

Animal Research – of Mice and Men

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Questions:

- How many animals are used in Canada each year in medical research? Which species used most?
- How long does it take a drug, device, or intervention to get to market? What \$\$\$? Failure rate?
- Which of the following was the most successful animal to human transfer project: tamoxifen, Gleevac, cyclosporine, HRT, fialuridine?

~2.9 Million Animals in Canada

(1996 - ~2 Million animals of which 25% were mice)

Issues for consideration - #1

(Aysha Akhtar, MD, MPH)

- Animals are not little humans
 - Methylprednisolone in cord injury:
 - Cats – yes
 - Dogs – yes
 - Rats – no
 - Mice – NO
 - Rabbits – yes/no

- Ancestor 80M y – 3.1 b base pair genome
- 5% related to protein coding
- Share 70% of protein coding genes
- Regulation is not the same

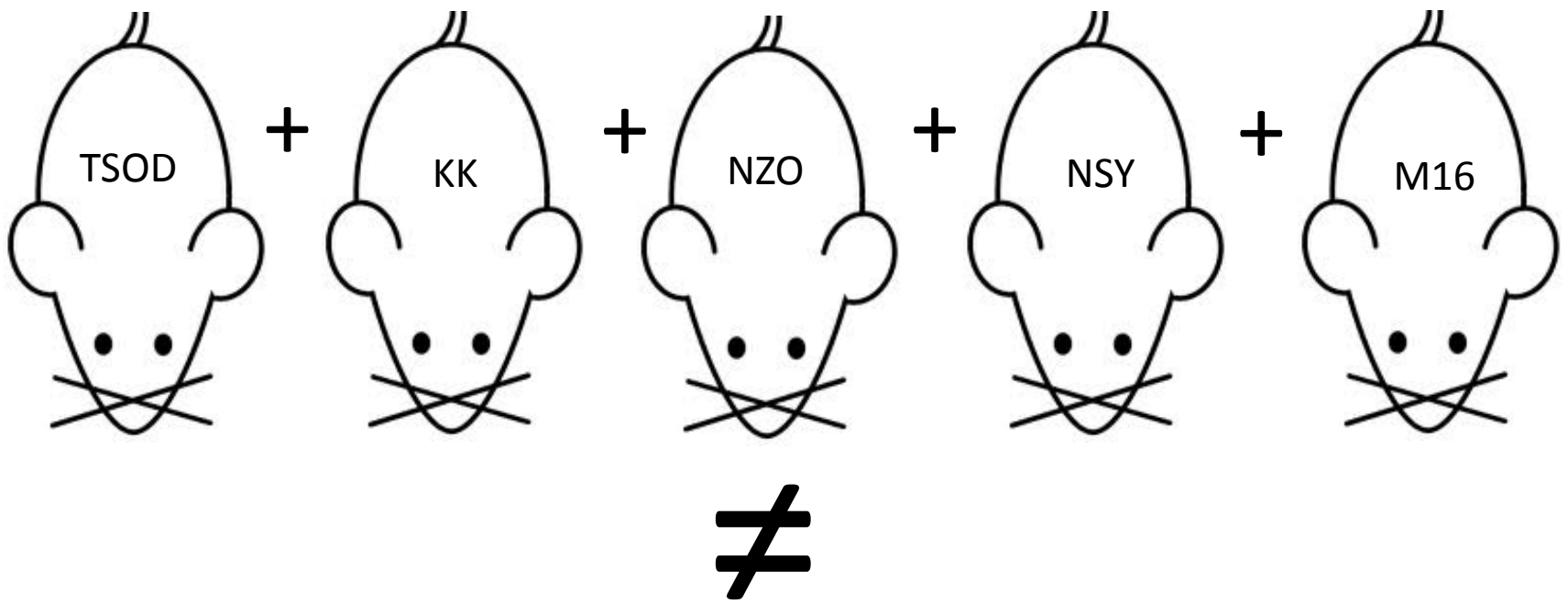
Discordant for disease
and response –
epigenetics and
environment

Issues for consideration - #2

- Animal don't get human diseases

Types of animal models

- **Experimental**
 - resemble human phenotype or response; induced
- **Negative**
 - control animals
- **Spontaneous**
 - analogous to human and occur naturally; rare
- **Orphan**
 - no human analog; exclusively in the animal species



We study the animal model
NOT the disease

Issues for consideration - #3

- Stressed animals yield poor data

“...scientific assessment of animal affect—emotions, pain, preference—is still in its infancy.”

Possible impacts

Developing a novel drug, device or other intervention:

- 14 years, \$2 billion, failure rate > 95%
- ~150 stroke drugs failed in human trials
- humans are injured (tamoxifen, gleevac, cyclosporine, HRT, fialuridine, TGN1421)

Moving forward...

- We rarely study basic anatomy and physiology – now subtle nuances of biology and diseases
- Many parallels – need to understand the differences not ignore them
- The more sophisticated the therapy – the more the differences matter

Moving forward...

- Develop important clinical endpoints in animal models, e.g. QOL
- Use preferred endpoints of clinical trials – survival versus progression free survival
- Back translate from clinical trials to animal models to fine tune predictive value in future studies

Moving forward...

- National Centre for Advancing Translational Sciences
- Human organs on a chip; non-invasive bio-physiological imaging

Moving forward...

- Expectations for animal models;



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Research Articles

Animal models in translational medicine: Validation and prediction

Tinneke Denayer, Thomas Stöhr  , Maarten Van Roy

- Go to the patient: cells, tissues

Thank you.