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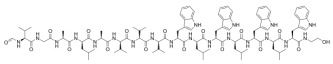
Gramicidin A



Cat. No.:	HY-P2324
CAS No.:	11029-61-1
Molecular Formula:	$C_{99}H_{140}N_{20}O_{17}$
Molecular Weight:	1882.29
Sequence:	{For}-Val-Gly-Ala-{D-Leu}-Ala-{D-Val}-Val-{D-Val}-Trp-{D-Leu}-Trp-{D-Leu}-Trp-{D-Leu}-Trp-{NHCH2CH2OH}
Target:	Bacterial; HIF/HIF Prolyl-Hydroxylase; Antibiotic
Pathway:	Anti-infection; Metabolic Enzyme/Protease
Storage:	Sealed storage, away from moisture Powder -80°C 2 years -20°C 1 year * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)

SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (53.13 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.5313 mL	2.6563 mL	5.3127 mL
	5 mM	0.1063 mL	0.5313 mL	1.0625 mL
	10 mM	0.0531 mL	0.2656 mL	0.5313 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Gramicidin A is a peptide component of gramicidin, an antibiotic mixture originally isolated from B. brevis. Gramicidin A is a highly hydrophobic channel-forming ionophore that forms channels in model membranes that are permeable to monovalent cations. Gramicidin A induces degradation of hypoxia inducible factor 1 α (HIF-1α)[1][2].

IC_{50} & Target

HIF-1α[2]

In Vitro

Gramicidin A displays potent broad-spectrum antibiotic activity against Gram-positive strains, even multidrug-resistant strains[1].
Gramicidin A has the disadvantage of high hemolytic activity[1].
Gramicidin A (0.1 nM-10 μM, 72 h) reduces the viability of RCC cell lines and affects cell viability comparable to Monensin (HY-N4302)[2].
Gramicidin A cellular sensitivity is significantly altered by neither VHL nor HIF-1α expression[2].
Gramicidin A (1 and 10 μM, 48 or 72 h) induces nonapoptotic cell death in RCC cells[2].

Gramicidin A (0-10 μM, 24 h) depletes cellular energy and induces metabolic dysfunction in RCC cells[2].
Gramicidin A (0-1 μM, 24-72 h) reduces HIF-1α and HIF-2α protein expression, reduces HIF transcriptional activity and target gene expression (24 h)[3]

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	A498, 786-O, Caki-1, SN12C, ACHN, UMRC6, UMRC6+VHL, HEK293T+pcDNA3, HEK293T+HA-HIF-1α, HEK293T+HA-HIF-1α-mut
Concentration:	0.1 nM-10 μM
Incubation Time:	72 h
Result:	Reduced the viability with IC_{50}s of 0.420, 0.430, 0.228, 0.104, 0.783, 0.253, 0.425, 0.057, 0.058 and 0.067 μM against A498, 786-O, Caki-1, SN12C, ACHN, UMRC6, UMRC6+VHL, HEK293T+pcDNA3, HEK293T+HA-HIF-1α, HEK293T+HA-HIF-1α-mut cells, respectively.

Western Blot Analysis[2][3]

Cell Line:	786-O, SN12C, Caki-1, ACHN
Concentration:	1 and 10 μM or 0.1, 0.5 and 1.0 μM
Incubation Time:	24, 48 or 72 h
Result:	PARP cleavage was not detected. Increased the phosphorylation of AMPKα and its substrate ACC at both 24 and 48 hours. Reduced HIF-1α and HIF-2α protein expression. Hypoxic expression of CA-IX, GLUT-1, and GAPDH were all decreased in a dose-dependent manner.

RT-PCR[3]

Cell Line:	SN12C, Caki-1, ACHN
Concentration:	0.1, 0.5 and 1.0 μM
Incubation Time:	24 h
Result:	Significantly altered transcript expression for only HIF-2α in SN12C cells.

In Vivo

Gramicidin A (0.11 mg/kg; intratumoral injection; twice weekly for 14 days) inhibits the growth of RCC tumor xenografts[2].
Gramicidin A (0.22 mg/kg; intratumoral injection; thrice weekly for 26 days) inhibits the growth and angiogenesis of VHL-expressing RCC tumor xenografts[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female hairless Nu/J mice, 6- to 8-week old, injected subcutaneously with a suspension of SN12C cells (1.0×10^6) in a 50% growth factor–reduced Matrigel solution[2]
Dosage:	0.11 mg/kg body weight
Administration:	Intratumoral injection, twice weekly for 14 days
Result:	The average tumor mass was reduced by approximately 40% without significant toxicity.

Animal Model:	Female hairless 6- to 8-week-old Nu/J mice, injected subcutaneously with a suspension of

	Caki-1-td-Tomato cells (1.5×10^6) in a 50% growth factor-reduced Matrigel solution[3].
Dosage:	0.22 mg/kg
Administration:	Intratumoral injection, thrice weekly for 26 days
Result:	Inhibited tumor growth. HIF-2α and GAPDH protein expression was substantially reduced.

CUSTOMER VALIDATION

- Cell Rep Med. 2023 Mar 2;100957.

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REFERENCES

[1]. Takada Y, et al. Discovery of gramicidin A analogues with altered activities by multidimensional screening of a one-bead-one-compound library. Nat Commun. 2020 Oct 1;11(1):4935.

[2]. David JM, et al. Gramicidin A induces metabolic dysfunction and energy depletion leading to cell death in renal cell carcinoma cells. Mol Cancer Ther. 2013 Nov;12(11):2296-307.

[3]. David JM, et al. Gramicidin A blocks tumor growth and angiogenesis through inhibition of hypoxia-inducible factor in renal cell carcinoma. Mol Cancer Ther. 2014 Apr;13(4):788-99.

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