Animal use in research – opportunities for replacement

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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)

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
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<tbody>
<tr>
<td></td>
<td>86%</td>
<td>58%</td>
<td>20%</td>
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<td>(67/78)</td>
<td>(76/132)</td>
<td>(27/134)</td>
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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 good news

Online resources: AltWeb
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 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

- Medical Advances Without Animals Trust (MAWA)
- 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
- ALTWEB - news, information, discussion and resources from the field of alternatives to animal testing
  http://altweb.jhsph.edu
- Peta International Science Consortium
  www.piscitld.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.
- NORINA
  http://oslovet.vets.no/NORINA/
- Interagency Coordinating Committee on the validation of Animal Models (ICCVAM)
  http://iccvam.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 Ca2+ 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

#### Journals

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What we can do

Institutional incentives and support

• 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

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