Table S1: The list of genes differentially expressed genes (DEGs) in resistant cell lines compared to sensitive cells. P-value is achieved by the Ranksam method, with a minimum value of 0.000155. Chemotherapy resistance mechanism drawn by text mining and the other genes in which have not yet been identified as chemotherapy resistance factors are suggested for further research.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene Name** | **mechanism** | **FC** | **Sorted result ranksum3** | **drug** | **ref** |
| RGS2 | amplification of endogenous cell growth and AKT signals PMID: 21044322, survival signaling pathways / PMID: 24475290 | Inf | 0.000155 | Ovarian cancer/cisplatin | [1, 2] |
| PITRM1 |  | Inf | 0.000155 | n/a |  |
| PDS5A | cohesin-associated proliferation PMID:24123833/ regulator of sister chromatid and DNA repair  | Inf | 0.000155 | DNA damaging agents | [3, 4] |
| MPC1 | Induction of metabolism reprogramming to aerobic glycolysis with reduced ATP production, proliferation, migration and resistant to both chemotherapy and radiotherapy,PMID: 24738035 | -4.72962 | 0.000155 | docetaxel | [5] |
| NUFIP2 | Cell proliferation induction | 4.35586 | 0.000155 | n/a | [6] |
| TM7SF3 | downstream transcriptional target of p53/TP53, pro-survival homeostatic factor through attenuation of the development of cellular stress PMID: 27740623 ,protein homeostasis maintainance and the subsequent induction of unfolded protein response (UPR)  PMID: 21853325 | -12.0 | 0.000155 | n/a | **[7] [8]** |
| EEF1A1 | apoptosis inhibition PMID: 14588074 | 6.59797 | 0.000155 | Cisplatin/ head and neck cancer cell line & ovarian carcinomas | [9] |
| DYNC1I2  | microtubule motor activity, G2/M transition of mitotic cell cycle | 3.04843 | 0.000155 | n/a | [10] |
| NID1 | Calcium ion binding, protein binding, extracellular matrix structural constituent, cell migration. extracellular matrix organization, cell adhesion | -3.78565 | 0.000155 | n/a | [11] |
| EXT2  | tumor suppressor | -4.2133 | 0.000155 | lapatinib, erlotinib, and AZD0530 sensitivity | [12] |
| SAP30 | negative regulation of transcription by RNA polymerase II, Transcription regulation | -3.86105 | 0.000155 | n/a | [13] [14] |
| COQ2 | tumor suppressors | 11.2629 | 0.000155 | n/a | [15] |
| JAG1 | mediation of Notch signaling (maintaining the balance of cell proliferation, survival, apoptosis, and differentiation) PMID: 24659709 | -4.74588 | 0.000155 | cisplatin | [16] |
| SOWAHC | n/a | -3.50855 | 0.000155 | n/a |  |
| NOTCH2 | Affection on the implementation of differentiation, proliferation and apoptotic programs (DOI: 10.1158/0008-5472.CAN-10-2719), Positively regulation of self-renewal of liver cancer cells (DOI: 10.1038/ncomms8122) | 5.13316 | 0.000155 | n/a | [17][18] |
| NOTCH2NL | function in the Notch signaling pathway | 4.02318 | 0.000155 | breastcancer/Paclitaxel, 5-Fluoroutacil, Doxorubicin | [19] |
| PAX9 | decreased proliferation growth and increase chemoresistance (DOI: [10.1038/modpathol.2009.92](https://doi.org/10.1038/modpathol.2009.92)) | 7.29978 | 0.000155 | Cisplatin/ovarian cancer | [20] |
| S100A10 |  mediate immune response evasion, angiogenesis, proliferation, invasion and metastasis | 3.21413 | 0.000155 | n/a | [21] |
| UBXN8 | Silencing of UBXD8 protein reduces Ras signal activity and downregulates the ERK and AKT pathways | 10.2519 | 0.000155 | n/a | [22] |
| TUB | n/a | -3.8407 | 0.000155 | n/a | n/a |
| SBNO1 | regulation of transcription, proliferation | 3.40396 | 0.000155 | n/a | [23] |
| SEC14L1  | lymphovascular invasion (doi.org/10.1038/s41379-018-0092-9) | 4.1419 | 0.000155 | Breast Cancer / n/a | [24] |
| FAM50A  | May be a DNA-binding protein or transcriptional factor(PMID: [29867487](https://www.ncbi.nlm.nih.gov/pubmed/29867487)) | 3.41068 | 0.000155 | n/a | [25] |
| DNM3 | involved in producing microtubule bundles and able to bind and hydrolyze GTP, Most probably involved in vesicular trafficking processes, in particular endocytosis | -31.4838 | 0.000155 | n/a | [26] |
| FEM1C | n/a | -4.86562 | 0.000155 |  | n/a |
| SOD2 | are toxic to biological systems/negative regulator of cell proliferation and the increase of apoptosis and chemosensitivity | -5.10462 | 0.000155 | Ovarian Cancer/ paclitaxel | [27] |
| CEP55 | regulation of phosphatidylinositol 3-kinase signaling/ cancer cell growth rate correlation(doi: 10.1074/jbc.M111.289108) | -6.23614 | 0.000155 | n/a | [28] |
| SEC11C  | regulators of metabolism through catalyzing the cleavage of N-terminal signal sequences of proteins targeted to the endoplasmic reticulum (PMID:  27107061) | -11.5314 | 0.000155 | pancreatic cancer n/a | [29] |
| TM9SF3 | TM9SF4 downregulation is associated with cell growth inhibition and susceptibility to apoptosis and inhibition of the invasive behavior (doi:10.1038/onc.2014.437) | -6.25425 | 0.000155 | Paclitaxel/ breast cancer cells/5-fu colon cancer | [30] |
| SPTY2D1 | n/a | 6.70572 | 0.000155 |  | n/a |
| PPP1R10 |  functions as a proto-oncogene by sequestering PTEN (PMID: 23117887) | 8.74526 | 0.000155 | n/a | [31] |
| MDC1 | Required for checkpoint mediated cell cycle arrest in response to DNA damage within both the S phase and G2/M phases of the cell cycle (doi: 10.1158/0008-5472.CAN-12-1394)Serves as a scaffold for the recruitment of DNA repair and signal transduction proteins to discrete foci of DNA damage phosphorylation , activation of the ATM, CHEK1 and CHEK2 kinases, and stabilization of TP53 and apoptosis([doi.org/10.1038/nature01447](https://doi.org/10.1038/nature01447)) | -7.52228 | 0.000155 | n/a | [32] **[33]** |
| ABCC4 | Multidrug resistance-associated protein 4/ May be an organic anion pump ovarian relevant to cellular detoxification([doi.org/10.1016/j.bcp.2009.12.002](https://doi.org/10.1016/j.bcp.2009.12.002)) | 8.00352 | 0.000155 | Ovarian cancer/ oxaliplatin | [34] |
| TPP2  | DNA repair/ TPP2 inhibition decreases the levels of active, di-phosphorylated extracellular signal-regulated kinase 1 (ERK1) and ERK2 in the nucleus, thereby down-regulating signal transduction downstream of growth factors and mitogenic stimuli([doi.org/10.1074/mcp.M114.043331](https://doi.org/10.1074/mcp.M114.043331)). | 7.36531 | 0.000155 | n/a | [35] |
| APC | sensitivity of colon cancer cells to histone deacetylase inhibitor-induced apoptosis (Tumor suppressor) (doi.org/10.3892/or.2013.2446) | 5.88223 | 0.000155 | Cisplatin/ ovarian cancer | [36] |
| CEBPD | Transcription activator | -12.1342 | 0.000155 | n/a | [37] |
| FAM208A |  | -3.42085 | 0.000155 | n/a |  |
| GEMIN2 | RNA splicing, via transesterification reactions | -8.00122 | 0.000155 |  | [38] |
| RAB27A | apoptosis induction (PMID:  28902788)/ a mediator of human bCSCs by promoting the growth of mammospheres and synergistic suppressor of Rab27A(PMID: [28928832](https://www.ncbi.nlm.nih.gov/pubmed/28928832)) | 7.05088 | 0.000155 | Pancreatic cancer /Breast cancer stem cell/na | [39][40] |
| PNISR | Rna binding | -4.12779 | 0.000155 | n/a |  |
| FAM168A | Reducing the cisplatin-induced apoptosis(PMID: 21334329 )/ activation of the PI3K/Akt/NF-κB signaling pathway([doi.org/10.1371/journal.pone.0051413](https://doi.org/10.1371/journal.pone.0051413)) | -8.5151 | 0.000155 | oral squamous cell carcinoma cell line/cisplatin | [41][42] |
| FAM171A1 |  | 4.4997 | 0.000155 | n/a |  |
| UHRF1BP1L | cellular proliferation and molecular pathogenesis of colorectal cancer involvement(doi.org/10.3892/or.2012.2064)/ bladder cancer cell invasion promotion by inhibiting KiSS1(doi.org/10.1371/journal.pone.0104252) | 8.85999 | 0.000155 | n/a | [43][44] |
| SLC6A8 | support survival of metastatic cells (PMID: [26191006](https://www.ncbi.nlm.nih.gov/pubmed/26191006)) | 8.16269 | 0.000155 | n/a | [45] |
| MAP4K4 | a novel positive regulator of MAPK/ERK signaling and  proliferation(PMID: [28306189](https://www.ncbi.nlm.nih.gov/pubmed/28306189)), may play a role in the response to environmental stress and cytokines such as TNF-alpha(DOI: 10.4172/2157-2518.1000284). Acts in upstream of the JUN N-terminal pathway | -5.92845 | 0.000155 | in lung adenocarcinoma/n/a | [46][47][48] |
| ARMCX5 |  | 10.5675 | 0.000155 |  |  |
| TRAPPC2 | n/a | -5.14049 | 0.000155 |  | n/a |
| RAB11FIP1 | Mediation of NF-κB signaling/ mediate response to ERBB2-targeting agents([doi.org/10.1038/onc.2013.41](https://doi.org/10.1038/onc.2013.41)) | 6.88623 | 0.000155 | Lapatinib & ERBB2-targeting agents/breast cancer | [49] |
| VKORC1L1 | n/a | -5.17368 | 0.000155 |  | n/a |
| AGPS | n/a | 8.92837 | 0.000155 |  | n/a |
| ZNF652 | n/a | -5.04376 | 0.000155 |  | n/a |
| RNF170 | n/a | 13.8601 | 0.000155 |  | n/a |
| FAM102B | n/a | 4.18346 | 0.000155 |  | n/a |
| MASTL |  Promotion of the cell proliferation in the presence of cisplatin by attenuating DNA damage signaling and cell death(PMID: [25373736](https://www.ncbi.nlm.nih.gov/pubmed/25373736))/Regulators of Mitotic Arrest ([doi.org/10.1016/j.ccr.2007.04.011](https://doi.org/10.1016/j.ccr.2007.04.011)) | 4.73429 | 0.000155 | neck squamous cell carcinoma/cisplatinPaclitaxel /ovarian cancer | [50][51] |
| ZNF77 | RNA polymerase II transcription factor activity, sequence-specific DNA binding | -7.63264 | 0.000155 | n/a | [52] |
| ID2 | A member of the helix‐loop‐helix protein family implicated in regulation of cellular growth, senescence, differentiation, apoptosis, angiogenesis, and neoplastic transformation ([doi.org/10.1002/ijc.24704](https://doi.org/10.1002/ijc.24704)) / is repressed by mutant p53 in proliferating cellsdoi.org/10.1186/s12964-016-0161-y | -6.57247 | 0.000155 | cisplatin //head and neck squamous cell carcinoma// colon cancer | [53][54][55] |
| SH3YL1 | n/a | -5.44056 | 0.000155 | n/a |  |
| TPGS2 | n/a | 4.81372 | 0.000155 | n/a |  |
| CKAP2L | Microtubule-associated protein which required for mitotic spindle formation and cell-cycle progression in neural progenitor cells | 6.07322 | 0.000155 | n/a | [56] |
| ACSL1 | acti-vate EMT in colorectal cancer, leading to increasedmigration, invasion and colony formation acti-vate EMT in colorectal cancer, leading to increasedmigration, invasion and colony formation acti-vate EMT in colorectal cancer, leading to increasedmigration, invasion and colony formation activation of EMT in leading to increased migration, invasion and colony formation(doi:10.1111/febs.14090) | -7.64993 | 0.000155 | CRC/N/A | [57] |
| ITCH |  Mediation of the antiapoptotic activity of epidermal growth factor through the ubiquitination and proteasomal degradation of p15 BID (doi:10.1111/j.1742-4658.2010.07562.x)/ the negative regulators of the Hippo pathway, induction of drug resistance/ protection from apoptosis and increase cell survival(doi:10.1016/j.bbrc.2007.06.104) / | 8.09749 | 0.000155 | OVARIAN CANCER/ CISPLATIN | [58, 59] |
| SHOX2 | modulator of embryonic EMT (DOI: 10.1158/0008-5472.CAN-10-2941) | -7.3082 | 0.000155 | N/A | [60] |
| CMC4 | n/a | 4.83781 | 0.000155 | n/a |  |
| RPL28 | n/a | -16.7386 | 0.000155 | n/a |  |
| EML4 | n/a | -7.26386 | 0.000155 | n/a |  |
| CC2D2A | n/a | 7.72493 | 0.000155 | n/a |  |
| KCNJ2 | cell growth and drug resistance modulation by regulating MRP1/ABCC1 expression and is simultaneously regulated by the Ras/MAPK pathway(PMID: [25880778](https://www.ncbi.nlm.nih.gov/pubmed/25880778)) | -4.29919 | 0.000155 | multidrug resistance of small-cell lung cancer  | [61] |
| DCLK1  | involvement in regulation of EMT and CSCs, radio-resistance and self-renewal/survival through paracrine regulation and activation of ATM mediated DNA Damage response | -6.29108 | 0.000155 |  | [62, 63] |
| HEY1 | Direct target gene of the Notch signal pathway/ involved in the regulation of liver cancer cells self-renewal/ NOTCH4-HEY1 pathway is specifically up-regulated in the HNSCC, induction of proliferation and cisplatin resistance, and EMT promotion (DOI: 10.1158/1078-0432.CCR-17-1366) | -6.61397 | 0.000155 | HNSCC / cisplatin | [64] |
| PDGFRL | Is a c-MET network genes (c-MET-AXL-PDGFR) that suppresses cell proliferation and invasion ([doi.org/10.1371/journal.pone.0134552](https://doi.org/10.1371/journal.pone.0134552)) | 7.40355 | 0.000155 |  bladder cancer/ sensitivity to cisplatin | [65] |
| ANTXR1 | is selectively expressed in tumor vasculature and promotes tumor angiogenesis/ is expressed at a higher level in breast cancer stem cells compared to mature cells / control the function of Wnt pathway in cancer stem cells ( PMID: [22340594](https://www.ncbi.nlm.nih.gov/pubmed/22340594))/ Inhibitors of ANTXR1, such as mutant protective antigen of anthrax or soluble ANTXR1 may inhibit ANTXR1 activity and sensitize cancer stem cells to chemotherapy | 5.68738 | 0.000155 | BREAST cancer | [66][67] |
| CD36 |  promote endothelial cell apoptosis and reduce tumor metastasis (PMID: 10329920) | -9.32482 | 0.000155 | leukemia / n/a | [68] |
| PDCD6IP | modulating apoptosis as it interacts with apoptosis-related proteins such as PDCD6 and endophilins (DOI 10.1074/mcp.M500140-MCP200) | -9.08568 | 0.000155 | Cisplatin Resistance in Ovarian Cancer Cells | [69] |
| PEG10 | promote or support cell proliferation/ inhibition of apoptosis and inhibition of TGF-β signaling (DOI: 10.1158/0008-5472.CAN-05-1553) | 7.89947 | 0.000155 | pancreatic carcinoma and hepatocellular carcinoma /na | [70] |
| B4GALT6 | induce apoptosis (PMID: [23744354](https://www.ncbi.nlm.nih.gov/pubmed/23744354)) | -8.14293 | 0.000155 | n/a | [71] |
| PDE3A | Is downregulated in chemoresistant NSCLC cells due to DNA hypermethylation. Enforced PDE3A expression can sensitize cisplatin resistant A549 cells to cisplatin (PMID: 28678321) | -6.53588 | 0.000155 | NSCLU/cisplatin | [72] |
| PSD3 | n/a | 7.0479 | 0.000155 |  | n/a |
| RINT1 | RINT-1 may be involved in cell cycle regulation after DNA damage (tumor suppressor gene) (doi: 10.1074/jbc.M008893200) | -8.68882 | 0.000155 | breast cancer n/a | [73] |
| SEMA6D | Activation of SEMA6D leads to Abl kinase activation (DOI: 10.1158/1535-7163.MCT-07-0390 )/ hypoxia related drug resistance(PMID: 26205780) | 8.64642 | 0.000155 | Ovarian cancer /cisplatin  | [74][75] |
| OXLD1 | n/a | 5.69523 | 0.000155 |  | n/a |
| HS6ST2 |  is associated with the progression of malignant tumors, and is upregulated in various tumor types (PMID: [29113266](https://www.ncbi.nlm.nih.gov/pubmed/29113266)) | 8.2576 | 0.000155 | Gastric cancer/n/a | [76] |
| TLE4 | Cell death (DOI: 10.1002/ijc.24704)/ Inhibits the transcriptional activation mediated by PAX5, and by CTNNB1 and TCF family members in Wnt signaling | -7.46448 | 0.000155 | cisplatin-resistance in head and neck squamous cell carcinoma | [77] |
| NAGA |  induced cytotoxicity in response to cisplatin (PMID: [29302211](https://www.ncbi.nlm.nih.gov/pubmed/29302211)) | 5.40837 | 0.000155 | ovarian cells / cisplatin | [78] |
| HIRIP3 | May play a role in chromatin function and histone metabolism via its interaction with HIRA and histones (doi:10.1016/j.ygyno.2013.05.002) | -7.77276 | 0.000155 | carboplatin resistance in ovarian cancer | [79] |
| ZMYM4 | inhibit interferon-gamma induced apoptosis./ cytoskeleton organization/multicellular organism development regulation of cell morphogenesis | 10.4861 | 0.000155 |  | [80] |
| CHML | In association with Rab proteins has been shown to mediate endocytosis and degradation of glucose and amino acid transporters in growth factor–deprived conditions, which in turn control cellular nutrient uptake and sensitivity to cell death(10.1158/0008-5472.CAN-05-0573) | 4.54585 | 0.000155 | Docetaxel/carboplatin /ovarian cancer | [81] |
| ETFDH | Transport/ response to oxidative stress([doi.org/10.1186/1471-2164-9-99](https://doi.org/10.1186/1471-2164-9-99)) | -8.37348 | 0.000155 | differentially expressed gene groups upon cisplatin treatment/ topotecan / paclitaxel | [82] |
| CMTM3 | Knockdown of CMTM3 promotes cell migration, invasion and tumor metastasis, increases MMP2 expression and enhances MMP2 activity. CMTM3 inhibits EMT along with the upregulation of E-cadherin and the downregulation of N-cadherin, Vimentin and Twist1 (doi.org/10.18632/oncotarget.8789) | -8.68542 | 0.000155 | oxaliplatin or irinotecan/CRC | [83] |
| BNIP2 | Implicated in the suppression of cell death. Interacts with the BCL-2 (PMID: 21242194) | -6.61485 | 0.000155 | colorectal adenocarcinoma/ 5-FU, L-OHP, and VM-26 sensitivity  | [84] |