

# NR162: A Chemical Probe for CASK

Version 1.0 (26<sup>th</sup> March 2021)

Web link for more details: <https://www.thesgc.org/chemical-probes/NR162>

## Overview

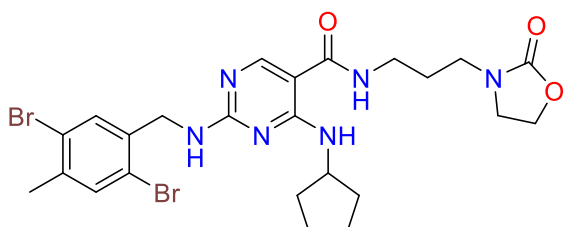
The pseudokinase [CASK](#) is a multi-domain scaffold protein and it has been shown to maintain some catalytic activity in the absence of metal ions. CASK is involved in a variety of cellular functions, including synaptic targeting of ion channels and synaptic adhesion molecules, dendritic spine formation, axonal outgrowth and differentiation and transcriptional control. High expression levels and mutations in CASK have been linked to colorectal cancer, Parkinson's disease and X-linked mental retardation, making CASK a potential drug target.

## Summary

Chemical Probe Name	NR162
Negative control compound	NR187
Target(s) (synonyms)	CASK (calcium/calmodulin dependent serine protein kinase)
Recommended cell assay concentration	Use at concentration of 1 $\mu$ M (and < 10 $\mu$ M) for NR162 and NR187; use with control for best interpretation of data.
Suitability for <i>in vivo</i> use and recommended dose	NR162 was not tested <i>in vivo</i> .
Publications	None at time of writing.
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	DSF, ITC
Cellular assay(s) for target-engagement	NanoBRET

## Chemical Probe & Negative Control Structures and Use

NR162 Chemical Probe



**SMILES:** O=C(C1=CN=C(N=C1NC2CCCC2)NCC3=CC(Br)=C(C)C=C3Br)NCCCN4CCOC4=O

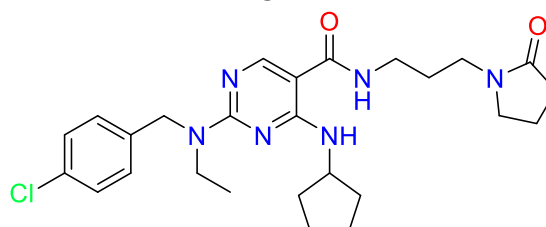
**InChiKey:** BPLPIBNWDLPUKP-UHFFFAOYSA-N

**Molecular weight:** 608.07

**Storage:** Stable as solid in the dark at -20°C. NB making aliquots rather than freeze-thawing is recommended

**Dissolution:** Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

NR187 Negative Control



**SMILES:** O=C(NCCCN1CCCC1=O)C2=CN=C(N(CC)CC3=CC=C(Cl)C=C3)N=C2NC4CCCC4

**InChiKey:** AYRUNBYNKCLGFI-UHFFFAOYSA-N

**Molecular weight:** 499.06

**Storage:** Stable as solid in the dark at -20°C. NB making aliquots rather than freeze-thawing is recommended

**Dissolution:** Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

## Chemical Probe Profile

### *In vitro* Potency & Selectivity:

NR162 shows potent activity on CASK with a  $K_d$  of 22 nM in ITC. NR162 has been shown to be selective in a DiscoverX KINOMEScan at 1  $\mu$ M. The closest off-target was TYRO3 ( $IC_{50}$  = 3.8  $\mu$ M) and ERBB3 ( $IC_{50}$  = 18.2  $\mu$ M).

### Potency in Cells and Cellular Target Engagement:

In NanoBRET assay using HEK293T cells NR162 binds CASK with an  $IC_{50}$  of 80 nM. In the full NCI-60 panel NR162 showed no significant cell toxicity as well as growth inhibition in a single high dose of 10  $\mu$ M in the full NCI-60.