
# Biomedical Replication Studies

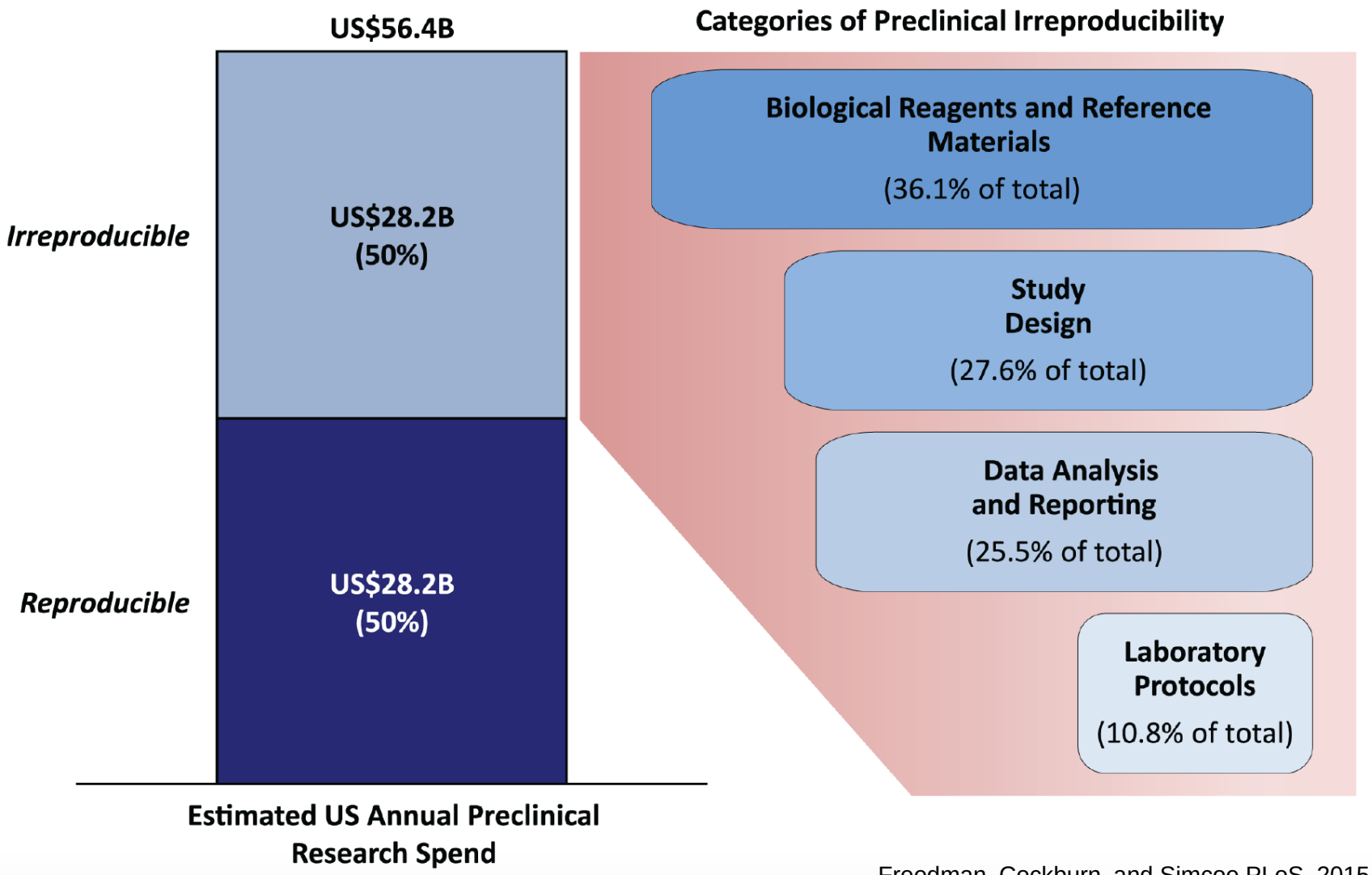
Elizabeth Iorns, PhD and Nicole Perfito, PhD

May 2017 – 5th World Conference on Research Integrity

# Annual Preclinical Spend

## $28B

Spent on irreproducible studies




Freedman, Cockburn, and Simcoe PLoS 2015

Science EXCHANGE

# Reproducibility rates in biomedical studies ranged between 0 to 21%


0%

- Re-tested 70+ drugs from 221 independent studies[1]
- Minocycline: effective in four separate ALS mouse studies worsened symptoms in a clinical trial of more than 400 patients[2]


11%

- Attempted to replicate 53 “landmark” oncology studies
- 6 of 53 fully reproduced


16%

- Sponsored replication of 12 spinal cord injury studies
- 2 of 12 fully reproduced


21%

- Conducted in-house target validation studies
- 14 of 67 fully reproduced

*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).*

# Defining Reproducibility

PERSPECTIVE | SCIENTIFIC INTEGRITY

## What does research reproducibility mean?

**Steven N. Goodman*, Daniele Fanelli and John P. A. Ioannidis**

+ See all authors and affiliations

*Science Translational Medicine* 01 Jun 2016:
Vol. 8, Issue 341, pp. 341ps12
DOI: 10.1126/scitranslmed.aaf5027

### Results reproducibility

Results reproducibility (previously described as replicability) refers to obtaining the same results from the conduct of an independent study whose procedures are as closely matched to the original experiment as possible.

.... Reproducibility is a minimum necessary condition for a finding to be believable and informative."

Science EXCHANGE

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

Science EXCHANGE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

# 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

Published: May 15, 2013 • https://doi.org/10.1371/journal.pone.0063221

| | |
|---|---|
| 124 Save | 52 Citation |
| 16,115 View | 146 Share |

## 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.

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

# 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

Published: May 15, 2013 • https://doi.org/10.1371/journal.pone.0063221

| 124 Save | 52 Citation |
|---|---|
| 16,115 View | 146 Share |

## 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.

Less than 30% of respondents who could not reproduce published findings published their failure

# Why don’t scientists publish their failures and enable self-correction?

- Replication experiments are not the norm
- Creates issues with retaliation from community of peers
- Can be difficult to interpret results, particularly from studies that were not originally designed as formal replications

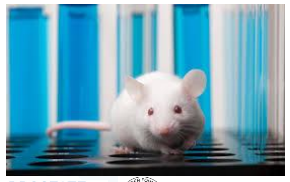
Science EXCHANGE

# Science Exchange: Replication Projects

Reproducibility Project: Cancer Biolo

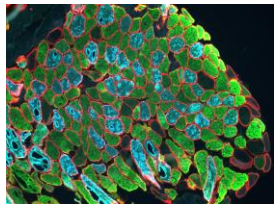
Independent Antibody Validation Initiative



PCF Movember Foundation Reproducibility Initiative

3ie Gates Foundation Reanalysis Studies

Reproducibility Initiative



Private pharmaceutical validations

HUMAN BIOLOGY AND MEDICINE

# The CD47-signal regulated protein alpha (SIRPa) interaction is a therapeutic target for human solid tumors

## ORIGINAL ARTICLE

April 24, 2012

SB Willingham, JP Volkmer, AJ Gentles, D Sahoo, P Dalerba, SS Mitra, J Wang, H Contreras-Trujillo, R Martin, JD Cohen et al.

*Proceedings of the National Academy of Sciences of USA* 2012;109:6662-6667

10.1073/pnas.1121623109

## REGISTERED REPORT

January 26, 2015

Denise Chroscinski, Nimet Maherali, Erin Griner, Reproducibility Project: Cancer Biology

eLife 2015;4:e04586

10.7554/eLife.04586

## REPLICATION STUDY

January 19, 2017

Stephen K Horrigan, Reproducibility Project: Cancer Biology

eLife 2017;6:e18173

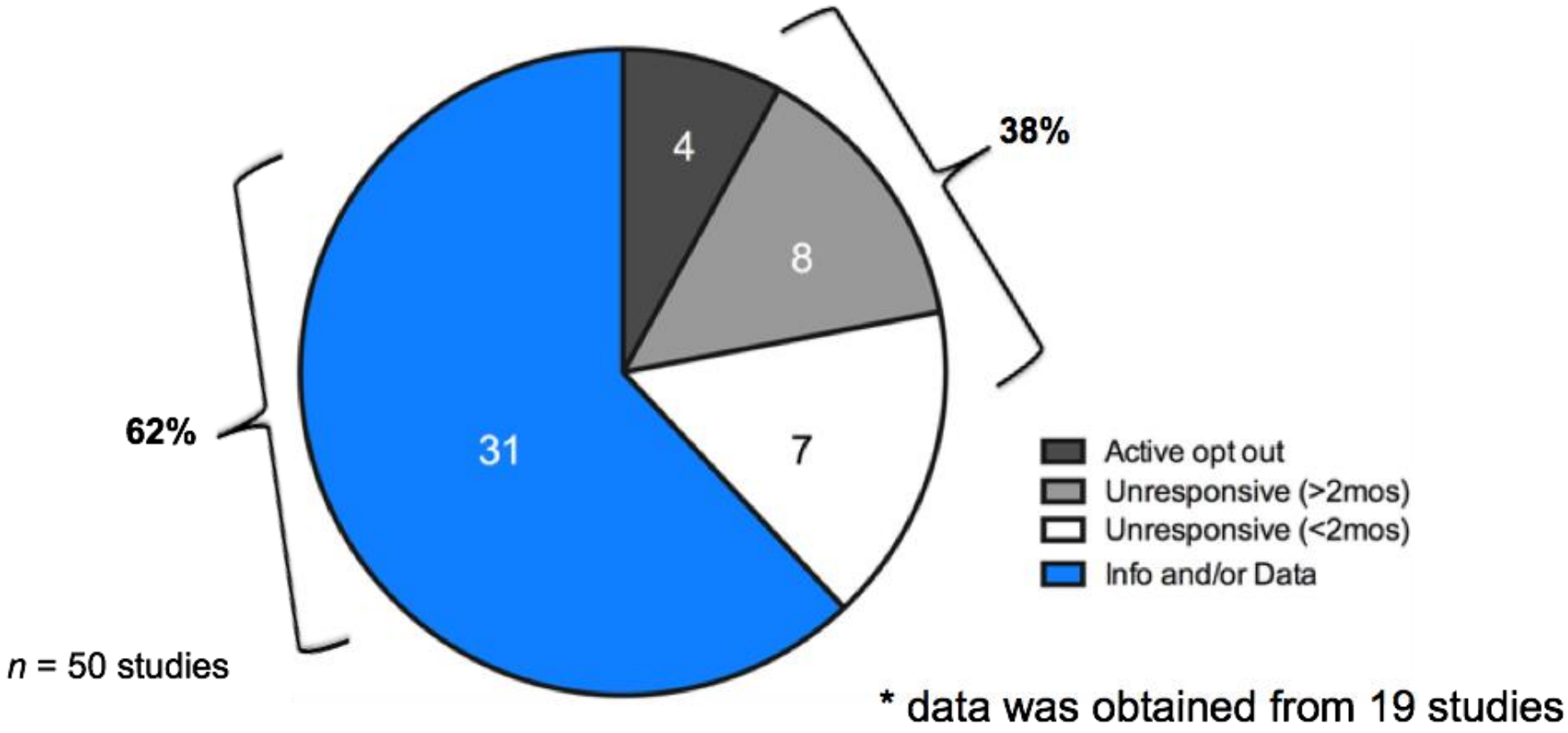
10.7554/eLife.18173

1. Where possible, we obtained input from the original authors (and unique non-commercial reagents as well as data)

# Replication study best practices

Author responsiveness:



HUMAN BIOLOGY AND MEDICINE

# The CD47-signal regulated protein alpha (SIRPa) interaction is a therapeutic target for human solid tumors

**ORIGINAL ARTICLE**

April 24, 2012

SB Willingham, JP Volkmer, AJ Gentles, D Sahoo, P Dalerba, SS Mitra, J Wang, H Contreras-Trujillo, R Martin, JD Cohen et al.

*Proceedings of the National Academy of Sciences of USA* 2012;109:6662-6667

10.1073/pnas.1121623109

**REGISTERED REPORT**

January 26, 2015

Denise Chroscinski, Nimet Maherali, Erin Griner, Reproducibility Project: Cancer Biology

eLife 2015;4:e04586

10.7554/eLife.04586

**REPLICATION STUDY**

January 19, 2017

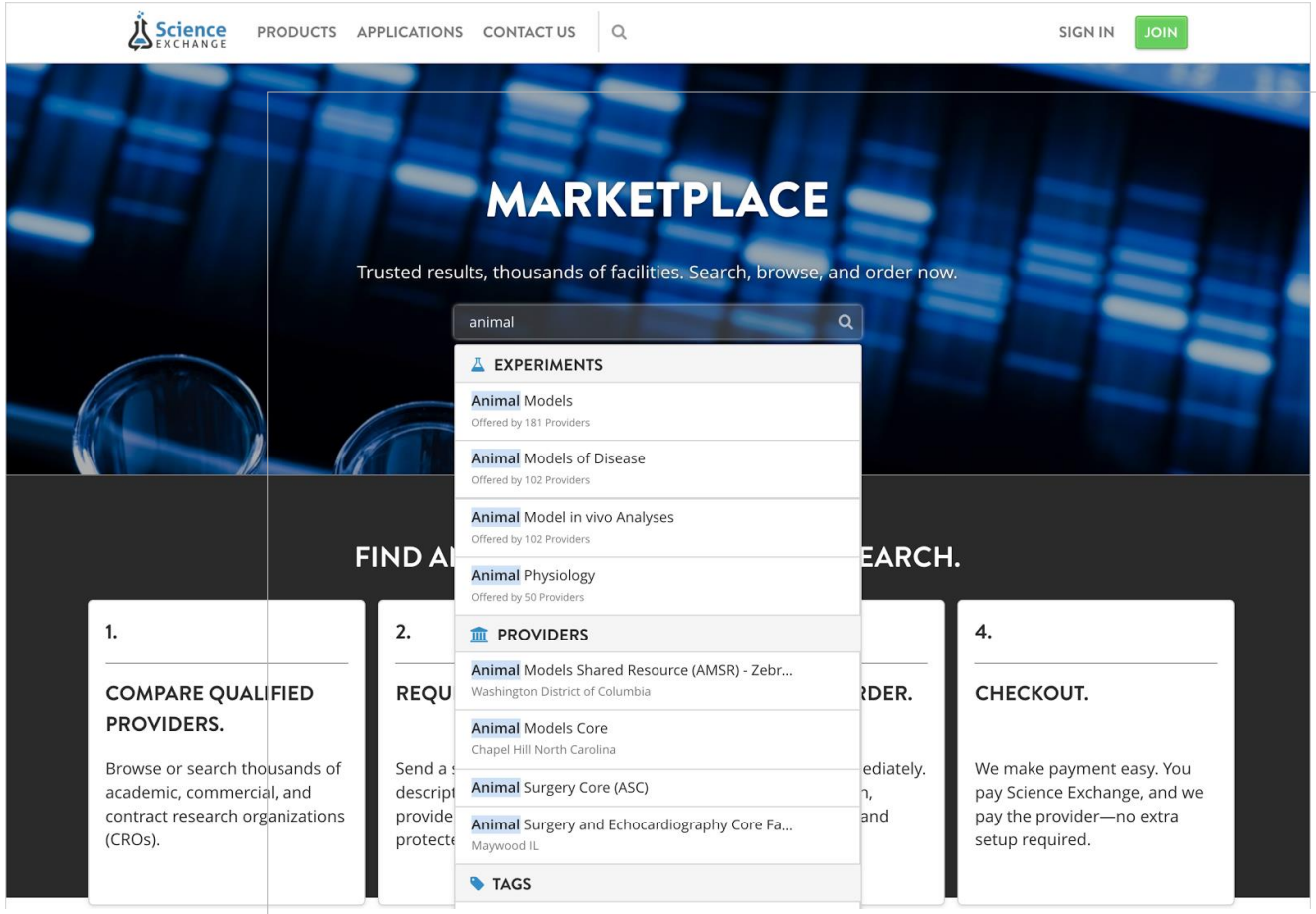
Stephen K Horrigan, Reproducibility Project: Cancer Biology

eLife 2017;6:e18173

10.7554/eLife.18173

2. Pre-establish (and pre-register) protocols and analysis plans
3. Use power calculations to ensure replication sample size is sufficient to detect the reported effect with sufficient power




4. Use expert, independent labs with extensive expertise in the techniques being replicated

Science EXCHANGE

Open Science Framework

HUMAN BIOLOGY AND MEDICINE

# The CD47-signal regulated protein alpha (SIRPa) interaction is a therapeutic target for human solid tumors

## ORIGINAL ARTICLE

April 24, 2012

SB Willingham, JP Volkmer, AJ Gentles, D Sahoo, P Dalerba, SS Mitra, J Wang, H Contreras-Trujillo, R Martin, JD Cohen et al.

*Proceedings of the National Academy of Sciences of USA* 2012;109:6662-6667

10.1073/pnas.1121623109

## REGISTERED REPORT

January 26, 2015

Denise Chroscinski, Nimet Maherali, Erin Griner, Reproducibility Project: Cancer Biology

eLife 2015;4:e04586

10.7554/eLife.04586

## REPLICATION STUDY

January 19, 2017

Stephen K Horrigan, Reproducibility Project: Cancer Biology

eLife 2017;6:e18173

10.7554/eLife.18173

5. Make all protocols, results, and data open and accessible to everyone
6. Results are published regardless of findings

# RP:CB Project Status

50 most impactful papers from 2010-2012 in cancer biology

31 Registered Reports submitted to eLife

- 29 accepted and published
- 2 rejected

8 replication studies completed

- 5 replication studies published
- 3 replication studies in review

21 replication studies ongoing

19 potential studies on hold

**Meta-Analysis for all Replication Studies**

- What were the main road-blocks to conducting replication studies
- How much do they cost on average?
- What factors were associated with studies that were more likely to replicate?

Science EXCHANGE

# Promoting a culture of replication

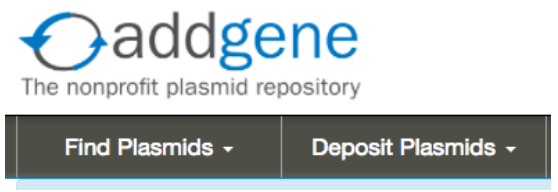
## 1. Reduce reliance on contacting original authors

Update journal formats to capture more information and data



Uniquely identify commercial reagents


Repositories for materials





# Promoting a culture of replication

**2. Divide research studies into different categories and identify studies in each category**

Exploratory
Novel Studies

- Multi-year Investigator initiated grants

Confirmatory
Studies

- Technical Experts
- May require different types of labs and scientists (e.g. Core Facilities)
- Rigorous QC Procedures

Science EXCHANGE

# Promoting a culture of replication

## 3. Provide funding for Replication

nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio & Video | For A

News & Comment > News > 2016 > September > Article

NATURE | NEWS

Dutch agency launches first grants programme dedicated to replication

**Three-year pilot devotes €3 million to verifying other studies.**

Monya Baker

20 July 2016 | Updated: 20 July 2016

Rights & Permissions

The Netherlands has launched what researchers say is the world's first national fund dedicated to replication studies: a pot of €3 million (US$3.3 million) over the next 3 years for Dutch scientists to test whether they can reproduce important research results in social and medical sciences.

Science EXCHANGE

# Thank you.


- RPCB Core Team
- Science Exchange labs
- Center for Open Science
- eLife
- Laura & John Arnold Foundation
- Reagent donors
- Prostate Cancer Foundation
- 3IE /Gates Foundation



Contact

Nicole Perfito

nicole@scienceexchange.com

| Published Studies | Were effects in the same direction? | Were effects statistically significant? |
|---|---|---|
| **Aird et al. 2017. Replication study: BET bromodomain inhibition as a therapeutic strategy to target c-Myc** | Yes | No |
| **Horrigan et al. Replication study: The CD47-signal regulatory protein alpha (SIRPa) interaction is a therapeutic target for human solid tumors** | No | No |
| **Horrigan et al. Replication study: Melanoma genome sequencing reveals frequent PREX2 mutations** | No | No |
| **Kandela, et al. Replication study: Discovery and preclinical validation of drug indications using compendia of public gene expression data** | Yes | Yes |
| **Mantis et al. Replication study: Coadministration of a tumor penetrating peptide enhances the efficacy of cancer drugs** | 2 of 3 | No |

Science EXCHANGE