Lucile Packard Children's Hospital AT STANFORD

ImmPort
Bioinformatics For The Future of Immunology

Discovering new drugs and diagnostics from 300 billion points of data

Atul Butte, MD, PhD abutte@stanford.edu

Chief, Division of Systems Medicine, @atulbutte
Department of Pediatrics, @ImmPortDB
Department of Medicine, and, by courtesy,
Computer Science

Center for Pediatric Bioinformatics, LPCH

Stanford University

Butte Lab
Systems Medicine • Stanford Pediatrics • Packard Children's Hospital

Disclosures

- Scientific founder and advisory board membership
  - Genstruct
  - NuMedii
  - Personalis
  - Carmenta
- Past or present consultancy
  - Lilly
  - Johnson and Johnson
  - Roche
  - NuMedii
  - Genstruct
  - Tercica
  - Ansh Labs
  - Prevendia
  - Samsung
  - Assay Depot
- Honoraria
  - Lilly
  - Pfizer
  - Siemens
  - Bristol Myers Squibb
- Speakers' bureau
  - None
- Companies started by students
  - Carmenta
  - Serendipity
  - NuMedii
  - Stimulomics
  - NunaHealth
  - Praedicat
  - Flipora


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GeneChip®
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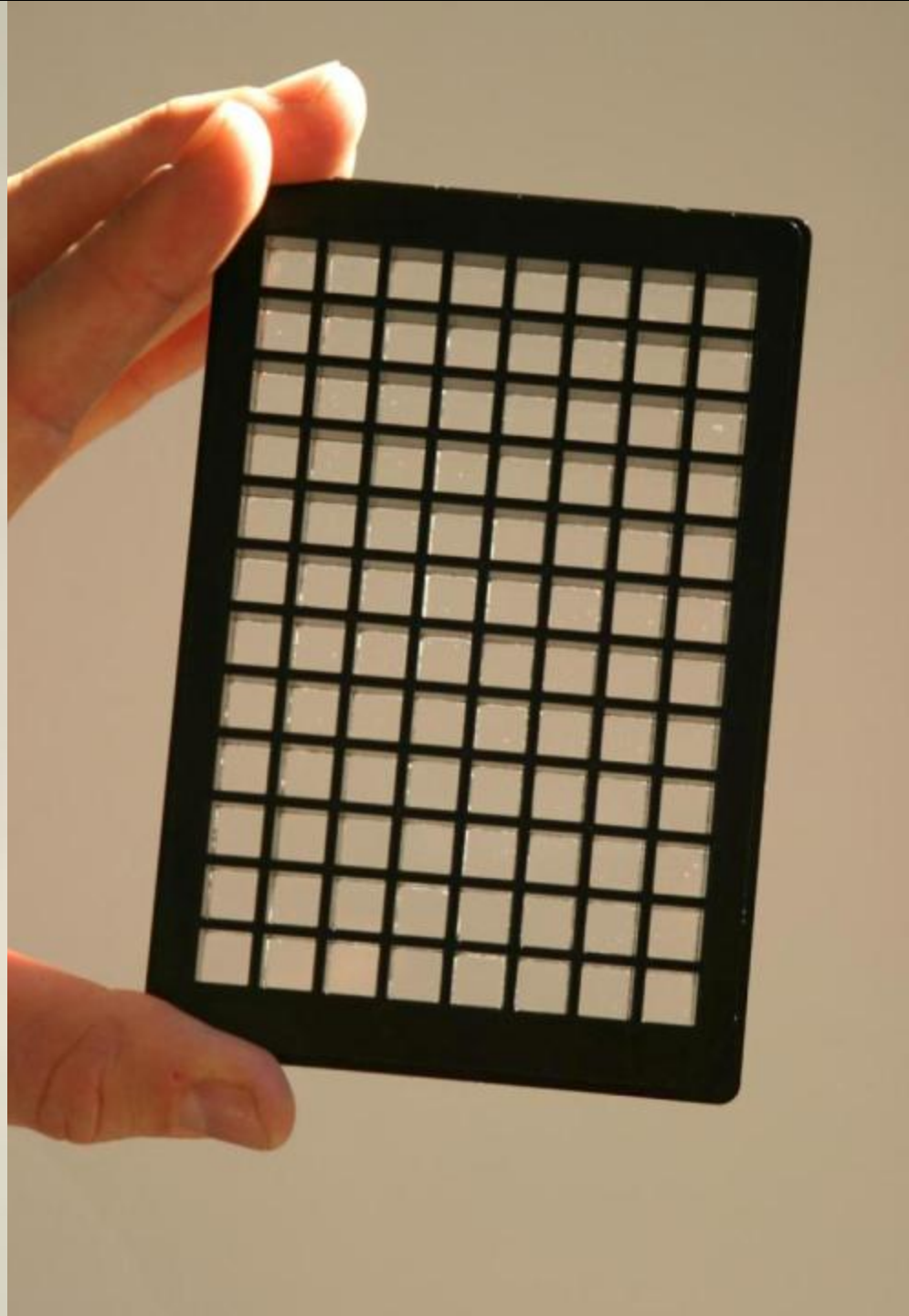

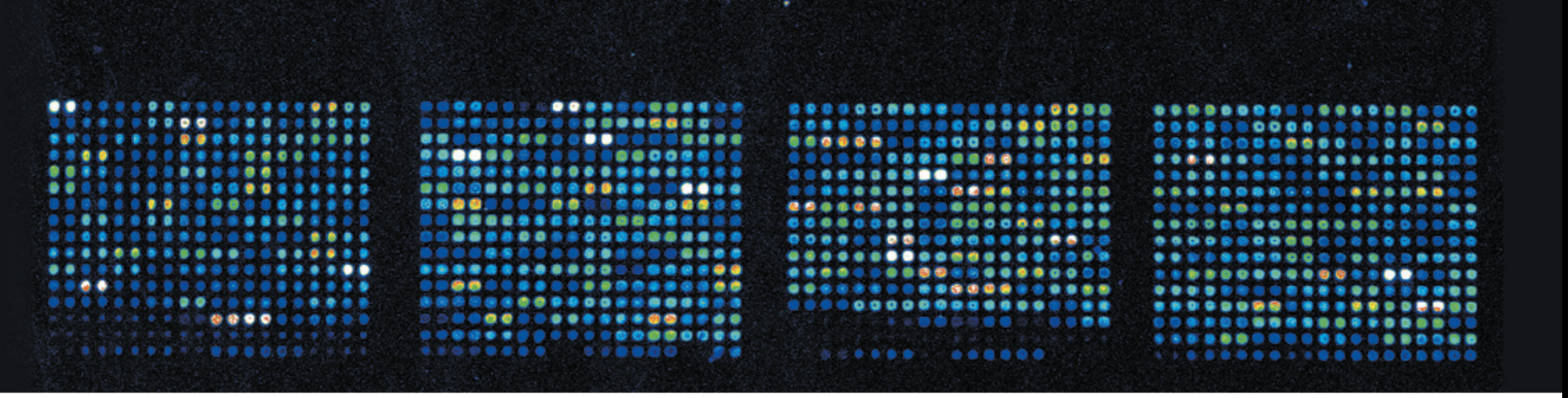

DNA microarrays allow researchers to analyse the expression of a huge number of genes simultaneously.

GENOMICS

Gene data to hit milestone

With close to one million gene-expression data sets now in publi researchers can identify disease trends without ever having to e

BY MONYA BAKER

Purvesh Khatri sits in front of an oversized computer screen, trawling for treasure in a sea of genetic data. Entering the search term 'breast cancer' into a public repository called the Gene Expression Omnibus (GEO), the postdoctoral researcher retrieves a list of 1,170 experiments, representing nearly 33,000 samples and a hoard of gene-expression data that could reveal previously unseen patterns.

That is exactly the kind of search that led Khatri's boss, Atul Butte, a bioinformatician at the Stanford School of Medicine in California, to identify a new drug target for diabetes. After downloading data from 130 gene-expression

for discovery," he says. Those are for validating hypotheses. The beauty of analysing data from multiple experiments is that biases and artefacts should cancel out between data sets, helping true relationships to stand out, Butte says. "There is safety in numbers."

And those numbers are rising rapidly. Since 2002, many scientific journals have required that data from gene-expression studies be deposited in public databases such as GEO, which is maintained by the National Center for Biotechnology Information in Bethesda, Maryland, and ArrayExpress, a large gene-expression

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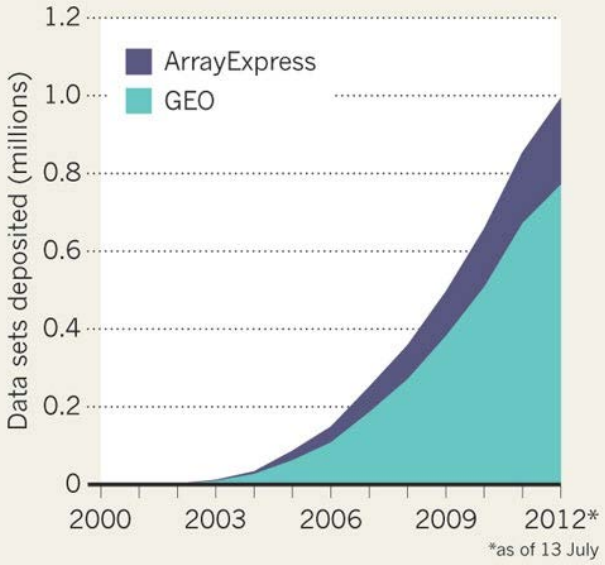
DATA DUMP

The number of gene-expression data sets in publicly available databases has climbed to nearly one million over the past decade.




NCBI
Gene Expression Omnibus
GEO Publications
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Gene Expression Omnibus: a public functional genomics data repository supporting MIAME-compliant data submissions. Array- and sequence-based data are accepted. Tools are provided to help users query and download experiments and curated gene expression profiles. More information »
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DataSets
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Platforms 10,789
Samples 841,339
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DataSets 2,720
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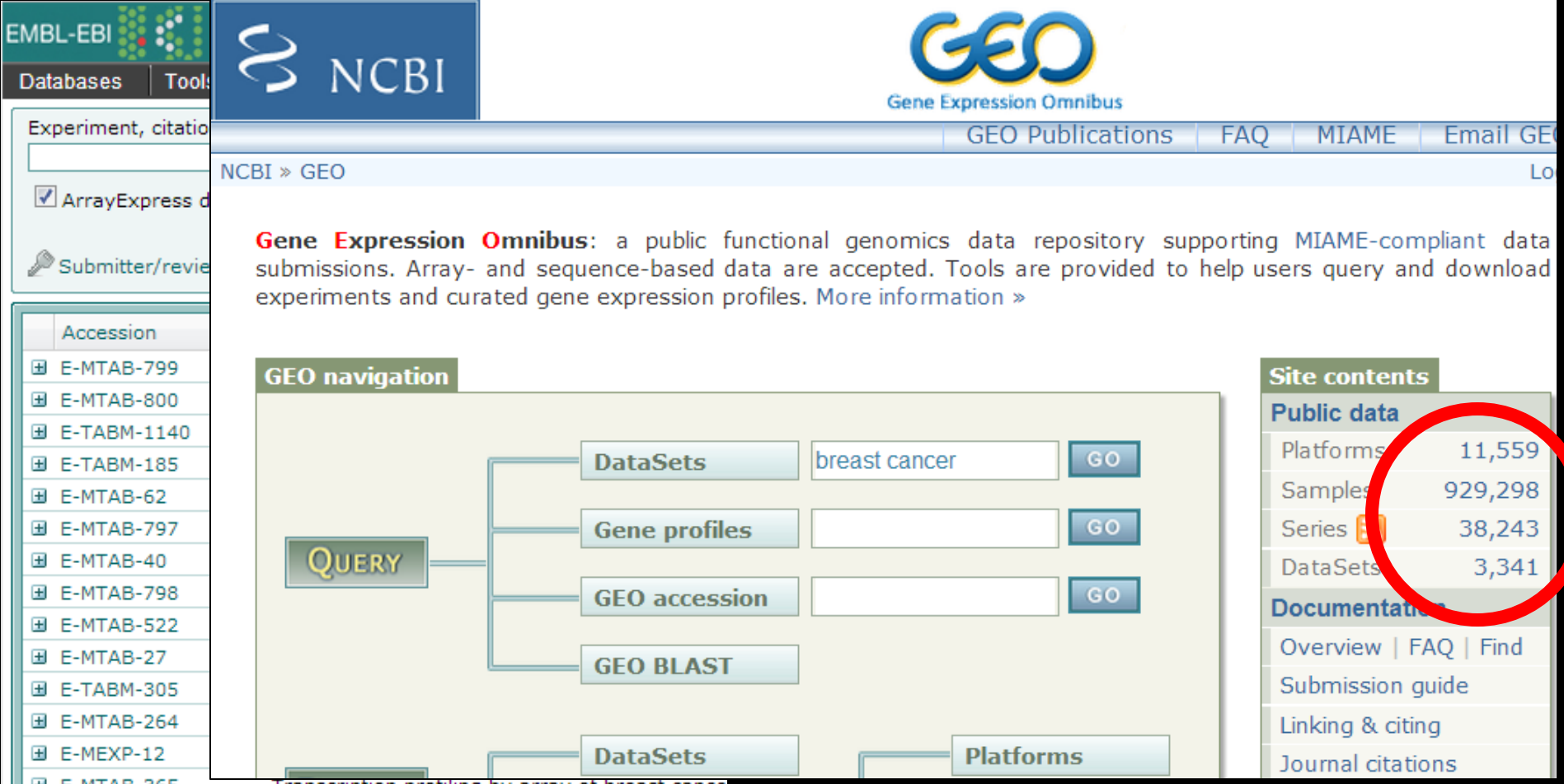


Total 1.2 million microarrays available

Doubles every 2-3 years

Butte AJ. Translational Bioinformatics: coming of age. *JAMIA*, 2008.

NCBI

Gene Expression Omnibus

Sign in to NCBI

GEO DataSets

GEO DataSets | breast cancer | Search

Save search Limits Advanced Help

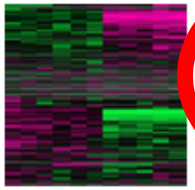
Display Settings: Summary, 20 per page, Sorted by Default order

Send to:

Results: 1 to 20 of 39372

<< First < Prev Page 1 of 1969 Next > Last >>

1. Leukemia inhibitory factor effect on Sin3a-silenced MCF7 **breast cancer** cell line



Analysis of SIN3 transcription regulator homolog A (Sin3a)-depleted MCF7 cells stimulated with LIF cytokine to activate signal transducer and activator of transcription 3 (STAT3). STAT3 transcription factor is a potent oncogene. Results provide insight into role of Sin3a in mediating STAT3 activity.

Organism: Homo sapiens

Type: Expression profiling by array, transformed count, 2 agent, 2 genotype/variation sets

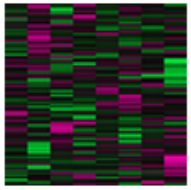
Platform: GPL570 Series: GSE35696 11 Samples

Download data: GEO (CEL)

DataSet Accession: GDS4388 ID: 4388

PubMed Full text in PMC Similar studies GEO Profiles Analyze DataSet

2. Co-expression of tyrosine kinase receptors HER2 and HER3 in mammary epithelial cells MCF10A grown in three-dimensional cultures



Analysis of MCF10A mammary epithelial cells expressing HER2, HER3, or HER2/HER3 heterodimer. Co-expression of HER2 and HER3 induced migration and invasion of MCF10A cells. Results provide insight into the role of HER2 and HER3 in **breast cancer**.

Organism: Homo sapiens

Type: Expression profiling by array, transformed count, 4 genotype/variation sets

Filter your results:

All (39372)

Platforms (34)

Samples (37742)

Series (1455)

Manage Filters

Top Organisms [Tree]

Homo sapiens *(36547)*

Mus musculus *(2686)*

Rattus norvegicus *(182)*

Canis lupus familiaris *(31)*

Human herpesvirus 8 *(5)*

More...

Find related data

Database: Select

Find items

ARTICLE

doi:10.1038/nature10983

The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups

Christina Curtis[1,2]†*, Sohrab P. Shah[3,4]*, Suet-Feung Chin[1,2]*, Gulisa Turashvili[3,4]*, Oscar M. Rueda[1,2], Mark J. Dunning[2], Doug Speed[2,5]†, Andy G. Lynch[1,2], Shamith Samarajiwa[1,2], Yinyin Yuan[1,2], Stefan Gräf[1,2], Gavin Ha[3], Gholamreza Haffari[3], Ali Bashashati[3], Roslin Russell[2], Steven McKinney[3,4], METABRIC Group‡, Anita Langerød[6], Andrew Green[7], Elena Provenzano[8], Gordon Wishart[8], Sarah Pinder[9], Peter Watson[3,4,10], Florian Markowetz[1,2], Leigh Murphy[10], Ian Ellis[7], Arnie Purushotham[9,11], Anne-Lise Børresen-Dale[6,12], James D. Brenton[2,13], Simon Tavaré[1,2,5,14], Carlos Caldas[1,2,8,13] & Samuel Aparicio[3,4]

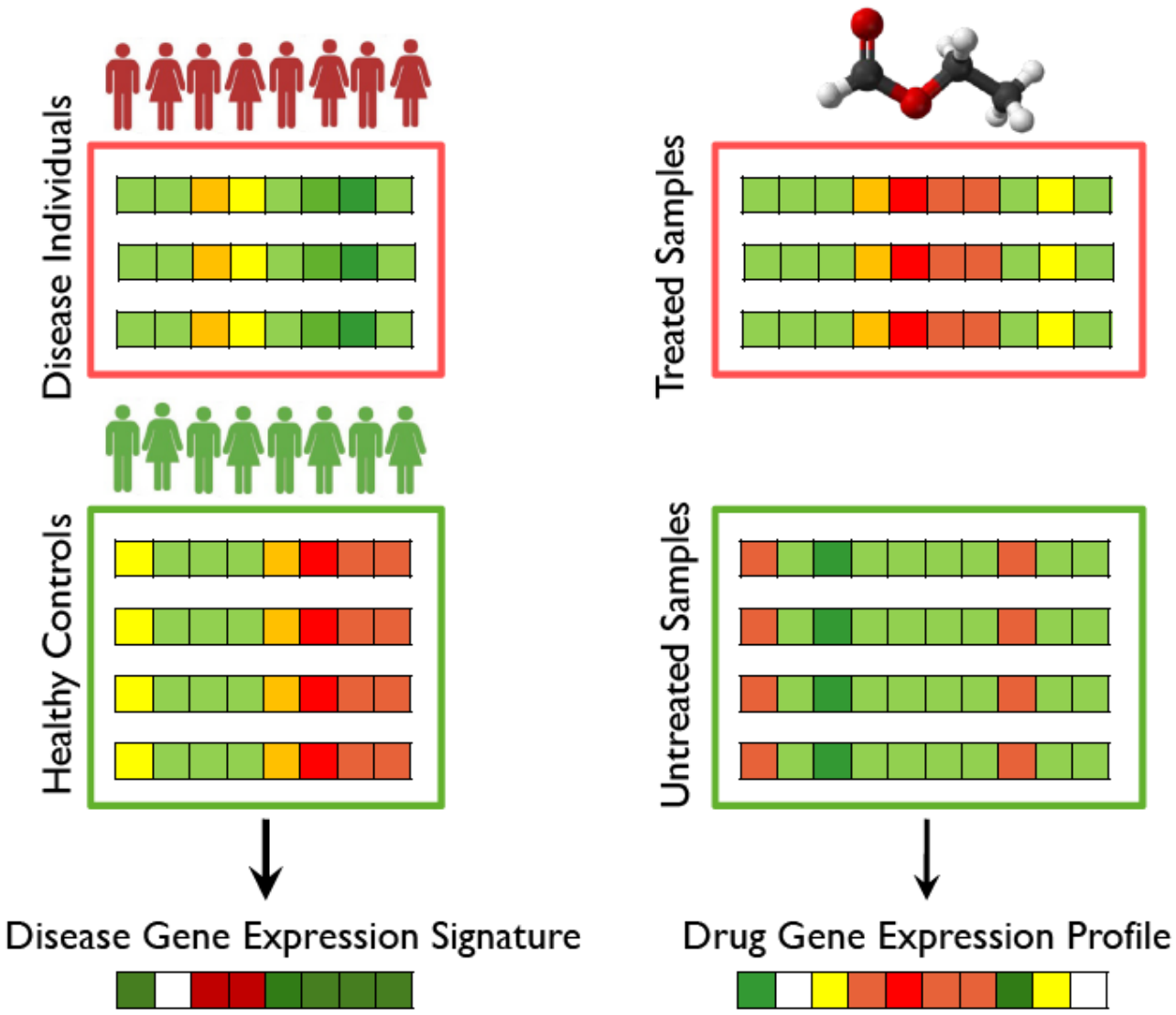
The elucidation of breast cancer subgroups and their molecular drivers requires integrated views of the genome and transcriptome from representative numbers of patients. We present an integrated analysis of copy number and gene expression in a discovery and validation set of 997 and 995 primary breast tumours, respectively, with long-term clinical follow-up. Inherited variants (copy number variants and single nucleotide polymorphisms) and acquired somatic copy number aberrations (CNAs) were associated with expression in ~40% of genes, with the landscape dominated by *cis*- and *trans*-acting CNAs. By delineating expression outlier genes driven in *cis* by CNAs, we identified putative cancer genes, including deletions in *PPP2R2A*, *MTAP* and *MAP2K4*. Unsupervised analysis of paired DNA–RNA profiles revealed novel subgroups with distinct clinical outcomes, which reproduced in the validation cohort. These include a high-risk, oestrogen-receptor-positive 11q13/14 *cis*-acting subgroup and a favourable prognosis subgroup devoid of CNAs. *Trans*-acting aberration hotspots were found to modulate subgroup-specific gene networks, including a TCR deletion-mediated adaptive immune response in the 'CNA-devoid' subgroup and a basal-specific chromosome 5 deletion-associated mitotic network. Our results provide a novel molecular stratification of the breast cancer population, derived from the impact of somatic CNAs on the transcriptome.

National Cancer Institute

The Cancer Genome Atlas

Understanding genomics to improve cancer care

Available Cancer Types	# Patients with Samples	# Downloadable Tumor Samples	Updated
Acute Myeloid Leukemia [LAML]	202	200	04/04/12
Bladder Urothelial Carcinoma [BLCA]	89	78	04/12/12
Brain Lower Grade Glioma [LGG]	144	80	04/10/12
Breast invasive carcinoma [BRCA]	861	866	04/08/12
Cervical squamous cell carcinoma and endocervical adenocarcinoma [CESC]	99	37	04/12/12
Colon adenocarcinoma [COAD]	423	422	03/26/12
Glioblastoma multiforme [GBM]	598	581	04/09/12
Head and Neck squamous cell carcinoma[HNSC]	312	292	04/13/12
Kidney renal clear cell carcinoma [KIRC]	502	501	04/12/12
Kidney renal papillary cell carcinoma [KIRP]	103	97	04/13/12
Liver hepatocellular carcinoma [LIHC]	84	55	03/24/12
Lung adenocarcinoma [LUAD]	374	351	04/12/12
Lung squamous cell carcinoma [LUSC]	290	283	04/13/12
Lymphoid Neoplasm Diffuse Large B-cell Lymphoma [DLBC]	27	0	04/12/12
Lymphoid Neoplasm Non-Hodgkins Lymphoma [LNNH]	2	0	11/16/11
Ovarian serous cystadenocarcinoma [OV]	597	591	04/13/12
Pancreatic adenocarcinoma [PAAD]	48	38	03/29/12
Prostate adenocarcinoma [PRAD]	153	153	04/13/12



Marina Sirota
Joel Dudley

Lamb J, ..., Golub TR. *Science*, 2006.
Sirota M, Dudley JT, ..., Sweet-Cordero A, Sage J, Butte AJ. *Science Translational Medicine*, 2011.

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Osteoporosis

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Coronary Artery Disease
Hypertension
Ischemia
Myocardial Infarction
Restenosis
Ventricular Tachycardia

Dermatology Models

Acne
Atopic Dermatitis
Hair Growth
Lupus
Psoriasis
Rosacea
Skin Graft
Wound Healing

Diabetes Models

BB/W Rats
Food Intake
Goto-Kakizaki Rats
Non Obese Diabetic Mice
Obese Mice
Primate Diabetes
Streptozotocin Mice
Streptozotocin Rats
More...

Genitourinary Models

Chronic Kidney Disease
Cystometry
Endometriosis
IGA Glomerulonephritis
Interstitial Cystitis
Spinalized Rats

In Vitro Models

In Vitro Bone Models
In Vitro CVD Models
In Vitro Diabetes Models
In Vitro Eye Models
In Vitro Oncology Models
In Vitro Skin Models

In Vivo Technologies

Cognition
EEG
Electrophysiology
Imaging
Microdialysis

Infectious Disease

Bacterial Infection
Dengue Virus
Hepatitis C Virus
Influenza
LCMV Mouse
Malaria

Inflammation Models

Arthritis
Delayed Type Hypersens
Edema
Hemophilia
Irritable Bowel Disease
Irritant
LPS Acute Response
Mucositis
More...

Neurological Models

Alzheimer's Disease
Anxiety
Behavioral Tests
Cerebral Palsy
Circadian Profiling
Depression
Epilepsy
Olfactory Testing
More...

Oncology Models

Angiogenesis
Cachexia

Ophthalmic Models

Cataract
Corneal Dystrophy

Otology Models

Hearing Loss
Meniere's Disease

Pain Models

General Pain
Inflammatory Pain

Respiratory Models

Ascaris Lung Allergy
Cough

ob/ob Diabetes Model - 16 Mice

Service Description

Provider: Links Biosciences is a US company with laboratories in Hangzhou, China. The laboratory has been offering exploratory (non-GLP) pharmacology services to US and Chinese biopharma since 2004.

Background: The obese mutant mouse model was first reported by Ingalls A *et al* from the Jackson Laboratory in 1951 (Obese, a New Mutation in the House Mouse [164 KB]). The obese mouse resulted from a spontaneous mutation in a gene that was named *ob* in the V stock. Mice homozygous for the obese spontaneous mutation, (Lep^ob^; commonly referred to as *ob* or *ob/ob*), are first recognizable at about 4 weeks of age. Homozygous mutant mice gain weight rapidly and may reach three times the weight of wild-type controls. In addition to obesity, mutant mice exhibit hyperphagia, a diabetes-like syndrome of hyperglycemia, glucose intolerance, elevated plasma insulin, subfertility, impaired wound healing, and an increase in hormone production from both pituitary and adrenal glands. Friedman J *et al* reported leptin in 1994, and demonstrated that leptin, the product of the *ob* gene, was produced in white adipose tissue and served as the peripheral signal to the central nervous system of nutritional status.

Service Details: This service offers a 28 day db/db mouse model of T2DM and obesity. Customer has various options that are conveyed to Links Biosciences using a Service Order Form. Customer assigns up to 16 mice to

ob/ob Diabetes Model - 16 Mice

$9,000.00 USD
per service

9 week
turn around time

Provided By
Links Biosciences

Request Info

Add to Cart

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Service Description

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Scroll down to browse a list of available research models for **Type I and Type II diabetes, hyperglycemia, insulin resistance, diet-induced obesity and related diseases**. Use the filters on the left to refine the list and then click on any listing to view technical information or to ask a question.

Click on the Vendors tab to view a complete list of CROs that offer diabetes and obesity pharmacology models.

VIEW SERVICES | VIEW VENDORS | **133 results** get help

Search Filters

Diabetes and Obesity

- BB/W Rats
- Food Intake
- Goto-Kakizaki Rats
- Non Obese Diabetic Mice
- Obese Mice
- Obese Primates
- Primate Diabetes
- Streptozotocin Mice
- Streptozotocin Rats
- db/db Diabetic Mice
- fa/fa Zucker Diabetic Rats

Certifications help

- GLP (48)
- AAALAC (28)
- GMP (20)
- ISO 9001 (7)
- GCP (7)
- FDA (5)
- USDA (4)

more

Locations

United States (64)

Univ. of Maryland School of Medicine Obesity and Diabetes Research Center

University of Maryland School of Medicine Obesity and Diabetes Research Center focuses on research of obesity, diabetes, and aging in nonhuman primates.

vendor info | Add

Transgenic Rabbit Models

Transgenic Rabbit Models offers transgenic rabbit models for the study of atherosclerosis, ophtalmology, hypertrophic myopathies, diabetes, obesity, hemostasis, respiratory diseases, AIDS, and cancer.

vendor info | Add

Ophthy-DS

Ophthy-DS offers ophthalmic model services for macular degeneration, diabetes, uveitis, and dry eye.

vendor info | Add

PharmaNess

PharmaNess offers pharmacokinetics, pharmacodynamics, formulations, behavioral assay, in vivo screening, ex vivo screening, microscopy, stereology and histology staining services.

vendor info | Add

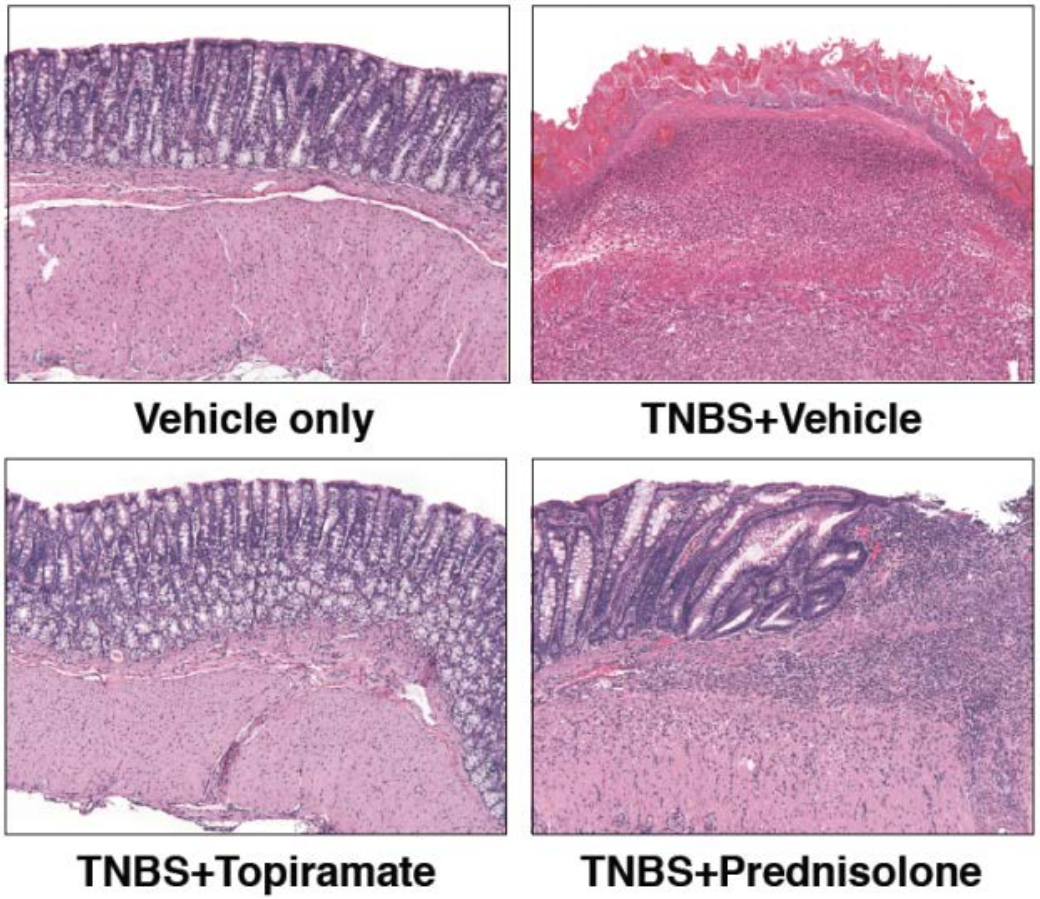
Wisconsin National Primate Research Center

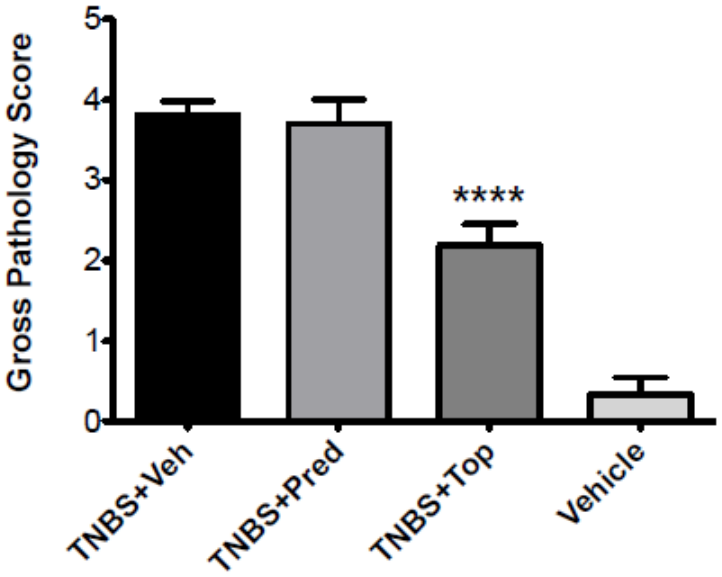
Wisconsin National Primate Research Center focuses on research of regenerative medicine, reproduction, immunology, virology, aging, and metabolic diseases.

vendor info | Add

Selected Vendors

Anti-seizure drug works against a rat model of inflammatory bowel disease





Marina Sirota
Joel Dudley
Mohan M Shenoy
Jay Pasricha

Dudley JT, Sirota M, ..., Pasricha J, Butte AJ. *Science Translational Medicine*, 2011.

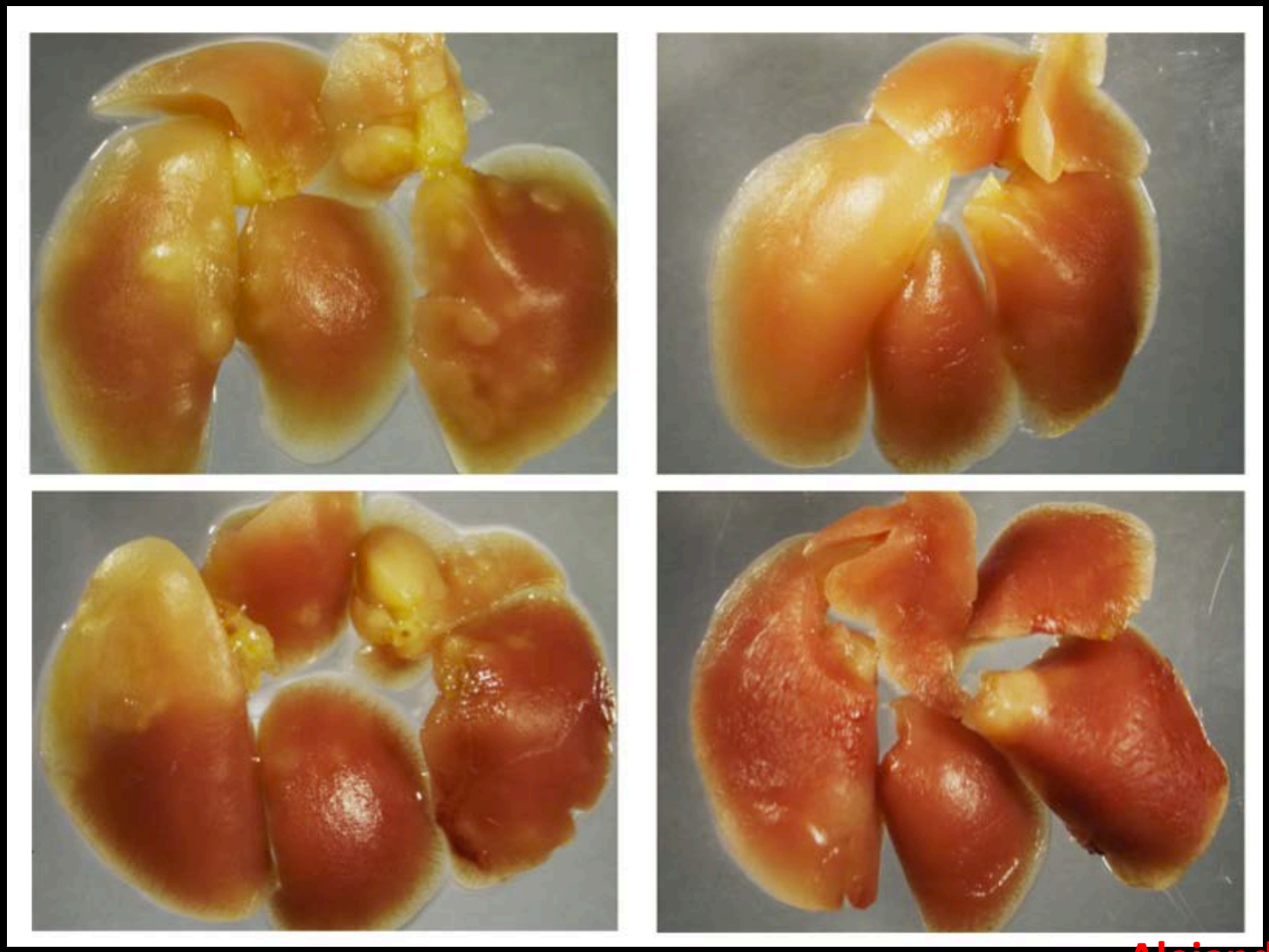
Rat colonoscopy

Rat with Inflammatory Bowel Disease

Inflammatory Bowel Disease After Anti-seizure Drug

Dudley JT, Sirota M, ..., Pasricha J, Butte AJ. *Science Translational Medicine*, 2011.

Drug X Shows Significant Activity Against Small Cell Lung Cancer



Control

Drug X

p53/Rb/p130 triple knockout model of SCLC

Mice dosed after tumor formation

Nadine Jahchan
Joel Dudley
Julien Sage
Joel Neal
Alejandro Sweet-Cordero
NuMedii

NuMedii

Translating Big Data into new medicines

Drug development

NuMedii lands 1st deal to spin drug data into product gold

San Francisco Business Times by Ron Leuty, Reporter

Date: Wednesday, October 3, 2012, 5:30am PDT - Last Modified: Wednesday, October 3, 2012, 6:27am PDT

Ron Leuty
Reporter- *San Francisco Business Times*

NuMedii Inc. is looking to make a big difference in drug development with Big Data.

The Mountain View company co-founded by Stanford University's Atul Butte and his wife, former Affymetrix executive Gini Deshpande, said Wednesday that it inked a deal to help drug developer Aptalis Pharma Inc. find new treatments for gastrointestinal disorders and cystic fibrosis.

Stanford University professor and NuMedii co-founder Atul Butte.

FierceBiotechIT NEWS TOPICS ANALYSIS FEATURES

Topics: Big Data

UPDATED: 'Big Data' startup wins deal with Aptalis Pharma

October 3, 2012 | By Ryan McBride

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NuMedii has landed a deal with Aptalis Pharma in which the Stanford University spinoff will apply its predictive "Big Data" technology. The companies aim to hunt down and advance drugs to combat gastrointestinal ailments and cystic fibrosis, which are two areas of focus at Aptalis. The deal boosts the commercial credentials of NuMedii, building on the startup's role in a pair of papers last year that showed how its computational method could quickly pair approved and generic drugs with new potential uses against diseases.

News

What's Next In Medical Innovation

Using data to find new drug-disease matches wins startup NuMedii its first pharma deal

October 3, 2012 4:02 pm by Deanna Pogorelc | 1 Comments

Pairing existing drugs with new disease applications, using not wet labs but computers, has landed a Stanford startup its first contract with a pharmaceutical company.

ScienceInsider

Breaking news and analysis from the world of science policy

White House Unveils Long-Awaited Public Access Policy

by Jocelyn Kaiser on 22 February 2013, 5:40 PM | 1 Comment

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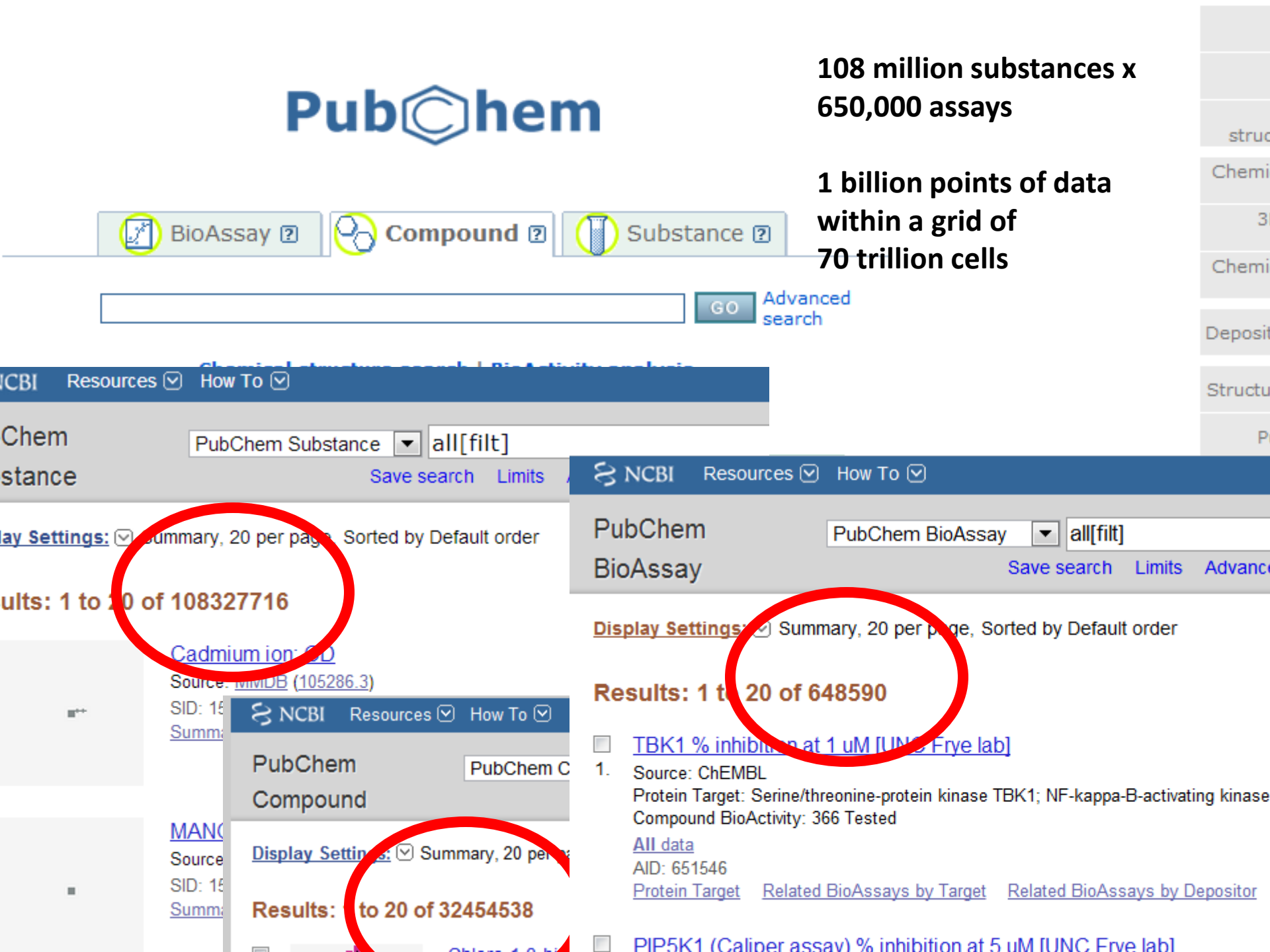
In a victory for open access advocates, the White House science office today released a long-awaited policy aimed at sharing the results of federally funded re
agencies make papers that they fund freely availa

The policy follows several years of consultations a
last year. It appears to have found a middle groun
"open access"—the issue of whether and when s
available, for free, to the public. Traditionally, publi
journals that charge fees for access to the papers
the advent of digital technologies and new researc
resisted complete and immediate open access, a
survive.

John Holdren, Director of the Office of Science and Technology Policy, "has directed Federal agencies with more than $100M in R&D expenditures to develop plans to make the published results of federally funded research freely available to the public within one year of publication and requiring researchers to better account for and manage the digital data resulting from federally funded scientific research."


PubChem
108 million substances x
650,000 assays
1 billion points of data
within a grid of
70 trillion cells
BioAssay
Compound
Substance
GO
Advanced search
NCBI Resources How To
PubChem Substance
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Save search Limits
Summary, 20 per page, Sorted by Default order
Results: 1 to 20 of 108327716
Cadmium ion; CD
Source: MMDB (105286.3)
NCBI Resources How To
PubChem Compound
Results: to 20 of 32454538
NCBI Resources How To
PubChem BioAssay
all[filt]
Save search Limits
Display Settings: Summary, 20 per page, Sorted by Default order
Results: 1 to 20 of 648590
TBK1 % inhibition at 1 uM [UNC Frye lab]
1. Source: ChEMBL
Protein Target: Serine/threonine-protein kinase TBK1; NF-kappa-B-activating kinase
Compound BioActivity: 366 Tested
All data
AID: 651546
Protein Target Related BioAssays by Target Related BioAssays by Depositor
PIP5K1 (Caliper assay) % inhibition at 5 uM [UNC Frye lab]

NIH LINCS PROGRAM

SEARCH SEARCH

Bin Chen

LIBRARY OF INTEGRATED NETWORK-BASED CELLULAR SIGNATURES

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LINCS aims to create a network-based understanding of biology by cataloging changes in gene expression and other cellular processes that occur when cells are exposed to a variety of perturbing agents

LINCS aims to create a network-based understanding of
cataloging changes in gene expression and other cellular
that occur when cells are exposed to a variety of perturbi
and by using computational tools to integrate this diverse
into a comprehensive view of normal and disease states
applied for the development of new biomarkers and thera
generating and making public data that indicates how cel
to various genetic and environmental stressors, the LINC
help us gain a more detailed understanding of cell pathw
efforts to develop therapies that might restore perturbed
and networks to their normal states.

5,178 compounds

- 1,300 off-patent FDA-approved drugs
- 700 bioactive tool compounds
- 2,000+ screening hits (MLPCN and others)

3,712 genes (shRNA + cDNA)

- targets/pathways of FDA-approved drugs (n=900)
- candidate disease genes (n=600)
- community nominations (n=500+)

15 cell types

- Banked primary cell types
- Cancer cell lines
- Primary hTERT immortalized
- Patient derived iPS cells
- 5 community nominated

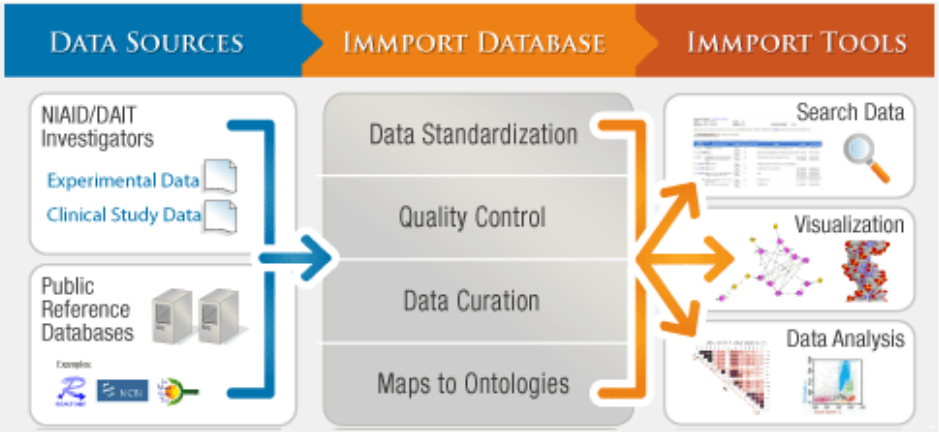
ImmPort

Bioinformatics For The Future of Immunology

About ImmPort

ImmPort, the Immunology Database and Analysis Portal, is a one stop shop to access reference and experiment data for immunologists. ImmPort provides advanced information technology support in the production, analysis, archiving, and exchange of scientific data for the diverse community of life science researchers supported by NIAID/DAIT.

What is ImmPort



Important Notice

We have completed the migration of ImmPort to the NIAID hosted facility. Thank you for your patience during the transition and for finding us at our new home, immport.niaid.nih.gov

Sign In

User Name:

Password:

SIGN IN Forgot Password?

Register for ImmPort

Benefits of Registration:

- Access to data visualization tools
- Compare data sets to other researchers
- Access to data analysis tools

What You Can Do:

Search Data | Visualize Data | Analyze Data

Genes

Access integrated information about genes and their protein products, including structural and functional attributes, biological pathway membership, protein-protein interactions and more.

SNPs

Search the ImmPort Single Nucleotide Polymorphism (SNP) database, a collection of NCBI dbSNP, Entrez Gene and HapMap data.

Pathways

Explore the biological pathways associated with particular genes or proteins using pathway information from KEGG. (BioCarta, Reactome, MGI

MHC Alleles

Find complete DNA and protein sequences, sequence features, and population frequencies of MHC, MIC and TAP alleles. Align MHC sequences to visualize extent of polymorphisms.

ImmPort Gene Lists

View detailed information about immunologically-relevant genes by category. Examine differential gene expression information from immunologically-relevant microarray data sets.

Immune Cells

Learn about immunologically relevant cell types and the surface markers expressed and the cytokines

FlowCAP

Flow Cytometry: Critical Assessment of Population Identification Methods project.

The goal of FlowCAP


National Cancer Institute
The Cancer Genome Atlas
Understanding ge
to improve cance
BY THE NUMBERS
The ENCODE project involved hundreds of people from around the world, and a lot of editing, disk space and phone calls.
32 INSTITUTES
442 CONSORTIUM MEMBERS
CCLE Cancer Cell Line Encyclopedia
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MEDWATCH
NIH LINCS PROGRAM
National Cancer Institute
Surveillance Epidemiology and End Results
providing information on cancer statistics to help reduce the burden of these diseases on the U.S. pop
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BioAssay
Compound
Substance
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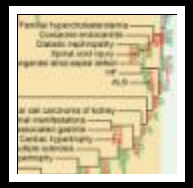
GENOTYPE and PHENOTYPE
PG KB
PharmGKB
GO
Advanced search

Take Home Points

- Big Data is out there: molecular, clinical, individual, epidemiological.
  We can get to new uses for therapeutics.



- More data is always better, but there is a lot to execute on today. Don't wait for perfection.

- Discoveries don't happen automatically. A new generation of investigators will have to "own" and follow these findings through validation.

Collaborators

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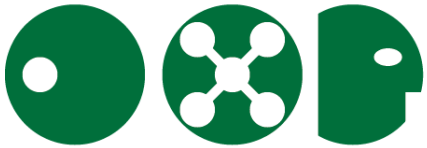

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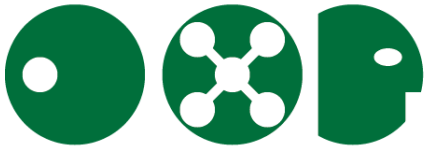

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