UNIVERSITY OF CALIFORNIA

Translating a Trillion Points of Open Data into Diagnostics, Therapies and New Insights in Health and Disease

Atul Butte, MD, PhD

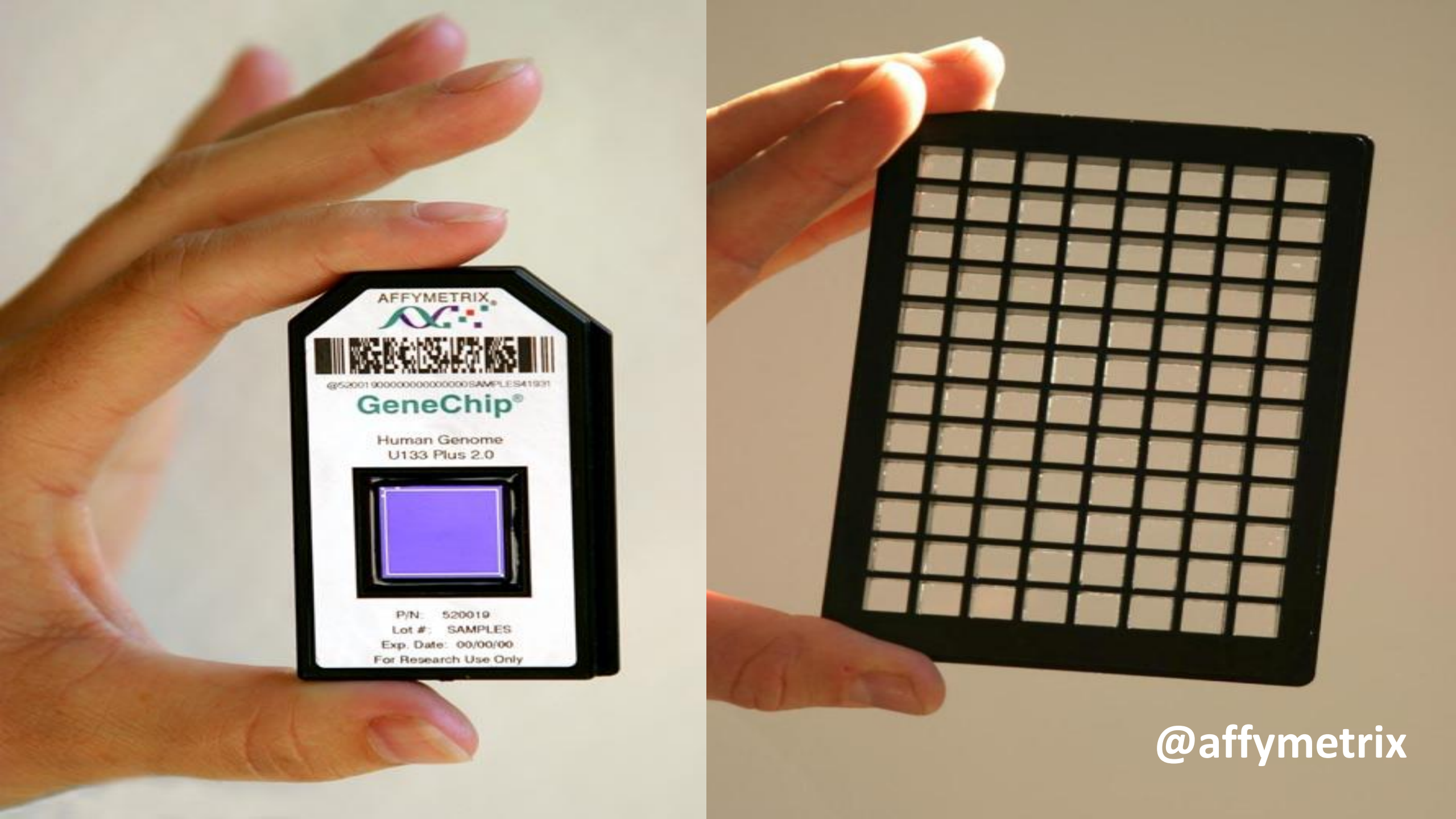
Chief Data Scientist, University of California Health (UC Health)

Director, Bakar Computational Health Sciences Institute, UCSF

Priscilla Chan and Mark Zuckerberg Distinguished Professor

Conflicts of Interest

- Scientific founder and advisory board membership
  - Genstruct
  - NuMedii
  - Personalis
  - Carmenta
- Honoraria for talks
  - Lilly
  - Pfizer
  - Siemens
  - Bristol Myers Squibb
  - AstraZeneca
  - Roche
  - Genentech
  - Warburg Pincus
  - CRG
  - AbbVie
  - Westat
- Past or present consultancy
  - Lilly
  - Johnson and Johnson
  - Roche
  - NuMedii
  - Genstruct
  - Tercica
  - Ecoeos
  - Helix
  - Ansh Labs
  - uBiome
  - Prevendia
  - Samsung
  - Assay Depot
  - Regeneron
  - Verinata
  - Pathway Diagnostics
  - Geisinger Health
  - Covance
  - Wilson Sonsini Goodrich & Rosati
  - Orrick
  - 10X Genomics
  - GNS Healthcare
  - Gerson Lehman Group
  - Coatue Management
- Corporate Relationships
  - Northrop Grumman
  - Genentech
  - Optum
  - Aptalis
  - Allergan
  - Astellas
  - Thomson Reuters
  - Intel
  - SAP
  - SV Angel
  - Progenity
  - Illumina
- Speakers' bureau
  - None
- Companies started by students
  - Carmenta
  - Serendipity
  - Stimulomics
  - NunaHealth
  - Praedicat
  - MyTime
  - Flipora
  - Tumbl.in
  - Polyglot
  - Iota Health
  - Ongevity Health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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 gen… …cly accessible repositories, researchers can identify dise… …ter a laboratory.

BY MONYA BAKER

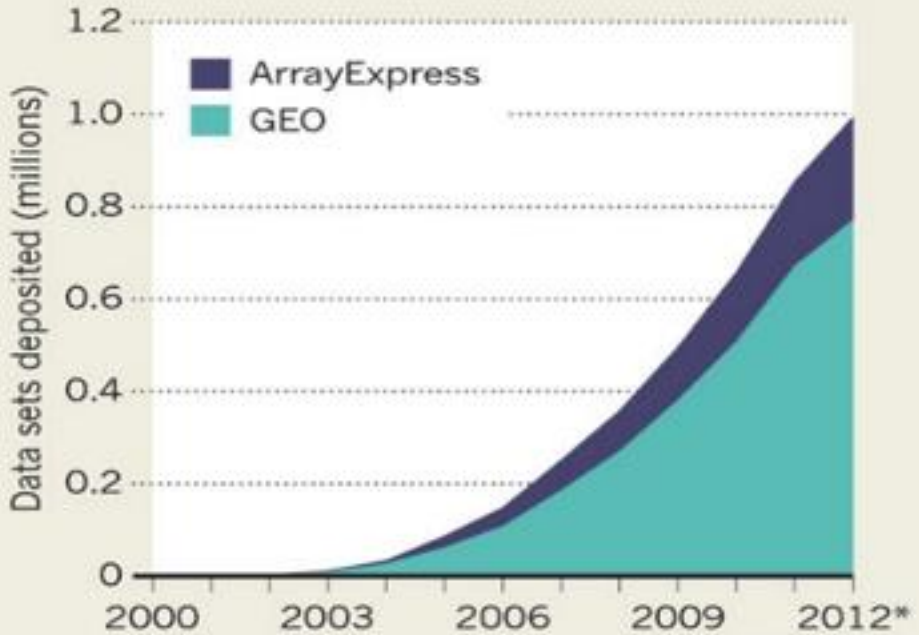
Purvesh Khatri sits in front of an oversize… computer screen, trawling for treasure i… a sea of genetic data. Entering the searc… term 'breast cancer' into a public repositor… called the Gene Expression Omnibus (GEO… the postdoctoral researcher retrieves a list … 1,170 experiments, representing nearly 33,00… samples and a hoard of gene-expression dat… that could reveal previously unseen patterns…

That is exactly the kind of search that le… Khatri's boss, Atul Butte, a bioinformatician … the Stanford School of Medicine in Californi… to identify a new drug target for diabetes. Afte… downloading data from 130 gene-expressio… studies in mice, rats and humans, Butte looke… for genes that were expressed at higher levels i…

…pository at the European Bioinformatics …titute (EBI) in Hinxton, UK. Some time in … next few weeks, the number of deposited …a sets will top one million (see 'Data dump'). …The result is an unprecedented resource that …mises to drive down costs and speed up pro- …ss in understanding disease. Gene-sequence …a are already shared extensively, but expres- …n data are more complex and can reveal …ich genes are the most active in, say, liver …sus brain cells, or in diseased versus healthy …ue. And because studies often look at many

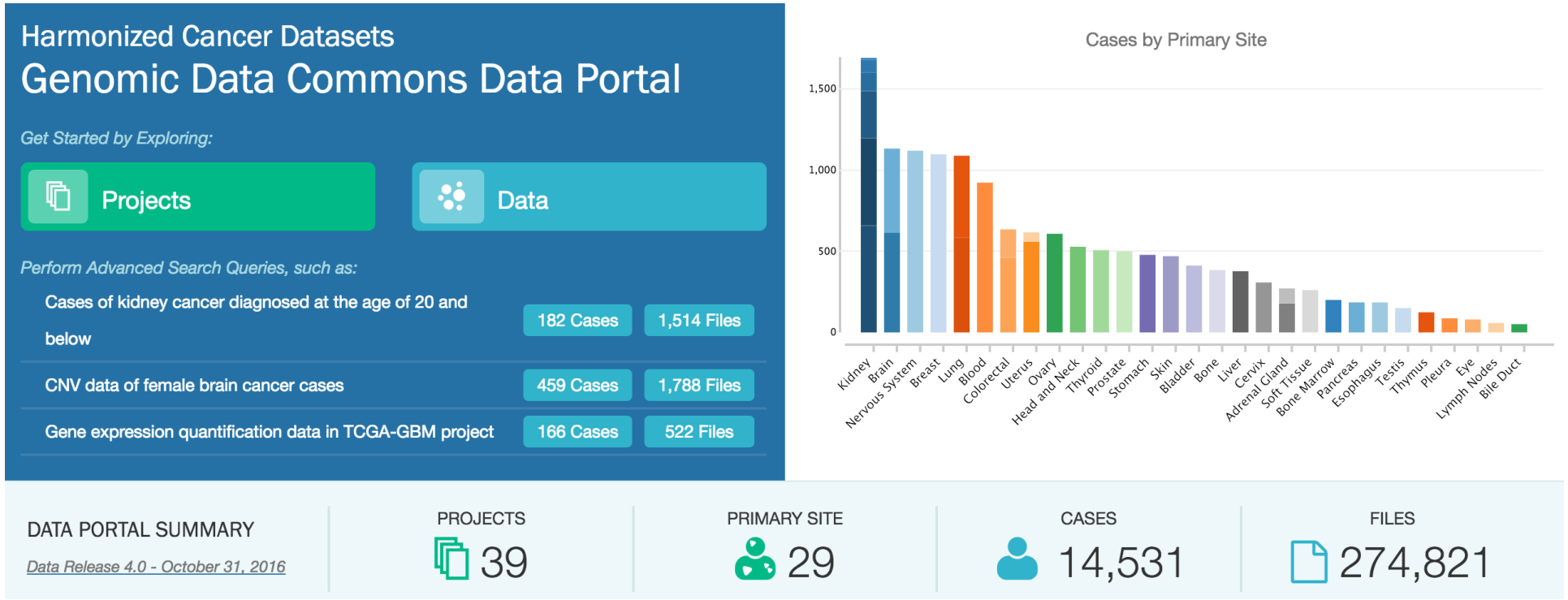
DATA DUMP

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



bit.ly/genedata

Cancer researchers share data



The Cancer Genome Atlas

- 14 thousand cases
- 39 types of cancers
- 13 types of data: molecular, clinical, sequencing

Browse dbGaP

db GaP GENOTYPE and PHENOTYPE

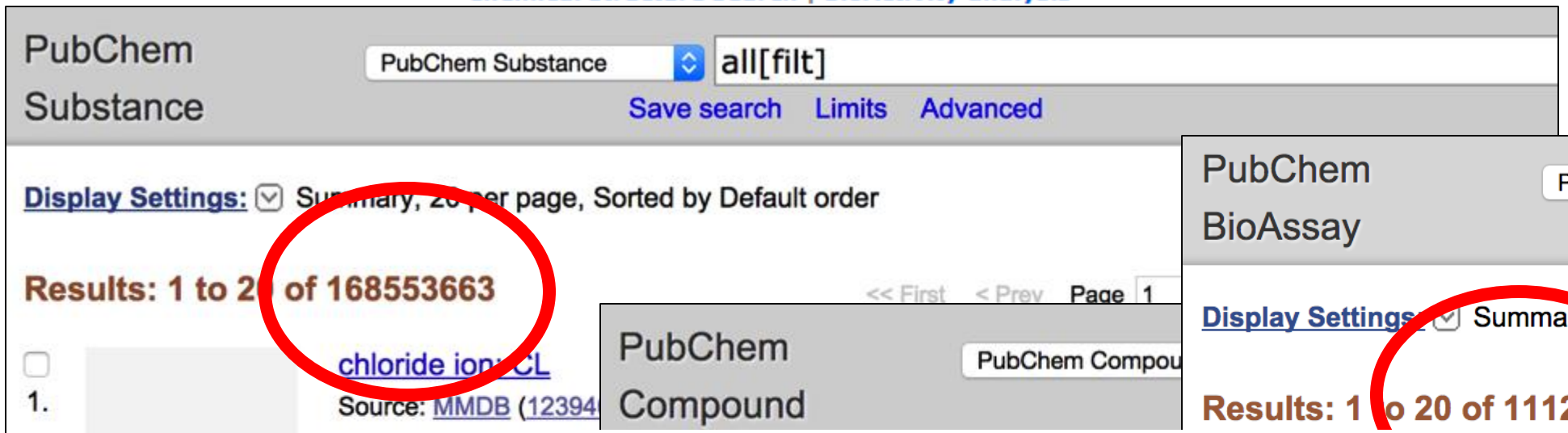
Study	Embargo Release	Details	Participants	Type of Study	Project
CIDR: Genome Wide Association Study in Familial Parkinson Disease (PD)	Feb 13, 2009	V D A	1991	Case-control	CIDR
Framingham SHARe	Version 1: Oct 19, 2008 Version 2: Feb 01, 2009 Version 3: Jul 08, 2009	V D A	14277	Longitudinal	SHARe
GAIN: Collaborative Association Study of Psoriasis	Aug 13, 2008	V D A	2875	Case-control	GAIN
GAIN: Genotyping the 270 HapMap samples for GAIN by Broad		V D A	-	Parent-offspring trios	
GAIN: Genotyping the 270 HapMap samples for GAIN by Perlegen		V D A	-	Parent-offspring trios	
GAIN: International Multi-Center ADHD Genetics Project	Mar 26, 2008	V D A	2835	Parent-offspring trios	GAIN
GAIN: Linking Genome-Wide Association Study of Schizophrenia	Version 1: Nov 07, 2008 Version 2: Dec 03, 2008	V D A	5066	Case-control	GAIN
GAIN: Major Depression: Stage 1 Genomewide Association in Population-Based Samples	Jul 09, 2008	V D A	3741	Case-control	GAIN
GAIN: Search for Susceptibility Genes for Diabetic Nephropathy in Type 1 Diabetes	Jul 09, 2008	V D A	1825	Case-control	GAIN
GAIN: Whole Genome Association Study of Bipolar Disorder	Version 1: Nov 25, 2008 Version 2: Dec 01, 2008	V D A	3261	Case-control	GAIN
GAW16 Framingham and Simulated Data	Oct 19, 2008	V D A	7130	Longitudinal, population-based	SHARe
Genome-wide Association Studies in the Hutterites		V D A	632	Population-based	University of Chicago
Genome-wide Association Study of Neuroblastoma		V D A	1032	Case-control	COG
Genome-wide Study in Amyotrophic Lateral Sclerosis and Controls: First Stage Analysis	Jun 26, 2008	V D A	544	Case-control	NINDS
Ischemic Stroke Genetics Study (ISGS)	Jun 26, 2008	V D A	485	Case-control	NINDS
Mayo-Perlegen LEAPS (Linked Efforts to Accelerate Parkinson's Solutions) Collaboration	Mar 03, 2008	V D A	1550	Case-control	MJFF
NEI Age-Related Eye Disease Study (AREDS)	Jun 11, 2007	V D A	600	Case-control	NEI
NINDS Parkinson's Disease	Oct 12, 2007	V D A	535	Case-control	NINDS
NINDS Parkinsonism Study	Oct 12, 2007	V D A	1283	Case-set	NINDS
NINDS Repository Cerebrovascular Disease/Stroke Study	Jun 26, 2008	V D A	870	Case-set	NINDS
NIND				Case-set	NINDS
NIND				Control-set	NINDS
POP				ulation samples, Control-set	NHGRI
SEARCH GWA Study of Statin-Induced Myopathy		V D A	175	Case-control	University of Oxford
Study of Irish Amyotrophic Lateral Sclerosis (SIALS)		V D A	432	Case-control	NINDS
The Finland-United States Investigation of NIDDM Genetics (FUSION) study		V D A	2335	Case-control	University of Michigan
Whole Genome Association Study of Systemic Lupus Erythematosus		V D A	4651	Case-control	

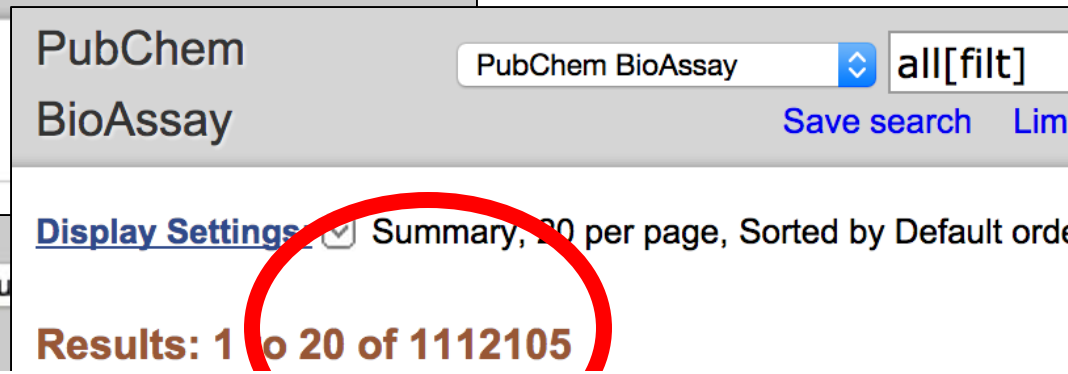
Genetics researchers share data

170 million substances x
1.1 million assays

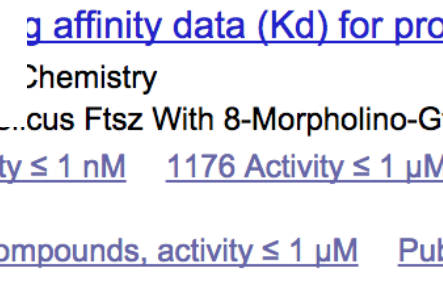
More than a billion measurements within a grid of 190 trillion cells

122 million meet Lipinski 5
1 million active substances



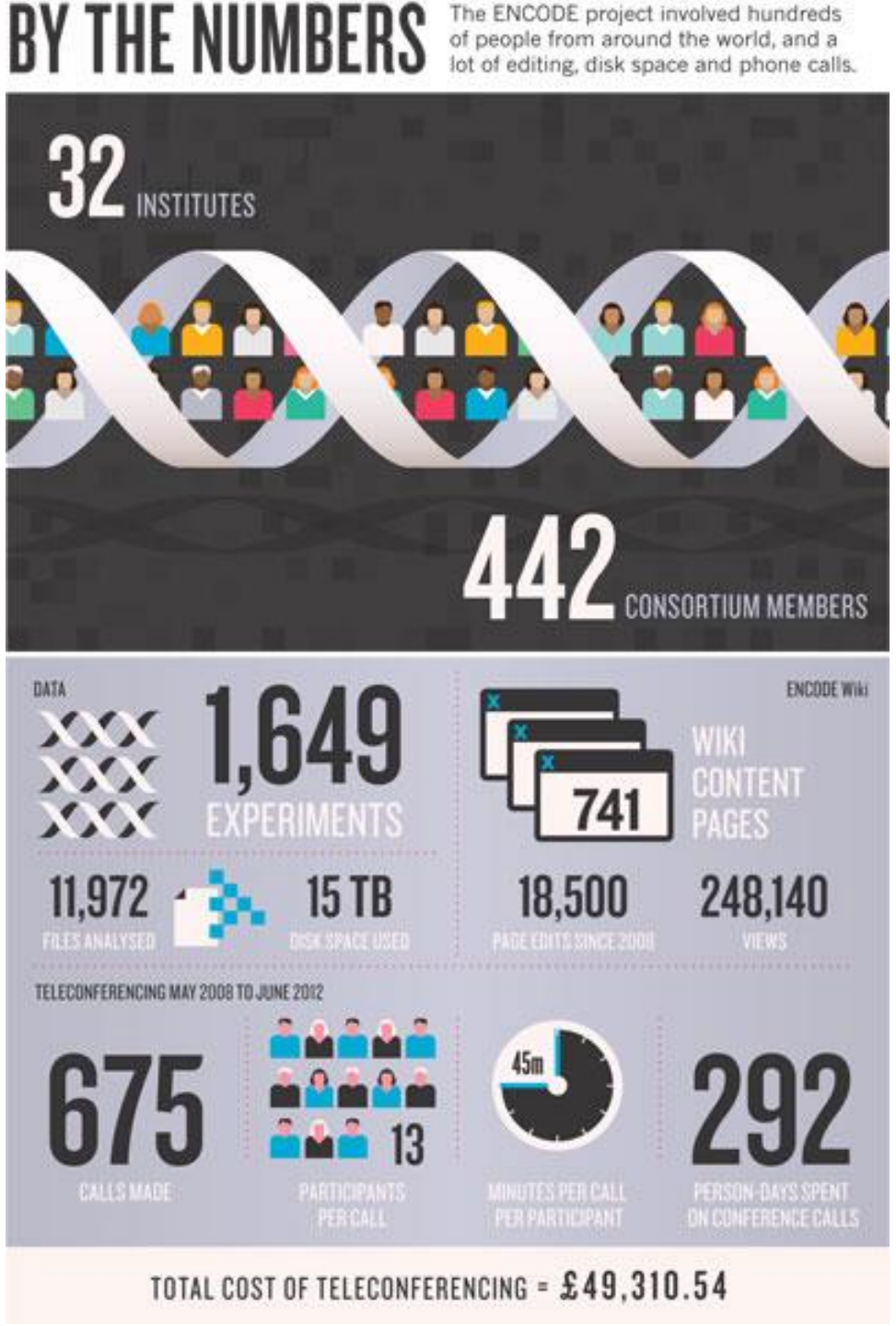


Chemical biologists share data



ENCODE

Molecular biologists share data



immport.org

Yes, clinical trialists can share data!

Download 300+ studies today

Clinical trials, new patient subsets, digital comparative effectiveness, more

Sanchita Bhattacharya
Elizabeth Thomson

NORTHROP GRUMMAN

UCSF

NIH National Institute of Allergy and Infectious Diseases

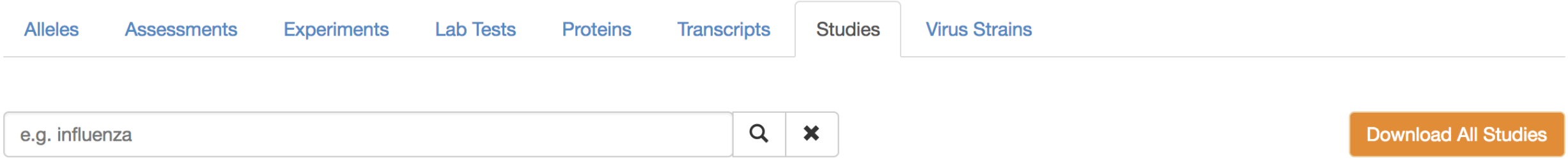
march of dimes

BILL & MELINDA GATES foundation

IMMPORT Shared Data

Your site for searching and downloading shared data

ImmPort Shared Data enables searching and downloa
funded from NIAID DAIT and DMID, other NIH age
Additional resources include step-by-step data reuse
analysis code, the Cell Ontology Visualizer, the Cyto
reference dataset for human immunology and Imm
interaction literature mining tool.



IMPROVING THE EFFICIENCY AND EFFECTIVENESS OF GENOMIC SCIENCE TRANSLATION

WORKSHOP SUMMARY

DRUG REPURPOSING AND REPOSITIONING

WORKSHOP SUMMARY

Olson, and

Sharing Clinical Trial Data

MAXIMIZING BENEFITS, MINIMIZING RISK

Committee on Strategies for Responsible Sharing of Clinical Trial Data

Board on Health Sciences Policy

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

clinical trial data submitted to the agency[3] once a marketing decision on the study products has been made (EMA, 2014).

- The AllTrials campaign was launched, calling for "all past and present clinical trials to be registered and their full methods and summary results reported" (AllTrials, 2013). As of December 2014, more than 81,000 people had signed the AllTrials petition, and 532 organizations had joined AllTrials (AllTrials, 2014).
- Astellas, Bayer, Boehringer Ingelheim, GlaxoSmithKline, Lilly, Novartis, Roche, Sanofi, Takeda, UCB, and ViiV Healthcare committed to sharing clinical trial data through ClinicalStudyDataRequest.com and allowing an independent review panel to make decisions on data requests (ClinicalStudyDataRequest.com, 2014).
- The *British Medical Journal* issued a policy requiring data sharing for clinical trials it publishes (BMJ, 2013).
- The Pharmaceutical Research and Manufacturers of America (PhRMA), the European Federation of Pharmaceutical Industries and Associations (EFPIA), and the Biotechnology Industry Organization (BIO) released principles documents signaling their support for sharing clinical trial data (BIO, 2014; PhRMA, 2013).
- The National Institute of Allergy and Infectious Diseases (NIAID) made de-identified data from 11 clinical trials available through the Immunology Database and Analysis Portal (ImmPort) (ImmPort, 2013).
- NIH issued a new policy on sharing of genomic data. The new policy outlines and emphasizes the expectation that investigators will obtain informed consent from study participants for potential future use of the participants' de-identified data for both research and broad sharing, and commit to sharing data no later than the date of first publication of the study results (NIH, 2014).

Numerous approaches and models for sharing clinical trial data are being implemented with varying levels of access control. At one end of the spectrum, ImmPort in the United States and the FreeBIRD website (FreeBIRD, 2014) in the United Kingdom make available some de-identified data sets from publicly funded clinical trials (NIAID and CRASH trials, respectively) with minimal restrictions; the data sets can be downloaded from the Web upon registration and acceptance of their terms

provide the data to an academic institution, whereupon that institution becomes the entity that discloses the data.

The term "adversary" is often used in the disclosure control literature to refer to the role of the individual or entity that is trying to re-identify data subjects. Other terms used are "attacker" and "intruder." Discussions about the QI being a potential adversary are not intended to paint QIs as having malicious objectives. Rather, in the context of a risk assessment, one must consider a number of possible data recipients as being potential adversaries and manage the re-identification risk accordingly.

Data Sharing Models

A number of different ways to provide access to IPD have been proposed and used, each with different advantages and risks (Mello et al., 2013). First, there is the traditional public data release where anyone can get access to the data with no registration or conditions. Examples of such releases include the publicly available clinical trial data from the International Stroke Trial (IST) (Sandercock et al., 2011) and data posted to the Dryad online open access data repository (Dryad, undated; Haggie, 2013).

A second form of data sharing, which is more restrictive, occurs when there exists a formal request and approval process to obtain access to clinical trial data, such as the GlaxoSmithKline (GSK) trials repository (Harrison, 2012; Nisen and Rockhold, 2013); Project Data Sphere (whose focus is on oncology trial data) (Bhattacharjee, 2012; Hede, 2013); the Yale University Open Data Access (YODA) Project, which is initially making trial data from Medtronic available (CORE, 2014; Krumholz and Ross, 2011); and the Immunology Database and Analysis Portal (ImmPort, n.d.), which is restricted to researchers funded by the Division of Allergy, Immunology, and Transplantation of the National Institute of Allergy and Infectious Diseases (DAIT/NIAID), other approved life science researchers, National Institutes of Health employees, and other preauthorized government employees (ImmPort, n.d.). More recently, pharmaceutical companies have created the ClinicalStudyDataRequest.com website, which facilitates data requests to multiple companies under one portal. Following this restrictive model, a request can be processed by the study sponsor or by a delegate of the sponsor (e.g., an academic institution).

A hybrid of the above approaches is a quasi-public release, in which

10 reasons to share study data openly

- Reproducibility
- Transparency
- Support public policy
- Return data to the community
- Visibility into failed trials
- Speed results reporting
- Enable learning
- Enable new ventures
- New science
- Trust and Believability

Reproducibility

Repeatability of published microarray gene expression analyses

John P A Ioannidis[1–3], David B A
Mario Falchi[8,9], Cesare Furlanell
Michael Nitzberg[5], Grier P Page[4]

Given the complexity of microarray-l
studies, guidelines er
data availability. Sev
and several public da
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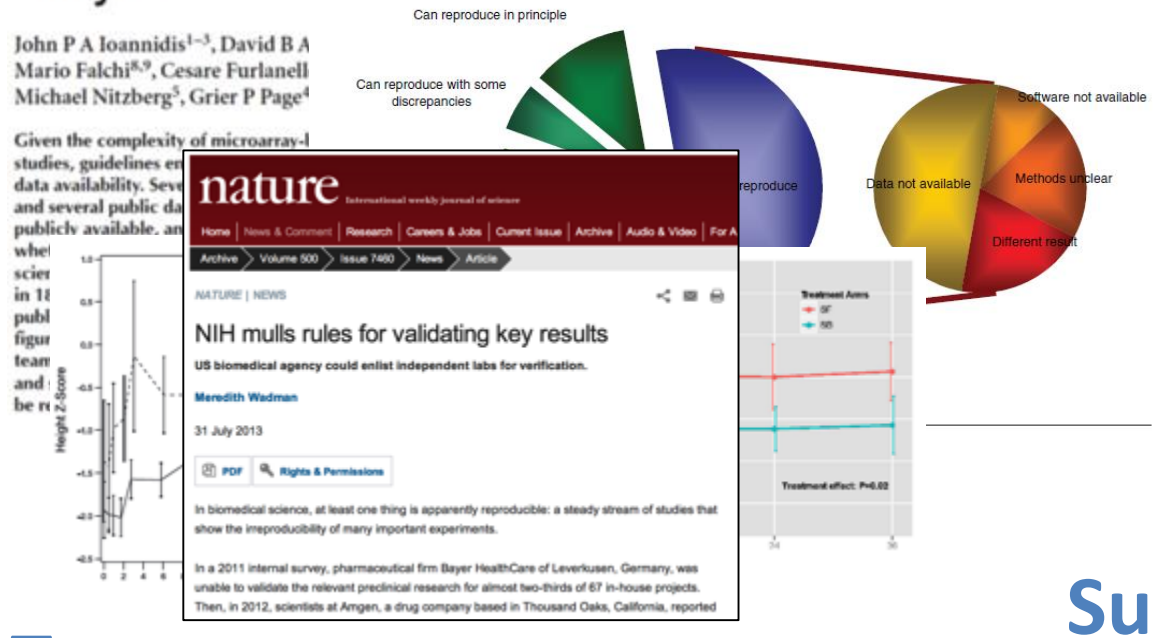

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International weekly journal of science
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NATURE | NEWS

NIH mulls rules for validating key results

US biomedical agency could enlist independent labs for verification.

Meredith Wadman

31 July 2013

PDF | Rights & Permissions

In biomedical science, at least one thing is apparently reproducible: a steady stream of studies that show the irreproducibility of many important experiments.

In a 2011 internal survey, pharmaceutical firm Bayer HealthCare of Leverkusen, Germany, was unable to validate the relevant preclinical research for almost two-thirds of 67 in-house projects. Then, in 2012, scientists at Amgen, a drug company based in Thousand Oaks, California, reported

Return data to the community

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The Scientist » Magazine » Features

Do-It-Yourself Medicine

**Patients are sidestepping clinical research and using themselves as guinea pi
treatments for fatal diseases. Will they hurt themselves, or science?**

By Jef Akst | March 1, 2013

9 Comments | Like 270 | Pin it 3 | +1 17 | Link this

On August 10,
Butler dilute
percent sodium ch
slightly salted wat
injected 1 liter of t

Transparency

Evolution of Translational Omics: Lessons Learned and the Path Forward

EVOLUTION OF TRANSLATIONAL
OMICS
Lessons Learned and the Path Forward

Committee on the Review of Omics-Based Tests for Predicting Patient Outcomes in Clinical Trials

Board on Health Care Services

Board on Health Sciences Policy

code — in protecting patient confidentiality, for example. In such cases, authors should justify the omission and assure independent reproducibility by alternative means.

The quality of scientific output will benefit from setting these standards. As a community, we owe it to patients and to the public to do what we can to ensure the validity of the research we publish.

Keith Baggerly *on behalf of 7 co-authors*, The University of Texas MD Anderson Cancer*

Support public policy

BMJ

BMJ 2013;346:f2157 doi: 10.1136/bmj.f2157 (Published 4 April 2013) Page 1 of 2

NEWS

Roche offers researchers access to all Tamiflu trials

Deborah Cohen

BMJ

More than three years after the Cochrane Collaboration first asked Roche for the full clinical study reports for its influenza drug oseltamivir (Tamiflu), the Swiss company has offered the

follows that regulators were in the same situation as we were: lacking data to come to firm conclusions."

Visibility into failed trials

BMJ

RESEARCH

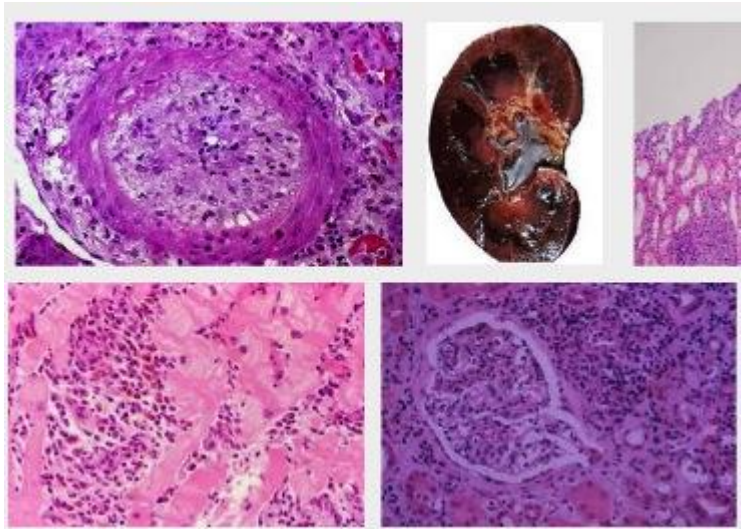
BMJ 2013;347:f6104 doi: 10.1136/bmj.f6104 (Published 29 October 2013)

Non-publication of large randomized clinical trials: cross sectional analysis

OPEN ACCESS

Christopher W Jones *attending physician*[1], Lara Handler *school of medicine liaison librarian*[2], Karen E Crowell *clinical information specialist*[2], Lukas G Keil *research assistant*[3], Mark A Weaver *assistant professor*[4], Timothy F Platts-Mills *assistant professor*[3]

Enable learning



Speed results reporting

Scientists voice fears over ethics of drug trials remaining unpublished

Almost a third of large clinical trials in the US still not published five years after being finished, scientists write in BMJ

Sarah Boseley
The Guardian, Tuesday 29 October 2013 19.30 EDT

Enable new ventures

NEXTBIO
now part of Illumina

Pathwork Diagnostics

All the world's genomic data

NHS National Institute for Health Research

Welcome to the UK Clinical Trials Gateway

New Science

nature genetics

ANALYSIS

An APOBEC cytidine deaminase mutagenesis pattern widespread in human cancers

Steven A Roberts[1], Michael S Lawrence[2], Leszek J Klimczak[3], Sara A Grimm[3], David Fargo[3], Petar Stojano
Adam Kiezun[2], Gregory V Kryukov[2,4], Scott L Carter[2], Gordon Saksena[2], Shawn Harris[5],
Ruchir R Shah[5], Michael A Resnick[1], Gad Getz[2,6–8] & Dmitry A Gordenin[1,8]

Recent studies indicate that a subclass of APOBEC cytidine deaminases, which convert cytosine to uracil during RNA editing and retrovirus or retrotransposon restriction, may induce mutation clusters in human tumors. We show here that throughout cancer genomes APOBEC-mediated mutagenesis is pervasive and correlates with APOBEC mRNA levels. Mutation clusters in whole-genome and exome
to the stringent criteria indicative of a
pattern. Applying these criteria to 954
exomes from 14 cancer types, mostly
Atlas (TCGA), showed a significant pr
mutation pattern in bladder, cervical,
and lung cancers, reaching 68% of all
samples. Within breast cancer, the HE
was clearly enriched for tumors with t
pattern, suggesting that this type of m
linked with cancer development. The
pattern also extended to cancer-associ
ubiquitous APOBEC-mediated mutage

Genome instability triggers the develo
cancers[1,2]. Radiation and chemical dama
as culprits in theories of carcinogeni
normal enzymatic activities can also be
and mutation. Cytidine deaminases, wh
to uracil, likely contribute to DNA da
cytidine deaminase (AID), a key enzyme
only initiates the hypermutation and cla
immunoglobulin genes but also can mu
a limited number of secondary targets,

implicated in carcinogenesis[5]. In addition to AID, the human
encodes several homologous APOBEC (apolipoprotein B
editing enzyme, catalytic polypeptide-like) cytidine deamin
function in innate immunity as well as in RNA editing[6].
human cell culture studies showed that a subclass of APOB
mutational specificity for TC motifs (with the mutated bas

[1]Laboratory of Molecular Genetics, National Insti
Sciences, Durham, North Carolina, USA. [2]The Br
Harvard, Cambridge, Massachusetts, USA. [3]Integ
Institute of Environmental Health Sciences, Durh
[4]Harvard Medical School, Boston, Massachusetts
Durham, North Carolina, USA. [6]Massachusetts G
Boston, Massachusetts, USA. [7]Department of Pa
Hospital, Boston, Massachusetts, USA. [8]These a
work. Correspondence should be addressed to D.A
G.G. (gadgetz@broadinstitute.org).

Received 28 January; accepted 20 June; publish
doi:10.1038/ng.2702

Methods

Abstract • Introduction • Results • Discussion • Methods • References • Acknowledgments • Author information • Supplementary information

Genome and exome data sets.

Genome and exome data sets were obtained from publications[20, 21] or from the TCGA data portal (see URLs; Controlled Data Access HTTP Directory). The catalog of base substitutions identified by whole-genome sequencing in 21 breast cancers was downloaded from the website provided in ref. 12 (seeURLs).

Hyperlinks to TCGA data sets and references to published mutation lists are provided in Supplementary Table 3.

Cluster analysis.

Clusters and colocalization between clusters and rearrangement breakpoints in whole-genome data sets were identified as described in ref. 13. Analysis of mutation clustering in exomes was conducted similarly to that in whole-genome data sets. Briefly, we first filtered out mutations identical to variants in dbSNP. These SNPs generally constituted a small percentage (0.9–12.1%) of all exome mutations for a given cancer type. However, LUSC, KIRC, PRAD and STAD samples contained somewhat higher numbers of mutations identical to variants in dbSNP (19.5–25.1%). Notably, each prefiltered mutation was included in the total number of mutations in the genome, which would thereby only increase the *P* values of clusters. We next identified groups of closely

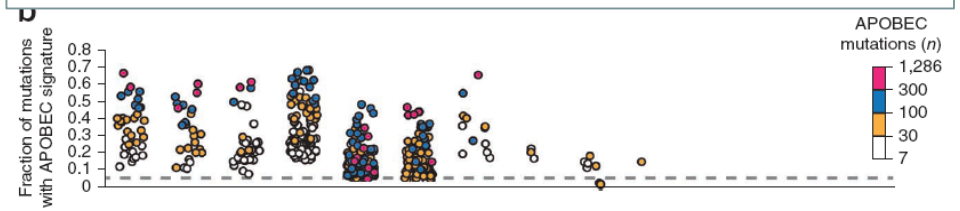
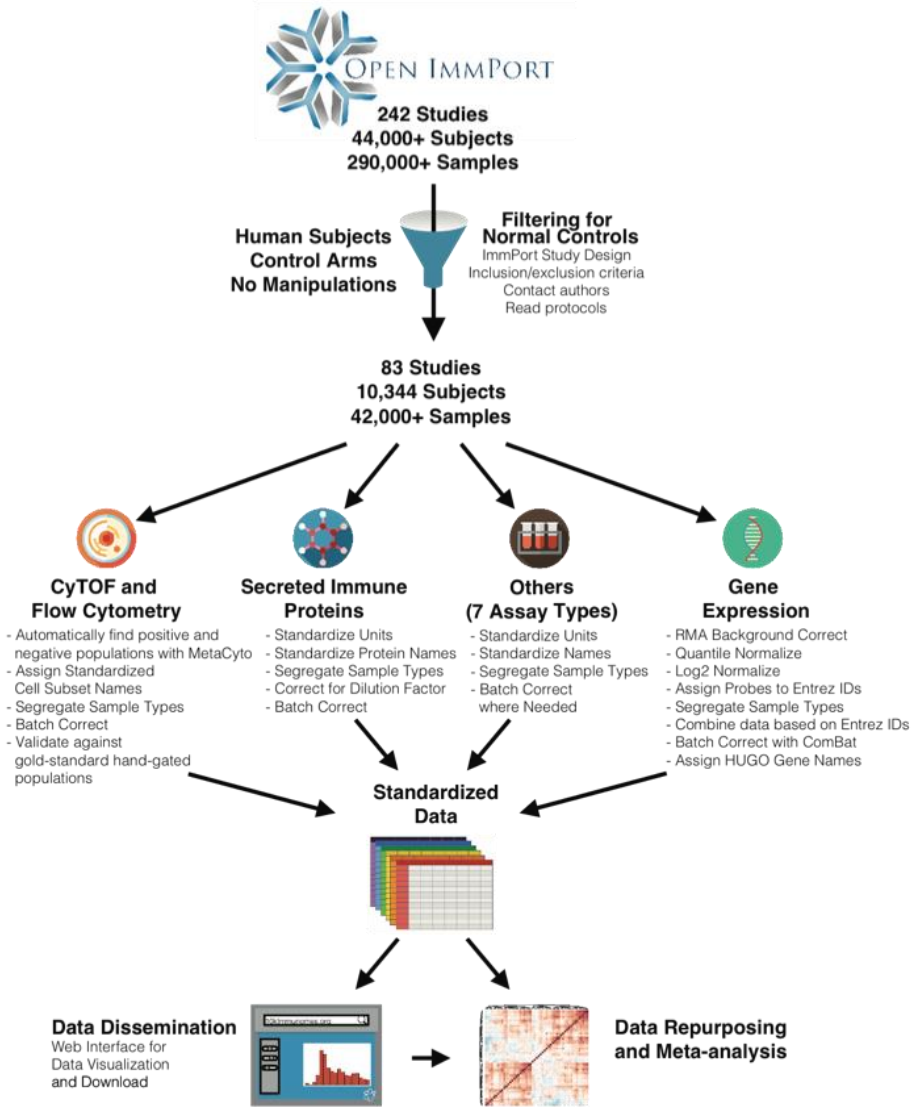
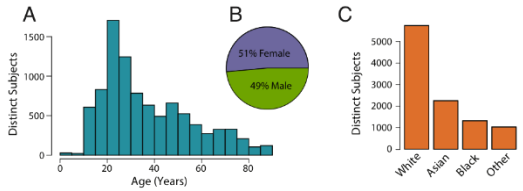


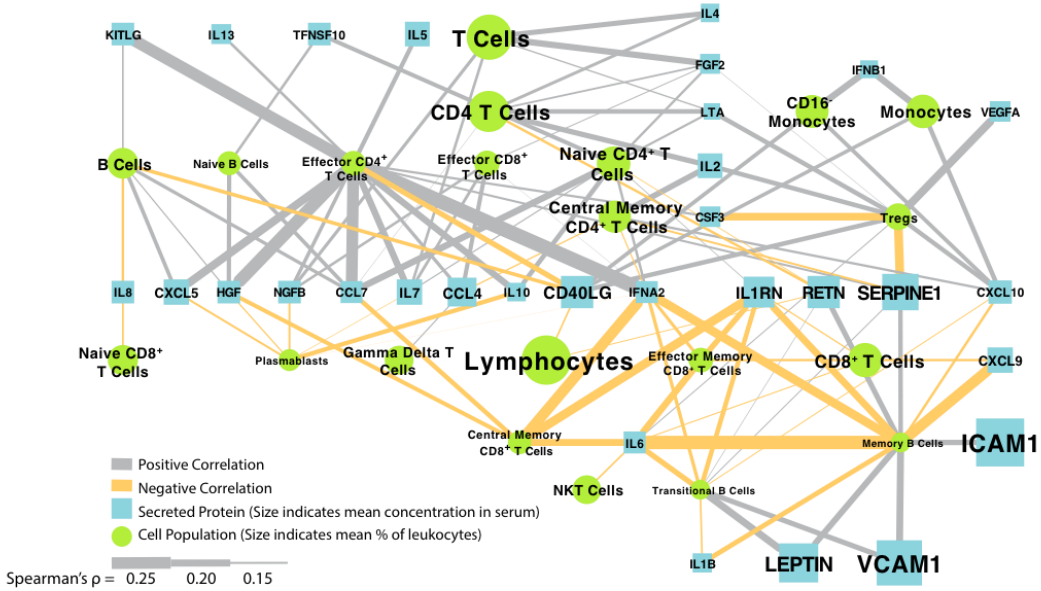
Figure 2 Presence of an APOBEC mutation pattern in exome data sets from different cancer types. (**a**,**b**) Fold enrichment (**a**) and mutation load (**b**) of the APOBEC mutation pattern were determined in each of 2,680 whole exome–sequenced tumors representing 14 cancer types. Samples were categorized by the statistical significance of the APOBEC mutation pattern and the magnitude of enrichment. The significance of the APOBEC mutation pattern was calculated by one-sided Fisher's exact test comparing the ratio of the number of C-to-T or C-to-G substitutions and complementary G-to-A or G-to-C substitutions that occur in and out of the APOBEC target motif (TCW or WGA) to an analogous ratio for all cytosines or guanines that reside inside and outside of the TCW or WGA motif within a sample fraction of the genome (Benjamini-Hochberg–corrected q value < 0.05). The number of tumor samples in each category is presented in each pie chart in **a**. Samples with q value > 0.05 are represented in black. These samples are excluded from the scatter graphs in **a**,**b**. Color scales indicate the magnitude of enrichment in **a** and the number of APOBEC signature mutations in **b** for samples with $q < 0.05$. Dashed lines indicate effects expected with random mutagenesis. Cancer types are abbreviated as in TCGA: cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), bladder urothelial carcinoma (BLCA), head and neck squamous cell carcinoma (HNSC), breast invasive carcinoma (BRCA), lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), uterine corpus endometrioid carcinoma (UCEC), ovarian serous cystadenocarcinoma (OV), stomach adenocarcinoma (STAD), rectum adenocarcinoma (READ), colon adenocarcinoma (COAD), prostate adenocarcinoma (PRAD), kidney renal clear-cell carcinoma (KIRC) and acute myeloid leukemia (LAML).

The 10,000 Immunome Project: From the control groups of 242 manually curated experiments





Data available in the 10,000 Immunomes Project	
Total Samples	**42117**
Total Distinct Subjects	**10344**
MEASUREMENT	**SUBJECTS**
Secreted Proteins	4835
ELISA	4035
Multiplex ELISA	1286
Virus Titer	3609
Virus Neutralization Titer	2265
HAI Titer	1344
Clinical Lab Tests	2639
Complete Blood Count	1684
Comprehensive Metabolic Panel	664
Fasting Lipid Profile	664
Questionnaire	1422
Cytometry	1415
Flow Cytometry (PBMC)	907
CyTOF (PBMC)	583
Flow Cytometry (Whole Blood)	164
HLA Type	1093
Gene Expression Array	476
Whole Blood	311
PBMC	165



Kelly Zalocusky
Sanchita Bhattacharya
@ImmPortDB

bit.ly/10kimpdf
http://10kimmunomes.org/

Share successful, failed, and so-so data

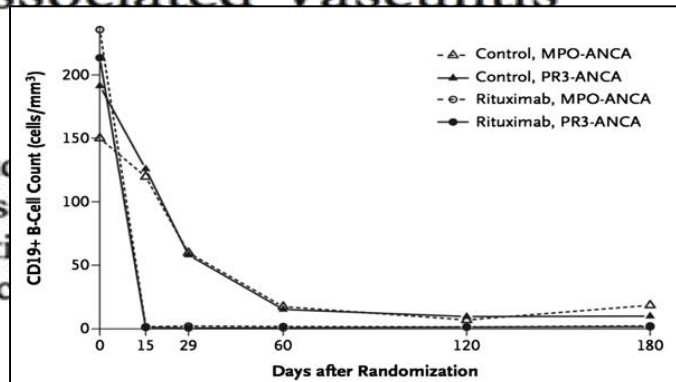
- Rituximab in ANCA-Associated Vasculitis (RAVE) trial of new approach to the induction of remission
- But even though rituximab was found to be non-inferior than cyclophosphamide, which drug is the right one to use?

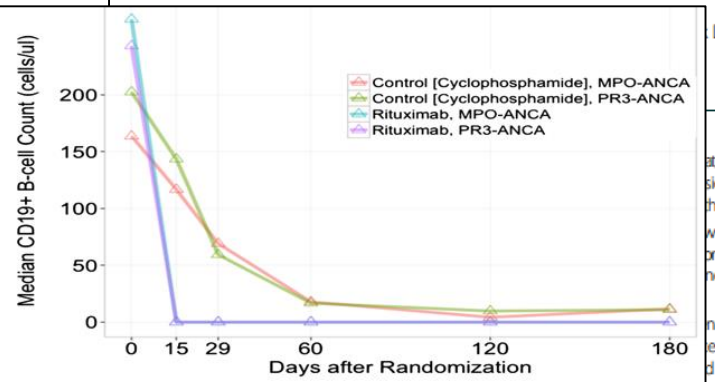
ORIGINAL ARTICLE

Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis

CONCLUSIONS

Rituximab therapy was not inferior t
tion of remission in severe ANCA-as
lapsing disease. (Funded by the Nati
eases, Genentech, and Biogen; Clinic





Nasrallah et al. Arthritis Research & Therapy (2015) 17:262
DOI 10.1186/s13075-015-0778-z

arthritis research&therapy

RESEARCH ARTICLE Open Access

Reanalysis of the Rituximab in ANCA-Associated Vasculitis trial identifies granulocyte subsets as a novel early marker of successful treatment

Dunn[5], Elizabeth Thomson[5], Jeffrey Wiser[5]

atients with anti-neutrophil cytoplasmic antibody
sion at 6 months following rituximab or
he Rituximab in ANCA-Associated Vasculitis (RAVE) trial.
wnloaded from the Immunology Database and
ories. Flow cytometry data were analyzed using
nd granulocyte populations were measured in patients

nt outcome with either treatment. We defined a
entage of hypergranular and hypogranular
d remission had a significantly higher GI at baseline

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Once-Daily Plazomicin for Complicated Urinary Tract Infections

Florian M.E. Wagenlehner, M.D., Daniel J. Cloutier, Pharm.D., Allison S. Komirenko, Pharm.D., Deborah S. Cebrik, M.S., M.P.H., Kevin M. Krause, M.B.A., Tiffany R. Keepers, Ph.D., Lynn E. Connolly, M.D., Ph.D., Loren G. Miller, M.D., M.P.H., Ian Friedland, M.D., and Jamie P. Dwyer, M.D., for the EPIC Study Group*

ABSTRACT

BACKGROUND

The increasing multidrug resistance among gram-negative uropathogens necessitates new treatments for serious infections. Plazomicin is an aminoglycoside with bactericidal activity against multidrug-resistant (including carbapenem-resistant) Enterobacteriaceae.

METHODS

We randomly assigned 609 patients with complicated urinary tract infections (UTIs), including acute pyelonephritis, in a 1:1 ratio to receive intravenous plazomicin (15 mg per kilogram of body weight once daily) or meropenem (1 g every 8 hours), with optional oral step-down therapy after at least 4 days of intravenous therapy, for a total of 7 to 10 days of therapy. The primary objective was to show the noninferiority of plazomicin to meropenem in the treatment of complicated UTIs, including acute pyelonephritis, with a noninferiority margin of 15 percentage points. The primary end points were composite cure (clinical cure and microbiologic eradication) at day 5 and at the test-of-cure visit (15 to 19 days after initiation of therapy) in the microbiologic modified intention-to-treat population.

RESULTS

Plazomicin was noninferior to meropenem with respect to the primary efficacy end points. At day 5, composite cure was observed in 88.0% of the patients (168 of 191 patients) in the plazomicin group and in 91.4% (180 of 197 patients) in the meropenem group (difference, –3.4 percentage points; 95% confidence interval [CI], –10.0 to 3.1). At the test-of-cure visit, composite cure was observed in 81.7% (156 of 191 patients) and 70.1% (138 of 197 patients), respectively (difference, 11.6 percentage points; 95% CI, 2.7 to 20.3). At the test-of-cure visit, a higher percentage of patients in the plazomicin group than in the meropenem group were found to have microbiologic eradication, including eradication of Enterobacteriaceae that were not susceptible to aminoglycosides (78.8% vs. 68.6%) and Enterobacteriaceae that produce extended-spectrum β-lactamases (82.4% vs. 75.0%). At late follow-up (24 to 32 days after initiation of therapy), fewer patients in the plazomicin group than in the meropenem group had microbiologic recurrence (3.7% vs. 8.1%) or clinical relapse (1.6% vs. 7.1%). Increases in serum creatinine levels of 0.5 mg or more per deciliter (≥40 μmol per liter) above baseline occurred in 7.0% of patients in the plazomicin group and in 4.0% in the meropenem group.

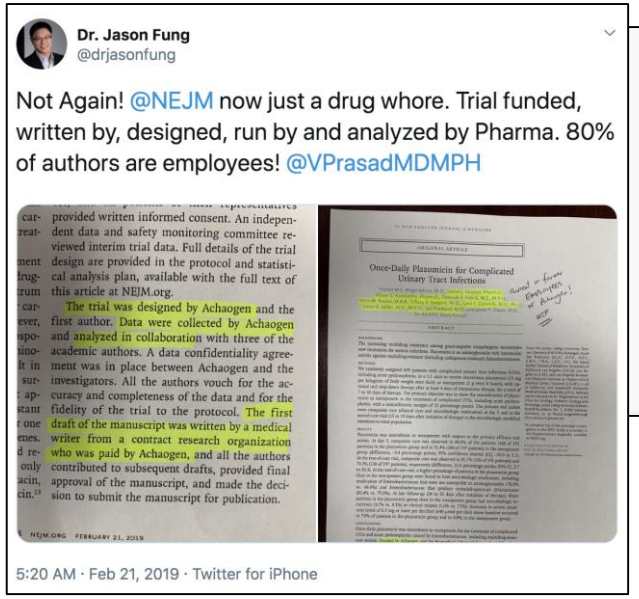
CONCLUSIONS

Once-daily plazomicin was noninferior to meropenem for the treatment of complicated UTIs and acute pyelonephritis caused by Enterobacteriaceae, including multidrug-resistant strains. (Funded by Achaogen and the Biomedical Advanced Research and Development Authority; EPIC ClinicalTrials.gov number, NCT02486627.)

From the Justus Liebig University, Giessen, Germany (F.M.E.W.); Achaogen, South San Francisco (D.J.C., A.S.K., D.S.C., K.M.K., T.R.K., L.E.C., I.F.), the David Geffen School of Medicine, University of California Los Angeles (UCLA), Los Angeles (L.G.M.), and Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center, Torrance (L.G.M.) — all in California; and Vanderbilt University Medical Center, Nashville (J.P.D.). Address reprint requests to Dr. Wagenlehner at the Clinic for Urology, Pediatric Urology and Andrology, Justus Liebig University Giessen, Rudolf-Buchheim Str. 7, 35392 Giessen, Germany, or at florian.wagenlehner@chiru.med.uni-giessen.de.

*A complete list of the principal investigators in the EPIC Study is provided in the Supplementary Appendix, available at NEJM.org.

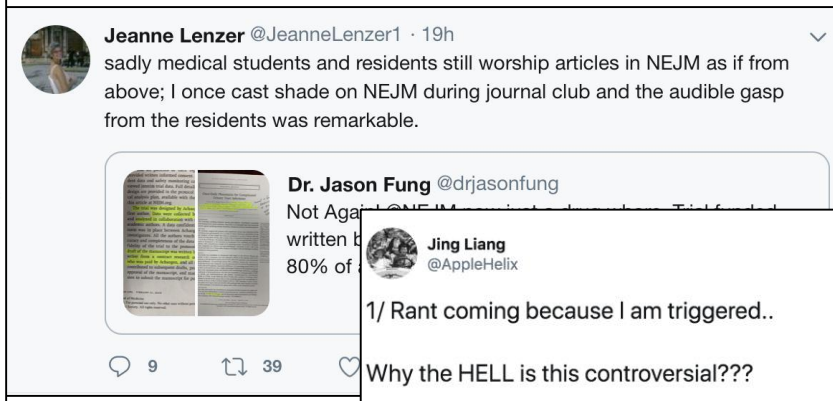
N Engl J Med 2019;380:729-40.
DOI: 10.1056/NEJMoa1801467



Dr. Jason Fung
@drjasonfung

Not Again! @NEJM now just a drug whore. Trial funded, written by, designed, run by and analyzed by Pharma. 80% of authors are employees! @VPrasadMDMPH

5:20 AM · Feb 21, 2019 · Twitter for iPhone



Jeanne Lenzer @JeanneLenzer1 · 19h
sadly medical students and residents still worship articles in NEJM as if from above; I once cast shade on NEJM during journal club and the audible gasp from the residents was remarkable.

Dr. Jason Fung @drjasonfung
Not Agai
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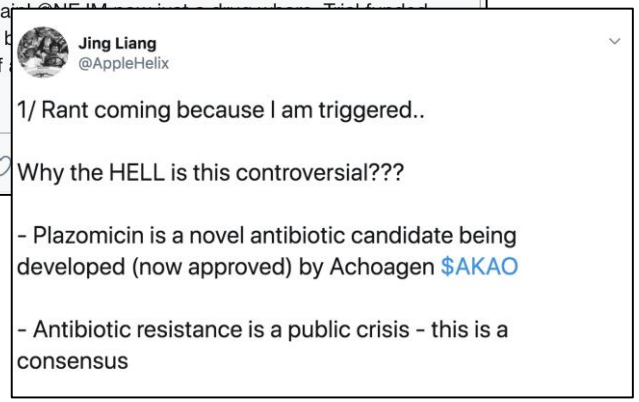


Jing Liang
@AppleHelix

1/ Rant coming because I am triggered..

Why the HELL is this controversial???

- Plazomicin is a novel antibiotic candidate being developed (now approved) by Achoagen $AKAO

- Antibiotic resistance is a public crisis - this is a consensus

Journal reputation is at a critical moment

- How are journals going to respond to professional skeptics?
- How does a journal respond to another journal's editor criticizing approval?
- How will journals respond to health systems (like University of California) who will now look at drug efficacy in real world clinical data? Will the data match?
- How will journals respond to payers incentivized to challenge expensive drug approvals, who will now want to see the raw data? $Billions riding on these papers.
- How will journals address the family ready to sell their house to pay for a drug for their family member?
- How will journals counter when government officials label them "fake news"?

"Trust us, it works, we've looked at the data"?! Really?

Preeclampsia: large cause of maternal and fetal death

- Incidence
  - 5-8% of all pregnancies in the U.S. and worldwide
  - 4.1 million births in the U.S. in 2009
  - Up to 300K cases of preeclampsia annually in the U.S.
- Mortality
  - Responsible for 18% of all maternal deaths in the U.S.
  - Maternal death in 56 out of every 100,000 live births in US
  - Neonatal death in 71 out of every 100,000 live births in US
- Cost
  - $20 billion in direct costs in the U.S annually
  - Average hospital stay of 3.5 days

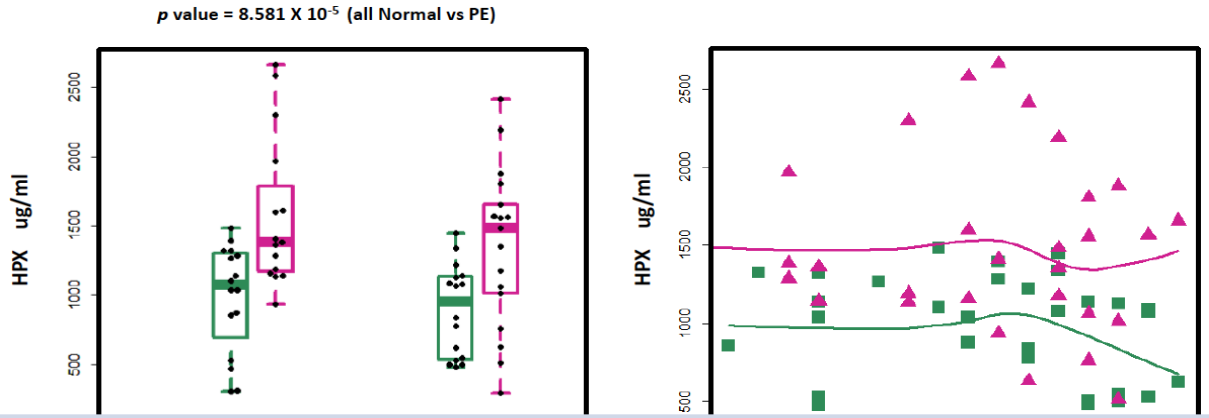
Linda Liu
Bruce Ling
Matt Cooper

Page 1 2 3 4 5 6 .. 11 Showing 1 - 25 of 266 experiments

Accession	Title	Type	Organism	Assays	Released
E-GEOD-32472	Oxygen induced complication of prematurity: from experimental data to prevention strategy	transcription profiling by array	Homo sapiens	299	01/11/2011
E-GEOD-27976	Calvarial osteoblast transcriptome analysis identifies genetic targets and extracellular matrix-mediated focal adhesion as potential biomarkers for single-suture craniosynostosis	transcription profiling by array	Homo sapiens	249	04/03/2012
E-GEOD-46510	New whole blood gene expression profile predictve of preterm birth	transcription profiling by array	Homo sapiens	154	15/05/2014
E-GEOD-37210	The application of nonsense-mediated mRNA decay inhibition to the identification of breast cancer susceptibility genes	transcription profiling by array	Homo sapiens	143	11/04/2012
E-TABM-682	Transcription profiling of human decidua basalis to identify pre-eclampsia susceptibility genes	transcription profiling by array	Homo sapiens	104	07/04/2009
E-GEOD-35574	Differentially expressed microRNAs revealed by molecular signatures of Preeclampsia and IUGR in human placenta	transcription profiling by array	Homo sapiens	94	07/02/2012
E-GEOD-41336	Cultured Cyto and Syncytio-trophoblast samples exposed to varying degrees of hypoxia (methylation)	methylation profiling by array	Homo sapiens	90	18/01/2013
E-GEOD-5999	Transcription profiling of human 27 non-	transcription	Homo sapiens	72	07/11/2008

march of dimes
prematurity research center
at STANFORD University School of Medicine

SPARK
AT STANFORD



Need a diagnostic for preeclampsia

Public big data available

March of Dimes Center for Prematurity Research

Data analyzed, diagnostic designed

SPARK grant ($50k)

Life Science Angels, other seed investors ($2 million)

Acquired by Progenity (La Jolla)

@CarmentaBio
progenity.com
bit.ly/carm_prog

STOCK WATCH Express, Wet Seal, Avago Jump

Carmenta Bioscience Secures Over $2 Million in Oversubscribed Seed Financing

Camille Samuels Accepts Seat on Carmenta Board of Di

BusinessWire

Press Release: Carmenta Bioscience, Inc. – Wed, A

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How Much Does Pharmaceutical Innovation Cost? A Look At 100 Companies

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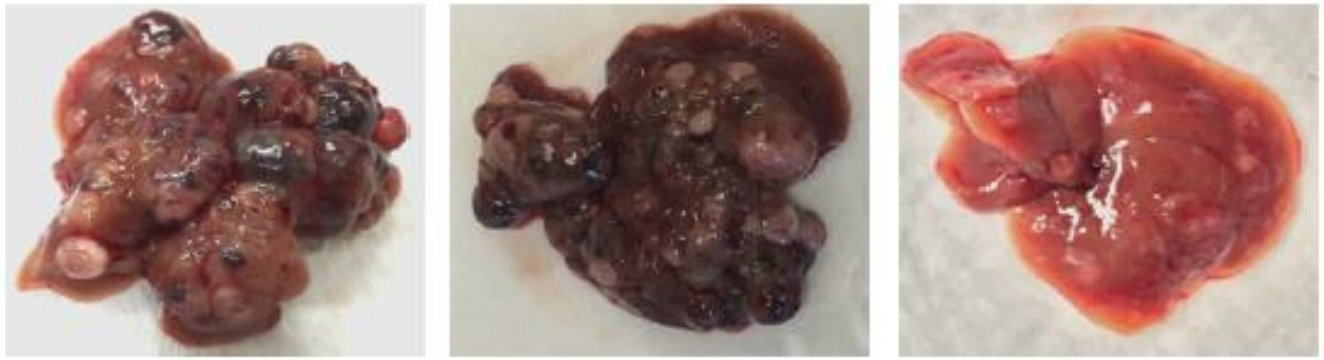
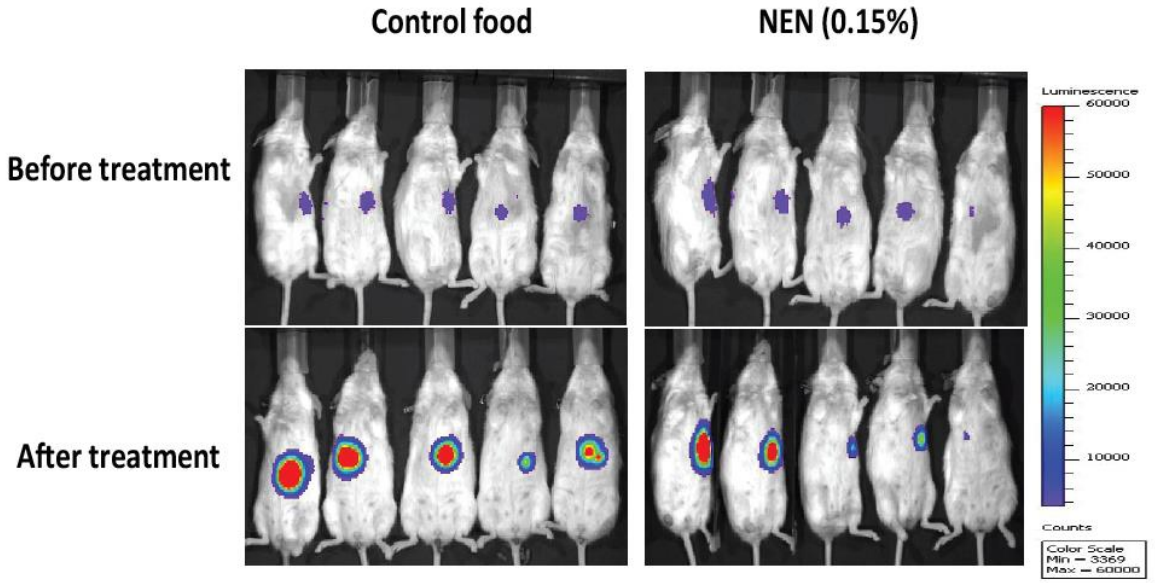
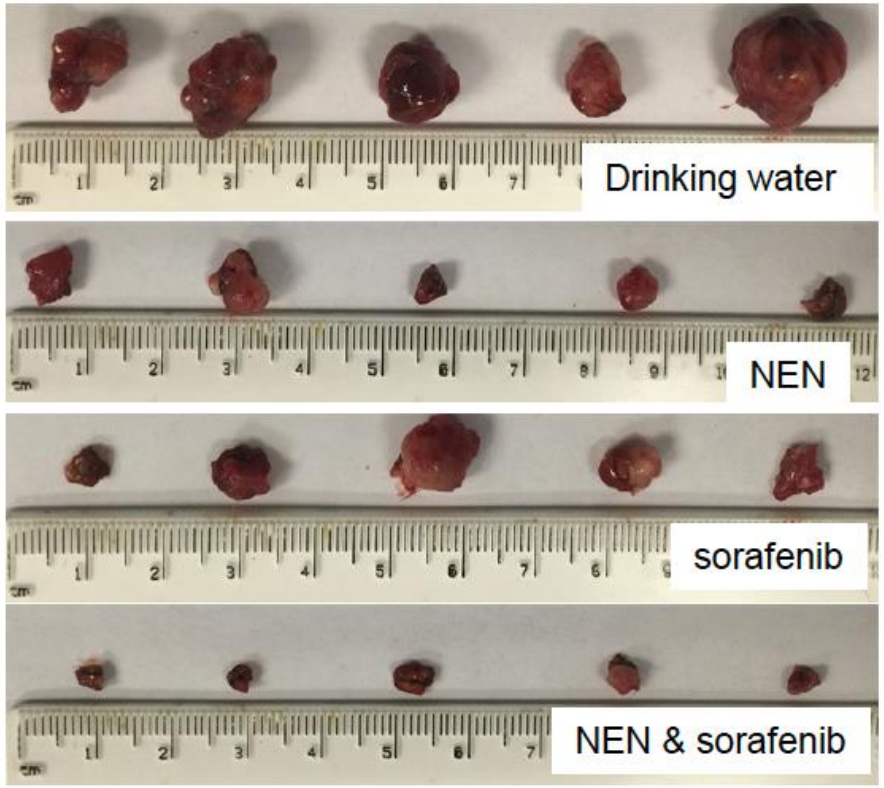
Company	Ticker	Number of drugs approved	R&D Spending Per Drug ($Mil)	Total R&D Spending 1997-2011 ($Mil)
AstraZeneca	AZN	5	11,790.93	58,955
GlaxoSmithKline	GSK	10	8,170.81	81,708
Sanofi	SNY	8	7,909.26	63,274
Roche Holding AG	RHHBY	11	7,803.77	85,841
Pfizer Inc.	PFE	14	7,727.03	108,178
Johnson & Johnson	JNJ	15	5,885.65	88,285
Eli Lilly & Co.	LLY	11	4,577.04	50,347
Abbott Laboratories	ABT	8	4,496.21	35,970
Merck & Co Inc	MRK	16	4,209.99	67,360
Bristol-Myers Squibb Co.	BMY	11	4,152.26	
Novartis AG	NVS	21	3,983.13	
Amgen Inc.	AMGN	9	3,692.14	

Sources: InnoThink Center For Research In Biomedical Innovation; Tho Fundamentals via FactSet Research Systems

@MatthewHerper
bit.ly/newdrug1







Bin Chen
Wei Wei
Li Ma
Bin Yang
Mei-Sze Chua
Samuel So

***Gastroenterology*, 2017**

Need more drugs for more diseases

Public big data available

NIH funding

Data analyzed, method designed

Company launched, ARRA, StartX, Stanford license, first deal

Claremont Creek, Lightspeed ($3.5 million)

@NuMedii

NuMedii
Translating Big Data into new medicines

Venture capital

'Digital drug development' company NuMedii snags $3.5 million

Ron Leuty
Reporter-
San Francisco Business Times
Email | Twitter | Google+ | Twitter

NuMedii Inc., the Palo Alto startup looking to convert pages of drug safety data into faster drug-development times, lined up $3.5 million in a Series A round.

Enlarge

NuMedii CEO Gini Deshpande: Tapping old data drugs.

The oversubscribed round was led by Claremont Creek Ventures and Lightspeed Ve Partners and included Life Science Angels and others.

NuMedii's data-into-gold approach rolls a wide range of data — from public scientific data bases and other sources — into an algorithm to predict if a compound will trans

THE WALL STREET JOURNAL. | U.S.

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2 of 12 U.S. Economy Contracted Last Quarter

U.S. NEWS

Researchers Show Gains in Finding Reus

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By AMY DOCKSER

August 18, 2011

In a bit of high-tec already-approved combat.

The scientists ha have benefits in t

FierceBiotechIT

Topics: R&D

Allergan taps NuMedii's digit platform for psoriasis R&D

October 5, 2015 | By Nick Paul Taylor

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NuMedii has landed a deal that could val discovery. Allergan ($AGN) is the compa tments fo

Astellas hooks up with NuMedii to continue drug repurposing deal drive

January 15, 2016 | By Nick Paul Taylor

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Email

NuMedii, Inc. Announces New Partnership To Discover An Advance New Treatments For Idiopathic Pulmonary Fibros

Future speculation

- Open data will democratize biomedical innovation, and that’s a good thing
- Open data is going to lead to more believability
- Digitalization of biomedicine will bring new players into the field
- DNA and other molecular measurements will be routine
- Less privacy, and less concern for privacy
- The entire world will be in continual study → more importance on continually acquired accurate data