

# SGC-SMARCA-BRDVIII: A Chemical Probe for SMARCA2/4 and PBRM1(BD5)

Version 1.0 (15<sup>th</sup> April 2021)

**Web link for more details:** <https://www.thesgc.org/chemical-probes/SGC-SMARCA-BRDVIII>

## Overview

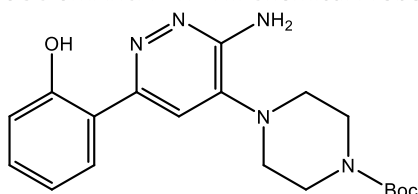
Either [SMARCA2](#) or [SMARCA4](#) is incorporated into the SWI/SNF (switch/sucrose non-fermenting) chromatin remodelling complexes, BAF and PBAF, that are crucial epigenetic regulators to control DNA accessibility. A unique feature of PBAF is the subunit [PBRM1](#) containing six tandem-acting bromodomains. SWI/SNF complexes are known to be strong tumor suppressors and their dysfunctions trigger substantial oncogenic programs or deregulate cell lineage differentiation mechanisms

## Summary

Chemical Probe Name	SGC-SMARCA-BRDVIII
Negative control compound	SGC-BRDVIII-NC
Target(s) (synonyms)	SMARCA2 (SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 2, BRM), SMARCA4, PBRM1 (PB1(5))
Recommended cell assay concentration	< 10 $\mu$ M for SGC-SMARCA-BRDVIII and SGC-BRDVIII-NC; use with negative control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	This chemical probe was not tested for <i>in vivo</i> use
Publications	<a href="#">PMID: 33216538</a>
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	ITC
Cellular assay(s) for target-engagement	Adipogenesis cell differentiation assay
ChemicalProbes.org	<a href="#">Link to chemicalprobes.org</a>

## Chemical Probe & Negative Control Structures and Use

SGC-SMARCA-BRDVIII Chemical Probe



SMILES: OC1=CC=CC=C1C2=CC(N3CCN(C(OC(C)(C)C)=O)CC3)=C(N)N=N2

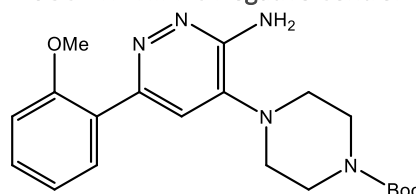
InChiKey: AQTNUGRRZDRZIA-UHFFFAOYSA-N

Molecular weight: 380.45

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

SGC-BRDVIII-NC Negative Control



SMILES: NC(N=N1)=C(N2CCN(C(OC(C)(C)C)=O)CC2)C=C1C3=CC=CC=C3OC

InChiKey: YOBVMDSDYHOOLN-UHFFFAOYSA-N

Molecular weight: 385.21

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:

SGC-SMARCA-BRDVIII binds potently to the SMARCA2/4 and PBRM1(BD5) bromodomains with a KD(ITC) of 35, 36 and 13 nM.

Selectivity of the SGC-SMARCA-BRDVIII probe within the bromodomain families was confirmed by an thermal shift assay containing 25 bromodomains. No activity was also observed on 85 protein kinases screened in an DSF assay.

### Potency in Cells and Cellular Target Engagement:

SGC-SMARCA-BRDVIII is non-toxic as demonstrated by the NCI-60 human tumor cell lines screen. The formation from 3T3-L1 mouse fibroblasts into adipocytes was impaired with an EC<sub>50</sub> < 1.0  $\mu$ M. SGC-BRDVIII-NC showed no cellular activity.

Bromodomain	SGC-SMARCA-BRDVIII K <sub>D</sub> [nM] (ITC)
SMARCA2	35
SMARCA4	36
PB1(5)	13
PB1(2)	3655
PB1(3)	1963