



MELVIN AND BREN SIMON CANCER CENTER

INDIANA UNIVERSITY

CHEMICAL GENOMICS CORE FACILITY

Core Director Zhong-Yin Zhang, Ph.D.



OVERVIEW

The Chemical Genomics Core Facility (CGCF) is a new shared facility of the IU Simon Cancer Center and the IU School of Medicine. This facility has been in full operation since July 2006. 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 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

COMPOUND COLLECTIONS

- A total of 160,000 structurally diverse, pharmacophore-rich collections of drug-like small molecules obtained from ChemDiv and ChemBridge
- A diversity set of 1,990 compounds selected from the NCI open collection of 140,000 compounds
- A challenge set of 57 compounds from NCI exhibiting unusual cellular activity
- 879 compounds representing a broad-spectrum of structural diversity and growth inhibition of the NCI 60 cancer cell lines

TYPE OF ASSAYS IMPLEMENTED

- Enzyme activity-based assay
- Affinity-based binding assay
- Protein-DNA interaction assay
- Cell proliferation assay
- Cell-based reporter gene assay

ASSAY DETECTION ABILITY

- Absorbance
- Fluorescence Intensity
- Fluorescence Polarization
- Time-Resolved Fluorescence
- Luminescence

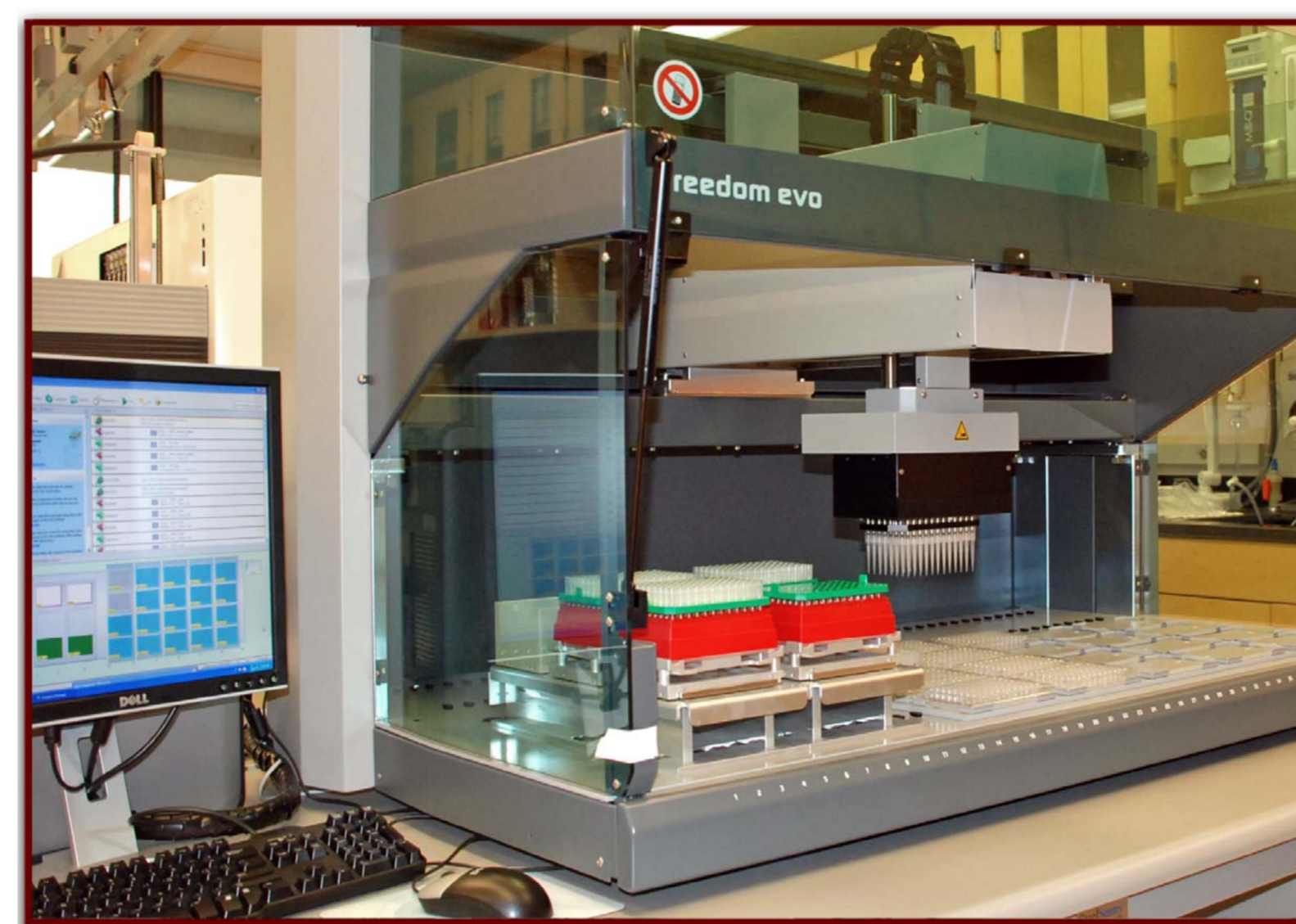
KEY PERSONNEL

- Lan Chen, Ph.D., Director of HTS
- Lily Wu, M.S., Facility Manager
- Andrea Gunawan, M.S., Research Analyst

FUTURE USERS

Johnny He (HIV), Tom Hurley (glycogen synthase), Mark Kelley (APE), Chao-Hung Lee (Caspase 9), Suk-hee Lee (Metnase), Samy Meroueh (uPAR), Claire Walczak (MCAK), Mu Wang (SOD1), Qizhuang Ye (DNA methyltransferase), Zhong-Yin Zhang (SHP2)

EQUIPMENT



Freedom EVO 150 MCA (Tecan)

An automatic liquid handling platform and a flexible robotic workstation. It is currently equipped with a robotic MultiChannel Arm (MCA), which is a 96-channel pipetting head. The MCA can also operate as an 8 or 12 channel head as desired, picking a column of 8 or a row of 12 tips to perform for example, in-plate serial dilution for IC50 assays. It works with various disposable and washable tips and can exchange them automatically during a run.

Genesis Workstation 150 (Tecan)

Another automatic liquid handling workstation, 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.

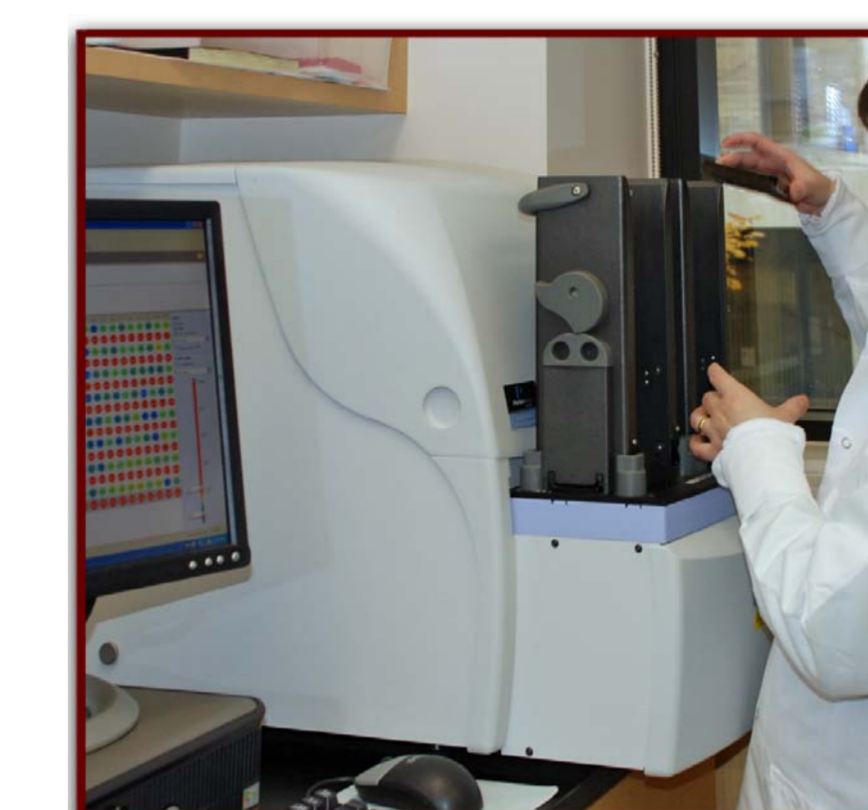


Precision™ Microplate Pipetting System (BioTek)

- Automated 8-channel pipettor
- Rapid Serial dilution function
- Cherry picking applications

Multidrop384 Dispensers/Titan Stackers (Titertek)

- Automated 8-channel pipettor
- Dispenses from 5 to 200 microliters
- Integrated with two Titan Microplate Stackers for automation



EnVision Multifunctional Plate Reader (PerkinElmer)

Filter based. Detects:

- Absorbance
- Fluorescence intensity
- Time-Resolved fluorescence
- Fluorescence polarization
- AlphaScreen™ technology
- Luminescence



Ultra384 Multifunctional Plate Reader (Tecan)

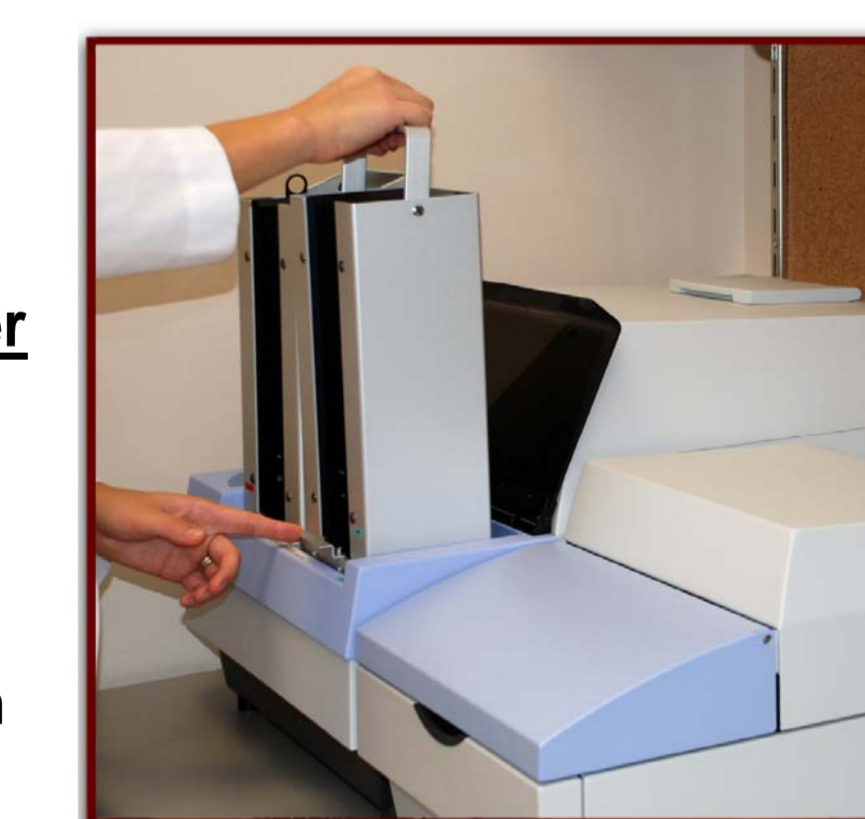
Filter based. Detects:

- Absorbance
- Fluorescence intensity
- Time-Resolved fluorescence
- Fluorescence polarization



SpectraMax384Plus Plate Reader (Molecular Device)

High performance absorbance plate reader. Possesses a full spectral range of 190 - 1000nm.



Victor Light luminescence counter (PerkinElmer)

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

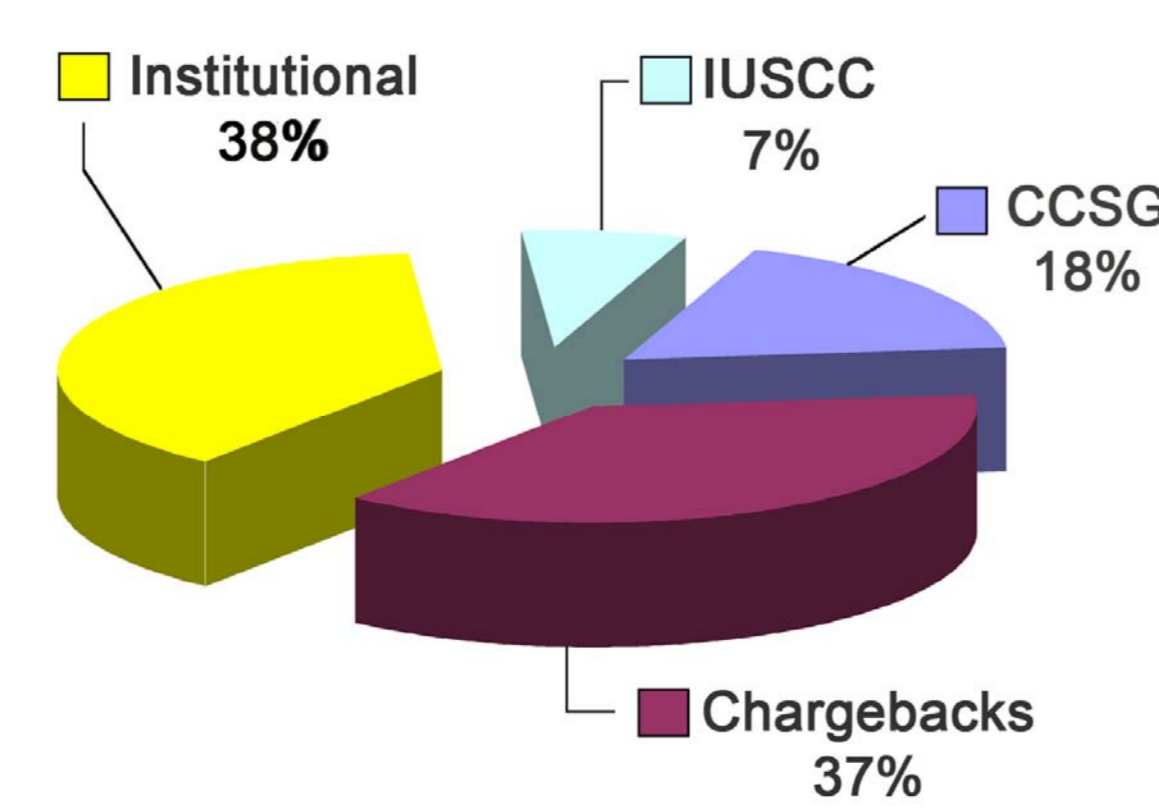
BenchCel Microplate Handling System (Velocity 11)

Features a high-speed plate shuttle that accesses four integrated microplate stacks with removable racks. Each rack can hold up to 70 standard microplates. A wide range of peripheral machines can also be integrated through BenchWorks.

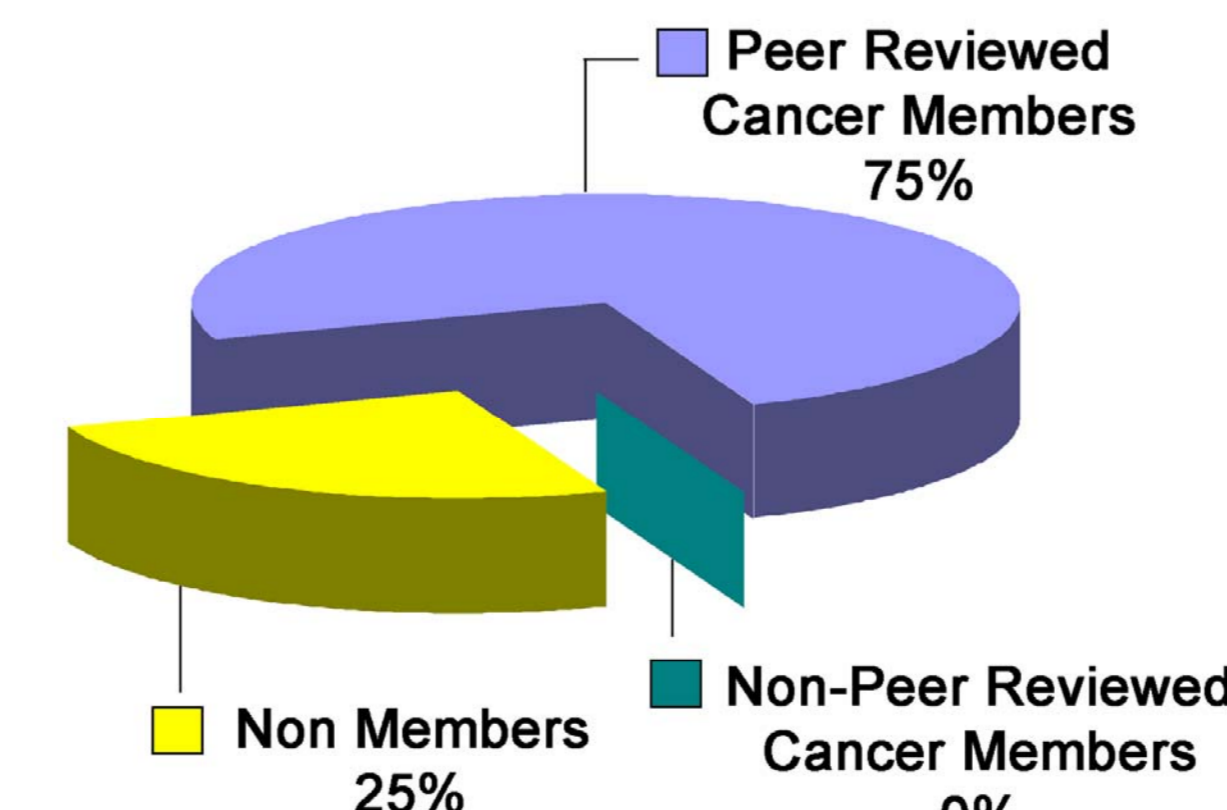
FUNDED RESEARCH PROJECTS UTILIZING OR LEVERAGING THE CGCF

Title	Investigators	Agency
Inhibition of s-nitrosoglutathione for the treatment of asthma (R21)	Paresh 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 (R01)	Qi-Zhuang Ye	NIH NIAID
Targeting PRL phosphatases for cancer therapy (R01)	Zhong-Yin Zhang	NIH NCI

CGCF Income Source



CGCF Utilization



FUTURE DIRECTION: MEDICINAL CHEMISTRY

In the near future, the CGCF will further develop its medicinal chemistry capabilities for targeted chemical synthesis. Currently, the core is equipped with three fume hoods as well as standard equipment required for organic synthesis. The CGCF will provide these facilities for targeted chemical synthesis. We envision that the medicinal chemistry component of the chemical genomics core facility will start with a Ph.D.-level chemist who will oversee the day-to-day operations of the synthetic activity. He/she will be assisted by two M.S./B.S. level chemists.

