



IOTA's Fragment Library Screening Programs

Fragment-based Drug Design

Fragment-based drug design - FBDD - is a paradigm shift for drug discovery.

Out! with expensive, million-component, high-throughput screening and combichem libraries.

In! with low complexity, target-focused chemical libraries, tailored to specific medchem and chemo applications.

Fragment libraries are a tried and tested starting point for pharma discovery. A multitude of recent publications illustrate their successful use in drug discovery - for details, see:

www.iotapharma.com/literature

Leveraged by smart screens, chemical fragments open a reliable and productive way to develop chemical probes and valuable drugs in your therapeutic programs.

IOTA's Fragment Libraries

IOTA's fragment libraries have been carefully assembled in collaboration with an expert in the FBDD area, Dr Iwan de Esch, head of Drug Design and Synthesis in the Medicinal Chemistry Department at the Free University in Amsterdam¹⁻⁶.

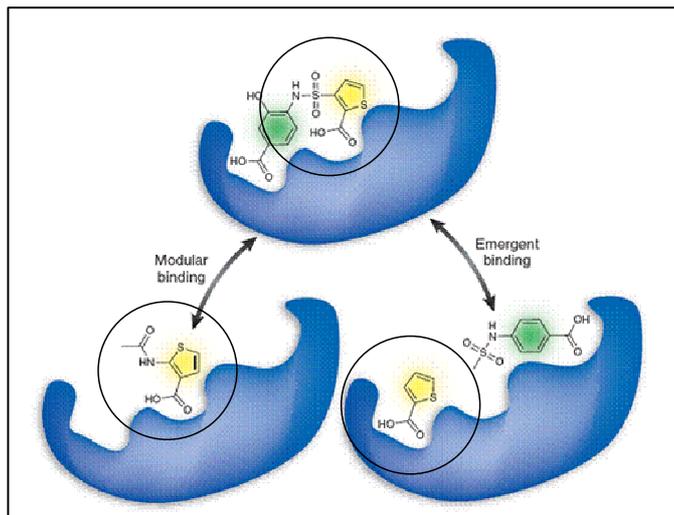
The majority of our compounds conform to criteria⁷ defined in the "Rule of 3". The only exception to this is the inclusion of certain compounds of ~350 MW whose SAR could be instructive for discovery applications (see below).

The compounds in **IOTA Diverse 1500** are unique heterocycles developed with the Free University in Amsterdam which can only be obtained from IOTA.

The compounds in **IOTA Vitas 4000** are a collection of new Rule-of-3 compliant scaffolds which have been selected from the Vitas-M Labs compound collections.

The compounds in **IOTA Family** libraries are target-focused fragments, derived by virtually screening large compound collections against pharmaceutical targets.

Available without any legal restrictions, these libraries can be used for screening at home in your lab, or in collaboration with IOTA in our labs.



The Principles of Fragment Screening

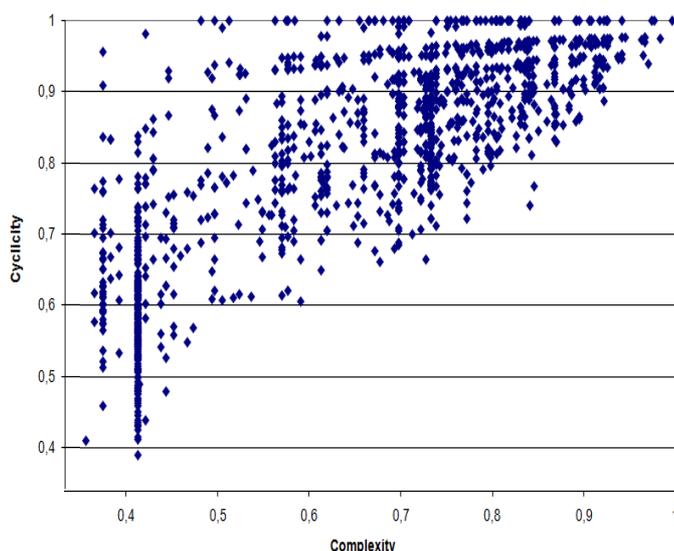
The diagram above, adapted from a recent review⁸ of FBDD, illustrates some features of the approach, including the provision of:

- a variety of novel medchem entrypoints
- alternative lead series by directed scaffold-hopping
- structure-driven elaboration of fragments into drug-like molecules for candidate selection

The power of the approach lies in its modularity - fragment-swapping within leads can fine-tune both potency and ADMET characteristics⁹.

IOTA Diverse 1500 covers scaffold space¹⁰ very broadly, uniquely containing almost 700 different scaffolds amongst its 1500 fragments (below). This makes IOTA Diverse a very valuable drug discovery resource for initial screening applications.

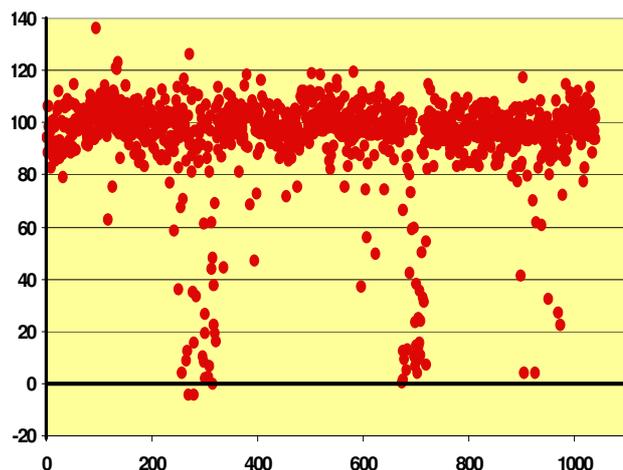
"IOTA Diverse" Scaffold Space



Using IOTA Libraries in Screening Applications

Because Fragment Libraries may contain weak hits, they are screened at high concentrations, which necessitates robust screens (Z' values of >0.6). The physico-chemical properties of the IOTA Fragment Libraries mean that there is little interference with typical screening assays.

Screening results using "IOTA Diverse 1500"

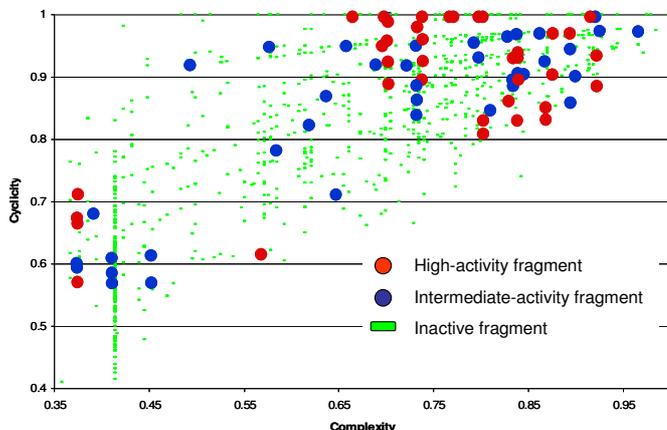


The SAR of actives can be explored later using small focussed combinatorial libraries, but there is usually enough information within the initial fragment screen to provide preliminary SAR.

Scaffold "Mapping" using IOTA Diverse 1500

The active fragments identified in such screens originate from a variety of scaffold families, reflecting the fact that **IOTA Diverse 1500** has been optimized for scaffold diversity, as illustrated in the analysis below.

Active Scaffold "mapping" from the "IOTA Diverse 1500" dataset above



Prices and Availability

Full descriptions of our Fragment Libraries, with chemical structures and property analyses, are available, under confidentiality, from IOTA.

Contact us at info@iotapharma.com for more information concerning screening options.

References

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IOTA's Discovery Strategy

IOTA believes that new chemical tools and genomic technologies are urgently required to accelerate drug discovery - today.

We aim to position ground-breaking technologies - such as FBDD - at the forefront of pharmacological research in every laboratory, making them available to researchers in formats appropriate to their widespread use.

We encourage you to visit IOTA's website for more information:

www.iotapharma.com