

Table SI. Single gene mutation rates of key genes in Hedgehog pathway in different tumor types (I).

Tumor type	Genes	Mutated samples	samples tested	Rate of mutagenesis
Adrenal cortical carcinoma	PTCH1	4	336	1.19%
	SMO	1	306	0.33%
	GLI3	1	164	0.61%
Neuroblastoma	SHH	1	1139	0.09%
	PTCH1	1	1232	0.08%
	GLI3	3	1139	0.26%
	GLI1	1	1219	0.08%
	SHH	2	457	0.44%
Bile duct adenocarcinoma	PTCH1	20	899	2.22%
	PTCH2	11	529	2.08%
	SUFU	3	771	0.39%
	SMO	4	1271	0.31%
	GLI1	18	728	2.47%
	GLI3	15	457	3.28%
	GLI2	12	460	2.61%
	SHH	1	120	0.83%
	PTCH1	7	202	3.47%
	PTCH2	2	120	1.67%
Gallbladder adenocarcinoma	SUFU	6	217	2.76%
	SMO	2	290	0.69%
	GLI1	5	173	2.89%
	GLI3	5	120	4.17%
	GLI2	3	120	2.50%
	Gallbladdersarcomatoid carcinoma	SMO	1	9
SHH		1	17	5.88%
PTCH1		1	17	5.88%
Gallbladder small cell carcinoma	PTCH2	1	17	5.88%
	SMO	1	17	5.88%
	GLI1	3	17	17.65%
	GLI3	1	17	5.88%
	PTCH1	69	1009	6.84%
Bone tumor	PTCH2	2	589	0.34%
	SUFU	5	762	0.66%
	SMO	23	1056	2.18%
	GLI3	7	589	1.19%
	GLI2	4	589	0.68%
	GLI1	2	726	0.28%
	SHH	10	3037	0.33%
	PTCH1	127	6584	1.93%
Breast cancer	PTCH2	61	3158	1.93%
	SUFU	74	5955	1.24%
	SMO	70	6709	1.04%
	GLI3	210	3075	6.83%
	GLI2	175	3038	5.76%
	GLI1	61	4583	1.33%

			PTCH1	6	362	1.66%
			PTCH2	4	191	2.09%
Triple-negative breast cancer			SUFU	1	205	0.49%
			SMO	5	421	1.19%
			GLI2	3	176	1.70%
			GLI3	1	176	0.57%
			SHH	2	318	0.63%
			PTCH2	7	318	2.20%
			PTCH1	7	412	1.70%
Cervical squamous cell carcinoma			SUFU	5	412	1.21%
			SMO	8	412	1.94%
			GLI2	10	318	3.14%
			GLI3	9	318	2.83%
			GLI1	6	329	1.82%
			SHH	5	1,910	0.26%
			PTCH1	34	2,597	1.31%
Brain glioma			PTCH2	17	1,910	0.89%
			SUFU	19	2,577	0.74%
			SMO	17	2,686	0.63%
			GLI3	36	1,910	1.88%
			GLI1	32	2,472	1.29%
			GLI2	20	1,910	1.05%
			PTCH1	45	763	5.90%
Brain medulloblastoma (include all)			PTCH2	2	509	0.39%
			SUFU	8	746	1.07%
			SMO	8	604	1.32%
			GLI3	16	509	3.14%
			GLI2	9	509	1.77%
			GLI1	1	513	0.19%
			SHH	5	2,152	0.23%
Central nervous system glioma			PTCH1	38	2,933	1.30%
			PTCH2	18	2,169	0.83%
			SUFU	19	2,871	0.66%
			SMO	20	3,007	0.67%
			GLI3	39	2,169	1.80%
			GLI1	34	2,747	1.24%
			GLI2	24	2,169	1.11%
Central nervous system medulloblastoma (include all)			PTCH1	82	1,025	8.00%
			PTCH2	2	562	0.36%
			SUFU	10	868	1.15%
			SMO	11	731	1.50%
			GLI3	16	562	2.85%
			GLI2	9	562	1.60%
			GLI1	1	566	0.18%
Central nervous system medulloblastoma (SHH subtype)			PTCH1	4	16	25.00%
			SUFU	1	14	7.14%
			SMO	1	15	6.67%
Endometrial carcinoma			SHH	17	756	2.25%
			PTCH1	75	1,072	7.00%

	PTCH2	35	756	4.63%
	SUFU	32	1,008	3.17%
	SMO	35	1,072	3.26%
	GLI3	87	751	11.58%
	GLI2	53	759	6.98%
	GLI1	40	977	4.09%
	PTCH1	24	2,304	1.04%
	PTCH2	4	2,085	0.19%
	SUFU	9	2,118	0.42%
Hematopoietic neoplasm	SMO	5	2,291	0.22%
	GLI2	17	2,085	0.82%
	GLI3	14	2,085	0.67%
	GLI1	9	2,087	0.43%
	PTCH1	12	1,263	0.95%
	PTCH2	4	1,251	0.32%
	SUFU	7	1,263	0.55%
Acute myeloid leukemia	SMO	5	1,304	0.38%
	GLI2	15	1,251	1.20%
	GLI3	11	1,251	0.88%
	GLI1	9	1,252	0.72%
	SHH	12	5,192	0.23%
	PTCH1	78	6,771	1.15%
	PTCH2	27	5,543	0.49%
	SUFU	46	5,752	0.80%
Lymphoid neoplasm	SMO	43	5,908	0.73%
	GLI3	182	5,347	3.40%
	GLI2	173	5,448	3.18%
	GLI1	21	5,552	0.38%
	SHH	1	1,396	0.07%
	PTCH1	13	1,454	0.89%
	PTCH2	2	1,396	0.14%
Acute lymphoblastic B cell leukemia	SUFU	4	1,454	0.28%
	SMO	1	1,454	0.07%
	GLI2	11	1,396	0.79%
	GLI3	8	1,396	0.57%
	GLI1	6	1,396	0.43%
	PTCH1	17	821	2.07%
	PTCH2	6	808	0.74%
	SUFU	2	809	0.25%
Acute lymphoblastic T cell leukemia	SMO	5	809	0.62%
	GLI3	13	808	1.61%
	GLI2	7	808	0.87%
	GLI1	1	809	0.12%
	PTCH1	7	1,365	0.51%
	PTCH2	1	359	0.28%
	SUFU	2	430	0.47%
Diffuse large B cell lymphoma	SMO	2	431	0.46%
	GLI2	7	359	1.95%
	GLI3	7	359	1.95%

			SHH	5	468	1.07%
			PTCH1	32	580	5.52%
			PTCH2	14	468	2.99%
Esophageal adenocarcinoma			SUFU	26	579	4.49%
			SMO	12	608	1.97%
			GLI3	190	468	40.60%
			GLI2	56	468	11.97%
			GLI1	7	575	1.22%
			SHH	4	1,335	0.30%
			PTCH1	62	1,427	4.34%
Esophageal squamous cell carcinoma			PTCH2	8	1,335	0.60%
			SUFU	7	1,349	0.52%
			SMO	10	1,525	0.66%
			GLI3	15	1,335	1.12%
			GLI2	12	1,335	0.90%
			GLI1	10	1,344	0.74%
			SHH	23	926	2.48%
Colon adenocarcinoma			PTCH1	119	1,657	7.18%
			PTCH2	29	926	3.13%
			SUFU	26	1,589	1.64%
			GLI3	113	943	11.98%
			GLI2	75	926	8.10%
			GLI1	65	1,529	4.25%
			SHH	2	462	0.43%
Rectal adenocarcinoma			PTCH1	24	926	2.59%
			PTCH2	8	462	1.73%
			SUFU	4	874	0.46%
			SMO	13	1,058	1.23%
			GLI3	43	470	9.15%
			GLI2	17	462	3.68%
			GLI1	15	857	1.75%
Intestinal adenocarcinoma			SHH	2	48	4.17%
			PTCH1	9	84	10.71%
			PTCH2	5	48	10.42%
			SUFU	5	84	5.95%
			SMO	5	106	4.72%
			GLI1	6	84	7.14%
			GLI2	5	48	10.42%
Gastric adenocarcinoma			GLI3	3	48	6.25%
			SHH	13	727	1.79%
			PTCH1	53	1,165	4.55%
			PTCH2	22	727	3.03%
			SUFU	15	1083	1.39%
			SMO	39	1,161	3.36%
			GLI3	96	728	13.19%
Pancreatic carcinoma			GLI2	46	727	6.33%
			GLI1	26	947	2.75%
			SHH	12	1,652	0.73%
			PTCH1	55	2,226	2.47%

	PTCH2	22	1,652	1.33%
	SUFU	44	2,132	2.06%
	SMO	32	2,453	1.30%
	GLI3	336	1,682	19.98%
	GLI2	128	1,652	7.75%
	GLI1	27	2,081	1.30%
	SHH	5	1,026	0.49%
	PTCH1	11	1,134	0.97%
	PTCH2	9	1,026	0.88%
Hepatocellular carcinoma	SUFU	12	1,128	1.06%
	SMO	19	1,431	1.33%
	GLI1	17	1,111	1.53%
	GLI2	48	1,029	4.66%
	GLI3	42	1,014	4.14%
	SHH	8	1,535	0.52%
	PTCH1	76	3,483	2.18%
	PTCH2	23	1,535	1.50%
Lung adenocarcinoma	SUFU	21	3,156	0.67%
	SMO	58	3,470	1.67%
	GLI3	111	1,347	8.24%
	GLI2	78	1,347	5.79%
	GLI1	75	2,648	2.83%
	SHH	8	899	0.89%
	PTCH1	26	1,250	2.08%
	PTCH2	19	899	2.11%
Lung squamous cell carcinoma	SUFU	15	1,073	1.40%
	SMO	19	1,111	1.71%
	GLI3	53	899	5.90%
	GLI2	33	899	3.67%
	GLI1	32	1,006	3.18%
	SHH	8	433	1.85%
	PTCH2	8	435	1.84%
	PTCH1	7	530	1.32%
Small cell lung carcinoma	SUFU	1	529	0.19%
	SMO	12	592	2.03%
	GLI3	16	435	3.68%
	GLI2	16	434	3.69%
	GLI1	13	510	2.55%
	SHH	1	293	0.34%
	PTCH1	24	352	6.82%
	PTCH2	15	273	5.49%
Meningioma	SUFU	82	938	8.74%
	SMO	153	1,583	9.67%
	GLI2	3	255	1.18%
	GLI1	2	285	0.70%
	GLI3	1	255	0.39%
	SHH	2	1,393	0.14%
Renal clear cell carcinoma	PTCH1	26	1,803	1.44%
	PTCH2	6	1,454	0.41%

	SUFU	9	1,789	0.50%
	SMO	11	1,799	0.61%
	GLI3	19	1,566	1.21%
	GLI2	16	1,461	1.10%
	GLI1	10	1,725	0.58%
Wilms tumour	PTCH1	2	338	0.59%
	GLI3	2	326	0.61%
	GLI2	1	325	0.31%
Uterine clear cell carcinoma	PTCH1	2	83	2.41%
	SUFU	1	64	1.56%
Endometrioid carcinoma	SMO	1	71	1.41%
	PTCH1	2	37	5.41%
	SMO	3	34	8.82%
Mucinous carcinoma of uterus	GLI1	1	8	12.50%
	PTCH1	1	84	1.19%
	SUFU	1	83	1.20%
	SMO	1	87	1.15%
	GLI3	5	59	8.47%
	SHH	2	673	0.30%
	PTCH1	14	913	1.53%
Uterine serous carcinoma	PTCH2	2	673	0.30%
	SUFU	2	875	0.23%
	SMO	6	925	0.65%
	GLI2	17	673	2.53%
	GLI1	14	831	1.68%
	GLI3	7	673	1.04%
	PTCH1	4	470	0.85%
Pleural mesothelioma	SUFU	5	485	1.03%
	SMO	2	483	0.41%
	GLI3	1	245	0.41%
	SHH	5	1505	0.33%
	PTCH1	45	2311	1.95%
	PTCH2	17	1505	1.13%
	SUFU	43	2255	1.91%
Prostatic adenocarcinoma	SMO	14	2295	0.61%
	GLI3	129	1505	8.57%
	GLI2	92	1505	6.11%
	GLI1	20	2202	0.91%
	PTCH1	2	493	0.41%
	SUFU	1	315	0.32%
Salivary gland carcinoma	SMO	5	494	1.01%
	GLI1	1	298	0.34%
	SHH	25	1589	1.57%
	PTCH1	190	2526	7.52%
Malignant melanoma	PTCH2	122	1682	7.25%
	SUFU	91	2493	3.65%
	SMO	92	2631	3.50%
	GLI2	190	1631	11.65%
	GLI3	119	1631	7.30%

	GLI1	111	1870	5.94%
	SHH	3	126	2.38%
	PTCH1	491	933	52.63%
	PTCH2	19	126	15.08%
Basal cell carcinoma	SUFU	33	338	9.76%
	SMO	154	578	26.64%
	GLI3	31	126	24.60%
	GLI2	23	126	18.25%
	GLI1	15	142	10.56%
	SHH	9	69	13.04%
	PTCH1	33	243	13.58%
	PTCH2	14	69	20.29%
Skin squamous cell carcinoma	SUFU	8	150	5.33%
	SMO	17	193	8.81%
	GLI1	25	147	17.01%
	GLI3	18	69	26.09%
	GLI2	18	69	26.09%
	PTCH1	2	564	0.35%
Testicular germ cell tumors	SMO	1	457	0.22%
	GLI1	3	457	0.66%
	PTCH1	1	96	1.04%
Thymic carcinoma	GLI2	1	21	4.76%
	SHH	16	1117	1.43%
	PTCH1	25	2148	1.16%
	PTCH2	22	1739	1.27%
Thyroid carcinoma	SUFU	11	2124	0.52%
	SMO	17	2415	0.70%
	GLI2	22	1117	1.97%
	GLI3	21	1117	1.88%
	GLI1	9	1988	0.45%
	SHH	15	802	1.87%
	PTCH1	45	1344	3.35%
	PTCH2	17	802	2.12%
Bladder cancer	SUFU	23	1221	1.88%
	SMO	22	1302	1.69%
	GLI3	40	820	4.88%
	GLI2	33	802	4.11%
	GLI1	26	1151	2.26%

Data was from the latest version of COSMIC v99 (released November, 28 2023; <https://cancer.sanger.ac.uk>).PTCH,Patched;SMO,Smoothened;GLI,glioma-associated oncogene;SHH;sonic Hedgehog;SUFU,suppressor of fused protein.

Table SII. Single gene mutation rates of key genes in Hedgehog pathway in different tumor types (II).

Tumor type	Gene	Rate of mutagenesis	Affects	Refs. (DOI)
Ameloblastoma	SMO	39%	carried in ameloblastomas arising in the maxilla predominantly	10.1038/ng.2986
Medulloblastoma	PTCH1	43-73%	intermediate prognosis	10.21873/anticancerres.15703
	SUFU	8-10%	TP53 mutations and MYC amplifications as the main predictors of prognosis;	10.1097/CMR.00000000000000789
	SMO	9-20%	GLI1 rs2228226 polymorphism had poorer overall survival and recurrence-free survival	10.1038/NG.3525
	GLI1 or GLI2 amplifications	9%		
Basal cell carcinoma	PTCH1	30-40%		
	SMO	6-13%	promote tumorigenesis	10.1016/j.jaad.2010.06.054
Gorlin syndrome / Nevoid basal cell carcinoma syndrome	PTCH1 (heterozygous germline mutations)	56%	promote tumorigenesis	10.21873/anticancerres.15703 10.1097/CMR.00000000000000789 10.1016/j.jaad.2010.06.054
	PTCH2	/	lose PTCH2 inhibitory function in the SHH signalling pathway	10.1136/jmg.2007.055343
Fetal rhabdomyomas and embryonal rhabdomyomas	PTCH	44.50%		
	SUFU	22%	haploinsufficiency for PTCH and SUFU promote tumorigenesis	10.1002/path.1882
Meningioma	SMO (in non-NF2 meningiomas)	5%	/	10.1126/science.1233009
	SUFU	<1%	SUFU mutations predispose to meningiomas	10.1016/j.ajhg.2012.07.015
Bladder cancer	PTCH1	5%		
	SMO	3%	/	10.1016/j.cell.2017.09.007
Breast cancer	SUFU	2.70%		
	SMO	33.3%	/	
Non-small-cell lung cancer	SMO (gain-of-function mutations) or	5.6%	/	
Ovarian cancer	PTCH1	14.3%	/	10.1200/JCO.2017.75.3780
Prostate cancer	(loss-of-function mutations)	20%	/	
Salivary gland carcinoma		16.7%	/	

Small intestinal carcinoma		16.7%	/		
Pancreatic cancer	GLI3	6%		NO association with PDA grade, presence of lymph node metastasis and adenosquamous histology	10.1038/ncomms7744
Pan-cancer	GLI1	10%		modulate the immune microenvironment, regulate of EMT;associate with poor prognosis in several cancers	10.18632/aging.205630
	GLI2	14%			
	GLI3	13%			
Gastrointestinal cancer	PTCH1	/		enriched INF- γ response, INF- α response, glycolysis and reactive oxygen species pathway gene sets; associated with better OS in patients receiving immunotherapy	10.1093/carcin/bgae007
Colorectal cancer	PTCH1	28.60%		associated with better OS and PFS in patients receiving immunotherapy	10.1007/s00262-021-02966-9
Pericytic Neoplasm	Actinbeta (ACTB1):GLI-1 fusion	1	/	inconsistent myopericytic characteristics and a propensity for metastasis	10.1097/PAS.0000000000001360
Malignant Epithelioid Neoplasm (submandibular soft tissue/neck)	PTCH1:GLI1 fusion		/	with lung metastases	10.1097/PAS.0000000000001010
Gastroblastoma	MALAT1:GLI1 fusion		/	overexpression of GLI1 protein, promote tumorigenesis	10.1038/modpathol.2017.68
Mesenchymal neoplasms of the gynecologic tract	PAMR1:GLI1 fusion		/	/	10.1002/gcc.23099

Data was from published studies. SMO, smoothened; PTCH, Patched; SUFU, suppressor of fused protein; GLI, glioma-associated oncogene; ACTB1 MALAT1, metastasis associated lung adenocarcinoma transcript 1; PAMR1, peptidase domain containing associated with muscle regeneration 1; ACTB1, actin beta.

Table SIII. The potential of differentially methylated regions for diagnosis of different tumor types.

Genes	Tumortypes	Types	ID	AUC*	
SHH	Bladder cancer	gene	SHH	0.917	
	Breast cancer	gene	SHH	0.934	
	Colon cancer	gene	SHH		0.992
		DMR	chr7	155809011-155812971	0.924
	Head and neck cancer	gene	SHH	0.979	
	Kidney clear cell carcinoma	gene	SHH	0.941	
	Kidney papillary cell carcinoma	gene	SHH	0.956	
	Lung adenocarcinoma	gene	SHH		0.985
		gene	SHH		0.998
		DMR	chr7	155802380-155803663	0.97
	Lung squamous cell carcinoma	DMR	chr7	155804650-155804779	0.904
		DMR	chr7	155805883-155808297	0.963
		gene	SHH		0.964
	Prostate cancer	gene	SHH	0.995	
	Endometrioid cancer	gene	SHH	0.995	
SMO	Liver cancer	gene	SMO	0.984	
	Head and neck cancer	gene	SMO	0.959	
	Kidney clear cell carcinoma	gene	SMO	0.966	
	Kidney papillary cell carcinoma	gene	SMO	0.969	
	Lung adenocarcinoma	gene	SMO		0.983
		gene	SMO		0.967
	Lung squamous cell carcinoma	gene	SMO		0.967
		DMR	chr7	129189639-129190227	0.936
	Prostate cancer	DMR	chr7	129189639-129190227	0.936
	Bladder cancer	gene	PTCH1	0.988	
PTCH1	Breast cancer	gene	PTCH1	0.993	
	Colon cancer	gene	PTCH1	0.968	
	Head and neck cancer	gene	PTCH1	0.932	
	Kidney clear cell carcinoma	gene	PTCH1	0.96	
	Kidney papillary cell carcinoma	gene	PTCH1	0.983	
	Liver cancer	gene	PTCH1	0.977	
	Lung adenocarcinoma	gene	PTCH1		0.977
		gene	PTCH1		0.987

	Lung squamous cell carcinoma	gene	PTCH1		0.978
	Prostate cancer	gene	PTCH1		0.92
	Breast cancer	gene	PTCH2		0.912
	Colon cancer	gene	PTCH2		0.938
	Head and neck cancer	gene	PTCH2		0.938
PTCH2	Kidney clear cell carcinoma	gene	PTCH2		0.974
	Liver cancer	gene	PTCH2		0.948
	Lung adenocarcinoma	gene	PTCH2		0.925
	Lung squamous cell carcinoma	gene	PTCH2		0.996
	Prostate cancer	gene	PTCH2		0.942
	Bladder cancer	gene	GLI1		0.988
	Breast cancer	gene	GLI1		0.956
	Colon cancer	gene	GLI1		0.917
	Head and neck cancer	gene	GLI1		0.92
	Kidney clear cell carcinoma	gene	GLI1		0.944
GLI1	Liver cancer	gene	GLI1		0.944
		DMR	chr12	57471942-57473404	0.912
	Lung adenocarcinoma	gene	GLI1		0.974
	Lung squamous cell carcinoma	gene	GLI1		0.981
	Prostate cancer	gene	GLI1		0.99
	Endometrioid cancer	gene	GLI1		0.959
	Bladder cancer	gene	GLI2		0.937
	Breast cancer	gene	GLI2		0.99
		DMR	chr2	120867253-120868346	0.917
	Colon cancer	gene	GLI2		1
	Head and neck cancer	gene	GLI2		0.991
GLI2	Kidney clear cell carcinoma	gene	GLI2		0.983
	Kidney papillary cell carcinoma	gene	GLI2		0.981
		gene	GLI2		0.9
	Liver cancer	DMR	chr2	120742559-120744613	0.921
		DMR	chr2	120783844-120791854	0.962
		DMR	chr2	120791988-120797125	0.989

		DMR	chr2	120797208-120798274	0.913
		DMR	chr2	120810301-120820229	0.907
		DMR	chr2	120855306-120862188	0.961
		DMR	chr2	120869637-120875001	0.942
		DMR	chr2	120912706-120913214	0.921
		DMR	chr2	120950123-120955720	0.962
		DMR	chr2	120982835-120986131	0.922
		DMR	chr2	120989088-120989482	0.912
		DMR	chr2	120990479-120996343	0.946
		gene	GLI2		1
	Lung adenocarcinoma	DMR	chr2	120765339-120766886	0.942
		DMR	chr2	120867794-120868289	0.974
		gene	GLI2		0.998
	Lung squamous cell carcinoma	DMR	chr2	120740885-120741392	0.919
		DMR	chr2	120765339-120766886	0.981
		DMR	chr2	120867794-120868289	0.97
		gene	GLI2		0.985
	Prostate cancer	DMR	chr2	120978152-120978462	0.929
	Thyroid cancer	gene	GLI2		0.95
	Bladder cancer	gene	GLI3		0.913
		gene	GLI3		0.979
	Breast cancer	DMR	chr7	42226218-42229436	0.978
		gene	GLI3		0.998
	Colon cancer	DMR	chr7	42227601-42228367	0.958
		DMR	chr7	42238113-42238356	0.94
GLI3	Head and neck cancer	gene	GLI3		0.986
	Kidney clear cell carcinoma	gene	GLI3		0.994
	Kidney papillary cell carcinoma	gene	GLI3		0.979
		gene	GLI3		0.957
	Liver cancer	DMR	chr7	41956340-41964058	0.952
		DMR	chr7	41967618-41969776	0.946
		DMR	chr7	41986179-41995798	0.903

	gene	GLI3		1
Lung adenocarcinoma	DMR	chr7	41957139-41963298	0.957
	DMR	chr7	41967794-41969007	0.978
	DMR	chr7	42223505-42226551	0.959
	gene	GLI3		0.99
Lung squamous cell carcinoma	DMR	chr7	41957139-41963298	0.905
	DMR	chr7	41967794-41969007	0.923
	DMR	chr7	42223505-42226551	0.947
	DMR	chr7	42227878-42228504	0.971
	DMR	chr7	42238166-42238603	0.916
Prostate cancer	gene	GLI3		0.929
	DMR	chr7	42238251-42238873	0.926
Endometrioid cancer	gene	GLI3		0.911

*AUC, DMR overlapped with protein in classifying cancer and normal samples in the TCGA cohort. SHH, sonic Hedgehog; SMO, smoothened; PTCH, patched; GLI, glioma-associated oncogene.

Table SIV. The potential of differentially methylated regions for prognosis of different tumor types.

Gene	Cancer type	Type	ID	Low methylation group	High methylation group	P-Value	HR (High)	P (HR)
SHH	Breast cancer	DMR	chr7 155804650-155904914	394	393	0.00993	0.6	0.011
	Kidney clear cell carcinoma	gene	SHH	160	160	0.019	0.63	0.02
	Acute myeloid leukemia	DMR	chr7 155806332-155806766	90	90	0.00303	0.58	0.0033
	Lung squamous cell carcinoma	gene	SHH	182	182	0.0409	0.72	0.042
	Lung adenocarcinoma	DMR	chr7 155802380-155803663	182	182	0.00522	0.64	0.0056
		DMR	chr7 155802380-155803663	226	225	0.0162	1.5	0.017
	Pancreatic cancer	gene	SHH	93	92	0.0346	1.5	0.036
		DMR	chr7 155804703-155805626	93	92	0.0307	1.6	0.032
Sarcoma	gene	SHH	133	132	0.0166	1.6	0.018	
SMO	Stomach cancer	gene	SMO	195	195	0.00378	0.62	0.0041
		DMR	chr7 129189058-129189778	195	195	0.00184	0.6	0.0021
	Kidney clear cell carcinoma	gene	SMO	160	160	0.00165	1.9	0.002
	Kidney papillary cell carcinoma	gene	SMO	138	137	0.0439	1.9	0.048
	Pancreatic cancer	DMR	chr7 129188102-129188362	93	92	0.0258	1.6	0.027
PTCH1	Uterine carcinosarcoma	gene	SMO	29	28	0.0374	2.1	0.041
	Adrenocortical cancer	gene	PTCH1	40	40	0.00209	3.4	0.0037
	Cervical cancer	DMR	chr9 95515602-95516593	155	154	0.0139	1.8	0.015
		gene	PTCH1	258	257	0.0331	3.2	0.044
PTCH2	Cervical cancer	DMR	chr1 44842499-44842830	155	154	0.0279	0.59	0.03
	Adrenocortical cancer	gene	PTCH2	40	40	0.0157	2.6	0.02
	Colon cancer	gene	PTCH2	148	148	0.046	1.6	0.048
GLI1	Lung adenocarcinoma	DMR	chr1 44831716-44831825	226	225	0.0277	1.4	0.028
	Cervical cancer	DMR	chr12 57474962-57476515	155	154	0.0117	0.55	0.013

	Liver cancer	DMR	chr12	57469483-57470576	189	189	0.0264	0.68	0.027
	Sarcoma	gene	GLI1		133	132	0.00293	0.54	0.0034
	Melanoma	gene	GLI1		229	229	0.00176	0.65	0.0019
	Thymoma	gene	GLI1		62	61	0.014	0.15	0.027
	Acute myeloid leukemia	DMR	chr12	120735486-120735690	90	90	0.000652	0.53	0.00079
	Cervical cancer	DMR	chr12	120792018-120792191	155	154	0.0439	0.62	0.046
		DMR	chr12	120863477-120864006	155	154	0.033	0.60	0.035
	Thymoma	gene	GLI2		62	61	0.00864	0.10	0.032
	Ocular melanomas	gene	GLI2		40	40	0.00189	0.25	0.004
GLI2	Colon cancer	DMR	chr12	120758389-120759215	148	148	0.000337	2.4	0.00052
	Kidney clear cell carcinoma	gene	GLI2		160	160	3.07E-05	2.3	5.20E-05
	Lung adenocarcinoma	DMR	chr12	120820224-120821206	226	225	0.00329	1.6	0.0036
	Lung squamous cell carcinoma	DMR	chr12	120792018-120792295	182	182	0.038	1.4	0.039
	Acute myeloid leukemia	DMR	chr7	41991908-41993148	90	90	0.044	0.69	0.046
	Lung adenocarcinoma	DMR	chr7	41957139-41963298	226	225	0.0299	0.71	0.031
		gene	GLI3		195	195	0.0218	0.68	0.023
	Stomach cancer	DMR	chr7	42235733-42236053	195	195	0.0106	0.65	0.011
		DMR	chr7	42236114-42237019	195	195	0.0012	0.58	0.0014
		DMR	chr7	42237016-42237257	195	195	0.0283	0.7	0.029
GLI3		DMR	chr7	42237263-42237476	195	195	0.00644	0.64	0.0069
	Thymoma	gene	GLI3		62	61	0.00454	0.087	0.023
	Colon cancer	DMR	chr7	42151259-42153610	148	148	0.0403	1.6	0.042
	Head and neck cancer	gene	GLI3		265	264	0.00936	1.4	0.0097
	Lung squamous cell carcinoma	gene	GLI3		182	182	0.0284	1.4	0.029

SMO, smoothened;PTCH, Patched;GLI, glioma-associated oncogene.

Table SV.HH pathway affect the expression of other pathway molecules by regulating ncRNAs to regulate tumor phenotypes

HH pathway	ncRNA	Targets	Affects	Tumor type	Phenotype	References (DOI)
GLI1	circ-0011536 (upregulate)	miR-451a VGF	/ sponge miR-451a / increase VGF expression	Pancreatic cancer	Promote peripheral neural remodeling	10.1186/s13046-023-02894-9
GLI1	circ-0005358 (generate from GLI1)	PTBP1 CDCP1	/ block polypyrimidine tract-binding protein 1 (PTBP1) from binding to and stabilizing CUB-domain-containing protein 1 (CDCP1) mRNA	Cervical cancer	Reduce tumor metastasis	10.1016/j.omtn.2021.11.020
GLI2	miR-124 (downregulate)	AURKA	increase AURKA expression	Glioma	Reduce tumor proliferation and colony formation.	10.1093/neuonc/nou217
PTCH1-3'UTR	miR-101-3p (downregulate)	SLC39A6	sponge miR-101-3p / increase SLC39A6 expression	Non-small cell lung cancer	Promote cell migration, invasion, and adhesion	10.18632/oncotarget.23219
SHH	lncRNA-TMEM105(upregulate)	lactate dehydrogenase A (LDHA)	SHH activation promote Myc-associated zinc finger protein (MAZ) binding to TMEM105 promoter / promote LDHA expression	Breast cancer	Promote glycolysis, tumor invasion and metastasis	10.1038/s41419-023-05628-z

HH, Hedgehog; PTBP1, polypyrimidine tract-binding protein 1; CDCP1, CUB-domain-containing protein 1; AURKA;aurora kinase A; LDHA, SLC39A6 lactate dehydrogenase A; MAZ, Myc-associated zinc finger protein; UTR, untranslated region.