T-10430: A Chemical Probe for LTB4R2

Version 1.0 (28th August 2024)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/T-10430

Overview

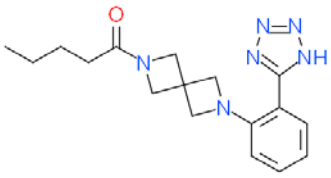
LTB4R2 is a lipid GPCR closely related to LTB4R. LTB4R2 has a lower affinity for LTB4 than LTB4R and is expressed ubiquitously in humans, with highest mRNA expression levels in the spleen, liver, ovaries, and leucocytes. LTB4R2 activation has been associated with treatment of intestine ulcers and inflammatory bowel disease, diabetic wound healing, corneal wound healing, and acute lung injury among others.

Summary

Chemical Probe Name	T-10430
Negative control compound	T-10404
Target(s) (synonyms)	LTB4R2 (BLT2 receptor)
Recommended *in vitro* assay concentration	Use at concentration up to 1 µM for T-10430 and T-10404; use with control for best interpretation of data
Suitability for *in* vivo use and recommended dose	Tested in mice with 3 mg/kg (iv) and 10 mg/kg (po, sc).
Publications	None at time of publication
In vitro assay(s) used to characterise	Tag-lite assay
Cellular assay(s) for target-engagement	IP-One assay

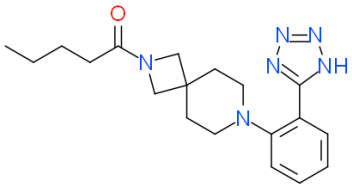
Chemical Probe & Negative Control Structures and Use

T-10430 Chemical Probe



SMILES: CCCCC(N1CC2(C1)CN(C2)c1ccccc1c1nnn[nH]1)=O
InChiKey: RIEBAXQZOMUWKX-UHFFFAOYSA-N
Molecular weight: 326.19 g/mol
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

T-10404 Negative Control



SMILES: CCCCC(N1CC2(CCN(CC2)c2ccccc2c2nnn[nH]2)C1)=O
InChiKey: FRDJKCFCJPPTGJ-UHFFFAOYSA-N
Molecular weight: 354.22 g/mol
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

T-10430 is a potent agonist of LTB4R2 with IC_{50} = 31 nM in the Tag-lite assay and shows no effect in the IP-One assay at up to 50 µM for the closely related targets LTB4R and AGTR1. The GPCR screen (314 receptors, Ca^{2+} Aequorin assay) shows no activity at 1 µM except for LTB4R2.

Potency in Cells and Cellular Target Engagement:

T-10430 shows an EC_{50} of 19 nM in the IP-One assay using CHO-K1 cells.