

Table S1. Details of included histone chaperones in human.

Histone chaperone	Histone preference	Complex (or complexes)	Related Tumors
ASF1A	H3.1–, H3.2–, H3.3–H4	Multiple	HCC, GIC
ASF1B	H3.1–, H3.2–, H3.3–H4	Multiple	HCC, GC, PC
MCM2	CENP-A–, H3.1–, H3.2–, H3.3–H4	MCM2–7 complex	HCC, EC, GC, CRC
TONSL	H3–H4	MMS22L–TONSL complex	GC
RBAP46	H3–H4	HAT, HDAC, NuRF, NuRD, PRC2	NR
sNASP	H3.1–, H3.2–, H3.3–H4, H1	HAT	HCC
IPO4	H3.1–, H3.2–, H3.3–H4	Nuclear import receptor	GC
SPT2	H3–H4	ND	CRC
SPT6	H3–H4	ND	CRC
ANP32E	H2A.Z–H2B	P400–TIP60	GC, PC
HJURP	CENP-A–H4 (Cse4–H4)	Centromere assembly	HCC, PC, CRC
SET	H3–H4	INHAT, Vps75–Rtt109	NR
NAP1L1	H2A–, H2A.Z–H2B, H3–H4, H1	Nuclear import importin 9, Kap114	HCC, CRC
NPM1	H3–H4, CENP-A–H4, H1	SWAP	HCC, GC, PC, CRC, EC
Nucleolin	H2A–H2B, H1	SWAP	HCC, GC, PC, CRC, EC
CHAF1A	H3.1–H4	CAF1	HCC, GC
CHAF1B	H3.1–H4	CAF1	HCC

Histone chaperone	Histone preference	Complex (or complexes)	Related Tumors
RBAP48	H3.1–, H3.2–, H3.3–H4	CAF1, HDAC, NuRF, NuRD, and PRC2	GC
HIRA	ND	HIRA/HIR	NR
UBN1	H3.3–H4	HIRA/HIR	NR
CABIN1	ND	HIRA/HIR	NR
SPT16	H2A–H2B, H3–H4	FACT	HCC
SSRP1	H2A–H2B, H3–H4	FACT	HCC, GC, CRC
DAXX	H3.3–H4	DAXX–ATRX	GC, CRC
ATRX	ND	DAXX–ATRX	CRC, PC
VPS72	H2A.Z–H2B	SRCAP/SWR-C, P400-TIP60	HCC

ANP32E: Acidic-leucine-rich nuclear phosphoprotein 32E; ASF1A: Anti-Silencing Function 1A; ASF1B: Anti-Silencing Function 1B; ATRX: Alpha-thalassaemia/mental retardation syndrome X-linked; CABIN: Calcineurin-binding protein cabin-1; CHAF1A: Chromatin Assembly Factor 1 Subunit A; CHAF1B: Chromatin Assembly Factor 1 Subunit B; CRC: colorectal cancer; DAXX: Death domain-associated protein 6; EC: esophageal cancer; GC: gastric cancer; HATs: Histone acetyltransferases; HCC: hepatocellular carcinoma; HDAC: Histone deacetylase; HIRA: Histone regulation A; HJURP: Holliday Junction Recognition Protein; hTERT: Human telomerase reverse transcriptase; INHAT: Inhibitor of histone acetyltransferases; IPO4: Importin 4; MCM2: Minichromosome maintenance protein 2; MMS22L: Methyl Methanesulfonate-Sensitivity Protein 22-Like; NAP1L1: Nucleosome Assembly Protein 1 Like 1; ND, not defined; NPM1: Nucleophosmin 1; NR: not reported; NuRF: Nucleosome Remodeling Factor; PC: pancreatic cancer; RBAP46: Retinoblastoma associated protein 46; RBAP48: Retinoblastoma associated protein 48; SET: Patient SE translocation; PRC2: Polycomb repressive complex 2; sNASP: Somatic nuclear autoantigenic sperm protein; SPT2: Suppressor of Ty 2; SPT16: Suppressor Of Ty 16; SSRP1: Structure Specific Recognition Protein 1. UBN1: Ubinuclein 1; VPS72: protein sorting 72 homologue; TONSL: Tonsuku Like.

Table S2. Included literature on selected histone chaperones in digestive cancer.

ID	Histone chaperone	First author	Year	Tumor	Reference number
1	ANP32E	Zhu	2022	GC	[1]
2		Zhang	2020	PDAC	[2]
3		Ma	2021	PDAC	[3]
4	ASF1A	Liang	2017	CRC	[4]
5		Qiu	2019	CRC	[5]
6		Wu	2019	HCC	[6]
7		Chen	2022	GC	[7]
8		Zhang	2022	HCC	[8]
9		Ouyang	2021	HCC	[9]
10		Zhan	2021	HCC	[10]
11		Kim	2022	PDAC	[11]
12		Wang	2022	PDAC	[12]
13	ATRX	Young	2019	PDAC	[13]
14		Li	2018	CRC	[14]
15	DAXX	Tzeng	2006	CRC	[15]
16		Chen	2019	CRC	[16]
17		Liu	2020	CRC	[17]
18		Huang	2022	CRC	[18]
19		Ko	2018	EC	[19]
20		Chen	2020	GC	[20]
21		Wu	2020	GC	[21]
22		Xu	2017	GC	[22]
23	CHAF1A	Zheng	2018	GC	[23]
24		Wang	2019	GC	[24]
25		Xu	2016	HCC	[25]
26	CHAF1B	Peng	2018	HCC	[26]
27	HJURP	Kang	2020	CRC	[27]
28		Chen	2019	HCC	[28]
29		Hu	2017	HCC	[29]
30		Yi	2021	HCC	[30]
31		Chen	2018	HCC	[31]
32		Wang	2020	PDAC	[32]
33	IPO4	Xu	2019	GC	[33]
34	MCM2	Wang	2020	CRC	[34]
35		Giaginis	2009	CRC	[35]
36		Hanna-Morris	2009	CRC	[36]
37		Kato	2003	EC	[37]

ID	Histone chaperone	First author	Year	Tumor	Reference number
38		Huang	2011	EC	[38]
39		Yang	2012	GC	[39]
40		Giaginis	2011	GC	[40]
41		Liu	2013	GC	[41]
42		Tokuyasu	2008	GC	[42]
43		Tang	2022	HCC	[43]
44		Ahmed	2019	HCC	[44]
45	NAP1L1	Queiroz	2020	CRC	[45]
46		Aydin	2020	CRC	[46]
47		Huang	2018	HCC	[47]
48		Chen	2018	HCC	[48]
49		Zhang	2021	HCC	[49]
50		Le	2019	HCC	[50]
		Schimmack	2014	PDAC	[51]
51	NPM1	Wang	2022	CRC	[52]
52		Wong	2013	CRC	[53]
53		Yu	2021	CRC	[54]
54		Grbčić	2021	CRC	[55]
55		Liu	2012	CRC	[56]
56		Nozawa	1996	CRC	[57]
57		Yang	2014	CRC	[58]
58		Tang	2018	CRC	[59]
59		Liu	2022	EC	[60]
60		Leal	2014	GC	[61]
61		Zhou	2016	GC	[62]
62		Zhou	2013	GC	[63]
63		Guo	2022	GC	[64]
64		Li	2014	GC	[65]
65		Lakshmi Ch	2021	GC	[66]
66		Yun	2007	HCC	[67]
67		Xu	2014	HCC	[68]
68		Lo	2013	HCC	[69]
69		Zhang	2022	HCC	[70]
70		Liu	2012	HCC	[71]
71		Li	2017	HCC	[72]
72		Ching	2015	HCC	[73]
73		Zhu	2015	PDAC	[74]
74		Hamilton	2014	PDAC	[75]
75	Nucleolin	Wu	2014	CRC	[76]
76		Reyes-Reyes	2008	CRC	[77]

ID	Histone chaperone	First author	Year	Tumor	Reference number
77		Wu	2020	CRC	[78]
78		Qi	2015	ESCC	[79]
79		Qiu	2013	GC	[80]
80		Devanand	2018	GC	[81]
81		Qiu	2015	HCC	[82]
82		Guo	2014	HCC	[83]
83		Chen	2015	HCC	[84]
84		Burbano De Lara	2021	HCC	[85]
85		Gilles	2016	PDAC	[86]
86		Peng	2010	PDAC	[87]
87		Xu	2019	PDAC	[88]
88	RBAP48	Jin	2018	GC	[89]
89	sNASP	Yu	2017	GC	[90]
90		Kang	2018	HCC	[91]
91	SPT2	Yin	2022	CRC	[92]
92	SPT6	Diao	2021	CRC	[93]
93	SPT16/SSRP1	Shen	2020	HCC	[94]
94	SSRP1	Song	2020	CRC	[95]
95		Wu	2019	CRC	[96]
96		Wang	2019	CRC	[97]
97		Huang	2019	CRC	[98]
98		Jin	2022	GC	[99]
99		Ding	2016	HCC	[100]
100		Min	2021	HCC	[101]
101		Zheng	2020	HCC	[102]
102	TONSL	Wang	2019	GC	[103]
103	VPS72	Chen	2022	HCC	[104]

Abbreviations: ANP32E: Acidic Nuclear Phosphoprotein 32 Family Member E; ASF1A: Anti-Silencing Function 1A; ASF1B: Anti-Silencing Function 1B; ATRX: ATRX Chromatin Remodeler; CHAF1A: Chromatin Assembly Factor 1 Subunit A; CHAF1B: Chromatin Assembly Factor 1 Subunit B; DAXX: Death Domain Associated Protein; HJURP: Holliday Junction Recognition Protein; HIRA; IPO4: Importin 4; MCM2: Minichromosome Maintenance Complex Component 2; NAP1L1: Nucleosome Assembly Protein 1 Like 1; NPM1: Nucleophosmin 1; NR: not reported; NS: not significant; sNASP: Nuclear Autoantigenic Sperm Protein; SPT2: Suppressor Of Ty 2; SPT6: Suppressor Of Ty 6; SPT16: Suppressor Of Ty 16; SSRP1: Structure Specific Recognition Protein 1; TONSL: Ton-soku Like.

Table S3. Clinical events of selected histone chaperones in digestive cancer.

Gene	Tumor	Role	Expression	Correlation with OS	Correlation with DFS	Reference number
ASF1A	HCC	promoter	High	Negative	Negative	[6]
	CRC	promoter	High	Negative	Negative	[4]
ASF1B	HCC	promoter	NR	Negative	Negative	[8]
	HCC	promoter	High	NR	NR	[9]
	GC	promoter	High	Negative	NR	[7]
SPT16	HCC	promoter	High	Negative	Negative	[105]
SSRP1	HCC	promoter	High	Negative	Negative	[105]
	HCC	promoter	High	Negative	Negative	[100]
	GC	promoter	High (RNA)	NR	NR	[99]
	CRC	promoter	High	NR	NR	[95]
	CRC	promoter	High	Negative	Negative	[96]
HJURP	HCC	promoter	High	Negative	NR	[31]
	HCC	promoter	High	NR	NR	[106]
	HCC	promoter	High	Negative	NR	[29]
	HCC	promoter	High	Negative	NR	[107]
	PDAC	promoter	High	NR	NR	[32]
	CRC	promoter	High	Negative	NR	[27]
NPM1	HCC	promoter	High	NR	NR	[108]
	HCC	NR	High	NR	NR	[68]
	HCC	promoter	High	Negative	NR	[109]
	GC	NR	Low	NR	NR	[110]
	GC	promoter	High	Negative	Negative	[62]
	GC	promoter	High	Negative	Negative	[63]
	GC	suppressor	Low	Positive	Positive	[64]
	GC	promoter	High	Negative	Negative	[65]
	PDAC	promoter	High	Negative	NR	[74]
	PDAC	promoter	High (NPM ^{S48ph})	NR	NR	[75]
	CRC	promoter	High	NR	NR	[53]
	CRC	promoter	High	Negative	NR	[54]
	CRC	promoter	High	NR	NR	[55]
	CRC	promoter	High	Negative	NR	[56]
	CRC	NR	High	NR	NR	[57]
	CRC	promoter	High	Negative	Negative	[58]
NAP1L1	HCC	promoter	High	Negative	NR	[49]
	HCC	promoter	High	Negative	NR	[50]
	CRC	suppressor	Low	Positive	NR	[45]

Gene	Tumor	Role	Expression	Correlation with OS	Correlation with DFS	Reference number
	CRC	NR	High in serum	NR	NR	[46]
CHAF1A	HCC	promoter	High	Negative	Negative	[25]
	GC	promoter	High	NR	NR	[23]
	GC	promoter	NR	Negative	Negative	[24]
Nucleolin	HCC	promoter	High	Negative	NR	[82]
	HCC	promoter	High	Negative	Negative	[111]
	HCC	promoter	High	Negative	NR	[84]
	GC	dependent on site	High	Dependent on site	NR	[80]
	GC	promoter	High	Negative	NR	[81]
	PDAC	promoter	High	Negative	NR	[86]
	PDAC	dependent on site	High in nucleolus	Positive	NR	[87]
	CRC	promoter	NS	NR	NR	[76]
	ESCC	dependent on site	High	Dependent on site	NR	[79]
DAXX	EC	promoter	High	Negative	NR	[19]
	GC	promoter	High in nucleolus	Negative	Negative	[20]
	GC	suppressor	Low	NR	NR	[21]
	GC	promoter	High in nucleolus	Negative	Negative	[22]
	CRC	NR	Low	NR	NR	[15]
	CRC	suppressor	Low	NR	NR	[16]
	CRC	suppressor	Low (RNA)	NR	NR	[17]
	CRC	promoter	High	NR	NR	[18]
ATRX	CRC	promoter	High (RNA)	NR	NR	[14]
MCM2	HCC	promoter	High	Negative	NR	[43]
	HCC	promoter	High (RNA)	NR	NR	[44]
	EC	promoter	NR	Negative	NR	[37]
	EC	NR	High	NR	NR	[38]
	GC	promoter	High	Negative	Negative	[39]
	GC	NR	High	NS	NR	[40]
	GC	NR	High	Negative	Negative	[41]
	GC	NR	High	Negative	NR	[42]
	CRC	NR	High	NR	NR	[35]

Gene	Tumor	Role	Expression	Correlation with OS	Correlation with DFS	Reference number
	CRC	NR	High	NR	NR	[36]
sNASP	HCC	promoter	High	NR	NR	[91]
IPO4	GC	promoter	High	NR	NR	[33]
SPT2	CRC	promoter	High	Negative	NR	[92]
SPT6	CRC	promoter	High	NR	NR	[93]
ANP32E	PDAC	promoter	High	NR	NR	[3]
	GC	promoter	High (RNA)	NR	NR	[1]

Abbreviations: ANP32E: Acidic Nuclear Phosphoprotein 32 Family Member E; ASF1A: Anti-Silencing Function 1A; ASF1B: Anti-Silencing Function 1B; ATRX: ATRX Chromatin Remodeler; CHAF1A: Chromatin Assembly Factor 1 Subunit A; CHAF1B: Chromatin Assembly Factor 1 Subunit B; DAXX: Death Domain Associated Protein; HJURP: Holliday Junction Recognition Protein; HIRA: IPO4: Importin 4; MCM2: Minichromosome Maintenance Complex Component 2; NAP1L1: Nucleosome Assembly Protein 1 Like 1; NPM1: Nucleophosmin 1; NR: not re-ported; NS: not significant; sNASP: Nuclear Autoantigenic Sperm Protein; SPT2: Suppressor Of Ty 2; SPT6: Suppressor Of Ty 6; SPT16: Suppressor Of Ty 16; SSRP1: Structure Specific Recognition Protein 1; TONSL: Tonsoku Like.

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