Table S1

ITEM TO CHECK	IMPORTANCE	Comments
EXPERIMENTAL DESIGN		
Definition of experimental and control groups	E	Table 1
Number within each group	E	4 Good responders & 5 Poor responders. Each patient with both normal and tumour tissue.
Assay carried out by core lab or investigator's lab?	D	Core lab
SAMPLE		
Description	E	FFPE tissues
Volume/mass of sample processed	D	10 to 30µm
Microdissection or macrodissection	E	microdissection
Processing procedure	E	Materials and Methods
Sample storage conditions and duration (especially for FFPE samples)	E	Stored at Room Temperature
NUCLEIC ACID EXTRACTION		
Procedure and/or instrumentation	E	Materials and Methods
Name of kit and details of any modifications	E	Quick-DNA/RNA™ FFPE Kit (Zymo Research)
Details of DNase or RNAse treatment	E	on-column DNase I treatment (Quick-DNA/RNA™ FFPE Kit)
Contamination assessment (DNA or RNA)	E	DNA contamination assessed by qPCR without RT step.
Nucleic acid quantification	E	Qubit RNA High Sensitivity Kit
Instrument and method	E	Qubit 4 Fluorometer
Purity (A260/A280)	D	Assessed by NanoDrop 8000 spectrophotometer
RNA integrity method/instrument	E	Agilent High Sensitivity ScreenTape and 4200 TapeStation Syste
RIN/RQI or Cq of 3' and 5' transcripts	E	RIN values of RNA samples and Cq values of 3' and 5' transcriptsdetailed in Table S1
Inhibition testing (Cq dilutions, spike or other)	E	Inhibition assessed by SPUD qPCR assay, Table S2
REVERSE TRANSCRIPTION		
Complete reaction conditions	E	cDNA was synthesized from FFPE total RNA using the Maxima H Minus cDNA Synthesis MasterMix with dsDNase Kit (Thermo Fisher) according to the manufacturer's protocol. All samples were prepared in 200 µL PCR-strip tubes. Approximately 100 ng of RNA was mixed with 1 µL of 10x dsDNase Buffer and 1 µL of dsDNase and diluted up to 10 µL with Nuclease-free water. Each sample was mixed gently and centrifuged briefly. All samples were then incubated in the Applied Biosystems 2720 Thermal Cycler (Thermo Fisher) at 37 °C for 2 min and stored on ice. Each dsDNase-treated RNA sample was then mixed with 4 µL of 5x Maxima cDNA H Minus Synthesis MasterMix and 6 µL of Nuclease-free water and incubated in a Applied Biosystems 2720 Thermal Cycler (Thermo Fisher) at the following settings: 10 min at 25 °C for priming, 15 min at 50 °C for reverse transcription to occur, 5 min at 85 °C for inactivation of reverse transcriptase. No-RT control samples were created at the same time in which RNA from the each FFPE sample was mixed with Maxima No RT Control mastermix containing no Maxima H Minus Reverse Transcriptase. A No template control (NTC) reaction was also included in which reverse trancription was carried out without any RNA template.
Amount of RNA and reaction volume	E	100 ng of RNA in a 20 µL of volume per sample.
Priming oligonucleotide (if using GSP) and concentration	E	No GSP was used. The Maxima H Minus cDNA Synthesis Master Mix used in this study contains oligo(dT) and random hexamers for priming cDNA synthesis.
Reverse transcriptase and concentration	E	Maxima H Minus cDNA Synthesis MasterMix with dsDNase Kit (Thermo Fisher)
Temperature and time	E	Specified in 'Complete reaction conditions'
Manufacturer of reagents and catalogue numbers	D	
Cqs with and without RT	D*	In all experiments, no Cq values were obtained for samples without RT compared to samples with RT.
Storage conditions of cDNA	D	All cDNA samples were stored at -20 °C.
qPCR TARGET INFORMATION		
If multiplex, efficiency and LOD of each assay.	E	Not Applicable
Sequence accession number	E	**ABCB1:** NM_001348945.2; **CYP1B:** NM_000104.4
Location of amplicon	D	
Amplicon length	E	Table 2
In silico specificity screen (BLAST, etc)	E	Primer specificity confirmed b Primer-BLAST
Pseudogenes, retropseudogenes or other homologs?	D	
Sequence alignment	D	
Secondary structure analysis of amplicon	D	
Location of each primer by exon or intron (if applicable)	E	Not Applicable
What splice variants are targeted?	E	No splice variants were targeted.
qPCR OLIGONUCLEOTIDES		
Primer sequences	E	Table 2
Probe sequences	D**	Not Applicable
Location and identity of any modifications	E	None
Manufacturer of oligonucleotides	D	Integrated DNA Technologies
Purification method	D	Standard Desalting

qPCR PROTOCOL		
Complete reaction conditions	**E**	qPCR was performed in a total reaction volume of 10 µL consisting of 2 µl diluted preamplified cDNA as template, 5µL of 2x PowerUp SYBR Green I Mastermix (Thermo Fisher), and both the forward and reverse primers to a final concentration of 500 nM. NTC reactions were included in all assays as negative controls. Each reaction was run in triplicate. Reactions were performed on the QuantStudio 12K Flex Real-Time PCR System (Applied Biosystems) using the following cycling parameters: 50°C for 2 min; initial denaturation at 95°C for 2 min followed by 40 cycles of 95°C for 15 secs and 57°C for 1 min. A melt curve analysis was performed on all reactions at the end of the PCR run using default parameters. Amplification data were analyzed with Life Technologies QuantStudio 12K Flex Software v1.2.4, applying user-defined thresholds to obtain Cq-values. Outliers in technical replicate reactions, reactions that showed no amplification and reactions that showed multiple Tm peaks during melt curve analysis were removed from analysis. Data was finally exported into Excel spreadsheets for further analysis.
Reaction volume and amount of cDNA/DNA	**E**	10 µL reaction with 2 µL diluted preamplified cDNA
Primer, (probe), Mg++ and dNTP concentrations	**E**	500 nM each primer with PowerUp SYBR Green Master Mix (Thermo Fisher)
Polymerase identity and concentration	**E**	PowerUp SYBR Green Master Mix (Thermo Fisher)
Buffer/kit identity and manufacturer	**E**	PowerUp SYBR Green Master Mix (Thermo Fisher)
Exact chemical constitution of the buffer	D	PowerUp SYBR Green Master Mix (Thermo Fisher)
Additives (SYBR Green I, DMSO, etc.)	**E**	PowerUp SYBR Green Master Mix (Thermo Fisher)
Manufacturer of plates/tubes and catalog number	D	MicroAmp™ Optical 384-Well Reaction Plate with Barcode, Catalog number: 4326270
Complete thermocycling parameters	**E**	See 'Complete reaction conditions'
Reaction setup (manual/robotic)	D	Manual
Manufacturer of qPCR instrument	**E**	Applied Biosystems QuantStudio™ 12K Flex thermocycler
qPCR VALIDATION		
Specificity (gel, sequence, melt, or digest)	**E**	Confirmed by melt curve analysis (single peak) for each primer set and gel electrophoresis
For SYBR Green I, Cq of the NTC	**E**	Cq of NTC was 'undetermined'
Standard curves with slope and y-intercept	**E**	Available on request
PCR efficiency calculated from slope	**E**	ABCB1, E= 98.4%; CYP1B: E= 108.1%; GAPDH, E= 99.7%; HPRT, E=92.9%; HSPCB, E=103.9%
r2 of standard curve	**E**	> 0,98 for all assays
DATA ANALYSIS		
qPCR analysis program (source, version)	**E**	QuantStudio™ 12K Flex Software 1.5
Cq method determination	**E**	Automatic baseline setting and manual threshold setting
Outlier identification and disposition	**E**	A Cq value was discarded if the melt curve was inconsistent with other samples in the experiment.
Results of NTCs	**E**	No Cq values were assigned to NTC for all assays except for HSPCB where Cq for NTC was > 10 cycles away from the experimental samples
Justification of number and choice of reference genes	**E**	The stability of three reference genes: GAPDH, HPRT and HSPCB was evaluated using RefFinder. Both GAPDH and HSPCB were used to normalized the qPCR data.
Description of normalisation method	**E**	qPCR data were analyzed in Microsoft Excel using both GAPDH and HSPCB as normalization controls and the Pfaffl (Pfaffl, 2001) method to calculate relative expression.
Number and stage (RT or qPCR) of technical replicates	**E**	3 technical qPCR replicates
Repeatability (intra-assay variation)	E	Standard deviation of triplicates < 0.5
Statistical methods for result significance	**E**	A significance level of p<0.05 was used
Software (source, version)	E	Microsoft Excel, SAS Version 9.2

Table.S2. Primer nucleotide sequences and product lengths for the target and reference genes amplification by qPCR

Gene Symbol	Primer Name	Primer Sequence (5'------ 3')	Amplicon Size	Reference
ABCB1	3-abcb1Fp1 3-abcb1Rp1	GGA CTG TAA CTG ACT GCC TTG C GGC AGT TTG GAC AAG ATG ACT CC	124 bp	This study
CYP1B1	CYP1B1pp3F CYP1B1pp3R	GCTGCAGTGGCTGCTCCT CCCACGACCTGATCCAATTCT	81 bp	(Finnström et al. 2001)
GAPDH	3-GAPDHFp 3-GAPDHRp	AGT CCC TGC CAC ACT CAG TAC TTT ATT GAT GGT ACA TGA CAA GG	123 bp	(Nolan et al. 2006)
HPRT1	HPRT1F HPRT1R	GAC CAG TCA ACA GGG GAC AT CCT GAC CAA GGA AAG CAA AG	132 bp	(Liu et al. 2015)
HSPCB	HSPCBF HSPCBR	TCT GGG TAT CGG AAA GCA AGC C GTG CAC TTC CTC AGG CAT CTT G	80 bp	(Jacob et al. 2013)

Table. S3: Molecular function and network analysis following gene enrichment.

Molecular function and pathways	Library	p-value	q-value	z-score	Combined score
MicroRNAs in cancer	KEGG_2021_Human	0.0002395	0.002155	39380	328300
Nuclear Receptors Meta-Pathway WP2882	WikiPathway_2021_Human	0.0002536	0.004599	39362	325900
Sulindac Metabolic Pathway WP2542	WikiPathway_2021_Human	0.0004999	0.004599	4999	37990
PMC5346035 Nihms844046F1	PFOCR_Pathways	0.0004999	0.002168	4999	37990
PMC4844852 Nihms-744712-F0001	PFOCR_Pathways	0.0004999	0.002168	4999	37990
PMC7235470 RMV-30-e2109-g001	PFOCR_Pathways	0.0004999	0.002168	4999	37990
PMC5953846 Nihms963973F8	PFOCR_Pathways	0.0004999	0.002168	4999	37990
PMC5896366 Dmd.118.080663F2	PFOCR_Pathways	0.0004999	0.002168	4999	37990
LncRNA-mediated mechanisms of therapeutic resistance WP3672	WikiPathway_2021_Human	0.0005999	0.004599	3999	29660
Benzo(a)pyrene metabolism WP696	WikiPathway_2021_Human	0.0008998	0.004827	2499	17520
Estrogen Receptor Pathway WP2881	WikiPathway_2021_Human	0.0013	0.004827	1666	11070
Tryptophan metabolism	KEGG_2021_Human	0.004196	0.01096	486.8	2664
ABC transporters	KEGG_2021_Human	0.004495	0.01096	453.5	2451
Ovarian steroidogenesis	KEGG_2021_Human	0.005094	0.01096	399	2106
Steroid hormone biosynthesis	KEGG_2021_Human	0.006091	0.01096	332.3	1695