For Research Use Only

AGI-5198

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Catalog Number: CM04693

产品信息

Catalog Number:
CM04693

CAS号:
1355326-35-0

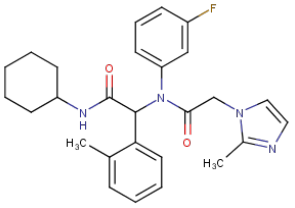
分子式:
$C_{27}H_{31}FN_4O_2$

主要靶点:
Dehydrogenase|Isocitrate Dehydrogenase (IDH)

主要通路:
代谢|代谢

分子量:
462.56

溶解度:
H2O:< 1 mg/mL (insoluble or slightly soluble);Ethanol:12 mg/mL (25.9 mM);DMSO:23 mg/mL (49.7 mM)



靶点活性

R132H-IDH1:70 nM|R132C-IDH1:0.16 μM

体外活性

在带有Ki-67蛋白抗体染色的小鼠体内,AGI-5198可使其肿瘤减少.但空白对照组和AGI-5198处理组的小鼠肿瘤中裂解的caspase-3无显著差异.AGI-5198（450 mg/kg/day）治疗R132H-IDH1胶质瘤移植瘤三周,可抑制50-60%的生长,但不影响IDH1野生型胶质瘤移植瘤的生长.

体内活性

AGI-5198对TS603胶质瘤细胞系有一定抗肿瘤疗效,且剂量依赖性抑制R-2HG产生。在R-2HG几乎被完全抑制的条件下,AGI-5198对组蛋白H3K9me3去甲基化有诱导作用,且诱导与胶质基因分化相关的基因表达。在全基因组DNA甲基化中,AGI-5198对mIDH1受损的IDH1突变型生长具有抑制作用,但野生型生长几乎没有受到影响。AGI-5198对突变型IDH1(R132H-IDH1 和 R132C-IDH1)有明显抑制作用,但对野生型IDH1 (IC50>100 μM) 或任何IDH2亚型(R140Q, R172K, 野生型) (IC50>100 μM)抑制作用非常弱。

细胞实验

AGI-5198 is dissolved in DMSO.TS603 cells are grown in medium containing either AGI-5198 (1.5 μM) or DMSO vehicle control.One week prior to harvest cells are ransferred to differentiation medium (DMEM F12; 15 mM HEPES; 0.06% glucose; B27 without vitamin A; N2; Insulin/transferrin; 1% FBS) containing freshly added retinoic acid (1 μM).ChIP of non-crosslinked cells is then carried out using established ChIP methods.350 μg of lysate is immunoprecipitated-using anti-H3K9Me3,H3K27me3 or Rabbit Control IgG.After washing,ChIP DNA is eluted from protein G beads and analyzed by RT-PCR using SYBR green.Relative occupancy is calculated using the standard curve method and fold enrichment versus IgG.Enrichment in AGI-5198-treated cells is normalized to vehicle control.Means and standard deviation are calculated from 4 technical replicates.

储存

Powder: -20°C for 3 years | In solvent: -80°C for 1 year | Shipping with blue ice.