

## **Supporting Information**

### **MATERIALS AND METHODS**

#### **Hydrodynamic injection, vector constructs**

For tumor generation, oncogenic plasmids and sleeping beauty transposase(1) (ratio of 10:1) were diluted in 2mL saline (0.9% NaCl), and injected into the tail vein of 6 - 8 week-old FVB/n female mice (NCI-Frederick, USA) in 5 - 7 seconds. For AKT-CAT tumors, plasmids encoding for activated AKT1 (myristoylated-AKT1) and b-catenin (truncated D90N-b-catenin) were used(2). For AKT-NRAS<sup>G12V</sup> tumors, AKT1 and N-Ras<sup>G12V</sup> plasmids were used(3). For chronic liver inflammation, mice received a diet containing 0.1% DDC (Bio-Serv, Flemington, NJ) or were treated intraperitoneally twice a week with carbon tetrachloride (CCl<sub>4</sub>; Sigma) diluted 1:10 in mineral oil (Sigma) at 5ml/g body weight. Mice were kept in accordance with the animal regulations at the NCI/NIH (Bethesda, USA).

#### **Statistics**

Data were analyzed using Student t test. P values < 0.05 were considered as significant.

**Cell lines and DDC treatment.** SNU-449 and PLC/PLR/5 were obtained from ATCC (Manassas, VA, USA). Media were supplemented with 10% heat-inactivated fetal bovine serum (FBS) 10%, 2mM Glutamine and 100 U/mL penicillin/streptomycin. Cell proliferation was assessed using the xCELLigence system (ACEA, Basel, Switzerland). 5000 cells/well were plated and DDC (Sigma, Switzerland) at different concentration was added to the wells. Cell proliferation was monitored with a 15 min frequency measured in real time starting 48h after start of DDC treatment until cell growth reached a plateau due to confluence. Proliferation rate was calculated as relative cell index and time 0 was considered as the time of DDC addition to the media.

**Immunoblotting.** Three tumors of each group (AKT-CAT, AKT-CAT+DDC, and AKT-CAT+CCl<sub>4</sub>) and untreated liver control tissue were used. Tumor specimens were homogenized in RIPA buffer [30 mM Tris (pH 7.5), 150 mM NaCl, 1% NP-40, 0.5%

Na deoxycholate, 0.1% SDS, 10% glycerol, and 2 mM EDTA] containing the Complete Protease Inhibitor Cocktail (Roche Molecular Biochemicals, Indianapolis, IN). The concentration of protein contained in the supernatants was assessed by employing the BCA assay method.

Subsequently, 60 µg of protein lysates for each sample were used to run SDS-PAGE by using gradient polyacrylamide gels (Life Technologies, Thermo Fischer Scientific, Waltham, MA, USA). Proteins were electro-blotted on nitrocellulose filters by using a semi-dry apparatus (Life Technologies, Thermo Fischer Scientific). Finally, after blocking in a solution containing 5% non-fat milk, filters were incubated overnight at 4 °C with AceCS1, ACSL1, Phospho-ATP-Citrate Lyase, Fatty Acid Synthase, phospho PS6 (Cell Signalling, USA) and b-Actin (Sigma Aldrich, USA) antibodies. After incubation and several washings in a solution of Tween-TBS, filters were incubated with secondary antibodies conjugated to the horseradish peroxidase for one hour at room temperature. Signals were finally detected by using Enhanced Chemiluminescent Kit (GE Healthcare, Buckinghamshire, United Kingdom) and signal was acquired with Azura C300 apparatus (Axon Lab AG, Switzerland).

### **Histology, Immunohistochemistry, Immunofluorescence**

Individual liver tumors ( $\geq 2$ mm in diameter) were macrodissected in half. One half was flash frozen and used for RNA or DNA isolation; the other half was used for histology and stained for H&E or Sirius red. Immunohistochemistry was performed on an entire tumor section or on a TMA, which was constructed after selecting a representative tumor area on an H&E-stained slide of the donor paraffin block. Afterwards, a core punch with a diameter of 0.6 mm was taken from the tumor. Core punches were transferred to a new paraffin recipient block by using a programmed tissue arrayer (Beecher Instruments, Silver Spring, MD, USA). TMAs were cut in sections of 4 mm thickness, deparaffinized and stained according to standard protocols using polyclonal antibodies against pAKT(Ser473), b-catenin (D10A8), CD31, CD3, Ly6.G (all Cell Signaling Technologies).

For visualization of GFP encoding plasmid, livers were perfused *in situ* with 4% paraformaldehyde and post fixed in the same fixative for 4 hours. Fixed tissue fragments were incubated in 30% sucrose overnight at 4°C and embedded in Tissue-Tec OCT (Fisher; Pittsburgh, PA). Five-µM frozen sections were prepared and examined with an immunofluorescence microscope.

### **Transposon replication assay**

A total of 4µg DNA was subjected to DpnI (10 units) digestion overnight at 37° C. Quantitative PCR was performed using SYBR Green (Applied Biosystems, Foster City, CA) with the following primers: pT3-AKT-FW GTGGGTGGAGACTGAAGTTAG and pT3-AKT-RW GAATTCCACCACACTGGACTA.

### **Cholesteryl and triglyceride measurement**

Cholesteryl-ester, free cholesterol, and triglyceride levels were determined using the Cholesterol/Cholesteryl Ester Quantification or Triglyceride Quantification assay Kit (Abcam, Cambridge, MA) according to the instructions.

### **Microarray data analysis**

Microarray analysis was performed from four mice per group and three mice per non-tumoral and control group. RNA was isolated from fresh frozen tissue using RNeasy kit from Qiagen (Valencia, CA, USA) and pooled from 3-4 histologically confirmed hepatocellular tumors per mouse and 1-2 locations of non-tumoral tissue and control liver tissue of age- and sex-matched mice on normal chow. RNA hybridized on Sentrix Mouse Ref-8v2.0 expression BeadChips (Illumina, San Diego, CA) and scanned on an iSCAN (Illumina). Data preprocessing and quantile normalization with background subtraction was performed with GenomeStudio2010 (Illumina). Signal intensity with a detection  $p > 0.05$  was treated as missing value, and only genes represented in at least 50% of all samples were included. Data analysis was performed with Qlucore (Lund, Sweden). Functional analyses were performed by GSEA and Ingenuity Pathway Analysis (IPA8.7; Ingenuity Systems, Redwood City CA). All microarray data was submitted to GEO (*accession number pending*). If not stated otherwise, significantly different expressed genes between two groups were identified using a p-value of 0.001 and fold change difference of 1.5.

### **RNA extraction and qRT-PCR analysis**

RNA was isolated from fresh frozen tissue using RNeasy kit from Qiagen (Valencia, CA, USA) according to the manufacturer's instructions. Complementary DNA was generated starting from 1 µg of RNA retrotranscribed with First-Strand cDNA Synthesis Kit (GE Healthcare, Little Chalfont, United Kingdom). qRT-PCR analyses

were performed in 384-well plates using ViiA™ 7 Real-Time PCR System (Life Technologies, Thermo Fischer Scientific, Waltham MA, USA). GAPDH expression was used as internal control and relative expression levels were calculated by applying the  $2^{-\Delta Ct}$  formula. Primer sequences are as follows:

**CXCL16:** CXCL16 Left 5'-CGTTGTCCATTCTTTATCAGGTTCC-3', CXCL16 Right: 5'-TTGCGCTCAAAGCAGTCC-3';

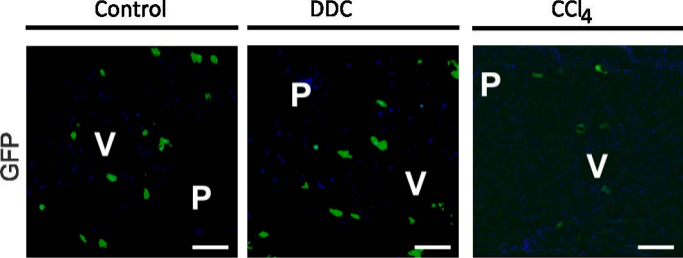
**Nedd9:** Nedd9 Left 5'-GACGACGCCAAACAACACTGACCAC-3', Nedd9 Right: 5'-GGCTTACTGTGGACCTGGGCTTT-3';

**Gal3:** Gal3 Left 5'-AGGTTCTTCATCCGATGGTTGT-3', Gal3 Right 5'-AGGTTCTTCATCCGATGGTTGT-3';

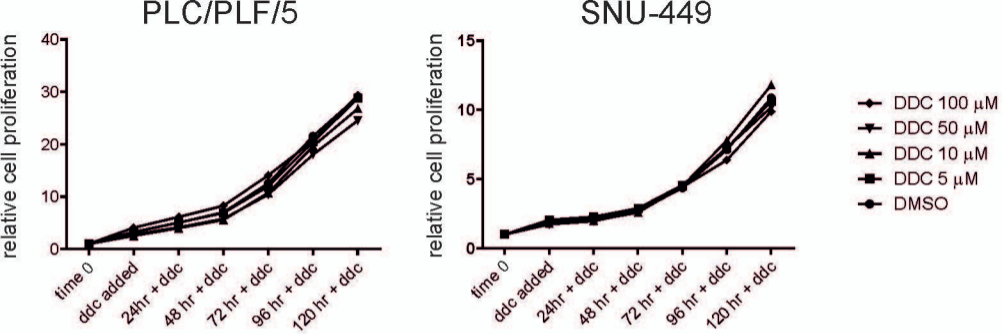
**GAPDH:** GAPDH Left 5'-CATGGCCTCCAAGGAGTAAG-3', GAPDH Right 5'-TGTGAGGGAGATGCTCAGTG-3'

## REFERENCES

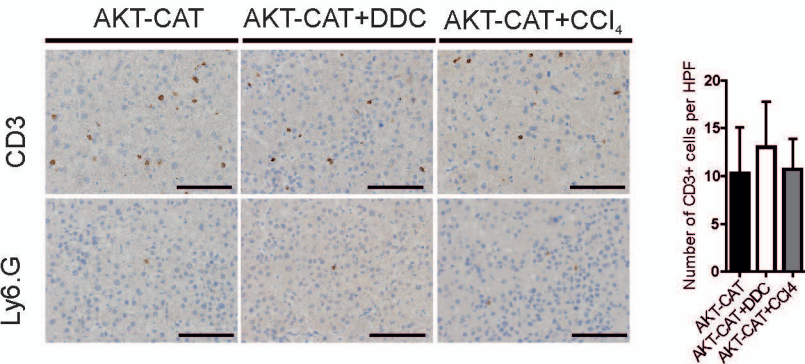
1. Yant SR, Park J, Huang Y, Mikkelsen JG, Kay MA. Mutational analysis of the N-terminal DNA-binding domain of sleeping beauty transposase: critical residues for DNA binding and hyperactivity in mammalian cells. *Mol Cell Biol* 2004;24:9239-9247.
2. Stauffer JK, Scarzello AJ, Andersen JB, De Kluver RL, Back TC, Weiss JM, Thorgeirsson SS, et al. Coactivation of AKT and beta-catenin in mice rapidly induces formation of lipogenic liver tumors. *Cancer Res* 2011;71:2718-2727.
3. Ho C, Wang C, Mattu S, Destefanis G, Ladu S, Delogu S, Armbruster J, et al. AKT (v-akt murine thymoma viral oncogene homolog 1) and N-Ras (neuroblastoma ras viral oncogene homolog) coactivation in the mouse liver promotes rapid carcinogenesis by way of mTOR (mammalian target of rapamycin complex 1), FOXM1 (forkhead box M1)/SKP2, and c-Myc pathways. *Hepatology* 2012;55:833-845.



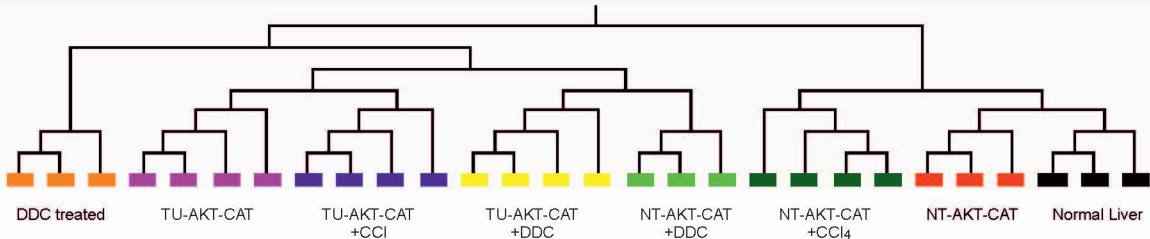
Supplementary Figure 1. Confocal immunofluorescence microscopy of liver tissue from FVB/n mice, 7 days after hydrodynamic injection with a GFP-labelled plasmid and 4 days after start with DDC diet or CCl<sub>4</sub> administration. Bar=100 $\mu$ m. P: portal tract; C: central vein, blue: DAPI. One representative picture from 3 mice/group.



Supplementary Fig. 2. Liver cancer cell lines SNU-449 and PLC/PLF/5 were treated with different concentrations of DDC and proliferation rate was measured using Xcelligence.



Supplementary Figure 3. Immunohistochemical analysis of intratumoral CD3+ and Ly6.G+ cells. Bar=50 $\mu$ m. One representative picture from 3-7 mice/group.

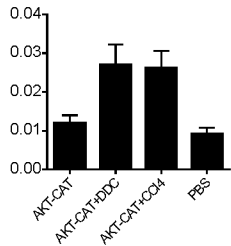


Supplementary Fig. 4. Unsupervised clustering (average linkage) of all samples analyzed (detected gene number n=9037).

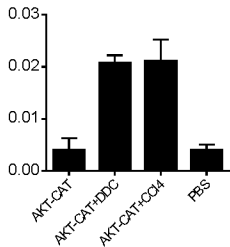


relative expression 2-dCt

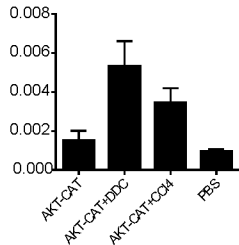
CXCL16



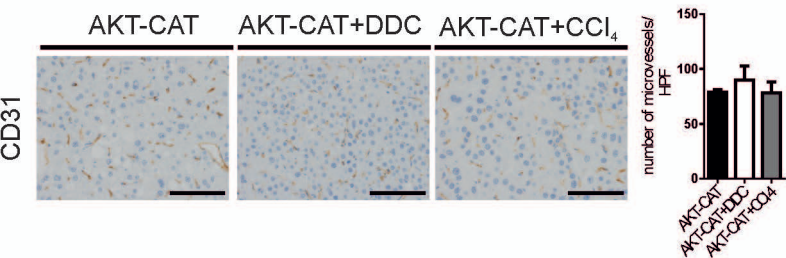
Galectin-3



Nedd9

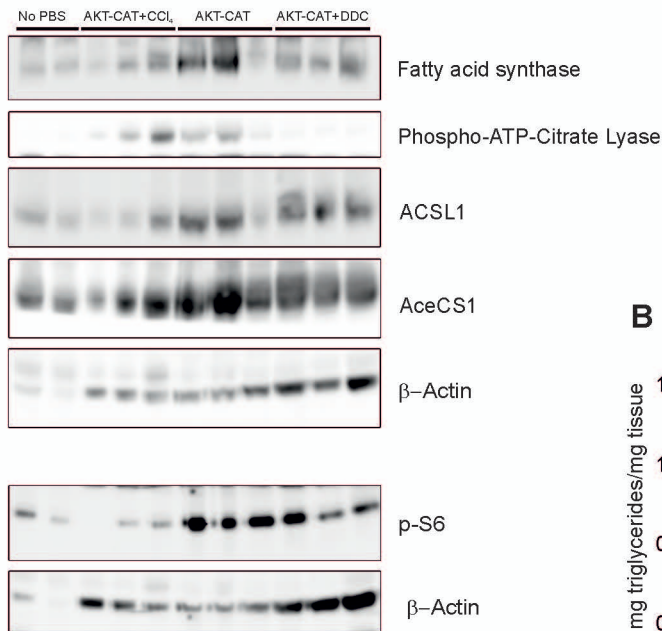
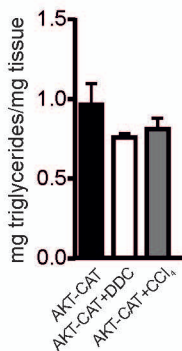


Supplementary Figure 5. Expression of CXCL-16, Galectin-3, and Nedd9 was evaluated by qRT-PCR in a panel of randomly selected AKT-CAT, AKT-CAT+DDC, and AKT-CAT+CCl4 tumors as well as normal liver (PBS). GAPDH was used as internal control and 2-dCt formula was applied to determine relative expression levels. Data represented as mean $\pm$  SEM.



Supplementary Figure 6. Immunohistochemical analysis of CD31+ microvessels. Bar=50 $\mu$ m.

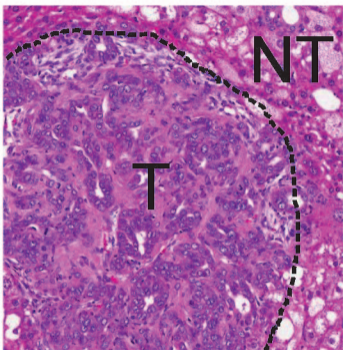
One representative picture from 4-7 mice/group.

**A****B**

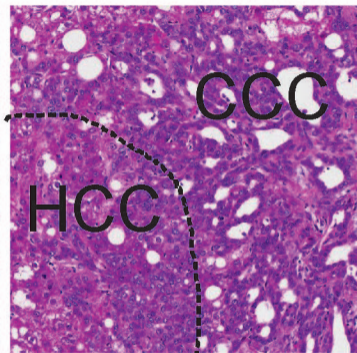
Supplementary Figure 7. A) AKT-CAT, AKT-CAT+DDC, AKT-CAT+CCl<sub>4</sub> tumors and normal liver (PBS) were measured for expression of several proteins by western blot.

B) Triglycerides were measured in AKT-CAT, AKT-CAT+DDC, and AKT-CAT+CCl<sub>4</sub> tumors.

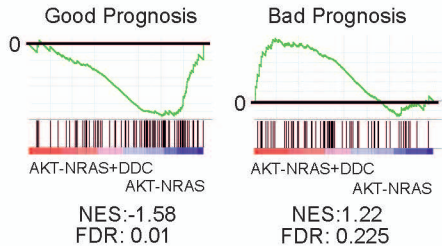
A



B



Supplementary Figure 8. AKT-NRAS tumors showing a CCC (A), and a mixed HCC-CCC (B).

**A****B**

Supplementary Figure 9. (A) Unsupervised hierarchical clustering of transcriptome from AKT-NRAS<sup>G12V</sup> and AKT-NRAS<sup>G12V</sup> + DDC tumors. (B) GSEA using good and bad prognosis gene sets as described before.

**Supplementary Table 1**

Genes differently expressed in AKT-CAT tumors in comparison to normal liver tissue ( $p < 0.001$ , fold change  $> 1.5$ )

Gene_Symbol	p-value	Fold change
A530050D06Rik	0.0001467	-11.2071
A730098D12Rik	0.00078798	-1.77633
AA407659	0.00030683	2.28304769
AI317395	2.31E-05	-2.28756
Abat	0.00063657	-2.8655
Abca6	0.00035737	-2.1021
Abcg5	0.00074825	-2.00181
Acot10	0.00075927	3.88039083
Actn3	0.00055552	-1.75191
Adam9	0.00014995	2.01617781
Adamtsl4	0.00089511	1.99240098
Adra1b	0.00075801	-3.69244
Afmid	0.00032711	-3.66423
Aifm1	0.00055673	1.87377853
Akr1b8	0.00062292	-3.37421
Aldh1l1	9.75E-05	-2.62692
Anapc2	0.00033067	1.55470703
Anxa2	1.30E-06	12.545981
Anxa5	4.28E-05	12.9250901
Aplp2	0.00039729	2.3369837
Arf14	0.00016035	-5.29923
Arhgap17	0.00046287	2.16482548
Arhgef19	0.00040546	2.64802457
Arl2bp	0.00075886	3.93318309
Arl6ip1	0.00068352	1.86724975
Arl8a	1.54E-05	4.3052787
Arpc5	0.00017492	1.57620312
Arpp19	3.16E-06	2.96644359
Arrdc2	0.00086608	-6.95873
Arsa	0.00024664	4.47499374
Art5	0.00091861	-1.98838
Asb13	1.85E-05	1.64372573
Ass1	0.00075706	-4.59167
Atp5sl	0.00042812	-3.33921
Atp6ap2	8.81E-05	1.50982367
Atp6v1a	0.00047124	1.73561393
B230339M05Rik	0.0004623	1.76858116
B230342M21Rik	0.00024275	-4.2556
BC046331	0.00013105	1.78627569
BC057552	0.00055546	3.46757471
Bat4	0.00094131	-1.786
Bcas2	0.00086032	1.84687214
C6	0.00040933	3.56746614

Cacna2d1	0.00011862	-1.50538
Cc2d1a	9.51E-05	2.23470678
Cd164	5.89E-06	1.94154399
Cd81	0.00029425	1.79388286
Cdc42se1	7.59E-06	3.48869662
Cdca3	0.0004697	9.92358837
Chaf1b	0.00056795	2.08374574
Chchd7	0.00059231	-2.5457
Clec2d	0.00065366	-2.76112
Cln3	0.00051038	1.84748631
Cmtm8	0.00085862	-2.43945
Col4a1	0.00072544	5.68734395
Coro1c	4.67E-05	2.24234352
Cpsf4	0.00080621	-2.76318
Cpsf4l	8.58E-05	-7.88538
Cs	0.00026994	3.12548836
Ctnna1	0.00030325	1.60245368
Ctnnal1	0.00084617	2.59525225
Ctsb	0.00016576	1.61413987
Cyp2d9	6.14E-05	18.2602709
Cyp4b1	0.00033447	-6.05147
Cyp4f15	0.00034366	-3.27699
Dab2ip	7.11E-05	3.47765606
Dbnidd2	1.76E-05	3.65203418
Dbt	0.00021108	-2.31158
Dcxr	0.00040588	-3.43194
Ddt	0.0001438	-2.05594
Ddx3x	0.00052266	1.53746101
Degs1	0.0002986	1.58071777
Dgcr6	7.66E-05	-2.06081
Dhx32	2.78E-05	1.8437224
Dpp7	0.00028918	2.38137763
Dscr1l2	6.91E-05	3.46416323
Dync1i2	7.88E-05	1.80625397
EG317677	0.00050143	-3.09292
Edg8	0.00076931	-2.01095
Efha1	0.00083733	2.42411314
Egln2	9.40E-05	-2.49171
Egln3	0.00083032	6.00488798
Ehd4	0.00044775	2.82194116
Eif2ak2	0.00026146	2.46236885
Elf3	0.00037378	3.49606343
Elmo1	2.98E-05	3.52322333
Emp1	0.00052741	7.66430351
Emp2	0.00078179	3.79572905
Endod1	1.59E-05	8.51317414
Ercc3	0.00025084	2.13541066
Erh	0.00040768	1.8347109
Ermp1	0.00011604	2.74704144

Es22	0.00052835	-4.33985
Espn	0.00072195	12.329468
Ets2	0.00029494	3.27046411
F2r	0.00016945	2.99224709
Fahd2a	0.0002186	-1.95798
Fam102a	0.00026582	2.0349482
Fam164a	0.00049495	5.05379768
Fbxo4	2.89E-05	1.86930563
Fbxo6	0.00090882	2.94159175
Fez2	0.00044826	1.50631447
Fkbp1a	0.00062218	2.9793738
Fkbp8	0.00050552	-2.4022
Fnbp1l	4.21E-05	2.44920352
Fntb	0.00050053	2.00650509
Foxa1	0.00036771	2.35101611
Galnt10	0.00016936	3.6608313
Gars	0.00056286	2.78483269
Gas6	0.00012836	4.26852433
Gchfr	0.0001919	-2.48064
Gde1	0.00061153	-2.08708
Gfer	2.08E-05	1.71053037
Ghdc	0.00033654	-2.16081
Glr2	0.00084817	-2.05124
Gls2	0.00060933	-6.62361
Gm129	0.00025626	-5.2766
Golm1	0.00024623	8.74860022
Gpt1	0.00039924	-2.34149
Gpx4	0.00070411	1.90334074
Grcc10	0.00082674	-2.23548
Gspt2	0.00045055	5.1129711
Gstm1	0.00028571	2.00281596
Gtpbp2	1.20E-05	2.11645139
Gypc	0.00060642	-3.11474
H2-M3	0.00017366	-1.65073
Hdgfrp2	0.00059353	1.87511719
Hint3	0.00015509	-2.08559
Hist1h1c	0.00027456	4.43606521
Hist1h2bc	2.86E-06	1.81373323
Hist1h4m	0.00098145	3.9529754
Hn1	0.0001511	10.5393291
Hn1l	0.00062367	2.62390747
Homez	0.00025499	-2.7938
Hpgd	0.00080484	-2.54824
Hspbap1	0.00021366	4.91067482
lah1	0.00081951	-2.05984
ldh2	0.00035443	2.90794888
lfit2	0.00022972	9.5848789
lft172	0.00014308	-1.59543
ll18bp	0.0006608	-2.16123



Il20ra	0.00043313	-2.14544
Inhbe	0.00058909	3.55021603
Inpp5f	0.00039439	1.59902012
Ivd	0.00041384	-2.25625
Jun	0.00052315	3.45889108
Kif22	0.00026542	8.23920047
Kif3a	0.00019683	1.91408074
Klf1	0.0002063	-5.7912
Klf6	0.00067604	4.95547506
Klhdc8b	1.72E-05	-2.83274
Klk1b4	0.000257	11.8059991
Kpnb1	2.94E-05	3.55792118
LOC100040592	3.29E-05	1.96481797
LOC100044221	0.00015242	3.80113958
LOC100044298	0.00089635	-2.677
LOC100047490	0.00025812	1.87185995
LOC100047911	0.00036668	2.10228013
LOC100048295	1.50E-05	-1.70232
LOC100048331	0.00089861	1.95324326
LOC100048622	0.00093017	1.81298021
LOC677317	0.000291	2.94228415
Lasp1	1.41E-06	3.56515136
Lgals1	0.00016822	7.14045999
Litaf	0.00016973	2.69545412
Lmo4	0.0003154	1.64497764
Lrp10	0.00028999	2.25077708
Ly6c1	0.00066315	3.40210114
Lym5	0.00019718	-2.34135
M6prbp1	0.00043317	2.43025768
MacroD1	0.0008634	-5.71388
Mad2l1bp	0.00014556	1.9223856
Magee1	0.00084982	1.92124804
Mark2	0.00059788	2.37501484
Mast2	2.18E-05	4.89339734
Mcl1	0.00055409	1.64793514
Mcoln1	0.00054269	-2.04155
Mdfic	0.00031086	4.83210839
Mea1	0.00062408	-1.90899
Mgmt	0.00035257	-2.49704
Mif	0.00025842	1.74717656
Mpv17l	0.00025873	-3.02653
Mrpl38	5.65E-05	1.78625335
Mtap7d1	0.00042832	2.31502381
Mtdh	0.00086878	1.55260216
Mthfd1	7.01E-05	-2.49556
Mylc2b	0.00029093	1.97769555
Myo5b	2.71E-05	4.54977683
Myo9b	0.00011479	2.96800197
Nans	0.00049712	2.3778442

Ndufb7	4.11E-05	-1.83585
Nfkbia	0.00012675	-2.63213
Ngef	0.00071526	-3.83174
Nid1	0.00011364	4.97136494
Nme3	0.00020179	-2.11392
Nr1i3	0.00074835	-4.72779
Nras	0.00011143	2.09323258
Ociad2	0.00097757	3.68735642
Olfm1	7.98E-05	-4.10583
Olfr1443	0.00054228	-2.02909
Olfr244	6.28E-05	-1.98993
Olfr497	0.00032311	-1.62597
Os9	0.00047179	-2.06542
Otc	0.00061788	-2.32973
Pacs2	0.00032883	2.13049722
Pak4	0.00055586	2.03751472
Pdlim7	5.30E-05	5.18672199
Pemt	6.99E-05	-2.0265
Pgp	0.00017031	2.49156605
Pgs1	0.00062592	2.32596545
Pi4ka	0.00098784	-1.88642
Pigyl	0.00089176	-2.73746
Pkp2	0.00040667	2.65428003
Plekha1	2.08E-05	3.6234641
Plrg1	0.00087433	1.5088623
Polr2g	0.00095113	2.3264687
Ppm1k	0.00058217	-3.49575
Ppp2ca	0.00033168	2.09910725
Ppp2cz	2.08E-05	-1.98615
Prei4	0.00022162	-2.96243
Prkx	4.48E-05	2.41563398
Prmt2	0.00052901	5.24535131
Proz	0.00046383	-1.72764
Prss8	0.00013548	14.0677842
Psm5	0.00052269	1.60501535
Pxmp2	1.64E-06	-2.99779
Pygb	0.00071085	4.41358856
Rab2a	0.00077981	1.51983999
Rab6	0.00040302	2.09457421
Rassf1	0.0008353	2.38605399
Rbx1	0.00037084	1.55087089
Rcan3	0.00013596	3.76151965
Reep5	0.00051668	1.86927418
Rela	0.00056692	1.61927586
Rell1	0.00040698	3.2013625
Rin3	0.00062791	2.39653557
Rit1	6.62E-06	2.11361974
Rpl22	4.69E-05	-2.2148
Rpn2	0.00020654	1.55783623

Rps6ka1	0.00047241	2.26061756
Rras	0.00030352	2.1044391
S100a11	9.58E-06	20.1896209
Samd9l	5.14E-06	3.28038787
Sardh	8.54E-05	-6.8931
Scamp5	5.67E-06	8.47127391
Scnn1a	5.10E-05	-11.354
Sdpr	0.00082162	-2.27242
Sec16b	0.00077491	-1.58962
Selk	0.00070824	2.44723756
Sema3b	0.00014412	-2.12769
Serpina3m	3.55E-05	-5.62556
Setdb2	0.00095995	-2.55889
Sfrs4	8.51E-05	-1.90947
Sipa1l1	0.00057032	2.43975036
Slc24a3	0.00031909	6.33850132
Slc25a38	0.00076283	-2.21953
Slc27a1	0.00048481	-3.65496
Slc27a5	0.00073793	-2.20446
Slc35a5	4.55E-05	-2.07827
Smox	0.00095584	2.54443215
Sntg2	0.0002276	-3.40503
Snurf	0.00020793	3.17505675
Snx7	0.00073005	3.82706269
Spata2L	0.00067134	-5.54556
Spns1	0.00078088	-1.53399
Spon2	0.00027226	27.2268871
Srrm2	0.00031753	-1.8627
Taf13	0.00045924	1.78259157
Tax1bp3	1.83E-05	3.86097405
Tcn2	0.00095325	-2.0379
Tctex1d2	0.00079511	2.04010437
Tjp2	0.00063412	3.07890305
Tjp3	0.00011915	9.8284928
Tk1	3.60E-05	-5.25065
Tmem176b	4.32E-05	3.86746955
Tmem183a	0.00049853	-1.97546
Tmem184a	0.00096728	3.82185566
Tmem43	4.79E-05	5.03101621
Tmem51	0.00078902	2.24571237
Tmem63a	0.00066592	-3.87228
Tmem65	0.0001378	2.15253278
Tnfaip1	0.00071858	2.41895883
Tnfaip2	0.00056619	5.22258664
Tnfrsf12a	0.00015617	8.03148341
Tnxb	0.00021388	-3.42594
Tpd52l2	0.00031028	1.51853832
Tpr	0.00034382	1.92621814
Tprkb	0.00032401	-1.68397

Tpst1	0.00070913	-3.33604
Tpst2	0.00077105	-1.85241
Trak1	0.0001498	-2.28932
Trappc6a	3.82E-05	-1.85138
Trmu	0.00026078	-1.71091
Ttc39a	0.00010749	3.53222092
Ttyh2	0.00047935	1.62675425
Tubb2b	2.15E-05	11.4957328
Tubb6	0.00041668	4.81065271
Uaca	0.00046498	1.96675399
Uap1l1	3.86E-05	5.3922018
Ube2d2	0.0008843	1.70023786
Ugt2b34	0.00022674	1.69088007
Unc13b	5.85E-06	8.43063693
Usp20	0.00026062	4.64136196
Vcl	0.00015528	2.53495706
Vkorc1	0.00040137	-1.81984
Wasl	0.00098401	1.57243088
Xpnpep1	0.00064862	1.97496924
Yif1b	2.58E-05	-1.69538
Ywhah	0.00067309	2.34969031
Zbtb33	0.00019816	2.13616789
Zdhhc14	0.00082726	-2.68867
Zfand2a	0.00085748	1.90044699
Zfp161	0.00022491	-1.64273
Zfp213	0.00064868	-1.83157
Zfp238	0.00015371	2.94320209
Zfp36	1.15E-05	-2.70242
Zfp41	8.54E-05	3.79757411
Zfp715	1.93E-05	-2.08469
Zkscan14	0.00024398	-2.07696
Zmym3	0.00025687	1.86317235
0610012D14Rik	0.00090552	-3.7858
1190003J15Rik	5.14E-05	-1.63114
1700029P11Rik	8.72E-05	-1.73657
1700047I17Rik1	0.00040948	3.37676985
1810049H13Rik	0.00099431	-2.50287
2010106G01Rik	0.00071534	2.05767668
2310045A20Rik	0.00060292	3.73329351
2810004N23Rik	7.63E-05	-2.03563
4933426M11Rik	0.00018288	-1.73781
5730502D15Rik	0.00085705	-2.01222
5930434B04Rik	2.82E-05	-2.36581
6330503K22Rik	7.92E-05	-1.83809
8430410K20Rik	0.00087695	1.69556762
9130005N14Rik	3.73E-05	3.19469425
9530008L14Rik	6.20E-05	-4.84501

**Supplementary Table 2**

Genes differently expressed in AKT-CAT+DDC tumors in comparison to normal PBS treated liver tissue ( $p < 0.001$ , fold change  $> 1.5$ )

<b>Gen_Symbol</b>	<b>p-value</b>	<b>Fold change</b>
A1bg	1.49E-06	-46.6299
A230050P20Rik	5.10E-04	2.01282573
A530050D06Rik	1.66E-06	-7.3574
AI316807	5.01E-04	-1.90517
AI317395	1.17E-04	-4.21205
AI467606	5.29E-04	-1.74403
AI595366	6.75E-05	3.24096581
AU040320	3.62E-04	1.97317274
AW146242	3.99E-04	3.51790614
Aadat	4.17E-04	-3.7298
Aass	3.27E-04	-5.83774
Abat	7.71E-05	-3.08927
Abcc6	5.78E-04	-3.42502
Abcg8	9.65E-04	-9.16427
Acad10	3.35E-04	-2.06148
Acat1	2.76E-04	-4.70545
Acat2	2.63E-06	2.33635034
Acot10	1.60E-05	4.61591012
Actn3	6.75E-05	-1.78481
Acvr2b	4.62E-04	-2.1785
Acy1	8.58E-05	-3.3611
Afmid	1.08E-04	-10.051
Agps	4.88E-04	2.17484444
Agrn	8.32E-04	2.61552787
Agxt2l1	4.56E-04	-12.3078
Ahcy	2.80E-04	-4.08223
Ahnak	6.03E-05	2.87416613
Akr1a4	2.63E-04	1.83138444
Akr1b8	3.44E-05	-4.95084
Aldh1l1	8.36E-05	-2.8896
Aldh3a2	1.75E-04	2.25259217
Amd2	1.14E-04	-2.05899
Amn	1.44E-04	6.55883935
Amt	8.94E-04	-1.77271
Ank	1.32E-04	-8.16363
Ank3	3.65E-04	3.12829449
Anks1	6.11E-04	-2.55589
Ano10	5.37E-04	2.61070703
Anxa2	1.42E-06	11.2908744
Anxa5	3.92E-06	21.1627671
Aof2	2.42E-04	1.93970994
Apcs	5.08E-05	-4.50238
Apom	4.15E-04	-9.48833

Appbp1	3.63E-04	1.73368516
App1	2.83E-04	4.20406533
Arhgef19	3.42E-04	2.47739992
Arhgef2	9.36E-05	2.55139791
Arl6ip1	3.20E-05	2.54791351
Arl6ip5	8.44E-04	2.77427141
Arl8a	1.67E-04	2.82440398
Arpc5	8.73E-05	1.86758452
Arpp19	1.28E-05	3.64947521
Arrdc2	9.01E-04	-6.27557
Arsa	4.34E-05	6.370847
Asns	3.35E-04	2.78072844
Atp9a	8.56E-04	2.16457713
Atpif1	1.24E-04	2.5501942
Axin2	3.61E-04	5.497375
B230342M21Rik	2.69E-04	-14.7425
B930041F14Rik	2.37E-05	22.0824648
BC014805	1.95E-04	-18.3189
BC025446	8.36E-04	-2.01629
Bahd1	9.63E-05	2.12216903
Bax	1.85E-05	1.99549019
Bdh2	2.24E-05	-34.9784
Bicc1	1.20E-04	18.7928948
Birc2	8.73E-04	1.81624339
Bmper	2.53E-04	-6.48621
Brp44	9.60E-05	-3.25658
Btbd12	4.27E-04	1.79148864
C430004E15Rik	1.13E-04	4.46482389
C6	5.37E-05	6.97413294
Cadps2	3.82E-04	-2.10327
Calca	3.03E-05	-3.48328
Calml4	1.21E-05	12.5252697
Casp2	1.21E-04	2.13072873
Cbr3	3.52E-05	8.77716533
Cbx7	5.64E-04	-4.02876
Cc2d1a	8.00E-04	1.78441103
Ccdc120	4.74E-05	3.40105977
Ccdc3	4.87E-04	3.45098905
Ccdc41	4.10E-05	1.84744877
Ccl2	2.82E-04	-2.98899
Ccl27	2.46E-05	-2.7014
Cd163	8.94E-04	-4.04234
Cd276	4.27E-04	8.80219703
Cd63	7.23E-06	8.35289302
Cd9	9.73E-04	4.66720495
Cdc42se1	8.68E-06	3.92948924
Cdca3	3.67E-04	6.43355744
Cdk5rap1	6.13E-04	1.72029396
Cdkl2	2.86E-04	2.09910725

Cenpm	2.90E-04	4.66733565
Cenpt	6.48E-04	4.83949805
Chrn1	9.89E-04	6.63706536
Cisd1	2.77E-04	-4.37976
Clcn2	9.62E-04	-4.11006
Clec11a	6.86E-06	-2.71002
Clec2d	6.93E-04	-4.10705
Clic6	1.33E-05	-6.4868
Cln6	3.30E-04	5.17804715
Clstn3	9.79E-04	8.67054529
Cml1	2.94E-04	-3.68198
Cmtm8	8.40E-04	-2.49685
Cnot6l	2.26E-04	-2.00346
Cnr2	4.73E-04	-7.94725
Col4a1	4.18E-05	12.3232993
Col4a2	1.35E-04	4.85410973
Commd10	2.47E-04	2.01412303
Cox15	1.77E-04	2.01174456
Cox19	4.90E-05	2.81211685
Cpne8	2.44E-05	7.18117383
Cpsf4l	3.27E-04	-11.8112
Cry2	4.45E-04	-2.31467
Cryl1	9.80E-06	-14.4113
Cs	3.20E-04	2.8295507
Csad	3.73E-04	8.04647645
Cstb	1.60E-05	4.37124073
Ctdspl	9.20E-04	1.73151478
Ctnna1	1.02E-04	1.86873274
Ctsc	2.10E-05	-6.63038
Cux2	8.98E-04	-16.5328
Cxcl16	2.00E-04	3.77847554
Cyp2b10	1.18E-05	-88.7287
Cyp2b13	1.76E-05	-48.2838
Cyp2b9	4.38E-05	-43.2179
Cyp2c37	8.36E-04	-8.96284
Cyp2d13	1.50E-04	-7.22417
Cyp2d22	5.66E-04	-1.82309
Cyp2d26	4.40E-05	-3.02588
Cyp2d40	5.74E-04	-3.42828
Cyp2d9	1.55E-06	46.377887
Cyp2f2	2.22E-05	-215.906
Cyp4b1	2.84E-04	-4.22471
Cyp4f15	8.74E-06	-4.31021
Cyp4f16	4.30E-04	2.04223756
D5Wsu178e	8.14E-05	1.91493843
D9Wsu20e	3.13E-04	-2.75465
Dab1	1.42E-04	3.20297236
Dab2ip	2.94E-04	2.49379668
Dact2	1.62E-06	2.3065284

Dalrd3	4.68E-04	-1.88149
Dbnidd2	9.24E-05	3.28393205
Dbt	1.12E-04	-3.78454
Dcun1d3	7.21E-05	-2.09216
Dcxr	7.15E-04	-3.40295
Ddt	5.87E-04	-3.21716
Ddx1	7.32E-04	1.84027516
Dhrs1	3.70E-04	-1.99509
Dhrs7b	1.02E-06	2.11608862
Dhx32	4.70E-05	1.93486846
Dpm1	1.46E-04	-2.02808
Dpp7	8.28E-04	1.81158764
Dscr1l2	5.29E-04	2.84494212
Dusp7	4.90E-04	-1.74276
Dusp8	7.19E-04	2.79794631
Dync1i2	9.65E-06	1.9527131
Dynll1	2.45E-04	3.10738501
Dyrk3	7.22E-04	3.95741818
EG13909	2.20E-04	-9.73038
EG317677	6.76E-04	-2.81457
EG381438	4.79E-04	-1.71127
EG622339	3.08E-04	1.9332899
Ecm1	3.21E-04	-13.5721
Efha1	9.73E-06	2.92920979
Eftud2	1.07E-05	1.89153915
Egln2	4.17E-04	-2.06385
Egln3	1.04E-04	4.86220511
Ehd4	4.48E-04	2.75529913
Elf3	5.52E-05	6.12369871
Emp1	1.24E-04	12.5514767
Emp2	1.12E-04	5.7664141
Endod1	1.42E-07	7.8486159
Entpd2	5.69E-04	2.90680774
Entpd5	1.99E-04	2.56830405
Epb4.1	5.58E-04	-1.80908
Epb4.1l1	5.57E-04	3.44698027
Epha1	2.71E-04	2.84566264
Ephx1	1.61E-05	2.80389292
Eps8l2	6.55E-05	6.86723573
Erh	2.79E-04	2.10784138
Ermp1	9.38E-05	4.55352671
Espn	6.26E-05	29.3903271
Ets2	7.25E-05	4.7681715
Evc2	4.41E-04	-2.32208
Expi	4.28E-05	-6.75794
F10	6.77E-04	-1.94964
F11	3.31E-04	-8.47234
F2r	2.62E-04	2.90232796
F7	3.12E-04	-2.98327



F8	1.54E-04	-5.92339
Fam110a	1.93E-04	4.30880332
Fam164a	4.06E-04	6.52609459
Fam173b	9.16E-04	-1.68183
Fblim1	5.22E-04	3.43576494
Fbxo25	9.29E-06	3.10852482
Fbxo31	7.47E-04	-4.52386
Fbxo6	3.43E-05	3.22176366
Fchsd1	3.83E-04	11.0545731
Fdps	2.90E-04	2.23265118
Fez2	8.53E-04	1.79814719
Fgf1	3.05E-04	-13.512
Fkbp11	2.14E-04	7.11409587
Fkbp1a	4.66E-04	3.45824515
Fmo3	9.04E-05	-71.3542
Fn3k	6.30E-04	-11.6692
Fnbp1l	1.00E-05	2.84447276
Folr2	3.50E-05	-6.81736
Foxa1	4.57E-05	2.916804
Foxo1	4.79E-04	-3.03203
Frap1	8.52E-04	1.85795558
Frk	2.01E-04	5.19458932
Ftcd	2.23E-04	-13.3403
Gadd45g	9.82E-05	-3.78526
Gal3st4	2.40E-04	-1.84154
Gale	2.46E-05	5.07073678
Gars	7.00E-06	3.70669652
Gas6	7.56E-05	5.51931207
Gas8	2.97E-05	2.62560914
Gca	9.60E-04	4.0888758
Gcdh	3.24E-04	-2.2368
Gchfr	3.18E-04	-2.07326
Gdf2	7.21E-04	-2.05376
Ghr	4.19E-04	-5.4207
Gipc2	1.19E-04	3.66277558
Gls2	5.44E-05	-62.6227
Gm2a	5.60E-04	-2.2614
Gmcl1	2.35E-04	2.07143982
Gnmt	6.02E-04	-6.18479
Gnptab	9.70E-06	1.81153841
Golm1	1.38E-05	9.83342183
Gpld1	9.75E-04	-3.43231
Gpr172b	1.19E-04	2.42380173
Gpr180	1.01E-04	-2.45283
Gpt1	4.61E-04	-2.12437
Gpx4	5.35E-04	2.48088478
Gpx7	1.08E-04	4.00729327
Gspt2	1.61E-05	6.08805767
Gstm1	2.46E-05	2.28291739

Gstm2	4.66E-05	6.44653885
Gstm4	7.11E-04	1.81189619
Gstm6	4.12E-05	4.13018338
Gstp1	1.39E-05	4.07247374
Gtf2h2	9.72E-04	1.77415063
Gtpbp2	2.34E-04	1.87302045
Guca2a	4.09E-04	2.03495234
Gzf1	7.43E-04	-1.721
H2-M3	3.44E-04	-2.36402
Hao1	1.97E-04	-2.9846
Hapln4	6.39E-04	3.08044901
Hbs1l	5.08E-04	-2.4788
Hexim1	6.32E-05	-4.40681
Hgfac	5.11E-05	-3.14928
Hist1h1c	4.66E-05	4.50174668
Hist1h2bf	3.34E-04	1.89451708
HK3	9.92E-04	-5.45138
Hmga1	6.39E-04	-1.86638
Hn1	7.85E-07	10.3701092
Hnrnpab	8.03E-04	1.77401529
Hnrpd1	2.24E-04	-1.83632
Hrg	4.75E-04	-4.86692
Hrsp12	7.73E-04	-3.05712
Hsd11b1	3.65E-05	-8.9528
Hsd17b7	6.22E-04	2.49131155
Hspbap1	4.68E-04	3.53454309
Htatif2	4.70E-05	2.47315391
Icam1	9.71E-04	3.78196231
Ick	5.20E-04	2.42059246
Igf2bp3	1.24E-04	2.73949336
Igfbp2	9.16E-04	-36.5345
Ihh	1.01E-04	4.49585707
Il11ra1	4.06E-04	-1.92636
Il18bp	7.27E-05	-2.9821
Inmt	9.69E-04	-14.5052
Ipo5	1.28E-04	2.34291351
Itpr3	2.16E-04	5.50769976
Ivd	6.61E-04	-2.09533
Jak3	4.21E-04	2.74153619
Kat2a	4.16E-04	1.76294087
Kcnk6	8.31E-04	-2.77698
Kif3a	7.11E-04	2.07202783
Klf1	6.43E-07	-8.34985
Klf15	2.56E-04	-4.00585
Klf6	2.47E-04	5.83699605
Klhl26	5.38E-06	-2.02032
Klhl7	8.85E-05	-2.01654
Klk1b4	7.71E-05	8.31310478
Klkb1	6.42E-04	-2.54297

Kng1	3.97E-05	-1.77951
Kras	1.55E-04	-3.02589
Krt18	1.32E-04	3.72223215
Krt8	1.08E-04	3.77058267
LOC100040592	1.43E-06	2.18863399
LOC100042777	6.02E-05	1.89604731
LOC100044101	4.87E-04	-1.74904
LOC100044221	8.60E-05	7.00942768
LOC100044475	2.57E-04	2.8846875
LOC100046120	8.32E-06	2.00887118
LOC100047046	3.35E-04	2.55862448
LOC100047167	8.63E-04	-2.99755
LOC100047173	8.52E-05	-4.77773
LOC100047749	6.24E-05	-2.45135
LOC100047762	6.71E-04	-11.0511
LOC100047911	9.20E-04	2.33775403
LOC100047934	6.68E-04	6.68060687
LOC100047937	9.79E-04	-2.52503
LOC100048295	7.31E-04	-1.9916
LOC100048331	1.34E-04	2.27949842
LOC626152	1.02E-04	4.71269081
Large	4.54E-04	3.2388664
Lasp1	3.15E-04	2.95115833
Lcn2	1.88E-04	33.0509679
Lgals1	2.59E-05	10.3626513
Lgals3	1.07E-04	5.65502109
Litaf	5.65E-04	2.55841501
Lmo2	6.56E-04	4.73408637
Lpl	4.03E-04	7.79137806
Lrp1	6.61E-04	-2.45637
Lrrc20	4.12E-04	2.54493723
Lrrc59	4.38E-04	2.42946651
Lrrc8	9.83E-04	-2.17121
Lrtm1	7.21E-05	-38.9861
Lsm3	8.93E-04	1.92906444
Lxn	1.69E-04	7.04379125
Ly6e	5.02E-04	3.67997468
Lym5	1.06E-05	-3.28435
Macrod1	1.32E-06	-5.21071
Maged2	6.39E-05	3.02988986
Magix	7.31E-04	-4.15551
Map1lc3b	9.50E-05	-2.20016
Map3k1	3.48E-04	4.64190058
Mapkap2	6.99E-04	2.69650802
Mapre2	4.03E-04	-2.09761
Mapt	8.43E-05	9.91158863
Mark2	6.33E-04	1.96377233
Masp2	3.49E-04	-1.78851
Mcc	9.62E-04	-3.70952

Mcl1	5.04E-04	1.73344474
Mcm10	4.28E-04	-4.33344
Mcoln1	6.05E-04	-1.96673
Med19	6.22E-04	2.05025167
Metrn	1.16E-04	-3.20154
Mfge8	1.16E-05	9.55465742
Mgat4b	1.60E-04	2.15810725
Mgmt	1.11E-04	-8.73689
Mif	6.42E-05	1.83993317
Mkln1	1.53E-04	1.81330896
Mrxip1	6.74E-04	-2.01998
Mmp24	6.62E-05	5.0303076
Morf4l2	4.46E-05	1.75547621
Mosc2	5.93E-04	-2.77778
Mpst	2.57E-04	-2.86036
Mrc1	7.02E-04	-4.82647
Mre11a	5.72E-05	3.42271175
Mrgpra2	4.53E-04	-2.1359
Mrpl39	2.82E-04	-1.80296
Msi2	4.14E-04	2.38220587
Mtdh	8.59E-05	1.79360615
Mthfd1	7.04E-04	-2.03068
Mug2	6.30E-04	-8.6757
Mupcdh	6.07E-04	2.16527079
Mvp	7.36E-05	3.82545226
Mylc2b	1.05E-04	3.07922539
Myo9b	2.26E-04	3.09672305
N4bp2	3.52E-04	-3.10433
Nadk	4.33E-04	2.09331583
Nans	1.15E-04	2.73383891
Ndrp2	6.63E-04	-4.11093
Ndufb10	6.29E-04	-2.31516
Ndufb2	6.80E-04	-2.7802
Ndufb5	3.77E-04	-2.04925
Ndufb7	9.07E-06	-2.18487
Nedd9	2.68E-04	4.43976789
Nek3	1.12E-04	1.99149631
Nfkbia	1.04E-04	-2.22916
Nhej1	5.66E-04	2.07562326
Nid1	2.85E-08	5.14178471
Noc3l	2.85E-04	2.29701296
Nola2	4.87E-04	2.16635435
Npal2	3.44E-06	4.05607113
Nr1i3	2.45E-04	-14.4542
Ntrk2	2.91E-04	-30.1584
Nudt18	9.85E-04	2.3830347
Nudt2	5.39E-06	2.16941857
Oasl1	4.52E-04	7.35337373
Olfml1	2.72E-04	1.8390534

Olfr1443	6.34E-04	-2.12648
Oprs1	8.59E-06	2.01932494
Orm1	7.41E-04	-2.02456
Osbpl3	3.68E-04	18.0922779
Ostb	4.02E-04	4.1935051
Otc	3.36E-04	-4.89165
Pacs2	3.15E-04	2.12057145
Pafah1b3	7.80E-04	4.59204291
Palmd	2.79E-04	2.10461184
Pank2	2.88E-04	1.69764299
Parp6	4.82E-04	-2.02717
Pdgfa	9.81E-05	5.74089064
Pdgfb	4.21E-04	6.18314475
Pdlim7	6.94E-05	5.0245449
Pdzk1ip1	9.48E-05	5.87095638
Pecr	2.10E-05	-2.68099
Pgd	8.87E-05	2.73574608
Pgp	2.15E-05	2.5542197
Pgs1	6.54E-04	2.35196165
Pigr	5.45E-05	-8.02032
Pim3	3.96E-04	-2.62671
Pkia	2.92E-05	4.89660812
Pkp2	2.04E-04	2.93200103
Pla1a	4.56E-04	-2.31842
Plekha1	2.41E-05	3.33456712
Pols	9.65E-04	-2.0273
Ppap2c	1.27E-05	4.67010386
Ppia	3.27E-04	1.9995561
Ppl	3.59E-04	13.0816768
Ppm1k	1.10E-04	-4.71149
Prdx6	5.47E-04	-2.0469
Prhoxnb	1.69E-04	-13.125
Prickle1	5.99E-04	-6.10051
Prkx	6.14E-05	2.82922247
Prss8	2.40E-04	9.71722865
Psmc10	4.33E-04	1.94670316
Ptpn14	6.54E-04	4.96563779
Ptprs	7.03E-04	2.97635878
Pxmp2	6.06E-06	-4.95416
Pygb	7.92E-05	12.0580135
Rab22a	1.79E-04	-1.72656
Rab27a	4.55E-04	-3.78577
Rab3ip	1.24E-04	-2.00089
Ramp1	3.05E-04	-4.83407
Rassf1	5.45E-06	2.85945493
Rassf3	3.82E-04	3.4622682
Rcan3	1.83E-04	3.82532056
Rcl1	8.43E-04	-1.69053
Rdh20	8.07E-04	-9.40044

Reep4	4.22E-04	5.67736661
Rhbdf1	3.79E-04	4.24212344
Rhoc	6.66E-05	3.52380684
Rhod	2.20E-04	2.3952899
Rnf44	4.56E-04	1.72153189
Rnpep	7.83E-04	3.19962116
Rpa1	5.84E-04	2.39617379
Rpia	2.68E-05	1.96997366
Rpl22	6.30E-04	-1.73259
Rps6kl1	7.09E-04	3.76917568
Rras	3.20E-05	4.48076854
Rxra	3.65E-04	-2.24654
S100a11	7.67E-07	34.0571615
Sall1	4.10E-04	-3.07941
Samd9l	3.40E-05	3.43362966
Samhd1	6.69E-04	-2.20887
Sardh	1.83E-06	-4.67937
Scamp5	1.33E-05	9.20759442
Scara3	4.03E-04	6.88122321
Scarf1	2.08E-06	-2.41693
Scd2	6.05E-04	6.79814275
Scnn1a	2.48E-04	-15.7552
Sdc2	2.39E-05	-2.42333
Sdcbp2	1.54E-05	8.9844838
Sdhb	4.16E-04	-1.91593
Sdpr	2.02E-04	-3.53426
Sds	2.60E-05	-126.897
Sdsl	1.68E-04	-22.0833
Sec14l4	4.04E-04	-4.52097
Sema3b	3.19E-04	-2.57577
Sepn1	4.95E-04	2.05764704
Serpina11	5.89E-04	-3.0292
Serpina12	1.87E-05	-12.6949
Serpina1a	1.05E-05	-31.6368
Serpina1b	3.40E-04	-2.80168
Serpina1c	2.87E-06	-62.6063
Serpina1d	2.98E-04	-3.30845
Serpina3k	9.41E-04	-98.5689
Serpina3m	3.40E-07	-34.8319
Serpinb6a	1.53E-04	4.23484771
Sftpd	6.16E-05	2.99782658
Sfxn1	2.58E-04	-5.85647
Sh3bgrl3	5.10E-04	1.9319117
Shroom3	9.06E-04	3.35828539
Siat9	5.32E-04	-7.67896
Sirpa	9.05E-04	3.21142754
Sirt3	3.37E-04	-2.03077
Skap2	1.32E-04	1.78979886
Slc13a4	7.58E-04	-4.31858

Slc17a2	9.45E-04	-3.36301
Slc22a7	2.87E-04	-3.5632
Slc24a6	7.94E-04	-2.74134
Slc25a38	6.48E-04	-2.19845
Slc27a5	2.37E-05	-2.08916
Slc29a1	1.26E-04	-2.26657
Slc2a9	6.19E-04	-3.19262
Slc35a5	8.18E-04	-2.06092
Slc38a2	7.95E-04	-3.11855
Slc38a3	7.92E-04	-5.26719
Slc6a6	3.46E-04	2.10417785
Slc6a8	3.22E-04	7.94274867
Slc7a4	4.28E-04	3.3043869
Slco2a1	3.94E-04	-3.76841
Smpd13b	4.20E-04	3.06668507
Snn	9.01E-05	3.98790866
Snora65	4.01E-04	2.31756693
Sntg2	2.56E-04	-11.8287
Snurf	2.55E-04	2.50050635
Snx24	5.98E-04	2.45162935
Sort1	2.29E-04	2.40353993
Spata2L	2.77E-04	-4.17405
Spire2	7.28E-04	4.02065006
Spon2	2.65E-04	24.0931925
Spp1	4.46E-05	6.81867772
Sqle	5.74E-05	5.32501211
Sqrdl	3.12E-04	-7.34294
Sqstm1	8.61E-04	2.06643591
Sra1	3.80E-04	-2.27861
Srd5a3	6.51E-05	2.15263935
Srebf2	8.52E-04	1.81301308
Srpk1	5.82E-04	1.83344273
Srxn1	8.13E-05	5.65093071
St3gal1	2.36E-04	-2.06157
St3gal5	4.02E-04	-4.50168
St6galnac2	5.38E-05	12.2217116
Stim1	9.72E-04	-2.45096
Stk19	7.53E-04	-1.89697
Stk39	6.95E-04	4.41506952
Stt3b	3.40E-05	1.83562695
Sult1d1	7.39E-05	-6.41907
Syt9	1.98E-04	-1.72246
Taldo1	1.54E-04	1.82235335
Tax1bp3	5.67E-06	4.15111727
Tbc1d2	7.43E-04	4.29826522
Tbcel	1.80E-04	2.9209361
Tctex1d2	8.59E-05	2.18366834
Tdrkh	5.52E-04	1.82715481
Tes	2.12E-05	22.4982001

Tfrc	3.97E-04	6.50376893
Tgfbr3	1.74E-04	-5.48013
Tgm2	6.29E-05	4.4237609
Thumpd1	4.24E-04	1.8077756
Timd2	3.23E-04	-1.73523
Timd4	6.89E-04	-5.18924
Tjp2	1.97E-04	2.96672521
Tjp3	1.52E-04	14.1780422
Tk1	1.04E-04	-4.98189
Tmem176b	1.08E-05	4.39129996
Tmem183a	8.63E-06	-1.93406
Tmem184a	4.78E-04	2.33863424
Tmem43	1.72E-05	6.06137751
Tmem45b	3.69E-04	3.04869683
Tmem63a	1.26E-04	-5.1447
Tmem97	3.48E-04	1.90284094
Tnfaip1	2.33E-04	1.99824155
Tnfrsf12a	3.25E-05	13.6314625
Tnfrsf19	6.21E-04	5.98021744
Tnip1	2.95E-04	5.0966841
Tnnc1	9.99E-04	-3.42942
Tpd52	1.04E-06	4.20638192
Tpd52l1	4.50E-04	-5.28516
Tpm4	1.56E-04	3.25967553
Tpp1	5.55E-04	-1.68965
Tpr	3.78E-05	2.78583348
Trim47	3.85E-04	3.73184458
Tsc22d3	6.08E-04	-4.17941
Tspan17	4.49E-04	5.21983328
Tssc1	3.30E-04	1.98398527
Ttc17	7.87E-04	-1.80439
Ttc39a	1.03E-04	4.19732463
Ttpa	6.82E-04	-1.85766
Tuba1b	5.61E-04	3.37355738
Tubb2b	1.81E-06	16.1140618
Tuft1	3.96E-04	3.44481916
Txnrd2	4.39E-04	-1.70926
Uap1l1	3.66E-05	8.85339661
Ube2e2	3.20E-04	1.78436327
Unc13b	1.87E-07	10.4844222
Uox	2.20E-04	-3.04812
Upp2	5.04E-05	-27.9343
Uroc1	3.75E-04	-15.2604
Usp20	3.33E-05	6.33147821
Usp22	1.96E-04	2.31539902
Vasn	1.40E-04	2.12743778
Vcl	5.50E-05	2.49875062
Vegfa	2.16E-04	-2.46239
Wfdc2	2.74E-04	17.2208331



Wfdc3	3.48E-04	-3.17354
Xpnpep1	7.77E-04	2.00852418
Ywhah	4.13E-05	3.18699705
Zap70	5.35E-04	-20.0686
Zbtb33	3.82E-04	1.8299735
Zcchc3	8.73E-04	1.87685574
Zfp276	6.29E-04	-3.38043
Zfp36	2.44E-04	-2.2902
Zfp41	9.58E-05	2.80676543
Zfp428	3.20E-05	1.82642064
Zfp704	7.76E-04	4.73428808
Zfp748	2.13E-04	-1.99739
Zmat3	8.05E-04	2.48852169
Znrf2	7.09E-04	1.76941982
0610012D14Rik	5.70E-05	-5.28578
1110001J03Rik	7.63E-04	-3.08507
1110012J17Rik	9.08E-05	-5.28578
1300007L22Rik	2.46E-04	-2.25719
1300017J02Rik	9.93E-04	-1.90638
1600016N20Rik	1.25E-04	2.04668069
1700001C19Rik	8.82E-04	-3.76203
1700003F12Rik	2.82E-04	5.15649977
1700029P11Rik	3.03E-04	-2.1714
1700088E04Rik	4.18E-04	2.15520493
1810014F10Rik	1.50E-05	-2.69606
1810049H13Rik	9.42E-04	-1.94905
2010001J22Rik	9.03E-05	-12.4782
2310003H01Rik	8.73E-05	2.86203284
2310016C08Rik	9.38E-04	2.63209151
2310016E02Rik	7.65E-04	1.68971152
2310036D22Rik	3.09E-04	-2.20467
2310045A20Rik	8.45E-04	7.18483712
2410015M20Rik	1.66E-04	-2.11094
2410022L05Rik	5.35E-06	3.18921281
2610029G23Rik	1.92E-04	2.23008202
2810007J24Rik	1.98E-04	-16.5503
4732429D16Rik	9.79E-04	-3.12541
4833426J09Rik	1.86E-04	-2.51247
4930506M07Rik	3.67E-04	1.8228317
4930570C03Rik	3.65E-05	1.88674617
4933426M11Rik	4.81E-04	-1.72543
5133400G04Rik	8.29E-04	3.05505826
5133401N09Rik	5.58E-04	-2.02583
5730596K20Rik	1.48E-04	2.50728995
5930434B04Rik	1.16E-04	-2.32978
9530008L14Rik	1.14E-04	-4.9925
9530058B02Rik	1.21E-04	-2.58032

**Supplementary Table 3**

Genes differently expressed in AKT-CAT+CCI4 tumors in comparison to normal PBS treated liver tissue ( $p < 0.001$ , fold change  $> 1.5$ )

<b>Gene_Symbol</b>	<b>p-value</b>	<b>Fold change</b>
A230050P20Rik	0.000933785	1.648003032
A330080J22Rik	0.000164682	-2.54129
AA415398	0.000187057	-3.85901
AI316807	1.69E-06	-2.44007
AI595366	0.000584557	2.384216487
AU040320	6.67E-05	2.312967653
Aatk	0.000901021	-3.42931
Abat	0.00048695	-4.37096
Abcc3	0.000692275	-1.84754
Abcg1	0.000247274	-2.03987
Abi1	0.00078521	1.694785991
Acad10	0.000213425	-3.65802
Acot10	5.91E-05	5.304195619
Acsl4	0.000514296	1.923409821
Acta2	0.000166493	3.591786303
Actn3	0.000885564	-1.66544
Acvr2b	0.000468227	-2.87719
Adam9	0.000557275	3.194806523
Adcy4	0.000902979	-3.75106
Adra1b	3.80E-05	-4.08988
Afmid	0.000732042	-9.13949
Agxt2l1	0.000715881	-8.04252
Ahnak	0.000146484	3.062955998
Aifm1	0.000282707	3.64495247
Aldh1a1	0.000223052	3.59590642
Aldh1a7	0.00025024	2.917884884
Alg1	0.000757181	-2.38175
Ambra1	0.000927261	-2.52232
Amigo2	0.0002666	-2.58337
Ank	0.000814545	-3.14639
Ankrd10	0.000424859	3.56477009
Anks1	0.00051499	-5.23779
Ankzf1	0.000108672	-2.57416
Anxa2	0.0001067	13.92738263
Anxa3	0.00065043	2.269544752
Anxa5	2.09E-05	16.56018468
Ap3m1	0.00093296	-1.88766
Ap4s1	0.000483519	-1.63456
Ap1p2	0.00083649	2.707195183
Ap1p1	0.000248425	3.69253038
Arfl4	0.000942981	-2.98663

Arg1	0.000974616	-2.01267
Arhgap17	0.000942654	2.409493404
Arhgef15	0.000468975	-3.39804
Arhgef19	0.000349687	1.609797874
Arl3	0.00075931	-2.06989
Arl6ip1	0.000107148	2.324343547
Arl8a	1.73E-05	5.277239792
Arpc1b	0.000792188	1.696698225
Arpc5	0.000610903	1.913578948
Arpp19	7.01E-06	4.082865845
Arrdc2	0.000374065	-7.46904
Arsa	7.88E-06	6.31771804
Asap3	0.000738795	2.109940563
Atp5a1	0.000430479	2.113119514
Atp5sl	0.00055888	-2.93047
Atp6v1a	0.000411433	2.360689794
Atpif1	0.000940717	1.734701666
Aven	0.000160833	-2.66044
B230342M21Rik	0.000811251	-6.80689
BC013529	6.04E-05	2.359586884
BC021381	0.000267085	-4.76723
BC030183	0.000358828	-6.59151
Bcap31	0.000220319	4.753416518
Bdh2	0.00069987	-5.04538
Bfar	0.000665431	-2.26018
Blmh	0.00017582	-1.72279
Brp44	8.49E-05	-2.20908
Bxdc1	0.000207898	1.939788951
C1galt1c1	0.000410633	2.364474247
C1qtnf4	3.76E-05	-2.10333
C430004E15Rik	0.00081957	2.307406544
C4bp	0.000128723	2.40663461
C6	0.000234202	5.731447305
Calml4	0.000913301	6.514530661
Casp4	0.000117286	7.735148515
Cbx7	0.000672306	-3.20614
Ccdc120	0.000345418	2.997772655
Ccl27	0.000750144	-2.03547
Cct8	0.000660755	1.643134246
Cd163	0.000731628	-4.30034
Cd63	0.000204252	6.596654177
Cd9	0.000171361	4.115243273
Cdc42se1	0.000408013	3.138131117
Cdca3	0.000208133	6.601270084
Cdipt	0.000541462	1.743183716
Cdt1	0.000839207	6.613362961
Cisd1	0.00037873	-2.57738

Cldn9	0.000251232	-3.33049
Clec2d	6.89E-05	-3.43629
Cml4	1.86E-05	69.34716578
Col18a1	8.07E-05	-2.2142
Col4a1	0.000167914	7.086619753
Col4a2	4.80E-05	4.471272077
Col6a1	0.000595509	3.181936781
Coro1c	0.000294701	2.293162477
Cox19	4.58E-05	2.692572807
Cpne8	0.00057891	5.349453018
Cs	9.47E-05	2.822984742
Cstb	0.000110304	4.55145419
Cstf2	0.00049118	1.601065669
Ctsb	8.50E-05	1.908112914
Cul1	0.000303293	1.812484027
Cux2	0.000578542	-8.39277
Cx3cl1	0.000165506	2.818290707
Cxcl16	0.000496488	3.66198421
Cyp2d9	2.74E-06	40.57140771
Cyp4b1	0.000165296	-5.40612
Cyp4f15	0.00034517	-5.0114
Cyp4f16	0.000444694	1.576173303
D10Jhu81e	0.000133682	-2.2049
D2Ertd391e	0.000301133	-1.7553
D430028G21Rik	0.000398914	-2.02196
D5Wsu178e	0.000392762	1.733387646
D830050J10Rik	0.000302346	-3.81764
D9Ertd402e	0.000470214	-1.60976
Dapk1	0.000809121	-2.30605
Dazap2	0.000187877	1.59804144
Dbi	0.000394125	1.636428201
Dbnidd2	7.02E-05	3.815628816
Dcakd	0.000921291	1.910230622
Ddc	0.000328284	2.924712062
Ddx3x	1.18E-05	2.555420686
Dgcr6	0.000599602	-3.23139
Dhdh	0.000230559	-1.81362
Dhrs7b	2.62E-05	1.739460176
Dhx32	0.000754135	2.765769728
Dnase1l1	0.000395623	3.194469734
Dnmt1	0.000993428	2.870651322
Dpm1	0.000517809	-2.11951
Dpp7	0.000253701	2.233987892
Dscr1l2	7.35E-05	2.969077062
Dstn	0.000617183	1.713367349
Dus4l	0.000961808	-3.84641
Dynll1	0.000231315	2.83318223

Dynlt3	0.000242743	2.439280217
EG277333	0.000200067	4.443160865
EG317677	0.000956628	-2.47036
EG381438	9.13E-05	-2.99687
EG622339	0.00024621	2.238879486
Ecm1	0.000350632	-10.3816
Efha1	3.75E-05	4.147966252
Egln3	0.000225964	4.698607803
Ehd4	0.000162709	3.204727614
Eif3k	0.000663226	1.65722051
Elf3	7.09E-05	8.562816824
Elmo1	0.000233906	3.55846559
Emp1	8.57E-06	16.94162931
Endod1	4.51E-05	6.592218545
Eno1	0.000697302	1.925342904
Enoph1	0.000723532	3.318896135
Ephx1	5.41E-05	2.534423811
Eps8l2	0.000389376	3.584152312
Ercc3	6.04E-05	2.079871214
Ermp1	2.96E-05	3.481991142
Ets2	0.000287081	4.287245445
Exdl1	0.000585075	-2.01638
Exosc8	9.49E-05	2.386925378
F10	0.000993861	-1.77978
F2r	0.000302227	2.519500937
F8a	0.000508237	1.672428182
Fads3	0.000587402	5.782419133
Fam102a	0.000478006	2.295194093
Fam116b	0.000311995	-3.90613
Fam164a	0.000437238	5.556111167
Fam178a	0.000828576	-1.83739
Fbp1	0.000493682	-1.82312
Fbxo25	0.000359539	4.230583736
Fbxo6	4.09E-05	3.061071436
Fen1	0.000548805	2.648529536
Fkbp11	0.000777533	4.207921834
Fkbp1a	0.000223919	4.080600011
Foxa1	0.000845147	1.992309685
Frk	7.74E-05	6.0673721
Ftcd	0.00073156	-3.47189
Gadd45g	0.00053197	-2.1684
Gale	0.000980291	3.940389783
Gbl	2.12E-05	1.671106239
Gca	0.000304272	5.800497683
Gcc2	0.000421878	1.769494968
Gipc2	0.000645679	2.255142288
Glrx3	4.53E-05	2.983925593

Gm129	0.000795925	-11.0169
Gm1821	0.000481333	1.57622796
Gmcl1	0.000939884	2.140951696
Gnmt	0.000337738	-5.64182
Golm1	2.01E-05	11.24953033
Gpc4	0.000946944	2.662236705
Gphn	0.000801875	-1.57661
Gpld1	0.000477448	-3.93183
Gpn2	0.000587206	3.061858732
Gpr108	2.44E-05	-1.84214
Gpr97	9.62E-05	-3.07015
Gpt1	0.000848719	-1.99389
Gpx7	2.67E-05	3.01716465
Grcc10	0.000529421	-2.23239
Gspt2	0.000244598	5.536454787
Gstm1	2.15E-05	2.187752959
Gstm2	0.000387465	3.817070704
Gstm3	7.67E-06	3.412456832
Gstm6	0.00073373	2.898886827
Gstp1	0.000123016	3.499170697
Gstt3	0.000567799	-2.02931
Gtf3a	0.000449502	-2.20429
Gusb	0.000261823	2.619439911
H1f0	0.000178981	4.110811022
H3f3b	1.68E-05	2.145324266
Hdac2	0.000665216	2.640368595
Hgsnat	0.000820774	-1.95185
Hisppd1	0.000136832	3.329570918
Hist1h1c	0.000252505	4.242537377
Hist1h2ad	0.000382946	4.179012165
Hist1h2af	0.000772917	3.772688002
Hist1h2ah	0.00072353	3.625579186
Hist1h2ak	0.000320981	3.378663738
Hist1h2an	0.000370576	5.373022056
Hist1h2bc	0.000355109	1.874069993
Hist1h2bf	0.000617277	1.644193285
Hist2h3b	8.88E-06	2.556139207
Hivep1	0.000344981	-2.43185
Hmox1	0.00073581	-2.01394
Hn1	2.99E-05	18.05458261
Hnrnph3	0.000300824	-2.18032
Hnrpd1	0.00064229	-2.80606
Homez	0.000246921	-2.57063
Hs3st3a1	0.000387142	-3.05834
Hsd3b2	0.00010513	-2.88721
Hspa4	0.000151721	5.421758602
Hspb8	0.000330635	-1.86271

Hspbap1	0.000609921	3.180145714
ldh2	0.00034205	3.555138419
lfngr1	0.000819516	2.382120754
lgf1	0.000475692	-2.42266
ll10rb	0.00074752	3.16228532
ll11ra1	0.000549017	-1.98819
ll15ra	0.000440019	-3.3745
ll18bp	5.89E-05	-2.39483
lmp3	2.53E-05	-1.64608
lnhbe	8.18E-05	2.650417838
lnpp5f	0.000747565	1.89890604
ltgb5	0.000715145	2.01243686
Jun	0.000324382	4.013936387
Kctd2	0.000152069	1.826423971
Kctd3	0.000525661	4.24224941
Kif22	0.000719255	5.952487247
Klf1	3.70E-06	-5.85257
Klf6	0.000978568	4.832808974
Klhl17	0.000171051	-2.03846
Klk1b4	0.000368072	17.3058885
Klkb1	0.00041104	-3.1198
Kpna3	0.000138086	6.440767482
Kpnb1	0.000189348	6.136512865
LOC100040592	1.02E-05	2.084036696
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LOC100042179	5.76E-06	-2.06938
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LOC100044221	0.000142608	6.219253565
LOC100044475	0.000342086	3.929010636
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LOC100044692	0.000174049	2.245117431
LOC100044779	4.95E-05	5.262243926
LOC100045343	0.000252049	2.870593639
LOC100046841	0.000263354	2.780063608
LOC100047619	0.000571271	-2.52374
LOC100047934	0.000587932	5.985586707
LOC100047963	0.000731316	3.74259901
LOC100048622	0.000216629	2.768794578
LOC100048733	0.000686549	2.065723044
LOC433801	0.000365105	4.451943496
LOC677317	0.000768228	3.874782528
Lasp1	0.00017458	3.278527286
Lcat	0.000296518	-2.23232
Lcn2	8.44E-05	30.68416482
Ldhd	0.000390251	-2.10279
Lgals1	0.000148194	11.15990469
Lgals3	0.000356388	5.883321959

Litaf	3.13E-05	2.946801394
Lmbr1l	0.000112095	-6.67142
Lmo2	0.000910454	3.709295123
Lpin1	0.000621129	-7.29604
Lrp10	9.33E-05	2.421729696
Lrrc8	0.000118669	-3.03839
Lsm3	0.000997965	1.859959899
Luc7l2	0.00091527	-2.9727
Lxn	0.000413324	5.709489743
Lyzs	0.000356056	5.888969371
M6pr	9.72E-05	1.978540747
Macrocl	0.000204703	-8.40134
Mad2l1bp	6.61E-06	1.657085948
Magee1	0.000348548	2.677662936
Man2a1	0.000340286	-1.98313
Map3k1	0.000914341	3.988910828
Mapt	4.29E-05	6.645843025
Mast2	0.000382736	4.810606425
Mcm4	6.97E-05	4.034779802
Mdfic	0.000469666	8.213889687
Memo1	0.000483859	2.402408174
Mfge8	0.000138701	6.443174423
Morf4l2	1.57E-05	1.561182752
Mosc2	0.000373841	-3.46736
Mpv17l	0.000743798	-4.48331
Mrpl38	0.000271228	2.091140257
Msh6	0.000335947	1.780518986
Mthfd1	0.000444303	-2.65232
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Mvp	0.000754939	2.958194791
Myl6	0.000535519	2.534976336
Mylc2b	0.000526653	2.522029931
Myo5b	0.000359396	5.703172675
Myo9b	0.00059238	2.10396977
Myst4	0.000266237	-1.59091
Nans	0.0001372	2.949452287
Ndufa8	0.00086706	1.518125661
Nedd9	0.000452951	2.752849199
Nfkbia	0.000183134	-3.31748
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Nme3	0.000305	-2.21318
Nola2	0.000883835	1.559245076
Nosip	0.000552443	-1.78531
Notch4	0.000117491	1.733892571
Npm3	0.00056616	-2.13944
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Nras	0.000518006	1.978846135



Nsf	0.000795022	1.687760865
Nt5c	0.000369165	2.821662467
Nuak1	0.000259929	1.840417407
Nudcd2	0.00012549	6.082022151
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Nudt6	6.61E-05	-1.67368
OTTMUSG00000007855	0.000139147	4.882502576
Ociad2	0.000121121	5.00931733
Olfm1	0.000146526	-3.604
Oprs1	0.000858982	2.180977514
Osgin1	0.000863502	2.151435222
Ostb	0.000401852	5.368118743
Otud6b	0.000157095	3.867664008
Pabpc1	0.000187693	2.333515348
Paip2	0.000932933	2.497982879
Pank4	0.000686618	-1.97918
Pcbd2	0.000214857	-1.70057
Pcyt1a	0.000149216	2.247473839
Pdcd10	0.000563596	1.543181299
Pdlim7	0.000127949	4.728355951
Pfkfb2	0.000297136	-2.21262
Pgd	0.000176253	2.337387922
Pgp	0.000712627	1.84550877
Pgs1	0.000473576	2.555923609
Phf7	0.000450011	-3.05359
Pkia	0.000406051	4.420358403
Pkp2	0.000715226	2.762980482
Plekha1	9.19E-05	2.903499297
Plrg1	9.74E-05	1.556773991
Polg2	0.000327853	-2.39213
Polr2d	2.30E-05	1.800196221
Polr2g	0.000163727	2.981434607
Porcn	0.000446899	-2.84005
Ppap2c	0.000467484	2.544859511
Ppargc1b	0.000650788	-4.06857
Ppp2ca	0.000818967	2.17238293
Prc1	0.00091089	14.1734203
Prei4	0.000207624	-4.93782
Prkx	5.37E-05	2.467089032
Prnpip1	0.000356568	-1.88623
Proz	0.000217287	-2.11675
Prss8	5.07E-05	9.519548393
Prune	0.00076403	3.892413686
Pter	0.000906222	1.924409206
Pthr1	6.87E-05	-2.17331
Ptpn1	0.000853257	2.436385963
Ptpra	0.000472092	4.177475886

Pygb	0.000811329	9.554566127
Qdpr	0.000954264	-2.5568
R3hdm2	0.000529607	3.24403584
Rab11fip5	6.35E-05	3.19144183
Rab22a	0.000917748	-2.11083
Rab32	0.0002029	1.723980395
Rabl4	0.000315183	-1.96302
Rassf1	0.00023916	2.073428393
Rassf3	4.39E-05	10.5065193
Rbl1	0.000473717	1.599511189
Rcan3	0.000678234	3.959627637
Reep5	1.24E-05	2.157455411
Rer1	0.000282442	5.484560961
Rgs16	0.000132459	-37.5667
Rhbdf1	0.000554047	3.937814041
Rhod	0.000704864	2.206974481
Ripk3	0.000229638	-2.20839
Rnpep	5.55E-05	2.942206243
Rpa1	7.11E-06	1.970257
Rpl22	9.73E-05	-2.40103
Rpl29	0.000470777	1.99179381
Rpn2	0.000609074	1.532975843
Rps6ka1	0.000265489	2.419661199
Rras2	0.000290165	3.345466224
Rxra	2.38E-05	-3.49805
S100a10	0.000491225	4.902369315
S100a11	8.84E-06	37.99218881
S100a6	6.62E-05	3.366844661
Sae1	0.000462637	1.758322139
Samd9l	8.71E-05	3.48959751
Scamp5	9.41E-05	7.387215685
Scand1	0.000332573	-1.70981
Scarf1	1.77E-05	-3.33935
Scnn1a	0.000368269	-12.1626
Scrn2	0.000890974	-2.90727
Sdcbp2	0.000335996	6.245901127
Sdsl	0.000437023	-5.17269
Sec14l2	4.48E-05	1.924861121
Selk	3.48E-05	2.996173886
Sepp1	0.000213699	2.990591599
Serhl	0.000899152	-2.10126
Serpina1e	0.000252864	-3.18087
Serpinb6a	0.000718011	5.530484028
Setd3	0.000429861	1.834428181
Setd4	3.27E-05	-5.60408
Setx	0.000268392	2.489382782
Sfrs4	0.000513978	-2.02196

Sfxn1	0.000103305	-2.77312
Shf	0.000513675	-2.45001
Siat9	0.000303523	-3.78103
Sirpa	0.000615193	2.850513377
Sirt5	0.000745842	1.937736646
Skap2	0.000290153	1.662433004
Skp1a	6.26E-05	3.137274587
Slc13a4	0.000406991	-4.2232
Slc15a4	0.000452663	-2.61518
Slc16a10	0.000155616	-3.31692
Slc25a15	0.000354138	-2.16804
Slc25a29	0.000594589	-3.0886
Slc25a32	0.000983359	-3.74494
Slc27a4	0.000524335	1.943241794
Slc2a9	0.000450153	-3.52971
Slc30a6	0.000989177	1.828521275
Slc41a2	8.28E-05	6.763886258
Slc6a12	0.000350214	-2.1262
Slc6a8	0.000168314	8.725698928
Smc3	0.000641986	1.854616604
Smpd1	0.000543456	-1.70962
Snn	5.64E-05	4.118870606
Sntg2	0.00023839	-8.06536
Snurf	5.61E-05	3.858679714
Snx24	0.000964047	2.626112487
Snx3	4.10E-05	6.144695285
Snx7	0.000173473	7.003487737
Sox5	0.000427435	-2.30045
Spon2	0.000384096	26.20984652
Spr	0.000968401	-1.86158
Spred1	6.33E-06	-3.01934
Sqstm1	0.00018795	1.566391504
Srd5a3	0.000124214	1.789312081
Sri	5.18E-05	1.56694621
Srpx2	0.000113079	2.150301795
St3gal5	0.00056269	-3.95692
St6galnac2	6.99E-06	13.41921632
Stab1	0.000788031	-2.7226
Suhw4	0.000460565	-2.67898
Taf13	5.33E-05	2.670669109
Taf15	0.000670741	-2.59458
Taldo1	0.000303049	1.823326915
Tatdn2	0.000334763	-3.50777
Tax1bp3	0.000117529	4.799639067
Tbccl	0.000167893	2.577645115
Tcf19	0.000692692	4.631859784
Tcf7l2	0.00077312	-3.07268
Tef	0.000698027	-2.22122

Tgm2	2.43E-05	5.434073816
Tha1	0.000980603	-2.10274
Thap4	0.00040323	4.102277995
Tjp2	7.28E-05	5.145356316
Tjp3	0.000219487	7.862191507
Tk1	0.000927254	-2.99868
Tle1	1.58E-05	-4.41396
Tmed4	0.000547119	1.556895177
Tmem128	0.00064767	1.674904405
Tmem176b	6.70E-05	5.585468844
Tmem183a	0.000762183	-1.67544
Tmem25	0.000314799	-2.54413
Tmem43	1.07E-05	4.969289789
Tmem49	0.000936019	1.771319155
Tmtc2	0.000174179	-2.04521
Tnfaip2	0.000100544	5.598947398
Tnfrsf12a	4.38E-05	8.75695083
Tnip1	0.000361778	5.416061873
Tomm22	6.11E-05	2.074525245
Tomm70a	0.000899964	2.725813178
Tor1aip1	0.000456213	-2.33122
Tpd52	3.88E-05	3.87688562
Tpd52l1	0.000762997	-4.10949
Tpst1	0.000796411	-3.54802
Trak1	0.000490564	-1.73361
Trip12	0.000865076	1.558032828
Trub1	6.38E-05	-1.81177
Tsc22d3	0.000359444	-2.4433
Tsn	6.66E-05	4.33805603
Tspan17	0.000987852	6.442178229
Tspan7	0.000638393	-3.87975
Tssc1	0.00093538	2.054214838
Ttc39a	5.43E-05	4.964553091
Ttyh2	0.000202643	1.769971026
Tuba1a	0.000701046	6.139979247
Tubb2b	3.75E-06	13.76545861
Tubb5	0.000203772	2.815045857
Tubb6	0.000303799	5.962353699
Tuft1	0.000944436	3.283899697
Tug1	0.000743273	2.680648931
Tulp4	0.00082518	1.560468952
Txndc1	0.000251891	-2.2109
Txndc12	0.000554342	2.535509815
Uap1	3.99E-05	1.995438428
Uap1l1	2.07E-06	6.951057603
Ubd	0.000662556	56.55149013
Ugt2b34	0.000674611	2.918336198
Unc13b	6.23E-06	12.00412462
Upp1	0.000713451	2.598165176

Usp20	0.000442694	3.042982122
Usp4	0.000416778	1.559836092
Vapa	2.39E-05	3.012166139
Vapb	0.000473318	-2.66653
Vcl	5.52E-06	3.236130753
Vkorc1	0.000200267	-1.60296
Vps4b	0.000177371	1.908265844
Wbp2	0.000104477	1.547542039
Wdr1	0.000562881	1.794494491
Wdr5b	0.000295595	-1.52978
Wdr9	0.000159386	-2.97838
Wfdc2	1.42E-05	26.93356029
Wisp2	0.000291272	4.659701965
Yipf4	0.000570703	-1.5793
Ywhab	0.000206598	1.636131008
Ywhah	6.60E-05	2.914941993
Ywhaz	0.000470916	2.445944624
Zbed4	0.000334223	3.276593653
Zbtb33	0.000217329	2.217766975
Zbtb7a	0.000617417	2.415954967
Zfand2a	0.00077164	1.979500295
Zfp238	4.03E-06	4.683555568
Zfp41	0.000591728	2.805206463
Zfp715	0.000498159	-2.9159
Zkscan14	0.000934503	-1.81936
Zmym5	0.000785254	-1.80859
1110001J03Rik	2.88E-05	-2.10229
1110002B05Rik	0.000620396	3.971437422
1110002N22Rik	0.000802548	-1.79246
1110006G06Rik	3.22E-05	-2.645
1300001I01Rik	0.000248462	-1.69349
1300017J02Rik	0.000940281	-1.91107
1700047I17Rik1	0.000310588	4.713957084
1700067K01Rik	0.000766821	-4.60563
1810014F10Rik	0.000395785	-1.71586
1810049H13Rik	0.00011748	-2.94805
2010001J22Rik	0.000127485	-5.94897
2010106G01Rik	0.000443416	2.757875112
2310003H01Rik	0.000797794	2.109179571
2310045A20Rik	0.000971918	4.471851928
2610029G23Rik	5.68E-05	2.17331302
2610208M17Rik	0.000562878	2.133651959
2810004N23Rik	0.000674207	-2.30894
2900064A13Rik	0.000307797	3.755600539
3930401K13Rik	0.000913373	-1.59167
4732471D19Rik	9.72E-05	-2.70146
4833418A01Rik	0.000451575	1.634008288
4833421E05Rik	0.000988682	-2.14135
4833426J09Rik	9.10E-05	-4.93879

4931406C07Rik	6.22E-05	2.060925067
4933417E01Rik	0.000222275	-4.22372
4933426M11Rik	0.000100614	-1.88884
5830404H04Rik	0.00035508	-2.19754
5930434B04Rik	0.000175461	-2.67351
6720456H20Rik	0.000367622	-1.84826
9030025P20Rik	0.000534069	-2.72556
9130005N14Rik	1.83E-05	4.033103715

#### Supplementary Table 4

Genes involved in cellular growth and proliferation and differently expressed in AKT-CAT+DDC tumors

in comparison to normal PBS treated liver tissue ( $p < 0.001$ , fold change  $> 1.5$ )

Gene_ID	Entrez Gene Name
Acat1	acetyl-CoA acetyltransferase 1
Agps	alkylglycerone phosphate synthase
Agrn	agrin
Ahcy	adenosylhomocysteinase
Ahnak	AHNAK nucleoprotein
Akr1b8	aldo-keto reductase family 1, member B10 (aldose reductase)
Aldh111	aldehyde dehydrogenase 1 family, member L1
Amd2	adenosylmethionine decarboxylase 1
Ank3	ankyrin 3, node of Ranvier (ankyrin G)
Anxa2	annexin A2
Appl1	adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 1
Arhgef2	Rho/Rac guanine nucleotide exchange factor (GEF) 2
Arl6ip5	ADP-ribosylation factor-like 6 interacting protein 5
Asns	asparagine synthetase (glutamine-hydrolyzing)
Atpif1	ATPase inhibitory factor 1
Axin2	axin 2
Bax	BCL2-associated X protein
Bicc1	BicC family RNA binding protein 1
Birc2	baculoviral IAP repeat containing 2
Bmper	BMP binding endothelial regulator
Calca	calcitonin-related polypeptide beta
Casp2	caspase 2, apoptosis-related cysteine peptidase
Cbx7	chromobox homolog 7
Ccl2	chemokine (C-C motif) ligand 2
Cd163	CD163 molecule
Cd276	CD276 molecule
Cd63	CD63 molecule
Cd9	CD9 molecule
Cisd1	CDGSH iron sulfur domain 1
Clcn2	chloride channel, voltage-sensitive 2
Clec11a	C-type lectin domain family 11, member A
Clec2d	C-type lectin domain family 2, member d
Cnot6l	CCR4-NOT transcription complex, subunit 6-like
Cnr2	cannabinoid receptor 2 (macrophage)
Col4a1	collagen, type IV, alpha 1
Col4a2	collagen, type IV, alpha 2
Ctdspl	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase-like
Ctnna1	catenin (cadherin-associated protein), alpha 1, 102kDa
Ctsc	cathepsin C
Cux2	cut-like homeobox 2

Cxcl16 chemokine (C-X-C motif) ligand 16  
Cyp2b10 cytochrome P450, family 2, subfamily B, polypeptide 6  
Dab2ip DAB2 interacting protein  
Dact2 dishevelled-binding antagonist of beta-catenin 2  
Dcun1d3 DCN1, defective in cullin neddylation 1, domain containing 3  
Dusp8 dual specificity phosphatase 8  
Ecm1 extracellular matrix protein 1  
Egln2 egl-9 family hypoxia-inducible factor 2  
Egln3 egl-9 family hypoxia-inducible factor 3  
Ehd4 EH-domain containing 4  
Elf3 E74-like factor 3 (ets domain transcription factor, epithelial-specific)  
Emp1 epithelial membrane protein 1  
Entpd5 ectonucleoside triphosphate diphosphohydrolase 5  
Epha1 EPH receptor A1  
Ets2 v-ets avian erythroblastosis virus E26 oncogene homolog 2  
F2r coagulation factor II (thrombin) receptor  
F7 coagulation factor VII (serum prothrombin conversion accelerator)  
Fblim1 filamin binding LIM protein 1  
Fgf1 fibroblast growth factor 1 (acidic)  
Fkbp1a FK506 binding protein 1A, 12kDa  
Folr2 folate receptor 2 (fetal)  
Foxa1 forkhead box A1  
Foxo1 forkhead box O1  
Frk fyn-related Src family tyrosine kinase  
Gadd45g growth arrest and DNA-damage-inducible, gamma  
Gas6 growth arrest-specific 6  
Gas8 growth arrest-specific 8  
Gdf2 growth differentiation factor 2  
Ghr growth hormone receptor  
Gnmt glycine N-methyltransferase  
Golm1 golgi membrane protein 1  
Gpld1 glycosylphosphatidylinositol specific phospholipase D1  
Gpx4 glutathione peroxidase 4  
Gstm2 glutathione S-transferase mu 1  
Gstp1 glutathione S-transferase pi 1  
Guca2a guanylate cyclase activator 2A (guanylin)  
Hao1 hydroxyacid oxidase (glycolate oxidase) 1  
Hexim1 hexamethylene bis-acetamide inducible 1  
Hgfac HGF activator  
H2-M3 major histocompatibility complex, class I, G  
Hmga1 high mobility group AT-hook 1  
Hnrnpab heterogeneous nuclear ribonucleoprotein A/B  
Hrg histidine-rich glycoprotein  
Hsd11b1 hydroxysteroid (11-beta) dehydrogenase 1  
Htatip2 HIV-1 Tat interactive protein 2, 30kDa  
Icam1 intercellular adhesion molecule 1  
Ick intestinal cell (MAK-like) kinase  
Igf2bp3 insulin-like growth factor 2 mRNA binding protein 3  
Igfbp2 insulin-like growth factor binding protein 2, 36kDa



lhh	indian hedgehog
Il11ra1	interleukin 11 receptor, alpha
Itpr3	inositol 1,4,5-trisphosphate receptor, type 3
Jak3	Janus kinase 3
Kat2a	K(lysine) acetyltransferase 2A
Kif3a	kinesin family member 3A
Klf1	Kruppel-like factor 1 (erythroid)
Klf15	Kruppel-like factor 15
Klf6	Kruppel-like factor 6
Klk1b4	kallikrein-related peptidase 3
Kng1	kininogen 1
Kras	Kirsten rat sarcoma viral oncogene homolog
Krt8	keratin 8, type II
Lasp1	LIM and SH3 protein 1
Lcn2	lipocalin 2
Lgals1	lectin, galactoside-binding, soluble, 1
Lgals3	lectin, galactoside-binding, soluble, 3
Litaf	lipopolysaccharide-induced TNF factor
Lmo2	LIM domain only 2 (rhombotin-like 1)
Lrp1	low density lipoprotein receptor-related protein 1
Lxn	latexin
Maged2	melanoma antigen family D2
Map3k1	mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase
Mapkapk 2	mitogen-activated protein kinase-activated protein kinase 2
Mapt	microtubule-associated protein tau
Mark2	MAP/microtubule affinity-regulating kinase 2
Mcc	mutated in colorectal cancers
Mcl1	myeloid cell leukemia 1
Mcm10	minichromosome maintenance 10 replication initiation factor
Mfge8	milk fat globule-EGF factor 8 protein
Mgat4b	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme B
Mgmt	O-6-methylguanine-DNA methyltransferase
Mif	macrophage migration inhibitory factor (glycosylation-inhibiting factor)
Mlxipl	MLX interacting protein-like
Mmp24	matrix metalloproteinase 24 (membrane-inserted)
Mre11a	MRE11 homolog A, double strand break repair nuclease
Msi2	musashi RNA-binding protein 2
Mtdh	metadherin
Mthfd1	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1, methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase
Mvp	major vault protein
Ndrp2	NDRG family member 2
Nedd9	neural precursor cell expressed, developmentally down-regulated 9
Nfkbia	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
Noc3l	NOC3-like DNA replication regulator
Nr1i3	nuclear receptor subfamily 1, group I, member 3
Ntrk2	neurotrophic tyrosine kinase, receptor, type 2
Pdgfa	platelet-derived growth factor alpha polypeptide

Pdgbf platelet-derived growth factor beta polypeptide  
 Pdzk1ip1 PDZK1 interacting protein 1  
 Pigr polymeric immunoglobulin receptor  
 Pim3 Pim-3 proto-oncogene, serine/threonine kinase  
 Pkp2 plakophilin 2  
 pleckstrin homology domain containing, family A (phosphoinositide binding specific)  
 Plekha1 member 1  
 Ppap2c phospholipid phosphatase 2  
 Ppia peptidylprolyl isomerase A (cyclophilin A)  
 Ppl periplakin  
 Prkx protein kinase, X-linked  
 Psm10 proteasome 26S subunit, non-ATPase 10  
 Ptpn14 protein tyrosine phosphatase, non-receptor type 14  
 Ptpns protein tyrosine phosphatase, receptor type, S  
 Rab22a RAB22A, member RAS oncogene family  
 Rab27a RAB27A, member RAS oncogene family  
 Rassf1 Ras association (RalGDS/AF-6) domain family member 1  
 Rassf3 Ras association (RalGDS/AF-6) domain family member 3  
 Rcl1 RNA terminal phosphate cyclase-like 1  
 Rhbdf1 rhomboid 5 homolog 1 (Drosophila)  
 Rhoc ras homolog family member C  
 Rhod ras homolog family member D  
 Rpa1 replication protein A1, 70kDa  
 Rras related RAS viral (r-ras) oncogene homolog  
 Rxra retinoid X receptor, alpha  
 Samhd1 SAM domain and HD domain 1  
 Scarf1 scavenger receptor class F, member 1  
 Sdc2 syndecan 2  
 Sdhb succinate dehydrogenase complex, subunit B, iron sulfur (lp)  
 sema domain, immunoglobulin domain (lg), short basic domain, secreted, (semaphorin)  
 Sema3b 3B  
 Serpina1c serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1  
 Serpina3k serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3  
 Sftpd surfactant protein D  
 Sirpa signal-regulatory protein alpha  
 Sirt3 sirtuin 3  
 Skap2 src kinase associated phosphoprotein 2  
 Slc29a1 solute carrier family 29 (equilibrative nucleoside transporter), member 1  
 Slc7a4 solute carrier family 7, member 4  
 Spp1 secreted phosphoprotein 1  
 Sqstm1 sequestosome 1  
 Sra1 steroid receptor RNA activator 1  
 Stim1 stromal interaction molecule 1  
 Stt3b STT3B, subunit of the oligosaccharyltransferase complex (catalytic)  
 Tax1bp3 Tax1 (human T-cell leukemia virus type I) binding protein 3  
 Tes testin LIM domain protein  
 Tfrc transferrin receptor  
 Tgfbr3 transforming growth factor, beta receptor III  
 Tgm2 transglutaminase 2

Timd2	T cell immunoglobulin and mucin domain containing 2
Timd4	T-cell immunoglobulin and mucin domain containing 4
Tjp2	tight junction protein 2
Tjp3	tight junction protein 3
Tnfrsf12a	tumor necrosis factor receptor superfamily, member 12A
Tnfrsf19	tumor necrosis factor receptor superfamily, member 19
Tpd52	tumor protein D52
Tpd52l1	tumor protein D52-like 1
Tpr	translocated promoter region, nuclear basket protein
Tsc22d3	TSC22 domain family, member 3
Ttpa	tocopherol (alpha) transfer protein
Txnrd2	thioredoxin reductase 2
Usp22	ubiquitin specific peptidase 22
Vcl	vinculin
Vegfa	vascular endothelial growth factor A
Zap70	zeta-chain (TCR) associated protein kinase 70kDa
Zfp36	ZFP36 ring finger protein
Zmat3	zinc finger, matrin-type 3

### Supplementary Table 5

Genes involved in cellular growth and proliferation and differently expressed in AKT-CAT+CCl<sub>4</sub> tumors

in comparison to normal PBS treated liver tissue ( $p < 0.001$ , fold change  $> 1.5$ )

Gene_ID	Entrez Gene Name
Aatk	apoptosis-associated tyrosine kinase
Abcc3	ATP-binding cassette, sub-family C (CFTR/MRP), member 3
Abcg1	ATP-binding cassette, sub-family G (WHITE), member 1
Abi1	abl-interactor 1
Acsl4	acyl-CoA synthetase long-chain family member 4
Adam9	ADAM metallopeptidase domain 9
Adra1b	adrenoceptor alpha 1B
Ahnak	AHNAK nucleoprotein
Aldh1a1	aldehyde dehydrogenase 1 family, member A1
Aldh1a7	aldehyde dehydrogenase family 1, subfamily A7
Ambra1	autophagy/beclin-1 regulator 1
Anxa2	annexin A2
App1	adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 1
Arg1	arginase 1
Arhgap1	
7	Rho GTPase activating protein 17
Arl3	ADP-ribosylation factor-like 3
	ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle
Atp5a1	
Atpif1	ATPase inhibitory factor 1
Bcap31	B-cell receptor-associated protein 31
C1galt1c	
1	C1GALT1-specific chaperone 1
Cbx7	chromobox homolog 7
Cd163	CD163 molecule
Cd63	CD63 molecule
Cd9	CD9 molecule
Cdt1	chromatin licensing and DNA replication factor 1
Cisd1	CDGSH iron sulfur domain 1
Clec2d	C-type lectin domain family 2, member d
Col18a1	collagen, type XVIII, alpha 1
Col4a1	collagen, type IV, alpha 1
Col4a2	collagen, type IV, alpha 2
Col6a1	collagen, type VI, alpha 1
Cstf2	cleavage stimulation factor, 3' pre-RNA, subunit 2, 64kDa
Ctsb	cathepsin B
Cul1	cullin 1
Cux2	cut-like homeobox 2
Cx3cl1	chemokine (C-X3-C motif) ligand 1
Cxcl16	chemokine (C-X-C motif) ligand 16
Dapk1	death-associated protein kinase 1
Dbi	diazepam binding inhibitor (GABA receptor modulator, acyl-CoA binding protein)
Ddx3x	DEAD (Asp-Glu-Ala-Asp) box helicase 3, X-linked
Dnmt1	DNA (cytosine-5-)-methyltransferase 1

Ecm1	extracellular matrix protein 1
Egln3	egl-9 family hypoxia-inducible factor 3
Ehd4	EH-domain containing 4
Elf3	E74-like factor 3 (ets domain transcription factor, epithelial-specific )
Emp1	epithelial membrane protein 1
Eno1	enolase 1, (alpha)
Ercc3	excision repair cross-complementation group 3
Ets2	v-ets avian erythroblastosis virus E26 oncogene homolog 2
F2r	coagulation factor II (thrombin) receptor
Fads3	fatty acid desaturase 3
Fbp1	fructose-1,6-bisphosphatase 1
Fen1	flap structure-specific endonuclease 1
Fkbp1a	FK506 binding protein 1A, 12kDa
Foxa1	forkhead box A1
Frk	fyn-related Src family tyrosine kinase
Gadd45g	growth arrest and DNA-damage-inducible, gamma
Gnmt	glycine N-methyltransferase
Golm1	golgi membrane protein 1
Gpc4	glypican 4
Gphn	gephyrin
Gpld1	glycosylphosphatidylinositol specific phospholipase D1
Gstm2	glutathione S-transferase mu 1
Gstp1	glutathione S-transferase pi 1
H3f3b	H3 histone, family 3A
Hdac2	histone deacetylase 2
Hmox1	heme oxygenase 1
Hspa4	heat shock 70kDa protein 4
Hspb8	heat shock 22kDa protein 8
Idh2	isocitrate dehydrogenase 2 (NADP+), mitochondrial
Ifngr1	interferon gamma receptor 1
Igf1	insulin-like growth factor 1 (somatomedin C)
Il11ra1	interleukin 11 receptor, alpha
Il15ra	interleukin 15 receptor, alpha
Inpp5f	inositol polyphosphate-5-phosphatase F
Itgb5	integrin, beta 5
Jun	jun proto-oncogene
Klf1	Kruppel-like factor 1 (erythroid)
Klf6	Kruppel-like factor 6
Klk1b4	kallikrein-related peptidase 3
Lasp1	LIM and SH3 protein 1
Lcat	lecithin-cholesterol acyltransferase
Lcn2	lipocalin 2
Lgals1	lectin, galactoside-binding, soluble, 1
Lgals3	lectin, galactoside-binding, soluble, 3
Litaf	lipopolysaccharide-induced TNF factor
Lmo2	LIM domain only 2 (rhombotin-like 1)
Lpin1	lipin 1
Lxn	latexin
Map3k1	mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase

Mapt microtubule-associated protein tau  
 Mcm4 minichromosome maintenance complex component 4  
 Memo1 mediator of cell motility 1  
 Mfge8 milk fat globule-EGF factor 8 protein  
 Mthfd1 methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1,  
 methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase  
 Mtss1 metastasis suppressor 1  
 Mvp major vault protein  
 Nedd9 neural precursor cell expressed, developmentally down-regulated 9  
 Nfkbia nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha  
 Nme3 NME/NM23 nucleoside diphosphate kinase 3  
 Nosip nitric oxide synthase interacting protein  
 Notch4 notch 4  
 Nras neuroblastoma RAS viral (v-ras) oncogene homolog  
 Nuak1 NUAK family, SNF1-like kinase, 1  
 Osgin1 oxidative stress induced growth inhibitor 1  
 Pcyt1a phosphate cytidyltransferase 1, choline, alpha  
 Pcd10 programmed cell death 10  
 Pkp2 plakophilin 2  
 pleckstrin homology domain containing, family A (phosphoinositide binding specific)  
 Plekha1 member 1  
 Ppap2c phospholipid phosphatase 2  
 Ppargc1b peroxisome proliferator-activated receptor gamma, coactivator 1 beta  
 Ppp2ca protein phosphatase 2, catalytic subunit, alpha isozyme  
 Prkx protein kinase, X-linked  
 Prune prune exopolyphosphatase  
 Ptpn1 protein tyrosine phosphatase, non-receptor type 1  
 Ptptra protein tyrosine phosphatase, receptor type, A  
 Rab22a RAB22A, member RAS oncogene family  
 Rassf1 Ras association (RalGDS/AF-6) domain family member 1  
 Rassf3 Ras association (RalGDS/AF-6) domain family member 3  
 Rbl1 retinoblastoma-like 1  
 Rgs16 regulator of G-protein signaling 16  
 Rhbdf1 rhomboid 5 homolog 1 (Drosophila)  
 Rhod ras homolog family member D  
 Ripk3 receptor-interacting serine-threonine kinase 3  
 Rpa1 replication protein A1, 70kDa  
 Rps6ka1 ribosomal protein S6 kinase, 90kDa, polypeptide 1  
 Rras2 related RAS viral (r-ras) oncogene homolog 2  
 Rxra retinoid X receptor, alpha  
 S100a10 S100 calcium binding protein A10  
 S100a6 S100 calcium binding protein A6  
 Sae1 SUMO1 activating enzyme subunit 1  
 Scarf1 scavenger receptor class F, member 1  
 Sec14l2 SEC14-like lipid binding 2  
 Selk selenoprotein K  
 Serpina1  
 e serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1  
 Sirpa signal-regulatory protein alpha  
 Skap2 src kinase associated phosphoprotein 2

Skp1a	S-phase kinase-associated protein 1
Slc30a6	solute carrier family 30 (zinc transporter), member 6
Smc3	structural maintenance of chromosomes 3
Smpd1	sphingomyelin phosphodiesterase 1, acid lysosomal
Snx3	sorting nexin 3
Sox5	SRY (sex determining region Y)-box 5
Spred1	sprouty-related, EVH1 domain containing 1
Sqstm1	sequestosome 1
Tax1bp3	Tax1 (human T-cell leukemia virus type I) binding protein 3
Tcf19	transcription factor 19
Tcf7l2	transcription factor 7-like 2 (T-cell specific, HMG-box)
Tgm2	transglutaminase 2
Tjp2	tight junction protein 2
Tjp3	tight junction protein 3
Tle1	transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila)
Tnfrsf12a	tumor necrosis factor receptor superfamily, member 12A
Tpd52	tumor protein D52
Tpd52l1	tumor protein D52-like 1
Tsc22d3	TSC22 domain family, member 3
Tsn	translin
Tuba1a	tubulin, alpha 1a
Tubb5	tubulin, beta class I
Ubd	ubiquitin D
Upp1	uridine phosphorylase 1
Usp4	ubiquitin specific peptidase 4 (proto-oncogene)
Vapa	VAMP (vesicle-associated membrane protein)-associated protein A, 33kDa
Vcl	vinculin
Vkorc1	vitamin K epoxide reductase complex, subunit 1
Wbp2	WW domain binding protein 2
Wisp2	WNT1 inducible signaling pathway protein 2
Ywhaz	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta
Zbtb7a	zinc finger and BTB domain containing 7A

**Supplementary Table 6:** Most significant diseases and function affected by DDC in AKT-CAT tumors in comparison to AKT-NRAS<sup>G12V</sup> tumors.

<u>Pathway</u>	<u>p-value</u>
Cellular Growth and Proliferation	3.51 E-06 - 1.5E-02
Cellular Assembly and Orgnization	1.21 E-05 - 1.5E-02
Cardiovascular System Development and Function	1.69E-05 - 1.5E-02
Organismal survival	3.21E-05 - 3.21E05
Cancer	1.06E-04 - 1.5E-02