Upregulation of peroxisome proliferator-activated receptor-α and the lipid metabolism pathway promotes carcinogenesis of ampullary cancer
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**Supplementary Table 1.** Demographics and clinical outcomes of five patients with ampullary cancer

| Age (years) | Sex | Staging | Tumor size (cm) | Morphology | Differentiation | Recurrence | Time to recurrence (months) | Condition | Time of survival/ expired (months) |
|-------------|-----|---------|----------------|------------|-----------------|-------------|---------------------------|-----------|----------------------------------|
| 51          | F   | T2N0, stage Ib | 2×1×1         | Polypoid   | Unknown         | No          | --                        | Survived  | 193                              |
| 58          | F   | T2N0, stage Ib | 2.4×1.5×0.6   | Mixed      | Good            | Yes         | 14                       | Expired   | 17                               |
| 68          | M   | T3N0, stage IIA | 4.5×3.5×1.2   | Polypoid   | Good            | No          | --                        | Survived  | 162                              |
| 66          | M   | T3N0, stage IIA | 1×1×0.8       | Ulcerative | Good            | Yes         | 64                       | Expired   | 227                              |
| 60          | M   | T3N0, stage IIA | 2×1.8×1       | Mixed      | Moderate        | Yes         | 5.6                      | Expired   | 16.7                             |
**Supplementary Table 2.** Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis of an ampullary cancer microarray using the Database for Annotation, Visualization and Integrated Discovery (DAVID). This table contains only pathways with \( p \) values that ranged 0.0001–0.05.

| KEGG Pathway                             | \( p \) value | Genes                                                                 |
|------------------------------------------|--------------|----------------------------------------------------------------------|
| Pentose and glucururonate interconversions | 1.50E-04     | UGT1A6, CRYL1, UGT1A8, AKR1B1, UGT2B11, UGT2A3, UGT2B10, UGT2B7, XYLB |
| Drug metabolism                          | 1.63E-04     | CYP3A4, XDH, UGT1A6, CYP3A5, CES2, CYP3A7, UGT1A8, NAT2, UGT2B11, DPYD, UGT2A3, UGT2B10, UGT2B7 |
| Maturity-onset diabetes of the young      | 2.43E-04     | HNF1A, HNF4A, SLC2A2, PKLR, NEUROD1, HNF4G, PDX1, NR5A2, NKX2-2 |
| Starch and sucrose metabolism            | 6.03E-04     | GBA3, UGT1A6, G6PC, UGT1A8, ENPP3, MGAM, SI, UGT2B11, TREH, UGT2A3, UGT2B10, UGT2B7 |
| Valine, leucine and isoleucine degradation| 8.94E-04     | ACA2, ALDH6A1, ACADSB, ACADM, HMGCS2, ACADS, ABAT, ACAT1, HADHA, ACA1, HADHB |
| Alanine, aspartate and glutamate metabolism | 1.21E-03   | ASPA, ACY3, GLS, ABAT, GPT, AGXT2, CPS1, AGXT, DDO |
| Glycine, serine and threonine metabolism  | 1.21E-03     | GLYCTK, SHMT1, CTH, MOA, AMT, BHMT, MAOB, AGXT2, AGXT |
| Fructose and mannose metabolism          | 2.30E-03     | KHK, AKR1B15, MPI, PFKFB4, AKR1B10, PFKFB2, ALDOC, ALDOB, AKR1B1, FBP1 |
| Glycolysis / Gluconeogenesis              | 3.20E-03     | G6PC, GALM, ADH4, ALDOC, PKLR, ALDOB, FBP1, ADH6, PGAM2, ACS2, PCK2, PCK1 |
| ABC transporters                         | 3.48E-03     | ABCA8, ABCG8, ABCG5, ABCB1, ABC2, ABCA4, ABCC8, ABCA5, ABCG2, ABCC6 |
| Androgen and estrogen metabolism          | 4.04E-03     | UGT1A6, UGT1A8, HSD17B2, UGT2B11, HSD11B2, HSD17B3, UGT2A3, UGT2B10, SULT1E1, UGT2B7 |
| Nitrogen metabolism                      | 4.71E-03     | CTH, CA7, AMT, GLS, CA4, CA2, CPS1 |
| Sulfur metabolism                        | 8.22E-03     | CHST13, SULT1A2, SULT1A4, SULT1E1, BPNT1 |
| Histidine metabolism                     | 1.54E-02     | DDC, ASPA, CNDP1, ACY3, MAOA, MAOB, FTCD |
| Pathway | p-value | Genes |
|---------|---------|-------|
| Pantothenate and CoA biosynthesis | 1.91E-02 | PANK3, PANK1, ENPP3, VNN1, DPYD |
| Tryptophan metabolism | 2.23E-02 | DDC, CYP1A1, MAOA, MAOB, HAAO, CAT, ACAT1, HADHA |
| Primary bile acid biosynthesis | 2.40E-02 | ACOX2, CYP27A1, CYP7A1, PIWIL2, SCP2 |
| Propanoate metabolism | 2.44E-02 | ALDH6A1, ACADM, SUCLG1, ABAT, ACSS2, ACAT1, HADHA |
| Porphyrin and chlorophyll metabolism | 2.81E-02 | UGT1A6, ALAD, UGT1A8, HMOX1, UGT2B11, UGT2A3, UGT2B10, UGT2B7 |
| Renin-angiotensin system | 2.97E-02 | ACE, ACE2, MME, ANPEP, ENPEP |
| Ascorbate and aldarate metabolism | 2.97E-02 | UGT1A6, UGT1A8, UGT2B11, UGT2A3, UGT2B10, UGT2B7 |
| Butanoate metabolism | 3.22E-02 | AKR1B15, HMGCS2, ACADS, AKR1B10, ABAT, BDH2, ACAT1, HADHA |
| Galactose metabolism | 3.52E-02 | GALK1, G6PC, AKR1B1, MGAM, GALT, LCT |
| Glycerolipid metabolism | 3.99E-02 | DGKA, GLYCTK, PNLI PRP2, DGAT1, DGAT2, DAK, AKR1B1, GK |
### Supplementary Table 3

Functional enrichment of Gene Ontology (GO) biological processes analysis in a cDNA microarray of ampullary adenocarcinomas by the Database for Annotation, Visualization and Integrated Discovery (DAVID)

| GO term                        | p value     | Genes                                                                 |
|-------------------------------|-------------|----------------------------------------------------------------------|
| Digestion                     | 1.35E-13    | SLC15A1, SLC5A1, PRSS1, VIPR1, SCTR, APOA4, VDR, SCT, UGT1A6, ACE, UGT1A8, PLA2G1B, NPC1L1, SOAT2, MOGAT2, PNLIPRP2, SULT2A1, PPARGC1A, ABCG8, SSTR2, ABCG5, AKR1B15, SSTR1, AKR1B10, MEP1A, ACE2, MEP1B, GHRL, FABP1, FABP2, SST |
| Fatty acid metabolic process  | 1.99E-13    | ACOX2, HACL1, ACOX1, PPARA, ACADSB, CYP2J2, CPT2, HNF1A, EDN2, ECHDC2, ACSF3, ACSF2, HADHA, HADHB, AKR1C3, PECR, CRYLI1, ACOT11, PLA2G1B, ETFDH, ELOVL7, BDH2, ACSL6, ACSS5, ACAA2, PTGR1, ACADM, LIPA, ACADS, EPHX2, DECR1, FADS6, PPARGC1A, CYP4F8, CYP4F3, FABP2, CYP4F2, SLC27A3, HPGD, SLC27A2, CROT, SLC27A4, ACA1 |
| Oxidation reduction           | 2.23E-13    | ALDH8A1, ACOX2, CYP3A4, ACOX1, CYP3A5, HTATIP2, CYP3A7, CYP2J2, CYP2C19, CYP2C18, CYP2SI, CYP2D6, AKR1C3, GSR, PECR, MSRA, HMOX1, CYP7A1, GPX3, AKR7A2, AKR7A3, PIWIL2, CAT, ALDH6A1, ACADM, CYP1A1, ACADS, CYB5A, DECR1, DHRS7C, PPARGC1A, DDO, POR, DHDH, RDH5, DHRS1, AKR1B15, CYP27A1, AKR1B10, CYBRD1, HSD11B2, PRODH, HSD17B11, ME1, XDH, ACADSB, HSD17B2, CYP2B6, ADH6, HADHA, ALDH1A1, FMO4, FMO5, CBR1, ADH4, ETFDH, HAAO, BDH2, HSD17B3, GLRX, AKR7L, GPD1, PAOX, PTGR1, CYP2C9, MAOA, MAOB, DHRS11, CYP4F11, CYP4F12, CYP4V2, PHYH, FADS6, IDH3A, IYD, CYP4B1, SDHA, ADD1, CYP4F8, AKR1B1, PRODH2, CYP4F3, DPYD, CYP4F2, ACAD11, HPGD, RETSAT, CRYZ1L |
| Carboxylic acid transport     | 1.55E-11    | SLC36A1, PPARA, CPT2, HNF1A, SLC16A10, DRD4, SLC7A9, SLC19A1, AGXT, SLC7A7, MIP, SLC25A20, SLC23A1, ACE, PLIN2, SLC1A7, SLC22A4, PLA2G1B, SLC22A5, SLC1A1, SLC6A12, SLC3A1, SLC10A2, SLC6A19, CD36, SLC26A8, SLC6A5, FABP1, FABP2, SLC25A15, PDZK1, SLC46A1, CROT, SLC27A4 |
| Organic acid transport        | 1.89E-11    | SLC36A1, PPARA, CPT2, HNF1A, SLC16A10, DRD4, SLC7A9, SLC19A1, AGXT, SLC7A7, MIP, SLC25A20, SLC23A1, ACE, PLIN2, SLC1A7, SLC22A4, PLA2G1B, SLC22A5, SLC1A1, SLC6A12, SLC3A1, SLC10A2, SLC6A19, CD36, SLC26A8, |
SLC6A5, FABP1, FABP2, SLC25A15, PDZK1, SLC46A1, CROT, SLC27A4

Lipid transport 2.39E-10 PPARA, CPT2, MSR1, HNF1A, ATP10A, DRD4, APOC2, ABCA4, APOA4, SLC25A20, APOB, ACE, APOA1, PLIN2, APOC3, APOH, PLA2G1B, NPC1L1, SCARB1, GLTPD2, APOM, SOAT2, MTTP, ABCG8, ABCG5, CD36, FABP1, FABP2, SCP2, CROT, APOL5, SLC27A4

Lipid localization 4.48E-10 PPARA, CPT2, MSR1, HNF1A, ATP10A, DRD4, APOC2, ABCA4, ACVR1C, APOA4, SLC25A20, APOB, ACE, APOA1, PLIN2, APOC3, APOH, PLA2G1B, NPC1L1, SCARB1, GLTPD2, APOM, SOAT2, MTTP, ABCG8, ABCG5, CD36, FABP1, FABP2, SCP2, CROT, APOL5, SLC27A4

Steroid metabolic process 4.87E-10 HSD17B11, CYP3A4, ACOX2, CYP3A5, HNF1A, HSD17B2, APOA4, SULT4A1, UGT1A6, APOB, APOA1, UGT1A8, CYP7A1, APOC3, NPC1L1, SULT1A2, PIWIL2, HSD17B3, SCARB1, CAT, SULT1E1, SULT1A4, SOAT2, ACAA2, LIPA, SULT2A1, CYP1A1, NR0B2, GBA2, G6PC, NR1I2, AKR1B15, HMGC52, CYP27A1, SULT1B1, AKR1B10, UGT2B11, HSD11B2, NR5A2, SCP2

Triglyceride metabolic process 1.02E-09 MOGAT2, PNLIPRP2, APOC2, CPS1, PCK1, MTTP, APOA4, APOB, G6PC, DGAT1, DGAT2, APOC3, AGPAT9, APOH, SLC22A4, CAT, NR1H3

Regulation of hormone levels 2.98E-09 ALDH8A1, HSD17B11, EDN3, HNF1A, FAM3B, PDX1, FKBP1B, PCSK2, UGT1A6, PCSK1, ACE, APOA1, UGT1A8, ADH4, SCARB1, SULT1E1, PCSK5, SHBG, CYP1A1, TBX3, DDO, DGAT1, LRAT, GHRH, SULT1B1, UGT2B11, ACE2, NEUROD1, HSD11B2, GHRL, SMPD3, RETSAT

Organic ether metabolic process 4.30E-09 MOGAT2, PNLIPRP2, CYP1A1, APOC2, CPS1, PCK1, MTTP, APOA4, APOB, G6PC, DGAT1, DGAT2, APOC3, AGPAT9, APOH, SLC22A4, CAT, NR1H3

Lipid catabolic process 5.68E-09 HSD17B11, ACOX2, ENPP6, HACL1, ACOX1, CPT2, APOC2, HADHA, HADHB, APOA4, PLCB3, APOB, SMPDL3B, SMPDL3A, CYP7A1, PLA2G12B, APOC3, ETFDH, PLA2G1B, SCARB1, BDH2, PLD1, ACADM, LIPA, PNLIPRP2, SULT2A1, ACADS, DECR1, CPS1, GBA2, PLA2G2A, SMPD3, ACAAI

Cellular lipid catabolic process 8.88E-09 ACOX2, HACL1, ACOX1, PLD1, ACADM, CPT2, ACADS, DECR1, CPS1, HADHA, HADHB, GBA2, PLCB3, APOB, SMPDL3B, SMPDL3A, APOC3, ETFDH, BDH2, SMPD3, ACAAI
Acylglycerol metabolic process 9.19E-09
MOGAT2, PNLPRT2, APOC2, CPS1, PCK1, MTTP, APOA4, APOB, G6PC, DGAT1, DGAT2, APOC3, AGPAT9, APOH, SLC22A4, CAT, NR1H3

Neutral lipid metabolic process 1.28E-08
MOGAT2, PNLPRT2, APOC2, CPS1, PCK1, MTTP, APOA4, APOB, G6PC, DGAT1, DGAT2, APOC3, AGPAT9, APOH, SLC22A4, CAT, NR1H3

Sterol homeostasis 1.33E-08
SOAT2, APOC2, MTTP, ABCG8, APOA4, APOB, G6PC, ABCG5, MALL, APOA1, APOC3, NPC1L1, SCARB1, NR5A2, APOM

Cholesterol homeostasis 1.33E-08
SOAT2, APOC2, MTTP, ABCG8, APOA4, APOB, G6PC, ABCG5, MALL, APOA1, APOC3, NPC1L1, SCARB1, NR5A2, APOM

Glycerol ether metabolic process 1.76E-08
MOGAT2, PNLPRT2, APOC2, CPS1, PCK1, MTTP, APOA4, APOB, G6PC, DGAT1, DGAT2, APOC3, AGPAT9, APOH, SLC22A4, CAT, NR1H3

Fatty acid transport 1.96E-08
PPARA, SLC25A20, ACE, CPT2, CD36, HNF1A, PLIN2, DRD4, PLA2G1B, FABP1, FABP2, CROT, SLC27A4

Cofactor metabolic process 3.23E-08
MOCS1, ME1, ALAD, HNF1A, ALDOB, GGT1, PDSS1, GCH1, TPK1, UGT1A6, GSR, CBRI, UGT1A8, HMOX1, ADH4, GPX3, HAAO, VNN1, ACSL6, MOCS1, GPD1, SHMT1, ACO2, CYP1A1, SUCLG1, FTC2D, IDH3A, SDHA, COQ4, CTH, PANK3, HNF4A, PANK1, QPRT, CRYZL1

Sterol transport 8.51E-08
SOAT2, HNF1A, MSR1, APOC2, ABCG8, APOA4, APOB, ABCG5, CD36, APOA1, APOC3, NPC1L1, SCARB1, APOM

Cholesterol transport 8.51E-08
SOAT2, HNF1A, MSR1, APOC2, ABCG8, APOA4, APOB, ABCG5, CD36, APOA1, APOC3, NPC1L1, SCARB1, APOM

Lipid homeostasis 1.29E-07
SOAT2, APOC2, MTTP, ABCG8, APOA4, APOB, G6PC, ABCG5, APOA1, MALL, HNF4A, APOC3, NPC1L1, SCARB1, NR5A2, APOM

Response to toxin 2.86E-07
DDC, TRPM6, PTGR1, CYP1A1, SLC6A4, EPHX2, BPHL, GUCY2C, AQP10, BAK1, SLC23A1, CDKN1A, PEBP1, HTR1D, PDZD3, MT1H, MPST

Secretion 3.52E-07
EDN3, SLC22A18, HNF1A, TRPV1, FAM3B, DRD4, NR3C2, CCL8, AQP7, PDX1, TEDP52, AMN, AGXT, FKBP1B, AQP3, STXBP5L, SCTR, SRT, ACE, HMOX1, KNCN5, PLA2G1B, SLC22A4, GUC2A2B, PCSK5, SCG2, SCAMP5, TBX3, BAIAP3, ABCG8, SLC26A3, ABCG5, TRIM36, DGAT1, GHRH, SCIN, GHRL, NEUROD1, CA2, DOC2B, SMPD3, MON1A

Chemical homeostasis 4.52E-07
JPH4, HNF1A, GRIK1, EDN2, GNA11, GRIK3, F2RL1, PDX1, APOA4, BAK1, APOB, APOA1, MALL, GRIN2B, AQP11, HMOX1,
| Process                        | FDR   | Genes                                                                 |
|-------------------------------|-------|----------------------------------------------------------------------|
| Monocarboxylic acid transport | 6.65E-07 | RGN, NPC1L1, CHRNA7, CHRFAM7A, APOM, OTC, MLXIPL, GRIN2A, SLC9A3R1, PPARGC1A, CCR9, G6PC, HNF4A, GHRH, GHRL, MON1A, CALCR, PRKCZ, CCK, SLC37A4, DRD4, NR3C2, APOC2, FKBPIB, VDR, APOC3, SCARB1, SLC39A4, MT1H, GAL3ST1, SOAT2, EPHX2, ATP1A4, AFG3L2, CPS1, CCL15, PCK1, MTP, ABCG8, ABCG5, ADRA1B, NEUROD1, NR5A2, SCARA5, IL2 |
| Lipoprotein particle clearance | 1.15E-06 | PPARA, HNF1A, CPT2, DRD4, SLC10A2, MIP, SLC25A20, ACE, CD36, PLIN2, PLA2G1B, FABP1, FABP2, CROT, SLC27A4 |
| Intestinal absorption         | 1.15E-06 | APOB, MSR1, CD36, APOA1, HMOX1, APOC3, APOC2, SCARB1, APOM |
| Lipid oxidation               | 1.38E-06 | ACOX2, ACOX1, HACL1, CPT2, ACADM, ACADS, DECR1, PPARC1A, HADHA, HADHB, ETFDH, BDH2, ACA1 |
| Fatty acid oxidation          | 1.38E-06 | ACOX2, ACOX1, HACL1, CPT2, ACADM, ACADS, DECR1, PPARC1A, HADHA, HADHB, ETFDH, BDH2, ACA1 |
| Organic acid catabolic process| 1.62E-06 | ACOX2, HACL1, SHMT1, ALDH6A1, ACOX1, ACADM, CPT2, SULT2A1, ACADS, AMT, DECR1, TAT, DDO, HADHA, HADHB, ASPA, GLS, ETFDH, PRODH2, BDH2, ACA1, PRODH |
| Carboxylic acid catabolic process| 1.62E-06 | ACOX2, HACL1, SHMT1, ALDH6A1, ACOX1, ACADM, CPT2, SULT2A1, ACADS, AMT, DECR1, TAT, DDO, HADHA, HADHB, ASPA, GLS, ETFDH, PRODH2, BDH2, ACA1, PRODH |
| Fatty acid beta-oxidation      | 2.28E-06 | ACOX2, ACOX1, CPT2, ACADM, ACADS, ETFDH, BDH2, DECR1, HADHA, ACA1, HADHB |
| Ion transport                 | 2.31E-06 | KCNJ16, SLC36A1, JPH4, SLC5A4, SLC22A18, CPT2, GRIK1, GABRB2, TRPV1, SLC20A2, SLC5A1, GRIK3, KCNJ13, KCNK10, SLC25A20, SLC23A1, GRIN2B, AQP11, KCNK5, SLC22A4, CHRNA7, ANO4, SLC22A5, TRPV6, SLC4A4, CHRFAM7A, SLC1A1, ANO9, GABRG1, SGK1, TRPM6, CLC1A, GRIN2A, CNGA1, SLC26A3, SLC26A8, CATSPER2, CATSPER3, CLC5, SLC41A2, KCNH6, AKAP7, SLC30A10, MPST, CAV2, SLC39A14, ORAI1, ENPP3, RHBG, CCL8, KCNA3, KCNJ3, FKBPIB, BEST4, VDR, TMEM37, SLC01A2, SLC4A7, SLC39A5, SLC39A4, HCN4, CAMK2A, SLC31A1, GABRA1, SLC04C1, ATP1A4, ATP1A1, SLC10A2, P2RX6, KCNJ6, SLC17A4, SLC13A4, KCTD16, PDZK1, SCARA5, ABCC8, PDZD3, SLC5A11, SLC5A12 |
| Process                           | Score | Genes                                                                 |
|----------------------------------|-------|----------------------------------------------------------------------|
| Coenzyme metabolic process       | 2.89E-06 | ME1, MOCOS, ALDOB, GGT1, PDSS1, GCH1, TPK1, GSR, GPX3, HAAO, VNN1, ACSL6, MOCS1, SHMT1, GPD1, ACO2, SUCLG1, FTCD, IDH3A, SDHA, COQ4, CTH, PANK3, HNF4A, PANK1, QPRT |
| Fatty acid catabolic process      | 4.12E-06 | ACOX2, HACL1, ACOX1, CPT2, ACADM, ACADS, ETFDH, BDH2, DECR1, HADHA, ACAA1, HADHB |
| Cholesterol efflux               | 5.75E-06 | APOA4, ABCG8, SOAT2, ABCG5, APOA1, APOC3, APOC2, SCARB1, APOM |
| Transmembrane transport          | 6.80E-06 | SLC5A4, SLC22A18, CPT2, TRPV1, SLC5A1, MFSD2A, AQP7, AQP3, SLC25A20, SLC2A7, SLC23A1, APOA1, SLC2A5, SLC23A3, SLC2A2, SLC22A4, TRPV6, SLC22A5, FLVCR2, FLVCR1, TRPM6, SLC25A5, ABCC13, CNGA1, SLC26A3, SLC26A8, SLC25A34, CATSPER2, CATSPER3, SLC37A2, KCNH6, SLC30A10, SLC2A12, SLC39A14, SLC37A4, RHBG, KCNA3, SLC19A1, SLC47A2, MIP, SCARB1, SLC39A5, HCN4, SLC39A4, SLC2A9, ATP1A4, ABCB1, AQP10, SLC17A4, SLC13A2, ABCC2, SLC46A3, SCARF5, SLC25A15, ABCC8, PDZK1, SLC46A1, SLC5A11, SLC25A18, ABCC6, SLC5A12 |
| Carbohydrate transport           | 8.73E-06 | SLC2A12, SLC2A9, SLC5A4, SLC5A1, SLC37A4, AQP7, SLC2A7, G6PC, SLC2A5, AQP11, SLC2A2, SLC37A2, PLA2G1B, SCARB1, SLC5A11 |
| Response to nutrient levels      | 1.20E-05 | PPARA, CCK, HSD17B2, ALDOB, AQP3, VDR, PCSK1, UGT1A6, UGT1A8, CDKN2B, HMOX1, APOM, SOAT2, CYP1A1, ACADS, SI, CPS1, PPARC1A, SLC6A19, SSTR2, G6PC, ABCG5, HMGCS2, GHRH, SSTR1, HSD11B2, GHRL, SST, LCT, KLF4 |
| Homeostatic process              | 1.23E-05 | XRC5, JPH4, HNF1A, GRIK1, TRPV1, PDIA2, GNA11, EDN2, GRIK3, F2RL1, PDX1, APOA4, GSR, BAK1, APOB, APOA1, MALL, GRIN2B, AQP11, HMOX1, RGN, NPC1L1, CHRNA7, SLC22A5, CHRFAM7A, APOM, MB, FLVCR1, OTC, MLXIP, GRIN2A, SLC9A3R1, PPARC1A, CCR9, G6PC, HNF4A, GHRH, GHRL, MON1A, CALCRL, XDH, PRKCC2, CCK, SLC37A4, DRD4, NR3C2, APOC2, SOX6, TRIM10, FKBP1B, VDR, APOC3, HAAO, SCARB1, SLC39A4, MT1H, GAL3ST1, GLRX, SOAT2, LIPA, TNFRSF13B, EPHX2, ATP1A4, AFG3L2, CPS1, CCL15, PCK1, MTTP, ABCG8, ABCG5, ADRA1B, NEUROD1, NR5A2, SCARF5, IL2 |
| Long-chain fatty acid transport   | 1.39E-05 | SLC25A20, ACE, CPT2, CD36, PLIN2, DRD4, PLA2G1B, FABP1, FABP2 |
| Process                                      | p-value | Genes                                                                 |
|----------------------------------------------|---------|----------------------------------------------------------------------|
| Digestive system process                     | 1.65E-05| ABCG8, VDR, SOAT2, SCT, MOGAT2, ABCG5, SLC5A1, NPC1L1, GHRL, FABP1, FABP2 |
| Vitamin metabolic process                    | 2.47E-05| ME1, CYP3A4, ALDH8A1, SHMT1, ACADM, CYP1A1, RBP2, SLC19A3, TPK1, CBRI, LRAT, ADH4, HAAO, SLC22A4, QPRT, RETSAT |
| Glycerolipid metabolic process               | 2.49E-05| PIP5K1B, APOC2, APOA4, APOB, PIP5KL1, APOA1, APOC3, AGPAT9, APOH, SLC22A4, PLA2G1B, CAT, NR1H3, GPD1, MOGAT2, PLD1, PNLIPRP2, CPS1, PCK1, MTTP, G6PC, DGAT1, DGAT2, SEMA6D, PLA2G2A |
| Protein-lipid complex assembly               | 2.73E-05| APOA4, SOAT2, APOB, APOA1, DGAT1, APOC3, APOM                         |
| Plasma lipoprotein particle assembly         | 2.73E-05| APOA4, SOAT2, APOB, APOA1, DGAT1, APOC3, APOM                         |
| Response to carbohydrate stimulus            | 3.51E-05| ME1, HNF1A, PFKFB2, SI, ALDOB, FKBPIB, ACVR1C, HKH, PCSK1, APOB, SARM1, HNF4A, NEUROD1, LCT |
| Response to extracellular stimulus           | 3.59E-05| PPARA, CCK, HSD17B2, ALDOB, AQP3, VDR, PCSK1, UGT1A6, UGT1A8, CDKN2B, HMOXI, APOM, SOAT2, CYP1A1, ACADS, SI, CPS1, PPARGC1A, SLC6A19, CDKN1A, SSTR2, G6PC, ABCG5, HMGCS2, GHRH, SSTR1, HSD11B2, GHRL, SST, LCT, KLF4 |
| Cellular amino acid derivative metabolic process | 3.74E-05| ENPP6, DRD4, GGT1, AGMAT, GCH1, APOA4, GSR, PADI6, APOA1, GPX3, SLC22A4, PLA2G1B, VNN1, SULT1A2, SULT1A4, DDC, ACADM, CYP1A1, MAOA, GRIN2A, CPS1, CKMT1A, CTH, SULT1B1, ABAT |
| Lipid modification                           | 3.87E-05| ACOX2, HACL1, SOAT2, ACOX1, ACADM, CPT2, ACADS, DECR1, PPARGC1A, HADHA, HADHB, ETFDH, B4GALNT2, BDH2, ACA1 |
| Cation transport                             | 4.40E-05| KCNJ16, SLC36A1, JPH4, SLC5A4, SLC22A18, CPT2, SLC20A2, TRPV1, SLC5A1, KCNK10, KCNJ13, SLC25A20, SLC23A1, GRIN2B, KCNK5, SLC22A4, CHRNA7, SLC22A5, TRPV6, CHRFAM7A, SLC4A4, TRPM6, SGK1, CLCA1, GRIN2A, CNGA1, CATSPER2, CATSPER3, SLC4A2, KCNH6, SLC30A10, SLC39A14, ORAI1, RHBG, CCL8, KCNA3, FKBPIB, KCNJ3, TMEM37, VDR, SLC4A7, SLC39A5, HCN4, SLC39A4, CAMK2A, SLC31A1, ATP1A4, ATP1A1, SLC10A2, KCNJ6, SLC17A4, |
| Function                        | p-value   | Gene Symbols                                                                 |
|--------------------------------|-----------|-------------------------------------------------------------------------------|
| Metal ion transport            | 4.81E-05  | SLC13A2, KCTD16, ABCC8, SCARA5, PDZK1, SLC5A11, SLC5A12                      |
| Peptide transport              | 5.36E-05  | EDN3, HNF1A, DGAT1, SLC15A1, TRPV1, CDH17, GHRH, FAM3B, NEUROD1, GHR, PDX1, FKB1B, SMPD3 |
| Gluconeogenesis                | 6.01E-05  | GPD1, G6PC, ALDOB, FBPI, PGAM2, GPT, PCK2, PPARGC1A, PCK1                   |
| Alditol metabolic process      | 6.01E-05  | GAL1, GP1, MOGAT2, DGAT2, DAK, GK, GDP1, PCK1, GDP2                         |
| Amino acid transport           | 6.13E-05  | SLC36A1, CPT2, SLC16A10, SLC6A12, SLC7A9, SLC3A1, SLC19A1, SLC6A19, SLC7A7, SLC25A20, SLC6A5, SLC22A4, SLC22A5, SLC25A15, SLC1A1, PDZK1, SLC46A1 |
| Response to drug               | 6.58E-05  | CAV2, APOBEC1, SLC22A18, AQP7, HADHA, SLC47A2, PCSK1, UGT1A6, UGT1A8, PLIN2, SLC22A5, NAT8B, NAT8, CYP1A1, GRN2A, ABC1, ATP1A1, CPS1, ABCG2, CDKN1A, ABCG5, HMGCS2, ABAT, PEBP1, NEUROD1, CA4, HSD11B2, SST, PDZK1, LCT, ABCC6 |
| Polyol metabolic process       | 7.76E-05  | GAL1, GP1, MOGAT2, DGAT2, DAK, PP1PK1, GK, ITPKA, GDP1, PCK1, GDP2           |
| Xenobiotic metabolic process   | 9.23E-05  | CYP3A4, FMO4, UGT1A6, NR1I2, UGT1A8, HNF4A, CYP1A1, UGT2B11, EPHX2           |
| Regulation of cellular ketone metabolic process | 9.40E-05 | APO4, SLC25A20, PPARA, CPT2, HNF4A, BHMT, APOC3, MLXIPL, APOC2, FABP1, STRADB, PPARGC1A, NR1H3 |
| Peptide secretion              | 9.73E-05  | EDN3, HNF1A, DGAT1, TRPV1, GHRH, FAM3B, NEUROD1, GHR, PDX1, FKB1B, SMPD3   |
| Hormone transport              | 9.91E-05  | SHBG, EDN3, HNF1A, DGAT1, TBX3, GHRH, FAM3B, NEUROD1, GHR, PDX1, FKB1B, SMPD3 |
| Regulation of fatty acid metabolic process | 9.91E-05 | APO4, SLC25A20, PPARA, CPT2, HNF4A, APOC3, MLXIPL, APOC2, FABP1, STRADB, PPARGC1A, NR1H3 |
| Process                                      | p-value | Genes                                                                 |
|----------------------------------------------|---------|----------------------------------------------------------------------|
| Monosaccharide metabolic process             | 1.07E-04| PFKFB4, PFKFB2, ALDOC, SLC37A4, ALDOB, PGAM2, PDX1, GALK1, GALM, B4GALNT2, GDP1, HKDC1, PDK4, GALT, FBP1, RBKS, CHST5, PCK2, PPP1CC, CPS1, PPPARGC1A, PCK1, KHK, G6PC, CHST6, PKLR, GHRL, GPT, XYLB |
| Excretion                                    | 1.12E-04| ABCG8, SLC26A3, ABCG5, SLC22A18, TRPV1, HMOX1, KCNK5, NR3C2, AQP7, AMN, GUCA2B, AQP3, SCTR |
| Pyruvate metabolic process                   | 1.21E-04| GPD1, G6PC, PFKFB2, ALDOB, FBP1, PGAM2, GPT, PCK2, AGXT, PPPARGC1A, PCK1 |
| Positive regulation of fatty acid metabolic process | 1.31E-04| APOA4, PPARA, HNF4A, MLXIP, APOC2, FABP1, PPPARGC1A, NR1H3 |
| Regulation of secretion                      | 1.33E-04| EDN3, HNF1A, GRIK1, PFKFB2, EDN2, DRD4, KRT20, ADA, ACVR1C, PCSK1, APOA1, GRIN2B, HMOX1, PLA2G1B, TRPV6, RAB26, CASP1, NRG1, CAMK2A, SCAMP5, SIRT4, GCG, GHRH, SCN, NEUROD1, GHRH, IL2 |
| Lipid digestion                              | 1.35E-04| APOA4, ABCG8, SOAT2, ABCG5, PLA2G1B, NPC1L1 |
| Hormone metabolic process                    | 1.38E-04| ALDH8A1, HSD17B11, CYP1A1, DDO, PCSK2, PCSK1, UGT1A6, ACE, APOA1, UGT1A8, LRAT, SULT1B1, ADH4, UGT2B11, HSD11B2, SCARB1, SULT1E1, PCSK5, RETSAT |
| Nitrogen compound biosynthetic process       | 1.79E-04| MOCOS, ME1, ALAD, SEPHS2, HNF1A, NAGS, ATP10A, AGMAT, AGXT, ADA, GCH1, TPK1, PADD6, ARG2, ENTPD8, HAAO, SULT1A2, GUCA2B, GCHFR, MOCS1, DDC, SHMT1, OTC, ATP1A4, ATP1A1, CPS1, GUUC2C, AMPD1, ADI1, CTH, ADCY9, BHMT, PRODH2, QPRT, DPYD, SLC25A15, PRODH |
| Drug metabolic process                       | 1.93E-04| CYP3A4, CBR1, CYP1A1, CYP2C19, CYP2C9, CYP2D6, EPHX2 |
| Reverse cholesterol transport                | 1.93E-04| APOA4, APOA1, HNF1A, APOC3, APOC2, SCARB1, APOH |
| Hormone secretion                            | 2.24E-04| EDN3, HNF1A, DGAT1, TBX3, GHRH, FAM3B, NEUROD1, GHRL, PDX1, FKBP1B, SMPD3 |
| Regulation of cholesterol storage            | 2.36E-04| PPARA, APOB, MSR1, CD36, SCARB1, NR1H3 |
| Response to xenobiotic stimulus              | 2.50E-04| CYP3A4, FMO4, UGT1A6, NR1H2, UGT1A8, HNF4A, CYP1A1, UGT2B11, EPHX2 |
| Process                                      | p-value | Genes                                                                 |
|----------------------------------------------|---------|-----------------------------------------------------------------------|
| Glycerol metabolic process                   | 2.50E-04| *GPD1, MOGAT2, DGAT2, DAK, GK, GDPD1, PCK1, GDPD2*                     |
| Endocrine process                            | 2.50E-04| *EDN3, ACE, TBX3, EDN2, ACE2, HSD11B2, GHRL, PCSK5*                    |
| Endocrine pancreas development               | 2.84E-04| *INSM1, HNF1A, ONECUT2, NEUROD1, IL6R, PDX1, NKK2-2*                  |
| Hexose biosynthetic process                  | 3.20E-04| *GPD1, G6PC, ALDOB, FBPI, PGAM2, GPT, PCK2, PPARGC1A, PCK1*           |
| Vitamin transport                            | 3.35E-04| *SLC25A20, SLC23A1, CPT2, SLC22A4, SLC22A5, SLC19A1, PDZK1, SLC46A1* |
| Peptide hormone secretion                    | 3.40E-04| *EDN3, HNF1A, DGAT1, GHRH, FAM3B, NEUROD1, GHRL, PDX1, FKBP1B, SMPD3 |
| Betaine transport                            | 3.57E-04| *SLC25A20, CPT2, SLC22A4, SLC22A5, PDZK1*                            |
| Carnitine transport                          | 3.57E-04| *SLC25A20, CPT2, SLC22A4, SLC22A5, PDZK1*                            |
| Amine transport                              | 5.13E-04| *SLC36A1, CPT2, SLC16A10, SLC6A12, SLC6A4, SLC7A9, SLC3A1, SLC19A1, SLC6A19, SLC7A7, SLC25A20, SLC6A5, SLC22A4, SLC22A5, SLC25A15, PDZK1, SLC1A1, SLC46A1* |
| Cellular hormone metabolic process           | 5.57E-04| *HSD17B11, ALDH8A1, UGT1A6, LRAT, APOA1, UGT1A8, CYP1A1, ADH4, UGT2B11, HSD11B2, SCARB1, SULT1E1, RETSAT* |
| Response to glucocorticoid stimulus          | 5.64E-04| *CALCR, ACADS, SI, ALDOB, IL6R, CPS1, AGXT, TAT, PPARGC1B, PCSK1, UGT1A6, CDKN1A, UGT1A8, HSD11B2, PEBP1* |
| Regulation of system process                 | 6.34E-04| *EDN3, PRK2CZ, CCK, CYP2J2, GRK1, GRK3, EDN2, DRD4, FKBP1B, ADA, SYP, APOA4, ACE, APOA1, GRIN2B, HMOX1, ARG2, SLC22A5, LGI1, HCN4, CAMK2A, EPHX2, GRIN2A, MYH7, ATP1A1, CPS1, ABCG8, SSTR2, ABCG5, ADRA1B, ACE2, PEBP1, GHRL, IL2* |
| Unsaturated fatty acid metabolic process     | 6.51E-04| *AKR1C3, CYP4F8, ACOX1, PTGR1, CYP2J2, EDN2, EPHX2, PLA2G1B, CYP4F3, CYP4F2, HPGD* |
| Cofactor transport                           | 7.64E-04| *SLC25A20, CPT2, SLC22A4, SLC22A5, SLC19A1, PDZK1, SLC46A1*         |
| Macromolecular complex remodeling            | 7.64E-04| *APOA4, APOB, APOC3, PLA2G2A, APOC2, SCARB1, APOM*                   |
| Process                                                                 | Score  | Genes                                                                 |
|------------------------------------------------------------------------|--------|----------------------------------------------------------------------|
| Plasma lipoprotein particle remodeling                                 | 7.64E-04 | APOA4, APOB, APOC3, PLA2G2A, APOC2, SCARB1, APOM                     |
| Regulation of cholesterol transport                                    | 7.64E-04 | APOA4, ABCG8, ABCG5, APOA1, APOC3, APOC2, NR1H3                       |
| Regulation of sterol transport                                          | 7.64E-04 | APOA4, ABCG8, ABCG5, APOA1, APOC3, APOC2, NR1H3                       |
| Protein-lipid complex remodeling                                       | 7.64E-04 | APOA4, APOB, APOC3, PLA2G2A, APOC2, SCARB1, APOM                     |
| Regulation of lipid metabolic process                                  | 8.14E-04 | PPARA, CPT2, MLXIPL, APOC2, ATP1A1, STRADB, PPARGC1A, SEC14L2, APOA4, SLC25A20, APOB, APOA1, HNF4A, APOC3, FABP1, APOM, NR1H3 |
| Amine biosynthetic process                                             | 8.17E-04 | ADI1, DDC, SHMT1, SEPHS2, CTH, NAGS, OTC, BHMT, PRODH2, SULT1A2, AGMAT, AGXT, PRODH, GCH1 |
| Hexose metabolic process                                               | 8.84E-04 | GPD1, PFKFB4, PFKFB2, ALDOC, HKDC1, SLC37A4, PDK4, ALDOB, GALT, FBP1, PGAM2, PDX1, PPP1CC, PCK2, CPS1, PPARGC1A, PCK1, KHK, GALK1, GALM, G6PC, PKLR, GHRL, GPT |
| Negative regulation of transport                                       | 9.10E-04 | EDN3, CRYAA, SLC15A1, EDN2, DRD4, SIRT4, APOC2, ADA, ACVR1C, ABCG8, ABCG5, APOA1, HNF4A, HMOX1, APOC3, GHRL, NRG1, NR1H3, SCAMP5 |
| Response to inorganic substance material                               | 9.57E-04 | XDH, APOBEC1, CYP1A1, ALDOB, PGAM2, MYH7, TAT, AQP3, ADA, APOA4, KHK, PCSK1, APOB, CDKN1A, HMOX1, GPX3, CYBRD1, HAAO, PEBP1, ABAT, CAT, CA2, MT1H, LCT, MB |
| Monosaccharide biosynthetic process                                     | 1.15E-03 | GPD1, G6PC, ALDOB, FBP1, PGAM2, GPT, PCK2, PPARGC1A, PCK1             |
| Triglyceride biosynthetic process                                       | 1.17E-03 | MOGAT2, DGAT1, DGAT2, AGPAT9, PCK1                                   |
| Positive regulation of lipid metabolic process                          | 1.22E-03 | APOA4, PPARA, APOA1, HNF4A, MLXIPL, APOC2, FABP1, PPARGC1A, SEC14L2, NR1H3 |
| Process                                                                 | p-value | Genes                      |
|------------------------------------------------------------------------|---------|----------------------------|
| Regulation of fatty acid biosynthetic process                          | 1.26E-03| APOA4, HNF4A, APOC3, MLXIPL, APOC2, NR1H3 |
| Response to corticosteroid stimulus                                     | 1.30E-03| CALCRI, ACADS, SI, ALDOB, IL6R, CPS1, AGXT, TAT, PPARC1B, PCSK1, UGT1A6, CDKN1A, UGT1A8, HSD11B2, PEBP1 |
| Lipid biosynthetic process                                             | 1.35E-03| ALDH8A1, HSD17B11, HNF1A, HSD17B2, EDN2, ACSS2, PDSS1, PECR, APOA1, B3GNT5, AGPAT9, PLA2G1B, PIWIL2, NPC1L1, HSD17B3, SCARB1, ELOVL7, PCYT2, GAL3ST1, ACA2, MOGAT2, PLD1, CYP1A1, CDS1, LPCAT3, FADS6, PCK1, DGAT1, HMGCS2, ST8SIA6, DGAT2, SEMA6D, HSD11B2, SCP2 |
| Cellular amide metabolic process                                       | 1.39E-03| ME1, GPD1, NAGS, ARG2, OTC, ALDOB, HAAO, QPRT, CPS1, SLC25A15, IDH3A |
| Icosanoid metabolic process                                            | 1.43E-03| AKR1C3, CYP4F8, ACOX1, PTGR1, CYP2J2, EDN2, PLA2G1B, CYP4F3, CYP4F2, HPGD |
| Response to monosaccharide stimulus                                     | 1.43E-03| KHK, PCSK1, SARM1, HNF1A, HNF4A, PFKFB2, SI, NEUROD1, FKBP1B, ACVR1C |
| Response to hexose stimulus                                            | 1.43E-03| KHK, PCSK1, SARM1, HNF1A, HNF4A, PFKFB2, SI, NEUROD1, FKBP1B, ACVR1C |
| Response to organic substance                                          | 1.48E-03| PPARA, HNF1A, APOBEC1, TLR3, FOXO4, AGXT, ACVR1C, APOB, CDKN2B, GRIN2B, HMOX1, PLA2G1B, CHRNA7, CREB3L3, CASP1, CHRFAM7A, APOM, MB, PLD1, CYP1A1, ACADS, FBP1, GRIN2A, IL6R, TAT, PPARC1B, HNF4A, ERN1, GHRL, HSD11B2, PEBP1, ABAT, CA4, CA2, LCT, ME1, CALCRI, CAV2, ALDOC, PFKFB2, DRD4, ALDOB, ADH6, LIN28A, FKBP1B, GCH1, UGT1A6, PCSK1, UGT1A8, LIN2, SCARB1, KAT2B, SI, CPS1, GNAT3, PCK1, GCG, KHK, CDKN1A, SARM1, ADCY9, HMGCS2, ADRA1B, NEUROD1, SST |
| Biogenic amine metabolic process                                       | 1.53E-03| ENPP6, DDC, ACDM, MAOA, DRD4, GRIN2A, AGMAT, GCH1, APOA4, APOA1, SULT1B1, PLA2G1B, SLC22A4, SULT1A2, SULT1A4 |
| Sodium ion transport                                                   | 1.55E-03| SGK1, SLC5A4, SLC20A2, SLC5A1, ATP1A4, ATP1A1, SLC10A2, SLC23A1, CATSPER3, SLC17A4, SLC22A4, SLC13A2, SLC4A7, SLC22A5, HCN4, SLC4A4, SLC5A11, SLC5A12 |
| **Process**                                    | **p-value** | **Genes**                                                                 |
|-----------------------------------------------|-------------|--------------------------------------------------------------------------|
| Glucose metabolic process                     | 1.57E-03    | GPD1, PFKFB2, ALDOC, HKDC1, SLC37A4, PDK4, ALDOB, GALT, FBP1, PGAM2, PDX1, PPP1CC, CPS1, PCK2, PPARGC1A, PCK1, G6PC, PKLR, GHRL, GPT |
| Response to endogenous stimulus               | 1.58E-03    | CALCR, ME1, CAV2, PPARA, APOBEC1, ALDOC, ALDOB, DRD4, FOXO4, AGXT, ACVR1C, UGT1A6, PCSK1, UGT1A8, HMOX1, PLA2G1B, MB, PLD1, KAT2B, ACADS, SI, GRIN2A, FBP1, IL6R, CPS1, TAT, PPARC1B, PCK1, KHK, GCG, CDKN1A, ADCY9, HMGCS2, ADRA1B, PEBP1, GHRL, HSD11B2, CA4, CA2, SST, LCT |
| Organic cation transport                      | 1.71E-03    | SLC25A20, CPT2, SLC22A18, SLC22A4, RHBG, SLC22A5, PDZK1                  |
| Positive regulation of cholesterol storage    | 1.84E-03    | APOB, MSR1, CD36, SCARB1                                               |
| Urea metabolic process                        | 1.86E-03    | NAGS, ARG2, OTC, CPS1, SLC25A15                                         |
| Urea cycle                                    | 1.86E-03    | NAGS, ARG2, OTC, CPS1, SLC25A15                                         |
| Lipoprotein transport                         | 1.86E-03    | APOB, MSR1, APOBEC1, CD36, MTTP                                         |
| Regulation of blood pressure                  | 2.05E-03    | EDN3, PPARA, EDN2, EPHX2, ATP1A1, GCH1, ACE, CHGA, HMOX1, ADRA1B, ACE2, ABAT, HSD11B2, GUCA2B, PCSK5 |
| Coenzyme biosynthetic process                 | 2.13E-03    | MOCOS, ME1, TPK1, COQ4, PANK3, PANK1, HAAO, GGT1, QPRT, PDSS1, MOCS1, GCH1 |
| Sterol metabolic process                      | 2.26E-03    | ACA2A, SOAT2, HNF1A, LIPA, NR0B2, APOA4, APOB, APOA1, CYP27A1, HMGCS2, CYP7A1, APOC3, NPC1L1, SCARB1, CAT |
| Fructose metabolic process                    | 2.35E-03    | KHK, PFKFB4, PFKFB2, ALDOC, ALDOB, FBP1                                 |
| Regulation of lipoprotein lipase activity     | 2.35E-03    | APOA4, APOC3, APOH, APOC2, FKBP1B, NR1H3                                |
| Cellular amino acid biosynthetic process      | 2.60E-03    | ADI1, SHMT1, CTH, SEPHS2, NAGS, OTC, BHMT, PRODH2, AGXT, PRODH          |
| Fat-soluble vitamin metabolic process         | 2.61E-03    | CYP3A4, ALDH8A1, CBRI, LRAT, CYP1A1, ADH4, RBP2, RETSAT                 |
| Process                                                                 | P-value  | Genes                                                                 |
|-------------|----------|----------------------------------------------------------------------|
| Cholesterol metabolic process | 2.69E-03 | ACAA2, SOAT2, HNF1A, NR0B2, APOA4, APOB, APOA1, CYP27A1, HMGCS2, CYP7A1, APOC3, NPC1L1, SCARB1, CAT |
| Regulation of digestive system process | 2.79E-03 | APOA4, ABCG8, ABCG5, APOA1, SLC22A5                                      |
| Amide biosynthetic process | 2.79E-03 | NAGS, ARG2, OTC, CPS1, SLC25A15                                       |
| Positive regulation of fatty acid biosynthetic process | 2.79E-03 | APOA4, HNF4A, MLXIPL, APOC2, NR1H3                                      |
| Response to hormone stimulus | 3.16E-03 | CALCR, ME1, CAV2, PPARA, APOBEC1, ALDOB, FOXO4, AGX7, ACVR1C, UGT1A6, PCSK1, UGT1A8, HMOX1, PLA2G1B, MB, PLD1, KAT2B, ACADS, SI, FBP1, IL6R, CPS1, TAT, PPARGC1B, PCK1, KHK, GCG, CDKN1A, ADcy9, HMGCS2, PEBP1, GHRL, HSD11B2, CA4, CA2, SST, LCT |
| Response to nutrient | 3.44E-03 | SOAT2, CYP1A1, HSD17B2, SI, SLC6A19, AQP3, VDR, UGT1A6, SSTR2, ABCG5, UGT1A8, CDKN2B, HMGCS2, SSTR1, HMOX1, SSTR, APOM, KLF4, LCT |
| Negative regulation of multicellular organismal process | 3.49E-03 | F11, GRIK1, GRIK3, APOC2, ATP1A1, IL6R, CXADR, FKBP1B, ADA, ABCG8, ABCG5, APOA1, HMOX1, ARG2, KLKB1, APOC3, APOH, GHRL, CHRNA7, CHRFAM7A, IL2 |
| High-density lipoprotein particle clearance | 3.52E-03 | APOA1, APOC2, SCARB1, APOM                                         |
| Regulation of intestinal cholesterol absorption | 3.52E-03 | APOA4, ABCG8, ABCG5, APOA1                                      |
| Very-low-density lipoprotein particle assembly | 3.52E-03 | SOAT2, APOB, DGAT1, APOC3                                        |
| Response to metal ion | 3.61E-03 | XDH, APOBEC1, CYP1A1, ALDOB, PGAM2, TAT, AQP3, KHK, PCSK1, APOB, CYBRD1, HAAO, ABAT, PEBP1, CA2, MT1H, LCT |
| Process                                | q-value | Genes                                                                 |
|----------------------------------------|---------|----------------------------------------------------------------------|
| Alcohol biosynthetic process           | 3.66E-03| GPD1, G6PC, ALDOB, FBP1, PGAM2, GPT, PCK2, PPARGC1A, PCK1              |
| Pancreas development                   | 3.71E-03| INSM1, PCSK1, HNF1A, ONECUT2, NEUROD1, IL6R, PDX1, NKKX2-2           |
| Phenol metabolic process               | 3.71E-03| DDC, SULT1B1, MAOA, DRD4, GRIN2A, SULT1A2, SULT1A4, GCH1             |
| Cellular carbohydrate catabolic process| 3.89E-03| GPD1, ALDOC, HKDC1, PFKFB2, ALDOB, PGAM2, CPS1, GBA3, GBA2, G6PC, PKLR, MGAM, TREH |
| Quaternary ammonium group transport    | 3.99E-03| SLC25A20, CPT2, SLC22A4, SLC22A5, PDZK1                               |
| Neutral lipid biosynthetic process     | 3.99E-03| MOGAT2, DGAT1, DGAT2, AGPAT9, PCK1                                   |
| Acylglycerol biosynthetic process      | 3.99E-03| MOGAT2, DGAT1, DGAT2, AGPAT9, PCK1                                   |
| Bile acid metabolic process            | 4.01E-03| ACOX2, GBA2, HNF1A, SULT2A1, PIWIL2, NR5A2                           |
| Regulation of systemic arterial blood pressure mediated by a chemical signal | 4.10E-03| EDN3, ACE, EDN2, ADRA1B, ACE2, HSD11B2, PCSK5                        |
| Regulation of lipid biosynthetic process| 4.23E-03| APOA4, APOB, HNF4A, APOC3, MLXIPL, APOC2, ATP1A1, SEC14L2, NR1H3     |
| Response to glucose stimulus           | 4.23E-03| KHK, PCSK1, SARM1, HNF1A, HNF4A, PFKFB2, NEUROD1, FKBPA1, ACVR1C    |
| Cofactor biosynthetic process          | 4.29E-03| ME1, MOCOS, ALAD, HNF1A, GGT1, PDSS1, GCH1, COQ4, TPK1, PANK3, PANK1, HAAO, QPRT, MOCS1 |
| Carboxylic acid biosynthetic process   | 4.29E-03| SHMT1, SEPHS2, PLD1, HNF1A, NAGS, OTC, EDN2, AGXT, FAD6, ADI1, PECR, CTH, BHMT, PLA2G1B, HAAO, PIWIL2, PRODH2, ELOVL7, PRODH |
| Process                                                                 | p-value | Genes                                                                 |
|------------------------------------------------------------------------|---------|----------------------------------------------------------------------|
| Organic acid biosynthetic process                                       | 4.29E-03| $SHMT1$, $SEPHS2$, $PLD1$, $HNF1A$, $NAGS$, $OTC$, $EDN2$, $AGXT$, $FADS6$, $AD11$, $PECR$, $CTH$, $BHMT$, $PLA2G1B$, $HAAO$, $PIWIL2$, $PRODH2$, $ELOVL7$, $PRODH$ |
| Negative regulation of secretion                                         | 4.40E-03| $EDN3$, $APOA1$, $HMOX1$, $EDN2$, $DRD4$, $SIRT4$, $GHRL$, $NRG1$, $ADA$, $ACVR1C$ |
| Cellular aldehyde metabolic process                                     | 4.97E-03| $ALDH1A1$, $ALDH8A1$, $AKR1B15$, $ADH4$, $AKR1B10$, $AKR7A2$, $AKR7A3$, $AGXT$ |
| Regulation of leukocyte migration                                        | 5.09E-03| $EDN3$, $HMOX1$, $EDN2$, $F2RL1$, $IL6R$, $ADA$                      |
| Regulation of systemic arterial blood pressure by hormone                | 5.09E-03| $EDN3$, $ACE$, $EDN2$, $ACE2$, $HSD11B2$, $PCSK5$                    |
| Quinone cofactor metabolic process                                      | 5.50E-03| $COQ4$, $CBR1$, $ADH4$, $PDSS1$, $CRYZL1$                           |
| Glycerol ether biosynthetic process                                      | 5.50E-03| $MOGAT2$, $DGAT1$, $DGAT2$, $AGPAT9$, $PCK1$                       |
| Regulation of cellular localization                                     | 5.83E-03| $EDN3$, $HNF1A$, $CRYAA$, $PFKFB2$, $EDN2$, $DRD4$, $SIRT4$, $KRT20$, $FKBP1B$, $ACVR1C$, $GCG$, $PCSK1$, $APOA1$, $HNF4A$, $GRIN2B$, $GHRH$, $HMOX1$, $PLA2G1B$, $NEUROD1$, $GHRL$, $TRPV6$, $RAB26$, $CASP1$, $CAMK2A$, $IL2$, $SCAMP5$ |
| Negative regulation of sterol transport                                 | 5.90E-03| $ABCG8$, $ABCG5$, $APOC3$, $APOC2$                                 |
| Negative regulation of cholesterol transport                             | 5.90E-03| $ABCG8$, $ABCG5$, $APOC3$, $APOC2$                                 |
| Positive regulation of lipoprotein lipase activity                      | 5.90E-03| $APOA4$, $APOH$, $APOC2$, $NR1H3$                                   |
| Glucose transport                                                       | 5.96E-03| $SLC2A9$, $G6PC$, $SLC2A5$, $SLC5A1$, $SLC2A2$, $SLC37A4$, $PLA2G1B$ |
| Regulation of lipid storage                                              | 6.37E-03| $PPARA$, $APOB$, $MSR1$, $CD36$, $SCARB1$, $NR1H3$                 |
| Positive regulation of lipid biosynthetic process | 6.37E-03 | APOA4, HNF4A, MLXIPL, APOC2, SEC14L2, NR1H3 |
| Endocrine system development | 6.70E-03 | INSM1, PCSK1, APOA1, HNF1A, GHRH, ONECUT2, NEUROD1, IL6R, PDX1, MDK, NKX2-2 |
| Lipoprotein metabolic process | 6.83E-03 | APOA4, PPARA, APOB, APOBEC1, CD36, APOA1, SEMA6D, APOC3, NPC1L1, APOM, APOL5, MTTP |
| Hexose transport | 7.09E-03 | SLC2A9, G6PC, SLC2A5, SLC5A1, SLC2A2, SLC37A4, PLA2G1B |
| Regulation of lipid transport | 7.09E-03 | APOA4, ABCG8, ABCG5, APOA1, APOC3, APOC2, NR1H3 |
| Carbohydrate homeostasis | 7.20E-03 | G6PC, HNF1A, SLC37A4, MLXIPL, ADRA1B, NEUROD1, PDX1, PPARGC1A, PCK1 |
| Glucose homeostasis | 7.20E-03 | G6PC, HNF1A, SLC37A4, MLXIPL, ADRA1B, NEUROD1, PDX1, PPARGC1A, PCK1 |
| Positive regulation of heart contraction | 7.34E-03 | EDN3, EDN2, ADRA1B, ATP1A1, ADA |
| Sulfur metabolic process | 7.36E-03 | SEPHS2, GGT1, SLC19A3, CHST5, ADI1, TPK1, SULT4A1, GSR, MSRA, CTH, CHST6, BHMT, GPX3, CHST13, SEPP1 |
| Regulation of heart rate | 7.85E-03 | EDN3, EDN2, ADRA1B, MYH7, FKBP1B, ADA |
| Water-soluble vitamin metabolic process | 7.97E-03 | ME1, TPK1, SHMT1, ACADM, SLC22A4, HAAO, SLC19A3, QPRT |
| Monosaccharide transport | 8.36E-03 | SLC2A9, G6PC, SLC2A5, SLC5A1, SLC2A2, SLC37A4, PLA2G1B |
| Response to peptide hormone stimulus | 8.93E-03 | PPARA, CAV2, PLD1, KAT2B, APOBEC1, SI, ALDOB, FBP1, IL6R, FOXO4, CPS1, PCK1, ACVR1C, KHK, PCSK1, HMGCS2, PLA2G1B, HSD11B2 |
| Intestinal cholesterol absorption | 9.03E-03 | ABCG8, SOAT2, ABCG5, NPC1L1 |
| Response to steroid hormone stimulus | 9.07E-03 | CALCR, CAV2, ACADS, SI, ALDOB, IL6R, CPS1, AGXT, TAT, PPARGC1B, PCSK1, UGT1A6, CDKN1A, UGT1A8, HMOX1, PEBP1, CA4, HSD11B2, GHRL, CA2, SST, LCT |
| Process                                                                 | p-value   | Gene Symbols |
|-------------------------------------------------------------------------|-----------|--------------|
| Positive regulation of multicellular organismal process                 | 9.13E-03  | MAVS, PRKCZ, EDN3, GRIK1, KL, TRPV1, EDN2, EPHX2, TLR3, ATP1A1, IL6R, CPS1, ADA, CARD11, GHRH, HMOXI, GATA4, ADRA1B, APOH, GHRL, SLC22A5, CA2, LGI1, NRG1, CASP1 |
| Vitamin A metabolic process                                             | 9.55E-03  | ALDH8A1, LRAT, CYP1A1, ADH4, RBP2, RETSAT |
| Negative regulation of lipid transport                                  | 9.55E-03  | ABCG8, ABCG5, APOC3, APOC2, NR1H3 |
| Carbohydrate biosynthetic process                                       | 9.77E-03  | B3GNT8, GP1, G6PC, GCNT2, ST8SIA6, CHST6, ALDOB, FBP1, CHST13, PGAM2, GPT, PCK2, PPARC1A, PCK1 |
| Stem cell differentiation                                               | 9.79E-03  | XRCC5, ACE, CDX2, PLA2G2A, PIWIL2, LIN28A, KLF4 |
| Glycoside catabolic process                                             | 9.92E-03  | GBA3, GBA2, TREH |
| Generation of a signal involved in cell-cell signaling                  | 1.07E-02  | EDN3, HNF1A, DGAT1, TBX3, BAIAP3, GHRH, FAM3B, NEUROD1, GHRL, PDX1, FKBP1B, SMPD3 |
| Steroid biosynthetic process                                            | 1.07E-02  | HSD17B11, ACAA2, APOA1, HNF1A, HSD17B2, HMGCS2, PIWIL2, HSD11B2, NPC1L1, SCARB1, HSD17B3, SCP2 |
| Phospholipid transport                                                  | 1.14E-02  | APOA4, ABCG8, APOA1, APOC3, ATP10A, APOC2, ABCA4 |
| Peptide metabolic process                                               | 1.15E-02  | GSR, PCSK1, CTH, ACE, ADAMTS13, GPX3, MME, GGT1, PCSK5 |
| Cell-cell signaling                                                    | 1.16E-02  | EDN3, HNF1A, GRIK1, GABRB2, FAM3B, SLC6A4, ENPEP, PDX1, VIPR1, WNT3, GRIN2B, GATA4, HTR1D, SLC1A1, GABRG1, BAIAP3, GRIN2A, IL26, NRXN1, SSTR2, DGAT1, GHRH, SSTR1, ABAT, PEBP1, GHRL, CAV2, DRD4, MME, CCL8, AKAP9, FKBP1B, PCSK1, PCSK5, GCHFR, MLN, BMP3, TRHDE, TBX3, CPNE6, MAOA, CCL15, CXCL14, SLC6A5, ADRA1B, MTNR1B, NEUROD1, SST, SMPD3, IL2 |
| Response to ethanol                                                     | 1.19E-02  | UGT1A6, APOBEC1, UGT1A8, GRIN2B, DRD4, GRIN2A, ADH6, ABAT, PEBP1, IL6R, LCT |
| Water transport                                                        | 1.22E-02  | MIP, AQP11, AQP7, PDZD3, AQP3 |
| Process                                                                 | P-value  |
|------------------------------------------------------------------------|----------|
| Monovalent inorganic cation transport                                  | 1.23E-02 |
| Positive regulation of lipid storage                                  | 1.30E-02 |
| Response to food                                                       | 1.30E-02 |
| Positive regulation of behavior                                        | 1.32E-02 |
| Diol metabolic process                                                 | 1.32E-02 |
| Catechol metabolic process                                            | 1.32E-02 |
| Catecholamine metabolic process                                       | 1.32E-02 |
| Dicarboxylic acid metabolic process                                   | 1.32E-02 |
| Isoprenoid metabolic process                                          | 1.34E-02 |
| Regulation of foam cell differentiation                               | 1.37E-02 |
| Protein oligomerization                                               | 1.37E-02 |
| Regulation of heart contraction                                       | 1.42E-02 |
| Heterocycle catabolic process                                         | 1.42E-02 |
| Regulation of hormone secretion                                       | 1.45E-02 |
| Regulation of systemic arterial blood pressure                        | 1.51E-02 |

| Genes                                                                 |          |
|-----------------------------------------------------------------------|----------|
| Monovalent inorganic cation transport                                  | KCNJ16, SLC36A1, SLC5A4, SLC20A2, SLC5A1, KCNA3, KCNJ3, KCNK10, KCNJ13, SLC23A1, KCNK5, SLC22A4, SLC4A7, SLC22A5, HCN4, SLC4A4, SGK1, ATP1A4, ATP1A1, SLC10A2, CNGA1, KCNJ6, CATSPER3, SLC17A4, KCNH6, SLC13A2, KCTD16, ABCC8, SLC5A11, SLC5A12 |
| Positive regulation of lipid storage                                  | APOB, MSR1, CD36, SCARB1 |
| Response to food                                                      | G6PC, CYP1A1, GHRH, HSD11B2 |
| Positive regulation of behavior                                       | EDN3, GHRH, EDN2, F2RL1, GHRL, IL6R, SCG2 |
| Diol metabolic process                                                | DDC, MAOA, DRD4, GRIN2A, SULT1A2, SULT1A4, GCH1 |
| Catechol metabolic process                                            | DDC, MAOA, DRD4, GRIN2A, SULT1A2, SULT1A4, GCH1 |
| Catecholamine metabolic process                                       | DDC, MAOA, DRD4, GRIN2A, SULT1A2, SULT1A4, GCH1 |
| Dicarboxylic acid metabolic process                                   | SDHA, ME1, SUCLG1, HAAO, QPRT, IDH3A, PCK1 |
| Isoprenoid metabolic process                                          | ALDH8A1, LRAT, CYP1A1, HMGCS2, ADH4, RBP2, PDSS1, RETSAT |
| Regulation of foam cell differentiation                               | PPARA, APOB, MSR1, CD36, PLA2G2A, NR1H3 |
| Protein oligomerization                                               | SHMT1, PRK CZ, CAV2, CRYAA, OTC, ALDOC, DECR1, PDSS1, GCH1, CTH, P2RX6, AQP11, GPX3, PEBP1, QPRT, CAT, SCARA5, SLC1A1, GCHFR |
| Regulation of heart contraction                                       | EDN3, CYP2J2, EDN2, ADRA1B, PEBP1, MYH7, ATP1A1, HCN4, FKBP1B, ADA, IL2 |
| Heterocycle catabolic process                                         | ALDH6A1, UGT1A6, UGT1A8, CYP1A1, HMOX1, PRODH2, MYH7, DPDY, ADA, PRODH, GCH1, ABCC6 |
| Regulation of hormone secretion                                       | GCG, EDN3, HNF1A, GHRH, PFKFB2, EDN2, SIRT4, NEUROD1, GHRH, ACVR1C |
| Regulation of systemic arterial blood pressure                        | EDN3, ACE, EDN2, ADRA1B, ACE2, HSD11B2, PCSK5 |
| Category                                      | p-value | Genes                                                                 |
|-----------------------------------------------|---------|-----------------------------------------------------------------------|
| Fluid transport                               | 1.52E-02| MIP, AQP11, AQP7, PDZD3, AQP3                                         |
| Response to zinc ion                          | 1.52E-02| KHK, APOBEC1, ALDOB, HAAO, CA2                                        |
| Cellular chemical homeostasis                 | 1.56E-02| CALCR, PRKCZ, JPH4, CCK, GRIK1, GRIK3, GNA11, EDN2, F2RL1, DRD4, NR3C2,FKBP1B, VDR, BAK1, GRIN2B, AQP11, RGN, CHRNA7, CHRFAM7A, SLC39A4, MT1H, GAL3ST1, GRIN2A, EPHX2, ATP1A4, SLC9A3R1, AFG3L2, CCL15, PPARGC1A, CCR9, GHRH, GHRL, SCARA5, MON1A, IL2 |
| Nitrogen compound catabolic process           | 1.59E-02| ALDH6A1, UGT1A6, UGT1A8, HMOX1, ENPP3, MYH7, DPYD, ADA, MPST, GCH1, ABCC6 |
| Ion homeostasis                               | 1.61E-02| CALCR, PRKCZ, JPH4, CCK, GRIK1, GRIK3, GNA11, EDN2, DRD4, F2RL1, NR3C2,FKBP1B, VDR, BAK1, GRIN2B, AQP11, HMOX1, RGN, CHRNA7, CHRFAM7A, SLC39A4, MT1H, GAL3ST1, OTC, GRIN2A, EPHX2, ATP1A4, CPS1, SLC9A3R1, AFG3L2, CCL15, CCR9, GHRH, GHRL, SCARA5, MON1A, IL2 |
| Secondary metabolic process                   | 1.68E-02| ME1, ALDH8A1, GDP1, LRAT, CYP1A1, ADH4, ALDOB, HAAO, QPRT, IDH3A, RETSAT |
| Regulation of peptide secretion               | 1.69E-02| GCG, HNF1A, GHRH, PFKFB2, SIRT4, NEUROD1, GHRL, ACVR1C                |
| Regulation of behavior                        | 1.69E-02| EDN3, GHRH, EDN2, F2RL1, GHRL, IL6R, ADA, SCG2                       |
| Positive regulation of leukocyte chemotaxis   | 1.77E-02| EDN3, EDN2, F2RL1, IL6R                                               |
| Positive regulation of heart rate             | 1.77E-02| EDN3, EDN2, ADRA1B, ADA                                               |
| Phospholipid efflux                           | 1.77E-02| APOA4, APOA1, APOC3, APOC2                                           |
| Acid secretion                                | 1.86E-02| ACE, DRD4, PLA2G1B, GHRL, AGXT                                       |
| Insulin secretion                             | 1.89E-02| HNF1A, DGAT1, FAM3B, NEUROD1, PDX1, FKBP1B                            |
| Cellular carbohydrate biosynthetic process    | 1.90E-02| B3GNT8, GDP1, G6PC, ALDOB, FBP1, PGAM2, GPT, PCK2, PPARGC1A, PCK1     |
| Metabolic Process                        | p-value | Genes                                                                 |
|-----------------------------------------|---------|-----------------------------------------------------------------------|
| Glycoside metabolic process             | 1.91E-02| GBA3, GBA2, TREH                                                       |
| Plasminogen activation                  | 1.91E-02| F11, KLKB1, APOH                                                      |
| Secretion by cell                       | 1.95E-02| EDN3, HNF1A, TBX3, BAIA3P, FAM3B, CCL8, PDX1, FKB1B, STXB5L, TRIM36, DGAT1, GHRH, SCIN, GHRL, NEUROD1, DOC2B, PCSK5, SMPD3, MON1A, SCG2, SCAMP5 |
| Calcium ion transport                   | 1.95E-02| ORAI1, JPH4, TRPM6, CLCA1, TRPV1, GRIN2A, CCL8, FKB1B, VDR, TMEM37, CATSPER2, GRIN2B, CATSPER3, CHRNA7, TRPV6, CHRFAM7A, CAMK2A |
| Cellular ion homeostasis                | 2.10E-02| CALCR, JPH4, PRKZ, CCK, GRIK1, GRIK3, GNA11, EDN2, F2RL1, DRD4, NR3C2, FKB1B, VDR, BAK1, GRIN2B, AQP11, RGN, CHRNA7, CHRFAM7A, SLC39A4, MT1H, GAL3ST1, GRIN2A, EPHX2, ATP1A4, SLC9A3R1, AFG3L2, CCL15, CCR9, GHRH, GHRL, SCARA5, MON1A, IL2 |
| Regulation of fatty acid oxidation      | 2.19E-02| SLC25A20, PPARA, CPT2, FABP1, STRADB, PPARGC1A                        |
| Vitamin biosynthetic process            | 2.19E-02| ME1, TPK1, ALDH8A1, CYP1A1, HAAO, QPRT                               |
| Prostaglandin metabolic process         | 2.25E-02| AKR1C3, CYP4F8, ACOXI, EDN2, HPGD                                    |
| Prostanoid metabolic process            | 2.25E-02| AKR1C3, CYP4F8, ACOXI, EDN2, HPGD                                    |
| Serine family amino acid biosynthetic   | 2.33E-02| SHMT1, CTH, SEPHS2, AGXT                                            |
| process                                 |         |                                                                       |
| Sphingomyelin metabolic process         | 2.33E-02| ENPP7, SMPDL3B, SMPDL3A, SMPD3                                       |
| Regulation of leukocyte chemotaxis      | 2.33E-02| EDN3, EDN2, F2RL1, IL6R                                              |
| Protein tetramerization                 | 2.49E-02| SHMT1, CTH, ALDOC, GPX3, DECR1, CAT, PDSS1                           |
| **Response to organic cyclic substance** | 2.51E-02 | **CYP1A1, ALDOC, DRD4, TAT, GNA T3, PCSK1, CDKN1A, PLIN2, CDKN2B, HMOX1, ADRA1B, PEBP1, ABAT, CHRNA7, CHRFAM7A** |
| **Sulfur compound biosynthetic process** | 2.58E-02 | **TPK1, ADI1, CTH, SEPHS2, CHST6, BHMT, CHST13, GGT1** |
| **Carbohydrate catabolic process** | 2.60E-02 | **GPD1, ALDOC, HKDC1, PFKFB2, ALDOB, PGAM2, CPS1, GBA3, GBA2, G6PC, PKLR, MGAM, TREH** |
| **Positive regulation of secretion** | 2.60E-02 | **EDN3, PCSK1, GRIN2B, GRIK1, GHRH, PFKFB2, EDN2, SCIN, PLA2G1B, GHRL, CASP1, IL2, SCAMP5** |
| **Organophosphate metabolic process** | 2.61E-02 | **GPD1, PLD1, ENPP7, GAL T, PIP5K1B, CDS1, LPCAT3, APOA4, PLCB3, APOA1, PIP5K1L1, SMPDL3B, SEMA6D, SMPDL3A, AGPAT9, PLA2G2A, PLA2G1B, GK, PCYT2, SMPD3** |
| **Regulation of vasodilation** | 2.69E-02 | **ACE, HMOX1, ACE2, EPHX2, CPS1** |
| **Regulation of insulin secretion** | 2.79E-02 | **GCG, HNF1A, PFKFB2, SIRT4, NEUROD1, GHRL, ACVR1C** |
| **Di-, tri-valent inorganic cation transport** | 2.97E-02 | **ORA11, SL C39A14, JPH4, TRPM6, CLCA1, TRPV1, GRIN2A, CCL8, FKBP1B, TMEM37, VDR, CATSPER2, GRIN2B, CATSPER3, CHRNA7, TRPV6, CHRFAM7A, SCARA5, CAMK2A** |
| **High-density lipoprotein particle remodeling** | 2.98E-02 | **APOA4, APOC3, SCAR B1, APO M** |
| **Regulation of very-low-density lipoprotein particle remodeling** | 3.06E-02 | **APOA1, APOC3, APOC2** |
| **Sphingomyelin catabolic process** | 3.06E-02 | **SMPDL3B, SMPDL3A, SMPD3** |
| **Oxidoreduction coenzyme metabolic process** | 3.13E-02 | **ME1, COQ4, GPD1, ALDOB, HAAO, QPRT, PDSS1, IDH3A** |
| **Cofactor catabolic process** | 3.28E-02 | **SDHA, UGT1A6, UGT1A8, ACO2, HMOX1, SUCLG1, IDH3A** |
Response to starvation
3.46E-02  UGT1A6, UGT1A8, ACADS, ALDOB, SI, CPS1, PPARGC1A, LCT

Phospholipid catabolic process
3.70E-02  PLCB3, PLD1, SMPDL3B, SMPDL3A, SMPD3

Nitric oxide metabolic process
3.70E-02  ARG2, CPS1, GCHFR, GCH1

Positive regulation of foam cell differentiation
3.70E-02  APOB, MSR1, CD36, PLA2G2A

Positive regulation of lipid catabolic process
3.70E-02  APOA4, PPARA, APOC2, FABP1

Drug transport
3.70E-02  SLC22A18, SLC22A5, PDZK1, SLC47A2

Regulation of body fluid levels
3.74E-02  F11, F10, ADAMTS13, F2RL1, MSTR, F13B, SCT, CD36, HNF4A, KLKB1, PROZ, SLC22A4, APOH, HSD11B2, GUCA2B

Response to oxygen levels
3.74E-02  PPARA, CYP1A1, PDIA2, ALDOC, ADA, ACE, CDKN1A, HMOX1, ABAT, HSD11B2, CHRNA7, CHRFAM7A, CASP1, LCT, DPP4, MB

Cellular homeostasis
3.77E-02  CALCR, PRKCA, JPH4, CCK, GRIK1, PDIA2, GRIK3, GNA11, EDN2, DRD4, F2RL1, NR3C2, FKBP1B, GSR, VDR, BAK1, GRIN2B, AQP11, HAAO, RGN, CHRNA7, CHRFAM7A, SLC39A4, MT1H, GAL3ST1, GLRX, GRIN2A, EPHX2, ATP1A4, SLC9A3R1, AFG3L2, CCL15, PPARGC1A, CCR9, GHRH, GHRL, SCARA5, MON1A, IL2

Amine catabolic process
3.85E-02  ALDH6A1, SHMT1, ASPA, MAOA, AMT, GLS, PRODH2, TAT, DDO, PRODH

Diterpenoid metabolic process
4.28E-02  ALDH8A1, LRAT, CYP1A1, ADH4, RETSAT

Retinoid metabolic process
4.28E-02  ALDH8A1, LRAT, CYP1A1, ADH4, RETSAT

Nucleobase metabolic process
4.28E-02  ALDH6A1, SHMT1, DPDY, ADA, AMPD1

Sulfur amino acid metabolic process
4.28E-02  ADI1, MSRA, CTH, SEPHS2, BHMT

Regulation of postsynaptic
4.28E-02  GRIN2B, GRIK1, DRD4, GRIN2A, GHRL
membrane potential
Cellular cation homeostasis 4.38E-02  CALCR, JPH4, EDN2, F2RL1, DRD4, EPHX2, NR3C2, ATP1A4, CCL15, FKBP1B, CCR9, BAK1, VDR, AQP11, GHRH, RGN, GHRL, CHRNA7, CHRFAM7A, SLC39A4, MT1H, SCARA5, IL2, MON1A

Regulation of triglyceride catabolic process 4.41E-02  APOA4, APOC3, APOC2

Negative regulation of lipoprotein metabolic process 4.41E-02  APOA4, APOM, HHATL

Cellular amino acid catabolic process 4.49E-02  ALDH6A1, SHMT1, ASPA, AMT, GLS, PRODH2, TAT, DDO, PRODH

Nitric oxide mediated signal transduction 4.51E-02  CD36, NEUROD1, PDX1, MT1H

Purine base metabolic process 4.51E-02  SHMT1, DPYD, ADA, AMPD1

Circulatory system process 4.64E-02  EDN3, CAV2, PPARA, EDN2, EPHX2, ATP1A1, GCH1, ACE, CHGA, NTS, HMOX1, ADRA1B, ACE2, ABAT, HSD11B2, GUCA2B, HCN4, PCSK5

Blood circulation 4.64E-02  EDN3, CAV2, PPARA, EDN2, EPHX2, ATP1A1, GCH1, ACE, CHGA, NTS, HMOX1, ADRA1B, ACE2, ABAT, HSD11B2, GUCA2B, HCN4, PCSK5

Negative regulation of phosphorylation 4.64E-02  BAK1, PRKcz, CDKN1A, HNF4A, CDKN2B, PEBP1, IL2

Regulation of response to external stimulus 4.69E-02  F11, EDN3, PPARA, CCK, EDN2, F2RL1, IL6R, ADA, KLKB1, ACE2, PLA2G2A, APOH, GHRL, CHRNA7, CHRFAM7A, IL2, SCG2

Nucleoside triphosphate catabolic process 4.90E-02  ENPP3, MYH7, ADA, GCH1, ABCC6
| Process                                      | p-value | Genes                                                                 |
|----------------------------------------------|---------|----------------------------------------------------------------------|
| Aspartate family amino acid metabolic process| 4.90E-02| ADI1, MSRA, ASPA, BHMT, DDO                                           |
| Brown fat cell differentiation                | 4.90E-02| PEX11A, ALDH6A1, PRDM16, PPARGC1A, MB                                |
| Visual perception                            | 5.09E-02| GJA10, CLRN1, CRYAA, KRT12, CYP4V2, CDS1, ABCA4, PHYH, CNGA1, RDH5, SFRP5, MIP, CRYGC, LRAT, NRL, CA4, USH1C, ACAD11, OAT, ABCC6 |
| Sensory perception of light stimulus          | 5.09E-02| GJA10, CLRN1, CRYAA, KRT12, CYP4V2, CDS1, ABCA4, PHYH, CNGA1, RDH5, SFRP5, MIP, CRYGC, LRAT, NRL, CA4, USH1C, ACAD11, OAT, ABCC6 |
**Supplementary Table 4.** Connectivity Map analysis of differentially expressed genes (DEGs) from ampullary cancer microarray. Chemicals with a negative correlation with DEGs of ampullary cancer are those with higher potential of cytotoxic ability.

| Rank | CMap name         | Dose | Cell  | Score | Up    | Down   | Instance id |
|------|-------------------|------|-------|-------|-------|---------|-------------|
| 5489 | fludrocortisone   | 9 µM | HL60  | 0     | -0.19 | -0.234 | 2368        |
| 5490 | SB-202190         | 1 µM | PC3   | 0     | -0.19 | -0.14  | 7058        |
| 5491 | tocainide         | 17 µM| MCF7  | 0     | -0.19 | -0.195 | 4838        |
| 5492 | diclofenamide     | 13 µM| MCF7  | 0     | -0.19 | -0.225 | 5286        |
| 5493 | tribenoside       | 8 µM | HL60  | 0     | -0.19 | -0.159 | 2946        |
| 5494 | (-)-isoprenaline | 16 µM| PC3   | 0     | -0.19 | -0.093 | 4495        |
| 5495 | harman            | 18 µM| HL60  | 0     | -0.191| -0.22  | 2150        |
| 5496 | phentolamine      | 12 µM| MCF7  | 0     | -0.191| -0.207 | 1138        |
| 5497 | rosiglitazone     | 10 µM| MCF7  | 0     | -0.191| -0.235 | 6950        |
| 5498 | rilmenidine       | 8 µM | PC3   | 0     | -0.191| -0.129 | 5107        |
| 5499 | bacampicillin     | 8 µM | MCF7  | 0     | -0.191| -0.238 | 3273        |
| 5500 | hydroflumethiazide| 12 µM| PC3   | 0     | -0.191| -0.139 | 1809        |
| 5501 | lobeline          | 11 µM| MCF7  | 0     | -0.191| -0.161 | 6258        |
| 5502 | megestrol         | 10 µM| HL60  | 0     | -0.191| -0.206 | 3091        |
| 5503 | iocetamic acid    | 7 µM | PC3   | 0     | -0.191| -0.169 | 4600        |
| 5504 | isoxicam          | 12 µM| PC3   | 0     | -0.191| -0.147 | 7268        |
| 5505 | haloperidol       | 10 µM| PC3   | 0     | -0.191| -0.119 | 1244        |
| 5506 | dihydroergocristine| 6 µM| MCF7  | 0     | -0.191| -0.195 | 7034        |
| 5507 | AG-013608         | 10 µM| PC3   | 0     | -0.191| -0.113 | 6440        |
| 5508 | acemetacin        | 10 µM| HL60  | 0     | -0.192| -0.207 | 2411        |
| 5509 | mefexamide        | 13 µM| PC3   | 0     | -0.192| -0.118 | 2121        |
| 5510 | ramifenazonne     | 14 µM| HL60  | 0     | -0.192| -0.209 | 2534        |
| 5511 | strophanthidin    | 10 µM| MCF7  | 0     | -0.192| -0.163 | 7182        |
| 5512 | nicardipine       | 8 µM | HL60  | 0     | -0.192| -0.18  | 1600        |
| 5513 | clofazimine       | 8 µM | PC3   | 0     | -0.192| -0.145 | 4682        |
| 5514 | fenofibrate       | 11 µM| MCF7  | 0     | -0.192| -0.2   | 7432        |
| 5515 | quipazine         | 9 µM | MCF7  | 0     | -0.193| -0.23  | 2782        |
| 5516 | pizotifen         | 9 µM | HL60  | 0     | -0.193| -0.167 | 3134        |
| 5517 | rilmenidine       | 8 µM | HL60  | 0     | -0.193| -0.2   | 3133        |
| 5518 | tetracycline      | 8 µM | MCF7  | 0     | -0.193| -0.209 | 6233        |
| 5519 | haloperidol       | 10 µM| MCF7  | 0     | -0.193| -0.22  | 6960        |
| 5520 | merbromin         | 5 µM | MCF7  | 0     | -0.193| -0.213 | 3439        |
| 5521 | carisoprodol      | 15 µM| HL60  | 0     | -0.193| -0.215 | 1314        |
| 5522 | benzathine benzylpenicillin | 4 µM | MCF7  | 0 | -0.193| -0.209 | 7359        |
| No. | Compound                  | Concentration | Tumor Cell Line | IC501 | IC502 | IC503 |
|-----|---------------------------|---------------|----------------|-------|-------|-------|
| 5523| octopamine                | 21 µM         | HL60           | 0     | -0.193| -0.119|
| 5524| haloperidol               | 10 µM         | MCF7           | 0     | -0.194| -0.175|
| 5525| vanoxerine                | 8 µM          | PC3            | 0     | -0.194| -0.098|
| 5526| estradiol                 | 10 nM         | MCF7           | 0     | -0.194| -0.206|
| 5527| pilocarpine               | 15 µM         | MCF7           | 0     | -0.194| -0.172|
| 5528| vigabatrin                | 31 µM         | HL60           | 0     | -0.194| -0.19  |
| 5529| ergocalciferol            | 10 µM         | MCF7           | 0     | -0.194| -0.177|
| 5530| hexylcaine                | 13 µM         | HL60           | 0     | -0.195| -0.169|
| 5531| tinidazole                | 16 µM         | MCF7           | 0     | -0.195| -0.209|
| 5532| fluoxetine                | 12 µM         | HL60           | 0     | -0.195| -0.191|
| 5533| PHA-00745360              | 1 µM          | PC3            | 0     | -0.195| -0.159|
| 5534| tiaprofenic acid          | 15 µM         | MCF7           | 0     | -0.195| -0.219|
| 5535| mebeverine                | 9 µM          | PC3            | 0     | -0.195| -0.118|
| 5536| sulfadimethoxine          | 13 µM         | MCF7           | 0     | -0.195| -0.204|
| 5537| adiphenine                | 11 µM         | MCF7           | 0     | -0.195| -0.208|
| 5538| thapsigargin              | 100 nM        | PC3            | 0     | -0.195| -0.146|
| 5539| guanabenz                 | 14 µM         | PC3            | 0     | -0.195| -0.14  |
| 5540| genistein                 | 10 µM         | HL60           | 0     | -0.195| -0.207|
| 5541| isomethysetene            | 8 µM          | HL60           | 0     | -0.195| -0.198|
| 5542| 3-hydroxy-DL-kynurenine   | 18 µM         | HL60           | 0     | -0.195| -0.225|
| 5543| methanthelinium bromide   | 10 µM         | HL60           | 0     | -0.195| -0.197|
| 5544| eticlopride               | 11 µM         | HL60           | 0     | -0.195| -0.156|
| 5545| telenzepine               | 9 µM          | MCF7           | 0     | -0.196| -0.194|
| 5546| merbromin                 | 5 µM          | PC3            | 0     | -0.196| -0.071|
| 5547| alprostadil               | 10 µM         | MCF7           | 0     | -0.196| -0.205|
| 5548| lisuride                  | 12 µM         | MCF7           | 0     | -0.196| -0.206|
| 5549| genistein                 | 10 µM         | MCF7           | 0     | -0.196| -0.207|
| 5550| co-dergocrine mesilate    | 6 µM          | MCF7           | 0     | -0.196| -0.193|
| 5551| prazosin                  | 10 µM         | PC3            | 0     | -0.196| -0.115|
| 5552| thiamphenicol             | 11 µM         | PC3            | 0     | -0.196| -0.112|
| 5553| convolamine               | 12 µM         | MCF7           | 0     | -0.196| -0.23  |
| 5554| lactobionic acid          | 11 µM         | HL60           | 0     | -0.196| -0.193|
| 5555| meteneprost               | 10 µM         | PC3            | 0     | -0.197| -0.139|
| 5556| pirenperone               | 10 µM         | PC3            | 0     | -0.197| -0.121|
| 5557| tretinoin                 | 1 µM          | MCF7           | 0     | -0.197| -0.239|
| 5558| carteolol                 | 12 µM         | MCF7           | 0     | -0.197| -0.203|
| 5559| terconazole               | 8 µM          | PC3            | 0     | -0.197| -0.133|
| 5560| disopyramide              | 12 µM         | PC3            | 0     | -0.197| -0.141|
|   | Compound          | Concentration | Cell Line  | IC50 [µM] | EC50 [µM] | Alpha [α] | Beta [β] | R²    |
|---|------------------|---------------|------------|-----------|-----------|-----------|---------|-------|
| 5561 | stachydrine      | 22 µM         | MCF7       | -0.198    | -0.218    | 2743      |
| 5562 | acemetacin       | 10 µM         | MCF7       | -0.198    | -0.243    | 7442      |
| 5563 | carbarsone       | 15 µM         | HL60       | -0.198    | -0.238    | 1313      |
| 5564 | estradiol        | 10 nM         | MCF7       | -0.198    | -0.199    | 7000      |
| 5565 | amitriptyline    | 13 µM         | PC3        | -0.198    | -0.099    | 1823      |
| 5566 | terazosin        | 9 µM          | MCF7       | -0.198    | -0.181    | 7187      |
| 5567 | valproic acid    | 500 µM        | MCF7       | -0.198    | -0.168    | 6999      |
| 5568 | estradiol        | 10 nM         | HL60       | -0.198    | -0.173    | 1182      |
| 5569 | moracizine       | 9 µM          | MCF7       | -0.198    | -0.111    | 6000      |
| 5570 | atracurium besilate | 3 µM    | PC3        | -0.198    | -0.116    | 1824      |
| 5571 | chlorpropamide   | 100 µM        | MCF7       | -0.198    | -0.166    | 144       |
| 5572 | alexidine        | 7 µM          | HL60       | -0.199    | -0.238    | 2576      |
| 5573 | Gly-His-Lys      | 1 µM          | PC3        | -0.199    | -0.108    | 6570      |
| 5574 | tretinoin        | 1 µM          | HL60       | -0.199    | -0.172    | 6170      |
| 5575 | ajmaline         | 12 µM         | MCF7       | -0.199    | -0.175    | 7484      |
| 5576 | betulinic acid   | 9 µM          | MCF7       | -0.199    | -0.196    | 3281      |
| 5577 | myricetin        | 13 µM         | HL60       | -0.2      | -0.169    | 1334      |
| 5578 | dosulepin        | 12 µM         | HL60       | -0.2      | -0.156    | 1713      |
| 5579 | ifosfamide       | 15 µM         | MCF7       | -0.2      | -0.2      | 3485      |
| 5580 | alprenolol       | 14 µM         | PC3        | -0.2      | -0.139    | 7141      |
| 5581 | iopromide        | 5 µM          | PC3        | -0.2      | -0.126    | 4504      |
| 5582 | hexetidine       | 12 µM         | HL60       | -0.2      | -0.209    | 2457      |
| 5583 | loracarbef       | 11 µM         | HL60       | -0.2      | -0.249    | 2970      |
| 5584 | tranexamic acid  | 25 µM         | PC3        | -0.2      | -0.123    | 2085      |
| 5585 | chlorogenic acid | 11 µM         | PC3        | -0.2      | -0.141    | 4024      |
| 5586 | erythromycin     | 5 µM          | MCF7       | -0.201    | -0.172    | 5329      |
| 5587 | streptozocin     | 15 µM         | MCF7       | -0.201    | -0.202    | 7193      |
| 5588 | mebhydrolin      | 5 µM          | HL60       | -0.201    | -0.207    | 1333      |
| 5589 | succinylsulfathiazole | 11 µM   | MCF7       | -0.201    | -0.109    | 2128      |
| 5590 | meclofenamic acid| 12 µM         | PC3        | -0.201    | -0.194    | 4421      |
| 5591 | lidocaine        | 15 µM         | MCF7       | -0.201    | -0.14     | 1808      |
| 5592 | acetazolamide    | 18 µM         | PC3        | -0.201    | -0.18     | 3543      |
| 5593 | levopropoxyphene  | 7 µM          | MCF7       | -0.201    | -0.182    | 7349      |
| 5594 | fursultiamine    | 9 µM          | MCF7       | -0.201    | -0.185    | 2821      |
| 5595 | bemethesulfathiazole | 20 µM   | PC3        | -0.201    | -0.108    | 5114      |
| 5596 | ceforanide       | 8 µM          | MCF7       | -0.201    | -0.178    | 5351      |
|   | Chemical Name      | Concentration | Cell Line | IC50 | EC50 |   |
|---|-------------------|---------------|-----------|------|------|---|
| 5599 | hexylcaine       | 13 µM         | MCF7      | 0    | -0.201 | -0.183 | 6244 |
| 5600 | primidone        | 18 µM         | HL60      | 0    | -0.201 | -0.179 | 3065 |
| 5601 | trihexyphenidyl  | 12 µM         | HL60      | 0    | -0.201 | -0.187 | 2158 |
| 5602 | 5186324          | 2 µM          | MCF7      | 0    | -0.201 | -0.198 | 900  |
| 5603 | Prestwick-1103   | 20 µM         | PC3       | 0    | -0.202 | -0.13  | 7317 |
| 5604 | meclocycline     | 6 µM          | HL60      | 0    | -0.202 | -0.218 | 1341 |
| 5605 | tetryzoline      | 17 µM         | MCF7      | 0    | -0.202 | -0.162 | 6769 |
| 5606 | khellin          | 15 µM         | PC3       | 0    | -0.202 | -0.116 | 6641 |
| 5607 | paromomycin      | 6 µM          | HL60      | 0    | -0.202 | -0.168 | 3017 |
| 5608 | ciclosporin      | 3 µM          | PC3       | 0    | -0.202 | -0.145 | 4586 |
| 5609 | mimosine         | 20 µM         | MCF7      | 0    | -0.202 | -0.216 | 5302 |
| 5610 | metoclopramide   | 12 µM         | PC3       | 0    | -0.202 | -0.132 | 3728 |
| 5611 | haloperidol      | 10 µM         | HL60      | 0    | -0.202 | -0.214 | 1185 |
| 5612 | chlorprothixene  | 11 µM         | MCF7      | 0    | -0.202 | -0.234 | 5291 |
| 5613 | pepstatin        | 6 µM          | MCF7      | 0    | -0.202 | -0.19  | 3264 |
| 5614 | Prestwick-642    | 14 µM         | MCF7      | 0    | -0.203 | -0.213 | 2815 |
| 5615 | enoxacin         | 12 µM         | HL60      | 0    | -0.203 | -0.22  | 1597 |
| 5616 | (+/-)-catechin   | 14 µM         | HL60      | 0    | -0.203 | -0.169 | 3012 |
| 5617 | mefenamic acid   | 17 µM         | HL60      | 0    | -0.203 | -0.229 | 1863 |
| 5618 | valproic acid    | 500 µM        | MCF7      | 0    | -0.203 | -0.194 | 1665 |
| 5619 | midodrine        | 14 µM         | PC3       | 0    | -0.203 | -0.117 | 7156 |
| 5620 | tolmetin         | 13 µM         | HL60      | 0    | -0.203 | -0.191 | 3009 |
| 5621 | meteneprost      | 10 µM         | MCF7      | 0    | -0.203 | -0.21  | 7552 |
| 5622 | piperine         | 14 µM         | HL60      | 0    | -0.204 | -0.187 | 1327 |
| 5623 | dyclonine        | 12 µM         | MCF7      | 0    | -0.204 | -0.195 | 7423 |
| 5624 | CP-690334-01     | 1 µM          | PC3       | 0    | -0.204 | -0.207 | 4561 |
| 5625 | letrozole        | 14 µM         | MCF7      | 0    | -0.204 | -0.213 | 4824 |
| 5626 | methyldopa       | 19 µM         | PC3       | 0    | -0.204 | -0.133 | 4677 |
| 5627 | dicloxacillin    | 8 µM          | MCF7      | 0    | -0.204 | -0.165 | 5012 |
| 5628 | arecoline        | 17 µM         | PC3       | 0    | -0.205 | -0.127 | 6322 |
| 5629 | iopamidol        | 5 µM          | MCF7      | 0    | -0.205 | -0.185 | 7189 |
| 5630 | cyclobenzaprine  | 13 µM         | HL60      | 0    | -0.205 | -0.21  | 1332 |
| 5631 | sulfamonomethoxine | 14 µM     | MCF7      | 0    | -0.205 | -0.213 | 7200 |
| 5632 | vinblastine      | 100 nM        | MCF7      | 0    | -0.205 | -0.2   | 7551 |
| 5633 | trimipramine     | 10 µM         | HL60      | 0    | -0.205 | -0.172 | 3004 |
| 5634 | metampicillin    | 10 µM         | PC3       | 0    | -0.205 | -0.104 | 2123 |
| 5635 | pergolide        | 10 µM         | PC3       | 0    | -0.205 | -0.13  | 7271 |
| 5636 | doxycycline      | 8 µM          | MCF7      | 0    | -0.205 | -0.203 | 7195 |
| ID  | Compound          | Concentration | Cell Line | IC50 | Slope 1 | Slope 2 | R²   | ID  |
|-----|-------------------|---------------|-----------|------|---------|---------|------|-----|
| 5637 | cefoperazone      | 6 µM          | PC3       | 0    | -0.205  | -0.104  | 6323 |
| 5638 | fulvestrant       | 1 µM          | PC3       | 0    | -0.205  | -0.124  | 7539 |
| 5639 | Prestwick-682     | 6 µM          | HL60      | 0    | -0.205  | -0.228  | 2164 |
| 5640 | isosorbide        | 17 µM         | PC3       | 0    | -0.206  | -0.108  | 3720 |
| 5641 | atractyloside     | 5 µM          | HL60      | 0    | -0.206  | -0.212  | 2573 |
| 5642 | lumicolchicine    | 10 µM         | HL60      | 0    | -0.206  | -0.21   | 1317 |
| 5643 | cefotiam           | 7 µM          | MCF7      | 0    | -0.206  | -0.198  | 5361 |
| 5644 | CP-863187         | 10 µM         | MCF7      | 0    | -0.206  | -0.232  | 7553 |
| 5645 | saquinavir        | 5 µM          | HL60      | 0    | -0.206  | -0.159  | 6127 |
| 5646 | pentoxifylline    | 14 µM         | PC3       | 0    | -0.206  | -0.118  | 7319 |
| 5647 | estradiol         | 10 nM         | MCF7      | 0    | -0.207  | -0.222  | 1666 |
| 5648 | nystatin          | 4 µM          | HL60      | 0    | -0.207  | -0.175  | 2500 |
| 5649 | geldanamycin      | 1 µM          | MCF7      | 0    | -0.207  | -0.208  | 864  |
| 5650 | iohexol           | 5 µM          | PC3       | 0    | -0.207  | -0.126  | 4643 |
| 5651 | monorden          | 100 nM        | HL60      | 0    | -0.207  | -0.18   | 2679 |
| 5652 | isotretinoin      | 13 µM         | MCF7      | 0    | -0.207  | -0.196  | 7438 |
| 5653 | alpha-ergocryptine| 7 µM          | HL60      | 0    | -0.207  | -0.215  | 2572 |
| 5654 | prochlorperazine  | 7 µM          | HL60      | 0    | -0.207  | -0.22   | 1286 |
| 5655 | Prestwick-692     | 7 µM          | HL60      | 0    | -0.207  | -0.2    | 2165 |
| 5656 | penbutolol        | 6 µM          | HL60      | 0    | -0.207  | -0.227  | 2972 |
| 5657 | rosiglitazone     | 10 µM         | MCF7      | 0    | -0.208  | -0.232  | 1071 |
| 5658 | dapsone           | 16 µM         | PC3       | 0    | -0.208  | -0.164  | 1827 |
| 5659 | primaquine        | 9 µM          | HL60      | 0    | -0.209  | -0.187  | 1343 |
| 5660 | carbenoxolone     | 7 µM          | HL60      | 0    | -0.209  | -0.188  | 3014 |
| 5661 | cyclopenthiazide  | 11 µM         | HL60      | 0    | -0.209  | -0.23   | 2905 |
| 5662 | ketotifen         | 9 µM          | MCF7      | 0    | -0.209  | -0.186  | 7199 |
| 5663 | brinzolamide      | 10 µM         | MCF7      | 0    | -0.209  | -0.219  | 5016 |
| 5664 | azacyclonol       | 15 µM         | MCF7      | 0    | -0.209  | -0.188  | 1520 |
| 5665 | minocycline       | 11 µM         | MCF7      | 0    | -0.209  | -0.195  | 1135 |
| 5666 | noscapine         | 10 µM         | MCF7      | 0    | -0.21   | -0.201  | 2745 |
| 5667 | hydroxyachillin   | 14 µM         | HL60      | 0    | -0.21   | -0.244  | 2157 |
| 5668 | genistein         | 10 µM         | MCF7      | 0    | -0.21   | -0.209  | 1660 |
| 5669 | calycanthine      | 12 µM         | MCF7      | 0    | -0.21   | -0.195  | 6221 |
| 5670 | androsterone      | 14 µM         | PC3       | 0    | -0.211  | -0.093  | 4635 |
| 5671 | cefotaxime        | 8 µM          | MCF7      | 0    | -0.211  | -0.185  | 7186 |
| 5672 | vitexin           | 9 µM          | HL60      | 0    | -0.211  | -0.223  | 2155 |
| 5673 | methyldopate      | 15 µM         | MCF7      | 0    | -0.211  | -0.208  | 7360 |
| 5674 | naftifine         | 12 µM         | PC3       | 0    | -0.211  | -0.129  | 7273 |
|   | Compound                  | Concentration | Cell Line | IC50  | IC50  | IC50  |   |
|---|--------------------------|---------------|-----------|-------|-------|-------|---|
| 5675 | pyrityldione             | 24 µM         | PC3       | -0.211 | -0.131 | 7153  |   |
| 5676 | bupivacaine              | 12 µM         | MCF7      | -0.212 | -0.192 | 7435  |   |
| 5677 | sulfadimethoxine         | 13 µM         | HL60      | -0.212 | -0.224 | 2578  |   |
| 5678 | tolnaftate               | 13 µM         | MCF7      | -0.212 | -0.224 | 1501  |   |
| 5679 | tacrine                  | 16 µM         | MCF7      | -0.212 | -0.211 | 5297  |   |
| 5680 | dapsone                  | 16 µM         | MCF7      | -0.212 | -0.218 | 1705  |   |
| 5681 | Prestwick-984            | 9 µM          | HL60      | -0.212 | -0.213 | 2903  |   |
| 5682 | timolol                  | 9 µM          | PC3       | -0.212 | -0.147 | 4685  |   |
| 5683 | pentoxifylline           | 14 µM         | PC3       | -0.213 | -0.138 | 2127  |   |
| 5684 | neostigmine bromide      | 13 µM         | MCF7      | -0.213 | -0.221 | 5335  |   |
| 5685 | naproxen                 | 17 µM         | PC3       | -0.213 | -0.125 | 6358  |   |
| 5686 | streptomycin             | 3 µM          | MCF7      | -0.213 | -0.247 | 7194  |   |
| 5687 | sulindac                 | 11 µM         | PC3       | -0.213 | -0.137 | 5103  |   |
| 5688 | halofantrine             | 7 µM          | HL60      | -0.214 | -0.231 | 3130  |   |
| 5689 | benzoic acid             | 24 µM         | HL60      | -0.214 | -0.208 | 2167  |   |
| 5690 | triamterene              | 16 µM         | PC3       | -0.215 | -0.116 | 1819  |   |
| 5691 | Gly-His-Lys              | 1 µM          | MCF7      | -0.215 | -0.214 | 6575  |   |
| 5692 | prednisone               | 11 µM         | PC3       | -0.215 | -0.132 | 4577  |   |
| 5693 | heptaminol               | 22 µM         | PC3       | -0.215 | -0.13  | 1825  |   |
| 5694 | Prestwick-692            | 7 µM          | PC3       | -0.215 | -0.138 | 4599  |   |
| 5695 | homatropine              | 11 µM         | MCF7      | -0.215 | -0.232 | 1684  |   |
| 5696 | PF-00539758-00           | 10 µM         | PC3       | -0.216 | -0.137 | 6421  |   |
| 5697 | meclofenamic acid        | 12 µM         | MCF7      | -0.216 | -0.18  | 7038  |   |
| 5698 | dapsone                  | 16 µM         | HL60      | -0.216 | -0.204 | 1868  |   |
| 5699 | propidium iodide         | 6 µM          | HL60      | -0.216 | -0.181 | 2541  |   |
| 5700 | epirizole                | 17 µM         | PC3       | -0.216 | -0.156 | 1803  |   |
| 5701 | procarbazine             | 16 µM         | HL60      | -0.217 | -0.23  | 2971  |   |
| 5702 | nifedipine               | 12 µM         | PC3       | -0.217 | -0.161 | 1814  |   |
| 5703 | isoniazid                | 29 µM         | MCF7      | -0.217 | -0.194 | 7197  |   |
| 5704 | lansoprazole             | 11 µM         | HL60      | -0.217 | -0.269 | 2967  |   |
| 5705 | clozapine                | 10 µM         | HL60      | -0.217 | -0.191 | 1170  |   |
| 5706 | xamoterol                | 5 µM          | MCF7      | -0.218 | -0.209 | 5363  |   |
| 5707 | gentamicin               | 3 µM          | PC3       | -0.218 | -0.112 | 5883  |   |
| 5708 | thiamphenicol            | 11 µM         | PC3       | -0.218 | -0.149 | 1826  |   |
| 5709 | estradiol                | 10 nM         | HL60      | -0.218 | -0.234 | 2701  |   |
| 5710 | ondansetron              | 12 µM         | HL60      | -0.219 | -0.201 | 6153  |   |
| 5711 | aconitine                | 6 µM          | PC3       | -0.219 | -0.168 | 7149  |   |
| 5712 | DL-PPMP                  | 2 µM          | MCF7      | -0.219 | -0.236 | 1121  |   |
| ID | Name                  | Concentration | Cell Line | IC50 | pIC50 | Active Hits |
|----|-----------------------|---------------|-----------|------|-------|-------------|
| 5713 | diphenhydramine       | 14 µM         | PC3       | 0    | -0.219 | 1830        |
| 5714 | viomycin              | 5 µM          | PC3       | 0    | -0.219 | 7278        |
| 5715 | dextubuprofen         | 19 µM         | HL60      | 0    | -0.219 | 3094        |
| 5716 | levopropoxyphene       | 7 µM          | HL60      | 0    | -0.219 | 2980        |
| 5717 | adiphene               | 11 µM         | PC3       | 0    | -0.219 | 1831        |
| 5718 | cefmetazole           | 8 µM          | HL60      | 0    | -0.22  | 2578        |
| 5719 | Prestwick-691         | 14 µM         | MCF7      | 0    | -0.22  | 7554        |
| 5720 | merbromin             | 5 µM          | HL60      | 0    | -0.22  | 2813        |
| 5721 | BCB000040             | 10 µM         | MCF7      | 0    | -0.22  | 5554        |
| 5722 | thiamazole            | 35 µM         | HL60      | 0    | -0.22  | 2570        |
| 5723 | propoxyxaine          | 12 µM         | PC3       | 0    | -0.22  | 7155        |
| 5724 | cefotiam               | 7 µM          | HL60      | 0    | -0.22  | 2458        |
| 5725 | ambroxol               | 10 µM         | MCF7      | 0    | -0.22  | 5319        |
| 5726 | tyrphostin AG-1478    | 32 µM         | MCF7      | 0    | -0.22  | 1141        |
| 5727 | Chicago Sky Blue 6B   | 4 µM          | HL60      | 0    | -0.22  | 1330        |
| 5728 | pyrithyldione         | 24 µM         | MCF7      | 0    | -0.22  | 3482        |
| 5729 | naproxen               | 17 µM         | MCF7      | 0    | -0.22  | 1706        |
| 5730 | nadide                 | 6 µM          | HL60      | 0    | -0.22  | 2529        |
| 5731 | clemastine             | 9 µM          | MCF7      | 0    | -0.22  | 7443        |
| 5732 | chlorpromazine         | 11 µM         | HL60      | 0    | -0.22  | 1864        |
| 5733 | isoflupredone          | 10 µM         | HL60      | 0    | -0.22  | 1873        |
| 5734 | naftidrofuryl         | 8 µM          | MCF7      | 0    | -0.22  | 5287        |
| 5735 | sirolimus             | 100 nM        | HL60      | 0    | -0.22  | 1183        |
| 5736 | heptaminol            | 22 µM         | HL60      | 0    | -0.22  | 1866        |
| 5737 | harpagoside           | 8 µM          | MCF7      | 0    | -0.22  | 7355        |
| 5738 | flucloxacillin        | 8 µM          | HL60      | 0    | -0.22  | 3128        |
| 5739 | dl-alpha tocopherol   | 9 µM          | HL60      | 0    | -0.22  | 1320        |
| 5740 | diethylcarbamazaine   | 10 µM         | MCF7      | 0    | -0.22  | 7425        |
| 5741 | alprostadil           | 11 µM         | MCF7      | 0    | -0.22  | 7358        |
| 5742 | dimenhydrinate        | 9 µM          | MCF7      | 0    | -0.22  | 7431        |
| 5743 | corticosterone        | 12 µM         | HL60      | 0    | -0.22  | 1307        |
| 5744 | haloperidol           | 10 µM         | MCF7      | 0    | -0.22  | 1082        |
| 5745 | clozapine             | 12 µM         | HL60      | 0    | -0.22  | 1289        |
| 5746 | vinburnine            | 14 µM         | PC3       | 0    | -0.22  | 7154        |
| 5747 | 3-acetamidocoumarin   | 20 µM         | MCF7      | 0    | -0.22  | 7361        |
| 5748 | SR-95639A             | 10 µM         | HL60      | 0    | -0.22  | 1336        |
| 5749 | betulin               | 9 µM          | HL60      | 0    | -0.23  | 2952        |
| 5750 | isoflupredone         | 10 µM         | PC3       | 0    | -0.23  | 1832        |
|                 | Concentration | Cell Line | Percentage Difference | IC50 | IC95 | IC90 |
|----------------|---------------|-----------|-----------------------|------|------|------|
| asiaticoside   | 4 µM          | HL60      | -0.232                | 0.22 | 2943 |
| bumetanide     | 11 µM         | MCF7      | -0.232                | 0.256 | 7440 |
| streptozocin   | 15 µM         | HL60      | -0.233                | 0.24  | 2535 |
| fulvestrant    | 10 nM         | HL60      | -0.235                | 0.233 | 1179 |
| podophyllotoxin| 10 µM         | MCF7      | -0.235                | 0.202 | 7198 |
| cyclic adenosine monophosphate | 12 µM | HL60 | -0.236                | 0.245 | 2969 |
| chlortalidone  | 12 µM         | PC3       | -0.236                | 0.179 | 7152 |
| diprophylline  | 16 µM         | HL60      | -0.236                | 0.173 | 1853 |
| enalapril      | 8 µM          | MCF7      | -0.238                | 0.235 | 7428 |
| viomycin       | 5 µM          | HL60      | -0.238                | 0.223 | 2979 |
| adiphenine     | 11 µM         | PC3       | -0.239                | 0.132 | 7279 |
| azapropazone   | 13 µM         | PC3       | -0.24                | 0.168 | 7277 |
| estradiol      | 10 nM         | MCF7      | -0.24                | 0.214 | 1021 |
| chlorogenic acid| 11 µM        | HL60      | -0.242                | 0.252 | 1346 |
| ozagrel        | 15 µM         | HL60      | -0.242                | 0.257 | 2942 |
| boldine        | 12 µM         | HL60      | -0.246                | 0.199 | 2148 |
| proguanil      | 14 µM         | HL60      | -0.249                | 0.234 | 2944 |
| homatropine    | 11 µM         | HL60      | -0.25                | 0.219 | 1848 |
| diphenhydramine| 14 µM         | HL60      | -0.251                | 0.262 | 1871 |
| adiphenine     | 11 µM         | HL60      | -0.261                | 0.275 | 1872 |
| metformin      | 24 µM         | HL60      | -0.262                | 0.256 | 1858 |
| NU-1025        | 100 µM        | MCF7      | -0.436                | 0.066 | 0.072 | 313 |
| iloprost       | 1 µM          | SKMEL5    | -0.47                | 0.086 | 0.082 | 314 |
| exisulind      | 50 µM         | MCF7      | -0.473                | 0.068 | 0.082 | 314 |
| tolnaftate     | 13 µM         | PC3       | -0.474                | 0.084 | 0.066 | 4221 |
| chlorhexidine  | 8 µM          | PC3       | -0.475                | 0.107 | 0.043 | 1942 |
| raloxifene     | 100 nM        | HL60      | -0.475                | 0.078 | 0.073 | 388 |
| monastrol      | 20 µM         | MCF7      | -0.477                | 0.075 | 0.076 | 614 |
| 0173570-0000   | 1 µM          | PC3       | -0.477                | 0.096 | 0.055 | 3693 |
| betonicine     | 25 µM         | PC3       | -0.486                | 0.106 | 0.047 | 4301 |
| ciclosporin    | 1 µM          | MCF7      | -0.486                | 0.066 | 0.088 | 261 |
| dicloxacillin  | 8 µM          | PC3       | -0.49                | 0.086 | 0.069 | 6666 |
| SC-58125       | 10 µM         | SKMEL5    | -0.495                | 0.075 | 0.081 | 507 |
| Prestwick-674  | 14 µM         | PC3       | -0.501                | 0.1   | 0.058 | 3716 |
| novobiocin     | 100 µM        | MCF7      | -0.514                | 0.083 | 0.08 | 342 |
| thioridazine   | 10 µM         | MCF7      | -0.515                | 0.067 | 0.096 | 5916 |
| tanespimycin   | 1 µM          | PC3       | -0.516                | 0.1   | 0.064 | 4450 |
| Compound           | Concentration | Cell Line | IC50  | IC50  | EC50  | IC50  | EC50  |
|--------------------|---------------|-----------|-------|-------|-------|-------|-------|
| karakoline         | 11 µM         | PC3       | -0.518 | -0.091 | 0.073 | 4297  |
| tetraethylenepentamine | 100 µM    | PC3       | -0.52  | -0.097 | 0.068 | 457   |
| ketoprofen         | 16 µM         | PC3       | -0.525 | -0.099 | 0.067 | 3729  |
| sirolimus          | 100 nM        | PC3       | -0.526 | -0.12  | 0.047 | 4466  |
| carbenoxolone      | 7 µM          | MCF7      | -0.528 | -0.072 | 0.095 | 4173  |
| PF-00562151-00     | 10 µM         | MCF7      | -0.53  | -0.078 | 0.09  | 5954  |
| mexiletine         | 19 µM         | MCF7      | -0.53  | -0.069 | 0.099 | 3973  |
| metrizamide        | 5 µM          | MCF7      | -0.531 | -0.092 | 0.076 | 4156  |
| tanspimycin        | 1 µM          | MCF7      | -0.533 | -0.095 | 0.074 | 381   |
| mebeverine         | 9 µM          | MCF7      | -0.535 | -0.098 | 0.072 | 3193  |
| labetalol          | 11 µM         | PC3       | -0.535 | -0.108 | 0.061 | 4473  |
| diclofenac         | 10 µM         | MCF7      | -0.539 | -0.082 | 0.088 | 333   |
| ciclopirox         | 15 µM         | PC3       | -0.541 | -0.098 | 0.073 | 6677  |
| diperodon          | 9 µM          | PC3       | -0.541 | -0.102 | 0.069 | 4498  |
| clindamycin        | 9 µM          | HL60      | -0.542 | -0.084 | 0.088 | 1373  |
| triamcinolone      | 10 µM         | MCF7      | -0.543 | -0.09  | 0.082 | 2241  |
| vincamine          | 11 µM         | MCF7      | -0.544 | -0.088 | 0.084 | 3865  |
| sulfamethizole     | 15 µM         | PC3       | -0.545 | -0.098 | 0.074 | 5798  |
| dexamethasone      | 1 µM          | MCF7      | -0.549 | -0.073 | 0.101 | 255   |
| xylazine           | 18 µM         | PC3       | -0.55  | -0.122 | 0.052 | 4066  |
| fendiline          | 11 µM         | MCF7      | -0.554 | -0.106 | 0.07  | 3190  |
| NU-1025            | 100 µM        | MCF7      | -0.554 | -0.093 | 0.082 | 608   |
| famprofazone       | 11 µM         | MCF7      | -0.554 | -0.089 | 0.086 | 3834  |
| quinpirolo         | 1 µM          | MCF7      | -0.556 | -0.099 | 0.077 | 456   |
| trimethadione      | 28 µM         | PC3       | -0.558 | -0.082 | 0.095 | 4086  |
| bendrofluimethiazide | 9 µM       | PC3       | -0.558 | -0.109 | 0.067 | 4315  |
| famotidine         | 12 µM         | PC3       | -0.56  | -0.108 | 0.069 | 1946  |
| tiratricol         | 6 µM          | MCF7      | -0.56  | -0.088 | 0.09  | 2259  |
| diphenamid metilsulfate | 10 µM | PC3       | -0.561 | -0.108 | 0.069 | 1912  |
| citiolone          | 25 µM         | MCF7      | -0.565 | -0.081 | 0.097 | 3836  |
| dioxybenzone       | 16 µM         | PC3       | -0.565 | -0.116 | 0.063 | 4638  |
| azathioprine       | 14 µM         | PC3       | -0.565 | -0.117 | 0.062 | 1945  |
| lidocaine          | 15 µM         | PC3       | -0.566 | -0.105 | 0.074 | 1917  |
| nystatin           | 4 µM          | PC3       | -0.567 | -0.111 | 0.068 | 4223  |
| ethisterone        | 13 µM         | MCF7      | -0.569 | -0.08  | 0.1   | 3975  |
| perphenazine       | 10 µM         | PC3       | -0.57  | -0.116 | 0.064 | 4637  |
| meclocycline       | 6 µM          | PC3       | -0.573 | -0.108 | 0.073 | 6637  |
| propofol           | 22 µM         | MCF7      | -0.573 | -0.096 | 0.085 | 3386  |
| Compound             | Concentration | Cell Line | IC50 (µM) | COMBINED (µM) | COMBINED (µM) | COMBINED (µM) | COMBINED (µM) |
|----------------------|---------------|-----------|-----------|---------------|---------------|---------------|---------------|
| metergoline          | 10 µM         | PC3       | -0.574    | -0.118        | 0.064         | 6744          |
| tanespimycin         | 1 µM          | MCF7      | -0.574    | -0.09         | 0.092         | 5914          |
| mesalazine           | 26 µM         | PC3       | -0.575    | -0.095        | 0.087         | 5888          |
| W-13                 | 10 µM         | MCF7      | -0.576    | -0.09         | 0.092         | 643           |
| gibberellic acid     | 12 µM         | PC3       | -0.576    | -0.103        | 0.079         | 4234          |
| amprolium            | 13 µM         | PC3       | -0.577    | -0.091        | 0.091         | 6738          |
| bucladesine          | 8 µM          | HL60      | -0.582    | -0.096        | 0.088         | 2741          |
| geldanamycin         | 1 µM          | PC3       | -0.582    | -0.117        | 0.067         | 4452          |
| norfloxacin          | 13 µM         | MCF7      | -0.586    | -0.09         | 0.095         | 2253          |
| oxantel              | 7 µM          | PC3       | -0.586    | -0.109        | 0.076         | 5825          |
| probucol             | 10 µM         | MCF7      | -0.587    | -0.102        | 0.084         | 603           |
| phenformin           | 10 µM         | MCF7      | -0.587    | -0.097        | 0.088         | 21            |
| meclofenoxate        | 14 µM         | MCF7      | -0.588    | -0.093        | 0.093         | 4729          |
| torasemide           | 11 µM         | PC3       | -0.59     | -0.104        | 0.083         | 5057          |
| hydrochlorothiazide  | 13 µM         | PC3       | -0.59     | -0.12         | 0.067         | 1906          |
| praziquantel         | 13 µM         | MCF7      | -0.594    | -0.107        | 0.081         | 3189          |
| thiethylperazine     | 6 µM          | PC3       | -0.595    | -0.133        | 0.055         | 5756          |
| proscillaridin       | 8 µM          | MCF7      | -0.595    | -0.094        | 0.095         | 4404          |
| helveticoside        | 7 µM          | MCF7      | -0.599    | -0.089        | 0.1           | 6047          |
| cicloheximide        | 14 µM         | PC3       | -0.599    | -0.107        | 0.082         | 5743          |
| oleandomycin         | 5 µM          | PC3       | -0.599    | -0.121        | 0.068         | 1935          |
| spiramycin           | 5 µM          | MCF7      | -0.6      | -0.085        | 0.105         | 3844          |
| tetrandrine          | 6 µM          | PC3       | -0.6      | -0.111        | 0.079         | 5821          |
| metixene             | 12 µM         | PC3       | -0.601    | -0.089        | 0.101         | 6672          |
| calmidazolium        | 5 µM          | MCF7      | -0.602    | -0.109        | 0.081         | 486           |
| loxapine             | 9 µM          | PC3       | -0.603    | -0.108        | 0.082         | 6694          |
| probucol             | 8 µM          | MCF7      | -0.604    | -0.088        | 0.103         | 3223          |
| tanespimycin         | 1 µM          | PC3       | -0.608    | -0.113        | 0.079         | 5958          |
| proxymetacaine       | 12 µM         | MCF7      | -0.608    | -0.112        | 0.08          | 5433          |
| altizide             | 10 µM         | MCF7      | -0.609    | -0.109        | 0.084         | 6089          |
| protriptyline        | 13 µM         | MCF7      | -0.609    | -0.094        | 0.099         | 6498          |
| N6-methyladenosine   | 14 µM         | PC3       | -0.609    | -0.139        | 0.054         | 6732          |
| levodopa             | 20 µM         | PC3       | -0.611    | -0.124        | 0.069         | 4571          |
| metitepine           | 8 µM          | MCF7      | -0.612    | -0.087        | 0.107         | 5413          |
| mefloquine           | 10 µM         | MCF7      | -0.612    | -0.082        | 0.112         | 2210          |
| trifluoperazine      | 10 µM         | HL60      | -0.613    | -0.103        | 0.091         | 2684          |
| Compound                        | IC₅₀ (µM) | Cell Line | EC₅₀ (M) | IC₅₀ (nM) |
|--------------------------------|-----------|-----------|----------|-----------|
| Mafenide                        | 18        | MCF7      | -0.615   | -0.093    | 101      | 5499 |
| Cinchonidine                    | 14        | PC3       | -0.615   | -0.105    | 0.089    | 5833 |
| Sulocidil                       | 12        | PC3       | -0.615   | -0.1      | 0.095    | 6675 |
| Isomethyptene                   | 8         | MCF7      | -0.616   | -0.099    | 0.096    | 6524 |
| Azacyclonol                     | 15        | MCF7      | -0.616   | -0.097    | 0.098    | 5398 |
| Phensuximide                    | 21        | PC3       | -0.616   | -0.121    | 0.074    | 5097 |
| Pempidine                       | 13        | MCF7      | -0.621   | -0.103    | 0.094    | 3832 |
| Felodipine                      | 10        | PC3       | -0.621   | -0.112    | 0.084    | 6695 |
| Levomepromazine                 | 9         | MCF7      | -0.622   | -0.117    | 0.08     | 7399 |
| Ascobic acid                    | 22        | MCF7      | -0.622   | -0.087    | 0.11     | 3225 |
| Ritodrine                       | 12        | PC3       | -0.623   | -0.127    | 0.071    | 4619 |
| Terguride                       | 9         | MCF7      | -0.624   | -0.111    | 0.086    | 4633 |
| Mianserin                       | 13        | MCF7      | -0.624   | -0.099    | 0.098    | 2231 |
| MK-886                          | 1         | MCF7      | -0.628   | -0.117    | 0.082    | 601  |
| Chlorpromazine                  | 1         | MCF7      | -0.629   | -0.124    | 0.075    | 426  |
| Ondansetron                     | 12        | MCF7      | -0.631   | -0.102    | 0.098    | 3575 |
| Ciprofloxacin                   | 11        | PC3       | -0.631   | -0.125    | 0.074    | 6700 |
| 16,16'-Dimethylprostaglandin E2 | 10        | PC3       | -0.632   | -0.111    | 0.089    | 6562 |
| Sulpiride                       | 12        | MCF7      | -0.634   | -0.088    | 0.113    | 4389 |
| Trapidil                        | 19        | MCF7      | -0.634   | -0.106    | 0.095    | 6515 |
| Prestwick-1100                  | 9         | MCF7      | -0.634   | -0.102    | 0.098    | 3880 |
| Tretinoin                       | 1         | PC3       | -0.636   | -0.132    | 0.069    | 1211 |
| Scopolamine                     | 12        | MCF7      | -0.637   | -0.096    | 0.105    | 4803 |
| Orlistat                        | 10        | MCF7      | -0.637   | -0.076    | 0.125    | 6383 |
| CP-319743                       | 10        | PC3       | -0.638   | -0.121    | 0.08     | 7537 |
| Paclitaxel                      | 5         | MCF7      | -0.638   | -0.115    | 0.087    | 1542 |
| Furaladone                      | 11        | HL60      | -0.639   | -0.104    | 0.098    | 2554 |
| Methylbenzethonium chloride     | 9         | MCF7      | -0.64    | -0.107    | 0.095    | 3850 |
| Hydrocotarnine                  | 13        | PC3       | -0.642   | -0.123    | 0.08     | 4489 |
| Danazol                         | 12        | PC3       | -0.644   | -0.108    | 0.095    | 1954 |
| Econazole                       | 9         | PC3       | -0.644   | -0.127    | 0.077    | 7305 |
| Megestrol                       | 10        | MCF7      | -0.646   | -0.103    | 0.101    | 6468 |
| Butyl hydroxybenzoate           | 21        | MCF7      | -0.646   | -0.1      | 0.104    | 5608 |
| Midecamycin                     | 5         | PC3       | -0.647   | -0.104    | 0.101    | 1943 |
| Proguanil                       | 14        | MCF7      | -0.648   | -0.109    | 0.096    | 3505 |
| Phentolamine                     | 13        | MCF7      | -0.648   | -0.103    | 0.102    | 2323 |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 5900 | urapidil | 9 µM | PC3 | -0.649 | -0.127 | 0.078 | 6696 |
| 5901 | diprophylline | 16 µM | MCF7 | -0.65 | -0.104 | 0.101 | 5482 |
| 5902 | aciclovir | 18 µM | PC3 | -0.652 | -0.125 | 0.081 | 1960 |
| 5903 | tenoxicam | 12 µM | PC3 | -0.652 | -0.15 | 0.056 | 4102 |
| 5904 | allantoin | 25 µM | MCF7 | -0.652 | -0.084 | 0.122 | 5471 |
| 5905 | josamycin | 5 µM | PC3 | -0.653 | -0.117 | 0.089 | 1950 |
| 5906 | clorsulon | 11 µM | HL60 | -0.655 | -0.119 | 0.089 | 1735 |
| 5907 | puromycin | 7 µM | MCF7 | -0.656 | -0.095 | 0.113 | 3310 |
| 5908 | bucladesine | 20 µM | MCF7 | -0.656 | -0.112 | 0.096 | 591 |
| 5909 | dextromethorphan | 11 µM | MCF7 | -0.658 | -0.105 | 0.104 | 5401 |
| 5910 | ivermectin | 5 µM | PC3 | -0.658 | -0.103 | 0.105 | 5853 |
| 5911 | pindolol | 16 µM | MCF7 | -0.658 | -0.106 | 0.102 | 6834 |
| 5912 | SC-19220 | 10 µM | PC3 | -0.659 | -0.132 | 0.076 | 7065 |
| 5913 | tanespimycin | 1 µM | HL60 | -0.66 | -0.103 | 0.106 | 2666 |
| 5914 | paclitaxel | 5 µM | PC3 | -0.66 | -0.112 | 0.097 | 1959 |
| 5915 | salsolinol | 15 µM | PC3 | -0.66 | -0.102 | 0.107 | 4232 |
| 5916 | chlorhexidine | 8 µM | PC3 | -0.661 | -0.125 | 0.084 | 6302 |
| 5917 | nefopam | 14 µM | MCF7 | -0.661 | -0.087 | 0.122 | 4752 |
| 5918 | flupentixol | 8 µM | MCF7 | -0.662 | -0.106 | 0.103 | 2643 |
| 5919 | pizotifen | 9 µM | MCF7 | -0.664 | -0.092 | 0.118 | 5491 |
| 5920 | PF-00562151-00 | 10 µM | PC3 | -0.665 | -0.11 | 0.1 | 6863 |
| 5921 | diprophylline | 16 µM | PC3 | -0.665 | -0.143 | 0.067 | 5063 |
| 5922 | ketoconazole | 8 µM | MCF7 | -0.665 | -0.1 | 0.111 | 2640 |
| 5923 | orphenadrine | 13 µM | MCF7 | -0.667 | -0.088 | 0.123 | 3883 |
| 5924 | flumequine | 15 µM | MCF7 | -0.668 | -0.11 | 0.102 | 5529 |
| 5925 | apomorphine | 6 µM | PC3 | -0.668 | -0.122 | 0.09 | 6683 |
| 5926 | mianserin | 13 µM | PC3 | -0.67 | -0.117 | 0.095 | 5786 |
| 5927 | leflunomide | 15 µM | MCF7 | -0.67 | -0.117 | 0.095 | 7238 |
| 5928 | ciprofloxacin | 11 µM | PC3 | -0.671 | -0.135 | 0.078 | 1939 |
| 5929 | terbutaline | 7 µM | PC3 | -0.671 | -0.138 | 0.075 | 5764 |
| 5930 | carbenoxolone | 7 µM | MCF7 | -0.672 | -0.122 | 0.091 | 3353 |
| 5931 | altretamine | 19 µM | PC3 | -0.672 | -0.108 | 0.104 | 4627 |
| 5932 | mesoridazine | 7 µM | PC3 | -0.673 | -0.124 | 0.089 | 7256 |
| 5933 | tanespimycin | 1 µM | PC3 | -0.674 | -0.143 | 0.07 | 1218 |
| 5934 | emetine | 7 µM | MCF7 | -0.675 | -0.111 | 0.103 | 2801 |
| 5935 | santonin | 16 µM | MCF7 | -0.677 | -0.12 | 0.094 | 3877 |
| 5936 | thioridazine | 10 µM | HL60 | -0.679 | -0.084 | 0.131 | 2690 |
| 5937 | sulfadimethoxine | 12 µM | MCF7 | -0.68 | -0.104 | 0.111 | 6788 |
| 5938 | erythromycin | 5 µM | PC3 | -0.681 | -0.113 | 0.103 | 1928 |
| 5939 | lanatoside C | 4 µM | MCF7 | -0.682 | -0.102 | 0.114 | 3852 |
| 5940 | MG-262 | 100 nM | PC3 | -0.683 | -0.133 | 0.083 | 7068 |
| 5941 | solanine | 5 µM | MCF7 | -0.683 | -0.134 | 0.082 | 4166 |
| 5942 | megestrol | 10 µM | MCF7 | -0.684 | -0.111 | 0.105 | 5013 |
| 5943 | securinine | 18 µM | MCF7 | -0.686 | -0.121 | 0.096 | 6831 |
| 5944 | cefotaxime | 8 µM | PC3 | -0.686 | -0.134 | 0.083 | 2072 |
| 5945 | alfadolone | 10 µM | PC3 | -0.686 | -0.138 | 0.079 | 7262 |
| 5946 | chloropyrazine | 35 µM | HL60 | -0.687 | -0.113 | 0.104 | 6148 |
| 5947 | niflumic acid | 14 µM | MCF7 | -0.687 | -0.088 | 0.13 | 5490 |
| 5948 | verapamil | 8 µM | MCF7 | -0.688 | -0.107 | 0.111 | 5387 |
| 5949 | isocarboxazid | 17 µM | HL60 | -0.688 | -0.115 | 0.103 | 2562 |
| 5950 | glafenine | 10 µM | PC3 | -0.688 | -0.129 | 0.089 | 7257 |
| 5951 | pirenzepine | 9 µM | PC3 | -0.689 | -0.113 | 0.105 | 5872 |
| 5952 | cyclobenzaprine | 13 µM | MCF7 | -0.693 | -0.097 | 0.122 | 4834 |
| 5953 | dicycloverine | 12 µM | PC3 | -0.694 | -0.14 | 0.08 | 4581 |
| 5954 | piromidic acid | 14 µM | PC3 | -0.694 | -0.139 | 0.08 | 4575 |
| 5955 | lasalocid | 7 µM | MCF7 | -0.695 | -0.129 | 0.09 | 4985 |
| 5956 | harmalol | 15 µM | MCF7 | -0.695 | -0.1 | 0.12 | 2892 |
| 5957 | dirithromycin | 5 µM | MCF7 | -0.696 | -0.118 | 0.102 | 2863 |
| 5958 | atropine oxide | 12 µM | MCF7 | -0.696 | -0.114 | 0.107 | 6812 |
| 5959 | withaferin A | 1 µM | MCF7 | -0.697 | -0.104 | 0.117 | 3902 |
| 5960 | diphenhydramine | 14 µM | PC3 | -0.7 | -0.137 | 0.084 | 7318 |
| 5961 | quipazine | 9 µM | MCF7 | -0.701 | -0.115 | 0.106 | 7240 |
| 5962 | strophanthidin | 10 µM | PC3 | -0.703 | -0.119 | 0.103 | 5826 |
| 5963 | SC-560 | 10 µM | PC3 | -0.703 | -0.142 | 0.08 | 6865 |
| 5964 | perhexiline | 10 µM | PC3 | -0.703 | -0.103 | 0.12 | 5081 |
| 5965 | tetracycline | 8 µM | HL60 | -0.704 | -0.112 | 0.11 | 1397 |
| 5966 | butoconazole | 8 µM | HL60 | -0.705 | -0.108 | 0.115 | 2427 |
| 5967 | alverine | 8 µM | MCF7 | -0.706 | -0.106 | 0.117 | 2273 |
| 5968 | (-)-isoprenaline | 16 µM | HL60 | -0.706 | -0.133 | 0.09 | 6149 |
| 5969 | fulvestrant | 1 µM | PC3 | -0.708 | -0.141 | 0.083 | 704 |
| 5970 | alverine | 8 µM | PC3 | -0.708 | -0.118 | 0.106 | 6345 |
| 5971 | pirlindole | 12 µM | HL60 | -0.708 | -0.11 | 0.114 | 3140 |
| 5972 | triamterene | 16 µM | PC3 | -0.708 | -0.149 | 0.075 | 7307 |
| 5973 | nocodazole | 13 µM | PC3 | -0.709 | -0.124 | 0.1 | 7145 |
| 5974 | flunixin | 8 µM | MCF7 | -0.711 | -0.102 | 0.123 | 4735 |
| 5975 | clebopride | 8 µM | PC3 | -0.712 | -0.136 | 0.089 | 6311 |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 5976 | rilmenidine | 8 µM | MCF7 | -0.713 | -0.116 | 0.11 | 6512 |
| 5977 | oxybenzone   | 18 µM | PC3 | -0.714 | -0.135 | 0.091 | 6309 |
| 5978 | colchicine   | 10 µM | MCF7 | -0.716 | -0.092 | 0.135 | 5675 |
| 5979 | vinburnine   | 14 µM | HL60 | -0.717 | -0.113 | 0.114 | 1788 |
| 5980 | azathioprine | 14 µM | MCF7 | -0.717 | -0.125 | 0.102 | 5262 |
| 5981 | piretanide   | 11 µM | HL60 | -0.718 | -0.13 | 0.097 | 6144 |
| 5982 | aminophenazine | 17 µM | PC3 | -0.718 | -0.129 | 0.098 | 2060 |
| 5983 | dipivefrine  | 10 µM | MCF7 | -0.722 | -0.107 | 0.121 | 2744 |
| 5984 | antazoline   | 13 µM | HL60 | -0.723 | -0.118 | 0.11 | 1556 |
| 5985 | orciptrenaline | 8 µM | MCF7 | -0.724 | -0.091 | 0.138 | 4831 |
| 5986 | neomycin     | 4 µM | PC3 | -0.727 | -0.122 | 0.108 | 5867 |
| 5987 | geldanamycin | 1 µM | MCF7 | -0.727 | -0.125 | 0.105 | 5225 |
| 5988 | haloperidol  | 10 µM | MCF7 | -0.728 | -0.14 | 0.091 | 5604 |
| 5989 | mafenide     | 18 µM | PC3 | -0.728 | -0.157 | 0.074 | 2124 |
| 5990 | ticarcillin  | 9 µM | PC3 | -0.73 | -0.111 | 0.12 | 5829 |
| 5991 | astemizole   | 9 µM | MCF7 | -0.73 | -0.105 | 0.126 | 6807 |
| 5992 | digitoxigenin | 11 µM | MCF7 | -0.73 | -0.129 | 0.102 | 4801 |
| 5993 | tanespimycin | 1 µM | MCF7 | -0.732 | -0.126 | 0.106 | 428 |
| 5994 | sulpiride    | 12 µM | MCF7 | -0.736 | -0.108 | 0.125 | 1467 |
| 5995 | harmine      | 16 µM | HL60 | -0.736 | -0.114 | 0.118 | 1758 |
| 5996 | thiamine     | 12 µM | HL60 | -0.737 | -0.126 | 0.107 | 1744 |
| 5997 | oxybenzone   | 18 µM | MCF7 | -0.739 | -0.116 | 0.118 | 5410 |
| 5998 | acetylsalicylsalicylic acid | 13 µM | MCF7 | -0.742 | -0.12 | 0.114 | 6778 |
| 5999 | sulfapyridine | 16 µM | PC3 | -0.742 | -0.132 | 0.102 | 7151 |
| 6000 | sulfaguanidine | 19 µM | MCF7 | -0.743 | -0.105 | 0.13 | 1495 |
| 6001 | fulvestrant  | 1 µM | PC3 | -0.744 | -0.164 | 0.071 | 6867 |
| 6002 | mianserin    | 13 µM | HL60 | -0.745 | -0.112 | 0.124 | 1385 |
| 6003 | streptozocin | 15 µM | PC3 | -0.747 | -0.16 | 0.076 | 5836 |
| 6004 | pioglitazone | 10 µM | MCF7 | -0.748 | -0.093 | 0.144 | 7523 |
| 6005 | ramipril     | 10 µM | PC3 | -0.748 | -0.131 | 0.106 | 7144 |
| 6006 | STOCK1N-28457 | 20 µM | MCF7 | -0.749 | -0.118 | 0.12 | 6869 |
| 6007 | etodolac     | 14 µM | PC3 | -0.75 | -0.162 | 0.076 | 2091 |
| 6008 | mebeverine   | 9 µM | HL60 | -0.751 | -0.122 | 0.115 | 1576 |
| 6009 | amodiaquine  | 9 µM | HL60 | -0.753 | -0.126 | 0.112 | 1570 |
| 6010 | tridihexethyl | 11 µM | MCF7 | -0.754 | -0.131 | 0.108 | 5486 |
| 6011 | chlorphenamine | 10 µM | MCF7 | -0.755 | -0.094 | 0.145 | 6773 |
| 6012 | pheneticillin | 10 µM | MCF7 | -0.757 | -0.117 | 0.122 | 6239 |
| 6013 | ranitidine   | 11 µM | HL60 | -0.759 | -0.123 | 0.117 | 1404 |
|   | Compound               | Concentration | Assay  | IC50 (nM) | EC50 (nM) | pIC50 | pEC50 | EC50 (nM) |
|---|------------------------|---------------|--------|-----------|-----------|-------|-------|-----------|
| 6014 | clebopride            | 8 µM MCF7     | -0.759 | 0.116     | 2646      |
| 6015 | cephahlenine          | 6 µM HL60     | -0.762 | 0.101     | 2429      |
| 6016 | fluspirilene          | 8 µM MCF7     | -0.762 | 0.131     | 5008      |
| 6017 | nicergoline           | 8 µM PC3      | -0.763 | 0.086     | 2058      |
| 6018 | metformin             | 24 µM MCF7    | -0.765 | 0.098     | 5487      |
| 6019 | hydroquinine          | 9 µM HL60     | -0.765 | 0.113     | 1775      |
| 6020 | nifurtimox            | 14 µM MCF7    | -0.765 | 0.118     | 7328      |
| 6021 | strophanthidin        | 10 µM HL60    | -0.767 | 0.133     | 2525      |
| 6022 | zomepirac             | 13 µM MCF7    | -0.768 | 0.126     | 6815      |
| 6023 | ethosuximide          | 28 µM PC3     | -0.769 | 0.09      | 7308      |
| 6024 | colforsin             | 500 nM MCF7   | -0.769 | 0.132     | 7055      |
| 6025 | 16,16-dimethylprostaglandin E2 | 10 µM MCF7 | -0.769 | 0.134     | 6597      |
| 6026 | pilocarpine           | 15 µM HL60    | -0.77  | 0.126     | 2438      |
| 6027 | ampicillin            | 10 µM MCF7    | -0.77  | 0.121     | 5408      |
| 6028 | etifenin              | 12 µM HL60    | -0.771 | 0.137     | 2477      |
| 6029 | epivincamine          | 11 µM MCF7    | -0.772 | 0.116     | 2775      |
| 6030 | isoconazole           | 10 µM HL60    | -0.774 | 0.127     | 1372      |
| 6031 | chloropyramine        | 12 µM PC3     | -0.774 | 0.127     | 4589      |
| 6032 | sulcotidil            | 10 µM HL60    | -0.775 | 0.101     | 6152      |
| 6033 | suramin sodium        | 10 µM MCF7    | -0.776 | 0.102     | 2651      |
| 6034 | prenylamine           | 10 µM MCF7    | -0.78  | 0.139     | 5489      |
| 6035 | terazosin             | 9 µM HL60     | -0.78  | 0.103     | 2530      |
| 6036 | bumataneide           | 11 µM HL60    | -0.78  | 0.112     | 2409      |
| 6037 | nomifensine           | 11 µM HL60    | -0.781 | 0.105     | 1378      |
| 6038 | (-)-isoprenaline      | 16 µM MCF7    | -0.781 | 0.144     | 3571      |
| 6039 | ciclopirox            | 15 µM HL60    | -0.782 | 0.126     | 2456      |
| 6040 | cisapride             | 9 µM HL60     | -0.782 | 0.136     | 2443      |
| 6041 | lycorine              | 12 µM HL60    | -0.783 | 0.121     | 2195      |
| 6042 | bambuterol            | 10 µM PC3     | -0.784 | 0.108     | 5885      |
| 6043 | cefamandole           | 8 µM PC3      | -0.788 | 0.122     | 7394      |
| 6044 | demecarium bromide    | 6 µM MCF7     | -0.789 | 0.149     | 2773      |
| 6045 | alprostadil           | 11 µM PC3     | -0.79  | 0.096     | 4099      |
| 6046 | flucytosine           | 31 µM HL60    | -0.791 | 0.136     | 3073      |
| 6047 | digoxigenin           | 10 µM MCF7    | -0.792 | 0.15      | 5275      |
| 6048 | isoxicam              | 12 µM MCF7    | -0.792 | 0.129     | 7028      |
| 6049 | emetine               | 7 µM HL60     | -0.793 | 0.09      | 2145      |
| ID  | Compound                        | Concentration | Cell Line | IC50  | CC50  | LC50  | Fold Change |
|-----|---------------------------------|---------------|-----------|-------|-------|-------|-------------|
| 6051| Guanethidine                    | 13 µM         | HL60      | -0.794| -0.119| 0.132| 1554        |
| 6052| Imipramine                      | 13 µM         | PC3       | -0.796| -0.165| 0.087| 1807        |
| 6053| H-89                            | 500 nM        | MCF7      | -0.801| -0.121| 0.133| 6878        |
| 6054| Proadifen                       | 10 µM         | MCF7      | -0.801| -0.117| 0.136| 3446        |
| 6055| Dobutamine                      | 12 µM         | HL60      | -0.805| -0.128| 0.127| 1589        |
| 6056| Tamoxifen                       | 7 µM          | HL60      | -0.808| -0.119| 0.137| 1366        |
| 6057| Prestwick-689                   | 10 µM         | MCF7      | -0.811| -0.119| 0.138| 7173        |
| 6058| Diphenamid metilsulfate         | 10 µM         | MCF7      | -0.814| -0.112| 0.146| 1494        |
| 6059| Doxepin                         | 13 µM         | MCF7      | -0.818| -0.13  | 0.129| 7415        |
| 6060| Anabasine                       | 25 µM         | MCF7      | -0.819| -0.113| 0.146| 6774        |
| 6061| Etamivan                        | 18 µM         | MCF7      | -0.819| -0.123| 0.136| 7021        |
| 6062| Cotinine                        | 23 µM         | HL60      | -0.821| -0.137| 0.123| 2011        |
| 6063| Hecogenin                       | 9 µM          | MCF7      | -0.821| -0.128| 0.132| 7175        |
| 6064| Clemastine                      | 9 µM          | MCF7      | -0.823| -0.13  | 0.131| 7485        |
| 6065| Glipizide                       | 9 µM          | HL60      | -0.825| -0.124| 0.137| 2008        |
| 6066| Diprophylline                   | 16 µM         | MCF7      | -0.826| -0.125| 0.137| 1689        |
| 6067| Alimemazine                     | 5 µM          | MCF7      | -0.826| -0.126| 0.136| 3478        |
| 6068| Phenformin                      | 17 µM         | HL60      | -0.828| -0.134| 0.128| 2350        |
| 6069| Homochlorcyclizine              | 10 µM         | PC3       | -0.829| -0.135| 0.127| 7295        |
| 6070| Artemisin                       | 14 µM         | HL60      | -0.83 | -0.126| 0.137| 1714        |
| 6071| Colchicine                      | 10 µM         | HL60      | -0.83 | -0.136| 0.126| 1598        |
| 6072| Praziquantel                    | 13 µM         | HL60      | -0.831| -0.133| 0.13  | 1572        |
| 6073| Lovastatin                      | 10 µM         | HL60      | -0.836| -0.133| 0.131| 2494        |
| 6074| Nadide                          | 6 µM          | MCF7      | -0.841| -0.119| 0.147| 7227        |
| 6075| 15-delta prostaglandin J2       | 10 µM         | MCF7      | -0.843| -0.136| 0.131| 6990        |
| 6076| Metanephrine                    | 17 µM         | MCF7      | -0.865| -0.138| 0.136| 5334        |
| 6077| Mesoridazine                    | 7 µM          | MCF7      | -0.866| -0.138| 0.136| 7017        |
| 6078| Ciprofloxacin                   | 11 µM         | MCF7      | -0.866| -0.141| 0.133| 5299        |
| 6079| Proscillaridin                  | 8 µM          | MCF7      | -0.871| -0.134| 0.141| 7340        |
| 6080| Naltrexone                      | 10 µM         | MCF7      | -0.873| -0.156| 0.12  | 6241        |
| 6081| Lanatoside C                    | 4 µM          | HL60      | -0.876| -0.147| 0.13  | 2193        |
| 6082| Benzydamine                     | 12 µM         | MCF7      | -0.877| -0.151| 0.126| 7169        |
| 6083| 11-deoxy-16,16-dimethylprostaglandin E2 | 10 µM | PC3 | -0.881| -0.16  | 0.118| 7538        |
| 6084| Monorden                        | 100 nM        | HL60      | -0.884| -0.128| 0.152| 1160        |
| 6085| Demecolcine                     | 12 µM         | MCF7      | -0.885| -0.143| 0.137| 1103        |
| 6086| 15-delta prostaglandin J2       | 10 µM         | MCF7      | -0.887| -0.147| 0.134| 1011        |
| 6087| Sulfaphenazole                  | 13 µM         | MCF7      | -0.895| -0.136| 0.147| 1673        |
|   |   |   |   |   |
|---|---|---|---|---|
|6088 | SR-95531 | 11 µM | HL60 | -0.897 -0.146 0.138 1316 |
|6089 | thioridazine | 10 µM | HL60 | -0.898 -0.132 0.152 1171 |
|6090 | nitrofural | 20 µM | MCF7 | -0.91 -0.158 0.13 5321 |
|6091 | cytochalasin B | 21 µM | MCF7 | -0.917 -0.134 0.156 1122 |
|6092 | cinnarizine | 11 µM | MCF7 | -0.938 -0.156 0.141 7174 |
|6093 | N-acetylmuramic acid | 14 µM | HL60 | -0.946 -0.157 0.142 1326 |
|6094 | 5162773 | 7 µM | MCF7 | -0.947 -0.132 0.168 892 |
|6095 | dihydroergotamine | 3 µM | PC3 | -0.949 -0.221 0.079 2081 |
|6096 | bucladesine | 2 µM | MCF7 | -0.958 -0.132 0.171 842 |
|6097 | N-acetyl-L-aspartic acid | 23 µM | HL60 | -0.958 -0.148 0.155 1329 |
|6098 | aminoglutethimide | 17 µM | MCF7 | -0.96 -0.143 0.161 7421 |
|6099 | alvespimycin | 100 nM | HL60 | -0.963 -0.157 0.148 1154 |
|6100 | digoxin | 5 µM | MCF7 | -1 -0.138 0.179 5324 |
**Supplementary Figure 1. Analytical algorithm used in the present study.** The study began with a complementary (c)DNA microarray of patient samples validated by the National Center for Biotechnology Information (NCBI) dataset. Upregulated genes, peroxisome proliferator-activated receptor alpha (*PPARA*), and lipid metabolism-related genes were explored with the Connectivity Map (CMap) to find potential drugs.
Supplementary Figure 2. Validation of target genes in cell lines from ampullary cancer and other cancers. mRNA expression levels of targeted genes from Figure 7 were examined in cell lines of different cancer types. (A) Expressions of PPARA, (B) ACAAI, (C) FABPI, and (D) FABP2 by a qPCR. The graph represents a one-time experiment. (E) Expression of PPARA by a semiquantitative RT-PCR. β-actin served as a loading control. (F) Ratios of PPARA/β-actin in (E). The graph represents three independent experiments. Ampullary cancer cell lines: TGBC-18 TKB and SNU-478. Gastric cancer cell lines: AGS and MKN45. Pancreatic cancer cell lines: Pan1 and MIA-Pan2. Colon cancer cell line: HCT116.
Supplementary Figure 3. Expression of peroxisome proliferator-activated receptor alpha (PPAR-α) protein in clinical samples of ampullary cancer by IHC staining. (A) Low expression of PPAR-α (×200). (B) High expression of PPAR-α (×200).
Supplementary Figure 4. Cell proliferation assay after treatment with potential drugs from Connectivity Map (CMap). An MTT assay was performed. (A) SNU-478 ampullary cancer cells treated with alvespimycin. (B) TGBC-18 TKB ampullary cancer cells treated with alvespimycin. (C) SNU-478 ampullary cancer cells treated with cytochalasin B. (D) TGBC-18 TKB ampullary cancer cells treated with cytochalasin B. (E) SNU-478 ampullary cancer cells treated with trichostatin A. (F) TGBC-18 TKB ampullary cancer cells treated with trichostatin A. Each graph represents three independent experiments.
Supplementary Figure 5. Effects of potential drugs on ampullary cancer cells. Ampullary cancer cells were treated with alvespimycin, cytochalasin B, or trichostatin A for 24 or 48 h, and cell growth was evaluated by an MTT assay. (A) SNU-478 cells treated for 24 h. (B) SNU-478 cells treated for 48 h. (C) TGBC-18 TKB cells treated for 24 h. (D) TGBC-18 TKB cells treated for 48 h. Values of the dose-response growth inhibitory concentration (IC₅₀) were calculated according to a nonlinear regression curve with a variable slope. Graphs from three independent experiments with mean IC₅₀ values ± standard deviation (SD) are shown.