THE UNIVERSITY OF CHICAGO MEDICAL CENTER

High-Throughput Screening at The University of Chicago Cellular Screening Center

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High-Throughput Screening at The University of Chicago

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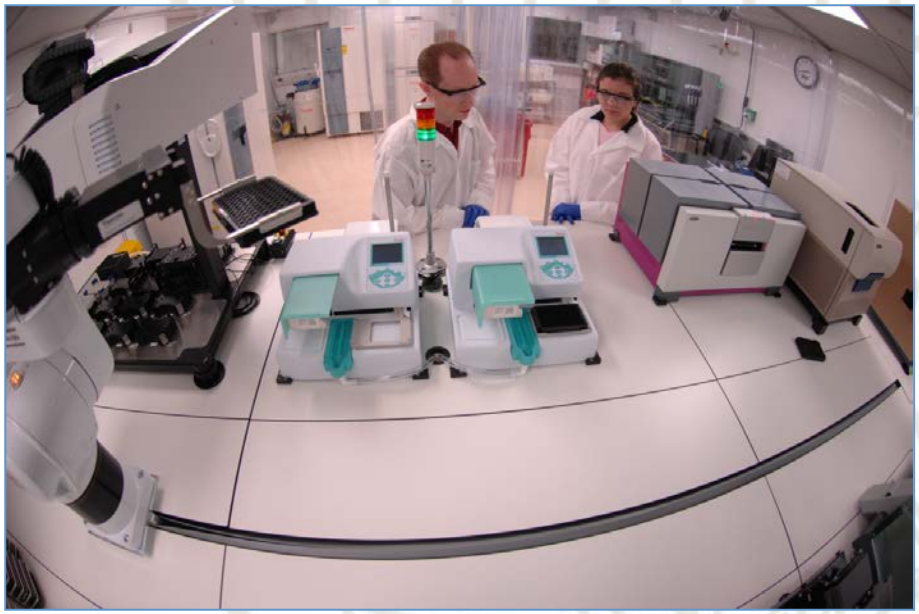
- Cellular Screening Center (CSC): Opened in January of 2007
  - In six years the CSC has run over 70 high-throughput screens
- Perform small molecule and siRNA screens for investigators throughout Chicago
  - Over 160,000 small molecules
  - Whole genome siRNA library (ThermoFisher Dharmacon)
- 900 ft^2 of cleanroom lab space: All screening areas are Class 100
- 8 liquid handlers and 3 readers (two high-content) with a multi-axis arm on a 3m rail



Available Chemical Libraries at The University of Chicago

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Cellular Screening Center
http://igsb.org/services/csc/
Sam Bettis, Technical Director

UCCCC Drug Discovery Core
Geoffrey Greene, Director

Compound Collections: Automated storage and retrieval for ~200,000 compounds; diverse scaffolds that cover as much chemical space as possible.

MicroSource Spectrum library: ~2,000 cpds - 50% (800 USP/USAN + 200 INN & BAN & JAN) known drugs, 30% (580) natural products, 20% (420) other bioactive compounds.
http://www.msdiscovery.com/spectrum.html

Prestwick Chemical Library: 1200 FDA approved drugs.
http://www.prestwickchemical.com/index.php?pa=26

The Prestwick Chemical Library® contains 1200 small molecules, 100% FDA approved drugs, thus it presents the greatest possible degree of “drug-likeliness”. The active compounds were selected for their high chemical and pharmacological diversity as well as for their known bioavailability and safety in humans. The Prestwick Chemical Library ® contains a limited number of highly diverse drug molecules for which bioavailability and toxicity studies have already been performed and which have proven usefulness in humans.

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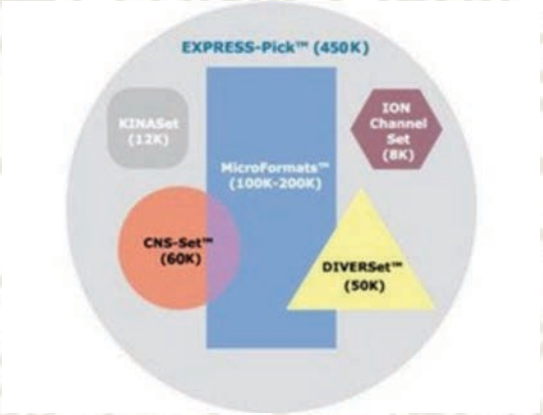
Chembridge Express-Pick collection:130,000 cpds from the MicroFormat library. Stock compounds are selected using novelty, diversity, drug-like property analysis, and medicinal chemistry expertise.
In addition, 50,000 compounds available as pooled plates - 8 cpds/well. These cpds come from the 130,000 cpd collection.
http://igsb.org/services/csc/



Chembridge DIVERSet Collection: 50,000 cpds
Extensive pharmacophore coverage for primary screening. Stringent drug-like and desirable chemical group filters coupled with a 3D conformer analysis are used in selecting a premium set of 50,000 drug-like compounds with maximum pharmacophore coverage and chemical diversity

CTCMLD collection: ~10,000 diverse cpds
Chicago Tri-Institutional Center for Chemical Methods and Library Development
Sergey Kozmin, Director
Karl Scheidt, Project 1 Leader
http://ctcmld.uchicago.edu

Diversity Analysis Using Principal Moments of Inertia (PMI) of CTCMLD Compounds

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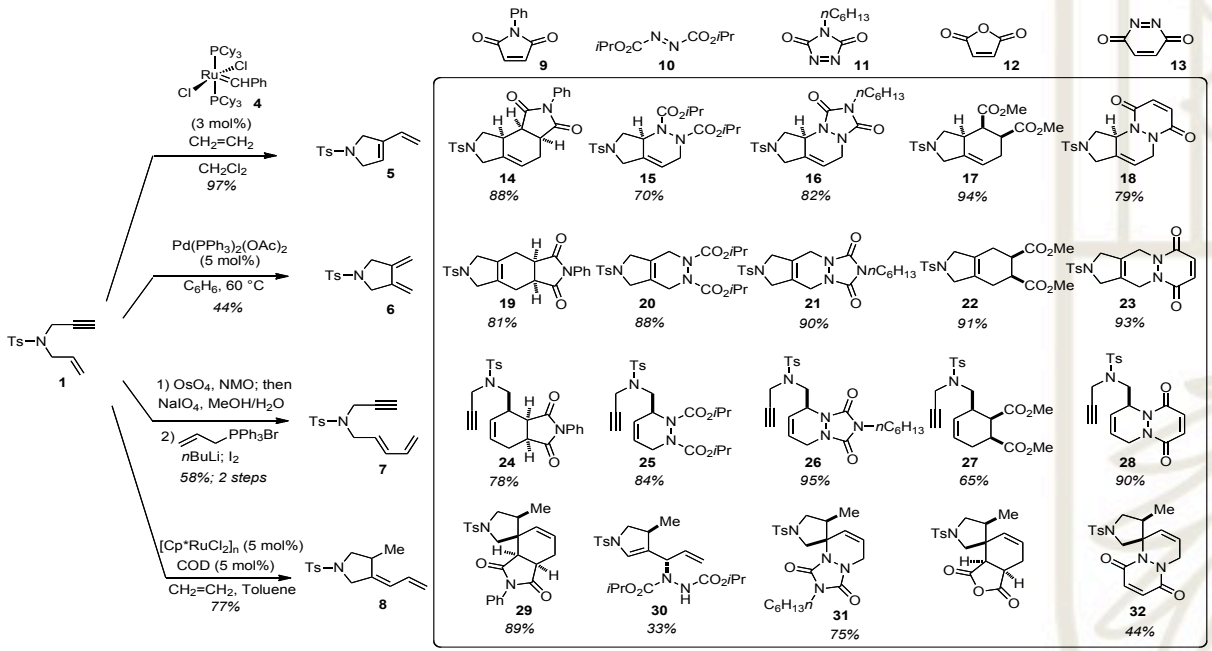
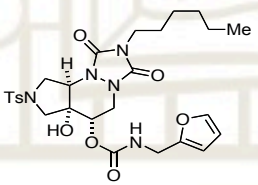
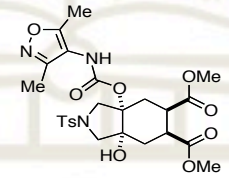
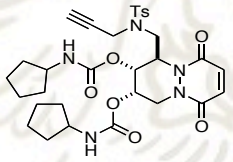




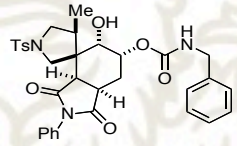
Yield: 18.0 mg (72%);
Purity (ELSD): 100%
MW: 589.7
Average ClogP: 2.41



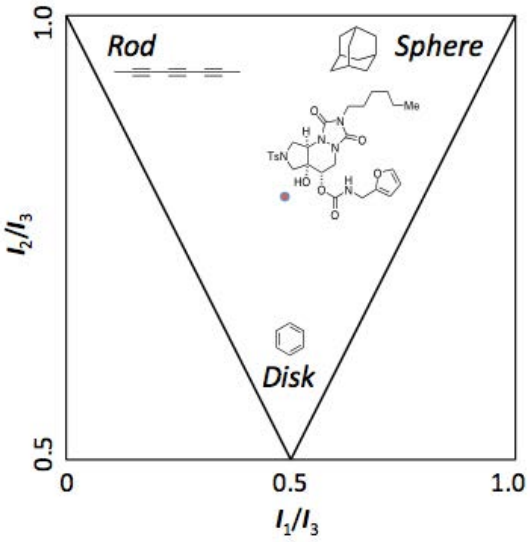
Yield: 23.0 mg (87%);
Purity (ELSD): 100%
MW: 565.6
Average ClogP: 1.09

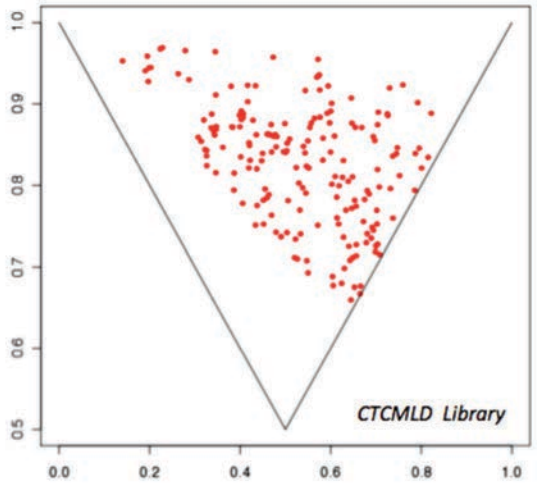


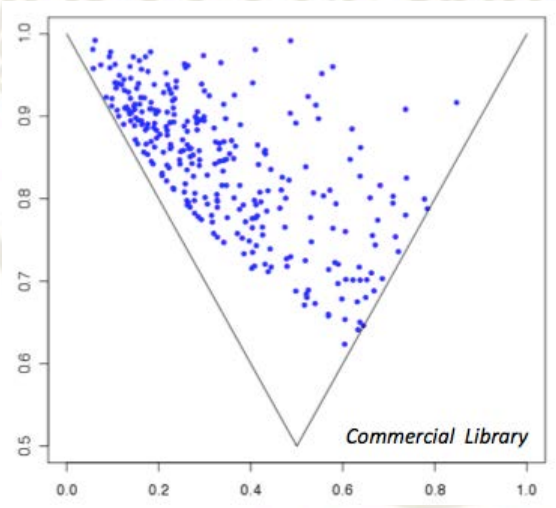
Yield: 21.9 mg (72%);
Purity (ELSD): 100%
Mw: 641.3
Average ClogP: 3.29



Yield: 19.7 mg (86%);
Purity (ELSD): 100%
MW: 589.7
Average ClogP: 3.39







Unique Capabilities at The University of Chicago

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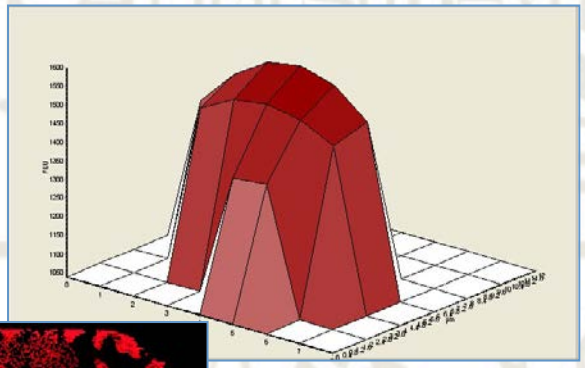
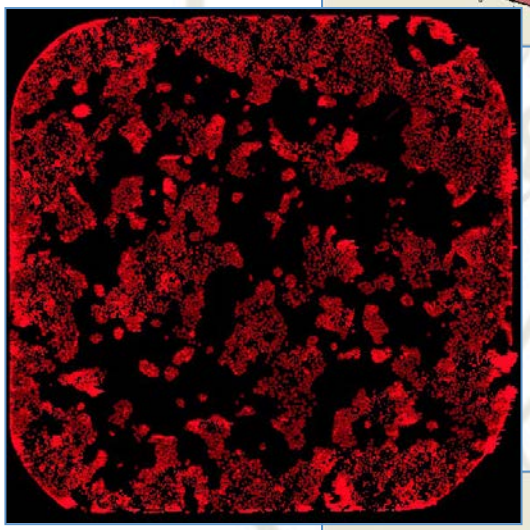
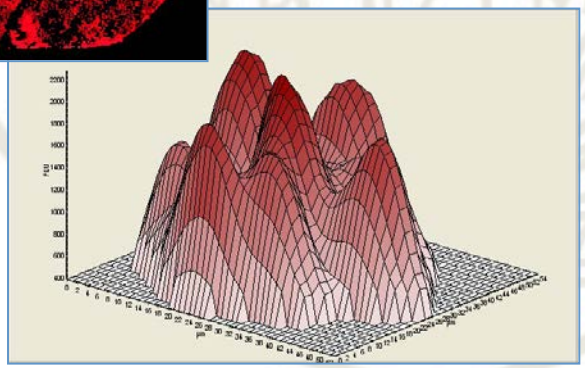
- Unique chemical libraries
- Flexible screening platform for enzymatic and cell-based screening
- Over 350 cell lines available in-house for immediate screening
- Class 100 clean room BSL2+ environment for sterility and reproducibility







Unique Capabilities at The University of Chicago

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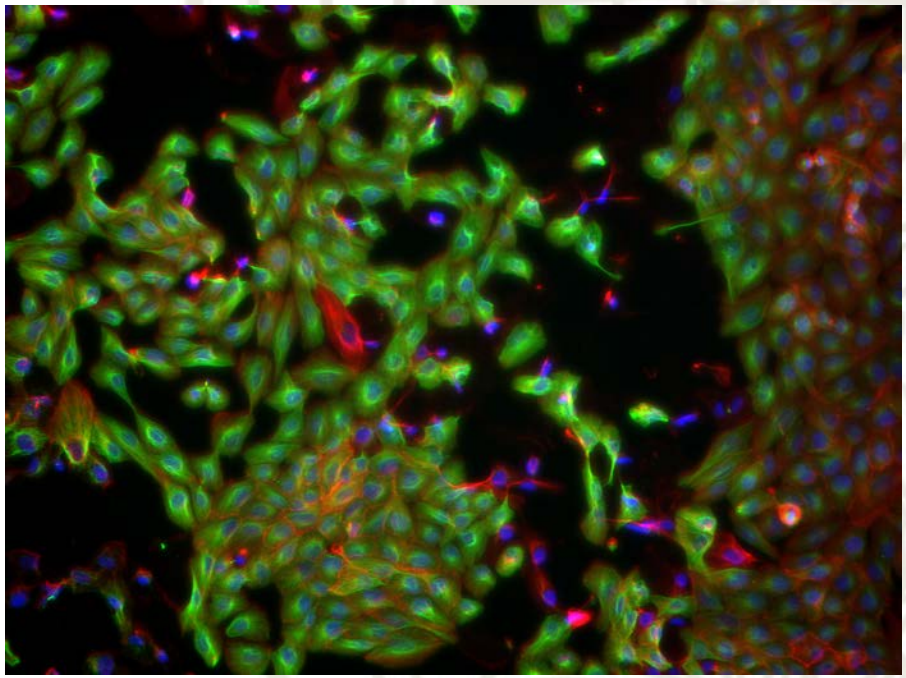
- Extensive screening experience in both compound screening and siRNA screening
  - Staff with experience in both industry and academia
- Work completed on unique targets and orphan diseases that are ignored by biotech/ pharma
- Two high-content readers are integrated for 24/7 reads with cutting-edge analysis tools and reliable data storage



Summary

THE UNIVERSITY OF CHICAGO MEDICAL CENTER

- We are discovering novel entities to further drug discovery in a wide variety of assays and disease areas
- We possess unique libraries, technology, and infrastructure to provide reliable and robust data for investigators
- We provide decades of experience in small molecule and siRNA screening
- Our setup is flexible and efficient which allows users to complete large screens in a reasonable time frame at a lower cost