

Animal use in research – opportunities for replacement

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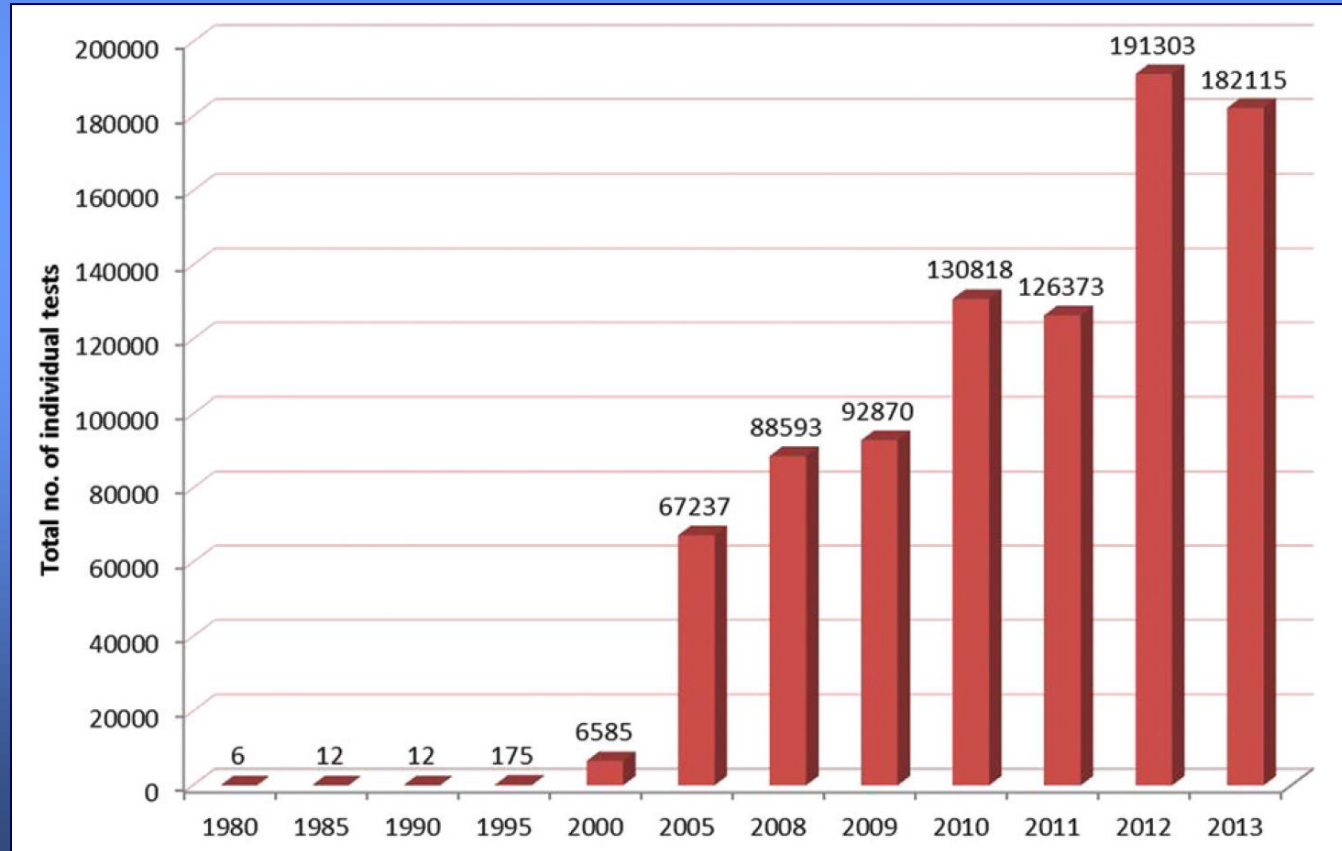
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Opportunities for replacement

- The good news
- The not quite so good news
- What we can do

The good news

Use of *in vitro* tests (1980 – 2013)



The good news

Single dose acute studies in animals prior to human clinical trials (UK)

2007	2011	2012	2013
86% (67/78)	58% (76/132)	20% (27/134)	16% (15/93)

The good news

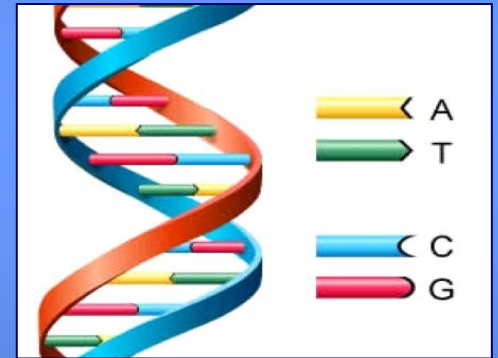
Human genome sequencing

Then:

- \$1,000,000,000
- 13 years
- International collaboration

Now:

- \$1,000
- A few hours
- 1 machine



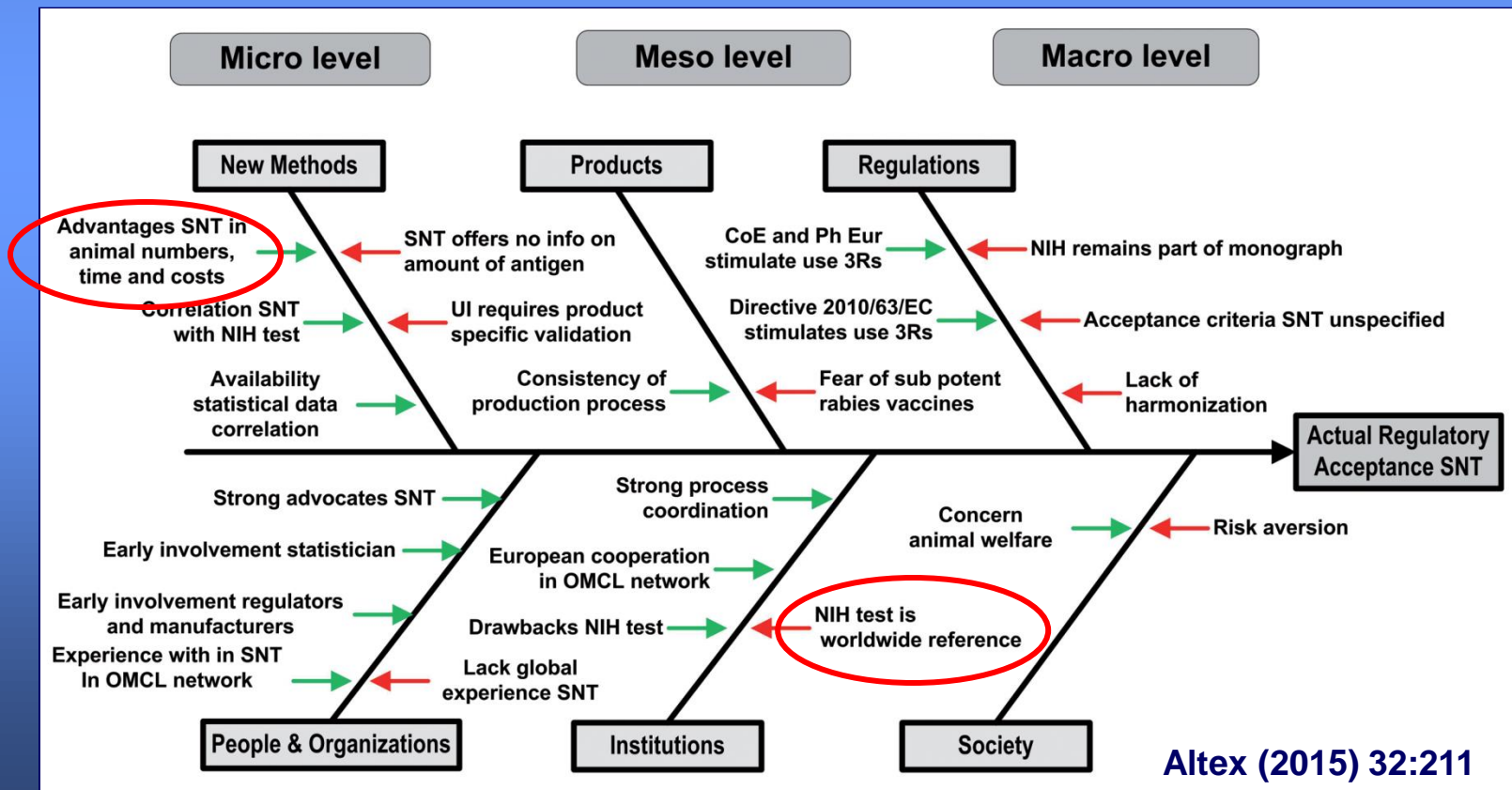
The good news

Vaccine safety & potency testing

- Now replaced: Hepatitis-B, rabies, Newcastle disease, diphtheria, tetanus
- New applications for 'old technology'

The good news

Vaccine safety & potency testing



The good news

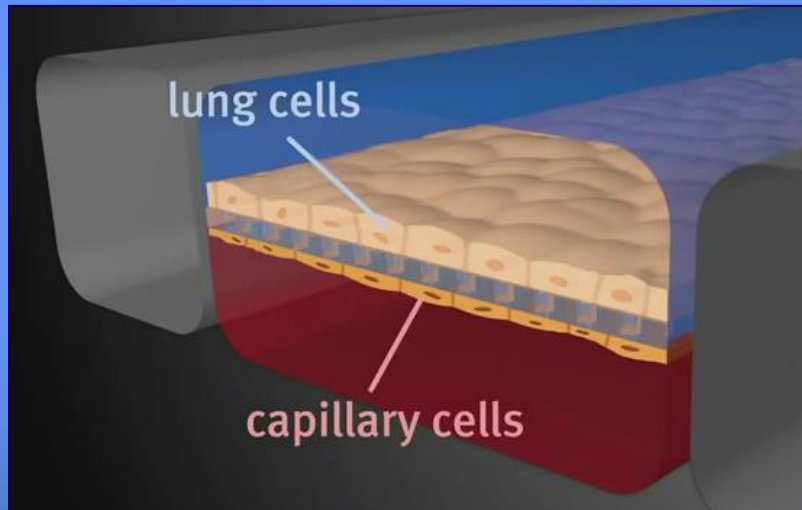
Organ-on-a-chip

- Human cells
- Multiple cell types in 3D:
 - e.g. lung and blood vessel
- Flowing media:
 - Nutrients or drug delivery
 - Waste removal
 - Exposure to infection
- Movement:
 - Breathing or peristalsis
- Mass production with 3D printing (Nature Protocols (2013) 8, 2135)

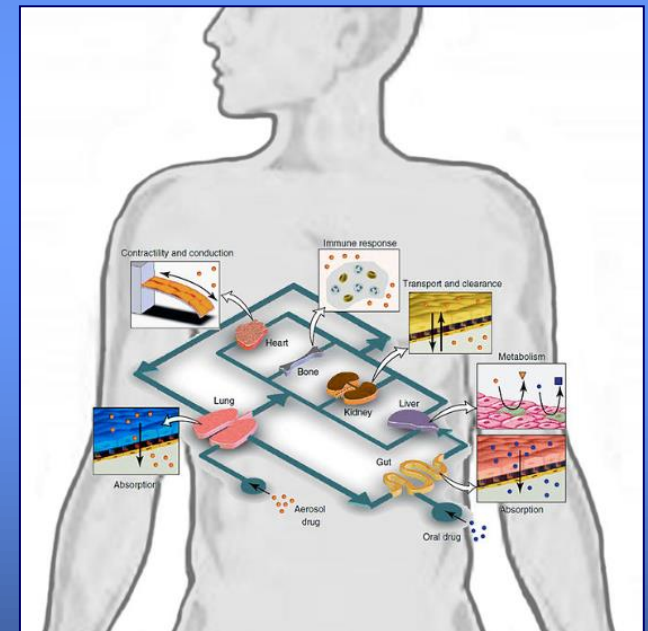


The good news

Organ-on-a-chip



Wyss Institute



Timothy Ruban

The good news

Organ-on-a-chip



The image shows a screenshot of a Business Insider Australia article. The header includes the logo and navigation tabs for Tech, Money & Markets, Briefing, Ideas, Executive Life, and Video. The article title is "A promising futuristic device is already starting to change medicine" by Ellie Kincaid, dated July 17, 2015. Social media sharing buttons for Facebook (5) and Twitter (8) are visible. The article content is partially obscured by a blue promotional banner for a World Congress event.

BUSINESS INSIDER AUSTRALIA

Tech Money & Markets Briefing Ideas Executive Life Video Search

BRIEFING: SMARTER HEALTH PARTNER SERIES

A promising futuristic device is already starting to change medicine

ELLIE KINCAID JUL 17 2015, 6:16 AM 84

f FACEBOOK 5 t TWITTER 8

SELECTBIO

ORGAN-ON-A-CHIP

World Congress

& 3D-Printing in the Life Sciences

8 - 9 July 2015 • Boston, MA, USA

The good news

Online resources: AltWeb



The screenshot displays the AltWeb website interface. At the top left is the Johns Hopkins Bloomberg School of Public Health logo. The main header features the 'ALT WEB' logo and a background image of petri dishes with orange agar. Below the header is the tagline: 'the global clearinghouse for information on alternatives to animal testing'. A left sidebar contains a search bar and a navigation menu with the following items: HOME, ABOUT US, RESOURCES, ALTEX, FEATURED ITEMS, PUBLICATIONS, and NEWSLETTER. The main content area features a banner for the 'Symposium on Social Housing of Laboratory Animals' held in March 2016 at UC Davis, CA, with images of mice and rabbits. Below this is a box for the 'LinZ 2015' event, the 19th European Congress on Alternatives to Animal Testing, organized by EUSAAT (European Society for Alternatives to Animal Testing) and The European 3Rs Society, held from September 20-23, 2015, at the University of Linz, Austria.

JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

ALT WEB

the global clearinghouse for information on alternatives to animal testing

SEARCH ALTWEB

HOME ▶

ABOUT US ▶

RESOURCES ▶

ALTEX ▶

FEATURED ITEMS ▶

PUBLICATIONS ▶

NEWSLETTER ▶

Symposium on Social Housing of Laboratory Animals March 17-18, 2016 UC Davis, CA

LinZ 2015
19th European Congress on Alternatives to Animal Testing

EUSAAT
European Society for Alternatives to Animal Testing

EUSAAT 2015
15th Annual Congress of EUSAAT

The European 3Rs Society

20 – 23 September 2015, University of Linz, Austria

The good news

Online resources: AltWeb

Specific databases

- AltTox
- DB-ALM
- ECVAM
- ICCVAM
- INVITTOX

General databases:

- CAB
- Jax
- PubMed

The good news

Online resources: NC3Rs

The screenshot displays the NC3Rs website interface. At the top left is the logo for the National Centre for the Replacement, Refinement & Reduction of Animals in Research. To the right are links for 'Login' and 'Register', and social media icons for LinkedIn, Twitter, Facebook, and YouTube. A search bar is positioned below these links. A horizontal navigation menu includes 'The 3Rs', 'Our science', 'Our resources', 'Funding', 'News', 'Events', and 'About us'. The main content area features three cards: a large image of laboratory equipment with a text box for the 'Non-Animal Technologies Special Interest Group', a card for 'ShARM: Shared Ageing Research Models' with a mouse image, and a card for 'Our resources' with an image of a laboratory cage.

NC 3Rs
National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

Login | Register

in | | f | You Tube

Search this site

Home | The 3Rs | Our science | Our resources | Funding | News | Events | About us

**Non-Animal Technologies
Special Interest Group**
Connecting the research and business
communities in the development of
technologies for more predictive efficacy
and safety testing.

**ShARM: Shared Ageing
Research Models**

Our resources

The good news

Online resources: [NC3Rs](#)

Technical information and training

Grants:

- Project grants
- Pilot studies
- Studentships
- Fellowships
- Infrastructure

Business case

The good news

Online resources: Animal Ethics Infolink

ANIMAL ETHICS INFOLINK

A NSW Department of Primary Industries and Animal Research Review

Home

Legislation

Australian Code

Accreditation and licensing

Three Rs »

Replacement

Replacement as one of the 3R's is higher animals of insentient mater

Medical Advances Without Animals Trust (MAWA)
www.mawa-trust.org.au/index.html

Fund for Replacement of Animals in Medical Experiments (FRAME)
www.frame.org.uk

The Centre for Alternatives to Animal Testing (CAAT)
<http://caat.jhsph.edu>

The European Centre for the Validation of Alternative Methods (ECVAM)
<http://ecvam.jrc.it/index.htm>

UC Davis Center for Animal Alternatives
www.vetmed.ucdavis.edu/Animal_Alternatives/main.htm

ALTWEB - news, information, discussion and resources from the field of alternatives to animal testing
<http://altweb.jhsph.edu>

Peta International Science Consortium
www.piscltd.org.uk

Alternative databases / searching for alternatives

The ECVAM Search Guide

A detailed guide, developed for untrained database users, to find high quality information on alternatives of animals in research.

<http://bookshop.europa.eu/en/the-ecvam-search-guide-pbLBNA24391>

NORINA

<http://oslovet.veths.no/NORINA/>

Interagency Coordinating Committee on the validation of Animal Models (ICCVAM)
<http://iccvam.niehs.nih.gov/>

The good news

Human clinical trials

**NHMRC Project Grants
Funding for top 100 grants**

- Human Trials
- Other Projects



The not quite so good news

Animal use in research

Animal use, citation or animal products

Nature Medicine

100%



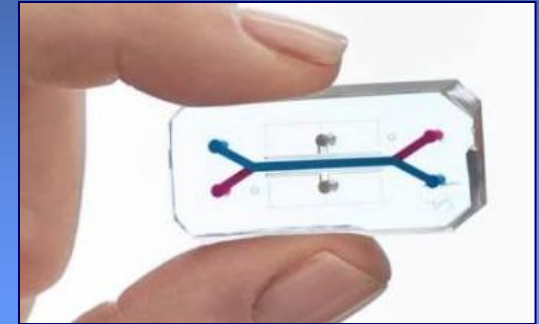
New England J Med

42%



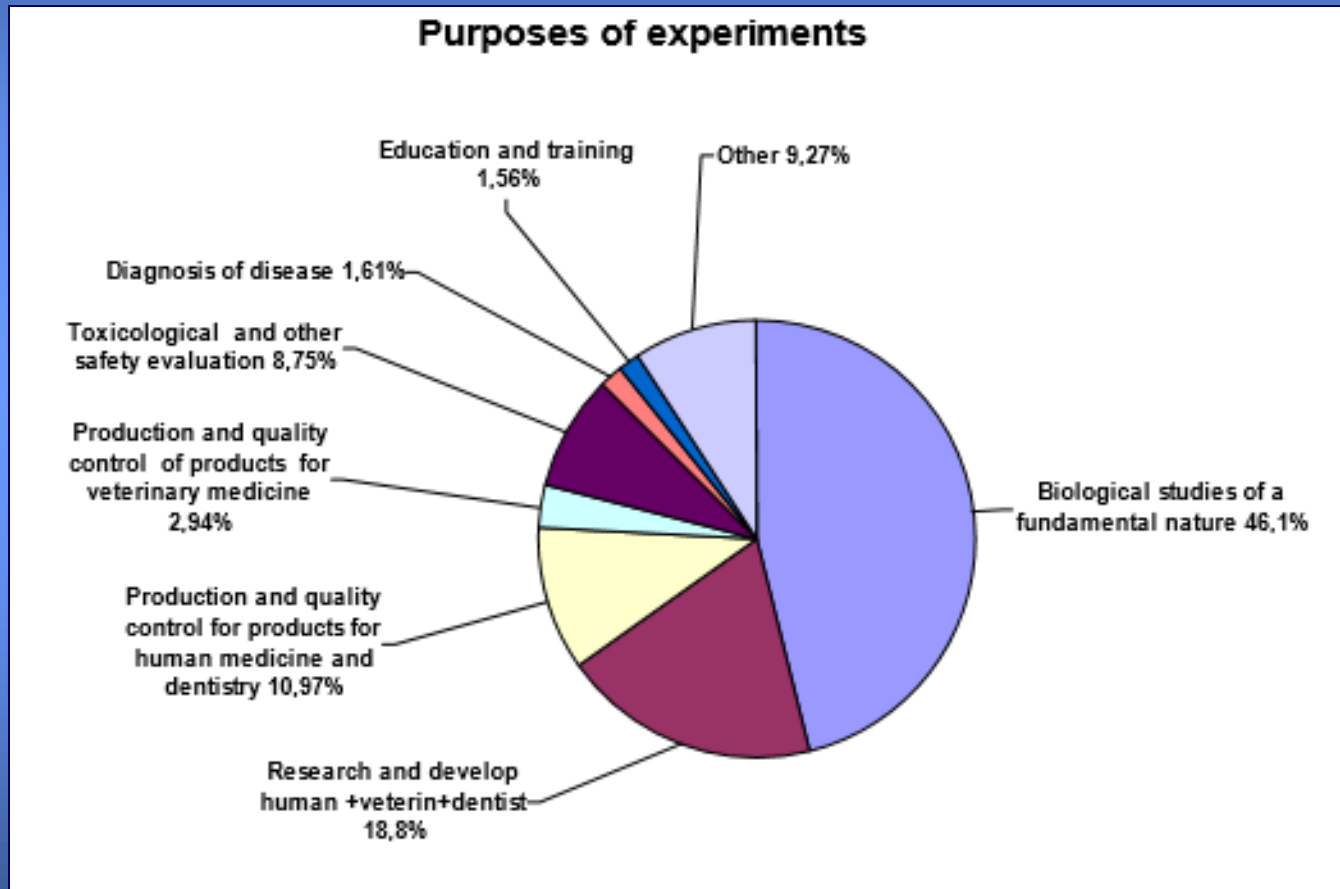
The not quite so good news

Organ-on-a-chip



- “What we’re **not building** is **complete organs**. We’re building the smallest amount of an organ that delivers a functional response.”
- “This is **not going to replace all animal models**...” Don Ingber
- “...**not necessarily cheaper** than animal experiments...”
- “[**Will require**] **integrated approaches** using 2D and 3D in vitro methods, as well as bioinformatics” Altex 31, 4/14

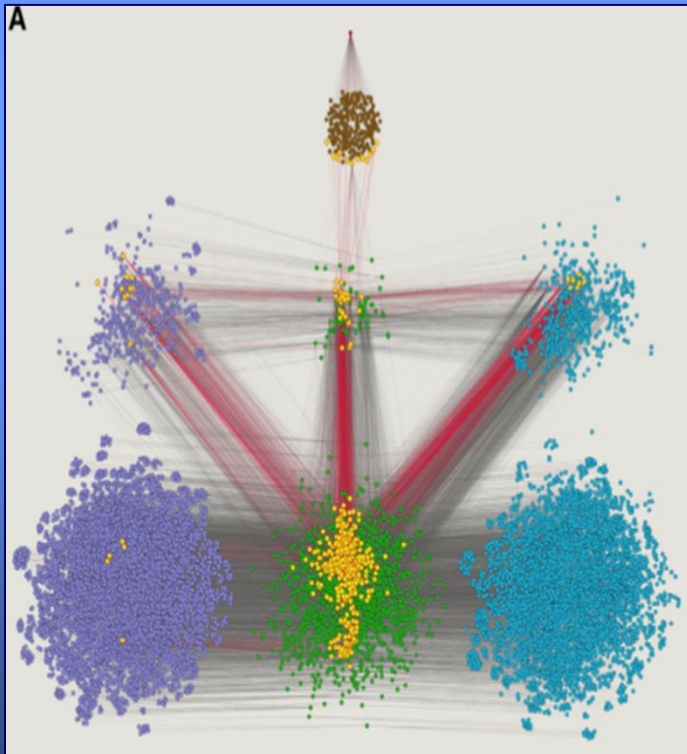
The not quite so good news



European Commission 2013

The not quite so good news

The tortuous path from bench to bedside



From Scientific Discovery to Cures: Bright Stars within a Galaxy

R. Sanders Williams,^{1,2,*} Samad Lotia,¹ Alisha K. Holloway,^{1,2} and Alexander R. Pico¹

Cell (2015) 163, 21

- 1 drug
- 7,000 Scientists
- 5,600 institutional departments
- 104 years

The not quite so good news

Papers from an 'Alternatives' journal

- *Dissociation of E-cadherin/ β -catenin complex by MG132 and bortezomib enhances CDDP induced cell death in oral cancer SCC-25 cells.*
- *Effect of the ostreolysin A/pleurotolysin B pore-forming complex on intracellular Ca^{2+} activity in the vascular smooth muscle cell line A10.*
- *N-acetyl cysteine protects human oral keratinocytes from Bis-GMA-induced apoptosis and cell cycle arrest by inhibiting reactive oxygen species-mediated mitochondrial dysfunction and the PI3K/Akt pathway.*

The not quite so good news

Conclusions (thus far)

- Current alternatives focus on toxicology, drug and vaccine development
- Reductionist approach is unavoidable
- Integrated approach is required
- Complicated

What we can do

Institutional incentives and support



The screenshot shows the University of Sydney's Research Support page. On the left is the university's crest and logo. Below it is a navigation menu for 'ANIMAL ETHICS' with links to 'What is ethics approval?', 'Who approves: Committee', 'Alternatives to using animals', and 'Award for reduction in the use of animals in research'. The main content area is titled 'AWARD FOR REDUCTION IN THE USE OF ANIMALS IN RESEARCH'. It states that the Australian Code for the Care and Use of Animals for Scientific Purposes requires techniques that replace animal use wherever possible. The university offers an award to recognize research that shows potential to reduce or replace animal use. Applicants must meet eligibility criteria and follow specific procedures. Applications close on Friday 30 October 2015.

- Interstate:
 - University of Western Australia: 3Rs Award (\$5k)
 - University of Melbourne: Ethics and Integrity Development Grant scheme (up to \$15k)

What we can do

(Human) Tissue banking



What we can do

(Human) Tissue banking Sydney Heart Bank

20,000 human cardiac samples

Collaborations with 12 institutions in Australia and 25 overseas

- Ischaemic Cardiomyopathy
- Dilated Cardiomyopathy
- Hypertrophic Cardiomyopathy
- Restrictive Cardiomyopathy
- Alcohol induced Cardiomyopathy
- Virus induced Cardiomyopathy
- Peripartum Cardiomyopathy
- Adriamycin induced Cardiomyopathy
- Others (Marfan, Sarcoid, Myocarditis, Eisenmengers, Rheumatic, Valvular)

MAWA Trust



ABOUT THE MAWA TRUST
DEVELOPING ALTERNATIVES TO ANIMAL RESEARCH

- “Work together with scientists for change”
- Scientific Advisory Panel
- Partnership with ANU
- Grants programs

MAWA Program	Support
Honours Research	\$10,000
Masters Research	\$10,000
Doctoral Research	\$75,000
Supplementary (NHMRC, APA)	\$10,000
Bridging	\$7,000
Research & Development Grant	\$30,000
Equipment Grant	\$30,000
Tissue banking	\$30,000
Fellowships	Salary & costs
ANU Partnership	On applic'n
Distinguished Scholars	On applic'n
Travel Bursaries	On applic'n
Conference Bursaries	On applic'n
Educational initiatives	On applic'n

What about the cost?

“The true cost of a test should be measured by the probability that a wrong decision is made”

Altex (2014) 31, 464

Thanks to...

Ms Sharyn Watson

MAWA Trust

Prof Tim Morris

University of Nottingham

Guest speaker, ANZLAA 2015