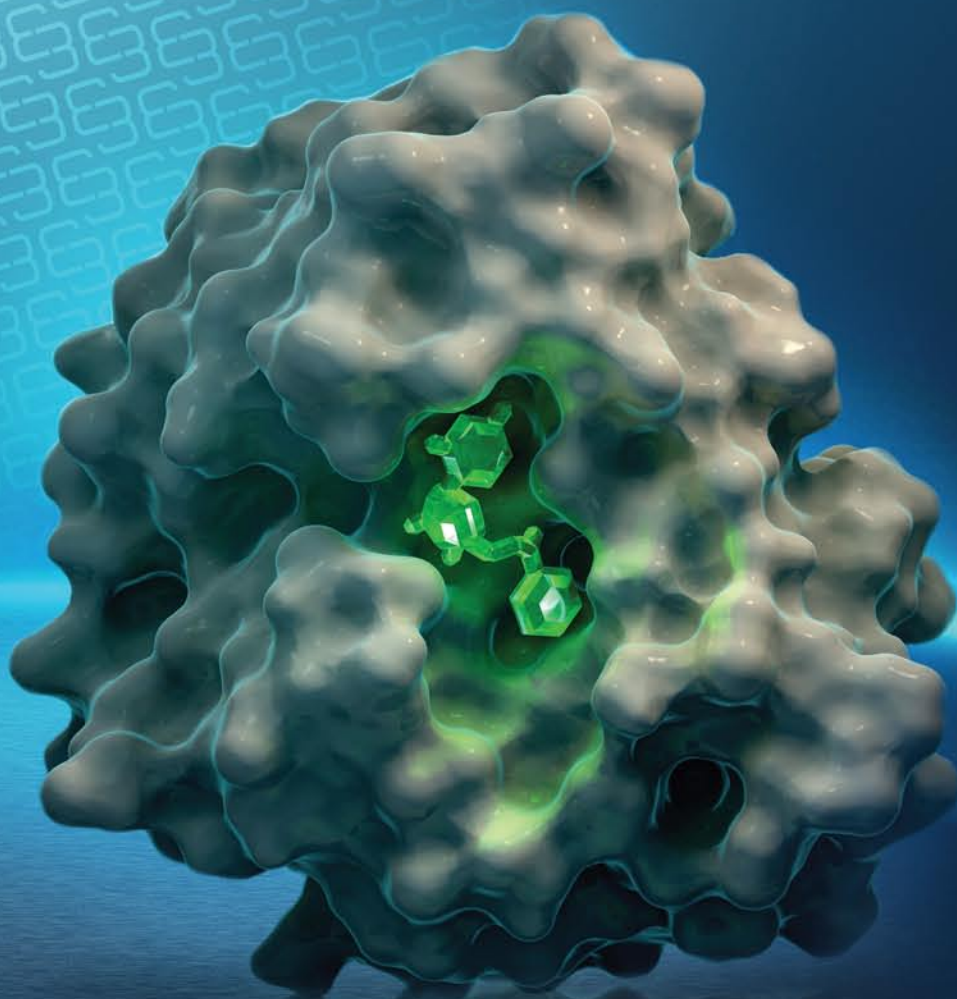


Optimize drug discovery

Fragments of Life™:

A proven and unique approach



Collaborate With Emerald BioStructures

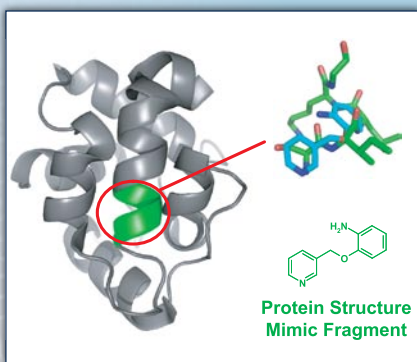
- Leader in fragment-based drug discovery (FBDD)
- Expert project management
- Proven success in accelerating clients' drug discovery programs, including delivery of clinical compounds

Accelerate Drug Discovery With Fragments of Life™ (FOL) Technology

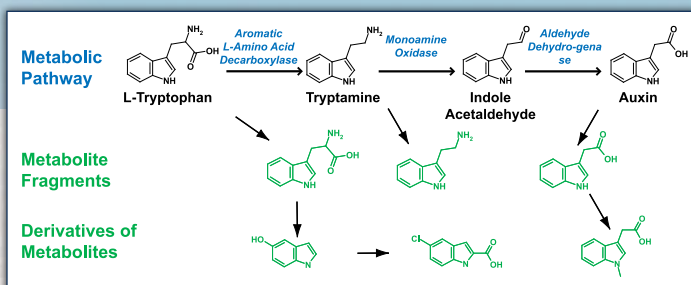
FOL is a proven, integrated approach that focuses on both the target and ligand perspectives:

- **Unique FOL library** provides critical starting points for lead compounds based on metabolites found naturally in cells
- **Proven structure-based drug design** includes:
 - X-ray crystallography
 - Nuclear magnetic resonance (NMR)
 - Computational chemistry

FOL Library: Optimized for Quality Hits and Leads



- Capitalizes on the fact that proteins have evolved binding surfaces interacting with myriad naturally occurring small molecules
- Contains >1500 naturally occurring metabolites/derivatives of metabolites (below) and protein mimetics (left)
- Follows “Rule of 3” guidelines,¹ tending toward more water solubility
 - Average molecular weight: 182.5
 - Average cLogP: 0.96
 - Less than 3 hydrogen bond donors or acceptors per molecule





Let Us Help Guide Your Drug Discovery

- Our solid expertise leads to the development of valuable drug discovery assets
- Our drug discovery experts drive chemistry efforts, translating fragment hits to leads
- Our tools secure intellectual property (IP) space, provide pharmacophore data and back-up compounds
- Our capabilities allow us to drive chemistry efforts to elaborate fragment hits to leads

Graduate From Theory to Practice With Fragment-Based Drug Discovery

Unique FOL library is designed to efficiently interact with proteins, and the fragments are highly amenable to lead optimization. FBDD is a proven approach with a growing track record:

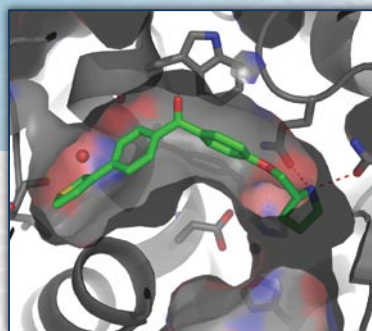
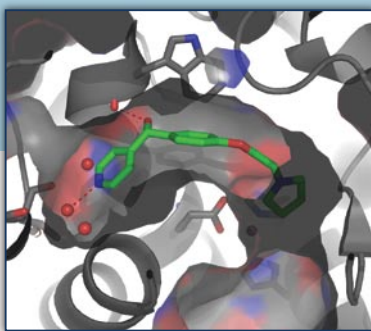
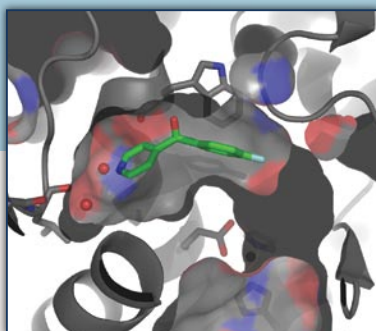
- An estimated 16 compounds progressing through clinical trials²
- Fragment screening hits generally have better ligand efficiency than hits from traditional high throughput screening (HTS)

Case Study: Fragments of Life Proof of Concept – Leukotriene A4 Hydrolase

Leukotriene A4 hydrolase (LTA4H) is an important drug target for treatment of inflammation and cardiovascular disease. The study demonstrated the flexible and efficient structure-guided drug discovery provided by our high-quality library.³

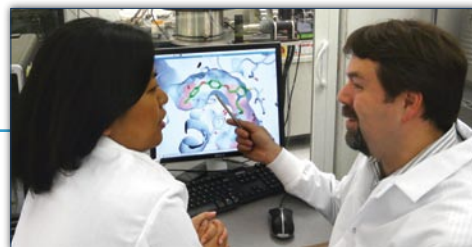
Moving From Quality Fragment Hits to Optimized Leads

We screened LTA4H with the FOL library using X-ray crystallography. The structures and binding affinities of 13 hits are described in *J Med Chem*. Figures below show the elaboration of a fragment hit with no detectable IC_{50} (left) to a lead with an IC_{50} of 135 nM (right).



Experience Quality Collaboration

- Expert project management
- Specialists in difficult targets
- Flexible, results-driven approach



Structural Biology & Biophysical Techniques

- Fully outfitted, proprietary protein crystallization and formulation laboratory, including data capture utilizing Crystal Miner™ database software
- State-of-the-art Rigaku X-ray generators, ACTOR robots, and CCD detectors capable of simultaneous collection on 4 samples
- Access to synchrotron X-ray data collection
 - Advanced Photon Source (APS)
 - Advanced Light Source (ALS)
 - Stanford Synchrotron Radiation Laboratory (SSRL)
- Varian Unity Inova 500 MHz NMR Spectrometer capable of multi-dimensional heteronuclear NMR experiments and medium- to high-throughput liquids sampling

Structure-Based Drug Discovery Experts

More than just sets of 3D coordinates for your protein and ligand, Emerald can deliver lead compounds for your drug discovery program using structural information as a guide. Through our FOL technology we:

- Offer the flexibility to leverage structural information at almost any stage of drug discovery
- Deliver more high-quality starting points and options
- Guide you every step of the way



Schedule an Emerald BioStructures Road Show Visit

- Learn about progress in structural biology, including fragment-based drug design, infectious disease, and difficult targets
- Discuss your challenges with experts (non-disclosure agreements available)

Register at www.EmeraldBioStructures.com/roadshow

Call: 1-206-780-8900

References

1. Congreve, M, Carr R, Murray C, Jhoti H. A "rule of three" for fragment-based lead discovery? *Drug Discov Today*. 2003; 8(19):876-877.
2. Practical Fragments Blog. Available at: <http://practicalfragments.blogspot.com/2009/01/fragments-in-clinic.html>. Accessed March 31, 2010.
3. Davies DR, Mamat B, Magnusson OT, et al. Discovery of leukotriene A4 hydrolase inhibitors using metabolomics biased fragment crystallography. *J Med Chem*. 2009;52(15):4694-4715.