# 产品名称：PLX7904
# 产品别名：PLX7904

## 生物活性：

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| **Description** | PLX7904 is a potent and selective BRAF inhibitor, with IC50 of appr 5 nM against BRAFV600E in mutant RAS expressing cells. |
| **$IC_{50}$ & Target** | $BRaf^{V600E}$ |
| | 5 nM ($IC_{50}$, in mutant RAS expressing cells) |
| **In Vitro** | PLX7904 inhibits the in vitro growth of two melanoma cell lines (A375 and COLO829) and an additional human colorectal cancer cell line COLO205 that expresses $BRAF^{V600E}$ with $IC_{50}$ values of 0.17 μM, 0.53 μM, and 0.16 μM, respectively, on a par with vemurafenib $IC_{50}$ values in the same assays (0.33 μM, 0.69 μM, and 0.25 μM, respectively)[1]. PLX7904 and PLX8394 potently inhibit ERK1/2-driven GAL4-Elk1 reporter activity in PRT cells as well as parental cells. PLX7904 and PLX8394 treatment at 1 μM concentration reduce colony formation and viability in parental cells to a similar level as PLX4720[2]. PPLX7904 potently inhibits phosphorylation of ERK1/2 in mutant BRAF melanoma cells without eliciting paradoxical activation in wild-type BRAF, mutant NRAS melanoma cells. PPLX7904 inhibits ERK1/2 in PLX470-resistant cell lines. PPLX7904 treatment promotes apoptosis and inhibits anchorage-independent growth of vemurafenib resistant cells[3]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO : ≥ 30 mg/mL (58.53 mM)**<br>* "≥" means soluble, but saturation unknown. |

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| | 1 mM | 1.9511 mL | 9.7555 mL | 19.5111 mL |
| | 5 mM | 0.3902 mL | 1.9511 mL | 3.9022 mL |
| | 10 mM | 0.1951 mL | 0.9756 mL | 1.9511 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: ≥ 2.5 mg/mL (4.88 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.88 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 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。



[1]. Zhang C, et al. RAF inhibitors that evade paradoxical MAPK pathway activation. Nature. 2015 Oct

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| **References** | 22;526(7574):583-586.<br>[2]. Basile KJ, et al. Inhibition of mutant BRAF splice variant signaling by next-generation, selective RAF inhibitors. Pigment Cell Melanoma Res. 2014 May;27(3):479-84<br>[3]. Le K, et al. Selective RAF inhibitor impairs ERK1/2 phosphorylation and growth in mutant NRAS, vemurafenib-resistant melanoma cells. Pigment Cell Melanoma Res. 2013 Jul;26(4):509-17 |

**实验参考：**

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| **Cell Assay** | For MTT assays, $2\times10^3$ cells are seeded in triplicate in 96 wells in their regular culture medium (containing PLX4720 for PRT lines). Next day, cells are washed twice with PBS and then the medium is replenished containing the indicated RAF inhibitor. Medium is changed 48 hours later and after a further 48 hours, 10 µL of 5 mg/mL MTT reagent is added to wells, and incubated for three hours. Formazan crystals are then solubilized overnight with a 1:10 dilution of 0.1 M glycine (pH 10.5) in DMSO. Wells are then analyzed at 450 nM in a Multiskan® Spectrum spectrophotometer. Results depicted are normalized to DMSO conditions and are a composite of three independent experiments. Error bars shown are representative of the standard error of mean (SEM). [2] |
| **Animal Administration** | COLO205 tumour cells are cultured in DMEM 10% FBS 1% penicillin/streptomycin supplemented with bovine insulin, at 37°C. Balb/C nude mice, female, 6-8 weeks old, weighing approximately 18-22 g, are inoculated subcutaneously at the right flank with COLO205 tumour cells ($5\times10^6$) in 0.1 mL of PBS mixed with matrigel (50:50) for tumour development. The treatment is started when mean tumour size reach approximately 100 $mm^3$, with eight mice in each treatment group randomized to balance the average weight and tumour size. B9 cells are expanded in DMEM 10% FBS 1% penicillin/streptomycin. Upon trypsinization the cells are washed three times with 20 mL RPMI, and after the final centrifugation are re-suspended, counted, and adjusted by volume to a final concentration of $5\times10^7$ cells per millilitre. B9 xenografts are started by injection of $5\times10^6$ cells subcutaneously in 6- to 7-week-old female nude Balb/c mice. Compound dosing starts when the average size of tumours reach 50-70 $mm^3$. Animals are equally distributed over treatment groups (n=10) to balance the average tumour size and body weight. Animals are dosed orally for days 1-14 twice daily and days 15-28 once daily with vehicle, vemurafenib 50 mg per kg, or PLX7904 50 mg per kg. 12-O-tetradecanoylphorbol-13-acetate (TPA) is put on the skin of all mice twice a week during weeks 3 and 4 at a dose of 2 µg in 200 µL acetone. [1] |
| **References** | [1]. Zhang C, et al. RAF inhibitors that evade paradoxical MAPK pathway activation. Nature. 2015 Oct 22;526(7574):583-586.<br>[2]. Basile KJ, et al. Inhibition of mutant BRAF splice variant signaling by next-generation, selective RAF inhibitors. Pigment Cell Melanoma Res. 2014 May;27(3):479-84<br>[3]. Le K, et al. Selective RAF inhibitor impairs ERK1/2 phosphorylation and growth in mutant NRAS, vemurafenib-resistant melanoma cells. Pigment Cell Melanoma Res. 2013 Jul;26(4):509-17 |