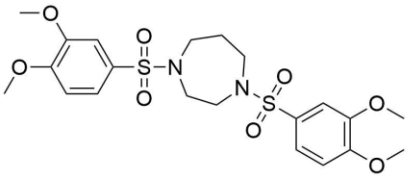
Kinase Screening Library (KSL)

Kinase modulators represent a very hot topic in drug discovery: 52 protein kinase inhibitors are approved drugs, with several hundred undergoing clinical trials [1]. Only in 2019, the US FDA approved four new small molecule protein kinase antagonists. Moreover, over the past 10 years, the number of protein kinase inhibitor chemotypes has dramatically expanded [2].

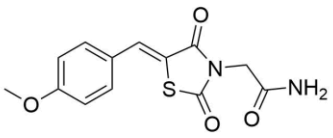
Life Chemicals offers its proprietary Kinase Screening Library (KSL) built by the front-end industry standards [3,4]. KSL was designed based on about 1,000 Markush structures and pharmacophore models of known kinase inhibitors derived from ChEMBL and PubChem databases. Our 2D similarity search allowed us to select **2,090** drug-like screening compounds of potential inhibitors and activators targeting key kinases in cancer and inflammation. Information on the closest homolog with its highest activity from the ChEMBL and PubChem databases was added to each compound entry (examples in Fig. 1).

KSL aims to provide high-quality hits for drug discovery projects related to kinases and other ATP-binding proteins. The Library contains:

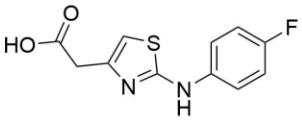
- Inhibitors of protein kinases heavily pursued by industry: ABL, AKT, ALK, AMPK, Aur, Bcr-ABL, Braf, BTK, CDK, cFMS, CHK, CK2, cKIT, cMET, EGFR, FLT3, Fyn, GSK3, HER, JAK, IGFR, IKK, ITK, KDR, LCK, LRRK, MEK, mTOR, p38α, PI3K, PIM, PKA, PKC, PKM2, ROCK, Src, Syk, Tie2, Trk, VEGFR
- ATP-competitive inhibitors
- DGF-out and αC-helix out non-ATP competitive inhibitors
- MEK non-ATP competitive inhibitors
- Covalent kinase inhibitors
- Allosteric kinase inhibitors
- Kinase activators: AMPK, ABL, DPK1, PKM2
- Generic hinge binders



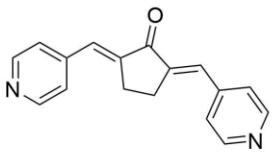
F1018-1711
Analog of DASA-58, allosteric PKM2 activator, Nature Chem.Biol. 2012,8,839-845



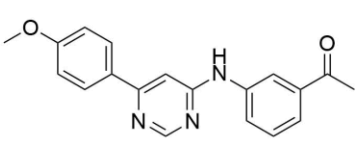
F1074-0296
Analog of allosteric inhibitor of ERK2



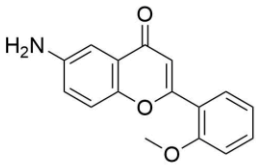
F2158-0418
Analog of allosteric AMPK activator, WO2009019600 (A2)



F0013-1066
Analog of SC66, allosteric ABL inhibitor, myristoyl agonist, facilitates autoinhibition state of ABL



F5759-0407
Analog of SC66, allosteric ABL inhibitor, myristoyl agonist, facilitates autoinhibition state of ABL



F2211-0008
Analog of PD98059, prevents inhibition of MEK1 by RAF

Figure 1. Examples of structures from the Kinase-Targeted Screening Library.

Reference:

1. Roskoski R Jr. Properties of FDA-approved small molecule protein kinase inhibitors: A 2020 update. *Pharmacol Res*. 2020;152:104609.
2. Bhullar KS, Lagarón NO, McGowan EM, et al. Kinase-targeted cancer therapies: progress, challenges and future directions. *Mol Cancer*. 2018;17(1):48.
3. Gagic Z, Ruzic D, Djokovic N, Djikic T, Nikolic K. *In silico* Methods for Design of Kinase Inhibitors as Anticancer Drugs. *Front Chem*. 2020;7:873.
4. Fabbro D, Cowan-Jacob SW, Moebitz H. Ten things you should know about protein kinases: IUPHAR Review 14. *Br J Pharmacol*. 2015;172(11):2675-2700.