Supplementary table IV. List of genes with the highest number of separate fusion partners as a measure of promiscuity. Only the genes with at least 3 different fusion partners were included in the table. Recurrence refers to the number of samples where the gene was observed forming transcript fusions. Role in cancer columns indicates whether the fusion gene is a known oncogene or tumor suppressor gene (TSG) included in COSMIC Cancer Gene Census (CGC).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Fusions** | **Promiscuity** | **Recurrence** | **Role in cancer** | **Literature evidence** |
| RNF213 | NUTM2A-AS1:RNF213; MAFG:RNF213; USP16:RNF213; HELZ2:RNF213 | 4 | 4 |  | RNF213 mutations in circulating DNA differentiate between early stage lung cancer from pulmonary nodules (PMID: 33200540). |
| ZBTB7A | DNAJC11:ZBTB7A; EIF4G2:ZBTB7A; NDST1:ZBTB7A; EXD3:ZBTB7A | 4 | 4 |  | ZBTB7A acts as tumor suppressor by regulating glycolysis. Reduced expression of ZBTB7A correlates with poor survival in colon cancer patients. ZBTB7A tumors show heightened sensitivity to glycolysis inhibition (PMID: 25184678). |
| CCDC91 | CCDC91:USP15; FTX:CCDC91; HIPK1:CCDC91 | 3 | 3 |  | Uknown |
| CERS6 | CERS6:SAP130; CERS6:MTX2; CERS6:IMPA2 | 3 | 3 |  | CERS6 is required for cell migration and metastasis in NSCLC (PMID: 32902157). |
| CHMP1A | TDRP:CHMP1A; MSR1:CHMP1A; CYP24A1:CHMP1A | 3 | 3 |  | CHMP1A acts as a tumor suppressor gene in that inhibits proliferation of renal cell carcinoma (PMID: 22261332). |
| CHST11 | CHST11:SUCLG2; CHST11:BICD1; CHST11:MAPKAPK5 | 3 | 3 |  | CHST11 plays a role in the induction of epithelial-to-mesenchymal transition and stem cell-like properties in breast cancer (PMID: 32344408). |
| HIF1A | CHIC2:HIF1A; HIF1A:PRKCH; HIF1A:TNPO2 | 3 | 3 |  | HIF1 is key factor involved in the metabolic switch in cancer tissues from oxidative phosphorylation to aerobic glycolysis (PMID: 33791987). |
| INPP4A | INPP4A:VWA3B; INPP4A:TTC3; INPP4A:RAPGEF1 | 3 | 3 |  | Lower nuclear localization of INPP4A correlates with increased cancerous growth, moreover constitutive expression of this gene leads to massive apoptosis (PMID: 30071275). |
| ITCH | RALY:ITCH; BCL2L1:ITCH; ITCH:ZNF217 | 3 | 3 |  | Circular RNA cir-ITCH promotes cell invasion and migration in osteosarcoma (PMID: 31960764). |
| MAD1L1 | MAD1L1:NBPF19; DNAAF5:MAD1L1; EIF3B:MAD1L1 | 3 | 3 |  | Gain of a region on 7p22.3, containing MAD1L1, is the most frequent event in small-cell lung cancer cell lines (PMID: 16130125). |
| MKL1 | MKL1:PVT1; MKL1:RHOT1; MKL1:MTFR1 | 3 | 3 |  | MKL1 potentiates lung cancer cell migration and invasion by epigenetically activating MMP9 transcription (PMID: 25746000). |
| MROH1 | MROH1:ZNF395; ABT1:MROH1; COL23A1:MROH1 | 3 | 3 |  | Unknown |
| N4BP2L2 | USP12:N4BP2L2; TRAPPC9:N4BP2L2; N4BP2L2:SH3BGRL | 3 | 3 |  | Unknown |
| NFIB | ENPP2:NFIB; CD302:NFIB; GPATCH2L:NFIB | 3 | 3 |  | NFIB promotes the migration and progression of kidney renal clear cell carcinoma by regulating PINK1 transcription (PMID: 33981484). |
| NPEPPS | AGPAT6:NPEPPS; ITFG3:NPEPPS; NPEPPS:SLC7A11 | 3 | 3 |  | Unknown |
| PCNX | ZFYVE28:PCNX; PCNX:SPTLC2; PCNX:SYNJ2BP-COX16 | 3 | 3 |  | PCNX-3' UTR promotes cell growth, proliferation and cell cycle progression, and suppresses apoptosis of lung cancer cells (PMID: 28789966). |
| PPP1R12C | PPP1R12C:SLC6A3; PPP1R12C:TNK2; PPP1R12C:SPPL2B | 3 | 3 |  | Unknown |
| PTPRF | PTPRF:CSMD2; ACSF3:PTPRF; ATXN2L:PTPRF | 3 | 3 |  | PTPRF as a novel tumor suppressor through deactivation of ERK1/2 signaling in gastric adenocarcinoma (PMID: 30464527). |
| RHOT1 | RHOT1:UTP6; SLFN5:RHOT1; MKL1:RHOT1 | 3 | 3 |  | Propofol suppresses non-small cell lung cancer tumorigenesis by regulation of circ-RHOT1/miR-326/FOXM1 axis (PMID: 33515563). |
| SVIL | LCOR:SVIL; SVIL:ZNF292; SVIL:MTPAP | 3 | 3 |  | SVIL promotes tumor angiogenesis in liver cancer (PMID: 32468064). |
| TBL1XR1 | TBL1XR1:COL14A1; NSUN3:TBL1XR1; TBL1XR1:KDM6A | 3 | 3 | Oncogene, TSG | TBL1XR1 is involved in c-Met-mediated tumorigenesis of human nonsmall cell lung cancer (PMID: 31243347). |
| TMCC1 | TMCC1:HMCES; TMCC1:CNBP; MIR205HG:TMCC1 | 3 | 3 |  | Unknown |
| TRAPPC9 | RSF1:TRAPPC9; TRAPPC9:N4BP2L2; CLK3:TRAPPC9 | 3 | 3 |  | Elevated NIBP/TRAPPC9 mediates tumorigenesis of cancer cells through NFκB signaling (PMID: 25704885). |
| ZBTB20 | CD96:ZBTB20; ZBTB20:BRAF; ATG3:ZBTB20 | 3 | 3 | Oncogene | Zinc finger protein ZBTB20 promotes cell proliferation in non-small cell lung cancer through repression of FoxO1 (PMID: 25311537). |