**Supplemental Materials**

**Multi-omics analysis reveals adipose-tumor crosstalk**

**in colorectal cancer patients**

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Fig.S1

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Fig. S1. Step-wise flowchart diagram of this study. Ingenuity Pathway Analysis (IPA) software was used to map transcripts to genes and remove duplicates. *PPARG*, *Peroxisome proliferator-activated receptors* *γ*. *COX‑2/PTGS2*, cyclooxygenase-2. R, correlation coefficient.

Table S1. Systemic inflammation and angiogenesis biomarker levels measured in patient sera (n=47) associated with differential VAT expression levels of *PPARG*, adjusted for patient sex, tumor site and stage. Biomarkers are ranked by P-value.

|  |  |  |
| --- | --- | --- |
| **Biomarker** | **Fold Change** | **P-Value** |
| *sICAM* | 0.81 | 0.08 |
| *VEGFA* | 0.77 | 0.15 |
| *sVCAM* | 0.89 | 0.30 |
| *CXCL12* | 1.16 | 0.42 |
| *TNFA* | 1.10 | 0.52 |
| *IL-6* | 0.72 | 0.58 |
| *CRP* | 0.86 | 0.79 |
| *MCP1* | 1.03 | 0.89 |
| *VEGFD* | 1.01 | 0.94 |
| *IL-8* | 0.99 | 0.97 |
| *SAA* | 0.99 | 0.98 |

Table S2. Plasma metabolite changes between *PPARG* VAT expression groups. Fold change and P-values were calculated for metabolites from models adjusted for patient age, sex, tumor site and stage. Metabolites ranked by P-value. PC aa, phosphatidylcholines di-alkyl; PC ae, phosphatidylcholines alkyl-acyl; Lyso PC a, lyso-phosphatidylcholines.

|  |  |  |
| --- | --- | --- |
| **Metabolite** | **Fold Change** | **P-value** |
| t4 OH Pro | 1.53 | 0.005 |
| PC ae C36 0 | 0.78 | 0.01 |
| PC aa C32 1 | 0.68 | 0.02 |
| PC aa C34 1 | 0.82 | 0.03 |
| lysoPC a C20 4 | 1.44 | 0.06 |
| C18 2 | 1.37 | 0.06 |
| Cit | 1.32 | 0.06 |
| PC ae C34 1 | 0.86 | 0.09 |
| Kynurenine | 1.18 | 0.10 |
| Gln | 1.12 | 0.13 |
| PC ae C32 2 | 0.86 | 0.13 |
| PC aa C42 2 | 0.85 | 0.14 |
| Creatinine | 1.11 | 0.15 |
| PC aa C36 1 | 0.85 | 0.15 |
| PC ae C32 1 | 0.88 | 0.16 |
| lysoPC a C17 0 | 1.33 | 0.16 |
| lysoPC a C18 0 | 1.29 | 0.18 |
| PC aa C38 4 | 1.14 | 0.20 |
| lysoPC a C18 2 | 1.36 | 0.20 |
| His | 1.10 | 0.20 |
| PC aa C30 0 | 0.85 | 0.21 |
| PC aa C42 0 | 0.88 | 0.21 |
| SDMA | 1.11 | 0.25 |
| PC aa C32 0 | 0.90 | 0.26 |
| PC ae C44 3 | 0.90 | 0.26 |
| PC aa C36 5 | 0.83 | 0.26 |
| lysoPC a C16 0 | 1.19 | 0.27 |
| PC ae C34 0 | 0.89 | 0.28 |
| C18 | 1.16 | 0.28 |
| PC ae C42 2 | 0.89 | 0.28 |
| PC ae C36 1 | 0.90 | 0.28 |
| C16 | 1.12 | 0.30 |
| PC aa C34 3 | 0.86 | 0.31 |
| PC ae C44 5 | 0.90 | 0.31 |
| lysoPC a C18 1 | 1.20 | 0.32 |
| C18 1 | 1.15 | 0.33 |
| PC ae C30 0 | 0.90 | 0.34 |
| SM C18 0 | 0.91 | 0.34 |
| PC ae C42 4 | 0.91 | 0.34 |
| Taurine | 1.12 | 0.35 |
| PC aa C34 2 | 0.93 | 0.35 |
| lysoPC a C20 3 | 1.18 | 0.36 |
| PC ae C36 4 | 1.12 | 0.36 |
| PC aa C28 1 | 0.91 | 0.36 |
| SM C16 0 | 0.92 | 0.36 |
| SM C24 1 | 0.91 | 0.37 |
| Ser | 1.08 | 0.39 |
| PC aa C36 4 | 1.08 | 0.39 |
| PC ae C38 4 | 1.10 | 0.39 |
| SM C26 1 | 0.90 | 0.41 |
| Orn | 1.12 | 0.41 |
| Sarcosine | 1.08 | 0.44 |
| PC aa C36 3 | 0.92 | 0.44 |
| PC ae C42 5 | 0.94 | 0.45 |
| PC aa C42 1 | 0.93 | 0.45 |
| Arg | 1.14 | 0.48 |
| PC ae C44 4 | 0.94 | 0.49 |
| Val | 1.07 | 0.50 |
| PC ae C40 1 | 1.10 | 0.52 |
| Gly | 1.07 | 0.53 |
| C3 | 1.07 | 0.54 |
| PC ae C42 3 | 0.94 | 0.55 |
| PC aa C40 2 | 0.93 | 0.55 |
| C4 | 1.07 | 0.57 |
| PC aa C36 2 | 0.94 | 0.57 |
| PC aa C32 2 | 0.90 | 0.58 |
| PC ae C44 6 | 0.95 | 0.58 |
| lysoPC a C28 1 | 0.94 | 0.58 |
| Lys | 1.04 | 0.59 |
| Ala | 1.05 | 0.59 |
| PC ae C36 5 | 1.07 | 0.60 |
| PC ae C38 2 | 0.94 | 0.60 |
| SM OH C16 1 | 0.94 | 0.60 |
| PC aa C34 4 | 1.11 | 0.60 |
| SM C26 0 | 1.07 | 0.60 |
| C2 | 1.06 | 0.61 |
| PC aa C40 4 | 1.06 | 0.62 |
| PC aa C36 6 | 0.92 | 0.64 |
| PC aa C38 6 | 0.95 | 0.64 |
| PC aa C38 3 | 0.95 | 0.65 |
| PC aa C38 0 | 0.94 | 0.65 |
| Leu | 1.05 | 0.65 |
| PC ae C42 1 | 1.05 | 0.66 |
| PC ae C40 2 | 0.96 | 0.66 |
| lysoPC a C16 1 | 1.08 | 0.68 |
| PC ae C38 5 | 1.05 | 0.68 |
| Asn | 1.03 | 0.69 |
| SM OH C22 1 | 1.04 | 0.71 |
| SM OH C14 1 | 0.96 | 0.72 |
| PC ae C34 3 | 1.05 | 0.73 |
| C0 | 1.03 | 0.73 |
| PC ae C30 2 | 1.04 | 0.74 |
| PC ae C36 2 | 0.96 | 0.75 |
| SM OH C22 2 | 1.03 | 0.78 |
| Pro | 1.03 | 0.78 |
| SM OH C24 1 | 0.98 | 0.79 |
| Phe | 1.02 | 0.79 |
| H1 | 1.03 | 0.82 |
| SM C24 0 | 0.98 | 0.82 |
| PC aa C32 3 | 0.97 | 0.82 |
| PC ae C40 6 | 0.98 | 0.84 |
| Tyr | 0.98 | 0.84 |
| PC ae C40 3 | 0.98 | 0.85 |
| SM C16 1 | 0.98 | 0.85 |
| PC aa C42 4 | 1.02 | 0.86 |
| PC aa C40 6 | 0.98 | 0.86 |
| C14 1 | 1.02 | 0.87 |
| Ile | 1.01 | 0.88 |
| PC ae C34 2 | 1.02 | 0.88 |
| PC aa C40 3 | 0.98 | 0.88 |
| PC ae C40 4 | 1.01 | 0.89 |
| PC ae C38 0 | 0.98 | 0.90 |
| Trp | 1.02 | 0.90 |
| PC aa C38 5 | 0.99 | 0.91 |
| Glu | 1.02 | 0.92 |
| SM C20 2 | 1.02 | 0.92 |
| PC aa C36 0 | 1.01 | 0.93 |
| Met | 1.01 | 0.94 |
| PC aa C40 5 | 1.01 | 0.95 |
| PC ae C38 3 | 1.00 | 0.97 |
| PC aa C42 5 | 1.00 | 0.98 |
| PC ae C40 5 | 1.00 | 0.98 |
| PC ae C38 6 | 1.00 | 0.98 |
| SM C18 1 | 1.00 | 0.99 |
| Thr | 1.00 | 0.99 |
| PC ae C36 3 | 1.00 | 0.99 |
| ADMA | 1.00 | 1.00 |

Table S3. Annotated transcriptomic sequencing data of 249 dysregulated colorectal tumor genes significantly associated with differential VAT expression of *PPARG*. Differential expression of tumor transcripts between high versus low *PPARG* VAT expression groups of patients was computed using Wald tests. Significance thresholds were set at fold change > 1.2 (absolute value) and *P*-value < 0.05. Regression model coefficients and *P*-values were estimated for tumor transcripts after adjustment for: patient age at surgery, sex, tumor site, and stage.

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene Symbol** | **Entrez Gene Name** | **Fold Change** | **P-value** |
| *A2M* | alpha-2-macroglobulin | 1.52 | 0.009 |
| *ACKR3* | atypical chemokine receptor 3 | 1.49 | 0.004 |
| *ACOT13* | acyl-CoA thioesterase 13 | 0.80 | 0.042 |
| *ACTA2* | actin, alpha 2, smooth muscle, aorta | 1.66 | 0.044 |
| *ADAMTS1* | ADAM metallopeptidase with thrombospondin type 1 motif 1 | 1.53 | 0.019 |
| *ADGRA2* | adhesion G protein-coupled receptor A2 | 1.24 | 0.013 |
| *ADGRE5* | adhesion G protein-coupled receptor E5 | 1.26 | 0.045 |
| *ADGRF5* | adhesion G protein-coupled receptor F5 | 1.34 | 0.011 |
| *AGRN* | agrin | 0.79 | 0.020 |
| *AHNAK* | AHNAK nucleoprotein | 1.39 | 0.049 |
| *ALDH3A2* | aldehyde dehydrogenase 3 family member A2 | 0.80 | 0.004 |
| *ALDOA* | aldolase, fructose-bisphosphate A | 0.77 | 0.033 |
| *ALOX5* | arachidonate 5-lipoxygenase | 1.39 | 0.020 |
| *ANTXR1* | anthrax toxin receptor 1 | 1.66 | 0.020 |
| *AP1S1* | adaptor related protein complex 1 sigma 1 subunit | 0.75 | 0.010 |
| *APLNR* | apelin receptor | 1.35 | 0.034 |
| *APOD* | apolipoprotein D | 1.76 | 0.026 |
| *APOL3* | apolipoprotein L3 | 1.22 | 0.007 |
| *ARHGAP4* | Rho GTPase activating protein 4 | 1.22 | 0.035 |
| *ARHGDIB* | Rho GDP dissociation inhibitor beta | 1.39 | 0.048 |
| *ARID5B* | AT-rich interaction domain 5B | 1.37 | 0.009 |
| *ARMCX3* | armadillo repeat containing, X-linked 3 | 1.23 | 0.021 |
| *ATP2A2* | ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 2 | 1.24 | 0.049 |
| *ATP5MF* | ATP synthase membrane subunit f | 0.80 | 0.018 |
| *AXL* | AXL receptor tyrosine kinase | 1.37 | 0.023 |
| *BCL2* | BCL2, apoptosis regulator | 1.22 | 0.016 |
| *BGN* | biglycan | 1.81 | 0.023 |
| *BICC1* | BicC family RNA binding protein 1 | 1.28 | 0.038 |
| *BZW2* | basic leucine zipper and W2 domains 2 | 0.78 | 0.018 |
| *C11orf96* | chromosome 11 open reading frame 96 | 2.09 | 0.002 |
| *C1QTNF5* | C1q and TNF related 5 | 1.40 | 0.020 |
| *C1R* | complement C1r | 1.41 | 0.036 |
| *C1S* | complement C1s | 1.53 | 0.044 |
| *C2CD4B* | C2 calcium dependent domain containing 4B | 1.44 | 0.028 |
| *CAT* | catalase | 1.22 | 0.029 |
| *CD248* | CD248 molecule | 1.57 | 0.006 |
| *CD34* | CD34 molecule | 1.32 | 0.041 |
| *CD93* | CD93 molecule | 1.43 | 0.012 |
| *CDH11* | cadherin 11 | 1.65 | 0.007 |
| *CDH5* | cadherin 5 | 1.28 | 0.005 |
| *CEBPD* | CCAAT/enhancer binding protein delta | 1.37 | 0.041 |
| *CHN1* | chimerin 1 | 1.24 | 0.006 |
| *CHSY1* | chondroitin sulfate synthase 1 | 1.44 | 0.002 |
| *CLDN11* | claudin 11 | 1.37 | 0.021 |
| *CLDND1* | claudin domain containing 1 | 1.26 | 0.008 |
| *CLEC14A* | C-type lectin domain containing 14A | 1.24 | 0.024 |
| *CMTM3* | CKLF like MARVEL transmembrane domain containing 3 | 1.35 | 0.026 |
| *CNN3* | calponin 3 | 1.34 | 0.028 |
| *COBL* | cordon-bleu WH2 repeat protein | 0.73 | 0.025 |
| *COL14A1* | collagen type XIV alpha 1 chain | 1.20 | 0.027 |
| *COL15A1* | collagen type XV alpha 1 chain | 1.47 | 0.028 |
| *COL16A1* | collagen type XVI alpha 1 chain | 1.35 | 0.030 |
| *COL18A1* | collagen type XVIII alpha 1 chain | 1.29 | 0.019 |
| *COL1A2* | collagen type I alpha 2 chain | 1.91 | 0.027 |
| *COL3A1* | collagen type III alpha 1 chain | 1.87 | 0.025 |
| *COL4A1* | collagen type IV alpha 1 chain | 1.49 | 0.035 |
| *COL5A2* | collagen type V alpha 2 chain | 1.71 | 0.017 |
| *COL6A1* | collagen type VI alpha 1 chain | 1.58 | 0.027 |
| *COL6A2* | collagen type VI alpha 2 chain | 1.55 | 0.012 |
| *COL6A3* | collagen type VI alpha 3 chain | 1.91 | 0.013 |
| *CPXM1* | carboxypeptidase X, M14 family member 1 | 1.20 | 0.032 |
| *CRISPLD2* | cysteine rich secretory protein LCCL domain containing 2 | 1.68 | 0.010 |
| *CTGF* | connective tissue growth factor | 1.47 | 0.048 |
| *CTSK* | cathepsin K | 1.74 | 0.012 |
| *CTSO* | cathepsin O | 1.21 | 0.021 |
| *CYBB* | cytochrome b-245 beta chain | 1.22 | 0.045 |
| *CYBRD1* | cytochrome b reductase 1 | 1.71 | 0.011 |
| *CYGB* | cytoglobin | 1.27 | 0.004 |
| *CYR61* | cysteine rich angiogenic inducer 61 | 1.73 | 0.025 |
| *DAB2* | DAB2, clathrin adaptor protein | 1.23 | 0.042 |
| *DACT1* | dishevelled binding antagonist of beta catenin 1 | 1.20 | 0.025 |
| *DCN* | decorin | 1.49 | 0.037 |
| *DDX5* | DEAD-box helicase 5 | 1.29 | 0.016 |
| *DEPP1* | DEPP1, autophagy regulator | 1.30 | 0.049 |
| *DKK3* | dickkopf WNT signaling pathway inhibitor 3 | 1.59 | 0.017 |
| *DPYSL2* | dihydropyrimidinase like 2 | 1.47 | 0.018 |
| *DRAM1* | DNA damage regulated autophagy modulator 1 | 1.23 | 0.030 |
| *EBF1* | early B cell factor 1 | 1.21 | 0.026 |
| *ECM2* | extracellular matrix protein 2 | 1.26 | 0.029 |
| *ECSCR* | endothelial cell surface expressed chemotaxis and apoptosis regulator | 1.20 | 0.015 |
| *EDNRA* | endothelin receptor type A | 1.21 | 0.028 |
| *EGFLAM* | EGF like, fibronectin type III and laminin G domains | 1.21 | 0.030 |
| *EGR2* | early growth response 2 | 1.40 | 0.027 |
| *EGR3* | early growth response 3 | 1.21 | 0.013 |
| *EIF3B* | eukaryotic translation initiation factor 3 subunit B | 0.80 | 0.023 |
| *EMILIN2* | elastin microfibril interfacer 2 | 1.26 | 0.011 |
| *ENG* | endoglin | 1.28 | 0.010 |
| *ENTPD6* | ectonucleoside triphosphate diphosphohydrolase 6 (putative) | 0.77 | 0.014 |
| *ESAM* | endothelial cell adhesion molecule | 1.25 | 0.002 |
| *ETS1* | ETS proto-oncogene 1, transcription factor | 1.48 | 0.002 |
| *F2R* | coagulation factor II thrombin receptor | 1.33 | 0.0005 |
| *FAM198B* | family with sequence similarity 198 member B | 1.23 | 0.041 |
| *FBLN2* | fibulin 2 | 1.54 | 0.041 |
| *FILIP1L* | filamin A interacting protein 1 like | 1.53 | 0.009 |
| *FKBP1A* | FK506 binding protein 1A | 0.76 | 0.016 |
| *FMOD* | fibromodulin | 1.27 | 0.036 |
| *FRZB* | frizzled related protein | 1.45 | 0.026 |
| *FTL* | ferritin light chain | 1.21 | 0.042 |
| *GAPDH* | glyceraldehyde-3-phosphate dehydrogenase | 0.76 | 0.020 |
| *GAPDHP33* | glyceraldehyde 3 phosphate dehydrogenase pseudogene 33 | 0.79 | 0.021 |
| *GEM* | GTP binding protein overexpressed in skeletal muscle | 1.60 | 0.009 |
| *GIMAP4* | GTPase, IMAP family member 4 | 1.34 | 0.023 |
| *GIMAP7* | GTPase, IMAP family member 7 | 1.33 | 0.035 |
| *GLT8D2* | glycosyltransferase 8 domain containing 2 | 1.27 | 0.049 |
| *GNE* | glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase | 1.61 | 0.010 |
| *GPNMB* | glycoprotein nmb | 1.42 | 0.043 |
| *GRAP* | GRB2-related adaptor protein | 1.20 | 0.017 |
| *GRK5* | G protein-coupled receptor kinase 5 | 1.27 | 0.032 |
| *GSTK1* | glutathione S-transferase kappa 1 | 0.77 | 0.013 |
| *H2AFY2* | H2A histone family member Y2 | 1.33 | 0.015 |
| *HEG1* | heart development protein with EGF like domains 1 | 1.29 | 0.025 |
| *HEYL* | hes related family bHLH transcription factor with YRPW motif-like | 1.30 | 0.005 |
| *HIF1A* | hypoxia inducible factor 1 alpha subunit | 1.25 | 0.047 |
| *HNRNPA0* | heterogeneous nuclear ribonucleoprotein A0 | 1.27 | 0.011 |
| *HNRNPA1P12* | heterogeneous nuclear ribonucleoprotein A1 pseudogene 12 | 1.31 | 0.038 |
| *HNRNPA1P39* | heterogeneous nuclear ribonucleoprotein A1 pseudogene 39 | 1.24 | 0.047 |
| *HNRNPA1P53* | heterogeneous nuclear ribonucleoprotein A1 pseudogene 53 | 1.21 | 0.046 |
| *HOXD11* | homeobox D11 | 0.80 | 0.026 |
| *HTRA1* | HtrA serine peptidase 1 | 1.57 | 0.049 |
| *IFI16* | interferon gamma inducible protein 16 | 1.40 | 0.012 |
| *IGFBP7* | insulin like growth factor binding protein 7 | 1.61 | 0.040 |
| *IL13RA1* | interleukin 13 receptor subunit alpha 1 | 1.26 | 0.013 |
| *IL1R1* | interleukin 1 receptor type 1 | 1.21 | 0.045 |
| *IRAK3* | interleukin 1 receptor associated kinase 3 | 1.21 | 0.023 |
| *ITGB5* | integrin subunit beta 5 | 1.29 | 0.033 |
| *ITPRIP* | inositol 1,4,5-trisphosphate receptor interacting protein | 1.34 | 0.012 |
| *JMJD1C* | jumonji domain containing 1C | 1.21 | 0.012 |
| *JUND* | JunD proto-oncogene, AP-1 transcription factor subunit | 1.29 | 0.004 |
| *KCTD12* | potassium channel tetramerization domain containing 12 | 1.33 | 0.027 |
| *KLF9* | Kruppel like factor 9 | 1.43 | 0.040 |
| *KRT6A* | keratin 6A | 0.73 | 0.022 |
| *LAMA4* | laminin subunit alpha 4 | 1.38 | 0.009 |
| *LAMB1* | laminin subunit beta 1 | 1.25 | 0.043 |
| *LAMP2* | lysosomal associated membrane protein 2 | 1.23 | 0.040 |
| *LAP3* | leucine aminopeptidase 3 | 1.22 | 0.017 |
| *LBH* | limb bud and heart development | 1.26 | 0.050 |
| *LDB2* | LIM domain binding 2 | 1.32 | 0.016 |
| *LEF1* | lymphoid enhancer binding factor 1 | 1.31 | 0.009 |
| *LHFPL6* | LHFPL tetraspan subfamily member 6 | 1.34 | 0.021 |
| *LIMS1* | LIM zinc finger domain containing 1 | 1.30 | 0.005 |
| *LINC01559* | long intergenic non-protein coding RNA 1559 | 0.68 | 0.030 |
| *LMCD1* | LIM and cysteine rich domains 1 | 1.35 | 0.034 |
| *LRRC26* | leucine rich repeat containing 26 | 1.58 | 0.013 |
| *LRRC32* | leucine rich repeat containing 32 | 1.52 | 0.001 |
| *LTBP2* | latent transforming growth factor beta binding protein 2 | 1.28 | 0.008 |
| *LTBP4* | latent transforming growth factor beta binding protein 4 | 1.28 | 0.012 |
| *LUM* | lumican | 1.85 | 0.017 |
| *LXN* | latexin | 1.34 | 0.048 |
| *MAF* | MAF bZIP transcription factor | 1.20 | 0.028 |
| *MEDAG* | mesenteric estrogen dependent adipogenesis | 1.22 | 0.009 |
| *MFGE8* | milk fat globule-EGF factor 8 protein | 1.40 | 0.047 |
| *MFNG* | MFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase | 1.21 | 0.011 |
| *MS4A7* | membrane spanning 4-domains A7 | 1.41 | 0.016 |
| *MYADM* | myeloid associated differentiation marker | 1.58 | 0.021 |
| *MYH9* | myosin heavy chain 9 | 1.21 | 0.036 |
| *NAA20* | N(alpha)-acetyltransferase 20, NatB catalytic subunit | 0.73 | 0.003 |
| *NCOA7* | nuclear receptor coactivator 7 | 1.44 | 0.007 |
| *NEDD9* | neural precursor cell expressed, developmentally down-regulated 9 | 1.26 | 0.026 |
| *NOX4* | NADPH oxidase 4 | 1.21 | 0.033 |
| *NR2F2* | nuclear receptor subfamily 2 group F member 2 | 1.50 | 0.002 |
| *NR2F6* | nuclear receptor subfamily 2 group F member 6 | 0.79 | 0.013 |
| *NRP1* | neuropilin 1 | 1.34 | 0.017 |
| *OLFML1* | olfactomedin like 1 | 1.23 | 0.003 |
| *OLFML2B* | olfactomedin like 2B | 1.26 | 0.043 |
| *PAPLN* | papilin, proteoglycan like sulfated glycoprotein | 1.22 | 0.024 |
| *PARP12* | poly(ADP-ribose) polymerase family member 12 | 0.80 | 0.018 |
| *PCDH18* | protocadherin 18 | 1.41 | 0.018 |
| *PCSK1* | proprotein convertase subtilisin/kexin type 1 | 1.36 | 0.026 |
| *PDGFRA* | platelet derived growth factor receptor alpha | 1.44 | 0.021 |
| *PDGFRB* | platelet derived growth factor receptor beta | 1.65 | 0.001 |
| *PECAM1* | platelet and endothelial cell adhesion molecule 1 | 1.42 | 0.006 |
| *PET100* | PET100 homolog | 0.80 | 0.012 |
| *PHLDB1* | pleckstrin homology like domain family B member 1 | 1.22 | 0.019 |
| *PLA1A* | phospholipase A1 member A | 1.22 | 0.001 |
| *PLA2G4C* | phospholipase A2 group IVC | 1.22 | 0.024 |
| *PLAU* | plasminogen activator, urokinase | 1.45 | 0.035 |
| *PLD3* | phospholipase D family member 3 | 1.25 | 0.040 |
| *PLVAP* | plasmalemma vesicle associated protein | 1.21 | 0.018 |
| *PLXDC2* | plexin domain containing 2 | 1.34 | 0.013 |
| *PMP22* | peripheral myelin protein 22 | 1.70 | 0.004 |
| *POLE4* | DNA polymerase epsilon 4, accessory subunit | 0.78 | 0.006 |
| *PON2* | paraoxonase 2 | 0.79 | 0.013 |
| *PPP1R18* | protein phosphatase 1 regulatory subunit 18 | 1.24 | 0.017 |
| *PRCP* | prolylcarboxypeptidase | 1.30 | 0.013 |
| *PRKAR1A* | protein kinase cAMP-dependent type I regulatory subunit alpha | 1.40 | 0.021 |
| *PROS1* | protein S | 1.42 | 0.008 |
| *PRUNE2* | prune homolog 2 | 1.65 | 0.043 |
| *RAB3IL1* | RAB3A interacting protein like 1 | 1.23 | 0.016 |
| *RAB8B* | RAB8B, member RAS oncogene family | 1.30 | 0.030 |
| *RCC1* | regulator of chromosome condensation 1 | 0.80 | 0.002 |
| *RFTN1* | raftlin, lipid raft linker 1 | 1.46 | 0.007 |
| *RFX5* | regulatory factor X5 | 1.22 | 0.028 |
| *ROMO1* | reactive oxygen species modulator 1 | 0.78 | 0.025 |
| *RPS10P14* | ribosomal protein S10 pseudogene 14 | 0.78 | 0.008 |
| *RPS26P55* | ribosomal protein S26 pseudogene 55 | 0.79 | 0.041 |
| *S1PR1* | sphingosine-1-phosphate receptor 1 | 1.24 | 0.006 |
| *SASH1* | SAM and SH3 domain containing 1 | 1.24 | 0.042 |
| *SCG5* | secretogranin V | 1.28 | 0.035 |
| *SEM1* | SEM1, 26S proteasome complex subunit | 0.79 | 0.014 |
| *SERPINF1* | serpin family F member 1 | 1.36 | 0.033 |
| *SERPING1* | serpin family G member 1 | 1.41 | 0.031 |
| *SERPINH1* | serpin family H member 1 | 1.32 | 0.034 |
| *SGCE* | sarcoglycan epsilon | 1.31 | 0.049 |
| *SH2B3* | SH2B adaptor protein 3 | 1.38 | 0.001 |
| *SHANK3* | SH3 and multiple ankyrin repeat domains 3 | 1.20 | 0.017 |
| *SLC7A5* | solute carrier family 7 member 5 | 0.72 | 0.021 |
| *SLFN11* | schlafen family member 11 | 1.37 | 0.013 |
| *SLPI* | secretory leukocyte peptidase inhibitor | 0.66 | 0.011 |
| *SMARCA2* | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2 | 1.28 | 0.011 |
| *SMOC2* | SPARC related modular calcium binding 2 | 1.36 | 0.042 |
| *SNORA61* | small nucleolar RNA, H/ACA box 61 | 0.78 | 0.015 |
| *SNORD3A* | small nucleolar RNA, C/D box 3A | 0.52 | 0.006 |
| *SNORD3C* | small nucleolar RNA, C/D box 3C | 0.60 | 0.010 |
| *SNORD3D* | small nucleolar RNA, C/D box 3D | 0.58 | 0.024 |
| *SNRK* | SNF related kinase | 1.22 | 0.033 |
| *SORBS3* | sorbin and SH3 domain containing 3 | 1.23 | 0.003 |
| *SOX18* | SRY-box 18 | 1.43 | 0.013 |
| *SPARC* | secreted protein acidic and cysteine rich | 1.65 | 0.043 |
| *SPRY1* | sprouty RTK signaling antagonist 1 | 1.46 | 0.001 |
| *SRXN1* | sulfiredoxin 1 | 0.80 | 0.008 |
| *ST3GAL5* | ST3 beta-galactoside alpha-2,3-sialyltransferase 5 | 1.22 | 0.003 |
| *SVEP1* | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | 1.36 | 0.041 |
| *SWAP70* | switching B cell complex subunit SWAP70 | 1.20 | 0.047 |
| *TAX1BP1* | Tax1 binding protein 1 | 0.79 | 0.001 |
| *TBC1D2B* | TBC1 domain family member 2B | 1.22 | 0.003 |
| *TCEAL9* | transcription elongation factor A like 9 | 1.35 | 0.029 |
| *TEK* | TEK receptor tyrosine kinase | 1.22 | 0.012 |
| *TFB2M* | transcription factor B2, mitochondrial | 0.79 | 0.003 |
| *TFPI* | tissue factor pathway inhibitor | 1.36 | 0.003 |
| *THBS1* | thrombospondin 1 | 1.71 | 0.014 |
| *THY1* | Thy-1 cell surface antigen | 1.54 | 0.026 |
| *TMBIM1* | transmembrane BAX inhibitor motif containing 1 | 0.80 | 0.012 |
| *TMEM119* | transmembrane protein 119 | 1.43 | 0.005 |
| *TPI1* | triosephosphate isomerase 1 | 0.80 | 0.033 |
| *TRAM2* | translocation associated membrane protein 2 | 1.24 | 0.006 |
| *TSEN2* | tRNA splicing endonuclease subunit 2 | 0.77 | 0.013 |
| *UGCG* | UDP-glucose ceramide glucosyltransferase | 1.24 | 0.048 |
| *VAMP8* | vesicle associated membrane protein 8 | 0.77 | 0.050 |
| *VASN* | vasorin | 1.54 | 0.003 |
| *VCAM1* | vascular cell adhesion molecule 1 | 1.56 | 0.010 |
| *VCAN* | versican | 1.65 | 0.030 |
| *VIM* | vimentin | 1.78 | 0.010 |
| *VWF* | von Willebrand factor | 1.36 | 0.038 |
| *WIPF1* | WAS/WASL interacting protein family member 1 | 1.23 | 0.048 |
| *WISP3* | WNT1 inducible signaling pathway protein 3 | 1.21 | 0.011 |
| *ZEB2* | zinc finger E-box binding homeobox 2 | 1.22 | 0.018 |
| *ZFAS1* | ZNFX1 antisense RNA 1 | 0.70 | 0.031 |
| *ZFP36L1* | ZFP36 ring finger protein like 1 | 1.40 | 0.028 |
| *ZMIZ1* | zinc finger MIZ-type containing 1 | 1.29 | 0.020 |

**Table S4.** **Ingenuity Pathway Analysis (IPA) results of molecular pathways significantly enriched in the n=249 colorectal tumor genes differentially expressed (absolute fold change >1.2; P<0.05) in patients by *PPARG* VAT expression group, after adjustment for patient sex, tumor site and stage. Canonical pathways ranked by Z-score and P-value.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Canonical Pathways** | **Z-score** | **-Log(P-value)** | **P-value** | **Molecules** |
| GP6 Signaling Pathway | 3.464 | 7.02 | 9.55E-08 | *COL1A2, COL16A1, COL5A2, COL6A1, COL4A1, COL6A2, COL6A3, LAMA4, LAMB1, COL18A1, COL15A1, COL3A1* |
| IL-8 Signaling | 2.828 | 2.39 | 0.004 | *VCAM1, NOX4, PLD3, CYBB, IRAK3, TEK, ITGB5, BCL2* |
| ILK Signaling | 2.236 | 1.96 | 0.011 | *MYH9, ACTA2, LIMS1, VIM, LEF1, HIF1A, ITGB5* |
| Neuroinflammation Signaling Pathway | 2.121 | 1.45 | 0.035 | *VCAM1, NOX4, PLA2G4C, CYBB, MFGE8, IRAK3, IL1R1, BCL2* |
| Signaling by Rho Family GTPases | 1.89 | 1.41 | 0.039 | *WIPF1, NOX4, CDH5, ACTA2, CYBB, VIM, CDH11* |
| Leukocyte Extravasation Signaling | 1.134 | 2.92 | 0.001 | *VCAM1, WIPF1, CLDN11, CDH5, ACTA2, CYBB, ARHGAP4, PECAM1, THY1* |
| Intrinsic Prothrombin Activation Pathway | 1 | 2.77 | 0.002 | *COL1A2, PROS1, COL18A1, COL3A1* |
| Osteoarthritis Pathway | 0.447 | 1.37 | 0.043 | *FRZB, DCN, LEF1, HIF1A, IL1R1, HTRA1* |
| Death Receptor Signaling | 0 | 1.54 | 0.029 | *ACTA2, PARP12, ARHGDIB, BCL2* |
| Coagulation System | -0.816 | 5.36 | 4.37E-06 | *F2R, PROS1, VWF, PLAU, TFPI, A2M* |
| Hepatic Fibrosis / Hepatic Stellate Cell Activation | -- | 12.8 | 1.58E-13 | *COL5A2, VCAM1, MYH9, COL4A1, CTGF, COL6A2, IL1R1, COL15A1, BCL2, COL16A1, COL1A2, COL6A1, COL6A3, ACTA2, PDGFRA, EDNRA, COL18A1, A2M, PDGFRB, COL3A1* |
| Atherosclerosis Signaling | -- | 3.04 | 0.0009 | *COL1A2, VCAM1, PLA2G4C, ALOX5, COL18A1, COL3A1, APOD* |
| Acute Phase Response Signaling | -- | 2.79 | 0.002 | *C1R, SERPING1, FTL, C1S, SERPINF1, VWF, IL1R1, A2M* |
| Agranulocyte Adhesion and Diapedesis | -- | 2.75 | 0.002 | *VCAM1, CLDN11, MYH9, CDH5, ACTA2, PECAM1, IL1R1, CD34* |
| Ethanol Degradation IV | -- | 2.66 | 0.002 | *ALDH3A2, CAT, CYGB* |
| Glycolysis I | -- | 2.49 | 0.003 | *TPI1, GAPDH, ALDOA* |
| Sucrose Degradation V (Mammalian) | -- | 2.38 | 0.004 | *TPI1, ALDOA* |
| Superoxide Radicals Degradation | -- | 2.38 | 0.004 | *CAT, CYGB* |
| Autophagy | -- | 2.33 | 0.005 | *LAMP2, CTSK, CTSO, BCL2* |
| Complement System | -- | 1.99 | 0.010 | *C1R, SERPING1, C1S* |
| Extrinsic Prothrombin Activation Pathway | -- | 1.78 | 0.017 | *PROS1, TFPI* |
| Granulocyte Adhesion and Diapedesis | -- | 1.72 | 0.019 | *VCAM1, CLDN11, CDH5, PECAM1, THY1, IL1R1* |
| Adipogenesis pathway | -- | 1.61 | 0.025 | *EBF1, EGR2, NR2F2, CEBPD, HIF1A* |
| Iron homeostasis signaling pathway | -- | 1.61 | 0.025 | *FTL, PDGFRA, CYBRD1, HIF1A, PDGFRB* |
| Phagosome Maturation | -- | 1.52 | 0.030 | *NOX4, LAMP2, CTSK, CTSO, CYBB* |
| Phospholipases | -- | 1.44 | 0.036 | *PLD3, PLA2G4C, PLA1A* |
| NADH Repair | -- | 1.43 | 0.037 | *GAPDH* |
| Gluconeogenesis I | -- | 1.41 | 0.039 | *GAPDH, ALDOA* |
| Clathrin-mediated Endocytosis Signaling | -- | 1.34 | 0.046 | *AP1S1, ACTA2, F2R, DAB2, ITGB5, APOD* |
| Uracil Degradation II (Reductive) | -- | 1.31 | 0.049 | *DPYSL2* |
| Phenylethylamine Degradation I | -- | 1.31 | 0.049 | *ALDH3A2* |
| Thymine Degradation | -- | 1.31 | 0.049 | *DPYSL2* |

Table S5. Over-representation analysis results of joint gene-metabolite pathways for the significant gene (n=249 genes from colorectal tumor tissue transcriptomic analysis) and plasma metabolite (n=4 metabolites from plasma metabolomics analysis by *PPARG* VAT expression group) set. Hypergeometric testing conducted using MetaboAnalyst version 4.0 software. Top ten canonical pathways are ranked by P-value.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Pathway** | **Total Molecules** | **Expected # of Molecules** | **Hits** | **Impact Score** | **P-value** | **-Log****(P-value)** |
| Glycolysis / Gluconeogenesis | 91 | 1.1154 | 4 | 0.30508 | 0.021325 | 3.8479 |
| Arginine and proline metabolism | 102 | 1.2502 | 3 | 0.096774 | 0.12376 | 2.0894 |
| Fructose and mannose metabolism | 55 | 0.67412 | 2 | 0.37838 | 0.14371 | 1.9399 |
| Glycosphingolipid biosynthesis | 14 | 0.17159 | 1 | 0.086957 | 0.15926 | 1.8372 |
| Glycosaminoglycan biosynthesis | 14 | 0.17159 | 1 | 0.57143 | 0.15926 | 1.8372 |
| Glutathione metabolism | 75 | 0.91925 | 2 | 0.16981 | 0.23331 | 1.4554 |
| Tryptophan metabolism | 80 | 0.98053 | 2 | 0.075 | 0.25657 | 1.3604 |
| alpha-Linolenic acid metabolism | 34 | 0.41673 | 1 | 0.05 | 0.34584 | 1.0618 |
| Linoleic acid metabolism | 34 | 0.41673 | 1 | 0.125 | 0.34584 | 1.0618 |
| Arachidonic acid metabolism | 100 | 1.2257 | 2 | 0.076923 | 0.34994 | 1.05 |

Table S6. Plasma metabolite changes between *PTGS2* tumor expression groups. Fold change and P-values were calculated for metabolites from models adjusted for patient age, sex, tumor site and stage. Metabolites ranked by P-value. PC aa, phosphatidylcholines di-alkyl; PC ae, phosphatidylcholines alkyl-acyl; Lyso PC a, lyso-phosphatidylcholines.

|  |  |  |
| --- | --- | --- |
| *Metabolite* | *Fold Change* | *P-value* |
|  Gly | 1.23 | 0.02 |
|  SM OH C24 1 | 0.85 | 0.047 |
|  C4 | 0.84 | 0.08 |
|  C3 | 0.85 | 0.09 |
|  Gln | 1.10 | 0.12 |
|  PC aa C36 1 | 0.86 | 0.14 |
|  PC ae C34 0 | 0.87 | 0.15 |
|  PC ae C36 0 | 0.88 | 0.15 |
|  PC ae C36 1 | 0.89 | 0.17 |
|  PC aa C42 4 | 0.88 | 0.18 |
|  PC ae C42 1 | 0.89 | 0.19 |
|  PC aa C34 1 | 0.90 | 0.21 |
|  Arg | 1.22 | 0.21 |
|  Ser | 1.10 | 0.23 |
|  PC aa C32 3 | 0.87 | 0.24 |
|  C0 | 0.93 | 0.25 |
|  Glu | 0.84 | 0.26 |
|  PC aa C40 3 | 1.12 | 0.28 |
|  Thr | 0.92 | 0.29 |
|  SM OH C22 1 | 0.92 | 0.30 |
|  PC ae C38 3 | 0.90 | 0.30 |
|  PC aa C30 0 | 0.89 | 0.32 |
|  lysoPC a C16 1 | 0.86 | 0.34 |
|  lysoPC a C20 3 | 0.86 | 0.35 |
|  lysoPC a C16 0 | 0.87 | 0.35 |
|  PC aa C42 5 | 1.10 | 0.35 |
|  H1 | 1.10 | 0.36 |
|  lysoPC a C28 1 | 0.91 | 0.37 |
|  PC aa C40 4 | 0.91 | 0.38 |
|  PC aa C34 4 | 0.86 | 0.39 |
|  PC ae C34 1 | 0.93 | 0.39 |
|  PC ae C44 6 | 1.08 | 0.39 |
|  His | 1.06 | 0.40 |
|  Phe | 1.06 | 0.40 |
|  C16 | 0.92 | 0.40 |
|  PC aa C32 1 | 0.88 | 0.41 |
|  Ile | 0.94 | 0.42 |
|  PC aa C38 3 | 0.93 | 0.44 |
|  PC ae C38 2 | 0.92 | 0.45 |
|  PC aa C36 3 | 0.93 | 0.46 |
|  Lys | 1.05 | 0.47 |
|  PC aa C40 5 | 0.93 | 0.47 |
|  PC aa C34 3 | 0.91 | 0.49 |
|  PC aa C28 1 | 0.94 | 0.50 |
|  Val | 1.06 | 0.50 |
|  PC ae C38 4 | 0.94 | 0.50 |
|  lysoPC a C18 0 | 0.89 | 0.50 |
|  lysoPC a C20 4 | 0.89 | 0.50 |
|  PC aa C36 4 | 0.95 | 0.51 |
|  PC ae C40 4 | 0.94 | 0.51 |
|  lysoPC a C18 1 | 0.90 | 0.52 |
|  PC ae C44 3 | 1.05 | 0.54 |
|  lysoPC a C17 0 | 0.89 | 0.54 |
|  C18 1 | 0.92 | 0.54 |
|  SM C18 0 | 0.95 | 0.55 |
|  Orn | 0.93 | 0.56 |
|  SDMA | 1.05 | 0.57 |
|  PC aa C38 4 | 0.95 | 0.57 |
|  SM C26 0 | 0.94 | 0.58 |
|  SM C24 0 | 0.96 | 0.60 |
|  PC ae C38 5 | 0.95 | 0.61 |
|  PC ae C40 2 | 0.95 | 0.61 |
|  PC ae C30 2 | 0.94 | 0.62 |
|  PC ae C40 1 | 0.94 | 0.62 |
|  PC ae C36 4 | 0.95 | 0.62 |
|  SM C24 1 | 1.05 | 0.63 |
|  PC ae C40 3 | 0.96 | 0.63 |
|  Tyr | 1.04 | 0.63 |
|  PC aa C32 0 | 0.96 | 0.64 |
|  ADMA | 1.03 | 0.64 |
|  Asn | 1.03 | 0.64 |
|  Leu | 1.04 | 0.65 |
|  PC aa C40 2 | 0.95 | 0.65 |
|  SM OH C16 1 | 0.96 | 0.66 |
|  C18 | 0.95 | 0.67 |
|  C2 | 1.04 | 0.67 |
|  C18 2 | 0.94 | 0.67 |
|  PC ae C40 5 | 0.96 | 0.68 |
|  PC aa C36 6 | 0.93 | 0.68 |
|  PC ae C42 2 | 0.96 | 0.69 |
|  PC ae C30 0 | 0.96 | 0.70 |
|  PC ae C36 5 | 0.96 | 0.70 |
|  Kynurenine | 1.04 | 0.70 |
|  PC aa C38 5 | 0.96 | 0.70 |
|  Taurine | 1.04 | 0.71 |
|  Cit | 1.05 | 0.72 |
|  PC ae C34 3 | 1.05 | 0.74 |
|  PC aa C42 0 | 1.03 | 0.79 |
|  PC aa C42 2 | 0.97 | 0.79 |
|  PC ae C44 5 | 1.03 | 0.79 |
|  PC aa C40 6 | 0.98 | 0.79 |
|  PC aa C32 2 | 0.96 | 0.80 |
|  SM C18 1 | 0.98 | 0.80 |
|  t4 OH Pro | 0.97 | 0.82 |
|  PC ae C32 2 | 1.02 | 0.83 |
|  PC aa C38 0 | 0.98 | 0.85 |
|  Creatinine | 0.99 | 0.85 |
|  PC ae C36 3 | 0.98 | 0.86 |
|  SM OH C14 1 | 0.98 | 0.86 |
|  SM C20 2 | 1.03 | 0.87 |
|  SM C16 0 | 1.01 | 0.87 |
|  Pro | 0.99 | 0.88 |
|  PC aa C38 6 | 1.01 | 0.88 |
|  Met | 1.01 | 0.89 |
|  PC ae C44 4 | 1.01 | 0.90 |
|  SM C26 1 | 1.01 | 0.90 |
|  PC ae C42 5 | 1.01 | 0.91 |
|  PC ae C36 2 | 0.99 | 0.91 |
|  Ala | 1.01 | 0.91 |
|  PC aa C36 5 | 0.99 | 0.93 |
|  PC aa C42 1 | 0.99 | 0.93 |
|  Sarcosine | 0.99 | 0.94 |
|  PC ae C38 0 | 0.99 | 0.94 |
|  SM OH C22 2 | 1.01 | 0.94 |
|  PC ae C40 6 | 0.99 | 0.95 |
|  SM C16 1 | 0.99 | 0.95 |
|  PC aa C36 2 | 0.99 | 0.95 |
|  PC ae C34 2 | 1.01 | 0.96 |
|  PC ae C38 6 | 1.00 | 0.97 |
|  PC ae C42 3 | 1.00 | 0.97 |
|  PC ae C42 4 | 1.00 | 0.98 |
|  PC aa C36 0 | 1.00 | 0.98 |
|  Trp | 1.00 | 0.98 |
|  PC ae C32 1 | 1.00 | 0.98 |
|  PC aa C34 2 | 1.00 | 0.99 |
|  lysoPC a C18 2 | 1.00 | 0.99 |
|  C14 1 | 1.00 | 0.99 |

Table S7. Systemic inflammation and angiogenesis biomarker levels measured in patient sera (n=47) associated with differential colorectal tumor expression levels of *PTGS2*, adjusted for patient sex, tumor site and stage. Biomarkers are ranked by P-value.

|  |  |  |
| --- | --- | --- |
| **Biomarker** | **Fold Change** | **P-Value** |
| *SAA* | 2.13 | 0.0398 |
| *IL-6* | 2.38 | 0.11 |
| *IL-8* | 0.71 | 0.32 |
| *sICAM* | 0.90 | 0.36 |
| *CRP* | 1.53 | 0.39 |
| *TNFA* | 0.89 | 0.40 |
| *CXCL12* | 1.15 | 0.43 |
| *MCP1* | 0.89 | 0.50 |
| *VEGFA* | 1.11 | 0.55 |
| *VEGFD* | 0.97 | 0.80 |
| *sVCAM* | 0.99 | 0.88 |

Table S8. Annotated transcriptomic sequencing data of 129 dysregulated VAT genes significantly associated with differential tumor expression of *PTGS2*. Differential expression of VAT transcripts between high versus low *PTGS2* tumor expression groups of patients was computed using Wald tests. Significance thresholds were set at fold change > 1.2 (absolute value) and *P*-value < 0.05. Regression model coefficients and *P*-values were estimated for tumor transcripts after adjustment for: patient age at surgery, sex, tumor site, and stage.

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene Symbol** | **Entrez Gene Name** | **Fold Change** | ***P*-value** |
| *ADA2* | adenosine deaminase 2 | 1.22 | 0.021 |
| *ADAP2* | ArfGAP with dual PH domains 2 | 1.23 | 0.006 |
| *AIF1* | allograft inflammatory factor 1 | 1.32 | 0.001 |
| *ALDH1A3* | aldehyde dehydrogenase 1 family member A3 | 1.34 | 0.031 |
| *ALPL* | alkaline phosphatase, liver/bone/kidney | 1.35 | 0.004 |
| *ANG* | angiogenin | 0.79 | 0.039 |
| *ARHGDIB* | Rho GDP dissociation inhibitor beta | 1.20 | 0.040 |
| *BASP1* | brain abundant membrane attached signal protein 1 | 1.37 | 0.002 |
| *BCHE* | butyrylcholinesterase | 0.75 | 0.040 |
| *C17orf58* | chromosome 17 open reading frame 58 | 1.31 | 0.015 |
| *CCL13* | C-C motif chemokine ligand 13 | 1.43 | 0.008 |
| *CCL18* | C-C motif chemokine ligand 18 | 1.21 | 0.017 |
| *CCL5* | C-C motif chemokine ligand 5 | 1.35 | 0.025 |
| *CCND1* | cyclin D1 | 1.22 | 0.036 |
| *CD14* | CD14 molecule | 1.48 | 0.001 |
| *CD209* | CD209 molecule | 1.27 | 0.018 |
| *CD248* | CD248 molecule | 1.31 | 0.014 |
| *CD68* | CD68 molecule | 1.28 | 0.032 |
| *CILP* | cartilage intermediate layer protein | 1.25 | 0.035 |
| *CKB* | creatine kinase B | 0.75 | 0.021 |
| *CLDN1* | claudin 1 | 0.74 | 0.034 |
| *COL1A1* | collagen type I alpha 1 chain | 1.63 | 0.020 |
| *COL1A2* | collagen type I alpha 2 chain | 1.61 | 0.008 |
| *COL3A1* | collagen type III alpha 1 chain | 1.53 | 0.009 |
| *COL5A1* | collagen type V alpha 1 chain | 1.30 | 0.020 |
| *COL6A1* | collagen type VI alpha 1 chain | 1.37 | 0.003 |
| *CPA3* | carboxypeptidase A3 | 1.45 | 0.001 |
| *CPVL* | carboxypeptidase, vitellogenic like | 1.26 | 0.010 |
| *CPXM1* | carboxypeptidase X, M14 family member 1 | 1.26 | 0.011 |
| *CRYAB* | crystallin alpha B | 0.72 | 0.048 |
| *CSN1S1* | casein alpha s1 | 1.24 | 0.015 |
| *CTSG* | cathepsin G | 1.43 | 0.002 |
| *CTSZ* | cathepsin Z | 1.41 | 0.000 |
| *CXCL12* | C-X-C motif chemokine ligand 12 | 1.29 | 0.014 |
| *CXCL8* | C-X-C motif chemokine ligand 8 | 1.92 | 0.012 |
| *CYBA* | cytochrome b-245 alpha chain | 1.34 | 0.024 |
| *CYBB* | cytochrome b-245 beta chain | 1.27 | 0.003 |
| *CYTH4* | cytohesin 4 | 1.20 | 0.002 |
| *DAB2* | DAB2, clathrin adaptor protein | 1.24 | 0.027 |
| *DCN* | decorin | 1.49 | 0.049 |
| *DSG2* | desmoglein 2 | 0.79 | 0.024 |
| *EGR2* | early growth response 2 | 1.32 | 0.039 |
| *EMILIN2* | elastin microfibril interfacer 2 | 1.22 | 0.001 |
| *EMP3* | epithelial membrane protein 3 | 1.23 | 0.027 |
| *ERAP2* | endoplasmic reticulum aminopeptidase 2 | 0.76 | 0.021 |
| *ERRFI1* | ERBB receptor feedback inhibitor 1 | 0.76 | 0.036 |
| *F13A1* | coagulation factor XIII A chain | 1.51 | 0.010 |
| *FCER1A* | Fc fragment of IgE receptor Ia | 1.22 | 0.036 |
| *FCER1G* | Fc fragment of IgE receptor Ig | 1.32 | 0.004 |
| *FCGR2A* | Fc fragment of IgG receptor IIa | 1.20 | 0.046 |
| *FCN1* | ficolin 1 | 1.33 | 0.012 |
| *FSCN1* | fascin actin-bundling protein 1 | 1.24 | 0.023 |
| *GBP5* | guanylate binding protein 5 | 1.22 | 0.00005 |
| *HDC* | histidine decarboxylase | 1.21 | 0.001 |
| *HLA-DMB* | major histocompatibility complex, class II, DM beta | 1.27 | 0.040 |
| *HLA-DRB3* | major histocompatibility complex, class II, DR beta 3 | 1.20 | 0.045 |
| *HSPA6* | heat shock protein family A (Hsp70) member 6 | 1.25 | 0.033 |
| *ID2* | inhibitor of DNA binding 2 | 1.22 | 0.014 |
| *IFI30* | IFI30, lysosomal thiol reductase | 1.20 | 0.014 |
| *IL1B* | interleukin 1 beta | 1.39 | 0.048 |
| *IL1RN* | interleukin 1 receptor antagonist | 1.23 | 0.027 |
| *ITGB2* | integrin subunit beta 2 | 1.28 | 0.031 |
| *LAPTM5* | lysosomal protein transmembrane 5 | 1.24 | 0.032 |
| *LBP* | lipopolysaccharide binding protein | 1.34 | 0.004 |
| *LCP1* | lymphocyte cytosolic protein 1 | 1.33 | 0.031 |
| *LGMN* | legumain | 1.27 | 0.043 |
| *LUM* | lumican | 1.32 | 0.034 |
| *LYZ* | lysozyme | 1.69 | 0.021 |
| *MAF* | MAF bZIP transcription factor | 1.20 | 0.009 |
| *MARCKS* | myristoylated alanine rich protein kinase C substrate | 1.23 | 0.003 |
| *MS4A6A* | membrane spanning 4-domains A6A | 1.34 | 0.024 |
| *MXRA5* | matrix remodeling associated 5 | 1.34 | 0.010 |
| *NINJ1* | ninjurin 1 | 1.30 | 0.0003 |
| *NR4A2* | nuclear receptor subfamily 4 group A member 2 | 1.51 | 0.021 |
| *OSM* | oncostatin M | 1.22 | 0.005 |
| *PCOLCE* | procollagen C-endopeptidase enhancer | 1.28 | 0.013 |
| *PDE4B* | phosphodiesterase 4B | 1.26 | 0.021 |
| *PDGFRB* | platelet derived growth factor receptor beta | 1.20 | 0.024 |
| *PLAU* | plasminogen activator, urokinase | 1.41 | 0.010 |
| *PLAUR* | plasminogen activator, urokinase receptor | 1.25 | 0.012 |
| *PLCXD1* | phosphatidylinositol specific phospholipase C X domain containing 1 | 1.24 | 0.043 |
| *PLEK* | pleckstrin | 1.32 | 0.003 |
| *PLIN3* | perilipin 3 | 1.25 | 0.0002 |
| *PLTP* | phospholipid transfer protein | 1.47 | 0.010 |
| *PPP2R1B* | protein phosphatase 2 scaffold subunit Abeta | 1.22 | 0.028 |
| *PRICKLE1* | prickle planar cell polarity protein 1 | 1.24 | 0.023 |
| *PROK2* | prokineticin 2 | 1.26 | 0.015 |
| *PSME2* | proteasome activator subunit 2 | 1.20 | 0.026 |
| *PTGS2* | prostaglandin-endoperoxide synthase 2 | 1.42 | 0.025 |
| *RNA5S9* | RNA, 5S ribosomal 9 | 1.23 | 0.034 |
| *RNASE1* | ribonuclease A family member 1, pancreatic | 1.38 | 0.045 |
| *RNU1-1* | RNA, U1 small nuclear 1 | 1.33 | 0.020 |
| *RNU1-3* | RNA, U1 small nuclear 3 | 1.33 | 0.047 |
| *RNU11* | RNA, U11 small nuclear | 1.24 | 0.002 |
| *RNU4-1* | RNA, U4 small nuclear 1 | 1.25 | 0.008 |
| *RNU4-2* | RNA, U4 small nuclear 2 | 1.37 | 0.0005 |
| *RNU6-1* | RNA, U6 small nuclear 1 | 1.35 | 0.002 |
| *RNU6-15P* | RNA, U6 small nuclear 15, pseudogene | 1.43 | 0.0004 |
| *RNVU1-18* | RNA, variant U1 small nuclear 18 | 1.36 | 0.035 |
| *RNVU1-7* | RNA, variant U1 small nuclear 7 | 1.37 | 0.023 |
| *S100A11P1* | S100 calcium binding protein A11 pseudogene 1 | 1.25 | 0.026 |
| *S100A4* | S100 calcium binding protein A4 | 1.45 | 0.003 |
| *SAA2* | serum amyloid A2 | 1.39 | 0.041 |
| *SAMSN1* | SAM domain, SH3 domain and nuclear localization signals 1 | 1.24 | 0.011 |
| *SCARNA9* | small Cajal body-specific RNA 9 | 1.25 | 0.017 |
| *SERPINH1* | serpin family H member 1 | 1.21 | 0.015 |
| *SH3BGRL3* | SH3 domain binding glutamate rich protein like 3 | 1.21 | 0.002 |
| *SLC25A24* | solute carrier family 25 member 24 | 1.21 | 0.020 |
| *SLC7A7* | solute carrier family 7 member 7 | 1.24 | 0.004 |
| *SLMAP* | sarcolemma associated protein | 0.78 | 0.016 |
| *SNORD13* | small nucleolar RNA, C/D box 13 | 1.57 | 0.002 |
| *SRPX* | sushi repeat containing protein, X-linked | 1.25 | 0.030 |
| *STAB1* | stabilin 1 | 1.26 | 0.002 |
| *SYNM* | synemin | 0.70 | 0.036 |
| *THBS2* | thrombospondin 2 | 1.39 | 0.029 |
| *TMOD1* | tropomodulin 1 | 0.78 | 0.0003 |
| *TNFSF13B* | TNF superfamily member 13b | 1.27 | 0.0001 |
| *TPSAB1/TPSB2* | tryptase alpha/beta 1 | 1.43 | 0.001 |
| *TSPAN6* | tetraspanin 6 | 0.79 | 0.003 |
| *TUBA1A* | tubulin alpha 1a | 1.28 | 0.035 |
| *TYMP* | thymidine phosphorylase | 1.38 | 0.003 |
| *TYROBP* | TYRO protein tyrosine kinase binding protein | 1.43 | 0.002 |
| *USP36* | ubiquitin specific peptidase 36 | 1.22 | 0.004 |
| *VCAN* | versican | 1.49 | 0.005 |
| *VTRNA1-1* | vault RNA 1-1 | 1.22 | 0.010 |
| *VTRNA2-1* | vault RNA 2-1 | 1.31 | 0.029 |
| *WAS* | Wiskott-Aldrich syndrome | 1.20 | 0.0495 |
| *WISP2* | WNT1 inducible signaling pathway protein 2 | 1.20 | 0.029 |
| *ZNF331* | zinc finger protein 331 | 1.23 | 0.042 |

**Table S9.** **Ingenuity Pathway Analysis (IPA) results of molecular pathways significantly enriched in the n=129 VAT genes differentially expressed (absolute fold change >1.2; P<0.05) in colorectal tumor tissues of patients by *PTGS2* tumor expression group, after adjustment for patient sex, tumor site and stage. Canonical pathways ranked by Z-score.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Canonical Pathways** | **Z-Score** |  **-Log** **(P-value)** | **P-value** | **Molecules** |
| PPAR Signaling | -2.00 | 2.46 | 0.0035 | *IL1RN, IL1B, PTGS2, PDGFRB* |
| LXR/RXR Activation | -1.41 | 5.99 | 0.000001 | *LYZ, IL1RN, CD14, IL1B, PLTP, LBP, PTGS2, SAA2* |
| LPS/IL-1 Mediated Inhibition of RXR Function | 1.00 | 2.66 | 0.0022 | *ALDH1A3, IL1RN, CD14, IL1B, PLTP, LBP* |
| Production of Nitric Oxide and Reactive Oxygen Species in Macrophages | 1.00 | 1.47 | 0.0339 | *LYZ, CYBA, CYBB, PPP2R1B* |
| Neuroinflammation Signaling Pathway | 1.89 | 3.19 | 0.0006 | *CXCL8, TYROBP, HLA-DMB, CYBB, CXCL12, IL1B, PTGS2, CCL5* |
| Intrinsic Prothrombin Activation Pathway | 2.00 | 3.93 | 0.0001 | *COL1A2, COL1A1, F13A1, COL3A1* |
| IL-6 Signaling | 2.00 | 3.67 | 0.0002 | *CXCL8, COL1A1, IL1RN, CD14, IL1B, LBP* |
| Leukocyte Extravasation Signaling | 2.00 | 2.71 | 0.0019 | *ITGB2, CLDN1, WAS, CYBA, CYBB, CXCL12* |
| Acute Phase Response Signaling | 2.00 | 2.31 | 0.0049 | *IL1RN, IL1B, OSM, LBP, SAA2* |
| Osteoarthritis Pathway | 2.00 | 2.04 | 0.0091 | *CXCL8, DCN, IL1B, PTGS2, ALPL* |
| Role of NFAT in Regulation of the Immune Response | 2.00 | 1.55 | 0.0282 | *FCGR2A, HLA-DMB, FCER1A, FCER1G* |
| NF-κB Signaling | 2.24 | 2.25 | 0.0056 | *IL1RN, FCER1G, IL1B, TNFSF13B, PDGFRB* |
| IL-8 Signaling | 2.24 | 2.04 | 0.0091 | *CXCL8, ITGB2, CYBB, PTGS2, CCND1* |
| GPVI/GP6 Signaling Pathway | 2.45 | 3.75 | 0.0002 | *COL5A1, COL1A2, COL1A1, COL6A1, FCER1G, COL3A1* |
| Dendritic Cell Maturation | 3.00 | 7.78 | 0.00000002 | *COL1A2, COL1A1, FCGR2A, TYROBP, IL1RN, FSCN1, HLA-DRB3, HLA-DMB, FCER1G, IL1B, COL3A1* |