

# PROMOTING TRANSPARENT RESEARCH METHODS, PROTOCOLS AND DATA TO REDUCE IRREPRODUCIBILITY

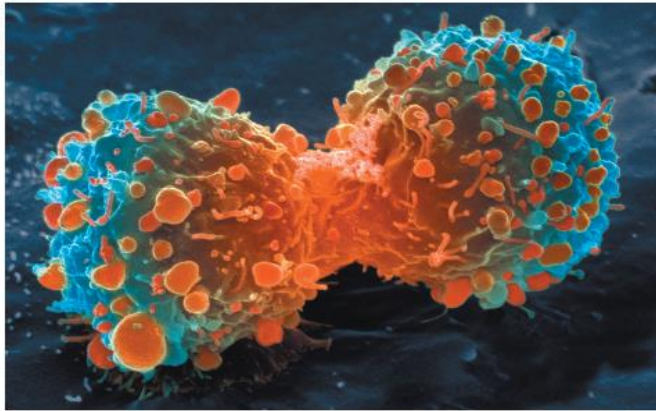
December 2015 | STM Innovations Seminar

Andrew L Hufton, PhD  
Managing Editor, *Scientific Data*  
Nature Publishing Group

**SPRINGER NATURE**

# Why Most Published Research Findings Are False

John P. A. Ioannidis



Many landmark findings in preclinical oncology research are not reproducible, in part because of inadequate cell lines and animal models.

## Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

*PloS Medicine* 2005  
doi: [10.1371/journal.pmed.0020124](https://doi.org/10.1371/journal.pmed.0020124)

*Nature* 2012  
doi: [10.1038/483531a](https://doi.org/10.1038/483531a)

*NRDD* 2011  
doi: [nrd3439](https://doi.org/10.1038/nrd3439)

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Believe it or not: how much can we rely on published data on potential drug targets?

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*Florian Prinz, Thomas Schlange and Khusru Asadullah*

# Transparency issues that undermine reproducibility

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- Methods descriptions  
Common issues: randomization, blinding, sample size determinations, independent experiments vs technical replicates
- Statistical clarity
- Gels, microscopy images unduly manipulated
- Missing controls and markers
- Reagent validity – antibodies, cell lines
- Animal studies description
- Data access, deposition & reusability

Needs joint approach from funders, publishers, institutions, researchers

# **Methodological details**

Reporting checklists

**1**

# Reporting checklist of statistical and methodological details

Please ensure that the answers to the following questions are reported in the manuscript itself. We encourage you to include a specific subsection in the Methods section for statistics, reagents and animal models. **Below, provide the page numbers (s) for where the information can be located.**

## Statistics and General Methods

## Reported in section/paragraph or page #:

1. How was the sample size chosen to ensure adequate power to detect a pre-specified effect size?  
(Give section/paragraph or page number)

For animal studies, include a statement about sample size estimate even if no statistical methods were used. *For example, "No statistical method was used to predetermine sample size."*

2. Describe inclusion/exclusion criteria if samples or animals were excluded from the analysis. Were the criteria pre-established?  
(Give section/paragraph or page number)

manuscript prior to formal acceptance.

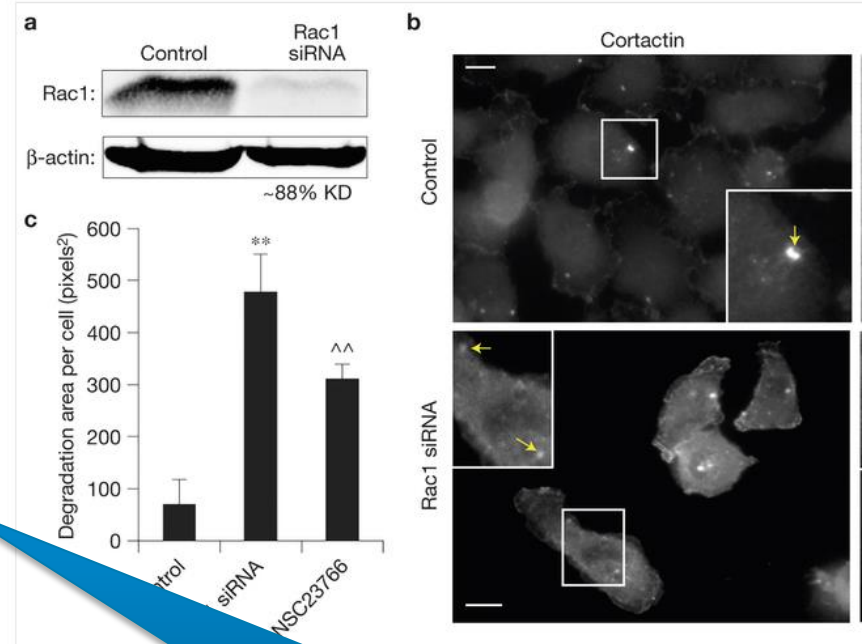
Reproducibility checklist also currently being trialled at various BMC journals, including *BMC Biology*, *BMC Neuroscience*, *Genome Biology*, and *GigaScience*.

# Raising reporting standards for data description

## Checklist to improve figure legends and reporting

**(a)** Western blot of cell lysates of control and Rac1-siRNA-treated MTLn3 cells, blotted for Rac1 and  $\beta$ -actin. **A representative image is shown from 3 blots.** **(b)** MTLn3 cells transfected with control or Rac1 siRNA and plated on Alexa-405-conjugated gelatin overnight. Arrows point to invadopodia and sites of degradation. Scale bars, 10  $\mu$ m. Representative image sets are shown from 50 image sets each for the control and Rac1 siRNA. **(c)** Quantification of mean degradation area per cell from **b**, including Rac1 inhibitor NSC23766 treatment at 100  $\mu$ M.  **$n = 60$  fields for each condition, pooled from 5 independent experiments;** error bars are s.e.m. Student's *t*-test was used. **\*\* $P = 0.00022$ ,  $\wedge \wedge P = 0.011639$ .** **Uncropped images** of blots are shown in Supplementary Fig. 9.

statement of replication



definition of  $n$

definition of statistic tests

raw source data

## **Maximizing the reuse of research techniques**

Protocol publication adds value and provides credit

# 2

A peer-reviewed journal of laboratory protocols. Each is presented in a 'recipe' style, with step-by-step descriptions which users can immediately apply in their own research.

Open resource maintained by NPG: collaborative, open (CC-NC), free to post and read

## Timing

Abstract • Introduction • Materials • Procedure • Tables of contents • References • Acknowledgments • Author contributions

Steps 1–3, protein storage and analysis: 1 d  
Steps 4–6, immunization: 6 weeks  
Steps 7–10, blood sampling and lymphocyte isolation: 6 weeks  
Steps 11 and 12, analysis of serum conversion: 2 weeks  
Steps 13–18, isolation of total RNA: 1 d  
Steps 19 and 20, cDNA synthesis: 4 h  
Steps 21–36, construction of the immune library: 6 weeks  
Steps 37–45, rescue and titration: 6 weeks  
Steps 46–61, antigen production and immunization: 6 weeks  
Steps 62–67, screening: 6 weeks  
Steps 68 and 69, selection: 6 weeks  
Steps 70–73, expression and purification: 6 weeks  
Box 1, ELISA: 2 d

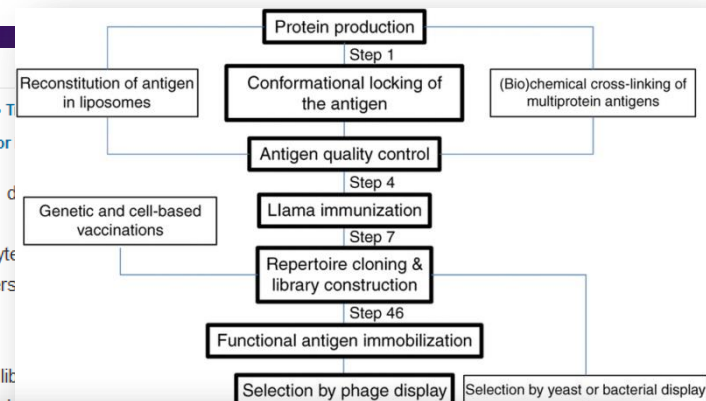
## REAGENTS

- Llamas

**Caution:** All vaccination experiments should be executed in accordance with the applicable animal welfare legislation, and they must be approved by the local ethics committee.

- Acetic acid, glacial (Merck, cat. no. 1.00058.2500)

**Caution:** Glacial acetic acid is corrosive. Avoid inhalation and exposure to skin and eyes.



## Production of neuron-preferential lentiviral vectors

Authors: Takashi Torashima, Chiho Koyama, Haruhiro Higashida, Hirokazu Hirai

Lab groups: H. Higashida Lab (Kanazawa Univ)

Associated Publications: [CD38 is critical for social behaviour by regulating oxytocin secretion](#)

Adenoviral vectors widely used to transfer foreign genes into neuronal cells possess tropism for glial cells 1, 2 and are toxic to infected cells. Alternatively, the use of lentiviral vectors for t...



## **Access to data underlying the paper**

Transparency for data

3

## Fundamental sharing policy for *Nature* and the Nature research journals

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An inherent principle of publication is that others should be able to replicate and build upon the authors' published claims. A condition of publication in a Nature journal is that **authors are required to make materials, data, code, and associated protocols promptly available** to readers without undue qualifications. Any restrictions on the availability of materials or information must be disclosed to the editors ... [and] ... in the submitted manuscript.

Supporting data must be made available to editors and peer-reviewers at the time of submission for the purposes of evaluating the manuscript.

See <http://www.nature.com/authors/policies/availability.html>

# Step one: removing barriers to sharing

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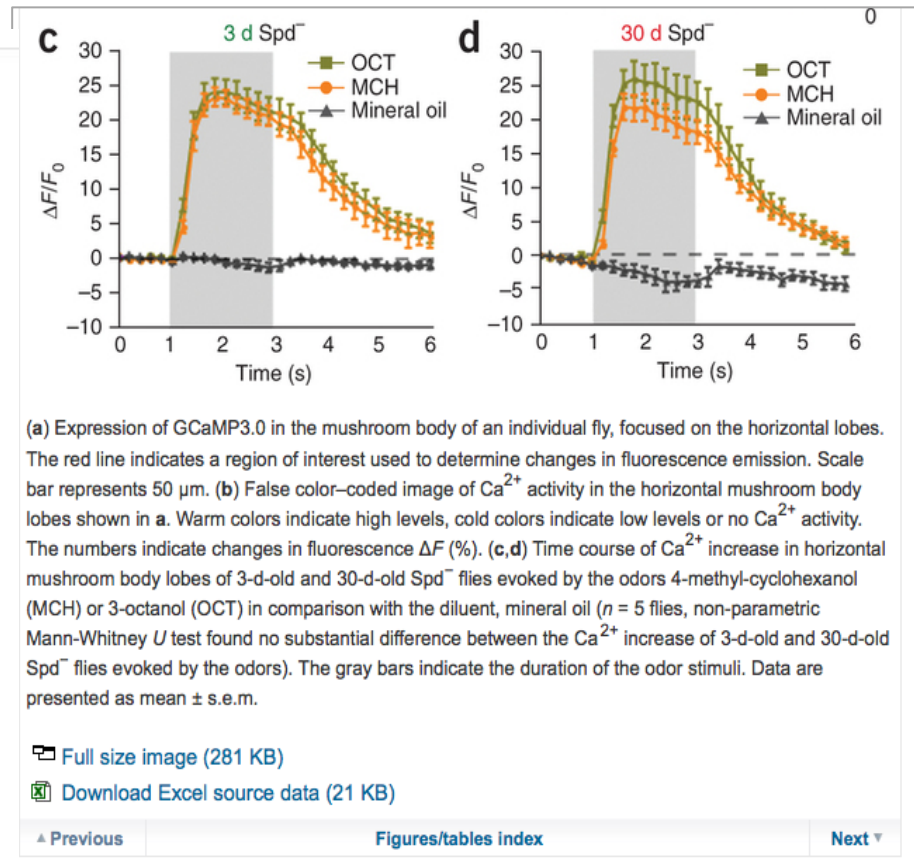
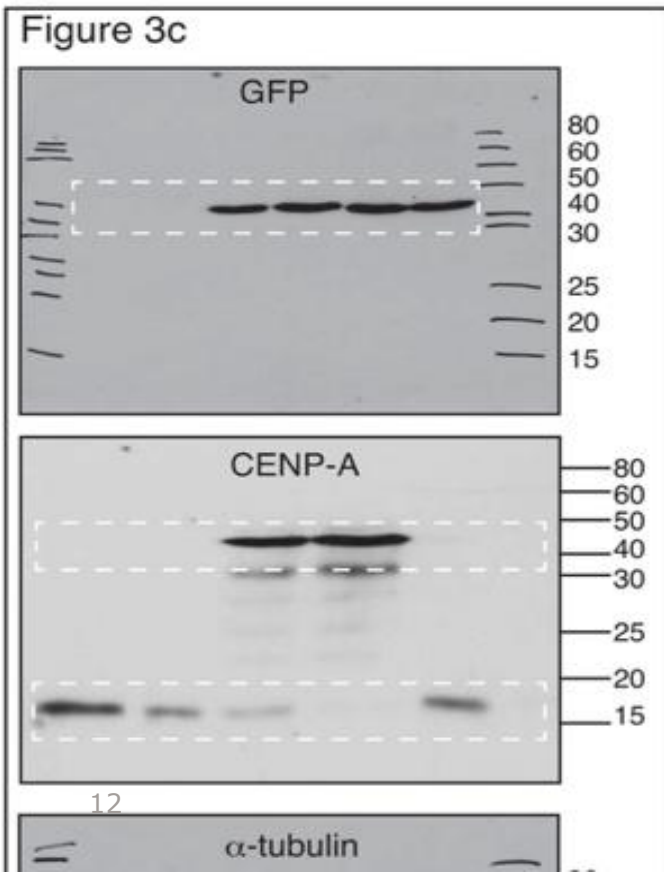
- Nature-titles and *Scientific Data* explicitly allow pre-publication sharing of data and article preprints
- Publication of data articles will not compromise novelty of subsequent research articles
- Similar policies at the BMC journals



# Solution for small datasets

## Source data – aka “data behind the graph”

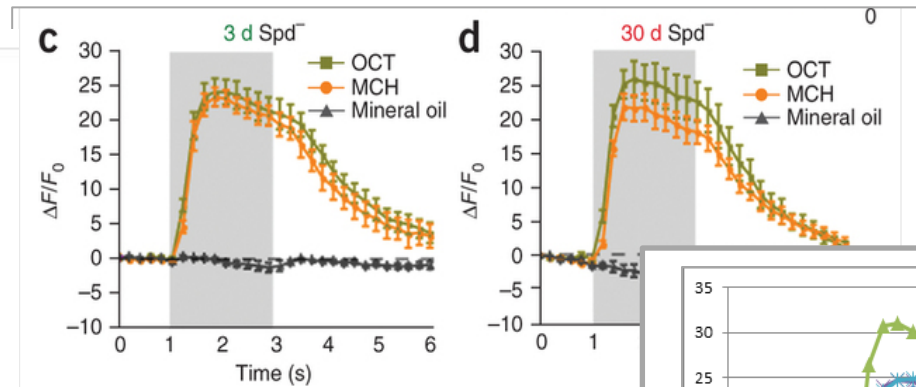
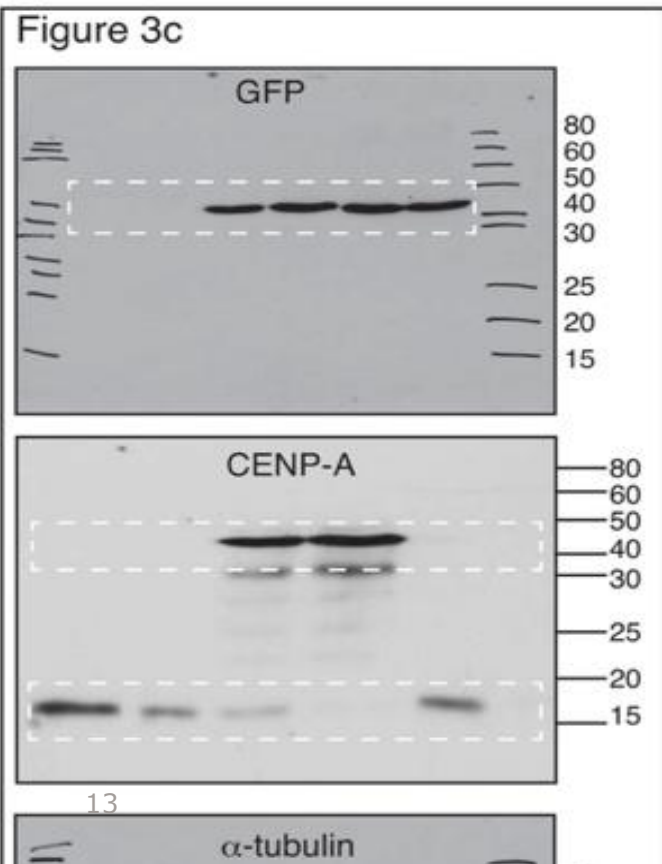
- Non-processed data and numerical values that went into making the figure
- presented in a file that can be downloaded from the figure legend



# Solution for small datasets

## Source data – aka “data behind the graph”

- Non-processed data and numerical values that went into making the figure
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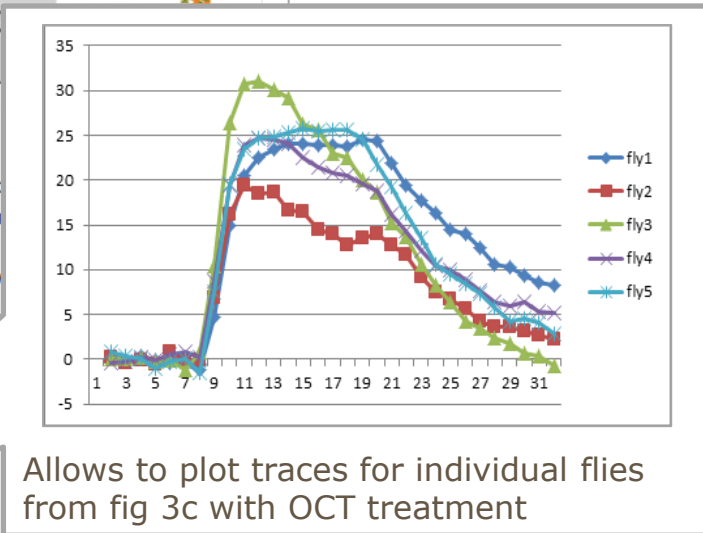
(a) Expression of GCaMP3.0 in the mushroom body of an individual fly, for the lobes shown in (b). The red line indicates a region of interest used to determine changes in fluorescence. The gray bar represents 50  $\mu$ m. (b) False color-coded image of Ca<sup>2+</sup> activity in the mushroom body lobes of 3-d-old and 30-d-old Spd<sup>-</sup> flies evoked by the odors (MCH) or 3-octanol (OCT) in comparison with the diluent, mineral oil. The numbers indicate changes in fluorescence  $\Delta F$  (%). (c, d) Time course of calcium activity in the mushroom body lobes of 3-d-old (c) and 30-d-old (d) Spd<sup>-</sup> flies evoked by the odors (MCH) or 3-octanol (OCT) in comparison with the diluent, mineral oil. The numbers indicate changes in fluorescence  $\Delta F$  (%). The gray bars indicate the time of odor presentation. The Mann-Whitney *U* test found no substantial difference between the responses of 3-d-old and 30-d-old Spd<sup>-</sup> flies evoked by the odors. The gray bars indicate the time of odor presentation. The numbers are presented as mean  $\pm$  s.e.m.

[Full size image \(281 KB\)](#)  
[Download Excel source data \(21 KB\)](#)

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[Figures/tables index](#)

[Next](#)



Allows to plot traces for individual flies from fig 3c with OCT treatment

# Data-access practices strengthened in Nature journals

*Nature* editorial (Nov 2014)

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- Clear preference for sharing large datasets via public repositories.
- Enforce data deposition in fields where there is strong community consensus
- List of public data repositories now maintained by *Scientific Data*
- Encourage authors to publish Data Descriptors at *Scientific Data*
  - before, with or after the analysis paper
  - editors work with authors

## Maximizing the reuse of data

Data journals add value and provide credit for reusable data

SCIENTIFIC DATA 

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## Data publication

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### Get Credit for Sharing Data

Publications will be listed in the major indexes and will be citeable



### Focused on Data Reuse

All the information others need to reuse the data; no interpretative analysis or hypothesis testing



### Open-access

The main article is published by default under the CC BY licence. Each publication supported by curated CC0 metadata



### Peer-reviewed

Rigorous peer-review by  
researchers ensures data

**Data Note** article-type available at  
two BMC journals



### Promoting Community

Data stored in communi

**(GIGA)<sup>n</sup>  
SCIENCE**

**BMC  
Research Notes**



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SCIENTIFIC DATA | DATA DESCRIPTOR **OPEN**

## Global integrated drought monitoring and prediction system

Zengchao Hao, Amir AghaKouchak, Navid Nakhjiri & Alireza Farahmand

Affiliations | Contributions | Corresponding author

Scientific Data 1, Article number: 140001 | doi:10.1038/sdata.2014.1  
Received 12 November 2013 | Accepted 10 January 2014 | Published online 11 March 2014

Associated Links

- Previously unpublished dataset
- Data in figshare
- Code in figshare
- Integrated figshare data viewer

*Cited 37 times, according to Google Scholar*

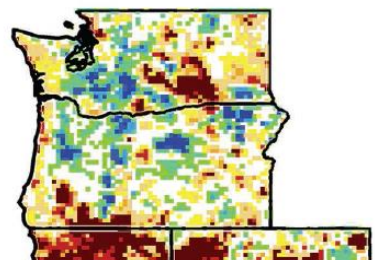
PDF ISA t

## LETTERS

edited by Jennifer Sills

### Australia's Drought: Lessons for California

MOST OF CALIFORNIA IS SUFFERING FROM AN extreme drought, and storage levels in the major reservoirs are well below historic levels. For the past several months, an unusually stubborn ridge of high pressure off the West Coast of the United States has been blocking normal winter storms and the rain they carry. California's history of drought has led to state-wide strategies to save water, but Californian residents and policy-makers can do even more: They can look to the story of Australia's experience with a drought so intense and long-lasting



sumptive activities watering and car wa ing efficient water: ments for shutoff those temporary restrictions grew. still restrict daytim most relevant for how the Australia changes. Studies goodwill and coop stress of drought (6

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\*Corresponding author. E-mail: amir.a@uci.edu

#### References

1. A. I. Dijk *et al.*, *Water Resources Res.* **49**, 1040 (2013).
2. Z. Hao *et al.*, *Sci. Data* **1**, 1 (2014).
3. S. Dolnicar, A. I. Schäfer, *J. Environ. Manage.* **90**, 888 (2009).

**Thank you for listening!**

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Thank you to colleagues:

Iain Hrynaszkiewicz, Head of Data and HSS Publishing  
Sowmya Swaminathan, Head of Editorial Policy

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