Gene symbol	Forward Primer (5' –> 3')	Reverse Primer (5' –> 3')
AKR1C1	GCCATATTGATTCTGCTCATTTAT	TGGGAATTGCTCCAAAGC
AKR1C2	AAGTAAAGCTCTAGAGGCCGT	GCTCCTCATTATTGTAAACATGT
AKR1C3	TGGAAAACTCACTGAAAAAAGC	CATTTTCATCTGTTGGTGAAAG
AKR1B1	GGATGAAGGGCTGGTGAA	GTGGCACTCAATCTGGTTA
AKR1B10	CCCAAAGATGATAAAGGTAATGCCATCGGT	CGATCTGGAAGTGGCTGAAATTGGAGA
ALDOB	CACCATTCAAGGGCTTGATGGCCT	TTCCTGGATAGCGAGGCTGGAT
HSD12B2	CAATGCTGCAGGACAGAGGA	GTTCACGGCCATGCATTGTT
PLAC8	GGAACAAGCGTCGCAATGAG	AAAGTACGCATGGCTCTCCTT
FGF21	GACTGTGGGTTTCTGTGCTG	GAATAACTCCCGGCTTCAAGG
CPXM2	GTGCGCGGGAAGAAATGAC	CCTCCCTTGAGTGATGACACC
TBC1D4	AGATGGCCTGCCACGTT	CTCTTTCATGGCCGCTTTAG
FREM2	TGAGCCAACTGTGTTTATTC	GTATAACAGACCACCATCAAC
ALDH1L2	TAACACATACAACAAGACAGAT	ATATTCATTTAGAGCTTCCTCA
MDR1	CCCATCATTGCAATAGCAGG	GTTCAAACTTCTGCTCCTGA
MRP1	CGG AAA CCA TCC ACG ACC CTA ATC	ACC TCC TCA TTC GCA TCC ACC TGG
XRCC1	ACT GCT GGA ACC TGG CCC TGC	GCA AAC CCC GAG GAG AAG GCA
ERCC1	AAG TGC TGC GAG CCC TGG GC	AAT AAG GGC TTG GCC ACT CC
GAPDH	CCCCTTCATTGACCTCAACTAC	GATGACAAGCTTCCCGTTCTC

Table S1. Primer sequences used in this study were listed.

Top 50 upregulated genes	Log 2 Fold change	Top 50 upregulated genes	Log 2 Fold change
ANKS1B	**10.00120701**	*DPEP1*	**4.010343936**
TMEM200B	**8.279903579**	*NCF1*	**3.976568327**
TMOD1	**7.411541132**	*TNNI2*	**3.975859619**
CXCL13	**6.582793746**	*CTD-3193O13.9*	**3.925505776**
CLDN22	**6.383369611**	*LPPR1*	**3.862463534**
SLC10A2	**6.221569778**	*AKR1C3*	**3.707357856**
ALDOB	**5.942942007**	*HPGD*	**3.704429688**
HSD17B2	**5.63596137**	*SRGAP3*	**3.667642121**
PLAC8	**5.5946095**	*GGTLC2*	**3.654972786**
CTD-3074O7.11	**5.579142468**	*CYP4F12*	**3.639574743**
AKR1C1	**5.565227132**	*PDZD3*	**3.553896042**
APOBEC1	**5.543903602**	*KRT20*	**3.484469377**
ENPP3	**5.381785846**	*GAGE12F*	**3.474989902**
AKR1C2	**5.295546827**	*GAGE12G*	**3.471310628**
ADAMTS18	**4.813060175**	*PADI2*	**3.470230902**
RP11-6N17.6	**4.74912944**	*CRYBB1*	**3.468425963**
DEFB1	**4.716958372**	*LGALS9C*	**3.395554164**
LGALS2	**4.546300171**	*APOD*	**3.331868841**
PHGR1	**4.412965345**	*ACSM3*	**3.295612591**
FAM3D	**4.393154683**	*CDH17*	**3.280257658**
REG4	**4.376451913**	*HTN1*	**3.254720797**
TM4SF5	**4.338300867**	*AKR1B15*	**3.247006572**
SPINK4	**4.20820479**	*LINC01088*	**3.245920558**
UGT1A5	**4.190219093**	*NMUR2*	**3.240752369**
PART1	**4.146625076**	*TGFBR3L*	**3.187284262**

Table S2. Top 50 upregulated differentially expressed genes (KATO/DDP vs KATOIII) analyzed by CLC genomic work bench.

Top 50 down regulated genes	Log 2 Fold change	Top 50 down regulated genes	Log 2 Fold change
DUX4L7	**-10.08529421**	*TBC1D4*	**-5.471998485**
MSANTD4	**-9.938113925**	*ANKRD20A3*	**-5.420006916**
GCOM1	**-9.004911443**	*SLITRK1*	**-5.303238935**
ZNF134	**-8.908232759**	*ASB3*	**-5.17177588**
TUBA3C	**-8.880048623**	*LUC7L2*	**-5.048251183**
GAGE12C	**-8.751851805**	*ALDH1L2*	**-4.990809922**
TUBA3E	**-8.72756069**	*CT45A5*	**-4.978625427**
RP11-544M22.13	**-7.961757733**	*PRSS1*	**-4.975307056**
PCYT1B	**-7.959000431**	*FAM157B*	**-4.965680434**
ATP10A	**-7.847628147**	*NECAB2*	**-4.931482747**
GAGE12D	**-7.638452541**	*GAGE2C*	**-4.918040046**
OLFM2	**-7.340402539**	*TGFB2*	**-4.917914633**
TNFRSF9	**-7.267109125**	*FREM2*	**-4.913189506**
DUX4L13	**-6.65803919**	*EYA4*	**-4.90850198**
FAM115B	**-6.510186858**	*ZNF469*	**-4.884203884**
PRSS3P2	**-6.415960084**	*SSX1*	**-4.829520825**
LINC00326	**-6.096395261**	*TBX20*	**-4.829215923**
FGF21	**-6.052656406**	*SOHLH2*	**-4.744286679**
ST6GALNAC5	**-6.031810226**	*SOX5*	**-4.539827753**
GDAP1L1	**-5.829606389**	*PLAC9*	**-4.517630046**
GGN	**-5.823501787**	*FAM200A*	**-4.465701387**
CPXM2	**-5.707164065**	*HCK*	**-4.456694213**
DUX4L4	**-5.686992478**	*THSD7A*	**-4.455646016**
POTEF	**-5.666120276**	*POTED*	**-4.437075994**
GAGE12J	**-5.518564693**	*PDE4B*	**-4.436759955**

Table S3. Top 50 downregulated differentially expressed genes (KATO/DDP vs KATOIII) analyzed by CLC genomic work bench.

Gene ontology biological process term	Genes Names
Oxidation reduction process	*STEAP2, ALDH1L2, AKR1B10, AKR1B15, AKR1C1, AKR1C2, AKR1C3, CBR3, CYP1A1, Cyp26B1, CYP4F12, CYP4F3, FAR2P1, HPGD, HSD17B2, IDP1, LPO, LOXL4, NCF1, PDPR, SOD3*
Digestion	*UGT1A1, ADM2, AKR1B10, AKR1C1, AKR1C2, PRSS1, PRSS3P2, TFF2, TFF3*
Positive regulation of gene expression	*PRDM1, SMAD1, WNT11, ADM2, ANK2, CAV1, CYP26B1, HMGN5, RPS6KA2, SLC26A9, TGFB2, VEGFA*
Angiogenesis	*ADM2, APOD, CAV1, NRXN1, RAMP1, SLC12A6, THSD7A, TGFB2, TNFSF12, UNC5B, VEGFA*
Negative regulation of cell proliferation	*CD33, ETS1, FOSL1, KLF10, SMAD1, TNFRSF9, CDKN2B, IFITM1, RARRES3, RPS6KA2, SSTR5, TES, TGFB2*
Steroid metabolic process	*UGT1A1, AKR1B10, AKR1C2, AKR1C3, CYP1A1, SULT1E1*
Regulation of apoptosis process	*BCL2L14, ETS1, IKZF3, TNFRSF9, CASP1, CARD16, DAPK1, INHPC, INHBE, SDF2L1*
Daunorubicin metabolic process	*AKR1B10, AKR1C1, AKR1C2, AKR1C3*
Doxorubicin metabolic process	*AKR1B10, AKR1C1, AKR1C2, AKR1C3*
Response to hypoxia	*DTIT4, ETS1, CA9, CASP1, CAV1, CYP1A1, SOD3, TGFB2, VEGFA*

Table S4. Genes involved in top ten gene ontology biological process by David gene function annotation.

GO term	Upregulated genes (KATO/DDP vs KATOIII)	Downregulated genes (KATO/DDP vs KATOIII)
Oxidation reduction Process	*ALDOB, AKR1C1, HSD17B2, AKR1C2, NCF1, CYP4F12, AKR1C3, HPGD, APOD, AKR1B15, CYP4F3, IDO1, AKR1B10, CBR3*	*SESN2, SOD3, MT-ND4L, LOXL4, STEAP2, PDPR, CYP1A1, CYP26B1, LPO, ALDH1L2*
Small molecule metabolic process	*ALDOB, AKR1C1, APOBEC1, ENPP3, AKR1C2, UGT1A5, DPEP1, CYP4F12, AKR1C3, HPGD, ADOP, ACSM3, TCN1, CYP4F3, IDO1, AKR1B10, CBR3, QPRT, UGT1A1, TFF3, UGT1A10, BAAT, PSMB10, DBI*	*SESN2, ABCA1, PDPR, CAV1, CYP1A1, GSTM2, OGT, CYP26B1, CTH, RIMKLB, SULT1E1, ST6GAL1, LPO, PDE4B, PRSS1, ALDH1L2*
Cofactor metabolic process	*ALDOB, AKR1C1, AKR1C2, DPEP1, GGTLC2, AKR1C3, ACSM3, TCN1, IDO1, AKR1B10, CBR3, QPRT, UGT1A1, BAAT, DBI*	*PDPR, CYP1A1, GSTM2, CHAC1, LPO, PRSS1, ALDH1L2*

Table S5. Genes involved in top GO terms by gene set enrichment analysis