WHY MICE?

Inbred strains

Over 100 different inbred strains of mice, each with a different genetic background

C57Bl6

C57LJ

129S1

CAST_EiJ

BALB/c

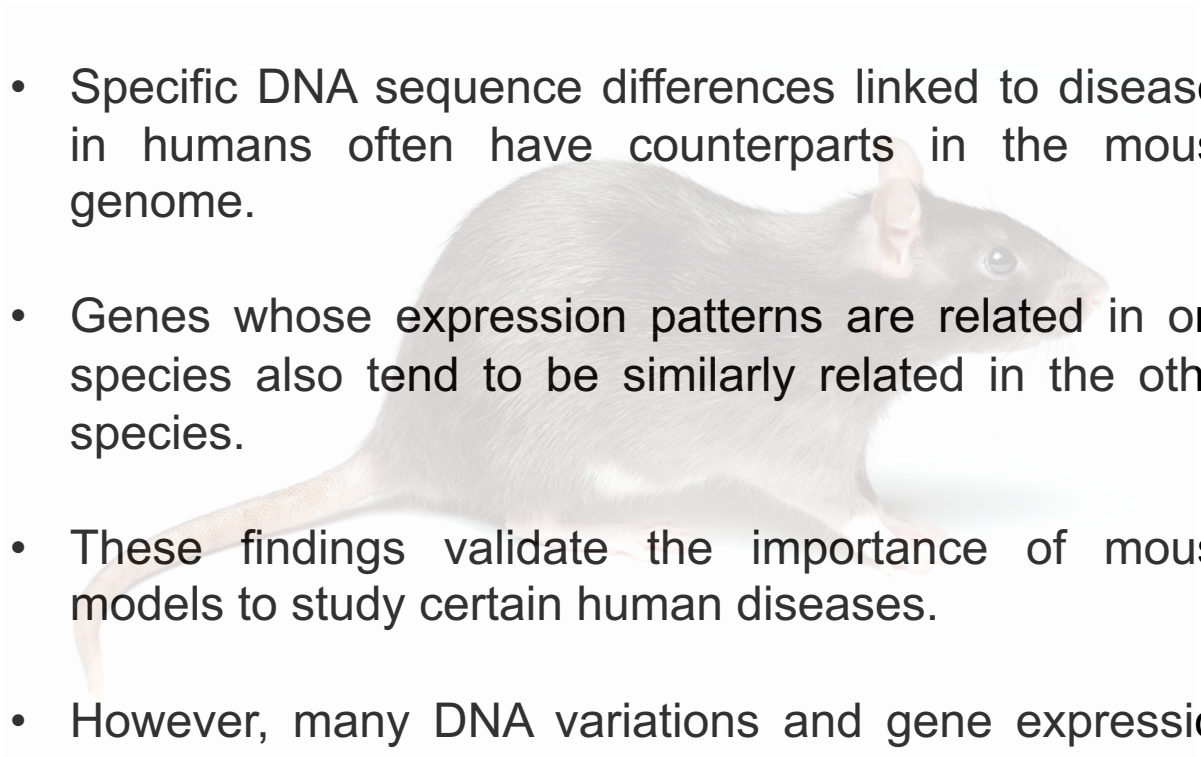
C3H

FVB

DBA2

Mice vs. Humans

- Gene regulation and other systems important to mammalian biology have many similarities between mice and humans.
- Specific DNA sequence differences linked to diseases in humans often have counterparts in the mouse genome.
- Genes whose expression patterns are related in one species also tend to be similarly related in the other species.
- These findings validate the importance of mouse models to study certain human diseases.
- However, many DNA variations and gene expression patterns are not shared between the species.
- Understanding these differences enhances the value of the mouse as a model organism.



The ENCODE Project

Humans and mice share many common genetic features and by examining the physiology, anatomy and metabolism of a mouse, scientists can gain a valuable insight into human functions.

Mouse genome & human genome: about 3.1 billion base pairs. Only about 5% of the sequence consist of protein-coding regions (genes).
On average, the protein-coding regions of the mouse and human genomes are 85% identical; some genes are 99% identical while others are only 60% percent identical. These regions are evolutionarily conserved because they are required for function.
In contrast, the non-coding regions are much less similar (only 50 % or less).

The ENCODE project: launched by NIH to build a comprehensive catalog of functional elements in the human and mouse genomes.

Mouse ENCODE Consortium., Stamatoyannopoulos, J.A., Snyder, M. et al. An encyclopedia of mouse DNA elements (Mouse ENCODE). Genome Biol 13, 418 (2012). https://doi.org/10.1186/gb-2012-13-8-418

From: Federica Cavallo, University of Torino

Benefits

- The mouse has many similarities to humans in terms of anatomy, physiology and genetics → useful for the study of human diseases.
- Mice are cost effective because they are cheap, easy to look after, small and convenient to house.
- Adult mice multiply quickly. They can reproduce as often as every three weeks, so scientists have lots of mice to work with. Moreover, the time between a mouse being born and giving birth (generation time) is short, usually around 10 weeks. This means several generations can be observed at once.
- The mouse has a short lifespan (one mouse year equals about 30 human years) which means scientists can easily measure the effects of ageing.
- Mice are extremely useful for studying complex diseases, as many of the genes responsible for these diseases are shared between mice and humans. Research in mice provides insights into the genetic risk factors for these diseases in the human population.
- It is relatively easy to manipulate the mouse genome, for example, adding or removing a gene to better understand its role in the body. This provides a powerful tool for modelling specific diseases when a mutated gene is known to play a role in the disease.

From: Federica Cavallo, University of Torino

Common strains

C57BL/6 mouse

BALB/c mouse

Nude mice
immunocompromised strain lacking a normal immune system and thymus gland. Commonly used model in cancer research.

strain	major features	advantages	main applications
C57BL/6	inbred, black	strain stability, easy breeding	physiological or pathological models for *in vivo* experiments, background strain for transgenics and congenics
BALB/c	inbred, albino, immunodeficient	easy breeding, tumor-prone	hybridoma and monoclonal antibody production, research models for cancer therapy and immunology.
CD-1	outbred, albino	genetic variability	positional cloning, genotypic selection, toxicology testing (questionable)
CB17 SCID	inbred, albino	no T and B cells, tumor transplantation	immunodeficient animal model for testing new cancer treatments and as hosts for human immune system tissues.

From: Johnson M. MATER METHODS 2012;2:113
DOI//dx.doi.org/10.13070/mm.en.2.113

C57BL/6J

Most widely used GENERAL PURPOSE strain
Generation of congenics carrying both spontaneous and induced mutations
DNA source for the first high quality draft sequence of the mouse genome

https://www.jax.org/strain/000664

Characteristics

- Low susceptibility to tumors
- High susceptibility to diet-induced obesity, moderate hyperglycemia and hyperinsulinemia
- High susceptibility to diet-induced atherosclerosis
- High incidence of hydrocephalus and malocclusion
- High incidence of microphthalmia and other eye defects
- Resistant to audiogenic seizures
- Low bone density
- Preference for alcohol and morphine
- Late-onset hearing loss

BALB/cJ

IMMUNOLOGICAL STUDIES, CANCER

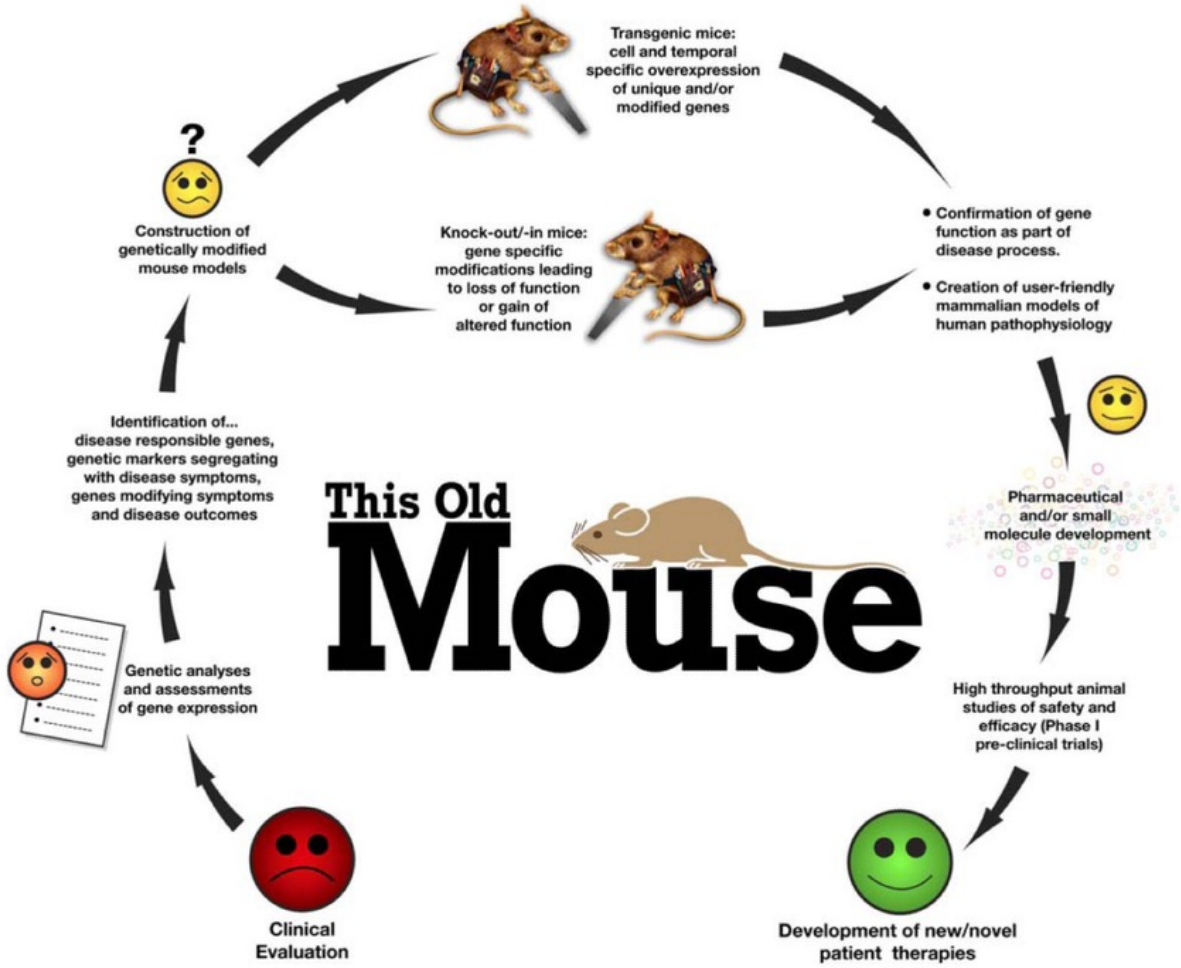
- TH2-biased immune responses
- Production of monoclonal antibodies
- Mammary tumor
- Cancers (reticular neoplasm, primary lung tumors, renal tumors, rare myoepitheliomas)

https://www.jax.org/strain/000651

Characteristics

- Commonly develops ulcerative blepharitis and periorbital abscess
- Exhibits incomplete penetrance of callosal agenesis
- Exhibits spontaneous dystrophic cardiac calcinosis
- Susceptible to pristane induced arthritis
- Exhibits TH-2-lymphocyte driven pulmonary inflammation, a model for asthma
- Susceptible to TMEV-induced demyelinating disease
- Relatively resistant to diet-induced atherosclerosis
- Male mice are resistant to multi-dose streptozotocin (STZ)-induced diabetes
- Resistant to the induction of experimental allergic encephalomyelitis (EAE)
- Useful in vaccine development and studies of infectious disease

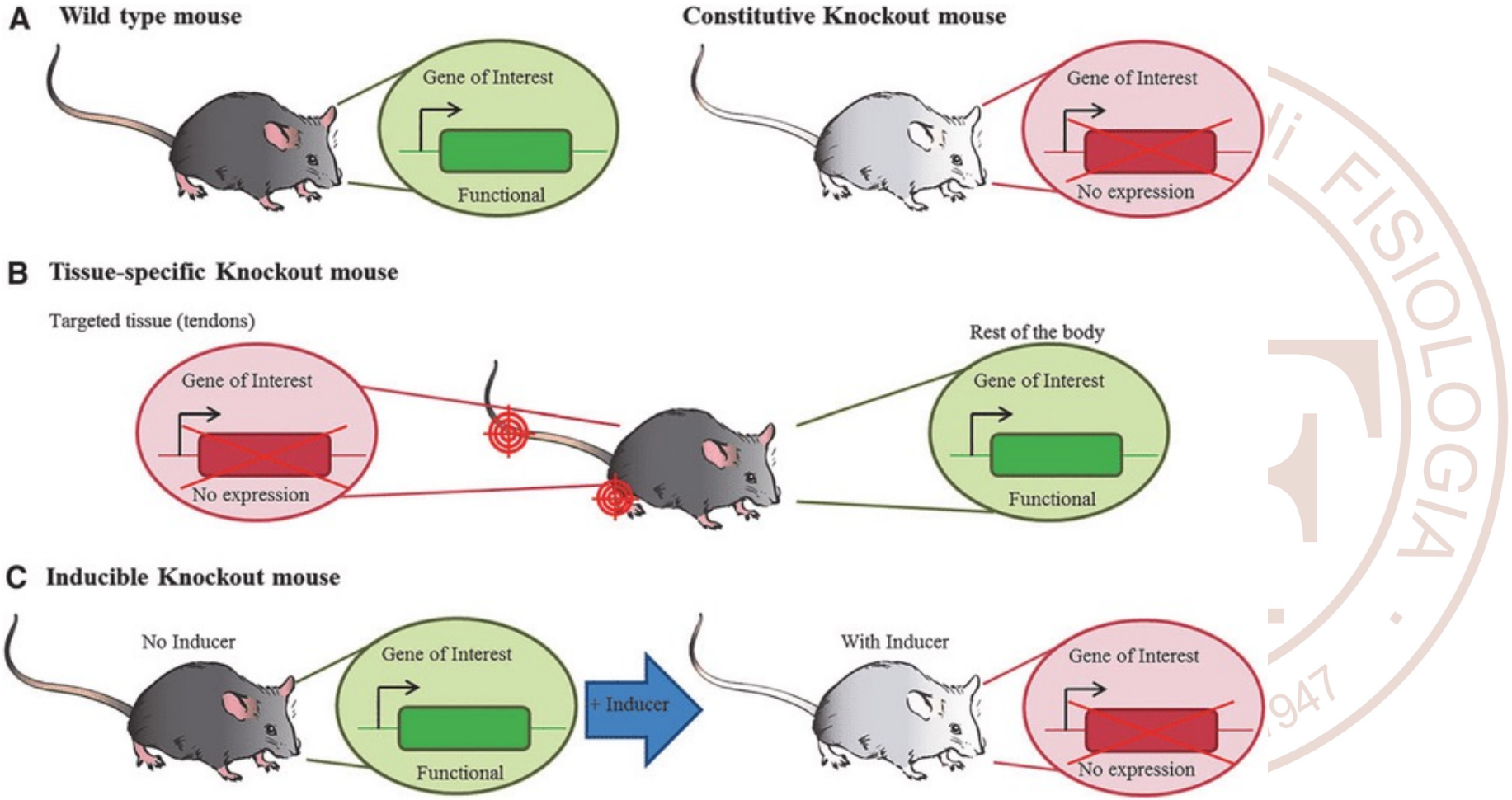
Mouse phenotypes



- Blood cancers – leukemia/lymphoma
- Bone defects
- Development (embryonic) disorders
- Diabetes
- Gastrointestinal defects
- Growth retardation
- Hematology defects
- Immune defects including autoimmunity
- Kidney disease
- Neurological disorders
- Obesity
- Solid tumors
- ETC….

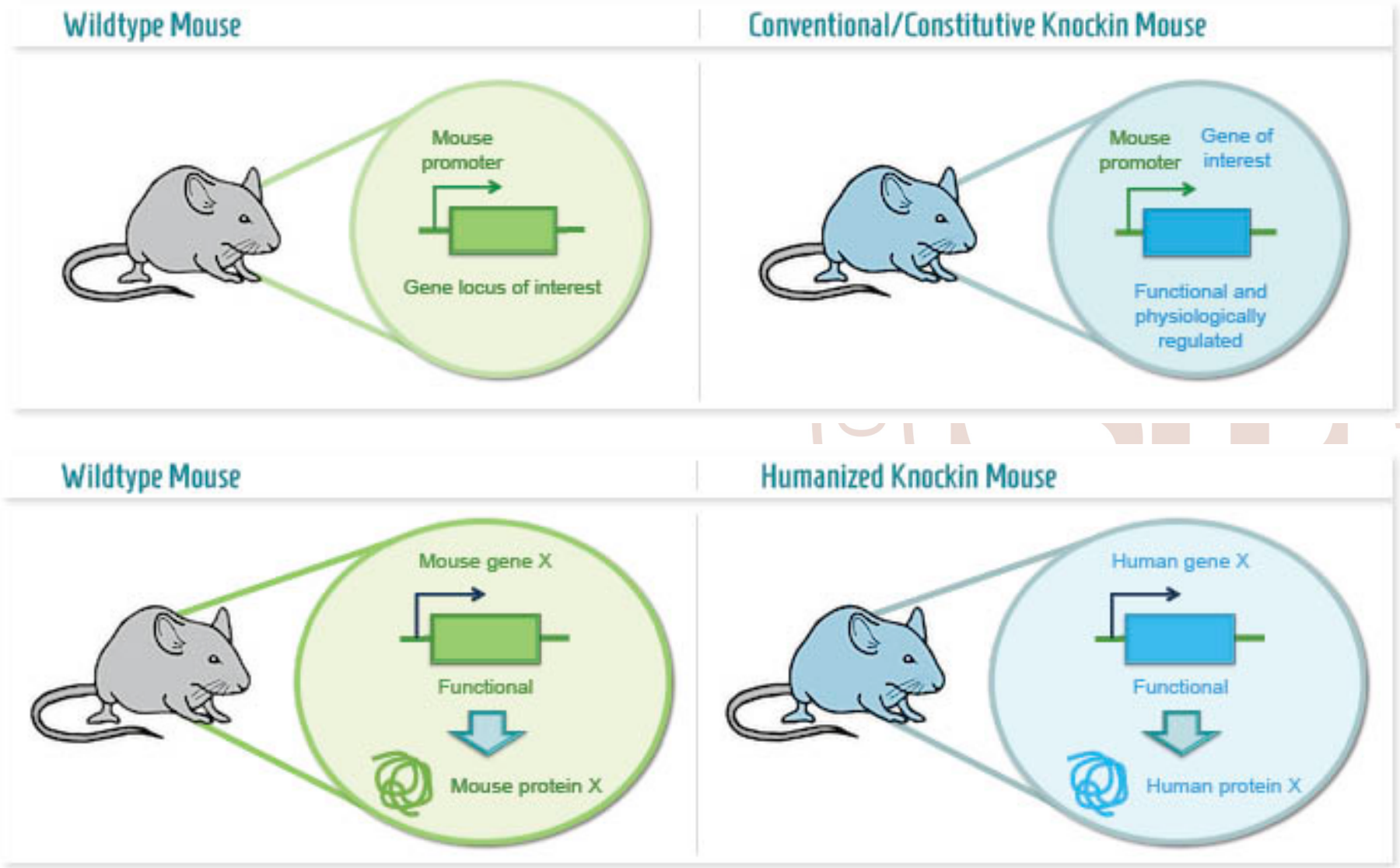
From Doyle et al, Transgenic Research, 2011

Knock-out mice



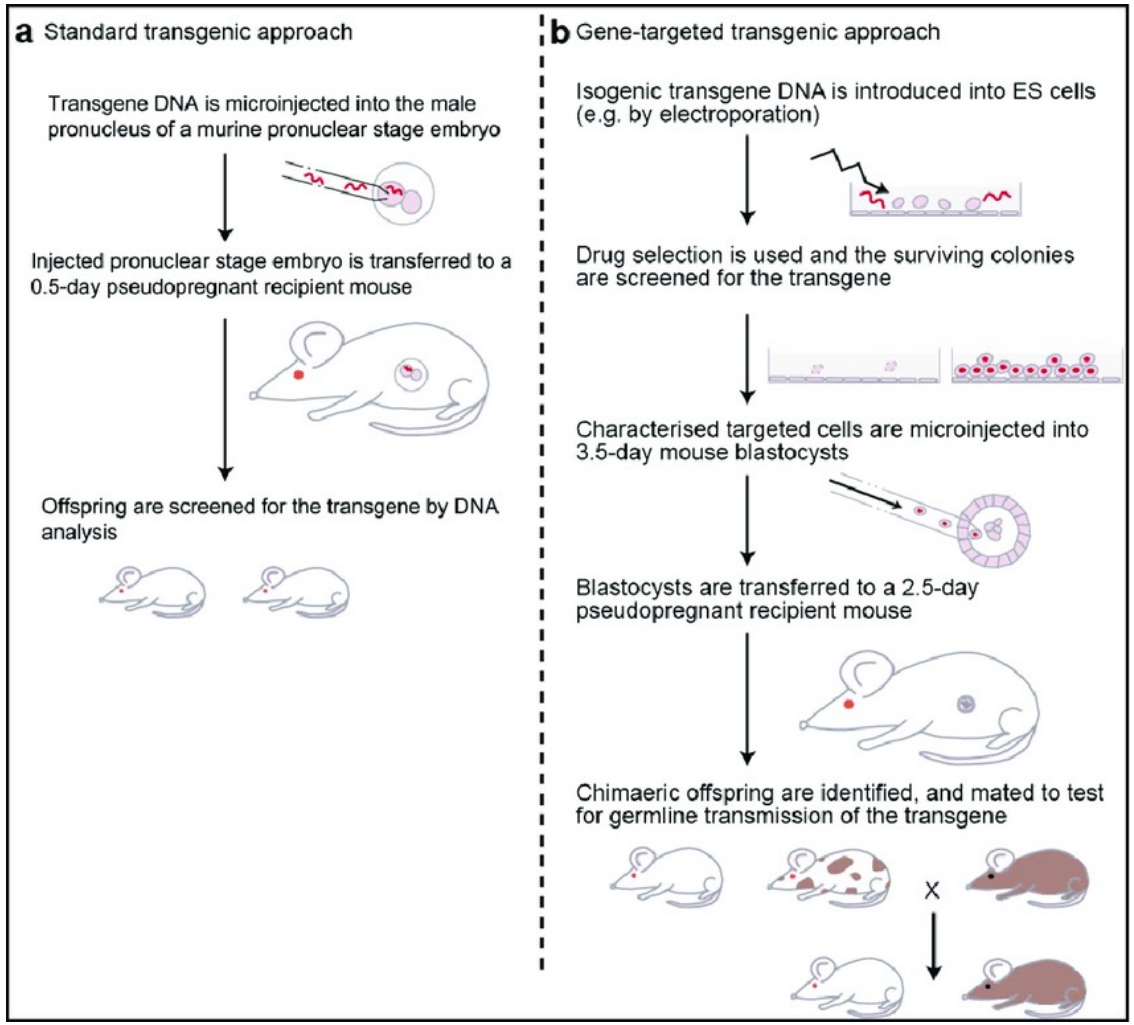
From Delgado Caceres et al. (2018). Stem Cells and Development. 27. 10.1089/scd.2018.0121.

Knock-in mice

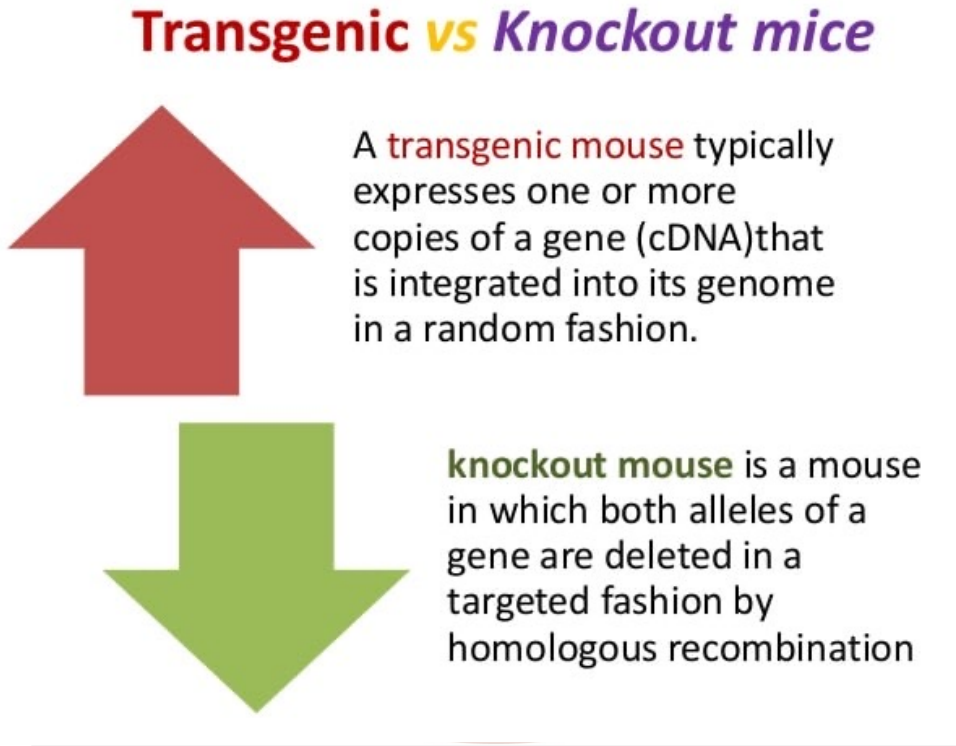


https://www.genoway.com/

Transgenic mice



A transgenic animal has part of another species' genome transferred into its own through the tecniques of genetic engineering.



From Boverhof et al. (2011). Transgenic Animal Models in Toxicology: Historical Perspectives and Future Outlook. Toxicological sciences : an official journal of the Society of Toxicology. 121. 207-33. 10.1093/toxsci/kfr075. /