

Catalog Number: CM04909

产品信息

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CM04909

CAS号:
540737-29-9

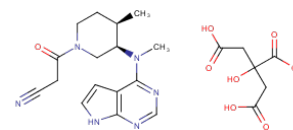
分子式:
C₂₂H₂₈N₆O₈

主要靶点:
Antifungal|Antibacterial|JAK|Apoptosis|Influenza
Virus

主要通路:
微生物学|表观遗传|蛋白酪氨酸激酶|干细胞|血管生成|JAK/STAT 信号通路|凋亡|微生物学|微生物学

分子量:
504.49

溶解度:
DMSO:55 mg/mL (109.02 mM)



靶点活性

JAK1:112 nM (cell free)|JAK2:20 nM (cell free)|JAK3:1 nM (cell free)

体外活性

虽然Tofacitinib (CP-690,550) 对JAK3的抑制作用极为强大 (酶抑制效力为1 nM), 但其对JAK2和JAK1的抑制作用分别低20至100倍。CP-690,550能以比GM-CSF诱导的增殖30倍更强的效力抑制IL-2诱导的增殖。CP-690,550在使用鼠、猴或人细胞的混合淋巴细胞反应中展现出强大的抑制效果。与其作用机制一致, 这些细胞活性与CP-690,550阻断IL-2诱导的JAK3及其关键底物STAT5的磷酸化能力相关[1]。在治疗含有人类野生型或V617F JAK2的鼠类因子依赖细胞Patersen-erythropoietin receptor (FDCP-EpoR)时, CP-690,550能抑制细胞增殖, 其IC50分别为2.1 μg/ml和0.25 μg/ml。对JAK2(V617F)-阳性PV患者体外扩增的红细胞祖细胞进行CP-690,550治疗, 表现出特异的抗增殖 (IC50: 0.2 μg/ml) 和促凋亡活性[2]。Tofacitinib对JAK3的药理抑制作用与IMA在CML细胞中的抗肿瘤效果协同增强[3]。

体内活性

CP-690,550治疗显著延长了与对照组相比的移植体存活时间。12只动物中有4只接受CP-690,550治疗 (每个剂量组各两只) 存活至研究结束, 且肾功能正常, 根据组织病理学判断只有轻度排斥反应[1]。用tofacitinib单药治疗小鼠能够抑制对由细菌蛋白质Pseudomonas exotoxin A衍生的免疫毒素以及模型抗原钥孔血蓝蛋白的抗体 (Ab) 反应。实验显示, 在免疫后21天观察到对两种抗原IgG1滴度的千倍降低。Tofacitinib治疗还导致CD127⁺前B细胞数量减少[4]。

动物实验

Mice received tofacitinib in PEG300 (100 mg/ml) or vehicle alone (PEG300) by osmotic pump infusion (Alzet Model 2004, 0.25 μl/hour, 28 days). Four days prior to immunization, mice were anesthetized and their dorsal surface was shaved. A one cm incision was made on the back to create a subcutaneous pocket and insert the pump. The incision site was closed with wound clips. Mice were injected weekly (i.p.) with SS1P recombinant immunotoxin (RIT; 5 μg/mouse) beginning on day 0; control mice received injections of saline alone. Every week before SS1P or vehicle immunization, ~50 μl of blood was drawn to obtain serum samples. Sera were stored at -80°C until analyzed [4].

细胞实验

Apoptotic cells were detected by flow cytometry using recombinant human Annexin-V conjugated with allophycocyanin. Briefly, after exposure to CP-690,550 for different periods of time, cells were washed in Ca²⁺-free PBS and resuspended in 100 μl of binding buffer (10 mM HEPES pH 7.4; 0.15 M NaCl; 5 mM KCl; 1 mM MgCl₂; 1.8 mM CaCl₂) to which Annexin-V-APC had been previously added. Cells were incubated for 20 min in the dark at room temperature, washed and resuspended in 0.3 mL binding buffer. Cells were analyzed on a FACSCalibur flow cytometer equipped with the Cell Quest Pro software [2].

储存

store at low temperature, keep away from moisture, keep away from direct sunlight | Powder: -20°C for 3 years | In solvent: -80°C for 1 year | Shipping with blue ice.