



MELVIN AND BREN SIMON CANCER CENTER

INDIANA UNIVERSITY

CHEMICAL GENOMICS CORE

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ABSTRACT

The Chemical Genomics Core Facility (CGCF) is a new shared facility of the IU Simon Cancer Center and the IU School of Medicine that was established less than two years ago. The mission of CGCF is to provide IU investigators with cost-effective access to high-throughput screening of structurally diverse, drug-like small molecules in biological assays provided by the investigators. This service enables the investigators to discover small molecule tools for basic research, therapeutic development and diagnostic applications. Facility staff will work closely with each investigator through all stages of the screening process, providing an opportunity for students and fellows to gain experience and training in high throughput screening at the facility.

SERVICES PROVIDED

- Consultation for assay development
- Assistance in assay implementation and validation
- Assistance in carrying out high-throughput screening of chemical libraries
- Provide compound libraries pre-plated, available for use in a 96- or 384-well format
- Provide training in the use of facility-maintained instrumentation
- Assistance with data analysis and compound selection

CHEMICAL LIBRARIES

ChemDiv 60K

ChemBridge 43K

ChemDiv 55K

- The three libraries consist of a total of 160,000 compounds obtained from ChemDiv and ChemBridge
- They are structurally diverse, pharmacophore-rich collections of drug-like small molecules
- Compounds generally obey Lipinski's "rule of five" and demonstrate good ADME (absorption, distribution, metabolism and excretion) profiles
- Purity of the compounds is typically greater than 90%

NCI01 and NCI02:

- The NCI01 library consists of 1,990 compounds selected from the NCI open collection of 140,000 compounds
- Compounds were selected based upon drug-likeness
- Library includes a challenge set of 57 compounds
- Novel structural types show unusual patterns of cell line sensitivity and resistance
- The NCI02 library consists of 879 compounds representing structural diversity

TYPE OF ASSAYS IMPLEMENTED

- In vitro enzymatic activity assay
- In vitro protein binding assay
- Cell proliferation assay
- Cell-based reporter gene assay

ASSAY DETECTION ABILITY

- Absorbance (ABS)
- Fluorescence Intensity (FI)
- Fluorescence Polarization (FP)
- Time-Resolved Fluorescence (TRF)
- Luminescence

DETECTION SPECTROMETERS



EnVision Plate Reader (Perkin Elmer)

Multifunctional filter based plate reader
Equipped with dual stackers
Equipped with dual detectors
Works independently to detect:

- Absorbance
- Fluorescence Intensity (FI)
- Time-Resolved fluorescence (TRF)
- Fluorescence polarization
- AlphaScreen™ technology
- Luminescence

Ultra 384

Multifunctional filter based plate reader
Works independently or integrated with Genesis Workstation.
Detects:

- Absorbance
- Fluorescence Intensity (FI)
- Time-Resolved fluorescence (TRF)
- Fluorescence polarization



SpectraMax Plus 384

- High performance absorbance plate reader
- Possesses a full spectral range of 190 - 1000nm
- Accommodates 96- and 384-well microplates



Victor Light

Microplate counter for luminescence
Equipped with stackers and dual injectors
Dedicated to detect:

- Flash luminescence
- Glow luminescence
- Dual luciferase assays
- Dual emission luminescence (such as BRET and BRET2)

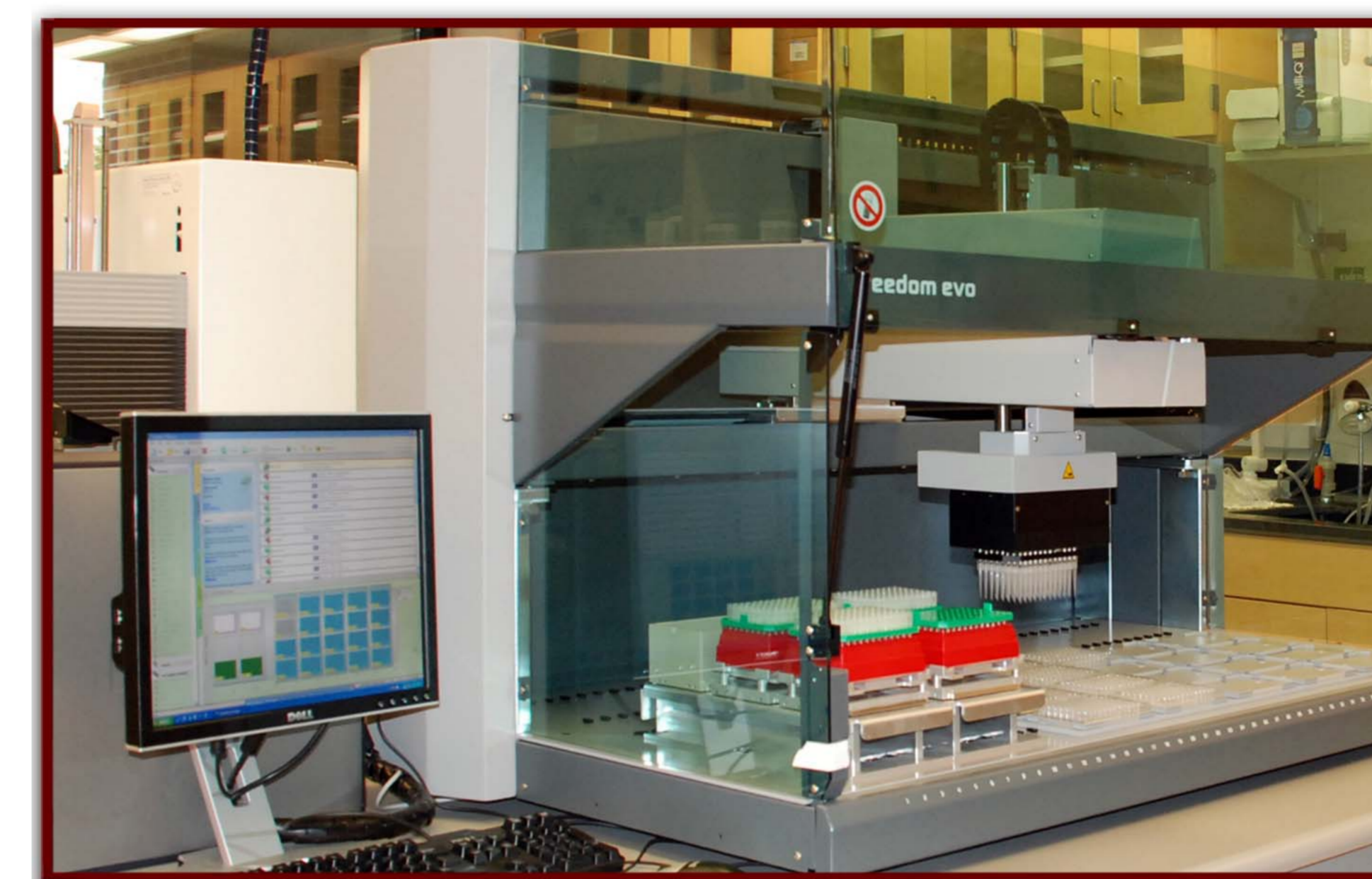


MAJOR EQUIPMENT

Freedom EVO 150 MCA (TECAN)

It is an automatic liquid handling platform and a flexible robotic workstation. It is currently equipped with an MCA robotic 96-channel pipetting head using disposable tips and 20 plate carrier and 6 service carrier, but it offers versatile configurations, including:

- Up to three liquid handling & robotic arm options.
- Choice of one or two high precision liquid handling arms that can each be equipped with one, two, four or eight washable or disposable pipetting tips
- 96- or 384- multi-channel pipetting head options.
- Freely configurable worktable that may include separation and detection devices, shakers and incubators in addition to standard labware carriers and is easily reconfigured for multiple applications or different users.
- Field upgradeability via additional options or, capacity extension via extensive storage options.

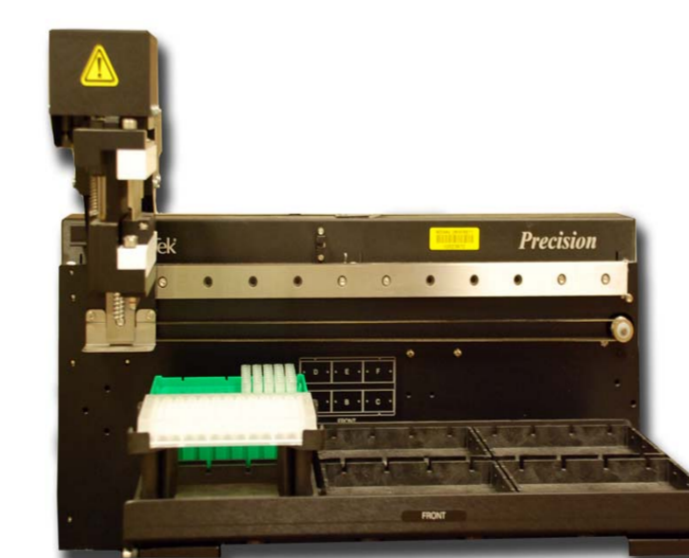


Genesis Workstation 150 (TECAN)

This is another automatic liquid handling workstation. It is equipped with three liquid handling and robotic arm options:

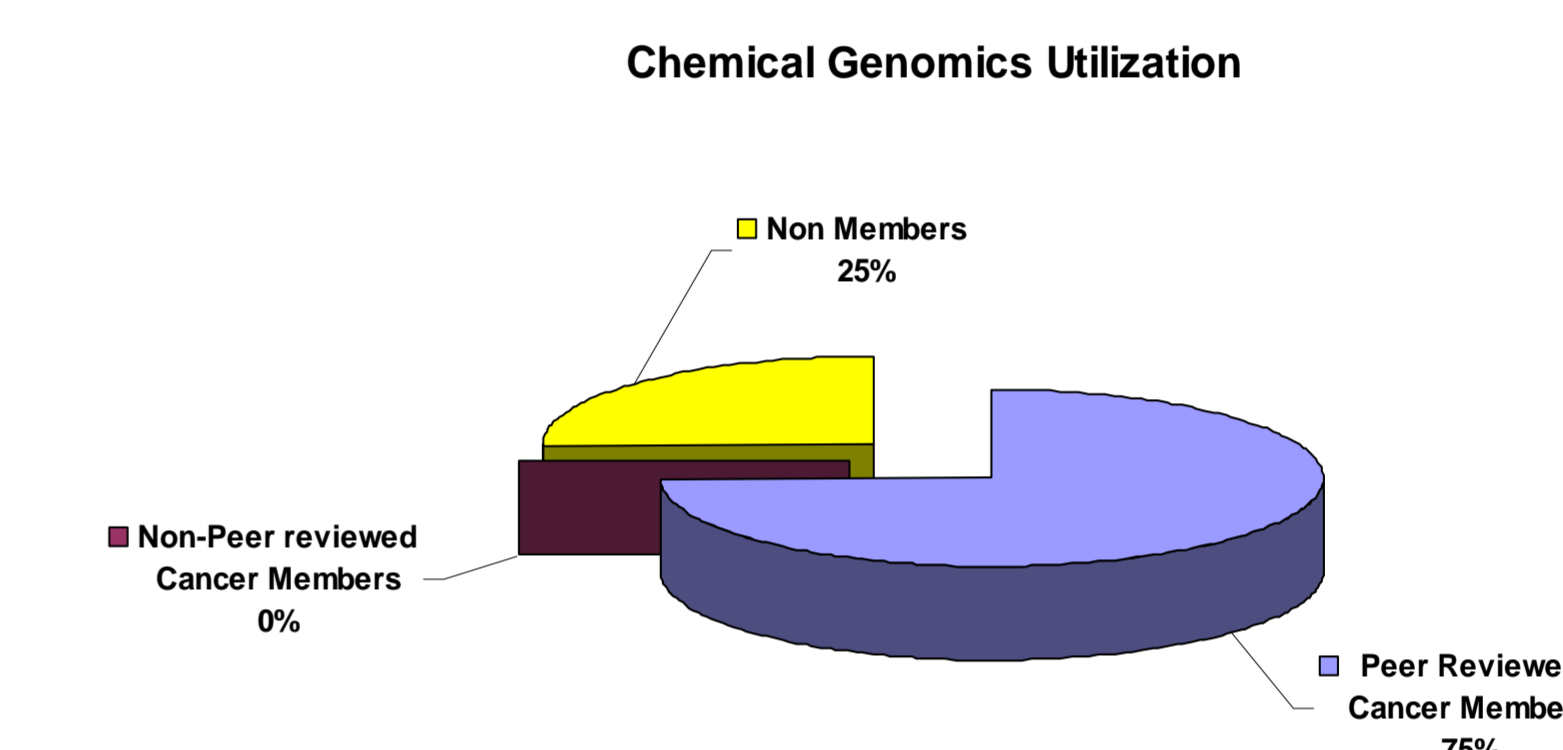
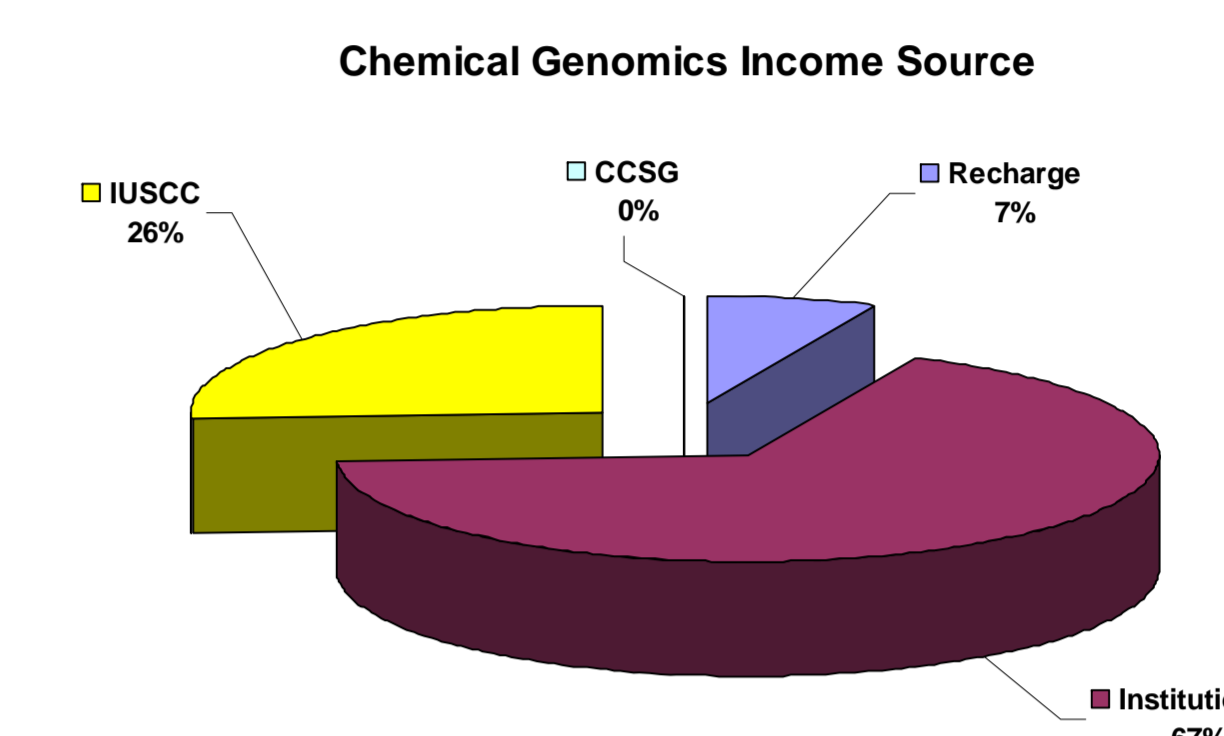
- LIHA: a liquid handling arm with eight washable pipetting tips that can reach any where on the station.
- TeMo: a 96-channel pipetting head that can use either fixed or disposable tips.
- ROMA: an arm with a 5-point rotational robotic gripper to move microplates between positions, devices, and storage.

- Precision**
- Automated 8-channel pipettor
 - Rapid Serial dilution function
 - Cherry picking applications
 - Accommodates 96- and 384-well microplates



Titertek Multidrop384

- Automated 8-channel pipettor
- Dispenses from 5 to 200 microliters
- Integrated with two Titan Microplate Stackers for automation
- Accommodates 96- and 384-well microplates



FUNDED RESEARCH PROJECTS UTILIZING OR LEVERAGING THE CGCF

Title	Investigators	Agency
Inhibition of s-nitrosoglutathione for the treatment of asthma (R21)	Pareesh Sanghani	NIH-NHLBI
APEs as novel drug targets in AIDs opportunist Toxoplasma (R21)	William Sullivan Millie Georgiadis Mark R. Kelley	NIH-AI
Chemosensitization of pancreatic tumors via inhibition of a DNA base excision repair enzyme, Ape 1 (R21)	Melisa Fishel Mark R. Kelley	NIH NCI
Antibacterial methionine aminopeptidase inhibitors	Qi-Zhuang Ye	NIH NIAID
Targeting PRL phosphatases for cancer therapy (R01)	Zhong-Yin Zhang	NIH NCI