Animal data reliance bias in peer review: a barrier to scientific progress

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https://app.sli.do/event/4zlwcyln

Early definition of publication bias

Publication Bias: The Problem That Won't Go Away

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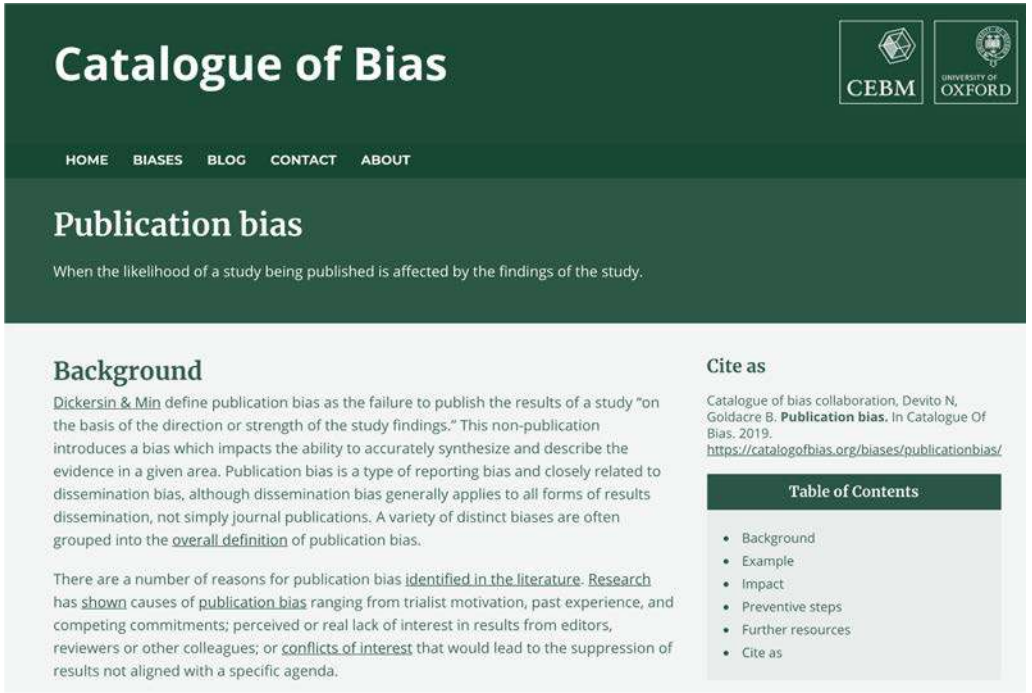
Publication bias: the problem that won't go away.Dickersin K, Min YI.Ann N Y Acad Sci. 1993 Dec 31;703:135-46; discussion 146-8. doi: 10.1111/j.1749-6632.1993.tb26343.x.PMID: 8192291

Catalogue of publication bias



Catalogue of Bias

CEBM | University of Oxford

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Publication bias

When the likelihood of a study being published is affected by the findings of the study.

Background

Dickersin & Min define publication bias as the failure to publish the results of a study "on the basis of the direction or strength of the study findings." This non-publication introduces a bias which impacts the ability to accurately synthesize and describe the evidence in a given area. Publication bias is a type of reporting bias and closely related to dissemination bias, although dissemination bias generally applies to all forms of results dissemination, not simply journal publications. A variety of distinct biases are often grouped into the overall definition of publication bias.

There are a number of reasons for publication bias identified in the literature. Research has shown causes of publication bias ranging from trialist motivation, past experience, and competing commitments; perceived or real lack of interest in results from editors, reviewers or other colleagues; or conflicts of interest that would lead to the suppression of results not aligned with a specific agenda.

Cite as

Catalogue of bias collaboration, Devito N, Goldacre B. **Publication bias.** In Catalogue Of Bias. 2019. https://catalogofbias.org/biases/publicationbias/

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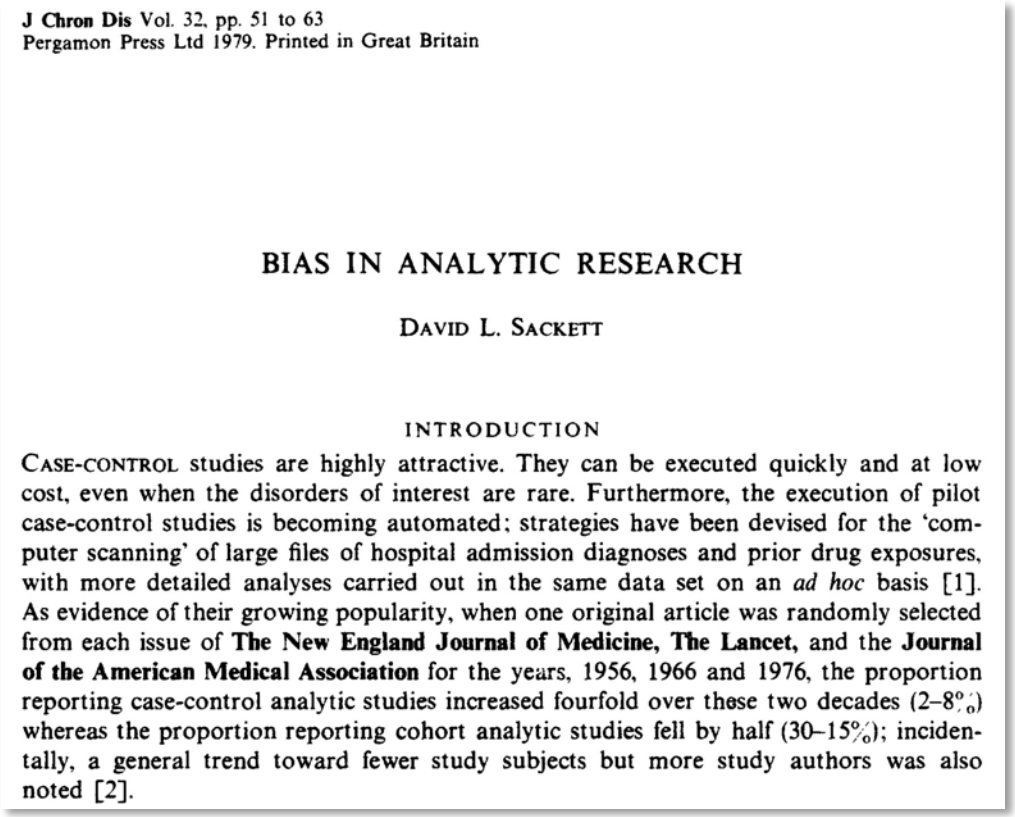
Catalogue of bias collaboration, Devito N, Goldacre B. **Publication bias.** In Catalogue Of Bias. 2019. https://catalogofbias.org

Seminal work on publication bias



J Chron Dis Vol. 32, pp. 51 to 63
Pergamon Press Ltd 1979. Printed in Great Britain

BIAS IN ANALYTIC RESEARCH

DAVID L. SACKETT

INTRODUCTION

CASE-CONTROL studies are highly attractive. They can be executed quickly and at low cost, even when the disorders of interest are rare. Furthermore, the execution of pilot case-control studies is becoming automated; strategies have been devised for the 'computer scanning' of large files of hospital admission diagnoses and prior drug exposures, with more detailed analyses carried out in the same data set on an *ad hoc* basis [1]. As evidence of their growing popularity, when one original article was randomly selected from each issue of **The New England Journal of Medicine, The Lancet,** and the **Journal of the American Medical Association** for the years, 1956, 1966 and 1976, the proportion reporting case-control analytic studies increased fourfold over these two decades (2–8%) whereas the proportion reporting cohort analytic studies fell by half (30–15%); incidentally, a general trend toward fewer study subjects but more study authors was also noted [2].

Early resistance to accept the failure of mice models

The New York Times

Mice Fall Short as Test Subjects for Some of Humans' Deadly Ills

285

Dr. H. Shaw Warren is one of the authors of a new study that questions the use of laboratory mice as models for all human diseases. Evan McGlinn for The New York Times

"They [the reviewers] were so used to doing mouse studies that they thought that was how you validate things."

PNAS

Genomic responses in mouse models poorly mimic human inflammatory diseases

Junhee Seok[a,1], H. Shaw Warren[b,1], Alex G. Cuenca[c,1], Michael N. Mindrinos[a], Henry V. Baker[c], Weihong Xu[a], Daniel R. Richards[d], Grace P. McDonald-Smith[e], Hong Gao[a], Laura Hennessy[f], Celeste C. Finnerty[g], Cecilia M. López[c], Shari Honari[f], Ernest E. Moore[h], Joseph P. Minei[i], Joseph Cuschieri[j], Paul E. Bankey[k], Jeffrey L. Johnson[h], Jason Sperry[l], Avery B. Nathens[m], Timothy R. Billiar[l], Michael A. West[n], Marc G. Jeschke[o], Matthew B. Klein[j], Richard L. Gamelli[p], Nicole S. Gibran[j], Bernard H. Brownstein[q], Carol Miller-Graziano[k], Steve E. Calvano[r], Philip H. Mason[e], J. Perren Cobb[s], Laurence G. Rahme[t], Stephen F. Lowry[r,2], Ronald V. Maier[j], Lyle L. Moldawer[c], David N. Herndon[g], Ronald W. Davis[a,3], Wenzhong Xiao[a,t,3], Ronald G. Tompkins[t,3], and the Inflammation and Host Response to Injury, Large Scale Collaborative Research Program[4]

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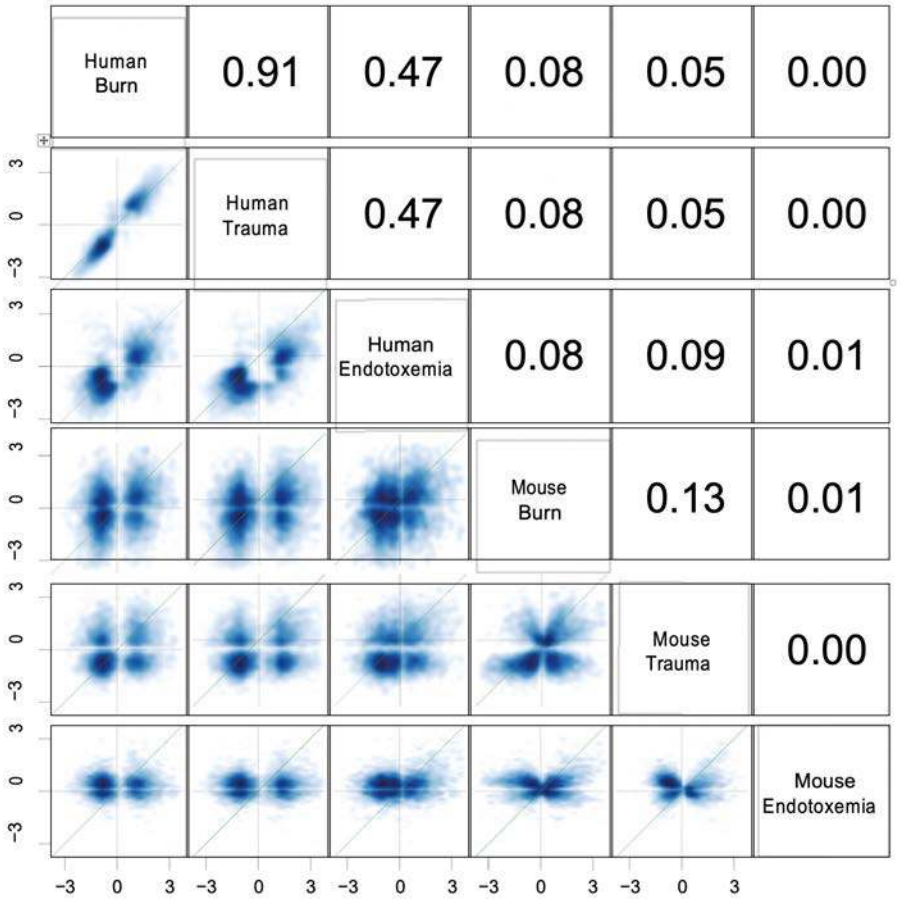
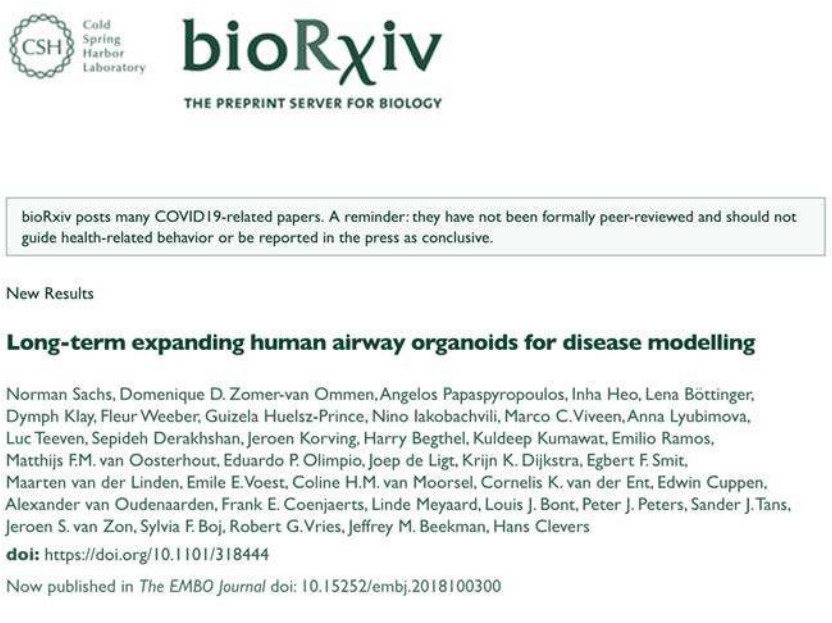
Contributed by Ronald W. Davis, January 7, 2013 (sent for review December 6, 2012)



Junhee Seok, H. Shaw Warren, Alex GC, Michael NM, Henry VB, Xu W, et al. Genomic responses in mouse models poorly mimic human inflammatory diseases. Proc Natl Acad Sci U S A. 2013;110: 3507–3512.

Evidence of animal data reliance bias



Cold Spring Harbor Laboratory

bioRxiv

THE PREPRINT SERVER FOR BIOLOGY

bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

Long-term expanding human airway organoids for disease modelling

Norman Sachs, Domenique D. Zomer-van Ommen, Angelos Papaspyropoulos, Inha Heo, Lena Böttinger, Dymph Klay, Fleur Weeber, Guizela Huelsz-Prince, Nino Iakobachvili, Marco C. Viveen, Anna Lyubimova, Luc Teeven, Sepideh Derakhshan, Jeroen Korving, Harry Begthel, Kuldeep Kumawat, Emilio Ramos, Matthijs F.M. van Oosterhout, Eduardo P. Olimpio, Joep de Ligt, Krijn K. Dijkstra, Egbert F. Smit, Maarten van der Linden, Emile E. Voest, Coline H.M. van Moorsel, Cornelis K. van der Ent, Edwin Cuppen, Alexander van Oudenaarden, Frank E. Coenjaerts, Linde Meyaard, Louis J. Bont, Peter J. Peters, Sander J. Tans, Jeroen S. van Zon, Sylvia F. Boj, Robert G. Vries, Jeffrey M. Beekman, Hans Clevers

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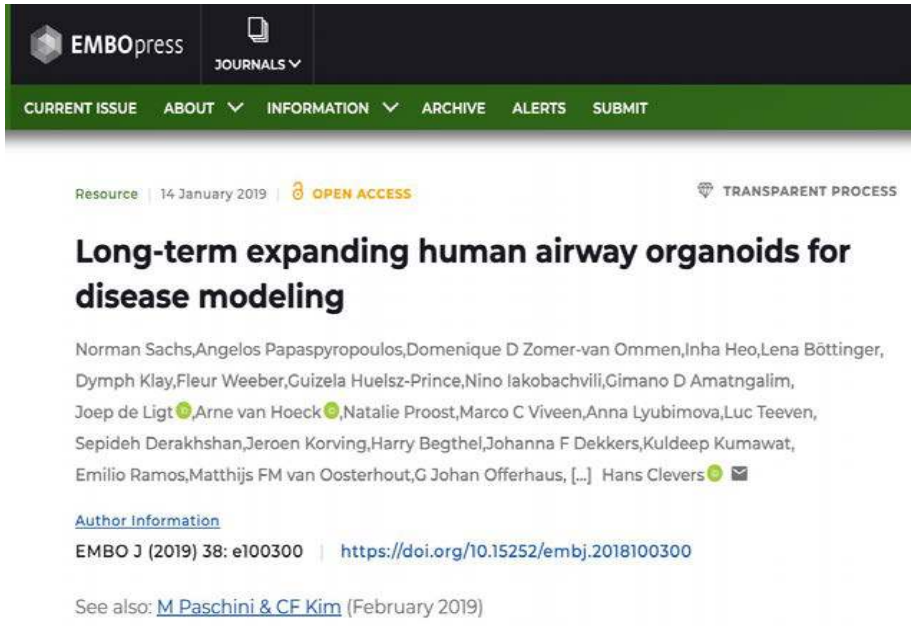

EMBOpress JOURNALS

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Resource | 14 January 2019 | OPEN ACCESS TRANSPARENT PROCESS

Long-term expanding human airway organoids for disease modeling

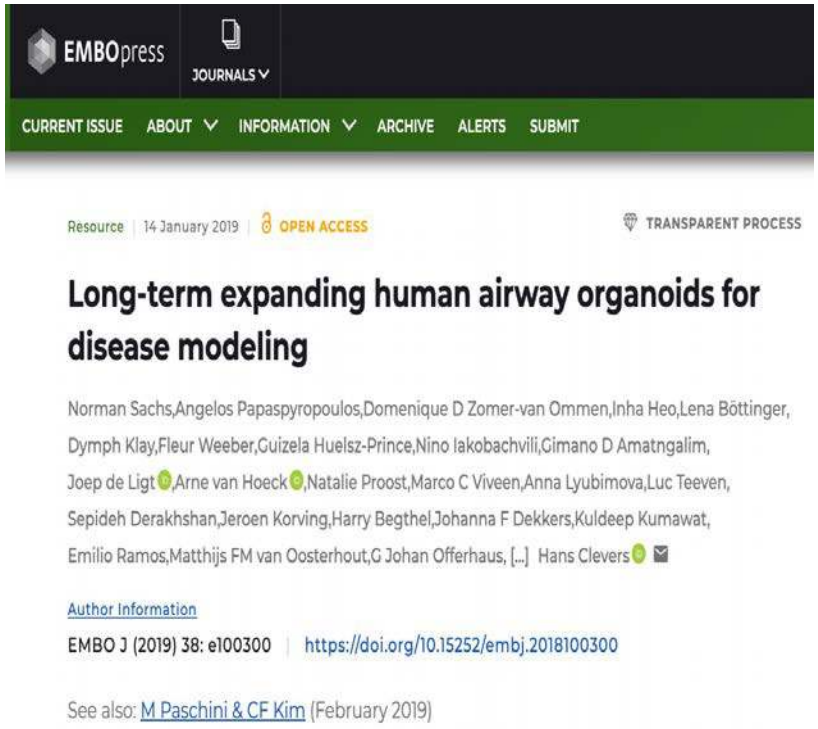
Norman Sachs, Angelos Papaspyropoulos, Domenique D Zomer-van Ommen, Inha Heo, Lena Böttinger, Dymph Klay, Fleur Weeber, Guizela Huelsz-Prince, Nino Iakobachvili, Gimano D Amatngalim, Joep de Ligt, Arne van Hoeck, Natalie Proost, Marco C Viveen, Anna Lyubimova, Luc Teeven, Sepideh Derakhshan, Jeroen Korving, Harry Begthel, Johanna F Dekkers, Kuldeep Kumawat, Emilio Ramos, Matthijs FM van Oosterhout, G Johan Offerhaus, [...] Hans Clevers

Author Information

EMBO J (2019) 38: e100300 | https://doi.org/10.15252/embj.2018100300

See also: M Paschini & CF Kim (February 2019)

"This is a popular paper that was very difficult to publish. We had to try three or four different journals, until we had it accepted. I don't recall exactly at what point we decided to add the animal experiments, but I believe it was done because of a request by an editor or referee from one of these journals," says Prof. Dr Clevers.



Scientists speak out

PROGRESS REPORT

ADVANCED SCIENCE

www.advancedscience.com

Is it Time for Reviewer 3 to Request Human Organ Chip Experiments Instead of Animal Validation Studies?

Donald E. Ingber

For the past century, experimental data obtained from animal studies have been required by reviewers of scientific articles and grant applications to validate the physiological relevance of in vitro results. At the same time, pharmaceutical researchers and regulatory agencies recognize that results from preclinical animal models frequently fail to predict drug responses in humans. This *Progress Report* reviews recent advances in human organ-on-a-chip (Organ Chip) microfluidic culture technology, both with single Organ Chips and fluidically coupled human "Body-on-Chips" platforms, which demonstrate their ability to recapitulate human physiology and disease states, as well as human patient responses to clinically relevant drug pharmacokinetic exposures, with higher fidelity than other in vitro models or animal studies. These findings raise the question of whether continuing to require results of animal testing for publication or grant funding still makes scientific or ethical sense, and if more physiologically relevant human Organ Chip models might better serve this purpose. This issue is addressed in this article in context of the history of the field, and advantages and disadvantages of Organ Chip approaches versus animal models are discussed that should be considered by the wider research community.

1. Introduction

their premise is that the results they generate in their cell cultures will translate to humans. Because in vitro studies generally lack the natural three dimensional (3D) context, vascular flow, and physico-chemical microenvironment of living tissues and organs, as well as the multi-organ physiology of whole organisms, many question the clinical relevance of findings obtained with these simplified models. For this reason, most researchers who submit a grant application or publication based on in vitro findings commonly expect to find at least one reviewer (the classic exasperating "Reviewer 3") who demands that additional animal experiments be carried out to validate their findings before the work could be acceptable for publication or funding. This article seeks to provoke a conversation in the scientific community by asking two simple questions: does this make sense, and if not, is there a better alternative? I address these questions by reviewing recent progress that has been made using organoids and engineered microphysiological systems (MPS) with a focus on microfluidic organ-on-a-chip (Organ Chip) culture technologies.

Ingber DE. Is it Time for Reviewer 3 to Request Human Organ Chip Experiments Instead of Animal Validation Studies? Adv Sci (Weinh). 2020 Oct 12;7(22):2002030.

HUMANE SOCIETY INTERNATIONAL

BIOMED 21

Physicians Committee for Responsible Medicine

Survey to Assess Journal and Reviewer Requests for Evidence in Animals

SurveyMonkey

Q: During manuscript submission peer review, how many times have you been asked for animal experimental data to be added to a study that otherwise had no animal-based experiments? Did you feel the requested additional animal-based experiments were justified?

"Sometimes the reviewers identify critical gaps in knowledge, these are valuable peer reviews. ***Other times it seems like they ask for animals out of habit. We refuse.*** *This is even more difficult and hard to deal with when it comes to grant reviews."*

"The study was about heterogeneity of cancer cells from human tissue samples. ***It was irrelevant to do an experiment on mice."***

"Referees ask for animal experiments because it is customary to do so in the field of biophysics, toxicology not because it is necessary. ***Many researchers are unaware about the potential of in vitro, in silico methods and human based models****."*

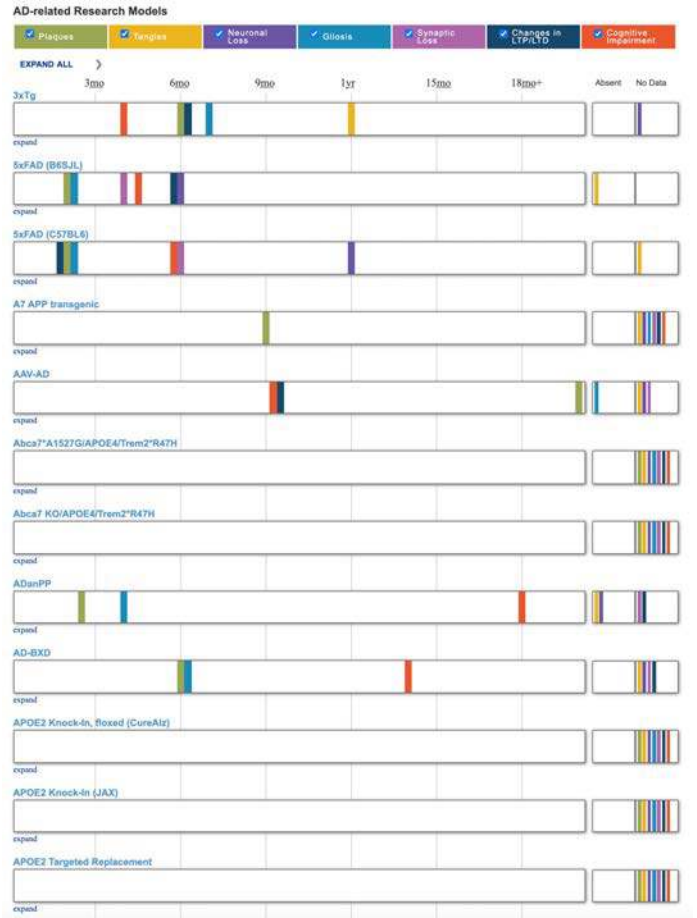
"The need for validation of human organoid data with animal studies... just because journal reviewers were used to this."

"They wanted human in vitro data to be "validated" against an animal model."

Possible reasons behind animal data reliance bias

- Lack of understanding of how advanced human-based technologies work
- Status quo
- Journal editorial policy
- Scientific justification
- Regulatory requirement
- Avoiding sunk costs and the bygones principle

More than 200 rodent models of Alzheimer's Disease



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How to prevent animal data reliance bias?

- Explore the scientific, ethical and economic advantages of advanced animal-free models
- Emphasize NAMs and non-animal research design in academic curricula and continuing education programs
- Recommend amendments to journal policies
- Discuss (challenge) scientific justifications (when claimed to exist) and regulation

Toward a new best practice

- Editors of scientific journals should **scrutinize** reviewer feedback requesting animal data to be supplied or generated *de novo* to validate or complement findings from advanced non-animal approaches as a condition for publication and **require a high level of justification** for such requests
- Journals should commit to **publicly disclose** when such requests are made

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