The BIONET Premium Fragment Library

Fragment-based lead discovery (FBLD) is now broadly practised throughout the drug research community and a number of compounds that evolved from fragments have now entered clinical trials. FBLD involves the screening of small libraries of fragments that typically obey the Rule of Three (Ro3). Pre-requisites for fragment screening are a diverse library of compounds with good aqueous solubility.

The BIONET Premium Fragment Library consists of 931 fragments with experimentally assured aqueous solubility, high purity (≥95%), excellent diversity (Diversity Coefficient = 0.78[1]) and were selected based on Ro3 criteria, chemical tractability and potential for fragment evolution.

Key features and benefits

- ☑ Ro3 compliant
- ☑ Measured solubility in PBS buffer (1mM)
- ☑ Soluble in DMSO at 200mM
- ☑ Purity ≥ 95%. NMR available for each fragment
- ☑ Filtered to remove toxic and reactive groups[2]
- ☑ Filtered for PAINS substructures[3]
- ☑ Diversity coefficient = 0.78[1]
- ☑ Low overlap (68 fragments) with the Maybridge Ro3 Diversity Fragment Library

The BIONET Premium Fragment characteristics are listed in the table below.

Characteristic	BIONET Premium Fragment
cLogP	≤ 3
Rotatable bonds	≤ 3
H Bond donors	≤ 3
H Bond acceptors	≤ 3
MW	≤ 300
TPSA	≤ 60Å^2
Purity	≥ 95%
Aqueous solubility	> 1mM
DMSO solubility	200mM
Diversity coefficient	0.78

Measured solubility

One of the key factors to be considered when constructing a fragment library is aqueous solubility. Factors contributing to solubility are difficult to predict and therefore this property can only safely be obtained through experiment. Solubility of the BIONET Premium Fragment Library was determined by Laser nephelometry. DMSO solubility at 200mM was determined by visual inspection.

Experimental details are available on request.

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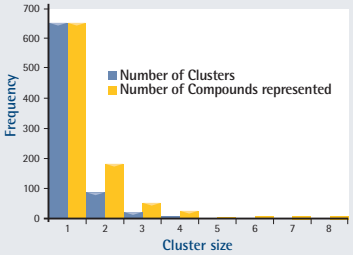
Diversity-Clustering Analysis

Compounds were fingerprinted with bit-packed MACCS keys and then Jarvis-Patrick clustering was applied with a Tanimoto similarity metric using an 85% threshold for similarity and cluster overlap. There are significant numbers of singletons illustrating the diversity of the BIONET Premium Fragment Library.

Diversity coefficient = 0.78[1]



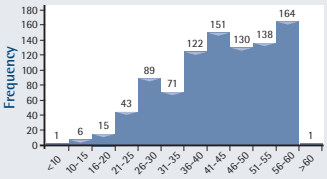
Toxicophores

Toxic properties can often be related to particular chemical substructures and application of criteria for toxicophore rule derivation and validation have been established[2]. Toxic/Reactive compounds were identified and removed from the fragment library using MOE (Chemical Computing Group).

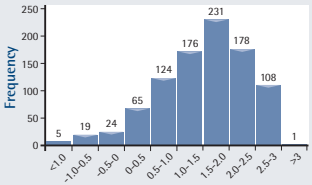
PAINS

Jonathan Baell and Georgina Holloway describe a number of substructure features which can help to identify compounds that are frequent hitters in many biochemical high throughput screens and named compounds with these features 'Pan-assay interference compounds', or PAINS[3]. The BIONET Premium Fragment Library has been visually inspected and PAINS compounds removed.

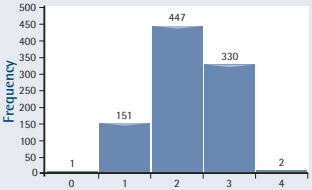
BIONET Premium Fragment Library
Physiochemical property distribution graphs



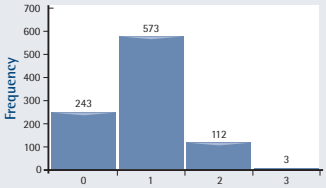
TPSA



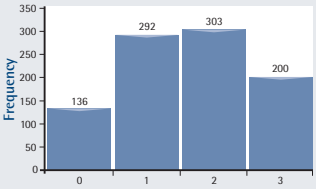
cLogP



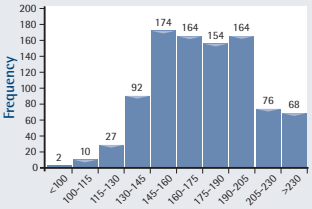
H bond acceptors



H bond donors



Rotatable bonds



Mol Wt

The BIONET Premium Fragment Library is available custom-weighed in milligram or micromolar quantities. Customers can purchase the entire library or select any number of compounds as required.

1 Turner D.B., Tyrell S.M., Willet P. J.Chem. Inf. Comput. Sci. 37 (2007) 18-22
2 Kazius J, McGuire R, and Bursi R. Derivation and Validation of Toxicophores for Mutagenicity Prediction. J. Med. Chem. 2005, 48:312-320
3 Baell J.B., Hollaway G.A. J. Med. Chem. 2010, 53:2719-2740

BIONET Fragment Libraries

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