High Fidelity Fragment Library

- *Fragments of high MedChem tractability*
- **1,920 compounds**

Fragment screening usually provides high numbers of hits and is one of the most affordable approaches to start drug discovery. However, subsequent steps involving hit-to-lead optimization may be challenging and require significant resources. It's even more painful when efforts result in false positives.

We have designed a new fragment library specifically addressing the quality of decision making when evaluating hits. Our **High Fidelity Fragment Set** features high medchem tractability enabling researchers to grow interesting hits with confidence.

High medchem tractability of this set was achieved through structure review and selection by FBDD experts at Takeda and Carmot Therapeutics. In particular, we would like to thank Dr. Dan Erlanson, Dr. Derek Cole, Dr. David Lawson and Dr. Xiaolun Wang for their involvement in the design of our **High Fidelity Fragment Library.**

High quality: All compounds selected for this library passed turbidity tests to assure high solubility in water at 1 mM; all aggregators were filtered out. In addition, the fragments in this set were screened by surface plasmon resonance (SPR) to remove any false positive fragments. SPR screening was kindly provided by Dr. Laure at Sailor at **HarkerBio**.

Optimal molecular properties: Fragments in this set all have 9–16 heavy atoms, are moderately complex and have suitable physiochemical and shape profiles.

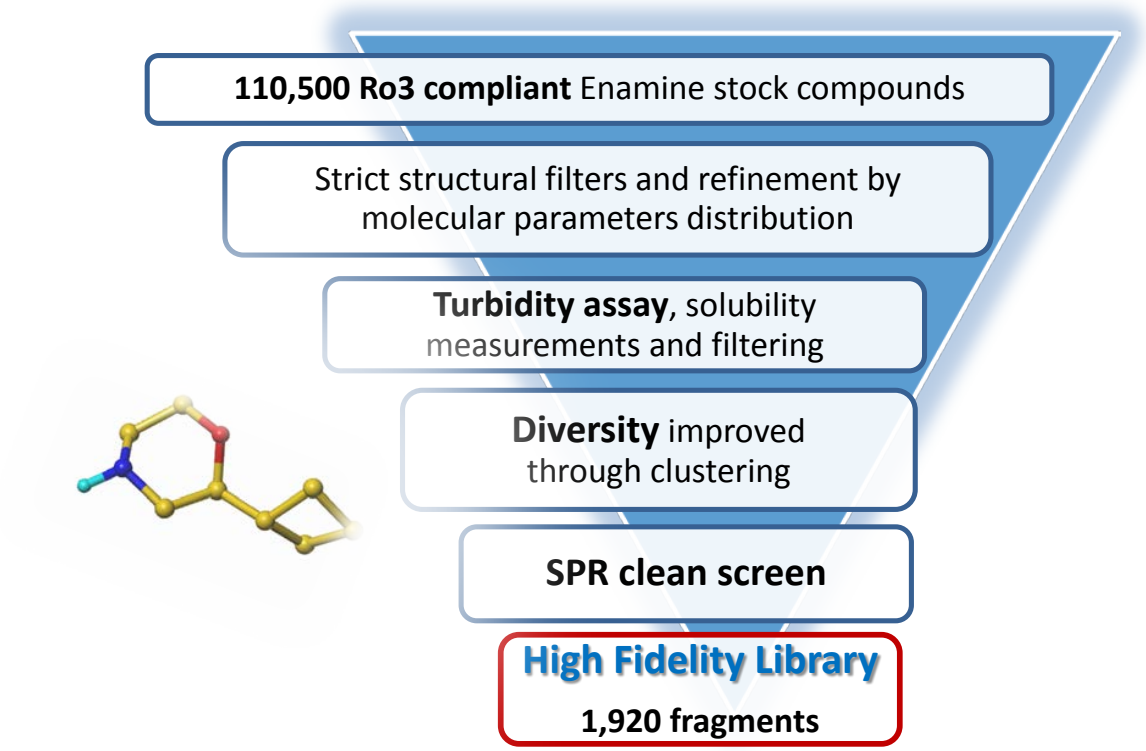
Our High Fidelity Fragment Library is available for prompt delivery in various formats.

Library Design

A complex iterative approach has been applied in the design of this library. Fragment selection was made from over 110k Ro3-compliant compounds in Enamine's stock collection. All industry recommended medchem filters, including PAINS, were applied. Diversity selection was performed using clustering algorithm and manual review of identified clusters to select the most representative structure within each cluster.

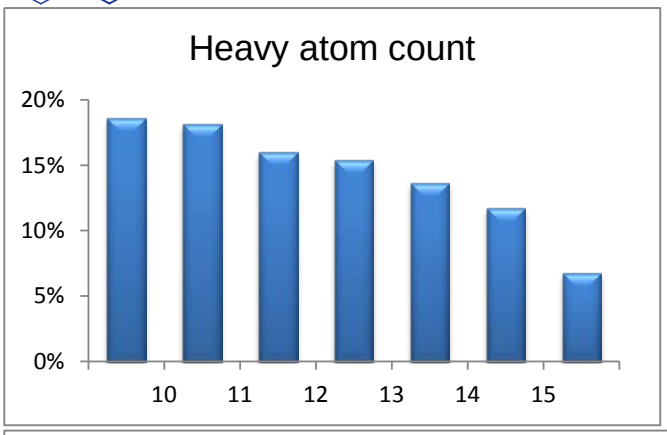
All compounds were tested for solubility in water and aggregation by laser nephelometry to remove compounds with solubility issues. The resulting set of fragments was then tested in clean SPR screens to exclude SPR "sticky" compounds.

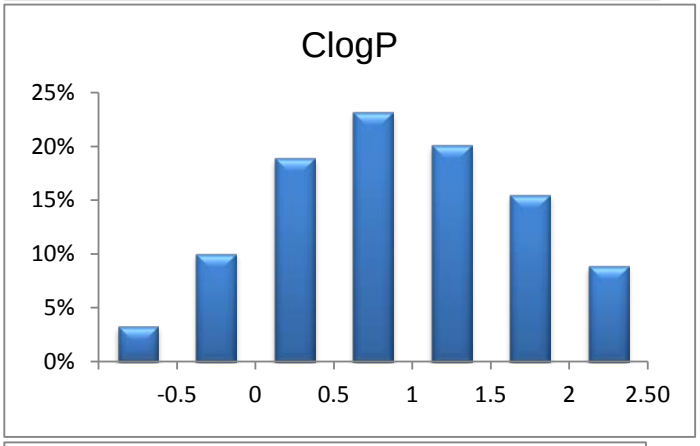
The selection process and resulting molecular parameters of our High Fidelity Fragment Set are described in the following scheme:

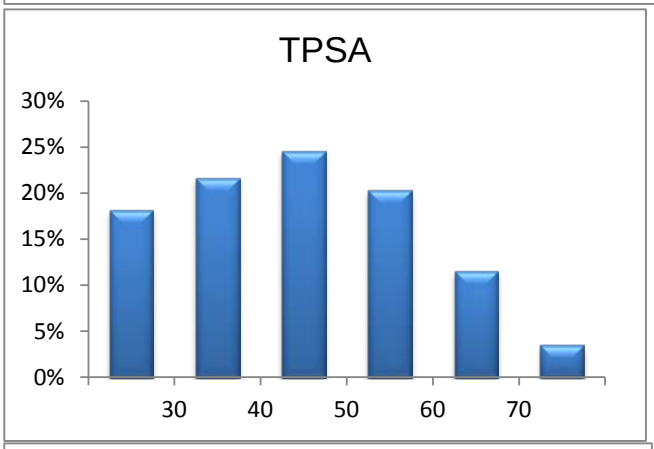


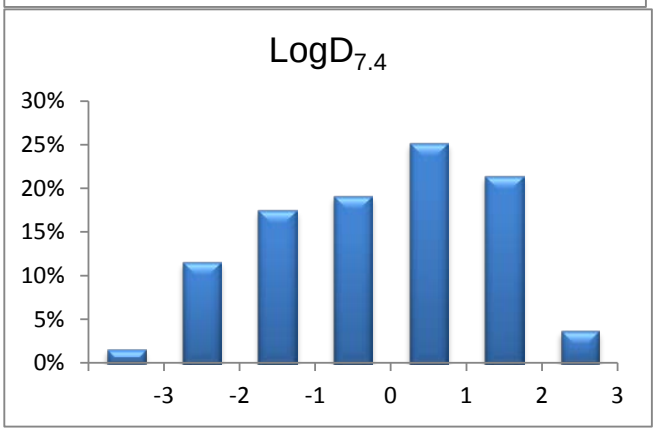
Molecular Parameters

Parameters	Range	Other restrictions
HAC	**9 - 16**	No reactive groups or undesirable cores, PAINS filters applied
MW	132 - 298	
HBD	0 – 2	No more than 1 Sulfur, 3 halogens (only F or Cl)
HBA	1 - 3	
ClogP	**-1.0 - 2.5**	Chemotype control
TPSA	20 – 100 Å^2	Optimal and even distribution of molecular parameters
logD$_{7.4}$	**≤ 2.5**	
Aromatic rings	0 – 2	Purity of samples (LCMS) ≥ 95%
Fused rings	≤ 2	


Heavy atom count
20%
15%
10%
5%
0%
10
11
12
13
14
15


ClogP
25%
20%
15%
10%
5%
0%
-0.5
0
0.5
1
1.5
2
2.50


TPSA
30%
25%
20%
15%
10%
5%
0%
30
40
50
60
70


LogD7.4
30%
25%
20%
15%
10%
5%
0%
-3
-2
-1
0
1
2
3