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***Research article***

**Network diffusion with centrality measures to identify disease-related genes**

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**Supplementary**

1. **Supplementary Figures**



1. (b)



 (c) (d)

**Figure F1.** Mean and standard error of (a) AUROC, (b) pAUROC, (c) AUPRC, and (d) Top100 of each centrality measures on all diseases.

1. **Supplementary Tables**

**Table T1. List of diseases with their number of corresponding gene.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No. | Disease | Disease ID | Disease Semantic Type | Number of genes |
| 1 | Adenocarcinoma | C0001418 | Neoplastic Process | 1334 |
| 2 | Glioblastoma | C0017636 | Neoplastic Process | 1482 |
| 3 | Schizophrenia | C0036341 | Mental or Behavioral Dysfunction | 1402 |
| 4 | Alzheimer's Disease | C0002395 | Disease or Syndrome | 1542 |
| 5 | Rheumatoid Arthritis | C0003873 | Disease or Syndrome | 1407 |
| 6 | Malignant neoplasm of breast | C0006142 | Neoplastic Process | 3674 |
| 7 | Malignant tumor of colon | C0007102 | Neoplastic Process | 1570 |
| 8 | Diabetes Mellitus | C0011849 | Disease or Syndrome | 1164 |
| 9 | Melanoma | C0025202 | Neoplastic Process | 1852 |
| 10 | Neoplasm Metastasis | C0027627 | Neoplastic Process | 2886 |
| 11 | Obesity | C0028754 | Disease or Syndrome | 1509 |
| 12 | Prostatic Neoplasms | C0033578 | Neoplastic Process | 1272 |
| 13 | Malignant neoplasm of lung | C0242379 | Neoplastic Process | 1817 |
| 14 | Malignant neoplasm of prostate | C0376358 | Neoplastic Process | 2407 |
| 15 | Prostate carcinoma | C0600139 | Neoplastic Process | 2302 |
| 16 | Breast Carcinoma | C0678222 | Neoplastic Process | 3605 |
| 17 | Liver carcinoma | C2239176 | Neoplastic Process | 2611 |
| 18 | Squamous cell carcinoma | C0007137 | Neoplastic Process | 1452 |
| 19 | Colorectal Carcinoma | C0009402 | Neoplastic Process | 2150 |
| 20 | Leukemia | C0023418 | Neoplastic Process | 1482 |
| 21 | Malignant neoplasm of stomach | C0024623 | Neoplastic Process | 1729 |
| 22 | Neuroblastoma | C0027819 | Neoplastic Process | 1343 |
| 23 | Pancreatic carcinoma | C0235974 | Neoplastic Process | 1444 |
| 24 | Malignant neoplasm of pancreas | C0346647 | Neoplastic Process | 1425 |
| 25 | Carcinogenesis | C0596263 | Neoplastic Process | 2953 |
| 26 | Carcinoma of lung | C0684249 | Neoplastic Process | 1834 |
| 27 | Colon Carcinoma | C0699790 | Neoplastic Process | 1637 |
| 28 | Stomach Carcinoma | C0699791 | Neoplastic Process | 1680 |
| 29 | Central neuroblastoma | C0700095 | Neoplastic Process | 1310 |
| 30 | Primary malignant neoplasm of lung | C1306460 | Neoplastic Process | 1693 |
| 31 | Mammary Neoplasms | C1458155 | Neoplastic Process | 1892 |
| 32 | Colorectal Cancer | C1527249 | Neoplastic Process | 2369 |
| 33 | Non-Small Cell Lung Carcinoma | C0007131 | Neoplastic Process | 1633 |
| 34 | Diabetes Mellitus, Non-Insulin-Dependent | C0011860 | Disease or Syndrome | 1226 |
| 35 | Glioma | C0017638 | Neoplastic Process | 1654 |
| 36 | Leukemia, Myelocytic, Acute | C0023467 | Neoplastic Process | 1293 |
| 37 | Ovarian Carcinoma | C0029925 | Neoplastic Process | 1631 |
| 38 | Tumor Progression | C0178874 | Neoplastic Process | 1618 |
| 39 | Malignant neoplasm of ovary | C1140680 | Neoplastic Process | 1524 |
| 40 | Intellectual Disability | C3714756 | Mental or Behavioral Dysfunction | 1887 |

**Table T2. The average value of *m* and standard deviation.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| No. | Degree | Closeness | Betweenness | Eigenvector |  | PageRank |
| 1 | 0.1764 ± 0.0098 | 0.1282 ± 0.0019 | 0.5788 ± 0.1456 | 0.1764 ± 0.0098 |  | 0.9942 ± 0.0006 |
| 2 | 0.1487 ± 0.0128 | 0.0853 ± 0.0032 | 0.4634 ± 0.2014 | 0.1487 ± 0.0128 |  | 0.9921 ± 0.0028 |
| 3 | 0.2047 ± 0.0124 | 0.1592 ± 0.0086 | 0.6210 ± 0.0609 | 0.2047 ± 0.0124 |  | 0.9945 ± 0.0004 |
| 4 | 0.2076 ± 0.0105 | 0.1527 ± 0.0113 | 0.5335 ± 0.2782 | 0.2076 ± 0.0105 |  | 0.9952 ± 0.0003 |
| 5 | 0.2082 ± 0.0090 | 0.1388 ± 0.0067 | 0.6445 ± 0.1149 | 0.2082 ±0.0090 |  | 0.9940 ± 0.0007 |
| 6 | 0.1586 ± 0.0033 | 0.0703 ± 0.0048 | 0.6292 ± 0.2818 | 0.1586 ± 0.0033 |  | 0.9938 ± 0.0009 |
| 7 | 0.1652 ± 0.0095 | 0.1071 ± 0.0065 | 0.3670 ± 0.2107 | 0.1652 ± 0.0095 |  | 0.9944 ± 0.0010 |
| 8 | 0.1781 ± 0.0086 | 0.1302 ± 0.0065 | 0.5340 ± 0.1134 | 0.1781 ± 0.0086 |  | 0.9830 ± 0.0253 |
| 9 | 0.1694 ± 0.0167 | 0.0967 ± 0.0097 | 0.3744 ± 0.3022 | 0.1694 ±0.0167 |  | 0.9938 ± 0.0009 |
| 10 | 0.1958 ± 0.0064 | 0.1316 ± 0.0038 | 0.6324 ± 0.2517 | 0.1958 ± 0.0064 |  | 0.9950 ± 0.0004 |
| 11 | 0.2112 ± 0.0094 | 0.1813 ± 0.0109 | 0.6781 ± 0.0262 | 0.2112 ± 0.0094 |  | 0.9950 ± 0.0004 |
| 12 | 0.1609 ± 0.0103 | 0.1051 ± 0.0123 | 0.3679 ± 0.2135 | 0.1609 ± 0.0103 |  | 0.9868 ± 0.0138 |
| 13 | 0.1577 ± 0.0165 | 0.0872 ± 0.0052 | 0.4900 ± 0.2514 | 0.1577 ± 0.0165 |  | 0.9932 ± 0.0006 |
| 14 | 0.1704 ±0.0162 | 0.0847 ± 0.0081 | 0.5903 ± 0.0896 | 0.1704 ± 0.0162 |  | 0.9937 ± 0.0007 |
| 15 | 0.1686 ± 0.0183 | 0.0938 ± 0.0160 | 0.6344 ± 0.0561 | 0.1686 ± 0.0183 |  | 0.9931 ± 0.0017 |
| 16 | 0.1664 ± 0.0129 | 0.0717 ± 0.0087 | 0.5134 ± 0.2328 | 0.1664 ± 0.0129 |  | 0.9948 ± 0.0007 |
| 17 | 0.1965 ± 0.0088 | 0.1219 ± 0.0083 | 0.7381 ± 0.0251 | 0.1965 ± 0.0088 |  | 0.9956 ± 0.0010 |
| 18 | 0.1867 ± 0.0138 | 0.1218 ± 0.0099 | 0.4917 ± 0.1557 | 0.1867 ± 0.0138 |  | 0.9869 ± 0.0150 |
| 19 | 0.1774 ± 0.0115 | 0.0860 ± 0.0086 | 0.5347 ± 0.1799 | 0.1774 ± 0.0115 |  | 0.9911 ± 0.0068 |
| 20 | 0.1382 ± 0.0122 | 0.0630 ± 0.0087 | 0.4879 ± 0.1168 | 0.1382 ± 0.0122 |  | 0.9927 ± 0.0033 |
| 21 | 0.1612 ± 0.0120 | 0.0871 ± 0.0092 | 0.5464 ± 0.0688 | 0.1612 ± 0.0120 |  | 0.9934 ± 0.0009 |
| 22 | 0.1515 ± 0.0184 | 0.0926 ± 0.0120 | 0.3589 ± 0.2325 | 0.1515 ± 0.0184 |  | 0.9853 ± 0.0145 |
| 23 | 0.1718 ± 0.0112 | 0.1066 ± 0.0036 | 0.3968 ± 0.3237 | 0.1718 ± 0.0112 |  | 0.9934 ± 0.0013 |
| 24 | 0.1742 ± 0.0103 | 0.1113 ± 0.0063 | 0.4606 ± 0.0658 | 0.1742 ± 0.0103 |  | 0.9874 ± 0.0116 |
| 25 | 0.1337 ± 0.0071 | 0.0279 ± 0.0092 | 0.6332 ± 0.1248 | 0.1337 ± 0.0071 |  | 0.9932 ± 0.0007 |
| 26 | 0.1707 ± 0.0180 | 0.0805 ± 0.0106 | 0.5655 ± 0.1402 | 0.1707 ± 0.0180 |  | 0.9935 ± 0.0011 |
| 27 | 0.1659 ± 0.0061 | 0.1097 ± 0.0084 | 0.3390 ± 0.2715 | 0.1659 ± 0.0061 |  | 0.9944 ± 0.0005 |
| 28 | 0.1725 ± 0.0101 | 0.1035 ± 0.0086 | 0.6519± 0.0169 | 0.1725 ± 0.0101 |  | 0.9907 ± 0.0035 |
| 29 | 0.1395 ± 0.0154 | 0.0873 ± 0.0088 | 0.4155 ± 0.2360 | 0.1395 ± 0.0154 |  | 0.9908 ± 0.0024 |
| 30 | 0.1470 ± 0.0140 | 0.0922 ± 0.0109 | 0.5261 ± 0.1406 | 0.1470 ± 0.0140 |  | 0.9925 ± 0.0022 |
| 31 | 0.1677 ± 0.0098 | 0.0948 ± 0.0067 | 0.4439 ± 0.2589 | 0.1677 ± 0.0098 |  | 0.9946 ± 0.0010 |
| 32 | 0.1760 ± 0.0140 | 0.0749 ± 0.0057 | 0.3030 ± 0.2506 | 0.1760 ± 0.0140 |  | 0.9942 ± 0.0007 |
| 33 | 0.1561 ± 0.0181 | 0.0766 ± 0.0100 | 0.6234 ± 0.0262 | 0.1561 ± 0.0181 |  | 0.9925 ± 0.0021 |
| 34 | 0.1800 ± 0.0106 | 0.1438 ± 0.0119 | 0.5936 ± 0.1024 | 0.1800 ± 0.0106 |  | 0.9930 ± 0.0017 |
| 35 | 0.1796 ± 0.0155 | 0.0962 ± 0.0052 | 0.3468 ± 0.2741 | 0.1796 ± 0.0155 |  | 0.9944 ± 0.0006 |
| 36 | 0.1430 ± 0.0178 | 0.0701 ± 0.0172 | 0.3649 ± 0.2581 | 0.1430 ± 0.0178 |  | 0.9935 ± 0.0010 |
| 37 | 0.1740 ± 0.0079 | 0.0913 ± 0.0052 | 0.3852 ± 0.2986 | 0.1740 ± 0.0079 |  | 0.9930 ± 0.0020 |
| 38 | 0.1715 ± 0.0150 | 0.0919 ± 0.0073 | 0.6354 ± 0.0444 | 0.1715 ± 0.0150 |  | 0.9922 ± 0.0015 |
| 39 | 0.1603 ± 0.0078 | 0.0905 ± 0.0037 | 0.4740 ± 0.2585 | 0.1603 ± 0.0078 |  | 0.9928 ± 0.0013 |
| 40 | 0.2071 ± 0.0135 | 0.1468 ± 0.0163 | 0.4648 ± 0.2127 | 0.2071 ± 0.0135 |  | 0.9938 ± 0.0030 |

**Table T3. The coefficients of each variable with its *p*-value.**

|  |  |  |
| --- | --- | --- |
| Disease No. | Network diffusion | Closeness centrality |
| Coefficient | p-value | Coefficient | p-value |
| 1 | 89.7205 | 1.27E-57 | 10.9733 | 2.09E-19 |
| 2 | 75.4822 | 1.10E-70 | 6.6080 | 1.70E-12 |
| 3 | 61.7714 | 3.70E-78 | 11.7078 | 6.32E-29 |
| 4 | 65.4430 | 1.74E-80 | 11.8676 | 1.47E-33 |
| 5 | 58.3955 | 7.48E-77 | 9.2199 | 9.05E-21 |
| 6 | 39.8197 | 1.20E-190 | 2.9024 | 2.20E-09 |
| 7 | 68.1501 | 7.63E-77 | 6.9317 | 2.99E-16 |
| 8 | 74.7951 | 1.53E-55 | 11.5282 | 4.01E-19 |
| 9 | 55.6828 | 2.15E-92 | 6.7613 | 1.24E-17 |
| 10 | 42.4504 | 4.68E-153 | 6.3725 | 2.07E-28 |
| 11 | 51.2400 | 5.47E-84 | 9.9155 | 9.80E-26 |
| 12 | 86.8299 | 1.01E-58 | 9.3054 | 2.97E-16 |
| 13 | 66.0736 | 1.46E-86 | 6.1005 | 3.50E-13 |
| 14 | 54.5727 | 1.75E-117 | 5.0196 | 1.80E-13 |
| 15 | 53.5064 | 1.07E-114 | 5.4648 | 1.82E-14 |
| 16 | 39.2577 | 1.52E-191 | 3.2016 | 6.60E-11 |
| 17 | 49.0418 | 3.76E-126 | 5.8870 | 4.42E-22 |
| 18 | 69.2273 | 2.04E-70 | 9.2184 | 4.55E-23 |
| 19 | 52.4609 | 2.35E-105 | 4.7713 | 4.45E-12 |
| 20 | 72.5452 | 8.78E-69 | 4.3527 | 4.00E-06 |
| 21 | 63.0143 | 1.04E-84 | 5.9132 | 5.98E-14 |
| 22 | 90.5107 | 1.12E-59 | 8.2155 | 2.74E-13 |
| 23 | 80.3135 | 2.22E-64 | 8.8364 | 3.61E-18 |
| 24 | 80.6129 | 3.55E-62 | 9.5488 | 9.93E-19 |
| 25 | 48.4311 | 5.69E-138 | 1.2060 | 0.040630831 |
| 26 | 66.5365 | 3.85E-86 | 7.1061 | 1.39E-17 |
| 27 | 67.3582 | 1.96E-78 | 7.9413 | 9.93E-19 |
| 28 | 65.4964 | 1.03E-80 | 6.6362 | 2.16E-15 |
| 29 | 92.6579 | 4.18E-57 | 9.5942 | 1.70E-15 |
| 30 | 75.5707 | 2.73E-77 | 5.9004 | 4.87E-11 |
| 31 | 60.6820 | 2.46E-90 | 6.1287 | 6.02E-15 |
| 32 | 56.5738 | 7.46E-112 | 4.2864 | 1.32E-10 |
| 33 | 75.0909 | 2.37E-74 | 5.4827 | 9.55E-11 |
| 34 | 67.4262 | 1.59E-62 | 12.4418 | 2.03E-24 |
| 35 | 61.9555 | 2.78E-82 | 7.8361 | 6.02E-19 |
| 36 | 77.2458 | 1.59E-60 | 5.3923 | 1.59E-07 |
| 37 | 65.9110 | 1.33E-79 | 7.8565 | 1.50E-19 |
| 38 | 67.5458 | 5.26E-78 | 7.8774 | 1.72E-17 |
| 39 | 66.6503 | 1.22E-73 | 7.3411 | 1.19E-14 |
| 40 | 48.2392 | 1.31E-96 | 9.6848 | 5.61E-35 |

**Table T4. Proposed disease-related genes found and not found in DisGeNET.**

|  |  |  |
| --- | --- | --- |
|  | Disease | Proposed disease-related genes |
| Found in DisGeNET | Not Found in DisGeNET |
| 1 | Adenocarcinoma | SFTPA1, SFTPD, CLDN3, SFTPA2, SFTPB, WT1, PTGS2 | SPINK6, CYP2R1, GSTM5, SCGB1D2, CLDN12, JAML, FJX1, PTGDS, GLO1, CLDN23, METAP1 |
| 2 | Glioblastoma | BSG, hEMMPRIN, MCL1, BCL2L2, IFNA1, POU5F1, AIFM1, BCL2L11, STAT3, BCL2L1, SPINT1 | PCSK2, NANP, JAML, CD6, PRDM14, PMAIP1, IL17RE, ZBTB33, XBP1, PFKFB2, MITF, BID, IL20RA |
| 3 | Schizophrenia | P2RX2, GABRG2, DLG2, NLGN1, DLGAP2, P2RX5, DLGAP3, SHANK1, DLG3, DLG4, NLGN4X, DLGAP1, HOMER2, NLGN2, GABRB1, SHANK2, HOMER1, HTR3A, GABRA1, GRIN1, GABRA4, GABRA6, GRIN2A, NR2A | GABRA2, DLGAP4, GABRA3, NLGN3, HOMER3 |
| 4 | Alzheimer's Disease | GFAP, PTGS2, C2, MAPT, STAT3, IL10, FCN2, CASP1, IL1B, APP, PON1 | TBXAS1, CNTFR, AKTIP, FTS, FAM160A2, FCN1, MAG, ZBTB33 |
| 5 | Rheumatoid Arthritis | BTLA, IL18BP, IL10, STAT3, IL18, CD2, IL1B, IL6ST, TNFRSF9, MEFV, IL4, IL18R1, IL17F, STAT5A, STAT4, STAT6 | IL20RB, SPN, TNFRSF4, JAML, SELPLG, IL20RA, TNFSF8 |
| 6 | Malignant neoplasm of breast | GSTM2, CYP1A1, PTGS2, PTGS1, EPHX1, UGT1A6, PRDX1, AKR1C3, CYP19A1, UGT1A8, HSD17B1, CYP3A4 | IL17RA, PRSS57, HSD17B3 |
| 7 | Malignant tumor of colon | POU5F1, FABP6, WT1, PTGS1, TNFRSF10B, APEX1 | JAML, PRDM14, S100PBP, POR, UGT1A10, PMAIP1, TBXAS1, RAG2 |
| 8 | Diabetes Mellitus | PDX1, NEUROG3, PTGS2, NOS1AP, ONECUT1, IFNA1, LPA | IL17RA, DUOXA2, NKX6-1, SCG5, SGNE1, CIDEA, POGZ, TRPM8, PPRC1, FABP6, TFR2, TBXAS1, BTLA |
| 9 | Melanoma | TYR, PMEL, MLANA, DCT, TYRP1, TNFSF4, TNLG2B, BCL2L1, TNFSF10, BID, TNFRSF4, STAT3, BCL2, TNFRSF10B, CASP8, FAS, STAT1, CYP27B1, TNFRSF10A, BAK1, IL10, CYP2R1 | NCR3, DIABLO, JAML, STAT5A, POGZ, TP53BP2, TIGAR |
| 10 | Neoplasm Metastasis | FBLN5, MITF, MSX1, STAT3, NRP1, TNFSF10, FAS, SOX2, POU5F1, ITGB1, SHC1, SRC, KDR, MMP2, IGF1 | MFAP2, MFAP5, CLDN12 |
| 11 | Obesity | UGT1A7, UGT1A10, UGT1A1, UGT1A9, UGT1A3, UCP1, UGT1A4, UGT1A8, UGT1A6, CYP1A1, CIDEA, CYP3A4, CYP2B6, CYP2C9 | TNFSF4, TNLG2B, EPHX1, HSD17B2 |
| 12 | Prostatic Neoplasms | HSD17B3, HSD3B2, CYP19A1, HSD3B1, SRD5A1, CYP17A1, AKR1C3, AKR1C1, SRD5A3, CYP1A1, SPINT1, EPHX1, HSD17B1, PTGS2, SULT1E1 | HSD17B2, HSD17B6, CYP11B1, AKR1C2, CYP2R1, AKR1C4, S100PBP, AKR1D1, CD6, HGFAC, WT1, ZBTB33, HSD11B1, PTGES, GSTM2 |
| 13 | Malignant neoplasm of lung | DUOX2, DUOXA2, DUOX1, DUOXA1, GSTM2, GSTM3, GSTM4, EPHX1, CYP1A1 | CHRNB2, GSTM5, JAML, DIABLO, MAP3K4, FJX1, GSR, HEL-75 |
| 14 | Malignant neoplasm of prostate | , HSD17B2, HSD17B3, CYP19A1, HSD3B2, CYP17A1, HSD17B6, SRD5A1, AKR1C3, HSD3B1, HSD17B1, SRD5A3, CYP11B2, EPHX1, SULT1E1, AKR1C2, PTGS2, CYP1A1, CYP1A2, CYP2B6 | AKR1C1, CYP11B1, AKR1D1, TXN2, PTGIS, HSD11B1 |
| 15 | Prostate carcinoma | CYP17A1, CYP19A1, HSD3B1, SPINT1, HSD17B6, HSD3B2, HSD17B2, AKR1C3, CYP1A1, HSD17B3, SRD5A1, ASCC2, SRD5A3, PTGS2, HSD17B1 | CYP11B2, CYP11B1, AKR1C1, AKR1D1, DNAJC1, ASCC3 |
| 16 | Breast Carcinoma | GSTM2, CYP1A1, PTGS2, HSD3B1, EPHX1, MCL1, SOX2, CYP17A1, CYP1A2, HSD17B2 | HSD3B2, HSD17B3, UGT1A4 |
| 17 | Liver carcinoma | EPHX1, CYP3A4, CYP2E1, TXN2, SREBF2, CYP1A1, CYP1A2, CYP2B6, CYP3A5 | HSD17B2, HSD17B7, HSD3B1 |
| 18 | Squamous cell carcinoma | UGT1A10, UGT1A3, UGT1A4, UGT1A1, UGT1A8, UGT1A6, UGT1A7, UGT1A9, DSP, CYP2E1, PKP1, DSG1, EPHX1, PTGS2, DSC2, CYP1A2, HAVCR2 | PKP2, CYP2B6, DSC1, PKP3, JAML, TBXAS1, CYP3A4, CYP2C9, CD6 |
| 19 | Colorectal Carcinoma | UGT1A6, UGT1A1, UGT1A9, PTGS2, EPHX1, CYP3A4, APEX1, CYP2C9, CYP1A2, GUCA2A, PTGS1, CYP1A1, TNFSF4, TNLG2B | UGT1A4, RTCB, UGT1A8, UGT1A3, C2orf49, ZNRF3, TBXAS1 |
| 20 | Leukemia | TNFRSF18, HOXB7, HOXC6, HOXC5, HOXA7, HOXA5, CD244, TCF3, HOXB4 | DUOXA2, HOXA6, HOXB5, HOXB6, FBXO45, TCF12 |
| 21 | Malignant neoplasm of stomach | OGG1, HAVCR2, APEX1, CYP2E1, LGALS9 | POGZ, PORCN, TBXAS1, PAX9, NAXE, FJX1, HGFAC |
| 22 | Neuroblastoma | P2RX6, P2RX4, P2RX5, P2RX7, P2RX2, TYR, P2RX3, MCL1, CSF3, LIN28A, MECP2, BCL2L11, ABCG2 | DCT, POGZ, PANX1, METAP1, PMEL, MITF, RAG2, CNTFR, NEUROG3, BID, MSRB2, DIABLO, AIFM1, BCL2L1, PAX9 |
| 23 | Pancreatic carcinoma | CYP27B1, IL17B, TNFSF10, STAT3 | IL17RA, IL25, S100P, RAG1, DHPS, NKX6-1, C1GALT1, BID, BTLA |
| 24 | Malignant neoplasm of pancreas | CYP2R1, CYP27B1, CYP24A1, TNFSF10, STAT3, TNFRSF10B | IL17RA, TRPA1, ASCC2, DHPS, BTLA, C1GALT1 |
| 25 | Carcinogenesis | P2RX7, P2RX2, P2RX6, P2RX5, GSTM2, IL17RA, APEX1, PTGS1, POU5F1, GSTM3, TNFSF10 | IL17RE, IL17B, UGT1A10, TXN2, TBXAS1, UGT1A9, TCF3, GSTM5 |
| 26 | Carcinoma of lung | DUOX2, DUOXA2, EPHX1, CYP27B1, CYP1A1, CYP2E1, CYP3A4, CYP1A2, STAT3 | SLC24A5, JAML, STK3, TRPV1, ZBTB33, NEIL1, QTRT2, CD6, CYP2C8 |
| 27 | Colon Carcinoma | FABP6, GUCA2B, CYP2R1, TNFRSF9, PTGS2, STAT3, NANOG, MCL1 | UGT1A4, UGT1A10, UGT1A3, HCST, PRDM14, JAML, UGT1A8, DIABLO, S100PBP, CD6, APPL1, HAVCR2 |
| 28 | Stomach Carcinoma | CYP2E1, FZD9, WNT8B, WNT1, STAT3 | CLDN12, POGZ, LHPP, WNT4, PTGIS, PORCN, WNT8A |
| 29 | Central neuroblastoma | P2RX6, P2RX3, P2RX7, P2RX5, TRPA1, P2RX2, P2RX4, TYR, IFNA1, MCL1, CSF3, PMAIP1, PRDX2, HEL-S-2a, STAT3, FAS | POGZ, METAP1, PMEL, MITF, PRDX1, ABCD4, BCL2L1, BID, IL17RE |
| 30 | Primary malignant neoplasm of lung | DUOX2, DUOXA2, DUOX1, EPHX1, CYP27B1, GSTM1, CYP1A1, CYP1A2, CYP2C9, GSTM2, APEX1 | GSTM5, TNFRSF8, TXN2, SFTPC, PCSK2, CD6, UGT1A3, UGT1A10, NEIL1 |
| 31 | Mammary Neoplasms | HSD3B1, CYP19A1, CYP1A1, PTGS2, PTGES, PTGS1, HSD17B2, ALOX5, SULT1E1, ALOX15, CYP1B1, WT1, CYP2C19, ERBB4 | EPHX1, TBXAS1, HSD3B2, SRD5A1, TNFRSF18, RERE, HPGDS, JAML, CYP4A11, CYP11B2, HSD17B3, CD6 |
| 32 | Colorectal Cancer | RTRAF, C14orf166, UGT1A9, PTGS2, PCSK2, PTGS1, CYP1A2, UGT1A6, UGT1A1, CYP3A4, CYP2C9, EPHX1, CYP2B6, CYP1A1, APEX1 | UGT1A3, RTCB, ZBTB8OS, UGT1A8, C2orf49, RSPO1, ZNRF3, TBXAS1, UGT1A4 |
| 33 | Non-Small Cell Lung Carcinoma | SFTPA1, SFTPA2, SFTPD, SFTPC, MCL1, PMAIP1, APEX1 | SPINK6, PUM2, PTGDS, DHPS, DIABLO, PRDM14, UGT1A3, TSNAX, UGT1A10, DOHH, BBC3 |
| 34 | Diabetes Mellitus, Non-Insulin-Dependent | ONECUT1, PDX1, EPHX1, CYP1A1, PTGS2, CYP2E1, LIPE, ADIPOR1, CYP19A1, PNLIP | NPPC, SCG5, SGNE1, ATP2A1, HSD17B6, SELPLG, CYP24A1 |
| 35 | Glioma | P2RX7, P2RX4, PANX1, P2RX2, P2RX6, P2RX5, LGI4, LGI1, TNFSF4, TNLG2B, P2RX3, TNFRSF4, TNFSF10, BSG, hEMMPRIN, MCL1, MAG, BCL2L1, CNTN1, STAT3, NRP1 | PCSK2, MLANA, IL17RE, LINGO1, POGZ, SPINT1, ZBTB33, BID, BCL2L11 |
| 36 | Leukemia, Myelocytic, Acute | CD2, HOXB7, CSF3, HOXA5, IFNA1, CD48, HOXB6, HOXB5, HOXB4, HOXA7, TNFSF10, ABCG2 | HOXA6, HOXC6, HOXC5, JAML, TNFRSF8, TNFRSF4, LGALS9, SECTM1, DRG1, BID |
| 37 | Ovarian Carcinoma | SPINT1, MFAP5, POU5F1, WT1, CSF3, HGFAC, BCL2L1, STAT3, PTGS2 | DNAJC1, MFAP2, JAML, POGZ, ZBTB33, FASLG, TNFSF6 |
| 38 | Tumor Progression | P2RX2, P2RX6, P2RX5, P2RX3, P2RX4, P2RX7, POU5F1, STAT3, NRP1, CAV1, IFNA1 | HCST, JAML, TRPV1, NCR3, DHPS, MYOCD, PANX1, IL22RA1, FBLN2, METAP1, NECTIN2 |
| 39 | Malignant neoplasm of ovary | SPINT1, MFAP5, CSF3, CYP1A1, IL13, IFNA1, FBLN1, ROPN1L, STAT3 | DNAJC1, MFAP2, CYP2R1, MST1, DHPS, PSTPIP1, TNFSF9, TNLG5A |
| 40 | Intellectual Disability | PIGL, PIGC, PIGH, PIGA, DPM2, DPM1, FKTN, USH1C, PIGQ, ALG3, PIGY, DPM3, POMK, PIGV, NRL, ETFA, MYO7A | ALG1, PIGP, PIGM, KCNJ8 |

**Table T5. Proposed disease-related genes with literature support.**

|  |  |  |  |
| --- | --- | --- | --- |
| No. | Disease | Genes | References |
| 1 | Adenocarcinoma | SPINK6  | [1], [2] |
|  |  | CYP2R1 | [3], [4], [5], [6], [7] |
|  |  | GSTM5 | [8], [9], [10], [11] |
|  |  | SCGB1D2 | [12], [13] |
|  |  | CLDN12 | [14], [15] |
|  |  | JAML | - |
|  |  | FJX1 | [16], [17] |
|  |  | PTGDS | [18], [19], [20], [21] |
|  |  | GLO1 | [22], [23], [24], [25], [26], [27], [28], [29], [30] |
|  |  | CLDN23 | [31] |
|  |  | METAP1 | [32] |
| 2 | Glioblastoma | PCSK2 | - |
|  |  | NANP | - |
|  |  | JAML | - |
|  |  | CD6 | - |
|  |  | PRDM14 | - |
|  |  | PMAIP1 | [33], [34], [35], [36] |
|  |  | IL17RE | - |
|  |  | ZBTB33 | - |
|  |  | XBP1 | [37], [38], [39], [40], [41], [42] |
|  |  | PFKFB2 | [43], [44] |
|  |  | MITF | [45], [46], [47], [48] |
|  |  | BID | [49], [50] |
|  |  | IL20RA | - |
| 3 | Schizophrenia | GABRA2 | [51], [52], [53], [54], [55], [56], [57], [58] |
|  |  | DLGAP4 | - |
|  |  | GABRA3 | [59], [60], [61], [62] |
|  |  | NLGN3 | [63] |
|  |  | HOMER3 | - |
| 4 | Alzheimer's Disease | TBXAS1 | - |
|  |  | CNTFR | [64], [65], [66] |
|  |  | AKTIP | - |
|  |  | FTS | [67], [68], [69], [70], [71] |
|  |  | FAM160A2 | - |
|  |  | FCN1 | - |
|  |  | MAG | [72], [73], [74] |
|  |  | ZBTB33 | [75] |
| 5 | Rheumatoid Arthritis | IL20RB | [76] |
|  |  | SPN | [77], [78], [79] |
|  |  | TNFRSF4 | [80], [81], [82], [83], [84], [85], [86], [87], [88] |
|  |  | JAML | - |
|  |  | SELPLG | [89] |
|  |  | IL20RA | [90] |
|  |  | TNFSF8 | [91] |
| 6 | Malignant neoplasm of breast | IL17RA | [92], [93] |
|  |  | PRSS57 | - |
|  |  | HSD17B3 | [94] |
| 7 | Malignant tumor of colon | JAML | - |
|  |  | PRDM14 | [95] |
|  |  | S100PBP | - |
|  |  | POR | [96], [97], [98] |
|  |  | UGT1A10 | [99], [100], [101], [102], [103], [104] |
|  |  | PMAIP1 | [105], [106], [107] |
|  |  | TBXAS1 | [108] |
|  |  | RAG2 | [109] |
| 8 | Diabetes Mellitus | IL17RA | [110], [111], [112], [113] |
|  |  | DUOXA2 | - |
|  |  | NKX6-1 | [114], [115], [116], [117], [118], [119], [120] |
|  |  | SCG5 | [121], [122], [123], [124], [125], [126] |
|  |  | SGNE1 | [123] |
|  |  | CIDEA | [127], [128], [129], [130], [131], [132], [133] |
|  |  | POGZ | - |
|  |  | TRPM8 | [134], [135], [136], [137] |
|  |  | PPRC1 | - |
|  |  | FABP6 | [138], [139] |
|  |  | TFR2 | [140], [141], [142], [143], [144], [145] |
|  |  | TBXAS1 | [146], [147] |
|  |  | BTLA | [148], [149], [150] |
| 9 | Melanoma | NCR3 | [151], [152], [153], [154], [155] |
|  |  | DIABLO | [156], [157], [158], [159] |
|  |  | JAML | - |
|  |  | STAT5A | [160], [161], [162] |
|  |  | POGZ | - |
|  |  | TP53BP2 | [163] |
|  |  | TIGAR | [164] |
| 10 | Neoplasm Metastasis | MFAP2 | - |
|  |  | MFAP5 | [165], [166], [167] |
|  |  | CLDN12 | [168,169] |
| 11 | Obesity | TNFSF4 | - |
|  |  | TNLG2B | - |
|  |  | EPHX1 | [170], [171], [172], [173], [174] |
|  |  | HSD17B2 | [175] |
| 12 | Prostatic Neoplasms | HSD17B2 | [176], [177], [178], [179], [180], [181], [182], [183], [184] |
|  |  | HSD17B6 | [185], [186], [187] |
|  |  | CYP11B1 | [188], [189], [190], [191] |
|  |  | AKR1C2 | [192], [193], [194], [195] |
|  |  | CYP2R1 | [196], [197], [198] |
|  |  | AKR1C4 | [199], [200] |
|  |  | S100PBP | - |
|  |  | AKR1D1 | - |
|  |  | CD6 | - |
|  |  | HGFAC | - |
|  |  | WT1 | [201], [202], [203], [204] |
|  |  | ZBTB33 | [205], [206], [207] |
|  |  | HSD11B1 | [192], [208] |
|  |  | PTGES | [209], [210], [211], [212], [213] |
|  |  | GSTM2 | [214], [215], [216] , [217] |
| 13 | Malignant neoplasm of lung | CHRNB2 | - |
|  |  | GSTM5 | [9] |
|  |  | JAML | - |
|  |  | DIABLO | [218], [219], [220], [221] |
|  |  | MAP3K4 | [222], [223] |
|  |  | FJX1 | [224], [225] |
|  |  | GSR | [226], [227] |
|  |  | HEL-75 | - |
| 14 | Malignant neoplasm of prostate | AKR1C1 | [199], [228], [229], [230], [231], [232] |
|  |  | CYP11B1 | [188], [189], [190], [191] |
|  |  | AKR1D1 | - |
|  |  | TXN2 | - |
|  |  | PTGIS | [233] |
|  |  | HSD11B1 | [192], [208] |
| 15 | Prostate carcinoma | CYP11B2 | [234], [235] |
|  |  | CYP11B1 | [234] |
|  |  | AKR1C1 | [236] |
|  |  | AKR1D1 | [237] |
|  |  | DNAJC1 | - |
|  |  | ASCC3 | - |
| 16 | Breast Carcinoma | HSD3B2 | [238], [239] |
|  |  | HSD17B3 | [94] |
|  |  | UGT1A4 | [240], [241], [242], [243], [244], [245], [246], [247] |
| 17 | Liver carcinoma | HSD17B2 | [248] |
|  |  | HSD17B7 | [249], [250] |
|  |  | HSD3B1 | [251] |
| 18 | Squamous cell carcinoma | PKP2 | [252], [253], [254] |
|  |  | CYP2B6 | - |
|  |  | DSC1 | [255], [256], [257], [258] |
|  |  | PKP3 | [253] |
|  |  | JAML | - |
|  |  | TBXAS1 | - |
|  |  | CYP3A4 | [259], [260], [261], [262] |
|  |  | CYP2C9 | [263], [264], [265], [266], [267] |
|  |  | CD6 | [268], [269] |
| 19 | Colorectal Carcinoma | UGT1A4 | [270] |
|  |  | RTCB | - |
|  |  | UGT1A8 | [271], [100], [103] |
|  |  | UGT1A3 | [272], [273] |
|  |  | C2orf49 | - |
|  |  | ZNRF3 | [274], [275], [276], [277] |
|  |  | TBXAS1 | [108] |
| 20 | Leukemia | DUOXA2 | - |
|  |  | HOXA6 | [278], [279] |
|  |  | HOXB5 | [280], [281], [282] |
|  |  | HOXB6 | [283] , [282] |
|  |  | FBXO45 | - |
|  |  | TCF12 | [284] |
| 21 | Malignant neoplasm of stomach | POGZ | - |
|  |  | PORCN | [285] |
|  |  | TBXAS1 | - |
|  |  | PAX9 | [286] |
|  |  | NAXE | - |
|  |  | FJX1 | - |
|  |  | HGFAC | [287] |
| 22 | Neuroblastoma | DCT | - |
|  |  | POGZ | [288] |
|  |  | PANX1 | [289], [290], [291], [292] |
|  |  | METAP1 | - |
|  |  | PMEL | - |
|  |  | MITF | [293], [294] |
|  |  | RAG2 | - |
|  |  | CNTFR | [295] |
|  |  | NEUROG3 | [296] |
|  |  | BID | [297] |
|  |  | MSRB2 | - |
|  |  | DIABLO | [298] |
|  |  | AIFM1 | [299] |
|  |  | BCL2L1 | [300], [301], [302], [303] |
|  |  | PAX9 | [304] |
| 23 | Pancreatic carcinoma | IL17RA | - |
|  |  | IL25 | - |
|  |  | S100P | [305], [306], [307], [308], [309], [310] |
|  |  | RAG1 | - |
|  |  | DHPS | - |
|  |  | NKX6-1 | - |
|  |  | C1GALT1 | - |
|  |  | BID | - |
|  |  | BTLA | - |
| 24 | Malignant neoplasm of pancreas | IL17RA | - |
|  |  | TRPA1 | [311], [312] |
|  |  | ASCC2 | - |
|  |  | DHPS | [313] |
|  |  | BTLA | [314], [315] |
|  |  | C1GALT1 | [316] |
| 25 | Carcinogenesis | IL17RE | - |
|  |  | IL17B | - |
|  |  | UGT1A10 | [271], [317], [318] |
|  |  | TXN2 | [319], [320], [321] |
|  |  | TBXAS1 | [322] |
|  |  | UGT1A9 | [323], [324], [325] |
|  |  | TCF3 | [326], [327] |
|  |  | GSTM5 | [328], [11] |
| 26 | Carcinoma of lung | SLC24A5 | - |
|  |  | JAML | - |
|  |  | STK3 | [329], [330] |
|  |  | TRPV1 | [331], [332], [333] |
|  |  | ZBTB33 | [334], [335] |
|  |  | NEIL1 | [336] |
|  |  | QTRT2 | - |
|  |  | CD6 | - |
|  |  | CYP2C8 | [337], [338] |
| 27 | Colon Carcinoma | UGT1A4 | [339] |
|  |  | UGT1A10 | [102], [103] |
|  |  | UGT1A3 | [340] |
|  |  | HCST | - |
|  |  | PRDM14 | - |
|  |  | JAML | - |
|  |  | UGT1A8 | [102], [103] |
|  |  | DIABLO | [341], [342] |
|  |  | S100PBP | - |
|  |  | CD6 | - |
|  |  | APPL1 | - |
|  |  | HAVCR2 | [343], [344] |
| 28 | Stomach Carcinoma | CLDN12 | [15] |
|  |  | POGZ | - |
|  |  | LHPP | - |
|  |  | WNT4 | - |
|  |  | PTGIS | - |
|  |  | PORCN | - |
|  |  | WNT8A | - |
| 29 | Central neuroblastoma | POGZ | - |
|  |  | METAP1 | - |
|  |  | PMEL | - |
|  |  | MITF | - |
|  |  | PRDX1 | - |
|  |  | ABCD4 | - |
|  |  | BCL2L1 | [345], [346] |
|  |  | BID | - |
|  |  | IL17RE | - |
| 30 | Primary malignant neoplasm of lung | GSTM5 | - |
|  |  | TNFRSF8 | - |
|  |  | TXN2 | - |
|  |  | SFTPC | [347], [348], [349] |
|  |  | PCSK2 | [350] |
|  |  | CD6 | - |
|  |  | UGT1A3 | - |
|  |  | UGT1A10 | - |
|  |  | NEIL1 | [351] |
| 31 | Mammary Neoplasms | EPHX1 | [352], [353], [354], [355] |
|  |  | TBXAS1 | [322], [356] |
|  |  | HSD3B2 | [94], [238] |
|  |  | SRD5A1 | [357], [358], [359] |
|  |  | TNFRSF18 | - |
|  |  | RERE | [360], [361] |
|  |  | HPGDS | [362] |
|  |  | JAML | - |
|  |  | CYP4A11 | [363] |
|  |  | CYP11B2 | [364], [365], [366], [367] |
|  |  | HSD17B3 | [94] |
|  |  | CD6 | [368] |
| 32 | Colorectal Cancer | UGT1A3 | [270] |
|  |  | RTCB | - |
|  |  | ZBTB8OS | - |
|  |  | UGT1A8 | [271], [369], [103], [104] |
|  |  | C2orf49 | - |
|  |  | RSPO1 | [370], [371], [372] |
|  |  | ZNRF3 | [277], [276], [373] |
|  |  | TBXAS1 | [108] |
|  |  | UGT1A4 | [374], [375] |
| 33 | Non-Small Cell Lung Carcinoma | SPINK6 | - |
|  |  | PUM2 | [376], [377] |
|  |  | PTGDS | [19] |
|  |  | DHPS | - |
|  |  | DIABLO | [378], [221] |
|  |  | PRDM14 | [379], [380], [381] |
|  |  | UGT1A3 | [382] |
|  |  | TSNAX | - |
|  |  | UGT1A10 | [382] |
|  |  | DOHH | - |
|  |  | BBC3 | [383], [384] |
| 34 | Diabetes Mellitus, Non-Insulin-Dependent | NPPC | - |
|  |  | SCG5 | [385] |
|  |  | SGNE1 | [123] |
|  |  | ATP2A1 | [386], [387], [388] |
|  |  | HSD17B6 | - |
|  |  | SELPLG | [389] |
|  |  | CYP24A1 | [390], [391] |
| 35 | Glioma | PCSK2 | - |
|  |  | MLANA | [392], [393] |
|  |  | IL17RE | - |
|  |  | LINGO1 | [394], [395], [396] |
|  |  | POGZ | - |
|  |  | SPINT1 | [397], [398], [399] |
|  |  | ZBTB33 | [400] |
|  |  | BID | - |
|  |  | BCL2L11  | [401], [402] |
| 36 | Leukemia, Myelocytic, Acute | HOXA6 | [278], [403], [279] |
|  |  | HOXC6 | [404], [405], [406] |
|  |  | HOXC5 | [406] |
|  |  | JAML | [407] |
|  |  | TNFRSF8 | [408] |
|  |  | TNFRSF4 | [409], [410], [411] |
|  |  | LGALS9 | [412], [413], [414] |
|  |  | SECTM1 | [415], [416] |
|  |  | DRG1 | - |
|  |  | BID | - |
| 37 | Ovarian Carcinoma | DNAJC1 | - |
|  |  | MFAP2 | - |
|  |  | JAML | - |
|  |  | POGZ | - |
|  |  | ZBTB33 | [417] |
|  |  | FASLG | [418] |
|  |  | TNFSF6 | - |
| 38 | Tumor Progression | HCST | - |
|  |  | JAML | - |
|  |  | TRPV1 | [419], [420], [333] |
|  |  | NCR3 | [152] |
|  |  | DHPS | [421], [422] |
|  |  | MYOCD | - |
|  |  | PANX1 | [423], [424], [425] |
|  |  | IL22RA1 [426] | [427],  |
|  |  | FBLN2 | [428], [429], [430] |
|  |  | METAP1 | [431], [432] |
| 39 | Malignant neoplasm of ovary | DNAJC1 | - |
|  |  | MFAP2 | - |
|  |  | CYP2R1 | [433], [434], [435] |
|  |  | MST1 | [436], [437] |
|  |  | DHPS | - |
|  |  | PSTPIP1 | - |
|  |  | TNFSF9 | [438] |
|  |  | TNLG5A | - |
| 40 | Intellectual Disability | ALG1 | - |
|  |  | PIGP | [439], [440], [441], [442], [443] |
|  |  | PIGM | [444] |
|  |  | KCNJ8 | [445] |

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