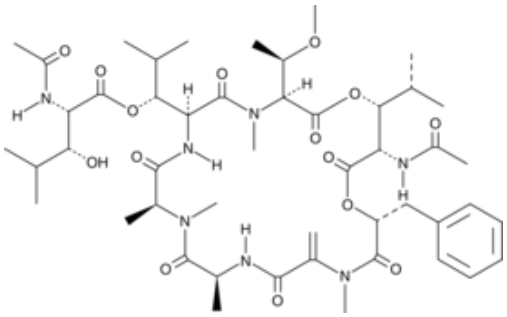
Product Data Sheet

Product Name: FR900359
Cat. No.: GC49089

Chemical Properties

Cas. No.	107530-18-7		
SMILES	CCC(N[C@@H]([C@H](O)C(C)C)C(O[C@@H]([C@@]1([H])C(N([C@@](C(O[C@@H]([C@@H](C(O[C@@H](C(N(C(C(N[C@H](C(N([C@H](C(N1)=O)C)C)=O)C)=O)=C)C)=O)CC2=CC=CC=C2)=O)NC(C)=O)C(C)C)=O)([H])[C@@H](C)OC)C)=O)C(C)C)=O)=O		
Formula	$C_{49}H_{75}N_7O_{15}$	M.Wt	1002.2
Solubility	Chloroform: soluble	Storage	-20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines Uveal melanoma cells

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Preparation Method	Uveal melanoma cells were plated on poly-L-lysine coated 96-well white bottom plates at 5 × 10^3 cells per well and allowed to sit overnight at 37°C and 5% CO2 in a humidified incubator. Cells were then treated with DMSO or 100nM, 300nM or 1μM FR900359 for 1–4 days and harvested by removing the media and lysing the cells with 100μl of cell-grade water for 1h at 37°C.
Reaction Conditions	100nM, 300nM or 1μM; 1–4days
Applications	FR900359 treatment of uveal melanoma cells induced cell growth arrest by inhibiting $G\alpha_q$ and decreasing levels of proteins involved in cell cycle and cell proliferation. FR900359 also induced cancer cell apoptosis.

Animal experiment [2]:

Animal models	Female Balb/c mice
Preparation Method	Female Balb/c mice at 10 weeks of age sensitized with intratracheal application of 1μg of house dust mite (HDM) (in 50μl of PBS) per mouse was performed on day 0. Then, mice were challenged by intratracheal application of 10μg of HDM (in 50μl of PBS) on days 7 to 11. Control mice received 50μl of PBS intratracheally on the respective days. Mice that received HDM were treated with either control solution or FR900359 (0.1mg/ml, 50μl) 4h before each HDM application on day 0 and days 7 to 11. Analysis was done on days 13 and 14.
Dosage form	0.1mg/ml, 50μl; i.t.; day 0 and day 7 to 11

Caution: Product has not been fully validated for medical applications. For research use only.
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Applications	FR900359 applied prevented increase in collagen deposition and airway hyperresponsiveness.

References:
[1] Serova M, Tijeras-Raballand A, Santos D C, et al. Effects of TGF-beta signalling inhibition with galunisertib (LY2157299) in hepatocellular carcinoma models and in ex vivo whole tumor tissue samples from patients. Oncotarget. 2015 Aug 28;6(25):21614-27.
[2] Matthey M, Roberts R, Seidinger A, et al.Targeted inhibition of Gq signaling induces airway relaxation in mouse models of asthma. Sci Transl Med. 2017 Sep 13;9(407):eaag2288.

Background

FR900359 is an inhibitor of G proteins $G\alpha_q$, $G\alpha_{11}$, and $G\alpha_{14}$ with IC_{50} values of 13.18, 10.47, and 10nM, respectively and is isolated from the leaves of the ornamental plant *Ardisia crenata*[1][2]. FR900359 has shown significant therapeutic potential in various disease models, including cancer, cardiovascular diseases, asthma and pulmonary arterial hypertension[3][4][5].

In vitro, FR900359 (0.01, 0.1, 1.0 and 10μM) incubated melanoma cell B16 for 72h reduced cell growth in a concentration-dependent manner without causing direct cytotoxicity but by arresting cell cycle in the G1 phase[2]. FR900359 (100nM, 300nM, 1μM) treated uveal melanoma cells for 1-4 days inhibited cancer cell growth by inhibiting $G\alpha_q$ and downregulating proteins involved in cell cycle and cell proliferation[3]. FR900359 (50nM) treated human patelets for 5min abolished platelet aggregation and secretion induced by lower concentration of the agonists as well. FR900359 treatment with higher concentrations (100nM) for 5min is required to cause a complete inhibition when used with murine platelets[4].

In vivo, FR900359 applied intratracheally (0.1mg/ml, 50μl) before each application of house dust mite allergen on mouse model of asthma prevented increase in collagen deposition and airway hyperresponsiveness[5]. FR900359 (2.5μg/mouse) or DMSO was applied to the lung via the intra-tracheal (i.t.) route 1h before hemodynamic measurements in mice with chronic hypoxia(Hx)-induced pulmonary hypertension (PH). FR900359 application reduced elevated basal right ventricular systolic

pressure and slightly attenuated basal heart rate in Hx-induced PH mouse model[6].

References:

[1]Fujioka, M, Koda S, Morimoto Y. Structure of FR900359, a cyclic depsipeptide from Ardisia crenata sims J. Org. Chem. 1988, 53 (12), 2820–2825.
[2] Schrage R, Schmitz L A, Gaffal E et.al. The experimental power of FR900359 to study Gq-regulated biological processes. Nat Commun. 2015 Dec 14;6:10156
[3] Lapadula D, Farias E, Randolph E C, et al. Effects of Oncogenic Gαq and Gα11 Inhibition by FR900359 in Uveal Melanoma. Mol Cancer Res. 2019 Apr;17(4):963-973.
[4] Inamdar V, Patel A, Bhanu Kanth Manne B K, et al. Characterization of UBO-QIC as a Gαq inhibitor in platelets.Platelets. 2015;26(8):771-8
[5] Matthey M, Roberts R, Seidinger A, et al.Targeted inhibition of Gq signaling induces airway relaxation in mouse models of asthma. Sci Transl Med. 2017 Sep 13;9(407):eaag2288.
[6] Seidinger A, Roberts R, Bai Y, et al. Pharmacological Gq inhibition induces strong pulmonary vasorelaxation and reverses pulmonary hypertension. EMBO Mol Med. 2024 Aug;16(8):1930-1956.