

Highlight

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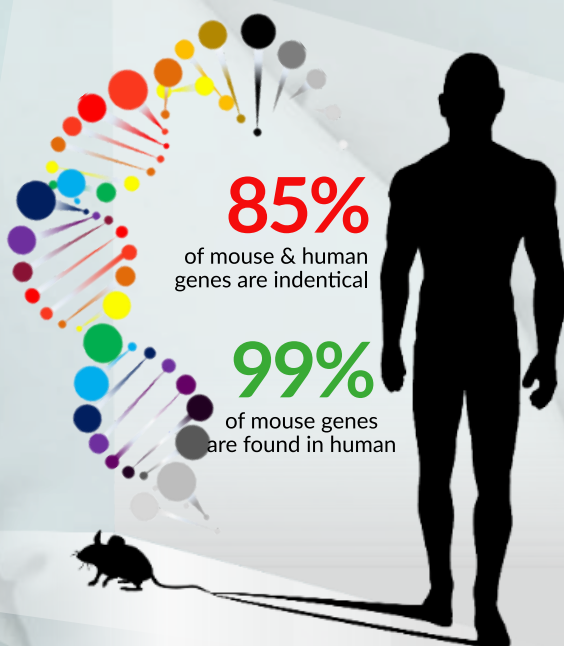


Photos of NODSCID/NSG (above, left) and C57BL6 (above, right)

“Mice are the most widely used experimental mammals, having made important contributions in most areas of biomedical research”.

(Festing and Lovell; Domestication and development of the mouse as a laboratory animal)

Laboratory Mice as Preclinical Animal Models in Biomedical Research



NO wonder mice suffer from similar diseases as us! They may be genetically modified to mimic our ailments too. In fact, tamoxifen and Herceptin® (common drugs for breast carcinoma), and gene-based treatment breakthroughs for Huntington disease, cystic fibrosis and sickle cell anaemia were discovered through mice studies.

Many diseases including cancers are complex diseases which cannot be fully studied using cells grown in the laboratory. The use of animal models in biomedical research would enable scientists to learn and understand more about human biology, health and for developing new treatment.

Research Areas



Comparative medicine is founded on the concept that other animal species share physiological, behavioural, or other characteristics with humans. Over 2,400 years ago it was recognized that by studying animals, we could learn much about ourselves. This technique has now developed to the point that animal models are employed in virtually all fields of biomedical research including, but not limited to, basic biology, immunology and infectious disease, oncology, and behaviour.

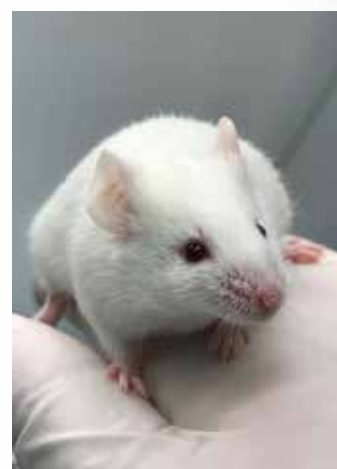
~Aaron C. Ericsson; A Brief History of Animal Model~

- » Behavioural
- » Immune studies
- » Chemotherapy research
- » Embryo transfer
- » Stem cell production
- » Antibody production
- » Drug testing
- » Gene functions in disease
- » Vaccine development

Animal Housing & Husbandry



Our laboratory mice are housed in individual ventilated cages at the Specific Pathogen Free (SPF) Facility. They are handled by well trained SPF staff and are always kept free from certain pathogens through routine health monitoring test.



Mouse Models in Drug Development

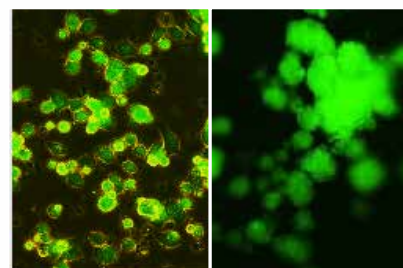


Despite large investments in drug development, the overall success rate of drugs during clinical development remains low. The use of animal models is pivotal to bridge the translational gap between the lab and the clinic. Therefore, the selection of a validated and predictive animal model is essential to address the clinical question.

The use of Nude mouse in drug development.

Replace, Reduce & Refine

In addition to the standard care and ethical use of mice for scientific purposes, we also practise the principle of 3Rs, i.e. replacement, reduction and refinement when conducting animal experiments in order to produce high quality research.

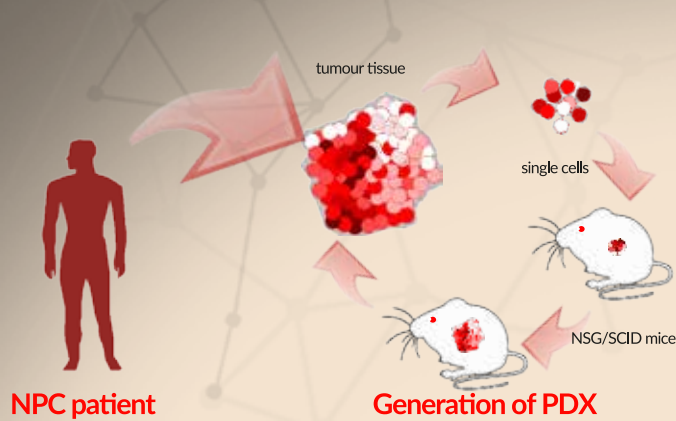


The use of 2D monolayer cells and 3D spheroid models using Patient-Derived Xenograft (PDX) is able to reduce and replace the application of mice in compound screening and hits validation.



Drug Discovery & Development

Establishment of Mice Models to Study Cancer of Nasopharynx

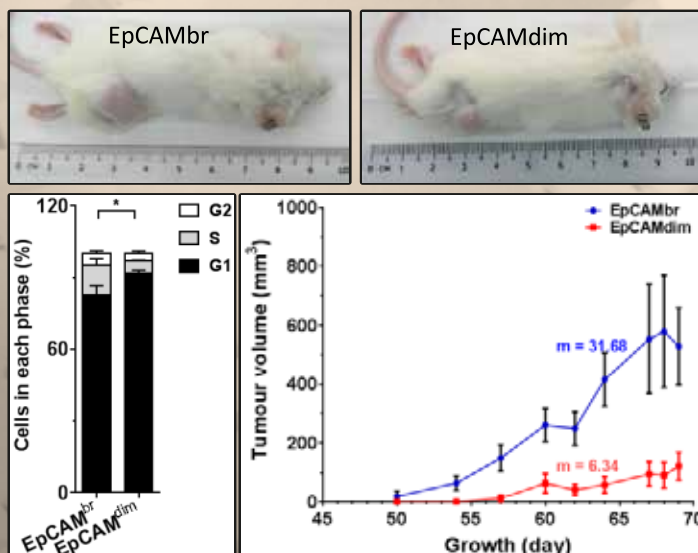


Patient-derived xenograft (PDX) is one of the most promising platforms to model human cancer and its complexity. To develop PDXs, tumour tissues from patients are implanted into immunodeficient mice. The established PDXs are then propagated for expansion and used in experiments. The cells are also cryopreserved in liquid nitrogen for future use.

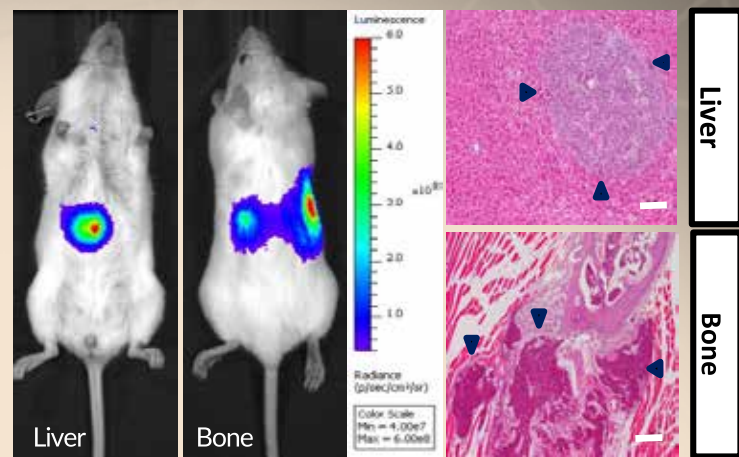
Applications of Mouse Models

NSG mice are excellent models for studies on cancer stem cells (CSCs). CSCs are a group of cancer cells that give rise to cancers more efficiently, have an almost indefinite lifespan and can also develop into other cell types. They are believed to be the seeds of cancers together with other contributing factors.

We used biomarkers to identify CSCs in a NPC PDX established in our lab. The PDX cells expressing high levels of EpCAM marker (EpCAM^{br}) seemed to be more consistent in behaving like CSCs. They grew faster and bigger, and could stably form new tumours in the mice for at least 3 consecutive generations. Altogether, the data were supportive of the presence of CSCs in our NPC PDX which contributed to repeated growths in the mice.



Growth properties of EpCAM cells from NPC PDX

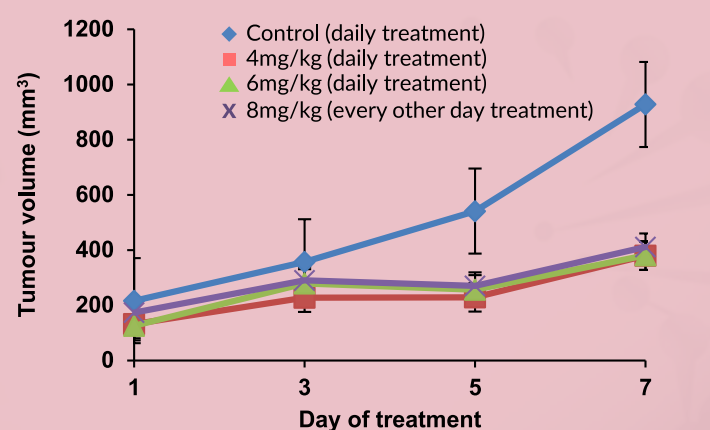


NPC metastatic models

The PDXs were labelled and inoculated into mice to model cancer metastasis. The mice were imaged using a non-invasive technique (bio-luminescence imaging i.e. measurement of light which allows highly sensitive real-time monitoring of the inoculated labelled cells.)

NSG mice are also routinely used as a study model for toxicity and efficacy testing of new drugs for NPC in our Unit. We had recently shown the effects of novel copper complexes against NPC cells grown in mice. Treated mice had smaller tumour growths than the control group at doses which did not show toxicity.

We had successfully developed a pipeline for drug discovery by using these cells and animal models (patent pending).



8mg/kg (every other day treatment)
6mg/kg (daily treatment)
4mg/kg (daily treatment)
Control (daily treatment)

Usage of a highly immunodeficient strain of mice (NSG) in drug discovery study

Summary

Laboratory mice are the most commonly used animal models in biomedical research. In IMR, immunodeficient mice such as NSG and SCID are housed in a clean environment. We practise the principle of 3Rs in our animal research.

The PDXs and mice models are important tools in cancer biology, drug discovery and other studies.

Ethical Approval

All animal procedures and protocols shown here were approved by the Animal Care and Use Committee (ACUC), Ministry of Health Malaysia

[ACUC/KKM/02(3/2013)

ACUC/KKM/02(05/2016)

ACUC/KKM/02(06/2013)

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