Dissecting molecular mechanisms of resistance to NOTCH1-targeted therapy in T-cell acute lymphoblastic leukemia xenografts

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SUPPLEMENTARY MATERIALS AND METHODS

Optical imaging

To perform *in vivo* imaging, PDTALL19 cells were transduced with a lentiviral vector encoding the Luciferase reporter gene, and bioluminescence images were acquired on IVIS Imaging System (Xenogen Corporation, Alameda, CA, USA) as described before (1).

Quantitative PCR (qPCR)

Primers used for qPCR analysis are:

ABCA1 – for CCAACCTCATCAGGAAGCAT
ABCA1 – rev GAGCCGGTCATCAATCTCAT

CYP51A1 – for CCAGAACTCCTCAGACTGT
CYP51A1 – rev CTCCAAATGGCACATAGGCA

SQLE – for AAACTTGGTGGCGAATGTGT
SQLE – rev GCAAAAATACACGGCATAGATTG

HMGCS1 – for GTCCCACTCCAAATGATGAC
HMGCS1 – rev TTCAGGTTCTGCTGCTGTG

β2-MICROGLOBULIN – for TGCTGTCTCCATGTTTGATGTATCT
β2-MICROGLOBULIN – rev TCTCTGCTCCCCACCTCTAAGT

HES4-for AGATGACCGTGAGACACCTG

HES4-rev GCCAGACACTCGTGGAAG

Primer sequences for *CR2*, *HES1*, *DELTEX1*, *pTa* and *NOTCH3* are reported in Agnusdei et al. Leukemia 2014.

Immunophenotype analysis and Ki67 staining

Ctrl Ab treated and OMP52M51 resistant PDTALL19 cells were analyzed by flow cytometry to evaluate possible phenotypic, cell size and growth rate changes. To this end, the following antibodies were used: CD4-FITC, CD8-PE, CD5-PeCy7, CD3-APC, CD64-FITC, CD11a-PE, DR-PeCy7, CD11b-PE, CD34-PeCy7, CD20-APC Cy7, Alexa Fluor 488 mouse anti-human Ki67 (from Becton Dickinson, Franklin Lakes,NJ), CD45-ECD, CD7-PeCy5, CD33-PeCy5, CD16-FITC, CD10-FITC, CD34-PeCy5 and CD19-PeCy7 (Coulter, Fullerton, CA, USA).

SNP array analysis

Genomic DNA was extracted from T-ALL cells derived from xenografts with Easy DNA kit (Life Technologies) according to the manufacturer's instructions. Whole-genome copy number variation (CNV) analysis was carried out using the CytoScan HD array (Affymetrix, Santa Clara, CA) according to the manufacturer's instructions. This array contains more than 2.6 million markers for copy number analysis and approximately 750,000 SNPs that fully genotype with greater than 99 percent accuracy. Copy number analysis was performed using the Chromosome Analysis Suite Software version 3.1 (Affymetrix, Santa Clara, CA): i) the raw data file (.CEL) was normalized using the default options; ii) an unpaired analysis was performed using as baseline 270 HapMap samples in order to obtain Copy numbers value from .CEL files. The amplified and/or deleted regions were detected using a standard Hidden Markov Model (HMM) method and base pair position were derived from the University of California Santa Cruz (UCSC) Genome Browser (http://genome.ucsc.edu/cgi-bin/hgGateway), build GRCh37 (hg19).

Gene expression profiling. Data were normalized following RMA algorithm (2) applying quantile normalization, implemented in R/Bioconductor (Version 3.4). Expression data were filtered to remove non-expressed (log2 intensity <5) or invariant (lowest 25% of standard deviation) genes (3). Statistically significant differentially expressed gene were determined using permutation tests (SAM) (4). Genes regulated at least two fold in comparison to untreated controls were considered. The delta value was set to return a median false significant number of zero. Hierarchical clustering was performed using Pearson correlation as distance measure and average linkage performed using MeV 4.0 software (http://www.tm4.org/mev/). Annotations were obtained through the Affymetrix database from Thermo

Fisher website. Microarray data have been deposited in NCBI's Gene Expression Omnibus (5) and are accessible through GEO accession number GSE123751.

Gene set enrichment analysis.

Gene enrichment analysis was performed using the EnrichR online tool (6) (7) and GSEA software version 3.0 (8, 9). For each group of gene sets, GSEA calculates and evaluates the statistical significance of an enrichment score (ES). The ES reflects the degree to which a gene set is overrepresented. GSEA analysis was performed, collapsing the probe sets to gene vectors and using the signal-to-noise metric, the gene-set permutation type and 1000 permutations. As recommended by GSEA guidelines, only gene sets with an FDR q-value<0.05 were considered.

Statistical analysis.

Results were expressed as mean value± S.D. Statistical analysis of data was performed using Student's t-test, when samples followed a normal distribution, or non-parametric Mann–Whitney–Wilcoxon test. Differences were considered statistically significant when P<0.05

BODIPY staining:

Cells were stained with 2 µM BODIPY 493/503 (Thermo Fisher Scientific , Waltham, MA, USA) for 15 minutes at 37°C and then were analyzed using LSRII flow cytometer (BD Biosciences, San Jose, CA, USA).

***FBW7* sequencing**

Genomic DNA was obtained from PDTALL cells with Easy DNA kit (Life Technologies) according to the manufacturer's instructions. DNA was then amplified by Titanium® DNA Amplification Kit (Clontech, Saint-Germain-en-Laye France) and sequenced by BigDye® Terminator v1.1 Cycle sequencing Kit (Applied Biosystems). Primers used are:

FBXW7ex9_for TGATGGGATCATTTTATACGGATG

FBXW7ex9_rev GACAAAACGCTATGGCTTTCC

FBXW7ex10_for CCCAACTTCCCATTCCCTTA

FBXW7ex10_rev TTTCTTCATGCCAATTTTAACG

FBXW7ex9_seq_for TTTAAATCACTTTTCCTTTCTACCC

FBXW7ex10_seq_for TGACTAAATCTACCATGTTTTCTCA.

Metabolomic analysis

Spleen samples recovered from Ctrl Ab or OMP52M51 treated mice were snap frozen and prepared for metabolomic analysis by Biocrates Life Sciences (Innsbruck, Austria). Measurements were done using proprietary sample preparation procedures and MS/MS (Tandem Mass Spectrometry) analytical methods for targeted classes of metabolites. “AbsoluteIDQ® p400 HR assay” and “Free Oxysterols Assay with Cholesterol” were used and the complete list of metabolites is reported in Supplementary Table I. Metabolomic data below the limit of detection (LOD) were replaced with a random number from a uniform distribution on the interval [LOD/2,LOD], provided that at least 80% valid values above LOD were available within each group. Otherwise, the analyte was excluded from the analysis. Variables were summarized as median and interquartile range (IQ) and their distribution was compared between control and treatment groups using the Kruskal-Wallis test. To control the False-Discovery-Rate, p-values were adjusted applying the Benjamini-Hochberg correction within each metabolite class. All statistical tests used a two-sided 5% significance level. Statistical analyses were performed using RStudio (RStudio: Integrated Development for R. RStudio, Inc., Boston, MA).

Western blot analysis

Western blot methods used in this study have been previously published (11). Immunoprobing was performed using rabbit primary Abs against NOTCH1 (C44H11) and Cleaved Notch1 Val1744, rabbit primary Ab against PTEN, mouse primary Ab against pAkt (Ser473) (Cell Signaling Technologies, Beverly, MA, USA), rabbit Ab against β-ACTIN, mouse Ab against α-TUBULIN (both from Sigma Aldrich, Saint Luis, MO, USA), mouse Ab against PAN-CADHERIN, rabbit primary antibody against Akt and mouse primary Ab against pAkt (Thr308) (Santa Cruz Biotechnology, Dallas, TX, USA), followed by hybridization with a horseradish peroxidase-conjugated anti-rabbit or anti-mouse secondary Ab (Perkin Elmer, Waltham, MA, USA).

Whole exome sequencing (WES) analysis

Whole exome sequencing was performed on six T-ALL xenograft derived cells, comprising three OMP52M51 resistant samples and three untreated controls. Genomic DNA was extracted with Easy DNA kit (Life Technologies), quantified with Qubit 2.0 Fluorometer (Invitrogen, Carlsbad, CA) and subjected to quality control using agarose gel prior to enzymatic DNA fragmentation. The samples were sequenced using the SureSelect^{XT} Low Input Human All Exon V7 48.2 Mb kit (Agilent, Santa Clara, CA) on NextSeq 500 (Illumina, San Diego, CA) in paired-end mode (2x100 bp). Sequencing reads were then analyzed with the Alissa Align & Call Software (version 1.0, Agilent Technologies, Santa Clara, CA). Specifically, fastq reads were trimmed and aligned to the human genomic reference (hg19) with default parameters. After reads de-duplication, aligned reads were used for somatic variant calling with Alissa SNPPET according to default threshold values. Single Nucleotide Variant (SNV) annotation and selection was performed using the Alissa Interpret module (version 1.0, Agilent Technologies, Santa Clara, CA). Briefly, exonic SNVs indicated as confident calls (PASS) were considered for further investigation and filtered considering the cut-off value of 10% for the variant allele frequency and a sequencing depth of 30 reads, excluding both common polymorphisms (MAF>5%) and synonymous SNVs (17, 18). To identify resistance associated genomic alterations, only variants shared among all the treated samples and absent in the controls were considered.

NOTCH1 sequencing

NOTCH1 variants identified by WES were validated by direct sequencing in both resistant samples (n=5) and controls (n=4). DNA was amplified by Titanium® DNA Amplification Kit (Clontech, Saint-Germain-en-Laye France) and sequenced by BigDye® Terminator v1.1 Cycle sequencing Kit (Applied Biosystems). Primers used are:

NOTCH1ex26_for: GCTGAGGGAGGACCTGAACTTGG

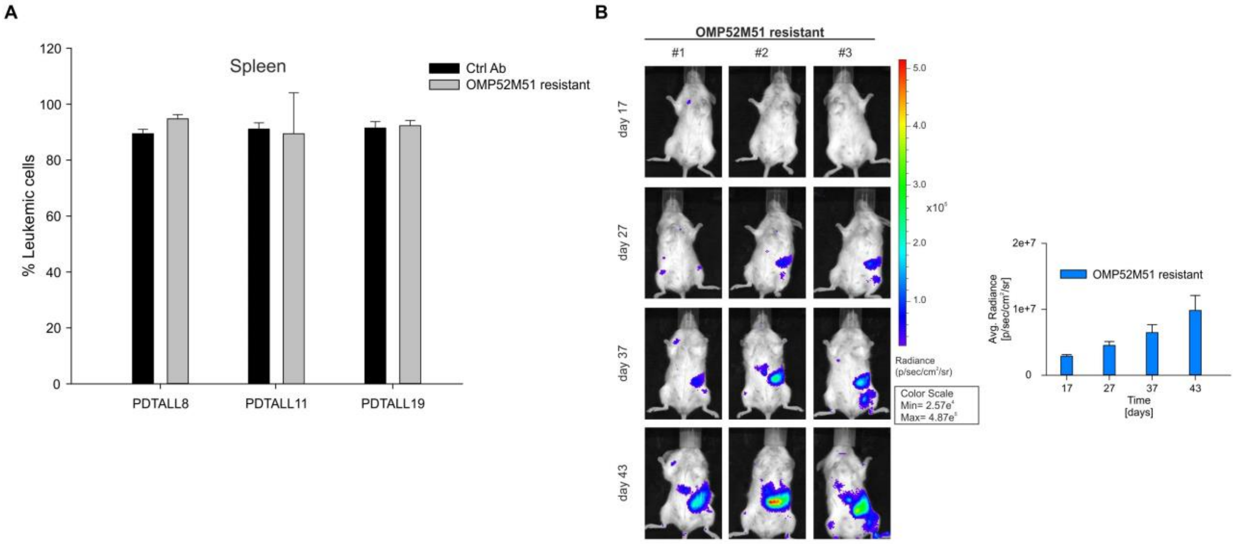
NOTCH1ex26_rev: CCTGAGCTGGAATGCTGCCTCTA

Target sequencing (NGS)

Candidate NOTCH1 variants were validated by deep sequencing using an in-house custom gene panel, which includes NOTCH1 gene. Gene panel libraries were prepared using the SureSelect$^{XT\text{-}HS}$ capture-based kit (Agilent Technologies, Santa Clara, CA) and sequenced on Illumina MiSeqDX platform (Illumina, San Diego, CA) with paired-end 151 reads. Sequencing reads were then analyzed with SureCall Software (version 4.0.1.46, Agilent Technologies, Santa Clara, CA) in single sample mode. Then, fastq reads were trimmed and aligned to the human genomic reference (hg19) with default parameters. After reads de-duplication, alignments were used for somatic variant calling with SureCall SNPPET (default threshold values; VAF cut-off=10%). To exclude false negative calls, SNPPET analysis was prelicated using a VAF cut/off value of 0.01% and candidate variants mapping to NOTCH1 gene were manually assessed with bam-readcount. Mean normalized coverage (i.e. without duplicated reads) in these genomic positions exceeded 300X.

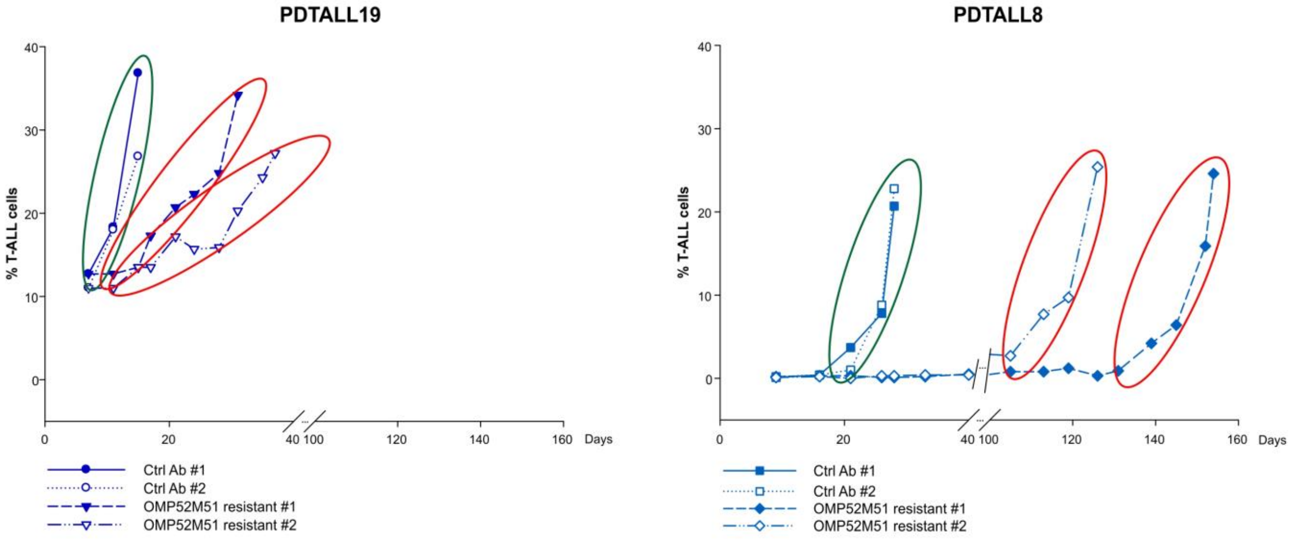
SUPPLEMENTARY FIGURES AND LEGENDS:

SUPPL. FIG. S1



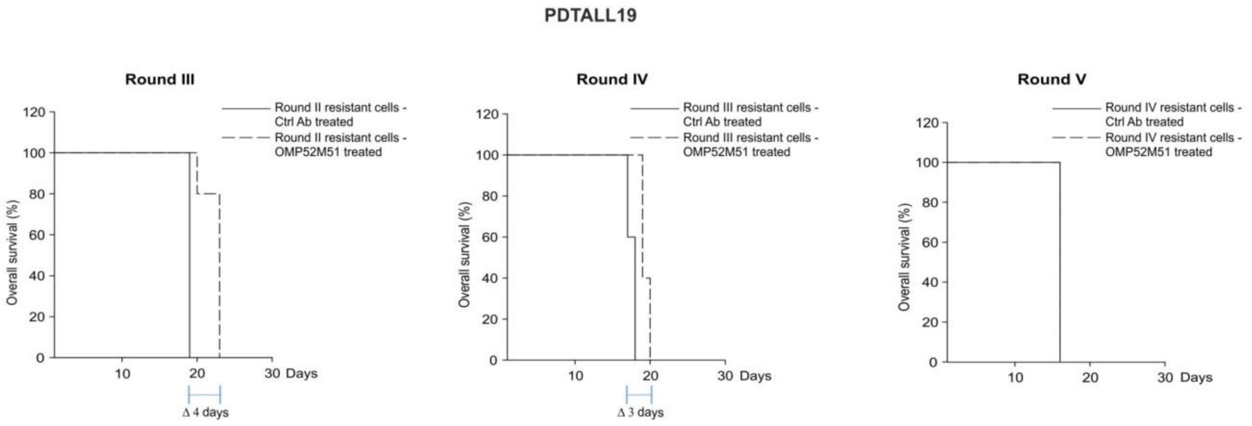
Suppl. Fig. S1: A. Measurement of leukemia by flow cytometry in the spleen of Ctrl Ab (black bars) and OMP52M51-treated mice (gray bars) at sacrifice (3-5 mice/group). **B.** Tracking leukemia outgrowth by optical imaging. PDTALL19 cells were labeled with the luciferase gene and i.v. injected into NOD/SCID mice (5x10^6 cells/mouse; n=5 mice/group). **Left:** Images of three representative OMP52M51-treated mice acquired at day 17, 27, 37 and 43. **Right**: Quantitative analysis of luciferase activity at various time points of measurement (n=5 mice/group).

SUPPL. FIG. S2



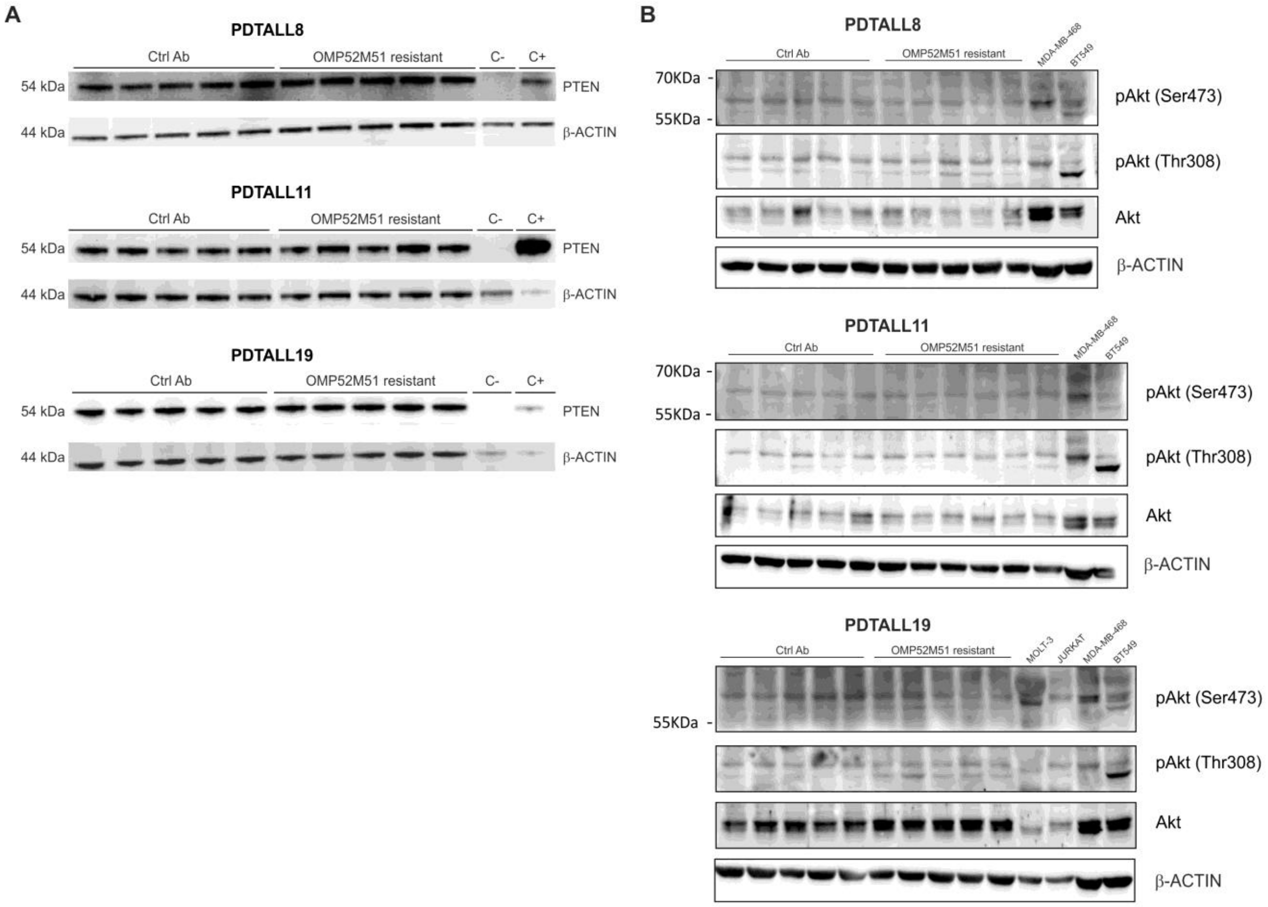
Suppl. Fig. S2: Measurement of leukemia outgrowth in mice by weekly blood drawings. The percentage of T-ALL cells in blood was measured by flow cytometry. Two representative mice for each model and treatment group are shown. The green and the red contouring indicate control and OMP52M51-treated mice, respectively.

SUPPL. FIG. S3



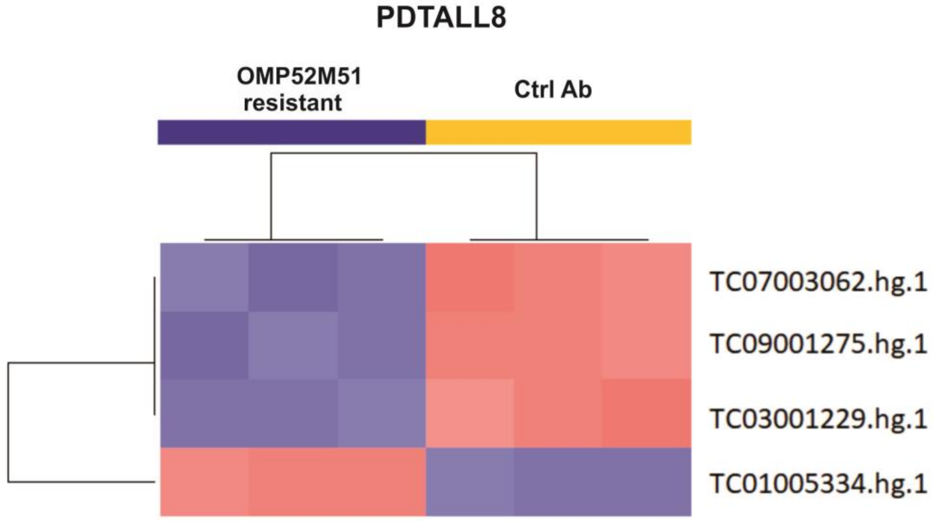
Suppl. Fig. S3: Survival of mice bearing PDTALL19 cells following repeated rounds of treatment with OMP52M51. Kaplan-Meier survival curves of leukemic mice after treatment with OMP52M51 (dotted lines) or Ctrl Ab (solid lines) of PDTALL19 xenografts (Round III *P*=0.0027; Round IV *P*=0.00313 log-rank test).

SUPPL. FIG. S4



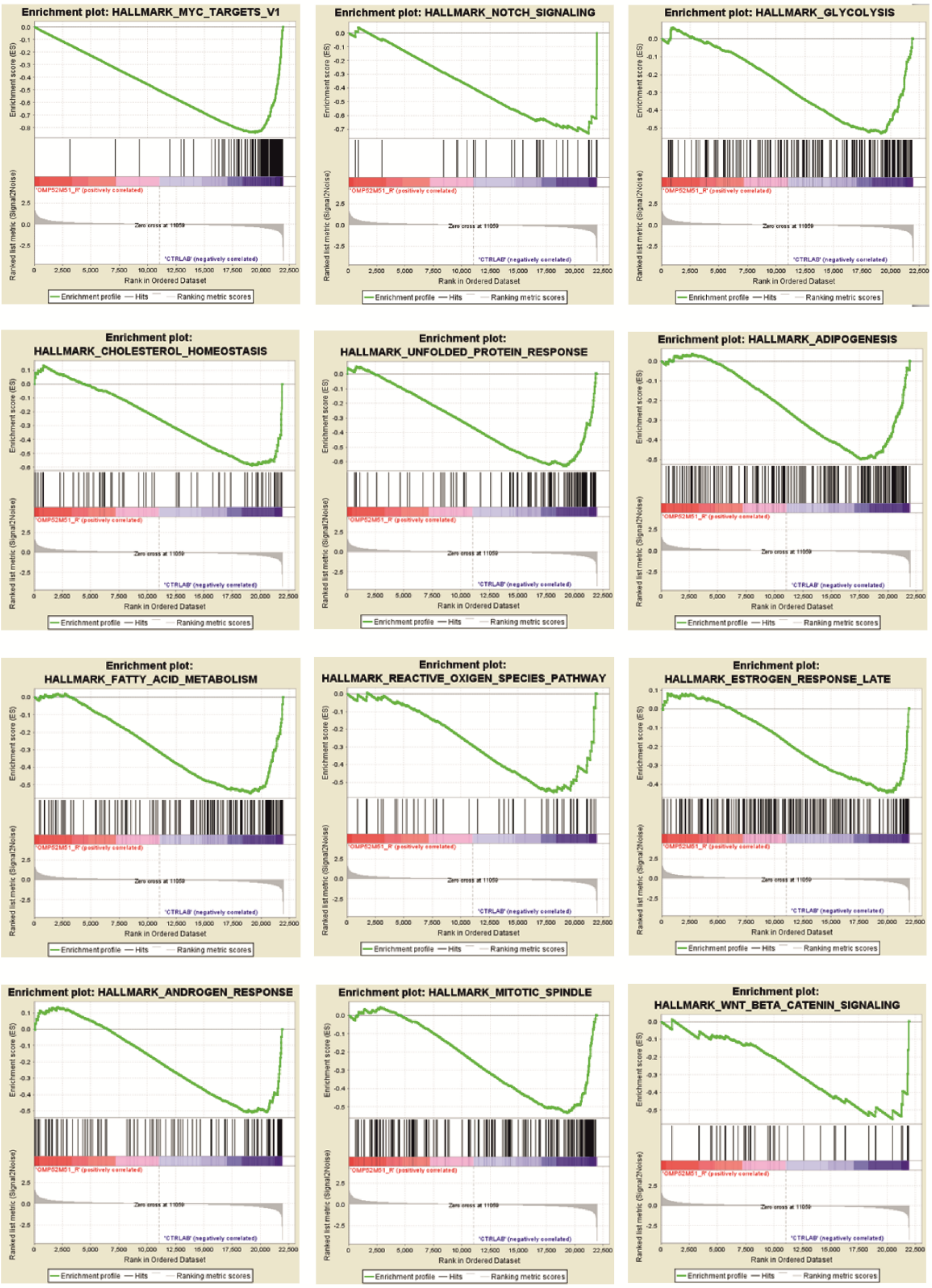
Suppl. Fig. S4: **Left panel:** WB analysis of PTEN protein expression in PDTALL8 (top), PDTALL11 (middle) and PDTALL19 (bottom) cells. MOLT-3 and TALL-1 cells, PTEN- and PTEN+ T-ALL cell lines, were used as negative and positive controls respectively. **Right panel:** WB analysis of pAkt (Ser473 and Thr308) protein expression in PDTALL8 (top), PDTALL11 (middle) and PDTALL19 (bottom) cells. MDA-MB-468 and BT549 cells were used as positive controls.

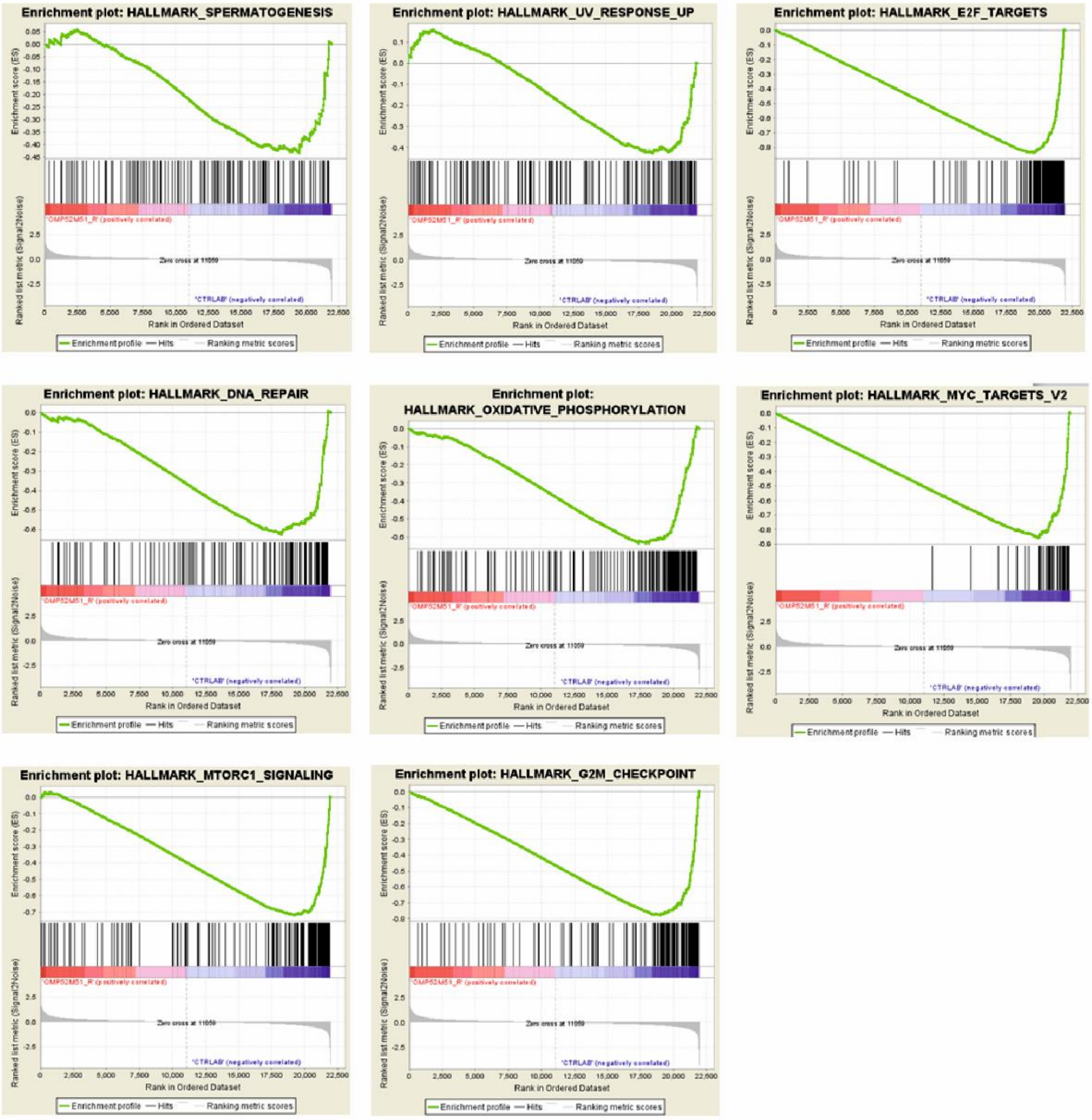
SUPPL. FIG. S5



Suppl. Fig. S5: **Transcriptome analysis of OMP52M51-resistant PDTALL8 cells. A.** Heat map of genes modulated comparing OMP52M51 resistant and control cells (3 samples/group). The ProbeSet IDs are reported instead of gene symbols, because their corresponding genes are not annotated. Red and blue indicate higher and lower expression levels, respectively. The columns represent individual samples.

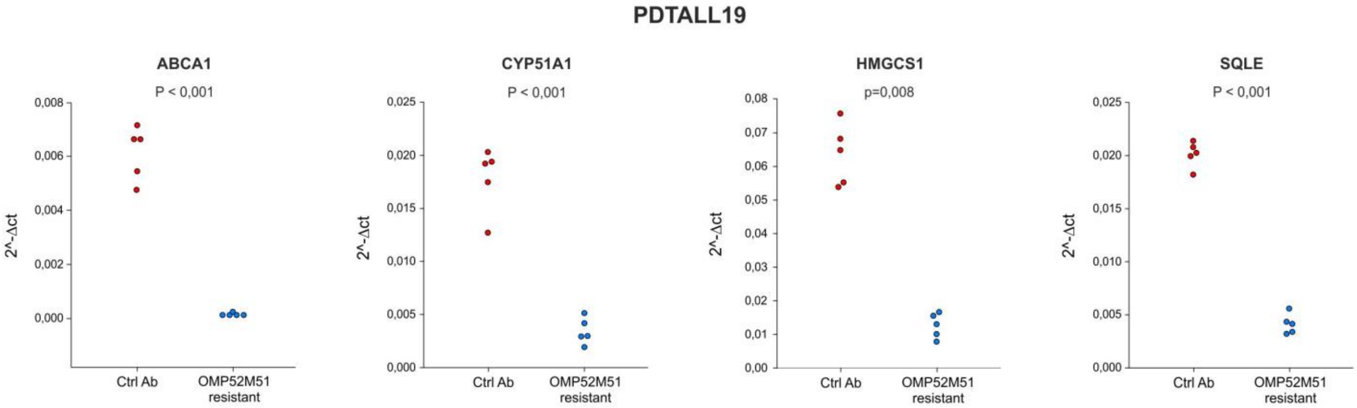
SUPPL. FIG. S6


Enrichment plot: HALLMARK_MYC_TARGETS_V1
Enrichment plot: HALLMARK_NOTCH_SIGNALING
Enrichment plot: HALLMARK_GLYCOLYSIS
Enrichment plot: HALLMARK_CHOLESTEROL_HOMEOSTASIS
Enrichment plot: HALLMARK_UNFOLDED_PROTEIN_RESPONSE
Enrichment plot: HALLMARK_ADIPOGENESIS
Enrichment plot: HALLMARK_FATTY_ACID_METABOLISM
Enrichment plot: HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY
Enrichment plot: HALLMARK_ESTROGEN_RESPONSE_LATE
Enrichment plot: HALLMARK_ANDROGEN_RESPONSE
Enrichment plot: HALLMARK_MITOTIC_SPINDLE
Enrichment plot: HALLMARK_WNT_BETA_CATENIN_SIGNALING
Enrichment score (ES)
Ranked list metric (Signal2Noise)
'OMP52M51_R' (positively correlated)
Zero cross at 11059
'CTRLAB' (negatively correlated)
Rank in Ordered Dataset
0
2,500
5,000
7,500
10,000
12,500
15,000
17,500
20,000
22,500
2.5
0.0
-2.5
Enrichment profile
Hits
Ranking metric scores



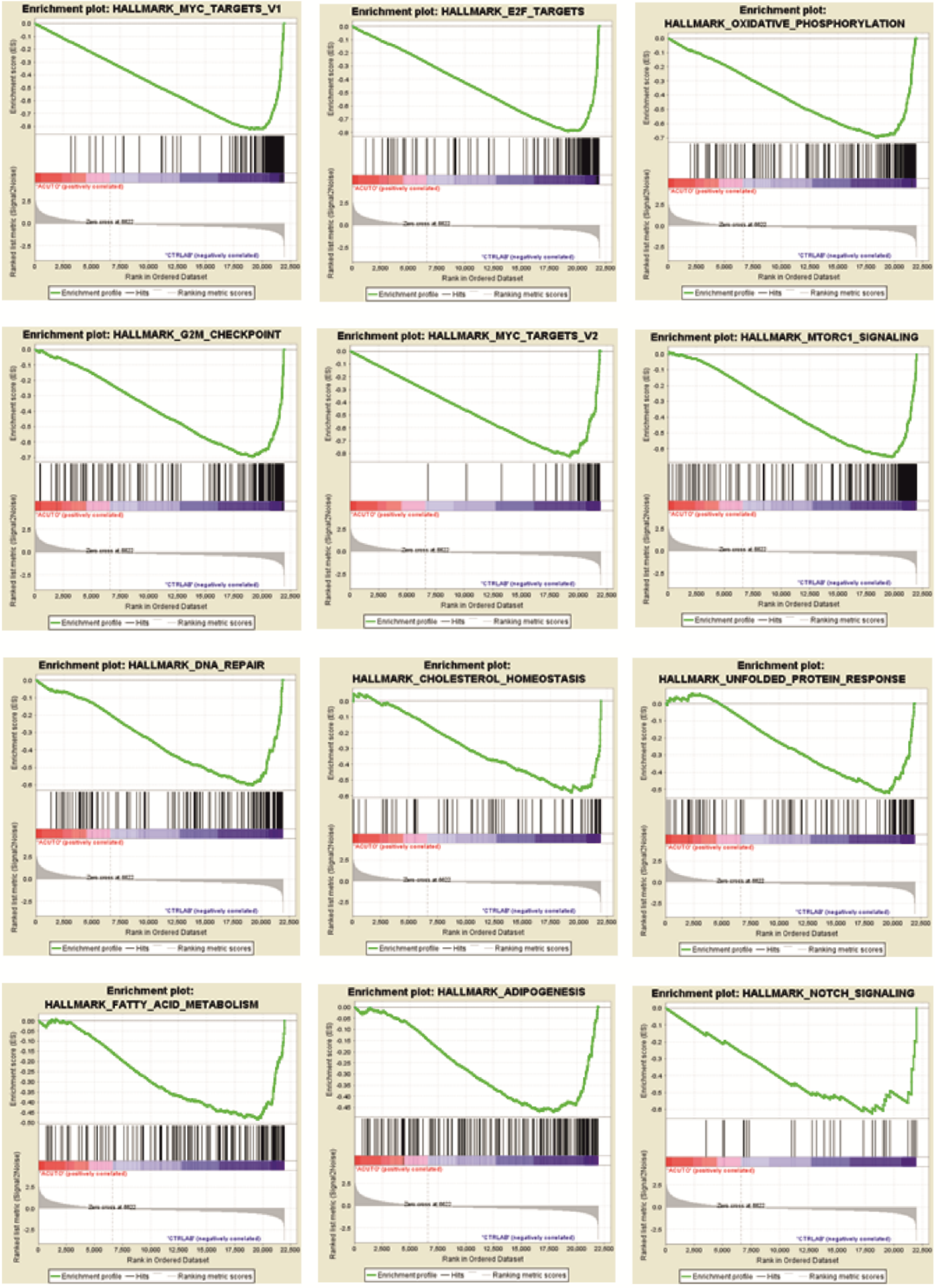
SUPPL. FIG. S6: Enrichment plots in OMP52M1 resistant *versus* control PDTALL19 cells by GSEA

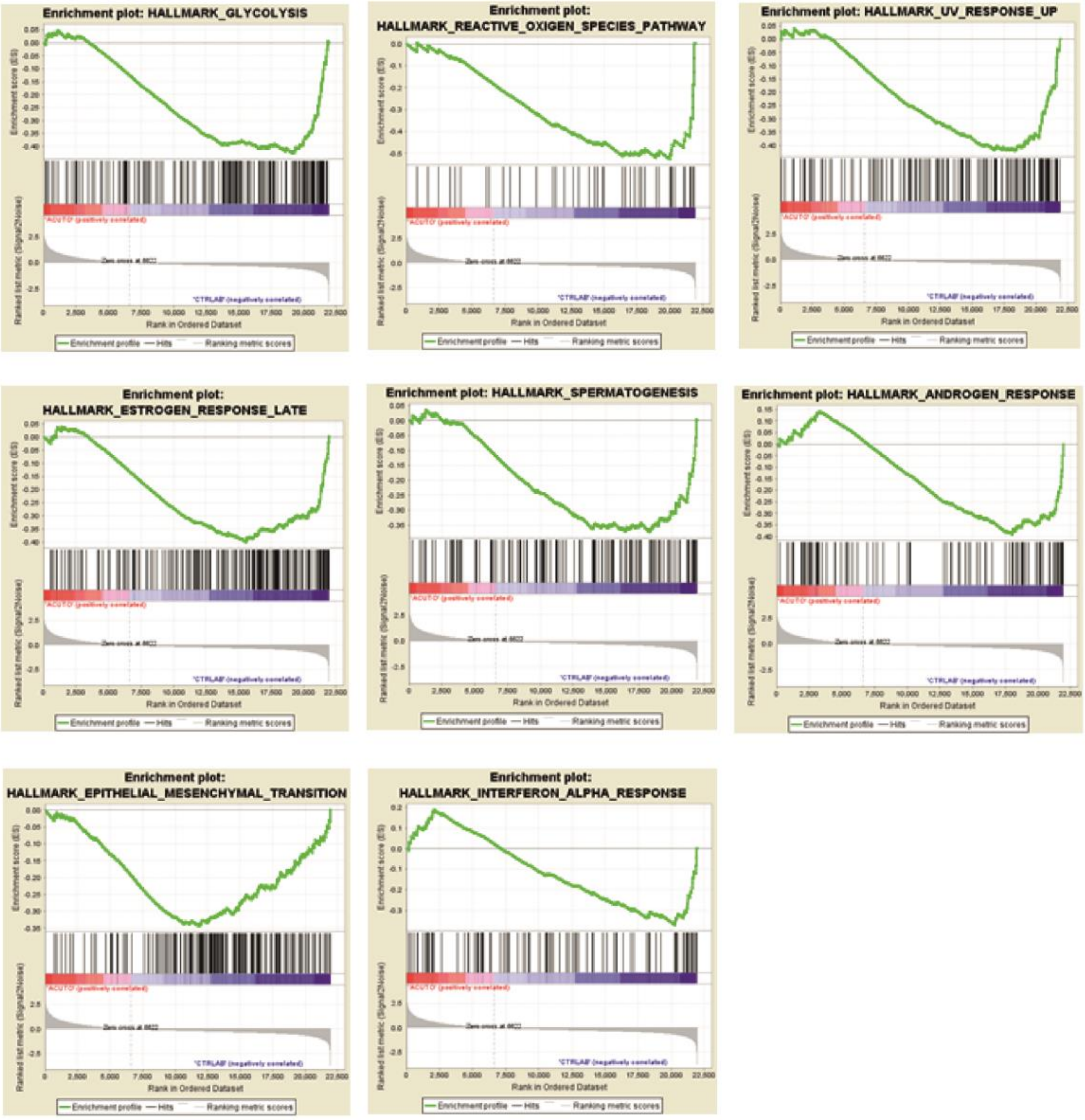
SUPPL. FIG. S7



Suppl. Fig. S7: Analysis of *ABCA1, CYP51A1, HMGCS1, SQLE* gene expression by qRT-PCR in PDTALL19 control and resistant cells (5 samples/group). Data are reported as $2^{-\Delta Ct}$ (ΔCt= Ct gene- Ct β2-microglobulin, the housekeeping gene). Statistically significant differences are indicated in the figure.

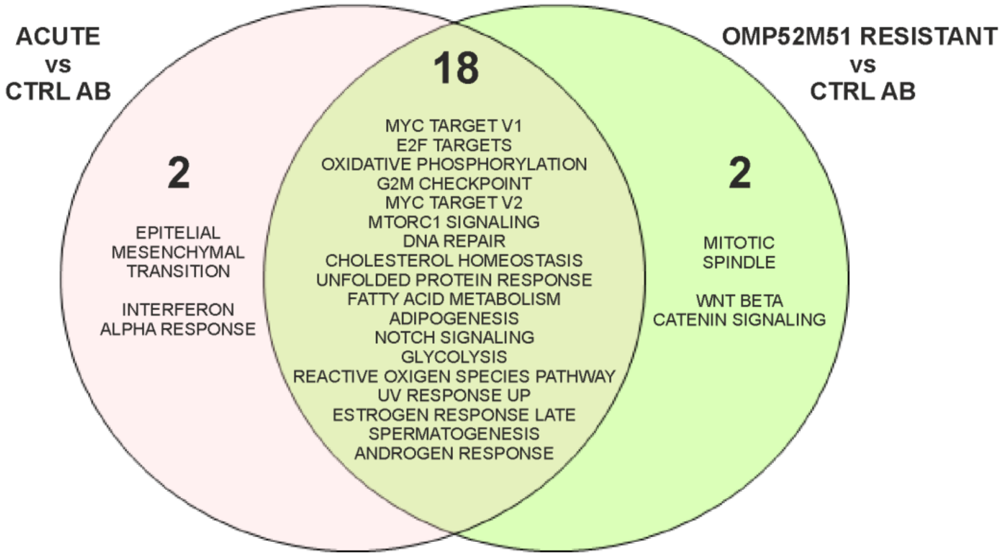
SUPPL. FIG. S8


Enrichment plot: HALLMARK_MYC_TARGETS_V1
Enrichment plot: HALLMARK_E2F_TARGETS
Enrichment plot: HALLMARK_OXIDATIVE_PHOSPHORYLATION
Enrichment plot: HALLMARK_G2M_CHECKPOINT
Enrichment plot: HALLMARK_MYC_TARGETS_V2
Enrichment plot: HALLMARK_MTORC1_SIGNALING
Enrichment plot: HALLMARK_DNA_REPAIR
Enrichment plot: HALLMARK_CHOLESTEROL_HOMEOSTASIS
Enrichment plot: HALLMARK_UNFOLDED_PROTEIN_RESPONSE
Enrichment plot: HALLMARK_FATTY_ACID_METABOLISM
Enrichment plot: HALLMARK_ADIPOGENESIS
Enrichment plot: HALLMARK_NOTCH_SIGNALING
Enrichment score (ES)
Ranked list metric (Signal2Noise)
'ACUTO' (positively correlated)
'CTRLAB' (negatively correlated)
Zero cross at 8822
Rank in Ordered Dataset
0
2,500
5,000
7,500
10,000
12,500
15,000
17,500
20,000
22,500
Enrichment profile
Hits
Ranking metric scores



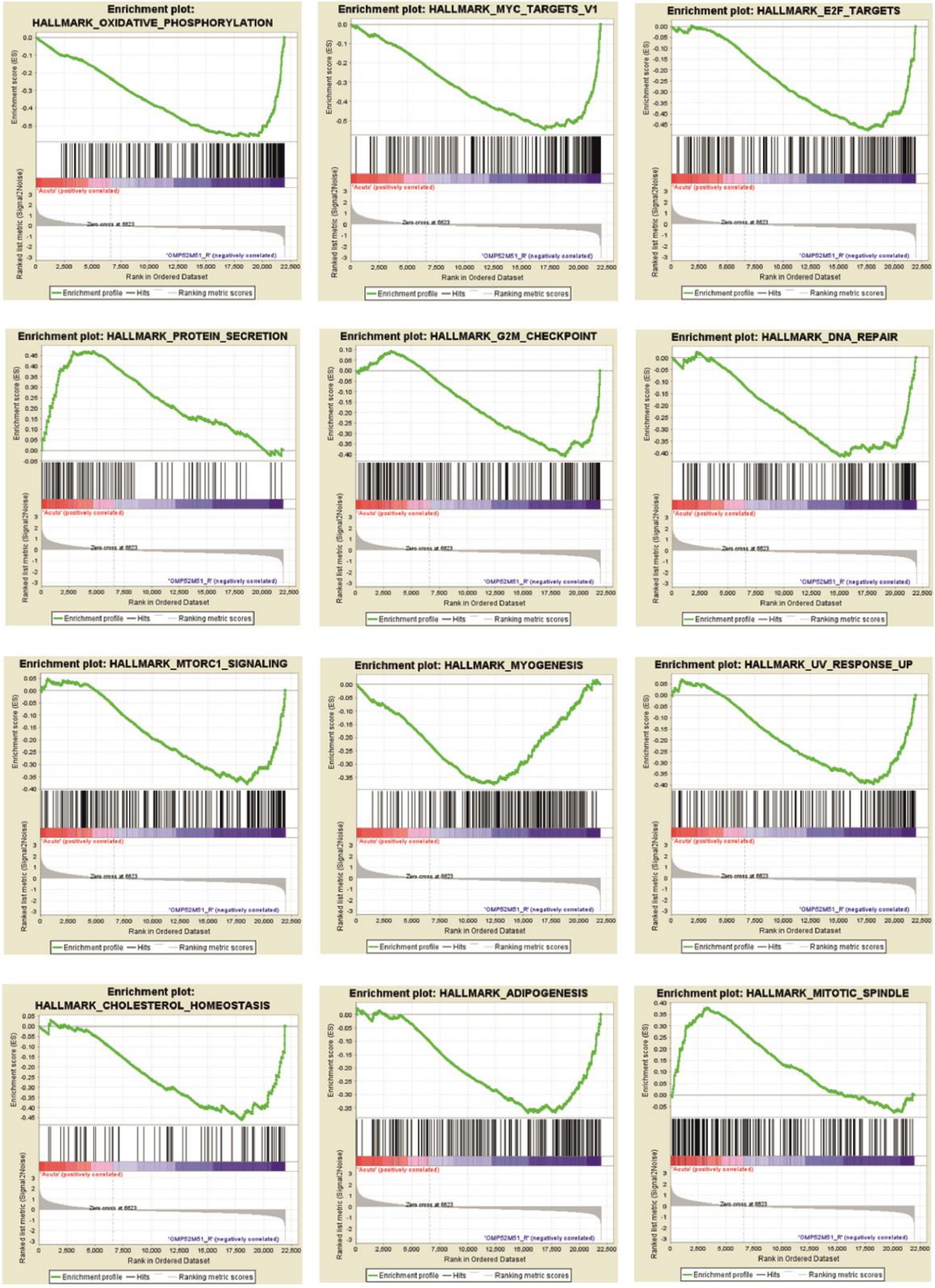
SUPPL. FIG. S8: Enrichment plots in PDTALL19 acute treatment *versus* Ctrl Ab by GSEA

SUPPL. FIG. S9



Suppl. Fig. S9: Venn diagram showing the intersection of pathways modulated in acute treatment *versus* control (pink circle) and in OMP52M51 resistant *versus* control PDTALL19 cells (green circle). Eighteen pathways identified by GSEA were shared, suggesting that they are a consequence of Notch signaling inhibition. Epitelial mesenchymal transition and interferon alpha response were pathways identified only in the comparison acute treatment *versus* control. On the contrary, mitotic spindle and WNT beta catenin signaling pathways emerged merely in OMP52M51 resistant *versus* control cells.

SUPPL. FIG. S10



Enrichment plot: HALLMARK_OXIDATIVE_PHOSPHORYLATION

Enrichment plot: HALLMARK_MYC_TARGETS_V1

Enrichment plot: HALLMARK_E2F_TARGETS

Enrichment plot: HALLMARK_PROTEIN_SECRETION

Enrichment plot: HALLMARK_G2M_CHECKPOINT

Enrichment plot: HALLMARK_DNA_REPAIR

Enrichment plot: HALLMARK_MTORC1_SIGNALING

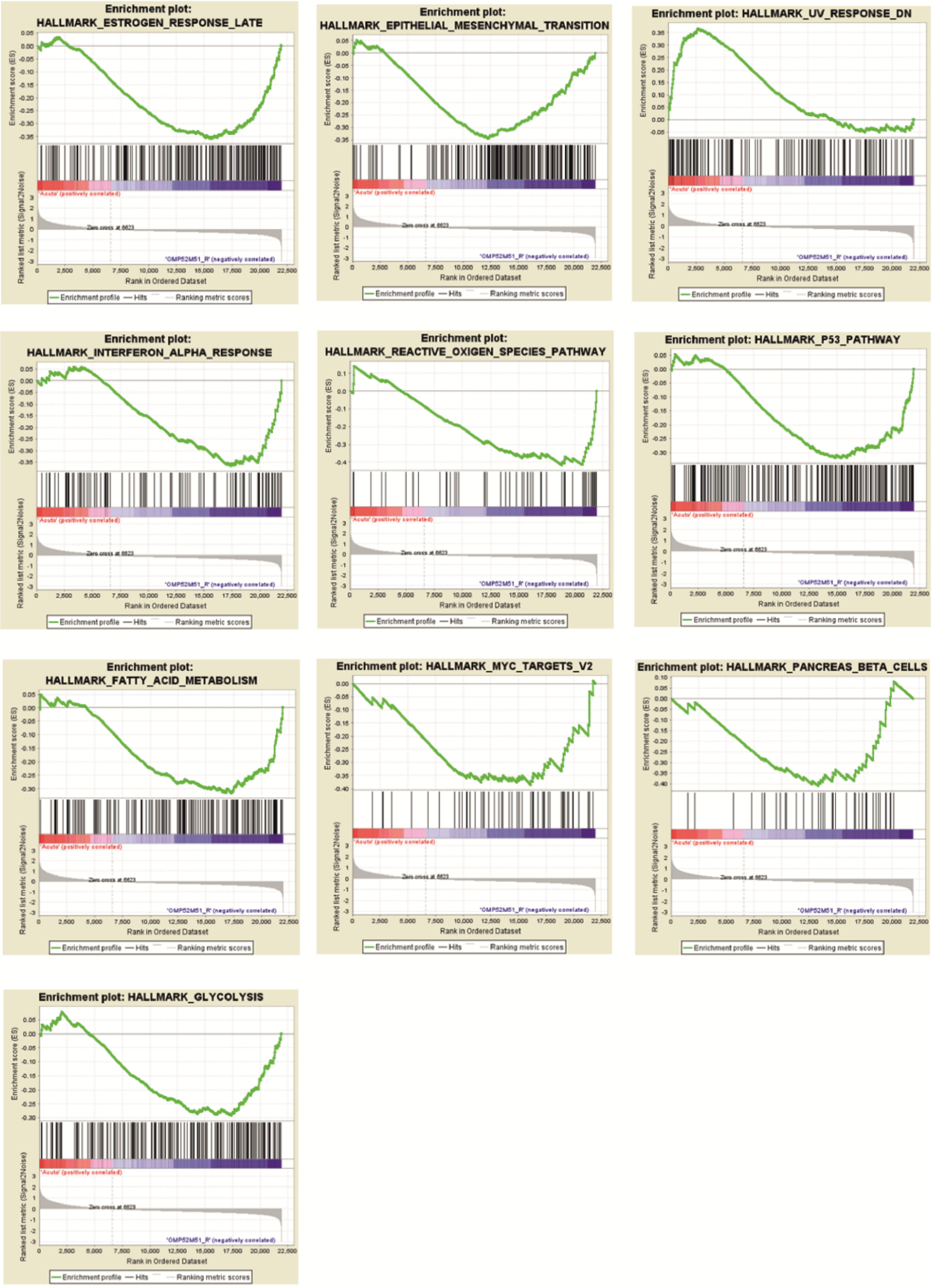
Enrichment plot: HALLMARK_MYOGENESIS

Enrichment plot: HALLMARK_UV_RESPONSE_UP

Enrichment plot: HALLMARK_CHOLESTEROL_HOMEOSTASIS

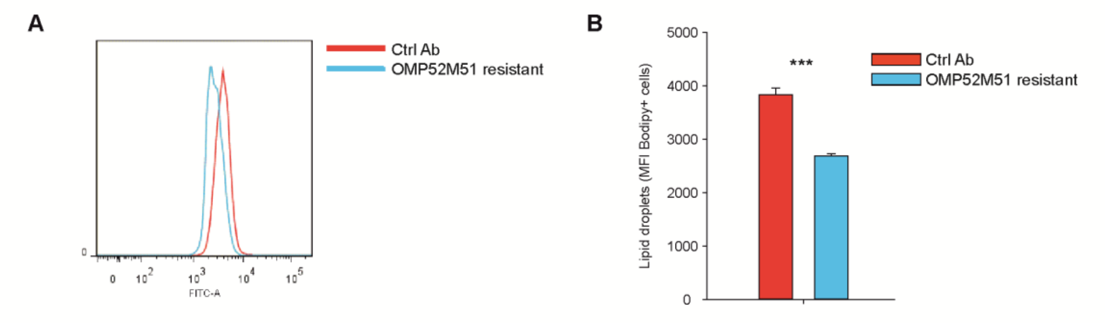
Enrichment plot: HALLMARK_ADIPOGENESIS

Enrichment plot: HALLMARK_MITOTIC_SPINDLE



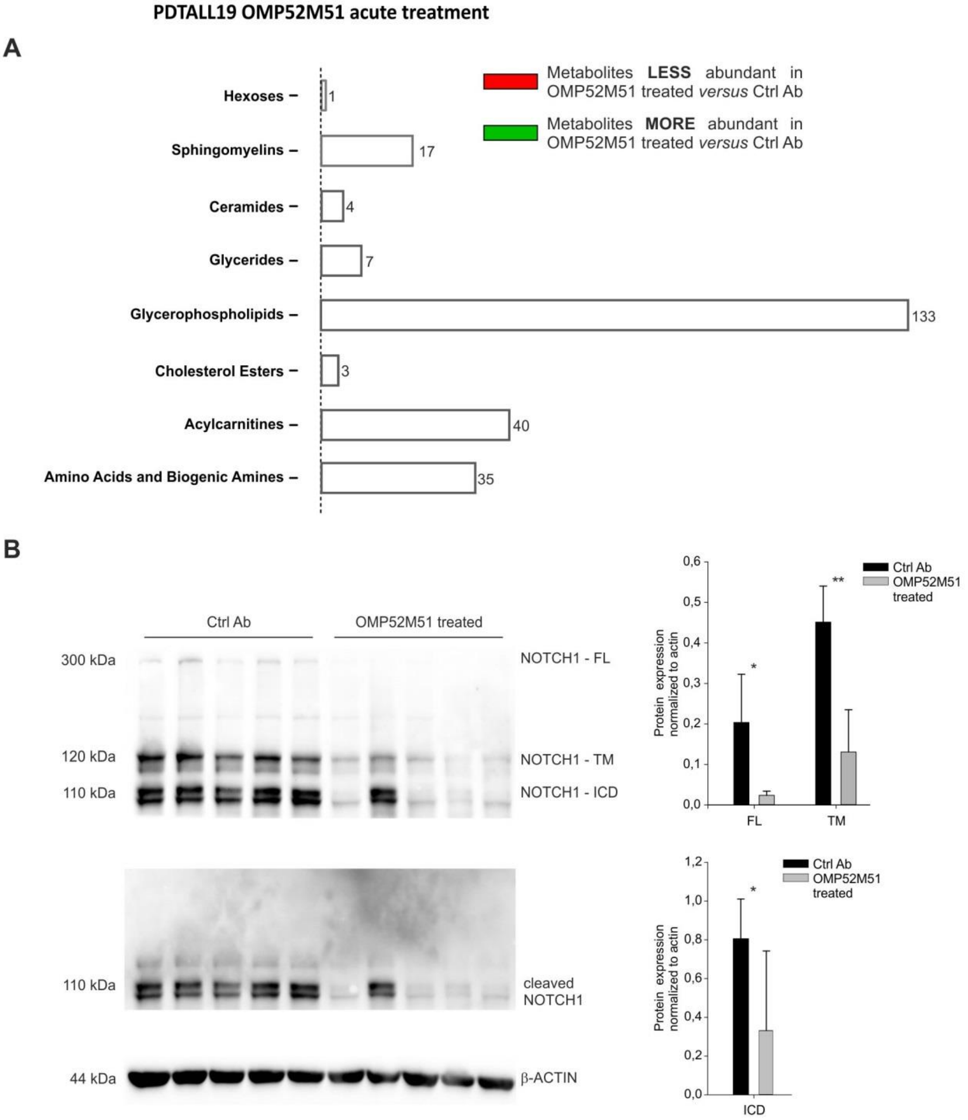
Suppl. Fig. S10: Pathways modulated in PDTALL19 cells from acute treated *versus* OMP52M1 resistant mice according to GSEA. Results indicate different intensity of gene modulation after acute or chronic treatment with OMP52M51 antibody. Most of the pathways (19 out of 22) were the same found down-regulated after acute treatment, suggesting that transcriptional effects of OMP52M51 are attenuated during resistance.

SUPPL. FIG. S11



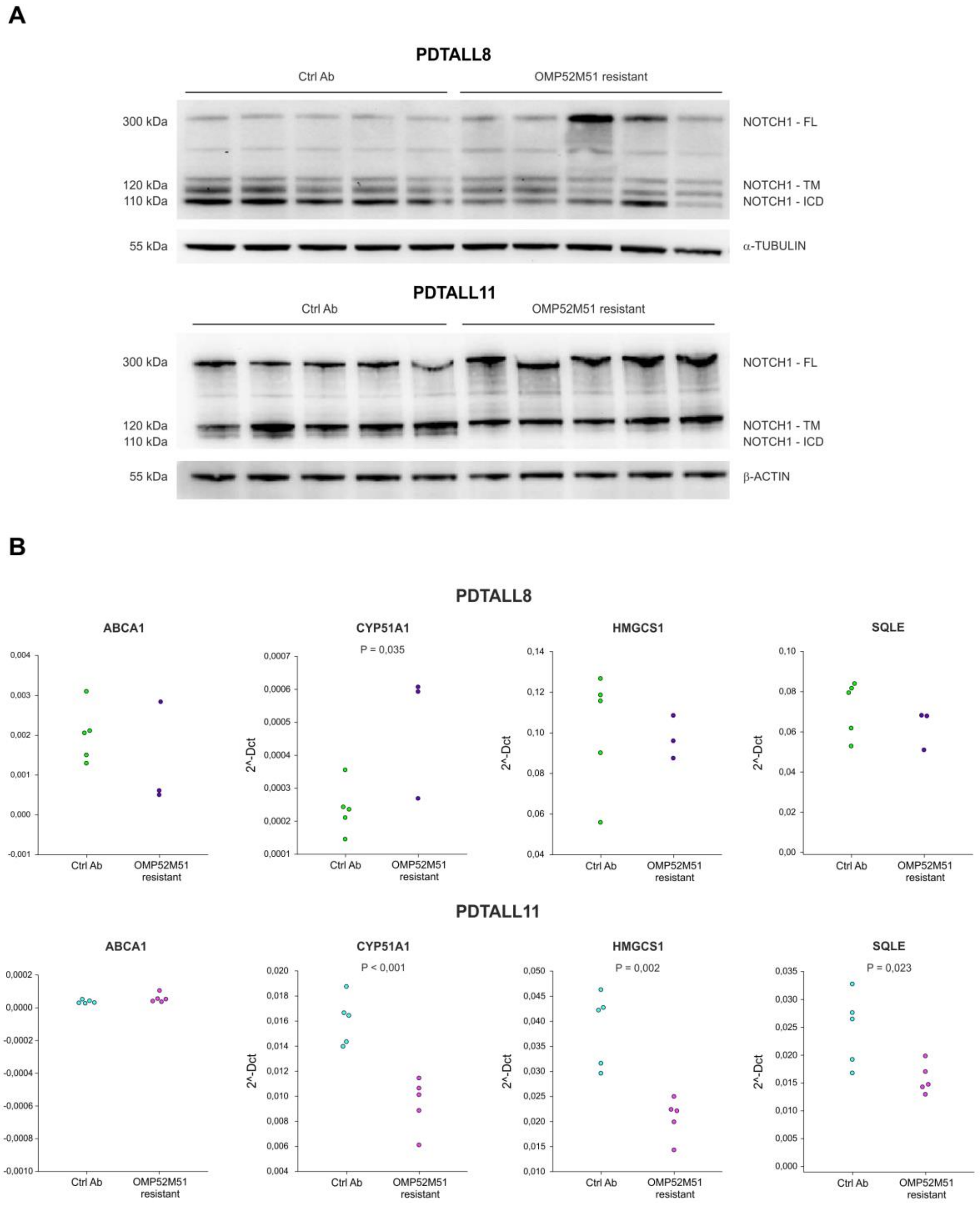
Suppl. Fig. S11: Evaluation of lipid droplets in PDTALL19 cells **A.** OMP52M51 resistant and control cells were stained with BODIPY 493/503 and analyzed by flow cytometry. One representative FACS histogram is shown. **B.** Histogram shows mean fluorescence intensity (MFI) ± SD of 5 samples/group (*** *P*<0.001).

SUPPL. FIG. S12



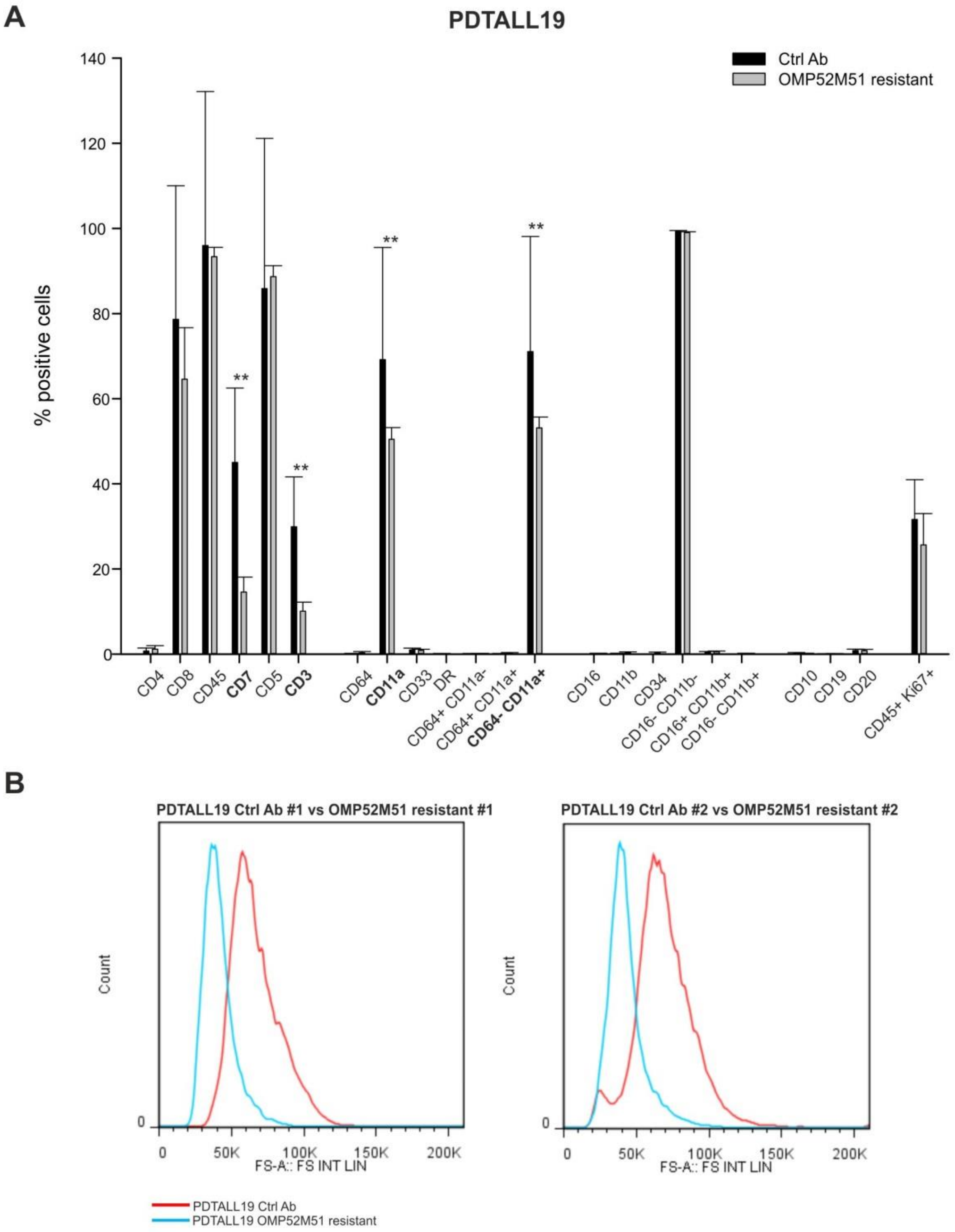
Suppl. Fig. S12: Lipidomic and Notch1 expression analysis of PDTALL19 cells following acute treatment with OMP52M51. A. The length of the columns is proportional to the abundance of analytes in the corresponding class. Numbers near columns represented the number of metabolites included in the analysis for each class. We found no metabolites significantly different between the two groups compared (adjusted p-value<0.05, 5 samples/group). **B. Left:** Notch1 full-length (FL), transmembrane (TM) and intra-cellular domain (ICD) expression levels were measured by Western-blot analysis on whole cell lysates. **Right:** quantification of Notch1 FL, TM and ICD levels normalized to β-actin expression (mean ± standard deviation) of control and resistant cells (5 samples/group. * *P*<0.05; ** *P*<0.001).

SUPPL. FIG. S13



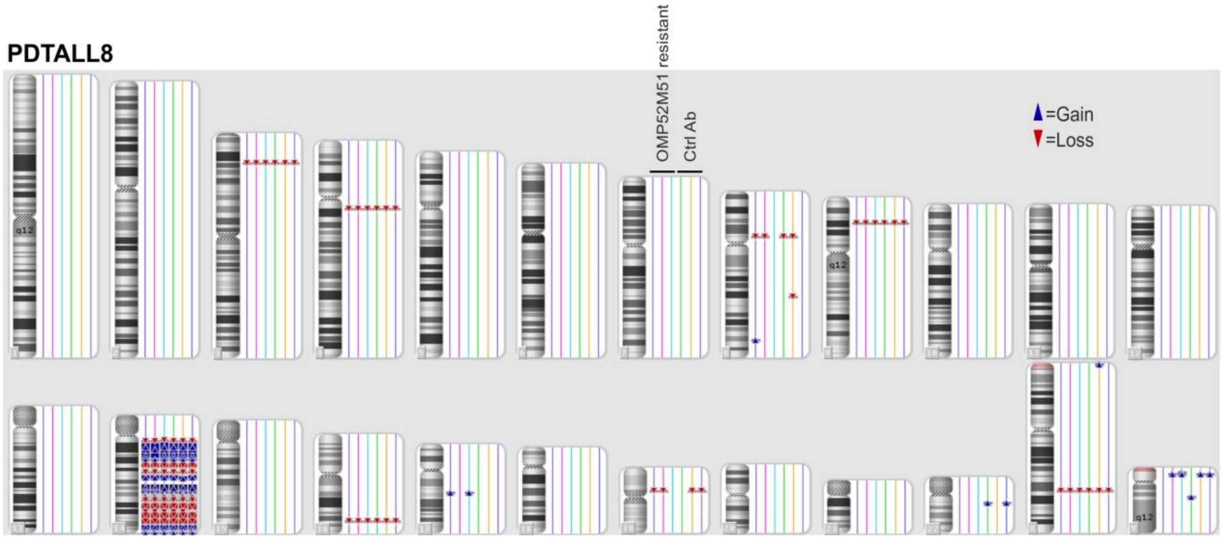
Suppl. Fig. S13: A. Western Blot analysis of Notch1 protein levels in PDTALL8 (top) and PDTALL11 (bottom) OMP52M51 resistant and control cells. **B.** Transcript levels of *ABCA1*, *CYP51A1*, *HMGCS1* and *SQLE* genes in PDTALL8 (top) and PDTALL11 (bottom) models analyzed by quantitative PCR (3-5 samples/group). Data are reported as $2^{-\Delta Ct}$ (ΔCt= Ct gene- Ct β2-microglobulin). Statistically significant differences are indicated.

SUPPL. FIG. S14



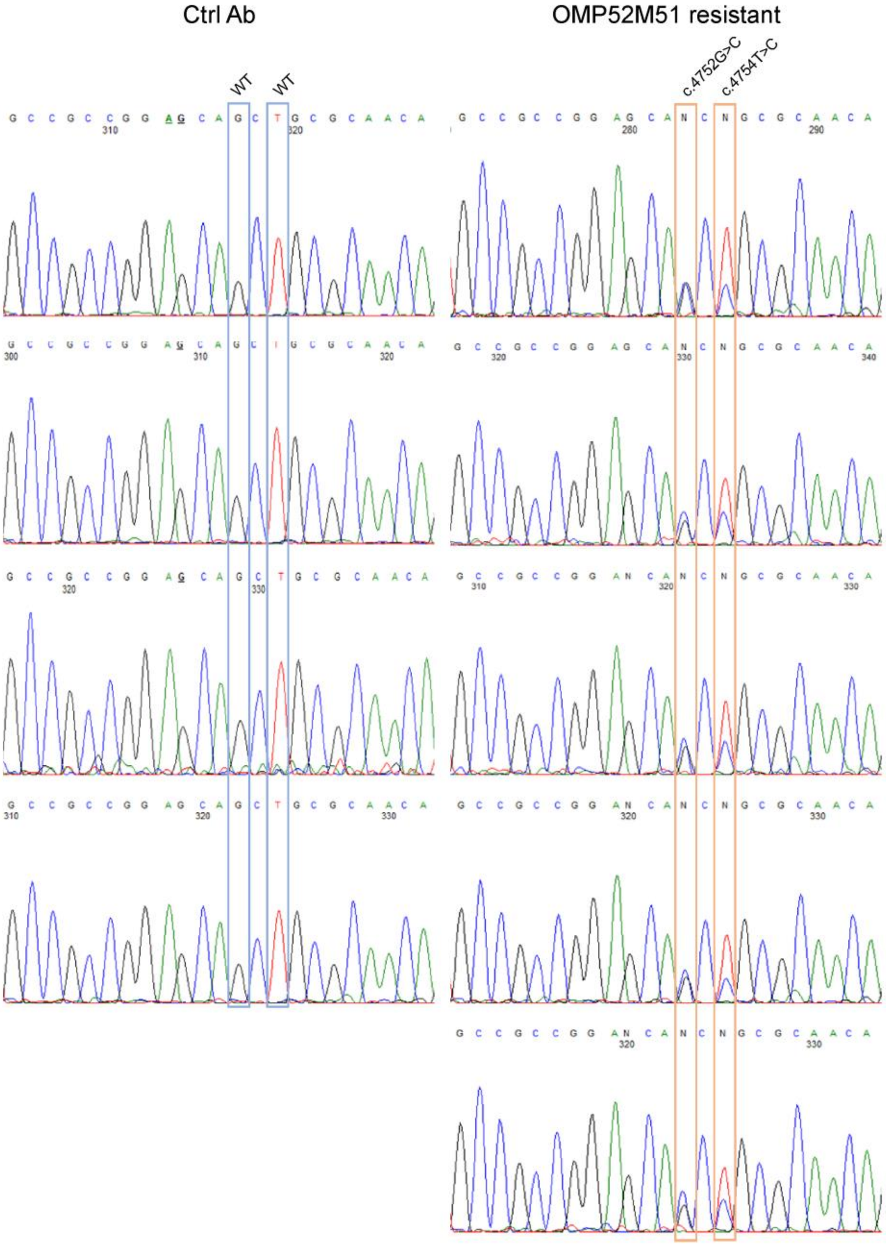
Suppl. Fig. S14: Immunophenotype and cell size of OMP52M51-resistant PDTALL19 cells. Following development of resistance to OMP52M51, T-ALL cells from the spleen of PDTALL19 mice were subjected to flow cytometric analysis for the markers shown in the figure (n=5 samples/group). ***P*<0.001. Cell size was determined by forward scatter analysis: two representative samples of each group are shown.

SUPPL. FIG. S15



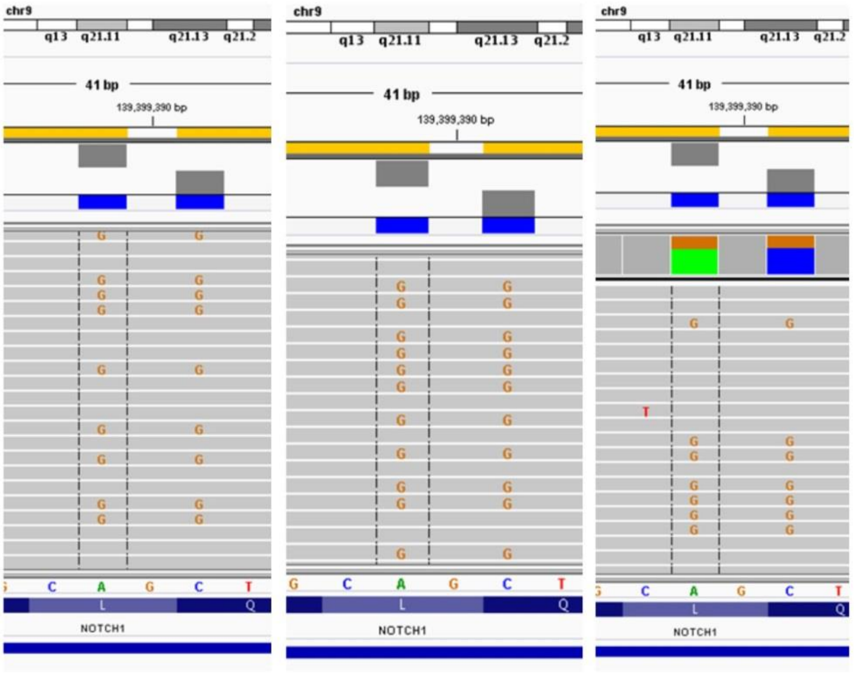
Suppl. Fig. S15: SNP arrays analysis performed on genomic DNA in PDTALL8 cells (3 samples/group). We found that some chromosomal alterations were common traits of the xenograft (shared by all samples), whereas others were specific of some subclones (and hence found in individual samples). Blue triangles represent the gain of specific regions (>2 copies), whereas the red ones are indicative of loss of genetic material (<2 copies).

SUPPL. FIG. S16



Suppl. Fig. S16: Sanger sequencing of *NOTCH1* exon 26 in 4 control (left panel) and 5 OMP52M51 resistant PDTALL8 samples (right panel). Positions of resistance-specific variants are highlighted by blue (control) and orange (resistant) boxes.

SUPPL. FIG. S17



PDTALL8
OMP52M51 resistant #5

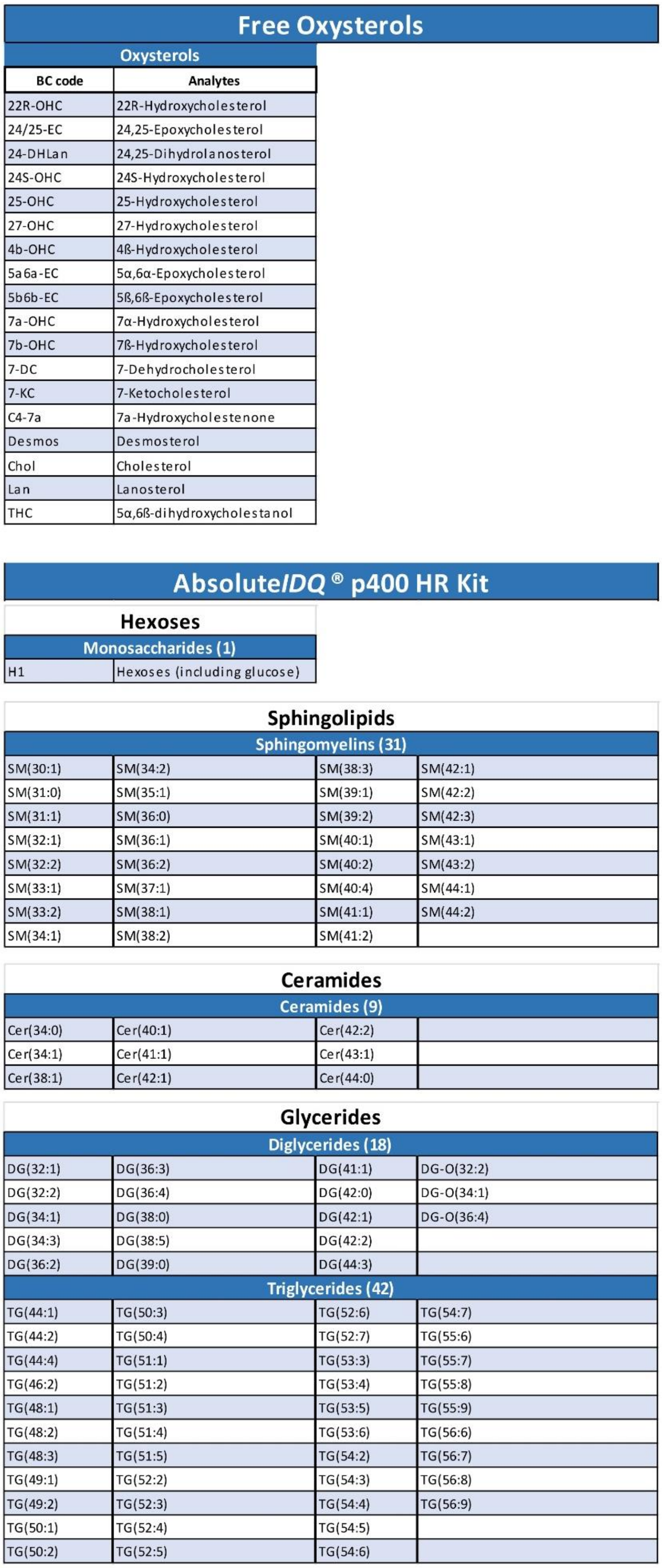
PDTALL8
OMP52M51 resistant #6

PDTALL8
OMP52M51 resistant #7

Suppl. Fig. S17: Target sequencing of Notch1 in PDTALL8 samples resistant to OMP52M51. IGV data showing that resistance-associated mutations are in cis: g.139399389:A>G; g.139399391:C>G.

SUPPLEMENTARY TABLES:

Supplementary Table I: List of metabolites included in the metabolomics analysis



Free Oxysterols

Oxysterols

BC code	Analytes
22R-OHC	22R-Hydroxycholesterol
24/25-EC	24,25-Epoxycholesterol
24-DHLan	24,25-Dihydrolanosterol
24S-OHC	24S-Hydroxycholesterol
25-OHC	25-Hydroxycholesterol
27-OHC	27-Hydroxycholesterol
4b-OHC	4ß-Hydroxycholesterol
5a6a-EC	5α,6α-Epoxycholesterol
5b6b-EC	5ß,6ß-Epoxycholesterol
7a-OHC	7α-Hydroxycholesterol
7b-OHC	7ß-Hydroxycholesterol
7-DC	7-Dehydrocholesterol
7-KC	7-Ketocholesterol
C4-7a	7a-Hydroxycholestenone
Desmos	Desmosterol
Chol	Cholesterol
Lan	Lanosterol
THC	5α,6ß-dihydroxycholestanol

Absolute*IDQ* ® p400 HR Kit

Hexoses

Monosaccharides (1)

H1	Hexoses (including glucose)

Sphingolipids

Sphingomyelins (31)

SM(30:1)	SM(34:2)	SM(38:3)	SM(42:1)
SM(31:0)	SM(35:1)	SM(39:1)	SM(42:2)
SM(31:1)	SM(36:0)	SM(39:2)	SM(42:3)
SM(32:1)	SM(36:1)	SM(40:1)	SM(43:1)
SM(32:2)	SM(36:2)	SM(40:2)	SM(43:2)
SM(33:1)	SM(37:1)	SM(40:4)	SM(44:1)
SM(33:2)	SM(38:1)	SM(41:1)	SM(44:2)
SM(34:1)	SM(38:2)	SM(41:2)	

Ceramides

Ceramides (9)

Cer(34:0)	Cer(40:1)	Cer(42:2)	
Cer(34:1)	Cer(41:1)	Cer(43:1)	
Cer(38:1)	Cer(42:1)	Cer(44:0)	

Glycerides

Diglycerides (18)

DG(32:1)	DG(36:3)	DG(41:1)	DG-O(32:2)
DG(32:2)	DG(36:4)	DG(42:0)	DG-O(34:1)
DG(34:1)	DG(38:0)	DG(42:1)	DG-O(36:4)
DG(34:3)	DG(38:5)	DG(42:2)	
DG(36:2)	DG(39:0)	DG(44:3)	

Triglycerides (42)

TG(44:1)	TG(50:3)	TG(52:6)	TG(54:7)
TG(44:2)	TG(50:4)	TG(52:7)	TG(55:6)
TG(44:4)	TG(51:1)	TG(53:3)	TG(55:7)
TG(46:2)	TG(51:2)	TG(53:4)	TG(55:8)
TG(48:1)	TG(51:3)	TG(53:5)	TG(55:9)
TG(48:2)	TG(51:4)	TG(53:6)	TG(56:6)
TG(48:3)	TG(51:5)	TG(54:2)	TG(56:7)
TG(49:1)	TG(52:2)	TG(54:3)	TG(56:8)
TG(49:2)	TG(52:3)	TG(54:4)	TG(56:9)
TG(50:1)	TG(52:4)	TG(54:5)	
TG(50:2)	TG(52:5)	TG(54:6)	

Glycerophospholipids

Lysophosphatidylcholines (24)

LPC(12:0)	LPC(17:1)	LPC(20:2)	LPC(24:1)
LPC(14:0)	LPC(18:0)	LPC(20:3)	LPC-O(16:1)
LPC(15:0)	LPC(18:1)	LPC(20:4)	LPC-O(17:1)
LPC(16:0)	LPC(18:2)	LPC(22:5)	LPC-O(18:0)
LPC(16:1)	LPC(20:0)	LPC(22:6)	LPC-O(18:1)
LPC(17:0)	LPC(20:1)	LPC(24:0)	LPC-O(18:2)

Phosphatidylcholines (172)

PC(24:0)	PC(36:1)	PC(41:5)	PC-O(34:0)
PC(25:0)	PC(36:2)	PC(41:8)	PC-O(34:1)
PC(26:0)	PC(36:3)	PC(42:0)	PC-O(34:2)
PC(27:0)	PC(36:4)	PC(42:1)	PC-O(34:3)
PC(27:1)	PC(36:5)	PC(42:2)	PC-O(34:4)
PC(28:1)	PC(36:6)	PC(42:3)	PC-O(35:3)
PC(29:0)	PC(37:0)	PC(42:4)	PC-O(35:4)
PC(29:1)	PC(37:1)	PC(42:5)	PC-O(36:0)
PC(29:2)	PC(37:2)	PC(42:6)	PC-O(36:1)
PC(30:0)	PC(37:3)	PC(42:7)	PC-O(36:2)
PC(30:1)	PC(37:4)	PC(42:10)	PC-O(36:3)
PC(30:2)	PC(37:5)	PC(43:2)	PC-O(36:4)
PC(30:3)	PC(37:6)	PC(43:6)	PC-O(36:5)
PC(31:0)	PC(37:7)	PC(44:1)	PC-O(36:6)
PC(31:1)	PC(38:0)	PC(44:3)	PC-O(37:6)
PC(31:2)	PC(38:1)	PC(44:5)	PC-O(37:7)
PC(31:3)	PC(38:2)	PC(44:6)	PC-O(38:0)
PC(32:0)	PC(38:3)	PC(44:7)	PC-O(38:1)
PC(32:1)	PC(38:4)	PC(44:10)	PC-O(38:2)
PC(32:2)	PC(38:5)	PC(44:12)	PC-O(38:3)
PC(32:3)	PC(38:6)	PC(46:1)	PC-O(38:4)
PC(32:4)	PC(38:7)	PC(46:2)	PC-O(38:5)
PC(32:5)	PC(39:0)	PC-O(26:0)	PC-O(38:6)
PC(32:6)	PC(39:1)	PC-O(26:1)	PC-O(40:0)
PC(33:0)	PC(39:2)	PC-O(28:0)	PC-O(40:1)
PC(33:1)	PC(39:3)	PC-O(28:1)	PC-O(40:2)
PC(33:2)	PC(39:4)	PC-O(29:0)	PC-O(40:3)
PC(33:3)	PC(39:5)	PC-O(30:0)	PC-O(40:4)
PC(33:4)	PC(39:6)	PC-O(30:1)	PC-O(40:5)
PC(33:5)	PC(39:7)	PC-O(30:2)	PC-O(40:6)
PC(34:0)	PC(40:1)	PC-O(31:0)	PC-O(40:7)
PC(34:1)	PC(40:2)	PC-O(31:1)	PC-O(40:8)
PC(34:2)	PC(40:3)	PC-O(31:3)	PC-O(42:0)
PC(34:3)	PC(40:4)	PC-O(32:0)	PC-O(42:1)
PC(34:4)	PC(40:5)	PC-O(32:1)	PC-O(42:2)
PC(34:5)	PC(40:6)	PC-O(32:2)	PC-O(42:3)
PC(35:0)	PC(40:7)	PC-O(32:3)	PC-O(42:4)
PC(35:1)	PC(40:8)	PC-O(33:0)	PC-O(42:5)
PC(35:2)	PC(40:9)	PC-O(33:1)	PC-O(42:6)
PC(35:3)	PC(41:1)	PC-O(33:2)	PC-O(44:3)
PC(35:4)	PC(41:2)	PC-O(33:3)	PC-O(44:4)
PC(35:5)	PC(41:3)	PC-O(33:4)	PC-O(44:5)
PC(36:0)	PC(41:4)	PC-O(33:6)	PC-O(44:6)

Cholesteryl Esters

Cholesteryl Esters (14)

CE(16:0)	CE(17:2)	CE(19:2)	CE(22:5)
CE(16:1)	CE(18:1)	CE(19:3)	CE(22:6)
CE(17:0)	CE(18:2)	CE(20:4)	
CE(17:1)	CE(18:3)	CE(20:5)	

Acylcarnitines

Acylcarnitines (55)

AC(0:0)	Carnitine	AC(10:2)	Decadienoylcarnitine
AC(2:0)	Acetylcarnitine	AC(10:3)	Decatrienoylcarnitine
AC(3:0)	Propionoylcarnitine	AC(11:0)	Dimethylnonanoylcarnitine
AC(3:0-DC)	Malonylcarnitine	AC(12:0)	Dodecanoylcarnitine
AC(3:0-OH)	Hydroxypropionylcarnitine	AC(12:0-DC)	Dodecanedioylcarnitine
AC(3:1)	Propenoylcarnitine	AC(12:1)	Dodecenoylcarnitine
AC(4:0)	Butyrylcarnitine	AC(13:0)	Tridecanoylcarnitine
AC(4:0-DC)	Methylmalonylcarnitine	AC(14:0)	Tetradecanoylcarnitine
AC(4:0-OH)	Hydroxybutyrylcarnitine	AC(14:0-OH)	Hydroxymyristoylcarnitine
AC(4:1)	Butenylcarnitine	AC(14:1)	Tetradecenoylcarnitine
AC(4:1-DC)	Fumarylcarnitine	AC(14:1-DC)	Carboxytridecenoylcarnitine
AC(5:0)	Valerylcarnitine	AC(14:1-OH)	Hydroxytetradecenoylcarnitine
AC(5:0-DC)	Glutarylcarnitine	AC(14:2)	Tetradecadienoylcarnitine
AC(5:0-OH)	Hydroxyvalerylcarnitine	AC(14:2-OH)	Hydroxytetradecadienoylcarnitine
AC(5:1)	Tiglylcarnitine	AC(15:0)	Pentadecanoylcarnitine
AC(5:1-DC)	Glutaconylcarnitine	AC(16:0)	Hexadecanoylcarnitine
AC(6:0)	Hexanoylcarnitine	AC(16:0-OH)	Hydroxyhexadecanoylcarnitine
AC(6:0-DC)	Adipoylcarnitine	AC(16:1)	Hexadecenoylcarnitine
AC(6:0-OH)	Hydroxyhexanoylcarnitine	AC(16:1-OH)	Hydroxyhexadecenoylcarnitine
AC(6:1)	Hexenoylcarnitine	AC(16:2)	Hexadecadienoylcarnitine
AC(7:0)	Heptanoylcarnitine	AC(16:2-OH)	Hydroxyhexadecadienoylcarnitine
AC(7:0-DC)	Pimeloylcarnitine	AC(17:0)	Heptadecanoylcarnitine
AC(8:0)	Octanoylcarnitine	AC(18:0)	Octadecanoylcarnitine
AC(8:1)	Octenoylcarnitine	AC(18:1)	Octadecenoylcarnitine
AC(8:1-OH)	Hydroxyoctenoylcarnitine	AC(18:1-OH)	Hydroxyoctadecenoylcarnitine
AC(9:0)	Nonaylcarnitine	AC(18:2)	Octadecadienylcarnitine
AC(10:0)	Decanoylcarnitine	AC(19:0)	Nonadecanoylcarnitine
AC(10:1)	Decenoylcarnitine		

Amino Acids and Biogenic Amines

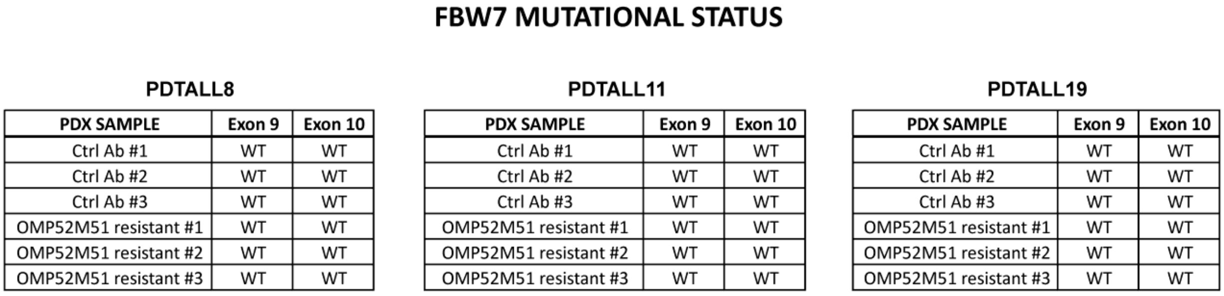
Amino Acids (21)

Ala	Alanine	Lys	Lysine
Arg	Arginine	Met	Methionine
Asn	Asparagine	Orn	Ornithine
Asp	Aspartate	Phe	Phenylalanine
Cit	Citrulline	Pro	Proline
Glu	Glutamate	Ser	Serine
Gln	Glutamine	Thr	Threonine
Gly	Glycine	Trp	Tryptophan
His	Histidine	Tyr	Tyrosine
Ile	Isoleucine*	Val	Valine
xLeu	Leucine + Isoleucine	* analyzed by additional LC-MS injection in parallel reaction monitoring (PRM) mode	

Biogenic Amines (21)

AcOrn	Acetylornithine	Nitro-Tyr	Nitrotyrosine
ADMA	Asymmetric dimethylarginine	PEA	Phenylethylamine
alpha-AAA	alpha-Aminoadipic acid	Putrescine	Putrescine
Carnosine	Carnosine	Sarcosine	Sarcosine
c4-OH-Pro	*cis*-4-Hydroxyproline	SDMA	Symmetric dimethylarginine
Creatinine	Creatinine	Serotonin	Serotonin
DOPA	Dihydroxyphenylalanine	Spermidine	Spermidine
Dopamine	Dopamine	Spermine	Spermine
Histamine	Histamine	Taurine	Taurine
Kynurenine	Kynurenine	t4-OH-Pro	*trans*-4-Hydroxyproline
Met-SO	Methionine sulfoxide		

Supplementary Table II: Analysis of FBW7 mutations in PDTALL8 (left), PDTALL11 (middle) and PDTALL19 (right) cells



FBW7 MUTATIONAL STATUS

PDTALL8

PDX SAMPLE	Exon 9	Exon 10
Ctrl Ab #1	WT	WT
Ctrl Ab #2	WT	WT
Ctrl Ab #3	WT	WT
OMP52M51 resistant #1	WT	WT
OMP52M51 resistant #2	WT	WT
OMP52M51 resistant #3	WT	WT

PDTALL11

PDX SAMPLE	Exon 9	Exon 10
Ctrl Ab #1	WT	WT
Ctrl Ab #2	WT	WT
Ctrl Ab #3	WT	WT
OMP52M51 resistant #1	WT	WT
OMP52M51 resistant #2	WT	WT
OMP52M51 resistant #3	WT	WT

PDTALL19

PDX SAMPLE	Exon 9	Exon 10
Ctrl Ab #1	WT	WT
Ctrl Ab #2	WT	WT
Ctrl Ab #3	WT	WT
OMP52M51 resistant #1	WT	WT
OMP52M51 resistant #2	WT	WT
OMP52M51 resistant #3	WT	WT

Supplementary Table III: list of 327 genes up-regulated in PDTALL19 OMP52M51 resistant compared to control Ab-treated cells.

ProbeSet ID	**Gene Symbol**
TC09001205.hg.1	ABHD17B
TC17000089.hg.1	ACAP1
TC16000493.hg.1	ADGRG1
TC0X000708.hg.1	AFF2
TC15001482.hg.1	ALDH1A2
TC02000547.hg.1	ANKRD36BP2
TC10002092.hg.1	ARID5B
TC03000171.hg.1	ARPP21
TC11000009.hg.1	ATHL1
TC01001685.hg.1	BTG2
TC01003759.hg.1	C1orf186
TC09001655.hg.1	C9orf78
TC06000136.hg.1	CASC15
TC01001022.hg.1	CD2
TC04000145.hg.1	CD38
TC01003405.hg.1	CD84
TC17000618.hg.1	CDK5RAP3
TC11002439.hg.1	ETS1
TC12003216.hg.1	GOLGA3
TC04000706.hg.1	HHIP
TC02002740.hg.1	IKZF2
TC01002977.hg.1	KCNA3
TC03002054.hg.1	LAMP3
TC01001642.hg.1	LINC01221
TC01003673.hg.1	LINC01222
TC12001640.hg.1	LOC100506844
TC04002272.hg.1	LOC100996286
TC15000954.hg.1	LRRC28

TC06003591.hg.1	LTB
TC01004964.hg.1	MDM4
TC03000846.hg.1	MME
TC07001348.hg.1	MYO1G
TC01005844.hg.1	PBXIP1
TC18000428.hg.1	PCAT18
TC04000663.hg.1	PCDH10
TC07002397.hg.1	PMS2P2
TC07000460.hg.1	PMS2P5
TC16000260.hg.1	PRKCB
TC13000147.hg.1	RGCC
TC04000242.hg.1	RHOH
TC09000338.hg.1	RORB
TC21000946.hg.1	RUNX1-IT1
TC02002491.hg.1	SCN3A
TC13000500.hg.1	SHISA2
TC15001192.hg.1	SLC12A6
TC07002413.hg.1	STAG3L1
TC07003024.hg.1	STAG3L2
TC07003013.hg.1	STAG3L3
TC03001849.hg.1	TFDP2
TC0Y000354.hg.1	TXLNGY
TC09000725.hg.1	USP20
TC17001552.hg.1	VAT1
TC02003138.hg.1	YPEL5
TC06001152.hg.1	IGF2R
TC16001704.hg.1	ACSF3
TC07002489.hg.1	STAG3L5P-PVRIG2P-PILRB
TC19000729.hg.1	CD37
TC03000106.hg.1	LOC339862
TC07003311.hg.1	DTX2P1-UPK3BP1-PMS2P11
TC0Y000184.hg.1	BCORP1
TC04001607.hg.1	HHIP-AS1
TC18000426.hg.1	KCTD1
TC16000480.hg.1	HERPUD1
TC01003479.hg.1	CD247
TC01002374.hg.1	RSRP1
TC03002064.hg.1	ABCC5
TC07000266.hg.1	STK17A
TC02005014.hg.1	UBE2F
TC13000867.hg.1	LIG4
TC01000909.hg.1	S1PR1
TC07001945.hg.1	TRBV7-6
TC01001724.hg.1	RASSF5
TC04001647.hg.1	FBXW7
TC11000734.hg.1	NADSYN1
TC10001676.hg.1	ABLIM1

TC02001030.hg.1	ITGA6
TC15000410.hg.1	TMOD2
TC12002225.hg.1	LOC642846
TC08000452.hg.1	PREX2
TC22000867.hg.1	LDOC1L
TC12003128.hg.1	LINC01089
TC12002748.hg.1	DDX12P
TC21000423.hg.1	RUNX1
TC17001442.hg.1	PLXDC1
TC07000521.hg.1	CROT
TC02000590.hg.1	LOC100506123
TC10000625.hg.1	PTEN
TC12002848.hg.1	LINC00938
TC07002414.hg.1	NSUN5P1
TC14001588.hg.1	YME1L1
TC12000812.hg.1	CHST11
TC07001285.hg.1	AOAH
TC12002734.hg.1	SLC2A3
TC12000109.hg.1	PEX5
TC06002155.hg.1	LOC100130476
TC12001988.hg.1	SLC8B1
TC12002253.hg.1	CDKN1B
TC19001169.hg.1	KRI1
TC14000794.hg.1	TNFAIP2
TC08001440.hg.1	TP53INP1
TC07003313.hg.1	PILRB
TC6_ssto_hap7000048.hg.1	HCP5
TC02000400.hg.1	ARHGAP25
TC17002788.hg.1	EXOC7
TC22000019.hg.1	IL17RA
TC22001491.hg.1	MFNG
TC07000273.hg.1	AEBP1
TC09000906.hg.1	PTPRD
TC05000565.hg.1	TNFAIP8
TC12001807.hg.1	BTG1
TC0X000356.hg.1	MIR223
TC02002136.hg.1	AFF3
TC20001593.hg.1	LINC01260
TC19002619.hg.1	SPPL2B
TC01001322.hg.1	TTC24
TC04001201.hg.1	CHIC2
TC07002640.hg.1	EPHB6
TC03000164.hg.1	CCR4
TC04000875.hg.1	LOC285500
TC07003297.hg.1	NSUN5P2
TC09002901.hg.1	S1PR3
TC15000329.hg.1	MAP1A

TC08001147.hg.1	FGFR1
TC03002780.hg.1	LOC100130207
TC09001618.hg.1	FAM102A
TC09000662.hg.1	RALGPS1
TC01000917.hg.1	RNPC3
TC17001445.hg.1	ARL5C
TC20000815.hg.1	SLA2
TC09000654.hg.1	MVB12B
TC10002951.hg.1	SLIT1
TC16000300.hg.1	SBK1
TC01001985.hg.1	ZBTB18
TC17001315.hg.1	TIAF1
TC22000372.hg.1	PARVG
TC22000546.hg.1	YPEL1
TC09001608.hg.1	SH2D3C
TC20000436.hg.1	TFAP2C
TC03002034.hg.1	ZMAT3
TC16000482.hg.1	NLRC5
TC12002894.hg.1	CALCOCO1
TC01001144.hg.1	NBPF15
TC17001111.hg.1	CTC1
TC12000147.hg.1	OVOS
TC15001233.hg.1	PLCB2
TC06003630.hg.1	MOCS1
TC09001401.hg.1	HEMGN
TC04002727.hg.1	LOC101927359
TC19000029.hg.1	HMHA1
TC01000342.hg.1	CD52
TC07000923.hg.1	EPHB6
TC17001595.hg.1	LOC339192
TC10001769.hg.1	BNIP3
TC01000921.hg.1	AMY1B
TC02002614.hg.1	SLC40A1
TC01000084.hg.1	KCNAB2
TC16001314.hg.1	COTL1
TC06000115.hg.1	FAM8A1
TC16000230.hg.1	SNX29P1
TC17000015.hg.1	SERPINF1
TC18000132.hg.1	RNF125
TC01000074.hg.1	DFFB
TC14001184.hg.1	DHRS7
TC05000782.hg.1	ARHGAP26
TC04001132.hg.1	SMIM14
TC18000468.hg.1	KC6
TC16000285.hg.1	HS3ST4
TC19001256.hg.1	RASAL3
TC17001301.hg.1	ALDOC

TC01000822.hg.1	CLCA1
TC15001540.hg.1	RPS27L
TC12000822.hg.1	TCP11L2
TC08002578.hg.1	LEPROTL1
TC09000378.hg.1	IDNK
TC12000081.hg.1	TAPBPL
TC07003360.hg.1	GATSL2
TC06002302.hg.1	LINC00473
TC07003081.hg.1	GATS
TC07001858.hg.1	UBE2H
TC06001732.hg.1	TRERF1
TC17000833.hg.1	RAB37
TC22000129.hg.1	BCR
TC10001594.hg.1	NDUFB8
TC11002092.hg.1	ARRB1
TC17000977.hg.1	SLC43A2
TC03000191.hg.1	XYLB
TC01001619.hg.1	RGS18
TC22001027.hg.1	BCRP3
TC01003029.hg.1	CD58
TC17001386.hg.1	TBC1D3B
TC09001508.hg.1	AKNA
TC17001187.hg.1	RASD1
TC17001391.hg.1	TBC1D3C
TC20000449.hg.1	RBM38
TC06000262.hg.1	LOC100131289
TC14002273.hg.1	IGHV5-51
TC15002498.hg.1	RAD51-AS1
TC6_qbl_hap6000232.hg.1	DDAH2
TC06001727.hg.1	CCND3
TC12003217.hg.1	CHFR
TC05000952.hg.1	ERGIC1
TC04001046.hg.1	LINC01096
TC02001490.hg.1	LINC01237
TC17001601.hg.1	PLEKHM1
TC07003312.hg.1	CCDC146
TC04001420.hg.1	DDIT4L
TC17002922.hg.1	PLEKHM1P
TC07000916.hg.1	TRBV27
TC01001314.hg.1	SEMA4A
TC09000350.hg.1	GCNT1
TC07002659.hg.1	LOC155060
TC05000469.hg.1	CAST
TC01006072.hg.1	C1orf132
TC05001102.hg.1	SLC12A7
TC20000338.hg.1	PABPC1L
TC10001461.hg.1	ANXA11

TC07000246.hg.1	TRG-AS1
TC15001992.hg.1	ADAMTS17
TC21000198.hg.1	ABCG1
TC15001783.hg.1	UBE2Q2P1
TC04000182.hg.1	TBC1D19
TC14002245.hg.1	IGHV1-3
TC16000045.hg.1	MAPK8IP3
TC11000265.hg.1	GAS2
TC22001495.hg.1	SUN2
TC06001293.hg.1	ATXN1
TC02001381.hg.1	ITM2C
TC17001523.hg.1	DHX58
TC01000918.hg.1	AMY2A
TC02001082.hg.1	LOC101927156
TC16001477.hg.1	SNX29P2
TC03001670.hg.1	ZBTB20
TC11001450.hg.1	PLEKHA7
TC01003775.hg.1	MIR29B2
TC03001358.hg.1	LRRC2
TC08001551.hg.1	SAMD12
TC19001075.hg.1	UHRF1
TC17000451.hg.1	TBC1D3
TC12001739.hg.1	LOC100507377
TC12001469.hg.1	LMBR1L
TC12001632.hg.1	AGAP2
TC12000543.hg.1	MARCH9
TC15000578.hg.1	TPM1
TC03001125.hg.1	SUMF1
TC03002826.hg.1	COL6A4P1
TC15002551.hg.1	LOC145783
TC14000090.hg.1	OR6C4
TC10000097.hg.1	OPTN
TC17000103.hg.1	CD68
TC01004071.hg.1	ZNF496
TC04000542.hg.1	TET2
TC05002122.hg.1	PHYKPL
TC20000486.hg.1	OSBPL2
TC07000280.hg.1	CCM2
TC15001989.hg.1	DNM1P46
TC15001507.hg.1	RORA
TC11000579.hg.1	NAA40
TC17000583.hg.1	MAP3K14-AS1
TC03001506.hg.1	FHIT
TC16000126.hg.1	DNASE1
TC04000069.hg.1	MAN2B2
TC01006359.hg.1	DAB1
TC22000423.hg.1	PPP6R2

TC01001777.hg.1	ATF3
TC01003378.hg.1	SPTA1
TC16000643.hg.1	PLCG2
TC03001252.hg.1	NEK10
TC04001280.hg.1	RASSF6
TC13000672.hg.1	DLEU7
TC22000699.hg.1	RBFOX2
TC01001928.hg.1	KCNK1
TC09000923.hg.1	TTC39B
TC07003404.hg.1	LOC401320
TC17000549.hg.1	TMEM106A
TC05000284.hg.1	MAST4
TC10001070.hg.1	CUBN
TC03003333.hg.1	ETV5
TC12001168.hg.1	SLC2A14
TC19001801.hg.1	ZNF528-AS1
TC20000582.hg.1	RNF24
TC21000479.hg.1	C2CD2
TC14000884.hg.1	TEP1
TC16001745.hg.1	ERVK13-1
TC04000517.hg.1	DAPP1
TC02005020.hg.1	CMPK2
TC01000271.hg.1	NBPF3
TC16001501.hg.1	CLUHP3
TC02000252.hg.1	SLC8A1-AS1
TC09002128.hg.1	LOC100499484
TC17001775.hg.1	TBC1D3P2
TC17000974.hg.1	MYO1C
TC02000427.hg.1	NAGK
TC22000659.hg.1	DUSP18
TC03000333.hg.1	DNAH1
TC01003096.hg.1	PDE4DIP
TC11002030.hg.1	SHANK2
TC19001812.hg.1	ZNF415
TC08001541.hg.1	TRPS1
TC15002793.hg.1	CAPN3
TC12001532.hg.1	KRT1
TC09000489.hg.1	CCDC180
TC15000756.hg.1	IL16
TC14001212.hg.1	MIR548H1
TC15000730.hg.1	HYKK
TC03000110.hg.1	KCNH8
TC02002492.hg.1	GALNT3
TC08002606.hg.1	C8orf44
TC04000040.hg.1	NOP14-AS1
TC14000277.hg.1	KLHDC1
TC03000607.hg.1	ARHGAP31

TC10000228.hg.1	CCDC7
TC06001927.hg.1	GJB7
TC11000921.hg.1	FUT4
TC03002033.hg.1	KCNMB2-AS1
TC02004694.hg.1	MLK7-AS1
TC10000143.hg.1	MALRD1
TC08001590.hg.1	FBXO32
TC02000318.hg.1	EML6
TC05000253.hg.1	GAPT
TC01003743.hg.1	DSTYK
TC04001176.hg.1	TEC
TC12000955.hg.1	P2RX7
TC0X001347.hg.1	TENM1
TC15000083.hg.1	SNORD115-10
TC09000005.hg.1	KANK1
TC04001380.hg.1	FAM13A
TC07001573.hg.1	KIAA1324L

Supplementary Table IV: list of 257 genes down-regulated in PDTALL19 OMP52M51 resistant compared to control Ab-treated cells.

ProbeSet ID	**Gene Symbol**
TC06000341.hg.1	ABCF1
TC09000335.hg.1	ANXA1
TC15000002.hg.1	BMS1P15
TC05000643.hg.1	CCNI2
TC05000072.hg.1	CCT5
TC01003371.hg.1	CD1B
TC01001340.hg.1	CD1E
TC17000831.hg.1	CD300A
TC11000374.hg.1	CD82
TC06001332.hg.1	CMAHP
TC06002794.hg.1	CNPY3
TC01001738.hg.1	CR1
TC01001737.hg.1	CR2
TC16001031.hg.1	DCTPP1
TC10002105.hg.1	DDX21
TC0X000779.hg.1	DKC1
TC19001125.hg.1	ELAVL1
TC11000541.hg.1	FEN1
TC12000028.hg.1	FKBP4
TC01001907.hg.1	GALNT2
TC07002868.hg.1	GGCT
TC12000642.hg.1	GLIPR1
TC08001110.hg.1	GSR
TC13000077.hg.1	GTF3A

TC04000788.hg.1	GUCY1B3
TC03003359.hg.1	GXYLT2
TC03002732.hg.1	HES1
TC02001202.hg.1	ICOS
TC14002263.hg.1	IGHV3-33
TC02000884.hg.1	LOC100507600
TC17001687.hg.1	LRRC59
TC03001352.hg.1	LZTFL1
TC22001090.hg.1	MCM5
TC07001654.hg.1	MCM7
TC14000388.hg.1	MTHFD1
TC20000320.hg.1	MYBL2
TC08000749.hg.1	MYC
TC18000016.hg.1	MYL12A
TC16001226.hg.1	NOB1
TC10000749.hg.1	NOLC1
TC19001250.hg.1	NOTCH3
TC03001188.hg.1	NUP210
TC02001570.hg.1	ODC1
TC17001960.hg.1	P4HB
TC15002776.hg.1	PKM
TC16000258.hg.1	PLK1
TC09002753.hg.1	POLE3
TC17000783.hg.1	PRKCA
TC14000371.hg.1	PRKCH
TC19000015.hg.1	PTBP1
TC09002738.hg.1	PTPN3
TC12000101.hg.1	PTPN6
TC04001163.hg.1	RAC1P2
TC09000545.hg.1	RAD23B
TC12001038.hg.1	RAN
TC01006343.hg.1	RHOU
TC14001101.hg.1	RPL36AL
TC02003665.hg.1	SCN2A
TC17002036.hg.1	SENP3-EIF4A1
TC12002398.hg.1	SHMT2
TC05000161.hg.1	SKP2
TC09000535.hg.1	SLC44A1
TC0X000101.hg.1	SMS
TC01002195.hg.1	SRM
TC20000636.hg.1	TASP1
TC17000958.hg.1	TBCD
TC17002468.hg.1	TP53
TC16001829.hg.1	TUFM
TC19000097.hg.1	UHRF1
TC16000852.hg.1	USP7
TC05003242.hg.1	VDAC1

TC12001227.hg.1	YBX3
TC07001540.hg.1	YWHAG
TC19000996.hg.1	POLR2E
TC19000169.hg.1	PPAN-P2RY11
TC02002591.hg.1	FRZB
TC03000159.hg.1	CMTM8
TC11003482.hg.1	SLC43A3
TC11002361.hg.1	HYOU1
TC04000979.hg.1	NOP14
TC19002608.hg.1	NUP62
TC02001573.hg.1	PDIA6
TC13000426.hg.1	TFDP1
TC22000046.hg.1	CDC45
TC07000764.hg.1	SND1
TC12000843.hg.1	UNG
TC22000859.hg.1	TTLL12
TC12000367.hg.1	TUBA1C
TC17000705.hg.1	MSI2
TC6_qbl_hap6000101.hg.1	KIFC1
TC06000614.hg.1	SLC29A1
TC11001738.hg.1	PSMC3
TC06000587.hg.1	PTCRA
TC02000851.hg.1	LINC01120
TC05000855.hg.1	LARP1
TC12001309.hg.1	BCAT1
TC06001684.hg.1	CCDC167
TC12001106.hg.1	FOXM1
TC03002319.hg.1	CCR9
TC01002511.hg.1	MRPS15
TC09000260.hg.1	FAM27E3
TC07001995.hg.1	PDIA4
TC16000879.hg.1	CPPED1
TC6_ssto_hap7000143.hg.1	VARS
TC02001685.hg.1	PPM1G
TC07002034.hg.1	ABCF2
TC05001772.hg.1	SEPT8
TC02000374.hg.1	SLC1A4
TC01000643.hg.1	GPX7
TC09001434.hg.1	ABCA1
TC17001571.hg.1	LSM12
TC09001161.hg.1	FAM27B
TC01001447.hg.1	UCK2
TC01002410.hg.1	FGR
TC06000074.hg.1	TMEM14C
TC07000969.hg.1	CUL1
TC02005042.hg.1	RFX8
TC15002181.hg.1	SORD

TC01005030.hg.1	RRP15
TC03001000.hg.1	EIF4G1
TC03000316.hg.1	MAPKAPK3
TC16000782.hg.1	RNPS1
TC01000245.hg.1	MRTO4
TC20000980.hg.1	PMEPA1
TC10002830.hg.1	XPNPEP1
TC02000035.hg.1	RNF144A
TC08000893.hg.1	CSMD1
TC01001030.hg.1	FAM46C
TC11003109.hg.1	WT1
TC05000010.hg.1	TRIP13
TC06000372.hg.1	LST1
TC22000233.hg.1	YWHAH
TC16000293.hg.1	IL4R
TC12002085.hg.1	CDK2AP1
TC07003399.hg.1	GIMAP1-GIMAP5
TC17002885.hg.1	P2RX5
TC03001456.hg.1	NT5DC2
TC21000204.hg.1	PDE9A
TC21000247.hg.1	PCBP3
TC07000815.hg.1	MEST
TC0X000826.hg.1	PUDP
TC15000837.hg.1	MRPS11
TC02001544.hg.1	RNF144A-AS1
TC16000133.hg.1	MGRN1
TC07003295.hg.1	REPIN1
TC15000949.hg.1	IGF1R
TC6_dbb_hap3000053.hg.1	MICB
TC08001361.hg.1	PAG1
TC6_mcf_hap5000121.hg.1	FLOT1
TC19000588.hg.1	CD79A
TC20000565.hg.1	CPXM1
TC01002149.hg.1	ACOT7
TC22000054.hg.1	RANBP1
TC11001442.hg.1	RRAS2
TC6_qbl_hap6000194.hg.1	WDR46
TC22000610.hg.1	TPST2
TC0X000821.hg.1	NLGN4Y
TC6_mcf_hap5000098.hg.1	TRIM27
TC02000082.hg.1	TRIB2
TC06000205.hg.1	ABT1
TC16000822.hg.1	TRAP1
TC0X001543.hg.1	GAB3
TC17000894.hg.1	TMC8
TC02003382.hg.1	MIR4435-2HG
TC14000297.hg.1	FRMD6

TC02000535.hg.1	LINC00152
TC14001509.hg.1	WARS
TC17000319.hg.1	TMEM97
TC19000663.hg.1	PPP5C
TC04000151.hg.1	LAP3
TC17000026.hg.1	RAP1GAP2
TC04001595.hg.1	RNF150
TC6_mcf_hap5000183.hg.1	TAPBP
TC15001476.hg.1	MNS1
TC11001194.hg.1	APLP2
TC05000209.hg.1	PARP8
TC17000136.hg.1	PFAS
TC04000028.hg.1	TACC3
TC02001923.hg.1	SPRED2
TC6_mcf_hap5000185.hg.1	DAXX
TC0Y000060.hg.1	FAM41AY1
TC05000641.hg.1	IL4
TC01001002.hg.1	DCLRE1B
TC11002205.hg.1	SESN3
TC02004923.hg.1	RNASEH1
TC15001643.hg.1	SEMA7A
TC02002207.hg.1	MIR4435-2HG
TC01000205.hg.1	SZRD1
TC09001668.hg.1	RAPGEF1
TC04000893.hg.1	STOX2
TC19000493.hg.1	WDR62
TC14001451.hg.1	LGMN
TC17001796.hg.1	ERN1
TC16000502.hg.1	GINS3
TC03001003.hg.1	POLR2H
TC09001008.hg.1	B4GALT1
TC06001552.hg.1	NELFE
TC17001584.hg.1	CCDC43
TC0X000033.hg.1	TBL1X
TC09000579.hg.1	ZNF618
TC01001731.hg.1	PFKFB2
TC10000820.hg.1	TCF7L2
TC17001129.hg.1	GAS7
TC03000672.hg.1	EEFSEC
TC20000600.hg.1	TRMT6
TC03001207.hg.1	SH3BP5
TC10001054.hg.1	FAM107B
TC6_ssto_hap7000064.hg.1	SAPCD1
TC09001490.hg.1	SUSD1
TC02001961.hg.1	FAM136A
TC03001772.hg.1	PLXND1
TC18000224.hg.1	PHLPP1

TC02001867.hg.1	EFEMP1
TC12001712.hg.1	BEST3
TC0X001042.hg.1	NUDT11
TC04000839.hg.1	PALLD
TC6_apd_hap1000074.hg.1	DHX16
TC22000658.hg.1	PES1
TC14002250.hg.1	IGHV3-11
TC03000248.hg.1	LIMD1
TC01003872.hg.1	SUSD4
TC01003477.hg.1	GPA33
TC04000903.hg.1	SNX25
TC15000153.hg.1	APBA2
TC06001499.hg.1	TRIM26
TC14002257.hg.1	IGHV3-23
TC09000319.hg.1	TJP2
TC18000160.hg.1	SETBP1
TC08001269.hg.1	GGH
TC01001736.hg.1	CD55
TC04001139.hg.1	APBB2
TC02000704.hg.1	FBLN7
TC09000899.hg.1	GLDC
TC16000870.hg.1	LITAF
TC08002611.hg.1	PINX1
TC17000898.hg.1	AFMID
TC11002002.hg.1	CHKA
TC17001536.hg.1	PSMC3IP
TC17000781.hg.1	RGS9
TC01001740.hg.1	CR1L
TC12000747.hg.1	ELK3
TC12000630.hg.1	TRHDE
TC17001014.hg.1	P2RX1
TC0X000025.hg.1	STS
TC08001408.hg.1	TMEM55A
TC02000675.hg.1	LOC100507334
TC22001461.hg.1	SEC14L2
TC08002590.hg.1	DOCK5
TC08000170.hg.1	SLC39A14
TC02002201.hg.1	LIMS3L
TC01006352.hg.1	MYCBP
TC17001820.hg.1	SLC16A6
TC05001519.hg.1	ARSB
TC08002617.hg.1	TPD52
TC0X000855.hg.1	MID1
TC0X001303.hg.1	KLHL13
TC03003332.hg.1	WDR49

Supplementary Table V: Summary of alignment and coverage metrics for each sequenced sample.

Sample	Nr. PF reads	HQ aligned bases	Duplication rate (%)	Usable bases on target regions	Mean coverage	Target regions 20X	Target regions 50X	Target regions 100X
R4	73716402	7327996997	7.36	0.46	116	95.26	88.24	72.69
R5	89575460	8914599284	8.12	0.44	137	95.90	90.78	78.03
R6	78288936	7784063247	8.07	0.46	123	95.49	89.02	74.13
C1	77398979	7684412397	8.57	0.47	124	95.75	89.79	75.73
C2	72867003	7246556123	7.49	0.46	114	95.16	88.05	71.96
C3	76091055	7574223494	7.75	0.45	118	92.51	77.20	49.12

The following information is listed: the number of passing sequencer quality filters (Nr. PF reads); the number of high quality aligned bases (HQ aligned bases); the fraction of aligned bases that were filtered out because they were in reads marked as duplicates (duplication rate); the percentage of aligned, de-duped, on-bait bases out of the passing-filter bases available (usable bases on target regions); the number of aligned reads mapping to bait regions (mean coverage); the fraction of all target bases achieving, 20X, 50X and 100X or greater coverage (in the last three columns). R4-6: PDTALL8 OMP52M51-resistant samples, C1-3: PDTALL8 control samples.

Supplementary Table VI: High impact variants resulting from WES analysis of PDTALL8 control and OMP52M51 resistant cells.

List of confident exonic variants shared among treated but absent in control mice. For simplicity, reported VAF and read depth refer to one sample per group (OMP52M51 resistant #4).

Chr	Start	Ref	Alt	Gene	Transcript	Exon	cDNA	Protein (pNomen)	dbSNP	Alt Allele Frequency	Alt Allele depth	Read depth	Filter status (filter)	COSMIC Id (cosmicId)	COSMIC CGC Tumor types (Somatic) (cgcTumorTypesSomatic)
1	45807197	A	G	TOE1	NM_025077.3	4	c.289A>G	p.I97V	rs778870256	0,114	20,976	184	PASS	_	_
1	67450386	A	G	MIER1	NM_001350530.1	16	c.1612A>G	p.T538A	_	0,116	11,02	95	PASS	_	_
1	152325628	C	A	FLG2	NM_001014342.2	3	c.4634G>T	p.G1545V	_	0,345	223,905	649	PASS	_	_
1	156830779	G	A	NTRK1	NM_002529.3	1	c.53G>A	p.G18E	rs1007211	0,433	12,99	30	PASS	COSM5762903	papillarythyroid, Spitzoidtumour
1	178861430	T	C	RALGPS2	NM_152663.4	15	c.1313T>C	p.M438T	_	0,4	12	30	PASS		
1	202124668	T	C	PTPN7	NM_002832.3	5	c.776A>G	p.Y259C	_	0,301	43,043	143	PASS	_	_
1	236189250	G	T	NID1	NM_002508.2	8	c.1930C>A	p.Q644K	_	0,101	13,938	138	PASS	_	_
3	49337950	C	T	USP4	NM_003363.3	11	c.1462G>A	p.V488I	rs147724381	0,131	17,947	137	PASS	_	_
3	195513324	C	G	MUC4	NM_018406.6	2	c.5127G>C	p.Q1709H	rs78921372	0,141	22,983	163	PASS	_	_
4	9356292	C	T	USP17L24	NM_001242327.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
4	9356292	C	T	USP17L25	NM_001242326.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
4	9356292	C	T	USP17L26	NM_001242328.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
4	9356292	C	T	USP17L27	NM_001242330.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
4	9356292	C	T	USP17L28	NM_001242331.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
4	9356292	C	T	USP17L29	NM_001242332.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
4	9356292	C	T	USP17L30	NM_001256867.1	1	c.929C>T	p.P310L	rs200799659	0,107	98,333	919	PASS	_	_
5	60214195	C	T	ERCC8	NM_001007233.2	5	c.122G>A	p.R41K	_	0,101	17,978	178	PASS	_	_
5	102355536	A	C	PAM	NM_001319943.1	24	c.2528A>C	p.Q843P	_	0,16	16	100	PASS	_	_
5	110443047	T	G	WDR36	NM_139281.2	12	c.1403T>G	p.L468R	_	0,105	9,975	95	PASS	_	_
5	139422098	A	G	NRG2	NM_013982.2	1	c.557T>C	p.V186A	_	0,109	16,023	147	PASS	_	_
5	140237183	A	T	PCDHA10	NM_018901.3	1	c.1550A>T	p.Y517F	_	0,129	14,964	116	PASS	_	_
5	153406874	C	A	FAM114A2	NM_001317994.1	7	c.651G>T	p.E217D	_	0,17	19,04	112	PASS	_	_
5	180795216	G	A	OR4F3	NM_001005224.1	1	c.929G>A	p.R310K	_	0,14	15,96	114	PASS	COSM5426378	_
6	15533570	T	G	DTNBP1	NM_183040.2	8	c.568A>C	p.M190L	rs536290179	0,113	26,103	231	PASS	_	_
6	30954890	A	G	MUC21	NM_001010909.4	2	c.938A>G	p.N313S	rs9262379	0,232	16,008	69	PASS	COSM3747665	_
6	43541286	C	T	XPO5	NM_020750.2	2	c.158G>A	p.R53K	rs373359039	0,107	16,05	150	PASS	_	_
6	82459682	C	G	TENT5A	NM_017633.2	3	c.1059G>C	p.E353D	rs780521689	0,104	29,952	288	PASS	_	_
6	86350217	C	T	SYNCRIP	NM_001159677.1	3	c.214G>A	p.G72S	_	0,261	42,021	161	PASS	_	_
7	86803913	T	G	DMTF1	NM_021145.3	9	c.447T>G	p.H149Q	_	0,136	11,016	81	PASS	_	_
7	97946538	T	A	BAIAP2L1	NM_018842.4	6	c.479A>T	p.E160V	_	0,374	54,978	147	PASS	_	_
8	30502893	A	C	SMIM18	NM_001206847.1	3	c.67A>C	p.K23Q	_	0,116	22,04	190	PASS	_	_
9	32543723	G	A	TOPORS	NM_005802.4	3	c.800C>T	p.A267V	_	0,12	25,92	216	PASS	_	_
9	139399389	A	G	NOTCH1	NM_017617.5	26	c.4754T>C	p.L1585P	_	0,253	39,974	158	PASS	COSM13046	T-cell acute lymphoblastic leukaemia, breast, bladder, skinSCC, lungSCC, headandneckSCC
9	139399391	C	G	NOTCH1	NM_017617.5	26	c.4752G>C	p.Q1584H	_	0,264	43,032	163	PASS	_	T-cell acute lymphoblastic leukaemia, breast, bladder, skinSCC, lungSCC, headandneckSCC
10	18690016	A	G	CACNB2	NM_201570.2	1	c.56A>G	p.N19S	_	0,108	11,988	111	PASS	_	_

10	96012246	C	G	PLCE1	NM_016341.3	9	c.3270C>G	p.I1090M	_	0,149	18,029	121	PASS	_	_
10	121436388	A	G	BAG3	NM_004281.3	4	c.1322A>G	p.N441S	_	0,106	9,964	94	PASS	_	_
10	125539688	G	A	CPXM2	NM_198148.2	7	c.973C>T	p.R325C	rs747723133	0,303	99,081	327	PASS	COSM915780	_
11	21594851	A	G	NELL1	NM_001288713.1	20	c.2362A>G	p.T788A	_	0,129	19,995	155	PASS	_	_
11	46563590	T	G	AMBRA1	NM_001267782.1	8	c.1707A>C	p.R569S	_	0,128	13,952	109	PASS	_	_
11	47605969	T	C	NDUFS3	NM_004551.2	7	c.731T>C	p.V244A	_	0,119	23,086	194	PASS	_	_
12	40880938	T	A	MUC19	NM_173600.2	56	c.14184T>A	p.D4728E	rs80222752	0,115	87,975	765	PASS	_	_
12	89917451	C	A	GALNT4	NM_003774.4	1	c.876G>T	p.Q292H	_	0,105	27,09	258	PASS	_	_
12	89917451	C	A	POC1B-GALNT4	NM_001199781.1	3	c.867G>T	p.Q289H	_	0,105	27,09	258	PASS	_	_
16	24788671	A	G	TNRC6A	NM_001351850.1	5	c.608A>G	p.N203S	_	0,108	14,04	130	PASS	_	_
16	26147507	T	A	HS3ST4	NM_006040.2	2	c.1309T>A	p.L437M	_	0,133	23,009	173	PASS	_	_
16	56468315	G	A	NUDT21	NM_007006.2	6	c.590C>T	p.P197L	_	0,105	15,015	143	PASS	_	_
19	52942307	C	A	ZNF534	NM_001143939.2	5	c.1633C>A	p.R545S	rs777652588	0,104	32,136	309	PASS	COSM1481436	_
19	55316320	G	T	KIR2DL4	NM_001080772.1	3	c.149G>T	p.R50L	rs377230503	0,121	20,933	173	PASS	_	_
20	3944568	T	C	RNF24	NM_007219.4	2	c.97A>G	p.I33V	rs765682596	0,127	10,033	79	PASS	_	_
X	48771497	C	T	PIM2	NM_006875.3	6	c.847G>A	p.D283N	_	0,157	13,031	83	PASS	_	_
X	48771506	T	C	PIM2	NM_006875.3	6	c.838A>G	p.I280V	rs35208542	0,146	11,972	82	PASS	_	_
X	117706393	A	C	DOCK11	NM_144658.3	11	c.1143A>C	p.Q381H	_	0,108	14,04	130	PASS	_	_
X	122319835	A	T	GRIA3	NM_000828.4	2	c.260A>T	p.K87I	_	0,106	24,062	227	PASS	_	_

List of confident exonic variants shared among control but absent in resistant mice. For simplicity, reported VAF and read depth refer to one sample per group (Ctrl Ab #1).

Chr	Start	Ref	Alt	Gene	Transcript	Exon	cDNA	Protein	dbSNP	Alt Allele Frequency	Alt Allele depth	Read depth	Filter status (filter)	COSMIC Id (cosmicId)	COSMIC tumor type (sample count) (cosmicTumorTypeSampleCount)
1	1168079	G	A	B3GALT6	NM_080605.3	1	c.421G>A	p.A141T		0,126	20,034	159	PASS		
1	1168095	A	G	B3GALT6	NM_080605.3	1	c.437A>G	p.H146R	rs750827414	0,13	21,97	169	PASS		
1	1168101	C	A	B3GALT6	NM_080605.3	1	c.443C>A	p.A148D	rs756325734	0,119	20,944	176	PASS		
1	1470807	C	T	TMEM240	NM_001114748.1	4	c.454G>A	p.A152T	rs146206869	0,101	21,917	217	PASS	COSM3750342	Colorectal adenocarcinoma (1)
1	1470810	C	G	TMEM240	NM_001114748.1	4	c.451G>C	p.A151P		0,108	22,896	212	PASS		
1	1565855	G	A	MIB2	NM_080875.2	20	c.3158G>A	p.S1053N	rs751553744	0,105	11,97	114	PASS		
1	2418669	A	G	PLCH2	NM_001303013.1	7	c.1028A>G	p.H343R		0,103	9,991	97	PASS		
1	2418670	T	A	PLCH2	NM_001303013.1	7	c.1029T>A	p.H343Q	rs373817416	0,105	9,975	95	PASS		
1	7723979	A	G	CAMTA1	NM_015215.3	9	c.1372A>G	p.T458A		0,127	12,954	102	PASS		
1	27092824	T	C	ARID1A	NM_006015.4	9	c.2845T>C	p.S949P		0,13	26,91	207	PASS		
1	27721119	C	G	GPR3	NM_005281.3	2	c.817C>G	p.H273D	rs750308556	0,116	9,976	86	PASS		
1	35827242	A	G	ZMYM4	NM_001350138.1	6	c.596A>G	p.N199S	rs749818676	0,126	11,97	95	PASS		
1	35827329	A	G	ZMYM4	NM_001350138.1	6	c.683A>G	p.K228R	rs767671002	0,118	12,036	102	PASS		
1	45101751	A	C	RNF220	NM_018150.3	8	c.1043A>C	p.E348A		0,105	17,01	162	PASS		
1	45101753	A	G	RNF220	NM_018150.3	8	c.1045A>G	p.N349D		0,108	17,064	158	PASS		
1	45101757	A	G	RNF220	NM_018150.3	8	c.1049A>G	p.N350S		0,114	18,012	158	PASS		
1	46751313	G	A	LRRC41	NM_006369.4	4	c.1216C>T	p.P406S	rs568255406	0,178	22,962	129	PASS		
1	46751331	C	G	LRRC41	NM_006369.4	4	c.1198G>C	p.A400P	rs751719630	0,165	15,015	91	PASS		
1	47144246	T	G	EFCAB14	NM_014774.2	11	c.1375A>C	p.I459L		0,106	11,024	104	PASS		
1	48764494	T	C	SPATA6	NM_019073.3	13	c.1358A>G	p.Y453C		0,116	14,036	121	PASS		
1	109635646	G	A	TMEM167B	NM_001322248.1	2	c.145G>A	p.E49K		0,135	12,015	89	PASS		
1	110563376	C	T	AHCYL1	NM_001242673.1	16	c.1348C>T	p.P450S		0,149	25,032	168	PASS		
1	113252888	G	A	PPM1J	NM_005167.5	10	c.1415C>T	p.T472I		0,122	24,034	197	PASS		
1	115262339	C	T	CSDE1	NM_001242891.1	19	c.2215G>A	p.G739R		0,11	13,97	127	PASS		
1	146465973	C	G	NBPF12	NM_001278141.1	37	c.4226C>G	p.P1409R	rs113829174	0,137	35,894	262	PASS	COSM4599309	Head and neck tumors (1)
1	147083642	T	C	BCL9	NM_004326.3	4	c.7T>C	p.S3P		0,106	11,978	113	PASS		
1	150444516	G	A	RPRD2	NM_015203.4	11	c.3092G>A	p.S1031N		0,104	19,032	183	PASS		
1	150444527	C	T	RPRD2	NM_015203.4	11	c.3103C>T	p.P1035S	rs767657944	0,102	17,034	167	PASS		
1	150915053	A	G	SETDB1	NM_001145415.1	6	c.562A>G	p.M188V		0,12	9,96	83	PASS		
1	151133398	C	T	LYSMD1	NM_212551.4	3	c.644G>A	p.R215Q		0,156	26,988	173	PASS	COSM1214125	Colorectal adenocarcinoma (1)
1	151341641	T	A	SELENBP1	NM_001258289.1	4	c.325A>T	p.N109Y		0,165	15,015	91	PASS		
1	151752471	G	A	TDRKH	NM_001083965.1	4	c.377C>T	p.S126F		0,107	22,898	214	PASS		
1	155851267	G	A	SYT11	NM_152280.4	4	c.1264G>A	p.V422M		0,107	14,017	131	PASS		
1	156811974	G	C	INSRR	NM_014215.2	19	c.3327C>G	p.N1109K	rs771963500	0,161	23,023	143	PASS		
1	156811974	G	C	NTRK1	NM_001007792.1	2	c.111G>C	p.L37F	rs771963500	0,161	23,023	143	PASS		

1	160012023	G	T	KCNJ10	NM_002241.4	2	c.300C>A	p.D100E	rs139069413	0,109	14,061	129	PASS		
1	160260430	T	C	COPA	NM_001098398.1	32	c.3494A>G	p.Y1165C		0,103	15,038	146	PASS		
1	167868684	C	T	ADCY10	NM_001297772.1	6	c.343G>A	p.V115I		0,173	12,975	75	PASS		
1	173839827	T	C	ZBTB37	NM_001122770.2	3	c.464T>C	p.V155A		0,12	21	175	PASS		
1	173839868	A	G	ZBTB37	NM_001122770.2	3	c.505A>G	p.T169A		0,106	13,992	132	PASS		
1	179013140	C	T	FAM20B	NM_014864.3	2	c.158C>T	p.A53V		0,14	13,02	93	PASS		
1	183891418	C	G	RGL1	NM_015149.4	18	c.2172C>G	p.D724E		0,126	11,97	95	PASS		
1	186147629	C	T	HMCN1	NM_031935.2	104	c.16025C>T	p.P5342L		0,104	9,984	96	PASS		
1	200378090	A	C	ZNF281	NM_001281293.1	2	c.744T>G	p.D248E		0,119	19,992	168	PASS		
1	201179173	G	A	IGFN1	NM_001164586.1	12	c.5152G>A	p.E1718K	rs76484008	0,107	25,894	242	PASS	COSM4143173	Head and neck tumors (19) Colorectal adenocarcinoma (1) Miscellaneous thyroid tumors (1)
1	201179497	G	A	IGFN1	NM_001164586.1	12	c.5476G>A	p.E1826K	rs369751827	0,187	34,034	182	PASS		
1	206773151	T	C	EIF2D	NM_006893.2	9	c.988A>G	p.I330V		0,194	19,012	98	PASS		
1	206773170	T	G	EIF2D	NM_006893.2	9	c.969A>C	p.Q323H		0,155	13,02	84	PASS		
1	216074215	A	C	USH2A	NM_206933.2	39	c.7333T>G	p.S2445A		0,169	11,999	71	PASS		
1	228476524	C	A	OBSCN	NM_001271223.2	43	c.11561C>A	p.A3854E		0,128	9,984	78	PASS		
1	229730306	T	A	TAF5L	NM_014409.3	5	c.1508A>T	p.Y503F		0,103	12,051	117	PASS		
2	14774605	G	C	FAM84A	NM_145175.3	2	c.502G>C	p.E168Q		0,196	10,976	56	PASS		
2	27276426	C	G	AGBL5	NM_021831.5	3	c.372C>G	p.D124E		0,171	12,996	76	PASS		
2	27600462	G	C	ZNF513	NM_144631.5	4	c.1576C>G	p.P526A		0,102	14,994	147	PASS	COSM4429654	Oesophageal Squamous cell carcinoma (1)
2	27607734	A	G	PPM1G	NM_177983.2	5	c.631T>C	p.Y211H		0,119	18,921	159	PASS		
2	27607736	G	C	PPM1G	NM_177983.2	5	c.629C>G	p.A210G		0,118	19,942	169	PASS		
2	27607779	T	A	PPM1G	NM_177983.2	5	c.586A>T	p.T196S		0,15	21	140	PASS		
2	27607870	G	C	PPM1G	NM_177983.2	5	c.495C>G	p.H165Q	rs773935463	0,126	16,002	127	PASS		
2	36739468	T	C	CRIM1	NM_016441.2	10	c.1711T>C	p.S571P		0,126	35,91	285	PASS		
2	54159136	A	T	PSME4	NM_014614.2	10	c.1152T>A	p.D384E		0,117	34,983	299	PASS		
2	54159170	T	A	PSME4	NM_014614.2	10	c.1118A>T	p.Y373F		0,119	30,94	260	PASS		
2	54197753	A	T	PSME4	NM_014614.2	1	c.169T>A	p.C57S		0,105	16,065	153	PASS		
2	54887205	G	T	SPTBN1	NM_178313.2	31	c.6450G>T	p.Q2150H	rs756795548	0,117	14,04	120	PASS		
2	54887206	C	T	SPTBN1	NM_178313.2	31	c.6451C>T	p.P2151S		0,121	14,036	116	PASS		
2	54887218	C	A	SPTBN1	NM_178313.2	31	c.6463C>A	p.L2155M		0,137	13,974	102	PASS		
2	55054857	A	C	EML6	NM_001039753.2	5	c.680A>C	p.N227T		0,105	26,88	256	PASS		
2	55471220	G	A	MTIF2	NM_001005369.1	12	c.1256C>T	p.T419I		0,113	18,984	168	PASS		
2	55800789	G	C	PPP4R3B	NM_001122964.2	12	c.1730C>G	p.A577G		0,139	20,989	151	PASS		
2	55800822	A	G	PPP4R3B	NM_001122964.2	12	c.1697T>C	p.I566T		0,124	16,988	137	PASS		
2	60679705	T	G	BCL11A	NM_138559.1	5	c.727A>C	p.I243L		0,108	12,96	120	PASS		
2	70315638	A	G	PCBP1	NM_006196.3	1	c.763A>G	p.T255A		0,103	15,038	146	PASS		
2	74300764	G	T	TET3	NM_001287491.1	4	c.2583G>T	p.E861D		0,131	11,004	84	PASS		

2	85280296	A	G	KCMF1	NM_020122.4	7	c.910A>G	p.T304A		0,222	15,984	72	PASS
2	98128387	G	T	ANKRD36B	NM_025190.3	39	c.2934C>A	p.D978E	rs370929832	0,101	23,028	228	PASS
2	98128473	G	A	ANKRD36B	NM_025190.3	39	c.2848C>T	p.R950C		0,107	20,972	196	PASS
2	149226059	G	A	MBD5	NM_018328.4	9	c.547G>A	p.V183I		0,106	15,052	142	PASS
2	149528431	G	A	EPC2	NM_015630.3	9	c.1301G>A	p.R434K		0,136	14,008	103	PASS
2	152350363	G	T	NEB	NM_001271208.1	176	c.24703C>A	p.L8235M		0,128	17,024	133	PASS
2	160006999	A	G	TANC1	NM_001350065.1	8	c.614A>G	p.N205S		0,103	19,055	185	PASS
2	170488402	G	C	PPIG	NM_004792.2	11	c.888G>C	p.E296D		0,157	10,99	70	PASS
2	171700638	G	A	GAD1	NM_000817.2	7	c.722G>A	p.S241N		0,116	20,996	181	PASS
2	216965099	A	G	TMEM169	NM_001142310.1	4	c.728A>G	p.Q243R		0,116	9,976	86	PASS
2	220113011	C	G	STK16	NM_001330213.1	7	c.754C>G	p.Q252E		0,122	25,986	213	PASS
2	233394819	G	A	CHRND	NM_000751.2	7	c.790G>A	p.V264I		0,299	23,023	77	PASS
3	14487337	A	G	SLC6A6	NM_001134367.3	4	c.653A>G	p.Y218C		0,149	12,963	87	PASS
3	14519994	G	A	SLC6A6	NM_003043.5	12	c.1368G>A	p.W456*		0,139	66,025	475	PASS
3	33135075	T	C	TMPPE	NM_001039770.2	2	c.613A>G	p.N205D		0,132	20,064	152	PASS
3	42573351	C	T	VIPR1	NM_001251882.1	10	c.785C>T	p.T262I	rs373034151	0,12	9,96	83	PASS
3	43095084	G	T	FAM198A	NM_001129908.2	3	c.1362G>T	p.R454S		0,104	13	125	PASS
3	49399977	A	G	RHOA	NM_001313947.1	3	c.239T>C	p.I80T		0,11	19,03	173	PASS
3	49399986	A	G	RHOA	NM_001313947.1	3	c.230T>C	p.I77T		0,117	24,102	206	PASS
3	49400010	G	A	RHOA	NM_001313947.1	3	c.206C>T	p.T69M	rs780868634	0,108	23,976	222	PASS
3	49400013	G	T	RHOA	NM_001313947.1	3	c.203C>A	p.P68Q	rs749741822	0,119	24,99	210	PASS
3	50311823	T	C	SEMA3B	NM_001005914.2	12	c.1163T>C	p.I388T		0,117	14,04	120	PASS
3	51399968	C	A	DOCK3	NM_004947.4	49	c.5156C>A	p.P1719H		0,112	19,04	170	PASS
3	53855731	T	C	CHDH	NM_018397.4	5	c.928A>G	p.I310V		0,104	19,032	183	PASS
3	62358366	C	T	FEZF2	NM_018008.3	2	c.178G>A	p.G60S	rs1034349324	0,19	15,01	79	PASS
3	64138992	T	C	PRICKLE2	NM_198859.3	6	c.653A>G	p.K218R		0,219	15,987	73	PASS
3	87027733	G	A	VGLL3	NM_016206.3	2	c.346C>T	p.L116F		0,215	16,985	79	PASS
3	122003125	T	C	CASR	NM_001178065.1	7	c.2354T>C	p.F785S		0,133	11,039	83	PASS
3	127298641	G	A	TPRA1	NM_001353004.1	5	c.200C>T	p.S67F	rs149024589	0,163	13,04	80	PASS
3	135870720	T	C	MSL2	NM_018133.3	2	c.1003A>G	p.I335V		0,124	32,116	259	PASS
3	140397243	T	G	TRIM42	NM_152616.4	1	c.172T>G	p.S58A		0,121	32,912	272	PASS
3	141464014	A	G	RNF7	NM_183237.2	3	c.230A>G	p.N77S		0,12	24	200	PASS
3	141464020	T	C	RNF7	NM_183237.2	3	c.236T>C	p.I79T		0,124	24,924	201	PASS
3	142681470	T	A	PAQR9	NM_198504.2	1	c.709A>T	p.T237S		0,106	16,96	160	PASS
3	143691400	G	A	C3orf58	NM_173552.3	1	c.226G>A	p.A76T		0,162	16,038	99	PASS
3	155282872	T	C	PLCH1	NM_001349252.1	8	c.901A>G	p.I301V		0,212	11,024	52	PASS
3	179094840	G	A	MFN1	NM_033540.2	11	c.1108G>A	p.V370M	rs759901191	0,105	13,02	124	PASS
3	182665065	T	A	DCUN1D1	NM_001308101.1	6	c.616A>T	p.T206S		0,122	10,98	90	PASS
3	184024572	A	C	PSMD2	NM_002808.4	16	c.1984A>C	p.M662L	rs562725422	0,111	11,988	108	PASS
3	184038751	A	T	EIF4G1	NM_182917.4	8	c.667A>T	p.T223S		0,105	9,975	95	PASS
3	195509606	C	T	MUC4	NM_018406.6	2	c.8845G>A	p.D2949N	rs200244334	0,142	37,914	267	PASS

4	1944105	C	T	NSD2	NM_133334.2	9	c.1921C>T	p.P641S		0,161	22,057	137	PASS		
4	3768911	A	G	ADRA2C	NM_000683.3	1	c.578A>G	p.Q193R		0,107	37,129	347	PASS		
4	4247954	G	A	TMEM128	NM_032927.3	2	c.142C>T	p.L48F	rs751176943	0,126	12,978	103	PASS		
4	22737625	A	G	GBA3	NM_020973.4	2	c.80A>G	p.K27R		0,126	13,986	111	PASS		
4	22737637	T	C	GBA3	NM_020973.4	2	c.92T>C	p.V31A		0,158	15,01	95	PASS		
4	26431542	C	A	RBPJ	NM_203284.2	10	c.908C>A	p.P303Q		0,278	10,008	36	PASS		
4	77818854	A	C	SOWAHB	NM_001029870.2	1	c.149T>G	p.L50R		0,183	21,045	115	PASS		
4	77977457	C	T	CCNI	NM_006835.2	4	c.263G>A	p.S88N		0,127	10,033	79	PASS		
4	79403651	T	C	FRAS1	NM_025074.6	58	c.8714T>C	p.F2905S		0,105	19,005	181	PASS		
4	95496941	A	G	PDLIM5	NM_006457.4	5	c.466A>G	p.T156A		0,126	21,042	167	PASS		
4	110442607	A	G	SEC24B	NM_001300813.2	15	c.2423A>G	p.N808S		0,13	13	100	PASS		
4	123813380	T	A	FGF2	NM_002006.5	3	c.696T>A	p.D232E		0,113	10,961	97	PASS		
4	155749032	A	G	RBM46	NM_144979.4	5	c.1415A>G	p.H472R		0,111	14,985	135	PASS		
4	184366756	C	T	CDKN2AIP	NM_017632.3	2	c.341C>T	p.T114I	rs551218956	0,148	22,052	149	PASS		
4	185329351	T	C	IRF2	NM_002199.3	6	c.490A>G	p.T164A	rs149340805	0,125	35,125	281	PASS		
4	185329381	G	A	IRF2	NM_002199.3	6	c.460C>T	p.L154F		0,121	30,976	256	PASS		
4	185329383	T	C	IRF2	NM_002199.3	6	c.458A>G	p.D153G	rs752688730	0,129	31,992	248	PASS		
4	186066318	G	A	SLC25A4	NM_001151.3	2	c.512G>A	p.R171K		0,141	12,972	92	PASS		
5	6449067	G	A	UBE2QL1	NM_001145161.2	1	c.61G>A	p.D21N		0,109	10,028	92	PASS		
5	39382839	T	C	DAB2	NM_001343.3	10	c.1222A>G	p.I408V		0,101	27,977	277	PASS		
5	39382892	G	T	DAB2	NM_001343.3	10	c.1169C>A	p.S390Y		0,14	34,02	243	PASS		
5	39382943	G	T	DAB2	NM_001343.3	10	c.1118C>A	p.P373Q		0,113	24,069	213	PASS		
5	56542128	A	C	GPBP1	NM_001331037.1	8	c.540A>C	p.E180D		0,102	13,056	128	PASS		
5	65440251	C	T	SREK1	NM_001077199.2	1	c.47C>T	p.T16I	rs201205648	0,157	18,055	115	PASS		
5	77423975	T	C	AP3B1	NM_001271769.1	17	c.1700A>G	p.H567R		0,298	14,006	47	PASS		
5	102326053	C	T	PAM	NM_001319943.1	17	c.1615C>T	p.P539S		0,103	11,948	116	PASS		
5	138209144	A	G	LRRTM2	NM_015564.2	2	c.1106T>C	p.V369A		0,103	39,14	380	PASS		
5	139921839	G	A	ANKHD1-EIF4EBP3	NM_020690.5	34	c.7652G>A	p.R2551Q	rs190820379	0,114	12,996	114	PASS		
5	139921856	C	T	ANKHD1-EIF4EBP3	NM_020690.5	34	c.7669C>T	p.P2557S		0,114	11,97	105	PASS		
5	139947173	T	C	SLC35A4	NM_080670.3	3	c.419T>C	p.V140A	rs748115397	0,113	15,029	133	PASS		
5	140051326	T	C	DND1	NM_194249.2	4	c.614A>G	p.H205R		0,2	17	85	PASS		
5	140174848	C	T	PCDHA2	NM_018905.2	1	c.299C>T	p.A100V	rs376518025	0,108	27,108	251	PASS	COSM1486354	Breast carcinoma (1) Gastric adenocarcinoma (1) Glioblastoma (1)
5	140482506	G	A	PCDHB3	NM_018937.4	1	c.2273G>A	p.G758D	rs202125784	0,112	29,008	259	PASS		
5	141035819	G	A	ARAP3	NM_022481.5	28	c.3814C>T	p.P1272S		0,102	12,954	127	PASS		
5	143586631	G	C	KCTD16	NM_020768.3	3	c.354G>C	p.L118F		0,115	10,005	87	PASS		
5	145719267	T	C	POU4F3	NM_002700.2	2	c.277T>C	p.S93P		0,171	20,007	117	PASS		
5	149429984	G	A	HMGXB3	NM_014983.2	19	c.3371G>A	p.R1124K		0,163	15,974	98	PASS		
5	156671385	C	G	ITK	NM_005546.3	13	c.1346C>G	p.T449S		0,104	13	125	PASS		
5	173317326	C	G	CPEB4	NM_030627.3	1	c.590C>G	p.A197G	rs760479707	0,138	11,04	80	PASS		

5	176396006	G	C	UIMC1	NM_001199297.2	7	c.750C>G	p.S250R	rs779047629	0,101	18,988	188	PASS		
6	10398690	T	C	TFAP2A	NM_001032280.2	7	c.1256A>G	p.N419S		0,167	23,046	138	PASS		
6	31795968	C	G	HSPA1B	NM_005346.4	1	c.241C>G	p.P81A		0,148	35,076	237	PASS		
6	32944041	G	A	BRD2	NM_001291986.1	7	c.265G>A	p.V89I	rs777979066	0,106	11,978	113	PASS		
6	43543531	T	C	XPO5	NM_020750.2	1	c.71A>G	p.N24S		0,143	20,02	140	PASS		
6	99848842	C	G	PNISR	NM_001322406.1	13	c.1992G>C	p.E664D		0,15	18	120	PASS		
6	131191157	C	T	EPB41L2	NM_001350299.1	17	c.2309G>A	p.S770N	rs149795029	0,135	19,035	141	PASS		
6	158924119	A	C	TULP4	NM_020245.4	13	c.3424A>C	p.T1142P		0,128	9,984	78	PASS		
6	158924126	G	T	TULP4	NM_020245.4	13	c.3431G>T	p.G1144V	rs751825544	0,125	10	80	PASS		
6	160188054	G	A	ACAT2	NM_001303253.1	3	c.295G>A	p.V99I		0,169	21,97	130	PASS		
6	160188055	T	C	ACAT2	NM_001303253.1	3	c.296T>C	p.V99A		0,178	22,962	129	PASS		
6	166779513	G	A	MPC1	NM_001270879.1	5	c.125C>T	p.A42V		0,136	17,952	132	PASS		
7	18633622	G	A	HDAC9	NM_001321868.1	7	c.691G>A	p.A231T		0,117	10,998	94	PASS		
7	18633623	C	G	HDAC9	NM_001321868.1	7	c.692C>G	p.A231G	rs201268507	0,132	12,012	91	PASS		
7	28997486	G	C	TRIL	NM_014817.3	1	c.177C>G	p.H59Q		0,113	15,029	133	PASS		
7	40173870	C	A	MPLKIP	NM_138701.3	1	c.297G>T	p.Q99H	rs867863192	0,311	13,995	45	PASS		
7	42063170	C	G	GLI3	NM_000168.5	10	c.1394G>C	p.G465A		0,107	13,054	122	PASS		
7	86541489	T	G	KIAA1324L	NM_001142749.2	15	c.2068A>C	p.S690R		0,103	19,055	185	PASS		
7	94057006	A	T	COL1A2	NM_000089.3	49	c.3335A>T	p.Y1112F		0,105	17,955	171	PASS		
7	99627954	G	A	ZKSCAN1	NM_001346581.1	6	c.755G>A	p.S252N		0,119	19,04	160	PASS	COSM4779792	Hepatic and intrahepatic bile duct carcinoma (1)
7	99686934	G	C	COPS6	NM_006833.4	2	c.98G>C	p.C33S		0,128	23,04	180	PASS		
7	100189474	G	C	FBXO24	NM_033506.2	4	c.507G>C	p.M169I		0,111	10,989	99	PASS		
7	102116666	G	C	POLR2J	NM_006234.4	2	c.105C>G	p.I35M	rs138574638	0,111	32,079	289	PASS	COSM5427926	Acute myeloid leukemia, NOS (1)
7	106820424	A	G	HBP1	NM_012257.3	2	c.86A>G	p.N29S		0,109	15,042	138	PASS		
7	106836407	A	G	HBP1	NM_012257.3	9	c.1196A>G	p.N399S		0,108	19,98	185	PASS		
7	116955288	A	T	WNT2	NM_003391.2	3	c.425T>A	p.M142K		0,109	18,966	174	PASS		
7	116955319	C	A	WNT2	NM_003391.2	3	c.394G>T	p.V132L	rs769771769	0,104	19,032	183	PASS		
7	127014009	T	C	ZNF800	NM_176814.4	5	c.1381A>G	p.T461A	rs139385030	0,156	33,072	212	PASS		
7	138968316	A	G	UBN2	NM_173569.3	15	c.2665A>G	p.T889A		0,105	29,085	277	PASS		
7	143657979	T	G	OR2F1	NM_012369.2	1	c.916T>G	p.W306G		0,12	12	100	PASS		
8	30916058	A	G	WRN	NM_000553.4	2	c.95A>G	p.K32R	rs34477820	0,341	13,981	41	PASS		
8	38287284	C	T	FGFR1	NM_001174064.1	4	c.250G>A	p.V84M	rs755828990	0,112	9,968	89	PASS		
8	38287292	T	C	FGFR1	NM_001174064.1	4	c.242A>G	p.Q81R	rs773938208	0,154	14,014	91	PASS		
8	64098758	A	G	YTHDF3	NM_001277815.1	5	c.35A>G	p.Q12R		0,109	20,056	184	PASS		
8	67341967	C	A	RRS1	NM_015169.3	1	c.601C>A	p.L201M		0,121	14,036	116	PASS		
8	67341976	G	T	RRS1	NM_015169.3	1	c.610G>T	p.A204S		0,117	12,051	103	PASS		
8	75276576	T	C	GDAP1	NM_018972.2	6	c.1051T>C	p.F351L		0,104	16,952	163	PASS		
8	77617485	A	C	ZFHX4	NM_024721.4	2	c.1162A>C	p.T388P		0,176	22	125	PASS		
8	87570561	C	T	CPNE3	NM_003909.4	17	c.1537C>T	p.P513S		0,128	16	125	PASS	COSM1673994	Malignant melanoma of skin (1)

8	106813556	A	G	ZFPM2	NM_001362837.1	8	c.850A>G	p.T284A		0,105	11,025	105	PASS		
8	124027760	C	T	DERL1	NM_024295.5	8	c.683G>A	p.R228K		0,122	11,956	98	PASS		
8	141930978	T	C	PTK2	NM_001352697.1	4	c.35A>G	p.K12R		0,107	16,05	150	PASS		
8	145772528	A	G	ARHGAP39	NM_001308207.1	6	c.1942T>C	p.Y648H		0,124	14,012	113	PASS		
9	8449785	T	C	PTPRD	NM_002839.3	34	c.3928A>G	p.I1310V		0,147	22,932	156	PASS		
9	35563282	A	G	FAM166B	NM_001164310.2	2	c.167T>C	p.V56A		0,121	16,94	140	PASS		
9	36357882	T	G	RNF38	NM_194328.2	5	c.379A>C	p.I127L		0,118	10,03	85	PASS		
9	91083304	G	T	SPIN1	NM_006717.2	5	c.373G>T	p.D125Y		0,211	16,036	76	PASS		
9	94486962	T	A	ROR2	NM_004560.3	9	c.1814A>T	p.Y605F		0,122	17,934	147	PASS		
9	94488964	T	G	ROR2	NM_001318204.1	8	c.1211A>C	p.H404P		0,133	9,975	75	PASS		
9	94488970	T	A	ROR2	NM_001318204.1	8	c.1205A>T	p.Q402L		0,118	10,03	85	PASS	COSM4931542	Hepatocellular carcinoma (1)
9	94488973	G	A	ROR2	NM_001318204.1	8	c.1202C>T	p.S401L	rs752218712	0,131	11,004	84	PASS		
9	94489014	T	C	ROR2	NM_004560.3	8	c.1195A>G	p.S399G		0,159	13,038	82	PASS		
9	106880516	C	G	SMC2	NM_001042550.1	15	c.1856C>G	p.A619G	rs143609098	0,133	22,078	166	PASS		
9	106880551	G	A	SMC2	NM_001042550.1	15	c.1891G>A	p.D631N		0,118	20,06	170	PASS		
9	113449489	C	T	MUSK	NM_005592.3	3	c.299C>T	p.T100M	rs35142681	0,187	14,025	75	PASS		
9	117072898	A	G	COL27A1	NM_032888.3	61	c.5506A>G	p.I1836V		0,159	17,967	113	PASS		
9	118989729	C	G	PAPPA	NM_002581.4	6	c.2131C>G	p.H711D		0,122	20,008	164	PASS		
9	130511853	C	T	SH2D3C	NM_170600.2	5	c.776G>A	p.R259H	rs575748112	0,112	9,968	89	PASS	COSM4725571	Colorectal adenocarcinoma (1)
9	131258486	T	C	ODF2	NM_001351580.1	19	c.2063T>C	p.V688A		0,14	24,08	172	PASS		
9	131258490	T	G	ODF2	NM_001351580.1	19	c.2067T>G	p.F689L		0,139	24,047	173	PASS		
9	131260720	A	G	ODF2	NM_001351580.1	20	c.2182A>G	p.I728V	rs769214843	0,136	11,968	88	PASS		
9	131260768	T	G	ODF2	NM_001351580.1	20	c.2230T>G	p.S744A		0,125	10	80	PASS		
9	132400637	T	G	ASB6	NM_017873.3	6	c.698A>C	p.Q233P		0,166	27,058	163	PASS		
9	132400648	T	C	ASB6	NM_177999.2	5	c.578A>G	p.K193R		0,155	26,97	174	PASS		
9	134136697	G	C	FAM78A	NM_033387.3	2	c.364C>G	p.Q122E		0,104	9,984	96	PASS		
9	138774783	A	C	CAMSAP1	NM_015447.3	2	c.302T>G	p.V101G		0,121	11,011	91	PASS		
10	21804911	T	C	SKIDA1	NM_207371.3	4	c.1841A>G	p.N614S		0,14	42,14	301	PASS		
10	24834873	T	G	KIAA1217	NM_019590.4	21	c.5452T>G	p.S1818A	rs750845049	0,113	15,933	141	PASS		
10	64575717	T	G	EGR2	NM_000399.3	1	c.73A>C	p.I25L		0,189	10,017	53	PASS		
10	64575726	A	G	EGR2	NM_000399.3	1	c.64T>C	p.S22P		0,231	12,012	52	PASS		
10	100995440	C	G	HPSE2	NM_001166246.1	1	c.120G>C	p.Q40H		0,114	12,996	114	PASS		
10	100995444	G	A	HPSE2	NM_001166246.1	1	c.116C>T	p.S39F		0,132	13,992	106	PASS		
10	101657987	C	T	DNMBP	NM_015221.3	9	c.2776G>A	p.V926I		0,114	12,996	114	PASS		
10	103898476	G	C	PPRC1	NM_015062.4	3	c.443G>C	p.S148T	rs749339735	0,105	30,975	295	PASS		
10	123325182	A	G	FGFR2	NM_022970.3	3	c.146T>C	p.V49A		0,122	23,058	189	PASS		
10	123353298	C	A	FGFR2	NM_022970.3	2	c.34G>T	p.V12L	rs143978938	0,181	13,032	72	PASS		
10	131557522	G	A	MGMT	NM_002412.4	4	c.424G>A	p.V142M		0,165	33,99	206	PASS		
10	131557523	T	C	MGMT	NM_002412.4	4	c.425T>C	p.V142A		0,167	34,068	204	PASS		
10	131557525	A	G	MGMT	NM_002412.4	4	c.427A>G	p.I143V		0,165	33	200	PASS		

11	239020	C	G	PSMD13	NM_002817.3	2	c.118C>G	p.Q40E		0,107	42,051	393	PASS		
11	13398236	T	C	ARNTL	NM_001351804.1	16	c.1372T>C	p.S458P		0,116	9,976	86	PASS		
11	14284276	C	G	SPON1	NM_006108.3	15	c.2014C>G	p.P672A	rs373661458	0,143	17,017	119	PASS		
11	36300145	G	A	COMMD9	NM_001307937.1	4	c.172C>T	p.L58F		0,141	10,998	78	PASS		
11	36300147	C	T	COMMD9	NM_001307937.1	4	c.170G>A	p.R57H	rs767617802	0,137	10,001	73	PASS	COSM4032601	Gastric adenocarcinoma (1)
11	47611407	G	C	C1QTNF4	NM_031909.2	2	c.956C>G	p.A319G		0,144	14,976	104	PASS		
11	56380715	T	G	OR5M1	NM_001004740.1	1	c.264A>C	p.E88D		0,11	16,94	154	PASS		
11	57427063	A	G	CLP1	NM_006831.2	2	c.115A>G	p.T39A	rs548787604	0,111	29,97	270	PASS		
11	62297773	A	C	AHNAK	NM_001620.2	5	c.4116T>G	p.D1372E		0,105	47,775	455	PASS		
11	62416921	C	A	INTS5	NM_030628.1	2	c.631G>T	p.A211S		0,127	20,955	165	PASS		
11	63883968	G	T	FLRT1	NM_013280.4	2	c.229G>T	p.A77S	rs770193280	0,104	22,048	212	PASS		
11	67132623	C	T	CLCF1	NM_013246.2	3	c.662G>A	p.G221E		0,107	13,054	122	PASS		
11	76814230	A	G	OMP	NM_006189.1	1	c.345A>G	p.I115M		0,126	14,994	119	PASS		
11	77301384	C	T	AQP11	NM_173039.2	1	c.347C>T	p.T116M		0,106	22,896	216	PASS		
11	94113625	C	T	GPR83	NM_016540.3	4	c.962G>A	p.R321H	rs145628763	0,102	18,054	177	PASS	COSM933476	Endometrial carcinoma (1) Glioblastoma (1)
11	111630571	C	G	PPP2R1B	NM_002716.4	5	c.644G>C	p.S215T		0,135	22,95	170	PASS		
11	118778288	G	T	BCL9L	NM_182557.2	3	c.436C>A	p.R146S	rs758711667	0,163	24,939	153	PASS		
11	118940999	T	C	VPS11	NM_001290185.1	4	c.497T>C	p.L166P		0,126	34,02	270	PASS		
11	118981313	G	A	C2CD2L	NM_014807.4	3	c.493G>A	p.V165I		0,157	10,99	70	PASS		
11	119027109	A	G	ABCG4	NM_022169.4	7	c.757A>G	p.I253V		0,104	9,984	96	PASS		
11	120351030	C	G	ARHGEF12	NM_015313.2	38	c.4128C>G	p.D1376E	rs773749077	0,119	14,042	118	PASS		
11	124489562	G	A	PANX3	NM_052959.2	4	c.910G>A	p.V304I		0,115	60,95	530	PASS		
12	319080	A	T	SLC6A12	NM_003044.4	4	c.73T>A	p.L25M		0,162	16,038	99	PASS		
12	6730087	T	G	LPAR5	NM_020400.5	2	c.328A>C	p.I110L		0,146	15,038	103	PASS		
12	6730126	T	A	LPAR5	NM_020400.5	2	c.289A>T	p.T97S		0,135	12,015	89	PASS		
12	8800698	T	C	MFAP5	NM_003480.3	10	c.511A>G	p.N171D		0,114	25,992	228	PASS		
12	8800713	C	T	MFAP5	NM_003480.3	10	c.496G>A	p.D166N		0,119	30,94	260	PASS		
12	8800716	C	T	MFAP5	NM_003480.3	10	c.493G>A	p.V165M		0,129	33,927	263	PASS		
12	10862510	T	C	YBX3	NM_003651.4	6	c.777A>G	p.I259M		0,156	14,976	96	PASS		
12	10862647	T	C	YBX3	NM_003651.4	6	c.640A>G	p.R214G		0,273	15,015	55	PASS		
12	10862653	T	C	YBX3	NM_003651.4	6	c.634A>G	p.T212A		0,267	16,02	60	PASS		
12	10862663	G	C	YBX3	NM_003651.4	6	c.624C>G	p.D208E		0,274	16,988	62	PASS		
12	12300362	C	T	LRP6	NM_002336.2	15	c.3335G>A	p.R1112K		0,135	12,015	89	PASS		
12	19443671	A	G	PLEKHA5	NM_001143821.2	13	c.1906A>G	p.I636V		0,132	10,032	76	PASS		
12	19646813	A	G	AEBP2	NM_153207.4	4	c.1067A>G	p.Q356R		0,104	11,96	115	PASS		
12	49392890	G	A	DDN	NM_015086.1	1	c.181C>T	p.H61Y	rs371650873	0,164	10,988	67	PASS		
12	49392902	A	T	DDN	NM_015086.1	1	c.169T>A	p.F57I		0,134	10,988	82	PASS		
12	49392911	G	A	DDN	NM_015086.1	1	c.160C>T	p.P54S		0,147	14,994	102	PASS		
12	49438695	A	C	KMT2D	NM_003482.3	19	c.4795T>G	p.L1599V		0,224	10,976	49	PASS		
12	52758792	A	C	KRT85	NM_002283.3	2	c.583T>G	p.S195A		0,267	12,015	45	PASS		

12	53613791	C	T	RARG	NM_001042728.2	1	c.94G>A	p.G32S		0,236	12,98	55	PASS		
12	53613795	G	A	RARG	NM_001243732.1	1	c.206C>T	p.P69L		0,236	12,98	55	PASS		
12	53613807	C	T	RARG	NM_001243732.1	1	c.194G>A	p.C65Y		0,182	16,016	88	PASS		
12	57652780	G	C	R3HDM2	NM_001351207.1	23	c.2320C>G	p.P774A		0,136	14,008	103	PASS		
12	65237233	A	C	TBC1D30	NM_015279.1	8	c.1006A>C	p.N336H		0,12	9,96	83	PASS		
12	65237235	T	G	TBC1D30	NM_015279.1	8	c.1008T>G	p.N336K		0,125	10	80	PASS		
12	70760666	A	C	KCNMB4	NM_014505.5	1	c.152A>C	p.E51A		0,124	26,908	217	PASS		
12	74932085	G	C	ATXN7L3B	NM_001136262.1	1	c.193G>C	p.E65Q	rs977284774	0,109	22,999	211	PASS		
12	102054963	C	A	MYBPC1	NM_002465.3	20	c.1955C>A	p.T652N		0,14	16,94	121	PASS		
12	108138328	T	C	PRDM4	NM_012406.3	7	c.1387A>G	p.I463V		0,177	16,992	96	PASS		
12	112641543	T	C	HECTD4	NM_001109662.3	54	c.7901A>G	p.N2634S		0,107	18,083	169	PASS		
12	121134249	A	G	MLEC	NM_001303628.1	3	c.545A>G	p.H182R		0,167	15,03	90	PASS		
12	125397065	G	A	UBC	NM_021009.6	2	c.1253C>T	p.P418L		0,111	108,447	977	PASS		
12	125397066	G	C	UBC	NM_021009.6	2	c.1252C>G	p.P418A		0,107	106,679	997	PASS		
13	21436926	T	C	XPO4	NM_022459.4	3	c.247A>G	p.I83V		0,104	14,04	135	PASS		
13	33629447	A	G	KL	NM_004795.3	3	c.1594A>G	p.I532V	rs371650258	0,118	19,942	169	PASS		
13	77700596	T	G	MYCBP2	NM_015057.4	53	c.7741A>C	p.M2581L	rs762244520	0,12	9,96	83	PASS		
13	77700601	T	C	MYCBP2	NM_015057.4	53	c.7736A>G	p.Q2579R		0,123	9,963	81	PASS		
13	77844544	T	C	MYCBP2	NM_015057.4	6	c.1075A>G	p.I359V	rs762953485	0,141	29,046	206	PASS		
13	99037961	A	G	FARP1	NM_005766.3	8	c.652A>G	p.I218V		0,105	26,88	256	PASS		
13	99037963	T	G	FARP1	NM_005766.3	8	c.654T>G	p.I218M		0,106	27,984	264	PASS		
13	110438238	C	T	IRS2	NM_003749.2	1	c.163G>A	p.A55T		0,131	12,969	99	PASS		
14	51239088	A	C	NIN	NM_020921.3	9	c.912T>G	p.H304Q		0,124	15,004	121	PASS		
14	54417573	T	C	BMP4	NM_001347916.1	4	c.404A>G	p.N135S		0,117	14,04	120	PASS		
14	70634002	C	T	SLC8A3	NM_183002.2	2	c.1138G>A	p.A380T	rs144693485	0,118	18,998	161	PASS	COSM109316	Malignant melanoma of skin (1)
14	75265858	G	A	YLPM1	NM_019589.2	5	c.3858G>A	p.M1286I		0,149	25,032	168	PASS		
14	102482274	C	A	DYNC1H1	NM_001376.4	36	c.7324C>A	p.Q2442K	rs866372089	0,132	25,08	190	PASS		
15	34355387	A	G	CHRM5	NM_001320917.1	2	c.469A>G	p.I157V		0,109	22,018	202	PASS		
15	41030727	C	T	RMDN3	NM_001323895.1	8	c.632G>A	p.R211K		0,11	11	100	PASS		
15	41030730	T	G	RMDN3	NM_001323895.1	8	c.629A>C	p.Q210P		0,108	11,016	102	PASS		
15	41030731	G	A	RMDN3	NM_001323895.1	8	c.628C>T	p.Q210*		0,111	10,989	99	PASS		
15	42702148	C	A	CAPN3	NM_000070.2	19	c.2070C>A	p.H690Q	rs560701241	0,12	48	400	PASS		
15	58306424	T	C	ALDH1A2	NM_001206897.1	3	c.110A>G	p.Y37C	rs141412807	0,111	16,983	153	PASS		
15	64983739	A	C	OAZ2	NM_002537.3	2	c.72T>G	p.I24M		0,197	13,002	66	PASS	COSM5983042	Head and neck tumors (1)
15	65822977	A	C	HACD3	NM_016395.2	1	c.8A>C	p.*3Sext*5		0,164	11,972	73	PASS		
15	65822985	T	C	HACD3	NM_016395.2	1	c.16T>C	p.W6R		0,174	12,006	69	PASS		
15	73045064	C	T	ADPGK	NM_031284.4	7	c.1109G>A	p.S370N		0,11	17,05	155	PASS		
15	73045068	T	C	ADPGK	NM_031284.4	7	c.1105A>G	p.K369E		0,102	16,014	157	PASS		
15	74177370	A	G	TBC1D21	NM_153356.2	6	c.505A>G	p.M169V		0,144	13,968	97	PASS		
15	76578058	T	C	ETFA	NM_000126.3	7	c.584A>G	p.E195G		0,119	29,036	244	PASS		

15	76578065	G	A	ETFA	NM_000126.3	7	c.577C>T	p.P193S		0,119	25,942	218	PASS
15	81648802	C	A	TMC3	NM_001080532.2	8	c.877G>T	p.V293L		0,207	18,009	87	PASS
15	83561526	T	C	HOMER2	NM_199330.2	2	c.73A>G	p.M25V	rs370099182	0,109	32,918	302	PASS
15	83926457	T	G	BNC1	NM_001301206.1	5	c.2701A>C	p.I901L	rs747965293	0,101	24,038	238	PASS
15	91485771	G	C	UNC45A	NM_001039675.1	10	c.747G>C	p.M249I	rs141749499	0,192	24	125	PASS
16	3832691	G	C	CREBBP	NM_004380.2	6	c.1567C>G	p.P523A	rs773829215	0,102	12,036	118	PASS
16	20926980	A	G	LYRM1	NM_001302836.1	4	c.103A>G	p.K35E		0,114	14,022	123	PASS
16	20970684	C	T	DNAH3	NM_001347886.1	54	c.10505G>A	p.R3502K		0,118	16,048	136	PASS
16	24950851	A	C	ARHGAP17	NM_001006634.2	17	c.1558T>G	p.S520A	rs899243714	0,143	12,012	84	PASS
16	29809718	G	A	KIF22	NM_001256270.1	3	c.86G>A	p.R29K	rs749908842	0,153	13,005	85	PASS
16	29809734	C	A	KIF22	NM_001256270.1	3	c.102C>A	p.D34E		0,115	11,96	104	PASS
16	29809735	A	G	KIF22	NM_001256270.1	3	c.103A>G	p.I35V		0,135	14,04	104	PASS
16	29809742	C	T	KIF22	NM_001256270.1	3	c.110C>T	p.A37V	rs746625772	0,185	22,015	119	PASS
16	30129068	C	A	MAPK3	NM_002746.2	5	c.698G>T	p.C233F		0,106	11,978	113	PASS
16	30376861	G	C	TBC1D10B	NM_015527.3	2	c.1011C>G	p.D337E		0,154	43,12	280	PASS
16	67286712	C	T	SLC9A5	NM_001323973.1	2	c.455C>T	p.A152V		0,105	9,975	95	PASS
16	68309086	C	A	SLC7A6	NM_001076785.2	4	c.457C>A	p.Q153K		0,182	14,014	77	PASS
16	68404842	T	C	SMPD3	NM_018667.3	3	c.1243A>G	p.I415V		0,133	25,935	195	PASS
16	68404863	G	A	SMPD3	NM_018667.3	3	c.1222C>T	p.L408F		0,128	24,064	188	PASS
16	71884793	G	A	ATXN1L	NM_001137675.3	3	c.1150G>A	p.A384T		0,111	10,989	99	PASS
16	71884803	C	T	ATXN1L	NM_001137675.3	3	c.1160C>T	p.A387V		0,108	10,044	93	PASS
16	75662559	T	C	KARS	NM_001130089.1	14	c.1687A>G	p.T563A		0,132	24,948	189	PASS
17	5286525	C	G	RABEP1	NM_004703.5	18	c.2596C>G	p.H866D	rs3026116	0,174	29,928	172	PASS
17	7473694	G	A	SENP3	NM_015670.5	8	c.1363G>A	p.V455I	rs760786721	0,122	24,034	197	PASS
17	26982425	A	T	SDF2	NM_006923.3	2	c.228T>A	p.S76R		0,111	12,987	117	PASS
17	26982426	C	G	SDF2	NM_006923.3	2	c.227G>C	p.S76T		0,113	14,012	124	PASS
17	27240093	C	G	PHF12	NM_001033561.1	9	c.1496G>C	p.G499A		0,11	14,96	136	PASS
17	27251133	C	T	PHF12	NM_001033561.1	4	c.509G>A	p.S170N	rs747408885	0,146	22,922	157	PASS
17	27614402	C	T	NUFIP2	NM_020772.2	2	c.610G>A	p.G204S	rs143075808	0,12	34,92	291	PASS
17	28545194	A	C	SLC6A4	NM_001045.5	5	c.640T>G	p.S214A		0,118	10,03	85	PASS
17	28545294	C	T	SLC6A4	NM_001045.5	5	c.540G>A	p.M180I		0,177	10,974	62	PASS
17	33353445	A	G	RFFL	NM_001017368.1	2	c.128T>C	p.L43S		0,146	21,024	144	PASS
17	36091657	C	T	HNF1B	NM_000458.3	4	c.974G>A	p.S325N	rs794727624	0,105	11,97	114	PASS
17	36909509	C	T	PSMB3	NM_002795.3	2	c.110C>T	p.T37M	rs748162148	0,117	49,14	420	PASS
17	37687336	C	T	CDK12	NM_016507.3	14	c.4240C>T	p.P1414S		0,14	19,04	136	PASS
17	37687363	G	T	CDK12	NM_016507.3	14	c.4267G>T	p.A1423S	rs201512860	0,119	15,946	134	PASS
17	38506158	A	C	RARA	NM_001024809.3	3	c.435A>C	p.E145D	rs762461183	0,179	34,905	195	PASS
17	44249377	C	A	KANSL1	NM_001193466.1	2	c.133G>T	p.A45S		0,105	25,095	239	PASS
17	53342865	C	A	HLF	NM_002126.4	1	c.20C>A	p.P7Q		0,213	10,011	47	PASS
17	54558153	C	A	ANKFN1	NM_153228.2	16	c.2074C>A	p.Q692K		0,142	23,998	169	PASS
17	56355351	C	G	MPO	NM_000250.1	7	c.1041G>C	p.E347D		0,106	20,988	198	PASS

17	57057871	G	A	PPM1E	NM_014906.4	7	c.1747G>A	p.A583T		0,119	23,919	201	PASS		
17	61864533	A	G	DDX42	NM_007372.3	3	c.124A>G	p.T42A		0,134	15,008	112	PASS		
17	62130282	T	C	ERN1	NM_001433.4	17	c.2111A>G	p.K704R		0,104	26,936	259	PASS		
17	72846436	C	T	GRIN2C	NM_000835.4	6	c.1400G>A	p.R467K		0,131	28,951	221	PASS		
17	74136410	G	T	FOXJ1	NM_001454.3	2	c.67C>A	p.L23M		0,123	9,963	81	PASS		
17	76046675	A	G	TNRC6C	NM_001142640.1	4	c.1532A>G	p.N511S		0,143	10,01	70	PASS		
17	76046707	G	A	TNRC6C	NM_001142640.1	4	c.1564G>A	p.G522S		0,145	11,02	76	PASS		
17	79684831	C	T	SLC25A10	NM_001270953.1	9	c.562C>T	p.P188S	rs760635043	0,15	12	80	PASS		
17	79684846	G	C	SLC25A10	NM_001270953.1	9	c.577G>C	p.G193R		0,174	16,008	92	PASS		
18	2674053	A	G	SMCHD1	NM_015295.2	5	c.547A>G	p.I183V	rs754881998	0,11	13,97	127	PASS		
18	29784275	T	G	MEP1B	NM_005925.2	7	c.499T>G	p.S167A		0,138	11,04	80	PASS		
18	47363917	A	G	MYO5B	NM_001080467.2	37	c.5108T>C	p.V1703A	rs138128932	0,131	25,938	198	PASS	COSM473883	Head and neck tumors (10) Malignant melanoma of skin (3) Clear cell renal cell carcinoma (RCC) (2) Colorectal adenocarcinoma (2) Endometrial carcinoma (2) Prostatic adenocarcinoma (acinar) (2) Basal cell carcinoma of skin (1) Extrahepatic bile duct carcinoma (1) Glioblastoma (1) Pulmonary squamous cell carcinoma (SCC) (1) Thymoma (1) Thyroid carcinoma (1)
18	56587312	T	C	ZNF532	NM_018181.5	4	c.1793T>C	p.I598T		0,131	25,021	191	PASS		
18	56615376	T	C	ZNF532	NM_018181.5	7	c.2783T>C	p.I928T		0,107	36,915	345	PASS		
18	56615380	A	C	ZNF532	NM_018181.5	7	c.2787A>C	p.E929D	rs752991034	0,11	37,84	344	PASS	COSM2881024	Head and neck tumors (1)
18	60237338	G	A	ZCCHC2	NM_017742.5	12	c.1849G>A	p.V617M		0,136	14,96	110	PASS		
18	76755097	T	G	SALL3	NM_171999.3	2	c.3106T>G	p.L1036V		0,107	17,013	159	PASS		
18	76755115	G	A	SALL3	NM_171999.3	2	c.3124G>A	p.A1042T	rs757315250	0,113	18,08	160	PASS		
19	2717513	C	T	DIRAS1	NM_145173.3	2	c.292G>A	p.G98R		0,106	22,896	216	PASS		
19	2717520	C	A	DIRAS1	NM_145173.3	2	c.285G>T	p.E95D		0,116	25,056	216	PASS		
19	10370304	C	T	MRPL4	NM_015956.2	9	c.751C>T	p.H251Y		0,259	15,022	58	PASS		
19	18245714	G	A	MAST3	NM_015016.1	16	c.1705G>A	p.V569I	rs766369438	0,186	21,018	113	PASS		
19	30936097	C	A	ZNF536	NM_001352260.1	2	c.1628C>A	p.P543Q		0,134	17,018	127	PASS		
19	31768282	A	C	TSHZ3	NM_020856.3	2	c.2417T>G	p.V806G		0,147	21,021	143	PASS		
19	33490564	G	T	RHPN2	NM_033103.4	10	c.1153C>A	p.L385I	rs147870656	0,165	17,985	109	PASS	COSM1129904	Soft tissue hemangioblastoma (2) Fibrillary diffuse astrocytoma (1) Glioblastoma (1) Head and neck tumors (1) Prostatic adenocarcinoma (acinar) (1)

19	41596333	T	A	CYP2A13	NM_000766.4	4	c.518T>A	p.F173Y		0,153	20,043	131	PASS		
19	44653044	T	G	ZNF234	NM_006630.2	4	c.136T>G	p.S46A		0,142	21,016	148	PASS		
19	47995366	T	C	NAPA	NM_003827.3	8	c.572A>G	p.N191S		0,204	9,996	49	PASS		
19	54964770	G	A	LENG8	NM_052925.3	5	c.361G>A	p.G121S	rs754237955	0,118	14,042	119	PASS	COSM1001141	Endometrial carcinoma (1)
20	2840412	G	A	VPS16	NM_022575.3	2	c.101G>A	p.R34K		0,102	11,016	108	PASS		
20	3571875	A	G	ATRN	NM_139321.2	19	c.3244A>G	p.N1082D		0,131	12,969	99	PASS		
20	10620243	T	C	JAG1	NM_000214.3	26	c.3560A>G	p.N1187S	rs755420729	0,121	19,965	165	PASS		
20	10620250	G	C	JAG1	NM_000214.3	26	c.3553C>G	p.P1185A		0,116	17,98	155	PASS		
20	21494120	T	C	NKX2-2	NM_002509.3	1	c.188A>G	p.N63S	rs755667448	0,104	23,088	222	PASS		
20	31315727	C	T	COMMD7	NM_053041.2	3	c.214G>A	p.V72M	rs754807110	0,104	11,024	106	PASS	COSM2889467	Colorectal adenocarcinoma (1)
20	31315735	C	T	COMMD7	NM_053041.2	3	c.206G>A	p.R69K	rs140188407	0,115	12,995	113	PASS		
20	31315742	A	G	COMMD7	NM_053041.2	3	c.199T>C	p.S67P		0,11	12,98	118	PASS		
20	31315762	G	C	COMMD7	NM_053041.2	3	c.179C>G	p.T60S		0,113	12,995	115	PASS		
20	35219335	C	T	TGIF2	NM_001199514.1	3	c.215C>T	p.A72V		0,105	24,045	229	PASS		
20	36147384	A	G	BLCAP	NM_001167820.1	3	c.193T>C	p.C65R		0,128	12,032	94	PASS		
20	37356854	A	C	SLC32A1	NM_080552.2	2	c.1150A>C	p.I384L		0,102	14,994	147	PASS		
20	47592663	A	G	ARFGEF2	NM_006420.2	14	c.1885A>G	p.T629A	rs143717062	0,117	18,954	162	PASS		
20	47881287	T	G	ZNFX1	NM_021035.2	5	c.2117A>C	p.N706T		0,129	14,964	116	PASS		
20	48503359	G	A	SLC9A8	NM_001260491.1	15	c.1610G>A	p.R537Q	rs373124036	0,108	17,064	158	PASS		
20	55088433	C	G	RTF2	NM_001283035.1	7	c.630C>G	p.D210E	rs552833396	0,112	12,992	116	PASS		
20	55088434	G	A	RTF2	NM_001283035.1	7	c.631G>A	p.V211M	rs758627888	0,117	14,04	120	PASS		
20	61340903	C	T	NTSR1	NM_002531.2	1	c.344C>T	p.T115I	rs766063233	0,154	10,01	65	PASS		
21	32638904	T	A	TIAM1	NM_001353693.1	5	c.385A>T	p.T129S		0,117	16,965	145	PASS		
21	32638949	T	C	TIAM1	NM_001353693.1	5	c.340A>G	p.S114G		0,101	15,958	158	PASS		
21	47966843	A	G	DIP2A	NM_001353942.1	21	c.2413A>G	p.I805V	rs201130788	0,102	12,036	118	PASS		
22	28394594	C	A	TTC28	NM_001145418.1	16	c.5053G>T	p.A1685S		0,118	10,03	85	PASS		
22	37771235	T	G	ELFN2	NM_052906.4	3	c.340A>C	p.K114Q		0,107	14,017	131	PASS		
22	38508263	T	C	PLA2G6	NM_001349867.1	18	c.1792A>G	p.T598A		0,119	14,042	118	PASS		
22	38508293	T	A	PLA2G6	NM_001349867.1	18	c.1762A>T	p.T588S		0,129	10,965	85	PASS		
22	42606088	C	A	TCF20	NM_005650.3	2	c.5224G>T	p.A1742S		0,155	17,05	110	PASS		
22	50832537	T	A	PPP6R2	NM_001351643.1	4	c.200T>A	p.L67Q		0,162	11,988	74	PASS		
X	23411270	G	C	PTCHD1	NM_173495.2	3	c.1635G>C	p.Q545H		0,125	37,875	303	PASS		
X	23411284	G	A	PTCHD1	NM_173495.2	3	c.1649G>A	p.S550N		0,111	34,965	315	PASS		
X	32834738	T	G	DMD	NM_004010.3	6	c.8A>C	p.N3T		0,111	19,98	180	PASS		
X	47511536	T	C	UXT	NM_153477.2	5	c.400A>G	p.N134D		0,116	12,992	112	PASS		
X	48458961	A	G	WDR13	NM_001166426.2	4	c.502A>G	p.S168G		0,184	18,952	103	PASS		
X	51639847	G	A	MAGED1	NM_001005333.1	5	c.1264G>A	p.V422I		0,127	13,97	110	PASS		
X	51639865	C	A	MAGED1	NM_001005333.1	5	c.1282C>A	p.L428M		0,121	12,947	107	PASS		
X	54013546	C	T	PHF8	NM_015107.2	16	c.1960G>A	p.V654I		0,126	13,986	111	PASS		
X	68748896	C	A	FAM155B	NM_015686.2	2	c.922C>A	p.R308S		0,158	12,008	76	PASS		

X	68748897	G	A	FAM155B	NM_015686.2	2	c.923G>A	p.R308H		0,156	12,012	77	PASS	COSM4682636	Colorectal adenocarcinoma (1)
X	70350062	C	A	MED12	NM_005120.2	28	c.4045C>A	p.Q1349K		0,132	13,992	106	PASS		
X	70367643	A	C	NLGN3	NM_181303.1	2	c.44A>C	p.K15T		0,171	11,97	70	PASS		
X	70596937	G	A	TAF1	NM_001286074.1	5	c.670G>A	p.E224K		0,112	19,936	178	PASS		
X	71350691	G	A	RTL5	NM_001024455.3	1	c.700C>T	p.P234S		0,106	16,96	160	PASS		
X	71350757	G	A	RTL5	NM_001024455.3	1	c.634C>T	p.P212S		0,118	18,054	153	PASS		
X	105970239	G	C	RNF128	NM_194463.1	1	c.96G>C	p.Q32H		0,14	19,04	136	PASS		
X	109697810	G	A	RTL9	NM_020769.2	3	c.3965G>A	p.S1322N		0,109	12,971	119	PASS		
X	109697818	C	G	RTL9	NM_020769.2	3	c.3973C>G	p.L1325V		0,134	15,008	112	PASS		
X	109697827	G	T	RTL9	NM_020769.2	3	c.3982G>T	p.A1328S		0,126	12,978	103	PASS		
X	109697858	G	A	RTL9	NM_020769.2	3	c.4013G>A	p.G1338E		0,141	10,998	78	PASS		
X	119694154	C	T	CUL4B	NM_003588.3	3	c.394G>A	p.A132T		0,156	19,032	122	PASS		
X	119694160	A	T	CUL4B	NM_003588.3	3	c.388T>A	p.F130I		0,153	16,983	111	PASS		
X	119694223	C	T	CUL4B	NM_003588.3	3	c.325G>A	p.A109T		0,148	19,98	135	PASS		
X	122536913	C	T	GRIA3	NM_000828.4	8	c.1148C>T	p.T383I	rs778109393	0,125	14	112	PASS	COSM1114262	Endometrial carcinoma (2)
X	122536919	G	A	GRIA3	NM_000828.4	8	c.1154G>A	p.G385E		0,116	12,992	112	PASS		
X	123518199	C	A	TENM1	NM_001163278.1	30	c.6582G>T	p.K2194N		0,102	46,206	453	PASS		
X	128709877	G	T	OCRL	NM_001318784.1	17	c.1720G>T	p.V574L		0,107	17,976	168	PASS		
X	129263974	T	C	AIFM1	NM_004208.3	15	c.1741A>G	p.I581V		0,11	10,01	91	PASS		
X	131205219	T	G	STK26	NM_016542.3	8	c.906T>G	p.D302E		0,104	14,976	144	PASS		
X	148693040	G	A	TMEM185A	NM_001282302.1	3	c.145C>T	p.H49Y		0,117	12,987	111	PASS		
X	154225338	A	G	F8	NM_000132.3	3	c.298T>C	p.Y100H		0,127	19,05	150	PASS		
X	155003786	G	T	SPRY3	NM_005840.2	2	c.253G>T	p.A85S	rs780957634	0,124	23,932	193	PASS		

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