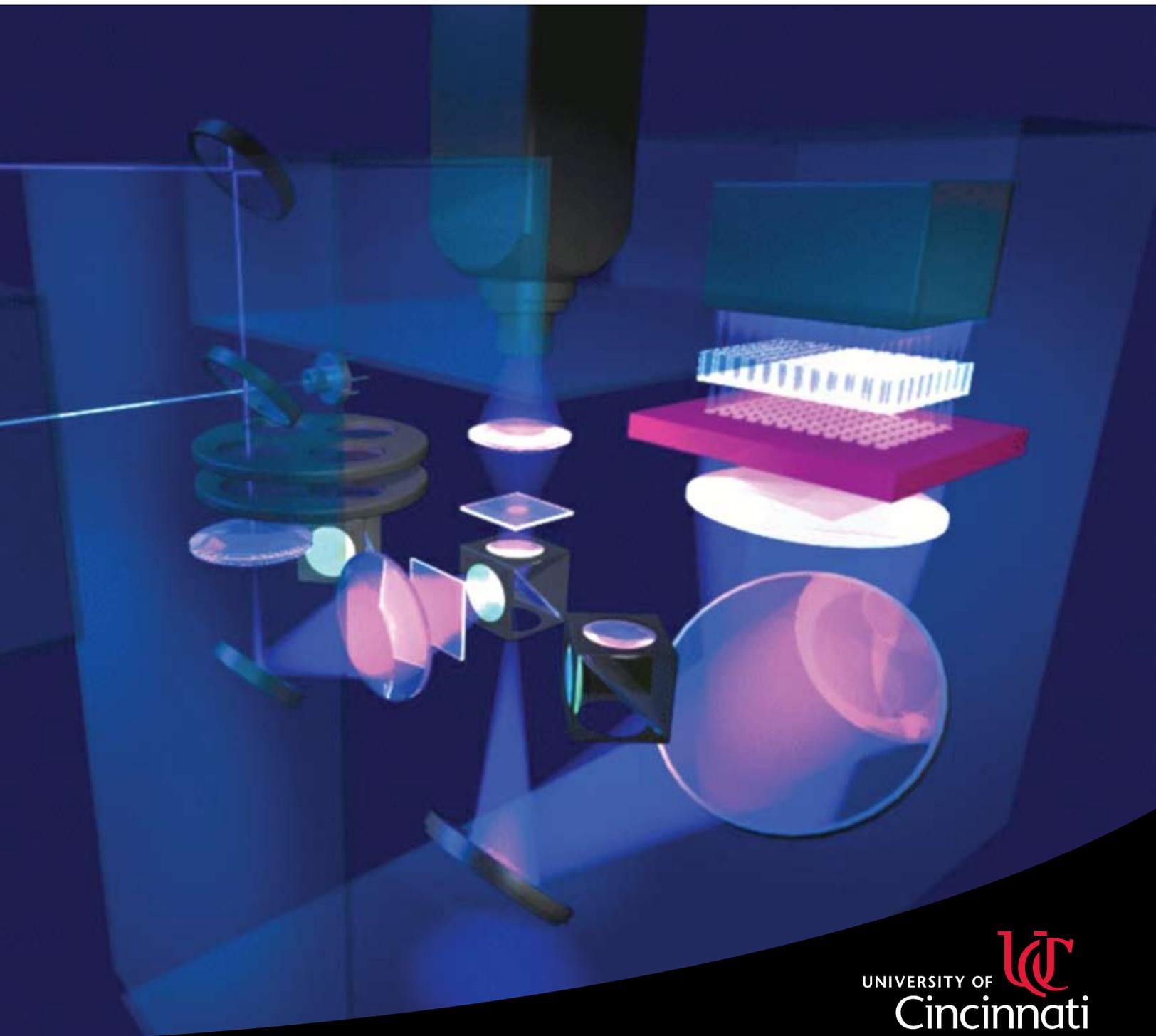


University of Cincinnati
Drug Discovery Center
www.drugdiscovery.uc.edu

Uniting Pharma Drug Discovery Capabilities with Academic Biomedical Research



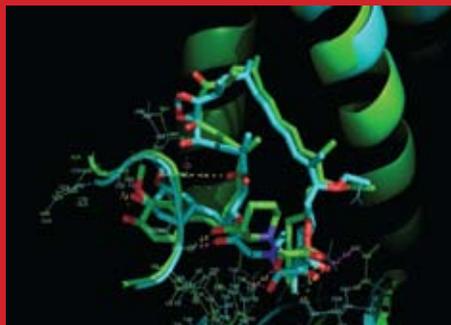
The Drug Discovery Center at the University of Cincinnati is dedicated to the discovery and early development of **novel and commercially viable therapeutic leads**.

The Drug Discovery Center offers academic and industry scientists access to **computational biology, high-throughput screening (HTS), medicinal chemistry** and a 250,000 pharma-quality **small molecule compound library**.

The Drug Discovery Center is managed by experienced pharmaceutical industry trained managers and staff. Strategically placed at the intersection of established academic and industrial entities. **Respecting complete confidentiality**, the Drug Discovery Center is designed to **fulfill both scientific and commercial objectives**.

These core capabilities and facilities allow scientists to **characterize drug targets** in terms of structure and function, and to **discover function-modulating chemical compounds**.

The Drug Discovery Center supports both hypothesis- and discovery-driven research, and provides the management infrastructure needed to **translate research discoveries into commercial opportunities**.

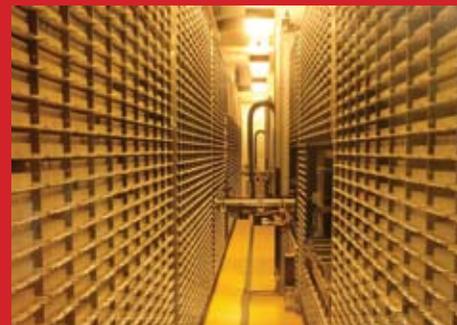


Computational Biology

Works with investigators to identify biologically active molecules for use as research tools or pharmaceutical leads.

- Homology modeling and protein structure refinement.
- Ligand and protein structure based *in silico* screening.
 - Database of over 4 million commercially available compounds.
 - Database of over 300,000 internally available compounds.
- High performance computing resource for custom code development and large-scale simulations.
- Custom computational chemistry software development.
- Developers of GRIDP, Ohio's statewide drug discovery web portal, now in beta release, hosted by the Ohio Supercomputer Center and the Ralph Regula School of Computational Science.

UC Drug



UC Compound Library

The UC Compound Library is a collection of drug-like compounds available to any investigator for use in finding a research tool or initial drug lead.

Compound Collection

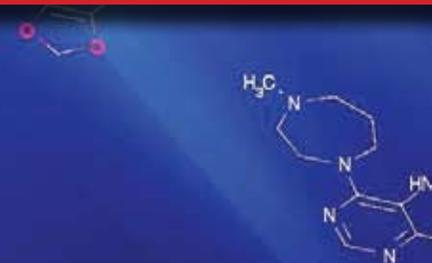
- 207,000 bottles of pure compounds
- 340,000 compounds in DMSO solution for rapid dispensing

Library constructed to ensure:

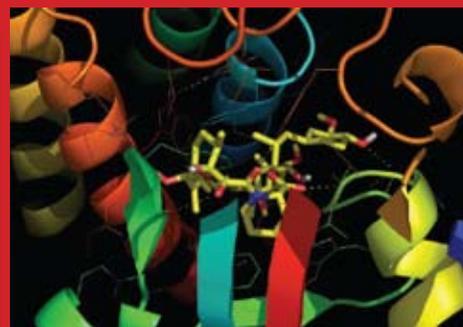
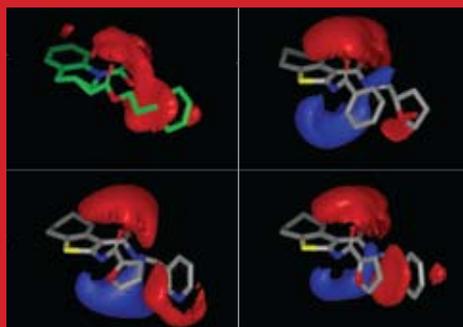
- Uniform distribution across "drug-like" structural space as defined by comparisons to Derwent's "World Drug Index."
- Added compound emphasis in certain classes (e.g. kinases, GPCRs, proteases) from selective purchases and internal synthesis.
- Compounds with reactive, unstable and other structural features associated with toxicities removed from library.

For additional information:

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Discovery Center Services



High-Throughput & High-Content Screening

Experts in assay development and high-throughput screening work with investigators to transition their laboratory assays to HTS-ready assays, and then conduct the screens on compound libraries from the UC collection or from other compound collections.

Capabilities

- Perkin Elmer Plate::Explorer™ Automated HTS system, Perkin Elmer Plate::Vision™, EnVision™ Detectors
 - Luminescence, fluorescence intensity, fluorescence polarization, FRET, time-resolved fluorescence, absorbance.
- Perkin Elmer Opera™ high content confocal imaging system
 - 4 CCD cameras, 4 lasers, 1 xenon lamp
- Capacity of 100,000 data points per day
- Data analysis software for single point, replicate and 10-pt dose-response data and associated statistics.
- MALDI - mass spec based label-free compound screening.

Computational Chemistry

Computational and medicinal chemistry personnel assist in overall evaluations of screening results and initial lead optimization efforts.

Cheminformatics

- Similarity (Nearest Neighbor), pharmacophore and structure based searching to find related internal and commercially available compounds closely related to a structural lead or HTS hits.
- Cluster Analysis of compounds into structurally related groups.
- Physical property calculations for ranking potential of compound classes.
 - Lipinski, Veber, PSA, solubility and related assessments of bioavailability.

Predictive Models

- Computational algorithms to predict various toxicities (e.g. hepatotoxicity, mutagenicity) and other biological properties (e.g. protein binding, CNS penetration, membrane permeability) for prioritization of compound classes.

Medicinal Chemistry

Experienced medicinal chemists to collaborate on analysis of HTS data, identification of early structure-activity relationships, and development of follow-up and optimization strategies.

Hit-to-Lead Capabilities

- Collaborative data analysis
- Cluster analysis
- Structure evaluations of hits
- Physical property predictions
- Literature background searches
- Synthetic accessibility

Lead Optimization Capabilities

- Peptide, small molecule and small library synthesis
- Medicinal chemistry and Modeling design input

We Provide

- Experienced staff recruited from pharma industry
- State-of-the-art high-throughput and high-content screening capability
- Access to a highly diverse library of drug-like compounds for screening
- Molecular modeling and in silico screening

We Seek

- Drug targets for screening
- Libraries of novel compounds
- Drug discovery collaborations
- Opportunities to create closer interactions with biotech and pharma companies

Our Leadership Team

Ruben Papoian, PhD

Ruben Papoian obtained his PhD in Experimental Pathology from the University of California, San Francisco. His early research focused on autoimmune diseases, T-cell activation and immunological tolerance. Over the past 20 years he has worked in the pharmaceutical industry primarily, in Switzerland, with Sandoz AG, Serono SA and Novartis AG. His main areas of research were related to target identification and drug discovery. Ruben moved from Novartis, Basel, to the University of Cincinnati in July 2005 as Research Professor and Director, Drug Discovery Center.

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Sandra Nelson, PhD

Sandra Nelson received a PhD in biochemistry from the University of North Carolina at Chapel Hill. Before joining the UC DDC in September 2006, Sandra was responsible for the HTS and Compound Repository facility for Procter & Gamble Pharmaceuticals. During her 18 year career with Procter & Gamble, she also performed research to develop new over-the-counter products for P&G (toothpaste, mouthwash, cough & cold medicines, gastrointestinal medicine), and developed and ran biochemical assays, including those for clinical studies, helping to develop new pharmaceutical products. Sandra is Head of High-throughput and High-content Screening and Assay Development.

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William Seibel, PhD

William Seibel received a PhD in Chemistry from Harvard University. He has 19 years of experience in the pharmaceutical industry and has led groups in the design and development of antibacterials, cardiovascular drugs, and anti-obesity agents. This work included optimization of known classes of drugs and explorations into emerging targets in disease,

several of which have progressed into clinical trials. William is Head of Medicinal and Computational Chemistry and Compound Library Services.

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Matt Wortman, PhD

Matt Wortman obtained his PhD from the University of Cincinnati. He has a background in molecular biology and metabolism with an emphasis on central nervous system control of obesity and metabolic disease and has conducted basic research related to the mechanisms of drug action. His group develops software applications and turn-key high performance computers for use in computational biology and drug discovery. He is currently Principal Investigator of GRIDP (GRI Discovery Platform), the State of Ohio's newly launched drug discovery web portal that enables students and researchers to apply high performance computational tools to biological and drug discovery projects. Matt is Head of Computational Biology and IT.

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Ken Greis, PhD

Ken Greis holds a PhD in Biochemistry from the University of Kentucky and has worked in the area of biological mass spectrometry for over 15 years. His research focuses on technology development and the application of mass spectrometry to understand biochemical and biomedical systems. He spent a decade building and leading protein characterization and proteomics mass spectrometry groups at Parke-Davis Pharmaceutical Research (now part of Pfizer) and Procter & Gamble Pharmaceuticals. Greis is the director of proteomics and mass spectrometry for UC and Cincinnati Children's Hospital Medical Center <<http://www.med.uc.edu/proteomics/>>. He has recently developed a novel MALDI mass spectrometry-based compound screening approach as a label-free alternative to traditional high-throughput screening assays.

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