

Table S1. List of peptide sequences predicted by AI

Sequence	Method	Treated cell	Inhibition index (μM)	Reference
GILSSIKGVAKGVAKNVAAQLDLTKCKITGC	ML	A549,	A549: 15.32 [IC_{50}],	[1]
		MCF7,	MCF7: 45.25 [IC_{50}],	
		HeLa,	HeLa: 37.23 [IC_{50}]	
		LoVo,	LoVo: 59.78 [IC_{50}],	
		293T	293T: 63.16 [IC_{50}]	
GIFDVVKGVKGVGKNVAGSLLEQLKCKLSGGC	ML	A549,	A549: 2.975 [IC_{50}],	
		MCF7,	MCF7: 25.74 [IC_{50}],	
		HeLa,	HeLa: 19.69 [IC_{50}]	
		LoVo,	LoVo: 8.05 [IC_{50}],	
		293T	293T: 5.832 [IC_{50}]	
GVLGAVKDLLIGAGKSAAQSVLTKLSCKLSNDC	ML	A549,	A549: 27.31 [IC_{50}],	
		MCF7,	MCF7: 41.21 [IC_{50}],	
		HeLa,	HeLa: 52.83 [IC_{50}]	
		LoVo,	LoVo: 55.22 [IC_{50}],	
		293T	293T: 48.7 [IC_{50}]	
GLFLDTLKGAADVAGKLEGLKCKIT	ML	A549,	A549: 24.01 [IC_{50}],	
		MCF7,	MCF7: 37.84 [IC_{50}],	
		HeLa,	HeLa: 23.26 [IC_{50}]	
		LoVo,	LoVo: 35.05 [IC_{50}],	
		293T	293T: 50.66 [IC_{50}]	
GLFDVVKGVKGVGAGKNVAGSLLEQLKCK	ML	A549,	A549: >128 [IC_{50}],	
		MCF7,	MCF7: >128 [IC_{50}],	
		HeLa,	HeLa: >128 [IC_{50}]	
		LoVo,	LoVo: 128 [IC_{50}],	
		293T	293T: >128 [IC_{50}]	
RLLRLIRKLII	ML	MCF7,	MCF7: 11 ± 1 [EC_{50}],	[2]
		A549,	A549: 21 ± 1 [EC_{50}],	
		LU1205,	LU1205: 9 ± 1 [EC_{50}],	
		Jurkat,	Jurkat: 39 ± 1 [EC_{50}],	
		HDMEC	HDMEC: 141 ± 1 [EC_{50}]	
RLLRLIRKLIL	ML	MCF7,	MCF7: 9 ± 1 [EC_{50}],	
		A549,	A549: 14 ± 1 [EC_{50}],	
		LU1205,	LU1205: 7 ± 1 [EC_{50}],	
		Jurkat,	Jurkat: 25 ± 1 [EC_{50}],	
		HDMEC	HDMEC: 125-250 [EC_{50}]	

LLLLLIRKLIK	ML	MCF7,	MCF7: 11 ± 1 [EC ₅₀],
		A549,	A549: 22 ± 1 [EC ₅₀],
		LU1205,	LU1205: 16 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 25 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 125-250 [EC ₅₀]
YLLYLIRKLIL	ML	MCF7,	MCF7: 13 ± 1 [EC ₅₀],
		A549,	A549: 29 ± 1 [EC ₅₀],
		LU1205,	LU1205: 14 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 22 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 256 ± 2 [EC ₅₀]
RLLRLIRKLIR	ML	MCF7,	MCF7: 14 ± 1 [EC ₅₀],
		A549,	A549: 27 ± 1 [EC ₅₀],
		LU1205,	LU1205: 16 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 27 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 138 ± 7 [EC ₅₀]
QLLQLIRKLII	ML	MCF7,	MCF7: 22 ± 1 [EC ₅₀],
		A549,	A549: 29 ± 1 [EC ₅₀],
		LU1205,	LU1205: 21 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 35 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 171 ± 1 [EC ₅₀]
QLLQLIRKLIM	ML	MCF7,	MCF7: 33 ± 1 [EC ₅₀],
		A549,	A549: 33 ± 1 [EC ₅₀],
		LU1205,	LU1205: 24 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 46 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 142 ± 2 [EC ₅₀]
MLLMLIRKLIL	ML	MCF7,	MCF7: 16 ± 1 [EC ₅₀],
		A549,	A549: 58 ± 1 [EC ₅₀],
		LU1205,	LU1205: 31 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 31 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 262 ± 1 [EC ₅₀]
QLLQLIRKLIR	ML	MCF7,	MCF7: 53 ± 1 [EC ₅₀],
		A549,	A549: 60 ± 1 [EC ₅₀],
		LU1205,	LU1205: 38 ± 1 [EC ₅₀],
		Jurkat,	Jurkat: 75 ± 1 [EC ₅₀],
		HDMEC	HDMEC: 260 ± 1 [EC ₅₀]
QLLQLIRKLIK	ML	MCF7,	MCF7: 50-100 [EC ₅₀],
		A549,	A549: 54 ± 1 [EC ₅₀],

		LU1205, Jurkat, HDMEC	LU1205: 39 ± 1 [EC ₅₀], Jurkat: 69 ± 1 [EC ₅₀], HDMEC: ≈250 [EC ₅₀]
QLLQLIRKLIY	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: 50-100 [EC ₅₀], A549: 61 ± 1 [EC ₅₀], LU1205: 29 ± 1 [EC ₅₀], Jurkat: 58 ± 1 [EC ₅₀], HDMEC: 349 ± 1 [EC ₅₀]
LLLQLIRKLIL	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: 10 ± 1 [EC ₅₀], A549: 30 ± 1 [EC ₅₀], LU1205: 12 ± 1 [EC ₅₀], Jurkat: 53 ± 1 [EC ₅₀], HDMEC: 154 ± 1 [EC ₅₀]
TLLLLIRKLIL	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: 38 ± 1 [EC ₅₀], A549: 79 ± 1 [EC ₅₀], LU1205: 16 ± 1 [EC ₅₀], Jurkat: 30 ± 1 [EC ₅₀], HDMEC: 348 ± 1 [EC ₅₀]
RLLLLIRKLIL	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: 24 ± 1 [EC ₅₀], A549: 35 ± 1 [EC ₅₀], LU1205: 18 ± 1 [EC ₅₀], Jurkat: 40 ± 1 [EC ₅₀], HDMEC: 160 ± 1 [EC ₅₀]
LLLLLIRKLIL	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: 25 ± 1 [EC ₅₀], A549: >100 [EC ₅₀], LU1205: 48 ± 1 [EC ₅₀], Jurkat: 50 ± 1 [EC ₅₀], HDMEC: 278 ± 1 [EC ₅₀]
QLLLLIRKLIL	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: 63 ± 1 [EC ₅₀], A549: >100 [EC ₅₀], LU1205: 44 ± 1 [EC ₅₀], Jurkat: 39 ± 1 [EC ₅₀], HDMEC: 271 ± 1 [EC ₅₀]
QLLLLIRKLIV	ML	MCF7, A549, LU1205, Jurkat,	MCF7: 77 ± 1 [EC ₅₀], A549: >100 [EC ₅₀], LU1205: 53 ± 1 [EC ₅₀], Jurkat: >100 [EC ₅₀],

		HDMEC	HDMEC: 339 ± 1 [EC ₅₀]
CLLLLIRKLIL	ML	MCF7, A549, LU1205, Jurkat, HDMEC	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀], LU1205: 76 ± 1 [EC ₅₀], Jurkat: >100 [EC ₅₀], HDMEC: ≈ 500 [EC ₅₀]
KLWKKIEKLIKLLTSIR	DL	MCF7	47 ± 3 [EC ₅₀], 236 ± 13 [HC ₅₀], 5.1 ± 0.6 [TI]
YIWARAERVWLWWGKFLSL	DL	MCF7	56 ± 3 [EC ₅₀], inactive [HC ₅₀], >7 [TI]
ELAKKLTCLKRQLHRIW	DL	MCF7	inactive [EC ₅₀], inactive [HC ₅₀], n.d. [TI]
DLFKQLQRLFLGILYCLYKIW	DL	MCF7	47 ± 4 [EC ₅₀], 132 ± 16 [HC ₅₀], 2.8 ± 0.6 [TI]
KLIDQWKKVLYHVE	DL	MCF7	inactive [EC ₅₀], inactive [HC ₅₀], n.d. [TI]
AIKKFGPLAKIVAKV	DL	MCF7	95 ± 4 [EC ₅₀], inactive [HC ₅₀], >4 [TI]
RWNGRIIKGFYNLVKIWKDLKG	DL	MCF7	42 ± 4 [EC ₅₀], 89 ± 6 [HC ₅₀], 2.1 ± 03 [TI]
KVWKIKKNIRLLHGIKRGWKG	DL	MCF7	34 ± 4 [EC ₅₀], inactive [HC ₅₀], >11 [TI]
GFWARIGKVFAAVKNL	DL	MCF7	101 ± 4 [EC ₅₀], inactive [HC ₅₀], >4 [TI]

[3]

AFLYRLTRQIRPWWRWLYKW	DL	MCF7	45.5 ± 0.8 [EC ₅₀], 34 ± 5 [HC ₅₀], 0.7 ± 0.1 [TI]
RIWGHKHSRYIKIVKRLIQ	DL	MCF7	50 ± 10 [EC ₅₀], inactive [HC ₅₀], >8 [TI]
QIWHKIRKLWQIIKDGF	DL	MCF7	16.1 ± 0.3 [EC ₅₀], 23 ± 5 [HC ₅₀], 1.4 ± 0.3 [TI]
ALFGILKKAFGKILTIFAGLPVV	ML	MCF7, A549	MCF7: 9.8 [EC ₅₀], A549: 8.6 [EC ₅₀]
GLGDFIKAIKHLGPLIGILPSKLVAA	ML	MCF7, A549	MCF7: 4.5 [EC ₅₀], A549: 11.3 [EC ₅₀]
GLKDPLKSVAKHLVK	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
GLVMLVKKAGLT	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549 >100: [EC ₅₀]
IIFGVIKALSG	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
FLGPTIGKIAKFILKHIVGLGDAALV	ML	MCF7, A549	MCF7: 2.6 [EC ₅₀], A549: 10.7 [EC ₅₀]
GIVTILKGAVGVILGGL	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
GLFKIISGIA	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
GLGMIAHGV	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
GLWKILKKGA	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
GLFAILKKLVNLVG	ML	MCF7, A549	MCF7: 2.3 [EC ₅₀], A549: 4.6 [EC ₅₀]

[4]

GLFKIISKLA KKA	ML	MCF7, A549	MCF7: 27.7 [EC ₅₀], A549: 36.3 [EC ₅₀]
GLPLFLKKLGS AV	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: >100 [EC ₅₀]
GLWGVIKALGGHVG	ML	MCF7, A549	MCF7: >100 [EC ₅₀], A549: 69.3 [EC ₅₀]
GLFLVALKQVATIKKLIGGLFAVVGVA	ML	MCF7, A549	Synthesis failed

IC₅₀: Half-inhibitory concentration, EC₅₀: half-effective concentration, HC₅₀: half-hemolytic concentration, TI: Therapeutic index (HC₅₀/ EC₅₀), AI: Artificial intelligence, n.d.: no data, ML: Machine learning, DL: Deep learning

References

1. Zhao, Y.; Wang, S.; Fei, W.; Feng, Y.; Shen, L.; Yang, X.; Wang, M.; Wu, M. Prediction of Anticancer Peptides with High Efficacy and Low Toxicity by Hybrid Model Based on 3D Structure of Peptides. *Int. J. Mol. Sci.* **2021**, *22*, 5630.
2. Grisoni, F.; Neuhaus, C.S.; Gabernet, G.; Müller, A.T.; Hiss, J.A.; Schneider, G. Designing anticancer peptides by constructive machine learning. *ChemMedChem.* **2018**, *13*, 1300-1302.
3. Grisoni, F.; Neuhaus, C.S.; Hishinuma, M.; Gabernet, G.; Hiss, J.A.; Kotera, M.; Schneider, G. De novo design of anticancer peptides by ensemble artificial neural networks. *J. Mol. Model.* **2019**, *25*, 112.
4. Lin, Y.C.; Lim, Y.F.; Russo, E.; Schneider, P.; Bolliger, L.; Edenharter, A.; Altmann, K.H.; Halin, C.; Hiss, J.A.; Schneider, G. Multidimensional design of anticancer peptides. *Angew. Chem. Int. Ed.* **2015**, *54*, 10370-10374.