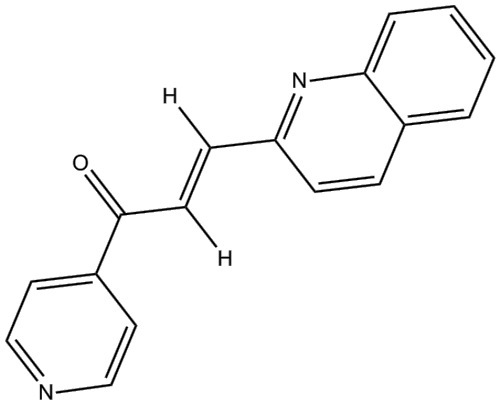
Product Data Sheet

Product Name: PFK-015
Cat. No.: GC16993

Chemical Properties

Cas. No.	4382-63-2		
SMILES	O=C(C1=CC=NC=C1)/C([H])=C([H])/C2=NC3=CC=CC=C3C=C2		
Formula	$C_{17}H_{12}N_2O$	M.Wt	260.29
Solubility	≥ 13mg/mL in DMSO	Storage	Store at -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	Peripheral blood mononuclear cells
Preparation Method	Peripheral blood mononuclear cells supplemented with 40ng/ml macrophage colony-stimulating factor (M-CSF) was used as a differentiation medium. To examine the role of PFKFB3 in macrophage polarization, PFKFB3 inhibitor PFK-015 (10μM) was used.

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Reaction Conditions	10μM; 80min
Applications	Treatment with PFK-015 during IFN-γ-induced macrophage polarization reduced the expression of M1 surface markers CD80, iNOS, and HLA-DR.

Animal experiment [2]:

Animal models	Xenograft modle
Preparation Method	LL cells were obtained from DMEM medium containing 10% FCS in the exponential growth phase. After washing twice, the cells were resuspended in PBS buffer. 0.1mL of cell suspension (1×10^6 cells) was subcutaneously injected into C57Bl6 mice. Mice carrying xenograft tumors (150–200mg) were randomly assigned to four groups: DMSO group, PFK-015 group (25mg/kg, intraperitoneal injection, every 3 days for 4 doses), irinotecan group (70mg/kg, intravenous injection, every 3 days for 4 doses), temozolomide group (30mg/kg, oral administration, 3 consecutive days followed by a 3-day break), and gemcitabine group (100mg/kg, every 3 days for 4 doses). Tumor size was measured daily using microcalipers.
Dosage form	25mg/kg; iv; every 3 days for 4 doses
Applications	PFK-015 inhibits the growth of Lewis lung carcinoma (LLC) xenografts by mediating the depletion of tumor-associated fructose-2,6-bisphosphate (F26BP), which consequently triggers apoptotic signaling and suppresses pulmonary metastasis of the subcutaneous tumors.

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References:
[1]. Chen R, Wang J, Dai X, et al. Augmented PFKFB3-mediated glycolysis by interferon-γ promotes inflammatory M1 polarization through the JAK2/STAT1 pathway in local vascular inflammation in Takayasu arteritis[J]. Arthritis research & therapy, 2022, 24(1): 266.
[2]. Clem B F, O'Neal J, Tapolsky G, et al. Targeting 6-phosphofructo-2-kinase (PFKFB3) as a therapeutic strategy against cancer[J]. Molecular cancer therapeutics, 2013, 12(8): 1461-1470.

Background

PFK-015 is a potent and selective inhibitor of PFKFB3 with an IC_{50} value of 110nM[1]. As a key regulator of glycolytic metabolism, PFK-015 disrupts fructose-2,6-bisphosphate production and demonstrates significant anti-proliferative effects across multiple tumor cell lines[2]. The compound also induces autophagy and exhibits synergistic activity with chemotherapeutic agents in vivo[3].

In Peripheral blood mononuclear cells treatment with PFK-015(10μM; 80min) during IFN-γ-induced macrophage polarization reduced the expression of M1 surface markers CD80, iNOS, and HLA-DR[4]. In the 786-O and OS-RC-2 cell lines, the expression levels of glycolytic regulatory enzymes, key enzymes, and PD-L1 decreased after the addition of the PFKFB3 inhibitor PFK-015(10μM; 24h)[5].

In Lewis lung carcinoma (LLC)-bearing mice, PFK-015(25mg/kg; iv; every 3 days for 4 doses) inhibits the growth of Lewis lung carcinoma (LLC) xenografts by mediating the depletion of tumor-associated fructose-2,6-bisphosphate (F26BP), which consequently triggers apoptotic signaling and suppresses pulmonary metastasis of the subcutaneous tumors[6]. In the Hu-NOG mouse model, PFK-015(25mg/kg; ip; 21d) combined with PD-1 mAb therapy significantly inhibits tumor growth in human PBMC-engrafted NOG mice[7].

References:
[1].Clem B, Tapolsky G H, O'Neal J, et al. Characterization of a novel small molecule antagonist of 6-phosphofructo-2-kinase that suppresses glucose metabolism and tumor growth[J]. Cancer Research, 2011, 71(8_Supplement): 2825-2825.
[2].Ling X, Liu L, Jiang A, et al. PFKFB3 promotes endometriosis cell proliferation via enhancing the

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protein stability of β-catenin[J]. Molecular and Cellular Endocrinology, 2024, 579: 112083.
[3].Brooke D G, van Dam E M, Watts C K W, et al. Targeting the Warburg Effect in cancer; relationships for 2-arylpyridazinones as inhibitors of the key glycolytic enzyme 6-phosphofructo-2-kinase/2, 6-bisphosphatase 3 (PFKFB3)[J]. Bioorganic & medicinal chemistry, 2014, 22(3): 1029-1039.
[4].Chen R, Wang J, Dai X, et al. Augmented PFKFB3-mediated glycolysis by interferon-γ promotes inflammatory M1 polarization through the JAK2/STAT1 pathway in local vascular inflammation in Takayasu arteritis[J]. Arthritis research & therapy, 2022, 24(1): 266.
[5].Yu Y, Liang Y, Li D, et al. Glucose metabolism involved in PD-L1-mediated immune escape in the malignant kidney tumour microenvironment[J]. Cell Death Discovery, 2021, 7(1): 15.
[6].Clem B F, O'Neal J, Tapolsky G, et al. Targeting 6-phosphofructo-2-kinase (PFKFB3) as a therapeutic strategy against cancer[J]. Molecular cancer therapeutics, 2013, 12(8): 1461-1470.
[7].Zheng J B, Wong C W, Liu J, et al. Glucose metabolism inhibitor PFK-015 combined with immune checkpoint inhibitor is an effective treatment regimen in cancer[J]. Oncoimmunology, 2022, 11(1): 2079182.

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