产品名称：雷特格韦钾盐
产品别名：Raltegravir potassium salt；MK 0518 potassium salt

生物活性：

Description	Raltegravir (potassium salt) is a potent integrase (IN) inhibitor, used to treat HIV infection.
In Vitro	PFV IN carrying the S217H substitution is 10-fold less susceptible to Raltegravir with IC50 of 900 nM. PFV IN displays 10% of WT activity and is inhibited by Raltegravir with an IC50 of 200 nM, indicating a appr twofold decrease in susceptibility to the IN strand transfer inhibitor (INSTI) compared with WT IN. S217Q PFV IN is as sensitive to Raltegravir as the WT enzyme[1]. Raltegravir is metabolized by glucuronidation, not hepatically. Raltegravir has potent in vitro activity against HIV-1, with a 95% inhibitory concentration of 31±20 nM, in human T lymphoid cell cultures. Raltegravir is also active against HIV-2 when Raltegravir is tested in CEMx174 cells, with an IC95 of 6 nM. Raltegravir metabolism occurs primarily through glucuronidation. Drugs that are strong inducers of the glucuronidation enzyme, UGT1A1, significantly reduce Raltegravir concentrations and should not be used. Raltegravir exhibits weak inhibitory effects on hepatic cytochrome P450 activity. Raltegravir does not induce CYP3A4 RNA expression or CYP3A4-dependent testosterone 6-β-hydroxylase activity[2]. Raltegravir cellular permeativity is reduced in the presence of magnesium and calcium[3]. Raltegravir and related HIV-1 integrase (IN) strand transfer inhibitors (INSTIs efficiently block viral replication[4]. In acutely infected human lymphoid $CD4^+$ T-cell lines MT-4 and CEMx174, SIVmac251 replication is efficiently inhibited by Raltegravir, which shows an EC90 in the low nanomolar range[5].
In Vivo	Raltegravir induces viro-immunological improvement of nonhuman primates with progressing SIVmac251 infection. One non-human primate shows an undetectable viral load following Raltegravir monotherapy[5].

Solvent&Solubility

In Vitro:

H_2O : 25 mg/mL (**51.81 mM**; Need ultrasonic)

DMSO : 6 mg/mL (**12.43 mM**; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0725 mL	10.3625 mL	20.7250 mL
	5 mM	0.4145 mL	2.0725 mL	4.1450 mL
	10 mM	0.2072 mL	1.0362 mL	2.0725 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 0.6 mg/mL (1.24 mM); Clear solution

此方案可获得 ≥ 0.6 mg/mL (1.24 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 6.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 0.6 mg/mL (1.24 mM); Clear solution 此方案可获得 ≥ 0.6 mg/mL (1.24 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 6.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 0.6 mg/mL (1.24 mM); Clear solution 此方案可获得 ≥ 0.6 mg/mL (1.24 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 6.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Hare, S., et al., Molecular mechanisms of retroviral integrase inhibition and the evolution of viral resistance. Proc Natl Acad Sci U S A, 2010. 107(46): p. 20057-62. [2]. Hicks C, et al. Raltegravir: the first HIV type 1 integrase inhibitor. Clin Infect Dis. 2009 Apr 1;48(7):931-9 [3]. Moss DM, et al. Divalent metals and pH alter raltegravir disposition in vitro. Antimicrob Agents Chemother. 2012 Jun;56(6):3020-6 [4]. Hare S, et al. Structural and functional analyses of the second-generation integrase strand transfer inhibitor dolutegravir (S/GSK1349572). Mol Pharmacol. 2011 Oct;80(4):565-72. [5]. Lewis, M.G., et al. Response of a simian immunodeficiency virus (SIVmac251) to raltegravir: a basis for a new treatment for simian AIDS and an animal model for studying lentiviral persistence during antiretroviral therapy. Retrovirology, 2010. 7: p. 21.

实验参考：

Cell Assay	Human MT-4 cells are infected for 2 hours with the SIVmac251, HIV-1 (IIIB) and HIV-2 (CDC 77618) stocks at a multiplicity of infection of, approximately, 0.1. Cells are then washed three times in phosphate buffered saline, and suspended at 5 × 10^5/mL in fresh culture medium (to primary cells 50 units/mL of IL-2 are added) in 96-well plates, in the presence or absence of a range of triplicate raltegravir concentrations (0.0001 μM-1 μM). Untreated infected and mock-infected controls are prepared too, in order to allow comparison of the data derived from the different treatments. Viral cytopathogeniciy in MT-4 cells is quantitated by the methyl tetrazolium (MTT) method (MT-4/MTT assay) when extensive cell death in control virus-infected cell cultures is detectable microscopically as lack of capacity to re-cluster. The capability of MT-4 cells to form clusters after infection. Briefly, clusters are disrupted by pipetting; and, after 2 hours of incubation at 37°C, the formation of new clusters is assessed by light microscopy (100× magnification). Cell culture supernatants are collected for HIV-1 p24 and HIV-2/SIVmac251 p27 core antigen measurement by ELISA. In CEMx174-infected cell cultures, which show a propensity to form syncytia induced by the virus envelope glycoproteins, syncytia are counted, in blinded fashion, by light microscopy for each well at 5 days following infection.［5］
	[1]. Hare, S., et al., Molecular mechanisms of retroviral integrase inhibition and the evolution of viral resistance. Proc Natl Acad Sci U S A, 2010. 107(46): p. 20057-62. [2]. Hicks C, et al. Raltegravir: the first HIV type 1 integrase inhibitor. Clin Infect Dis. 2009 Apr

References	1;48(7):931-9 [3]. Moss DM, et al. Divalent metals and pH alter raltegravir disposition in vitro. Antimicrob Agents Chemother. 2012 Jun;56(6):3020-6 [4]. Hare S, et al. Structural and functional analyses of the second-generation integrase strand transfer inhibitor dolutegravir (S/GSK1349572). Mol Pharmacol. 2011 Oct;80(4):565-72. [5]. Lewis, M.G., et al. Response of a simian immunodeficiency virus (SIVmac251) to raltegravir: a basis for a new treatment for simian AIDS and an animal model for studying lentiviral persistence during antiretroviral therapy. Retrovirology, 2010. 7: p. 21.