

The future of animal experimentation



Jan-Bas Prins

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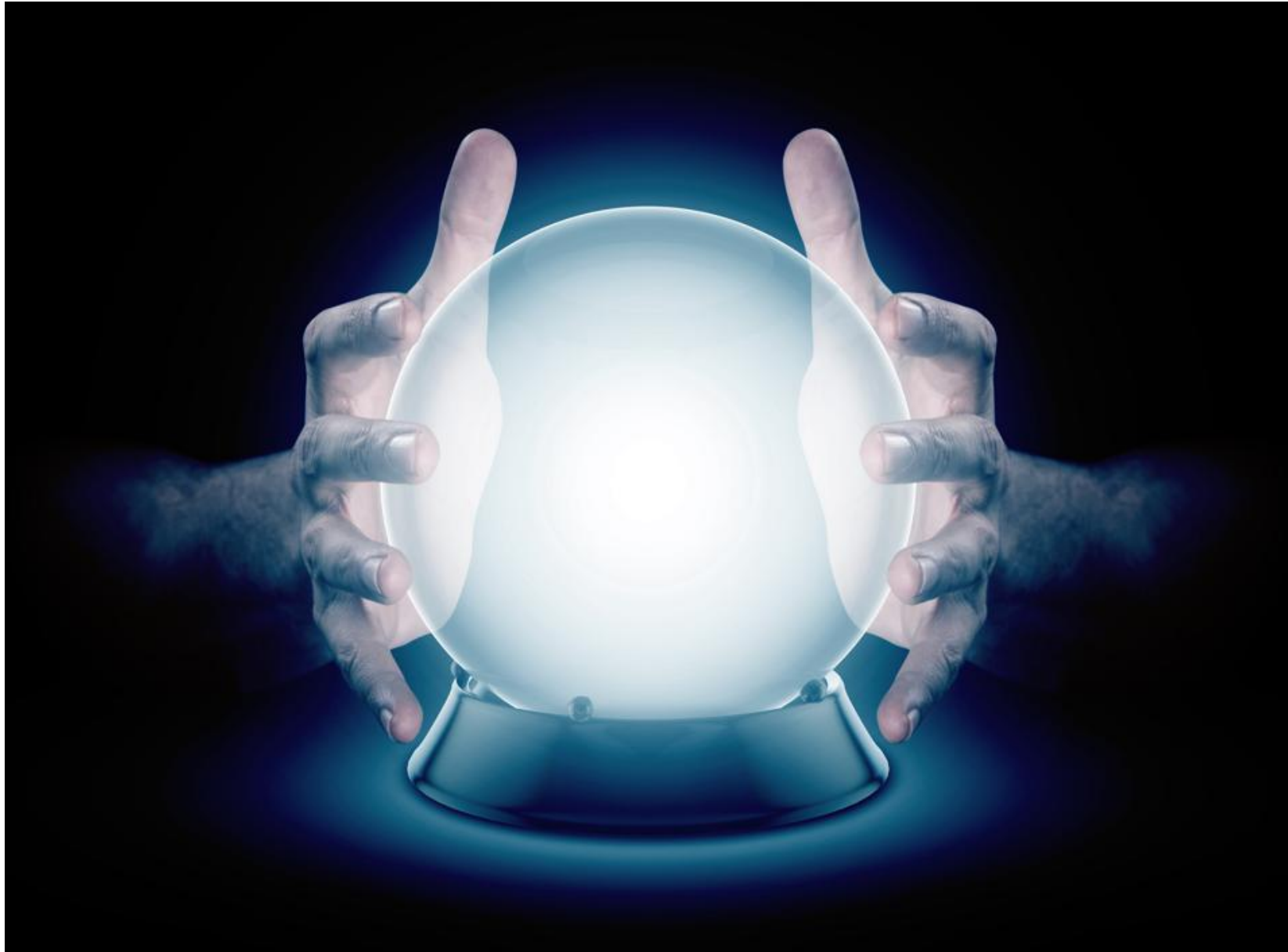
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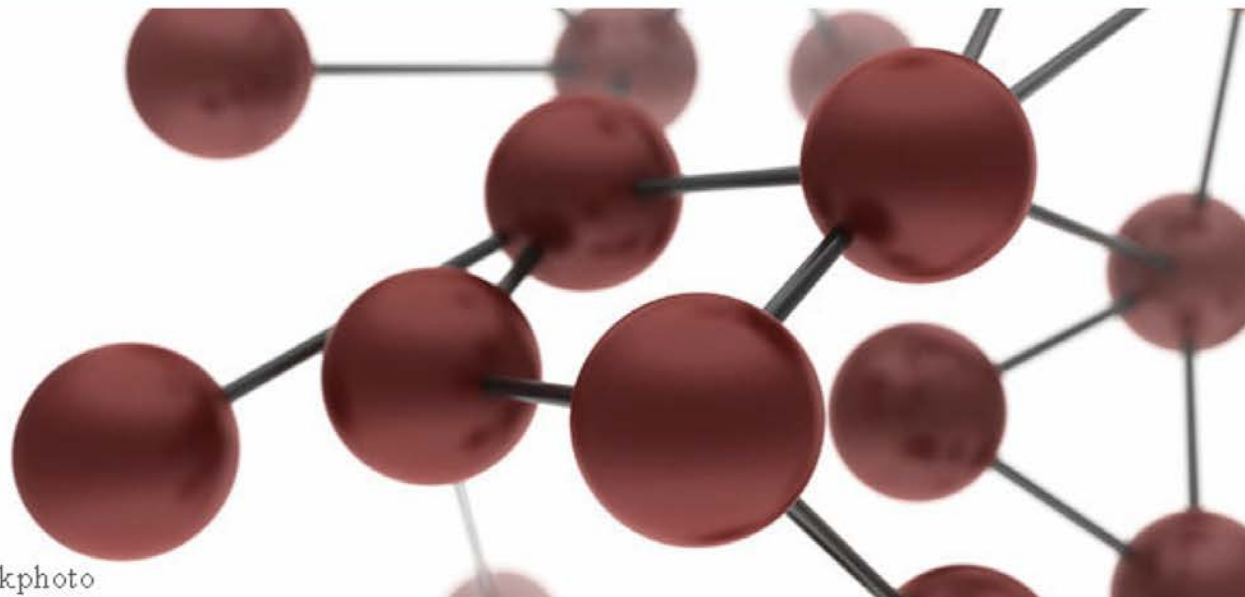


The future of animal experimentation



The future of animal experimentation





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Scientific Conference: Non-Animal Approaches - The Way Forward

December 6-7, 2016, Brussels, Belgium

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Scientific Conference: Non-Animal Approaches - The Way Forward

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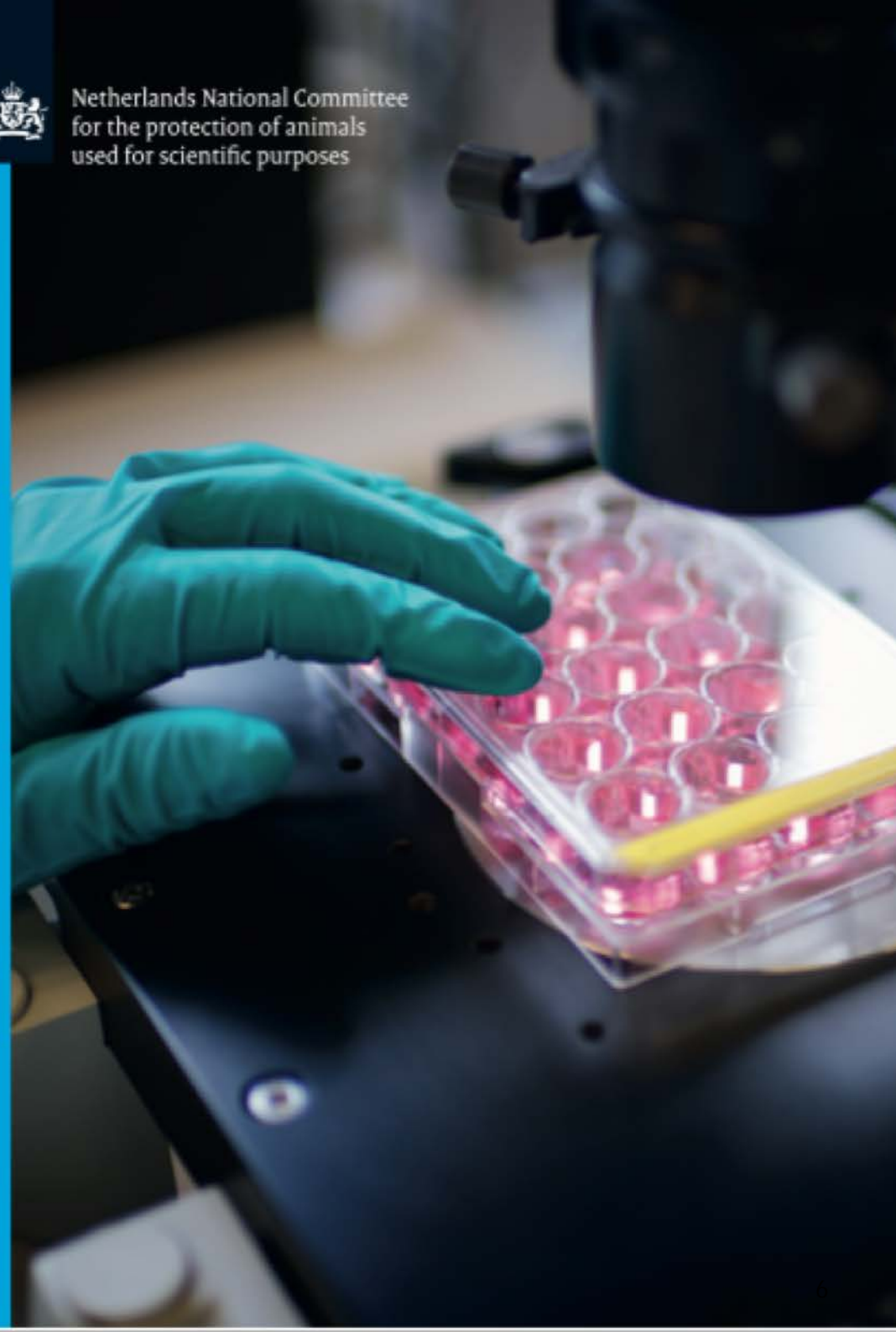
Netherlands National Committee
for the protection of animals
used for scientific purposes

Transition to non-animal research

*on opportunities for the phasing out of
animal procedures and the stimulation
of innovation without laboratory
animals*

Opinion of the Netherlands National Committee for the
protection of animals used for scientific purposes (NCad)

<https://english.ncadierproevenbeleid.nl/>





triggered by our competitive instincts for access to resources. The final chapter is a transition from the rigorous scholar to the logical dreamer of a better future. Sachs appeals to our cooperative nature as the means to approach sustainable development, equality for human diversity and the eradication of extreme poverty, as well as for peace.

A 'big bang' that inevitably unleashes in the background of the sequence of historical events in Sachs's book is that modern humans have displaced Darwinian reproductive success to instate our own version of currency for success: wealth. Fitness in humans is not exactly weighted by the genetic footprint left by an individual's reproductive success but rather by a form of social footprint built on their relative financial success. Sachs's account defogs the window's glass to reveal a form of 'financial selection' whereby differential wealth leads the way of modern human evolution instead.

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Essay

How the COVID-19 pandemic highlights the necessity of animal research

Lisa Genzel^{1,4}, Roger Adan², Anton Berns³, Jeroen J.J.P. van den Beucken⁴, Arjan Blokland⁵, Erik H.W.G.M. Boddeke^{5,7}, Willy M. Bogers⁵, Ronald Bontrop⁸, R. Bulthuis⁹, Teun Bousema⁴, Hans Clevers¹⁰, Tineke C.J.J. Coenen¹¹, Anne-Marie van Dam¹², Peter M.T. Deen¹, K.W. van Dijk¹¹, Bart J.L. Eggen^{6,7}, Ype Elgersma¹³, Izet Erdogan⁴, Bernhard Englitz¹, J. Martje Fentener van Vlissingen¹³, Susanne la Fleur^{12,14}, Ron Fouchier¹⁵, Carlos P. Fitzsimons¹⁶, Wilbert Frieling¹⁶, Bart Haagsmans¹³, Balthasar A. Heesters¹⁵, Marloes J.A.G. Henckens¹, Sander Herfst¹³, Elly Hol², Daniel van den Hove³, Marien I. de Jonge⁴, Jos Jonkers^{13,17}, Leo A.B. Joosten⁴, Andries Kalsbeek¹⁴, Maarten Kamermans^{12,14}, Harm H. Kampinga⁷, Martien J. Kas⁸, Jaap Keijer¹⁸, Sander Kersten¹⁸, Amanda J. Kilian⁴, Taco W.A. Kooij⁴, Sander Kooijman¹¹, Werner J.H. Koopman⁴, Aniko Korosi¹⁵, Harm J. Krugers¹⁵, Thijs Kuiken¹⁵, Steven A. Kushner¹³, Jan A.M. Langemans^{15,19}, Heidi M.B. Lesscher¹⁸, Paul J. Lucassen¹⁵, Esther Lutgens¹⁹, Mihai G. Netea^{1,20}, Lucas P.J.J. Noldus¹, Jos W.M. van der Meer⁴, Frank J. Meye², Joram D. Mul¹⁵, Kees van Oers^{18,21}, Jocelien D.A. Olivier¹, R. Jeroen Pasterkamp¹, Ingrid H.C.H.M. Philippens⁴, Jos Prickaerts⁵, B.J.A. Pollux¹⁸, Patrick C.N. Rensen¹¹, Jacco van Rheenen³, Ronald P. van Rijn⁴, Laila Ritsma¹¹, Barry H.G. Rockx¹³, Benno Roozendaal⁴, Evert M. van Schothorst¹⁸, K. Stittelaar²², Norbert Stockhofe^{18,23}, Dick F. Swaab¹⁶, Rik L. de Swart¹³, Louk J.M.J. Vanderschuren¹⁹, Taco J. de Vries¹², Femke de Vrij¹³, Richard van Wezel¹, Corette J. Wierenga¹⁹, Maximilian Wiesmann⁴, Ingo Willuhn^{12,14}, Chris I. de Zeeuw^{13,14}, and Judith R. Homberg^{4,6}

Recently, a petition was offered to the European Commission calling for an immediate ban on animal testing. Although a Europe-wide moratorium on the use of animals in science is not yet possible, there has been a push by the non-scientific community and politicians for a rapid transition to animal-free innovations. Although there are benefits for both animal welfare and researchers, advances on alternative methods have not progressed enough to be able to replace animal research in the foreseeable future. This trend has led first and foremost to a substantial increase in the administrative burden and hurdles required to make timely advances in research and treatments for human and animal diseases. The current COVID-19 pandemic clearly highlights how much we actually rely on animal research. COVID-19 affects several organs and systems, and the various animal-free alternatives currently available do not come close to this complexity. In this Essay, we therefore argue that the use of animals is essential for the advancement of human and veterinary health.

With the implementation of the European Directive to protect animals used in scientific procedures [1] around 10 years ago, the European Union set high ambitions regarding the protection of animals for research purposes. This directive focused on the development and implementation of the '3Rs' (reduction, refinement and replacement), transparency (public information about the use of animals) and their harmonization across Europe. The implementation of this directive into national legislation has revived intense political discussions

in many countries. For example, the Dutch government has expressed its ambition that the Netherlands "lead the way in the international transition with animal-free innovations" [2]. Further, in response [3] to a petition to immediately ban animal research, the European Commission has stated that more investments will be made in the development of alternatives, the goal of which is to ultimately replace all use of animals in research. The European Union directive, combined with political pressure, has mainly resulted in a substantial increase in

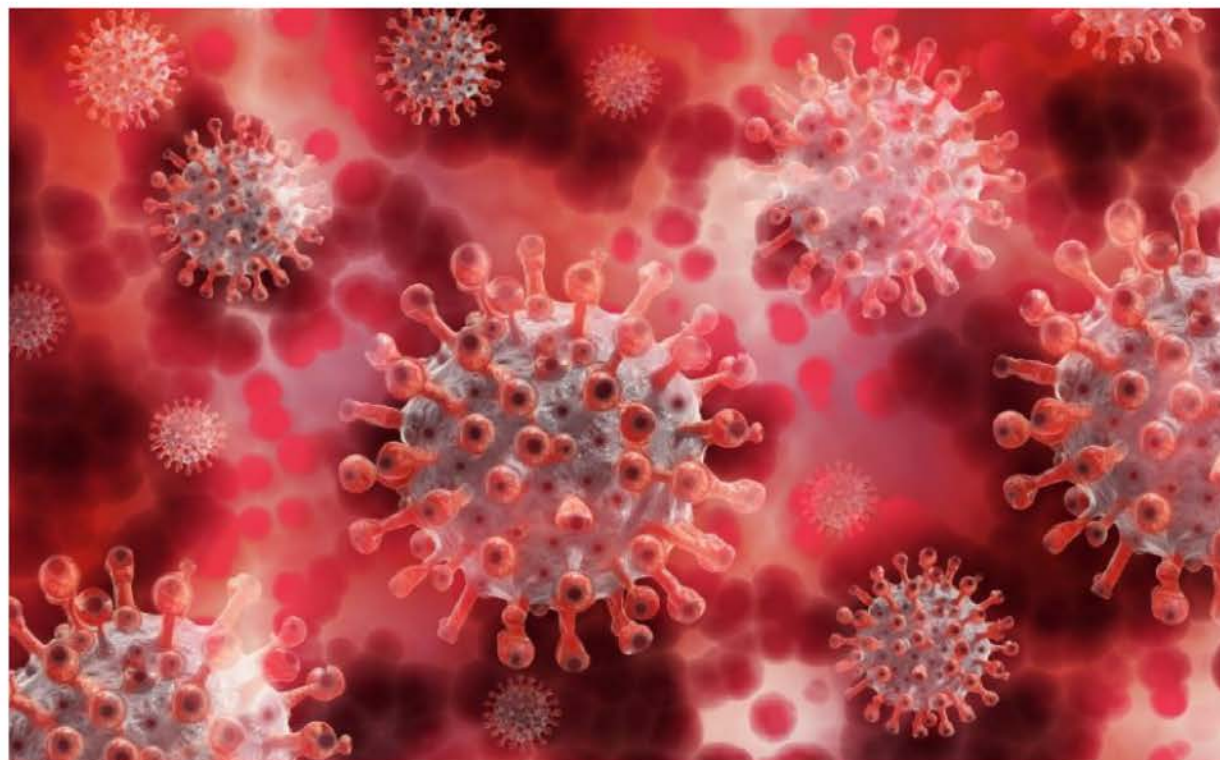
se to antibody



European Animal
Research Association

and animal-derived
have 'serious impact
life-saving drugs'

response to EURL ECVAM Recommendation
Animal-Derived Antibodies, November 2020



9th September 2020

COVID-19: an opportunity to review the bigger picture of animal research

In the first article in a series looking at the current pandemic, FRAME Scientific Liaison Officer Amy Beale discusses the current COVID-19 crisis and how it may provide unique insights into the value of non-animal approaches in vaccine development.

The COVID-19 opportunity

The current COVID-19 pandemic has had a huge impact on our way of life during 2020. Many of us have had to change our routines and habits to help slow down the spread of a virus which is deadly to many and currently has no effective vaccine or treatment. Google tells me



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The EU-Directive is rather clear about the direction



Article 4

Principle of replacement, reduction and refinement

1. Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure.
2. Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.
3. Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.

Article 13

Choice of methods

1. Without prejudice to national legislation prohibiting certain types of methods, Member States shall ensure that a procedure is not carried out if another method or testing strategy for obtaining the result sought, not entailing the use of a live animal, is recognised under the legislation of the Union.



What are the key goals?



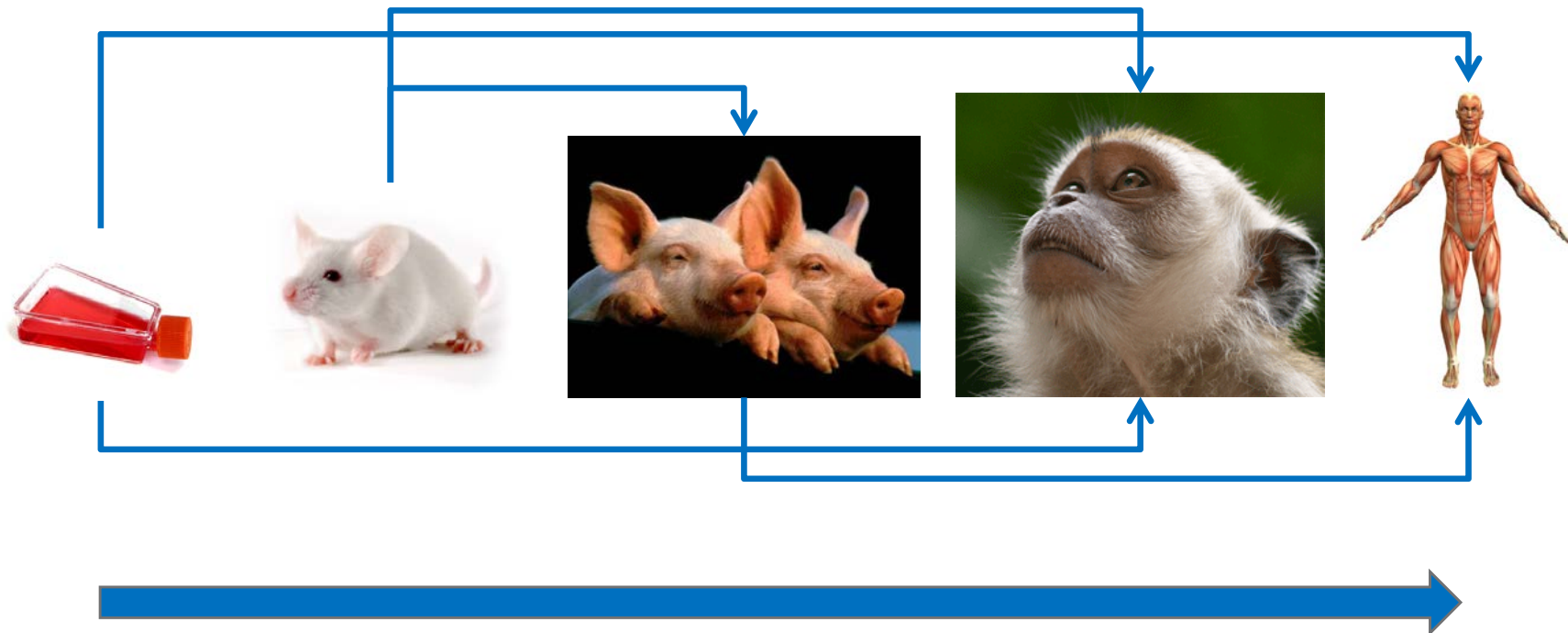
The best science

The least number of animals

The least suffering

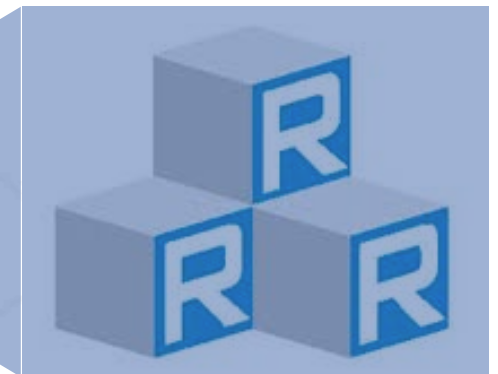
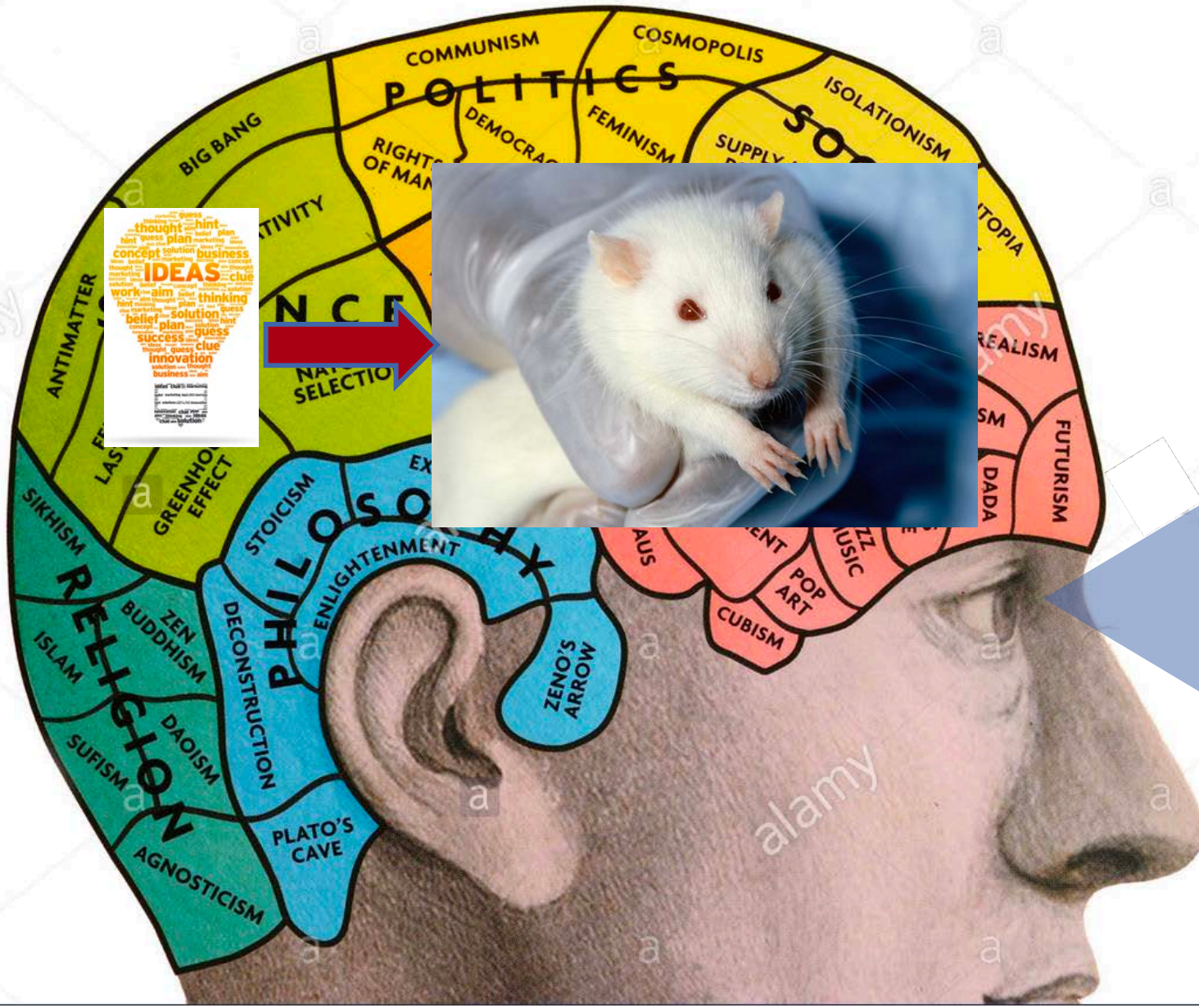
Validity of models, 'translationability' of results ...

"The art of science is to pose a research question
to the right model system"

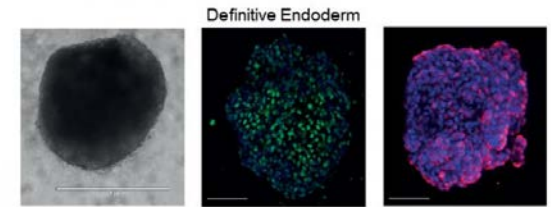


!!! EXTRAPOLATION !!!

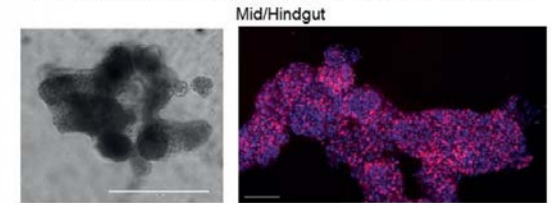
1. Perspective ... ?



2. The choice of model



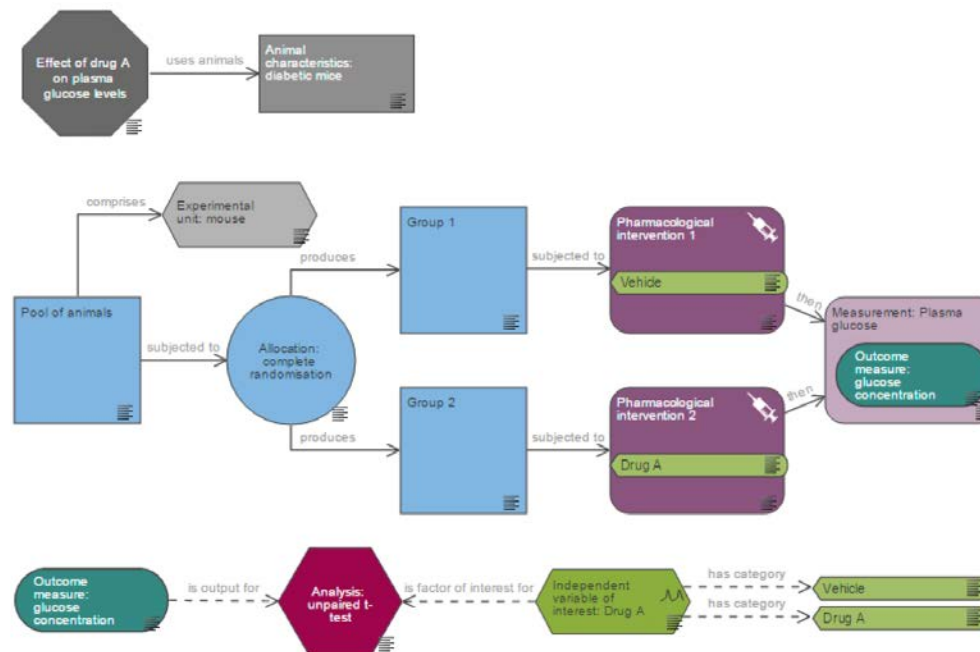
Representative photomicrographs of definitive endoderm spheroids. SOX17 (middle) and CXCR4 (right) expression with Hoechst nuclei counterstain.



Representative photomicrographs of mid/hindgut spheroids. CDX2 stained spheroid with Hoechst nuclei counterstain (right).



3. The methodology



KI-Seminar – Stuart Richie:
"Science Fictions: The Problems of Fraud, Bias,
Negligence and Hype in Science"



Science Fictions

How **FRAUD, BIAS,**
NEGLIGENCE, and
HYPE Undermine the
Search for Truth

**STUART
RITCHIE**



Reproducibility

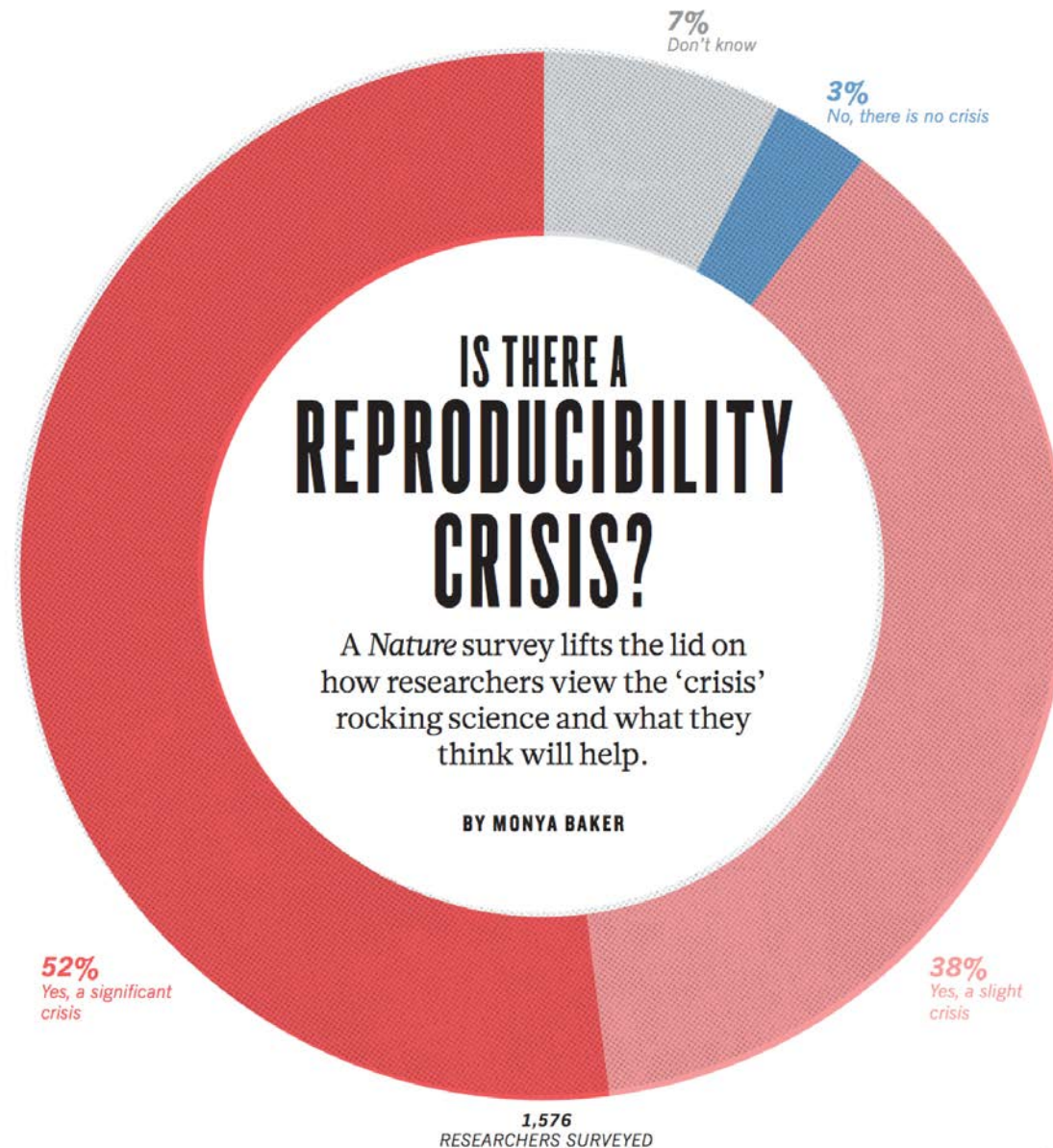
Publication bias

(Forced) retraction

Spin

Questionable research practices

Problems with the science: Reproducibility crisis



Frequency of Crisis Narrative in Web of Science Records

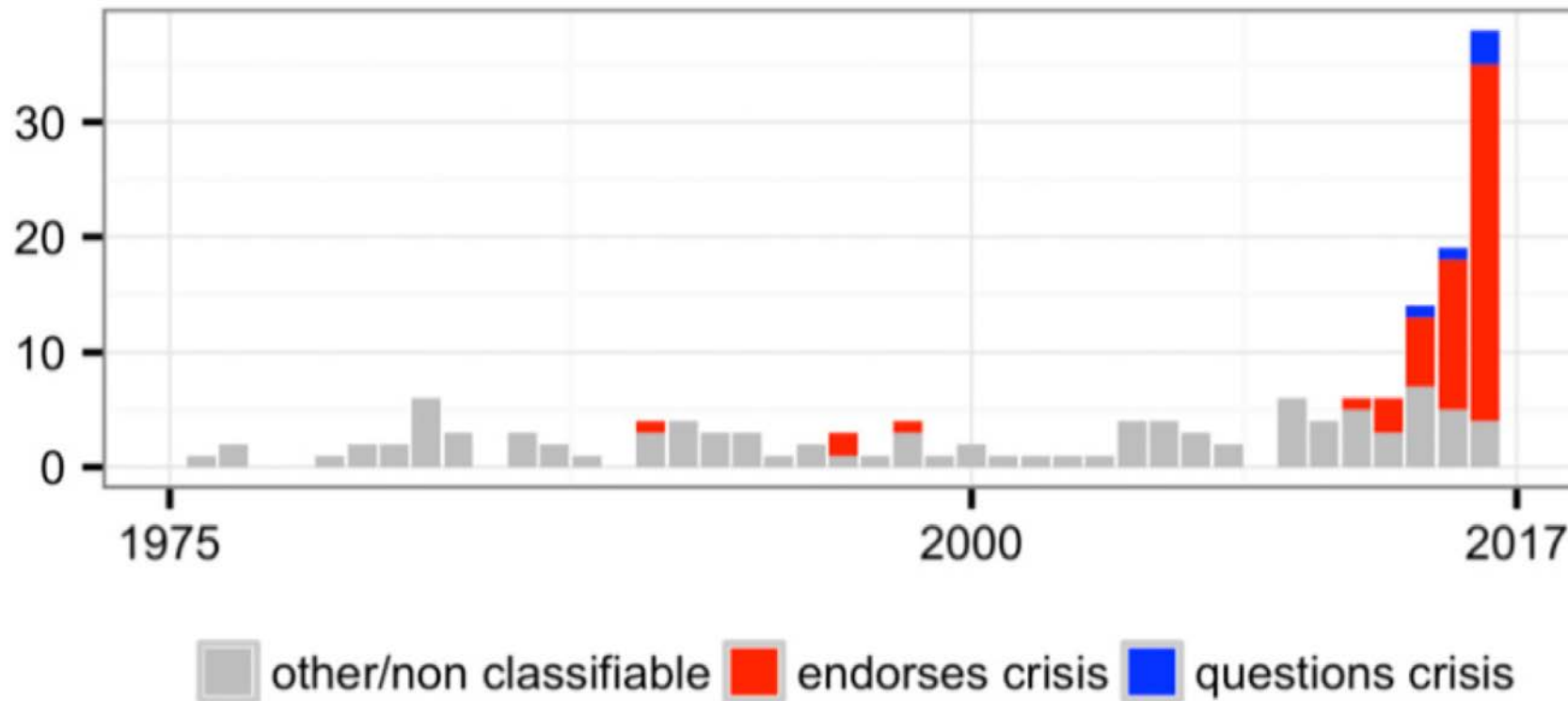
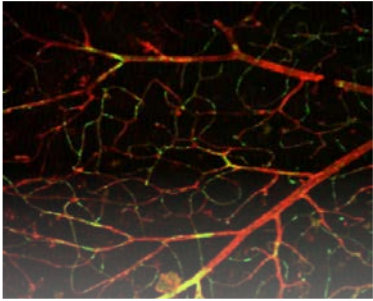


Fig. 1. Number of Web of Science records that in the title, abstract, or keywords contain one of the following phrases: "reproducibility crisis," "scientific crisis," "science in crisis," "crisis in science," "replication crisis," "replicability crisis."

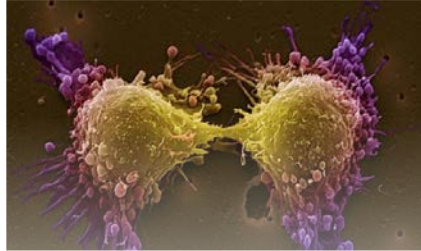
Is science really facing a reproducibility crisis, and do we need it to?

Daniele Fanelli^{a,1}

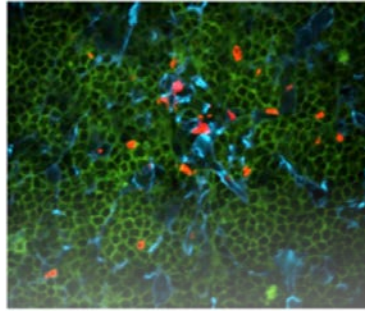
Lab Animal Science is a full-partner of the other sciences!



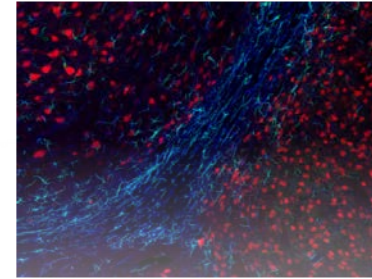
Vascular and
regenerative
medicine



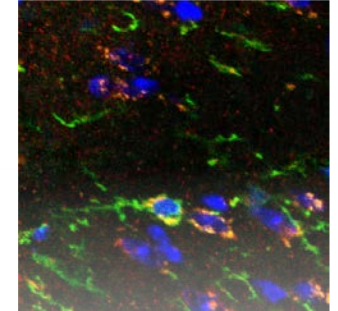
Oncology



Immunity, infection
and tolerance



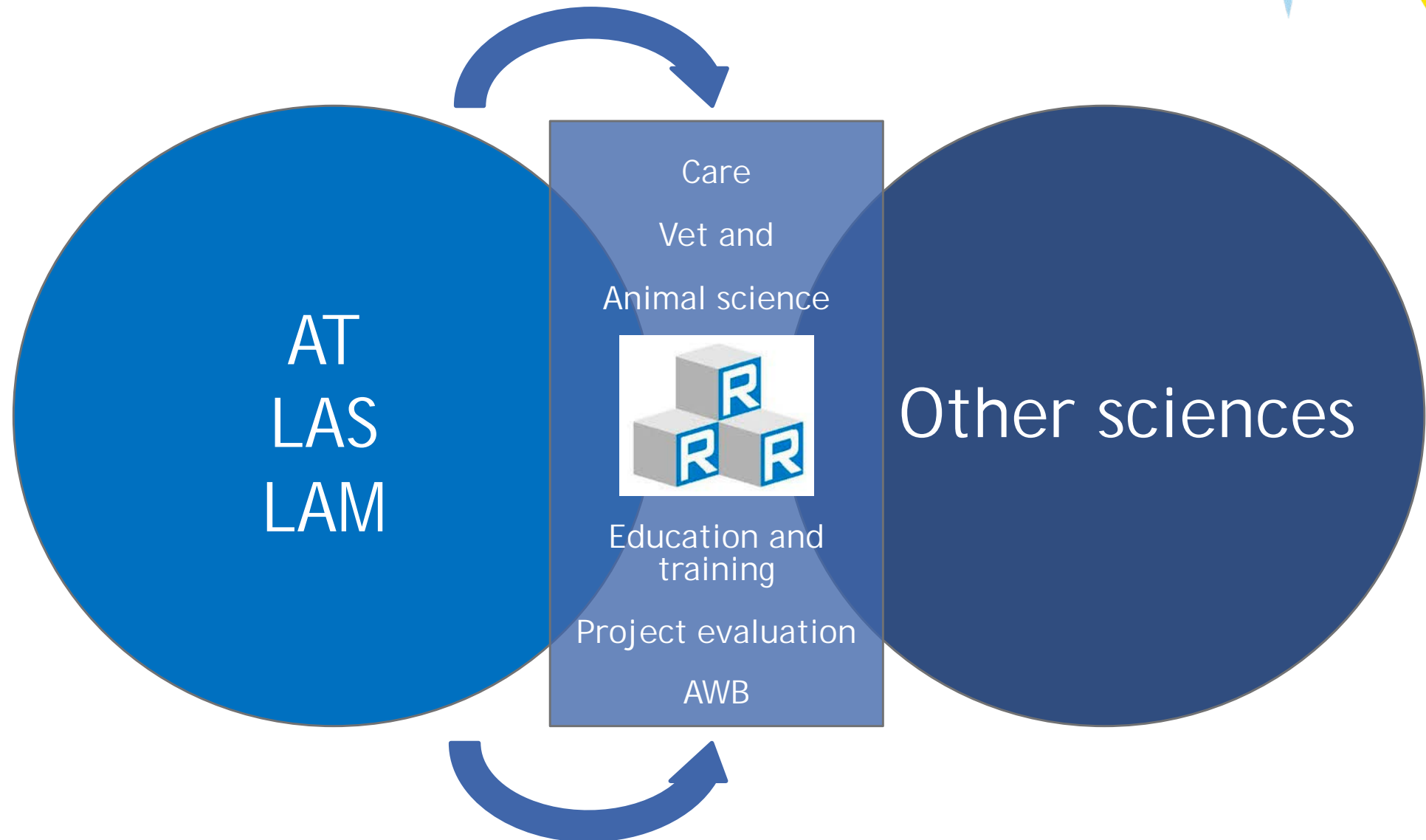
Neuroscience



Ageing and
reproduction



The essential and specific roles of the lab animal scientist, veterinarian, and animal technician



Happy animals make good science

Trevor Poole

Universities Federation for Animal Welfare, 8 Hamilton Close, Potters Bar, Hertfordshire EN6 3QD, UK

Summary

In this paper the question is posed whether it is not only better for the animal to be happy, but whether its state of mind may also have the potential to influence the scientific results derived from it. To ensure good science, the animal should have a normal physiology and behaviour, apart from specific adverse effects under investigation. There is a growing body of evidence from a wide variety of sources to show that animals whose well-being is compromised are often physiologically and immunologically abnormal and that experiments using them may reach unreliable conclusions. On scientific, as well as ethical grounds, therefore, the psychological well-being of laboratory animals should be an important concern for veterinarians, animal technicians and scientists.

Keywords Well-being; laboratory animals; endocrine; immune response; handling; experimental method





Send in the germs

Lab mice are usually kept squeaky clean, but some immunologists think a dose of dirt could make them more useful for science.

BY CASSANDRA WILLYARD

On an unseasonably warm February morning, Mark Pierson takes a 20-minute drive to one of Minneapolis's larger pet shops. Pierson, a researcher in an immunology laboratory at the University of Minnesota, often comes here to buy mice, so most of the staff know him. Today he asks for ten, and an employee fishes them out of a glass box. Pierson requests the smaller mice because they're typically younger, but he isn't too picky. They probably all have what he wants: germs.

These mice are about to enter one of the most tightly controlled labs in the country, a facility normally reserved for studying dangerous pathogens such as tuberculosis and chikungunya virus. The rodents probably don't carry serious human infections, but they do harbour

ILLUSTRATION BY ODESA HERBA

Overview

To Treat or Not to Treat: The Effects of Pain on Experimental Parameters

Norman C Peterson,^{1,*} Elizabeth A Nunamaker,² and Patricia V Turner³

A common dilemma faced by all animal bioethics committees arises when exceptions are proposed to the use of analgesics in painful procedures. The committee and researcher must weigh the possible confounding effects of including additional drugs (analgesics) in their treatment regimen against the moral obligation to perform humane research. Often neglected in these considerations are the potential confounding effects of unrelieved pain and consistency with pain-relieving practices in human medicine. In this review, we summarize what is currently known regarding the molecular and physiologic effects of pain and analgesics in common animal models used across several therapeutic areas. This work is intended to help provide guidance and assurance that a comprehensive approach has been taken when contemplating how pain relief will be applied in animal research protocols.

Abbreviations: CLP, cecal ligation and puncture; TBSA, total body surface area

e health

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PLOS ONE

RESEARCH ARTICLE

Rat tickling: A systematic review of applications, outcomes, and moderators

Megan R. LaFollette^{1,*}, Marguerite E. O'Haire², Sylvie Cloutier³, Whitney B. Blankenberger⁴, Brianna N. Gaskill¹

1 Department of Animal Sciences, Center for Animal Welfare Science, College of Agriculture, Purdue University, West Lafayette, Indiana, United States of America, **2** Department of Comparative Pathobiology, Center for the Human-Animal Bond, College of Veterinary Medicine, Purdue University, West Lafayette, Indiana, United States of America, **3** Canadian Council on Animal Care, Assessment and Accreditation Section, Ottawa, ON, Canada, **4** Department of Comparative Medicine, Stanford University, Stanford, California, United States of America

* meglafollette@gmail.com

Weninger, J., Wilcke, J., 2017, 9, 10,

Original Article

A comparison of various methods of blood sampling in mice and rats: Effects on animal welfare

VS Harikrishnan^{1,2}, Axel K Hansen², Klas SP Abelson³ and Dorte B Sørensen²



Laboratory Animals
0101 1–12
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SAGE



PERSPECTIVES

Reproducibility of animal research in light of biological variation

Bernhard Voelkl , Naomi S. Altman , Anders Forsman , Wolfgang Forstmeier , Jessica Gurevitch , Ivana Jaric , Natasha A. Karp , Martien J. Kas , Holger Schielzeth , Tom Van de Castele and Hanno Würbel

Abstract | Context-dependent biological variation presents a unique challenge to the reproducibility of results in experimental animal research, because organisms' responses to experimental treatments can vary with both genotype and environmental conditions. In March 2019, experts in animal biology, experimental design and statistics convened in Blonay, Switzerland, to discuss strategies addressing this challenge. In contrast to the current gold standard of rigorous standardization in experimental animal research, we recommend the use of systematic heterogenization of study samples and conditions by actively incorporating biological variation into study design through diversifying study samples and conditions. Here we provide the scientific rationale for this approach in the hope that researchers, regulators, funders and editors can embrace this paradigm shift. We also present a road map towards better practices in view of improving the reproducibility of animal research.

Effects of Cage Enrichment on Behavior, Welfare and Outcome Variability in Female Mice

Jeremy D. Bailoo ^{1*}, Eimear Murphy ¹, Maria Boada-Sañá ¹, Justin A. Varholick ¹, Sara Hintze ², Caroline Baussière ¹, Kerstin C. Hahn ³, Christine Göpfert ³, Rupert Palme ⁴, Bernhard Voelkl ¹ and Hanno Würbel ¹

¹Division of Animal Welfare, Veterinary Public Health Institute, University of Bern, Bern, Switzerland, ²Division of Livestock Sciences, Department of Sustainable Agricultural Systems, University of Natural Resources and Life Sciences Vienna (BOKU), Vienna, Austria, ³Institute for Animal Pathology, University of Bern, Bern, Switzerland, ⁴Department of Biomedical Sciences, University of Veterinary Medicine Vienna, Vienna, Austria

SCIENTIFIC REPORTS

nature research



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Effects of weaning age and housing conditions on phenotypic differences in mice

Jeremy D. Bailoo ^{1,2,3,4}, Bernhard Voelkl ¹, Justin Varholick ^{1,4}, Janja Novak ¹, Eimear Murphy ⁵, Marianna Rosso ¹, Rupert Palme ⁶ & Hanno Würbel ^{1,3}

Poor reproducibility is considered a serious problem in laboratory animal research, with important scientific, economic, and ethical implications. One possible source of conflicting findings in laboratory animal research are environmental differences between animal facilities combined with rigorous environmental standardization within studies. Due to phenotypic plasticity, study-specific differences in environmental conditions during development can induce differences in the animals' responsiveness to experimental treatments, thereby contributing to poor reproducibility of experimental results. Here, we studied how variation in weaning age (14–30 days) and housing conditions (single versus group housing) affects the phenotype of SWISS mice as measured by a range of behavioral and physiological outcome variables. Weaning age, housing conditions, and their interaction had little effect on the development of stereotypies, as well as on body weight, glucocorticoid metabolite concentrations, and behavior in the elevated plus-maze and open field test. These results are surprising and partly in conflict with previously published findings, especially with respect to the effects of early weaning. Our results thus question the external validity of previous findings and call for further research to identify the sources of variation between replicate studies and study designs that produce robust and reproducible experimental results.

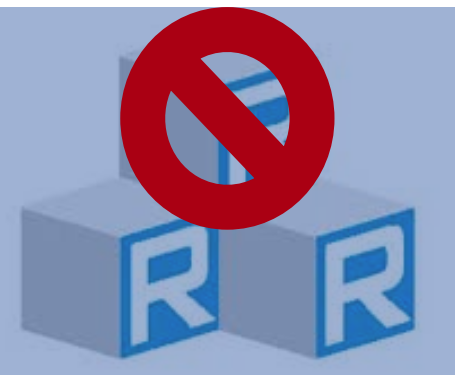
The 3Rs



W.M.S. Russell and R.L. Burch
(1959) The principles of
humane experimental
techniques

Reduction
Refinement

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Scientific Conference: Non-Animal Approaches - The Way Forward

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Brussels, 6-7 December 2016

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Transition to non-animal research

*on opportunities for the phasing out of
animal procedures and the stimulation
of innovation without laboratory
animals*

Opinion of the Netherlands National Committee for the
protection of animals used for scientific purposes (NCad)



Netherlands National Committee
for the protection of animals
used for scientific purposes



Every animal was here for
good reason experiencing
maximum welfare (given the
circumstances)!



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