

WC11 Virtual Congress



Breaking the lock-in to animal research within academia

Dr Pandora Pound
Safer Medicines Trust, UK

Session: Animal Experimentation: Working Towards a Paradigm Change

The problem

Animal research has failed to:

- Reduce human suffering – huge unmet need – chronic illnesses for which no treatments
- Safeguard humans – medicines tested on animals go on to cause ADRs etc

At same time:

- Increasing public unease about animal research
- Flourishing of new approach methodologies (NAMs)

BUT proving difficult to replace animal research with NAMs – AR is locked-in

- Focus on *academia*



Plan of talk



- What is lock-in?
- How animal research became locked in within academia
- Breaking lock-in

Technology becomes locked in due to positive feedback, regardless of worth

Technological:

- e.g. data, experience, off the shelf methodologies etc. accumulated from prior animal experiments

Institutional:

- enormous industry with key beneficiaries protecting interests
- massive infrastructure
- academics conforming to discipline norms rewarded

Psychological

- Desire to believe research is morally justified
- Belief becomes entrenched due to continually defending it



Research Article

Tradition, Not Science, Is the Basis of Animal Model Selection in Translational and Applied Research

Désirée H. Veening-Griffioen¹, Guilherme S. Ferreira¹, Wouter P. C. Boon², Christine C. Gispen-de Wied³, Huub Schellekens¹, Ellen H. M. Moors² and Peter J. K. van Meer^{1,4}

¹Utrecht Institute of Pharmaceutical Sciences, Utrecht, The Netherlands; ²Copernicus Institute of Sustainable Development, Utrecht, The Netherlands; ³Gispen/RegulatoryScience, advies en educatie, Bilthoven, The Netherlands; ⁴Medicines Evaluation Board, Utrecht, The Netherlands

Abstract

National and international laws and regulations exist to protect animals used for scientific purposes in translational and applied research, which includes drug development. However, multiple animal models are available for each disease. We evaluated the argumentation behind the selection of a specific animal model using thematic content analysis in project applications issued in 2017-2019 in the Netherlands. In total, 125 animal models for translational and applied



How it happened: seen as 'hard science'



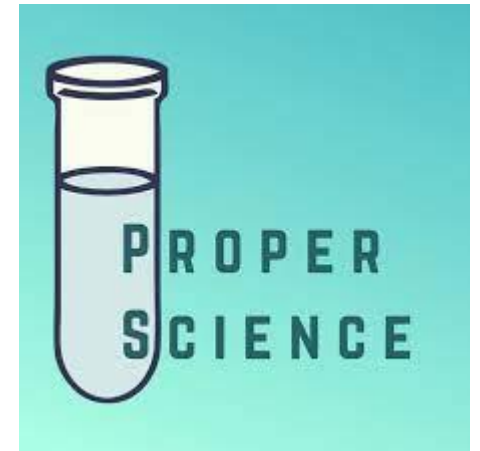
Physiologist Claude
Bernard 1813-1878

- Wanted to place physiology on firm scientific footing
- Believed:
 - Biomedical science should be conducted in lab
 - In testable hypotheses
 - Animal experiments relevant to humans
 - Species differences are differences of degree only
- Rejected evolutionary theory
- Academic animal research still under Bernard's influence



How it happened: little challenge from fellow academics

- Animal experiments:
 - created distance from patient's bedside, making biomedicine 'more scientific'
 - acquired a scientific veneer (statistics etc)
 - came to be seen as robust scientific approach
- Consequent reluctance to criticise/ challenge the practice – still clearly evident within academia
- Lacking challenge from fellow academics those conducting animal research have free rein within their universities



How it happened: insularity



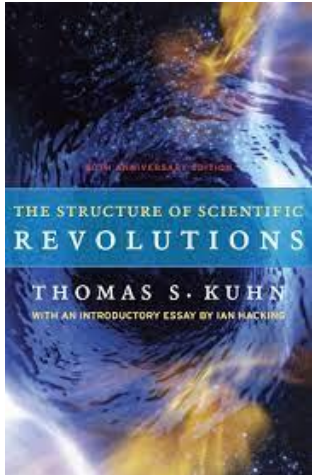
- Specific nature of animal research creates insularity:
 - secrecy – access to labs / info tightly controlled
 - lack of collaboration across disciplines
 - little exposure to external influences/ ideas
- Difficult for to reach/ influence/ challenge academics in ivory tower

Unreceptive to innovation

- Many animal researchers within academia don't perceive need for NAMs
- Universities unreceptive to change - NAMs seen as disruptive



Breaking lock-in: emphasise species differences



- Failure to translate a significant anomaly for preclinical animal research
- Kuhn: when faced with anomalies, scientists modify theory to eliminate conflict

BUT anomalies must reveal real inadequacy to provoke radical change

- Reproducibility crisis regarded as superficial issue that can be resolved
- Species differences more challenging because insurmountable

Breaking lock-in: emphasise species differences

'Every lineage has undergone its own independent history of adaptation and specialisation. Every species is special. That's why we call them species. It's the same root for the same reason. (...) So this idea that a given species is somehow representative of all other species is very difficult to rationalise based on modern evolutionary principles.'

Todd Preuss, Professor of Pathology, Emory University School of Medicine, Atlanta



Breaking lock-in: emphasise species differences



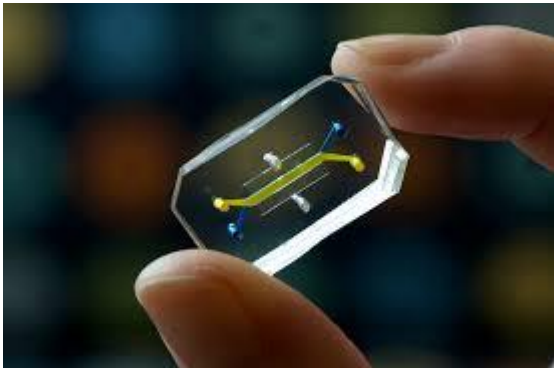
- Even if quality issues resolved, species differences would still make extrapolation to humans unreliable
- Issue of species differences reveals *the* fundamental inadequacy in paradigm

BUT insufficiently acknowledged as serious anomaly

- Vital to highlight tension between AR's mechanistic paradigm and evolutionary theory
- Highlight that ignoring species differences violates accepted, basic biological principles / shows disregard for evolutionary theory

Breaking lock-in: role of NAMs

Kuhn: a paradigm will only be declared invalid if an alternative paradigm available to take its place



- To be successful, alternative paradigm will need to solve problems that prompted crisis (lack of predictivity to humans)
- Will be persuasive if permits prediction of unsuspected phenomena, i.e. knowledge not possible to obtain within old paradigm
 - *if NAMs can do this we need to highlight examples*
- NAMs have to be valid, robust, reproducible and properly reported

Breaking lock-in: the need for dialogue

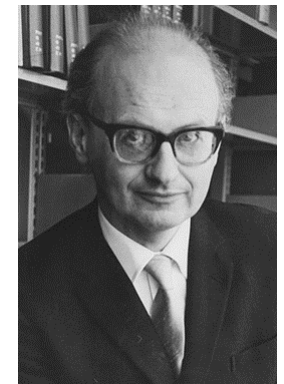


- Appeal to what animal researchers and NAMs developers may have in common – desire to advance human medicine
- Attend AR conferences to network/ open channels of communication/ thrash things out/ debate/ exchange views
- Organise friendly discussions, workshops, invite animal researchers to NAMs conferences, offer to give talks within universities
- Be imaginative – take inspiration from Dutch Helpathons
- Explore sticking points (e.g. arguments re intact systems)



Breaking lock-in: is it already happening slowly?

- Slow pace is not surprising – scientific revolutions / adoption of innovations take time
- Animal research *is* in decline
 - A research programme in decline is unable to extend to new cases – it's only advances relate to existing problems (Imre Lakatos, philosopher of science)
- Academics ruled by funding, so vital to push to divert funding from AR to NAMs
 - Most AR is blue-skies research, but funding increasingly impact-based - 'demonstrable impact' now the goal – potentially problematic for previously dominant academics
 - blue skies research may become increasingly less fundable



*Lakatos & Musgrave
1970: Criticism and
the growth of
knowledge*

Breaking lock-in: conclusions

To accelerate process:



- Emphasise ability of NAMs to discover new phenomena not predicted by animal research
- Ensure NAMs research & reporting practices watertight
- Open channels of communication with academic animal researchers
- Continue push for diversion of funding towards NAMs / away from animal research
- Stress animal research involves rejection of evolutionary theory - unacceptable in 21st century

Thank you

pandora@safermedicines.org

