The potential role of small nucleolar RNAs in cancers

- an evidence map

(Supplementary materials)

Content

Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Cui C	NSCLC	SNORA65, SNORA7A, SNORA7B	NOP10 predicts lung cancer prognosis and its associated small nucleolar RNAs drive proliferation and migration
Liu Z	HCC	SNORA23	SNORA23 inhibits HCC tumorigenesis by impairing the 2'-O-ribose methylation level of 28S rRNA
Shang X	ccRCC	SNORD63, SNORD96A	SNORD63 and SNORD96A as the non-invasive diagnostic biomarkers for clear cell renal cell carcinoma
Dong X	NSCLC	SNORD55	Tumor-educated platelet SNORD55 as a potential biomarker for the early diagnosis of non-small cell lung cancer
Su X	BC	SNORD50A, SNORD50B	The noncoding RNAs SNORD50A and SNORD50B-mediated TRIM21-GMPS interaction promotes the growth of p53 wild-type breast cancers by degrading p53
He JY	Colon cancer	SNORD16	Small Nucleolar RNA, C/D Box 16 (SNORD16) Acts as a Potential Prognostic Biomarker in Colon Cancer
Li C	HCC	SNORD52	The C/D box small nucleolar RNA SNORD52 regulated by Upf1 facilitates Hepatocarcinogenesis by stabilizing CDK1
Roychowdhury A	Cervical carcinoma	SNORD97, SNORD3A, SNORD3C, SNORD3D, SNORA12, SCARNA9	Deregulation of H19 is associated with cervical carcinoma
Guerrieri AN	BC	SNORA67	DKC1 Overexpression Induces a More Aggressive Cellular Behavior and Increases Intrinsic Ribosomal Activity in Immortalized Mammary Gland Cells

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Zhang L	OC	SNORA72	SNORA72 Activates the Notch1/c-Myc Pathway to Promote Stemness Transformation of Ovarian Cancer Cells
Mao LH	HCC	SNORD72	LncRNA-LALR1 upregulates small nucleolar RNA SNORD72 to promote growth and invasion of hepatocellular carcinoma
Xia XR	Glioma	SNORD44	Effects of small nucleolar RNA SNORD44 on the proliferation, apoptosis and invasion of glioma cells
Ding Y	HCC	SNORD31	Revealing the clinical significance and prognostic value of small nucleolar RNA SNORD31 in hepatocellular carcinoma
Zhang Z	CRC	SNORA71A	SNORA71A Promotes Colorectal Cancer Cell Proliferation, Migration, and Invasion
Pauli C	AML	SNORD42A	Site-specific methylation of 18S ribosomal RNA by SNORD42A is required for acute myeloid leukemia cell proliferation
Wu H	CRC	SNORD12C, SNORD78	Long noncoding RNA ZFAS1 promoting small nucleolar RNA-mediated 2'-O-methylation via NOP58 recruitment in colorectal cancer
Godel M	Osteosarcoma	SNORD3A, SNORA13, SNORA28	Small Nucleolar RNAs Determine Resistance to Doxorubicin in Human Osteosarcoma
Ding Y	HCC	SNORA71A	Identification of snoRNA SNORA71A as a Novel Biomarker in Prognosis of Hepatocellular Carcinoma
Duan S	BC	SNORA71B	SNORA71B promotes breast cancer cells across blood-brain barrier by inducing epithelial-mesenchymal transition
Oliveira V	MM	ACA11	The snoRNA target of t(4;14) in multiple myeloma regulates ribosome biogenesis
McMahon M	SH-HCC	SNORA24	A single H/ACA small nucleolar RNA mediates tumor suppression downstream of oncogenic RAS
Kitagawa T	PDAC	SNORA74A, SNORA25	Circulating pancreatic cancer exosomal RNAs for detection of pancreatic cancer

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Li Y	GC	SNORA42,SNORA74A,SNORD10	SRPK1 facilitates tumor cell growth via modulating the small nucleolar RNA expression in gastric cancer
Wang X	GC	U66, ACA47, ACA10, E2, SNORA58, HBII-316, U70, U8	Identification of Eight Small Nucleolar RNAs as Survival Biomarkers and Their Clinical Significance in Gastric Cancer
Qin Y	Gallbladder cancer	SNORA21	Overexpression of SNORA21 suppresses tumorgenesis of gallbladder cancer in vitro and in vivo
Sun Y	BC	SNORA7B	H/ACA box small nucleolar RNA 7B acts as an oncogene and a potential prognostic biomarker in breast cancer
Zhu W	OC	SNORA2B, SNORD19, SNORD116-4, SNORD89	SNORD89 promotes stemness phenotype of ovarian cancer cells by regulating Notch1-c-Myc pathway
Tang G	NSCLC	SNORA71A	Small Nucleolar RNA 71A Promotes Lung Cancer Cell Proliferation, Migration and Invasion via MAPK/ERK Pathway
Zhang C	GC	SNORD105B	C/D-Box Snord105b Promotes Tumorigenesis in Gastric Cancer via ALDOA/C-Myc Pathway
Yi C	PCa	SNORA42	SNORA42 enhances prostate cancer cell viability, migration and EMT and is correlated with prostate cancer poor prognosis
Liu CX	GC	SNORA21	The SNORA21 expression is upregulated and acts as a novel independent indicator in human gastric cancer prognosis
Wang H	HCC	snoU2_19	Small nucleolar RNA U2_19 promotes hepatocellular carcinoma progression by regulating Wnt/β-catenin signaling
Yang Y	OC	SNORD114-10	Preliminary screening and identification of differentially expressed metastasis-related ncRNAs in ovarian cancer
Cao P	HCC	SNORA18L5	Germline Duplication of SNORA18L5 Increases Risk for HBV-related Hepatocellular Carcinoma by Altering Localization of Ribosomal Proteins and Decreasing Levels of p53

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Zhou F	Leukaemia	SNORD14D, SNORD34, SNORD35A, SNORD43, SNORD53, SNORD104	AML1-ETO requires enhanced C/D box snoRNA/RNP formation to induce self-renewal and leukaemia
Li G	HCC	SNORA47	Small nucleolar RNA 47 promotes tumorigenesis by regulating EMT markers in hepatocellular carcinoma
Savelyeva AV	NSCLC	U1, U5, U6	Variety of RNAs in Peripheral Blood Cells, Plasma, and Plasma Fractions
Siprashvili Z	Melanoma, NSCLC	SNORD50A, SNORD50B	The noncoding RNAs SNORD50A and SNORD50B bind K-Ras and are recurrently deleted in human cancer
Su Y	NSCLC	SNORD66, SNORD78	Small non-coding RNA biomarkers in sputum for lung cancer diagnosis
Crea F	PCa	SNORA55	Integrated analysis of the prostate cancer small-nucleolar transcriptome reveals SNORA55 as a driver of prostate cancer progression
Xu G	HCC	SNORD113-1	Small nucleolar RNA 113-1 suppresses tumorigenesis in hepatocellular carcinoma
Mannoor K	NSCLC	SNORA3, SNORA42	Small nucleolar RNA signatures of lung tumor-initiating cells
Chu L	MM	ACA11	Multiple myeloma-associated chromosomal translocation activates orphan snoRNA ACA11 to suppress oxidative stress
Valleron W	Acute leukemia	SNORD114-1	Specific small nucleolar RNA expression profiles in acute leukemia
Valleron W	PTCL	U3, HBII-239, U59B, U90, HBII-438A, U80	Small nucleolar RNA expression profiling identifies potential prognostic markers in peripheral T-cell lymphoma
HE Gee	BC、HNSCC	RNU44, RNU43, RNU48, RNU6B	The small-nucleolar RNAs commonly used for microRNA normalisation correlate with tumour pathology and prognosis
Liao J	NSCLC	SNORD33, SNORD66, SNORD76	Small nucleolar RNA signatures as biomarkers for non-small-cell lung cancer
Dong XY	BC	snoRNA U50	Implication of snoRNA U50 in human breast cancer.

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Dong XY	PCa	snoRNA U50	SnoRNA U50 is a candidate tumor-suppressor gene at 6q14.3 with a mutation associated with clinically significant prostate cancer.
Wu L	HCC	ACA11	Small nucleolar RNA ACA11 promotes proliferation, migration and invasion in hepatocellular carcinoma by targeting the PI3K/AKT signaling pathway.
Ma P	HCC	SNORD78	Up-regulation of small nucleolar RNA 78 is correlated with aggressive phenotype and poor prognosis of hepatocellular carcinoma
Fang X	HCC、CRC	SNORD126	SNORD126 promotes HCC and CRC cell growth by activating the PI3K-AKT pathway through FGFR2
Gao L	NSCLC	SNORA47, SNORA68, SNORA78, SNORA21, SNORD28, SNORD66	Genome-wide small nucleolar RNA expression analysis of lung cancer by next-generation deep sequencing
Su J	NSCLC	SNORA80E, SNORD33, SNORD66, SNORD78	Analysis of small nucleolar RNAs in sputum for lung cancer diagnosis
Langhendries JL	NSCLC、BC	U3、U8	The human box C/D snoRNAs U3 and U8 are required for pre-rRNA processing and tumorigenesis
Blenkiron C	BC	SNORD29, SNORD34, SNORD68, SNORD33	Links between the oncoprotein YB-1 and small non-coding RNAs in breast cancer
Su H	BC	-	Elevated snoRNA biogenesis is essential in breast cancer
Patterson DG	BC	snoRNA-93	Human snoRNA-93 is processed into a microRNA-like RNA that promotes breast cancer cell invasion
Mei YP	NSCLC	SNORA42	Small nucleolar RNA 42 acts as an oncogene in lung tumorigenesis
Xu B	Glioblastoma	SNORD47	SNORD47, a box C/D snoRNA, suppresses tumorigenesis in glioblastoma
Okugawa Y	CRC	SNORA42	Clinical significance of SNORA42 as an oncogene and a prognostic biomarker in colorectal cancer

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Yoshida K	CRC	SNORA21	SNORA21—an oncogenic small nucleolar RNA, with a prognostic biomarker potential in human colorectal cancer
Yang X	CRC	SNORA15, SNORA41, SNORD33	SnoRNAs are involved in the progression of ulcerative colitis and colorectal cancer
Chen L	Glioblastoma	SNORD76	SNORD76, a box C/D snoRNA, acts as a tumor suppressor in glioblastoma
Wu L	HCC	SNORD76	Clinical significance of C/D box small nucleolar RNA U76 as an oncogene and a prognostic biomarker in hepatocellular carcinoma.
Martens-Uzunova ES	PCa	SNORD78	C/D-box snoRNA-derived RNA production is associated with malignant transformation and metastatic progression in prostate cancer
Cui L	PDAC	SNORA23	Small nucleolar noncoding RNA SNORA23, up-regulated in human pancreatic ductal adenocarcinoma, regulates expression of spectrin repeat-containing nuclear envelope 2 to promote growth and metastasis of xenograft tumors in mice.
Zou AE	HNSCC	SNORD35B	Transcriptome sequencing uncovers novel long noncoding and small nucleolar RNAs dysregulated in head and neck squamous cell carcinoma
Krell J	CRC	U44,U47	Growth arrest-specific transcript 5 associated snoRNA levels are related to p53 expression and DNA damage in colorectal cancer.
Yuan S	CRC	SNORD44	An oncolytic adenovirus expressing SNORD44 and GAS5 exhibits antitumor effect in colorectal cancer cells
Teittinen KJ	Leukemic	-	Expression of small nucleolar RNAs in leukemic cells
Ronchetti D	CLL	SNORA74A, SNORD116-18, SNORD56	Small nucleolar RNAs as new biomarkers in chronic lymphocytic leukemia

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Berquet L	CLL	SNORA12,SNORA22,SNORA27,SNORA56,SNORA70,SNORD1A,SNORD,SNORD105B,SCARNA8,SNORA80	Small nucleolar RNA expression profiles refine the prognostic impact of IGHV mutational status on treatment-free survival in chronic lymphocytic leukaemia
Boone DN	BC	SNORA17, SNORA43	SNHG7 is a lncRNA oncogene controlled by Insulin-like Growth Factor signaling through a negative feedback loop to tightly regulate proliferation
Schulten HJ	BC	SNORA1,SNORA2A,SNORA9,SNORA10,SNORA22,SNORA24,SNORA30,SNORA37,SNORA38,SNORA52,SNORA71A,SNORA71B,SNORA71C,SNORD13P2,SNORD15A,SNORD34,SNORD35A,SNORD41,SNORD53,SCARNA22	Comprehensive molecular biomarker identification in breast cancer brain metastases
Krishnan P	BC	SNORD46, SNORD89	Profiling of small nucleolar RNAs by next generation sequencing:Potential new players for breast cancer prognosis
Gong J	NSCLC、BC	SNORD46	A pan-cancer analysis of the expression and clinical relevance of small nucleolar RNAs in human cancer
Yu F	BC	SNORD28, SNORD25	p53 represses the oncogenic Sno-MiR-28 derived from a SnoRNA
Zhao Y	Renal clear cell carcinoma	SNORA2, SNORD12B, SNORA59B, SNORA70B, SNORD93, SNORD116-2	Expression signature of six-snoRNA serves as novel non-invasive biomarker for diagnosis and prognosis prediction of renal clear cell carcinoma
Kothari C	BC	SNORD115,SNORD114	Identification of a gene signature for different stages of breast cancer development that could be used for early diagnosis and specific therapy

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Liu Y	CRC	SNORD1C	Overexpression of small nucleolar RNA SNORD1C is associated with unfavorable outcome in colorectal cancer
Zheng D	NSCLC	SNORD78	Small nucleolar RNA 78 promotes the tumorigenesis in non-small cell lung cancer
Li H	GBM	SNORD76	SnoRNA SNORD76 is downregulated in glioblastoma and inhibits cell proliferation through cyclinD1 and p21
Shan Y	ESCC	SNORA42	SNORA42 promotes oesophageal squamous cell carcinoma development through triggering the DHX9/p65 axis
Qiao S	HCC	snoRA23	snoRNA23 enhances the progression of hepatocellular carcinoma via regulation of the Wnt/?-catenin pathway
Hu T	BC	SNORA71A	Small nucleolar RNA SNORA71A promotes epithelial-mesenchymal transition by maintaining ROCK2 mRNA stability in breast cancer
Li JN	BC	U50A（SNORD50A）	Expression of SnoRNA U50A Is Associated with Better Prognosis and Prolonged Mitosis in Breast Cancer
Wang G	HCC	SNORA42	Small nucleolar RNA 42 promotes the growth of hepatocellular carcinoma through the p53 signaling pathway
Liang J	HCC	SNORD17	Non-coding small nucleolar RNA SNORD17 promotes the progression of hepatocellular carcinoma through a positive feedback loop upon p53 inactivation
Ding Y	HCC	SNORA52	Downregulation of snoRNA SNORA52 and Its Clinical Significance in Hepatocellular Carcinoma
Appaiah HN	BC	U6	Persistent upregulation of U6:SNORD44 small RNA ratio in the serum of breast cancer patients
Pacilli A	CRC	SNORD50A	SnoRNA U50 Levels Are Regulated by Cell Proliferation and rRNA Transcription
Xu L	CRC	snord12B	Distinct Profiles for Mitochondrial t-RNAs and Small Nucleolar RNAs in Locally Invasive and Metastatic Colorectal Cancer

Supplementary materials - Table S1. List of included studies

Author	Cancer	SnoRNA	Title
Langhendries J-L	LUAD, BC	U3、U8	The human box C/D snoRNAs U3 and U8 are required for prer-RNA processing and tumorigenesis
Fang X	HCC,CRC	SNORD126	SNORD126 promotes HCC and CRC cell growth by activating the PI3K-AKT pathway through FGFR2
Bagheri A	NSCLC	SNORD37	Altered miR-223 expression in sputum for diagnosis of non-small cell lung cancer
Tian B	ESCC	SNORD12B	Oncogenic SNORD12B activates the AKT-mTOR-4EBP1 signaling in esophageal squamous cell carcinoma via nucleus partitioning of PP-1 α
Chen X	HCC	SNORD105	An SNP reducing SNORD105 and PPAN expression decreases the risk of hepatocellular carcinoma in a Chinese population
Xu W	HCC	SNORD126	SnoRD126 promotes the proliferation of hepatocellular carcinoma cells through transcriptional regulation of FGFR2 activation in combination with hnRNPK
Wang K	NSCLC	SNORD83A	Plasma SNORD83A as a potential biomarker for early diagnosis of non-small-cell lung cancer
Faucher-Giguère L	OC	SNORA81, SNORA19, SNORA56	High-grade ovarian cancer associated H/ACA snoRNAs promote cancer cell proliferation and survival
Wan R	LUAD	SNORD14A,SNORD59A, SNORD99,SNORD100, SNORD63, SNORD19	Discovery of tumor immune infiltration-related snoRNAs for predicting tumor immune microenvironment status and prognosis in lung adenocarcinoma

Abbreviations: NSCLC = non-small cell lung cancer, HCC = hepatocellular carcinoma, SH-HCC = resembles human steatohepatitic HCC, ccRCC = clear cell renal cell carcinoma, BC = Breast cancer, OC = ovarian cancer, PCa = Prostate cancer, GC = Gastric cancer, MM = Multiple myeloma, PTCL = Peripheral T-cell lymphoma, HNSCC = Head and neck squamous cell carcinoma, CRC = Colorectal cancer, PDAC = Pancreatic ductal adenocarcinom, CLL = Chronic lymphocytic leukemia, AML = Acute myeloid leukemia, ESCC = Esophageal Squamous Cell Carcinoma LUAD = Lung adenocarcinoma.

Table S2. Risk signature based on snoRNAs.

Author	Cancer	Risk formula	Expression data of snoRNAs	Clinical validation	HR (95%CI, P value)	AUC
Gao L[1]*	NSCLC	(411.959 * expression of snoRA78) + (2.34241 * expression of snoRA47) - (0.30167 * expression of snoRA68) - 0.7693.	Next-generation deep sequencing in 12 NSCLC tissues	training set of 77 cases; testing set of 49 cases	-	1 year: 0.701 3 year: 0.721 5 year: 0.744 7 year: 0.759
Wang X[2]*	Gastric cancer	(0.0496 * expression of U66) + (-0.0191 * expression of ACA47) + (0.0363 * expression of ACA10) + (-0.1711 * expression of E2) + (0.0650 * expression of SNORA58) + (0.0953 * expression of HBII-316) + (-0.4749 * U70) + (-0.2352 * expression of U8).	SNORic	-	3.43 (1.93–6.09, P=2.72e-05)	0.828
Zhao Y[3]*	Renal clear cell carcinoma	(-0.2791 * expression of SNORA2) + (-0.2461 * expression of SNORD116-2) + (-0.1322 * expression of SNORA59B) + (0.2680 * expression of SNORD93) + (0.2330 * expression of SNORD12B) + (0.4199 * expression of SNORA70B).	TCGA	64 clinical tissue cases; 50 serum samples	-	-

Supplementary materials - Table S2. Risk signature based on snoRNAs.

Author	Cancer	Risk formula	Expression data of snoRNAs	Clinical validation	HR (95%CI, P value)	AUC
Cao R[4]#	Bladder cancer	(0.01794 * expression of SNORD113-9) + (0.02659 * expression of U3) + (0.00104 * expression of U49A) + (0.0002 * expression of SNORD114-1) + (- 0.0031 * expression of SNORD19B)	SNORic	-	Training cohort: 2.14 (1.48–3.08, $P <$ 0.0001) Testing cohort: 2.03 (1.19–3.47, $P <$ 0.0001)	1 year: 0.702 3 year: 0.664 5 year: 0.710
Huang L[5]#	Colon adenocarcinoma	(0.263 * expression of SNORD14E) + (-0.079 * expression of SNORD67)	TCGA	-	7.489 (1.567-35.793, P= 0.012)	-
Liu J[6]#	Sarcoma	(-0.1803 * expression of U3) + (0.1826 * expression of SNORA73B) + (0.2846 * expression of SNORD46) + (0.1613 * expression of SNORA26)	TCGA	-	2.378 (1.560-3.625, $P <$ 0.001)	1 year: 0.727
Yi Q[7]#	Uveal melanoma	(-1.602 * ACA17) + (0.803 * ACA45) + (0.603 * HBII-276) + (1.348 * SNORD12)	SNORic	-	-	-
Yang H[8]#	Hepatocellular carcinoma	(0.0655 * expression of SNORA24) + (0.0991 * expression of SNORA7) + (0.1196 * expression of SNORA63) + (0.2590 * expression of U3_chr8-2) + (0.2464 * expression of U3_chr9) + (0.0613 * expression of SNOR19B) + (0.1653 * expression of hTR) + (0.0830 * expression of SNORD36C) + (0.0964 * expression of U44)	SNORic	-	2.778 (1.904-4.051, $P <$ 0.001)	0.731

Supplementary materials - Table S2. Risk signature based on snoRNAs.

Author	Cancer	Risk formula	Expression data of snoRNAs	Clinical validation	HR (95%CI, P value)	AUC
He RQ[9]#	Bladder carcinoma	(-0.168 * expression of SNORD114-11) + (0.201 * expression of SNORD114-14) − (0.229 * expression of SNORD114-15) + (0.543 * expression of SNORD114-9) − (0.198 * expression of SNORA55) − (0.192 * expression of SNORA60) − (0.167 * expression of SNORD88A) − (0.314 * expression of SNORD69) − (0.226 * expression of SNORD20) + (0.432 * expression of U49A) − (0.335 * expression of SNORD51) + (0.514 * expression of U74)	SNORic	-	2.5 (1.828–3.420, P＜0.001)	0.719
Xing L[10]#	HNSCC	SNORD114－17, SNORA36B, SNORD78, U3(chr2), U3(chr17) (The authors did not provide specific details of the signature.)	UCSC Xena, CGHub	-	2.41 (1.8–3.21, P＜0.0001)	1 year: 0.674 3 year: 0.704 5 year: 0.66
Zhang L[11]#	Lung adenocarcinoma	(0.1293 * expression of snoU109) + (0.1046 * expression of SNORA5A) + (−0.2012 * expression of SNORA70) + (−0.1005 * expression of SNORD104) + (−0.1155 * expression of U3)	TCGA	-	1.476 (1.096–1.987, P=0.0064)	1 year: 0.61 5 year: 0.618 9 year: 0.666

Supplementary materials - Table S2. Risk signature based on snoRNAs.

Author	Cancer	Risk formula	Expression data of snoRNAs	Clinical validation	HR (95%CI, P value)	AUC
Wan R[12]	Lung adenocarcinoma	SNORD14A, SNORD59A, SNORD99, SNORD100, SNORD63, SNORD19 (The authors did not provide specific details of the signature.)	GEO, TCGA, CCLE project	-	TCGA-LUAD: 4.605 (3.259 - 6.508,P<0.001); GSE81089: 2.044 (1.134 - 3.684, P=0.017)	3 year: 0.83 5 year: 0.82

* Included studies.

Supplementary studies, bioinformatics articles without subsequent validation by wet lab methods.

Abbreviations: HR = Hazard ratio; CI = Confidence interval; AUC = Area under curve; NSCLC = Non - small cell lung cancer; SNORic = snoRNA in cancers; TCGA = The cancer genome atlas; HNSCC = Head and neck squamous cell carcinoma; CGHub = the Cancer Genomics Hub GEO = Gene Expression Omnibus, CCLE = Cancer Cell Line Encyclopedia.

References

1. Gao, L., et al., Genome-wide small nucleolar RNA expression analysis of lung cancer by next-generation deep sequencing. Int J Cancer, 2015. 136(6): p. E623-9.

2. Wang, X., et al., Identification of Eight Small Nucleolar RNAs as Survival Biomarkers and Their Clinical Significance in Gastric Cancer. Front Oncol, 2019. 9: p. 788.

3. Zhao, Y., et al., Expression signature of six-snoRNA serves as novel non-invasive biomarker for diagnosis and prognosis prediction of renal clear cell carcinoma. J Cell Mol Med, 2020. 24(3): p. 2215-2228.

4. Cao, R., et al., Small nucleolar RNAs signature (SNORS) identified clinical outcome and prognosis of bladder cancer (BLCA). Cancer Cell Int, 2020. 20: p. 299.

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10. Xing L ., et al., Expression scoring of a small‐nucleolar‐RNA signature identified by machine learning serves as a prognostic predictor for head and neck cancer. J Cell Physiol. 2020;235: 8071–8084.

11. Zhang L., et al., Identification of a novel snoRNA expression signature associated with overall survival in patients with lung adenocarcinoma: A comprehensive analysis based on RNA sequencing dataset. Math Biosci Eng. 2021 Sep 10;18(6):7837-7860.

12. Wan R., et al., Discovery of tumor immune infiltration-related snoRNAs for predicting tumor immune microenvironment status and prognosis in lung adenocarcinoma. Comput Struct Biotechnol J. 2021 Nov 25;19:6386-6399.

Table S3. Capability of the snoRNAs to discriminate malignant tumor, other disease and healthy individuals.

Author	Tumor	Specimen	snoRNA	AUC; 95% CI	Sensitivity	Specificity	Remark
Shang X[1]	ccRCC	plasma	SNORD63	0.5161	95%	27.30%	
			SNORD96A	0.8909	90%	80%	
			combination	0.9205	80.00%	97.50%	
		US	SNORD63	0.7055	47.90%	86.70%	
			SNORD96A	0.6788	53.10%	77.30%	
			combination	0.71	43.70%	89.30%	
	early ccRCC	plasma	SNORD63	0.6144	95%	39.10%	
			SNORD96A	0.9359	95%	87%	
			combination	0.937	82.60%	97.50%	
		US	SNORD63	0.6884	47.90%	82.10%	
			SNORD96A	0.6701	53.10%	79.50%	
			combination	0.6944	92.30%	39.60%	
Dong X[2]	NSCLC	plasma	TEP SNORD55	0.803	79.30%	68.30%	
	early NSCLC	plasma	SNORD55	0.784	91.20%	49.70%	
			TEP SNORD55 and CEA	0.828	66.30%	90.00%	
	LUAD	plasma	TEP SNORD55	0.791	77.90%	68.30%	
	early LUAD	plasma	TEP SNORD55	0.759	89.70%	49.70%	
	LUSC	plasma	TEP SNORD55	0.826	72.40%	77.70%	
	early LUSC	plasma	TEP SNORD55	0.854	68.40%	93.10%	
He JY[3]	CC	tissues	SNORD16	0.7 (0.53-0.86)			

Supplementary materials - Table S3. Capability of the snoRNAs to discriminate malignant tumor, other disease and healthy individuals.

Author	Tumor	Specimen	snoRNA		AUC; 95% CI	Sensitivity	Specificity	Remark
Kitagawa T[4]	PDAC	serum	SNORA74A		0.909 (0.807–1.000)			
			SNORA25		0.903 (0.795–1.000)			
			SNORA22		0.883 (0.774–0.993)			
			SNORA14B		0.875 (0.759–0.990)			
			SNORD22		0.862 (0.750–0.973)			
Su Y[5]	NSCLC	sputum	SNORDs-66,78		0.86	73.91%	83.64%	
			miRs-21,31,210	and	0.94	89.13%	89.09%	
			SNORDRDs-66,78					
Liao J[6]	NSCLC	plasma	SNORD33		0.8233	72.97%	86.36%	1
			SNORD66		0.8139	75.68%	77.27%	
			SNORD76		0.8064	70.27%	90.91%	
			combination		0.89	83.78%	95.45%	
			SNORD33		0.82	72.97%	84.62%	2
			SNORD66		0.7903	72.97%	80.77%	
			SNORD76		0.8149	70.27%	88.46%	
			combination		0.88	81.08%	96.15%	
Gao L[7]	NSCLC	tissues	SNORA12		0.7456	75%	70%	
			SNORA64		0.9025	80%	75%	
			SNORA68		0.8325	75%	90%	
			SNORA70		0.8925	70%	85%	
			SNORA71A		0.8850	80%	80%	
			SNORA71C		0.9425	95%	75%	
			SNORD10		0.8850	95%	80%	
			SNORD74		0.8750	70%	95%	
			SNORD80		0.8625	80%	85%	

Supplementary materials - Table S3. Capability of the snoRNAs to discriminate malignant tumor, other disease and healthy individuals.

Author	Tumor	Specimen	snoRNA	AUC; 95% CI	Sensitivity	Specificity	Remark
			SNORD96A	0.8225	80%	80%	
			SNORA21	0.8900	80%	85%	
			SNORD28	0.8475	80%	80%	
			SNORA34	0.7475	80%	75%	
			SNORA38B	0.7569	75%	80%	
			SNORA47	0.7567	80%	75%	
			SNORD66	0.7975	75%	80%	
Su J[8]	NSCLC	sputum	SNORD33	0.7230 (0.630-0.816)			
			SNORA42	0.7431 (0.655-0.831)			
			SNORD66	0.8065 (0.725-0.888)			
			SN0RD78	0.8112 (0.731-0.891)			
			SNORDs-66,78	0.86			
Yang X[9]	CRC	tissues	SNORA15	0.808	59.09%	92.86%	3
			SNORA41	0.875	84.09%	64.29%	
			SNORD33	0.938	86.36%	89.99%	
			combination	0.995	90.84%	94.00%	
			SNORA15	0.648	43.18%	99.99%	4
			SNORA41	0.716	70.45%	71.43%	
			SNORD33	0.845	84.09%	82.14%	
			combination	0.841	75.47%	31.58%	
Wu L[10]	HCC	tissues	SNORD76	0.73 (0.64-0.81)			

Supplementary materials - Table S3. Capability of the snoRNAs to discriminate malignant tumor, other disease and healthy individuals.

Author	Tumor	Specimen	snoRNA	AUC; 95% CI	Sensitivity	Specificity	Remark
Zhao Y[11]	ccRCC	tissues	SNORA2, SNORD12B, SNORA59B, SNORA70B, SNORD93, SNORD116-2	0.800			
		serum	SNORA2, SNORD12B, SNORA59B, SNORA70B,SNORD93, SNORD116-2	0.747			
Liu Y[12]	CRC	serum	SNORD1C	0.748(0.670–0.826)	79.80%	57.45%	
			SNORD1C and CEA	0.838(0.774–0.901)	85.86%	62.26%	
Hu T[13]	BC	tissue	SNORA71A	0.72	76.92%	61.54%	
Wang K[14]	NSCLC	plasma	SNORD83A	0.7387	76%	60%	
	early NSCLC	plasma	SNORD83A	0.7016	84.7%	52.4%	
Bagheri A[15]	NSCLC	sputum	SNORD37	0.82(0.72–0.93)	93.3%	63.3%	

Abbreviations: ccRCC = clear cell renal cell carcinoma, NSCLC = non‐small cell lung cancer, LUAD = lung adenocarcinoma, LUSC = lung squamous cell carcinoma, CC = colon cancer, PDAC = Pancreatic ductal adenocarcinom, HCC = hepatocellular carcinoma, COPD = chronic obstructive pulmoriary disease, UC = ulcerative colitis, HC = healthy control, US = urinary sediment, TEP = tumor‐educated platelet, CEA = carcinoembryonic antigen.

Note: 1. Distinguishing NSCLC from healthy subjects; 2. Distinguishing NSCLC from COPD; 3. Distinguishing CRC from HC; 4. Distinguishing CRC from UC.

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Supplementary materials - Table S3. Capability of the snoRNAs to discriminate malignant tumor, other disease and healthy individuals.

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Fig.S1 Trends in articles published from January 2008 to February 2022.

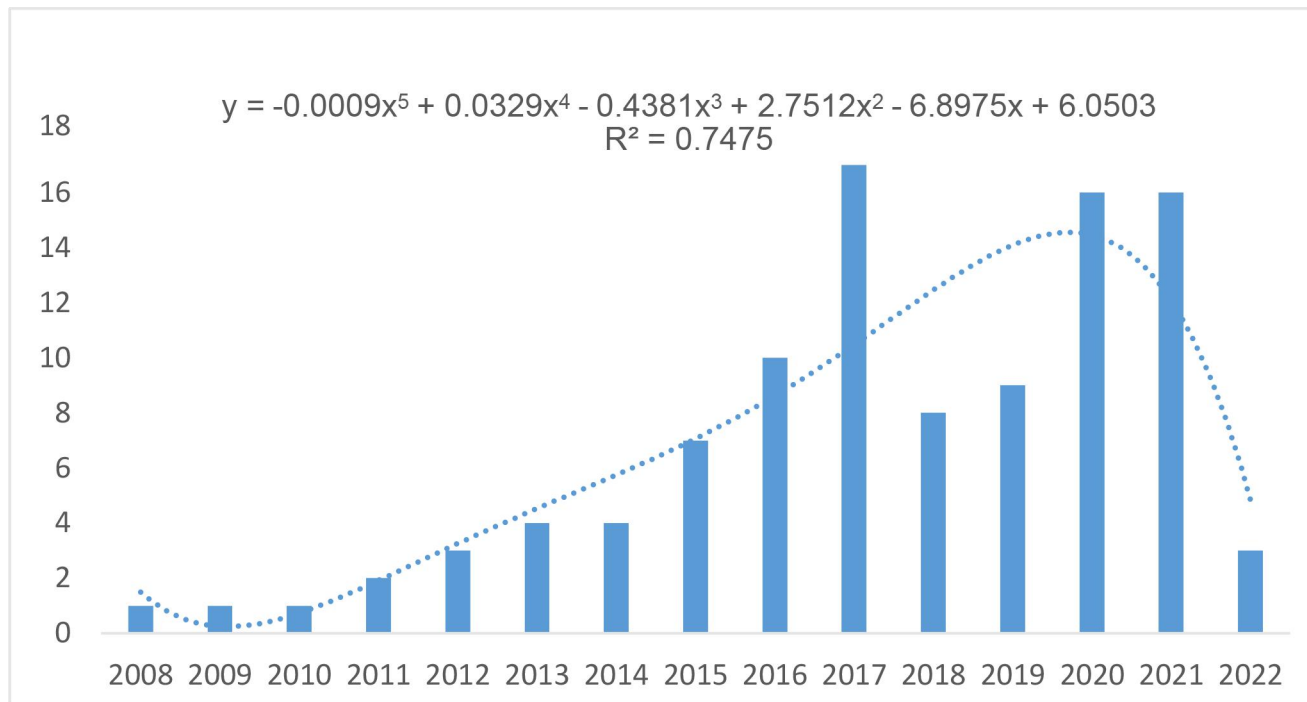$$y = -0.0009x^5 + 0.0329x^4 - 0.4381x^3 + 2.7512x^2 - 6.8975x + 6.0503$$
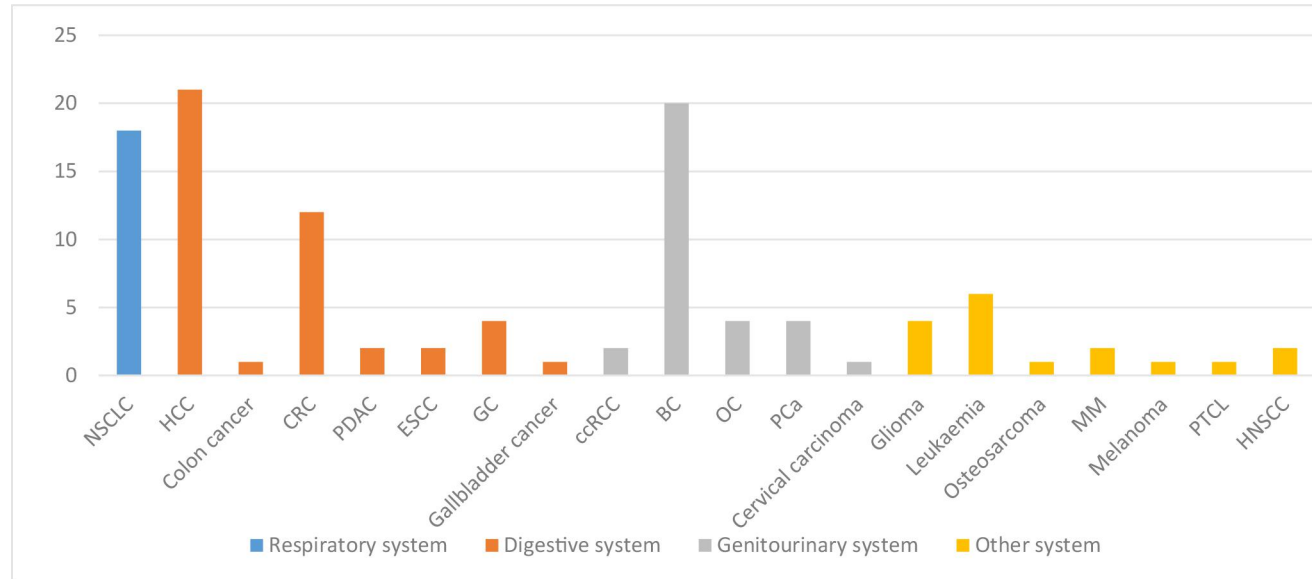$$R^2 = 0.7475$$

Fig.S2 Distribution of cancer types.
Abbreviations: NSCLC = Non-small cell lung cancer, HCC = Hepatocellular carcinoma, CRC = Colorectal cancer, PDAC = Pancreatic ductal adenocarcinoma, GC = Gastric cancer, ccRCC = Clear cell renal cell carcinoma, BC = Breast cancer, OC = Ovarian cancer, PCa = Prostate can- -cer, MM = Multiple myeloma, PTCL = Peripheral T-cell lymphoma, HNSCC = Head and neck squamous cell carcinoma, ESCC = Esophageal squamous cell carcinoma.

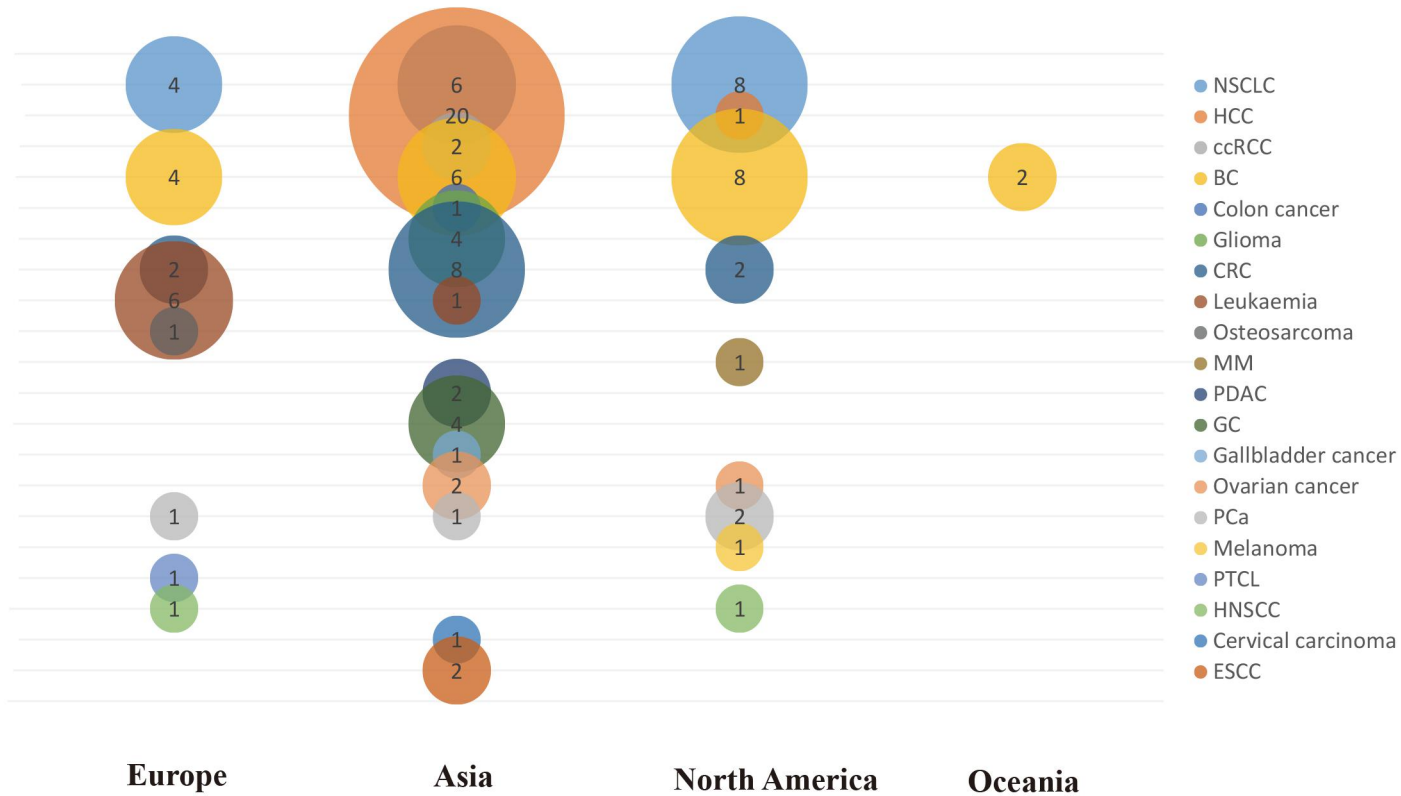Fig.S3 Fractions of articles from each continent from January 2008 to February 2022.

Fig.S4 Publication of articles on different cancer types in four continents.
Abbreviations: NSCLC = Non-small cell lung cancer, HCC = Hepatocellular carcinoma, ccRCC = Clear cell renal cell carcinoma, BC = Breast cancer, CRC = Colorectal cancer, MM = Multiple myeloma, PDAC = Pancreatic ductal ade--nocarcinoma, GC = Gastric cancer, PCa = Prostate cancer, PTCL = Peripheral T-cell lymphoma, HNSCC = Head and neck squamous cell carcinoma, ESCC = Esophageal squamous cell carcinoma.
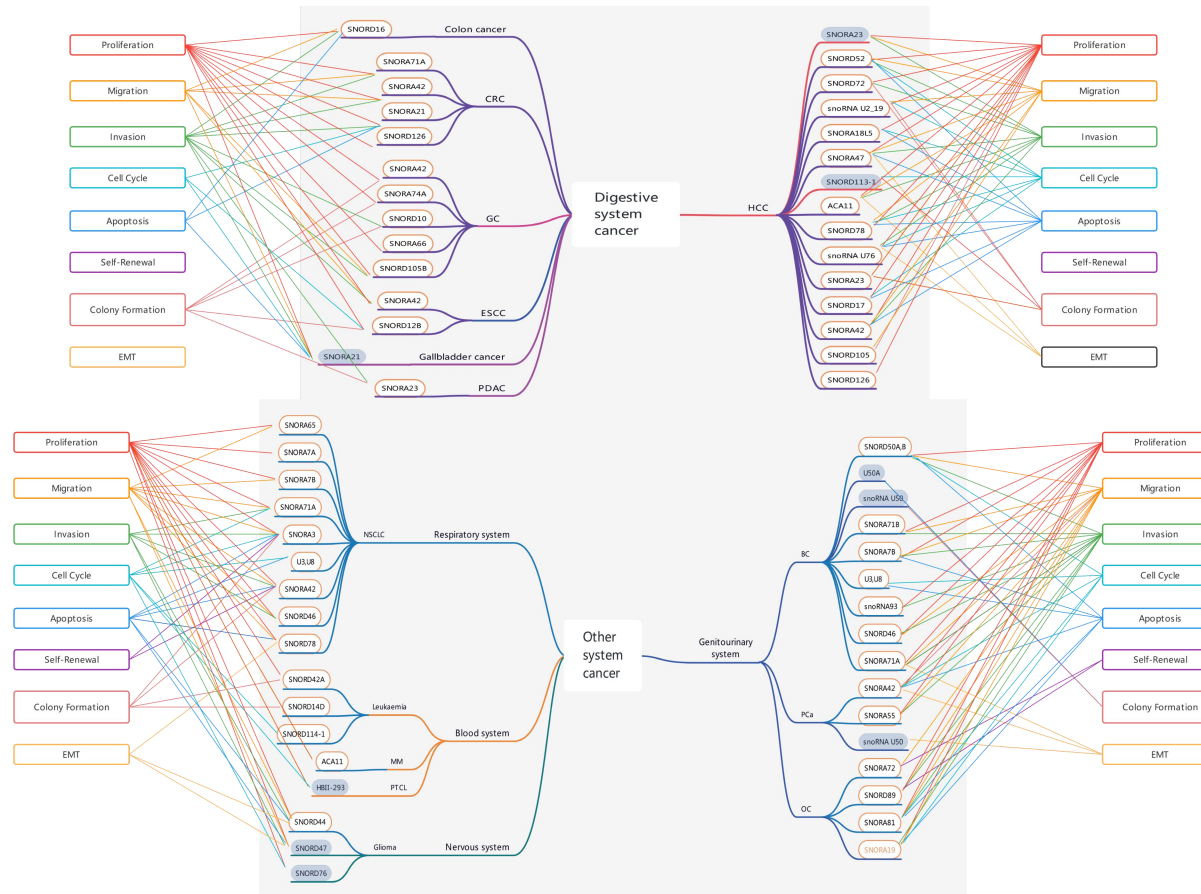
Fig.S5 The relationship between deregulated snoRNAs and cancer cell phenotype.
Abbreviations: HCC = hepatocellular carcinoma, PDAC = pancreatic ductal adenocarcinoma, CRC = colorectal cancer,
BC = Breast cancer, PCa = Prostate cancer, OC = Ovarian cancer, NSCLC = Non-small cell lung cancer, MM = Multiple
myeloma, PTCL = Peripheral T-cell lymphoma, EMT = epithelial-mesenchymal transition, ESCC = Esophageal squam-
-ous cell carcinoma.