Cysteine Focused Covalent Inhibitors Library

The Cys focused compound set of potential covalent inhibitors was created on the base of specific structure moieties that could react reversibly or irreversibly with active site cysteine residues. On the basis of literature data [1-8] we selected the most important functional groups that are known to target binding pocket of proteins through formation of covalent bonds with Cys amino acid residues. Michael acceptors are typical functionalities that often introduced in structures of this type of covalent inhibitors as well as fragments capable for nucleophilic displacement or addition.

The following structural fragments were used for selection of possible covalent inhibitors focused on Cys residue from Life Chemicals compounds collection:

- α,β-unsaturated ketones
- α-chloracetamides
- phenylsulphonate esters
- vinylsulfonamides
- acrylamides
- acrylonitriles
- aminomethyl methyl acrylathes
- methyl vinylsulfones
- epoxides
- activated acetylenes
- sulfonyl fluorides

Compounds from Life Chemicals' Stock Collection were pre-filtered with "Rule of five" restrictions:

- MW from 150 to 500
- clogP from -1 to 5
- Hb donor: 0-5
- Hb acceptor: 0-10
- rotatable bonds: no more than 10

Total number of compounds in the selected set: **1,300.**

References

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5. D. S. Johnson, E. Weerapana, B. F. Cravatt Future Med. Chem., Vol. 2 (6), 2010, pp. 949–964
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To download a file with compound structures for this library, please follow this link:

http://www.lifechemicals.com/downloads/Screening_Libs/13062/Covalent_inhibitors