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### **The Scientific Record**

### The basis for:

Current and future research (including clinical trials)

Public policy (medical, environmental, etc)

#### Healthcare



Johannes Kepler 1627

### **The Scientific Record**

### The basis for:

## Current and future research (including clinical trials)

Public policy (medical, environmental, etc)

### Healthcare

### The Poldermans case

"...European Society of Cardiology guideline recommending the liberal use of beta-blockers [...] was partly based on unreliable research."

#### Forbes / Pharma & Healthcare

JAN 15, 2014 @ 12:37 PM 45,237 VIEWS

Medicine Or Mass Murder? Guideline Based on Discredited Research May Have Caused 800,000 Deaths In Europe Over The Last 5 Years

#### The Wakefield Case

- Falsified vaccination-autism claims
- Measles epidemics



#### MMR and measles

"Fifty-three papers were deemed 'landmark' studies [...] scientific findings were confirmed in only 6 (11%) cases."

#### -Amgen USA





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.

Fiforts over the past decade to characterize the genetic alterations in human cancers have led to a better understanding of molecular drivers of this complex set of diseases. Although we in the cancer field hoped that this would lead to more effective drugs, historically, our ability to translate cancer research to clinical success has been remarkably (not "Sadly, cally cally

to trials in oncology have the highest failure one rate compared with other therapeutic areas. Given the high unmet need in oncology, it is understandable that barriers to clinical the development may be lower than for other disease areas, and a larger number of drugs with suboptimal pre-clinical wildation with uccace ease its on sustainable or acceptable, and enter oncology trials. However, this low sucing the substantial substantial substantial substantial ease areas in substainable or acceptable, and succount of the substantial substantial substantial substantial substantials. However, this low succoust net is not sustainable or acceptable, and substantials. investigators must reassess their approach to translating discovery research into greater clinical success and impact.

Many factors are responsible for the high failure rate, notwithstanding the inherently difficult nature of this disease. Certainly, the limitations of preclinical tools such as inadequate cancer-cell-line and mouse models' make it difficult for even **>** 

29 MARCH 2012 | VOL 483 | NATURE | 531 © 2012 Macmillan Publishers Limited. All rights reserved

Nature 2012

In 67 projects only 33% of published preclinical studies could be validated to the point at which projects could continue.

-Bayer HealthCare Germany

#### CORRESPONDENCE

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

Florian Prinz, Thomas Schlange and Khusru Asadullah

Nature Rev Drug Discovery 2011

"100 experimental and correlational studies published in three psychology journals.

39% of effects were subjectively rated to have replicated the original result"



#### **RESEARCH ARTICLE SUMMARY**

PSYCHOLOGY

## Estimating the reproducibility of psychological science

**Open Science Collaboration**\*

Science 2015

"...the complex system for ensuring the reproducibility of biomedical research is failing and is in need of restructuring."

#### NATURE | COMMENT

#### Policy: NIH plans to enhance reproducibility

Francis S. Collins & Lawrence A. Tabak

27 January 2014

Francis S. Collins and Lawrence A. Tabak discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

Nature 2014

### **Pressure to Publish**

"best" journals = career success (e.g. jobs, funding, promotions, etc.)

Potentially "high-impact" research at expense of careful work



Conflicts of interest impede correcting the scientific record

#### Authors / Journals / Institutions

"It is difficult to get a man to understand something, when his salary depends upon his not understanding it!" - Upton Sinclair

## Bypass conflicts of interest



Researcher to researcher - no intermediaries

#### > 70,000 comments

#### 14,000 articles

### 2300 journals



### Anonymous with Layered Safeguards

- Comments based on PUBLICLY VERIFIABLE information
- Comments moderated (not scientific review)
- Facilities for reporting abuse
- Permanent right of reply (author alerts)
- Show original data (full access coming!)
- Community surveillance
- Remember: publication was authors' choice



#### Another anti-vaxxer

- Published September 5th
- First PubPeer comment on September 20th
- Retracted October 10th



Subcutaneous injections of aluminum at vaccine adjuvant levels activate innate immune genes in mouse brain that are homologous with biomarkers of autism

Dan Li<sup>a</sup>, Lucija Tomljenovic<sup>a</sup>, Yongling Li<sup>a</sup>, Christopher A. Shaw<sup>a,b,c,\*</sup>

<sup>a</sup> Dept. of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, British Columbia, Canada <sup>b</sup> Program in Experimental Medicine, University of British Columbia, Vancouver, British Columbia, Canada <sup>c</sup> Program in Neuroscience, University of British Columbia, Vancouver, British Columbia, Canada



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## Put comments directly on journals

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Journal of Inorganic Biochemistry Volume 177, December 2017, Pages 39-54



Subcutaneous injections of aluminum at vaccine adjuvant levels activate innate immune genes in mouse brain that are homologous with biomarkers of autism Dan Li<sup>a</sup>, Lucija Tomljenovic<sup>a</sup>, Yongling Li<sup>a</sup>, Christopher A. Shaw<sup>a, b, c</sup> A Show more

https://doi.org/10.1016/j.jinorgbio.2017.08.035

35 comments on PubPeer (by: Calathus Mollis, Crepis Bursifolia, Mitracarpus Capitatus, Macrophthalmus Grandidieri, Sidymella Angulata, Caulanthus Californicus, Asclepias Macropus, Peristrophe Hyssopifolia, Caloptilia Kadsurae, Condylocarpon Amazonicum, Hoya Camphorifolia, Maniola Telmessia, Michael J. I. Brown, Centropyge Aurantia)

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#### Highlights

Mechanisms underlying aluminum adjuvant neurotoxicity have

#### **Browser Add-ons**

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Text availability Abstract Free full text Free full text Full text Commons Reader comments Trending articles Publication dates 5 years 10 years Custom range Species Humans Other Animals	<ul> <li>Items: 1 to 20 of 258</li> <li>w Fint Prov Page of 13 Next&gt; Last&gt;&gt;</li> <li>Meta-analysis of pharmacogenetic interactions in amyotrophic lateral sclerosis clinical trials.</li> <li>van Eijk RPA, Jones AR, Sproviero W, Shatunov A, Shaw PJ, Leigh PN, Young CA, Shaw CE, Mora G, Mandrioli J, Borghero G, Volanti P, Diekstra FP, van Rheenen W, Verstraete E, Eijkemans MJC, Veldinki JH, Chio A, Al-Chalabi A, van den Berg LH, van Es MA; For UKMND-LiCALS and LITALS Study Group.</li> <li>Neurology. 2017 Oct 4. pii: 10.1212/WNL.000000000004666. doi: 10.1212/WNL.000000000004666. [Epub ahead of print]</li> <li>PMID-28978660</li> <li>Similar ancies</li> <li>CSorf72 poly GA RAN-translated protein plays a key role in Amyotrophic Lateral Sclerosis via</li> <li>aggregation and toxicity.</li> <li>Lee YB, Baskaran P, Gomez J, Chen HJ, Nishimura A, Smith B, Troakes C, Adachi Y, Stepto A, Petrucelli L, Gallo JM, Hirth F, Rogelj B, Guthrie S, Shaw CE: Hum Mol Genet. 2017 Sep 13. doi: 10.1093/hmgldxd50. [Epub ahead of print]</li> <li>PMID-2897380</li> </ul>	Download CSV Find related data Database: Select • Find lenns Search details Shaw, Christopher [Full Author Name] OR Shaw, Christopher [Full Investigator Name]
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	Toxicology. 2017 Sep 1:390:159. doi: 10.1016/j.tox.2017.09.010. Epub 2017 Sep 18. No abstract available.           Image: state of the	Recent Activity
	Subcutaneous injections of aluminum at vaccine adjuvant levels activate innate immune genes in     mouse brain that are homologous with biomarkers of autism.     Li D, Tomljenovic L, Li Y, Shaw CA.     Jinorg Biochem. 2017 Sep 5:177:39-54. doi: 10.1016/j.jinorgbio.2017.08.035. [Epub ahead of print]	<ul> <li>Robotic esophagectomy: modified McKeown approach.</li> <li>PubMed</li> <li>A man with COPD, fever, and leucocytosis.</li> <li>PubMed</li> </ul>
	<ul> <li>35 comments on PubPeer (by: Calathus Mollis, Crepis Bursifolia, Mitracarpus Capitatus, Macrophthalmus Grandidieri, Sidymelia Angulata, Caulanthus Californicus, Asclepias Macropus, Peristorphe Hysosopholia, Calopitila Kadsurae, Condylocarpon Amazonicum, Hoya Camphorifolia, Maniola Telmessia, Michael J. I. Brown, Centropyge Aurantia)</li> <li>PMID: 28923356 Free Article</li> <li>Similar articles</li> </ul>	Kemp Kernstine (102) PubMed     Self-control relies on glucose as a limited     energy source: willpower is more tha PubMed     See more
	Skeletal trauma reflects hunting behaviour in extinct sabre-tooth cats and dire wolves.	See note

5. Brown C, Balisi M, Shaw CA, Van Valkenburgh B.

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#### Updated Jun 28, 2018

#### **Theoretical neuroscience**

Theory of spike initiation, sensory systems, autonomous behavior, epistemology

Editor Romain Brette

#### 66 Shares f

This journal highlights a number of papers that the editor personally finds interesting for computational or theoretical neuroscience, in particular but not limited to spike initiation, sensory systems, autonomous behavior and epistemology of neuroscience. These are not necessarily theoretical papers, but somehow relevant to theoretical neuroscientists (or more accurately, to the editor).

#### Published

#### Can robots make good models of biological behaviour? (2001-12) B Webb

http://www.ncbi.nlm.nih.gov/pubmed/12412325

Jun 28, 2018 - This is an essay about the epistemology of biorobotics, which consists in making robotic models of animals with the goal of understanding biology (as opposed to solving robotics problems). It is a mine of references about the epistemology of modelling, and in particular what we mea...

#### What Might Cognition Be, If Not Computation? (1995)

Tim Van Gelder

http://dx.doi.org/10.2307/2941061

Jun 22, 2018 - Because we are so used to think of the brain as a computer, some physical thing implementing computations (hence the name of the field « computational neuroscience »), a typical reaction to criticisms of that view is : « what else could it be, if not computation ? ». The ambition o…

#### Causal Circuit Explanations of Behavior: Are Necessity and Sufficiency Necessary and Sufficient? (2017)

Alex Gomez-Marin

http://dx.doi.org/10.1007/978-3-319-57363-2\_11

Jun 21, 2018 - This epistemological paper makes a number of important points about what constitutes an explanation in neuroscience, with many interesting pointers to relevant ideas in philosophy and psychology. A strong tendency in current literature is to identify neural circuits that are « nece...

Necessary and sufficient' in biology is not necessarily necessary - confusions and erroneous conclusions resulting from misapplied logic in the field of biology, especially neuroscience

Motojiro Yoshihara, Motoyuki Yoshihara

http://dx.doi.org/10.1080/01677063.2018.1468443

May 20, 2018 - This epistemological paper criticizes the lack of rigor in the use of the words "necessary"



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Subjects

Neuroscience (miscellaneous) Behavioral Neuroscience Cellular and Molecular Neuroscience Cognitive Neuroscience

Developmental Neuroscience Sensory Systems

Multidisciplinary Computational Systems



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- . Quickly pass information between scientists
- . Put focus on the data
- . Encourage wider use of preprints (arXiv, bioRxiv)



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