

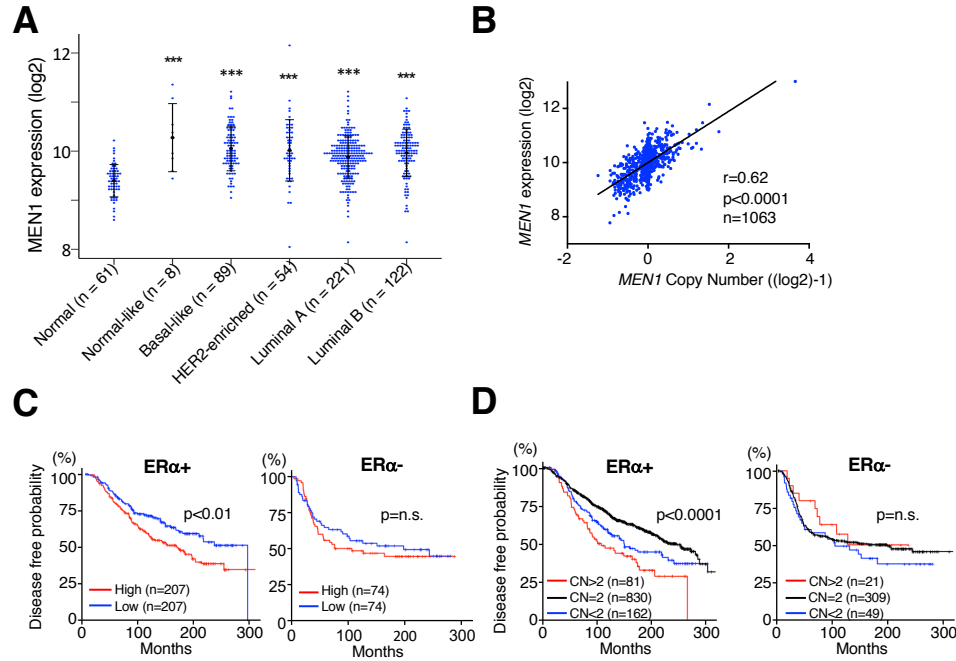
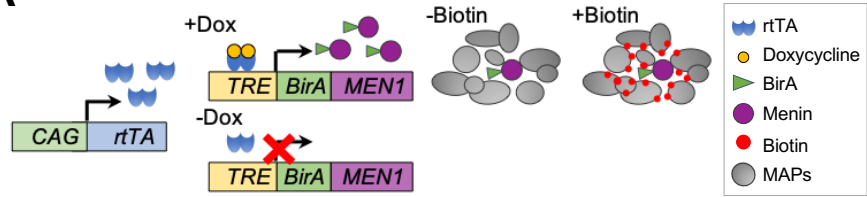
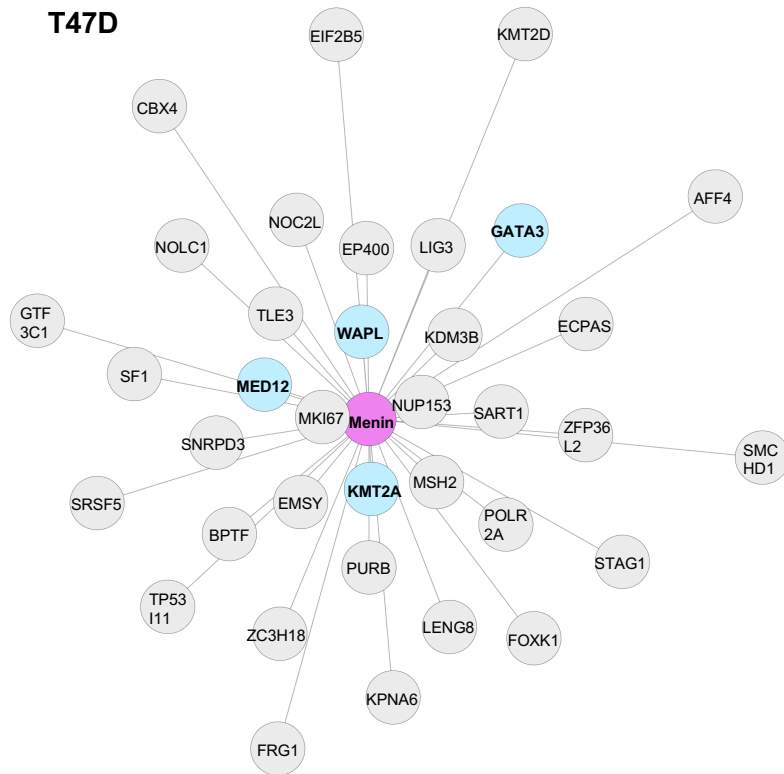


Figure S1.

Increased *MEN1* expression and copy number are related to poor prognosis of ERα+ breast cancer patients. **(A)** *MEN1* expression in different breast cancer PAM50 subtypes in TCGA breast cancer cohort. Significant levels were based on Duncan's multiple range tests (*** $P < 0.001$). **(B)** Scatter plot and linear regression of *MEN1* expression and copy number in TCGA breast cancer cohort. Significant levels were based on Pearson correlation coefficient. **(C)** and **(D)** Kaplan-Meier survival analyses and significant levels were based on logrank tests from Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) cohort based on *MEN1* expression (**c**) or copy number (**D**).

A**B**

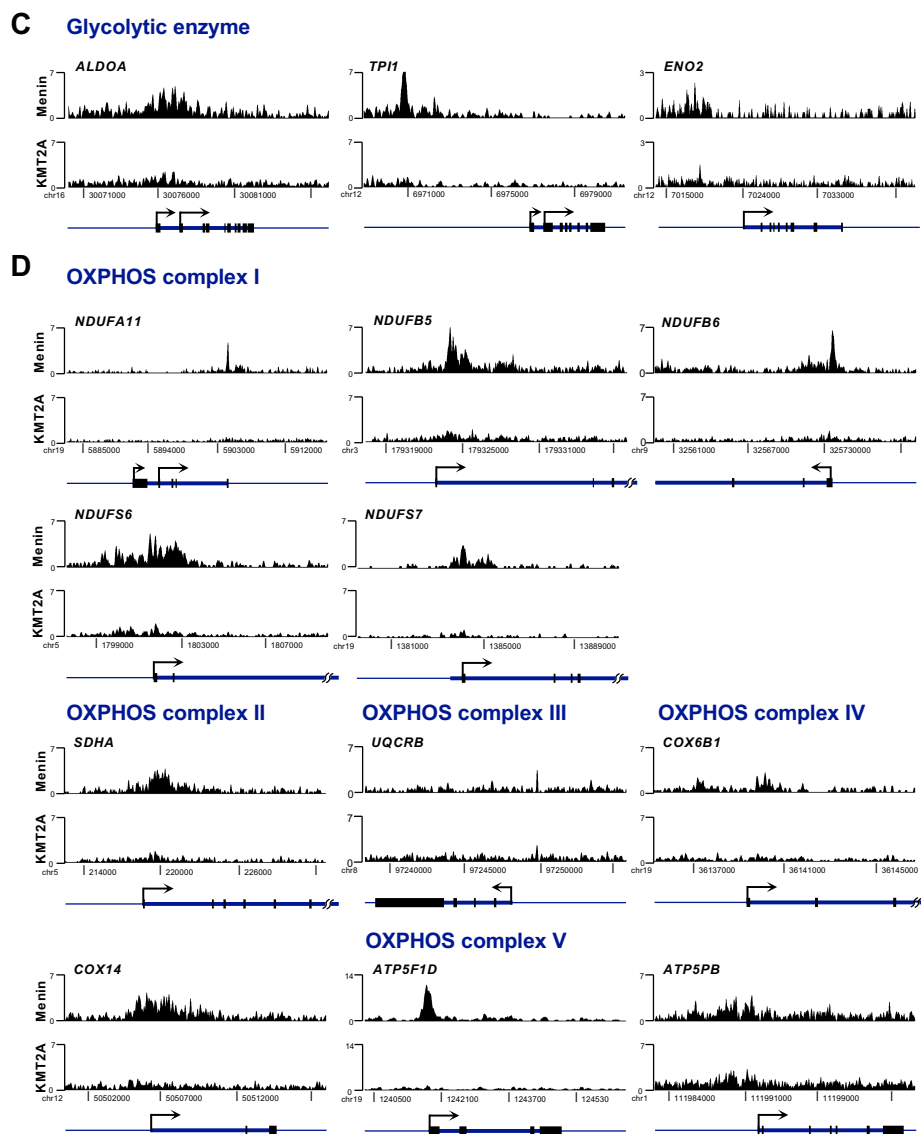


Figure S2.

The BioID system, network analysis of 35 MAPs in T47D and *in silico* analysis of anti-menin and anti-KMT2A ChIP-seq. **(A)** Schematic illustration of biotin labeling of MAPs using BioID proximity-dependent biotinylation with a doxycycline-inducible biotin ligase *BirA-MEN1* fused gene. **(B)** Network analysis of 35 MAPs in T47D cells. The distance between menin and MAPs represented the protein quantitative ratio of each MAP and menin. MAPs marked in blue were further validated by WES. **(C)** *In silico* analysis of anti-menin and anti-KMT2A ChIP-seq data indicates that anti-Menin immunoprecipitation enriched the promoter and gene body DNA sequence of the representative glycolytic genes and **(D)** OXPHOS genes in MCF-7 cells.

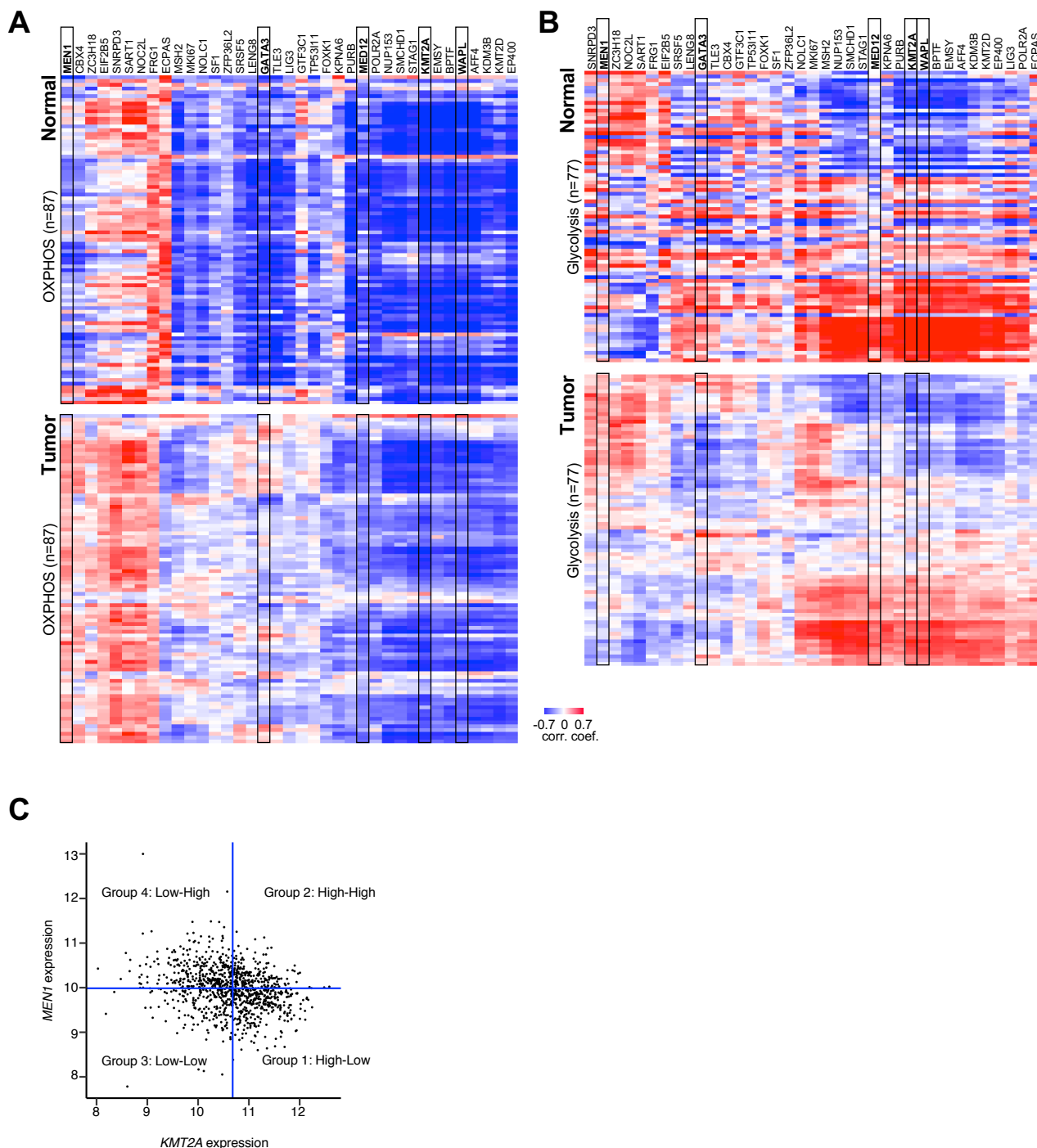


Figure S3.

Expression correlation relationship of MAPs and OXPPOS/glycolytic genes. **(A)** and **(B)**, Heatmaps of gene expression correlations of 37 MAPs (including *MEN1*) genes with OXPPOS genes **(A)** or glycolytic genes **(B)** in normal and tumor samples from TCGA breast cancer cohort. **(C)** Scatter plot of *MEN1* and *KMT2A* expression in TCGA breast tumors. The tumors are grouped into 4 groups (1-4) as in Figure 3E according to median values of both genes' expression. Similar groupings are also applied based on the median expression of *MEN1* and the other three MAP genes (*MED12*, *WAPL* and *GATA3*).

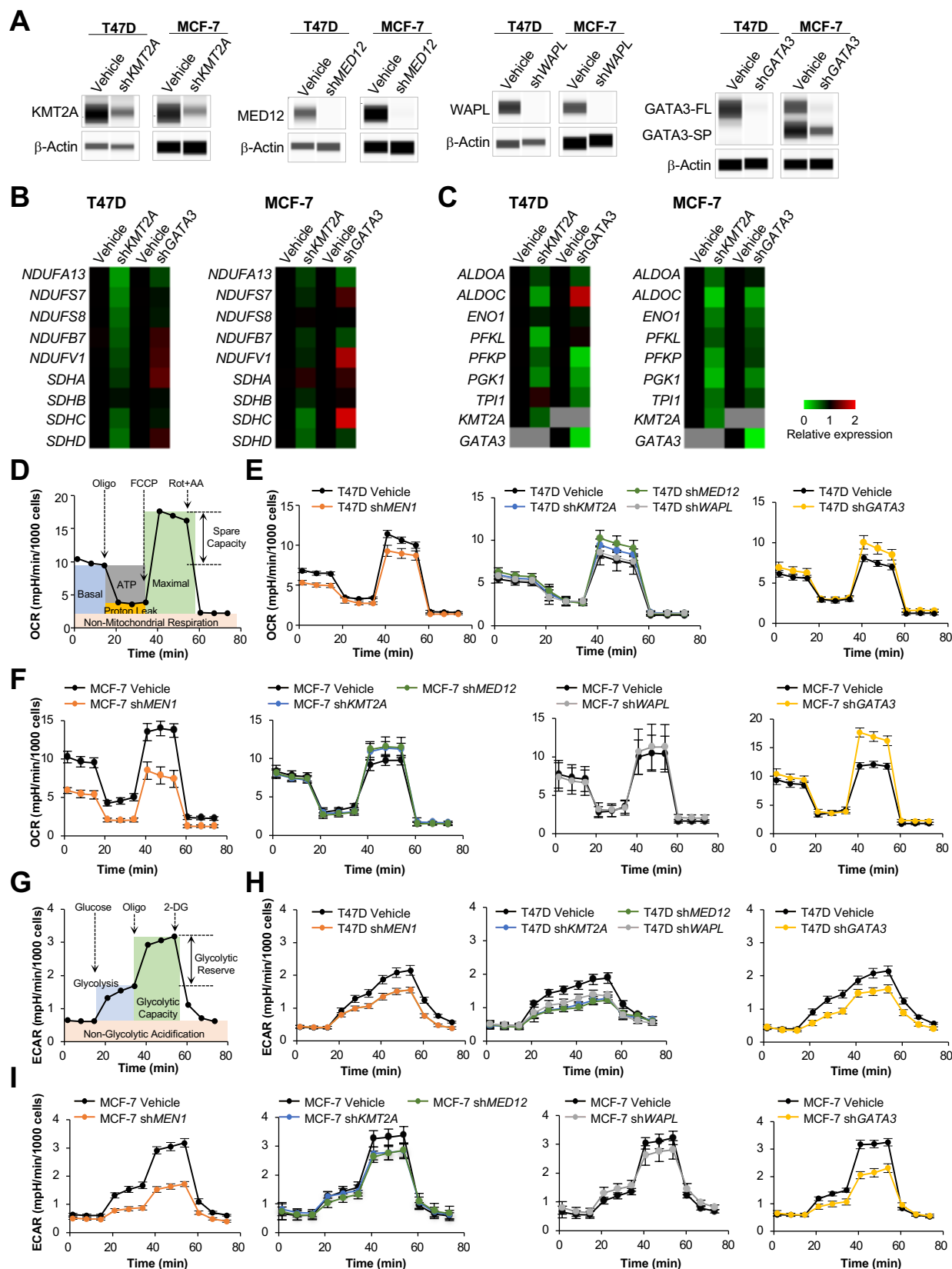


Figure S4.

Gene and protein expressions and extracellular-flux analysis in MAP shRNA knockdown cells. **(A)** WES of total lysate from T47D or MCF-7 cells subject to vehicle or MAP shRNA lentivirus infection. **(B)** and **(C)** Heat maps of RT-qPCR of OXPHOS genes **(B)** or glycolytic genes **(C)** in T47D or MCF-7 cells. The expression in vehicle control is normalized as 1 ($n = 3$). **(D)** Seahorse mitochondrial stress test profile. **(E)** and **(F)** Line charts of OCR for mitochondrial functions in T47D **(E)** and MCF-7 **(F)** cells. **(G)** Seahorse glycolytic stress test profile. **(H)** and **(I)** Line charts of ECAR for glycolytic functions in T47D **(H)** and MCF-7 **(I)** cells. Data are presented as mean $\pm$ S.D. ($n = 15$ -20 technical-replicate wells).

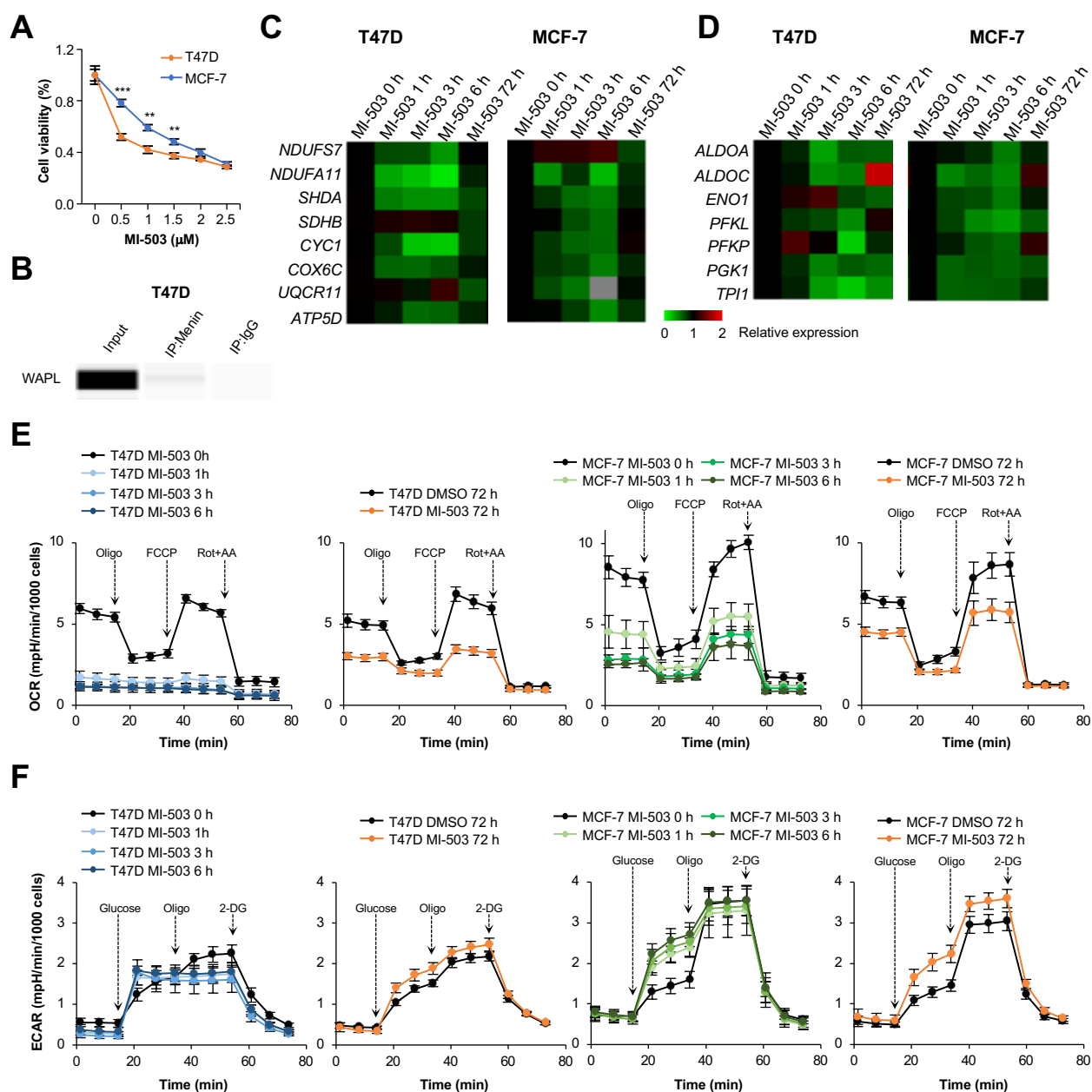


Figure S5.

Gene expressions and extracellular-flux analysis in cells treated with MI-503. **(A)** Cell viability of T47D and MCF-7 cells under different dosages of MI-503 for 3 days ($n = 5$). **(B)** Co-immunoprecipitation of WAPL, another MAP, with menin pulled down by anti-menin but not anti-IgG. **(C)** and **(D)** Heat maps of relative expression of OXPHOS **(C)** and glycolytic **(D)** genes by RT-qPCR in T47D or MCF-7 cells subject to 1 μ M MI-503 for 0, 1, 3, 6, 72 h, or DMSO for 72 h. Gene expressions post MI-503 treatment for 1, 3, and 6 h were normalized to that of the 0 h control; gene expressions post MI-503 treatment for 72 h were normalized to that of DMSO treatment for 72 h. The expressions in 0 h of MI-503 treated cells and 72 h of DMSO treated cells were normalized as 1 ($n = 3$). **(E)** and **(F)** Line charts of extracellular-flux analysis for mitochondrial **(E)** and glycolytic **(F)** functions in T47D or MCF-7 cells treated by MI-503 for 0, 1, 3, 6, 72 h, or DMSO for 72 h. Data are presented as mean $\pm$ S.D. ($n = 15$ -20 technical-replicate wells).

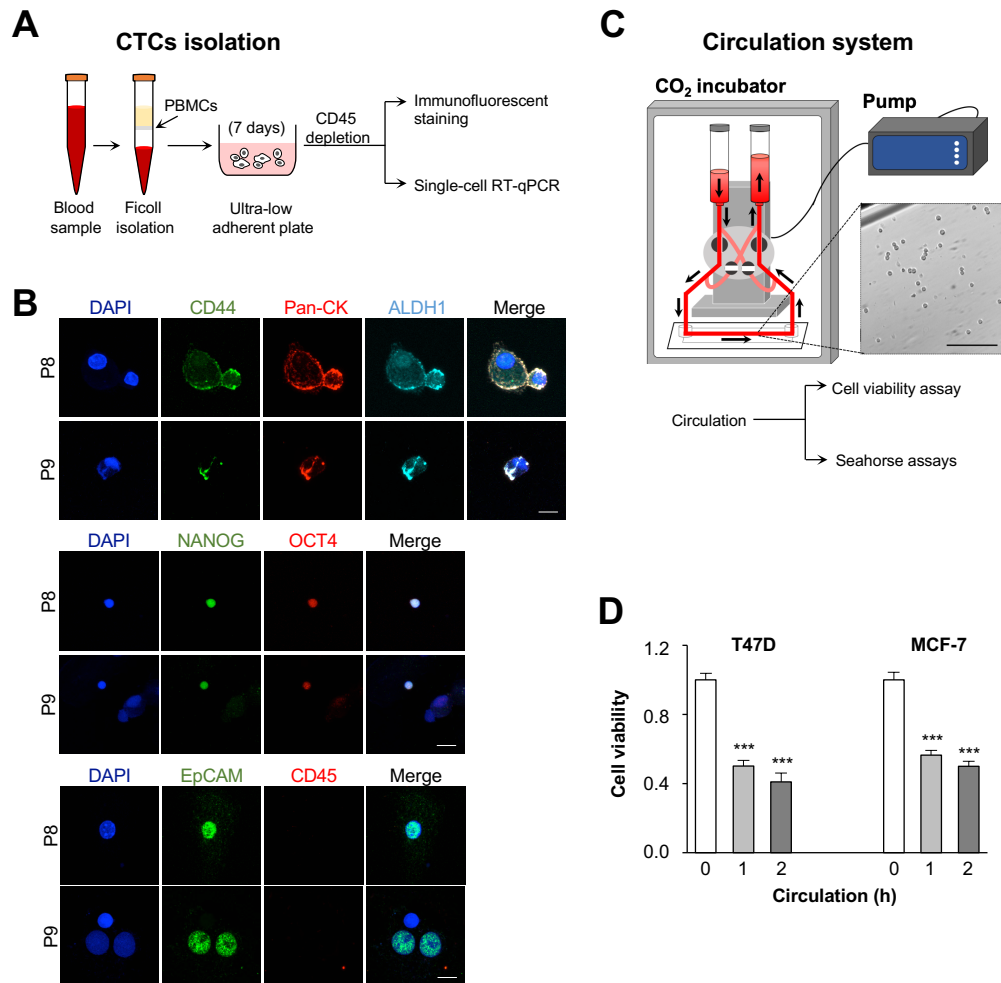


Figure S6.

CTCs isolation and *in vitro* circulation system. **(A)** Schematic workflow of CTC isolation, expansion, and subsequent experiments. **(B)** Representative images of CTCs staining with stem cell or epithelial markers. Scale bar, 10 μm . **(C)** Scheme of the circulation system and experimental assays. **(D)** Bar chart of cell viability of T47D and MCF-7 cells after circulation ($n = 5$ technical-replicate wells). Data are presented as mean $\pm$ S.D. Unpaired two-tailed Student's *t*-test was used for statistical significance determination of 0 h and each treatment ($***P < 0.001$).

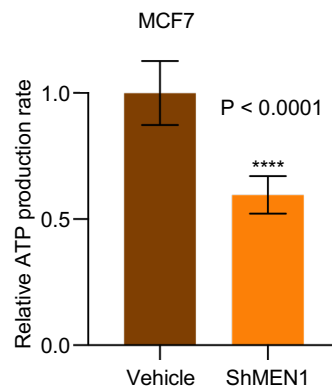


Figure S7.

Validation of ATP quantitation by Seahorse Seahorse XFe96 analyzer using CellTiter-Glo Luminescent Cell Viability Assay Kit. ATP reduction is observed in MCF7 cells treated with menin shRNA, consistent with the measurement result by Seahorse in Fig. 4A.

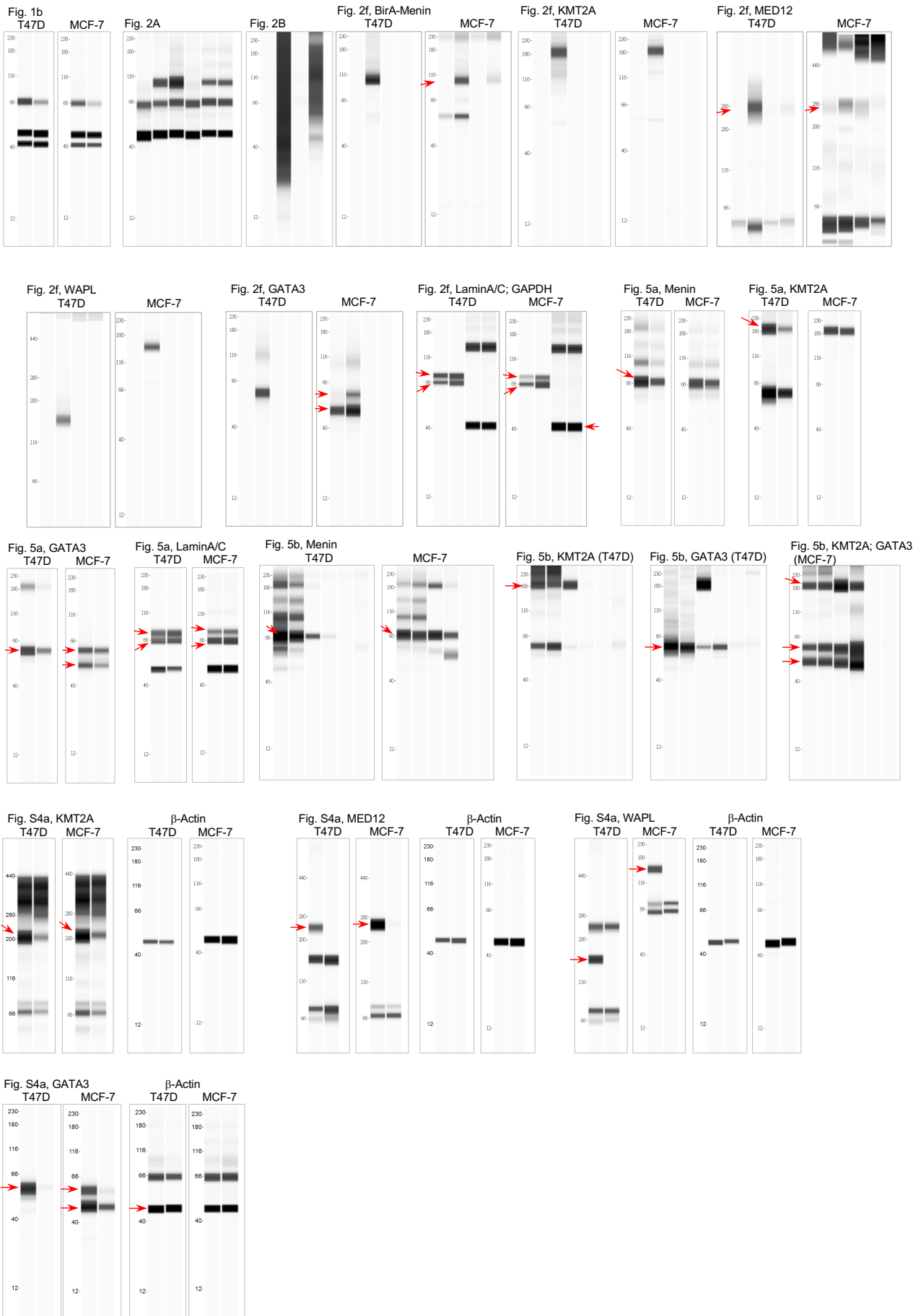


Figure S8. The original WES images.

Table S1. Biotin labelled nuclear proteins in T47D and MCF-7 cells. Related to Figure 2C.

	T47D	MCF-7
Class 1: Basal transcription factor complexes	ACIN1, AFF4, BPTF, BTAF1, CCNT1, CHD8, DHRS7B, EIF2B5, EIF3C, ELMSAN1, GTF2F2, GTF3C1, HP1BP3, INTS1, INTS9, LIG3, MED1, MED12, MED14, NELFE, NOC3L, ORC2, PAF1, PAPOLA, POLA1, POLR2A, POLR2B, RFC5, SENP3, SUPT16H, TAF7, TOX4, WAC, WDR82, ZC3H4, ZHX3, ZMYND8.	AFF4, BPTF, CHD1, CHD3, EIF2B5, EIF5B, GRHL2, GTF3C1, HCFC1, HIRA, INTS8, LIG3, MED12, MED24, NCOR1, POLR1D, POLR2A, POLR2E, SMC6, WDHD1.
Class 2: DNA repair complexes	ARID1B, BAZ1B, DCAF13, DDB1, EMSY, MSH2, NBN, PMS2, RBBP8, RIF1, SSBP1, XRCC1.	ARID1A, EMSY, FANCI, MDC1, MSH2, TNKS1BP1.
Class 3: mRNA modeling; RNA helicase; spliceosomes	C17orf85, C19orf43, CMTR1, CPSF6, DDX10, DDX23, DDX27, DDX41, DDX42, DDX46, DDX54, DDX56, DHX36, DHX38, DHX40, DIS3, EIF2AK2, FIP1L1, FRG1, FUBP1, MCM3AP, MRTO4, NHP2L1, NUFIP2, PARN, PLRG1, PRCC, PRPF31, PRPF6, RAE1, RBM10, RBM17, RBM26, RBM28, RBM7, SART1, SART3, SF1, SF3A1, SF3B5, SF3B6, SMN1, SNRPD1, SNRPD3, SRBD1, SRSF5, TFIP11, TTC37, WDR33, XAB2, ZFP36L2, ZNF638.	ATXN2L, CNOT2, CPSF2, DCP1A, EDC4, ESRP1, FRG1, GEMIN4, GEMIN6, KHDRBS1, KHSRP, PCID2, RANGAP1, SART1, SF1, SF3A2, SF3B2, SKIV2L2, SNRPD3, SRRM2, SRSF3, SRSF5, THOC1, THRAP3, TRA2A, UPF2, ZCCHC8, ZFP36L2.
Class 4: Nuclear scaffold complexes relate	DRG1, DRG2, ECM29, KPNA6, MISP, MKI67, NDC1, NSFL1C, NUP107, NUP153, NUP188, NUP205, NUP85, PPP1R10, SMC1A, SMC4, SMCHD1, SUN2, SURF6, TUBB6, TUBGCP2, WDR3, WDR46.	ECM29, EHD4, KPNA6, MAD1L1, MKI67, MYH10, NOP14, NUP153, NUP210, NUP88, PLK1, POM121C, SAFB2, SEC13, SMCHD1, SYMPK, TPX2.
Class 5: Site-specific transcription factors	CHAMP1, NCAPD2, NCAPD3, PDS5A, PDS5B, POGZ, STAG1, TOP1, TOP2B, WAPL.	STAG1, WAPL.
Class 6: Cohesin related complexes and mediators	ADNP, AQR, ARFGEF1, BDH1, CBX4, CRK, DNAJA3, FOXK1, FOXK2, GATA3, GREB1, JAK1, MKL2, MLLT11, MYBBP1A, NCOA6, NFIC, NKRF, PARP14, PEG10, PURB, RFX1, SBNO1, SCML2, SCYL1, SENP1, SIN3A, STAT2, TCF20, TLE3, TP53I11, YAP1, YY1AP1, ZC3H18, ZNF148, ZNF281, ZNF687.	CBX4, CHCHD3, DIDO1, ERBB2IP, FOXK1, G3BP1, GATA3, GATAD2B, GSE1, ILF3, MBD3, MYEF2, PPM1D, PURB, SAMD1, SPEN, TCF25, TLE3, TP53BP1, TP53I11, TRPS1, TSC2, ZC3H18, ZMYM2, ZNF384, ZNF644.
Class 7: Histone modifying enzymes	EP400, EZH2, GRWD1, HDAC2, JMJD1C, KDM2A, KDM3B, KMT2A, KMT2D, NOC2L, PHF8, RSBN1, RSBN1L, SETD1A, SMARCAD1, TRRAP, WIZ.	BAZ2A, EP400, HIST1H2BB, HIST1H2BC, KAT6B, KDM3B, KMT2A, KMT2D, NOC2L, OGT, PAXIP1, SAP130, SMARCAL1, SMARCC2, SRCAP, STK19, SUDS3.
Class 8: tRNA modification, ubiquitination, and others	ACOT13, BCLAF1, CRNKL1, CUL4B, CUL5, DARS2, DERA, EARS2, EBP, FAM120C, FBXL6, FDPS, GNL2, GPATCH1, IMP4, IPO11, ITPR2, KARS, KIF13B, L1RE1, LENG8, NFS1, NOL6, NOLC1, NOP2, PCNP, PDCD6, PPP2R5D, PPT1, PRKACG, PRKCD, PSPC1, QIL1, RANBP3, RBBP6, RNF213, RPF2, RPP30, RPP38, RSL1D1, SRP14, SUGT1, TAOX2, TCOF1, TRMT1L, TRMT5, TRNT1, UBE2L6, UBE3A, UBE4B, UBR4, UBXN7, UGDH, UNC45A, UTP6, WDR75, YARS2, YIF1B, YLPM1.	AP3D1, BAG2, BOLA2, CBS, DUT, IMPDH2, LAS1L, LENG8, NOLC1, PARL, PISD, PUS1, SRRT, UNC50.

Table S2. shRNA sequences used in this study.

sh <i>MEN1</i>	CCGGGCTGCGATTCTACGACGGCATCTCGAGATGCCGTCGTAGAATCGCAGCTTTTTG
sh <i>KMT2A</i>	CCGGCGCCTAAAGCAGCTCTCATTTCTCGAGAAATGAGAGCTGCTTTAGGC GTTTTT
sh <i>MED12</i>	CCGGGCAGAGAAATTACGTTGTAATCTCGAGATTACAACGTAATTTCTCTGCT TTTT
sh <i>WAPL</i>	CCGGACGTACTGTAGGGCCAATAAACTCGAGTTTATTGGCCCTACAGTACGT TTTTTG
sh <i>GATA3</i>	CCGGCATCCAGACCAGAAACCGAAACTCGAGTTTCGGTTTCTGGTCTGGAT GTTTTT

Table S3. RT-qPCR and Bio-mark primers used in this study.

Gene	F1 (5'- sequence -3')	R1 (5'- sequence -3')	R2 (5'- sequence -3')
<i>MEN1</i>	CCAGACAGTCAATGCCG	CAGGTCAATGGAAGGGTT	TGAACGCCACCTCCATC
<i>KMT2A</i>	AAATGAGAGTAATGATAGG AGAAGC	GTGGAGGTGGAGACGAG	TGGGGGGCACTTTGTAGA
<i>MED12</i>	TCAGTCAACAAGCACGC	AGGAGGATGGTCTGTAGG	GGGCACATAAGCAGGTC
<i>WAPL</i>	GTGACAAATCGGGGCTC	GGGTGGGTAGAAGGAAG AAA	TCAAAAATAGGAAGACAAT AGAAGGC
<i>GATA3</i>	CCACCACAACCACACTC	GGATTTGCTAGACATTTTT CGG	TGCCTTCCTTCTTCATAGT CAG
<i>ALDOA</i>	TCAAATCCAAGGGCGGT	CAATCTTCAGCACACAAC G	CTTGGGTGGTAGTCTCG
<i>ALDOC</i>	TTCACCTGGCACCAACT	GCCATCCTGTTCTGACTT CTA	GCTCCCTATCCTCCCATC
<i>ENO1</i>	GGAAAGATGCCACCAATG	CCCAGACCTGAAGAACT	CCAATAGCAGTCTTCAGC AG
<i>PFKL</i>	CGACTGGCTGTTTCATCC	GAGATGGGCTTCCCGTT	CCCACGGCTCCGAGTCT
<i>PFKP</i>	GGAGAAGCACGAGGAGT	GCAGGTGTGCGTGATAGT	AGTGTTCAAGGGCGGTGT
<i>PGK1</i>	TCGGGGCTAAGCAGATTGT	CAAGTGGCAGTGTCTCC	GCTTTCACCACCTCATCC
<i>TPI1</i>	GAGCAGACAAAGGTCATC G	TGGACTTCAGCCATCCTC	CAGTCTTGCCAGTACCAA T
<i>NDUFA7</i>	ACTACTTTGCCTCCTTGG	GCCTGGGAAACATGGTG	AAAAGTAGAAGTGATACCT GAGC
<i>NDUFA11</i>	AGTGAAACCCTGTCTCTAC TAT	GTGACATGATCTCGGCTC	TTCTCATGCCTCAGCCTC
<i>NDUFA13</i>	TACAGGCAGAAACCGACC	GTACAGCTCCCCGATCAA G	GAACACAGACTCCCCCAC
<i>NDUFB7</i>	CACACAGCAGGAGATGAT	GCAGTAGTCCCAGTCGT	CGCTTGCACTTGAGCAG
<i>NDUFS7</i>	GCACACTACCAACAAGA	GATGTAGATGTCCACGGG	CATGGAGACCACGTAGCG
<i>NDUFS8</i>	ATCCCGAGATGGACATGA A	GTAGTTGATGGTGGCCG	GAACAGGTAGCTCAGGGT
<i>NDUFV1</i>	CTGTGGAGGAGGAGATGT	GGGGATCAGTGGGGTAG	AGTGGGGTAGACGAGCC
<i>SDHA</i>	CATTCCCACCAACTACAAG G	GACAACCAGGTCCAAGAG	TGTACCGAGGCACAGGC
<i>SDHB</i>	GAGAAGGCATCTGTGGC	GCATAGAAGTTGCTCAAA TCG	GTGTGGAAGAGGGTAGAT TT
<i>SDHC</i>	GTGGGTAGGGTTGAGGGA	ACATACAGTGGTTTGGGT G	CCAGAAATGACCAAGAGA AAG
<i>SDHD</i>	AACTATCACGATGTGGGC	CTTATCTGTTATTTCTTCC TTATTGTGAG	AAGCAGAGGCCAAAGAGG
<i>CYC1*</i>	CGGAGGTGGAGGTTCAA	CACGATGTAGCTGAGGTC	
<i>COX6C*</i>	CGTATCAAGGACAGTAAC TACCA	ATCAGCCACACGAACTT A	
<i>UQCR11*</i>	GCTGACAGAACTGCCTA	CCCAGATACATCACTCCC AA	
<i>ACTB</i>	CATGTACGTTGCTATCCAG GC	CTCCTTAATGTCACGCAC GAT	CTCCTTAATGTCACGCAC GAT

*RT-qPCR only, F1 and R1 was used. For *ACTB*, same primer set was used for outer and inner primer.