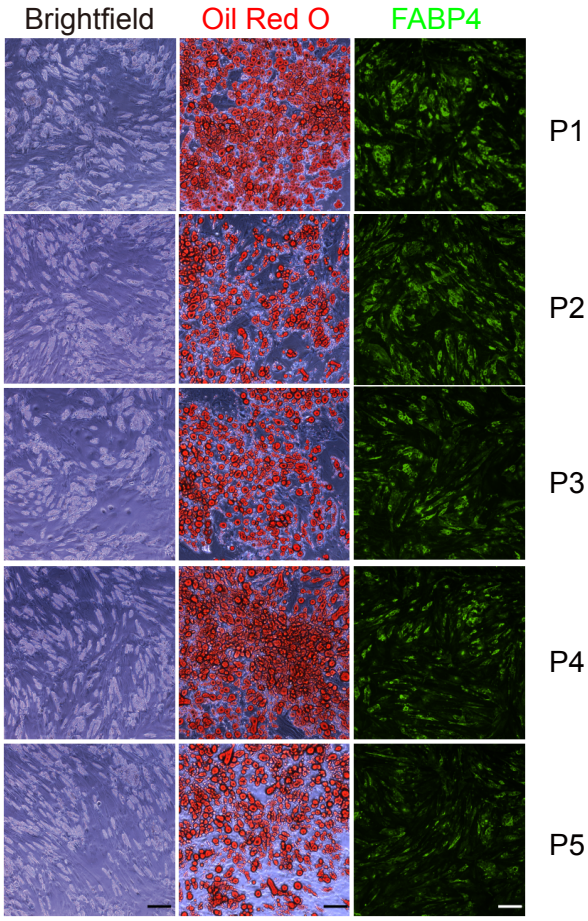
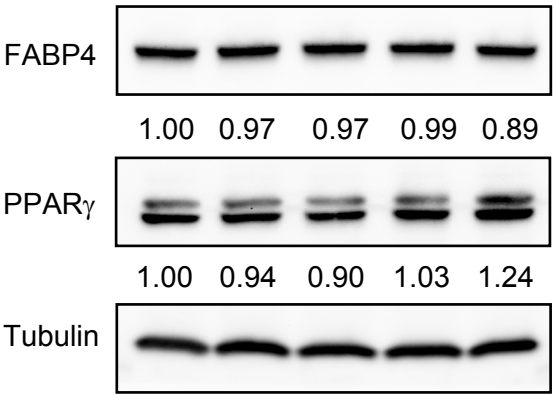
A

Subject	Age	Gender	Race	BMI
P1	46	Female	Black	37.2
P2	35	Female	Black	44.2
P3	22	Female	White	41.6
P4	49	Female	White	48.2
P5	49	Female	Black	54.9

B

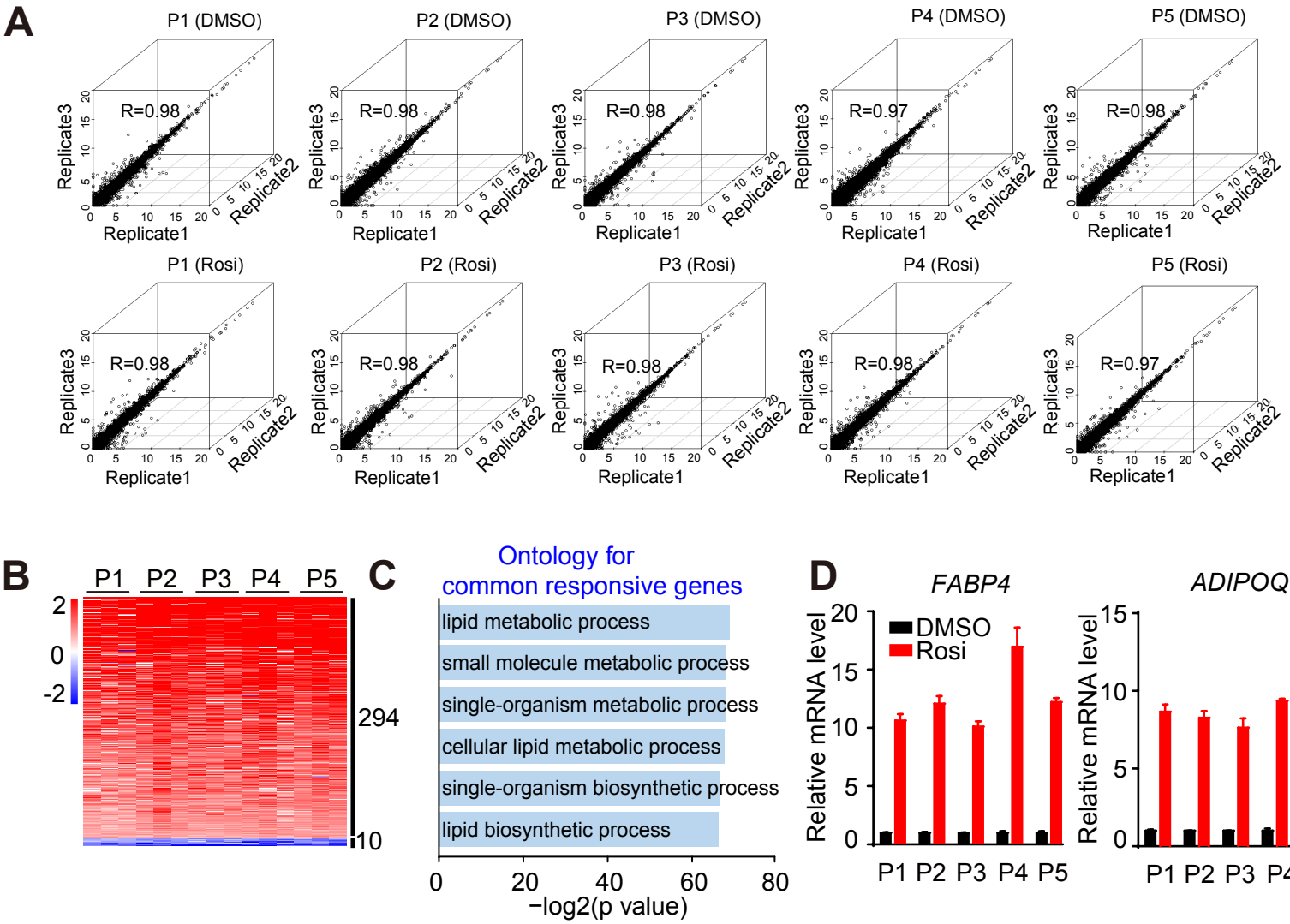


C



Supplemental Figure 1, related to Figure 1

Figure S1. Derive human adipocytes from obese patients, Related to Figure 1.
(A) Information about the 5 patients studied, including age, gender, race, and BMI.
(B) Representative images of morphology, Oil Red O staining and FABP4 immunostaining of adipocytes from five patients at day 21. Scale bar, 100 μm.
(C) Protein expression level of adipocyte marker genes *FABP4* and *PPARγ* in adipocytes from five patients at day 21. The values below the western blot represent the relative expression level of each protein after normalization to tubulin.



Supplemental Figure 2, related to Figure 1

Figure S2. Patient-derived adipocytes differentially respond to rosi treatment, Related to Figure 1.

(A) The correlation among three replicates in each patient and each condition. Each dot represents a gene. X-axis, Y-axis and Z-axis represent the normalized expression value of genes in three replicates.

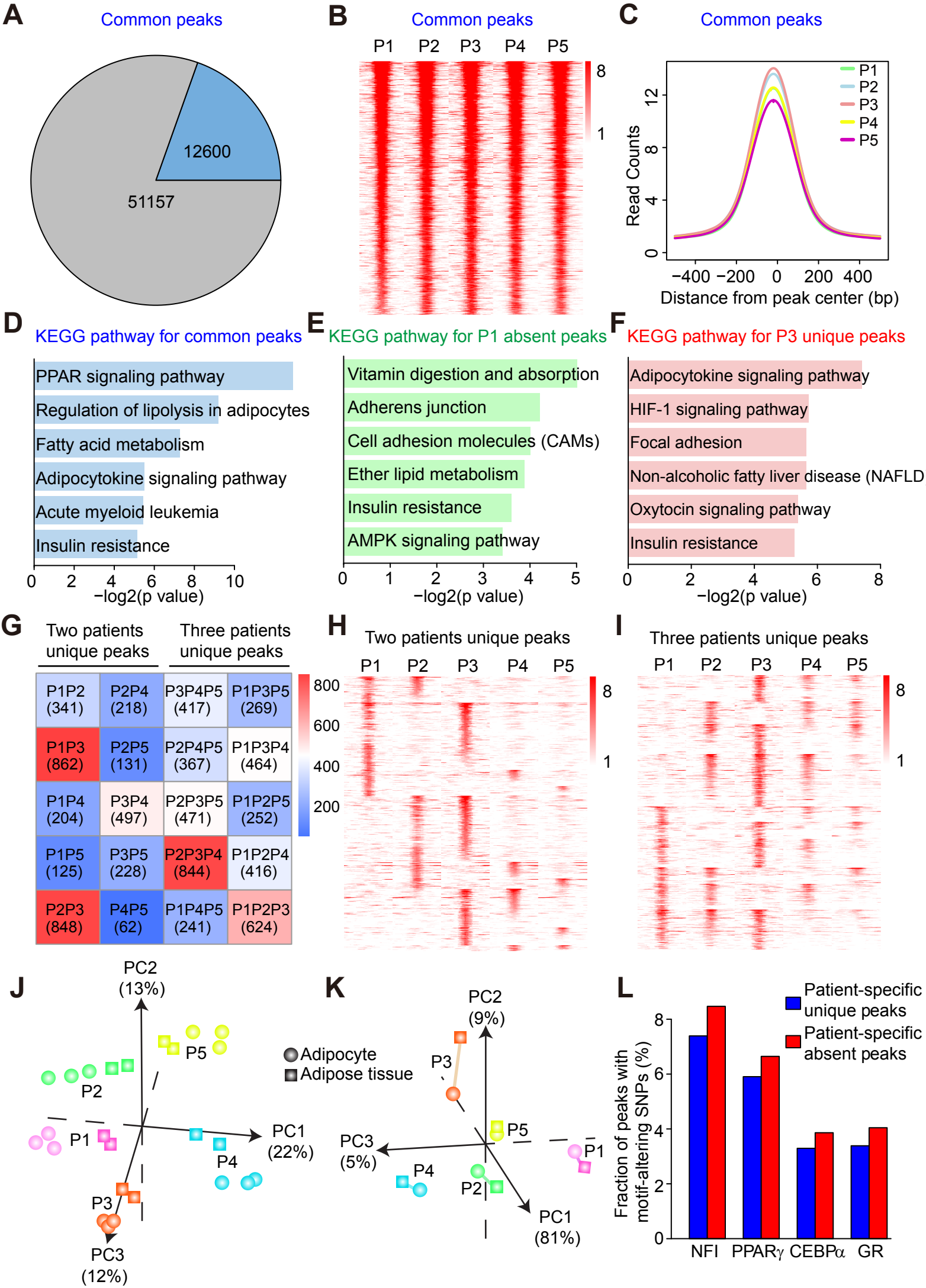
(B) Heat map of common rosi-responsive genes that are regulated by rosi in five patients. The color bar indicates the scale used to show log2FC(Rosi/DMSO) of genes across samples. Differentially expressed genes were identified using edgeR with adjusted *p* value < 0.01 and fold change≥1.5.

(C) Gene ontology for common rosi-responsive genes.

(D) mRNA expression of common rosi-responsive genes *FABP4* and *ADIPOQ* in adipocytes from five patients, normalized to *HPRT*, DMSO was set to 1, as measured by RT-qPCR.

(E-G) Proportion of common responsive genes (E), patient-specific unresponsive genes (F), and patient-specific responsive genes (G) in all five patients.

(H-J) KEGG pathways enriched in common responsive genes (H), P1-specific unresponsive genes (I), and P3-specific responsive genes (J).



Supplemental Figure 3, related to Figure 1

Figure S3. Common PPARγ binding sites shared by these five patients, Related to Figure 1.

(A and B) Proportion (A) and Heat map (B) of common PPARγ peaks that are detected similarly in all five patients. The color bar indicates the scale of relative normalized tag counts.

(C) For common PPARγ peaks, the average binding profiles are shown in 1 kb windows across patients.

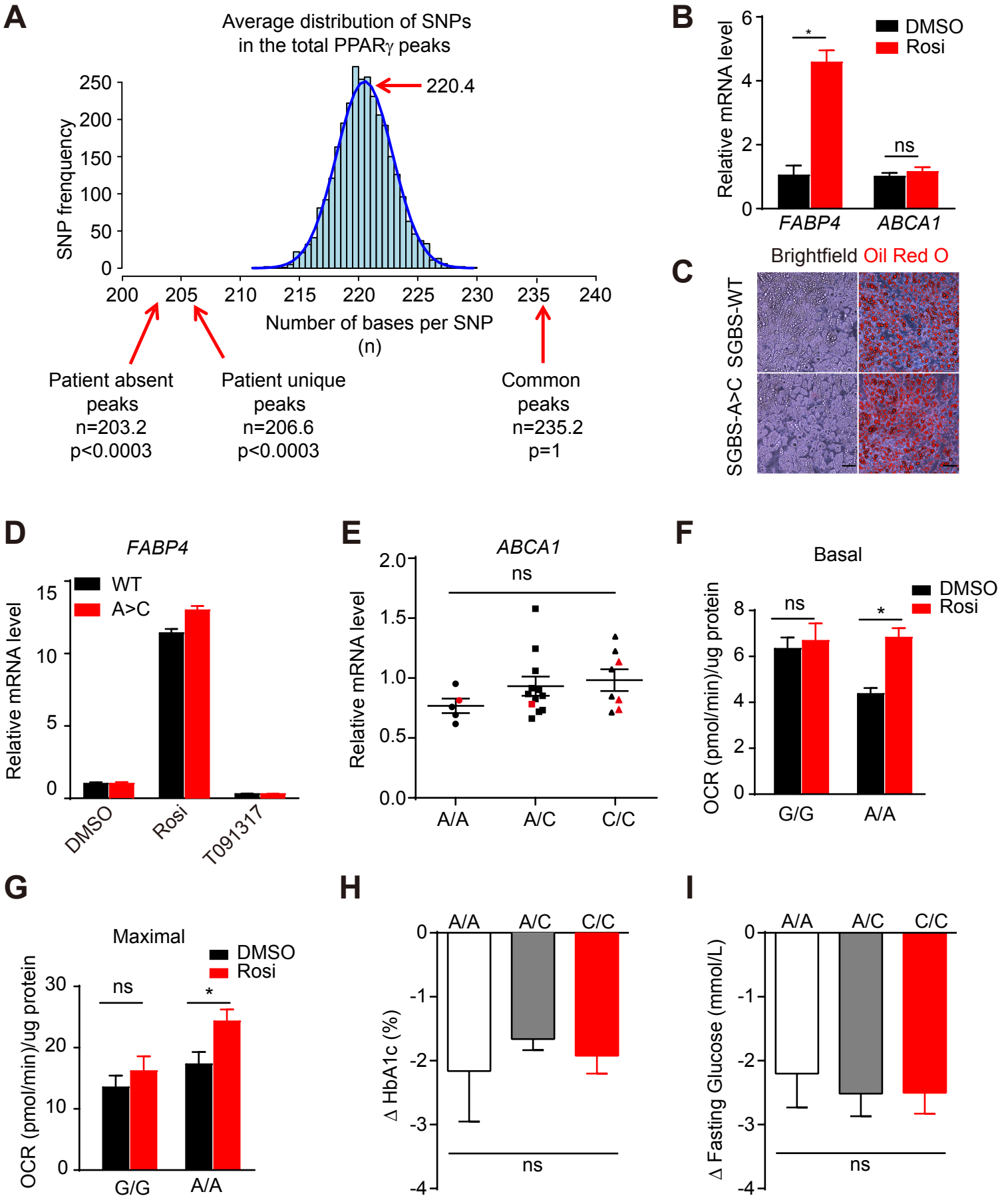
(D-F) KEGG pathways enriched in the genes surrounding common PPARγ peaks (D), patient-specific absent peaks (E) and patient-specific unique peaks (F).

(**G-I**) The numbers of patient-specific sites shared by a subset of two or three individuals are shown in table (G). Heat map of PPARγ peaks observed only in 2 patients (H) or 3 patients (I) with at least 2-fold differences in read counts compared to other patients.

(J) Principal component analysis (PCA) with computation of closest neighboring samples under ANOVA (p=0.02) showed more than 1000 genes with preserved patient-specific expression in adipocytes (circle) and adipose tissues (quadrilateral).

(K) PCA with computation of closest neighboring samples under ANOVA (p=0.05) showed more than 1000 PPARγ binding sites with preserved patient-specific pattern in adipocytes (circle) and adipose tissues (quadrilateral).

(L) Fraction of PPARγ binding sites that contain SNPs affecting PPARγ motif and its cofactors NFI, CEBPα and GR motifs.



Supplemental Figure 4, related to Figure 3 and 4

Figure S4. SNPs were enriched in patient-specific absent and unique sites and modulated rosi effect, Related to Figure 3 and 4.

(A) SNPs are enriched in patient-specific absent PPARγ peaks, patient-specific unique PPARγ peaks, but not enriched in common PPARγ peaks based on random test. The length of bases in patient-specific sites or common peaks that contains one SNP was indicated by red arrows. *P*-values are determined by random test.

(B) mRNA expression of *FABP4* and *ABCA1* in SGBS-differentiated adipocytes, normalized to *HPRT*, as measured by RT-qPCR. Data are expressed as mean ± SEM. (*) $p < 0.05$, (ns) $p > 0.05$ in Student's t-test. n = 3 per group.

(C) Representative images of morphology and Oil Red O staining of adipocytes from SGBS WT and SGBS A>C cell lines. Scale bar, 100 μm.

(D) mRNA expression of *FABP4* in SGBS WT and SGBS A>C adipocytes treated with DMSO, 1μM rosi or 10μM T091317 (n=3), normalized to *HPRT*, as measured by RT-qPCR. Data are expressed as mean ± SEM.

(E) mRNA expression of *ABCA1* in hASC-derived adipocytes from 25 patients without rosi treatment. Red dots represent patients P1-P5. Normalized to *HPRT*. (ns) $p > 0.05$ in one-way ANOVA test.

(F and G) Basal (F) and maximal (G) respiration calculated from OCRs in 3 rs2106146 G/G and 3 A/A patient adipocytes treated with DMSO or 1μM rosi. Data were normalized to total protein content per well. Data are expressed as mean ± SEM from n = 7 technical replicates. (*) $p < 0.05$, (ns) $p > 0.05$ in Student's t-test.

(**H and I**) The change of HbA1c (H) and fasting glucose (I) levels after rosi treatment of patients carrying different rs4743771 genotypes. (ns) $p > 0.05$ in one-way ANOVA test.

Table S1. Primers used in this study, Related to STAR Methods.

Primer for RT-qPCR		
Primers	**Forward (5'-3')**	**Reverse (5'-3')**
FABP4	TCATGAAAGGCGTCACTTCC	GCTTGCTAAATCAGGGAAAACA
ADIPOQ	GATGAAGTCCTGTCTTGGAAGG	CAGCACTTAGAGATGGAGTTGG
HPRT	TGACACTGGCAAAACAATGCA	GGTCCTTTTCACCAGCAAGCT
ANGPTL4	CCTTCTCCACTTGGGACCAG	AAACCACCAGCCTCCAGAGA
AGPAT2	GAGGGTACTCGCAACGACAA	CCTGCACTGTGACTGTTCCT
DGKQ	TGAGCCAGACGCGGTTCTA	CAGGCAACGTCCAACACTAC
GUK1	GTATGGCACGAGCAAGGTG	GCGGCTGCACAGAGATGTAG
SLC7A10	CCGAGGAGATGGTTGACGC	ATGGCCGTGAAGTAGGCAATG
FAM160B2	CACATGCCTGCTGAGACCG	CCACCCGACTCTTCTTGCTC
ABCA1	ACCCACCCTATGAACAACATGA	GAGTCGGGTAACGGAAACAGG
SLC25A1	ACGGGGTTAGGGAGATTGTG	GCCTGCAATAGCTCCGAAGA
MSX1	ACACAAGACGAACCGTAAGCC	CACATGGGCCGTGTAGAGTC
NFIA	GCAGGCCCGAAAACGAAAATA	TTTGCCAGAAGTCGAGATGCC
Primer for ChIP-qPCR		
Primers	**Forward (5'-3')**	**Reverse (5'-3')**
ABCA1	CCTGTAAACAGCTTTTATGCTAG	CACCTCAGTGCATGATAGTTA
ALAS2	GGGAGGGGGTACACTAGAGG	GGGTTAGGACCTGGCATTTA
INS2	GCCCACCCTCTGATGTATCT	AAAGTGACCAGCTCCCTGTG
PDK4	GCAGAGTCAACAAGGGGAAG	ACTAGATGCCTGGGAGCTGA
Primer for SNaPshot		
Primers	**Forward (5'-3')**	**Reverse (5'-3')**
ABCA1 PCR	GCAACATACGGTTCTGTGATTG	AGAACACCTCAGTGCATGATAG
ABCA1 SNaPshot	GACTGACTtactgaattgtcctcctgc	
Primer for Genotyping		
Primers	**Forward (5'-3')**	**Reverse (5'-3')**
rs4743771-F	GCAACATACGGTTCTGTGATTG	AGAACACCTCAGTGCATGATAG
rs2106146-F	AGCCCTAAATCATAAATCACCAGAG	GAACCATGCCCTCTCTCAGAT
rs76932545-F	GGATTTCACTGAGCCCCACA	TCACCGATCGTGTTCCTGTC
3C probe and primers		
Primers/Probe	**Forward (5'-3')**	**Reverse (5'-3')**
ABCA1 probe	ctggaagtgcatgtggagg	
ABCA1_constant_F	catagaagaggcccaagcag	
ABCA1_1R		ggacatcttggagtatagatgcaaa
ABCA1_2R		aagcaatgcatgactctattgac
ABCA1_3R		gtgccccttttaactgtcca
ABCA1_4R		tccctttcctctgatacactgac
ABCA1_5R		cttcaaggcagtgtcagcag
ABCA1_6R		gagaagagcaatcctcaagattaga
TBP probe	tggaaccccaactaggttcgg	
TBP_constant_F	tcttttcctgctgtctgctgag	
TBP_1R		tgaccagccacagttacttatc
Oligos for CRISPR		
ABCA1 sgRNA	5' CACCgagttgcagagaatatgtgc 3'	5' AAACgcacatattctctgcaactc 3'
ssODN	5'atacggttctgtgattggatttagcaacacagagacatttatactgaattgtcctcctgcccatattctctgca actctcagctctgcctgtttcctgtaaacagcttttatgctagagca 3'	
gBlocks Gene for Luciferase reporter cloning		

rs4743771-A (5'-3')	CCGCTCGAGAGATGCACTGAATGAGTTCAACAATCAAGCACTTGAGAGA GCAACATACGGTTCTGTGATTGGATTTAGCAACACAGAGACATTTATACT GAATTGTCCTCCTGCACATATTCTCTGCAACTCTCAGCTCTGCCTGTTTC CTGTAAACAGCTTTTATGCTAGAGCAGGCATCTCCAACAGTGAATCAAG AGAAATCCTTCTATCAGAGATCTTCC
rs4743771-C (5'-3')	CCGCTCGAGAGATGCACTGAATGAGTTCAACAATCAAGCACTTGAGAGA GCAACATACGGTTCTGTGATTGGATTTAGCAACACAGAGACATTTATACT GAATTGTCCTCCTGCCCATATTCTCTGCAACTCTCAGCTCTGCCTGTTTC CTGTAAACAGCTTTTATGCTAGAGCAGGCATCTCCAACAGTGAATCAAG AGAAATCCTTCTATCAGAGATCTTCC
rs2106146-A (5'-3')	CCGCTCGAGGCGTGATCACGGCTCAGTGCAGCTTTGACCTCCTTGGCT CATGCGATCCTCTCATTTCAACCTTCCCAATAGCTGGGACTACAGACAT GTGCCACTTTACCCAGTTAAATTTTTAAATTTTTTGTACAGACAGATTCTC CTTATGTTGCCCATGATGGTGTTGAACTGGGCTCAAGTGATGCACCTCG GCCTCAGATCTTCC
rs2106146-G (5'-3')	CCGCTCGAGGCGTGATCACGGCTCAGTGCAGCTTTGACCTCCTTGGCT CATGCGATCCTCTCATTTCAACCTTCCCAATAGCTGGGACTACAGACAT GTGCCACTTTGCCCAGTTAAATTTTTAAATTTTTTGTACAGACAGATTCT CCTTATGTTGCCCATGATGGTGTTGAACTGGGCTCAAGTGATGCACCTC GGCCTCAGATCTTCC
rs76932545-A (5'-3')	CCGCTCGAGGGTCCTGACACGCAGTGGGAACTCAGCGCTGTTAAATGT GGATTTCACTGAGCCCCACAGGCAGCCCTTTAGGACCTCGACCCAAGG TCATTCTGGCCAAAGGCCGCTAGAGGGCAGCGGTGCTTTTCCCTCTGC ATGAAGTTTGGGACAACGTCCGCAGTCAGCCTCGTCTGGTCCCAGGAG ATCTTCC
rs76932545-G (5'-3')	CCGCTCGAGGGTCCTGACACGCAGTGGGAACTCAGCGCTGTTAAATGT GGATTTCACTGAGCCCCACAGGCAGCCCTTTAGGACCTCGGCCCAAGG TCATTCTGGCCAAAGGCCGCTAGAGGGCAGCGGTGCTTTTCCCTCTGC ATGAAGTTTGGGACAACGTCCGCAGTCAGCCTCGTCTGGTCCCAGGAG ATCTTCC