

# Translational Research and the AEC: The Value of Basic Research

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Without “basic research”, there is no translational research

"Translational research transforms scientific discoveries arising from laboratory, clinical, or population studies into clinical applications to reduce cancer incidence, morbidity, and mortality."

*National Cancer Institute*

aka

"From bench to bedside (and back)"

*By these definitions, not really much of an issue for the AEC....*

# Code: Governing Principles

Scientific or educational merit

Obtain/establish information relevant to:

- Understanding humans or animals*
- Maintain or improve human/animal health or welfare
- Improve animal management or production
- Understanding/maintaining/improving the natural environment

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*Like with human studies, the benefits do not necessarily accrue to those taking the risks...*

# Briefly...

Consider protocols involving interference/capture/tagging and even euthanasia of wildlife.

(including pest species)

Outcomes ?

- climate change
- environmental degradation
- loss of species



# Benefits ?

We know more about animals, ecosystems, relationships between the living and the earth...

Does it save lives ?

Does it make *our* lives better ?

We are animals...understanding our environment is essential for our life (food, water, disease)

...but contributes to our happiness

## Basic Research

Consider animal-based research into physiology\* or pharmacology:

Is it enough that the research produces knowledge ?

or

Must that knowledge have a direct clinical application ?

*\* You can't understand disease without understanding "normal" functioning of a system*

**Basic Research** includes research that investigates biology that could be relevant to human disease

e.g. investigating elevated intraocular pressure in rats to provide clues for factors in glaucoma in humans

versus

**“Translational”**

e.g. this is a humanized mouse suffering from Alzheimer's disease or motor neuron disease..

Research that investigates biology that *could* be relevant to human disease:

- delineation of broad principles of physiology (e.g. adult neurogenesis)

- delineation of finer points of physiology (role of neurotransmitter spillover in lactation priming)

- investigation of animal disease models in order to determine their suitability for translational research

Research that investigates biology that *could* be relevant to human disease....but might not be

“Testing” a compound in animals without a clear idea of what it might be doing

Looking for an animal model that maximizes drug effects (without thinking about the underlying biology)

Using animals as “screens” for desired activity OR premature surrogates for drug development

- receptor activity
- ADME
- off target effects

## Direct translational research

Is it even possible using animals ?

*May be useful for “3<sup>rd</sup> party” experiments (anthrax/tetanus)*

“Humanized” animals ? (e.g. neurodegenerative diseases)

Usually made by transgenic overexpression of a pathogenic human protein – so by definition not an animal disease

If there is no animal equivalent, can the physiology ever be relevant ?

Does it matter – if the results are good....

## Direct translational research

What about animal experiments that are specifically pitched as being about human health ?

-immediately remove the “pro” of contributing to animal health or welfare (unless incidental)

-how do you weigh human outcomes versus animal adversity ?

-what do you need to know about before you give the go ahead ?

## Direct translational research

- the model must be understood (us and them)
- the model should be validated (but there is always a first time)

Research must: be appropriately controlled

have defined outcomes

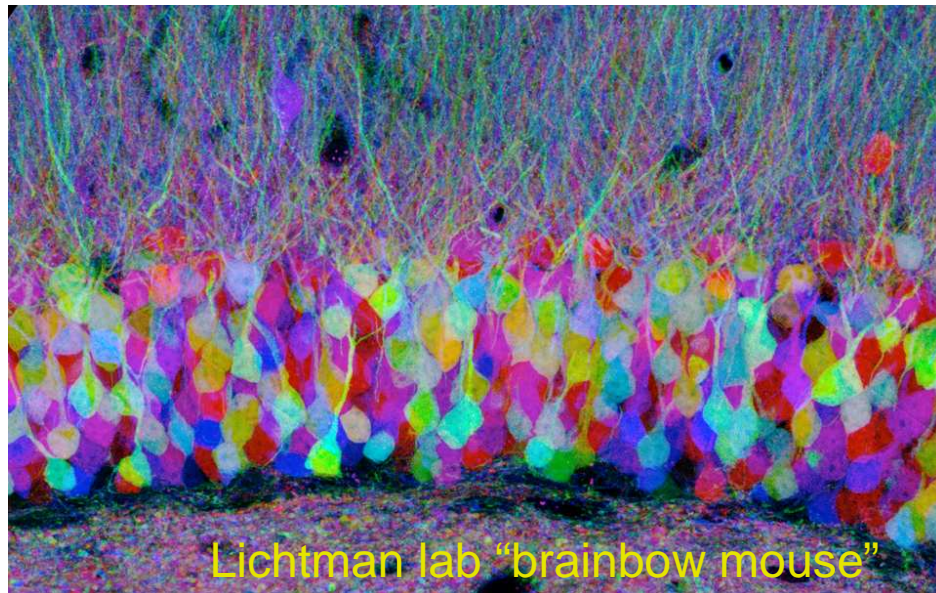
***Exactly the same as if it were any other piece of work coming before an AEC***



But....or finally....

There are things we cannot investigate in people:

The brain....~ 100 billion neurons ( ± baboon)



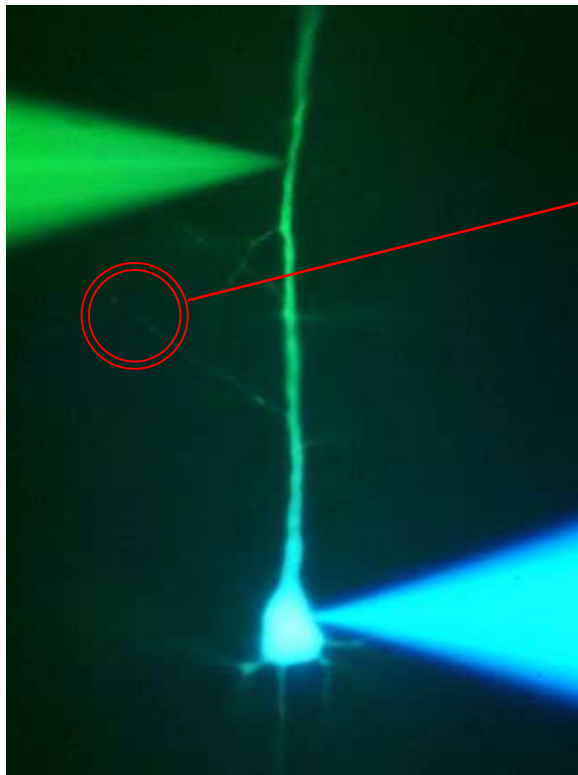
Resolution of fMRI:

2-3 mm<sup>3</sup>

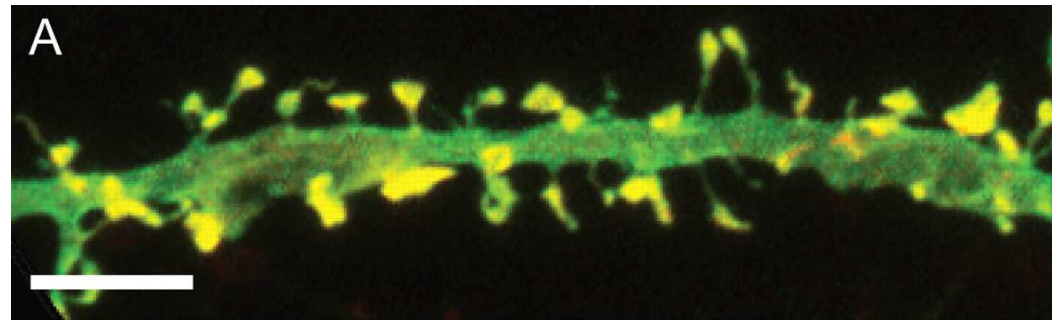
1 mm

The brain....~ 100 billion neurons

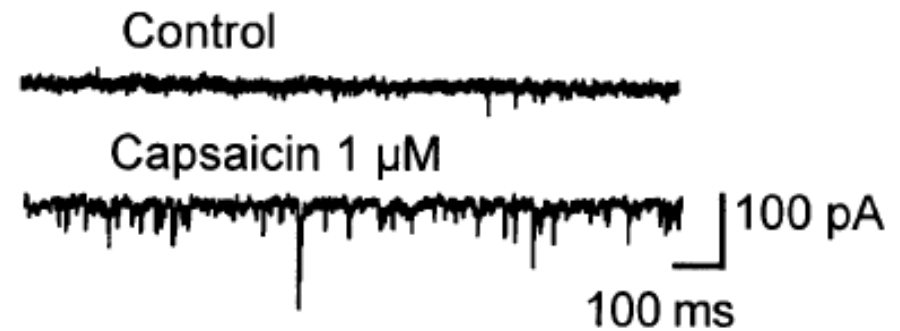
Maybe 5 - 10,000 connections each



Nature 367, 69



J Cell Biol, 189, 619



J Physiol 543, 431

## Summary

*Basic research* is essential for any translation

*Translational research* must be based on understanding of animal and human physiology/pathophysiology

Some kind of research can only be done in animals

Translational research does **not** require special consideration by AECs