Table SI. Representative examples of snoRNA functions and mechanisms in human cancers.

| Cancer | snoRNAs | Expression | Function | Mechanisms | (Refs.) |
|---|---|---|---|---|---|
| CRC | SNORA28 | Upregulated | Promotes proliferation and confers radioresistance. | Recruits BRD4 to increase H3K9 acetylation at the LIFR promoter and activates JAK1/STAT3 signaling. | (64) |
|  | SNORA56 | Upregulated | Inhibits ferroptosis and promotes survival. | Guides pseudouridylation of 28S rRNA at U1664 to facilitate GCLC translation. | (65) |
|  | SNORD11B | Upregulated | Enhances ribosome biogenesis, suppresses let-7a. | Mediates 2′-O-methylation of 18S rRNA (G509) and MIRLET7A1HG (G225). | (66) |
|  | SCARNA12 | Upregulated | Accelerates CRC progression. | Activates PI3K/AKT pathway. | (67) |
|  | SNORA21 | Upregulated | Enhances proliferation, invasion, and migration. | Regulates Hippo and Wnt signaling pathways. | (68) |
|  | SNORA24 | Upregulated | Promotes proliferation and xenograft tumor growth. | Promotes $G_1$/S phase transition and modulates p53 stability via the ubiquitin-proteasome pathway. | (69) |
|  | SNORA71A | Upregulated | Promotes proliferation, migration, and invasion. | Modulates NF-κB and Toll-like receptor pathways. | (71) |
|  | SNORD12C<br>SNORD78 | Upregulated | Promote migration and survival. | Mediate 2’-O-methylation of 28S rRNA and stabilize EIF4A3 and LAMC2. | (72) |
|  | SNORD1C | Upregulated | Enhances stemness and metastasis. | Suppression reduces β-catenin/TCF7 expression. | (73) |
|  | SNORD44 | Downregulated | Suppresses tumor progression. | Modulates the PI3K/Akt signaling pathway. | (74) |
| HCC | SNORA55 | Upregulated | Reprograms metabolism. | Disrupts oxidative phosphorylation by targeting ATP synthase subunits ATP5A1 and ATP5B. | (81) |
|  | SNORD17 | Upregulated | Enhances growth and tumorigenicity. | Sequesters NPM1/MYBBP1A in nucleolus, suppressing p53 activation. | (87) |
|  | SNORD88B | Upregulated | Regulates liver CSC self-renewal. | Regulates Hippo signaling pathway. | (91) |
|  | SNORD126 | Upregulated | Drives proliferation. | Activates PI3K/AKT/mTOR signaling via phosphorylation of AKT (Ser473), GSK-3β (Ser9), and p70S6K. | (82-84) |

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|---|---|---|---|---|---|
| | snoU2_19 | Upregulated | Promotes aggressive phenotypes. | Relocates β-catenin to cytoplasm, disrupting Wnt/β-catenin signaling. | (85) |
| | SNORA18L5 | Upregulated | Facilitates proliferation. | Alters RPL5/RPL11 localization, promoting MDM2-mediated p53 degradation. | (88) |
| | ACA11 | Upregulated | Enhances proliferation, migration, and invasion. | Activates PI3K/AKT signaling pathway. | (84) |
| | SNORD76 | Upregulated | Enhances proliferation and invasion. | Activates Wnt/β-catenin pathway. | (86) |
| | SNORD52 | Upregulated | Promotes tumorigenesis. | Elevates and stabilizes CDK1 levels. | (90) |
| | SNORA42 | Upregulated | Drives proliferation and suppresses apoptosis. | Modulates p53 signaling and facilitates cell cycle progression. | (89) |
| | SNORA24 | Upregulated | Promotes ribosome fidelity. | Guides pseudouridylates at 18S rRNA positions 609 and 863. | (93) |
| | SNORD72 | Upregulated | Enhances proliferation, colony formation, and invasion. | Stabilizes ID2 mRNA and counteractes lncRNA-LALR1-mediated suppression. | (92) |
| | SNORA23 | Downregulated | Suppresses tumor progression. | Guides 2′-O-methylation of 28S rRNA (C4506) and inhibits 4EBP1 phosphorylation. | (94) |
| GC | SNORD113-1 | Downregulated | Suppresses tumor progression. | Inactivates the MAPK/ERK and TGF-β signaling pathways. | (101) |
| | SNORA37 | Upregulated | Promotes proliferation, invasion and metastasis. | Interacts with CMTR1 and modulates CD44 alternative splicing. | (106) |
| | SNORD105B | Upregulated | Enhances proliferation. | Interacts with ALDOA and activates c-Myc signaling. | (107) |
| | SNORD88C | Upregulated | Promotes proliferation and metastasis. | Guides 2'-O-methylation of 28S ribosomal RNA (C3680) and enhances SCD1 translation. | (110) |
| NSCLC | SNORA42 | Upregulated | Regulates apoptosis. | Modulates p53-dependent apoptotic mechanism. | (111) |
| | SNORA71A | Upregulated | Stimulates growth, invasiveness and metastasis. | Activates MEK/ERK pathway. | (112) |
| | SNORA38B | Upregulated | Promotes immunosuppression and growth. | Activates GAB2/AKT/mTOR pathway and recruits regulatory T cells. | (114) |
| BC | SNORA71A | Upregulated | Facilitates proliferation, migration, invasion, and EMT. | Interacts with G3BP1, stabilizes ROCK2 and modulates TGF-β signaling. | (122) |

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|---|---|---|---|---|---|
| | U50A | Upregulated | Diminishes everolimus sensitivity. | Downregulates c-Myc and mTOR. | (127) |
| | SNORA68 | Upregulated | Enhances stemness, tumorigenesis. | Binds to U2AF2, increases nucleolar RPL23 retention, and upregulates c-Myc. | (123) |
| | SNORA51 | Upregulated | Maintains stem cell-like properties. | Reduces nucleolar RPL3 expression and increases c-MYC expression. | (124) |
| | SNORD50A/B | Homozygous deletion (p53-WT) | Inhibits proliferation, induces apoptosis. | Degrades p53 via TRIM21-GMPS interaction pathway. | (120) |
| OC | SNORA70E | Upregulated | Promotes tumor progression. | Pseudouridylates RAP1B and regulates alternative splicing of PARPBP. | (133) |
| | SNORA72 | Upregulated | Enhances stemness and migration. | Activates Notch1/c-Myc signaling axis. | (134) |
| | SNORD89 | Upregulated | Promotes proliferation, invasion, migration. | Upregulates c-Myc and Notch1 expression. | (135) |
| | SNORA73B | Upregulated | Promotes proliferation, migration and invasion. | Pseudouridylates MIB1 mRNA, activates Notch signaling and regulates RCC1 splicing. | (139) |
| EC | SNORD60 | Upregulated | Drives tumor progression. | Binds fibrillarin, methylates PIK3CA mRNA and enhances PI3K/AKT/mTOR activation. | (140) |
| | SNORD89 | Upregulated | Inhibits apoptosis. | Mediates 2'-O-methylation of Bim mRNA to disrupt Bcl-2/Bax balance. | (141) |
| | SNORD15B | Upregulated | Enhances proliferation, invasion, and migration. | Promotes TRIM25 upregulation and cytoplasmic p53 accumulation. | (144) |
| | SNORD104 | Upregulated | Accelerates tumor growth. | Guides 2'-O-methylation of PARP1 mRNA. | (142) |
| Glioma | U3 snoRNA | Upregulated | Promotes aerobic glycolysis, and proliferation. | Establishes U3/ZBTB7A/HK2/LDHA axis. | (145) |
| | SNORD88C | Upregulated | Enhances proliferation, migration, invasion. | Modulates DNA/RNA-related processes. | (148) |
| | SNORA71B | Upregulated | Promotes proliferation, invasion, migration. | Downregulates of mesenchymal and cell cycle markers. | (149) |

Presentation of selected representative examples of both oncogenic (upregulated) and tumor-suppressive (downregulated/deleted) snoRNAs, focusing primarily on their *in vitro* and *in vivo* mechanistic evidence.

snoRNA, small nucleolar RNA; SNORA, H/ACA box snoRNA; SNORD, C/D box snoRNA; sdRNA, snoRNA-derived fragment; SCARNA, small Cajal body-specific RNA; CRC, colorectal cancer; HCC, hepatocellular carcinoma; GC, gastric cancer; NSCLC, non-small cell lung cancer; BC, breast cancer; OC, ovarian cancer; EC, endometrial cancer; LUAD, lung adenocarcinoma; TNBC, triple-negative breast cancer; ESCA, esophageal cancer; PDAC, pancreatic ductal adenocarcinoma; rRNA, ribosomal RNA; lncRNA, long non-coding RNA; BRD4, bromodomain-containing protein 4; LIFR, leukemia inhibitory factor receptor; STAT3, signal transducer and activator of transcription 3; GCLC, glutamate-cysteine ligase catalytic subunit; PI3K/AKT, phosphoinositide 3-kinase/protein kinase B; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; EIF4A3, eukaryotic initiation factor 4A-III; LAMC2, laminin subunit gamma 2; TCF7, transcription factor 7; ATP, adenosine triphosphate; NPM1, nucleophosmin 1; MYBBP1A, MYB binding protein 1a; MDM2, mouse double minute 2 homolog; CDK1, cyclin-dependent kinase 1; CSC, cancer stem cell; mTOR, mechanistic target of rapamycin; GSK-3β, glycogen synthase kinase 3 beta; p70S6K, ribosomal protein S6 kinase beta-1; ID2, inhibitor of DNA binding 2; LALR1, liver-specific abundant lncRNA 1; 4EBP1, eukaryotic translation initiation factor 4E-binding protein 1; MAPK/ERK, mitogen-activated protein kinase/extracellular signal-regulated kinase; TGF-β, transforming growth factor-β; CMTR1, cap methyltransferase 1; ELAVL1, ELAV-like RNA binding protein 1; ALDOA, aldolase A; CHK1, checkpoint kinase 1; PERP, TP53 apoptosis effector; SRPK1, serine/arginine-rich protein-specific kinase 1; SCD1, stearoyl-CoA desaturase-1; GAB2, GRB2-associated binding protein 2; EMT, epithelial-mesenchymal transition; G3BP1, G3BP stress granule assembly factor 1; ROCK2, Rho-associated coiled-coil containing protein kinase 2; U2AF2, U2 small nuclear RNA auxiliary factor 2; RPL, ribosomal protein L; TRIM, tripartite motif containing; GMPS, guanosine monophosphate synthetase; RAP1B, RAP1B, member of RAS oncogene family; PARPBP, PARP1 binding protein; METTL3, methyltransferase like 3; IGF2BP2, insulin-like growth factor 2 mRNA binding protein 2; NFYA, nuclear transcription factor Y subunit alpha; MIB1, mindbomb E3 ubiquitin protein ligase 1; RCC1, regulator of chromosome condensation 1; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PARP1, poly(ADP-ribose) polymerase 1; HK2, hexokinase 2; LDHA, lactate dehydrogenase A.

Table SII. snoRNAs as clinical biomarkers and therapeutic targets in human cancers.

| Cancers | snoRNA | Expression | Biomarker type | Sample type | Clinical relevance | (Refs.) |
|---|---|---|---|---|---|---|
| CRC | SNORA28 | Upregulated | Prognostic | Tissue | High expression correlates with poor prognosis and confers radioresistance. | (64) |
| | SNORA51 | Upregulated | Diagnostic | Fecal samples | Potential non-invasive screening marker, especially in FIT$^+$ patients | (76) |
| | SNORD1C | Upregulated | Diagnostic | Serum | AUC=0.748 for CRC vs. controls; combined with CEA improves AUC to 0.838 | (78) |
| | SNORD57 | Upregulated | Diagnostic | Serum | Sensitive biomarker for early CRC detection | (79) |
| | SNORA33 | Upregulated | Diagnostic | Serum | Levels correlate with vascular invasion; decrease after resection | (80) |
| | SNORD15B, SNORA5C | Upregulated | Prognostic | Tissue | Independent prognostic markers associated with lymphatic invasion and colon polyp history | (77) |
| | SNORA13 | Upregulated | Therapeutic | N/A | ASO-mediated inhibition synergizes with 5-FU, enhancing antitumor effect | (174) |
| HCC | SNORA47 | Upregulated | Prognostic | Tissue | High expression correlates with poor OS and high recurrence rate | (96) |
| | SNORD78 | Upregulated | Prognostic | Tissue | Associated with increased tumor burden, advanced stage, and distant metastasis | (97) |
| | SNORA71A | Downregulated | Prognostic | Tissue | Reduced expression predicts higher recurrence risk and reduced OS | (102) |
| | SNORD113-1 | Downregulated | Prognostic | Tissue | Decreased expression associated with worse survival outcomes | (101) |
| | SNORA11, SNORD124, SNORD46 | Variable | Diagnostic/ Prognostic | Tissue | Linked to spliceosome and Notch signaling; robust diagnostic utility | (103) |
| | SNORD88B | Upregulated | Therapeutic | N/A | ASO-mediated inhibition reduces tumor burden in PDX models | (91) |

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|---|---|---|---|---|---|---|
| NSCLC | SNORA74A | Upregulated | Therapeutic | N/A | ASO targeting SNORA74A shows significant therapeutic efficacy in preclinical models | (172) |
| | SNORD42B,<br>SNORD111 | Upregulated | Diagnostic | Plasma | Early-stage detection; potential non-invasive biomarkers | (115) |
| | SNORD83A | Upregulated | Diagnostic | Plasma | Combined with CEA enhances early-stage diagnostic capability | (116) |
| | SNORA21 | Upregulated | Diagnostic/ Prognostic | Tissue | Identified by NGS as potential biomarker for early detection and prognosis | (118) |
| | SNORD60 (in LUAD) | Upregulated | Diagnostic | Tissue | 74.2% sensitivity, 75.3% specificity for LUAD detection | (117) |
| | SNORD116,<br>SNORA21 | Downregulated (exosomal) | Diagnostic | Serum exosomes | AUC=0.738 and 0.761; combined with CYFRA21-1/CEA gives AUC=0.917 | (167) |
| | SNORA38B | Upregulated | Therapeutic | N/A | LNA targeting SNORA38B enhances CD8$^+$ T-cell infiltration and sensitizes to ICB | (114) |
| BC | SNORD16,<br>SNORA73B,<br>SCARNA4,<br>SNORD49B | Upregulated | Diagnostic | Tissue/Plasma | AUC=0.7521 for BC detection; early-stage AUC=0.7305 | (130) |
| | SNORD33 | Upregulated | Predictive | Plasma | Circulating levels correlate with platinum-based chemotherapy response in TNBC | (132) |
| | 6-snoRNA signature (SNORD93, SNORA16A, SNORD113-6, SNORA7A, SNORA57, SNORA18A) | Variable | Prognostic | Tissue | Discriminates locoregional metastasis and predicts clinical outcomes | (129) |
| | SNORA38 | Upregulated | Prognostic | Tissue | Associated with advanced disease, poor OS, and OCT4 expression | (131) |

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|---|---|---|---|---|---|---|
| | SNORD50A/B | Homozygous deletion | Prognostic | Tissue | Deletion inhibits proliferation and induces apoptosis in p53-WT BC | (120) |
| OC | 9-snoRNA signature (SNORA11B, SNORA36C, SNORA58, SNORA70J, SNORA75B, SNORD105B, SNORD126, SNORD3C, SNORD89) | Variable | Prognostic | Tissue | Independent predictor of OC outcomes | (138) |
| | SNORA81, SNORA19, SNORA56 | Upregulated | Diagnostic | Tissue | Distinguish HGSOC from serous borderline tumors and normal tissues | (137) |
| EC | SNORD89 | Upregulated | Prognostic | Tissue | Elevated in tumors with lymph node metastasis | (141) |
| Glioma | 7-snoRNA signature (SNORA32, SNORA36B, SCARNA15, SNORA63E, SNORA63D, SNORD88C, SNORD38A) | Variable | Prognostic | Tissue | Predicts survival in LGG patients with high sensitivity and specificity | (148) |
| | 5-methylated-snoRNA signature (SNORA14B, SNORD113-4, SNORA71B, SNORA80B, SNORD97) | Variable | Prognostic | Tissue | Independent prognostic indicator for glioma | (149) |
| RCC | SNORD15A, SNORD35B, SNORD60 | Upregulated | Diagnostic | Tissue/urine | AUC=0.7421 for RCC vs. controls; early-stage AUC=0.7465 | (151) |

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|---|---|---|---|---|---|---|
| | SNORD63 | Upregulated | Diagnostic | Urine | AUC=0.7055 | (152) |
| | SNORD96A | Upregulated | Diagnostic | Plasma | AUC=0.8909 | (152) |
| | 6-snoRNA panel (SNORA2, SNORD116-2, SNORA59B, SNORD93, SNORD12B, SNORA70B) | Upregulated | Prognostic | Tissue | Combined with TNM stage (AUC=0.792) or Fuhrman grade (AUC=0.800) outperforms clinical parameters alone | (153) |
| ESCA | SNORA58, SNORA68, SNORD93 | Upregulated | Diagnostic | TEPs | AUC=0.846 for ESCA; early-stage AUC=0.857 | (160) |
| | SNORA80B | Upregulated | Therapeutic | N/A | Inhibitor clinofibrate synergizes with cisplatin to overcome chemotherapy resistance | (159) |
| PDAC | SNORA23 | Upregulated | Therapeutic | N/A | ASO-mediated silencing impedes tumor progression in PDX models | (173) |
| | WASF2, ARF6, SNORA74A, SNORA25 | Upregulated | Diagnostic | Plasma exosomes | AUC >0.9, surpassing CA19-9 (0.897); early-stage detection (stage 0-IIA) AUC >0.9 | (168) |

snoRNA, small nucleolar RNA; SNORA, H/ACA box snoRNA; SNORD, C/D box snoRNA; FIT, fecal immunochemical test; CRC, colorectal cancer; SCARNA, small Cajal body-specific RNA; HCC, hepatocellular carcinoma; GC, gastric cancer; NSCLC, non-small cell lung cancer; BC, breast cancer; TNBC, triple-negative breast cancer; OC, ovarian cancer; HGSOC, high-grade serous ovarian carcinoma; EC, endometrial cancer; RCC, renal cell carcinoma; ESCA: esophageal cancer; PDAC, pancreatic ductal adenocarcinoma; LUAD, lung adenocarcinoma; CEA, carcinoembryonic antigen; AUC, area under the curve; ASO, antisense oligonucleotide; 5-FU, 5-fluorouracil; OS, overall survival; PDX, patient-derived xenograft; CYFRA21-1, cytokeratin 19 fragment 21-1; LNA, locked nucleic acid; NGS, next-generation sequencing; ICB, immune checkpoint blockade; TNM, tumor, node, metastasis; TEPs, tumor-educated platelets; OCT4, octamer-binding transcription factor 4; N/A, not applicable.