



**Order experiments from
the world's best labs**

Elizabeth Iorns, Ph.D

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[@elizabethiorns](https://twitter.com/elizabethiorns)

TRENDS IN RESEARCH

A rapidly changing industry

Wednesday, May 29, 2013

The Crisis of Research Funding in the US

Bad Statistics, and Bad Training, Are Sabotaging Drug Discovery

Stewart Lyman | 1/6/14

Unreliable research

Trouble at the lab

Scientists like to think of science as self-correcting. To an alarming degree, it is not
Oct 17th 2013, 15:02 | From the print edition

PHARMA & HEALTHCARE

4/19/2012 @ 4:05PM | 31,531 views

Culture as a Culprit of the Pharma R&D Crisis

CROs globally employ more personnel than pharma and biotech companies

Science policy

High Cost and Pace Driving Collaborative Science

Science, once siloed and hyper-competitive, is becoming increasingly collaborative the face of the high cost of research and the need for speed in discovery.

San Diego's Mini-Cluster of Virtual Biotechs Without Labs on High Bluff Drive

SCIENCE

345 COMMENTS

Billionaires With Big Ideas Are Privatizing American Science

By WILLIAM J. BROAD MARCH 15, 2014

71% of senior industry executives say their companies will increase the use of CROs in the next three years



ONLINE



COLLABORATIVE



VERIFIED



ONLINE

*“Software is eating
the world”*

Marc Andreessen
(Founder, Andreessen Horowitz)

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Software is eating the world

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Reputation



academia.edu



Publishing

PeerJ



Fundraising



experiment

Design



Purchasing

antibodies-online.com

QUARTZY

Collaborating



Protocols/ELN



labguru do more science



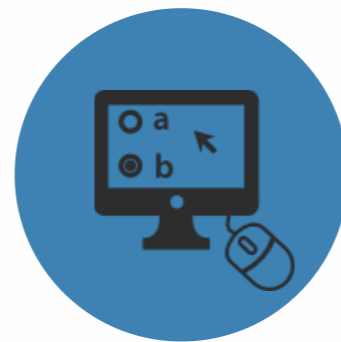
Peer review



Data storage



Research 2.0



- Real-time
 - potential for ‘open lab book science’
- Access to all information
 - including raw and analyzed data
 - enables re-analysis of data
 - full protocols and unique identification of research reagents
 - enables replication of experiments
- Wisdom of the crowd
 - poor quality products and results will be rapidly identified and flagged by the research community
 - e.g. Antibodypedia / Knoepfler Lab Stem Cell Blog



COLLABORATIVE

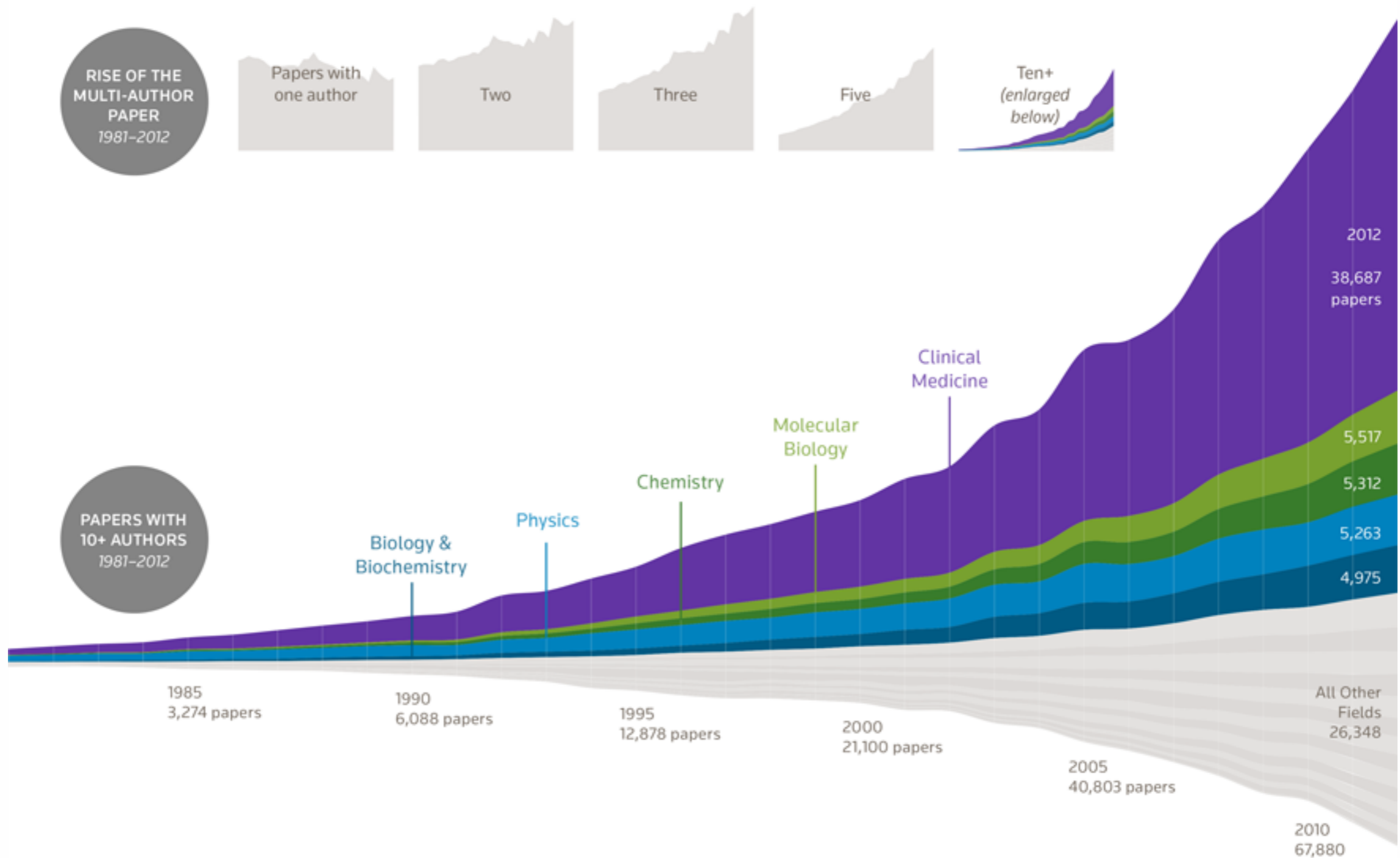
Science policy

High Cost and Pace Driving Collaborative Science

Science, once siloed and hyper-competitive, is becoming increasingly collaborative in the face of the high cost of research and the need for speed in discovery.

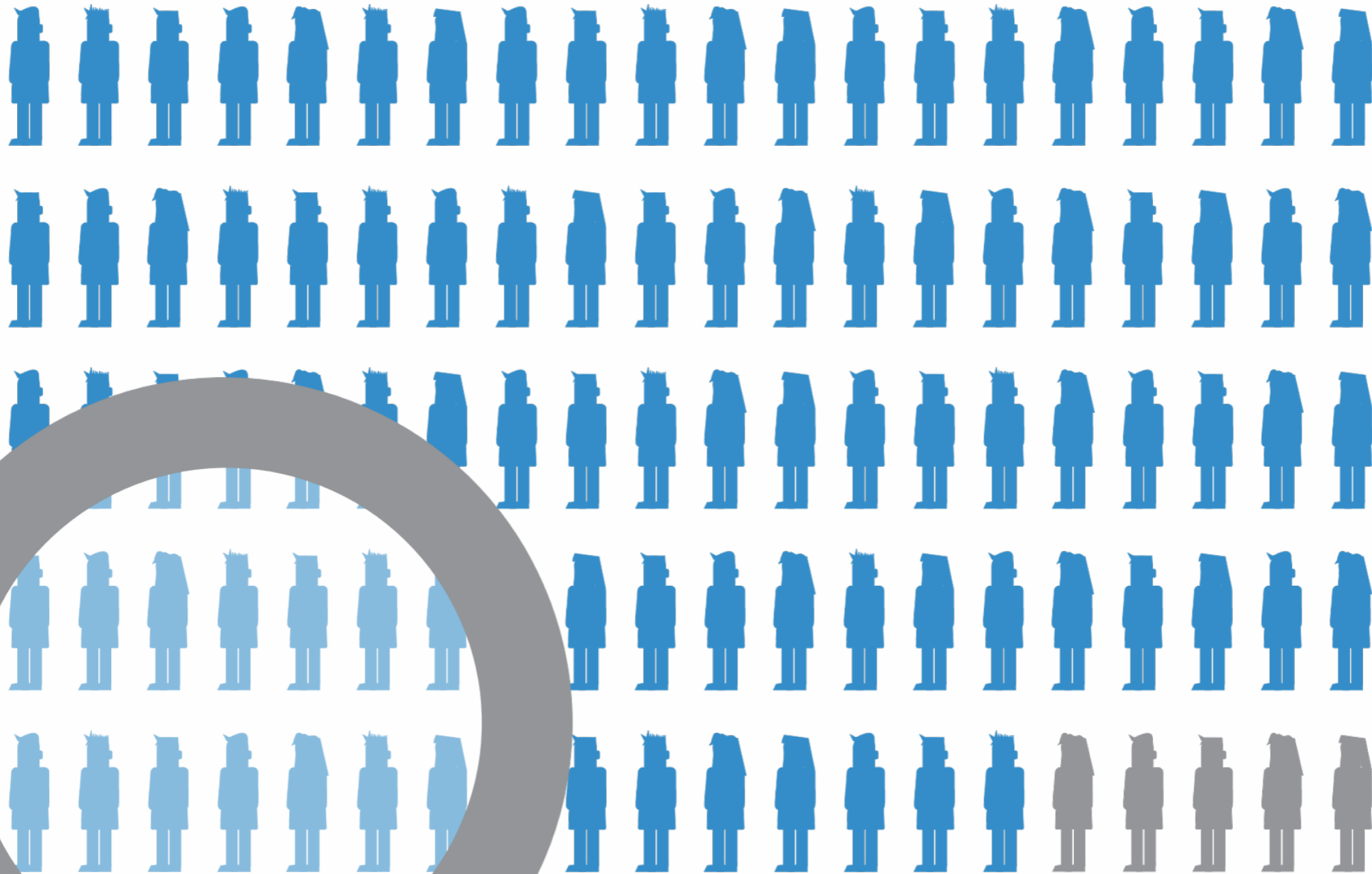
The
Economist

Collaboration is increasingly important



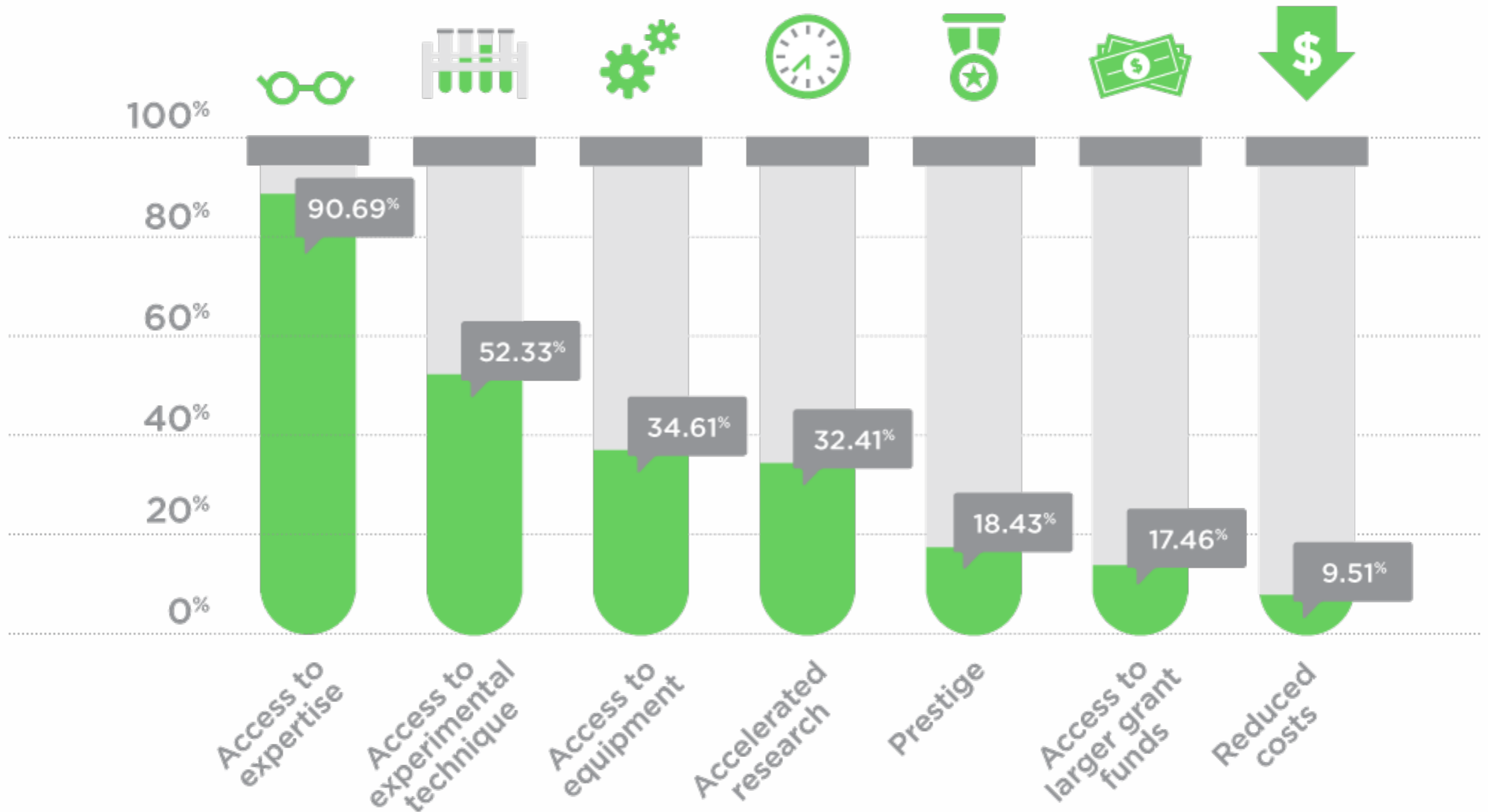
Source: <http://ar.thomsonreuters.com/story3.html>

Collaboration is increasingly important



95% of our surveyed scientists had been asked to collaborate or sought collaborators for their research.

Why do scientists collaborate?



Why do scientists collaborate?

To access specialized
equipment and expertise

Why do scientists collaborate?

[Journal home](#) > [Archive](#) > [Letter](#) > [Full Text](#)

Journal content

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- [Current issue](#)
- [Nature News](#)
- [Archive](#)
- [Supplements](#)
- [Web focuses](#)

Letter

Nature **464**, 431-435 (18 March 2010) | doi:10.1038/nature08833; Received 29 September 2009; Accepted 18 January 2010; Published online 3 February 2010

RAF inhibitors prime wild-type RAF to activate the MAPK pathway and enhance growth

Georgia Hatzivassiliou¹, Kyung Song¹, Ivana Yen¹, Barbara J. Brandhuber², Daniel J. Anderson¹, Ryan Alvarado¹, Mary J. C. Ludlam¹, David Stokoe¹, Susan L. Gloor², Guy Vigers², Tony Morales², Ignacio Aliagas¹, Bonnie Liu¹, Steve Sideris¹, Klaus P. Hoeflich¹, Bijay S. Jaiswal¹, Somasekar Seshagiri¹, Hartmut Koeppen¹, Marcia Belvin¹, Lori S. Friedman¹ & Shiva Malek¹

Author Contributions G.H. and S.M. designed the studies, interpreted the data and wrote the manuscript. K.S., I.Y., B.L., S.S. and D.S. conducted cellular experiments and dimerization assays. D.J.A., M.J.C.L. and R.A. conducted microscopy experiments. B.J.B., G.V., T.M. and I.A. conducted crystallography and provided structural input. S.L.G. conducted enzymology. K.P.H. and H.K. conducted *in vivo* experiments and immunohistochemistry. B.S.J. and S.S. generated inducible shRNA cell lines. M.B. and L.S.F. interpreted the data and wrote the manuscript.

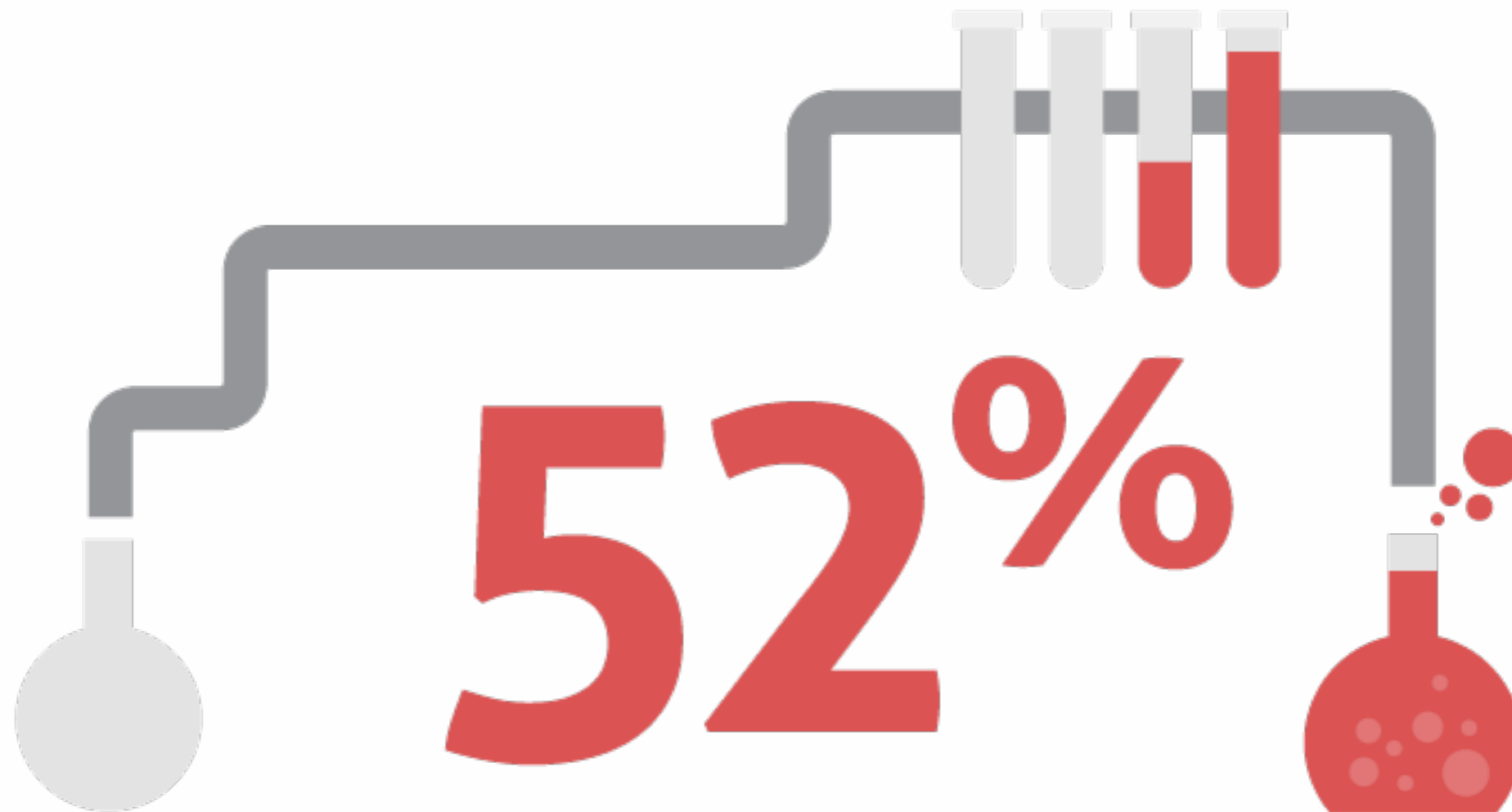
Barter for potential
future co-authorship

How do scientists collaborate?

But bartering is:

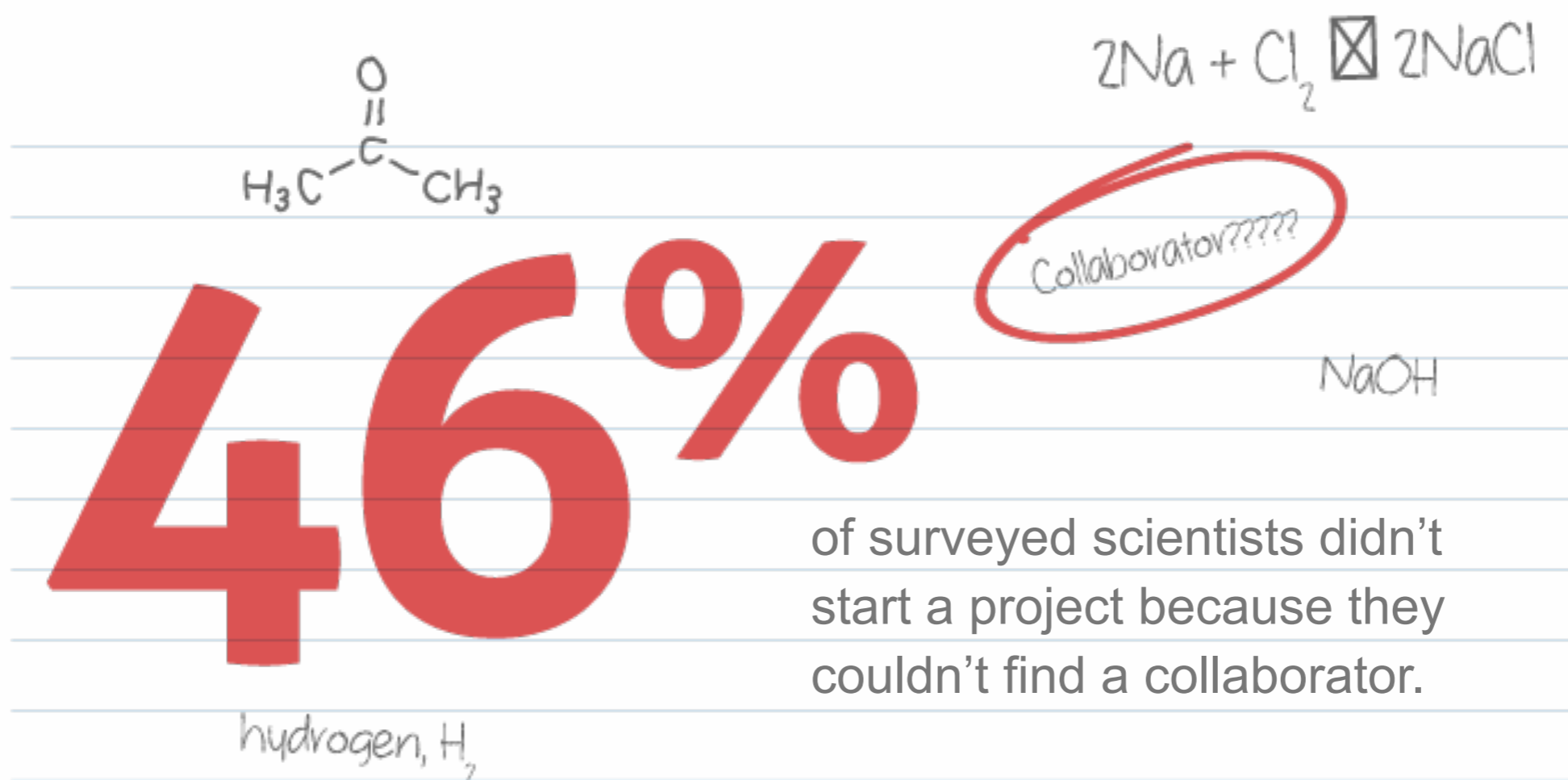
- Inefficient
 - time intensive to find and convince a professional colleague to help
- Unscalable
 - maintaining a professional network large enough to contain all expertise required
- Poor incentives
 - may not incentivize best experts to conduct experiments

Collaboration has poor incentives

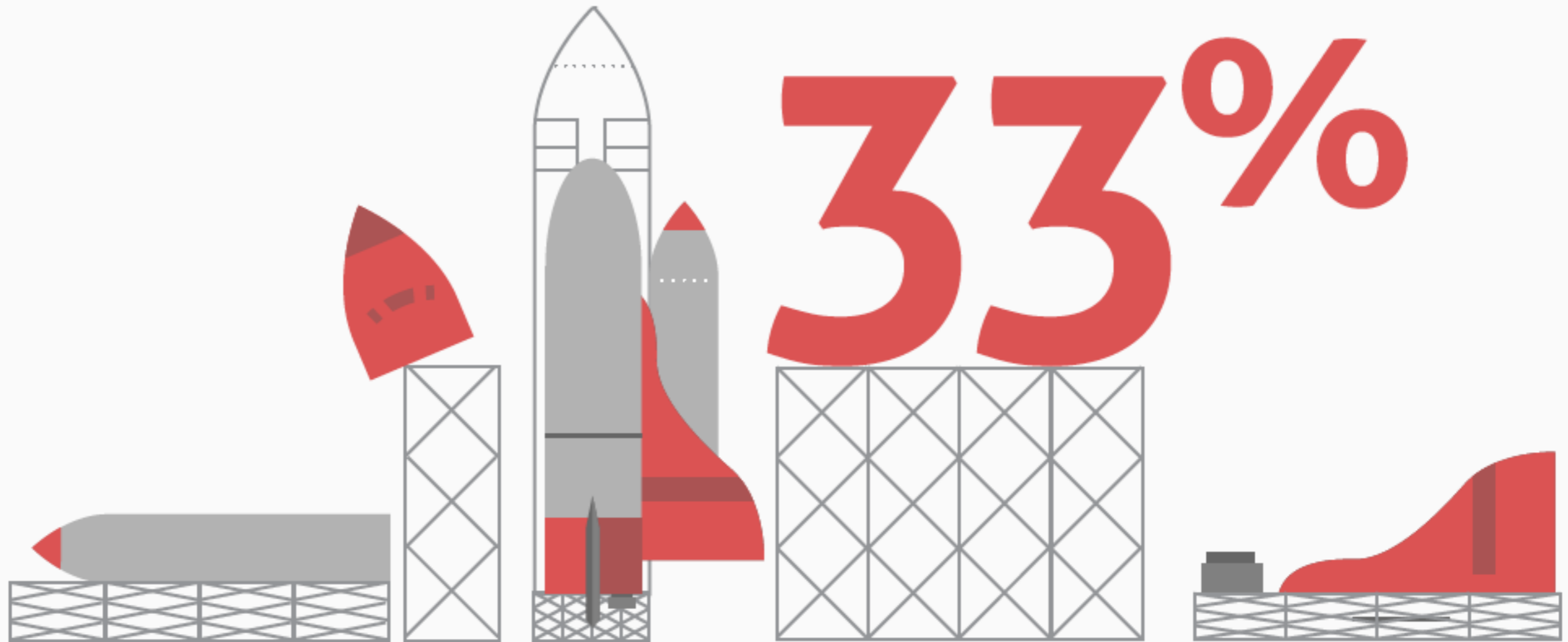


of surveyed scientists have felt that
collaboration was one-sided.

Collaboration has poor incentives



Collaboration has poor incentives



33% of surveyed scientists didn't complete a project because they couldn't find a collaborator.

Source: Science Exchange Collaboration Survey 2014

Marketplace for collaboration

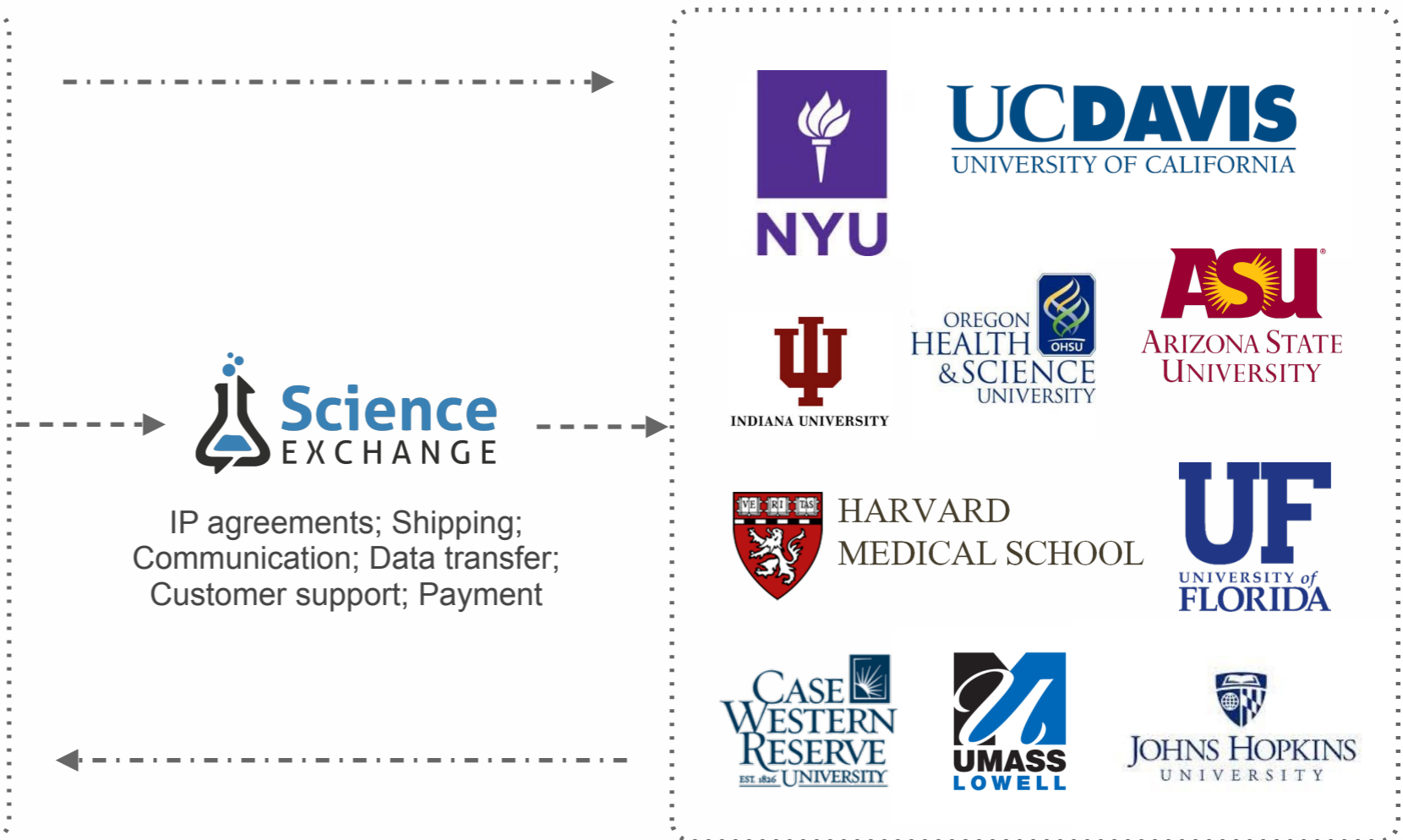
Demand Side



Researchers

Academics; Government;
Biotech & industry; Citizen scientists

Supply Side



Labs

CROs; Core Facilities;
individual scientists

Solution

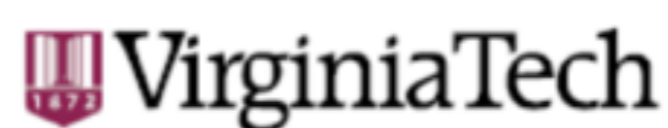


Simplifies collaboration to ordering an experiment from the world's best labs

UNIVERSITY



EST. 1862 UNIVERSITY



Consequences of greater collaboration



Speed

Distributed research

Collaborating with experts enables distributed research

Cost

Access the most cost effective expert

No investment in training/infrastructure required

Control

Maintain ownership

IP and confidentiality protected

Quality

Specialists for specialized research

Network of verified specialist labs ensures quality

Consequences of greater collaboration



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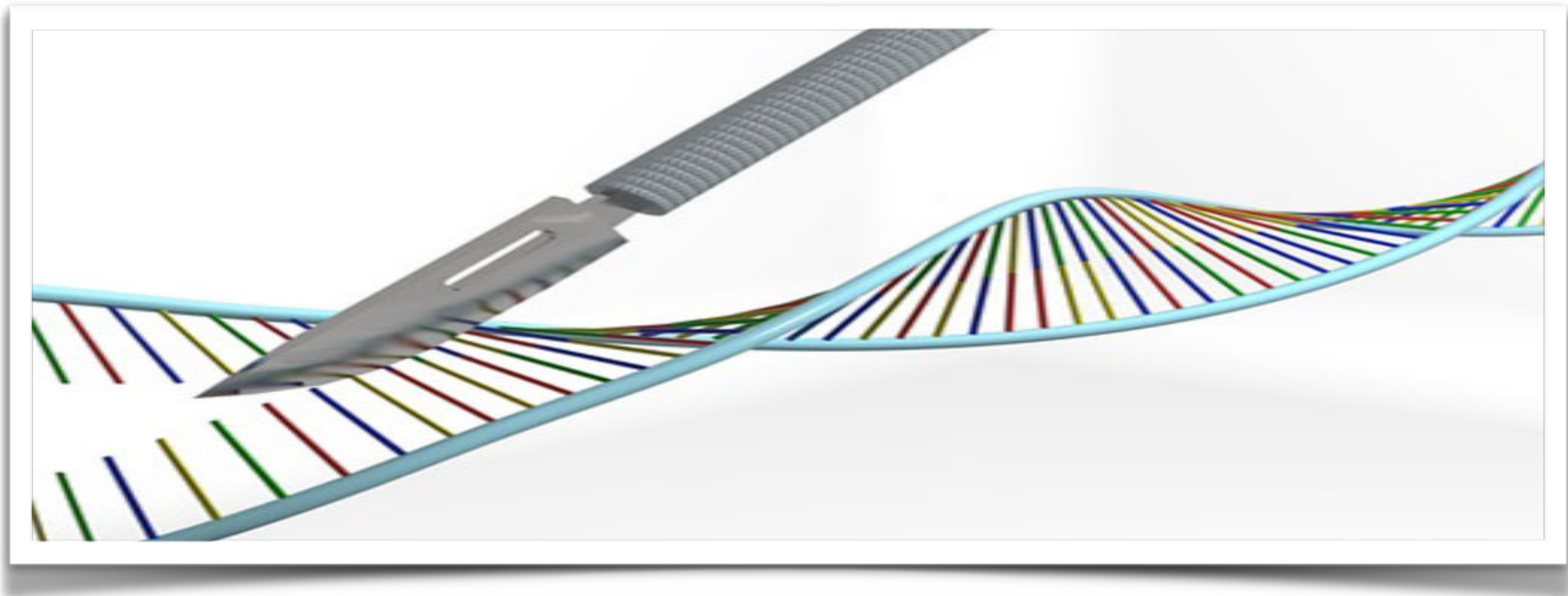
Speed

Platforms like Science Exchange provide one point of contact for a vast network of contract labs allowing research to be distributed and parallelized



Speed

Greater use of experts also enables more rapid adoption of new technologies (e.g. Illumina HiSeq X Ten and CRISPR now widely available)



Consequences of greater collaboration



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Specialists can be more cost effective than in-house



In House Methods

Doing experiments in house can be costly and time consuming. The cost of reagents have been obtained from major reagent suppliers. Labor costs have been ascertained by the university standard



Reagents

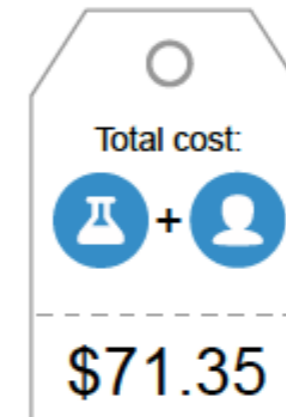
Reagent	Cost (per sample)
RNeasy Maxi Kit	\$27.00
2-Mercaptoethanol	\$0.19
Ethanol	\$12.88
RNase free tips	\$10.20
RNase free eppendorf	\$0.10

Total cost of reagents for 1 sample = \$50.35



Labor

Cost of Post Doc's Labor for 1 hour = \$21.00



Science EXCHANGE

Science Exchange allows you to browse and post projects in over 2000 categories for free. The labs listed are the world's best and are committed to providing expertise in knowledge and techniques.



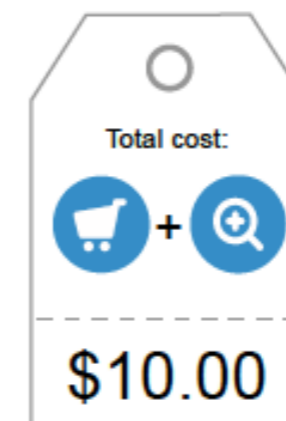
Browse

Browse over 40 labs for RNA Extraction services



Order

Save your time and money by ordering from one of the world's best labs!



Save 86% on RNA Extraction by using Science Exchange

Consequences of greater collaboration



Speed

Distributed research

Collaborating with experts enables distributed research

Cost

Access the most cost effective expert

No investment in training/infrastructure required

Control

Maintain ownership

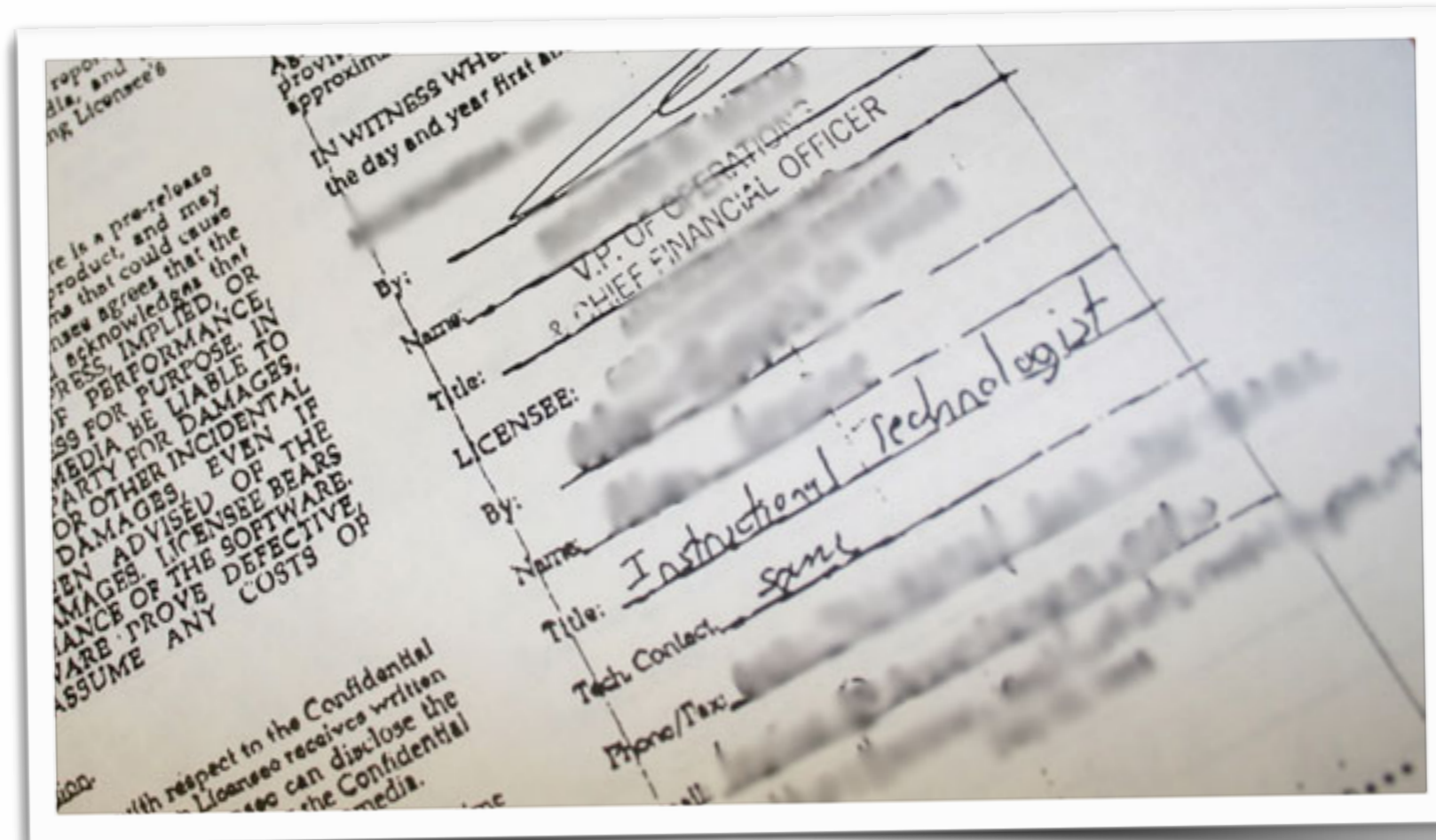
IP and confidentiality protected

Quality

Specialists for specialized research

Network of verified specialist labs ensures quality

IP and confidentiality agreements with expert labs protects research



Consequences of greater collaboration



Speed

Distributed research

Collaborating with experts enables distributed research

Cost

Access the most cost effective expert

No investment in training/infrastructure required

Control

Maintain ownership

IP and confidentiality protected

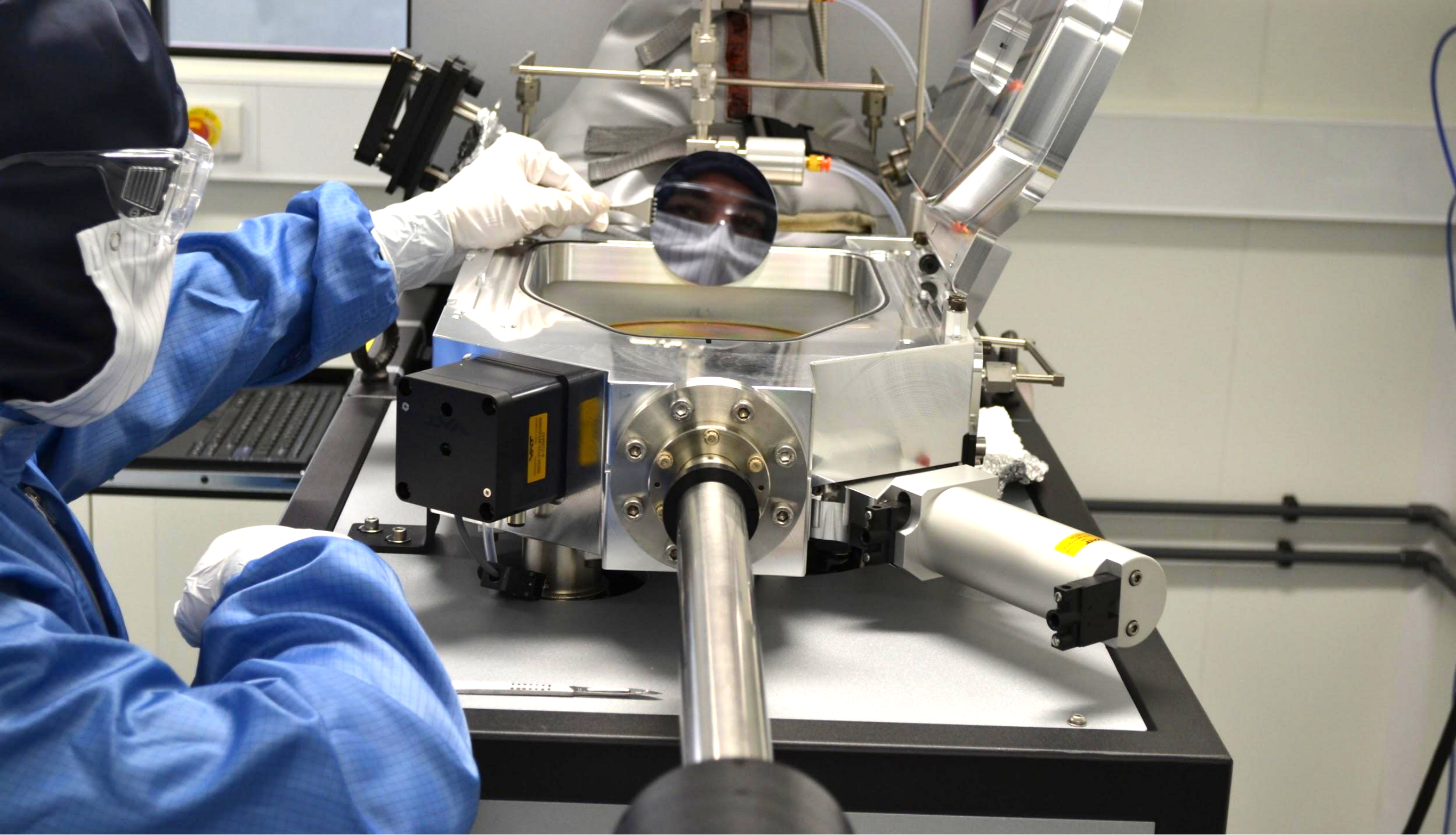
Quality

Specialists for specialized research

Network of verified specialist labs ensures quality

Using expert verified labs ensures high quality research

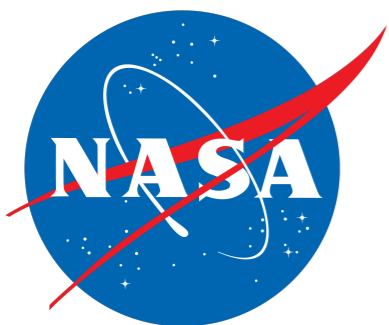
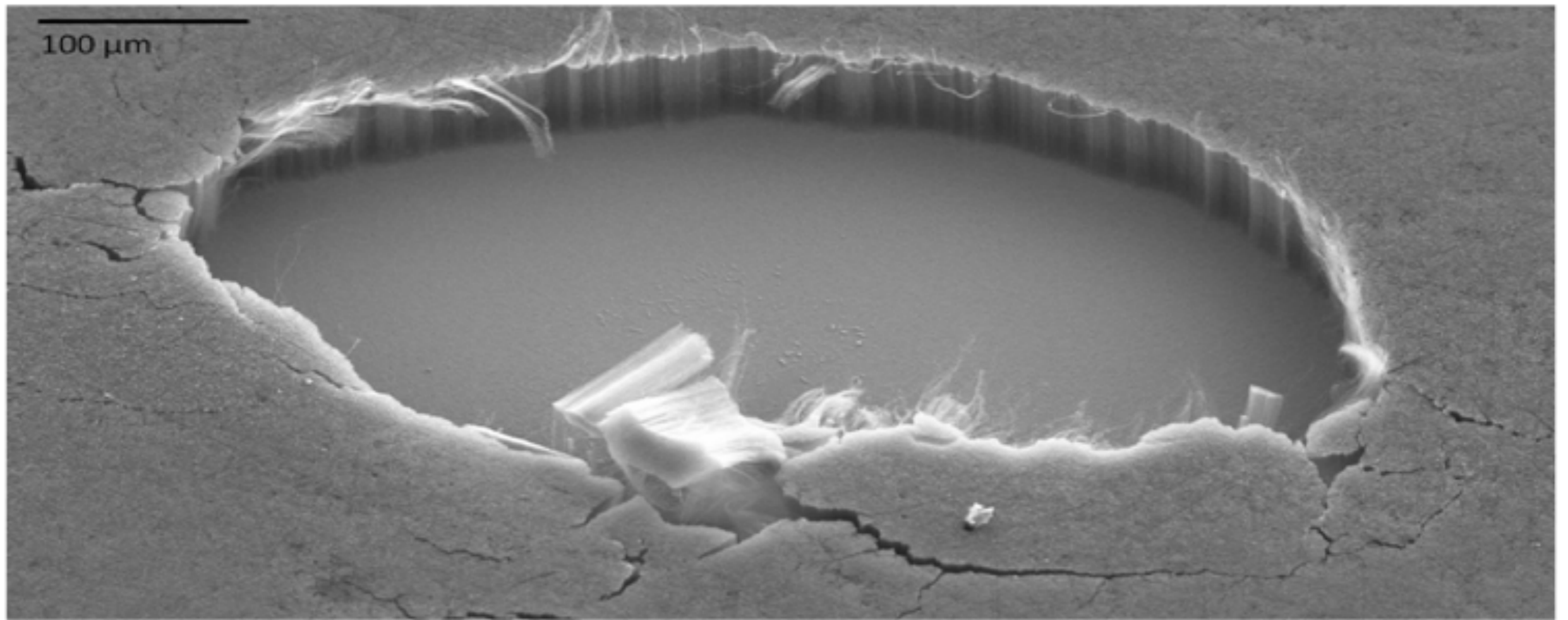




Australian National Fabrication Facility

Services offered:

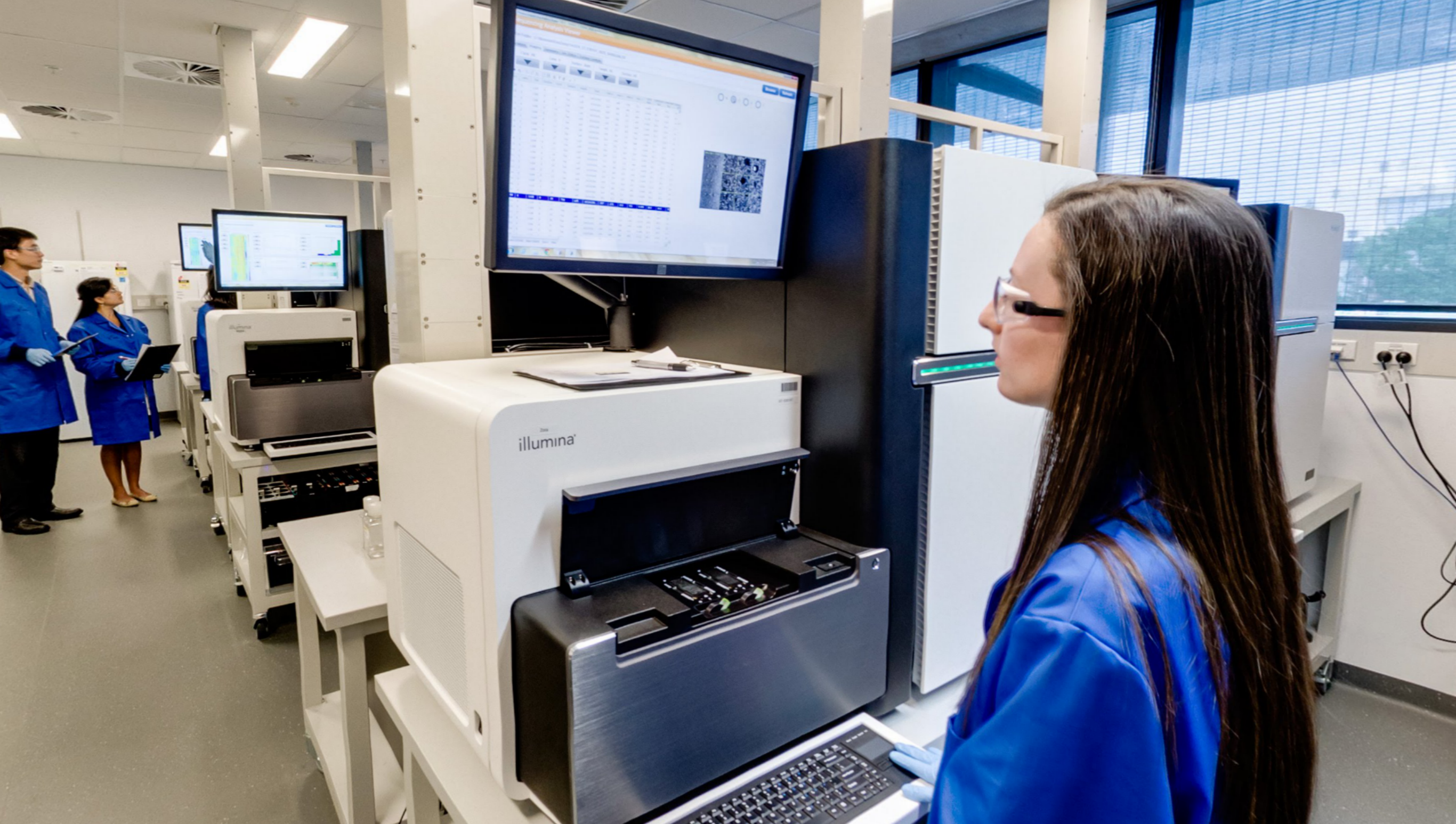
Chemical vapor deposition (CVD), Electron beam lithography (EBL), Focused ion beam tomography (FIB), Flip-chip bonding, Inductively coupled plasma etching, Digital Holographic microscopy and 80 others



2011-2013: NASA (unsuccessfully) attempts to increase the blackness of their nanotubes in order to improve the robustness and application of nanotube technology (at a cost of several million dollars).



2013: Through a collaboration formed via Science Exchange, NASA was able to produce carbon nanotube forests – the blackest materials ever measured. Project cost \$3,000 and took 3 months.



Kinghorn Centre for Clinical Genomics

Services offered:

Illumina next generation sequencing, Whole genome sequencing, Bioinformatics



WIRED

Jan 15th: “Illumina’s HiSeq X Ten Sequencing System will prove affordable for only a few. The system...costs a whopping \$10 million.”



Feb 8th: HiSeq X Ten at Kinghorn Center for Clinical Genomics listed on Science Exchange and available to any researcher in the world



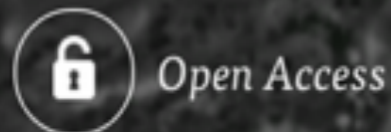
Sanford Burnham Medical Research Institute

Services offered:

Viral research BSL4; in vitro and in vivo experimentation; lentiviral, retroviral and adenoviral viral vector production

Can We Defeat EBOLA with an Experimental CANCER Drug?

Dr. W. Shawn Carbonell | Dr. Elizabeth Iorns
OncoSynergy, Inc.



\$5,031

Pledged

100% \$5,000 0
Funded Goal Days

Success! This project was funded on
21 September 2014

OncoSynergy

Aug 22nd: OncoSynergy discovers cancer drug (OS2966) targets the same pathway used by the ebola virus to infect cells. Starts crowdfunding project.



Oct 10th: Work starts with a BSL4 certified lab at Sanford Burnham Medical Institute to test whether OS2966 can be used as a treatment for ebola. Initial results show OS2966 is a potent inhibitor of ebola entry.

- Improvement of data quality through use of experts
- Need for tools to facilitate collaboration, workflow provenance, data integrity and sharing between collaborators
- Researchers will develop professional brands around technical expertise



VERIFIED



VERIFIED

“One of the most important principles of the scientific method is reproducibility, the ability to replicate an experimental result.”

The scientific method

Scientific method

From Wikipedia, the free encyclopedia

"Scientific study" redirects here. For observational studies, see *observational study*.



The **neutrality of this article is disputed**. Relevant discussion may be found on the [talk page](#). Please do not remove this message until the [dispute is resolved](#). (January 2013)

The **scientific method** is a body of [techniques](#) for investigating [phenomena](#), acquiring new [knowledge](#), or correcting and integrating previous knowledge.^[1] To be termed scientific, a method of inquiry must be based on [empirical](#) and [measurable](#) evidence subject to specific principles of reasoning.^[2] The *Oxford English Dictionary* defines the scientific method as: "a method or procedure that has characterized natural science since the 17th century, consisting in systematic observation, measurement, and experiment, and the formulation, testing, and modification of [hypotheses](#)."^[3]

The chief characteristic which distinguishes the scientific method from other methods of acquiring knowledge is that scientists seek to let reality speak for itself,^[discuss] supporting a theory when a theory's predictions are confirmed and challenging a theory when its predictions prove [false](#). Although procedures vary from one [field of inquiry](#) to another, identifiable features distinguish scientific inquiry from other methods of obtaining knowledge. Scientific researchers propose hypotheses as explanations of phenomena, and conduct [studies](#) to test these hypotheses via predictions which can be derived from them. These steps must be repeatable and verifiable by other experimenters. [Theories](#) that encompass wider domains of inquiry may bind many independently derived hypotheses into context. [Theories](#), in turn, may help form new hypotheses or place groups of hypotheses

Scientific inquiry is generally intended to be [documented](#), [archived](#), and [peer-reviewed](#), giving them the opportunity to verify the [reliability](#) of these data to be established (when data is sampled or compared to chance).

Part of a series on Science

Formal sciences	[show]
Physical sciences	[show]
Life sciences	[show]
Social sciences	[show]
Applied sciences	[show]
Interdisciplinarity	[show]
Philosophy and history of science	[show]

[Outline](#) · [Portal](#) · [Category](#)

[V](#) · [T](#) · [E](#)

propose hypotheses as explanations of phenomena. **These steps must be repeatable**, to give them the opportunity to verify the reliability of these data to be established (when data is sampled or compared to chance). Scientific inquiry may bind many independently derived hypotheses into context. Scientific inquiry is generally intended to be documented, archived, and peer-reviewed, giving them the opportunity to verify the reliability of these data to be established (when data is sampled or compared to chance).

Reproducibility

From Wikipedia, the free encyclopedia

Reproducibility is the ability of an entire **experiment** or study to be reproduced, either by the researcher or by someone else working independently. It is one of the main principles of the **scientific method**. The result values are said to be *commensurate* if they are obtained (in distinct experimental trials) according to the same reproducible experimental description and procedure.

Reproducibility is determined from controlled interlaboratory test programs.^{[3][4]}

Are published results
reproducible?

Are published results reproducible?

Unreliable research

Trouble at the lab

Scientists like to think of science as self-correcting. To an alarming degree, it is not

Oct 17th 2013, 15:02 | From the print edition



RESEARCH ARTICLE

VIEWS

ACADEMIC
BOOKMARKS

3
SI

A Survey on Data Reproducibility in Cancer Research Provides Insights into Our Limited Ability to Translate Findings from the Laboratory to the Clinic

Aaron Mobley, Suzanne K. Linder, Russell Braeuer, Lee M. Ellis , Leonard Zwelling 

Methods and Findings

To examine a microcosm of the academic experience with data reproducibility, we surveyed the faculty and trainees at MD Anderson Cancer Center using an anonymous computerized questionnaire; we sought to ascertain the frequency and potential causes of non-reproducible data. We found that ~50% of respondents had experienced at least one episode of the inability to reproduce published data; many who pursued this issue with the original authors were never able to identify the reason for the lack of reproducibility; some were even met with a less than “collegial” interaction.

<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0063221>

Reproducibility problems



Re-tested 70+ drugs from 221 independent studies¹

→ 0 reproduced

→ Minocycline: effective in four separate ALS mouse studies worsened symptoms in a clinical trial of more than 400 patients²



Sponsored replication of 12 spinal cord injury studies

→ 2/12 fully reproduced³



Conducted in-house target validation studies

→ 14/67 reproduced⁴



Attempted to reproduce 53 “landmark” oncology publications

→ 6/53 reproduced⁵

1. Scott et al. Amyotroph Lateral Scler. 9, 4-15 (2008).

2. Gordon et al. Lancet Neurol. 6, 1045–1053 (2007).

3. Stuart et al. Experimental Neurology 233, 597–605 (2012).

4. Prinz et al. Nat Rev Drug Discov. 10, 712 (2011).

5. Begley and Ellis. Nature. 483, 531-3 (2012).

Are published results
reproducible?

Not always

But doesn't the literature
correct itself?

But doesn't the literature
correct itself?

Not often

Retraction?

- Only 0.2% of the literature (vs 70%+ irreproducibility)

Negative findings?

- Less than 30% of researchers who could not reproduce published findings published their failure¹
- Only 14% of the literature reports any negative results²

Additional publications?

“We didn’t see that a target is more likely to be validated if it was reported in ten publications or in two publications”³

Example: Retraction of PLOS⁴ and Science⁵ papers by Pamela Ronald at UC Davis

- Self retraction due to reagent error
- Results had been ‘confirmed’ independently by three other groups⁶⁻⁸

1. Mobley et al. PLOS ONE. 8, e63221 (2013)

2. Fanelli. Scientometrics. 90, 891 (2012)

3. Prinz et al. Nat Rev Drug Discov. 10, 712 (2011)

4. Han et al. PLOS ONE. 6, e29192 (2011)

5. Lee et al. Science. 326, 850 (2009)

6. McCarthy et al. J Bacteriology. 193, 6375 (2011)

7. Shuguo et al. Appl Biochem Biotechnol. 166, 1368 (2012)

8. Qian et al. J Proteome Res. 12, 3327 (2013)

What about citations?

None of the replication studies reported have found any correlation with citations (or journal impact factor):

- NINDS - No significant difference¹
- Bayer - No significant difference²
- Amgen - *“We saw no significant difference in citation rates between papers that were reproducible versus non-reproducible”*³

1. Stuart et al. Experimental Neurology 233, 597–605 (2012).

2. Prinz et al. Nat Rev Drug Discov. 10, 712 (2011).

3. Begley and Ellis. Nature. 483, 531-3 (2012).

Many published results may be irreproducible and we do not have a mechanism to identify reproducible results

“As a funding agency, the NIH is deeply concerned about this problem.”

Francis S. Collins (Director, NIH)
Lawrence A. Tabak (Deputy Director, NIH)



nature

Reproducibility solution



nature International weekly journal of science

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Archive > Volume 496 > Issue 7443 > Column: World View > Article

NATURE | COLUMN: WORLD VIEW



عربي



Jocelyn Filley

If a job is worth doing, it is worth doing twice

Researchers and funding agencies need to put a premium on ensuring that results are reproducible, argues [Jonathan F. Russell](#).

03 April 2013



PDF



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Verify key results by
independent replication

RP: Cancer Biology

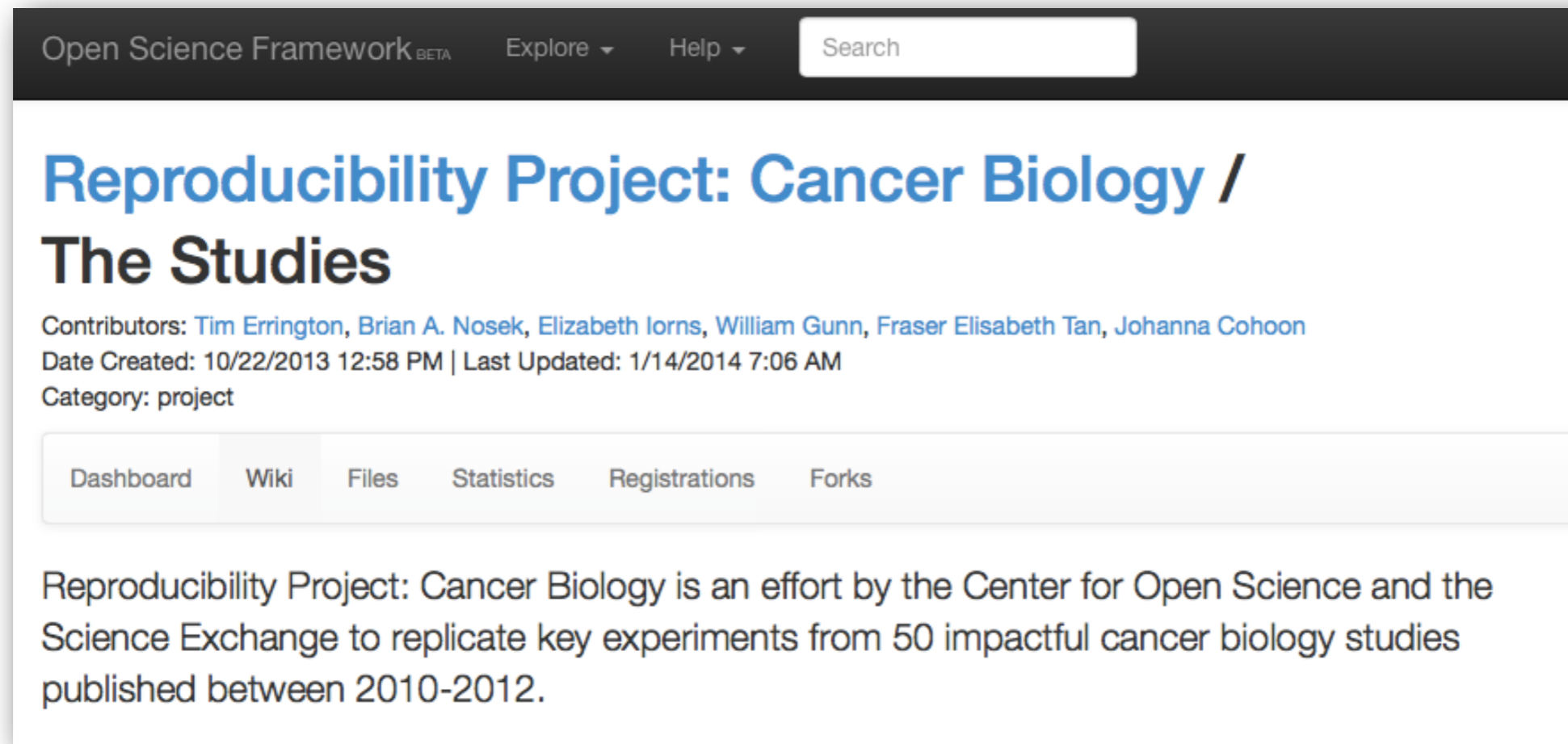
Reproducibility Project: Cancer Biology



RP: Cancer Biology

Project 1. Reproducibility Project: Cancer Biology

Independently replicating key experimental results from the top 50 cancer biology studies from 2010-2012



Open Science Framework^{BETA} Explore ▾ Help ▾ Search

Reproducibility Project: Cancer Biology / The Studies

Contributors: [Tim Errington](#), [Brian A. Nosek](#), [Elizabeth Iorns](#), [William Gunn](#), [Fraser Elisabeth Tan](#), [Johanna Cohoon](#)
Date Created: 10/22/2013 12:58 PM | Last Updated: 1/14/2014 7:06 AM
Category: project

Dashboard Wiki Files Statistics Registrations Forks

Reproducibility Project: Cancer Biology is an effort by the Center for Open Science and the Science Exchange to replicate key experiments from 50 impactful cancer biology studies published between 2010-2012.

Learn more at cos.io/cancerbiology

Project 1. Cancer Biology Reproducibility Project

Goals:

- Show direct replication is possible in a cost-effective and scalable manner
- Demonstrate replication studies provide an approach to identify reproducible results
- Generate an open dataset of high value replicated studies
- Identify best practices that maximize reproducibility

Track progress at cos.io/cancerbiology

Project 1. Cancer Biology Reproducibility Project

Selection:

- 50 studies from 2010, 2011, 2012
- most cited for cancer biology related terms in WoS and Scopus
- retrieved Mendeley readers and altmetric.com data & ranked by combined score
- excluded reviews, clinical trials, case studies, sequencing papers

Project 1. Cancer Biology Reproducibility Project

Replication:

- Identify key experiments
 - no initial exploratory work ensures timeliness and cost effectiveness
- Conduct a direct replication (using the same materials and methods as closely as possible, including any additional controls as necessary)
- Obtain input from the original author on proposed replication protocols
- Pre-register and peer review protocols and analysis plans
- Use power calculations to ensure replication sample size is sufficient to detect the reported effect with at least 80% power
- Use expert, independent labs with extensive expertise in the techniques being replicated
- Publish all protocols, results, and data in the Open Science Framework for review by any interested party

Project 1. Cancer Biology Reproducibility Project

Status:

- Replication experiments are currently underway for 9 studies
- Registered reports are currently being peer reviewed for 12 studies
- Awaiting information from authors and/or labs for remaining studies

<http://elifesciences.org/collections/reproducibility-project-cancer-biology>

REPRODUCIBILITY PROJECT Cancer Biology

The Reproducibility Project: Cancer Biology is a collaboration between the [Center for Open Science](#) and [Science Exchange](#) to independently replicate selected results from [50 papers in cancer biology](#). For each paper a Registered Report detailing the proposed experimental designs and protocols for the replications is peer reviewed and published prior to data collection. The results of these experiments will be published in a Replication Study. [The project](#) will provide evidence about reproducibility in cancer biology, and an opportunity to identify factors that influence reproducibility more generally.

Articles

HUMAN BIOLOGY AND MEDICINE

Discovery and Preclinical Validation of Drug Indications Using Compendia of Public Gene Expression Data



ORIGINAL ARTICLE

M Sirota, JT Dudley, J Kim, AP Chiang, AA Morgan, A Sweet-Cordero, J Sage, AJ Butte

Science Translational Medicine
2011;3:96ra77
[10.1126/scitranslmed.3001318](https://doi.org/10.1126/scitranslmed.3001318)



REGISTERED REPORT

May 5, 2015

Irawati Kandela, Ioannis Zervantonakis,
Reproducibility Project: Cancer Biology

eLife 2015;4:e06847
[10.7554/eLife.06847](https://doi.org/10.7554/eLife.06847)

HUMAN BIOLOGY AND MEDICINE | MICROBIOLOGY AND INFECTIOUS DISEASE

Intestinal inflammation targets cancer-inducing activity of the

Project 1. Cancer Biology Reproducibility Project

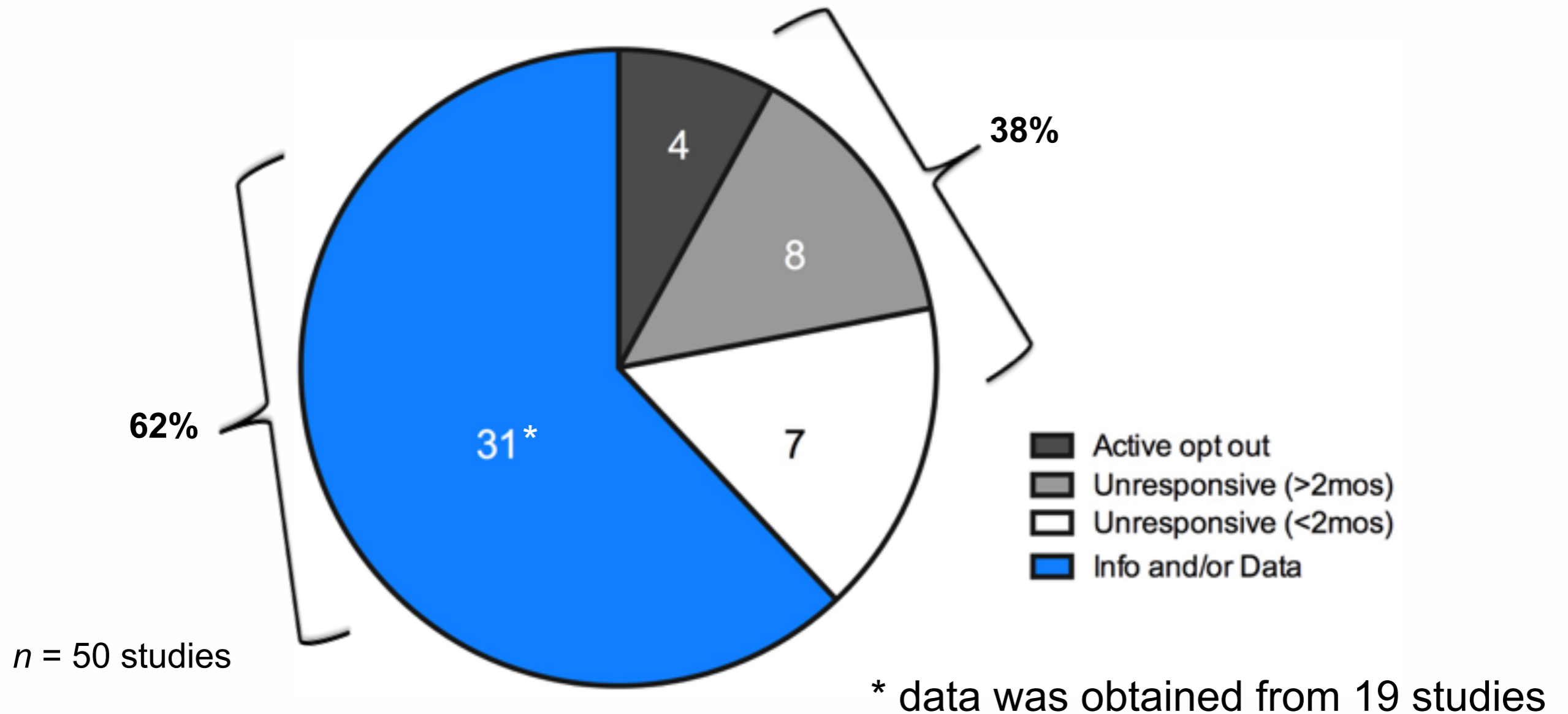
Key learnings to date:

- Publications have insufficient documentation to enable replication or follow on studies
 - all studies required additional information from original authors
 - frequently the only author with the required knowledge is the first author and they are often not able to be contacted
- Reagents are often not uniquely identified, not available or cannot be easily shared due to bureaucratic MTA requirements
 - need for centralized repositories and deposition requirements for research materials
- Raw data is infrequently stored or available
 - need for data repositories linked to published figures
- Replications are cost effective

RP: Cancer Biology

Project 1. Cancer Biology Reproducibility Project

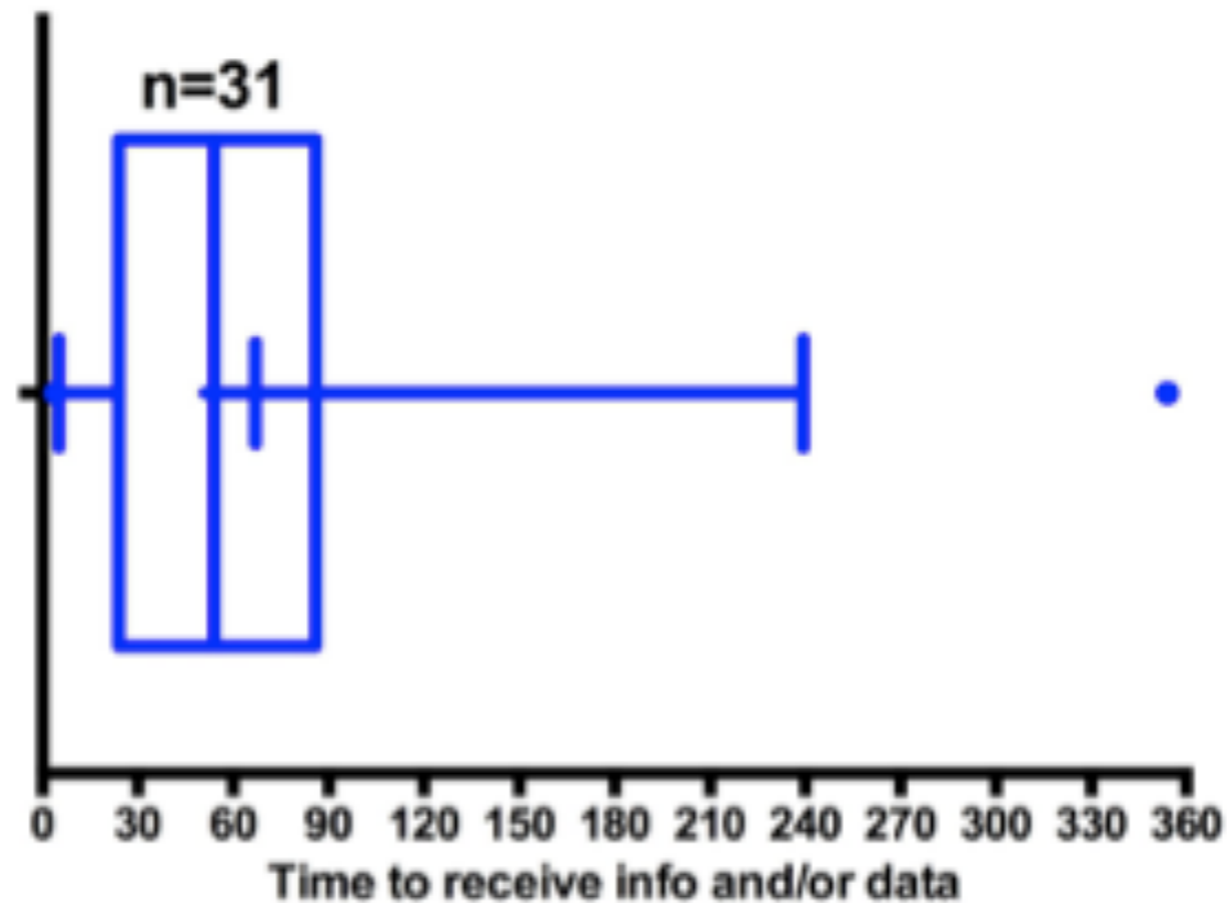
Author responsiveness:



RP: Cancer Biology

Project 1. Cancer Biology Reproducibility Project

Author responsiveness:

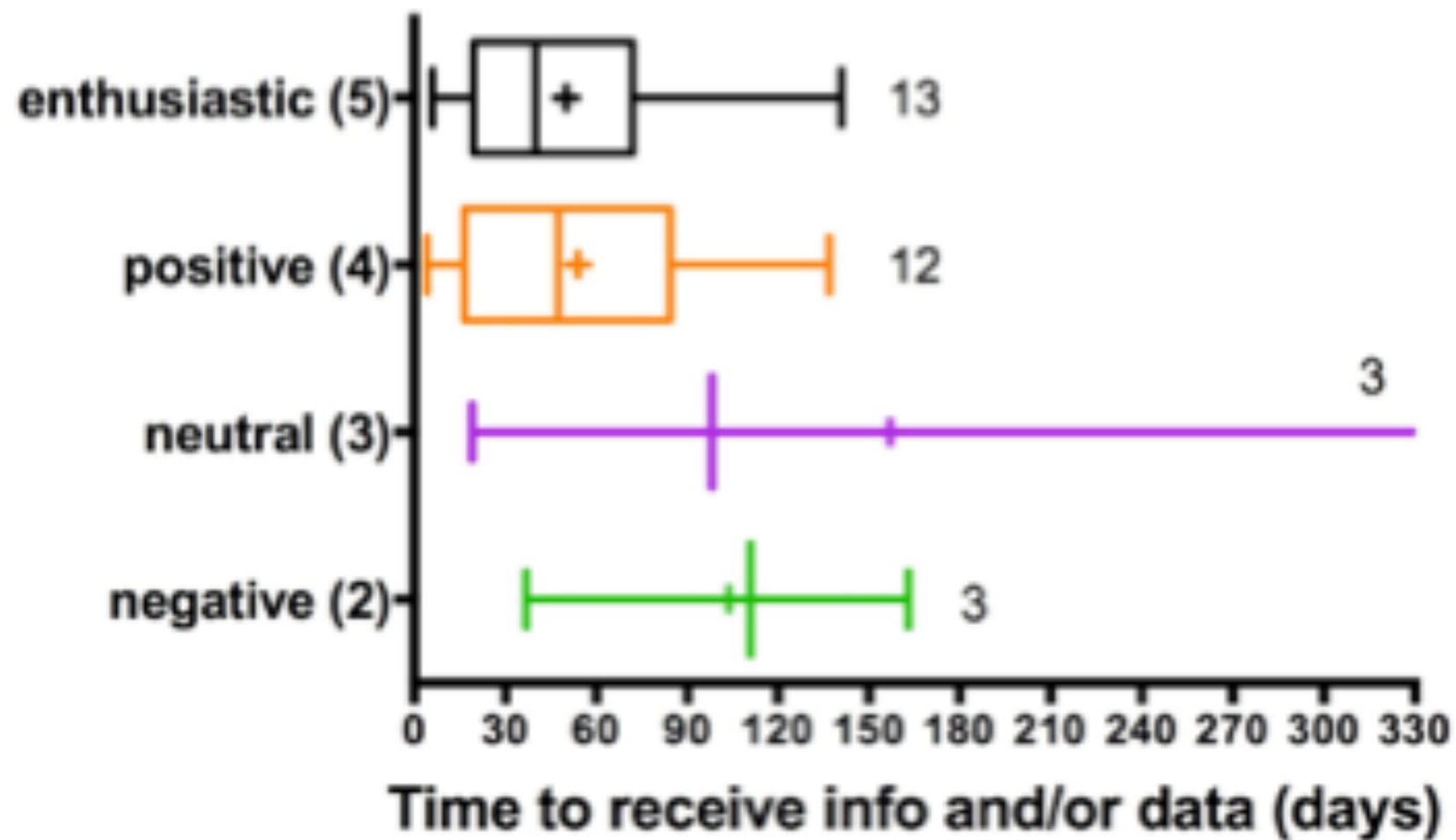


Mean = 67 days, max 354 days

RP: Cancer Biology

Project 1. Cancer Biology Reproducibility Project

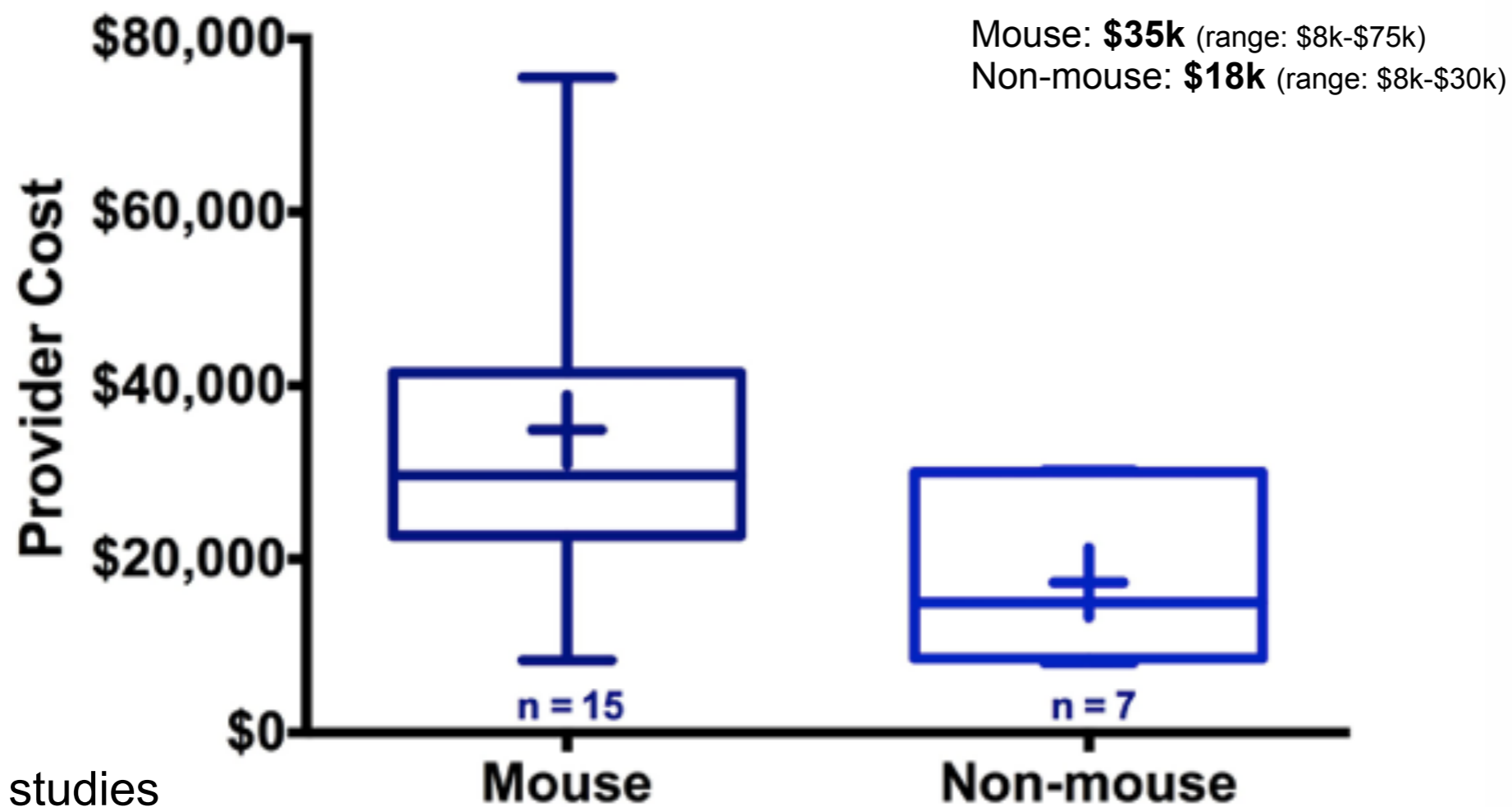
Author supportiveness:



RP: Cancer Biology

Project 1. Cancer Biology Reproducibility Project

Cost of replication studies:



n = 22 studies

RP: Prostate Cancer

Project 2. Reproducibility Project: Prostate Cancer



“Science Exchange, in collaboration with PCF, will identify faster high-impact biomedical research findings that could speed earlier detection and new cures.”

Reagent verification

antibodies -online.com

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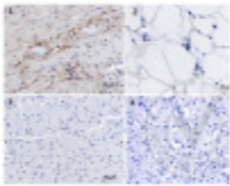
Details for Product No. ABIN734003
Elastin (ELN) (C-Term) antibody



Successfully validated
by Beth Israel Deaconess Medical
Center Confocal Imaging Core
No. 028751
Date 09/24/2013

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Antigen	Elastin (ELN)	
Synonyms	SVAS, WBS, WS, AI385707, AI480567, E030024M20Rik, Trela, TREL11, Trela26, RATTREL11, ELN	
Epitope	C-Term	

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- Reproducibility will become a primary metric for researchers
- Reproducibility requirements will promote greater documentation and sharing of reagents, equipment, protocols and data
 - potential opportunities to automate and facilitate this process
- Quality control of reagents will become increasingly important
 - certification as a means to build trust



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