AA74-1

Category | Parameter | Description
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Compound | Additional names | None
Citation | From: Click-generated triazole ureas as ultrapotent in vivo–active serine hydrolase inhibitors
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Chemical descriptors | SMILES: O=C(N1N=C(C(O)(CC(C)C)CC(C)C)C=N1)N2

InChIKey: GXBVPGCIMCIASQ-UHFFFAOYAL

Chemical compound page | 23

Entries in chemical databases | PubChem SID: 119526594

Availability | Compound was synthesized as described in the Supplementary Methods. Compound is available from the laboratory of Dr. Cravatt

Additional comments | In vitro profiling
Target | Human, mouse, and rat orthologs of Acyl-peptide hydrolase (APEH)
Potency | 5 nM IC_{50} by gel-based ABPP (see Figure 4 and Supplementary Fig. 12)
Selectivity | Selective in mouse T-cell hybridoma, B103 (rat), and MDA-MB-231(human) cell proteomes at concentrations up to 100 nM (see Figure 4a and Supplementary Fig. 6)
Potential reactivities | None to our knowledge
SAR | Pyrrolidine group essential for high potency. Bulky, aliphatic triazole group essential for selectivity over serine hydrolase PAFAH2.
Mechanism of action | Covalent, active-site directed inhibitor
Structure of target-probe complex | Not determined
Additional comments | The N1 regiosomer of AA74-1 is also a potent APEH inhibitor (8 nM IC_{50} by gel-based ABPP; see Supplementary Fig. 4c)

Cellular profiling | Validation of cellular target | Proteomic target validated by gel- and MS-based ABPP both in cells and in mice.
Validation of cellular specificity | Selective for APEH over 43 serine hydrolases in situ in mouse T-cell hybridoma cells as validated by ABPP-SILAC experiment; see Figure 4b). Selective in vivo in mouse brain and heart proteomes (see Figures 5a and 5b)

Additional comments