The NIH Chemical Genomics Center

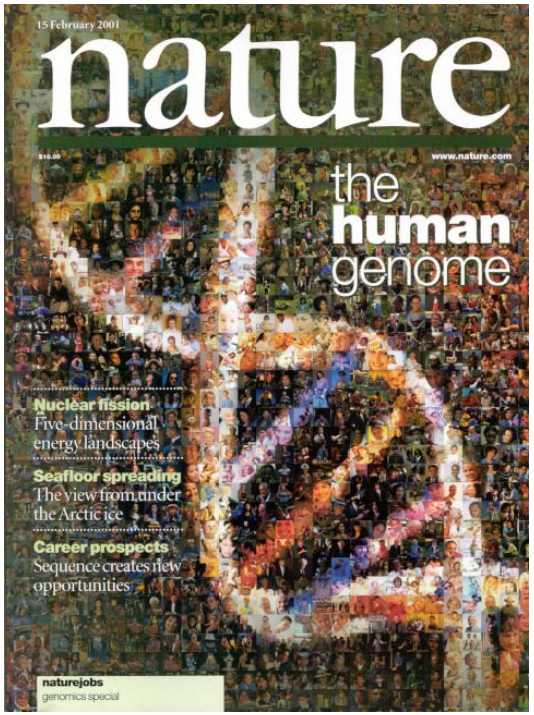
Bringing Biopharmaceutical Technologies to Academic Chemical Biology and Drug Discovery

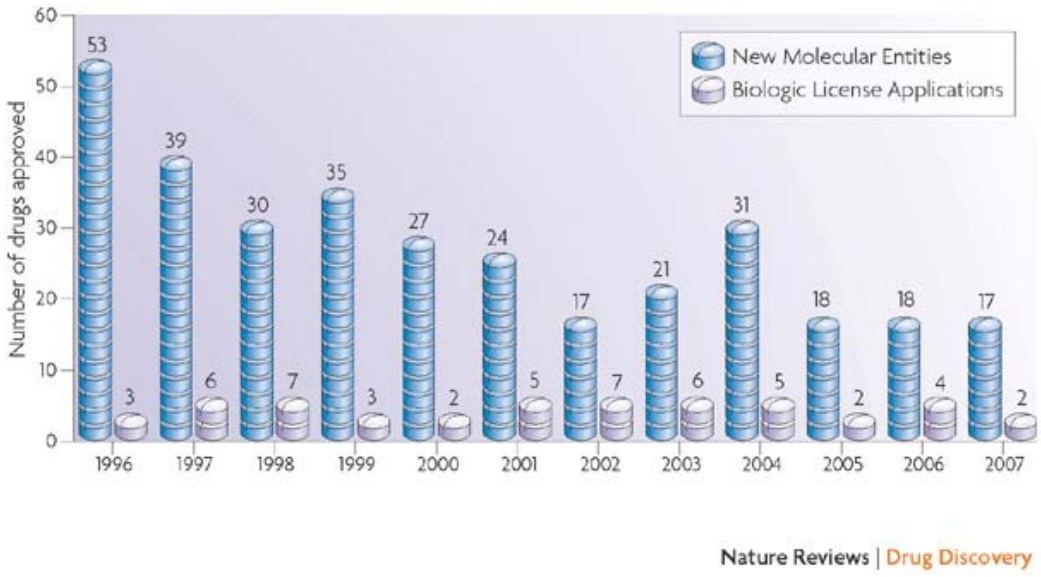
Christopher P. Austin, M.D.
Director, NIH Chemical Genomics Center
National Institutes of Health

Visit of UK House of Lords
4 June 2008

NIH Chemical Genomics Center

The best of times, the worst of times

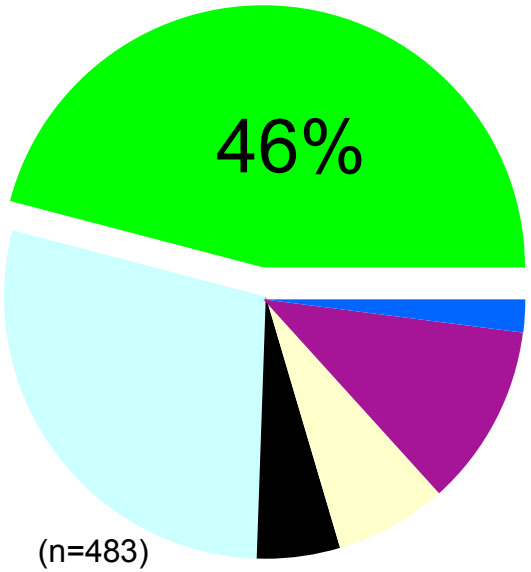




How to translate the genome into biological insights and therapeutics?

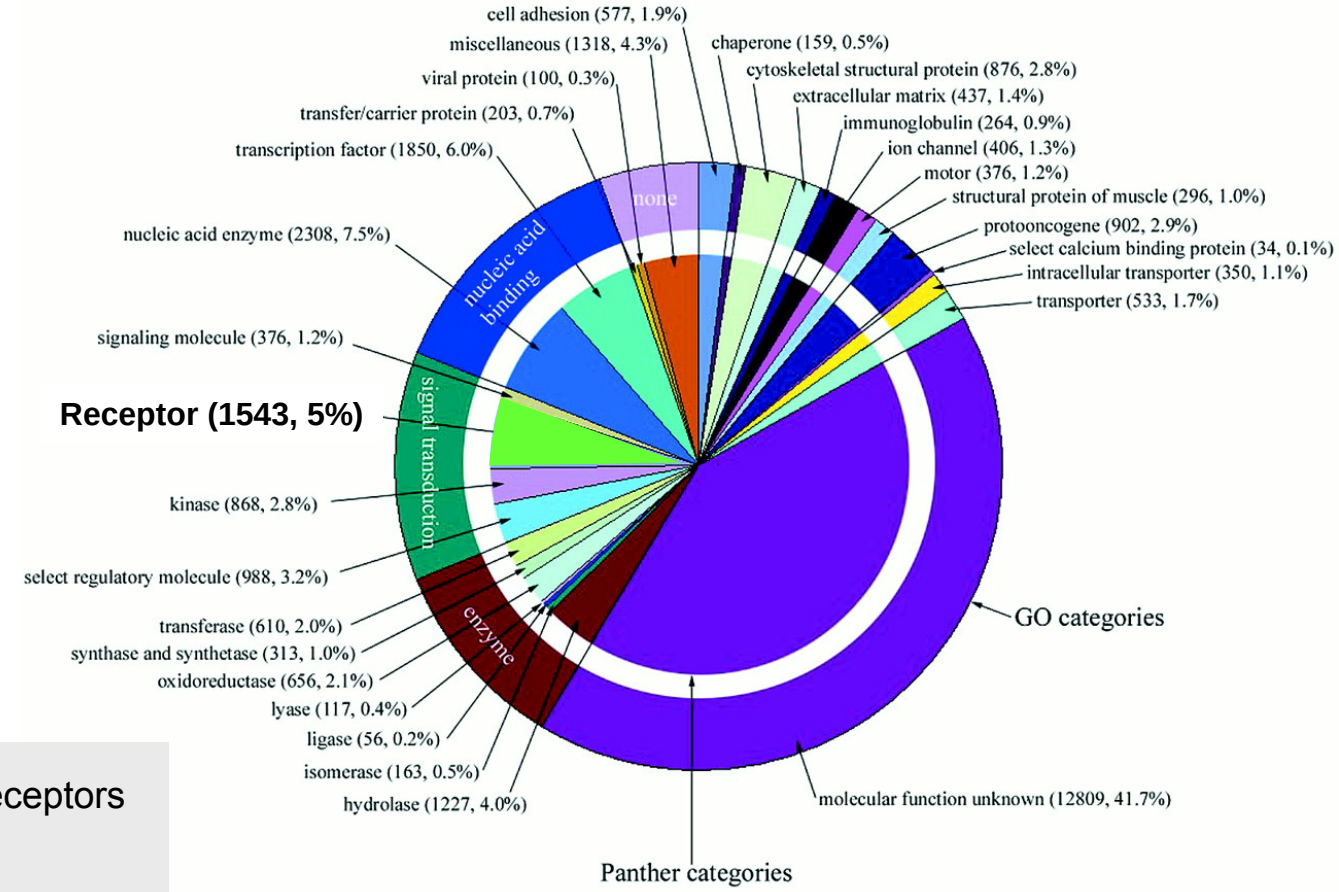
The “Non-Druggable” Genome Problem

Drug Target Classes



GPCRs
Enzymes
Ion Channels
Nuclear Receptors
Other
Unknown

Human Genome



Drews, J. (2000) *Science* **287**:1962

Venter et al., (2001) *Science* **291**:1304

NIH Roadmap ACCELERATING MEDICAL DISCOVERY TO IMPROVE HEALTH

Home Page

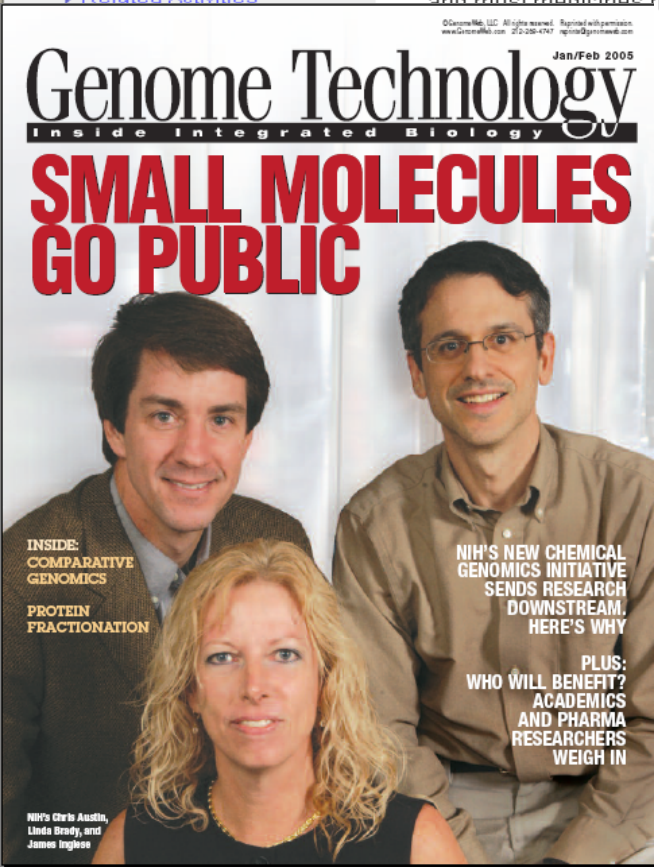
Molecular Libraries and Imaging

- Overview
- Implementation Group Members
- Funding Opportunities
- Funded Research
- Related Activities

Molecular Libraries and Imaging

OVERVIEW

Small molecules, often with molecular weights of 500 or below, have proven to be extremely important to researchers to explore function at the molecular, cellular, and in vivo level. Such molecules have also been proven to be valuable for treating diseases, and most medicines marketed today are from this class.



"…To empower the research community to use small molecule compounds in their research, whether as tools to perturb genes and pathways, or as starting points to the development of new therapeutics for human disease."

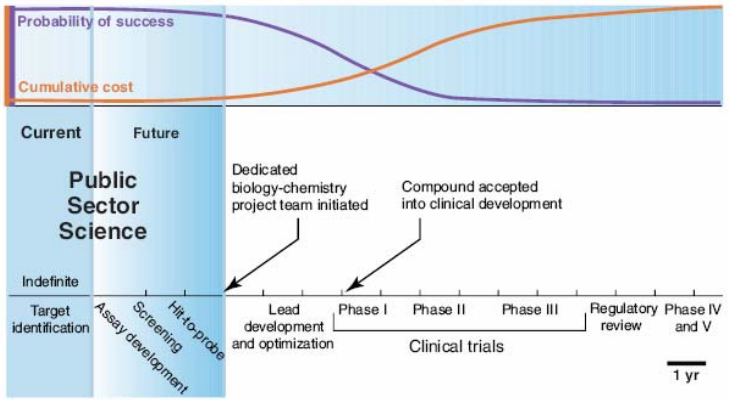
POLICY FORUM

MOLECULAR BIOLOGY

NIH Molecular Libraries Initiative

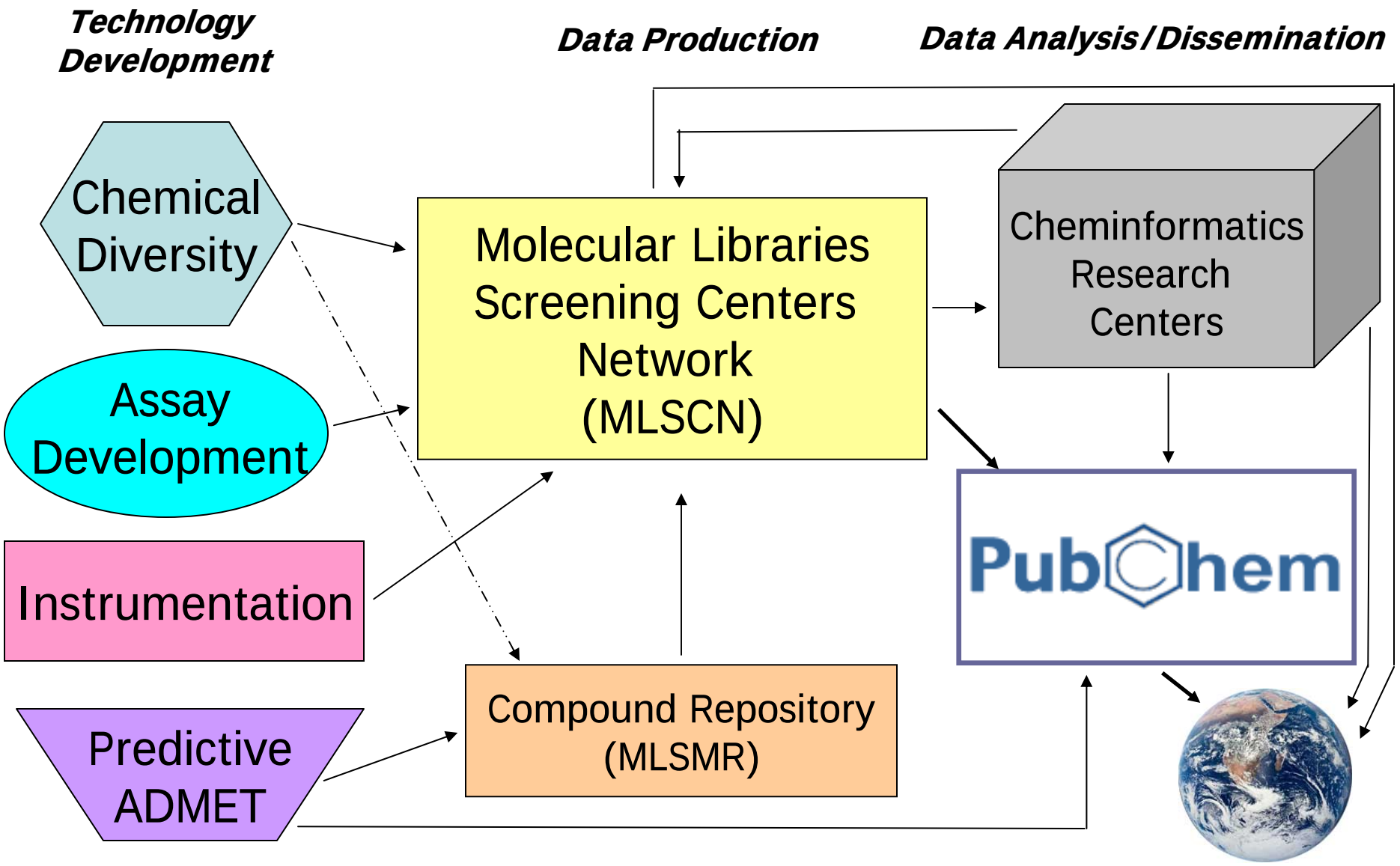
Christopher P. Austin,[1*] Linda S. Brady,[2] Thomas R. Insel,[2] and Francis S. Collins[1]

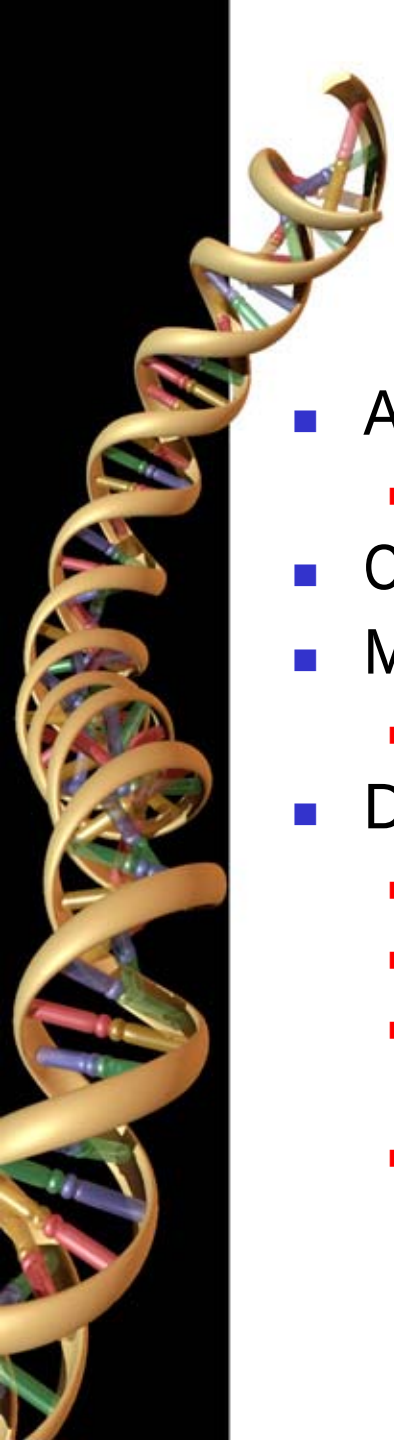
12 NOVEMBER 2004 VOL 306 SCIENCE www.sciencemag.org



Interface of the MLI and drug development.

The Molecular Libraries Roadmap: An Integrated Initiative

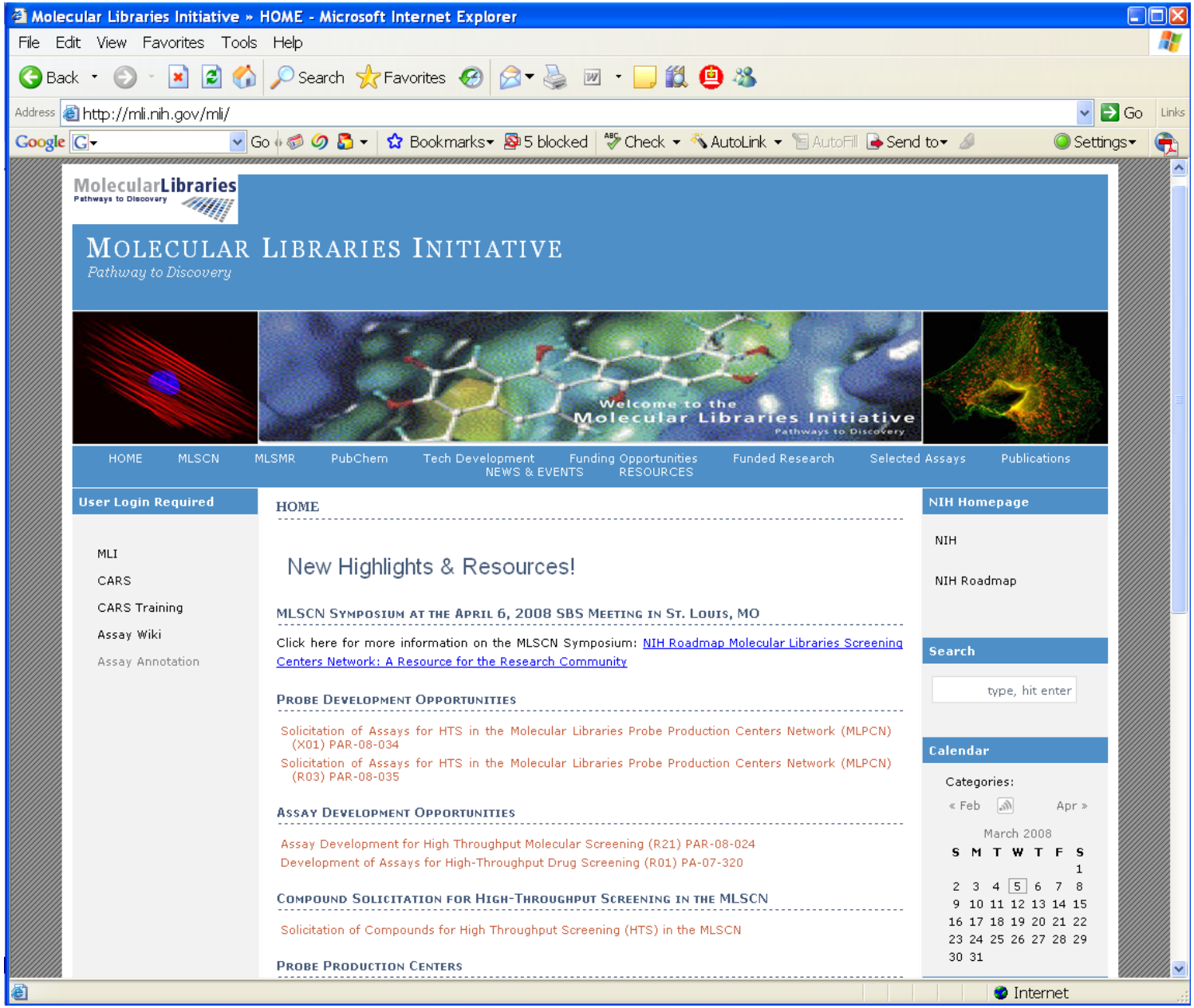




Unique features of the MLSCN

- All Centers screen same compound collection
  - Allows comparison of compounds' activities in many assays
- Capability to screen very wide variety of assay types
- Medicinal chemistry to transform hits into probes
  - Chemical probes of gene, pathway, and cell functions
- Data are released without restriction
  - *PubChem*: Screening data
  - *Probe reports*: activity, SAR, purity, compound source data
  - Enabling for all researchers to use probes and compute on the data
  - Sharing is catalytic to the transformation of data into information

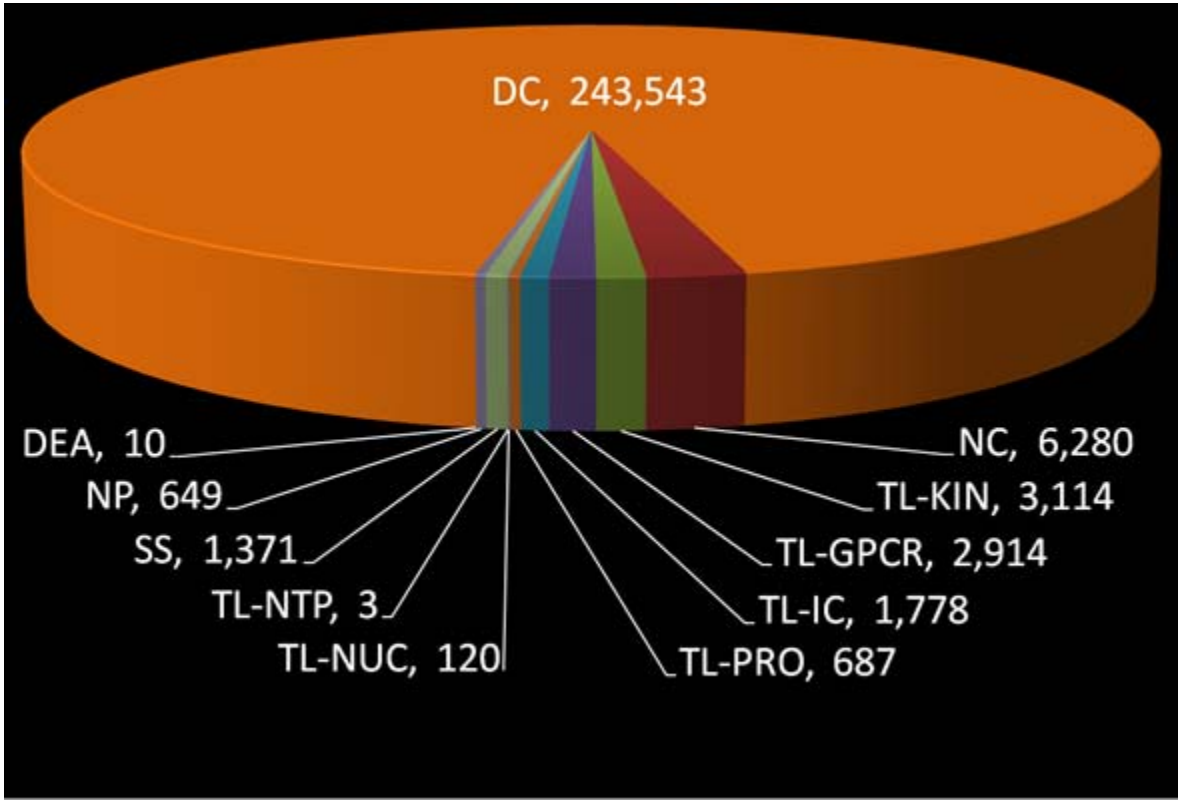
http://mli.nih.gov



MLSMR Compound Collection
(260,000 Compounds)

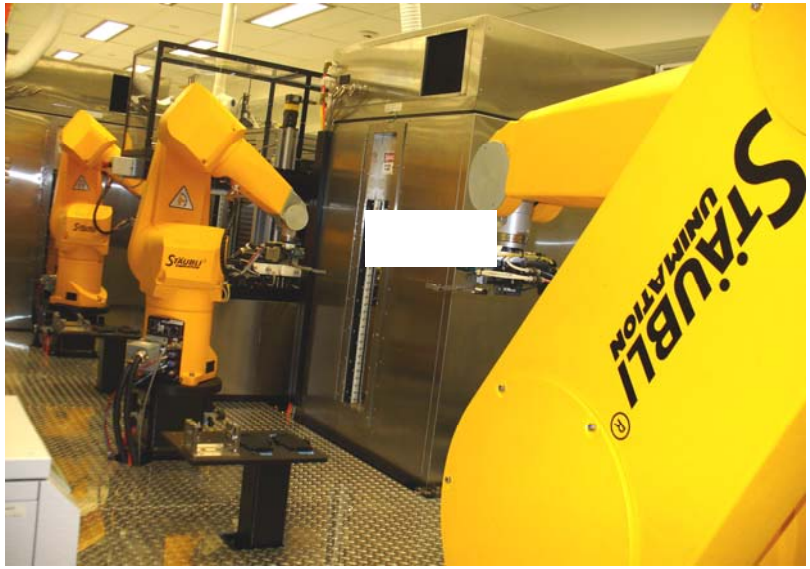
DC = Diversity Compounds
NC = Non-commercial
TL-KIN = Kinase Targeted Library
TL-GPCR = GPCR Targeted Library
TL-IC = Ion Channel Targeted Library

TL-PRO = Protease Targeted Library
TL-NUC = Nuclear Receptor Targeted
TL-NTP = National Toxicology Program
SS = Known Bioactives
NP = Natural Products
DEA = DEA Controlled Substances



NIH Chemical Genomics Center

- Founded 2004
- 54 scientists – biologists, chemists, informaticians, engineers
- Collaborates with >100 investigators worldwide
  - 60% NIH extramural
  - 25% NIH intramural
  - 15% Foundations, Research Consortia
- Focus on novel targets, rare and orphan diseases
  - Equal number of projects for basic research chemical probes and starting points for disease drug development

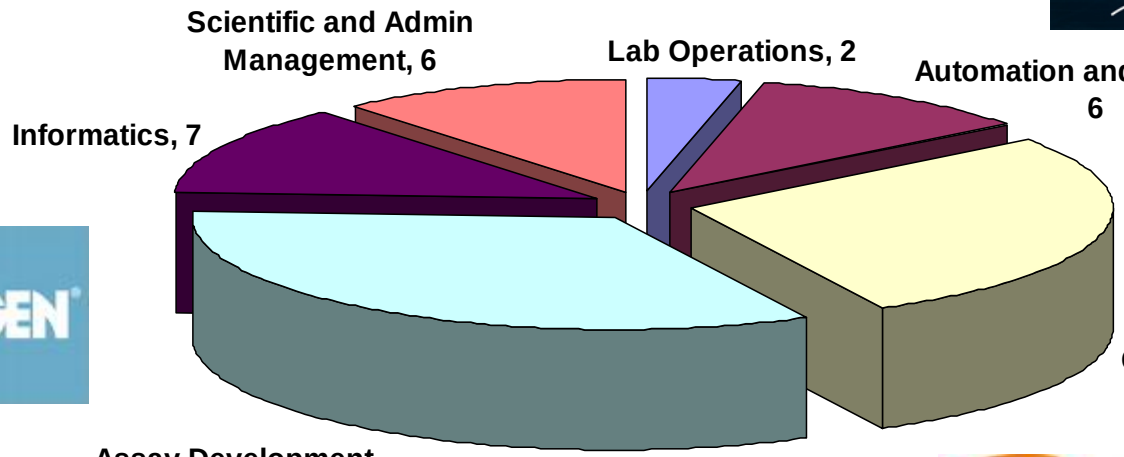


NIH Chemical Genomics Center: Founding Principles

- Bring the best of the **technologies, equipment, experience, and people** from pharma and biotech, and apply them to the 95% of the genome and 95% of human diseases not worked on by biopharma
- **Scale** must be equal to or greater than a pharma
- **Automate** everything
  - Cheaper, faster, more accurate
  - Allows recruitment and retention of finest scientists
- **Collaborate** extremely widely
- Produce **chemical probes of demonstrated biological utility**
  - Requires major Medicinal Chemistry presence

NCGC
NIH Chemical Genomics Center

NCGC Staff May 2008



Amphora

CELERA
an Applera Corporation Business

Pfizer

HGS

LARGE SCALE BIOLOGY

NORTHROP GRUMMAN
DEFINING THE FUTURE

AMGEN

ArQule

Johnson & Johnson

gsk GlaxoSmithKline

Caliper LifeSciences

MERCK

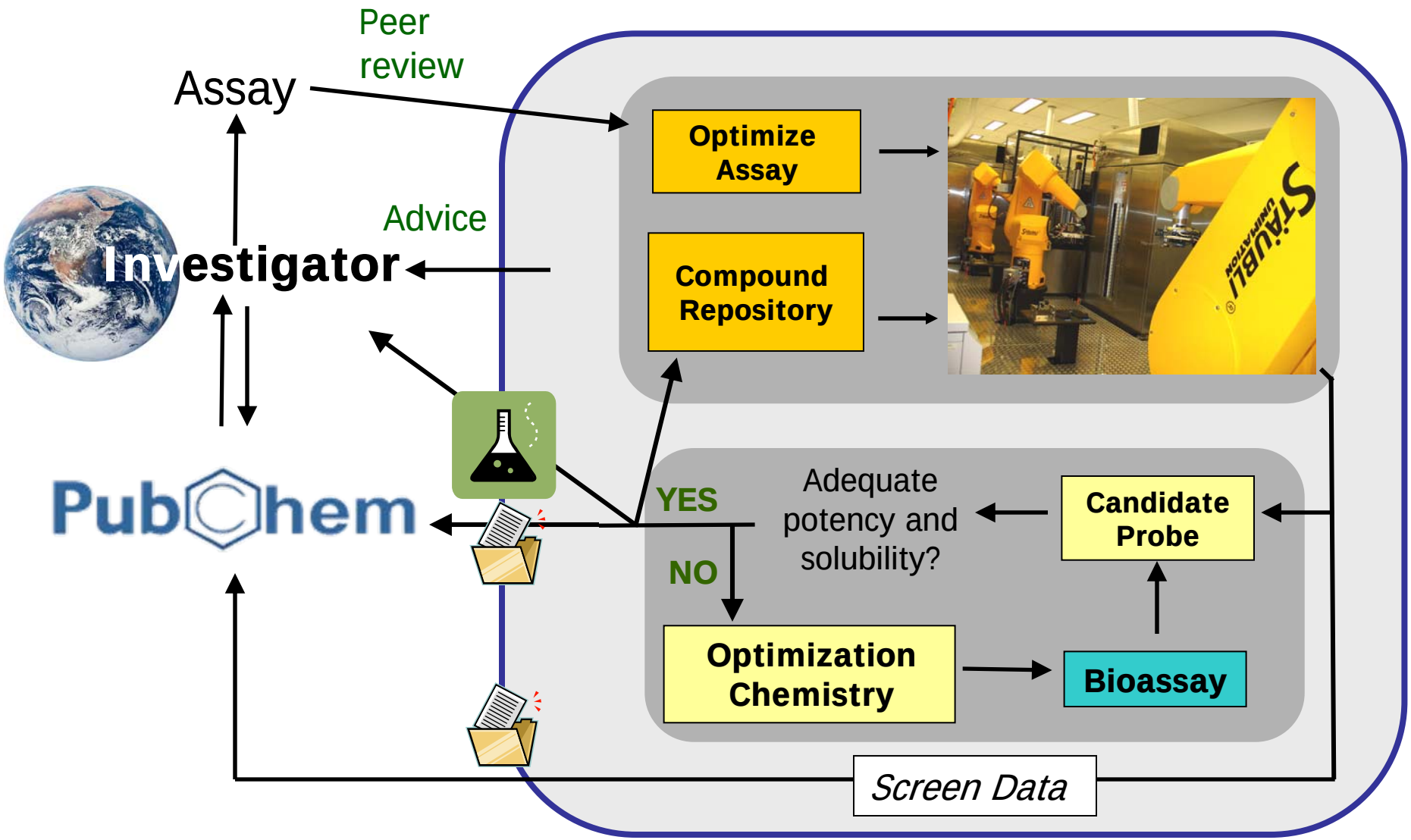
Pharmacopeia

BD
BD Biosciences

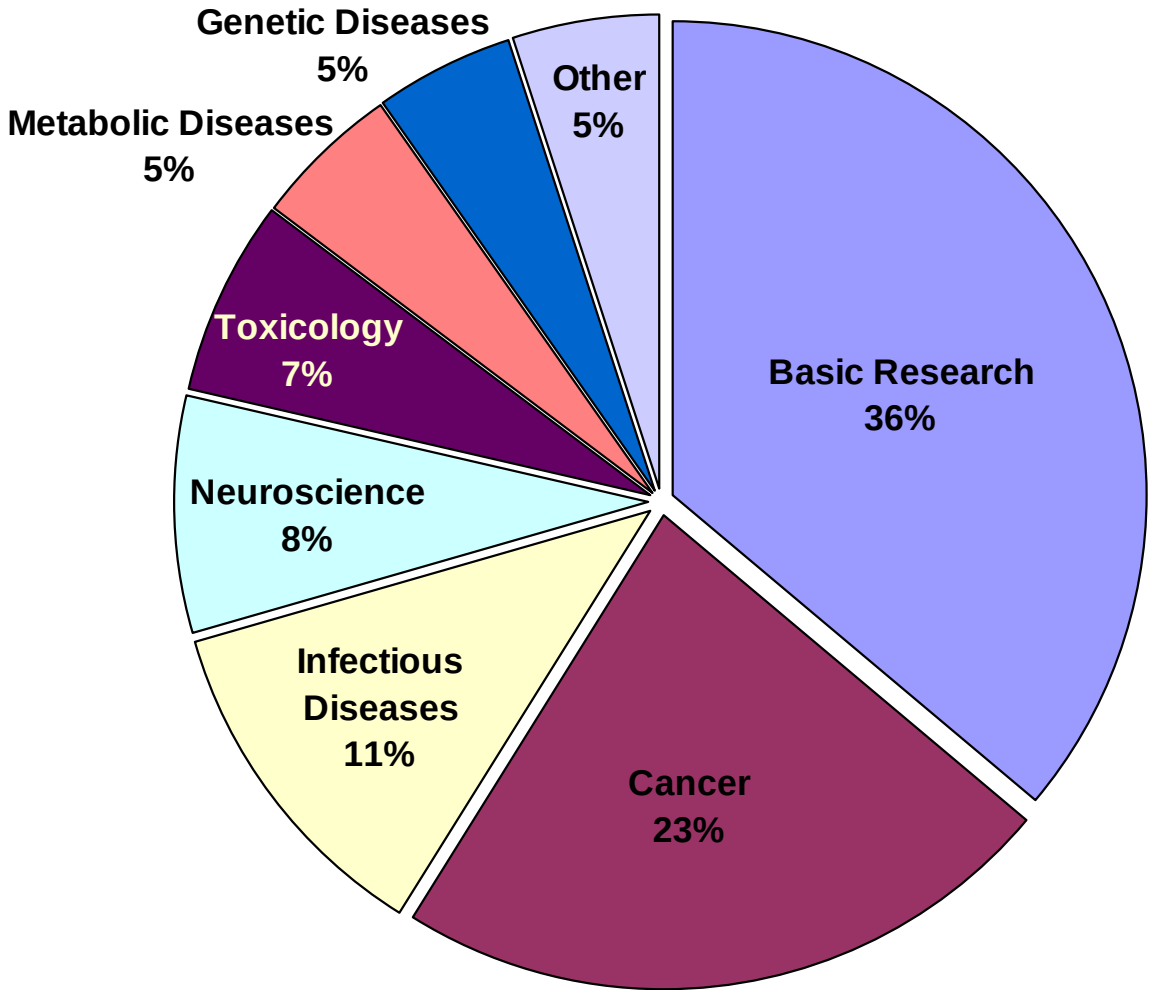
NCGC
NIH Chemical Genomics Center

NIH Chemical Genomics Center

NCGC Operation



Disease areas of NCGC projects 2005-2007



NIH Chemical Genomics Center

Establishing a paradigm for chemical genomics

For each assay, **efficiently** and **comprehensively** describe the biological activity of a chemical library

1. Direct us toward chemical series:
   - suitable probes
   - probe potential
     - ❖ SAR for probe optimization

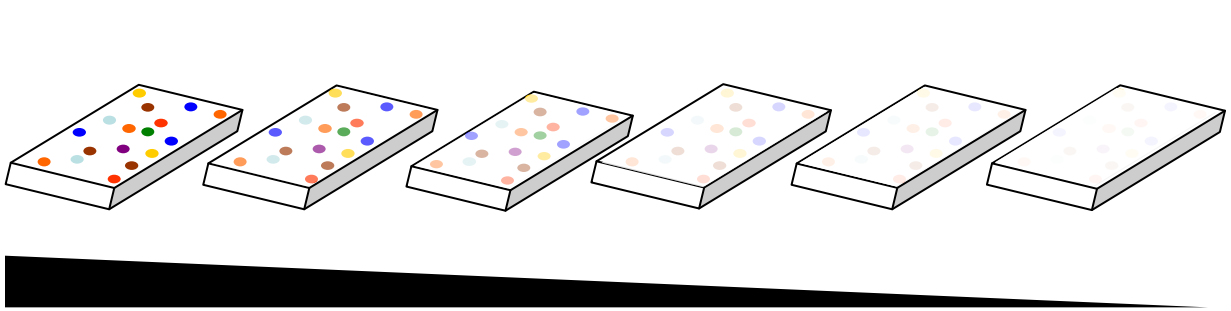
2. Populating a “Chemical Genomics” database
   - reliable activity of all library members

   for all assays that are screened at NCGC
   - → useful for profiling actives against all subsequent assays

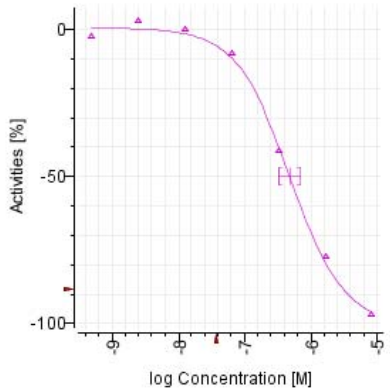
NIH Chemical Genomics Center

Quantitative high-throughput screening (qHTS)

- Conventional HTS: done at one concentration (typically 10 uM)
- qHTS: All compounds tested in titration
  - 15 concentrations
  - Concentration range 0.5 nM to 92 uM
  - Concentration-response curve generated for each compound
- Assay volumes ~5 uL
- 1536-well plate format
- Informatics pipeline for data processing, curve fitting & classification
- Higher quality data



Compound concentration



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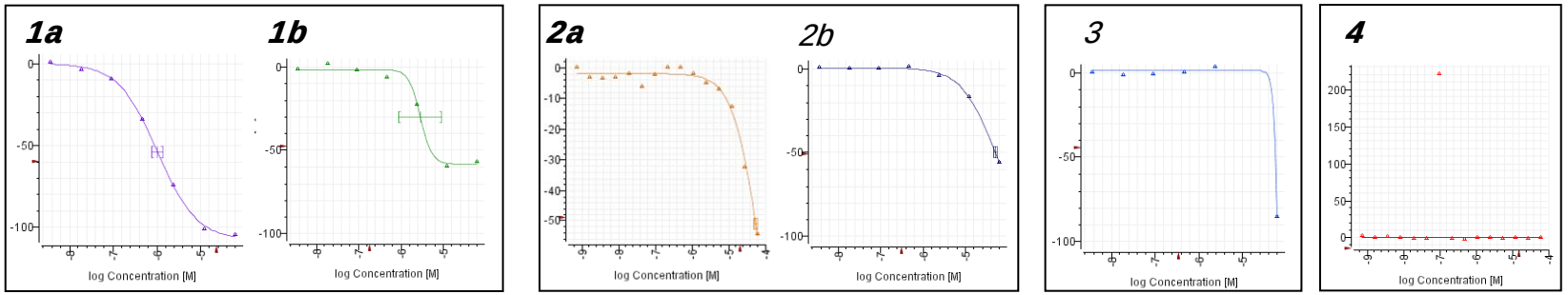
qHTS curve classification criteria

Curve Class	Description	Efficacy	r^2	Asymptotes	Inflection
1*	Complete curve (a) Partial curve (b)	> 80% (a) ≤ 80% (b)	≥ 0.9	2	yes
2†	Incomplete curve	> 80% (a) < 80% (b)	> 0.9 (a) < 0.9 (b)	1	yes
3	Single pt activity	> Min‡	NA	1	no
4	Inactive	NA	NA	0	no

NOTES: *AC_{50} derived from data; †AC_{50} extrapolated from data; ‡Min is > 3 SD from the mean activity of the sample field at the highest tested concentration

Examples

Lower confidence data



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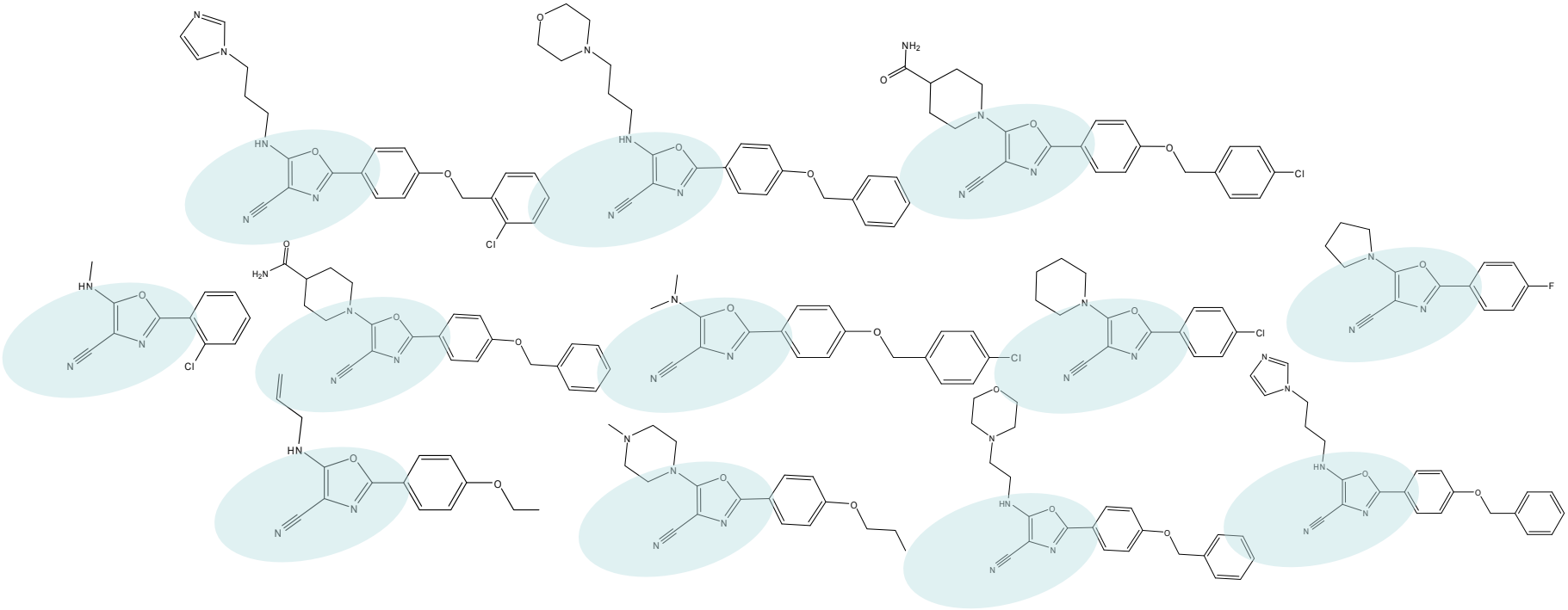
Derivation of nascent SAR from qHTS

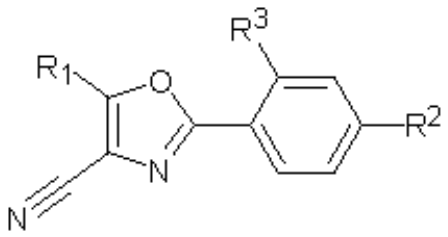
- Class 1 and 2a – Hierarchical clustering
  - Leadscope fingerprints
  - Tanimoto cutoff = 0.7
    - 55 clusters
- Maximal common substructure (MCS) extracted for each cluster
  - MCS used to search entire screening collection
    - 40 series composed of 4-25 active analogs
  - Results associated with biological data

Classes 1a, b and 2 ►12 cpds

Cluster 5, 2-phenyloxazole-4-carbonitrile



MCS



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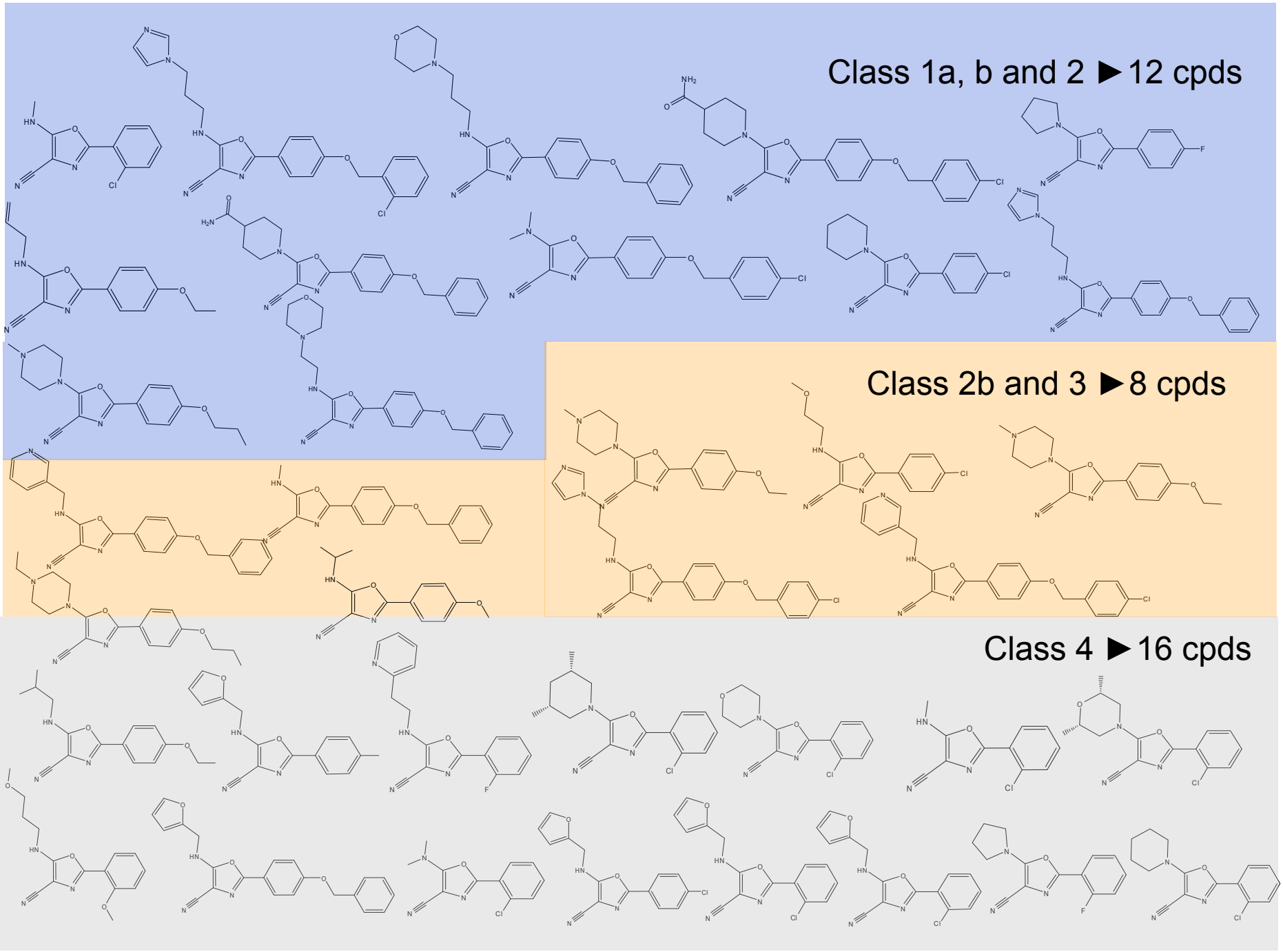
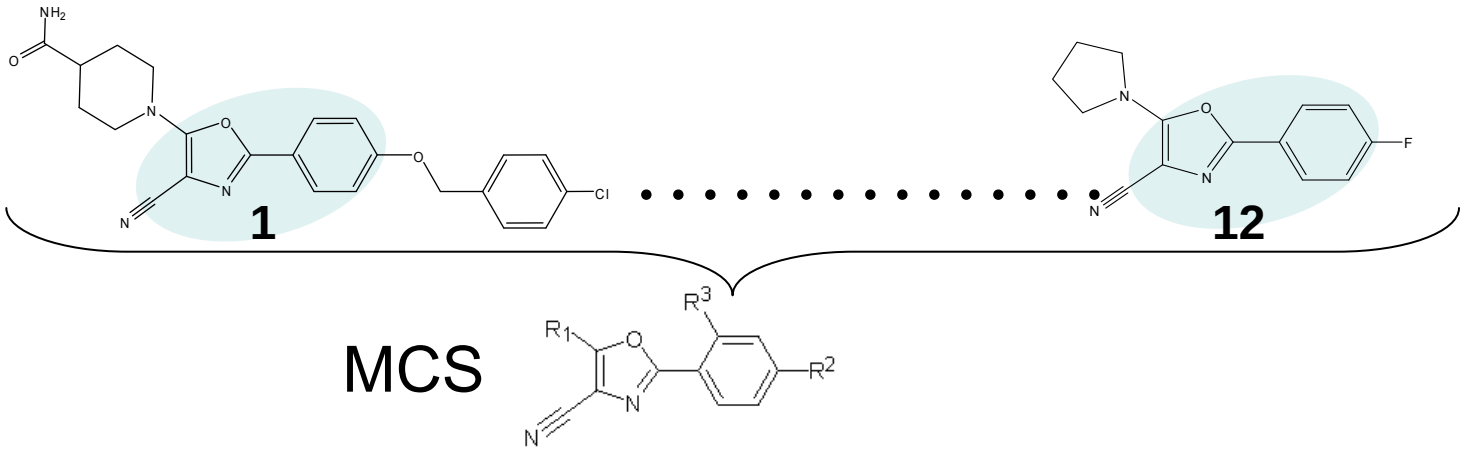
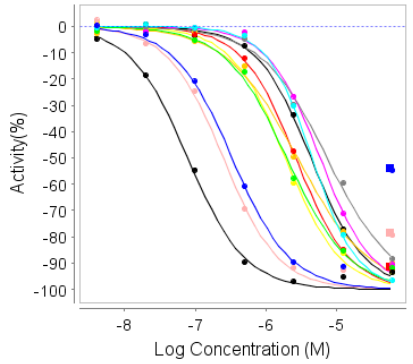
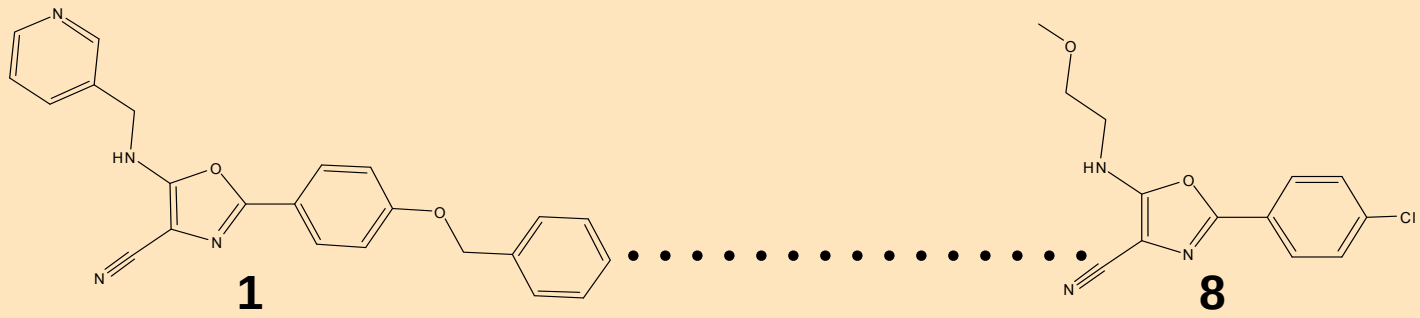
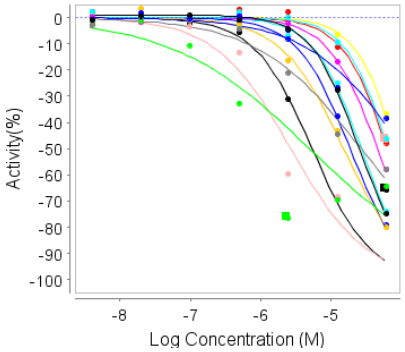

Class 1a, b and 2 ►12 cpds
Class 2b and 3 ►8 cpds
Class 4 ►16 cpds

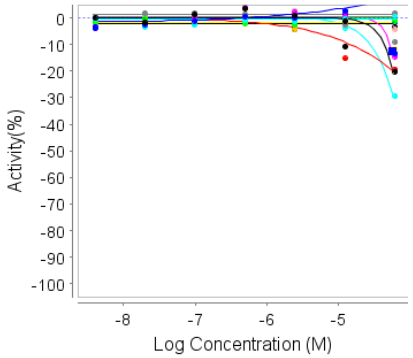
Classes 1a, b and 2 ►12 cpds, Cluster 5



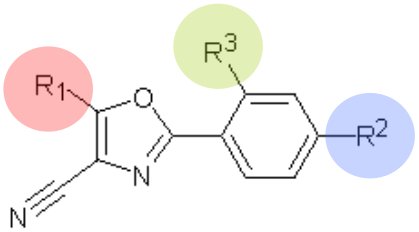






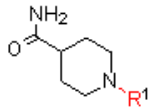
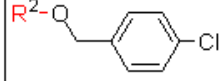
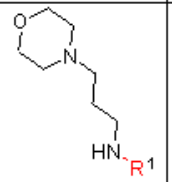
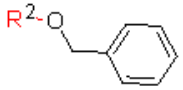
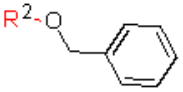
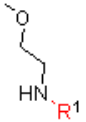
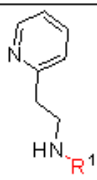
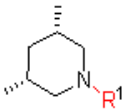


Structure-Activity Relationship (SAR) Report



2-phenyloxazole-4-carbonitrile series

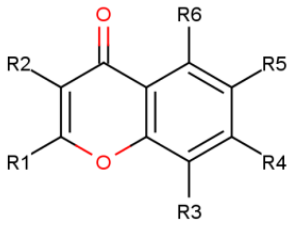
- The SAR report is a ‘map’ to enabling chemical optimization of a lead series

#	R1	R2	R3	NCGC ID	Curve Class	Rank	AC50 (uM)	Act Max Conc	hill Coeff
1			H	NCGC00067413-01	1.1	1/20	0.08	-92	1.1
2			H	NCGC00067270-01	1.1	5/20	1.9	-93	1.1
10			H	NCGC00067494-01	2.1	12/20	4.5	-96	1.4
21		F	H	NCGC00023889-01	3	20/20	42	-32	1.6
30		H	F	NCGC00039456-01	4		inactive	1	
39		H	Cl	NCGC00052762-01	4		inactive	1	

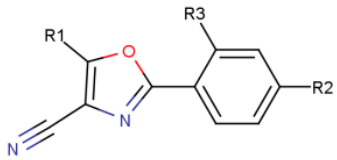
Electronic counterscreens across >100 assays

Active Chemical Series For Kinase Assay

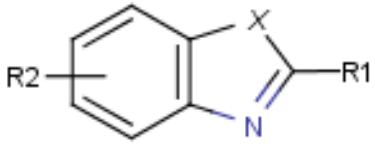
Series 1



Series 2



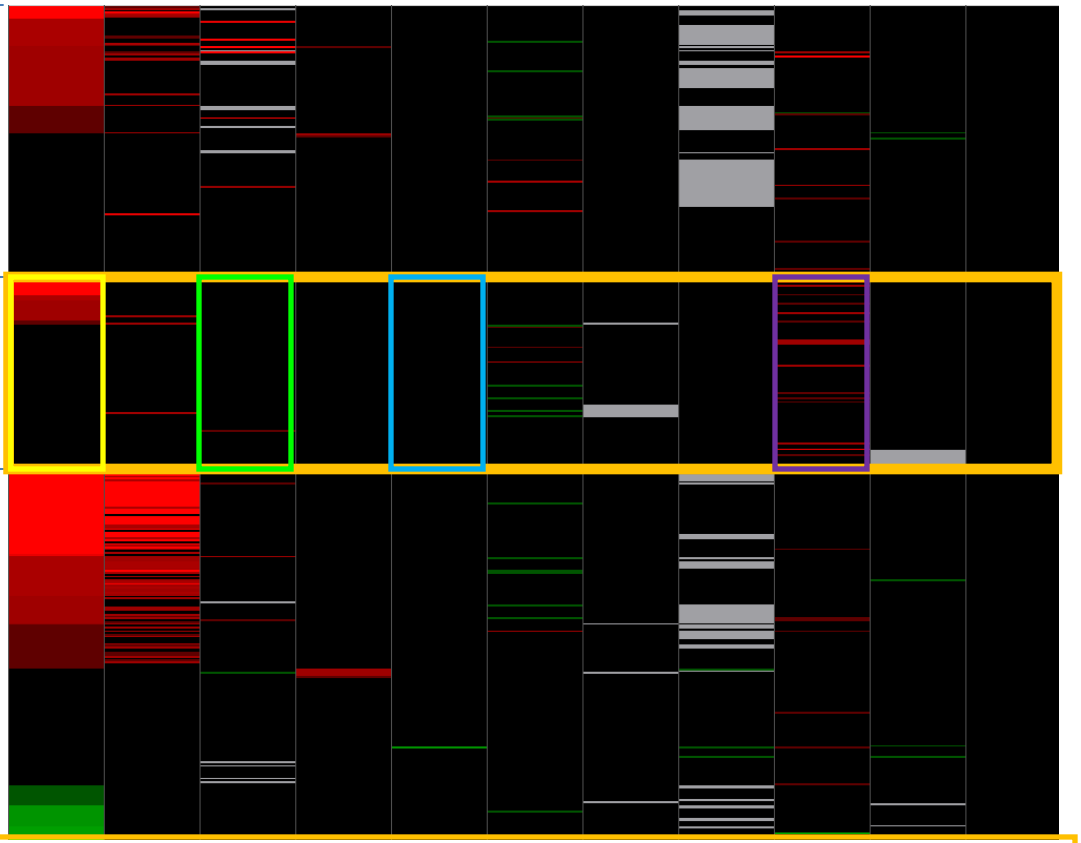
Series 3

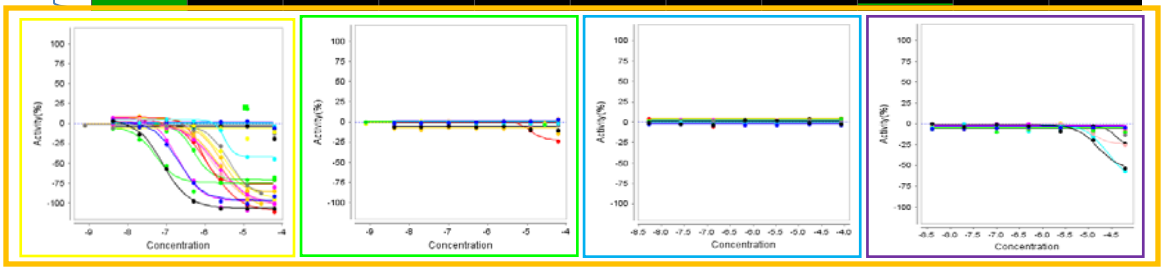


X = [O, S, or N]

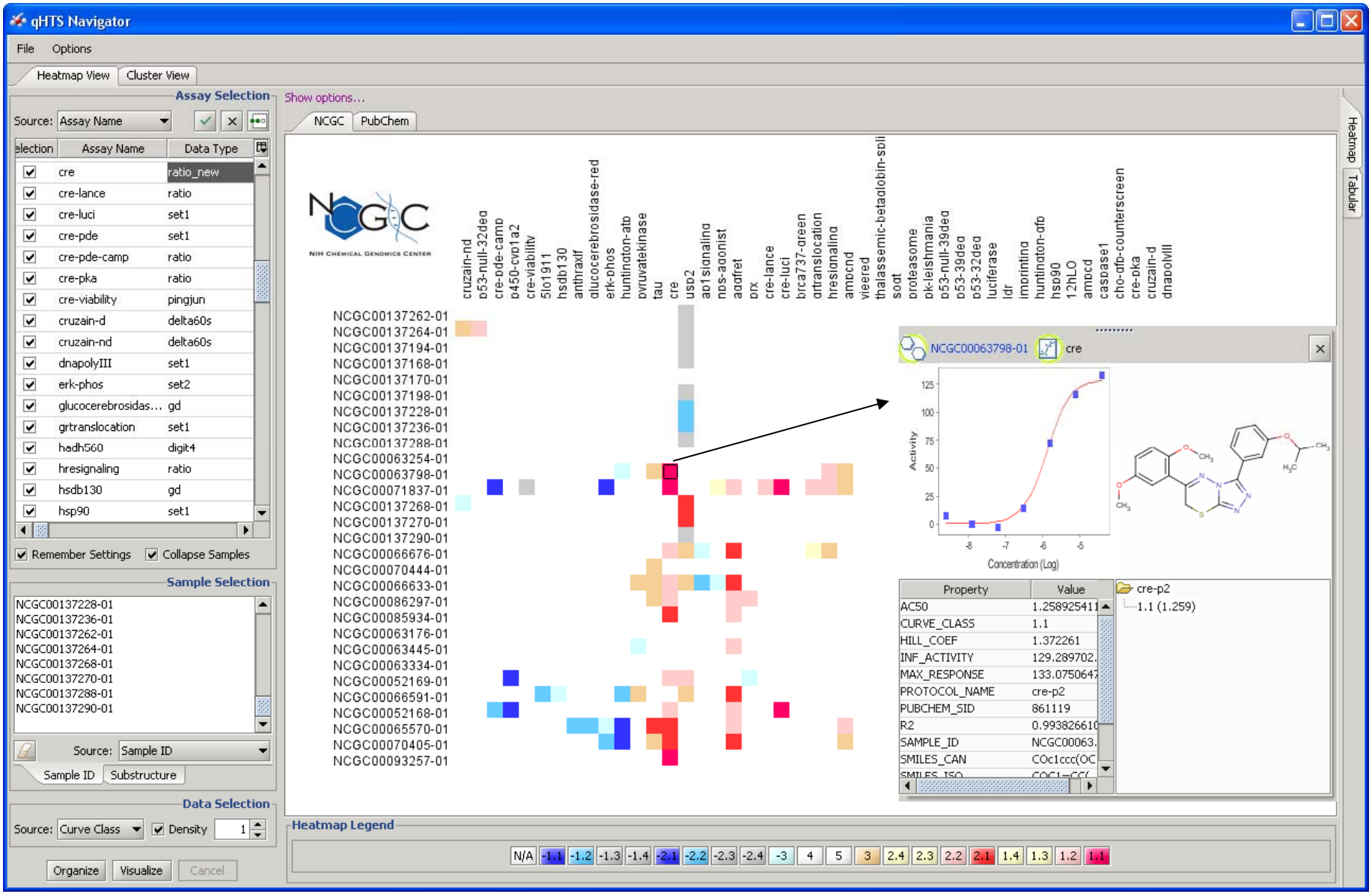
~300,000

Pk | Luc | Pol III | sOGT | YjeE | Prx2 | Prot | β-Thal | Hsp90 | LDR | AmpC | >100



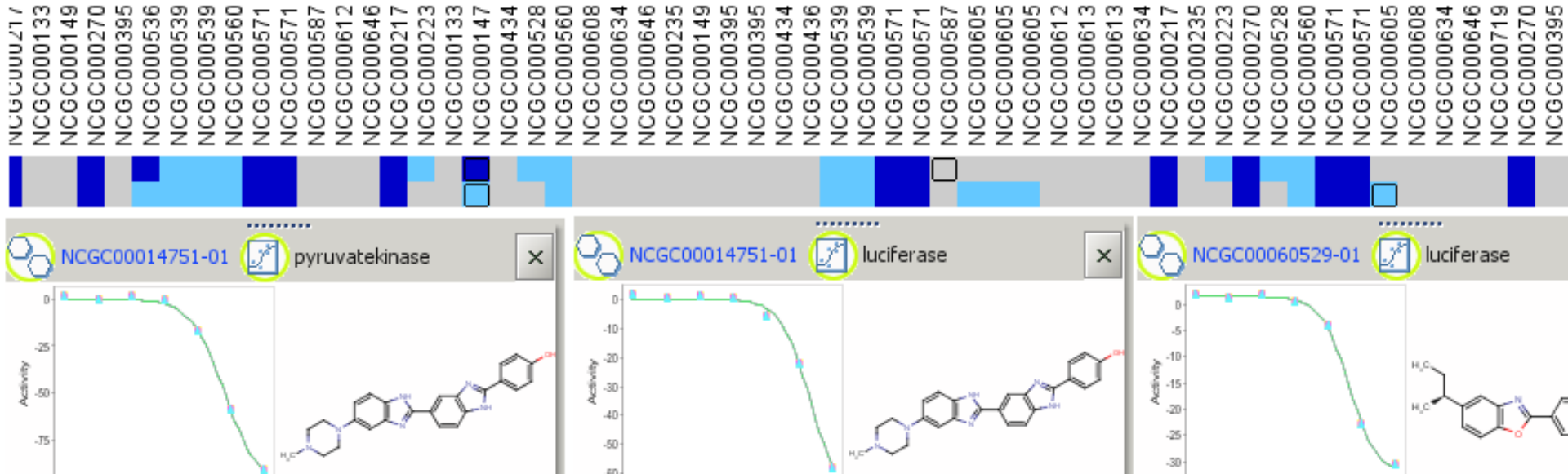


NCGC Chemical Genomics Browser



NCGC Stats

- 174 Assays deposited in PubChem (since Feb05)
- Wells tested: 42.5 million
  - Number of data points: 302 million
- Concentration-response (CR) profiles: 4.4 million
  - Data fields deposited into PubChem: >40M
- 32 probe projects / 34 probes/33 publications
- Screening throughput 2.5 million wells/wk



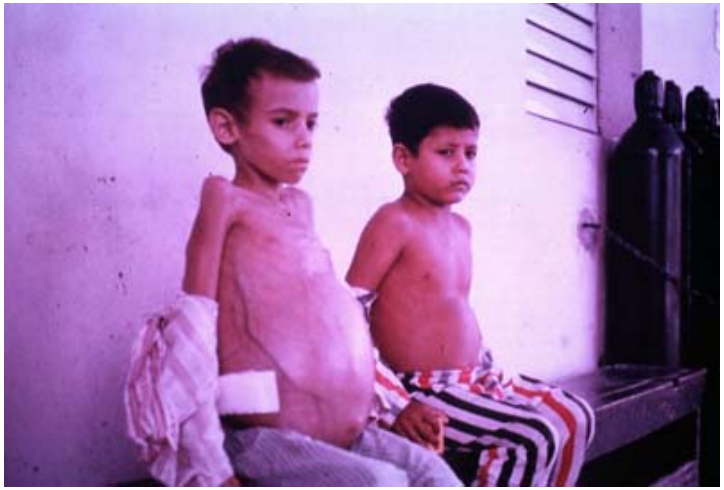
Case Study: Development of Inhibitors of *Schistosoma mansoni* Peroxiredoxins

NCGC Collaboration with
David Williams
Department of Biological Sciences
Illinois State University, Normal, IL

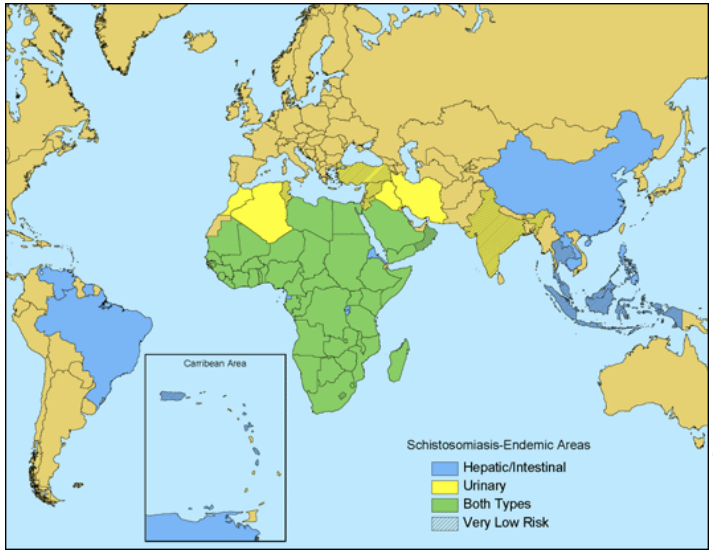
ILLINOIS STATE UNIVERSITY

NIH CHEMICAL GENOMICS CENTER

Schistosomiasis



- 250,000,000 infections
- 20,000,000 with significant pathology
- 280,000 deaths/year



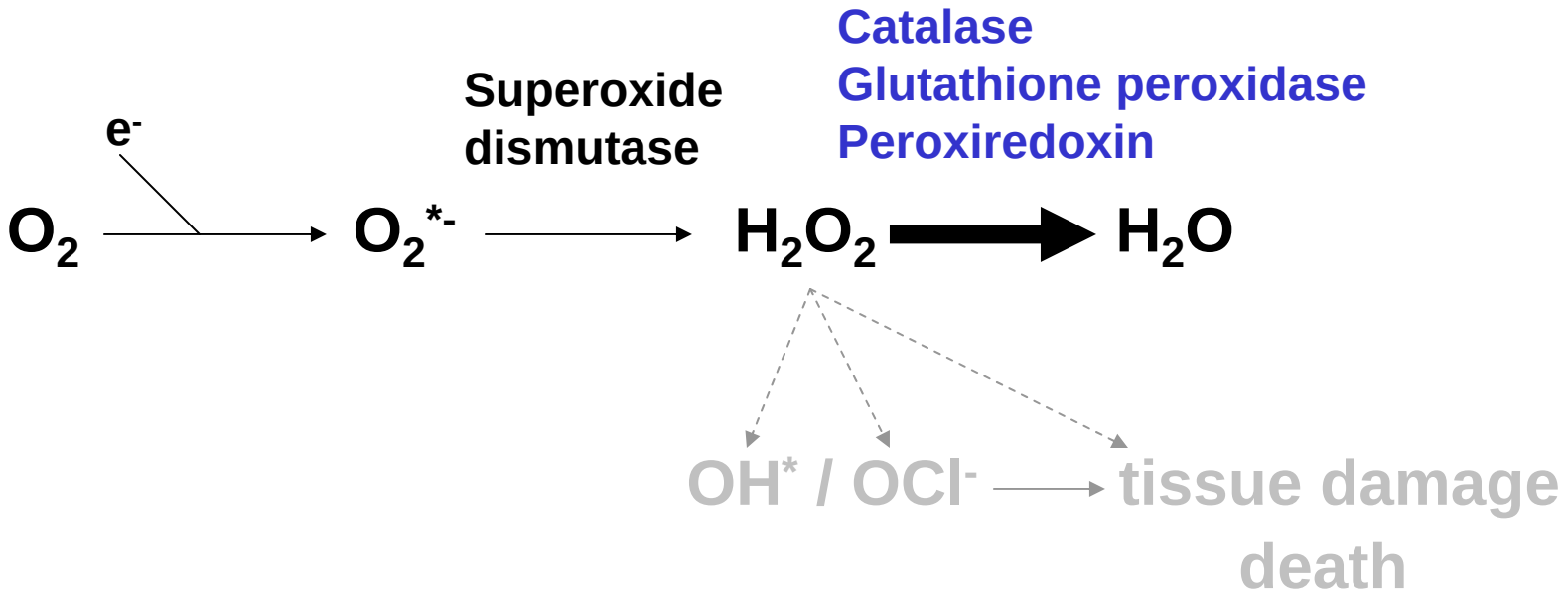
CDC©

- Major cause of morbidity
- Endemic in 75 countries
- > 80% infections in sub-Saharan Africa

NIH Chemical Genomics Center

Targeted Redox Pathway

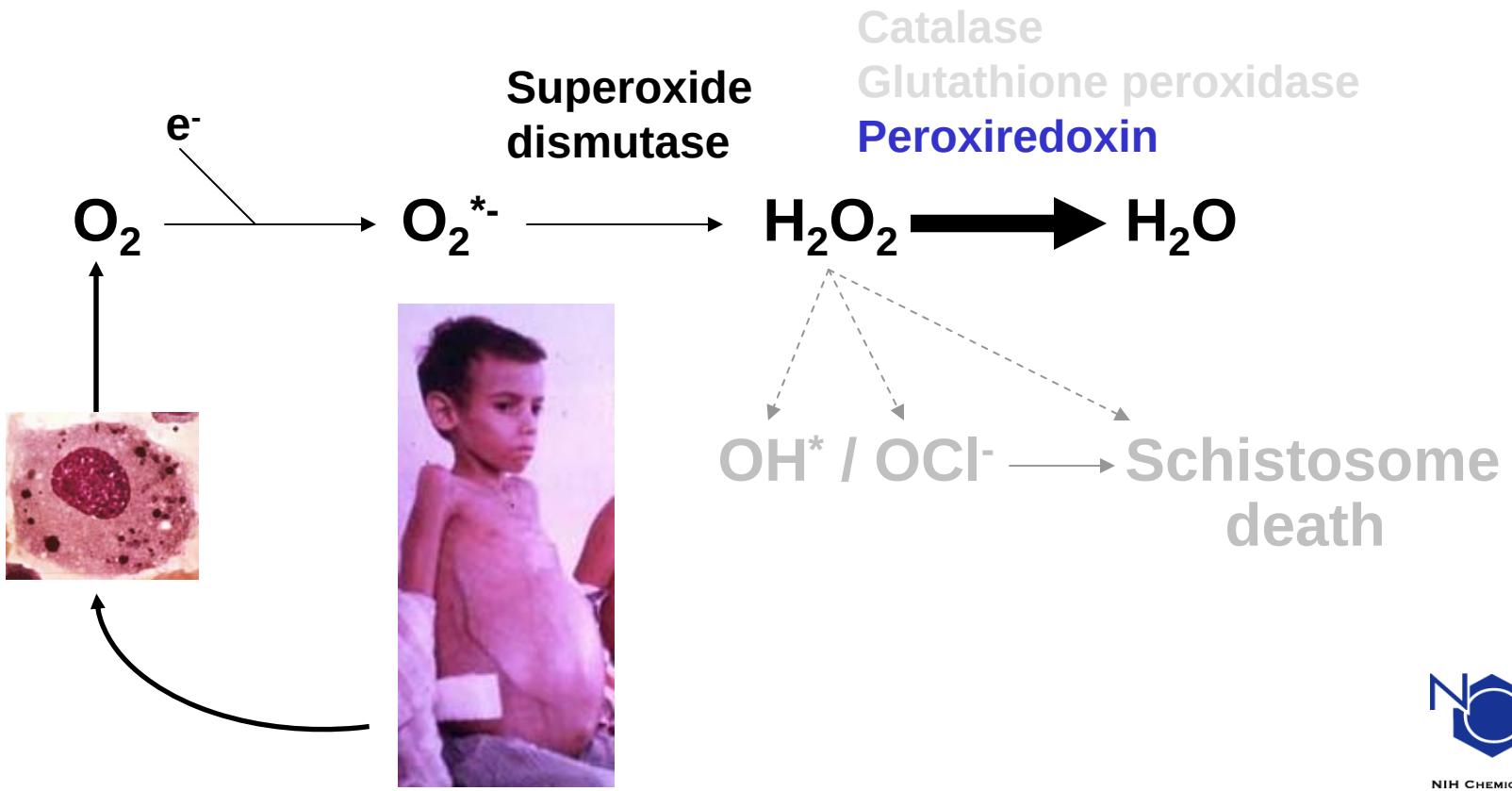
Humans have three enzymes that degrade hydrogen peroxide made from superoxide radicals



NIH Chemical Genomics Center

Targeted Redox Pathway

- *S. mansoni* has no catalase or glutathione peroxidase.
- Survives in humans due to parasite-specific peroxiredoxin that degrades reactive oxygen species produced by human innate immune response.



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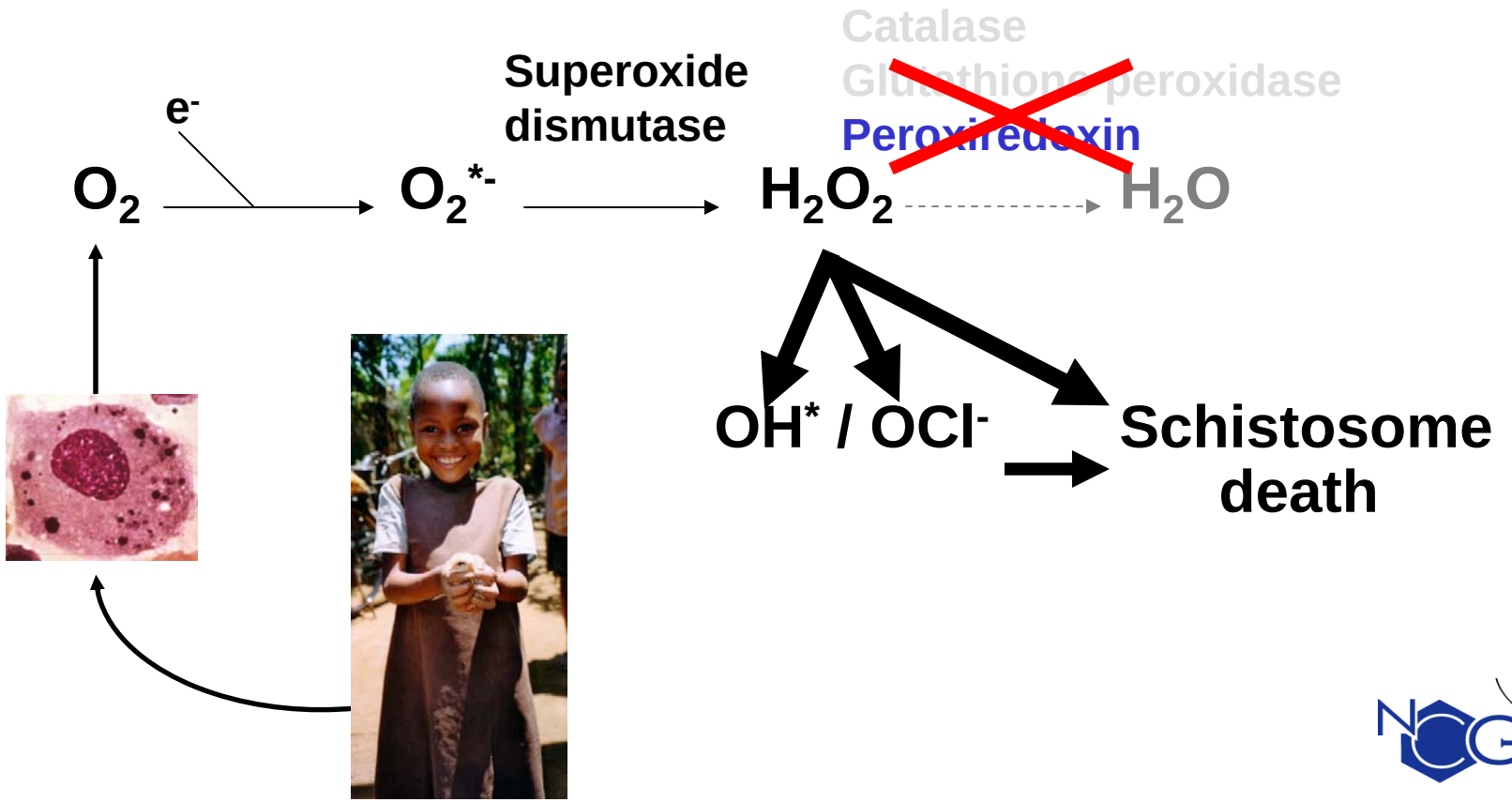
Targeted Redox Pathway

Inhibition of *S. mansoni* peroxiredoxin would prevent worm degradation of hydrogen peroxide and kill schistosomes



Discovery of Pathway: 2002

ELSEVIER

Molecular & Biochemical Parasitology 121 (2002) 129–139

MOLECULAR & BIOCHEMICAL PARASITOLOGY

www.parasitology-online.com

The disulfide redox system of *Schistosoma mansoni* and the importance of a multifunctional enzyme, thioredoxin glutathione reductase☆

Heather M. Alger, David L. Williams *

Department of Biological Sciences, Illinois State University, Normal, IL 61790-4120, USA

Received 26 December 2001; accepted in revised form 8 February 2002

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Identification of Target: 2006

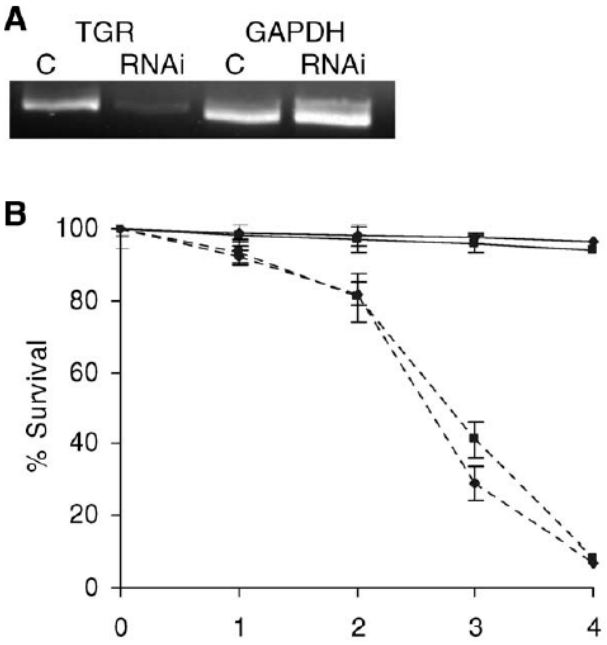
OPEN ACCESS Freely available online

PLOS MEDICINE

Thioredoxin Glutathione Reductase from *Schistosoma mansoni:* An Essential Parasite Enzyme and a Key Drug Target

Angela N. Kuntz[1], Elisabeth Davioud-Charvet[2,3], Ahmed A. Sayed[1], Lindsay L. Califf[1], Jean Dessolin[2,4], Elias S. J. Arnér[5], David L. Williams[1*]

1 Department of Biological Sciences, Illinois State University, Normal, Illinois, United States of America, **2** Biochemie-Zentrum der Universität Heidelberg, Heidelberg, Germany, **3** Centre National de la Recherche Scientifique (CNRS), Paris, France, **4** Institut Européen de Chimie et Biologie, CNRS UMR 5144, Bordeaux University, Pessac Cedex, France, **5** Medical Nobel Institute for Biochemistry, Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden



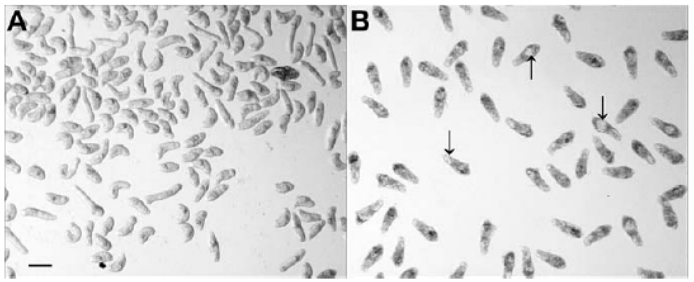
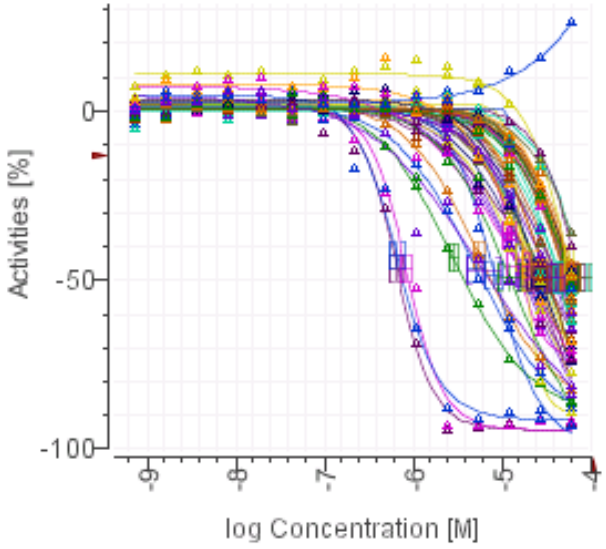


Figure 8. Photomicrographs (100×) of Irrelevant dsRNA-Treated Schistosomula (left image) and TGR dsRNA-Treated Schistosomula (right image) after Three Days of Treatment

All organisms in the left image are alive; parasites have different shapes, elongated, contracted, and curved during movement. In the right image, all of the parasites are dead and have roughly the same shape (no movement) and internal vacuoles (arrows). The bar represents 250 μm.
doi:10.1371/journal.pmed.0040206.g008

Quantitative HTS:2007

- **70,000 compounds at 7 concentrations (qHTS)**
  - **Dose-response curve for all compounds (PNAS 103, 11473-8 (2006))**
  - **~10,000,000 data points (16 Time-Point Reads)**
  - **31 hours of robot time**
- **Results: 100 compounds with IC50 < 40 μM**
  - **71 compounds**
  - **6 different structural classes**



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Report of chemical probes: Jan 2008

OPEN ACCESS Freely available online

PLoS NEGLECTED TROPICAL DISEASES

Quantitative High-Throughput Screen Identifies Inhibitors of the *Schistosoma mansoni* Redox Cascade

Anton Simeonov[1], Ajit Jadhav[1], Ahmed A. Sayed[2], Yuhong Wang[1], Michael E. Nelson[1], Craig J. Thomas[1], James Inglese[1], David L. Williams[2]*, Christopher P. Austin[1]*

1 NIH Chemical Genomics Center, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland, United States of America, **2** Department of Biological Sciences, Illinois State University, Normal, Illinois, United States of America

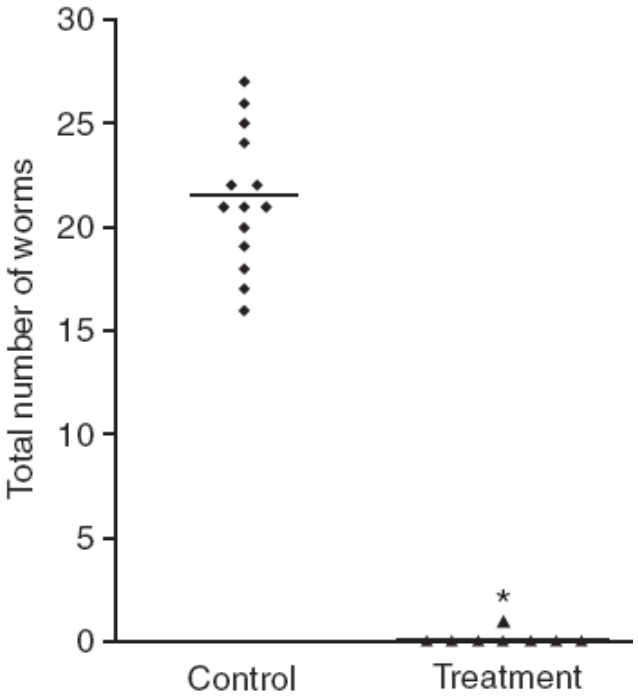
Abstract

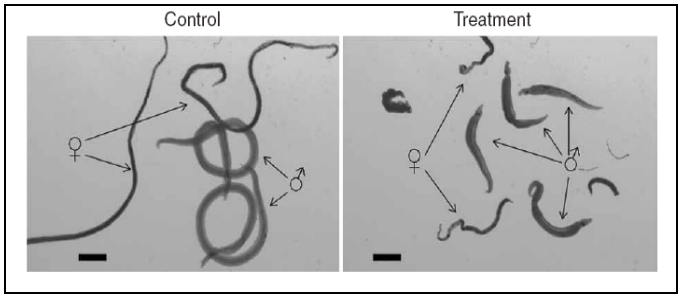
Schistosomiasis is a tropical disease associated with high morbidity and mortality, currently affecting over 200 million people worldwide. Praziquantel is the only drug used to treat the disease, and with its increased use the probability of developing drug resistance has grown significantly. The *Schistosoma* parasites can survive for up to decades in the human host due in part to a unique set of antioxidant enzymes that continuously degrade the reactive oxygen species produced by the host's innate immune response. Two principal components of this defense system have been recently identified in *S. mansoni* as thioredoxin/glutathione reductase (TGR) and peroxiredoxin (Prx) and as such these enzymes present attractive new targets for anti-schistosomiasis drug development. Inhibition of TGR/Prx activity was screened in a dual-enzyme format with reducing equivalents being transferred from NADPH to glutathione via a TGR-catalyzed reaction and then to hydrogen peroxide via a Prx-catalyzed step. A fully automated quantitative high-throughput (qHTS) experiment was performed against a collection of 71,028 compounds tested as 7- to 15-point concentration series at 5 μL reaction volume in 1536-well plate format. In order to generate a robust data set and to minimize the effect of compound autofluorescence, apparent reaction rates derived from a kinetic read were utilized instead of end-point measurements. Actives identified from the screen, along with previously untested analogues, were subjected to confirmatory experiments using the screening assay and subsequently against the individual targets in secondary assays. Several novel active series were identified which inhibited TGR at a range of potencies, with IC_{50}s ranging from micromolar to the assay response limit (~25 nM). This is, to our knowledge, the first report of a large-scale HTS to identify lead compounds for a helminthic disease, and provides a paradigm that can be used to jump-start development of novel therapeutics for other neglected tropical diseases.

Identification of oxadiazoles as new drug leads for the control of schistosomiasis

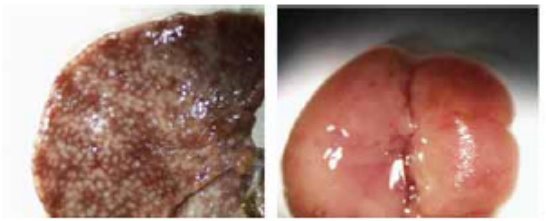
Ahmed A Sayed[1], Anton Simeonov[2], Craig J Thomas[2], James Inglese[2], Christopher P Austin[2] & David L Williams[1]

[1]Department of Biological Sciences, Illinois State University, Normal, Illinois 61790, USA. [2]NIH Chemical Genomics Center, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland 20892-3370, USA. Correspondence should be addressed to D.L.W. (dlwilli@ilstu.edu) or C.P.A. (austinc@mail.nih.gov).





Treated worms



Livers of treated mice

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BioAssay Summary:

AID: 448

Name: Schistosoma Mansoni Peroxiredoxins (Prx2).
Data Source: NCGC (prx2)
Activity Outcome Method: Confirmatory, Concentration-Response Relationship Observed

BioAssay Results: Data Table(Active Substances) Data Table(All Substances)

BioActive Compounds: 40
BioActivity Summary Structure-Activity Analysis Structure Clustering

Related BioAssays: Target Similarity (1) Activity Overlap (159)

Links:

Compounds: All: 63787 Active: 40 Inactive: 63393 Inconclusive: 364
Substances: All: 64651 Active: 44 Inactive: 64241 Inconclusive: 366
Protein Target: 1 Link
Taxonomy: 1 Link
Related BioAssay, Depositor: 2 Links

Description:

NIH Molecular Libraries Screening Centers Network [MLSCN]
NIH Chemical Genomics Center [NCGC]
David Williams [Illinois State University]

NCGC Assay Overview:
Schistosoma mansoni, a causative agent of schistosomiasis, resides in the bloodstream of their host up to 30 years without being eliminated by the host immune attack. One proposed survival mechanism is the production of an antioxidant "firewall" that neutralizes the oxidative assault of the host's immune attack. Schistosoma mansoni peroxiredoxins (Prx) are important parasite antioxidant proteins that play a crucial role in redox balance mechanisms. Data strongly suggest the possible use of Prx as novel drug targets. First, the proteins are essential for the parasite survival. Second, the proteins exhibit sufficient biochemical

PubChem BioActivity Analysis: Data Table - Microsoft Internet Explorer

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Address http://pubchem.ncbi.nlm.nih.gov/assay/assay.cgi?q=r&queue=t&qstatus=done&reqid=4835918962933304 82&version=1.2 Go Links

NCBI PubChem

PubChem BioAssay GO

PubMed | Entrez | Structure | PubChem | Help

PubChem » BioAssay Services » BioActivity Analysis: Data Table

BioActivity Analysis: 1 BioAssay and 63787 Compounds

Summary | Data Table | Structure-Activity

AID: 448

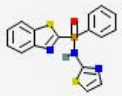
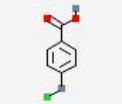
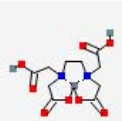
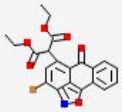
Total BioAssay Result Count: 63787

Data Table, Concise | Data Table, Complete | Plot | Select

MORE

Page: 1 of 3190 Display: 20 Go To Page 1

Sort: (Click the result table header to sort.)

#	Structure	SID	CID	Score	Outcome	Links	Activity Direction	Activity Qualifier	Qualified AC50	Log of AC50	Hill Coefficient	Curve R2	Data Type	Compound QC	Data Analysis QC	NCGC Comment	Curve Fit Model	Hill S0	Hill Sinf	Hill dS	Log AC50 Std Error	Exclu Poir
1		3715577	2311082	74	Active		decreasing	=	3.74e-008	-7.428	2.86	0.97	qHTS Primary	QC'd by DPI	Verified	Full Curve	3pHill (AC50, n, Sinf)	0	-77	77	0.119	{:
2		11110959	1730	64	Active		decreasing	=	4.41e-007	-6.355	3.31	0.99	qHTS Primary		Verified	Full Curve	3pHill (AC50, n, Sinf)	0	-81	81	0.022	{:
3		4253459	16683706	63	Active		decreasing	=	4.96e-007	-6.304	2.33	1	qHTS Primary		Verified	Full Curve	3pHill (AC50, n, Sinf)	0	-82	82	0.03	{:
4		857882	659226	63	Active		decreasing	=	5.3e-007	-6.276	10.72	0.98	qHTS Primary	QC'd by DPI	Verified	Full Curve	3pHill (AC50, n, Sinf)	0	-78	78		{:

Internet

PubChem BioActivity Analysis: Data Table - Microsoft Internet Explorer

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Address http://pubchem.ncbi.nlm.nih.gov/assay/assay.cgi?q=r&queue=t&qstatus=done&reqid=4835918962933304 82&version=1.2 Go Links Go Links

Full Concentration-Response

Number of Points	Activity at 0.732nM [%]	Activity at 1.636nM [%]	Activity at 3.658nM [%]	Activity at 8.18nM [%]	Activity at 18.291nM [%]	Activity at 0.041uM [%]	Activity at 0.091uM [%]	Activity at 0.204uM [%]	Activity at 0.457uM [%]	Activity at 1.022uM [%]	Activity at 2.286uM [%]	Activity at 5.111uM [%]	Activity at 11.429uM [%]	Activity at 25.556uM [%]	Activity at 0.057mM [%]	Compound Type
7			2		-9		-72		-81		-66		-81		-81	qHTS MLSMR
15	-4	-1	0	-3	3	-4	0	-5	-43	-75	-86	-85	-78	-75	-84	qHTS ECL - SigmaAldrich
7			1		0		1		-37		-78		-79		-86	qHTS ECL - NCI
7			-8		-1		-1		-13		-78		-84		-72	qHTS MLSMR

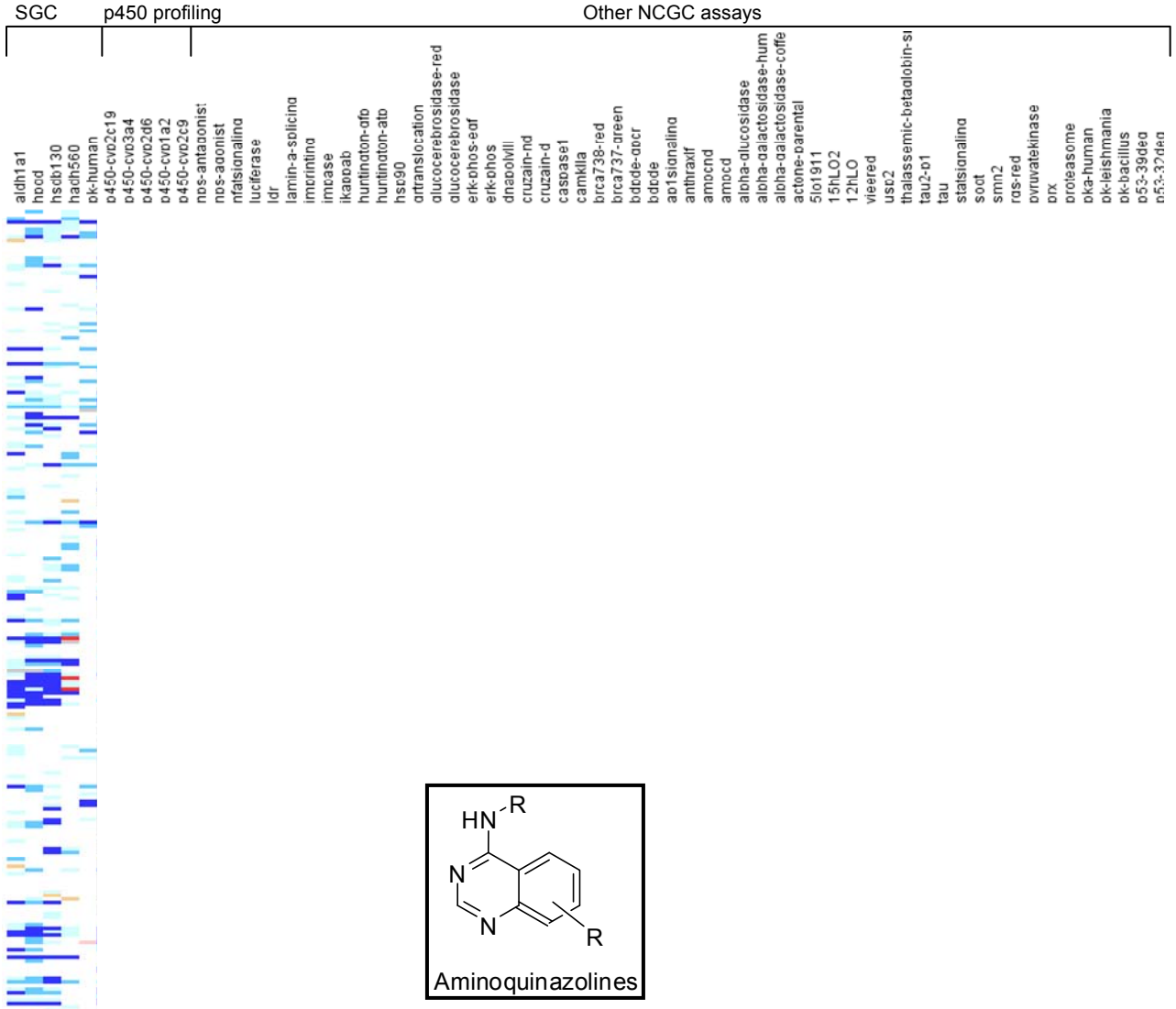
Internet Internet

SGC Collaboration: Chemical Probes of Gene Families

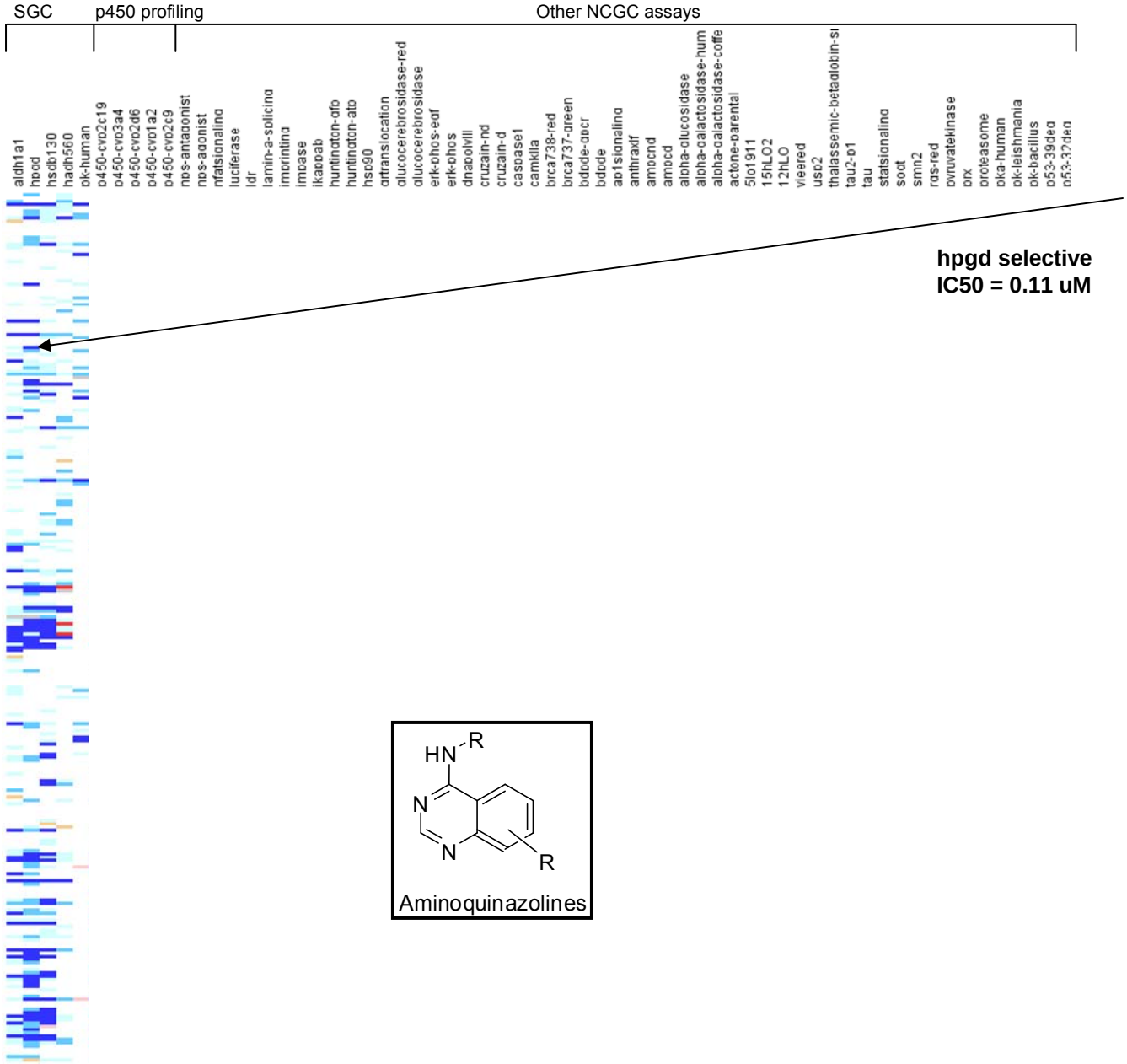
- Discussions started 4Q 2004 (Edwards)
- Dehydrogenases (SGC-Oxford) chosen as first targets, enzymes received 1Q 2006
  - 4 enzymes screened against the full collection
- Collaboration expanded 2Q 2007 to new targets from all SGC sites
- Epigenetics collaboration begun 4Q 2007
  - Joint application to WT submitted last week
- NCGC PIs
  - Anton Simeonov
  - Doug Auld (Human PK)

NIH Chemical Genomics Center

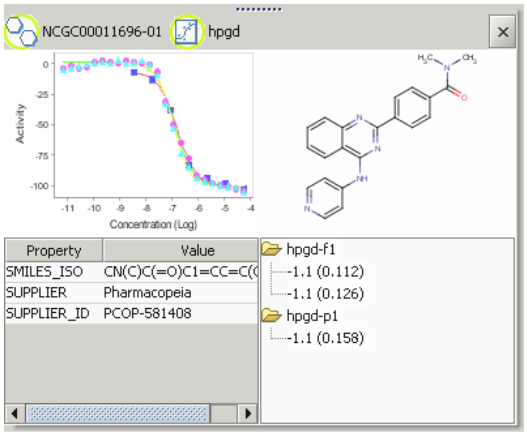
High Content Scaffold ‘Family’ Profiling of SGC Target Families



High Content Scaffold ‘Family’ Profiling of SGC Target Families

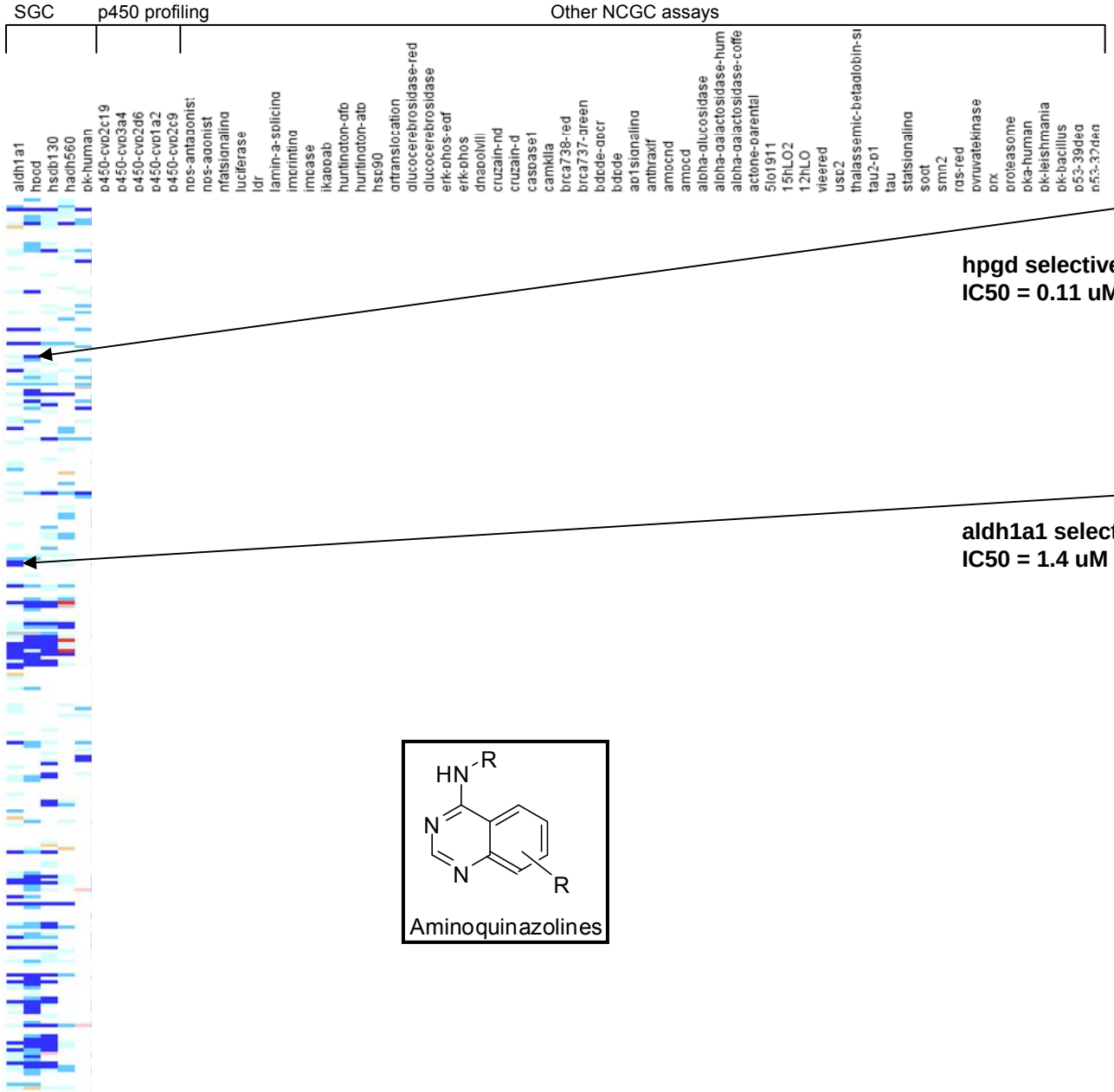


hpgd selective
IC50 = 0.11 uM

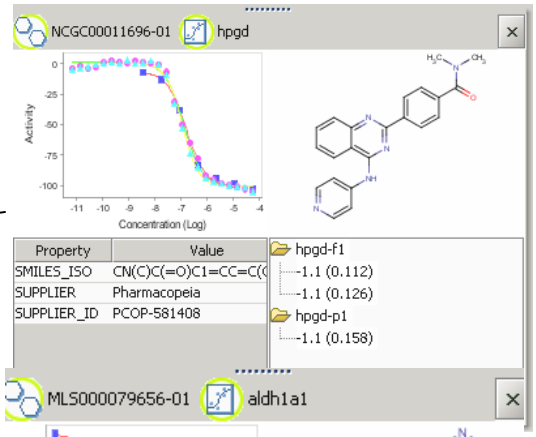


Aminoquinazolines

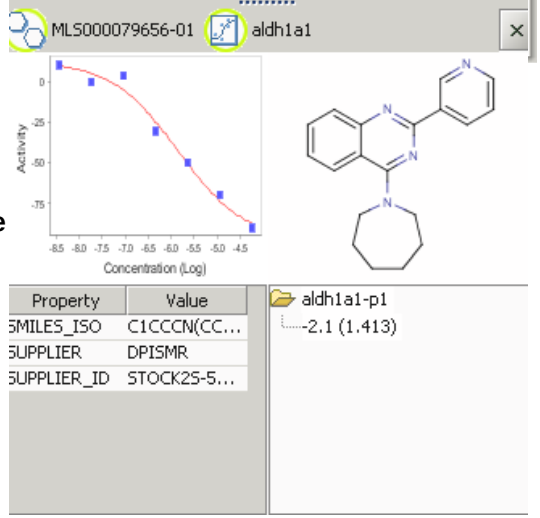
High Content Scaffold ‘Family’ Profiling of SGC Target Families



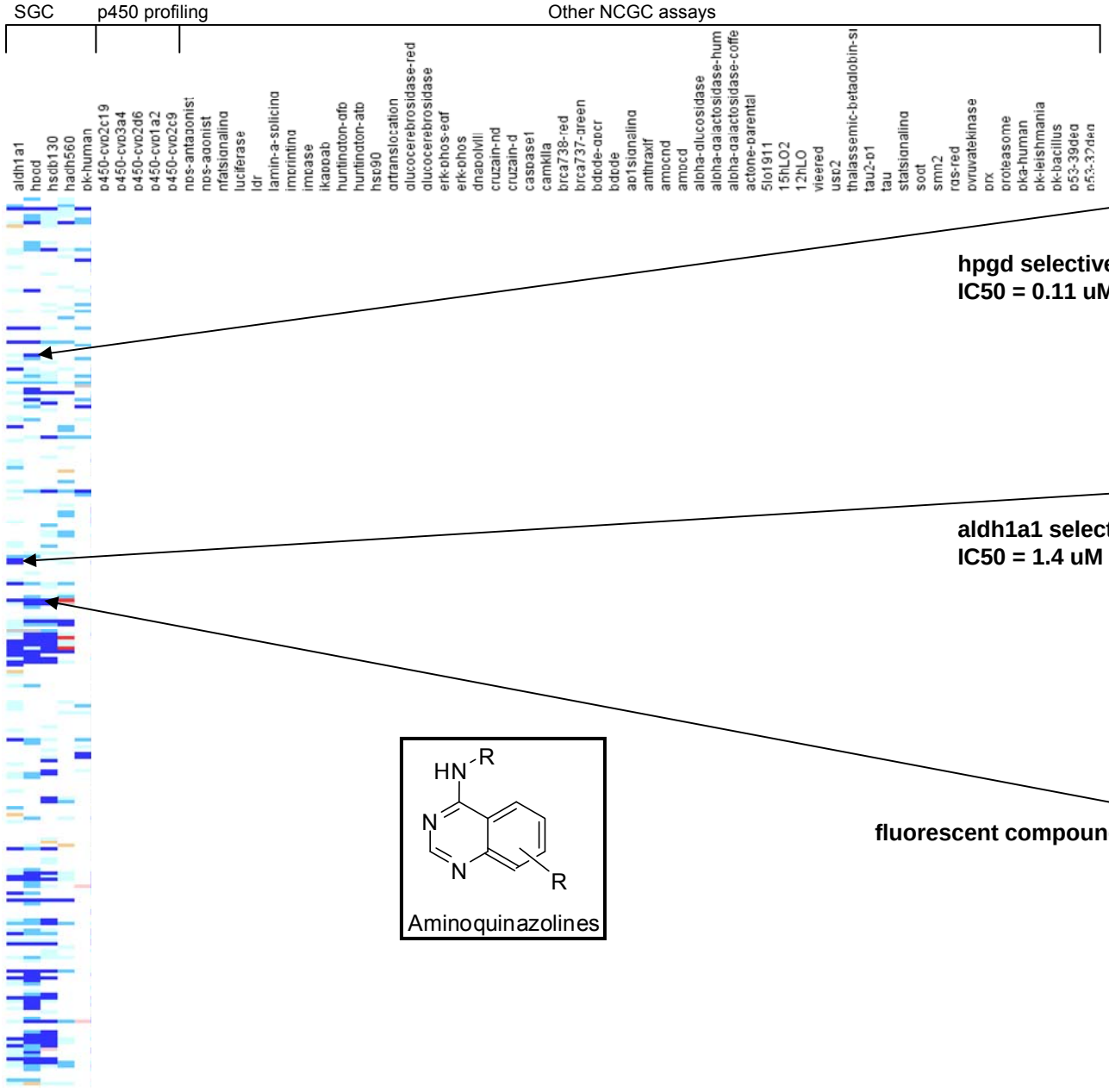
hpgd selective
IC50 = 0.11 uM



aldh1a1 selective
IC50 = 1.4 uM



High Content Scaffold ‘Family’ Profiling of SGC Target Families

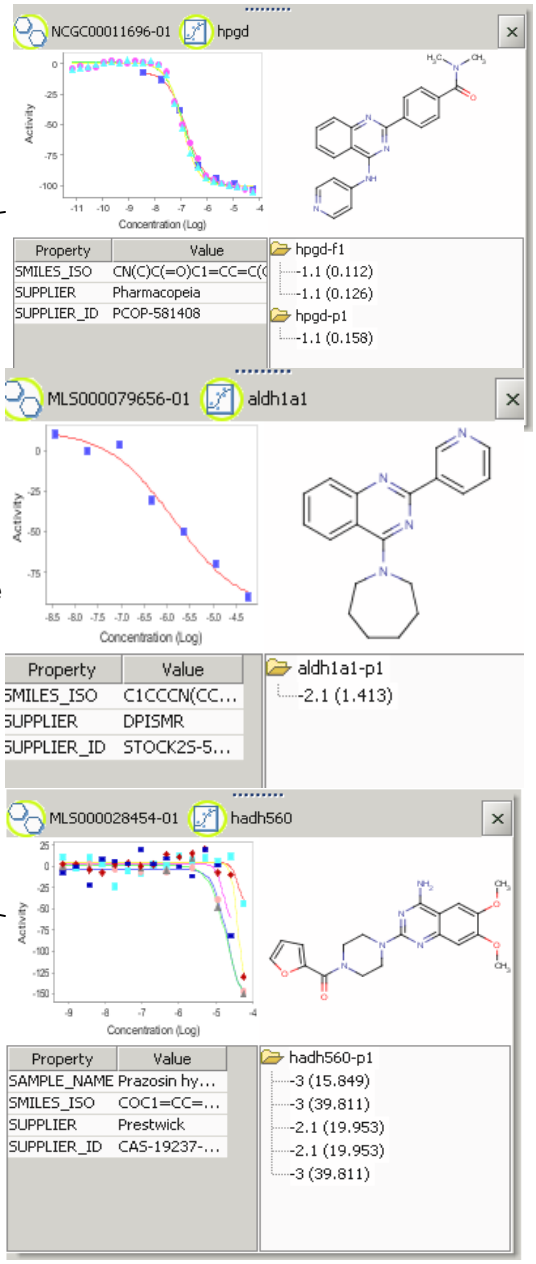


hpgd selective
IC50 = 0.11 uM

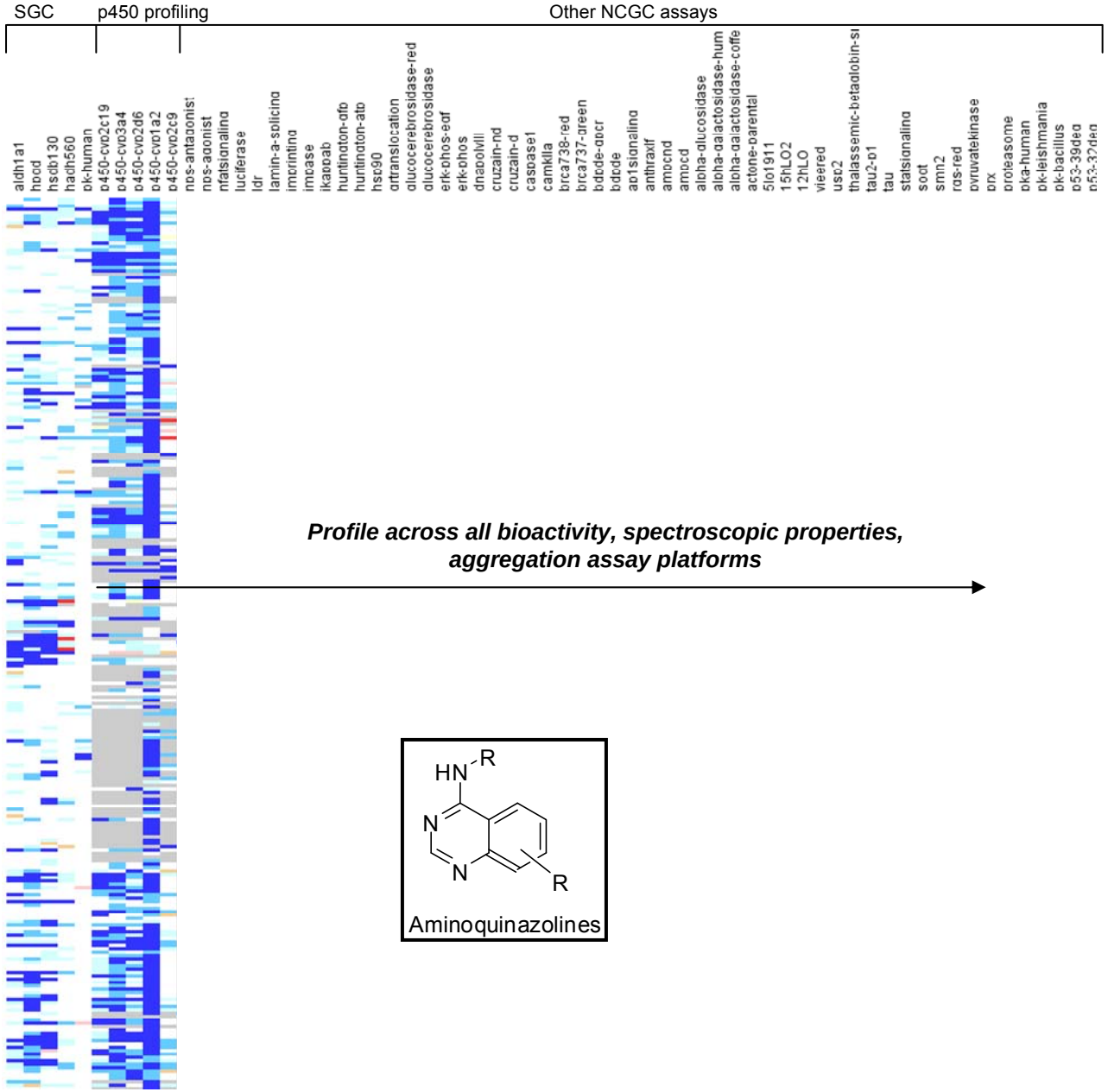
aldh1a1 selective
IC50 = 1.4 uM

fluorescent compound

Aminoquinazolines



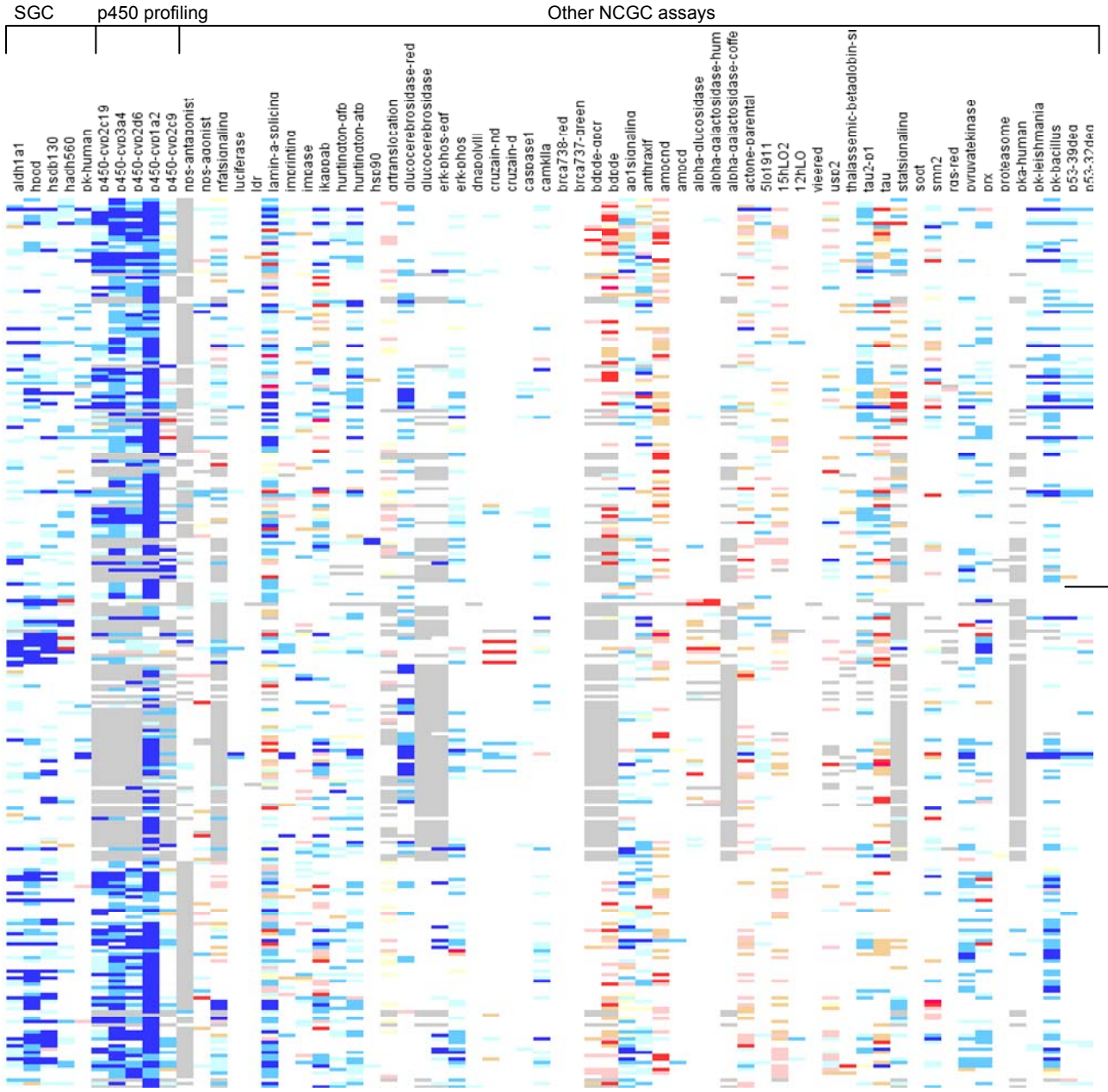
High Content Scaffold ‘Family’ Profiling of SGC Target Families

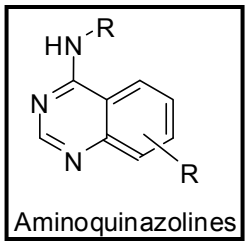


Profile across all bioactivity, spectroscopic properties, aggregation assay platforms

Aminoquinazolines

High Content Scaffold ‘Family’ Profiling of SGC Target Families





Aminoquinazolines

- Profiles mined for each scaffold tested, known drugs, etc

-Annotated assays organized by:
biological relationships,
assay platform, or
activity profiles

Education

REVIEW

nature chemical biology

High-throughput screening assays for the identification of chemical probes

James Inglese, Ronald L Johnson, Anton Simeonov, Menghang Xia, Wei Zheng, Christopher P Austin & Douglas S Auld

High-throughput screening (HTS) assays enable the testing of large numbers of chemical substances for activity in diverse areas of biology. The biological responses measured in HTS assays span isolated biochemical systems containing purified receptors or enzymes to signal transduction pathways and complex networks functioning in cellular environments. This Review addresses factors that need to be considered when implementing assays for HTS and is aimed particularly at investigators new to this field. We discuss assay design strategies, the major detection technologies and examples of HTS assays for common target classes, cellular pathways and simple cellular phenotypes. We conclude with special considerations for configuring sensitive, robust, informative and economically feasible HTS assays.

COMMENTARY

Reporting data from high-throughput screening of small-molecule libraries

James Inglese, Caroline E Shamu & R Kiplin Guy

Publications reporting results of small-molecule screens are becoming more common as academic researchers increasingly make use of high-throughput screening (HTS) facilities. However, no standards have been formally established for reporting small-molecule screening data, and often key information important for the evaluation and interpretation of results is omitted in published HTS protocols. Here, we propose concise guidelines for reporting small-molecule HTS data.

NCGC NIH Chemical Genomics Center

NIH Chemical Genomics Center

Free software and code for public use

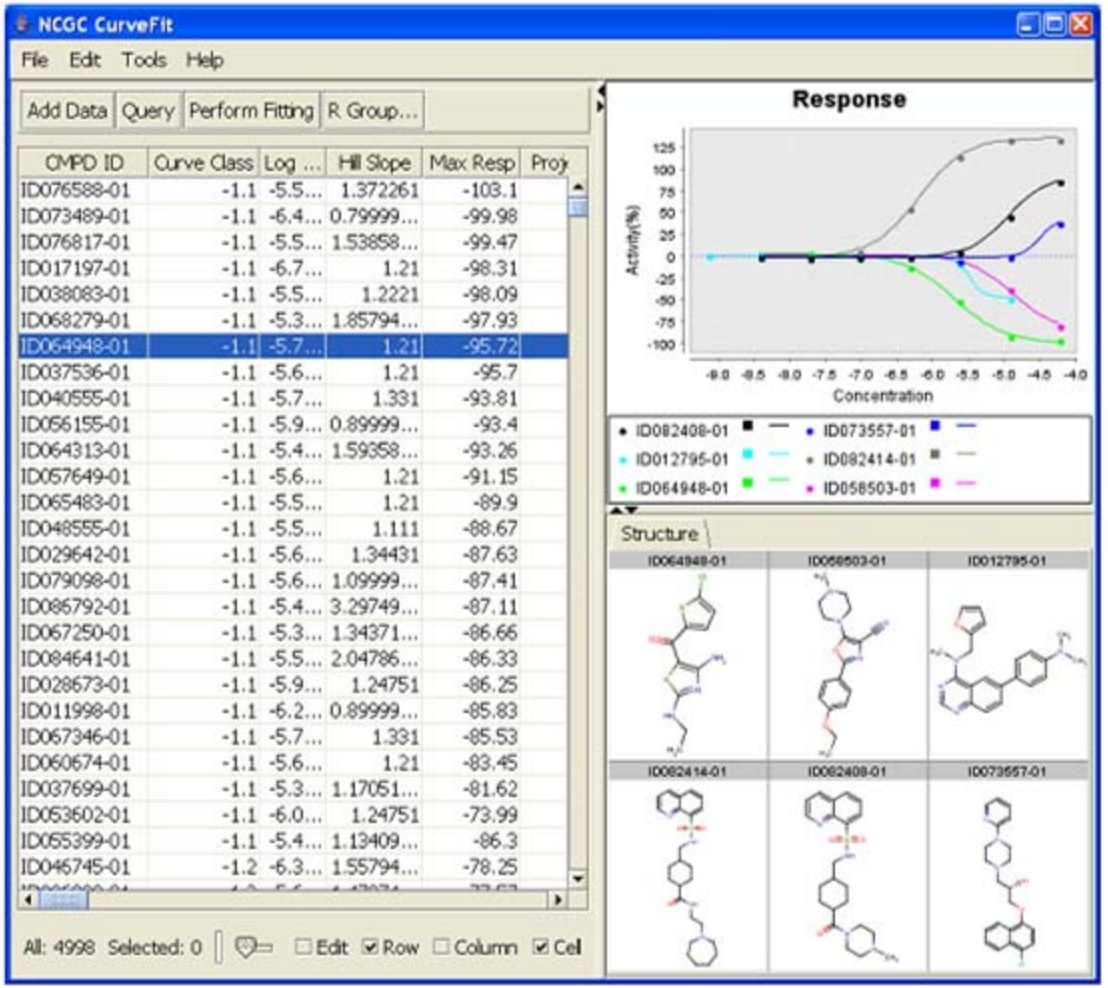
NCGC CurveFit

Large scale dose response curve fitting and curve classification software

Download: Application. (requires Java WebStart)
Download: Sample Data File.
Download: Source Code.

Software Features

- Automated curve fitting and classificatoin software
- Algorithm recognizes bell shaped curves, implements standard Hill equation, extensible for other models; distinguishes activation vs inhibition
- Stand alone tool designed explicitly for public use and for source code reference
- Analyzes 10k curves with good performance, capacity to handle >100k curves with memory usage on user machine being the limit
- Provides activity ranking of complete and incomplete curves
- Fast chemical similarity and substructure searching (including smarts support) enabled using path-based fingerprints
- Ability to export results, curve images
- Web deployed software, keeps users current with latest features



>> Assay Guidance

Assay Guidance Manual - Version 4.1

Introduction

Transfer of Validated Assays

Assay Operations for SAR Support

Enzymatic Assays

Receptor Binding Assays

GTPγS Binding Assays

Tissue Culture Assays

Cell-Based Elisa (C-Elisa) and Westerns Blots for Quantitative Antigen Detection

FLIPR™ Assays to Measure GPCR and Ion Channel Targets

Immunoassay Methods

Data Standardization for Results Management

Glossary of Quantitative Biology Terms

Comment Form

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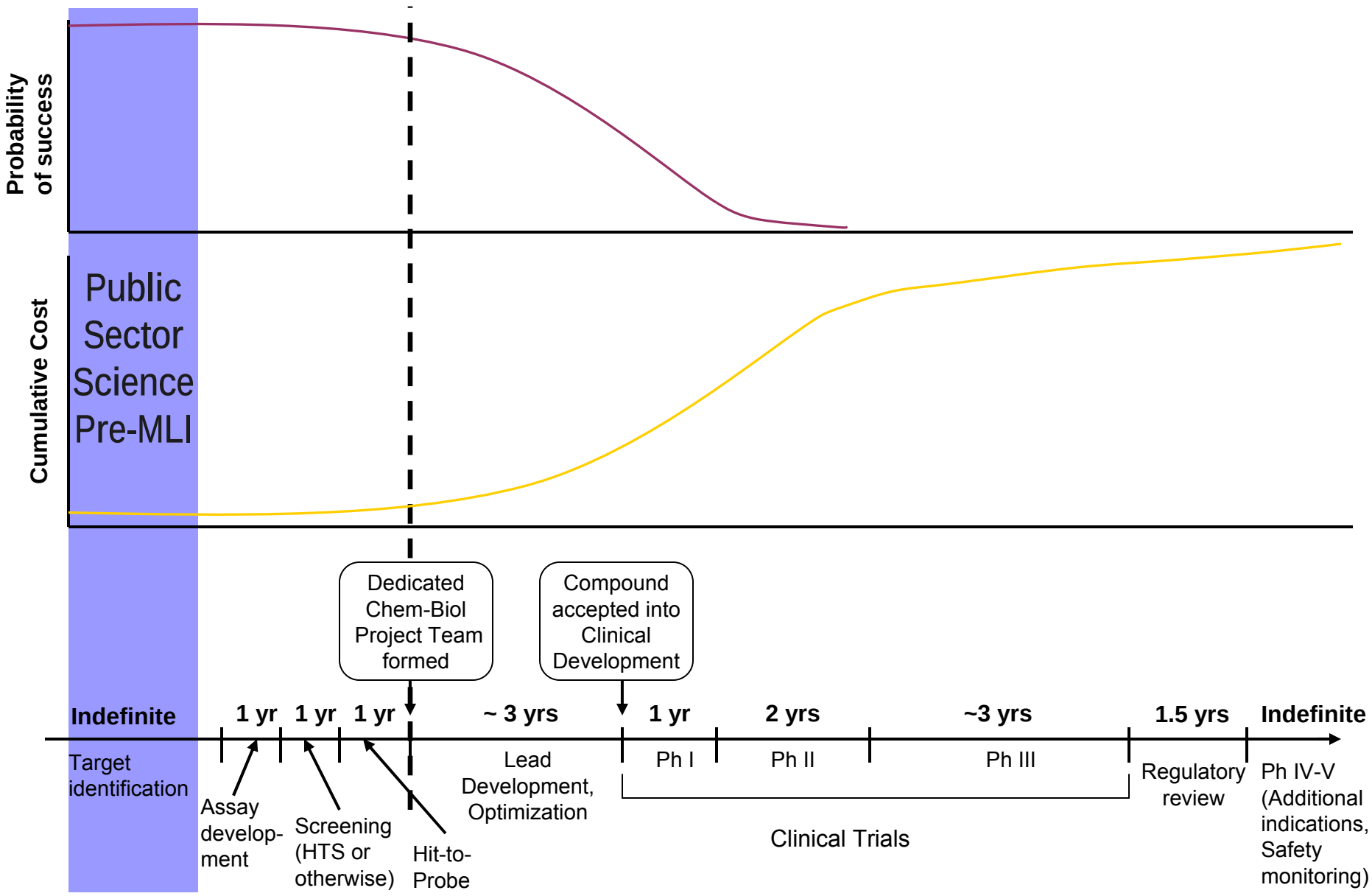
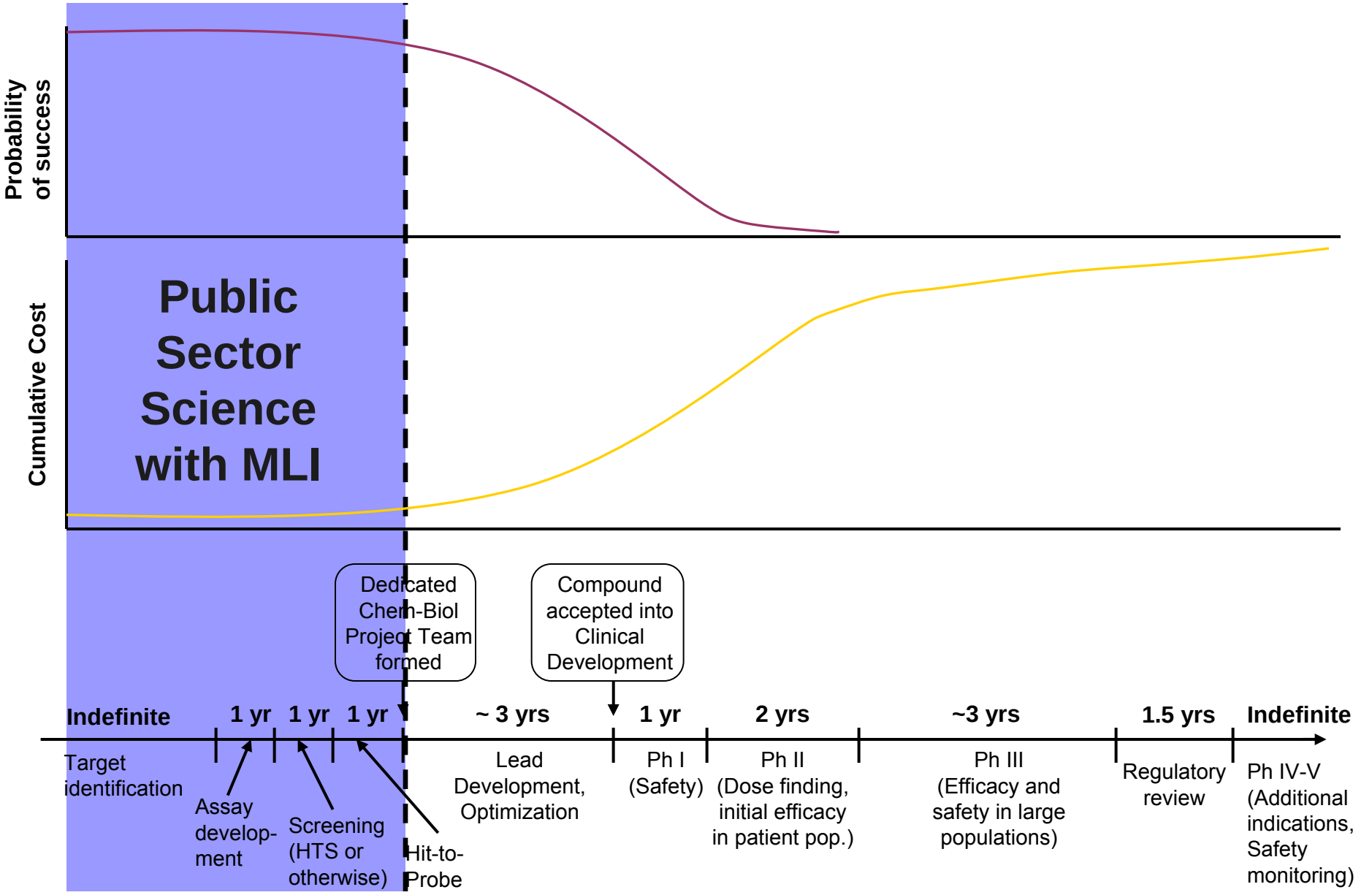
Probes are just the start of drug development



Probes are just the start of drug development



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[d]IRTA

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NIH Roadmap for Medical Research and the Intramural program of the NHGRI

More Information

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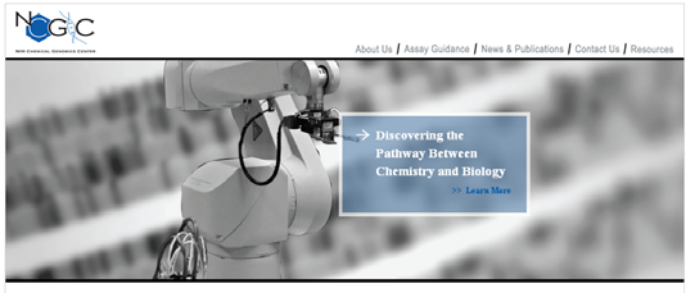

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