Reference: http://dx.doi.org/10.1155/2015/237969

pI, sequence, and structures of HS-binding cell penetrating peptides.

	Peptide name pI	Sequence and predicted secondary structure*	Heparan sulfate binding region	Internalization mechanism	Ref.
		Viral protein-derived CPP			
1	TAT peptide (49–57) pI: 12.70	**RKKRRQRRR** CCCCCCCCC	RKKRRQRR	Lipid raft-mediated macropinocytosis	[25, 26]
2	Nucleoplasmin NLS (155–170) pI: 11.47	**KRPAAIKKAGQAKKKK** CcHHHHHHHHhHHHhCC	Not reported	Not reported	[58]
3	HTLV-II Rex (4–16) pI: 12.85	**TRRQRTRRARRNR** CCCCHHHHCCCCC	TRRQRT	Direct translocation	[21, 22]
4	Lambda-N (48–62) pI: 11.83	**QTRRRERRAEKQAQW** CCHHHHHHHHHHCCC	RRRERR	Not reported	[22]
5	Phi21 N (12–29) pI: 11.45	**TAKTRYKARRAELIAERR** CCCCCCCHHHHHHHHHHH	KTRYKARRA	Not reported	[22]
6	Delta N (1–22) pI: 11.44	**MDAQTRRRERRAEKQAQWKAAN** CCCCHHHHHHHHHHHHHHHHHH	TRRRERRA	Not reported	[22]
7	FHV coat (35–49) pI: 13.00	**RRRRNRTRRNRRRVR** CCCCCCCCCCCCCCC	RRRRNRTRRNRRRVR	Not reported	
8	BMV coat (8–26) pI: 12.78	**KMTRAQRRAAARRNRWTAR** CcCHHHHHHHHHHHhccccC	ARRNRW	Not reported	
9	HIV-1 Rev (35–46) pI: 12.85	**RQARRNRRRRWR** CCCCCCCHHHHH	RQARRNRRRRWR	Not reported	[22]
10	Rev (26–42) pI: 12.54	**TRQARRNRRRRWRERQF** CCCCCCCCHHHHHHHHH	TRQARRNRRRRWRERQF	Energy dependent lipid raft-mediated macropinocytosis	[27, 28]
11	CPP from pestivirus envelope glycoprotein (Erns) (194–220) pI: 11.72	**ENARQGAARVTSWLGRQLRIAGKRLEGRSKTWFGAYA** CCCcchHHHHHHHHHHHHHHHHHhhhCCCCccccccC	Basic residues	Direct translocation	[23]
12	gp41 fusion sequence pI: 11.33	**GALFLGWLGAAGSTMGAWSQPKKKRKV** HHHHHHHHHHHHHHHHHHHCCCCCCCCCC	WSQPKKKRKV	Direct translocation	[24]
13	VP22 pI: 12.10	**DAATATRGRSAASRPTERPRAPARSASRPRRPVD** CCCccCCCCCCCCCCCCCCCCCCCCCCCCCCCC	SRPRRP	Energy dependent lipid raft-mediated macropinocytosis	[27, 29]
14	SV40 NLS pI: 11.33	**PKKKRKV** CCCCCCC	PKKKRKV	Not reported	[59, 60]
		Animal homeostatic modulator-derived CPP			
15	Penetratin pI: 12.31	**RQIKIWFQNRRMKWKK** CCCHHHHHHHCCCCCC	NRRMKW	Direct translocation Endocytosis	[61]
16	CPP*ecp* pI: 10.05	**NYRWRCKNQN** CCCCCCCCCC	RWRCK	Macropinocytosis	[12, 62]

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	Peptide name pI	Sequence and predicted secondary structure*	Heparan sulfate binding region	Internalization mechanism	Ref.
17	Apolipoprotein B binding domain pI: 9.82	**SVKAQYKKNSDKHRLMRKRGLK** CCccccCCCCCCCCCCcCCCC	Basic residues	Endocytosis	[63, 64]
18	hCT (9~32) pI: 6.74	**LGTYTQDFNKFHTFPQTAIGVGAP** HHHHHHHHHHHHHHHCHHHHHCCCC	Not reported	Endocytosis	[63, 65]
19	pVEC (615–632) pI: 12.48	**LLIILRRRIRKQAHAHSK** ChhHHHHHHHHHHHhcCC	LRRRIRK	Macropinocytosis and clathrin mediated endocytosis	[66–68]
20	hLF peptide pI: 10.93	**KCFQWQRNMRKVRGPPVSCIKR** CCCchhHHHHhCCCCCcececC	MRKVRG	Lipid raft-mediated endocytosis	[69]
21	PDX-1-PTD pI: 12.31	**RHIKIWFQNRRMKWKK** ChhhhHhhhhhhhhcC	NRRMKWKK	Caveolae-dependent endocytosis and lipid raft-mediated macropinocytosis	[70]
		Antimicrobial peptide			
22	LL-37 (1–37) pI: 10.61	**LLGDFFRKSKEKIGKEFKRIVQRIKDFLRNLVPRTES** HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHCCCCC	FRKSKEKI	Endocytosis	[30, 31, 71]
23	SynB1 (1–18) pI: 12.30	**RGGRLSYSRRRFSTSTGR** CCCCEEEEECCEEEEECC	Basic residues	Endocytosis	[32]
24	SynB3 pI: 12.18	**RRLSYSRRRF** CCCCcccCCC	Basic residues	Endocytosis	[32]
		Toxin-derived CPP			
25	bPrPp (1–28) pI: 10.03	**MVKSKIGSWILVLFVAMWSDVGLCKKRP** CCCCCCCCHHHHHHHHHHHHHHHHCCCC	Basic residues	Macropinocytosis	[33]
26	Crotamine (1–42) pI: 9.51	**YKQCHKKGGHCFPKEKICLPPSSDFGKMDCRWRWKCCKKGSG** CCHHHHHCEEEECCCCCCCCCCCCEECCCCCCCCCEEEECCCC	RWRWK	Endocytosis	[34]
27	Maurocalcine (MCa) (1–33) pI: 9.46	**GDCLPHLKLCKENKDCCSKKCKRRGTNIEKRCR** CCCCCCCCCCCCHHHCCCCEEECCCCCCCCEEE	SKKCKR and EKRCR	Macropinocytosis	[35, 36]

*The confidence of the prediction is denoted by scaling the predictions from week (lower-case letter) to strong (upper-case letter). "H," "E," and "C" refer to α-helical, β-strand, and random coil propensities, respectively.

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Multifunctional CPPs for tumor suppression.

Name/sequence	Function	Mechanism	Cell line	Tumor mouse model	Ref.
CPP*ecp*/**NYRWRCKNQN**	Cell penetrating HS binding Antimigration Antiangiogenesis Tumor targeting	Block putative HS coreceptor for growth factor	CT-26 HUVEC	Murine colon carcinoma CT-26	[12–14]
Crotamine/**YKQCHKKGGHCFPKEKICLPPSSDFGKMDCRWRWKCCKKGSG**	Cell penetrating HS binding Antiproliferation Tumor targeting	Interact with lysosomes to trigger intracellular Ca^{2+} transients and alter mitochondrial membrane potential	B16F10 CHO-K1	Murine melanoma (B16F10) Murine mammary carcinoma (TS/A-pc, TS/A-pc-pGL3)	[34, 57]
NFL-TBS. (40–63)/**YSSYSAPVSSSLSVRRSYSSSSGS**	Cell penetrating Antimigration Antiproliferation Apoptosis-inducing Antitumor growth	Inhibit polymerization of microtubules	Human glioblastoma (T98G) Rat glioblastoma (F98) Rat gliosarcoma (9L)	Murine glioblastoma (F98)	[72, 73]
TAT peptide (46–57)/**SYGRKKRRQRRR**	Cell penetrating HS binding Antiangiogenesis Apoptosis-inducing	Inhibit VEGF binding to HUVEC and inhibit phosphorylation of ERK	HUVEC	×	[25, 74]
p28/**LSTAADMQGVVTDGMASGLDKDYLKPDD**	Cell penetrating Antiangiogenesis Antitumor growth	Inhibit phosphorylation of VEGFR-2, FAK, and Akt	HUVEC	Human melanoma (UISO-Mel-6)	[75]