradation III	1.43		0.167	NT5C3A,XDH
PEDF Signaling	1.39	0.447213595	0.0612	CASP8,FGFR3,FLT3,PIK3R6,SRF,TCF7
Urate Biosynthesis/Inosine 5'-phosphate Degradation	1.37		0.154	NT5C3A,XDH
Granulocyte Adhesion and Diapedesis	1.37		0.0503	CCL18,CCL20,CLDN4,CXCR4,FPR1,MMP1,MMP9,SELL,SELPLG
TREM1 Signaling	1.36	1.341640786	0.0667	CASP5,CD86,FCGR2B,NLRP3,TLR5
Colorectal Cancer Metastasis Signaling	1.35	1.414213562	0.0449	CCND1,FGFR3,FLT3,GRK3,MMP1,MMP9,PIK3R6,RHOBTB2,RHOQ,TCF7,TLR5,WNT5A
Ovarian Cancer Signaling	1.32		0.0516	CCND1,CD44,FGFR3,FLT3,MMP9,PIK3R6,TCF7,WNT5A

Supplementary table 11. Raw data TUMOR ssGSEA analysis in the peritumoral fat cohort (appendix p 15).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
Tcm_cells	0.649	0.125	0.923	0.905
Th2_cells	0.533	0.172	0.923	0.765
DC	0.525	0.283	0.923	0.548
Tgd_cells	0.359	0.432	0.923	0.365
aDC	0.355	0.385	0.923	0.414
ImmuneScore	0.326	0.615	0.923	0.211
Neutrophils	0.297	0.560	0.923	0.252
Mast_cells	0.283	0.560	0.923	0.252
NK_CD56dim_cells	0.275	0.231	0.923	0.637
Cytotoxic_cells	0.259	0.432	0.923	0.365
Macrophages	0.246	0.615	0.923	0.211
Treg_cells	0.217	0.888	0.989	0.051
Eosinophils	0.206	0.587	0.923	0.231
PDL1	0.202	0.934	0.989	0.030
B_cells	0.146	1.000	1.000	0.000
CYT	0.126	0.763	0.989	0.117
TIS	0.117	0.888	0.989	0.051
IIS	0.088	0.888	0.989	0.051
APM2	0.061	0.984	1.000	0.007
T_helper_cells	0.046	0.794	0.989	0.100
T_cells	-0.042	0.888	0.989	0.051
Tfh_cells	-0.047	0.763	0.989	0.117
ImmuneCheckpoint	-0.085	0.733	0.989	0.135
APM1	-0.141	0.533	0.923	0.274
CD8_T_cells	-0.149	0.321	0.923	0.493
Tem_cells	-0.151	0.533	0.923	0.274
PD1	-0.168	0.481	0.923	0.318
Th1_cells	-0.215	0.587	0.923	0.231
iDC	-0.218	0.456	0.923	0.341
CTLA4	-0.235	0.456	0.923	0.341
Teff_Score	-0.246	0.432	0.923	0.365
pDC	-0.270	0.920	0.989	0.036
NK_CD56bright_cells	-0.386	0.506	0.923	0.296
Angiogenesis	-0.470	0.321	0.923	0.493
Th17_cells	-0.640	0.200	0.923	0.699
NK_cells	-0.769	0.215	0.923	0.668

Supplementary table 12. Raw data PNA ssGSEA analysis in the peritumoral fat cohort (appendix p 15).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
ImmuneScore	1.870	0.029	0.318	1.531
Tgd_cells	1.716	0.029	0.318	1.531
IIS	1.627	0.015	0.318	1.833
Teff_Score	1.474	0.088	0.318	1.054
ImmuneCheckpoint	1.394	0.088	0.318	1.054
TIS	1.372	0.059	0.318	1.230
T_cells	1.247	0.088	0.318	1.054
APM2	1.175	0.176	0.424	0.753
Cytotoxic_cells	1.173	0.132	0.367	0.878
APM1	1.147	0.059	0.318	1.230
Mast_cells	1.117	0.132	0.367	0.878
NK_CD56dim_cells	1.016	0.368	0.602	0.435
Neutrophils	0.992	0.176	0.424	0.753
CYT	0.985	0.132	0.367	0.878
Th1_cells	0.981	0.088	0.318	1.054
B_cells	0.934	0.059	0.318	1.230
PD1	0.929	0.368	0.602	0.435
CD8_T_cells	0.900	0.294	0.588	0.531
Macrophages	0.811	0.368	0.602	0.435
T_helper_cells	0.807	0.235	0.498	0.628
Th2_cells	0.796	0.235	0.498	0.628
CTLA4	0.657	0.529	0.681	0.276
Tem_cells	0.644	0.441	0.611	0.355
PDL1	0.638	0.368	0.602	0.435
Treg_cells	0.624	0.441	0.611	0.355
Tfh_cells	0.469	0.441	0.611	0.355
Eosinophils	0.466	0.941	0.941	0.026
pDC	0.458	0.529	0.681	0.276
Angiogenesis	0.418	0.441	0.611	0.355
aDC	0.412	0.618	0.741	0.209
Tcm_cells	0.226	0.721	0.837	0.142
iDC	0.179	0.824	0.898	0.084
DC	0.021	0.824	0.898	0.084
Th17_cells	-0.105	0.941	0.941	0.026
NK_CD56bright_cells	-0.290	0.941	0.941	0.026
NK_cells	-0.538	0.618	0.741	0.209

Supplementary table 13. Raw data PNN ssGSEA analysis in the peritumoral fat cohort (appendix p 15).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
APM2	1.827	0.00001	0.0003	5.073
ImmuneScore	1.574	0.0002	0.0027	3.655
Tem_cells	1.436	0.002	0.013	2.623
IIS	1.435	0.001	0.006	3.172
Cytotoxic_cells	1.362	0.002	0.013	2.623
Treg_cells	1.360	0.003	0.013	2.554
B_cells	1.254	0.000	0.000	4.708
APM1	1.236	0.011	0.035	1.947
ImmuneCheckpoint	1.223	0.003	0.013	2.554
TIS	1.183	0.003	0.013	2.486
Tgd_cells	1.104	0.006	0.021	2.232
CYT	1.061	0.013	0.035	1.893
Neutrophils	1.038	0.016	0.039	1.790
Teff_Score	0.988	0.013	0.035	1.893
T_cells	0.967	0.025	0.054	1.595
Th1_cells	0.962	0.031	0.063	1.504
pDC	0.922	0.014	0.037	1.841
iDC	0.808	0.023	0.051	1.642
DC	0.786	0.047	0.084	1.332
Macrophages	0.785	0.038	0.073	1.416
Tfh_cells	0.783	0.073	0.114	1.136
PDL1	0.777	0.067	0.110	1.174
aDC	0.712	0.061	0.105	1.212
CD8_T_cells	0.678	0.087	0.130	1.063
PD1	0.666	0.119	0.165	0.925
Th2_cells	0.655	0.128	0.171	0.892
Mast_cells	0.642	0.171	0.205	0.767
Tcm_cells	0.606	0.223	0.251	0.652
Eosinophils	0.588	0.159	0.198	0.797
Angiogenesis	0.452	0.183	0.213	0.738
T_helper_cells	0.306	0.528	0.576	0.277
NK_CD56dim_cells	0.200	0.843	0.867	0.074
CTLA4	0.152	0.843	0.867	0.074
NK_CD56bright_cells	-0.079	0.900	0.900	0.046
Th17_cells	-0.567	0.159	0.198	0.797
NK_cells	-0.673	0.102	0.147	0.992

Supplementary table 14. Raw data OBESE ssGSEA analysis in the peritumoral fat cohort (appendix p 15).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
CD8_T_cells	0.903	0.002	0.043	2.624
Eosinophils	0.870	0.002	0.043	2.624
Th1_cells	0.594	0.035	0.316	1.455
CTLA4	0.588	0.061	0.346	1.215
Neutrophils	0.567	0.086	0.346	1.063
Cytotoxic_cells	0.547	0.128	0.385	0.891
ImmuneScore	0.531	0.033	0.316	1.479
IIS	0.496	0.086	0.346	1.063
APM1	0.442	0.075	0.346	1.124
PDL1	0.406	0.079	0.346	1.104
pDC	0.405	0.118	0.385	0.928
APM2	0.394	0.184	0.474	0.734
TIS	0.382	0.345	0.539	0.463
ImmuneCheckpoint	0.310	0.323	0.539	0.490
B_cells	0.300	0.247	0.539	0.607
Tem_cells	0.280	0.334	0.539	0.476
Tfh_cells	0.269	0.313	0.539	0.504
Th17_cells	0.260	0.489	0.652	0.311
Treg_cells	0.254	0.391	0.587	0.408
PD1	0.238	0.413	0.589	0.384
CYT	0.229	0.425	0.589	0.371
T_cells	0.225	0.572	0.710	0.243
NK_CD56bright_cells	0.160	0.293	0.539	0.533
Th2_cells	0.131	0.834	0.883	0.079
Angiogenesis	0.124	0.706	0.820	0.151
Teff_Score	0.124	0.345	0.539	0.463
aDC	0.109	0.572	0.710	0.243
Mast_cells	0.062	0.950	0.977	0.022
DC	0.042	0.983	0.983	0.007
Tgd_cells	-0.004	0.802	0.875	0.096
iDC	-0.025	0.753	0.848	0.123
Macrophages	-0.112	0.706	0.820	0.151
Tcm_cells	-0.192	0.293	0.539	0.533
T_helper_cells	-0.306	0.323	0.539	0.490
NK_CD56dim_cells	-0.357	0.171	0.473	0.768
NK_cells	-0.433	0.104	0.373	0.985

Supplementary table 15. Raw data NORMAL ssGSEA analysis in the peritumoral fat cohort (appendix p 15).

Immune Feature	mean_Z_diff	pvalue	p.adjust	-LOG10(P)
CTLA4	1.263	0.071	1.000	1.146
Eosinophils	0.995	0.286	1.000	0.544
CD8_T_cells	0.957	0.429	1.000	0.368
Neutrophils	0.856	0.429	1.000	0.368
Mast_cells	0.820	0.429	1.000	0.368
Th17_cells	0.799	0.643	1.000	0.192
Teff_Score	0.542	0.429	1.000	0.368
Th1_cells	0.514	0.857	1.000	0.067
PDL1	0.452	0.643	1.000	0.192
Tgd_cells	0.428	0.643	1.000	0.192
Th2_cells	0.416	1.000	1.000	0.000
T_cells	0.258	0.857	1.000	0.067
NK_CD56dim_cells	0.157	0.857	1.000	0.067
PD1	0.116	1.000	1.000	0.000
ImmuneCheckpoint	0.115	0.857	1.000	0.067
Angiogenesis	0.099	1.000	1.000	0.000
TIS	0.057	1.000	1.000	0.000
IIS	-0.019	1.000	1.000	0.000
NK_CD56bright_cells	-0.051	0.857	1.000	0.067
Tfh_cells	-0.101	1.000	1.000	0.000
APM1	-0.105	0.429	1.000	0.368
T_helper_cells	-0.143	1.000	1.000	0.000
ImmuneScore	-0.145	0.857	1.000	0.067
pDC	-0.168	0.857	1.000	0.067
Cytotoxic_cells	-0.193	0.643	1.000	0.192
NK_cells	-0.306	0.857	1.000	0.067
CYT	-0.330	0.857	1.000	0.067
Macrophages	-0.391	0.643	1.000	0.192
Treg_cells	-0.421	1.000	1.000	0.000
B_cells	-0.518	0.643	1.000	0.192
aDC	-0.601	0.857	1.000	0.067
Tcm_cells	-0.733	0.643	1.000	0.192
Tem_cells	-0.844	0.286	1.000	0.544
iDC	-0.922	0.429	1.000	0.368
DC	-0.961	0.429	1.000	0.368
APM2	-1.216	0.071	1.000	1.146