

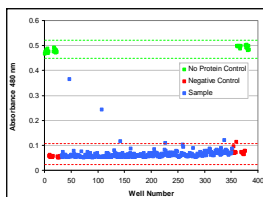
The Screening Process

- Discussion** Understanding your screening goals, we work with you to identify or suggest screening reagents compatible with our instruments.
- Manual optimization** We help you survey assay conditions, using multichannel pipetman, collecting signal and variability data in 384-well plates to quantify and improve assay performance.



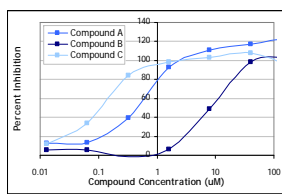
- Robotic method development** We transfer the robust manually-developed assay to a robotic method and test it.

- Pilot screen** Typically, researchers screen the bioactive collection (960 compounds) first.



- Larger screen** Robotic methods are adapted to handle stacks of plates, and the larger collection (20,000 compounds) is screened.

- Dose-response** Small molecule activity as a function of concentration is determined to confirm the primary screen and rank order compounds by potency. Analogs, or compounds sharing chemical features of screen hits, can also be tested.



The Center is located on the 7th floor of Kline Biology Tower in **KBT 724**. It houses equipment for mammalian tissue culture, liquid handling and compound storage, in addition to standard laboratory equipment.

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The facility was established with a grant from the university, which was used to purchase compound libraries and state-of-the-art instruments. Laboratories performing screens bear costs for reagents and consumables required for their assays, in addition to user-fees for the screens.

<http://cgp.yale.edu/index.htm>

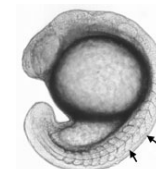
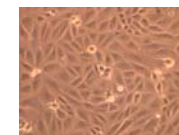
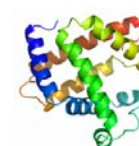
Yale University Center for Chemical Genomics



The Center for Chemical Genomics is available for use by Yale researchers to conduct biochemical and cell-based high throughput screens (HTS) to identify small molecules that modify the activities of biological systems of interest.

In the Center, Yale researchers have performed a variety of assays to discover small molecules with specific activities for targets, cells or organisms including:

- enzymatic inhibitors
- inhibitors of protein-protein interactions
- modifiers of protein polymerization states
- inducers and promoters of gene expression
- toxic responses
- developmental modifiers in model organisms



Liquid Handling

The Center houses several liquid handling instruments.



The **Multidrop** is a simple-to-use liquid dispenser for 96- and 384-well plates. In the tissue culture hood, it performs sterile transfers of suspended cells and media

to screening plates for cell-based assays.

The **Aquarius** is the main screening liquid handler. It can transfer reagents from reservoirs or deep 96-well plates into stacks of 384-well assay plates using disposable tips. Compound transfers using steel pins are performed here. It can also be used to create 384-well plates from 96-well stocks.



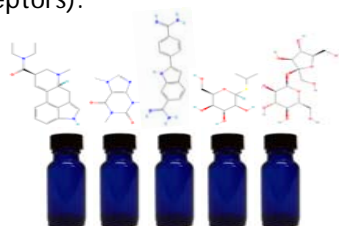
The **EVO** has fixed-tips, ideal for serial dilutions, dose-response or creating plates from samples in Eppendorf tubes. A robotic arm can

move plates around the deck and to components such as the plate washer, plate shaker, incubator and plate reader.

Compound Libraries

The **MicroSource Gen-Plus** collection is a set of 960 compounds with known bioactivity, including medicines currently in use, arrayed in three 384-well plates. It is an excellent library for pilot screening because only small amounts of reagents are required. In many cases, compounds identified are known effectors of the assay.

The **Maybridge Diversity** collection is a set of 20,000 compounds arrayed in 63 384-well plates. It is a chemically diverse library, that has been filtered for those chemical properties consistent with oral availability (small size, numbers of hydrogen bond donors and acceptors).

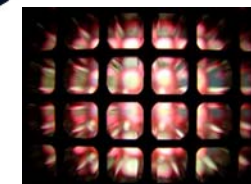
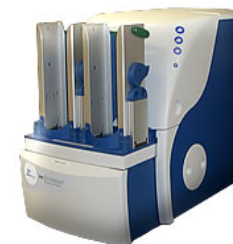


The **Yale Compound Repository** is a collection of compounds synthesized by Yale chemists. We are actively building this collection and would be happy to include your compounds. We need mg quantities of each compound, and the structure in ChemDraw format. These compounds are available, free of charge, for use in screens by the Yale community.

Coming soon... a **natural product** collection derived from extracts isolated from rainforest plants and the endophytes that live within them.

Plate Reading

The **Envision** plate reader is a filter-based instrument that can quantify signals from colorimetric, fluorescent intensity, fluorescent polarization, FRET, time-resolved fluorescent and luminescent assays. It is extremely sensitive and therefore ideal for reading 384-well plates with assay volumes ~20 uL.



Filters with the following spectral properties (in nm) are available:

<u>Center Wavelength</u>	<u>Bandwidth</u>
330	75
355	40
380	10
405	8
430	8
450	10
480	30
486	10
535	25
570	100
579	25
595	60
615	8.5
620	10
665	7.5