

Table S1. Tudor-SN-associated clinical diseases

N	Disease type	First author, year	Structural property	Spatiotemporal specificity	Binding partners	Cellular function alteration	Targeted intervention or therapy	Ref.
1	ADPKD	Low, 2006	NA	Tudor-SN↑ [partially basal bodies/cilia]	PC1/STAT6	RNA transcription	NA	[1]
2	Autism	Holt, 2010	rs1881084	NA	NA	NA	NA	[2]
3	Autism	Magini, 2019	CNV	NA	NA	NA	NA	[3]
4	NAFLD	Del Río, 2019	NA	NA	NA	RNA splicing	NA	[4]
5	Skin keloid	Qin, 2021	PAX5 [TF]	PAX5 ↑ Tudor-SN↑ [keloid]	NA	Tudor-SN↑ Telomerase activity↑ Proliferation ↑ Inflammation↑ [keloid fibroblasts]	NA	[5]
6	Hidradenitis suppurativa	Hessam, 2017	NA	Tudor-SN↓ [lesional HS skin]	NA	NA	NA	[6]
7	Osteoarthritis	Lv, 2022	NA	NA	3'UTR of <i>HSPA5</i>	Tudor-SN↑ <i>HSPA5</i> mRNA↓ GPX4↓	NA	[7]

						ferroptosis in chondrocytes↑		
8	Liver cancer	Yoo, 2011	NA	Tudor-SN↑ [HCC tissues with different stages]	MTDH/AGO2	Tudor-SN↑ RISC activity↑ Tumor suppression↓ Proliferation↑ Viability↑	NA	[8]
9	Liver cancer	Santhekadur, 2012	NA	Tudor-SN↑ [HCC cells]	NA	Tudor-SN↑ NF-κB↑ miR-221↑ CXCL16↑ Tumor angiogenesis↑	NA	[9]
10	Liver cancer	Yin, 2013	NA	Tudor-SN↑ [HCC tissue]	NA	Tudor-SN↑ IGFBP3↓ Proliferation↑ [SMMC-7721]	NA	[10]
11	Liver cancer	Armengol, 2014	ATF6 [TF]	ATF6↑ Tudor-SN↑	NA	Tudor-SN↑ ER stress↑ [HEPG2]	NA	[11]
12	Liver cancer	Santhekadur, 2014	NA	Tudor-SN↑ [HCC tissues different	AT1R mRNA	Tudor-SN↑ AT1R stability↑	ERK inhibition [PD184352]	[12]

				stages]		ERK/Smad2/TGFβ↑ EMT↑ [HCC cells]	AT1R blocker [Losartan potassium]	
13	Liver cancer	Arretxe, 2015	NA	TNFα↑ NF-κB↑ Tudor-SN↑	glycerolipid metabolic gene promoter	Tudor-SN↑ Glycerolipid metabolic gene transcription↑ [HepG2]	NA	[13]
14	Liver cancer	Navarro-Imaz, 2016	NA	Major in Cytoplasm [MMcA-S]	NA	Tudor-SN↑ SREBP2 activation↑ Cholesterol synthesis↑↓	NA	[14]
15	Liver cancer	Rajasekaran, 2016	NA	Major in Cytoplasm [QGY-7703 cells]	MGLL	Tudor-SN↑ MGLL↓ Hepatocarcinogenesis↑ [HCC cells]	NA	[15]
16	Liver cancer	Armengol, 2017	SREBP2 [TF]	SREBP2↑ Tudor-SN↑	NA	Tudor-SN↑ [HepG2 cells]	NA	[16]
17	Liver cancer	Jariwala, 2017	NA	NA	NA	Tudor-SN↑ AKT↑ NF-κB↑ Spontaneous HCC↑ Inflammation↑	pdTp	[17]

						TIC formation↑ Proliferation↑ HCC xenografts↑ [Alb/Tudor-SN mice]		
18	Liver cancer	Cui, 2018	NA	Tudor-SN↑ [HPA/TCGA]	MYB	Tudor-SN↑ MYB↑UCA1↑ 5-Fu-induced apoptosis↓ [HCC cells]	NA	[18]
19	Liver cancer	Jariwala, 2019	NA	NA	3'UTR of <i>PTPN23</i>	Tudor-SN↑ PTPN23↓ Proliferation↑ Migration/invasion↑ Tumorigenesis↑	NA	[19]
20	Liver cancer	Navarro-Imaz, 2019	NA	NA	NA	Tudor-SN↑ Triglyceride synthesis↓ Cholesterol Cholesterogenesis↑ [McA-S2 cell]	NA	[20]
21	Liver cancer	Liang, 2022	NA	mitochondrion-localization	PGAM5	Tudor-SN/PGAM5↑ Mitophagy↑ Tumor growth↑	NA	[21]

22	Liver cancer	Noureldeen, 2022	NA	NA	NA	NA	ruthenium(III)-pyrimidine Schiff base↑ Tudor-SN↓ apoptosis↑ [HepG2]	[22]
23	Breast cancer	Ho, 2009	NA	NA	NA	Tudor-SN↑ Invasive and metastatic lesions↑	NA	[23]
24	Breast cancer	Blanco, 2011	NA	NA	MTDH	Tudor-SN+MTDH↑ lung metastasis↑ apoptosis↓ chemoresistance↑ cell survival↑	NA	[24]
25	Breast cancer	Quintana, 2011	c-Myb [TF]	c-Myb↑ Tudor-SN↑ [MCF-7]	NA	NA	NA	[25]
26	Breast cancer	Zhao, 2013	NA	Tudor-SN↑ [MDA-M-231]	NA	Tudor-SN↑ miR-127↓ BCL6↑ Migration, invasion↑ Proliferation↑ [MDA-M-231]	NA	[26]
27	Breast cancer	Wan, 2014	NA	MTDH↓	MTDH	Tudor-SN-MTDH↑	NA	[27]

				Tudor-SN+MTDH↓ Tudor-SN↓		MTDH-mediated tumor initiation↑ survival↑		
28	Breast cancer	Kochan, 2015	NA	Circadian disruption↑ NF-κB activity↑ Tudor-SN↑ [rat mammary gland tissues]	NA	NA	NA	[28]
29	Breast cancer	Yu, 2015	Smad2/3	TGFβ1↑ Smad2/3↑ Tudor-SN↑ [breast cancer tissue, MDA-MB-231; BT549]	<i>Smurf1</i> mRNA	Tudor-SN↑ <i>Smurf1</i> ↑ RhoA↓ cell adhesion↓ migration/invasion↑ metastasis↑ [MCF-7, MDA-MB-213]	NA	[29]
30	Breast cancer	Yu, 2017	NA	Tudor-SN↑ [patients with metastasis]	GCN5 <i>Smad2/3/4</i> promoters	Tudor-SN↑ H3K9 acetylation↑ Smad2/3/4↑ TGFβ1 response↑ metastasis↑	NA	[30]

31	Breast cancer	Gu, 2018	NA	TNM stage ↑ metastasis ↑ Tudor-SN ↑	NA	Tudor-SN ↑ prognosis ↓	NA	[31]
32	Breast cancer	Qian, 2020	NA	NA	Linc00668	Tudor-SN+Linc00668 ↑ migration, invasion, stem cell-like capacity ↑ [MCF-7]	Tudor-SN+Linc00668 ↑ doxorubicin resistance ↑ [MCF-7]	[32]
33	Breast cancer	Li, 2021	NA	NA	MTDH CPP-4-2	NA	CPP-4-2 ↑ Tudor-SN/MTDH ↓ Tudor-SN ↓ Cell survival ↓	[33]
34	Breast cancer	Chen, 2022	NA	NA	MTDH	NA	Stabilized Peptide Inhibitors ↑ Tudor-SN/MTDH ↓ antitumor bioactivity ↑	[34]
35	Prostate cancer	Kuruma, 2009	NA	Tudor-SN ↑ [tissues]	NA	Tudor-SN ↑ cell growth ↑ [PC-3]	NA	[35]
36	Prostate cancer	Cappellari, 2014	NA	Tudor-SN ↑ [PC-3]	SAM68 <i>CD44</i>	Tudor-SN+ SAM68 ↑ Oncogenic CD44 variants ↑	NA	[36]

					pre-mRNA	Proliferation/migration↑ Cell growth/survival↑		
37	Prostate cancer	Sowalsky, 2015	Tudor-SN:BR AF	NA	NA	CRPC	NA	[37]
38	Prostate cancer	Ngollo, 2017	NA	NA	NA	H3K27me3	NA	[38]
39	Prostate cancer	Alhamar, 2020	Tudor-SN:BR AF	NA	NA	NA	NA	[39]
40	Prostate cancer	Chen, 2020	NA	LINC00665↑ miR-1224-5p↓ Tudor-SN↑	NA	Tudor-SN↑ Proliferation↑ Migration/invasion↑ [PC cells]	NA	[40]
41	Prostate cancer	Kaikkonen, 2020	NA	NA	ANO7	NA	NA	[41]
42	Prostate cancer	Fenor, 2022	Tudor-SN:BR AF	NA	NA	NA	Tudor-SN:BRAF↑ MEK inhibitor sensitivity↑	[42]
43	Gliomas	Emdad, 2015	NA	miR-184↑ Tudor-SN ↓ [T98G, U87]	NA	Tudor-SN↑ Invasion/progression↑ senescence-induced cell death↑	NA	[43]

				Tudor-SN ↑ [tissues]				
44	Gliomas	Tong, 2016	NA	MTDH ↑ NF-κB ↑ Tudor-SN ↑	MTDH	NA	NA	[44]
45	Gliomas	Li, 2017	miR-320a	miR-320a ↓ Tudor-SN ↑	NA	Tudor-SN ↑ Proliferation ↑ Migration/invasion ↑	NA	[45]
46	Gliomas	Liu, 2018	miR-361-5p	miR-361-5p ↓ Tudor-SN ↑	<i>MMP2</i> promoter	Tudor-SN ↑ MMP2 ↑ Migration/invasion ↑	NA	[46]
47	Gliomas	Yu, 2019	NA	WHO grade ↑ Tudor-SN ↑	<i>RhoA</i> promoter	Tudor-SN ↑ RhoA ↑ G1/S phase transition ↑ Proliferation/invasion ↑	NA	[47]
48	Gliomas	Zhu, 2019	NA	NA	NA	Tudor-SN ↑ <i>PTBP1</i> mRNA Stability ↑ Progression ↑	NA	[48]
49	Gliomas	Chen, 2019	NA	NA	tTmod3-C/Tudo r-SN	RhoA/CDKs pathway ↑ Proliferation ↑	NA	[49]

50	Colorectal cancer	Tsuchiya, 2007	NA	Tudor-SN↑ [tissues/cells at early stage]	NA	Tudor-SN↑ APC protein↓ Cell growth↑ Early-stage colon carcinogenesis↑	NA	[50]
51	Colorectal cancer	Tsuchiya, 2010	NA	NA	miR-34a/ <i>E2F5</i> mRNA	Tudor-SN↑ APC protein↓ miR-34a-mediated <i>E2F5</i> repression↑ [HCT 116] colon carcinogenesis↑	NA	[51]
52	Colorectal cancer	Wang, 2012	NA	Tudor-SN↑ [tissue]	MTDH	Tudor-SN+MTDH↑ prognosis↓	NA	[52]
53	Colorectal cancer	Naumov, 2013	cg09296001 methylation	NA	NA	NA	NA	[53]
54	Colorectal cancer	Ma, 2015	miR-361-5p	miR-361-5p↑ Tudor-SN↓	pre-miR-361-5p	Tudor-SN↑ Tudor-SN+pre-miR-361-5p↑ miR-361-5p↓ Tudor-SN↑ lung metastasis↑	NA	[54]

						[HCT116]		
55	Colorectal cancer	Azuara, 2018	cg26642667 methylation	NA	NA	NA	NA	[55]
56	Colorectal cancer	Diao, 2020	NA	NA	SPT6 <i>hTERT</i> promoter	Tudor-SN+SPT6↑ hTERT↑ Proliferation/metastasis↑ Stemness/growth↑	NA	[56]
57	Colorectal cancer	Meng, 2020	rs118049207	rs118049207 +DMRT3↑ Tudor-SN↑	NA	NA	NA	[57]
58	Colorectal cancer	Lehmusvaara, 2022	NA	NA	NA	NA	Suramin↑ Tudor-SN RNA binding ↓ miR-1-3p↑ Navitoclax sensitivity↑	[58]
59	Lung cancer	Chiosea, 2007	NA	Tudor-SN↑ [NCI-H520]	NA	NA	NA	[59]
60	Lung cancer	Surova, 2012	NA	Tudor-SN✘ [NSCLC/SCLC]	NA	NA	Tudor-SN↓ Ionizing Radiation sensitivity ✘	[60]

							[NSCLC cells]	
61	Lung cancer	Jang, 2015	Tudor-SN:BR AF [LUAD from never Smokers]	NA	NA	Tudor-SN: BRAF↑ MEK/ERK phosphorylation↑ Cell proliferation and Spheroid formation↑ [H1299]	NA	[61]
62	Lung cancer	Zagryazhskaya, 2015	NA	Tudor-SN↑ [NSCLC cells/tissues]	NA	NA	Tudor-SN↑ S100A11↑ Cell death in response to cisplatin↓ [NSCLC cells]	[62]
63	Lung cancer	Jang, 2016	Tudor-SN:BR AF [LUAD]	NA	NA	NA	NA	[63]
64	Lung cancer	Xing, 2018	miR-320a	miR-320a↓ Tudor-SN↑	NA	Tudor-SN↑ Migration↑ [H1299/SPC-A-1]	NA	[64]
65	Ovarian cancer	Permeth, 2016	rs185455523 [T>A]	NA	NA	rs185455523[AT/AA]↑ EOC risk↓	NA	[65]
66	Ovarian	Xin, 2019	NA	NA	GCN5+	Tudor-SN+ GCN5+ CBP/p300↑	NA	[66]

	cancer				CBP/p300+ <i>SLUG</i> promoter	SLUG↑ EMT↑ Invasion and migration↑ [SKOV3]		
67	Ovarian cancer	Wang, 2020	miR- 1224- 5p	miR- 1224- 5p↓ Tudor-SN↑	NA	Tudor-SN↑ Proliferation/invasion↑ [SKOV3/OVCAR3]	NA	[67]
68	Pancreatic cancer	Chmielecki, 2014	Tudor-SN:BR AF [PACC]	NA	NA	Tudor-SN:BRAF↑ MAPK pathway↑	Tudor-SN:BRAF↑ Sensitive to trametinib↑	[68]
69	Pancreatic cancer	Milochau, 2014	NA	NA	syt11+AGO2	Tudor-SN+syt11+AGO2 [clonal pancreatic b-cells]	NA	[69]
70	Pancreatic cancer	Wang, 2018	Tudor-SN:BR AF [PACC]	NA	NA	NA	NA	[70]
71	Melanoma	Sand, 2012	NA	Tudor-SN↑ [CMMM>BMN>PCMM]	NA	NA	NA	[71]
72	Melanoma	Lee, 2017	<i>Tudor-SN</i> pre-mRNA	NA	NA	NA	NA	[72]

			+SPRIGHTLY					
73	Melanoma	Wang, 2020	NA	NA	HLA-A	Tudor-SN↑ HLA-A↓ CD ⁸⁺ T cell infiltration↓ Tumor size↑ [B16F10]	NA	[73]
74	Osteosarcoma	Bilbao-Aldaiturriaga, 2015	rs3823994	NA	NA	NA	NA	[74]
75	Osteosarcoma	Zhou, 2019	NA	Tudor-SN↑ [tissues]	NA	Tudor-SN↑ NF-κB/COX-2↑ Cell proliferation↑ Tumor growth↑	NA	[75]
76	Osteosarcoma	Huang, 2021	miR-296-5p	miR-296-5p↓ Tudor-SN↑ [tissues/cells]	NA	Tudor-SN↑ Proliferation↑ Migration/invasion↑	NA	[76]
77	Cervical cancer	Zhan, 2020	NA	Tudor-SN↑ [tissues]	<i>Smurf1</i> promoter#	Tudor-SN↑ <i>Smurf1</i> ↑ FOXA2↓ Invasion/migration↑ EMT↑	NA	[77]

						lung metastasis↑ [CaSKI/MS-751]		
78	Cervical cancer	Zhang, 2021	NA	NA	Circ SMARCA5 YWHAB	SMARCA5↓ Tudor-SN↑ YWHAB↑ Proliferation/invasion↑ Apoptosis↓ Metastasis↑	NA	[78]
79	Gastric cancer	Dillon, 2011	Tudor-SN:BR AF	NA	NA	NA	Tudor-SN-BRAF↑ Resistance to PF-04217903↑ [GTL-16]	[79]
80	Gastric cancer	Lee, 2012	Tudor-SN:BR AF	NA	NA	NA	Resistance to PF-04217903↑ [GTL-16] Tudor-SN:BRAF↑ MAPK pathway↑	[80]
81	Gastric cancer	Ma, 2015	NA	miR-361-5p↑ Tudor-SN↓	pre-miR-361-5p	Tudor-SN↑ Tudor-SN+pre-miR-361-5p↑ miR-361-5p↓	NA	[54]

						Tudor-SN↑ Cell growth↑ [MKN45]		
82	Bladder cancer	Elbarbary, 2017	NA	NA	CA/UA miRNA +UPF1+AGO2	Tudor-SN↑ CA/UA miRNA↓ [T24 human urinary bladder cancer cells]	NA	[81]
83	Thyroid cancer	Chu, 2020	Tudor-SN:BR AF [two cases]	NA	NA	NA	NA	[82]
84	Oral cancer	Damani, 2020	rs3757769	NA	NA	NA	NA	[83]
85	MIFS	Klubickova, 2022	Tudor-SN:BR AF [one cases]	NA	NA	NA	NA	[84]
86	Pan cancer	Cui, 2020	~5% "amplification " [ovarian cancer] >8%	Tudor-SN↑ [BRCA/COAD/KICH/KIRC/KIRP/LIHC/LUAD/LUSC/PRAD/READ/HNSC/STAD/UCEC/DLBC/GBM/LGG/SKCM/TGC]	NA	NA	Tudor-SN↑ TMB↓ [THCA/COAD] TMB↑ [LGG/LUAD/PRAD, LIHC/STAD]	[85]

		<p>“mutation”</p> <p>[uterine tumors]</p> <p>~2% copy number deletion</p> <p>[AML]</p> <p>P723Lfs*</p> <p>[3STAD+1UC EC]</p> <p>Methylation</p> <p>[TGCT]</p> <p>S426 phosphorylation</p> <p>[breast cancer/clear cell RCC/LUAD/ovarian</p>	<p>T/THYM]</p> <p>[TCGA+GTEx+CPTAC]</p>			<p>MSI↓</p> <p>[PRAD/DLBC/LGG, THCA/COAD]</p> <p>MSI↑</p> <p>[OV/ACC/KIRC, STAD/SARC/CESC, LIHC]</p>	
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↑ upregulation or effect enhancement; ↓ downregulation or effect decrease; × no change or no difference; # Mechanism of speculation.

N, number; Ref., reference; NA, not available; Tudor-SN, Tudor staphylococcal nuclease; ADPKD, autosomal-dominant polycystic kidney disease; PC1, Polycystin-1; STAT6, signal transducer and activator of transcription 6; CNV, copy number variant; NAFLD, nonalcoholic fatty liver disease; PAX5, Paired-box gene 5; UTR, untranslated regions; HSPA5, Heat shock protein family A member 5; GPX4, Glutathione peroxidase 4; TF, transcription factor; HS, hidradenitis suppurativa; HCC, hepatocellular carcinoma; MTDH, Metadherin; AGO2, Argonaute RISC Catalytic Component 2; RISC, RNA-induced silencing complex; NF-κB, nuclear factor kappa-B; CXCL16, C-X-C Motif Chemokine Ligand 16; IGFBP3, Insulin Like Growth Factor Binding Protein 3; ATF6, Activating Transcription Factor 6; ER, endoplasmic reticulum; *AT1R*, *angiotensin II type 1 receptor*; ERK, Extracellular signal-regulated kinase; Smad2, SMAD Family Member 2; TGFβ, transforming growth factorβ; EMT, epithelial–mesenchymal transition; SREBP2, Sterol Regulatory Element Binding Transcription Factor 2; MGLL, Monoglyceride Lipase; TIC, Tumor-initiation cells; pdTp, 3',5'-deoxythymidine bisphosphate; HPA, human protein atlas; TCGA, the cancer genome atlas; MYB, MYB proto-oncogene, transcription factor; 5-Fu, 5-fluorouracil; UCA1, urothelial cancer associated 1; PTPN23, protein tyrosine phosphatase nonreceptor type 23; PGAM5, phosphoglycerate mutase 5; BCL6, BCL6 Transcription Repressor; TNM, Tumor/Node/metastasis; CRPC, castration-resistant prostate cancer; ANO7, Anoctamin 7; MMP2, Matrix Metalloproteinase 2; GCN5, General Control Of Amino-Acid Synthesis 5-Like; SAM68, Src-associated in mitosis of 68 kDa; WHO, World Health Organization; RhoA, Ras Homolog Family Member A; PTBP1, Polypyrimidine Tract Binding Protein 1; CDKs, Cyclin Dependent Kinases; E2F5, E2F Transcription Factor 5; SPT6, Suppressor Of Ty 6 Homolog; hTERT, Human telomerase reverse transcriptase; DMRT3, Doublesex And Mab-3 Related Transcription Factor 3; NSCLC, nonsmall cell lung carcinoma; SCLC, small cell lung carcinoma; BRAF, B-Raf Proto-Oncogene, Serine/Threonine Kinase; LUAD, Lung adenocarcinoma; S100A11, S100 Calcium Binding Protein A11; EOC, epithelial ovarian cancers; SLUG, SNAI2; syt11, Synaptotagmin 11; CMMM, cutaneous malignant melanoma metastases; PCMM, primary cutaneous malignant melanoma; BMN, benign melanocytic nevi; HLA-A, Major Histocompatibility Complex, Class I, A; COX-2, cyclooxygenase-2; FOXA2, Forkhead Box A2; YWHAB, Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Beta; UPF1, UPF1 RNA Helicase And ATPase; MIFS, Myxoinflammatory fibroblastic sarcoma; AML, Acute myeloid leukemia; STAD, Stomach adenocarcinoma; UCEC, Uterine corpus endometrial carcinoma; TGCT, Testicular germ cell tumors; RCC, Renal cell carcinoma; UCEC, Uterine corpus endometrial carcinoma; BRCA, Breast invasive carcinoma; COAD, Colon adenocarcinoma; KICH, Kidney chromophobe; KIRC, Kidney renal clear cell carcinoma; KIRP, Kidney renal papillary cell carcinoma; LIHC, Liver hepatocellular carcinoma; LUSC,

Lung squamous cell carcinoma; PRAD, Prostate adenocarcinoma; READ, Rectum adenocarcinoma ; HNSC, Head and neck squamous cell carcinoma; DLBC, Lymphoid neoplasm diffuse large B-cell lymphoma; GBM, Glioblastoma multiforme; LGG, Brain lower grade glioma; SKCM, Skin cutaneous melanoma; THYM, Thymoma; CPTAC, Clinical proteomic tumor analysis consortium; GTEx, Genotype-tissue expression; TMB, Tumor mutational burden; THCA, Thyroid carcinoma; MSI, Microsatellite instability; OV, Ovarian serous cystadenocarcinoma; ACC, Adrenocortical carcinoma; SARC, Sarcoma; CESC, Cervical squamous cell carcinoma and endocervical adenocarcinoma.

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