

# A Complexidade da Ética em Pesquisa, e a influência no ensino.

Jose Carlos Costa BAPTISTA Silva

Professor Titular e Livre Docente  
do Departamento de Cirurgia  
Escola Paulista de Medicina  
2026

Sem conflito de interesse

<https://profbaptistavascul.com.br/>





## William Stewart Halsted (1852-1922) A Lecture by Dr. Peter D. Olch

- Father of modern Surgery  
Professor at Johns Hopkins  
University
- Residência Médica

Annals of Surgery • Volume 243,  
Number 3, March 2006

Angels and Demons: The Peculiar  
and Haunted Genius of Dr Halsted

<https://hub.jhu.edu/magazine/2022/fall/william-halsted-breakthru...sted—his%20full,infinite%20and%20somewhat%20untamed%20curiosity>

FIGURE 2. Dr. Halsted by Stocksdales from W. G. MacCallum's book, *William Stewart Halsted* (Johns Hopkins Press, 1930). (Reproduced with permission from the Johns Hopkins Archives, Johns Hopkins Press.)

# The Founding Physicians

Every one of the "Big Four," as they are known at Johns Hopkins, was a character, a larger-than-life personality.

- [Pathologist William Henry Welch](#) was a stout bachelor who loved swimming, carnival rides and five-dessert dinners in Atlantic City.
- [Surgeon William Stewart Halsted](#) was known for being tough on students, but his severity masked an almost debilitating shyness.
- [Internist William Osler](#) was a known prankster.
- [Gynecologist Howard Kelly](#) collected snakes and was an evangelical Christian.

Each of the doctors, in his own way, had a profound and lasting influence on American medical education and research.

Welch Halsted Osler Kelly



As Johns Hopkins' most famous medical school professors, they sat in the London studio of famed painter John Singer Sargent in 1905 for a portrait that now hangs in the Welch Medical Library. (Lore has it that much of Halsted's figure was painted in disappearing pigment, so disgusted was Sargent with Halsted's strident objection to having blue shadows painted under his eyes. Halsted does, in fact, appear a bit fuzzier than his colleagues, but curators and art experts insist that is only because Sargent painted him farther in the background, and used a thinner wash, for perspective.)

# Finalidade da Pesquisa

A principal finalidade da pesquisa é a **geração de novo conhecimento e a descoberta e/ou confirmação de informações** sobre um determinado assunto, visando responder perguntas, resolver problemas, testar hipóteses e ampliar o entendimento da realidade em diversas áreas como ciência, academia, indústria e sociedade. Através de um processo sistemático de coleta e análise de dados, a pesquisa contribui para o avanço do conhecimento e para a tomada de decisões mais informadas

Objetivo

Melhorar a Sociedade ???

“The most important attribute that the University of Melbourne would like to see in its graduates is a profound respect for **truth**, and for the **ethics of scholarship**...we want our graduates to be capable of independent thought, to be able to do their own work, and to know how to acknowledge the work of **others**.”

*Professor Peter McPhee* (Provost 2007-9)



Australia

<https://researchinsiders.blog/2014/07/15/hyper-anxiety-4-doing-it-wrong/>

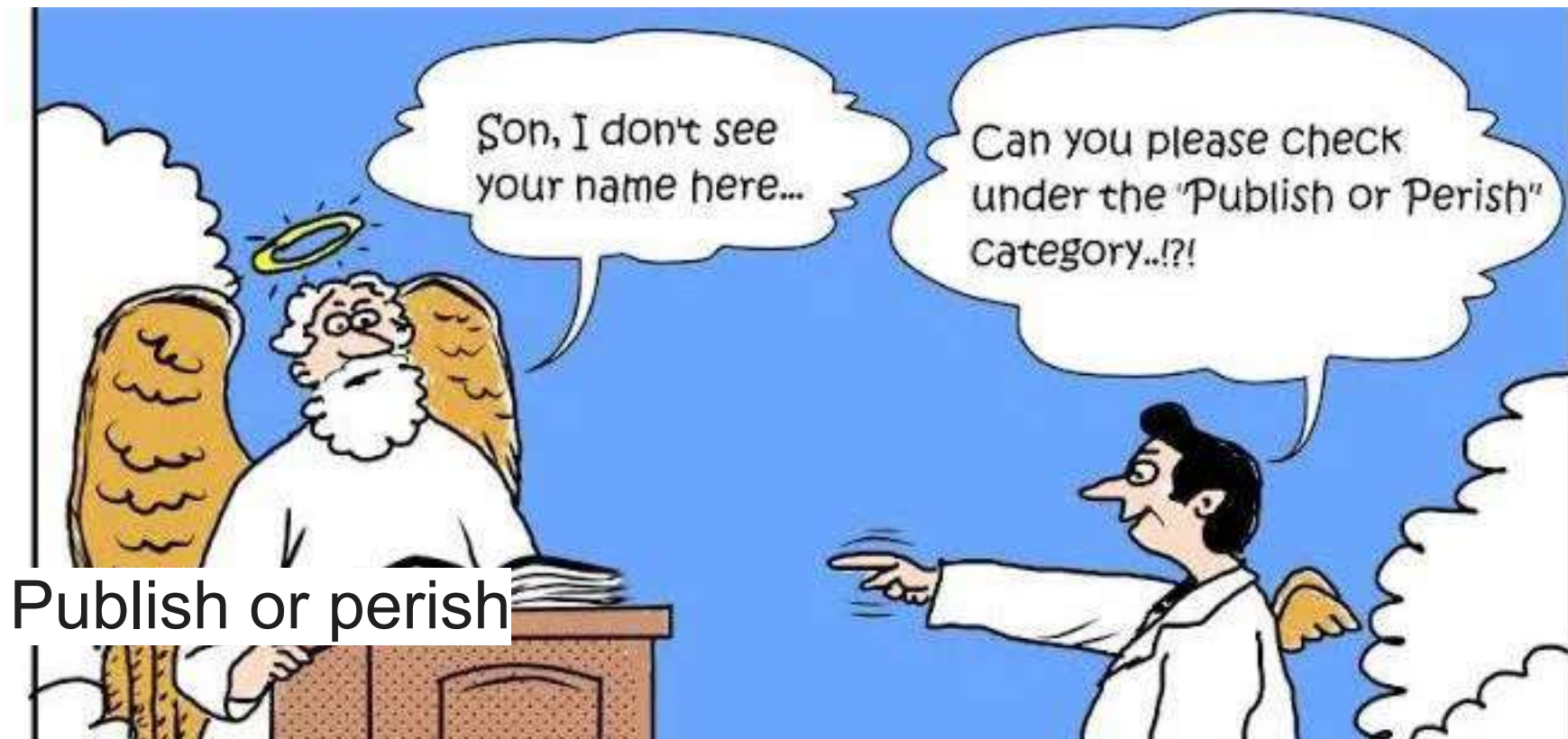


## **Professor Emeritus Peter McPhee AM**

*Honorary Professorial Fellow*  
Melbourne CSHE



- 1- Publish or Perish (Publicar ou Perecer)
- 2- Pressão do Financiador
- 3- Falta de Supervisão da Instituição
- 4- Falta de Treinamento Adequado
- 5- Desvio Moral e Ético



"Publicar ou perecer" é um aforismo que descreve a pressão para publicar trabalhos acadêmicos para ter sucesso na carreira acadêmica. Essa pressão institucional é geralmente mais forte nas universidades de pesquisa.

The phrase "publish or perish" is often attributed to American geographer **William Morris Davis** (1850–1934), who urged the Association of American Geographers to "publish or perish" as early as 1904. While commonly used in academia, it was often cited as a known aphorism by the 1930s, rather than having one single documented author.

**Early Written Uses:** Researchers have found early mentions in a 1928 journal article by Clarence Marsh Case and a 1932 book, *Archibald Cary Coolidge: Life and Letters*, by Harold Jefferson Coolidge

# Responsáveis pelas condutas éticas e não éticas em pesquisa

Autores

Instituição

CEP

CONEP/**SINEP**

Órgãos de Fomento (público ou privado)

País ou Países

PARA PROJETOS ENVOLVENDO

<u>Seres Humanos</u> <u>CEP/PLATAFORMA BRASIL</u>	<u>Uso de Animais Vertebrados</u> <u>CEUA</u>	<u>Outros Projetos que não envolvem</u> <u>Seres Humanos ou Animais Vertebrados</u>
		
<p><u>Área de Saúde:</u> Estudos envolvendo seres humanos diretamente (clínicos, obtenção de amostras biológicas, etc.) ou indiretamente (uso de prontuários, revisões bibliográficas, análises documentais, etc.)</p> <p><u>Outras áreas:</u> Qualquer estudo, independentemente da área, em que haja alguma interação com seres humanos (entrevistas, aplicação de questionários, estudos etnográficos)</p>	<p>Estudos envolvendo animais vertebrados vivos ou não, ou parte deles (tecidos, órgãos, etc.).</p>	<p><u>Biológica e Química</u> Estudos de bioquímica, biologia molecular, biofísica e química, que não envolvam diretamente seres humanos ou animais vertebrados (bactérias, parasitas, plantas, outros invertebrados, células comercializadas, etc.).</p> <p><u>Humanas</u> Estudos de História, Geografia, Filosofia, Letras, Artes, Educação, Administração e outras áreas afins.</p> <p><u>Exatas</u> Matemática, Física, Ciências da Terra, Informática, Engenharia e outras áreas afins.</p>



# COMITÊ DE ÉTICA EM PESQUISA

[HOME](#) [SOBRE](#) ▼ [LINKS ÚTEIS](#) [MODELOS](#) [ORIENTAÇÕES](#) [DOCUMENTOS](#)

No content in response.

## Localização e Contato

R. Sena Madureira, 1500 - 2º andar • Vila Clementino - São Paulo - SP - CEP: 04021-001

Horário de atendimento presencial e telefônico: Segundas a Sexta das 08:00 às 13:00hs.

E-mail: [cep@unifesp.br](mailto:cep@unifesp.br)

Telefone:(11) 3385-4343 ramal 8699/8557.

**Fabricação:** fabricar resultados sem tê-los  
células tronco de Wang

**Falsificação:** manipulação de materiais de investigação, equipamentos ou processos, ou alterar ou omitir resultados de tal forma que a pesquisa não é representada com precisão no registro.

Automotivos= controles de emissão de Gases

**Plágio:** a apropriação de idéias de outro, processos, resultados, ou seja, sem dar o devido crédito.

Dupla hélice de DNA (Watson, Crick, 1953)

Rosalind Franklin

Nature 1953

**Duplicidade:** publicar o mesmo artigo em locais diferentes -revistas ou livros ou na internet como sendo coisas novas ou inéditas.

Exceção: protocolos, diretrizes (guidelines) ou artigo com autorização dos autores, da revista etc.

**Fator Salame**

**Conflito de interesse** (indústria, revisor, comitê de ética)

**Citação cruzada**

<http://www.retractiondatabase.org/RetractionSearch.aspx?>

<http://www.retractiondatabase.org>

# Journal policies and editors' opinions on peer review

## Abstract

Peer review practices differ substantially between journals and disciplines. This study presents the results of a survey of 322 editors of journals in ecology, economics, medicine, physics and psychology. We found that 49% of the journals surveyed checked all manuscripts for plagiarism, that 61% allowed authors to recommend both for and against specific reviewers, and that less than 6% used a form of open peer review. Most journals did not have an official policy on altering reports from reviewers, but 91% of editors identified at least one situation in which it was appropriate for an editor to alter a report. Editors were also asked for their views on five issues related to publication ethics. A majority expressed support for co-reviewing, reviewers requesting access to data, reviewers recommending citations to their work, editors publishing in their own journals, and replication studies. Our results provide a window into what is largely an opaque aspect of the scientific process. We hope the findings will inform the debate about the role and transparency of peer review in scholarly publishing.

DANIEL G HAMILTON\*, HANNAH FRASER, RINK HOEKSTRA AND FIONA FIDLER

Hamilton et al. eLife 2020;9:e62529. DOI: <https://doi.org/10.7554/eLife.62529>

1. Interdisciplinary Metaresearch Group, School of BioSciences, University of Melbourne, Australia; Department of Educational Sciences, University of Groningen, Netherlands; School of Historical and Philosophical Studies, University of Melbourne, Australia

eLife (Max Planck e Wellcome Trust) IF=8,71

## Editors' *in principle* stances on the following topics

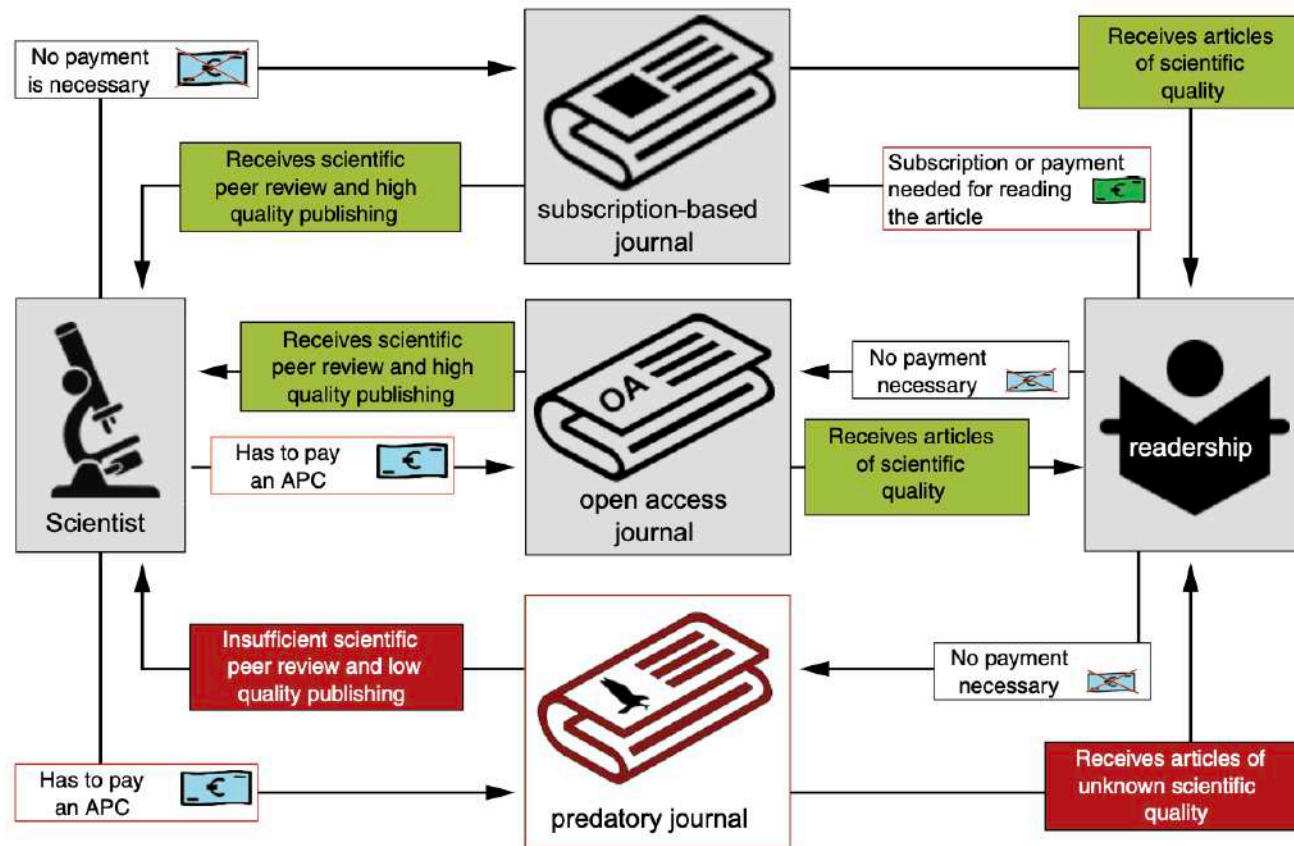


**Figure 1.** Participating editors' *in principle* stances on the six topics raised in Survey B. The figures presented are limited to statements that provided a clear view for or against the topic of interest. An interactive version of this figure reporting results by discipline can be viewed at <https://plotly.com/~dghamilton/9/> (**Supplementary file 1**). Source data for the figure can be found at <https://doi.org/10.17605/osf.io/cy2re>.

The online version of this article includes the following figure supplement(s) for figure 1:

**Figure supplement 1.** Survey response rate by discipline.

**Figure supplement 2.** Distribution of impact factors among invited and participating journals by discipline.



**Figure 1** The relationship between researcher, journal and readership. Subscription-based journal: Scientist submits his or her work to the journal without costs, and the journal provides high-quality peer review to the authors to ensure the scientific quality of the submitted paper. Members of the readership receive peer review articles of high scientific quality, but have to pay a fee to access the journal's content. Open access journal: Same standards as a subscription-based journal, but the author has to pay an article processing charge (APC) in this model, and the content is freely available to the readership in return. Predatory journal: Copy the open access publishing model by levying APCs on authors, but do not deliver high-quality, peer reviewed articles (and other services) and do not ensure the scientific quality of submitted articles. Therefore, they are fooling the scientific system as well as members of the readership.

## An exploratory analysis of 4844 withdrawn articles and their retraction notes.

Catalin Toma<sup>1</sup>, Liliana Padureanu<sup>2</sup>

<sup>1</sup> Romedchim International S.R.L., Iasi, Romania ([catalin.toma@gmail.com](mailto:catalin.toma@gmail.com)), <sup>2</sup> Emergency Clinical Hospital 'St. Spiridon', Iasi, R.O.

### Abstract.

The objective of our study was to obtain an updated image of the dynamic of retractions and retraction notes, retraction reasons for questionable research and publication practices, countries producing retracted articles, and the scientific impact of retractions by studying 4844 PubMed-indexed retracted articles published between 2009 and 2020 and their retraction notes.

#### RESULTS.

Mistakes/inconsistent data account for 32% of total retractions, followed by images(22,5%), plagiarism(13,7%) and overlap(11,5%).

Thirty countries account for 94,79% of 4844 retractions. Top five are: China(32,78%), United States(18,84%), India(7,25%), Japan(4,37%) and Italy(3,75%).

The total citations number for all articles is 140810(Google Scholar), 96000(Dimensions).

Average exposure time(ET) is 28,89 months. Largest ET is for image retractions(49,3 months), lowest ET is for editorial errors(11,2 months).

The impact of retracted research is higher for Spain, Sweden, United Kingdom, United States, and other nine countries and lower for Pakistan, Turkey, Malaysia, and other six countries, including China.

#### CONCLUSIONS.

Mistakes and data inconsistencies represent the main retraction reason; images and ethical issues show a growing trend, while plagiarism and overlap still represent a significant problem. There is a steady increase in QRP and QPP article withdrawals. Retraction of articles seems to be a technology-dependent process.

The number of citations of retracted articles shows a high impact of papers published by authors from certain countries. The number of retracted articles per country does not always accurately reflect the scientific impact of QRP/QPP articles.

The country distribution of retraction reasons shows structural problems in the organization and quality control of scientific research, which have different images depending on geographical location, economic development, and cultural model.

questionable research practices(QRP)  
questionable publication practices(QPP)



## Research ethics: a profile of retractions from world class universities

Caroline Lievore<sup>1</sup> · Priscila Rubbo<sup>1</sup> · Celso Bijnkievycz dos Santos<sup>2</sup> ·  
Claudia Tânia Picinin<sup>1</sup> · Luiz Alberto Pilatti<sup>1</sup>

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### Abstract

This study aims to profile the scientific retractions published in journals indexed in the Web of Science database from 2010 to 2019, from researchers at the top 20 World Class Universities according to the Times Higher Education global ranking of 2020. Descriptive statistics, Pearson's correlation coefficient, and simple linear regression were used to analyze the data. Of the 330 analyzed retractions, Harvard University had the highest number of retractions and the main reason for retraction was data results. We conclude that the universities with a higher ranking tend to have a lower rate of retraction.

**Keyword** Retraction · Research Anti-ethics · World Class Universities · Ranking

times higher education (THE) ranking (2020)

### Introduction

Unethical research undermines confidence in researchers, universities, journals, and in science itself. In this sense, the peer review process, along with the responsible and transparent correction of articles, aims to guarantee the quality of knowledge available (Fang & Casadevall, 2011; Fennell, 2019; Lei & Zhang, 2018). However, even if research is submitted to peer review, this process may fail (Van Leeuwen & Luwel, 2014), and research with honest or dishonest errors does get published, as well as those with scientific dishonesty.

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✉ Caroline Lievore  
carolievore1@gmail.com

Priscila Rubbo  
rubbo.priscila@gmail.com

Celso Bijnkievycz dos Santos  
bilynkievycz@globo.com

Claudia Tânia Picinin  
claudiapicinin@utfpr.edu.br

Luiz Alberto Pilatti  
lapilatti@utfpr.edu.br

<sup>1</sup> Federal University of Technology – Paraná (UTFPR), Ponta Grossa, Brazil

<sup>2</sup> State University of Ponta Grossa (UEPG), Ponta Grossa, Brazil

**Table 4** Number of retractions per university in the period from 2010 to 2019. *Source:* Authors (2020)

Rank	University	Published articles	Retractions	Retraction ratio %	Distribution of retractions per University %
1	Oxford University	89,731	11	0.012	3.33
2	California Institute of Technology	32,736	2	0.006	0.61
3	Cambridge University	79,220	7	0.009	2.12
4	→ Stanford University	85,892	20	0.023	6.06 ←
5	Massachusetts Institute of Technology	63,187	13	0.021	3.94
6	Princeton University	31,952	3	0.009	0.91
7	→ Harvard University	204,072	59	0.029	17.87 ←
8	Yale University	61,340	12	0.020	3.64
9	University of Chicago	57,632	9	0.016	2.73
10	Imperial College of London	68,670	17	0.025	5.15
11	University of Pennsylvania	75,823	19	0.025	5.76
12	Johns Hopkins University	89,462	15	0.017	4.55
13	University of California, Berkeley	68,336	5	0.007	1.52
14	ETH Zurich	50,388	8	0.016	2.42
15	→ University College London	93,036	23	0.025	6.97 ←
16	Columbia University	72,214	10	0.014	3.03
17	University of California, Los Angeles	78,132	14	0.018	4.24
18	→ University of Toronto	110,689	26	0.023	7.88 ←
19	→ Cornell University	61,870	23	0.037	6.97 ←
20	→ Duke University	60,884	34	0.056	10.30 ←
	Total	1,535,266	330	0.021	100
Summary statistics	$\mu$	76,763.30	16.50	0.020	5.00
	$\pm$	35,619.55	12.90	0.011	3.91

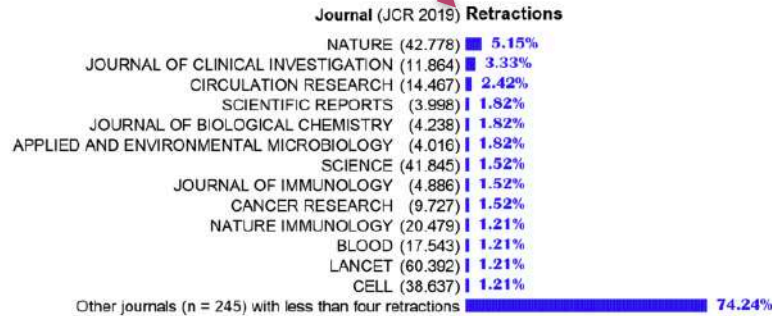


Fig. 3 Distribution of retractions per Journal. Source: Authors (2020)

Fig. 4 Distribution by type of retraction. Source: Authors (2020)

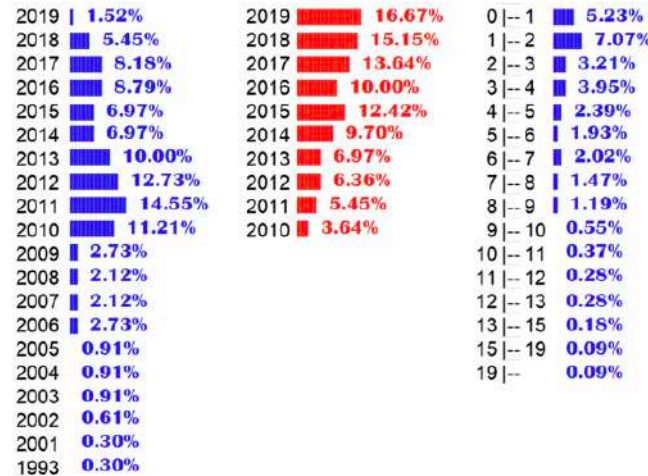


Fig. 5 Year of publication of the paper (a), year of retraction(b), and time between publication and retraction in years (c). Source: Authors (2020)

### Person responsible for the retraction

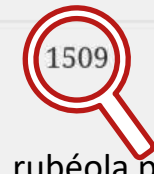
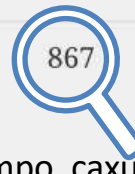
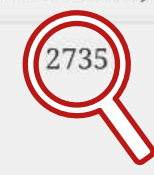
Figure 7 shows the person responsible for the retractions. In almost half of the retractions (43.64% of the cases), the author was listed as responsible.

# Top 10 most highly cited retracted papers

Ever curious which retracted papers have been most cited by other scientists? Below, we present the list of the 10 most highly cited retractions as of December 2020. Readers will see some familiar entries, such as the infamous *Lancet* paper by Andrew Wakefield that [originally suggested a link between autism and childhood vaccines](#). You'll note that several papers — including the #2 most cited paper — received more citations after they were retracted, which [research has shown is an ongoing problem](#).

<https://retractionwatch.com/the-retraction-watch-leaderboard/top-10-most-highly-cited-retracted-papers/>

Article	Year of retraction	Citing Articles before retraction	Citing Articles after retraction	Total cites (journals indexed by Web of Science)
<p><b>1. <u>Primary Prevention of Cardiovascular Disease with a Mediterranean Diet.</u> N ENGL J MED; APR 2013.</b></p> <p>IF= 91,24</p> <p><i>Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella, D, Aros F, Gomez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pinto X, Basora J, Munoz MA, Sorli JV, Martinez JA, Martinez-Gonzalez MA, et al., for the PREDIMED Study Investigators</i></p>	2018	1919	816	2735
<p><b>2. <u>Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children.</u> LANCET; FEB 28 1998.</b></p> <p>IF= 79, 32</p> <p><i>Wakefield AJ, Murch SH, Anthony A, Linnell L, Casson DM, Malik M,</i></p>	2010	642	867	1509



Barcelona University  
Navarra University, Spain

Vacinas MMR sarampo, caxumba, rubéola poderiam levar ao Autismo

Royal Free Hospital and School of Medicine, London NW3 2QG, UK

IF= Impact Factor of the Journal

## CORRESPONDENCE



## Article 1

Retraction and Republication: Primary Prevention  
of Cardiovascular Disease with a Mediterranean Diet.  
N Engl J Med 2013;368:1279-90.

**TO THE EDITOR:** Because of irregularities in the randomization procedures, we wish to retract the following article: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *N Engl J Med* 2013;368:1279-90. DOI: 10.1056/NEJMoa1200303.<sup>1</sup> We have reanalyzed the data and have published a new report: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med*. DOI: 10.1056/NEJMoa1800389.<sup>2</sup>

Ramón Estruch, M.D., Ph.D.

CIBEROBN  
Madrid, Spain

Emilio Ros, M.D., Ph.D.

Instituto de Investigaciones Biomédicas Augusto Pi Sunyer  
Barcelona, Spain

Jordi Salas-Salvadó, M.D., Ph.D.

Rovira i Virgili University  
Tarragona, Spain

Maria-Isabel Covas, D.Pharm., Ph.D.

Hospital del Mar Medical Research Institute  
Barcelona, Spain

Dolores Corella, D.Pharm., Ph.D.

University of Valencia  
Valencia, Spain

Fernando Arós, M.D., Ph.D.

University Hospital Araba  
Vitoria, Spain

Enrique Gómez-Gracia, M.D., Ph.D.

University of Malaga  
Malaga, Spain

Valentina Ruiz-Gutiérrez, Ph.D.

Instituto de la Grasa  
Seville, Spain

Miquel Fiol, M.D., Ph.D.

Institute of Health Sciences  
Palma de Mallorca, Spain

José Lapetra, M.D., Ph.D.

Distrito Sanitario Atención Primaria  
Seville, Spain

Rosa M. Lamuela-Raventos, D.Pharm., Ph.D.

University of Barcelona  
Barcelona, Spain

Lluís Serra-Majem, M.D., Ph.D.

Research Institute of Biomedical and Health Sciences  
Las Palmas, Spain

Xavier Pintó, M.D., Ph.D.

Bellvitge University Hospital  
Barcelona, Spain

Josep Basora, M.D., Ph.D.

Miguel A. Muñoz, M.D., Ph.D.

Instituto de Investigación en Atención Primaria J. Gol  
Barcelona, Spain

## THIS WEEK'S LETTERS

**2441 Retraction and Republication: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *N Engl J Med* 2013;368:1279-90.**

**2442 Molecular Minimal Residual Disease in Acute Myeloid Leukemia**

**2444 High-Flow Oxygen Therapy in Infants with Bronchiolitis**

**2447 Are We Prepared for Nuclear Terrorism?**

## Early report

## Article 2

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and  
pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

## Summary

**Background** We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

**Methods** 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

**Findings** Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities ranging from lymphoid nodular hyperplasia to granuloid ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible postviral or vaccinal encephalitis (two). There were no focal neurological abnormalities and MRI and EEG tests were normal. Abnormal laboratory results were significantly raised urinary methylmalonic acid compared with age-matched controls (mean 1003), low haemoglobin in four children, and low serum IgA in four children.

**Interpretation** We identify associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

*Lancet* 1998; **351**: 637–41

See Commentary page

**Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, A P Dillon MRCPsych, S E Davies MRCPsych) and the University Departments of Paediatric Gastroenterology (S H Murch MA, D M Casson MRCP, M Malik MRCP, M A Thomson FRCP, J A Walker-Smith FRCP), Child and Adolescent Psychiatry (M Berelowitz FRCPsych), Neurology (P Harvey FRCP), and Radiology (A Valentine FRCP), Royal Free Hospital and School of Medicine, London NW3 2QG, UK**

Correspondence to: Dr A J Wakefield

## Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and bloating and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

## Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for a week, accompanied by their parents.

## Clinical investigations

We took histories, including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases the history was obtained by the senior clinician (JW-S). Neurological and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.<sup>1</sup> Developmental assessments included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made this possible), and lumbar puncture were done.

## Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.<sup>2</sup> Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomyesal antibodies and boys were screened for fragile-X if this had not been done

# The discredited doctor hailed by the anti-vaccine movement

Article 2

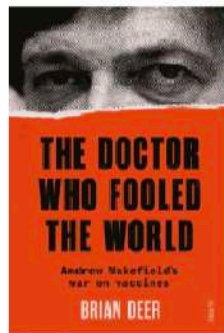
Riveting biography is a cautionary lesson in the legacy of hubris. **By Saad B. Omer**

Wakefield, foi cancelado o registro Médico por má conduta.

**S**ince Edward Jenner's first scientific description of vaccination in 1798 – using cowpox pus to protect against smallpox – there has been pushback. Throughout the nineteenth century, in the United States and the United Kingdom, there were cycles of increased smallpox vaccination, rising opposition, drops in immunization coverage, outbreaks, better appreciation of vaccination, more of it, and more protests. This stand-off eased around the start of the twentieth century when, with sanitation and medical care improving, public health placed less emphasis on compulsory vaccination. Probably the last time the world waited with bated breath for a vaccine – against polio in the 1950s – it was welcomed with open arms. The modern wave of vaccine scepticism has

its origins in the 1970s. That was when concerns (later determined to be unfounded) about the safety of a whole-cell vaccine against pertussis, or whooping cough, came to the fore in many high-income countries. In the 1980s and 1990s, a few organized groups opposed to vaccines emerged in many countries, including the United Kingdom.

It was in this context that, in 1998, Andrew Wakefield and his colleagues published a now-infamous and retracted paper in *The Lancet*, following which, in 2010, Wakefield was struck off the UK medical register for misconduct by the country's General Medical Council. The fraudulent work on 12 children promoted a non-existent connection between autism and the MMR vaccine, used against measles, mumps and rubella. It propelled Wakefield to notoriety and turbocharged the anti-vaccine movement. He remains a headliner on the international vaccine-sceptic circuit as diseases once vanquished return because of falling rates of immunization. Many large epidemiological studies have found no difference in risk of developmental delays between children who receive the MMR vaccine and those who don't.



**The Doctor Who Fooled the World: Andrew Wakefield's War on Vaccines**  
Brian Deer  
Scribe UK (2020)

**3. Visfatin: A protein secreted by visceral fat that mimics the effects of insulin. SCIENCE; JAN 2005.**

IF= 47, 72

*Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, Matsuki Y, Murakami M, Ichisaka T, Murakami H, Watanabe E, Takagi T, Akiyoshi M, Ohtsubo T, Kihara S, Yamashita S, Makishima M, Funahashi T, Yamanaka S, Hiramatsu R, Matsuzawa Y, Shimomura I.*

2007



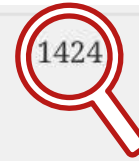
232



1192



1424



Sumitomo Pharmaceutics, Kyoto, Japan

**4. An enhanced transient expression system in plants based on suppression of gene silencing by the p19 protein of tomato bushy stunt virus. PLANT J; MAR 2003.**

IF= 6,14

*Voinnet O, Rivas S, Mestre P, Baulcombe D.*

2015

896

375



1271



Imperial College London, 59-61 North Wharf Road, London W2 1LA, UK  
Strasbourg, Cedex, France

## Retraction

[ATSUNORI FUKUHARA](#), [MORIHIRO MATSUDA](#), [MASAKO NISHIZAWA](#), [KATSUMORI SEGAWA](#), [MASAKI TANAKA](#), [KAE KISHIMOTO](#), [YASUSHI MATSUKI](#), [MIREI MURAKAMI](#)

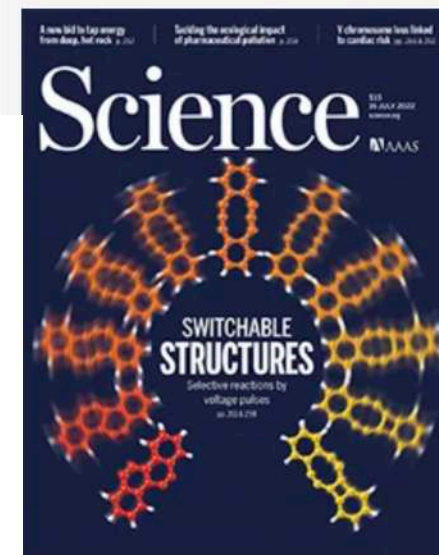
### Article 3



The visfatin work performed in our laboratory was recently investigated by the Committee for Research Integrity (CRI) of Osaka University Graduate School of Medicine. On the basis of the CRI report, which focused largely on our biochemical experiments examining visfatin-s interaction with the insulin receptor, the Faculty Council of Osaka University Medical School recommended that we retract the entire paper. At the suggestion of the Editor of *Science*, we have agreed to retract the paper, even though we continue to stand by our conclusions. We note that over a dozen subsequent publications have shown that plasma visfatin levels in humans correlate with various metabolic states, including obesity, visceral fat mass, and diabetes [for example, (4,6)]. We note also that another laboratory recently reported that visfatin has insulin mimetic effects in cultured osteoblasts (7). We acknowledge that, since publication of the *Science* Report, we have found that not all preparations of visfatin bind to and activate the insulin receptor. Thus far, we have found four different lots of purified recombinant visfatin protein that have both adipogenic and insulin mimetic activities. We still have the preparations of visfatin that show insulin mimetic activity, although the amount is limited, and we are willing to send them to other investigators for independent validation. We are continuing to investigate the significance of this molecule.

We regret any inconvenience caused by this retraction to researchers and readers. The corresponding author is responsible for the retraction.

### CURRENT ISSUE



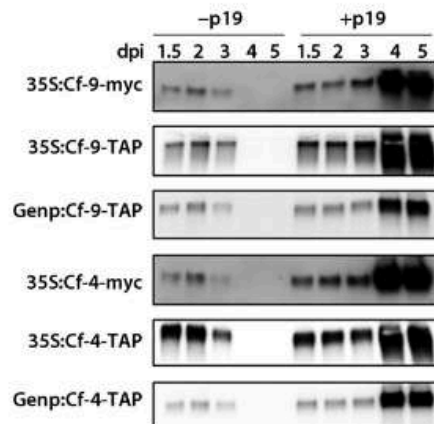
Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure

## Retraction: 'An enhanced transient expression system in plants based on suppression of gene silencing by the p19 protein of tomato bushy stunt virus'

The above article, first published online on 28 February 2003 in Wiley Online Library (wileyonlinelibrary.com), and in volume 33, pp. 949–956, has been retracted by agreement between the authors, the journal Editor in Chief, Christoph Benning, and John Wiley & Sons Ltd.

This notice updates and replaces a recent correction notice, published on 8 June 2015.

In the above article, it has recently been noted that the original Figure 3b in this paper was assembled incorrectly and included image duplications. As the original data are no longer available for assembly of a corrected figure, the experiment was repeated, in agreement with the editors, by co-author S. Rivas. The data from the repeated experiment, presented below together with the original figure legend, lead to the same interpretation and conclusions as in the original paper.



**Figure 3.** (b) Enhanced transient expression of tagged Cf proteins in the presence of P19. *Agrobacterium* cells carrying the indicated Cf tagged constructs were mixed together with (+p19) or without (-p19) the 35S:p19 strain and infiltrated into *Nicotiana benthamiana* leaves. At the times indicated, samples were harvested and total solubilised protein extracts were prepared. Proteins (50 µg) were separated by SDS-PAGE and analysed by immunoblot using a PAP or anti-c-myc antibody for detection of TAP- and c-myc-tagged Cf-9, respectively.

Since publication of the above notice the corresponding author has become aware of additional image duplications involving the loading control lanes of Figures 2g, 3a, 4e and 4f.

The authors accept that integrity of the scientific literature is compromised by the data manipulation and, for that reason, they wish to retract the article. However, researchers wishing to use the method described in this paper can still obtain the necessary clones from the corresponding author (dcb40@cam.ac.uk).

The authors apologise for having allowed this flawed article to be published.

### REFERENCE

Voinnet, O., Rivas, S., Mestre, P. and Baulcombe, D. (2003) An enhanced transient expression system in plants based on suppression of gene silencing by the p19 protein of tomato bushy stunt virus. *The Plant J.* 33, 949–956.

**5. Lysyl oxidase is essential for hypoxia-induced metastasis. NATURE; APR 2006.** IF= 49, 96

*Erler JT, Bennewith KL, Nicolau M, Dornhöfer N, Kong C, Le QT, Chi JT, Jeffrey SS, Giaccia AJ.*

2020



977



81



1058



Stanford, California 94305, USA.  
University of Leipzig, Leipzig 04103, Germany.  
Duke University, Durham, North Carolina, USA.

**6. TREEFINDER: a powerful graphical analysis environment for molecular phylogenetics. BMC EVOL BIOL; JUN 2004.** IF= 3,14

*Jobb G, von Haeseler A, Strimmer K.*

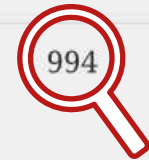
2015

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158



994



Dusseldorf University, Germany

## LETTERS

## Lysyl oxidase is essential for hypoxia-induced metastasis

Janine T. Erler<sup>1</sup>, Kevin L. Bennewith<sup>1</sup>, Monica Nicolau<sup>2</sup>, Nadja Dornhöfer<sup>4</sup>, Christina Kong<sup>3</sup>, Quynh-Thu Le<sup>1</sup>, Jen-Tsan Ashley Chi<sup>5</sup>, Stefanie S. Jeffrey<sup>2</sup> & Amato J. Giaccia<sup>1</sup>

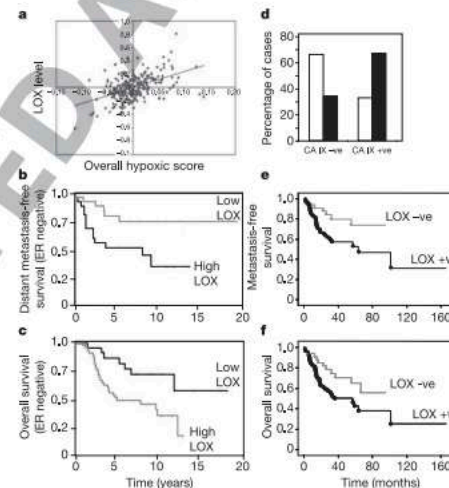
Metastasis is a multistep process responsible for most cancer deaths, and it can be influenced by both the immediate microenvironment (cell–cell or cell–matrix interactions) and the extended tumour microenvironment (for example vascularization)<sup>1</sup>. Hypoxia (low oxygen) is clinically associated with metastasis and poor patient outcome, although the underlying processes remain unclear<sup>2</sup>. Microarray studies have shown the expression of lysyl oxidase (LOX) to be elevated in hypoxic human tumour cells<sup>3</sup>. Paradoxically, LOX expression is associated with both tumour suppression and tumour progression, and its role in tumorigenesis seems dependent on cellular location, cell type and transformation status<sup>4–9</sup>. Here we show that LOX expression is regulated by hypoxia-inducible factor (HIF) and is associated with hypoxia in human breast and head and neck tumours. Patients with high LOX-expressing tumours have poor distant metastasis-free and overall survivals. Inhibition of LOX eliminates metastasis in mice with orthotopically grown breast cancer tumours. Mechanistically, secreted LOX is responsible for the invasive properties of hypoxic human cancer cells through focal adhesion kinase activity and cell to matrix adhesion. Furthermore, LOX may be required to create a niche permissive for metastatic growth. Our findings indicate that LOX is essential for hypoxia-induced metastasis and is a good therapeutic target for preventing and treating metastases.

First we validated LOX as a hypoxia-responsive gene and found it to be regulated at the messenger RNA level by hypoxia-inducible factor-1 (HIF-1) through a functional hypoxia-responsive element identified and tested in the LOX promoter (Supplementary Fig. 1). To examine the clinical relevance of hypoxia-induced LOX, we performed a retrospective breast cancer and a prospective head and neck cancer study<sup>10,11</sup>. There was significant correlation between the LOX expression level and hypoxia in patients (Fig. 1a, d). LOX expression was statistically associated with oestrogen receptor (ER) status (Supplementary Table 1), consistent with the finding that highly hypoxic tumours are most likely to be ER-negative<sup>12</sup>. This is of clinical importance because ER-negative breast cancer patients generally have a worse prognosis<sup>13</sup>. LOX expression was associated with lower distant metastasis-free survival and overall survival in breast cancer patients with ER-negative tumours, and in head and neck cancer patients (Fig. 1b–f).

To study the way in which hypoxia-induced LOX could influence metastasis and survival, we generated LOX short hairpin RNA (shRNA) expressing human MDA231 breast and SiHa cervical cancer cells. These cells expressed significantly less LOX mRNA and protein than cells expressing a scrambled control sequence, but grew at similar rates *in vitro* and *in vivo* (Supplementary Fig. 4). MDA231 cells were grown as orthotopic tumours in nude mice. Hypoxic

regulation of LOX was confirmed in tumours by staining for LOX and pimonidazole (Fig. 2a). Mice bearing shRNA-expressing tumours had significantly fewer lung metastases and no liver metastases, in contrast with wild-type tumours (Fig. 2b, c).

To evaluate the therapeutic usefulness of inhibiting LOX, mice



**Figure 1 | Cancer patients expressing high levels of LOX have poor outcome.** **a**, Correlation between the LOX expression level (y axis) and average hypoxia score (x axis) among breast cancer patients ( $n = 295$ )<sup>10</sup>,  $P < 0.0001$ . **b, c**, Kaplan–Meyer plots showing that patients with ER-negative breast tumours with high LOX expression levels had statistically significant reduced metastasis-free survival (**b**;  $P = 0.009$ ) and overall survival (**c**;  $P = 0.015$ ) than patients with low LOX expression levels. **d**, Comparison of LOX protein expression levels with those of CA-IX in a tissue array study from head and neck cancer patients ( $n = 91$ )<sup>11</sup>. Filled bars, LOX positive; open bars, LOX negative.  $P = 0.006$ . **e, f**, Kaplan–Meyer plots showing that head and neck cancer patients whose tumours stained positive for LOX had statistically significant reduced metastasis-free survival (**e**;  $P = 0.02$ ) and overall survival (**f**;  $P = 0.046$ ) than patients whose tumours stained negative for LOX.

<sup>1</sup>Department of Radiation Oncology, <sup>2</sup>Department of Surgery, <sup>3</sup>Department of Pathology, Stanford University School of Medicine, Stanford, California 94305, USA. <sup>4</sup>Department of Obstetrics and Gynecology, University of Leipzig, Leipzig 04103, Germany. <sup>5</sup>Department of Molecular Genetics and Microbiology, Duke University, Durham, North Carolina 27708, USA.

Software

Open Access

**TREEFINDER: a powerful graphical analysis environment for molecular phylogenetics**Gangolf Jobb<sup>\*1</sup>, Arndt von Haeseler<sup>2,3</sup> and Korbinian Strimmer<sup>1</sup>Address: <sup>1</sup>Department of Statistics, University of Munich, Ludwigstr. 33, D-80539 Munich, Germany, <sup>2</sup>Department of Computer Science, University of Düsseldorf, Universitätsstr. 1, D-40225 Düsseldorf, Germany and <sup>3</sup>John von Neumann Institute for Computing, Forschungszentrum Jülich, D-52425 Jülich, GermanyEmail: Gangolf Jobb<sup>\*</sup> - gangolf@treefinder.de; Arndt von Haeseler - haeseler@cs.uni-duesseldorf.de; Korbinian Strimmer - strimmer@stat.uni-muenchen.de<sup>\*</sup> Corresponding author

Published: 28 June 2004

BMC Evolutionary Biology 2004, 4:18 doi:10.1186/1471-2148-4-18

This article is available from: <http://www.biomedcentral.com/1471-2148/4/18>

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Received: 16 March 2004

Accepted: 28 June 2004

**Abstract****Background:** Most analysis programs for inferring molecular phylogenies are difficult to use, in particular for researchers with little programming experience.**Results:** TREEFINDER is an easy-to-use integrative platform-independent analysis environment for molecular phylogenetics. In this paper the main features of TREEFINDER (version of April 2004) are described. TREEFINDER is written in ANSI C and Java and implements powerful statistical approaches for inferring gene tree and related analyzes. In addition, it provides a user-friendly graphical interface and a phylogenetic programming language.**Conclusions:** TREEFINDER is a versatile framework for analyzing phylogenetic data across different platforms that is suited both for exploratory as well as advanced studies.**Background**

Computational inference of molecular phylogenies has a wide spectrum of applications in the analysis of DNA sequences, ranging from systematic biology to population genetics and comparative genomics [1].

As a result, a large body of theoretical methodology has developed [2], along with numerous specialist software packages. However, often the most advanced of these computer programs typically provide only a very Spartan user interface and hence are too difficult to use without additional training, especially for novices in phylogeny. One notable exception is the popular commercially distributed PAUP<sup>\*</sup> software [3] that implements both powerful probabilistic methods for modeling and inferring gene trees and at the same time offers a friendly graphical

user interface (GUI). Unfortunately, this GUI is currently available only on the Macintosh platform.

On the other hand, a more experienced user will quickly outgrow the limits of a graphical user interface. Consequently, to facilitate complex sequence analysis corresponding scripting languages have been developed. For example, in PAUP<sup>\*</sup> all elements of its GUI can also be invoked on the command line. However, for the rapid deployment of specialized phylogenetic analysis tools one still needs the additional flexibility of a *programming* rather than scripting language.

Therefore, in an integrative general-purpose phylogenetic analysis environment ideally several complementary objectives are taken into account:

Page 1 of 9

(page number not for citation purposes)

Jobb et al. BMC Evolutionary Biology (2015) 15:243  
DOI 10.1186/s12862-015-0513-z

## RETRACTION NOTE

Open Access

**Retraction Note: TREEFINDER: a powerful graphical analysis environment for molecular phylogenetics**Gangolf Jobb<sup>1\*</sup>, Arndt von Haeseler<sup>2,3</sup> and Korbinian Strimmer<sup>1</sup>**Retraction**The editors of *BMC Evolutionary Biology* retract this article [1] due to the decision by the corresponding author, Gangolf Jobb, to change the license to the software described in the article. The software is no longer available to all scientists wishing to use it in certain territories. This breaches the journal's editorial policy on software availability [2] which has been in effect since the time of publication. The other authors of the article, Arndt von Haeseler and Korbinian Strimmer, have no control over the licensing of the software and support the retraction of this article.**Author details**<sup>1</sup>Department of Statistics, University of Munich, Ludwigstr. 33, D-80539 Munich, Germany, <sup>2</sup>Department of Computer Science, University of Düsseldorf, Universitätsstr. 1, D-40225 Düsseldorf, Germany, <sup>3</sup>John von Neumann Institute for Computing, Forschungszentrum Jülich, D-52425 Jülich, Germany.

Received: 19 October 2015 Accepted: 20 October 2015

Published online: 05 November 2015

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2. BMC Evolutionary Biology's Instructions for Authors of Software Articles: <http://www.biomedcentral.com/bmcevolbio/authors/instructions/software>. Accessed 15 October 2015.

<sup>\*</sup> Correspondence: gangolf@treefinder.de

The online version of the original article can be found under doi:10.1186/1471-2148-4-18.

<sup>1</sup>Department of Statistics, University of Munich, Ludwigstr. 33, D-80539 Munich, Germany

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**7. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial. LANCET, NOV 2011.**

IF= 79, 32

*Bolli R, Chugh AR, D'Amario D, Loughran JH, Stoddard MF, Ikram S, Beache GM, Wagner SG, Leri A, Hosoda T, Sanada F, Elmore JB, Goichberg P, Cappetta D, Solankhi NK, Fahsah I, Rokosh DG, Slaughter MS, Kajstura J, Anversa P.*

2019



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71



988



University of Louisville, Louisville, KY, USA; and Departments of Anesthesia and Medicine and Division of Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

**8. Purification and ex vivo expansion of postnatal human marrow mesodermal progenitor cells.**

**BLOOD: NOV 2001.** IF= 25,47

*Reyes M, Lund T, Lenvik T, Aguiar D, Koodie L, Verfaillie CM.*

2009

596

315



911



University of Minnesota Medical School, Minneapolis.

been implemented at national and global levels, and have sparked national dialogue on the Global Strategy and challenges of moving toward UHC in multiple countries.

3 years into the SDGs, clear and shared understandings of accountability are needed. The IAP is a small panel, with an enormous mandate. The replication of accountability mechanisms will fragment and dilute meaningful oversight. UHC should be the umbrella for all these bodies that should agree on principles and priorities so that promises made in the SDGs will be delivered.

\*Alicia Ely Yamin, Elizabeth Mason, on behalf of the IAP†  
Petrie-Flom Center for Health Law Policy, Biotechnology and Bioethics at Harvard Law School, and Global Health Education and Learning Incubator at Harvard University, Boston, MA 02138, USA (AEY); and Faculty of Epidemiology and Population Health, Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK (EM)  
ayamin@hsph.harvard.edu

†The members of the Independent Accountability Panel (IAP) are: Alicia Ely Yamin (USA); Elizabeth Mason (UK); co-chairs Joy Phumaphi (Botswana) and Kul Gautam (Nepal); Brenda Kilen (Ireland); Giorgi Khakadze (Georgia); Nicolas Kojouharova (Ghana); Dame Carol Kido (Papua New Guinea); Gita Sen (India); and Jovana Rios (Panama).

We declare no competing interests.

## Retraction—Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial

Following a communication from Harvard Medical School in 2014, we published an Expression of Concern<sup>1</sup> about the above-referenced SCIPIO trial.<sup>2</sup> We promised to inform readers when further investigations were complete.<sup>3</sup> The results of these investigations persuade us that the laboratory work undertaken by Piero Anversa and colleagues at Harvard cannot be held to be reliable. Specifically, there are issues with the data presented in figures 2 and 3 and in supplemental figures 2 and 3. SCIPIO was a collaboration between Anversa's laboratory in Boston, MA, USA, and Roberto Bolli's team in Louisville, KY, USA. Anversa's laboratory isolated, expanded, and characterised the c-kit positive cells, which were then shipped to Louisville, where they were

- 1 UN Secretary-General. Global Strategy for Women's and Children's Health 2014. [http://www.who.int/gmnch/topics/maternal/20100914\\_gswch\\_en.pdf?ua=1](http://www.who.int/gmnch/topics/maternal/20100914_gswch_en.pdf?ua=1) (accessed Feb 12, 2019).
- 2 WHO. Commission on Information and Accountability for Women and Children's Health. Final report. 2011. [http://www.who.int/woman\\_child\\_accountability/about/coia/en/](http://www.who.int/woman_child_accountability/about/coia/en/) (accessed Feb 12, 2019).
- 3 UN Secretary-General. The Global Strategy for Women's, Children's and Adolescents' Health (2016–2030). 2015. <http://www.int/ife-course/partners/global-strategy/globalstrategyreport2016-2030-lowres.pdf> (accessed Feb 12, 2019).
- 4 Independent Accountability Panel. Old challenges, new hopes: accountability for the Global Strategy for Women's, Children's and Adolescents' Health. 2016. [http://www.iapreport.org/downloads/IAP\\_Report\\_September2016.pdf](http://www.iapreport.org/downloads/IAP_Report_September2016.pdf) (accessed Feb 12, 2019).
- 5 Independent Accountability Panel. Transformative accountability for adolescents: accountability for the health and human rights of women, children and adolescents. 2017. [http://iapreport.org/files/IAP%20Annual%20Report%202017-online-final-web\\_with%20endnotes.pdf](http://iapreport.org/files/IAP%20Annual%20Report%202017-online-final-web_with%20endnotes.pdf) (accessed Feb 12, 2019).
- 6 Independent Accountability Panel. Who is accountable?: private sector accountability for the Global Strategy for Women's, Children's and Adolescents' Health. 2018. <https://iapewc.org/reports/2018report/> (accessed Feb 12, 2019).
- 7 Hunt P. The importance of formal independent review: an opportunity for health to lead the way. *Health and Human Rights* 9(6), Sept 2, 2015. <http://www.hhrjournal.org/2015/09/sdg-series-sdgs-and-the-importance-of-formal-independent-review-an-opportunity-for-health-to-lead-the-way/> (accessed Feb 12, 2019).
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- 9 WHO. International Code of Marketing of Breast-milk Substitutes. [https://www.who.int/nutrition/publications/code\\_english.pdf](https://www.who.int/nutrition/publications/code_english.pdf) (accessed Feb 12, 2019).

administered to patients and all the clinical work was done. The Louisville team was not involved with the manufacturing and characterisation of c-kit positive cells. Although we do not have any reservations about the clinical work in Louisville that used the preparations from Anversa's laboratory in good faith, the lack of reliability regarding the laboratory work at Harvard means that we are now retracting this paper.

The Lancet Editors  
The Lancet, London EC2Y 5AS, UK

- 1 The Lancet Editors. Expression of concern: the SCIPIO trial. *Lancet* 2014; **383**: 1279.
- 2 Bolli R, Chugh AR, D'Amario D, et al. Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial. *Lancet* 2011; **378**: 1847–57.

### Plenary paper

## Purification and ex vivo expansion of postnatal human marrow mesodermal progenitor cells

Morayma Reyes, Troy Lund, Todd Lenvik, Dean Aguiar, Lisa Koodie, and Catherine M. Verfaillie

It is here reported that mesenchymal stem cells known to give rise to limb-bud mesoderm can, at the single-cell level, also differentiate into cells of visceral mesoderm and can be expanded extensively by means of clinically applicable methods. These cells were named mesodermal progenitor cells (MPCs). MPCs were selected by depleting bone marrow mononuclear cells from more than 30 healthy human donors of CD45<sup>+</sup>/glycophorin-A (GlyA)<sup>+</sup> cells. Cells were cultured on fibronectin with epidermal growth factor and platelet-derived growth factor BB and

2% or less fetal calf serum. It was found that 1/5 × 10<sup>5</sup> CD45<sup>+</sup>-GlyA<sup>-</sup> cells, or 1/10<sup>6</sup> bone marrow mononuclear cells, gave rise to clusters of small adherent cells. Cell-doubling time was 48 to 72 hours, and cells have been expanded in culture for more than 60 cell doublings. MPCs are CD34<sup>-</sup>, CD44<sup>low</sup>, CD45<sup>-</sup>, CD117 (cKit)<sup>-</sup>, class I-HLA<sup>-</sup>, and HLA-DR<sup>-</sup>. MPCs differentiated into cells of limb-bud mesoderm (osteoblasts, chondrocytes, adipocytes, stroma cells, and skeletal myoblasts) as well as visceral mesoderm (endothelial cells). Retroviral marking was used to

definitively prove that single MPCs can differentiate into cells of limb bud and visceral mesoderm. Thus, MPCs that proliferate without obvious senescence under clinically applicable conditions and differentiate at the single-cell level not only into mesenchymal cells but also cells of visceral mesoderm may be an ideal source of stem cells for treatment of genetic or degenerative disorders affecting cells of mesodermal origin. (*Blood*. 2001;98:2615-2625)

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### Introduction

Embryonic stem (ES) cells are pluripotent cells derived from blastocysts that can be propagated indefinitely undifferentiated in vitro, can differentiate to all cell lineages in vivo, and can be induced to differentiate to most cell types in vitro.<sup>1,4</sup> Although ES cells have been isolated from humans,<sup>2,3</sup> their use in research as well as therapeutics is encumbered by ethical considerations.<sup>5</sup> The ability to purify, culture, and manipulate multipotent stem cells from nonembryonic origin would provide investigators with an invaluable cell source to study cell and organ development. In addition, such cells could serve to develop replacement tissues for congenital or degenerative disorders. Stem cells have been identified in most organ tissues, including hematopoietic,<sup>6</sup> neural,<sup>7</sup> gastrointestinal,<sup>8</sup> epidermal,<sup>9</sup> hepatic,<sup>10</sup> and mesenchymal stem cells (MSCs).<sup>11–14</sup>

MSCs were first identified by Friedenstein,<sup>11</sup> who demonstrated that when bone marrow (BM) is plated in fetal calf serum (FCS)-containing medium, colonies of adherent fibroblastlike cells develop that differentiate into bone and adipocytes. Since then, several investigators have shown that these cells can also differentiate into chondrocytes, adipocytes, and, at least in rodents, skeletal myocytes.<sup>12–15</sup> MSCs can be purified on the basis of their ability to adhere to plastic-coated wells in the presence of monoclonal antibodies (SH2 and SH4, or Stro1).<sup>13,14</sup> Here, we describe for the first time the isolation and ex vivo expansion of cells from postnatal BM that can differentiate at the single-cell level not only into MSCs, but also into cells of visceral mesodermal origin, such as endothelium, which we termed mesodermal progenitor cells (MPCs).

From the Stem Cell Institute, Department of Medicine, and Cancer Center, University of Minnesota Medical School, Minneapolis.

Submitted April 9, 2001; accepted June 25, 2001.

Supported by National Institutes of Health grants PO1-CA-65493-1 (C.M.V.) and 1F31AI/GM10291 (M.R.); Children's Cancer Research Fund; and the University of Minnesota Bone Marrow Transplant Research Fund; C.M.V. is a Scholar of the Leukemia Society of America.

### Materials and methods

#### Bone marrow

BM was obtained from 30 healthy donors (ages 2 to 50 years) following informed consent according to guidelines from the University of Minnesota Committee on the Use of Human Subjects in Research. BM mononuclear cells (BMMNCs), obtained by Ficoll-Paque density gradient centrifugation (Sigma Chemical, St Louis, MO), were depleted of CD45<sup>+</sup> and glycophorin-A-positive (GlyA<sup>+</sup>) cells by means of micromagnetic beads (Miltenyi Biotec, Sunnyvale, CA). The eluted cells were 99.5% CD45p<sup>-</sup>GlyA<sup>-</sup>.

#### Cytokines

Epidermal growth factor (EGF) was from Sigma and platelet-derived growth factor BB (PDGF-BB), insulinlike growth factor (IGF), transforming growth factor β (TGF-β1), basic fibroblast growth factor (bFGF), acidic FGF (aFGF), bone morphogenetic protein 4 (BMP-4), interleukin-1α (IL-1α), IL-3, and IL-6 were from R&D Systems (Minneapolis, MN). Fetal liver tyrosine kinase 3 (Flt3) and granulocyte-macrophage colony-stimulating factor (GM-CSF) were from Immunex (Seattle, WA), and stem cell factor (SCF), granulocyte CSF (G-CSF), erythropoietin, and thrombopoietin were from Amgen (Thousand Oaks, CA). Vascular endothelial growth factor B (VEGF-B) was a gift from Dr S. Ramakrishnan, University of Minnesota.

#### Antibodies

Antibodies against fast-twitch skeletal myosin, sarcomeric actin, β-actin, fibroblast surface antigen (IB10), and control mouse immunoglobulin G (IgG) were from Sigma. Antibodies against Tie, Tek, Flt1, fms-related

Reprints: Catherine M. Verfaillie, Professor of Medicine, University of Minnesota, MMC 716, 420 Delaware St SE, Minneapolis, MN 55455; e-mail: verfa001@umn.edu.

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**9. Viral pathogenicity determinants are suppressors of transgene silencing in *Nicotiana benthamiana*. EMBO J; NOV 1998. IF= 11,5**

*Brigneti G, Voinnet O, Li WX, Ji LH, Ding SW, Baulcombe DC*

2015



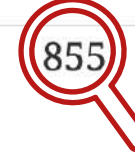
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EMBO= The European Molecular Biology Organization

The Sainsbury Laboratory, John Innes Centre, Colney Lane, Norwich NR4 7UH, UK and 1Molecular Virology Laboratory, Institute of Molecular Agrobiolgy, National University of Singapore, 1 Research Link, Singapore 117604

**10. Selective killing of cancer cells by a small molecule targeting the stress response to ROS. NATURE: JUL 2011. IF= 49, 96**

*Raj L, Ide T, Gurkar AU, Foley M, Schenone M, Li X, Tolliday NJ, Golub TR, Carr SA, Shamji AF, Stern AM,*

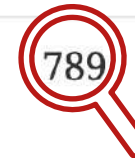
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ROS= Reactive oxygen species

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## Viral pathogenicity determinants are suppressors of transgene silencing in *Nicotiana benthamiana*

Gianinna Brigneti, Olivier Voinnet, Wan-Xiang Li<sup>1</sup>, Liang-Hui Ji<sup>1</sup>, Shou-Wei Ding<sup>1</sup> and David C.Baulcombe<sup>2</sup>

The Sainsbury Laboratory, John Innes Centre, Colney Lane, Norwich NR4 7UH, UK and <sup>1</sup>Molecular Virology Laboratory, Institute of Molecular Agrobiology, National University of Singapore, 1 Research Link, Singapore 117604

<sup>2</sup>Corresponding author  
e-mail: david.baulcombe@bbsrc.ac.uk

G. Brigneti and O. Voinnet contributed equally to this work

Post-transcriptional gene silencing (PTGS) of a green fluorescent protein (GFP) transgene is suppressed in *Nicotiana benthamiana* plants infected with potato virus Y (PVY) or with cucumber mosaic virus (CMV), but not in plants infected with potato virus X (PVX). By expressing PVY and CMV-encoded proteins in a PVX vector we have shown that the viral suppressors of gene silencing are the HCPro of PVY and the 2b protein of CMV. The HCPro acts by blocking the maintenance of PTGS in tissues where silencing had already been set, whereas the 2b protein prevents initiation of gene silencing at the growing points of the plants. Combined with previous findings that viruses are both activators and targets of PTGS, these data provide compelling evidence that PTGS represents a natural mechanism for plant protection against viruses. **Keywords:** cucumber mosaic virus/gene silencing/potato virus X/potato virus Y/virus resistance

### Introduction

Post-transcriptional gene silencing (PTGS) in transgenic plants involves sequence-specific degradation of RNA. The targeted RNA species are similar to the transcribed part of a silencer transgene and, in plants exhibiting PTGS, there is only a low level of the transgene RNA even if transcription is at a high level (Depicker and Van Montagu, 1997). In addition, if the silencer transgene is similar to an endogenous gene, there is only a low level of the corresponding endogenous gene RNAs (Matzke and Matzke, 1995). PTGS can also be targeted against viral RNA (Lindbo *et al.*, 1993; Smith *et al.*, 1994; Guo and Garcia, 1997) and extrapolating from this finding, it has been proposed that PTGS is a manifestation of a natural virus resistance mechanism in plants (Baulcombe, 1996; Pruss *et al.*, 1997). According to this idea, PTGS is activated in plants when the transgene, or its RNA, is perceived as a virus (Ratcliff *et al.*, 1997).

In support of the proposed relationship between PTGS and natural virus resistance, it has been shown that tobamovirus, potex- and geminiviruses are activators as well

as targets of gene silencing, provided they share sequence homology with a nuclear gene (Kumagai *et al.*, 1995; English *et al.*, 1996; Kjemtrup *et al.*, 1998; M.T.Ruiz *et al.*, 1998). Furthermore, caulimovirus and nepoviruses induce a PTGS-like resistance mechanism even if there is no sequence similarity between the virus and nuclear genes (Covey *et al.*, 1997; Ratcliff *et al.*, 1997). This mechanism causes the systemically infected leaves to be symptom-free, to have only low levels of the virus and to have RNA sequence-specific resistance against challenge virus infection (Ratcliff *et al.*, 1997).

If there is a natural PTGS-like virus resistance in plants, it is likely that viruses would evolve strategies to avoid or suppress this mechanism. This idea was first developed based on the analysis of plants infected with two viruses in which the disease symptoms were more severe than in plants infected with either of the two viruses alone (Pruss *et al.*, 1997). In plants infected with a potyvirus this synergism was due to suppression of a host defense mechanism by the P1-HC-protease (P1-HCPro) (Pruss *et al.*, 1997). Following from this discovery, it was suggested that P1-HCPro is targeted against a PTGS-like resistance mechanism.

A second candidate suppressor of a PTGS-like resistance mechanism is the 2b protein encoded in cucumber mosaic virus (CMV) (Ding *et al.*, 1995). This protein is required for long distance transport of CMV (Ding *et al.*, 1995) and is now thought to act by suppressing a host resistance mechanism (L.H.Ji, W.X.Li and S.W.Ding, in preparation). In the absence of this suppressor, the resistance mechanism would prevent entry, translocation or exit of CMV from the phloem of infected plants. It is conceivable that this resistance could rely on a PTGS-like mechanism.

Here, we test the hypothesis that the P1-HCPro and 2b proteins are suppressors of PTGS. Plants exhibiting PTGS of a green fluorescent protein (GFP) transgene were infected with a potyvirus (potato virus Y, PVY) or with CMV. We also infected silenced plants with potato virus X (PVX) and with chimeric constructs carrying coding sequences from PVY and CMV in a PVX vector. If PVY or CMV produce suppressors of a PTGS-like resistance mechanism we predicted that infection by PVY, CMV or the PVX vectors would interfere with PTGS. The outcome of these experiments was consistent with this prediction and reveals that HCPro and the 2b protein suppress different stages of PTGS. The results implicate a PTGS-like mechanism as a limiting factor in the accumulation and spread of PVY, PVX and CMV. Moreover, as these are unrelated viruses, it is likely that this mechanism is a generalized anti-viral defense in plants.

### Results

#### Reversion of GFP silencing by wild-type PVY

From the analysis of plants infected with a potyvirus and a second virus, it had been shown that potyviruses encode

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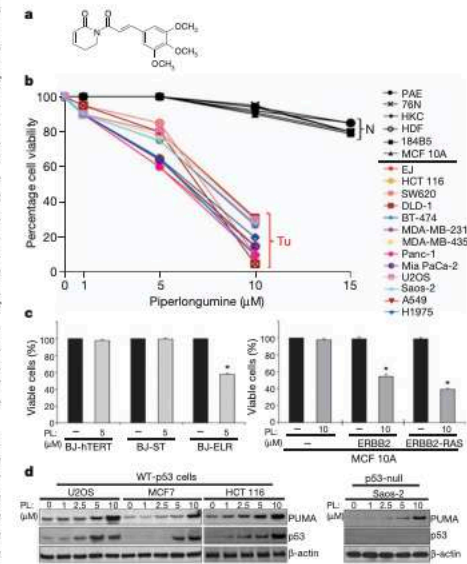
## Selective killing of cancer cells by a small molecule targeting the stress response to ROS

Lakshmi Raj<sup>1</sup>, Takao Ide<sup>1</sup>, Aditi U. Gurkar<sup>1</sup>, Michael Foley<sup>2</sup>, Monica Schenone<sup>2</sup>, Xiaoyu Li<sup>2</sup>, Nicola J. Tolliday<sup>2</sup>, Todd R. Golub<sup>2</sup>, Steven A. Carr<sup>2</sup>, Alykhan F. Shamji<sup>2</sup>, Andrew M. Stern<sup>2</sup>, Anna Mandinova<sup>1,2</sup>, Stuart L. Schreiber<sup>2</sup> & Sam W. Lee<sup>1,2</sup>

**Malignant transformation, driven by gain-of-function mutations in oncogenes and loss-of-function mutations in tumour suppressor genes, results in cell deregulation that is frequently associated with enhanced cellular stress (for example, oxidative, replicative, metabolic and proteotoxic stress, and DNA damage)<sup>1</sup>. Adaptation to this stress phenotype is required for cancer cells to survive, and consequently cancer cells may become dependent upon non-oncogenes that do not ordinarily perform such a vital function in normal cells. Thus, targeting these non-oncogene dependencies in the context of a transformed genotype may result in a synthetic lethal interaction and the selective death of cancer cells<sup>2</sup>. Here we used a cell-based small-molecule screening and quantitative proteomics approach that resulted in the unbiased identification of a small molecule that selectively kills cancer cells but not normal cells. Piperlongumine increases the level of reactive oxygen species (ROS) and apoptotic cell death in both cancer cells and normal cells engineered to have a cancer genotype, irrespective of p53 status, but it has little effect on either rapidly or slowly dividing primary normal cells. Significant antitumour effects are observed in piperlongumine-treated mouse xenograft tumour models, with no apparent toxicity in normal mice. Moreover, piperlongumine potentially inhibits the growth of spontaneously formed malignant breast tumours and their associated metastases in mice. Our results demonstrate the ability of a small molecule to induce apoptosis selectively in cells that have a cancer genotype, by targeting a non-oncogene co-dependency acquired through the expression of the cancer genotype in response to transformation-induced oxidative stress<sup>3–5</sup>.**

Using a luciferase reporter gene fused with the *CD1P* (cell death involved p53 target, also known as 5730403B10Rik) promoter<sup>6</sup>, we performed a small-molecule screen (Supplementary Fig. 1) to identify compounds acting through novel pro-apoptotic mechanisms. The compound with the highest composite Z value was piperlongumine (Supplementary Fig. 2a), which increased luciferase activity from the reporter gene at levels comparable to the positive control, etoposide (Supplementary Figs 2b and 3). Piperlongumine is a natural product isolated from the plant species *Piper longum* L. (Fig. 1a) and it was previously shown to have cytotoxic effects<sup>7</sup>. We examined the effects of piperlongumine on the viability of cultured cancer cells and normal cells (Fig. 1b and Supplementary Figs 4 and 6). Piperlongumine treatment markedly induced cell death in cancer cells with both wild-type p53 and mutant p53. When primary normal cells and non-transformed immortalized cells with diverse proliferative capacities were incubated with highly purified piperlongumine (Supplementary Fig. 5) for 24 h (under the indicated conditions, which avoid spontaneous transformation and minimize stress), there was little apparent reduction in cell viability, even at the highest concentration tested (15  $\mu$ M, a concentration of piperlongumine that approaches its solubility limit). This indicated that piperlongumine may have a cancer-cell-selective killing property, and that sensitivity to piperlongumine may result from the process of malignant transformation. To test this hypothesis, we used a

defined model<sup>8</sup> of oncogenic conversion of normal cells through ectopic expression of the telomerase catalytic subunit (*hTERT*) in combination with small T antigen and an oncogenic allele of *HRAS* (Fig. 1c), and



**Figure 1 | Selective killing effect of piperlongumine in cancer cells.** a, Structure of piperlongumine. b, Piperlongumine treatment induces cell death in cancer cells but not in normal cells. Normal human cells (N), including aortic endothelial cells (PAE), breast epithelial cells (76N), keratinocytes (HKC) and skin fibroblasts (HDF), as well as two immortalized breast epithelial cell lines (184B5 and MCF 10A), were grown in 12-well or 24-well plates and treated with piperlongumine at 1–15  $\mu$ M for 24 h. A variety of human cancer cell lines (Tu) were also treated with piperlongumine or DMSO (control) for 24 h. Cytotoxicity was measured by trypan blue exclusion staining (average of three independent experiments). Piperlongumine was HPLC-purified (~99% purity) before the treatment. c, Selective cell death caused by piperlongumine (PL) in oncogenically transformed human BJ skin fibroblasts (left panel) and MCF 10A cell lines (right panel). A representative graph for cell viability is shown (mean  $\pm$  s.d. of three independent experiments; \*,  $P < 0.0001$ ). d, The effects of piperlongumine on p53 and its target PUMA were measured by western blot analyses in several cancer cell lines.  $\beta$ -actin expression was used as a loading control.

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# Evolution of the myth of the human *rete mirabile* traced through text and illustrations in printed books: The case of Vesalius and his plagiarists

Douglas J. Lanska <https://doi.org/10.1080/0964704X.2021.2024406>

Published online: 07 Mar 2022

Andreas Vesalius initially accepted Galen's ideas concerning the *rete mirabile* in humans. In 1538, Vesalius drew a diagram of the human *rete mirabile* as a plexiform termination of the carotid arteries, where the vital spirit is transformed into the animal spirit, before being distributed from the brain along the nerves to the body. In 1540, Vesalius demonstrated the *rete mirabile* at a public anatomy, using a sheep's head (due to his nascent realization that he could not demonstrate this adequately in a human cadaver, potentially eliciting ridicule). By 1543, Vesalius had fully reversed himself, denied the existence of the *rete mirabile* in humans, and castigated himself for his prior failure to recognize this error in Galen's works. Vesalius nevertheless illustrated both the Galenic conception of the *rete mirabile* in humans and a schematic of the *rete mirabile* in ungulates. He intended the 1543 diagram of the human *rete mirabile* as an example of a *mistake* that resulted from Galen's overreliance on animals as models of human anatomy. However, in spite of Vesalius's intentions, for more than a century afterward, his figure was repeatedly and perversely plagiarized by advocates for Galenic doctrine, who misused it as a purportedly realistic representation of human anatomy and generally omitted the contrary opinions of Berengario da Carpi and Vesalius. The protracted use of stereotyped representations of the *rete mirabile* in extant printed illustrations provides tangible documentation of the stagnation in anatomical thought in the sixteenth and seventeenth centuries.

Galeno (129-199 d.C)

Vesalius (1514 -1564 d.C).

[Rete mirabile – Wikipédia, a enciclopédia livre](https://pt.wikipedia.org/wiki/Rete_mirabile)  
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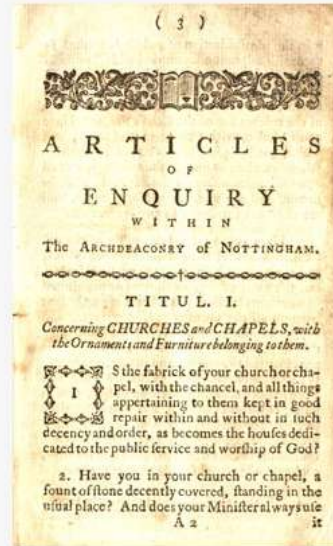
This page can be found conjectured articles asked of the churchwardens of Nottingham at Easter 1596 and Easter 1663; and an abridged version of original articles issued by the Archdeacon of Nottingham at Easter 1775, which are now part of the Drury-Lowe collection. Answers to numbered articles are also given in the East and West Leake presentment bills submitted at Easter 1733 (AN/PB 323/114 and AN/PI 323/148).



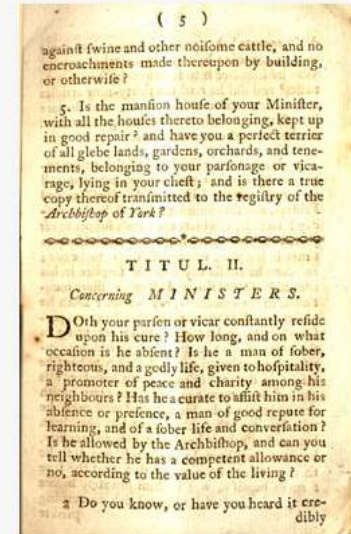
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Printed 1775 (De X 3)



First section - concerning churches and chapels, ornaments and furniture



Second section - concerning Ministers



# 50 Years of DNA

Edited by  
**Julie Clayton and  
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Julie Clayton

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equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

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## MOLECULAR STRUCTURE OF NUCLEIC ACIDS

### A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey<sup>1</sup>. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Praser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining  $\beta$ -D-deoxy-ribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furlberg's model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furlberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There

is a residue on each chain every 3-4 Å. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally<sup>2,4</sup> that the ratio of the amounts of adenine to thymine, and the ratio of guanines to cytosines, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data<sup>5,6</sup> on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material. Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON  
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge, April 2.

<sup>1</sup> Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **49**, 84 (1953).

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### Molecular Structure of Deoxypentose Nucleic Acids

WHILE the biological properties of deoxypentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here (cf. Astbury<sup>1</sup>) show the basic molecular configuration has great simplicity. The purpose of this communication is to describe, in a preliminary way, some of the experimental evidence for the polynucleotide chain configuration being helical, and existing in this form when in the natural state. A fuller account of the work will be published shortly.

The structure of deoxypentose nucleic acid is the same in all species (although the nitrogen base ratios alter considerably) in nucleoprotein, extracted or in cells, and in purified nucleate. The same linear group of polynucleotide chains may pack together parallel in different ways to give crystalline<sup>2,3</sup>, semi-crystalline or paracrystalline material. In all cases the X-ray diffraction photograph consists of two regions, one determined largely by the regular spacing of nucleotides along the chain, and the other by the longer spacings of the chain configuration. The sequence of different nitrogen bases along the chain is not made visible.

Oriented paracrystalline deoxypentose nucleic acid ('structure B' in the following communication by Franklin and Gosling) gives a fibre diagram as shown in Fig. 1 (cf. ref. 4). Astbury suggested that the strong 3-4 Å. reflexion corresponded to the inter-nucleotide repeat along the fibre axis. The  $\sim 34$  Å. layer lines, however, are not due to a repeat of a polynucleotide composition, but to the chain configuration repeat, which causes strong diffraction as the nucleotide chains have higher density than the interstitial water. The absence of reflexions on or near the meridian immediately suggests a helical structure with axis parallel to fibre length.

#### Diffraction by Helices

It may be shown<sup>5</sup> (also Stokes, unpublished) that the intensity distribution in the diffraction pattern of a series of points equally spaced along a helix is given by the squares of Bessel functions. A uniform continuous helix gives a series of layer lines of spacing corresponding to the helix pitch. A uniform distribution along the  $n$ th layer line being proportional to the square of  $J_n$ , the  $n$ th order Bessel function. A straight line may be drawn approximately through

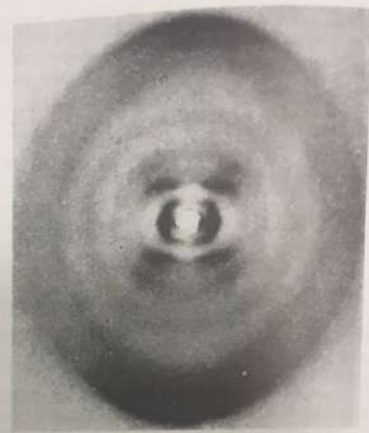


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical.

the innermost maxima of each Bessel function and the origin. The angle this line makes with the equator is roughly equal to the angle between an element of the helix and the helix axis. If a unit repeats  $n$  times along the helix there will be a meridional reflexion ( $J_n^2$ ) on the  $n$ th layer line. The helical configuration produces side-bands on this fundamental frequency, the effect being to reproduce the intensity distribution about the origin around the new origin, on the  $n$ th layer line, corresponding to  $C$  in Fig. 2.

We will now briefly analyse in physical terms some of the effects of the shape and size of the repeat unit or nucleotide on the diffraction pattern. First, if the nucleotide consists of a unit having circular symmetry about an axis parallel to the helix axis, the whole diffraction pattern is modified by the form factor of the nucleotide. Second, if the nucleotide consists of a series of points on a radius at right-angles to the helix axis, the phases of radiation scattered by the helices of different diameter passing through each point are the same. Summation of the corresponding Bessel functions gives reinforcement for the inner-

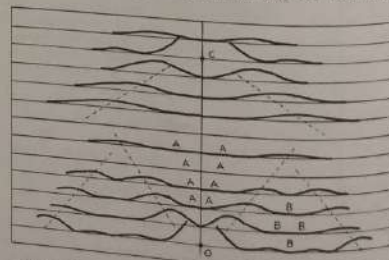


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel at second, third and fifth layer lines (on the equator and on the first, second and fifth layer lines (or half of the nucleotide mass) at a given radius) being proportional to the radius, the  $O$  on the tenth layer line similar functions are plotted for an angle of  $36^\circ$ .

most maxima and, in general, owing to phase difference, cancellation of all other maxima. Such a system core removed) diffracts mainly over a limited angular range, behaving, in fact, like a periodic arrangement of flat plates inclined at a fixed angle to the axis. Third, if the nucleotide is extended as an arc of a circle in a plane at right-angles to the helix axis, and with centre at the axis, the intensity of the system of Bessel function layer-line streaks emanating from the origin is modified owing to the phase differences point on the nucleotide. The form drawn through each of the series of points in which the helices intersect a plane drawn through the helix axis. This part of the diffraction pattern is then repeated as a whole with shape affects the central and peripheral regions of each layer line differently.

#### Interpretation of the X-Ray Photograph

It must first be decided whether the structure consists of essentially one helix giving an intensity distribution along the layer lines corresponding to  $J_1, J_2, J_3, \dots$ , or two similar co-axial helices of twice the above size and relatively displaced along the axis a distance equal to half the pitch giving  $J_2, J_4, J_6, \dots$ , or three helices, etc. Examination of the width of the layer-line streaks suggests the intensities correspond more closely to  $J_1^2, J_2^2, J_3^2$  than to  $J_2^2, J_4^2, J_6^2, \dots$ . Hence the dominant helix has a pitch of  $\sim 34$  A., and, from the angle of the helix, its diameter is found to be  $\sim 20$  A. The strong equatorial reflexion at  $\sim 17$  A. suggests that the helices have a maximum diameter of  $\sim 20$  A. and are hexagonally packed with little interpenetration. Apart from the width of the Bessel function streaks, the possibility of the helices having twice the above dimensions is also made unlikely by the absence of an equatorial reflexion at  $\sim 34$  A. To obtain a reasonable number of nucleotides per unit volume in the fibre, two or three intertwined coaxial helices are required, there being ten nucleotides on one turn of each helix.

The absence of reflexions on or near the meridian (an empty region *AAA* on Fig. 2) is a direct consequence of the helical structure. On the photograph there is also a relatively empty region on and near the equator, corresponding to region *BBB* on Fig. 2. As discussed above, this absence of secondary Bessel function maxima can be produced by a radial distribution of the nucleotide shape. To make the layer-line streaks sufficiently narrow, it is necessary to place a large fraction of the nucleotide mass at  $\sim 20$  A. diameter. In Fig. 2 the squares of Bessel functions are plotted for half the mass at the diameter, and the rest distributed along a radius, the mass at a given radius being proportional to the radius.

On the zero layer line there appears to be a marked  $J_{11}^2$ , and on the first, second and third layer lines,  $J_2^2 + J_{11}^2, J_4^2 + J_{11}^2, J_6^2 + J_{11}^2$ , respectively. This means that, in projection on a plane at right-angles to the fibre axis, the outer part of the nucleotide is relatively concentrated, giving rise to high-density regions spaced c. 6 A. apart around the circumference of a circle of 20 A. diameter. On the fifth layer line two functions overlap and produce a strong reflexion. On the sixth, seventh and eighth layer lines the maxima correspond to a helix of diameter  $\sim 12$  A. Apparently it is only the central region of the helix structure which is well defined by the 3.4-A. spacing, the outer

parts of the nucleotide overlapping to form a continuous helix. This suggests the presence of nitrogen bases arranged like a pile of pennies<sup>1</sup> in the central regions of the helical system.

There is a marked absence of reflexions on layer lines beyond the tenth. Disorientation in the specimen will cause more extension along the layer lines of the Bessel function streaks on the eleventh, twelfth and thirteenth layer lines than on the ninth, eighth and seventh. For this reason the reflexions on the higher-order layer lines will be less readily visible. The form factor of the nucleotide is also probably causing diminution of intensity in this region. Tilting of the nitrogen bases could have such an effect.

Reflexions on the equator are rather inadequate for determination of the radial distribution of density in the helical system. There are, however, indications that a high-density shell, as suggested above, occurs at diameter  $\sim 20$  A.

The material is apparently not completely paracrystalline, as sharp spots appear in the central region of the second layer line, indicating a partial degree of order of the helical units relative to one another in the direction of the helix axis. Photographs similar to Fig. 1 have been obtained from sodium nucleate from calf and pig thymus, wheat germ, herring sperm, human tissue and *T. bacteriophage*. The most marked correspondence with Fig. 2 is shown by the exceptional photograph obtained by our colleagues, R. E. Franklin and R. G. Gosling, from calf thymus deoxyribose nucleate (see following communication).

It must be stressed that some of the above discussion is not without ambiguity, but in general there appears to be reasonable agreement between the experimental data and the kind of model described by Watson and Crick (see also preceding communication).

It is interesting to note that if there are ten phosphate groups arranged on each helix of diameter 20 A. and pitch 34 A., the phosphate ester backbone chain is in an almost fully extended state. Hence, when sodium nucleate fibres are stretched<sup>2</sup>, the helix is evidently extended in length like a spiral spring in tension.

#### Structure in vivo

The biological significance of a two-chain nucleic acid unit has been noted (see preceding communication). The evidence that the helical structure discussed above does, in fact, exist in intact biological systems is briefly as follows:

**Sperm heads.** It may be shown that the intensity of the X-ray spectra from crystalline sperm heads is determined by the helical form-function in Fig. 2. Centrifuged trout semen give the same pattern as the dried and rehydrated or washed sperm heads used previously<sup>3</sup>. The sperm head fibre diagram is also given by extracted or synthetic<sup>4</sup> nucleoprotamine or extracted calf thymus nucleohistone.

**Bacteriophage.** Centrifuged wet pellets of *T. phage* photographed with X-rays while sealed in a cell with mica windows give a diffraction pattern containing the main features of paracrystalline sodium nucleate as distinct from that of crystalline nucleoprotein. This confirms current ideas of phage structure.

**Transforming principle** (in collaboration with H. Eprussi-Taylor). Active deoxyribose nucleate allowed to dry at  $\sim 60$  per cent humidity has the same crystalline structure as certain samples<sup>5</sup> of sodium thymonucleate.

We wish to thank Prof. J. T. Randall for encouragement; Prof. E. Chargaff, R. Signer, J. A. V. Butler and Drs. J. D. Watson, J. D. Smith, L. Hamilton, J. C. White and G. R. Wyatt for supplying material without which this work would have been impossible; also Drs. J. D. Watson and Mr. F. H. C. Crick for stimulation, and our colleagues R. E. Franklin, R. G. Gosling, G. L. Brown and W. E. Seeds for discussion. One of us (H. R. W.) wishes to acknowledge the award of a University of Wales Fellowship.

M. H. F. WILKINS  
Medical Research Council Biophysics  
Research Unit,

A. R. STOKES  
H. R. WILSON

Wheatstone Physics Laboratory,  
King's College, London,  
April 2.

<sup>1</sup> Astbury, W. T., *Symp. Soc. Exp. Biol.*, 1, Nucleic Acid (Cambridge Univ. Press, 1947).

<sup>2</sup> Riley, D. P., and Oster, G., *Biochim. et Biophys. Acta*, 7, 526 (1951).

<sup>3</sup> Wilkins, M. H. F., Gosling, R. G., and Seeds, W. E., *Nature*, 167, 729 (1951).

<sup>4</sup> Astbury, W. T., and Bell, F. O., *Cold Spring Harb. Symp. Quant. Biol.*, 8, 109 (1938).

<sup>5</sup> Cochran, W., Crick, F. H. C., and Vand, V., *Acta Cryst.*, 5, 581 (1952).

<sup>6</sup> Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, 10, 192 (1953).

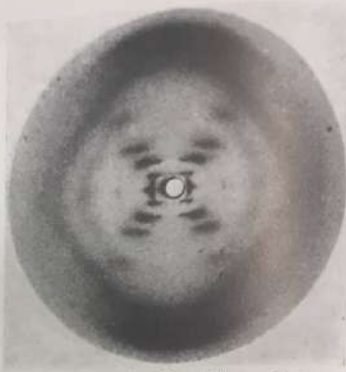
#### Molecular Configuration in Sodium Thymonucleate

SODIUM thymonucleate fibres give two distinct types of X-ray diagram. The first corresponds to a crystalline form, structure *A*, obtained at about 75 per cent relative humidity; a study of this is described in detail elsewhere<sup>1</sup>. At higher humidities a different structure, structure *B*, showing a lower degree of order, appears and persists over a wide range of ambient humidity. The change from *A* to *B* is reversible. The water content of structure *B* fibres which undergo this reversible change may vary from 40–50 per cent to several hundred per cent of the dry weight. Moreover, some fibres never show structure *A*, and in these structure *B* can be obtained with an even lower water content.

The X-ray diagram of structure *B* (see photograph) shows in striking manner the features characteristic of helical structures, first worked out in this laboratory by Stokes (unpublished) and by Crick, Cochran and Vand<sup>2</sup>. Stokes and Wilkins were the first to propose such structures for nucleic acid as a result of direct studies of nucleic acid fibres, although a helical structure had been previously suggested by Furberg (thesis, London, 1949) on the basis of X-ray studies of nucleosides and nucleotides.

While the X-ray evidence cannot, at present, be taken as direct proof that the structure is helical, other considerations discussed below make the existence of a helical structure highly probable.

Structure *B* is derived from the crystalline structures *A* when the sodium thymonucleate fibres take up quantities of water in excess of about 40 per cent of their weight. The change is accompanied by an increase of about 30 per cent in the length of an fibre, and by a substantial re-arrangement of the molecule. It therefore seems reasonable to suppose that in structure *B* the structural units of sodium thymonucleate (molecules or groups of molecules) are relatively free from the influence of neighbouring



Sodium deoxyribose nucleate from calf thymus. Structure *B*

molecules, each unit being shielded by a sheath of water. Each unit is then free to take up its least-energy configuration independently of its neighbours and, in view of the nature of the long-chain molecules involved, it is highly likely that the general form will be helical<sup>3</sup>. If we adopt the hypothesis of a helical structure, it is immediately possible, from the X-ray diagram of structure *B*, to make certain deductions as to the nature and dimensions of the helix.

The innermost maxima on the first, second, third and fifth layer lines lie approximately on straight lines radiating from the origin. For a smooth single-strand helix the structure factor on the *n*th layer line is given by:

$$F_n = J_n(2\pi r) \exp i n(\psi + \frac{1}{2}\pi),$$

where  $J_n(u)$  is the *n*th-order Bessel function of *u*, *r* is the radius of the helix, and *R* and  $\psi$  are the radial and azimuthal co-ordinates in reciprocal space<sup>4</sup>; this expression leads to an approximately linear array of intensity maxima of the type observed, corresponding to the first maxima in the functions  $J_1, J_2, J_3$ , etc.

If, instead of a smooth helix, we consider a series of residues equally spaced along the helix, the transform in the general case treated by Crick, Cochran and Vand is more complicated. But if there is a whole number, *m*, of residues per turn, the form of the transform is as for a smooth helix with the addition, only, of the same pattern repeated with its origin at heights  $me^*$ ,  $2mc^*$ , ... etc. (*c* is the fibre-axis period).

In the present case the fibre-axis period is 34 A. and the very strong reflexion at 3.4 A. lies on the tenth layer line. Moreover, lines of maxima radiating visible on the fifth and lower layer lines, having a  $J_5$  maximum coincident with that of the origin series which apparently radiate from the 3.4-A. maximum are not, however, so easily explained. This suggests of the helix. If this is so, then from a measurement of  $R_n$  the position of the first maximum on the *n*th layer line (for *n*  $\leq 5$ ), the radius of the helix, can be obtained. In the present instance, measurements of  $R_1, R_2, R_3$  and  $R_4$  all lead to values of *r* of about





Francis Harry Compton Crick  
British

1953

James Dewey Watson  
American



Cavendish Laboratory,  
Cambridge University,  
Cambridge  
England



| James Watson, seen here in 2009, apologised in 2007 after making similar remarks

**Nobel Prize-winning American scientist James Watson has been stripped of his honorary titles after repeating comments about race and intelligence.**

**Nobel Prize-winning American scientist James Watson has been stripped of his honorary titles after repeating comments about race and intelligence.**

In a TV programme, the pioneer in DNA studies made a reference to a view that genes cause a difference on average between blacks and whites on IQ tests.

Cold Spring Harbor Laboratory said the 90-year-old scientist's remarks were “unsubstantiated and reckless”. Dr Watson had made similar claims in 2007 and subsequently apologized.

He shared the Nobel in 1962 with Maurice Wilkins and Francis Crick for their 1953 discovery of the DNA's double helix structure.

[Dr Watson sold his gold medal](#) in 2014, saying he had been ostracized by the scientific community after his remarks about race.

**Luc Montagnier** accuses **Robert Gallo** misappropriating an **HIV strain**. Gallo is found innocent of misconduct. Gallo and Montagnier also have a dispute about who should be credited with discovering HIV and who can patent a test for the virus. **The U.S. and French governments reach an agreement to settle the controversy. 1984 - 1993.**

<https://www.niehs.nih.gov/research/resources/bioethics/timeline/index.cfm>

<https://www.nytimes.com/1990/10/06/us/possible-misconduct-is-seen-in-discovery-of-aids-virus.html>

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<https://www.nbcnews.com/id/wbna27049812>

## Book Reviews

### SCIENCE FICTIONS: A SCIENTIFIC MYSTERY, A MASSIVE COVER-UP, AND THE DARK LEGACY OF ROBERT GALLO

By John Crewdson. 670 pp., illustrated. Boston, Little, Brown, 2002.  
\$27.95. ISBN 0-316-13476-7.

A NOBEL prize has yet to be awarded for the discovery of the human immunodeficiency virus (HIV) or for the blood test to detect antibodies to the virus. Although the actual reasons are not known, it is widely speculated that the Nobel committee for medicine wants to stay away from the harsh battle over credit for the discovery between Robert Gallo of the National Cancer Institute and Luc Montagnier of the Institut Pasteur in Paris.

Gallo is one of the most famous scientists in the world, although he is in the spotlight less frequently now than a decade ago. John Crewdson is an investigative reporter who works for the *Chicago Tribune*. Crewdson has written a very critical book about Gallo's role in the discovery of HIV. In November 1989, the *Tribune* published a detailed account of the discovery written by Crewdson. He has continued to pursue the story, and this book is the result.

According to Crewdson, Gallo not only falsely claimed that he was the first to isolate HIV and to develop the HIV-antibody test, but also denigrated and obfuscated the role of Montagnier and his colleagues at the Institut Pasteur. Gallo's "discovery" was based on a sample of HIV supplied by Montagnier. (At the time, the French virus was known as lymphadenopathy-associated virus, or LAV.) Either Gallo's laboratory deliberately used the LAV sample without crediting the French investigators, or the French sample accidentally contaminated other viral cultures in Gallo's laboratory,

manufactured with the French virus. In March 1987, after considerable controversy and negotiations, President Ronald Reagan and French Prime Minister Jacques Chirac signed an agreement that the Department of Health and Human Services and the Institut Pasteur would share the patent rights to the blood test for AIDS. The dispute, however, was far from settled.

In the preface to his book, Crewdson states, "This is not a book about AIDS. Nor is it really about science. It is a book about how scientists behave when the stakes are high, and the stakes were never higher than the search for the cause of AIDS." The account, however, is about both Crewdson and Gallo. Although Crewdson writes about himself and the *Tribune* in the third person, much of the information in his book would never have become public if he had instead devoted more than 10 years of his life to something else.

In January 1990, soon after the *Tribune* article was published, the Office of Scientific Integrity at the National Institutes of Health opened an inquiry into Gallo's AIDS research. Gallo's actions were tentatively found to "warrant significant censure," but the office's findings were then substantially revised. Subsequently, the Office of Research Integrity in the Department of Health and Human Services replaced the Office of Scientific Integrity. In February 1992, the Office of Research Integrity found Gallo guilty of scientific misconduct for "falsely reporting that LAV had not been transmitted to a permanently growing cell line."

In November 1993, a review board reversed a related finding of misconduct against Mikulas Popovic, a virologist working in Gallo's laboratory, because it concluded that the burden of proof had not been met. Days later, the Office of Research Integrity withdrew its determination that Gallo had committed scientific misconduct. In July 1994, the Department of Health and Human Services agreed to provide the French with additional millions of dollars in patent royalties and acknowledged that "a virus provided by Institut Pasteur was used by National Institutes of Health scientists

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REPORTS



# Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts

WOO SUK HWANG, SUNG IL ROH, BYEONG CHUN LEE, SUNG KEUN KANG, DAE KEE KWON, SUE KIM, SUN JONG KIM, SUN WOO PARK, HEE SUN KWON, (...) GERALD SCHATTEN

+16 authors [Authors Info & Affiliations](#)

SCIENCE • 17 Jun 2005 • Vol 308, Issue 5729 • pp. 1777-1783 • DOI:10.1126/science.1112286

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## somatic cell nuclear transfer (SCNT)

Immune-matched human embryonic stem cells (hESCs) are antic-  
 : biomedical importance for studies of disease and develop-  
 e clinical deliberations regarding stem cell transplantation.  
 ere established by somatic cell nuclear transfer (SCNT) of skin  
 cells from patients with disease or injury into donated oocytes. These lines, nu-  
 clear transfer (NT)â€hESCs, grown on human feeders from the same NT donor or  
 from genetically unrelated individuals, were established at high rates, regardless of

### CURRENT ISSUE



**Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure**  
 BY CATHERINE J. REYNOLDS, GORINNA PADE, ET AL.

IF= 47, 72

SCNT= somatic cell nuclear transfer

Hwang- University of South Korea

Schatten - Pittsburgh University



SOUTH KOREA Sentenced for fraud Hwang Wo...

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2 **Hwang WS**, Lee BC, Lee CK, Kang SK.

Cite [Stem Cell Rev. 2005;1\(2\):99-109. doi: 10.1385/SCR:1:2:099.](#)

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IF= 5.316

[Dogs cloned from adult somatic cells.](#)

3 Lee BC, Kim MK, Jang G, Oh HJ, Yuda F, Kim HJ, Hossein MS, Kim JJ, Kang SK, Schatten G, **Hwang WS**.

Cite [Nature. 2005 Aug 4;436\(7051\):641. doi: 10.1038/436641a.](#)

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IF= 49, 96

[Endangered wolves cloned from adult somatic cells.](#)

4 Kim MK, Jang G, Oh HJ, Yuda F, Kim HJ, **Hwang WS**, Hossein MS, Kim JJ, Shin NS, Kang SK, Lee BC.

Cite [Cloning Stem Cells. 2007 Spring;9\(1\):130-7. doi: 10.1089/clo.2006.0034.](#)

Share [PMID: 17386020](#)

The first cloned wolf was delivered by cesarean section on October 18, **2005**, 60 days after embryo transfer. The second cloned wolf was delivered on October 26, **2005**, at 61 days postembryo transfer. ...

## somatic cell nuclear transfer

[Patient-specific embryonic stem cells derived from human SCNT blastocysts.](#)

5 **Hwang WS**, Roh SI, Lee BC, Kang SK, Kwon DK, Kim S, Kim SJ, Park SW, Kwon HS, Lee CK, Lee JB, Kim JM, Ahn C, Paek SH, Chang SS, Koo JJ, Yoon HS, Hwang JH, Hwang YY, Park YS, Oh SK, Kim HS, Park JH, Moon SY, Schatten G. ←

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[PMID: 15905366](#)

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Hwang Woo Suk



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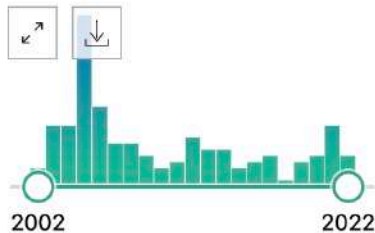
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2 [Impact of co-transfer of embryos produced by somatic cell nuclear transfer using two types of donor cells on pregnancy outcomes in dogs.](#)

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## University clears scientist of misconduct but says his conduct was misbehaviour

Jane Parry

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The University of Pittsburgh has cleared Gerald Schatten, director of its department of obstetrics, gynaecology, and reproductive sciences, of any scientific misconduct in his collaboration with the disgraced Korean stem cell researcher Hwang Woo-suk. The university's research integrity panel has investigated Dr Schatten's role in a paper published in

Science (2005;308:1777-83), which was one of two withdrawn by the journal in January after revelations that they were based on falsified data.

Although the panel concluded that Dr Schatten was not involved in the falsification of data and that he was not aware of the misconduct that led to Professor Hwang's resignation from Seoul National University, it accused him of shirking his responsibilities as co-author of the paper.

Its criticism of Dr Schatten centred on why he did not take greater steps to ensure the veracity of the data supporting the paper's claims. During the course of the investigation, Dr Schatten also sought to downplay his role as senior author of the paper, but his attempts to deny that he was not strictly speaking a



senior author were dismissed by the panel as disingenuous.

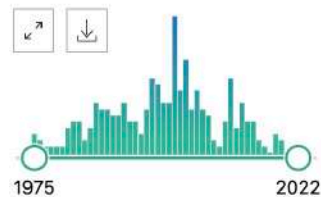
“Taken together with written comments to the committee, this appears to be part of a concerted and deliberate effort on the part of Dr Schatten to further distance himself from Dr Hwang and their joint publications. This is in sharp contrast to the full participation of Dr Schatten in the media spotlight following publication of the paper,” the panel wrote in its investigative report summary.

“Regardless of the adjective used to describe Dr Schatten's co-authorship, whether senior or not, he did invest a tremendous amount of time and energy in working over the several drafts of the manuscript, more than in many papers of his own students, according to his testimony. We feel that he did not

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2 **Fertilization and Cleavage Axes Differ In Primates Conceived By Conventional (IVF) Versus Intracytoplasmic Sperm Injection (ICSI).**  
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Share Eur J Med Genet. 2019 Aug;62(8):103682. doi: 10.1016/j.ejmg.2019.103682. Epub 2019 May 29.  
PMID: 31150829 **Review.**

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Author manuscript

*F S Sci.* Author manuscript; available in PMC 2021 December 29.

Published in final edited form as:

*F S Sci.* 2021 November ; 2(4): 365–375. doi:10.1016/j.xfss.2021.09.001.

## **Blastocyst development after fertilization with in vitro spermatids derived from nonhuman primate embryonic stem cells**

**Sujittra Khampang, Ph.D.<sup>a,b</sup>, In Ki Cho, Ph.D.<sup>a,c,d</sup>, Kanchana Punyawai, Ph.D.<sup>a</sup>, Brittany Gill, B.S.<sup>c,d</sup>, Jacqueline N. Langmo, B.S.<sup>c,d</sup>, Shivangi Nath, Ph.D.<sup>g</sup>, Katherine W. Greeson, B.S.<sup>c,d</sup>, Krista M. Symosko, B.S.<sup>c,d</sup>, Kristen L. Fowler, M.S.<sup>c,d</sup>, Siran Tian, B.S.<sup>a</sup>, John P. Statz, B.S.<sup>f,h</sup>, Alyse N. Steves, Ph.D.<sup>a,d</sup>, Rangsun Parnpai, Ph.D.<sup>b</sup>, Michael A. White, Ph.D.<sup>g</sup>, Jon D. Hennebold, Ph.D.<sup>f,h</sup>, Kyle E. Orwig, Ph.D.<sup>e</sup>, Calvin R. Simerly, Ph.D.<sup>e</sup>, Gerald Schatten, Ph.D.<sup>e</sup>, Charles A. Easley IV, Ph.D.<sup>a,c,d</sup>**

<sup>a</sup>Division of Neuropharmacology and Neurologic Diseases; Yerkes National Primate Research Center; Atlanta, Georgia;

<sup>b</sup>Embryo Technology and Stem Cell Research Center, School of Biotechnology, Suranaree University of Technology, Nakhon Ratchasima, Thailand;

<sup>c</sup>Department of Environmental Health Science, College of Public Health, University of Georgia; Athens, Georgia;

<sup>d</sup>Regenerative Bioscience Center; University of Georgia; Athens, Georgia;

<sup>e</sup>Magee-Womens Research Institute and Departments of Obstetrics, Gynecology, and Reproductive Sciences, Cell Biology and Bioengineering; University of Pittsburgh; Pittsburgh, Pennsylvania;

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## Gerald P. Schatten, PhD



Professor Gerald Schatten is Director of the Pittsburgh Development Center, Professor of Obstetrics, Gynecology and Reproductive Sciences, Cell Biology, Bioengineering and Director of the Division of Developmental and Regenerative Medicine. Dr. Schatten has directly trained >50 doctoral and postdoctoral fellows, along with several MD, MD-PhD, and DVM trainees. He is active in advanced research training and was the founding director of the FRONTIERS IN REPRODUCTION, the premier reproduction training vehicle for MD and PhDs.

He is currently President of UNESCO's International Cell Research Organization. With extensive funding from the National Institutes of Health, Dr. Schatten is the recipient of an NIH MERIT, and earlier a Research Career Development Award, was honored by the Czech Academy of Sciences with their Purkinje Medal of Science, elected as a Delegate of the American Association for the Advancement of Sciences, a Mentor Awardee of the American Society for Cell Biology, Elected Australian Society for Reproductive Biology President's Lecturer, awarded the Daniel Mazia Award from Stanford University and a Doctor Honoris Causa (Honorary Doctorate) from the University of Nova Gorica, presented by the President of the Republic of Slovenia.

**Retraction: Stimulus-triggered fate conversion of somatic cells into pluripotency**  
1 **Obokata H, Wakayama T, Sasai Y, Kojima K, Vacanti MP, Niwa H, Yamato M, Vacanti CA.**  
Cite Nature. 2014 Jul 3;511(7507):112. doi: 10.1038/nature13598.  
share PMID: 24990753 No abstract available.

**Retraction: Bidirectional developmental potential in reprogrammed cells with acquired pluripotency.**  
2 **Obokata H, Sasai Y, Niwa H, Kadota M, Andrabi M, Takata N, Tokoro M, Terashita Y, Yonemura S, Vacanti CA, Wakayama T.**  
Cite Nature. 2014 Jul 3;511(7507):112. doi: 10.1038/nature13599.  
share PMID: 24990752 No abstract available.

**Bidirectional developmental potential in reprogrammed cells with acquired pluripotency.**  
3 **Obokata H, Sasai Y, Niwa H, Kadota M, Andrabi M, Takata N, Tokoro M, Terashita Y, Yonemura S, Vacanti CA, Wakayama T.**  
Cite Nature. 2014 Jan 30;505(7485):676-80. doi: 10.1038/nature12969.  
share PMID: 24476891 **Retracted.**

**Stimulus-triggered fate conversion of somatic cells into pluripotency.**  
4 **Obokata H, Wakayama T, Sasai Y, Kojima K, Vacanti MP, Niwa H, Yamato M, Vacanti CA.**  
Cite Nature. 2014 Jan 30;505(7485):641-7. doi: 10.1038/nature12968.  
share PMID: 24476887 **Retracted.**

# What pushes scientists to lie? The disturbing but familiar story of Haruko Obokata

The spectacular fall of the Japanese scientist who claimed to have triggered stem cell abilities in regular body cells is not uncommon in the scientific community. The culprit: carelessness and hubris in the drive to make a historic discovery


**John Rasko and Carl Power**

Wed 18 Feb 2015 13.30 GMT



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 Riken researcher Haruko Obokata working at her laboratory in Kobe. Photograph: Jiji

## Haruko Obokata

**Born** September 25, 1983 (age 38)  
Matsudo City, Chiba Prefecture,  
Japan<sup>[1]</sup>

**Nationality** Japanese

**Alma mater** Waseda University

**Known for** STAP cells

### Scientific career

**Fields** Stem cell research

**Institutions** RIKEN

**Thesis** *Isolation of pluripotent adult stem cells discovered from tissues derived from all three germ layers*<sup>[2]</sup> (2011 (revoked in 2015))

**Doctoral advisor** Satoshi Tsuneda<sup>[2]</sup>



<sup>1</sup>Laboratory for Cellular Reprogramming, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan. <sup>2</sup>Laboratory for Genomic Reprogramming, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan. <sup>3</sup>Laboratory for Tissue Engineering and Regenerative Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA. <sup>4</sup>Laboratory for Organogenesis and Neurogenesis, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan. <sup>5</sup>Laboratory for Pluripotent Stem Cell Studies, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan. <sup>6</sup>Genome Resource and Analysis Unit, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan. <sup>7</sup>Electron Microscopy Laboratory, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan. <sup>8</sup>Faculty of Life and Environmental Sciences, University of Yamanashi, Yamanashi 400-8510, Japan.

regimens. Instead, one and her coauthors including her mentor Harvard's Charles Vacanti claimed that a simple procedure of low pH treatment would do the trick to get to pluripotency. They called the resulting cells "STAP cells" or "STAP stem cells".



Vacanti and Obokata in happier days before STAP crashed and burned.

STAP= Stimulus-Triggered Acquisition of Pluripotency (cells)

Actually, the whole STAP claim was bogus and never able to be replicated. Science did a good job of addressing this situation, but many wondered how the two faulty papers could have been published in the first place in *Nature*. This blog The Niche played some role in trying to elucidate the facts about STAP cells. I **posted a review** of the papers here the day they came out and registered growing skepticism about them within just days and weeks.

Over time it became clear, amongst much cloudiness, that Obokata had committed some research misconduct. Embryonic stem cells were likely mixed with the cells supposedly undergoing reprogramming by stress.

The complete facts of the case were never quite resolved, but STAP cells remain one of the most troubling stem cell-related scandals of all time.

<https://ipsell.com/2015/01/stapanniversary/>

<https://www.statnews.com/2015/09/23/stem-cell-claim-involving-brigham-research-debunked-once-more/>



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## Charles Alfred Vacanti, M.D.

**Title** Vandam/Covino Professor of Anaesthesia, Emeritus

**Institution** Brigham and Women's Hospital

**Department** Emeritus

**Address** Brigham and Women's Hospital  
Anaesthesia  
75 Francis St  
Boston MA 02115

**Phone** 617/732-8211

**Fax** 617/730-9534

**Email** [cvacanti@partners.org](mailto:cvacanti@partners.org)

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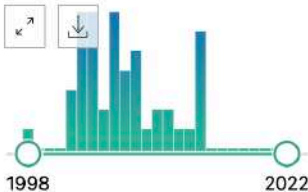
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- Meta-Analysis
- Randomized Controlled Trial
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- Systematic Review

PUBLICATION DATE

1 Peccora CD, Gimlich R, Cornell RP, **Vacanti CA**, Ehrenfeld JM, Urman RD.  
Cite J Med Syst. 2014 Sep;38(9):105. doi: 10.1007/s10916-014-0105-2. Epub 2014 Jul 20.  
Share PMID: 25038890

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[Retraction: Stimulus-triggered fate conversion of somatic cells into pluripotency.](#)  
2 Obokata H, Wakayama T, Sasai Y, Kojima K, Vacanti MP, Niwa H, Yamato M, **Vacanti CA**.  
Cite Nature. 2014 Jul 3;511(7507):112. doi: 10.1038/nature13598.  
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[Retraction: Bidirectional developmental potential in reprogrammed cells with acquired pluripotency.](#)  
3 Obokata H, Sasai Y, Niwa H, Kadota M, Andrabi M, Takata N, Tokoro M, Terashita Y, Yonemura S, **Vacanti CA**, Wakayama T.  
Cite Nature. 2014 Jul 3;511(7507):112. doi: 10.1038/nature13599.  
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[Bidirectional developmental potential in reprogrammed cells with acquired pluripotency.](#)  
4 Obokata H, Sasai Y, Niwa H, Kadota M, Andrabi M, Takata N, Tokoro M, Terashita Y, Yonemura S, **Vacanti CA**, Wakayama T.  
Cite Nature. 2014 Jan 30;505(7485):676-80. doi: 10.1038/nature12969.  
Share PMID: 24476891 **Retracted.**

[Stimulus-triggered fate conversion of somatic cells into pluripotency.](#)  
5 Obokata H, Wakayama T, Sasai Y, Kojima K, Vacanti MP, Niwa H, Yamato M, **Vacanti CA**.  
Cite Nature. 2014 Jan 30;505(7485):641-7. doi: 10.1038/nature12968.  
Share PMID: 24476887 **Retracted.**



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Yoshiki Sasai, right, deputy director of the Riken's Center for Developmental Biology, poses for a photo with Haruko Obokata on Jan. 28, 2014. *Kyodo/Reuters*

# Stem cell scientist found dead in apparent suicide

By Jonathan Webb

Science reporter, BBC News



The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group

[D Poldermans 1](#), [E Boersma](#), [J J Bax](#), [I R Thomson](#), [L L van de Ven](#), [J D Blankensteijn](#), [H F Baars](#), [T I Yo](#), [G Trocino](#), [C Vigna](#), [J R Roelandt](#), [H van Urk](#)

DOI: [10.1056/NEJM199912093412402](https://doi.org/10.1056/NEJM199912093412402)

Don Poldermans is a Dutch former cardiovascular medicine researcher who was fired **for scientific misconduct and ethics concerns over informed consent**. He was employed by Erasmus Medical Center in Rotterdam, Netherlands, where he was the head of the perioperative cardiac care unit.

[Don Poldermans - Wikipedia](#)

[https://en.wikipedia.org/wiki/Don\\_Poldermans](https://en.wikipedia.org/wiki/Don_Poldermans)



[Breaking news: Prolific Dutch heart researcher fired over ...](#)

<https://retractionwatch.com/breaki...>

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17 de nov. de 2011 — **Don Poldermans**, a leading heart specialist, has been **fired** over concerns that he committed research misconduct. According to a report on the .

# THE EFFECT OF BISOPROLOL ON PERIOPERATIVE MORTALITY AND MYOCARDIAL INFARCTION IN HIGH-RISK PATIENTS UNDERGOING VASCULAR SURGERY

→ DON POLDERMANS, PH.D., ERIC BOERSMA, PH.D., JEROEN J. BAX, PH.D., IAN R. THOMSON, PH.D., LOUIS L.M. VAN DE VEN, PH.D., JAN D. BLANKENSTEIJN, PH.D., HUBERT F. BAARS, M.D., TIK-IEN YO, PH.D., GIUSEPPE TROCINO, M.D., CARLO VIGNA, M.D., JOS R.T.C. ROELANDT, PH.D., AND HERO VAN URK, PH.D., FOR THE DUTCH ECHOCARDIOGRAPHIC CARDIAC RISK EVALUATION APPLYING STRESS ECHOCARDIOGRAPHY STUDY GROUP\*

## ABSTRACT

**Background** Cardiovascular complications are the most important causes of perioperative morbidity and mortality among patients undergoing major vascular surgery.

**Methods** We performed a randomized, multicenter trial to assess the effect of perioperative blockade of beta-adrenergic receptors on the incidence of death from cardiac causes and nonfatal myocardial infarction.

**Conclusions** Bisoprolol reduces the perioperative incidence of death from cardiac causes and nonfatal myocardial infarction in high-risk patients who are undergoing major vascular surgery. (N Engl J Med 1999;341:1789-94.)

©1999, Massachusetts Medical Society.

PATIENTS undergoing major vascular surgery are at risk for serious perioperative cardiac complications, such as nonfatal myocardial infarction and death.<sup>1</sup> A combination of clinical assessment and noninvasive cardiac testing can be used to identify patients at high risk.<sup>2</sup> Various interventions have been proposed to reduce the risk of cardiac complications in such patients after noncardiac surgery, but none have been found to be efficacious.

---

From Erasmus Medical Center, Rotterdam, the Netherlands (D.P., E.B., J.J.B., L.L.M.V., J.R.T.C.R., H.U.); the University of Manitoba, Winnipeg, Canada (I.R.T.); University Hospital, Utrecht, the Netherlands (J.D.B.); Twee Steden Ziekenhuis, Tilburg, the Netherlands (H.F.B.); Sint Clara Ziekenhuis, Rotterdam, the Netherlands (T.-I.Y.); San Gerardo Hospital, Monza, Italy (G.T.); and Istituto di Ricovero e Cura a Carattere Scientifico Hospital, San Giovanni Rotondo, Italy (C.V.). Address reprint requests to Dr. Poldermans at the Department of Vascular Surgery, Erasmus University Medical Center, Dr. Molewaterplein 40, 3015 GD Rotterdam, the Netherlands, or at poldermans@hkd.azr.nl.

Other authors were Paolo M. Fioretti, Ph.D., Istituto di Cardiologia, Azienda Ospedaliera, Santa Maria della Misericordia, Udine, Italy; and Bernard Paelinck, M.D., Ziekenhuis Middelheim, Antwerp, Belgium.

\*The members of the study group are listed in the Appendix.

# Should Major Vascular Surgery Be Delayed Because of Preoperative Cardiac Testing in Intermediate-Risk Patients Receiving Beta-Blocker Therapy With Tight Heart Rate Control?

Don Poldermans, MD, PhD,\* Jeroen J. Bax, MD, PhD,† Olaf Schouten, MD,‡ Aleksandar N. Neskovic, MD, PhD,§ Bernard Paelinck, MD, PhD,|| Guido Rocci, MD, PhD,¶ Laura van Dortmont, MD, PhD,# Anai E. S. Durazzo, MD, PhD,\*\* Louis L. M. van de Ven, MD, PhD,†† Marc R. H. M. van Sambeek, MD, PhD,‡ Miklos D. Kertai, MD, PhD,\* Eric Boersma, PhD,‡‡ for the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study Group  
*Rotterdam, Leiden, Schiedam, and Amsterdam, the Netherlands; Belgrade, Serbia and Montenegro; Antwerp, Belgium; Bologna, Italy; and São Paulo, Brazil*

**OBJECTIVES** The purpose of this study was to assess the value of preoperative cardiac testing in intermediate-risk patients receiving beta-blocker therapy with tight heart rate (HR) control scheduled for major vascular surgery.

**BACKGROUND** Treatment guidelines of the American College of Cardiology/American Heart Association recommend cardiac testing in these patients to identify subjects at increased risk. This policy delays surgery, even though test results might be redundant and beta-blockers with tight HR control provide sufficient myocardial protection. Furthermore, the benefit of revascularization in high-risk patients is ill-defined.

**METHODS** All 1,476 screened patients were stratified into low-risk (0 risk factors), intermediate-risk (1 to 2 risk factors), and high-risk ( $\geq 3$  risk factors). All patients received beta-blockers. The 770 intermediate-risk patients were randomly assigned to cardiac stress-testing (n = 386) or no testing. Test results influenced management. In patients with ischemia, physicians aimed to control HR below the ischemic threshold. Those with extensive stress-induced ischemia were

**CONCLUSIONS** Cardiac testing can safely be omitted in intermediate-risk patients, provided that beta-blockers aiming at tight HR control are prescribed. (J Am Coll Cardiol 2006;48:964–9)  
© 2006 by the American College of Cardiology Foundation

## **Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery**

**The Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA)**

**Authors/Task Force Members: Don Poldermans; (Chairperson) (The Netherlands)\*; Jeroen J. Bax (The Netherlands); Eric Boersma (The Netherlands); Stefan De Hert (The Netherlands); Erik Eeckhout (Switzerland); Gerry Fowkes (UK); Bulent Gorenek (Turkey); Michael G. Hennerici (Germany); Bernard Jung (France); Malte Kelm (Germany); Keld Per Kjeldsen (Denmark); Steen Dalby Kristensen (Denmark); Jose Lopez-Sendon (Spain); Paolo Pelosi (Italy); François Philippe (France); Luc Pierard (Belgium); Piotr Ponikowski (Poland); Jean-Paul Schmid (Switzerland); Olav F.M. Sellevold (Norway); Rosa Sicari (Italy); Greet Van den Berghe (Belgium); Frank Vermassen (Belgium)**

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

Larry Husten

Contributor ⓘ

*I'm a medical journalist covering cardiology news.*



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This article is more than 8 years old.

**(Updated)**– Last summer British researchers provoked concern when they published a paper raising the possibility that by following an established guideline UK doctors may have caused as many as 10,000 deaths each year. Now they have gone a step further and published an estimate that the same guideline may have led to the deaths of as many as 800,00 people in Europe over the last five years. The finding, they write, “is so large that the only context in the last 50 years comes from the largest scale professional failures in the political sphere.” The



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In their new article published in the *European Heart Journal*, Graham Cole and Darrel Francis continue to explore the extent and implications of the damage caused by the Don Poldermans research misconduct case. **[Update: the EHJ article has been removed from the EHJ website. For more on this see the bottom of the story.]** The earlier paper demonstrated the potentially large and lethal consequences of the current European Society of Cardiology guideline recommending the liberal use of beta-blockers to protect the heart during surgery for people undergoing



Jan 15, 2014, 12:37pm

# Suspect Drug Research Blamed for Massive Death Toll

Research misconduct can ruin everything from scientific careers to institutional reputations and public confidence in science. But in a paper published 2 weeks ago, two British cardiologists claimed that misconduct in their field may have had a far greater toll. Tainted research by Don Poldermans, a disgraced cardiologist who was at Erasmus MC in the Netherlands, may have led to the deaths of 800,000 people in Europe, Darrel Francis and Graham Cole of Imperial College London wrote in a provocative article that appeared briefly in the *European Heart Journal (EHJ)* and was then withdrawn.

Poldermans, a prominent researcher who published more than 300 papers, was fired in November 2011 after a university investigation concluded that he had engaged

in misconduct, including data fabrication. He was the lead author on two influential trials examining whether  $\beta$ -blocker drugs can protect patients undergoing surgery that doesn't directly involve the heart; those studies helped shape guidelines adopted in 2009 by the European Society of Cardiology (ESC) that recommended using the drugs. (U.S. guidelines are more cautious.) When Poldermans's studies are omitted, Francis and Cole say, the evidence shows that the recommendations don't save lives but endanger them.

The accusatory paper was removed from the *EHJ*'s website less than 48 hours after it appeared. It hadn't undergone peer review, as it should have, says Thomas Lüscher of the University of Zurich in Switzerland, the

journal's editor; an official retraction was posted on 23 January, and the paper is now under review. But Cole and Francis say the staggering number of deaths they calculated was based on published data, and their claim has reignited a debate about giving  $\beta$  blockers to patients about to undergo surgery that might stress the heart. It is also a reminder, some scientists say, of the huge effects that a few uncertain and potentially flawed studies can have on clinical practice. "This is unfortunately what happens when you write a guideline that affects large numbers of people in a relatively common situation," Francis says.

Defenders of the guidelines counter that the estimate of 800,000 deaths is wildly inflated. It disregards explicit cautions in

www.sciencemag.org **SCIENCE** VOL 343 31 JANUARY 2014

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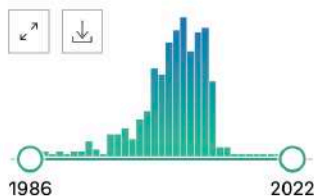
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ARTICLE ATTRIBUTE

- Associated data

ARTICLE TYPE

- Diet and kidney disease in high-risk individuals with type 2 diabetes mellitus.**  
1 Dunkler D, Dehghan M, Teo KK, Heinze G, Gao P, Kohl M, Clase CM, Mann JF, Yusuf S, Oberbauer R; ONTARGET Investigators.  
Cite JAMA Intern Med. 2013 Oct 14;173(18):1682-92. doi: 10.1001/jamainternmed.2013.9051.  
Share PMID: 23939297 Clinical Trial.
- Don Poldermans MD PhD, replies to European heart journal editorial.**  
2 **Poldermans D.**  
Cite Eur Heart J. 2013 Jun;34(23):1698.  
Share PMID: 23926606 No abstract available.
- Scientific fraud or a rush to judgment?**  
3 **Poldermans D.**  
Cite Am J Med. 2013 Apr;126(4):e5-6. doi: 10.1016/j.amjmed.2012.10.018.  
Share PMID: 23507217 No abstract available.
- [ESC guidelines for treatment of cardiovascular disease in pregnancy].**

# 3ª Diretriz de Avaliação Cardiovascular Perioperatória da Sociedade Brasileira de Cardiologia 2017

## 1. Definição do Problema

### A) Objetivo desta Diretriz

O objetivo principal desta diretriz é atualizar os conceitos difundidos por suas duas antecessoras, as diretrizes I e II, de avaliação perioperatória, da Sociedade Brasileira de Cardiologia (SBC), publicadas, respectivamente, em 2007 e 2011.<sup>1</sup> Ao realizar uma revisão sistemática das evidências acumuladas no período de 5 anos, ou seja, desde a última publicação, percebemos o notável crescimento do conhecimento do assunto, em especial na Cardiologia.

Em um ambiente perioperatório, o médico precisa reunir, a um só tempo, conceitos de diversas especialidades, para compreender facetas diferentes de um mesmo problema e otimizar a linguagem entre clínicos, cirurgiões, anesthesiologistas e intensivistas. Por outro lado, ainda que problemas mais relacionados com outras disciplinas sejam tratados nesta III diretriz, decidimos que o ponto de vista adotado no texto é o do cardiologista. Para ser fiel a esta decisão, esta diretriz incorporou o termo 'cardiovascular', passando a se denominar *Diretriz de Avaliação Cardiovascular Perioperatória*.

Ainda, algumas novidades foram incluídas em função de novas evidências, como os Novos Anticoagulantes Orais (NOAC) e a situação de intervenções cirúrgicas em pacientes com Dupla Antiagregação Plaquetária (DAP) em portadores de stents de última geração. A questão dos anticoagulantes e dos antiagregantes foi discutida com detalhe no caso de procedimentos cirúrgicos específicos, como odontológicos, dermatológicos, endoscópicos e oftalmológicos.

### B) Metodologia e Evidências

A revisão sistemática realizada para a elaboração desta diretriz considerou os aspectos relacionados às graves denúncias de fraude envolvendo um grupo de trabalhos do pesquisador Don Poldermans, do *Erasmus Medical Center*, na Holanda. Conhecidos sob o nome de DECREASE trials, estes estudos analisaram, em grupos significativos de pacientes, aspectos importantes no meio perioperatório, como o uso de betabloqueadores, a estratificação invasiva e o uso de biomarcadores.

O relatório divulgado pelo *Erasmus Medical Center* descreve diversos problemas, incluindo negligência e incorreções científicas nestes estudos, em especial no DECREASE IV.<sup>2</sup> Outros estudos do mesmo grupo, como o DECREASE V e VI, apresentaram problemas semelhantes, embora em menor quantidade.<sup>3,4</sup>

As conclusões do relatório levaram à demissão de Don Poldermans da instituição e à notificação das revistas as quais estes trabalhos foram publicados. Até a data da publicação desta diretriz, entretanto, os trabalhos publicados permaneciam nos sites das revistas.

Os membros do comitê redator desta diretriz discutiram o assunto e decidiram (não por unanimidade) que as recomendações da III diretriz **não** deveriam levar em conta as evidências provenientes dos estudos DECREASE IV, V e VI, e que tal decisão deveria ser informada aos leitores.

A metodologia e os níveis de evidência adotados para a *Diretriz de Avaliação Cardiovascular Perioperatória* foram os seguintes:

Retraction of Poehlman et al. *Journal of Applied Physiology* 76: 2281–2287, 1994

**RE: Poehlman, Eric T., Andrew W. Gardner, Paul J. Arciero, Michael I. Goran, and Jorge Calles-Escandon.** Effects of endurance training on total fat oxidation in elderly persons. *J Appl Physiol* 76: 2281–2287, 1994.

*To the Editor:* In the above referenced paper, we presented data purportedly showing the influence of endurance training (ET) on in vivo changes in total fat oxidation and its relationship to changes in sympathetic nervous system activity (SNSA) and resting metabolic rate (RMR) in elderly persons. We concluded that ET may be of benefit in regulation of energy balance via its impact on RMR and substrate oxidation.

This study was purported to be an extension of two earlier studies (1, 2). I have requested retraction of the 1992 *Metabolism* paper (2) because I intentionally omitted a material data point from the norepinephrine results for one of the seven subjects in that paper.

I now wish to report that I also intentionally omitted norepinephrine data from Table 3, Figure 1, Figure 2, and associated text of the above referenced *Journal of Applied Physiology* paper in order to make the association between increased

sympathetic nervous system activity and endurance training, resting metabolic rate, and change in fat oxidation appear significant when the actual data did not show significance. My coauthors were unaware of my actions and I now publicly exonerate them. I take sole responsibility for the intentional omission and request that you publish this letter of retraction.

Since both the 1992 and 1994 papers relied upon results where data were intentionally omitted, it is evident that we did not replicate the results reported in the 1991 paper.

#### REFERENCES

1. **Poehlman E and Danforth E Jr.** Endurance training increases metabolic rate and norepinephrine appearance rate in older individuals. *Am J Physiol Endocrinol Metab* 261: E233–E239, 1991.
2. **Poehlman E, Gardner A, and Goran M.** Influence of endurance training on energy intake, norepinephrine kinetics, and metabolic rate in older individuals. *Metabolism* 41: 941–948, 1992.

Eric T. Poehlman  
(formerly)Professor of Medicine  
University of Vermont  
College of Medicine  
Burlington, Vermont

<http://www.sciencemag.org/news/2006/06/poehlman-sentenced-1-year-prison>

## Poehlman Sentenced to 1 Year of Prison



Researcher Eric Poehlman was sentenced to prison today for **fabricating** research. UNIVERSITY OF VERMONT  
Researcher Eric Poehlman was sentenced to a year and a day in federal prison today for making a false statement on a federal grant application in 1999. The action by U.S. District Judge William Sessions in Burlington, Vermont, ends the most extensive case of scientific misconduct in the history of the National Institutes of Health (NIH). Experts say the case marks the first time a U.S. scientist will serve jail time for research misconduct not linked to fatalities.

Poehlman admitted in a plea agreement last year to falsifying 15 federal grant applications in addition to as many as 10 articles beginning in 1992 and spanning a decade (*Science*, 25 March 2005, p. 1851) while he was a scientist at the University of Vermont College of Medicine in Burlington and, before then, the University of Maryland, Baltimore. The work involved obesity, metabolism, and menopause. Eight journals have run retractions of his papers, including the *Annals of Internal Medicine*. More than 200 other articles he authored remain in the literature. Prosecutors said that Poehlman made what a clerk called "factual misstatements" in an earlier federal hearing; that offense worsened the sentence.

In a letter to the judge earlier this month, Poehlman explained that he was "motivated by my own desire to advance as a respected scientist" and added that he was "ashamed of myself for falsifying and fabricating data. ... I believed that because the research questions I had framed were legitimate and worthy of study, it was okay to misrepresent 'minor' pieces of data to increase the odds that the grant would be awarded."

Poehlman faced up to 5 years in jail and has already paid a \$180,000 fine. He has also been barred for life from receiving federal research funding.

The first questions about Poehlman's conduct were raised by a 24-year-old research assistant in Poehlman's lab at the University of Vermont. The university found falsifications in three papers, and a 2-year probe by NIH uncovered the rest of the crimes. A university review of Poehlman's scientific work at the University of Montreal, which he joined in 2001, found no wrongdoing in work he'd done there.

**A number of scientists joined his friends in appealing to the judge for leniency. "I do believe he still has a great deal to offer the scientific community," wrote Ross Andersen, an obesity expert at Johns Hopkins University School of Medicine in Baltimore, Maryland.**

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Retraction of Publication > Ann Intern Med. 2003 Oct 21;139(8):702.  
doi: 10.7326/0003-4819-139-8-200310210-00017.

## Notice of retraction

Harold C Sox

PMID: 14568863 DOI: 10.7326/0003-4819-139-8-200310210-00017

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### Retraction of

Changes in energy balance and body composition at menopause: a controlled longitudinal study.

Poehlman ET, Toth MJ, Gardner AW.

Ann Intern Med. 1995 Nov 1;123(9):673-5. doi: 10.7326/0003-4819-123-9-199511010-00005.

PMID: 7574222 **Retracted.**

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Menopause, energy expenditure, and body composition.

20 Poehlman ET.

Cite Acta Obstet Gynecol Scand. 2002 Jul;81(7):603-11. doi: 10.1034/j.1600-0412.2002.810705.x.

PMID: 12190834 **Retracted.** Review.

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# Research misconduct, retraction, and cleansing the medical literature: lessons from the Poehlman case

[Harold C Sox](#)<sup>1</sup>, [Drummond Rennie](#)

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PMID: 16522625 DOI: [10.7326/0003-4819-144-8-200604180-00123](https://doi.org/10.7326/0003-4819-144-8-200604180-00123)

**Free article**

## Abstract

The scientific literature is a record of the search for truth. Publication of faked data diverts this search. The scientific community has a duty to warn people to ignore an article containing faked data and must try to prevent inadvertent citation of it. The scientific community accomplishes these tasks by publishing a retraction and linking it to the fraudulent article's citation in electronic indexes of the medical literature, such as PubMed. This mechanism is far from perfect, as shown by a case history of scientific fraud perpetrated by Eric Poehlman, PhD. His institution notified 3 journals that they had published tainted articles. Two journals failed to retract. The third journal retracted immediately, but other authors continued to cite the retracted article. Another duty of the scientific community is to verify the integrity of other articles published by the author of a fraudulent article. This task falls to the author's institution and requires coauthors to vouch for their article's integrity by convincing institutional investigators that the suspect author could not have altered the raw scientific data from their study. Two universities are currently investigating Poehlman's published research. Maintaining the integrity of the scientific literature requires governmental institutions that have the authority to investigate and punish guilty scientists and

# Misconduct Policies in High-Impact Biomedical Journals

Xavier Bosch<sup>1\*</sup>, Cristina Hernández<sup>1</sup>, Juan M. Pericas<sup>1</sup>, Pamela Doti<sup>1</sup>, Ana Marušić<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Institut d'Investigacions Biome`diques August Pi i Sunyer, Hospital Cl`inic, University of Barcelona, Barcelona, Spain, <sup>2</sup>Department of

## Abstract

**Background:** It is not clear which research misconduct policies are adopted by biomedical journals. This study assessed the prevalence and content policies of the most influential biomedical journals on misconduct and procedures for handling and responding to allegations of misconduct.

**Methods:** We conducted a cross-sectional study of misconduct policies of 399 high-impact biomedical journals in 27 biomedical categories of the Journal Citation Reports in December 2011. Journal websites were reviewed for information relevant to misconduct policies.

**Results:** Of 399 journals, 140 (35.1%) provided explicit definitions of misconduct. Falsification was explicitly mentioned by 113 (28.3%) journals, fabrication by 104 (26.1%), plagiarism by 224 (56.1%), duplication by 242 (60.7%) and image manipulation by 154 (38.6%). Procedures for responding to misconduct were described in 179 (44.9%) websites, including retraction, (30.8%) and expression of concern (16.3%). Plagiarism-checking services were used by 112 (28.1%) journals. The prevalences of all types of misconduct policies were higher in journals that endorsed any policy from editors' associations, Office of Research Integrity or professional societies compared to those that did not state adherence to these policy-producing bodies. Elsevier and Wiley-Blackwell had the most journals included (22.6% and 14.8%, respectively), with Wiley journals having greater a prevalence of misconduct definition and policies on falsification, fabrication and expression of concern and Elsevier of plagiarism-checking services.

**Conclusions:** Only a third of top-ranking peer-reviewed journals had publicly-available definitions of misconduct and less than a half described procedures for handling allegations of misconduct. As endorsement of international policies from policy-producing bodies was positively associated with implementation of policies and procedures, journals and their publishers should standardize their policies globally in order to increase public trust in the integrity of the published record in biomedicine.

**Citation:** Bosch X, Hernández C, Pericas JM, Doti P, Marušić A (2012) Misconduct Policies in High-Impact Biomedical Journals. PLoS ONE 7(12): e51928. doi:10.1371/journal.pone.0051928

**Editor:** Lamberto Manzoli, University of Chieti, Italy

• [10.1371/journal.pone.0051928](https://doi.org/10.1371/journal.pone.0051928)

# Retractions in the scientific literature: do authors deliberately commit research fraud?

R Grant Steen <sup>1</sup>

Steen RG. J Med Ethics. 2011. PMID: 21081306

Affiliations + expand

IF= 2.21

PMID: 21081306 DOI: [10.1136/jme.2010.038125](https://doi.org/10.1136/jme.2010.038125)

## Retractions in the scientific literature: do authors deliberately commit research fraud?

### Abstract

**Background:** Papers retracted for fraud (data fabrication or data falsification) may represent a deliberate effort to deceive, a motivation fundamentally different from papers retracted for error. It is hypothesised that fraudulent authors target journals with a high impact factor (IF), have other fraudulent publications, diffuse responsibility across many co-authors, delay retracting fraudulent papers and publish from countries with a weak research infrastructure.

**Methods:** All 788 English language research papers retracted from the PubMed database between 2000 and 2010 were evaluated. Data pertinent to each retracted paper were abstracted from the paper and the reasons for retraction were derived from the retraction notice and dichotomised as fraud or error. Data for each retracted article were entered in an Excel spreadsheet for analysis.

**Results:** Journal IF was higher for fraudulent papers ( $p < 0.001$ ). Roughly 53% of fraudulent papers were written by a first author who had written other retracted papers ('repeat offender'), whereas only 18% of erroneous papers were written by a repeat offender ( $\chi^2 = 88.40$ ;  $p < 0.0001$ ). Fraudulent papers had more authors ( $p < 0.001$ ) and were retracted more slowly than erroneous papers ( $p < 0.005$ ). Surprisingly, there was significantly more fraud than error among retracted papers from the USA ( $\chi^2(2) = 8.71$ ;  $p < 0.05$ ) compared with the rest of the world.

**Conclusions:** This study reports evidence consistent with the 'deliberate fraud' hypothesis. The results suggest that papers retracted because of data fabrication or falsification represent a calculated effort to deceive. It is inferred that such behaviour is neither naïve, feckless nor inadvertent.



Interest in research misconduct has not only continued but, as [Figure 1](#) shows, has escalated. The increase in absolute numbers is still striking, while the annual rate of increase in the later years is even faster than it was earlier. It rose 5.89 times from 2012 to 2019 and 1.61 times from 2006 to 2011. Without putting a great deal of emphasis on the precise numbers shown here, it is fair to conclude that the phenomenon of scientific misconduct has clearly captured a good deal of scholarly attention.

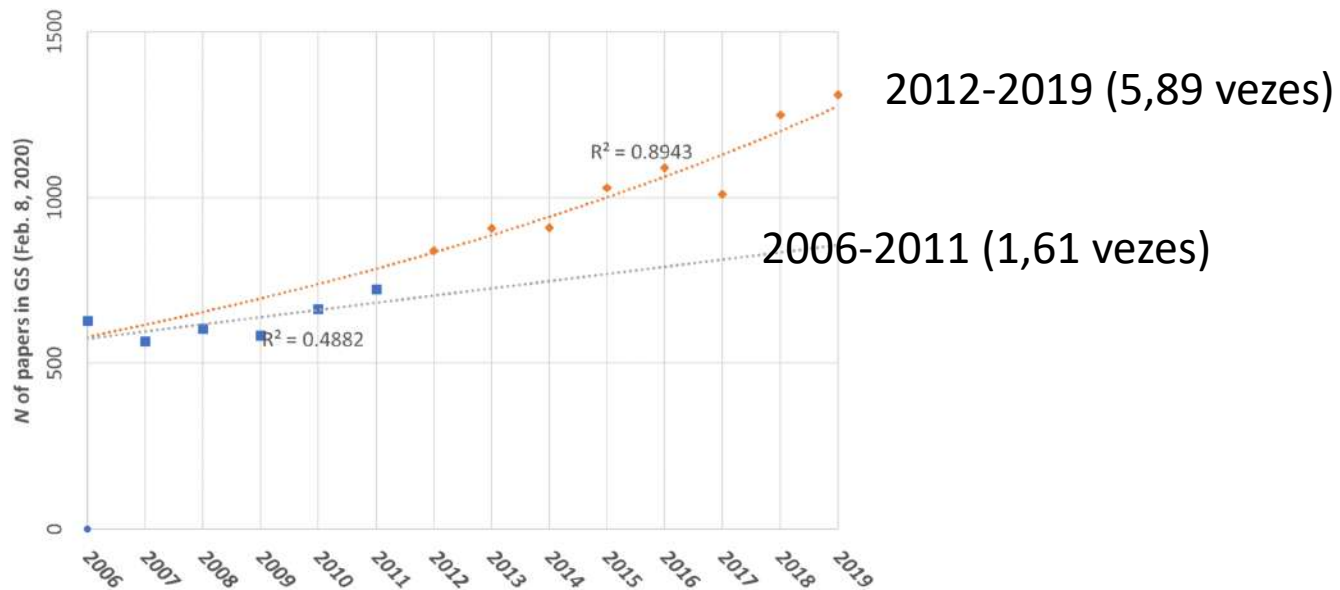


Figure 1.

**Figure Legend:**

Listings in Google Scholar of scientific misconduct 2006–2020. Source: The figure is based on Ben-Yehuda and Oliver-Lumerman (2017, Figure 4.1, p. 96), but was amended and redesigned for this paper by Loet Leydesdorff, February 8, 2020.

Citation: Zuckerman, H. (2020). Is “the time ripe” for quantitative research on misconduct in science? *Quantitative Science Studies*, 1(3), 945–958 [https://doi.org/10.1162/qss\\_a\\_00065](https://doi.org/10.1162/qss_a_00065)

The background of the slide is an abstract, textured pattern. It features a complex network of orange and reddish-brown lines that resemble veins or a cracked surface, set against a base of teal and blue. The overall effect is organic and somewhat chaotic, with the lines forming irregular, interconnected shapes.

# **FRAUD AND MISCONDUCT IN RESEARCH**

Detection, Investigation, and  
Organizational Response

**NACHMAN BEN-YEHUDA and  
AMALYA OLIVER-LUMERMAN**

2017



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# Effectiveness and safety of structured exercise vs. no exercise for asymptomatic aortic aneurysm: systematic review and meta-analysis

Efetividade e segurança de exercícios estruturados versus sem exercício em pacientes assintomáticos com aneurisma de aorta: revisão sistemática e metanálise

Ricardo de Ávila Oliveira Eliza Nakajima Vladimir Tonello de Vasconcelos Rachel Riera  
José Carlos Costa Baptista-Silva

ABOUT THE AUTHORS

J. Vasc. Bras  
2020



Cochrane Database of Systematic Reviews

Prehabilitation exercise therapy before elective abdominal aortic aneurysm repair (Review)

Fenton C, Tan AR, Abaraogu UO, McCaslin JE

2021



## Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery

F.L. Moll <sup>a,\*</sup>, J.T. Powell <sup>b</sup>, G. Fraedrich <sup>c</sup>, F. Verzini <sup>d</sup>, S. Haulon <sup>e</sup>,  
M. Waltham <sup>f</sup>, J.A. van Herwaarden <sup>a</sup>, P.J.E. Holt <sup>g</sup>, J.W. van Keulen <sup>a,h</sup>,  
B. Rantner <sup>c</sup>, F.J.V. Schlösser <sup>h</sup>, F. Setacci <sup>i</sup>, J.-B. Ricco <sup>j</sup>

<sup>a</sup> Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, The Netherlands

### Management of Abdominal Aortic Aneurysms

S17

angiography will have to be obtained after the placement of a stent graft, to investigate the stent graft position, the patency of sidebranches and the presence of endoleaks.

Iodinated contrast agents are the medium of choice for angiography, but they carry the risk of nephrotoxicity or anaphylaxis.<sup>226</sup> Low-osmolality iodinated contrast agents are generally preferred since they reduce the incidence of such adverse events, when compared to high-osmolality agents. Carbon dioxide arteriography is a non-nephrotoxic alternative, but the obtained images are frequently inadequate.<sup>227</sup> Gadolinium is another non-nephrotoxic contrast medium, and is considered to be an alternative for iodinated contrast agents in patients with renal insufficiency.<sup>226</sup> \*

An alternative for periprocedural angiography is IVUS, allowing for perioperative real-time diameter and length measurements. Perioperatively, IVUS can be a useful tool in patients without, or with an indecisive, pre-operative CTA or MRA. IVUS can help in reducing the amount of perioperative contrast used. However, as discussed earlier, this technique is not widely available, difficult to perform, and adds time to the procedure.

Quite recently, a newer imaging technique, the on-table angiographic CT modality has been introduced. This imaging technique acquires CT-like images and might help in the detection of complications which are possibly missed by unipolar angiography. Currently, the field of view of these techniques is still limited and the acquired images have a lower resolution, compared to CTA. Nevertheless, the on-table angiographic CT is still evolving and is a promising technique for the near future.<sup>228,229</sup>

Body temperature should be kept at a physiological level (>36 °C) during AAA repair to avoid perioperative complications. Level 3b, Recommendation B.

*Intraoperative fluid resuscitation and blood conservation*  
Loss of fluid during aortic surgery is on one hand due to blood loss, and on the other hand extracellular loss, due to the development of tissue edema, typically 1 L per hour during surgery and continuing into the immediate post-operative period. Especially before 'declamping' an adequate volume regimen is important to avoid the declamping shock with the blood release into a vasodilated ischaemic periphery. Although there are 38 randomised trials following the question of the best fluid management during aortic surgery, there is not enough evidence on the benefits of any particular individual or combination fluid therapy. Crystalloid solutions and colloids are commonly used with few differences in important outcomes, such as the need for allogenic blood transfusion, complications of organ failure, and length of post-operative hospital stay.<sup>235</sup>

Intraoperative blood salvage during aortic aneurysm repair either with red-blood-cell processors or haemofiltration devices is widely used. Although the centrifugation product of the cell processors is pure and efficient, platelets and clotting factors are lost. A review of the available literature shows that cell salvage techniques are not able to reduce the need of transfusion and do not help to reduce costs<sup>236</sup> in AAA repair. The use of cell salvage and ultrafiltration devices might nevertheless be recommended if large blood loss is likely, and if the risk of transfusion-related complications or disease transmission from banked blood is considered high. Transfusions of red blood cells should be considered if blood loss is ongoing and if the haematocrit is lower than 30%.<sup>237</sup>

Herwaarden JA. Validation of a new standardized method to measure proximal aneurysm neck angulation. *J Vasc Surg* 2010;51(4):821–8.

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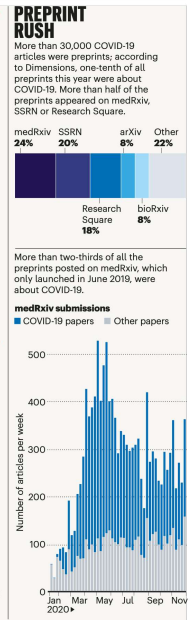
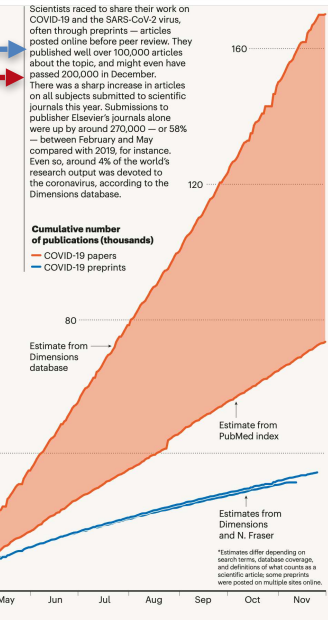
231 Stewart AH, Evers PS, Earnshaw JJ. Prevention of infection in peripheral arterial reconstruction: a systematic review and meta-analysis. *J Vasc Surg* 2007;46:148–55.

Scientists raced to share their work on COVID-19 and the SARS-CoV-2 virus, often through preprints — articles posted online before peer review. They published well over 100,000 articles about the topic, and might even have passed 200,000 in December. There was a sharp increase in articles on all subjects submitted to scientific journals this year. Submissions to publisher Elsevier's journals alone were up by around 270,000 — or 58% — between February and May compared with 2019, for instance. Even so, around 4% of the world's research output was devoted to the coronavirus, according to the Dimensions database.

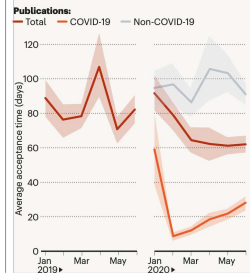
# COVID IN PAPERS: A TORRENT OF SCIENCE

An unprecedented flood of research on the coronavirus swept websites and journals this year.

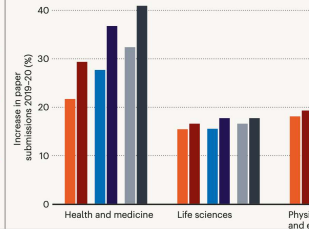
By Holly Else



**SPEEDY REVIEW**  
 Journals rushed to get COVID-19 articles through peer review. A study of 11 medical journals in the first half of the year found that they had published coronavirus papers much faster than normal, but at the expense of publishing other research more slowly.



**UNEQUAL BURDEN**  
 Growth in submissions from female authors trailed behind growth from male authors across all subject areas, according to an analysis of hundreds of thousands of papers sent to Elsevier journals between February and May. This is probably because women shouldered the burden of childcare and home-schooling during lockdowns, says Flaminio Squazzoni, a social scientist at the University of Milan, Italy, who co-authored the preprint analysis. "We need to make sure these things are taken into account when promoting and hiring in the years ahead," he says.



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Home > News > COVID-19 research update: How many pandemic papers have been published?

Alguns links sobre retratação ou retiradas de artigos sobre COVID-19 (19/07/2022)

<https://retractionwatch.com/retracted-coronavirus-covid-19-papers/>

Mais de 250 artigos  
COVID-19 Retratos  
25/07/2022



[https://www.science.org/content/article/mysterious-company-s-coronavirus-papers-top-medical-journals-may-be-unraveling?](https://www.science.org/content/article/mysterious-company-s-coronavirus-papers-top-medical-journals-may-be-unraveling?adobe_mc=MCMID%3D62452948724624662362245129327316184070%7CMCORGID%3D242B6472541199F70A4C98A6%2540AdobeOrg%7CTS%3D1658403973&_ga=2.162377983.2138212402.1658357768-1066406710.1655229479)

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<https://www.science.org/content/article/two-elite-medical-journals-retract-coronavirus-papers-over-data-integrity-questions>



## Review

## Obesity and mortality of COVID-19. Meta-analysis

Abdulzahra Hussain<sup>a,\*</sup>, Kamal Mahawar<sup>b</sup>, Zefeng Xia<sup>c</sup>, Wah Yang<sup>d</sup>, Shamsi EL-Hasani<sup>e</sup><sup>a</sup> Doncaster and Bassetlaw Teaching Hospitals, Doncaster, UK, Honorary Lecturer at Sheffield University, Sheffield, UK<sup>b</sup> Bariatric Unit, Department of General Surgery, Sunderland Royal Hospital, Sunderland, UK<sup>c</sup> Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Avenue, Wuhan, Hubei Province, China<sup>d</sup> The First Affiliated Hospital of Jinan University, 613 Huangpu Avenue West, Guangzhou, Guangdong Province, China<sup>e</sup> Bariatric Unit, Princess Royal University Hospital, King's College Hospitals NHS Foundation Trust, London, UK

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## ABSTRACT

**Background:** Obesity is a global disease with about 2.8 million people dying each year as a result of being overweight or obese according to the World Health Organization figures. This paper aims to explore the links between obesity and mortality in COVID-19.

**Methods:** Electronic search was performed for the papers showing obesity as a risk factor for mortality following COVID-19 infection. Three authors independently selected the papers and agreed for final inclusion. The outcomes were the age, gender, body mass index, severe comorbidities, respiratory support and the critical illness related mortality in COVID-19. 572 publications were identified and 42 studies were selected including one unpublished study. Only 14 studies were selected for quantitative analysis.

**Results:** All the primary endpoints but age were significantly associated with COVID-19 mortality. The age >70, [odds ratio (OR): 1.84, CI: 95%, P-value: <0.00001], gender [OR: 0.89; CI: 95%, P-value: 0.32], BMI > 25 kg/m<sup>2</sup> [OR: 3.68, CI: 95%, P-value: <0.003], severe comorbidities [OR: 1.84, CI: 95%, P-value: <0.00001], advanced respiratory support [OR: 0.98, CI: 95%, P-value: <0.00001], and critical illness [OR: 2.03, CI: 95%, P-value: <0.001].

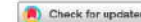
**Conclusions:** Patients with obesity are at high risk of mortality from COVID-19 infection.

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\* Corresponding author.  
E-mail address: [abdulzahra.hussain@nhs.net](mailto:abdulzahra.hussain@nhs.net) (A. Hussain).



OPEN

# GraphCovidNet: A graph neural network based model for detecting COVID-19 from CT scans and X-rays of chest

Pritam Saha<sup>1,7</sup>, Debadyuti Mukherjee<sup>2,7</sup>, Pawan Kumar Singh<sup>3</sup>, Ali Ahmadian<sup>4,5,6</sup>,  
Massimiliano Ferrara<sup>6</sup> & Ram Sarkar<sup>2</sup>

COVID-19, a viral infection originated from Wuhan, China has spread across the world and it has currently affected over 115 million people. Although vaccination process has already started, reaching sufficient availability will take time. Considering the impact of this widespread disease, many research attempts have been made by the computer scientists to screen the COVID-19 from Chest X-Rays (CXRs) or Computed Tomography (CT) scans. To this end, we have proposed GraphCovidNet, a Graph Isomorphic Network (GIN) based model which is used to detect COVID-19 from CT-scans and CXRs of the affected patients. Our proposed model only accepts input data in the form of graph as we follow a GIN based architecture. Initially, pre-processing is performed to convert an image data into an undirected graph to consider only the edges instead of the whole image. Our proposed GraphCovidNet model is evaluated on four standard datasets: SARS-COV-2 CT-Scan dataset, COVID-CT dataset, combination of covid-chestxray dataset, Chest X-Ray Images (Pneumonia) dataset and CMSC-678-ML-Project dataset. The model shows an impressive accuracy of 99% for all the datasets and its prediction capability becomes 100% accuracy for the binary classification problem of detecting COVID-19 scans. Source code of this work can be found at [GitHub-link](#).

Recently, Coronavirus (COVID-19) disease has created an unprecedented situation across the world. Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), a novel virus enveloped with large single stranded RNA genome<sup>1</sup> is the root cause for this disease<sup>2</sup>. Although this virus is originated from Wuhan in China, in December 2019, after America and several other countries of Europe have severely affected in early days of the year 2020. According to recent statistics, both America and India have more number of confirmed cases than other affected countries. World Health Organization (WHO)<sup>3</sup> announced COVID-19 as a global health emergency on January 30, 2020 considering the adverse effects of this situation.

To diagnose the SARS-CoV-2, it has been observed that both CXRs as well as CT-scans are found to be beneficial<sup>4,5</sup>. CXR images are more appreciated by the medical practitioners, since it can be obtained easily from the radiology departments. According to radiologists, CXR images help to understand the chest pathology clearly<sup>4</sup>. However, CT scans provide high sensitivity, for example, 97% of the positive CT scans are confirmed in a case study in Wuhan<sup>7</sup>. Due to the exponential growth in cases, it is required to develop an automated and fast paced system which can identify COVID-19 from chest CT-scans or CXR images. Figure 1 shows some samples of these CT-scan and CXR images.

SARS-CoV-2 generally affects the lungs and turbid formation of cough around lungs can be detected from CT-scans and CXRs. The usual symptoms of COVID-19 are related to fever, dry cough and tiredness. The severity of COVID-19 symptoms can range from very mild to critical. Some people may show only a few symptoms, and sometimes no symptoms can be observed at all. In some cases, symptoms start worsen mere after a week and

<sup>1</sup>Department of Electrical Engineering, Jadavpur University, Kolkata 700032, India. <sup>2</sup>Department of Computer Science and Engineering, Jadavpur University, Kolkata 700032, India. <sup>3</sup>Department of Information Technology, Jadavpur University, Kolkata 700105, India. <sup>4</sup>Institute of IR 4.0, The National University of Malaysia, Bangi 43600 UKM, Selangor, Malaysia. <sup>5</sup>School of Mathematical Sciences, College of Science and Technology, Wenzhou-Kean University, Wenzhou, China. <sup>6</sup>CRIOS-The Invernizzi Centre for Research in Innovation, Organization, Strategy and Entrepreneurship, Department of Management and Technology, Bocconi University, Via Sarfatti, 25, 20136 Milan (MI), Italy. <sup>7</sup>These authors contributed equally: Pritam Saha and Debadyuti Mukherjee. ✉email: ahmadian.hosseini@gmail.com

ORIGINAL ARTICLE

# Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19

Mandeep R. Mehra, M.D., Sapan S. Desai, M.D., Ph.D.,  
SreyRam Kuy, M.D., M.H.S., Timothy D. Henry, M.D., and Amit N. Patel, M.D.

## ABSTRACT

### BACKGROUND

Coronavirus disease 2019 (Covid-19) may disproportionately affect people with cardiovascular disease. Concern has been aroused regarding a potential harmful effect of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) in this clinical context.

### METHODS

Using an observational database from 169 hospitals in Asia, Europe, and North America, we evaluated the relationship of cardiovascular disease and drug therapy with in-hospital death among hospitalized patients with Covid-19 who were admitted between December 20, 2019, and March 15, 2020, and were recorded in the Surgical Outcomes Collaborative registry as having either died in the hospital or survived to discharge as of March 28, 2020.

### RESULTS

Of the 8910 patients with Covid-19 for whom discharge status was available at the time of the analysis, a total of 515 died in the hospital (5.8%) and 8395 survived to discharge. The factors we found to be independently associated with an increased risk of in-hospital death were an age greater than 65 years (mortality of

Explicação Retratação  
Deste Artigo  
Próximo Slide

From Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston (M.R.M.); Surgisphere, Chicago (S.S.D.); Baylor College of Medicine and Department of Veterans Affairs, Houston (S.K.); Christ Hospital, Cincinnati (T.D.H.); the Department of Biomedical Engineering, University of Utah, Salt Lake City (A.N.P.); and HCA Research Institute, Nashville (A.N.P.). Address reprint requests to Dr. Mehra at Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115, or at mmehra@bwh.harvard.edu.

This article was published on May 1, 2020, and updated on May 8, 2020, at NEJM.org.

N Engl J Med 2020;382:e102.  
DOI: 10.1056/NEJMoA2007621

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# Retraction: Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2007621.

**TO THE EDITOR:** Because all the authors were not granted access to the raw data and the raw data could not be made available to a third-party auditor, we are unable to validate the primary data sources underlying our article, “Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19.”<sup>1</sup> We therefore request that the article be retracted. We apologize to the editors and to readers of the *Journal* for the difficulties that this has caused.

Mandeep R. Mehra, M.D.

Brigham and Women’s Hospital Heart and Vascular Center  
Boston, MA  
mmehra@bwh.harvard.edu

Sapan S. Desai, M.D., Ph.D.

Surgisphere  
Chicago, IL

SreyRam Kuy, M.D., M.H.S.

Baylor College of Medicine  
Houston, TX

Timothy D. Henry, M.D.

Christ Hospital  
Cincinnati, OH

Amit N. Patel, M.D.

University of Utah  
Salt Lake City, UT

Retratação do  
Artigo  
Anterior

This letter was published on June 4, 2020, at NEJM.org.

1. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. *N Engl J Med* 2020;382:e102.

DOI: 10.1056/NEJMc2021225

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**CORRECTION**

Prevention of Early Ventilator-Associated Pneumonia (*N Engl J Med* 2020;382:1671-1674). In the third letter in the Correspondence regarding the article by François et al. (page 1672), the first author’s surname should have been Llitjos, rather than Llithos. The letter is correct at NEJM.org.

N ENGL J MED 382;26 NEJM.ORG JUNE 25, 2020

The New England Journal of Medicine

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RESULTS BY YEAR



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Cite [No authors listed]

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PMID: 35900448

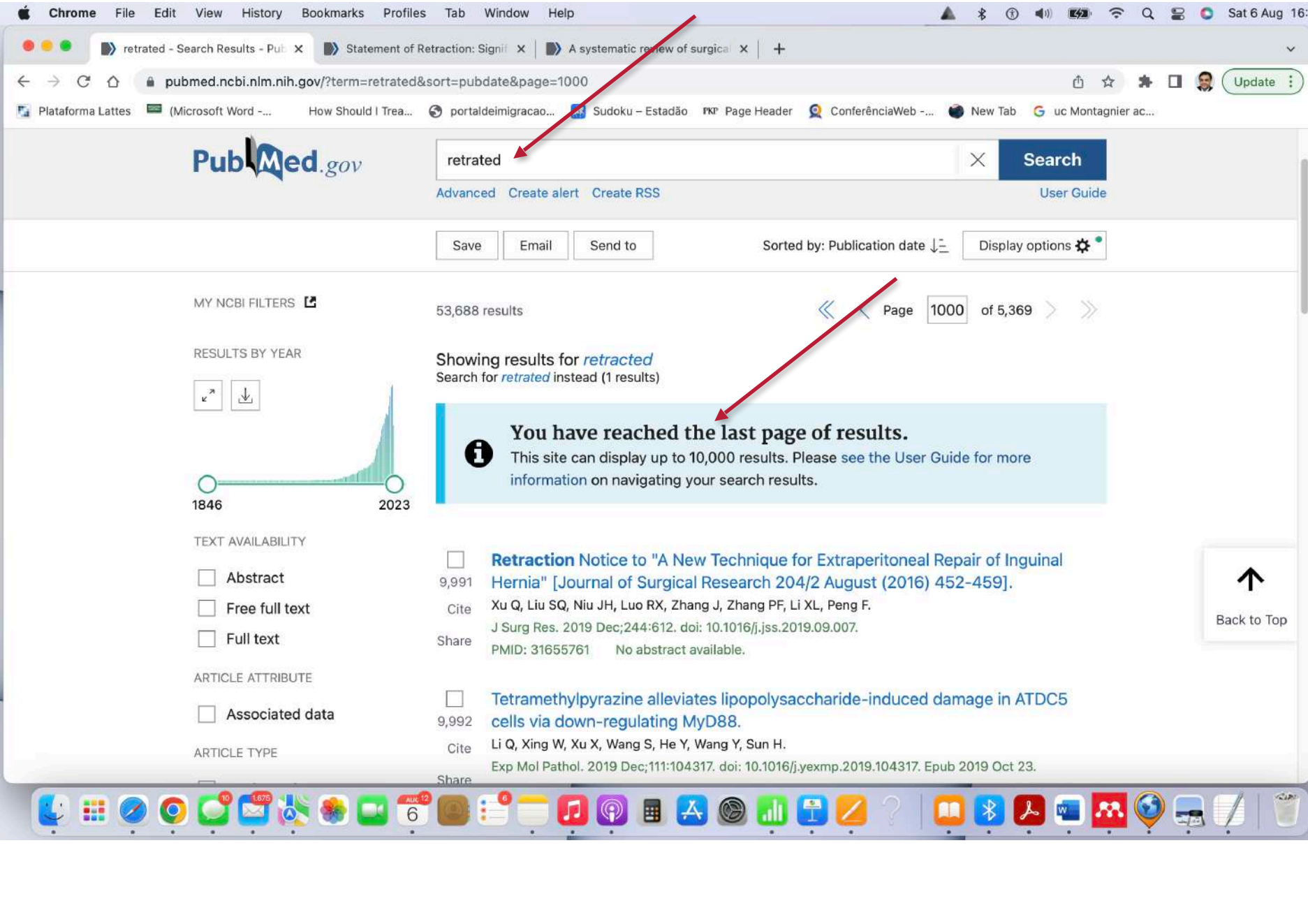
**Optic nerve injury-induced regeneration in the adult zebrafish is accompanied by spatiotemporal changes in mitochondrial dynamics.**

Cite Beckers A, Masin L, Van Dyck A, Bergmans S, Vanhunsel S, Zhang A, Verreet T, Poulain FE, Farrow K, Moons L.

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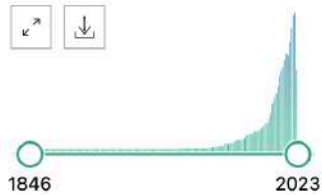
We previously showed that in adult zebrafish, subjected to an optic nerve crush, an antagonistic axon-dendrite interplay exists wherein the **retraction** of retinal ganglion cell dendrites is a



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Retraction Notice to "A New Technique for Extraperitoneal Repair of Inguinal Hernia" [Journal of Surgical Research 204/2 August (2016) 452-459]. Xu Q, Liu SQ, Niu JH, Luo RX, Zhang J, Zhang PF, Li XL, Peng F. J Surg Res. 2019 Dec;244:612. doi: 10.1016/j.jss.2019.09.007. PMID: 31655761 No abstract available.

ARTICLE ATTRIBUTE

- Associated data

Tetramethylpyrazine alleviates lipopolysaccharide-induced damage in ATDC5 cells via down-regulating MyD88. Li Q, Xing W, Xu X, Wang S, He Y, Wang Y, Sun H. Exp Mol Pathol. 2019 Dec;111:104317. doi: 10.1016/j.yexmp.2019.104317. Epub 2019 Oct 23.

ARTICLE TYPE





# One in 277 PubMed-indexed papers in 2026 shows fabricated references, says analysis

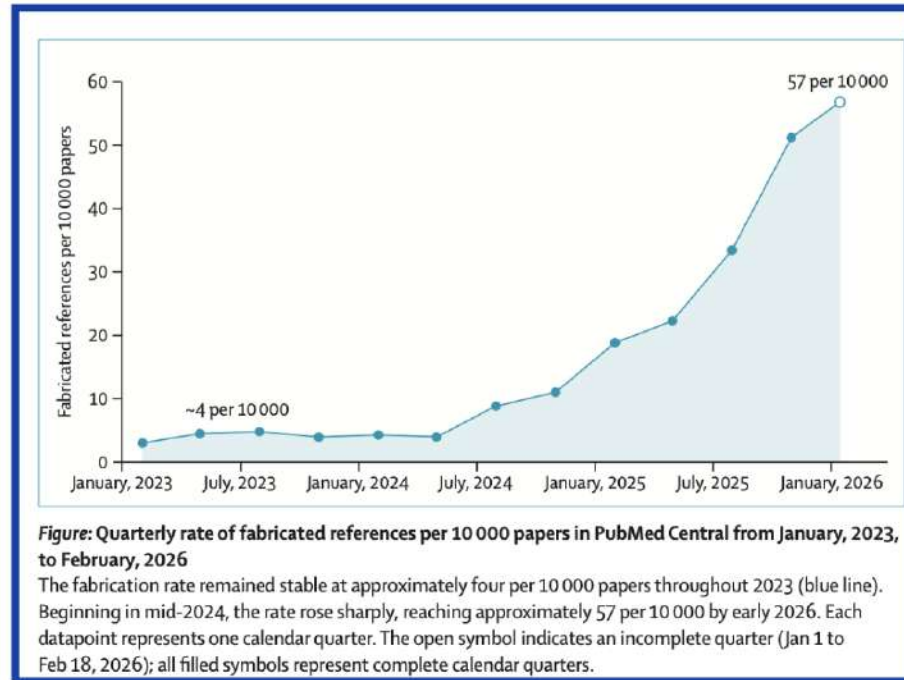


Figure from correspondence to *The Lancet* by Maxim Topaz and colleagues.

Fabricated citations in the biomedical literature have increased 12-fold in two years, according to an audit of nearly 2.5 million papers published as a letter to *The Lancet* today.

The analysis of articles indexed in PubMed found that about one in 277 papers published in the first seven weeks of 2026 referenced a paper that didn't exist. That was a jump from 2025's rate of one in 458 and 2023's one in 2,828. The researchers, led by Maxim Topaz of Columbia

# Mapping retracted articles and exploring regional differences in China, 2012–2023

Liping Shi<sup>1</sup>✉, Xue Zhang<sup>1</sup>✉, Xiaojun Ma<sup>1</sup>, Xian Sun<sup>1,2</sup>, Jiangping Li<sup>1,2\*</sup>, Shulan He<sup>1,2\*</sup>

**1** Department of Epidemiology and Health Statistics, School of Public Health, Ningxia Medical University, Yinchuan, Ningxia, China, **2** Key Laboratory of Environmental Factors and Chronic Disease Control, Ningxia Medical University, Yinchuan, Ningxia, China

✉ These authors contributed equally to this work.

\* [ljip@nxmu.edu.cn](mailto:ljip@nxmu.edu.cn) (JL); [heshulan0954@163.com](mailto:heshulan0954@163.com) (SH)



## OPEN ACCESS

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**Peer Review History:** PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0314622>

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**Data Availability Statement:** The original dataset can be downloaded from the Figshare public repository (<https://doi.org/10.6084/m9.figshare.27044899>).

## Abstract

### Background

China is one of the top countries with the most significant number or proportion of retracted publications, which has garnered significant attention.

### Methods

Using the Retraction Watch Database, we collected retracted articles written by Chinese authors from 31 provinces in mainland China, spanning the period between January 1, 2012, and December 31, 2023. We used Geographical Information Science to analyze spatial distribution characteristics of retracted articles by Chinese authors and identify high-risk clusters of retracted areas.

### Results

A total of 14,445 retracted articles authored by researchers from 31 provinces in China between 2012 and 2023 were analyzed. The Spatial trend surface analysis and Gravity center movement indicated a gradual increase in the number of retracted articles from the west to the east. The spatial autocorrelation analysis showed that revealed significant spatial clustering in the distribution of retracted articles across the 31 provinces. The results of the spatial-temporal clustering analysis showed that the hotspots were primarily concentrated in Shandong, Jiangsu, Shanghai, Henan, and Anhui.

### Conclusion

There is a discernible spatial clustering among these retractions, with a gradual increase in the number of retracted articles from west to east. Shandong, Jiangsu, Shanghai, Henan, and Anhui are the hotspots for retractions.

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# *Stanford President Will Resign After Report Found Flaws in His Research*

Marc Tessier-Lavigne was cleared of accusations of scientific fraud and misconduct. But the review said his work had “multiple problems” and “fell below customary standards of scientific rigor.”

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Marc Tessier-Lavigne announced his resignation as president of Stanford University on July 19, 2023, effective August 31, 2023.



Marc Tessier-Lavigne, a noted scientist, announced he would resign as president of Stanford University. Carolyn Fong for The

# The forces behind Harvard President Claudine Gay's resignation

*Gay will continue to work as a professor at the university.*

By [Kiara Alfonseca](#)

January 5, 2024, 6:01 AM ET • 12 min read



Harvard president resigns over plagiarism allegations  
Claudine Gay announced her resignation on Tuesday amid accusations of plagiarism and controversy over her testimony before Congress last month.  
Steven Senne/AP

# Ex-Harvard Medical School Morgue Chief to Plead Guilty in Sale of Body Parts

Cedric Lodge stole organs from cadavers that had been donated for medical research, prosecutors said. The university fired him in 2023.

## Harvard morgue manager who sold body parts like 'baubles' gets 8-year prison term

DEC 17, 2025  
By Associated Press

"bugigangas"



# Former HMS Morgue Manager Sentenced to 8 Years in Prison for Selling Human Remains



Former Harvard Medical School morgue manager Cedric Lodge was sentenced to eight years in prison for stealing and selling human remains donated for medical research. | By [Jonathan G. Yuan](#)

By [Juliana L. Yao](#), Crimson Staff Writer

December 18, 2025

**Former Harvard Medical School morgue manager Cedric Lodge was sentenced to eight years in prison for the interstate sale and transport of human body**

In mid-2023, a major scandal was uncovered involving the **theft and sale of human body**

justice.gov/usao-mdpa/pr/former-harvard-morgue-manager-pleads-guilty-trafficking-stolen-human-remains

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Justice.gov > U.S. Attorneys > Middle District of Pennsylvania > Press Releases > Former Harvard Morgue Manager Pleads Guilty To Trafficking Stolen Human Remains

PRESS RELEASE

# Former Harvard Morgue Manager Pleads Guilty To Trafficking Stolen Human Remains

Thursday, May 22, 2025

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**For Immediate Release**  
U.S. Attorney's Office, Middle District of Pennsylvania

# Errors Today and Errors Tomorrow

Donald M. Berwick, M.D.

If the Institute of Medicine is right, then at the very least, 100 patients will die in hospitals in the United States today because of injuries from their care, not from their diseases. How many will die tomorrow?

Tom Nolan, one of the leading quality-improvement scholars of our time, identifies three essential preconditions for improvement: will, ideas, and execution.<sup>1</sup> Improvement requires will, because durable improvement is not an accident; it takes effort. Left alone, systems tend to deteriorate. Roads decay until someone decides to repair them. Patients will suffer injuries from care until someone decides otherwise.

that may take 90,000 lives per year<sup>3</sup>; the report by Gandhi and her colleagues showing that adverse drug events are more common, though less severe, in outpatient settings than in inpatient settings<sup>4</sup>; and the disturbing findings by Blendon and his colleagues on the relative blindness of physicians to the frequency and severity of medical errors, even though they often notice errors in their own care or that of family members.<sup>5</sup> Ideas for change also abound in the series, both in terms of technical changes (such as minimizing the occurrence of retained instruments and sponges after surgery<sup>6</sup> and exploiting the power of innovations in information technology to reduce the rate of patient injuries<sup>7</sup>)

N ENGL J MED 348:25 WWW.NEJM.ORG JUNE 19, 2003

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### Study Suggests Medical Errors Now Third Leading Cause of Death in the U.S.

Physicians advocate for changes in how deaths are reported to better reflect reality

Release Date: May 3, 2016

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-  10 percent of all U.S. deaths are now due to medical error. - [Click to Tweet](#)
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#### FOR THE MEDIA

##### Contacts:

**Vanessa McMains**

410-502-9410

[vmcmain1@jhmi.edu](mailto:vmcmain1@jhmi.edu)

**Lauren Nelson**

410-955-8725

[laurennelson@jhmi.edu](mailto:laurennelson@jhmi.edu)

# A New, Evidence-based Estimate of Patient Harms Associated with Hospital Care

*John T. James, PhD*

Dr. **John T. James** is the Chief Toxicologist for the National Aeronautics & Space Administration NASA. He leads the Space Toxicology Office located at Lyndon B. Houston, Tx.

**Objectives:** Based on 1984 data developed from reviews of medical records of patients treated in New York hospitals, the Institute of Medicine estimated that up to 98,000 Americans die each year from medical errors. The basis of this estimate is nearly 3 decades old; herein, an updated estimate is developed from modern studies published from 2008 to 2011.

**Methods:** A literature review identified 4 limited studies that used primarily the Global Trigger Tool to flag specific evidence in medical records, such as medication stop orders or abnormal laboratory results, which point to an adverse event that may have harmed a patient. Ultimately, a physician must concur on the findings of an adverse event and then classify the severity of patient harm.

**Results:** Using a weighted average of the 4 studies, a lower limit of 210,000 deaths per year was associated with preventable harm in hospitals. Given limitations in the search capability of the Global Trigger Tool and the incompleteness of medical records on which the Tool depends, the true number of premature deaths associated with preventable harm to patients was estimated at more than 400,000 per year. Serious harm seems to be 10- to 20-fold more common than lethal harm.

**Conclusions:** The epidemic of patient harm in hospitals must be taken more seriously if it is to be curtailed. Fully engaging patients and their advocates during hospital care, systematically seeking the patients' voice in identifying harms, transparent accountability for harm, and intentional correction of root causes of harm will be necessary to accomplish this goal.

**Key Words:** patient harm, preventable adverse events, transparency, patient-centered care, Global Trigger Tool, medical errors

(*J Patient Saf* 2013;9: 122–128)

the national level. The amount of new knowledge generated each year by clinical research that applies directly to patient care can easily overwhelm the individual physician trying to optimize the care of his patients.<sup>1</sup> Furthermore, the lack of a well-integrated and comprehensive continuing education system in the health professions is a major contributing factor to knowledge and performance deficiencies at the individual and system level.<sup>2</sup> Guidelines for physicians to optimize patient care are quickly out of date and can be biased by those who write the guidelines.<sup>3–5</sup> At the system level, hospitals struggle with staffing issues, making suitable technology available for patient care, and executing effective handoffs between shifts and also between inpatient and outpatient care.<sup>6</sup> Increased production demands in cost-driven institutions may increase the risk of preventable adverse events (PAEs). The United States trails behind other developed nations in implementing electronic medical records for its citizens.<sup>7</sup> Hence, the information a physician needs to optimize care of a patient is often unavailable.

At the national level, our country is distinguished for its patchwork of medical care subsystems that can require patients to bounce around in a complex maze of providers as they seek effective and affordable care. Because of increased production demands, providers may be expected to give care in suboptimal working conditions, with decreased staff, and a shortage of physicians, which leads to fatigue and burnout. It should be no surprise that PAEs that harm patients are frighteningly common in this highly technical, rapidly changing, and poorly integrated industry. The picture is further complicated by a lack of transparency and limited accountability for errors that harm patients.<sup>8,9</sup>

There are at least 3 time-based categories of PAEs recognized in patients that are or have been hospitalized. The broadest

# Estimating deaths due to medical error: the ongoing controversy and why it matters

Kaveh G Shojania,<sup>1</sup> Mary Dixon-Woods<sup>2</sup>

<sup>1</sup>Department of Medicine, Centre for Quality Improvement and Patient Safety, University of Toronto, Toronto, Ontario, Canada

<sup>2</sup>Cambridge Centre for Health Services Research, University of Cambridge, Institute of Public Health, Cambridge, UK

## Correspondence to

Dr Kaveh G Shojania, Sunnybrook Health Sciences Centre, Room H468, 2075 Bayview Avenue, Toronto, Ontario, Canada M4N 3M5; kaveh.shojania@sunnybrook.ca

Accepted 26 September 2016  
Published Online First  
12 October 2016

One important reason for the widespread attention given to the 1999 US Institute of Medicine (IOM) report *To Err Is Human*<sup>1</sup> lie in its estimate that medical error was to blame for 44 000–98 000 deaths each year in the US hospitals. This striking claim established patient safety as a public concern, strengthened the case for improving the science underlying safety and motivated providers, policy-makers, payers and regulators to take safety seriously. Some did express disquiet about the validity of the figures cited,<sup>2</sup> including one of the principal investigators of the two studies that provided the data for these estimates.<sup>3</sup>

A decade and a half later, Makary and Daniel<sup>4</sup> attribute an even higher toll to medical error: 251 454 deaths in US hospitals per year, making, they say, medical error the third-leading cause of death in the USA. Unsurprisingly, this claim generated widespread coverage in multiple media channels. It also ignited scientific controversy about the basis of the esti-

Inspector General (OIG)<sup>6</sup> and two peer-reviewed articles (table 1).<sup>7 8</sup> The paper did not apply any established methodology for quantitative synthesis nor did it include a discussion either of the intrinsic limitations of the studies used or of the errors associated with the extrapolation process. To bolster their claims, Makary and Daniel did highlight the agreement between their estimates and that of a similar analysis published a few years ago by James.<sup>9</sup> The apparent consensus is not, however, surprising, since they use mostly the same studies (listed in table 1, together with a more recent analysis commissioned by the Leapfrog group<sup>10</sup>).

## ISSUES WITH THE STUDIES ON WHICH ESTIMATES OF DEATHS DUE TO MEDICAL ERROR ARE BASED

Some of the widely quoted estimates of deaths due to medical error, including the IOM estimates,<sup>1</sup> Makary and Daniel<sup>4</sup>

# Your Health Care May Kill You: Medical Errors

James G Anderson <sup>1</sup>, Kathleen Abrahamson <sup>1</sup>

Affiliations + expand

PMID: 28186008

## Abstract

Recent studies of medical errors have estimated errors may account for as many as 251,000 deaths annually in the United States (U.S.), making medical errors the third leading cause of death. Error rates are significantly higher in the U.S. than in other developed countries such as Canada, Australia, New Zealand, Germany and the United Kingdom (U.K). At the same time less than 10 percent of medical errors are reported. This study describes the results of an investigation of the effectiveness of the implementation of the MEDMARX Medication Error Reporting system in 25 hospitals in Pennsylvania. Data were collected on 17,000 errors reported by participating hospitals over a 12-month period. Latent growth curve analysis revealed that reporting of errors by health care providers increased significantly over the four quarters. At the same time, the proportion of corrective actions taken by the hospitals remained relatively constant over the 12 months. A simulation model was constructed to examine the effect of potential organizational changes resulting from error reporting. Four interventions were simulated. The results suggest that improving patient safety requires more than voluntary reporting. Organizational changes need to be implemented and institutionalized as well.

What Are Surgical Errors, And When Could I Claim?

How Much Compensation Could I Receive Following A Surgical Mistake?

Special Damages In Surgical Error Claims

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compensation brackets that correspond with different mental and physical injuries.

Below, you can find some examples of these guidelines. Please be aware that the first entry has not been taken from the JCG.

Injury	Severity	Guideline Compensation Amount
Multiple Severe Injuries & Special Damages	Very Severe	Up to £1,000,000+
Brain or Head Injury	Very Severe (a)	£344,150 to £493,000
	Moderately Severe (b)	£267,340 to £344,150
	Less Severe (d)	£18,700 to £52,550
Kidney	Permanent Damage To Both Kidneys	£206,730 to £256,780
	Loss of One Kidney	£37,550 to £54,760
Chest	Severe	£122,850 to £183,190
Bladder	Serious Impairment	£78,080 to £97,540
Bowels	Faecal Urgency and Passive Incontinence	In the region of £97,530



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# Wrong site surgery: the most common NHS "Never Event"



Arti Shah

28/01/2026



In medicine, the term "Never Event" refers to a patient safety incident so serious and preventable that it should never happen. These are shocking errors that go far beyond rare mishaps.

**NHS England** has just released provisional data for Never Events between April and

NHS

This article is more than 2 months old

## NHS medical negligence persisting in England 'despite 24 years of warnings'

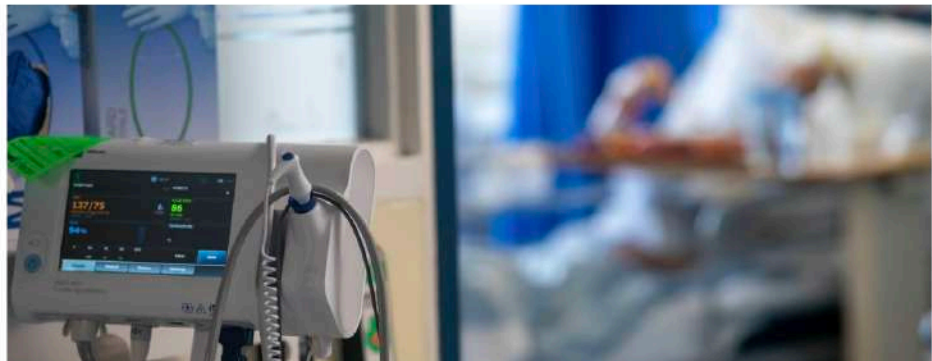
MPs on influential committee excoriate health department and NHS England for errors costing £3.6bn a year

**Denis Campbell** Health policy editor

Fri 30 Jan 2026 00.01 GMT

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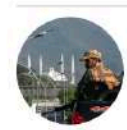
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Pakistan acts as backchannel to help US and Iran inch towards deal, experts say



## Cases of wrong-site surgery in England have risen from 69 in 2020 to 101 last year, with 7% involving serious harm to patients.

Between 2020 and last year, 661 cases of surgery performed on the wrong patient or body part were reported in English hospitals, according to new data from [Medical Negligence Assist](#).

The phenomenon, known as wrong-site surgery, is a medical error where an invasive procedure is performed on the wrong patient, the wrong body part or the wrong site on the body – such as operating on the left limb instead of the right. Many of these incidents are classified as “never events” by the NHS, meaning they are considered entirely preventable.

Obtained via Freedom of Information requests, 117 NHS Trusts were contacted. Of the 72 that responded, 661 cases were reported in total over the five-year period. While 69 incidents were recorded in 2020, that had jumped to 101 last year, marking a 46% increase in cases during that time.



**Around 1 in every 10 patients is harmed in health care and more than 3 million deaths occur annually due to unsafe care. In low-to-middle income countries, as many as 4 in 100 people die from unsafe care (1).**

**Above 50% of harm (1 in every 20 patients) is preventable; half of this harm is attributed to medications (2,3).**

**Some estimates suggest that as many as 4 in 10 patients are harmed in primary and ambulatory settings, while up to 80% (23.6–85%) of this harm can be avoided (4).**

# Why Most Published Research Findings Are False

John P. A. Ioannidis

## Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

factors that influence this problem and some corollaries thereof.

## Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a  $p$ -value less than 0.05. Research is not most appropriately represented and summarized by  $p$ -values, but, unfortunately, there is a widespread notion that medical research articles

**It can be proven that most claimed research findings are false.**

should be interpreted based only on  $p$ -values. Research findings are defined here as any relationship reaching formal statistical significance, e.g., effective interventions, informative predictors, risk factors, or associations. “Negative” research is also very useful. “Negative” is actually a misnomer, and the misinterpretation is widespread.

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is  $R/(R + 1)$ . The probability of a study finding a true relationship reflects the power  $1 - \beta$  (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate,  $\alpha$ . Assuming that  $c$  relationships are being probed in the field, the expected values of the  $2 \times 2$  table are given in Table 1. After a research finding has been claimed based on achieving formal statistical significance, the post-study probability that it is true is the positive predictive value, PPV. The PPV is also the complementary probability of what Wacholder et al. have called the false positive report probability [10]. According to the  $2 \times 2$  table, one gets  $PPV = (1 - \beta)R/(R - \beta R + \alpha)$ . A research finding is thus

John Ioannidis's 2005 paper, "[Why Most Published Research Findings Are False](#)," argues that most claimed research findings—especially in medicine and psychology—are likely false positive results. This occurs because many studies are small, have low power, have high bias, and engage in multiple hypothesis testing and data manipulation to reach a statistical significance of  $p < 0,05$ . PubMed Central (PMC) (.gov)



*Fisher, R. A. (1925). Statistical methods for research workers. Edinburgh: Oliver and Boyd.*

# John Ioannidis's 2005 paper

## Key Reasons Research Findings Are Often False:

- **Small Sample Sizes & Low Power:** Small studies have lower power to detect real effects, making it more likely that significant findings are just noise.
- **Small Effect Sizes:** If a field has a low ratio of true relationships to non-true relationships, many "discoveries" are false positives.
- **Flexibility in Design and Analysis:** Known as "p-hacking," Researchers may alter definitions, outcomes, or analysis methods to make findings look more significant than they are.
- **Bias and Financial Interest:** Greater financial, political, or professional interest in a topic leads to higher bias, which produces false findings.
- **"Hot" Fields:** As more teams work on the same topic, the race to publish means findings are less likely to be true.
- [PubMed Central \(PMC\) \(.gov\)](#)

John P. A. Ioannidis is in the Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece, and Institute for Clinical Research and Health Policy Studies, Department of Medicine, Tufts-New England Medical Center, Tufts University School of Medicine, Boston, Massachusetts, United States of America. E-mail: jioannid@cc.uoi.gr



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## John P.A. Ioannidis

PROFESSOR OF MEDICINE (STANFORD PREVENTION RESEARCH CENTER), OF EPIDEMIOLOGY AND POPULATION HEALTH AND, BY COURTESY, OF BIOMEDICAL DATA SCIENCE



Original Investigation | Medical Journals and Publishing

# Retracted Randomized Clinical Trials From Superretractors and Top-Cited Scientists With Multiple Retractions

Published Online: April 15, 2026  
2026;9;(4):e267424.

Chunwei Lyu, MSc; Mino Matbouriahi, MSc; Florian Naudet, MD, PhD; John P. A. Ioannidis, MD, DSc; Ioana Alina Cristea, PhD

doi:10.1001/jamanetworkopen.2026.7424



## Abstract

**IMPORTANCE** Multiple retractions from the same author often uncover issues affecting their entire work, such as having systematically altered or fabricated data.

**OBJECTIVES** To evaluate the contribution of authors with the most retractions (ie, superretractors) and top-cited scientists with multiple retractions to the retracted randomized clinical trial (RCT) literature.

**DESIGN, SETTING, AND PARTICIPANTS** This retrospective cohort study linked an openly available cohort of retracted RCTs (VITALITY) to 3 lists of scientists: (1) superretractors, totaling most retractions in the Retraction Watch Leaderboard; (2) scientists in the top 100 000 or 2% of their subfield in terms of citations (ie, top-cited scientists) over their entire careers who accumulated 10 or more retractions not due to editor or publisher errors; and (3) top-cited scientists in the most recent year (ie, 2024) who accumulated 10 or more retractions not due to editor or publisher errors. The VITALITY cohort was updated up to November 2024. The 3 author lists were updated in August 2025.

**MAIN OUTCOMES AND MEASURES** The main outcomes were authorship and the characteristics of retracted RCTs (publication and retraction year, time between publication and retraction, number of citations).

**RESULTS** A total of 30 superretractors, 163 career-long top-cited scientists with 10 or more retractions, and 174 recent-year top-cited scientists with 10 or more retractions were included; 1330 retracted RCTs were included. Overall, 6 superretractors (20%), representing anesthesiology as well as endocrinology and metabolism, coauthored 290 retracted RCTs (22%); 18 career-long top-cited scientists with at least 10 retractions, representing 10 fields, coauthored 327 trials (25%), 275 (84%) of which were also coauthored by a superretractor; 7 single-year top-cited scientists with at least 10 retractions coauthored 50 retracted RCTs (4%), all of which were also included in the list of articles authored by career-long top-cited scientists with at least 10 retractions. Articles with superretractor

## Key Points

**Question** How many retractions have authors with the most retractions (ie, superretractors) and top-cited authors with multiple retractions contributed to the retracted randomized clinical trial literature?

**Findings** In this cohort study of 367 authors and 1330 retracted randomized clinical trials, 6 superretractors, from anesthesiology as well as endocrinology and metabolism, coauthored one-fifth of all retracted trials, while 18 top-cited scientists with more than 10 retractions coauthored one-quarter of them. Articles coauthored by superretractors or by top-cited scientists with multiple retractions were published and retracted earlier, took longer to retract, and accumulated more citations.

**Meaning** This study found that retracted randomized clinical trials were disproportionately associated with a small number of influential authors, often coauthors, and concentrated across few subfields of medicine.



ioannidis J



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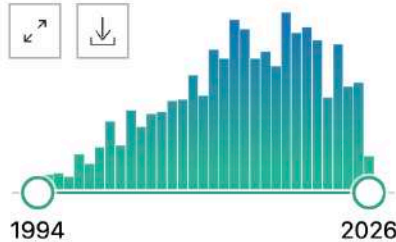


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RESULTS BY YEAR



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1,449 results

Page 1 of 145

1  Retracted Randomized Clinical Trials From Superretractors and Top-Cited Scientists With Multiple Retractions.

Cite Lyu C, Matbouriahi M, Naudet F, **Ioannidis JPA**, Cristea IA. JAMA Netw Open. 2026 Apr 1;9(4):e267424. doi: 10.1001/jama.2026.7424. PMID: 41984475 Free PMC article.



2  The Food and Drug Administration approval and clearance process for orthodontic devices.

Cite Seehra J, Pandis N, **Ioannidis J**. Am J Orthod Dentofacial Orthop. 2026 Apr;169(4):544-548. doi: 10.1016/j.ajodo.2026.01.008. PMID: 41887817 No abstract available.

3  An atlas of exposome-phenome associations in health and disease risk.

Cite Patel CJ, **Ioannidis JPA**, Manrai AK. Nat Med. 2026 Apr;32(4):1501-1510. doi: 10.1038/s41591-026-04266-0. Epub 2026 Mar 18. PMID: 41951210

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 1,446 **Ioannidis JP**, Skolnik PR, Chalmers TC, Lau J.  
 Cite AIDS. 1995 Jun;9(6):649-51. doi: 10.1097/00002030-199506000-00019.  
 PMID: 7662207 No abstract available.

[Aspergillus fumigatus infection of a biloma.](#)  
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 Cite Clin Infect Dis. 1995 May;20(5):1427-8. doi: 10.1093/clinids/20.5.1427.  
 PMID: 7620038 No abstract available.

[Insulin-dependent diabetes in AIDS.](#)  
 1,448 **Ioannidis JP**, Iacoviello VR, Samore MH.  
 Cite AIDS. 1994 Apr;8(4):556-7. doi: 10.1097/00002030-199404000-00022.  
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[Risk of gastrointestinal bleeding from dexamethasone in children with bacterial meningitis.](#)  
 1,449 **Ioannidis JP**, Samarel MD, Lau J, Drapkin MS.  
 Cite Lancet. 1994 Mar 26;343(8900):792. doi: 10.1016/s0140-6736(94)91867-8.  
 PMID: 7907747 No abstract available.


1,449 results

# John P.A. Ioannidis

**h-index**, 286, 189. **i10-index**, 1465, 1105. 0. 77000. 38500. 19250. 57750. 200520062007 ... **John P.A. Ioannidis**. Professor of Medicine/Health Research & Policy ...

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John P.A. Ioannidis is one of the most highly cited scientists globally, with an h-index of approximately **278–286** on [Google Scholar](#) as of early 2026. He is a professor at Stanford University, recognized for his work in meta-research, medicine, and epidemiology, with over 500,000 citations.  Google Scholar +3

## Key Citation Metrics (approximate):

- **Google Scholar:** ~286 h-index
- **Scopus:** ~205 h-index
- **Exaly:** ~177 h-index  Google Scholar +2



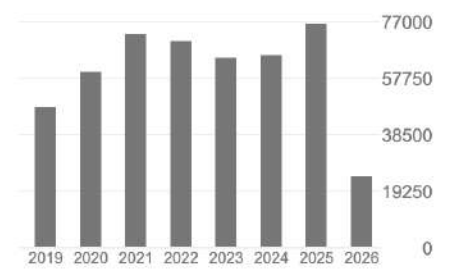
# John P.A. Ioannidis

Professor of Medicine/Health Research & Policy/Biomedical Data Science/Statistics, [Stanford Univ](#)  
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i10-index	1464	1106



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TITLE	CITED BY	YEAR
<a href="#">Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement</a> D Moher, A Liberati, J Tetzlaff, DG Altman, P Group PLoS med 6 (7), e1000097	142957	2009
<a href="#">The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies</a> E Von Elm, DG Altman, M Egger, SJ Pocock, PC Gøtzsche, ... The lancet 370 (9596), 1453-1457	74043	2007
<a href="#">The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration</a> A Liberati, DG Altman, J Tetzlaff, C Mulrow, PC Gøtzsche, JPA Ioannidis, ... Bmj 339	59778	2009
<a href="#">CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials</a> KF Schulz, DG Altman, D Moher BMC medicine 8 (1), 18	23852	2010
<a href="#">Why most published research findings are false</a> JPA Ioannidis PLoS medicine 2 (8), e124	15673	2005

[Strengthening the Reporting of explanation and elaboration](#)

**Total H Index Rankings**

- World Rank **40**
- United States Rank **18**
- Institution **2**

World Ranking: **40**

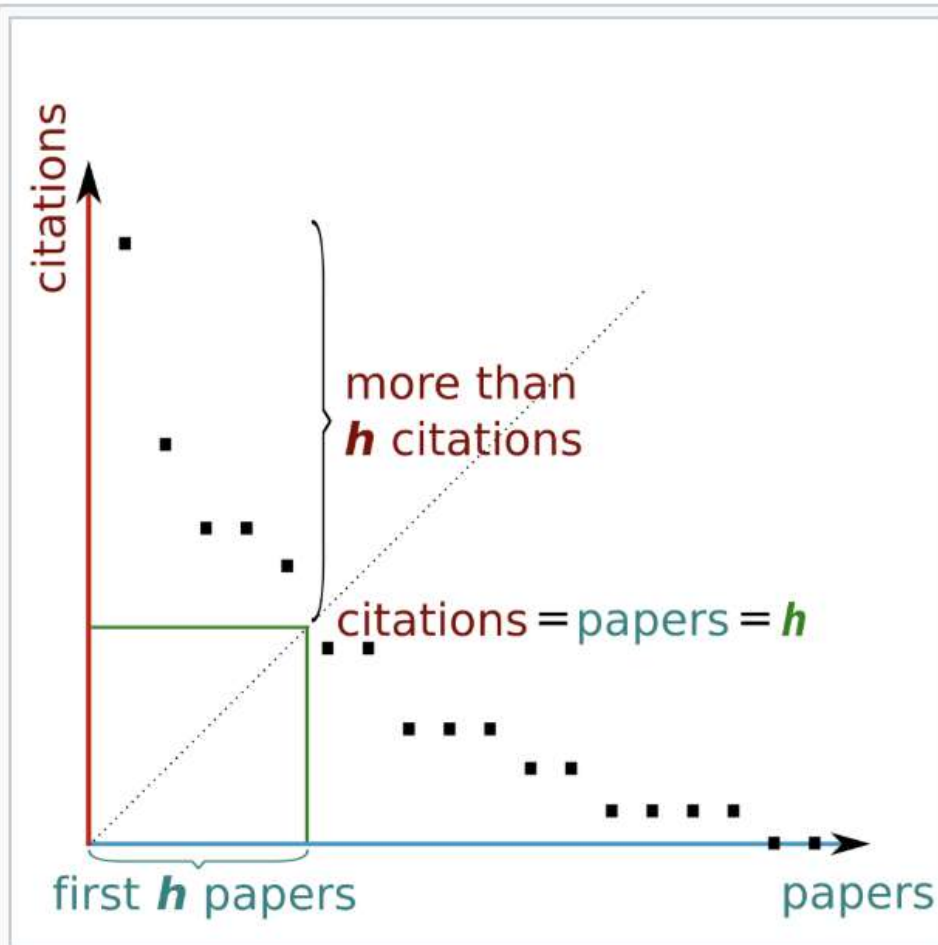


**John PA Ioannidis**  
[Stanford University, United States](#)  
[Medical and Health Sciences](#) / [Biostatistics](#)  
Meta-research | Clinical Epidemiology | Evidence-based Medicine  
| Research Methods | Meta-analysis



**H-Index Metrics**

- 286** Total H-Index
- 189** Last 5 Years H-Index
- 66.1%** H-Index Momentum Score



Hirsh Index, 2005  
Jorge E. Hirsh


$h$ -index from a plot of numbers of citations for an author's numbered papers (arranged in decreasing order)


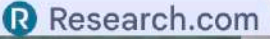


Exibindo resultados para **Top of *Hirsch* Index**

Em vez disso, pesquisar por **Top of Hirsh Index**

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The top of the Hirsch index (h-index) **identifies the most impactful researchers based on citation metrics**, with leading figures often reaching h-index values over 300. As of 2026, top-ranked scientists include **Francisco Matorras** ( $h = 382$ ), **Alberto Ruiz Jimeno** ( $h = 365$ ), and **HJ Kim** ( $h = 364$ ). 

- **Top Scientist Rankings:** According to the [AD Scientific Index](#), Francisco Matorras (Universidad de Cantabria, Spain) holds a leading global ranking with a total h-index of 382. 
- **Other Highly Cited Researchers:** Other top researchers often cited for high h-indexes include Frank B. Hu (Harvard University,  $h=309$ ), Michael Grätzel (EPFL,  $h=292$ ), and Bert Vogelstein (Johns Hopkins,  $h=290$ ). 



## Tweet



**Mayana Zatz**

@Mayanazatz

O absurdo de se pagar 11.000 dólares para publicar um artigo na revista Nature

# Protocolos de Pesquisa

1 - Seres Humanos

2- Animais

4- Vegetais

3- Indústria

4- Meio Ambiente

Sempre - medir o risco e o Benefício  
a curto e longo prazo



## [Sistema Nacional de Ética em Pesquisa - SINEP](#)

# Comissão Nacional de Ética e Pesquisa



A **Comissão Nacional de Ética em Pesquisa - CONEP** está diretamente ligada ao Conselho Nacional de Saúde - CNS. A composição multi e transdisciplinar reúne representantes de diferentes áreas do conhecimento para cumprir sua principal atribuição, que é a avaliação dos aspectos éticos das pesquisas que envolvem seres humanos no Brasil. Em cumprimento à sua missão, a Comissão elabora e atualiza as diretrizes e normas para a proteção dos participantes de pesquisa e coordena o Sistema CEP/CONEP.

O Sistema CEP/CONEP é formado pela CONEP (instância máxima de avaliação ética em protocolos de pesquisa envolvendo seres humanos) e pelos CEP (Comitês de Ética em Pesquisa), instâncias regionais dispostas em todo território brasileiro. O Sistema também envolve pesquisadores, assistentes de pesquisa, professores e universitários em iniciação científica, instituições de ensino, centros de pesquisa, fomentadores de pesquisa e

<https://www.gov.br/saude/pt-br/composicao/orgaos-colegiados/inaep>

<https://www.gov.br/conselho-nacional-de-saude/pt-br/camaras-tecnicas-e-comissoes/conep>

## Documentos regulatórios no Brasil

- **Nota Técnica 01/2026:** Orientações acerca da tramitação de protocolos de pesquisa com seres humanos, da definição de competências no âmbito do Sistema Nacional de Ética em Pesquisa com Seres Humanos, da análise ética de protocolos com o Ministério da Saúde como instituição proponente, da prorrogação excepcional do credenciamento dos Comitês de Ética em Pesquisa e dos procedimentos aplicáveis a biobancos, no contexto da implementação da Instância Nacional de Ética em Pesquisa.
- **Decreto 12.651/2025:** Regulamenta a Lei nº 14.874, de 28 de maio de 2024, que dispõe sobre a pesquisa com seres humanos e institui o Sistema Nacional de Ética em Pesquisa com Seres Humanos.
- **Lei 14.874/2024:** Dispõe sobre a pesquisa com seres humanos e institui o Sistema Nacional de Ética em Pesquisa com Seres Humanos
- **Resolução 580/2018:** Regulamenta o disposto no item XIII.4 da Resolução CNS nº 466, de 12 de dezembro de 2012, que estabelece que as especificidades éticas das pesquisas de interesse estratégico para o Sistema Único de Saúde (SUS) serão contempladas em Resolução específica, e dá outras providências.
- **Resolução 510/2016:** Esta Resolução dispõe sobre as normas aplicáveis a pesquisas em Ciências Humanas e Sociais cujos procedimentos metodológicos envolvam a utilização de dados diretamente obtidos com os participantes ou de informações identificáveis ou que possam acarretar riscos maiores do que os existentes na vida cotidiana, na forma definida nesta Resolução.
- **Norma Operacional CNS 01/2013:** Aprova as normas regulamentadoras de pesquisas envolvendo seres humanos
- **Resolução 466/2012:** Aprova as normas regulamentadoras de pesquisas envolvendo seres humanos



# Instância Nacional de Ética em Pesquisa

Toda pesquisa realizada com seres humanos deve passar por avaliação ética para assegurar respeito, proteção e cuidado aos participantes. Para fortalecer essa garantia, a [Lei nº 14.874, de 28 de maio de 2024](#), instituiu o **Sistema Nacional de Ética em Pesquisa com Seres Humanos (SINEP)**.

O SINEP é composto por duas instâncias:

- **Instância Nacional de Ética em Pesquisa (INAEP):** responsável por orientar e estabelecer diretrizes para o sistema.
- **Comitês de Ética em Pesquisa (CEP):** responsáveis pela análise ética dos projetos de pesquisa nas instituições.

## Instância Nacional de Ética em Pesquisa (INAEP)

A **Instância Nacional de Ética em Pesquisa (INAEP)** é um órgão colegiado vinculado ao Ministério da Saúde, instituída pela [Lei nº 14.874, de 28 de maio de 2024](#), conhecida como Lei de Ética em Pesquisa com Seres Humanos.

a [Comissão Nacional de Ética em Pesquisa](#) (Conep) foi substituída pelo novo [Sistema Nacional de Ética em Pesquisa](#) (Sinep) e pela nova [Instância Nacional de Ética em Pesquisa](#) (Inaep). A mudança decorre da [Lei nº 14.874/2024](#), que moderniza a pesquisa clínica, com regulamentação em 2025. [[1](#), [2](#), [3](#), [4](#)]



# COMITÊ DE ÉTICA EM PESQUISA

HOME SOBRE ▾ LINKS ÚTEIS MODELOS ORIENTAÇÕES DOCUMENTOS

No content in response.

O Comitê de Ética em Pesquisa não analisa projetos já iniciados (NORMA OPERACIONAL CNS No. 001/2013).

## Localização e Contato

R. Sena Madureira, 1500 - 2º andar • Vila Clementino - São Paulo - SP - CEP: 04021-001

 Horário de atendimento presencial e telefônico: Segundas a Sexta das 08:00 às 13:00hs.

E-mail: [cep@unifesp.br](mailto:cep@unifesp.br)

Telefone:(11) 3385-4343 ramal 8699/8557.

<https://site.unifesp.br/cep/>

Orientações

Passo a Passo

Uso de dados ou de projetos já encerrados

Participante/Coparticipante

Projetos patrocinados

Resposta de pendências

Submissão de emendas

Envio de relatório parcial e final

Eventos adversos

Troca de pesquisador principal

Cancelamento de projetos

Projetos sem humanos/animais

Biobanco e Biorrepositório

Indígenas

## Passo a Passo

## Plataforma Brasil

Para realizar a submissão da pesquisa na Plataforma Brasil, siga os passos abaixo:

**ETAPA 1** - Acesse a Plataforma Brasil: <http://plataformabrasil.saude.gov.br/login.jsf>

**O cadastro do projeto na Plataforma Brasil deve ser feito no login do(a) Professor(a) Orientador(a), o aluno deve ser incluído na Plataforma Brasil como equipe de pesquisa.**

- Caso você ainda não tenha um cadastro, clique em "Cadastre-se" (maiores informações sobre como se cadastrar na Plataforma, acessar a página 6 do Manual do Pesquisador da Plataforma Brasil ou assista ao vídeo "Cadastro de Usuário" publicado pela Conep).

- **Atenção:** durante o seu cadastro, na página 4, no campo: "Instituição" deverá ser selecionada a Unifesp. Realize a busca da instituição pelo CNPJ 60.453.032/0001-74.

- No campo "Perfil, selecione a opção "Pesquisador"

- Ao término do seu cadastro como pesquisador, você receberá por e-mail uma senha de acesso à Plataforma Brasil.



# Acreditação de CEPs

**A Resolução nº 506 de 2016**, publicada pelo Conselho Nacional de Saúde, versa sobre o processo de acreditação de Comitês de Ética em Pesquisa (CEP) que compõem o Sistema CEP/Conep. Tal processo visa estimular a descentralização do Sistema, mantendo-se a uniformidade dos critérios de análise ética estabelecidos pelo CNS.

A ***acreditação de CEPs***, uma ação inédita para o Sistema, promove maior eficiência na gestão da análise ética dos protocolos de pesquisa. Para isso, haverá um processo de avaliação de conformidades, com vistas à certificação concedida pela Comissão Nacional de Ética em Pesquisa (Conep) aos CEPs, que realizarão a análise ética dos protocolos envolvendo seres humanos. Destaca-se ainda que, além de estar prevista nas normas do Conselho Nacional de Saúde, a acreditação de CEPs também está definida na **Lei nº 14.874, de 28 de maio de 2024**.

## Lista de CEPs Acreditados

0082 – Centro Universitário FMABC. UF: SP. Município: Santo André.

5432 – Fundação Antônio Prudente - A.C. Camargo Cancer Center. UF: SP. Município: São Paulo.

5462 – Instituto Dante Pazzanese de Cardiologia (IDPC). UF: SP. Município: São Paulo.

0071 – Hospital Israelita Albert Einstein (HIAE). UF: SP. Município: São Paulo.

0068 – Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP). UF: SP. Município: São Paulo.

5415 – Faculdade de Medicina de São José do Rio Preto – FAMERP. UF: SP. Município: São José do Rio Preto.

8083 – Faculdade Ceres - FACERES. UF: SP. Município: São José do Rio Preto.

CEP 5411 - Faculdade de Medicina de Botucatu (FMB). UF: SP. Município: Botucatu.

## Sistema Nacional de Ética em Pesquisa \_SINEP

# Sistema Nacional de Ética em Pesquisa com Seres Humanos (SINEP).

### COMITÊS DE ÉTICA EM PESQUISA

#### CEP credenciado

Comitê autorizado pela INAEP a analisar pesquisas de **baixo risco**, aquelas em que quase não há chances de causar desconforto ou danos aos participantes; e **médio risco**, que envolvem procedimentos um pouco mais complexos, como o uso de novos exames, medicamentos já conhecidos em novas doses ou estudos que exigem acompanhamento mais próximo dos participantes.

#### CEP acreditado

Comitê reconhecido pela INAEP por sua excelência técnica e estrutura operacional, habilitado a avaliar pesquisas de **alto risco**, que são aquelas que testam novos medicamentos, vacinas ou procedimentos ainda não utilizados em pessoas, podendo causar efeitos desconhecidos. Por isso, precisam de uma avaliação ética mais detalhada e rigorosa. Também analisar pesquisas de risco médio e baixo.

<https://www.gov.br/saude/pt-br/composicao/orgaos-colegiados/inaep>



## Comitê de Ensino, Pesquisa e Extensão

O Comitê de Ensino, Pesquisa e Extensão foi criado no escopo do acordo celebrado entre a UNIFESP e a SPDM em 11 de fevereiro de 2020, relativo a Gestão e Missão do Hospital São Paulo (HSP), a fim de acompanhar as atividades de natureza acadêmica do HU, conforme a cláusula décima quinta. Está vinculado ao Conselho Estratégico do HSP/HU, criado no mesmo acordo, a quem auxilia nas atividades acadêmicas.

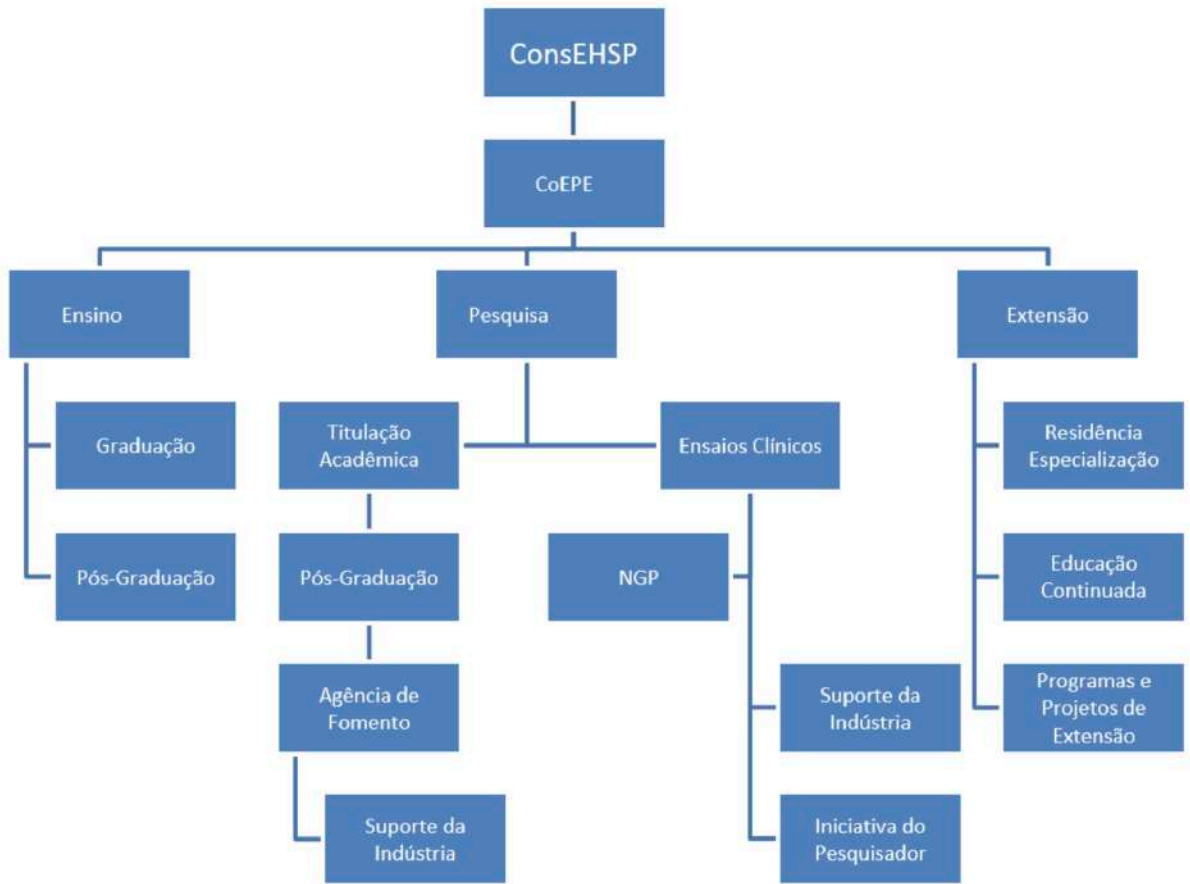
<https://sites.google.com/huhsp.org.br/ensino-pesquisa-hsp/p%C3%A1gina-inicial?authuser=0>

## Acordo UNIFESP - SPDM

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REGULAMENTO INTERNO DO COMITÊ DE ENSINO, PESQUISA E EXTENSÃO do  
HOSPITAL SÃO PAULO – HOSPITAL UNIVERSITÁRIO.

[https://drive.google.com/file/d/1mDlx6UKOLM3uuzTaGSS9oEL7Zp\\_qilZ2/view](https://drive.google.com/file/d/1mDlx6UKOLM3uuzTaGSS9oEL7Zp_qilZ2/view)



### Comitê de Ensino, Pesquisa e Extensão (CoEPE)

(11) 5576-4848 ramal 7253

[coep@huhsp.org.br](mailto:coep@huhsp.org.br)

Horário de Funcionamento: De segunda à sexta das 08 às 17h  
16h

### Núcleo de Gestão em Pesquisa Clínica (NGP)

(11) 5576-4848 ramal 8030 / 8031

[nucleodepesquisa@huhsp.org.br](mailto:nucleodepesquisa@huhsp.org.br)

Horário de Funcionamento: De segunda à sexta das 07 às

# Parte 1: Elaboração do Protocolo Ético

O protocolo não é apenas burocracia; é o mapa que garante que ninguém sairá ferido (física ou moralmente) do seu estudo.

## A. Pesquisa Clínica (Envolvendo Seres Humanos)

Aqui, o foco é a proteção do participante. O protocolo deve detalhar:

- **Riscos e Benefícios:** Descrição honesta do que pode dar errado e como isso será mitigado.
- **TCLE (Termo de Consentimento Livre e Esclarecido):** O documento mais importante. Deve ser escrito em linguagem acessível (nada de "juridiquês" ou termos médicos densos).
- **Crterios de Inclusão/Exclusão:** Justificativa ética de quem participa para evitar discriminação ou exploração de vulneráveis.
- **Privacidade:** Como os dados serão anonimizados? Onde serão guardados?

## Parte 3: Conclusão e Debate

**Resumida: A ética deve ser pensada antes da coleta de dados. Uma vez que o erro ético acontece, ele é quase impossível de consertar sem invalidar todo o trabalho.**

**Nota de Rodapé:** No Brasil, o sistema que rege isso é a plataforma **CEP/ CONEP/SINEP**. **Todo protocolo clínico deve ser submetido antes de começar qualquer contato com participantes.** **Sempre via CEP local.**

Protocolo Nacional CEP/ **CONEP/SINEP**

Protocolo Internacional **CONEP/SINEP**

Protocolo - menor de idade - < 18 anos **CONEP/SINEP**

Protocolo - Incapazes < 16 anos **CONEP/SINEP**

Protocolo - Portador de necessidades especiais (física e mental) **CONEP/SINEP**

Protocolo Genoma - total ou partes - **CONEP/SINEP**

População indígena, Novos Fármacos- **CONEP/SINEP**

# 1. Modelo Estruturado de TCLE (Padrão 2026)

O **Termo de Consentimento Livre e Esclarecido (TCLE)** evoluiu de um simples formulário para um documento de proteção jurídica e ética mútua. Em 2026, a ênfase está na **literacia em saúde** (garantir que o paciente realmente entendeu) e na **segurança de dados (LGPD)**.

## Seções Obrigatórias do Modelo:

- 1. Convite e Justificativa:** Texto direto explicando por que aquele indivíduo foi escolhido.
- 2. Procedimentos:** Descrição passo a passo do que será feito. *Dica: Use fluxogramas se for complexo.*
- 3. Riscos e Desconfortos:** Devem ser detalhados por ordem de probabilidade e gravidade, incluindo o que será feito para remediá-los.
- 4. Benefícios:** Devem ser reais. Se não houver benefício direto ao participante deve-se declarar o benefício para a ciência.



## **Anexo III. Nota Técnica n.º 42/2026-CGRAR/DAET/SAES/MS.**

### **Termo de Consentimento Livre e Esclarecido (TCLE) para tratamento com Onasemnogeno Abeparvoveque - Onasemnogeno Abeparvoveque (Zolgensma®)**

Eu, \_\_\_\_\_ (nome completo do paciente ou  
responsável legal), \_\_\_\_\_ responsável legal paciente), portador  
(a) do CPF \_\_\_\_\_, fui informado(a) e esclarecido(a)  
pelo(a) Dr(a). \_\_\_\_\_ (nome do médico responsável), CRM  
\_\_\_\_\_, sobre a necessidade e os riscos do tratamento com  
Onasemnogeno Abeparvoveque (Zolgensma®) para Atrofia Muscular Espinhal (AME)  
tipo 1.

#### **1. Esclarecimento e objetivos da terapia**



- A terapia gênica é um tipo de tratamento feito com um produto biológico que

## B. Revisão da Literatura

Muitos acham que revisões não precisam de ética, mas precisam!

- **Transparência e Reprodutibilidade:** No protocolo de uma Revisão Sistemática (como o PRISMA), a ética reside em não "escolher a dedo" apenas os artigos que confirmam sua tese (viés de seleção).
- **Uso de Dados Secundários:** Se a revisão utiliza bases de dados de acesso restrito, é necessário citar a conformidade com a LGPD (Lei Geral de Proteção de Dados).

## Parte 2: Integridade Acadêmica e Prevenção de Má Conduta

Pesquisa ética também trata da **honestidade do pesquisador** perante a comunidade científica.

- **Plágio e Autoplágio:** A apropriação de ideias ou a "reciclagem" de textos próprios sem citação.
- **Fabricação e Falsificação:** Inventar dados ou alterar resultados para que a hipótese pareça verdadeira.
- **Conflito de Interesses:** Declarar quem financiou a pesquisa. Se uma farmacêutica paga um estudo sobre seu próprio remédio, o leitor precisa saber disso.
- **Crítérios de Autoria:** Só deve assinar quem realmente contribuiu intelectualmente. "Cortesias" em autoria são consideradas má conduta ética.

Para verificar a ética de artigos e protocolos em 2026, a conferência mudou: saímos da simples conferência manual para o uso de **ecossistemas de integridade digital**.


Aqui estão as ferramentas e diretrizes mais atualizadas, divididas por categoria:

## **1. Plataformas de Diretrizes de Relato (Checklists Gold Standard)**

Antes de submeter a qualquer comitê, o protocolo deve seguir roteiros internacionais que garantem a transparência ética. A rede **EQUATOR Network** continua sendo o hub principal, mas com ferramentas mais dinâmicas:

- **SPIRIT (para Protocolos Clínicos):** Checklist essencial para montar o desenho do estudo.
- **PRISMA 2020/2026 (Revisões Sistemáticas):** Agora inclui extensões específicas para **revisões que utilizam IA e busca automatizada**.
- **CONSORT:** Para o relato de ensaios clínicos randomizados.

**5. Assistência e Indenização:** Declaração explícita de que o pesquisador e a instituição se responsabilizam por danos decorrentes da pesquisa, **pelo tempo que for necessário.**

**6. Contatos:** Telefone 24h do pesquisador principal e o contato do **CEP**  **Comitê de Ética em Pesquisa)** da instituição.

**Regra de Ouro do TCLE:** Nunca use termos como "eu entendo que não há riscos". O correto é "fui informado sobre os riscos de...".

O ônus da informação é sempre do pesquisador.

# Resumo das Penalidades em 2026

Se você usar IA (como ChatGPT, Claude ou Gemini) para escrever partes do seu protocolo ou artigo e **não declarar**, estas são as consequências prováveis:

Nível de Falha	Ação Tomada pela Editora/Instituição
<b>Omissão Leve</b> (ajuste de gramática não declarado)	Advertência e exigência de correção ( <i>Corrigendum</i> ).
<b>Omissão Grave</b> (texto de discussão/metodologia gerado)	<b>Retratação do artigo</b> e notificação ao empregador.
<b>Falsificação de Dados</b> (IA criando resultados ou imagens)	<b>Banimento permanente</b> da editora e processo administrativo disciplinar.
<b>Fraude em Revisão por Pares</b> (usar IA para fingir ser revisor)	Exclusão do nome de todas as bases de dados científicas e perda de financiamentos (CNPq/FAPESP).

## **Como evitar isso na sua aula ou pesquisa?**

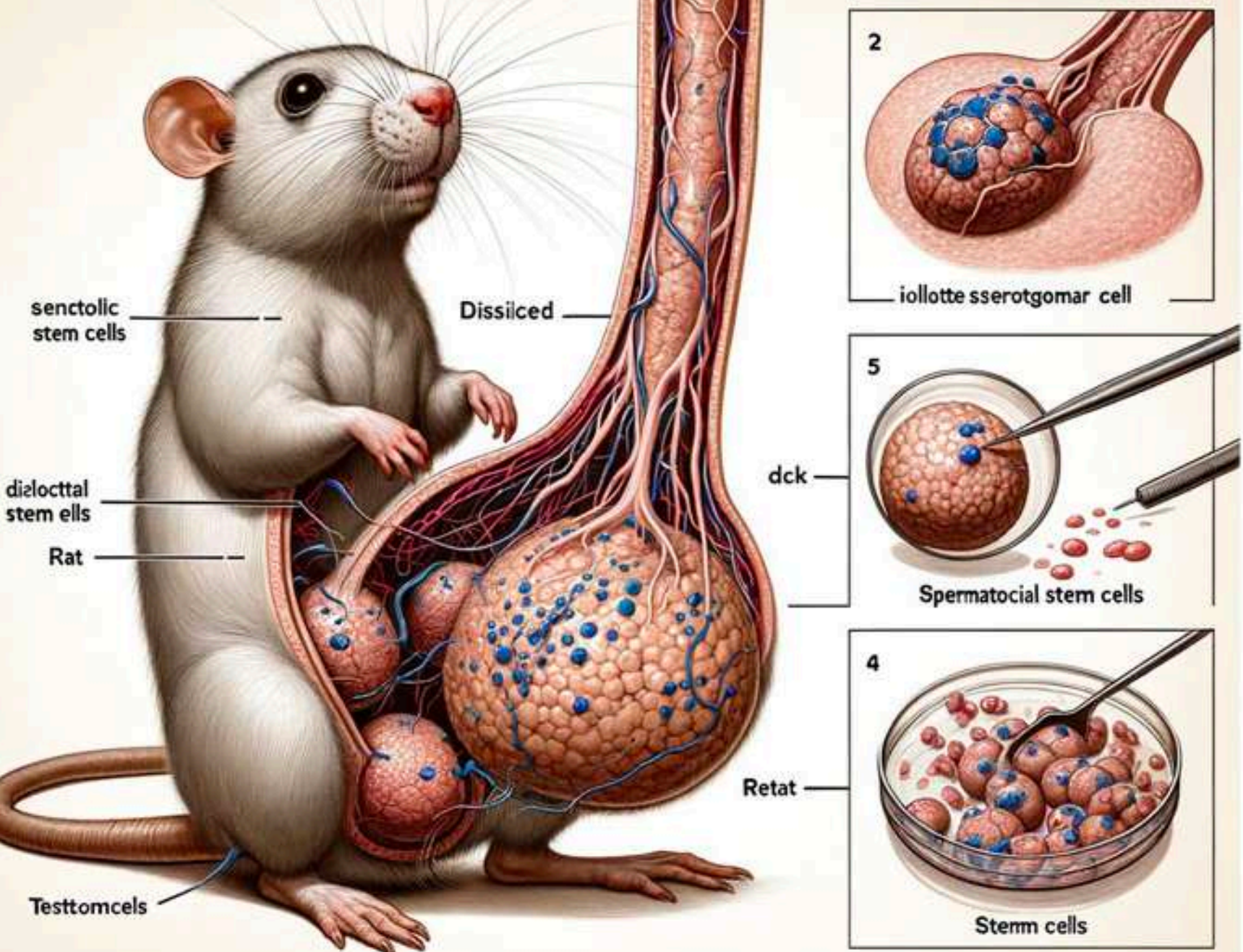
A regra atual (Portaria 2664/2026 do CNPq) é clara: **Transparência Total**. Se usou IA para estruturar os slides, para traduzir o abstract ou para revisar o texto, coloque uma seção de "Agradecimentos" ou "Declaração de Uso de IA" detalhando exatamente qual ferramenta foi usada e para quê.

**O crime ético não é usar a IA, é esconder o uso dela.**

# 1. O Caso da "Rata Gigante" (Revista *Frontiers in Cell and Developmental Biology*, 2024)

Este é talvez o caso mais famoso de uso "ilegal" (contra as normas editoriais) de IA generativa de imagens (Midjourney/DALL-E).

- **O erro:** O artigo continha um diagrama de uma rata com órgãos genitais gigantescos e desconexos, além de textos sem sentido como "*dck dck*" e "*stern cells*".
- **A falha:** Os autores usaram IA para gerar as figuras, não declararam e, pior, não revisaram. Os revisores por pares e editores também falharam no controle de qualidade.
- **Resultado:** O artigo foi **retratado** em poucos dias após viralizar nas redes sociais, e a revista sofreu um enorme dano de reputação.



The paper by Xinyu Guo et al., [Cellular functions of spermatogonial stem cells in relation to JAK/STAT signaling pathway](#), *Frontiers in Cell and Developmental Biology* 2024, DOI 10.3389/fcell.2023.1339390 [link to [PDF](#), in case the publisher removes it], easily passed editorial and peer review.

## 2. O Caso "As an AI language model..." (Várias revistas da Elsevier, 2024-2025)

Vários artigos foram identificados e retratados porque os autores deram "copiar e colar" diretamente do ChatGPT, esquecendo-se de apagar as frases de sistema da IA.

- **Exemplos:** Artigos publicados em revistas de engenharia e medicina que continham frases como: "*Certainly, here is a possible introduction for your paper...*" ou "*As an AI language model, I don't have access to real-time data*".
- **O problema ético:** Isso configura **falsidade ideológica acadêmica**, pois o autor assina um trabalho que ele sequer leu com atenção suficiente para notar que a IA estava "falando" com ele.

### 3. Retratação Massiva na *Neurosurgical Review* (Janeiro de 2026)

Como mencionei anteriormente, este caso é um marco recente.

- **O fato:** Mais de 120 artigos foram retratados de uma só vez.

**A "ilegalidade":** Descobriu-se que eram produtos de **Paper Mills** (

- fábricas de artigos) que usavam IA para criar estudos fictícios e burlar o sistema de revisão.
- **Penalidade:** Banimento dos autores e investigação institucional profunda em universidades na Índia e China.



The screenshot shows a webpage for a retraction note. The breadcrumb navigation at the top reads "Home > Neurosurgical Review > Article". The main title is "Retraction Note: Reoperation rate and risk factors of reoperation for ossification of the posterior longitudinal ligament (OPLL): a systematic review and meta-analysis". Below the title, it says "Retraction Note | Published: 25 March 2026" and "Volume 49, article number 302, (2026) Cite this article". At the bottom left, there are two buttons: "Download PDF" with a download icon and "Save article" with a bookmark icon. On the right side, there is a thumbnail image of the journal cover for "Neurosurgical Review" featuring a blue and red abstract design with the Springer logo. Below the thumbnail, the text "Neurosurgical Review" is displayed, followed by two links: "Aims and scope" with a right-pointing arrow and "Submit manuscript" with a right-pointing arrow.

Home > [Neurosurgical Review](#) > Article

## Retraction Note: Reoperation rate and risk factors of reoperation for ossification of the posterior longitudinal ligament (OPLL): a systematic review and meta-analysis

Retraction Note | Published: 25 March 2026

Volume 49, article number 302, (2026) [Cite this article](#)

[Download PDF](#) ↓ [Save article](#)

[Neurosurgical Review](#)

[Aims and scope](#) →

[Submit manuscript](#) →

## Estatísticas de 2026 (O "Raio-X" do Problema)

De acordo com dados recentes de plataformas como o *Retraction Watch* e o *Problematic Paper Screener*:

- **Volume:** Em 2024 e 2025, houve um aumento de **45% nas retratações** ligadas "erros de integridade", onde a IA não declarada foi o principal motor.
- **Áreas mais afetadas:** Engenharia (30%), Medicina Clínica (22%) e Ciências Ambientais (15%).
- **As "Marcas da IA":** Ferramentas de detecção identificaram que cerca de **1 a cada 500 artigos** publicados atualmente contém "frases torturadas" (sinônimos estranhos usados por IAs para evitar detectores de plágio comuns).

## Por que esses casos são considerados "ilegais" na academia?

Não existe uma "lei" penal comum para isso (a menos que envolva verba pública, o que pode ser considerado estelionato), mas viola os **Contratos de Publicação**:

- 1. Quebra de Autoria:** IAs não podem ser autores porque não têm responsabilidade jurídica.
- 2. Violação de Originalidade:** Copiar da IA sem citar é considerado uma forma de plágio (apropriação de produção não original).
- 3. Falsificação de Dados:** Se a IA inventa uma referência bibliográfica (alucinação) e o autor a mantém, isso é **falsificação**.

o caso da "Rata da Frontiers" como quebra-gelo. Ele ilustra perfeitamente como a falta de ética (omissão do uso de IA) caminha de mãos dadas com a falta de rigor científico.

# **Normas para protocolo de pesquisa para revisões Sistemáticas**

Para as **revisões sistemáticas**, as normas são focadas em **transparência e reprodutibilidade**. A grande dúvida sobre a necessidade de aprovação ética (CEP/CONEP) é um dos pontos mais debatidos em bancas de pós-graduação.

Aqui estão as diretrizes atualizadas para 2026:

**Resolução CNS nº 510/2016, Portaria 2664/2026 do CNPq**

# 1. Precisa de aprovação no sistema CEP/CONEP? Revisão Sistemática

A resposta curta é: **Geralmente, NÃO**. De acordo com a **Resolução CNS nº 510/2016** (ainda a base legal no Brasil), pesquisas que utilizam apenas informações de **acesso público** ou de **domínio público** não precisam de registro ou avaliação pelo sistema CEP/CONEP.

Quando **NÃO** precisa:

- **Revisão de Literatura Comum:** Uso de artigos já publicados em bases de dados (PubMed, Scielo, Cochrane).
- **Dados Secundários Públicos:** Uso de dados do DATASUS ou IBGE sem identificação dos indivíduos.

Quando **PRECISA (As Exceções)**:

- **Revisão de prontuários não publicados:** Se você vai coletar dados de prontuários no arquivo de um hospital para fazer sua própria análise antes de comparar com a literatura, isso é pesquisa com seres humanos.
- **Dados Secundários Identificados:** Se os dados que você está revisando permitem identificar quem são as pessoas (violação da LGPD).
- **Revisões Sistemáticas de Dados de Pacientes Individuais (IPD Meta-analysis):** Quando os autores originais enviam os dados brutos de cada paciente para você.

## 2. Normas de Protocolo para Revisões Sistemáticas

Mesmo que não passe pelo comitê de ética, uma revisão sistemática exige um **protocolo ético-metodológico** rigoroso para ser aceita por revistas de alto impacto.

### A. Registro no PROSPERO

O **PROSPERO** (International Prospective Register of Systematic Reviews) é o "comitê de ética" virtual das revisões.

- Você deve registrar seu protocolo **antes** de começar a extração de dados.
- Isso evita o "viés de publicação" e impede que outros pesquisadores publiquem exatamente a mesma pergunta que você está trabalhando.

**Cuidado:** Revisão Sistemática - Artigo publicado e que está com **restrição conhecida/retratação** - **Não** pode ser usado na revisão / Pesquisa Clínica.

## **B. Diretriz PRISMA 2020 (e atualizações 2026)**

O **PRISMA** (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) é o checklist obrigatório. Ele dita como o protocolo deve ser escrito:

- **Estratégia de Busca:** Deve ser descrita de forma que qualquer pessoa possa repetir e achar os mesmos resultados.
- **Crterios de Elegibilidade (PICO):** Definição clara de População, Intervenção, Comparação e *Outcomes* (Desfechos).
- **Avaliação de Risco de Viés:** Você deve declarar como verificou se os artigos incluídos são confiáveis (usando ferramentas como a da Cochrane ou Newcastle-Ottawa).

### 3. A Ética na Revisão da Literatura

Se não há pacientes "vivos" sendo testados, onde está a ética? Em 2026, a ética na revisão foca na **Integridade dos Dados**:

- 1. Viés de Seleção:** É antiético excluir um artigo apenas porque o resultado dele contradiz a sua hipótese.
- 2. Transparência na IA:** Se você usou ferramentas de IA (como Rayyan, Covidence ou modelos de linguagem) para triar os artigos, isso **deve** ser declarado no protocolo.
- 3. Plágio de Ideias:** Respeitar a autoria dos artigos revisados, garantindo que a síntese seja original e não uma colcha de retalhos de frases alheias.

# Ética em Pesquisa: Protocolos e Integridade

<b>Tipo de Estudo</b>	<b>Registro Obrigatório</b>	<b>Aprovação CEP/CONEP</b>
<b>Pesquisa Clínica</b>	Registro de Ensaio Clínico	<b>Sim</b>
<b>Revisão Sistemática</b>	PROSPERO	<b>Não</b> (em regra)
<b>Revisão Narrativa</b>	Opcional	<b>Não</b>



Artigos selecionados  
Já avaliados p/ CEP

**Dica Prática:** Muitas revistas agora exigem o número do registro no PROSPERO logo na submissão. Se você terminar a revisão e não tiver o registro, pode ter o artigo recusado por "falha ética de protocolo".

Faz sentido para a estrutura da sua aula ou quer que eu detalhe como funciona o fluxo do PROSPERO?

O **PROSPERO** (*International Prospective Register of Systematic Reviews*) funciona como o "cartório" da sua revisão. O objetivo central é evitar a duplicidade de esforços e o **viés de relato** (quando o autor muda o desfecho planejado porque os resultados não foram os esperados).

## **Fluxo de Registro no PROSPERO**

### **1. Preparação (O que ter em mãos antes de abrir o site)**

Não se abre o formulário do PROSPERO sem o protocolo metodológico pronto. Você precisará de:

- **Pergunta PICO** clara.
- **Estratégia de busca** definida para pelo menos uma base de dados principal (ex: PubMed).
- **Crterios de inclusão e exclusão** bem delimitados.
- **Método de extração de dados** e avaliação de qualidade (Risco de Viés).

## 2. Verificação de Duplicidade (O "Search")

Antes de registrar, você deve pesquisar no próprio PROSPERO se já não existe uma revisão em andamento sobre o mesmo tema.

- **Regra Ética:** Se houver um registro idêntico recente, você deve justificar por que a sua revisão é necessária (ex: atualização de dados ou subpopulação diferente).

### 3. Submissão do Registro

O registro deve ser feito **antes de iniciar a extração de dados**.

- **O "Ponto sem Retorno"**: O PROSPERO geralmente não aceita registros de revisões que já foram concluídas ou que já iniciaram a análise de dados.
- **Campos Obrigatórios**: Em 2026, houve um aumento no rigor sobre a descrição dos desfechos (*outcomes*) primários e secundários.

### 4. Revisão e Publicação do Registro

A equipe do PROSPERO revisa o formulário (isso pode levar de alguns dias a algumas semanas).

- Uma vez aprovado, você recebe um **Número de Registro** (ex: CRD42026XXXXX).
- **Este número deve constar no Abstract e na Metodologia do seu artigo final.**

# Regras de Ouro e Ética no Fluxo

Fase do Fluxo	Ação Ética Necessária
<b>Durante a Pesquisa</b>	Se você precisar mudar o método (ex: mudar a ferramenta de risco de viés), você <b>deve atualizar</b> o registro no PROSPERO. O histórico de alterações fica visível para os editores.
<b>Uso de IA</b>	Em 2026, o PROSPERO exige que você declare se usará ferramentas de IA (como o <i>Rayyan</i> ou <i>ASReview</i> ) para a triagem de títulos e resumos.
<b>Finalização</b>	Após publicar o artigo, você deve voltar ao PROSPERO e adicionar o link da publicação final para encerrar o ciclo do registro.

## Por que isso é vital para o pesquisador?

- 1. Proteção de Propriedade:** O registro prova que você teve a ideia e iniciou o trabalho naquela data.
- 2. Facilitação da Publicação:** Revistas de alto impacto (Q1 e Q2) raramente aceitam revisões sistemáticas sem o número do PROSPERO.
- 3. Transparência:** Demonstra que você não manipulou os critérios de inclusão para "forçar" um resultado estatístico após ver os dados.

O registro no **PROSPERO** é para a **Revisão Sistemática**, já a aprovação do **CEP/CONEP** é para a **Pesquisa Clínica**: uma salvaguarda contra a má conduta e um selo de qualidade científica.

# Checklist de Pré-Submissão: PROSPERO (Versão 2026)

Antes de acessar o portal, garanta que todos os itens abaixo estejam definidos. O PROSPERO rejeitará registros incompletos ou feitos após o início da extração de dados.

## 1. Etapa de Planejamento (Pré-requisitos)

- **Busca de Duplicidade:** Realizei uma busca no PROSPERO e na *Cochrane Database* para garantir que não há uma revisão idêntica publicada ou em andamento nos últimos 2 anos.
- **Equipe Definida:** Tenho pelo menos dois revisores independentes (obrigatório para garantir a isenção na triagem).
- **Status da Revisão:** Confirmando que a extração de dados **ainda não começou**.

## 2. Definição Metodológica (O Coração do Registro)

- [ ] **Pergunta PICO/PECO:** \* **P**opulação (quem?), **I**ntervenção (o quê?), **C**omparação (contra o quê?) e **O**utcome (qual desfecho?).
- [ ] **Estratégia de Busca:** Tenho a linha de busca completa para pelo menos uma base principal (ex: *PubMed/Medline*), incluindo os termos MeSH e operadores booleanos (AND/OR).
- [ ] **Bases de Dados:** Liste todas as bases que serão consultadas (ex: Embase, Cochrane, Scielo, LILACS).
- [ ] **Critérios de Elegibilidade:** Defini claramente quais tipos de estudo serão incluídos (ex: apenas Ensaio Clínico Randomizado) e quais serão excluídos (ex: relatos de caso, estudos em animais).

### 3. Procedimentos de Triagem e Extração

- [ ] **Triagem:** Especifiquei que dois revisores olharão títulos e resumos de forma independente.
- [ ] **Resolução de Conflitos:** Defini se haverá um terceiro revisor sênior ou se o consenso será por discussão.
- [ ] **Uso de IA (Novo 2026):** Se for usar ferramentas como *Rayyan* ou *Covidence* com funções de automação, descrever como a IA será utilizada (ex: "apenas para ordenação de relevância").

## 4. Análise e Qualidade

- [ ] **Risco de Viés:** Escolhi a ferramenta de avaliação (ex: RoB 2 para ensaios clínicos ou ROBINS-I para não-randomizados).
- [ ] **Síntese de Dados:** Descrevi se farei Metanálise (síntese quantitativa) ou apenas uma síntese narrativa.

## 5. Transparência e Financiamento

- [ ] **Fontes de Financiamento:** Identifiquei se há bolsas (CNPq/FAPESP) ou conflitos de interesse comerciais.
- [ ] **Idioma:** Definido em qual idioma o artigo final será redigido.

Muitos alunos esquecem de **salvar o PDF do registro aprovado**. Oriente-os a guardar esse documento, pois muitos periódicos exigem o PDF do protocolo original anexado como "Material Suplementar" para conferir se os autores não mudaram as regras do jogo no meio do caminho.

# 1. A Sequência de Nomes (Hierarquia da Autoria)

Diferente de outras áreas, na medicina e ciências biológicas, a posição do nome no artigo conta uma história sobre a função de cada um:

- **Primeiro Autor (First Author):** É quem mais trabalhou. Geralmente o pesquisador que executou a maior parte da coleta de dados, análise e escreveu rascunho principal. É o nome mais valorizado para fins de currículo.
- **Co-autores Intermediários:** São listados por ordem decrescente de contribuição. Se as contribuições forem iguais, utiliza-se a ordem alfabética (embora isso deva ser declarado nas notas de rodapé).
- **Último Autor (Senior/Corresponding Author):** Geralmente é o orientador, o chefe do laboratório ou o pesquisador sênior que concebeu a ideia, garantiu financiamento e supervisionou todo o projeto. É uma posição de grande prestígio.
- **Autor Correspondente (Corresponding Author):** É quem assume a responsabilidade administrativa (submissão, resposta aos revisores). Pode ser primeiro ou o último autor.

## Os 4 Critérios de Autoria (Norma ICMJE)

Para ser considerado autor, não basta ser o "chefe do departamento". É preciso cumprir **TODOS** os quatro requisitos:

1. Contribuição substancial na concepção/design **OU** na coleta/análise de dados.
2. Redação do artigo ou revisão crítica de conteúdo intelectual importante.
3. Aprovação final da versão a ser publicada.
4. Compromisso de ser responsável por todos os aspectos do trabalho (integridade).

## 2. Como são colocados os Agradecimentos (Acknowledgements)

A seção de agradecimentos serve para dar crédito a quem ajudou, mas **não cumpre** os 4 critérios de autoria acima. Em 2026, a transparência aqui é rigorosa.

### Quem incluir nos Agradecimentos?

- **Apoio Técnico:** Técnicos de laboratório, enfermeiros ou estatísticos que apenas rodaram os dados sem participar do desenho do estudo.
- **Apoio Administrativo:** Chefes de departamento que apenas forneceram o espaço físico.
- **Revisores de Texto/Tradutores:** Pessoas que corrigiram o inglês ou a gramática.
- **Financiadores:** Agências de fomento (CNPq, FAPESP, CAPES) e o número do processo/bolsa. **Isso é obrigatório.**
- **Participantes da Pesquisa:** Um agradecimento geral aos pacientes ou voluntários (sem citar nomes para preservar o sigilo).

## Regras de Ouro:

- 1. Consentimento:** Você deve ter permissão por escrito das pessoas que cita nos agradecimentos (algumas revistas exigem isso), pois ser citado ali pode implicar endosso aos resultados.
- 2. Uso de IA:** Em 2026, é aqui que você deve declarar: "*Os autores agradecem o suporte do modelo de linguagem [Nome da IA] para a revisão gramatical e estruturação do manuscrito*".

Tive a colaboração da IA - Gemini

## Tabela Comparativa: Autor vs. Agradecimento

Atividade	Autor	Agradecimento
Idealizou a pergunta da pesquisa	✓	✗
Coletou dados clínicos	✓	✗
Apenas revisou a gramática	✗	✓
Emprestou o laboratório	✗	✓
Escreveu a primeira versão do texto	✓	✗
Analisou estatisticamente os dados	✓	✗*

## Tabela Comparativa: Autor vs. Agradecimento

*\*Se o estatístico apenas rodou o teste solicitado, vai nos agradecimentos. Se ele ajudou a escolher o teste e interpretar o sentido biológico dos dados, deve ser coautor.*

**Dica para os alunos:** Conflitos de autoria são a maior causa de brigas em grupos de pesquisa. Defina a ordem dos nomes **antes** de começar a escrever o artigo, baseando-se no esforço estimado de cada um.

Tive a colaboração da IA - Gemini

# Regras Internacionais de Publicação

*Recommendations for the Conduct, Reporting, Editing, and Publication*

Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journal

**PROSPERO** (*International Prospective Register of Systematic Reviews*)

**How to Publish a Research Paper in a Journal: A Beginner's Guide**

**Best Scientific Documentation Tools in 2026**

# 1. Literature Search and Journal Selection Tools

Before writing, you need to identify the right journal and ensure your research is novel.

- **Google Scholar:** A global search engine for literature search, citation tracking, and journal metrics.
- **Elsevier Journal Finder / Springer Journal Suggester:** Tools that use your manuscript title and abstract to suggest suitable journals within their portfolios.
- **Directory of Open Access Journals (DOAJ):** A database of trusted open-access journals, useful for ensuring compliance with international open-access mandates.
- **Jane (Journal/Author Name Estimator):** A free web-based tool that compares your abstract against PubMed data to find relevant journals.
- **Scopus/Web of Science:** Databases for identifying high-impact, reputable journals.

## 2. Manuscript Writing and Preparation Tools

- **Overleaf:** An online collaborative LaTeX editor that allows you to use pre-built templates for many international journals.
- **Microsoft Word / Google Docs:** Common word processors used to draft manuscripts, increasingly utilizing collaborative features.
- **Scrivener:** A tool tailored for writing long-form, complex papers.
- **Manchester Academic Phrasebank:** A resource for academic phrases and terminology, especially useful for non-native English speakers.

### 3. Citation and Reference Management

- **Mendeley:** A free reference manager and academic social network that automatically formats citations and bibliographies.
- **Zotero:** A powerful, free tool for collecting, organizing, and citing sources.
- **EndNote:** A robust, paid reference management software often used by experienced researchers.

• [ResearchGate](#)  
+3

## 4. Language, Paraphrasing, and Editing Tools

- **Grammarly:** A cloud-based typing assistant that checks grammar, spelling, and style.
- **Paperpal:** AI-based editing software tailored for academic writing, assisting with grammar, word choice, and sentence structure.
- **Quillbot:** A paraphrasing tool that helps rewrite sentences to avoid plagiarism.
- **Hemingway Editor:** Improves readability by highlighting complex sentences, passive voice, and unnecessary adverbs.

## 5. Ethical Standards and Specialized Tools

- **EQUATOR Network:** Provides reporting guidelines (e.g., CONSORT, STROBE, PRISMA) to ensure high-quality, transparent reporting in research papers.
- **ORCID:** A persistent digital identifier (iD) that distinguishes you from other researchers, required by most international journals.
- **Turnitin/iThenticate:** Professional tools used by journals to check for plagiarism before publication.
- **Zenodo/Figshare:** Repositories for storing and sharing research data, providing a citable Digital Object Identifier (DOI).

.

## Summary Checklist for Submitting

1. **Draft:** Use Overleaf (LaTeX) or Word.
2. **Cite:** Manage with Zotero or Mendeley.
3. **Polish:** Check with Grammarly/Paperpal.
4. **Find Journal:** Use DOAJ or Journal Finders.
5. **Check Ethics:** Use EQUATOR Network guidelines.
6. **Submit:** Via journal portals (e.g., Editorial Manager, ScholarOne).

# Home | ClinicalTrials.gov

ClinicalTrials.gov

<https://clinicaltrials.gov>

ClinicalTrials.gov

<https://clinicaltrials.gov>

A structured online system, such as the **ClinicalTrials.gov** results database, that provides the public with access to registration and summary results ...

## International Clinical Trials Registry Platform (ICTRP)

World Health Organization (WHO)

<https://www.who.int> › Tools and toolkits

World Health Organization (WHO)

<https://www.who.int> › Tools and toolkits

In order to register a trial, please **contact one of the Primary registries**. What is a clinical trial? For the purposes of registration, a clinical trial is any ...[Read more](#)

## EU Clinical Trials Register - Update

EU Clinical Trials Register

<https://www.clinicaltrialsregister.eu>

EU Clinical Trials Register

<https://www.clinicaltrialsregister.eu>

The EU Clinical Trials Register **provides a free and accurate search of clinical trials** in European Union member states and the European Economic Area.

# Brazilian Registry of Clinical Trials (ReBEC)

Brazilian Registry of Clinical Trials

<https://ensaiosclinicos.gov.br>

Brazilian Registry of Clinical Trials

<https://ensaiosclinicos.gov.br>

The Brazilian Registry of **Clinical Trials** (ReBEC) is a free access virtual platform for recording experimental and **non-experimental** studies.[Read more](#)

## ReBec (Registro Brasileiro de Ensaio Clinicos)

World Health Organization (WHO)

<https://www.who.int> › ... › Primary registries

World Health Organization (WHO)

<https://www.who.int> › ... › Primary registries

Brazilian **Clinical Trials** Registry. Registry Profile. General Information. Address: Av. Brasil, 4.365 - Pavilhão Haity Moussatché sala 214 Manguinhos, Rio de ...[Read more](#)

## REBEC

Brazilian Registry of Clinical Trials

<https://ensaiosclinicos.gov.br> › faq

Brazilian Registry of Clinical Trials

<https://ensaiosclinicos.gov.br> › faq

Registering your clinical trial is mandatory to meet ethical, legal, and publication requirements. It ensures transparency, reduces publication bias by preventing the suppression of negative results, and helps avoid unnecessary duplication of research. Registration makes studies searchable, aids participant recruitment, and strengthens scientific integrity.

World Health Organization (WHO)

+4

Key reasons for registration include:

- **Ethical Obligation & Accountability:** It is often a condition of ethical approval and ensures accountability for research involving human subjects.
- **Publishing Requirements:** Most medical journals, adhering to ICMJE guidelines, require prior registration for a trial to be considered for publication.
- **Transparency and Trust:** It ensures that study protocols, including pre-specified outcome measures, are public, preventing researchers from changing them later to produce more favorable results.
- **Reduced Research Waste:** It allows other researchers to see what is already being studied, reducing duplication and identifying research gaps.
- **Participant Recruitment:** Public registries, such as [ClinicalTrials.gov](https://clinicaltrials.gov) and [WHO registries](#), help potential participants find relevant trials.

World Health Organization (WHO)

+5

# Nova Lei do CNPq sobre IA ✨

Portaria CNPq nº 2.664, de 6 de março de 2026



Institui a Política de Integridade na Atividade Científica do CNPq, incluindo regras específicas para o uso de Inteligência Artificial (IA) na pesquisa. ✨



## FOCO NA INTEGRIDADE

Estabelece regras de educação, prevenção, apuração e sanção para garantir a integridade científica apoiada pelo CNPq.



## REGULAMENTAÇÃO DA IA GENERATIVA

Torna obrigatória a declaração do uso de ferramentas de IA em qualquer etapa da pesquisa, especificando a ferramenta e a finalidade.

### EXEMPLOS DE USO:

- ✓ Geração de texto
- ✓ Análise de dados
- ✓ Tradução
- ✓ Revisão de literatura
- ✓ Outros...



## INTEGRIDADE CIENTÍFICA & IA

O que muda na pesquisa?



## RESPONSABILIDADE

O pesquisador é totalmente responsável pela integridade dos dados, análises e resultados, mesmo quando utiliza IA.



## MÁ CONDUTA

Define e combate:

- Fabricação
- Falsificação
- Plágio (FFP)
- Autoplágio
- "Salami Science" (fragmentação indevida de publicações).



## ABRANGÊNCIA

Aplica-se a bolsistas, pesquisadores e todos os envolvidos no fomento do órgão.

## TRANSPARÊNCIA É CIÊNCIA!

Cite a IA que você usa. Valorize sua pesquisa. Fortaleça a ciência.



## Onde encontrar?

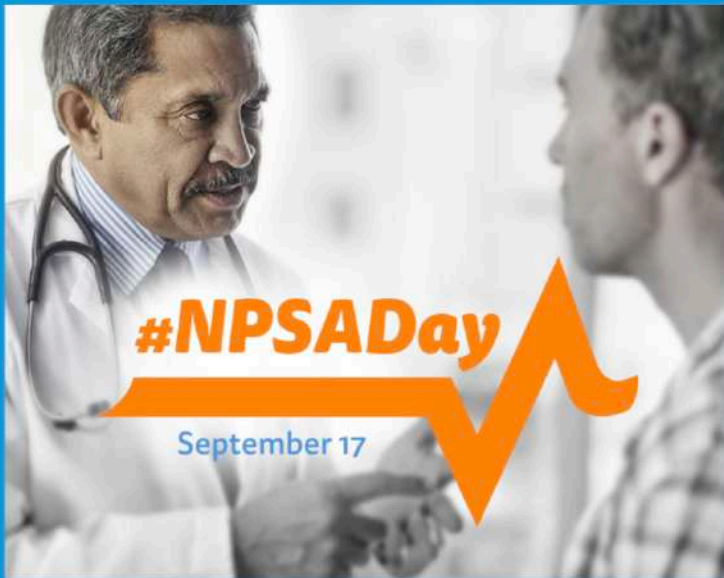
O texto integral está disponível na seção de "Notícias" ou "Legislação" no portal do CNPq:

[gov.br/cnpq](http://gov.br/cnpq)

## LEMBRE-SE:

Usou IA? Declare!  
É obrigatório.





## ACT NOW

While physician suicide was a crisis long before COVID-19, the demands of the pandemic have created a sense of urgency to better support physicians' mental health and wellbeing.

**National Physician Suicide Awareness Day (#NPSADay)** is a reminder and call to action. In 2021, #NPSADay reached 1.2 million people and received sign-on support from 54 organizations that resulted in a total of 26,000 actions taken to prevent suicide. But it doesn't have to stop there – with your help, everyday we can make time to talk – and to act – so physicians' struggles don't become mental health emergencies. We can all help prevent physician suicide by learning the signs, starting the conversations, understanding the underlying barriers and sharing the resources that can help those in distress seek mental health care.

# Doctors' Suicide Rate Highest of Any Profession

By Pauline Anderson

FROM THE WEBMD ARCHIVES 

May 8, 2018 -- One doctor commits suicide in the U.S. every day -- the highest [suicide](#) rate of any profession. And the number of doctor suicides -- 28 to 40 per 100,000 -- is more than twice that of the general population, new research shows. The rate in the general population is 12.3 per 100,000.

Doctors who die by suicide often have untreated or undertreated [depression](#) or other mental illnesses, a fact that underscores the need for early diagnosis and treatment, says study researcher Deepika Tanwar, MD, of the psychiatric program at Harlem Hospital Center in New York.

"It's very surprising" that the suicide rate among physicians is higher than among those in the military, which is considered a very stressful occupation, Tanwar says.



## Practice Management

[Surprise Billing and Patient Notice](#)

[Telehealth and Virtual Care](#)

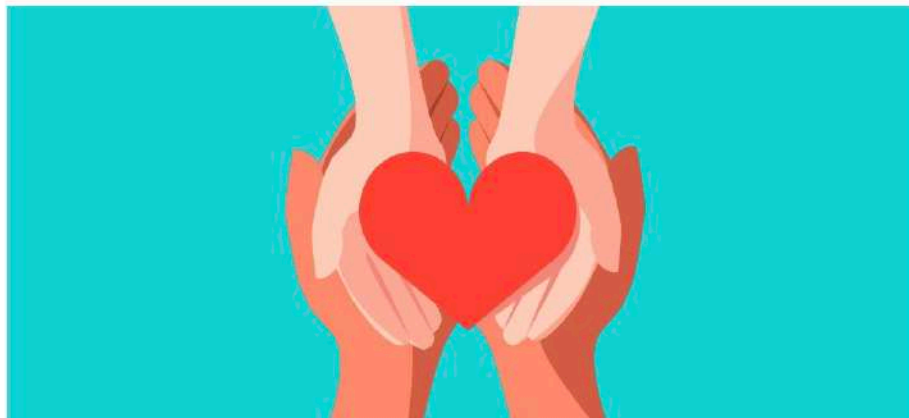
[Legal and Regulatory](#)

[Employed Physicians](#)

**[Physician Wellness](#)**

[Personal and Financial Resources](#)

## Physician Suicide Awareness



**National Physician Suicide Awareness Day (#NPSADay), taking place on September 17, 2022, is a call to action to prevent physician suicide.**

The rising rates of physician burnout, depression, and suicide have

Print  
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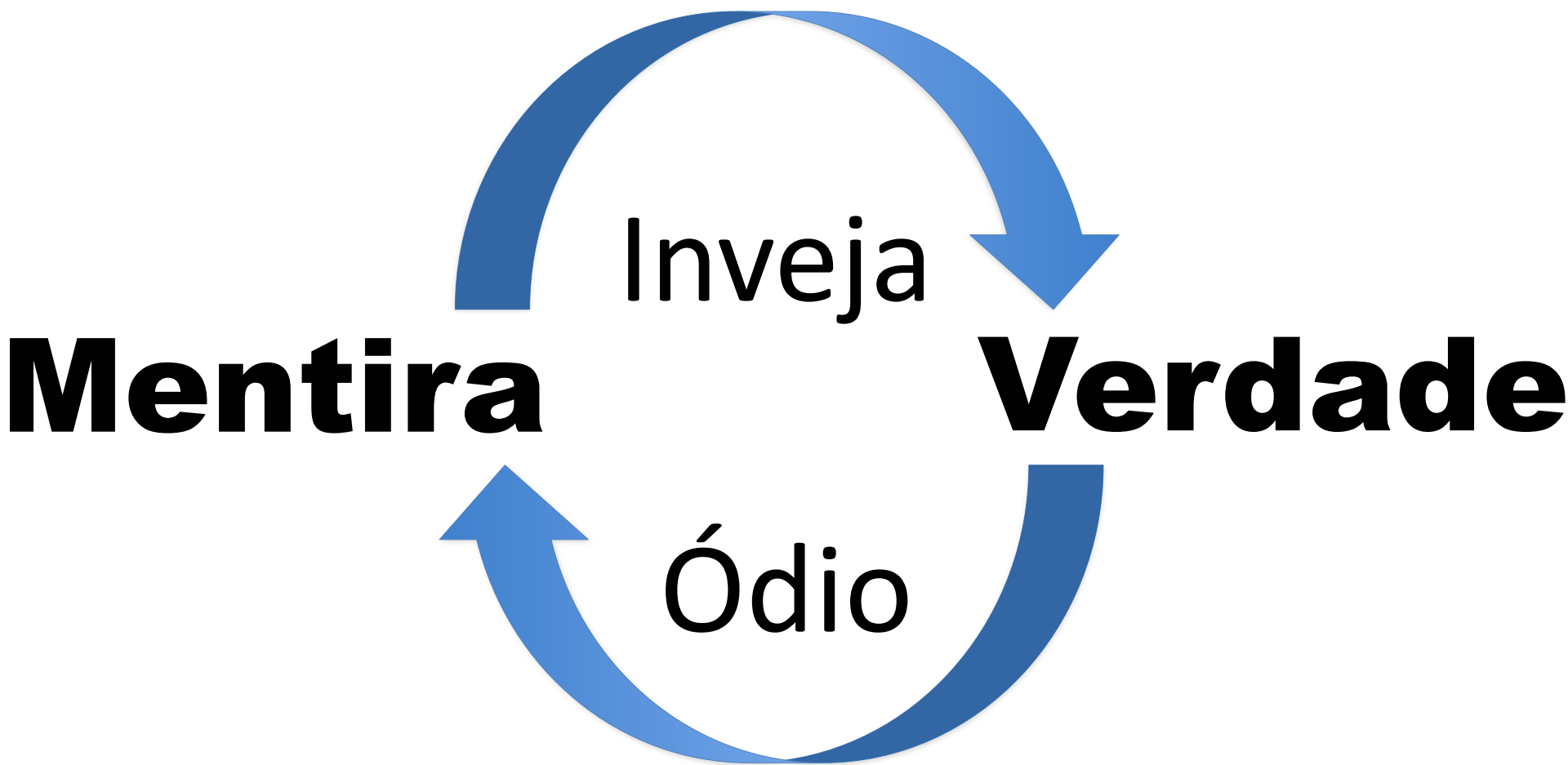
**Physicians Insurance** **Cover Your Assets.**

**LEARN MORE**

a subsidiary of the  
Massachusetts Medical Society

**Boston Medical Library**

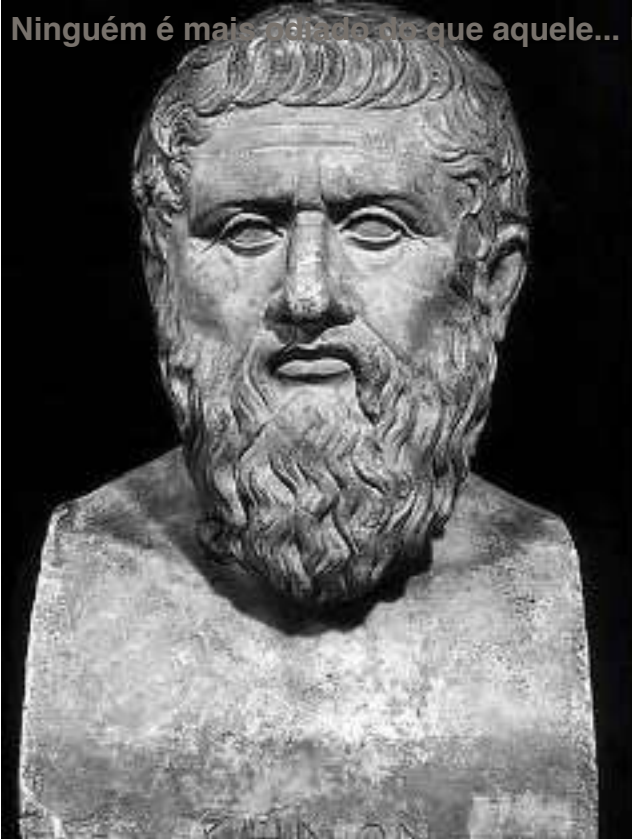
Members have access to the Waltham branch of the [Boston Medical Library](#) and the [Countway](#)



Cuidado para não chamar de inteligentes  
apenas aqueles que pensam como você.  
Ugo Ojetti (1871-946) escritor Italiano

Palavras que circulam a vida

Ninguém é mais odiado do que aquele... Platão



ninguém é  
mais odiado do  
que aquele que  
fala a verdade

Platão



PENSADOR

428 a.C.-347 a.C.



## Departamento de Cirurgia

<https://sp.unifesp.br/epm/cirurgia/>

<https://sp.unifesp.br/epm/cirurgia/acontece/historia-da-fundacao-epm-documentada>