

# JP3000: A Chemical Probe for RXR

Version 1.0 (25<sup>th</sup> October 2023)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/JP3000>

## Overview

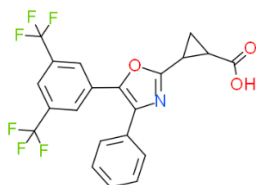
The nuclear retinoid X receptors ([RXRA](#), [RXRB](#), [RXRG](#)) regulate gene expression in response to ligands like 9-cis retinoic acid and other fatty acids. Due to their central role as universal heterodimer partner in nuclear receptor regulation, RXRs are widely distributed over all tissues and linked to multiple pathologies including metabolic and inflammatory diseases, cancer and neurodegeneration.

## Summary

Chemical Probe Name	JP3000
Negative control compound	JP3001
Target(s) (synonyms)	RXRA, RXAB, RXRG
Recommended <i>in vitro</i> assay concentration	Use at concentration of 0.1 to 1 $\mu$ M for JP3000 and JP3001; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Not tested in vivo
Publications	None at time of publication
<i>In vitro</i> assay(s) used to characterise	ITC
Cellular assay(s) for target-engagement	Hybrid reporter gene assay, full-length RXR reporter gene assay

## Chemical Probe & Negative Control Structures and Use

JP3000 Chemical Probe



**SMILES:** C1C(C1c1nc(c2ccccc2)c(c2cc(cc2)C(F)(F)F)C(F)(F)F)C(F)(F)F)C(F)(F)F)O1)C(O)=O

**InChiKey:** CRLZRGXSDBAEFD-UHFFFAOYSA-N

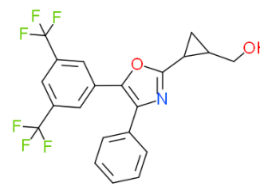
**Molecular weight:** 441.08 g/mol

**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

JP3001 Negative Control



**SMILES:** C1C(CO)C1c1nc(c2ccccc2)c(c2cc(cc2)C(F)(F)F)C(F)(F)F)C(F)(F)F)O1)C(O)=O

**InChiKey:** GQHICRTXIJFNDU-UHFFFAOYSA-N

**Molecular weight:** 427.10 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

### Selectivity:

JP3000 shows a  $K_D < 10$  nM in the ITC assay for RXRA. A panel with 27 related nuclear receptors at 1  $\mu$ M (in-house panel) is clean with > 100-fold selectivity.

### Potency in Cells and Cellular Target Engagement:

The Hybrid reporter gene assay yields the following data:  $EC_{50} = 5 \pm 1$  nM ( $38 \pm 1$ -fold) for RXRA,  $EC_{50} = 1.4 \pm 0.4$  nM ( $69 \pm 3$ -fold) for RXRB and  $EC_{50} = 4 \pm 1$  nM ( $24 \pm 1$ -fold) for RXRG. The full-length RXR reporter gene assay results in  $EC_{50} = 2.6 \pm 0.3$  nM for the RXR:RXR homodimer and  $EC_{50} = 29 \pm 2$  nM for the RXR:RAR heterodimer. The induction of RXR-regulated gene expression (GDE1) shows an  $EC_{50} \approx 10$  nM (qRT-PCR).