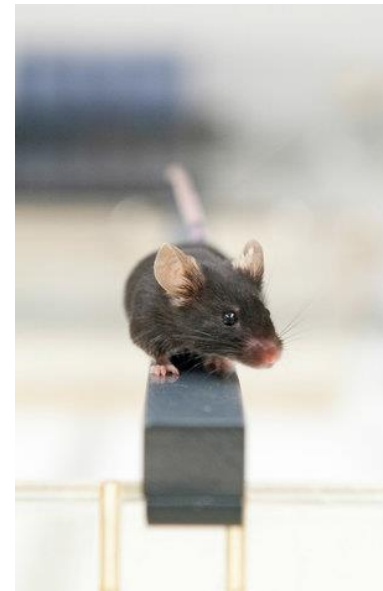


Model organisms: Mouse



Hans Bluysen, 01.04.2021



What are model organisms?



A model organism is a species that has been widely studied, usually because it is easy to maintain and breed in a laboratory setting and has particular experimental advantages.

Model organisms are non-human species that are used in the laboratory to help scientists understand biological processes.



What are model organisms?

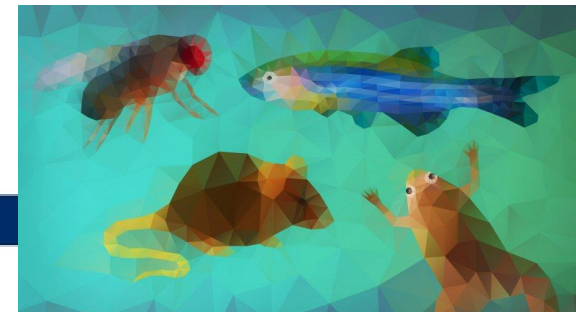
For example, they may have particularly robust embryos? that are easily studied and manipulated in the lab, this is useful for scientists studying development.

Or they may occupy a pivotal position in the evolutionary tree, this is useful for scientists studying evolution.?

Why are model organisms useful in genetics research?

Many model organisms can breed in large numbers. Some have a very short generation time, which is the time between being born and being able to reproduce, so several generations can be followed at once

Mutants allow scientists to study certain characteristics or diseases. These are model organisms that have undergone a change or mutation[?] in their DNA[?] that may result in a change in a certain characteristic.



Why are model organisms useful in genetics research?

Some model organisms have similar genes[?] or similar-sized genomes[?] to humans.

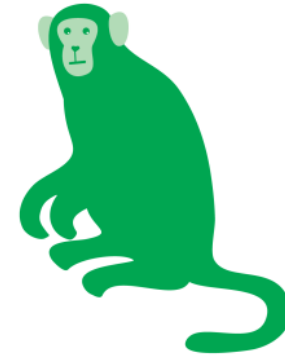
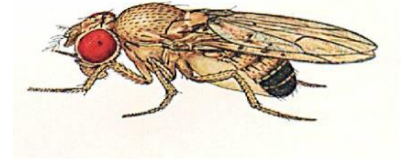
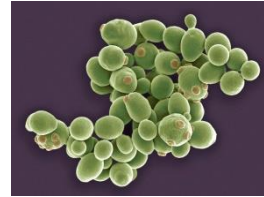
Model organisms can be used to create highly detailed genetic maps:

Genetic maps are a visual representation of the location of different genes on a chromosome[?], a bit like a real map but one where the key landmarks are areas of interest in the genome. For example, areas of DNA that differ between individuals in the same species (SNPs[?]) or genes.

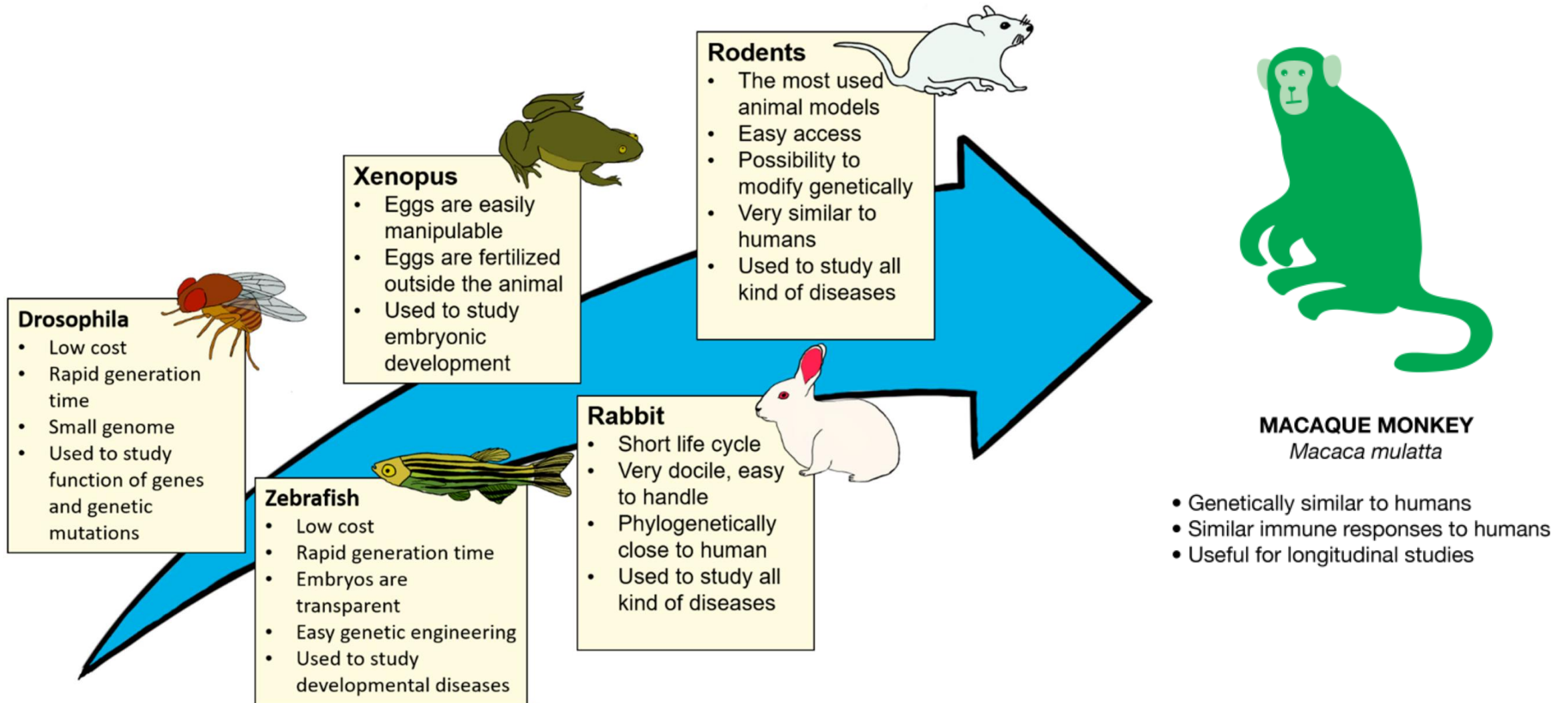


Examples of model organisms used to study genetics

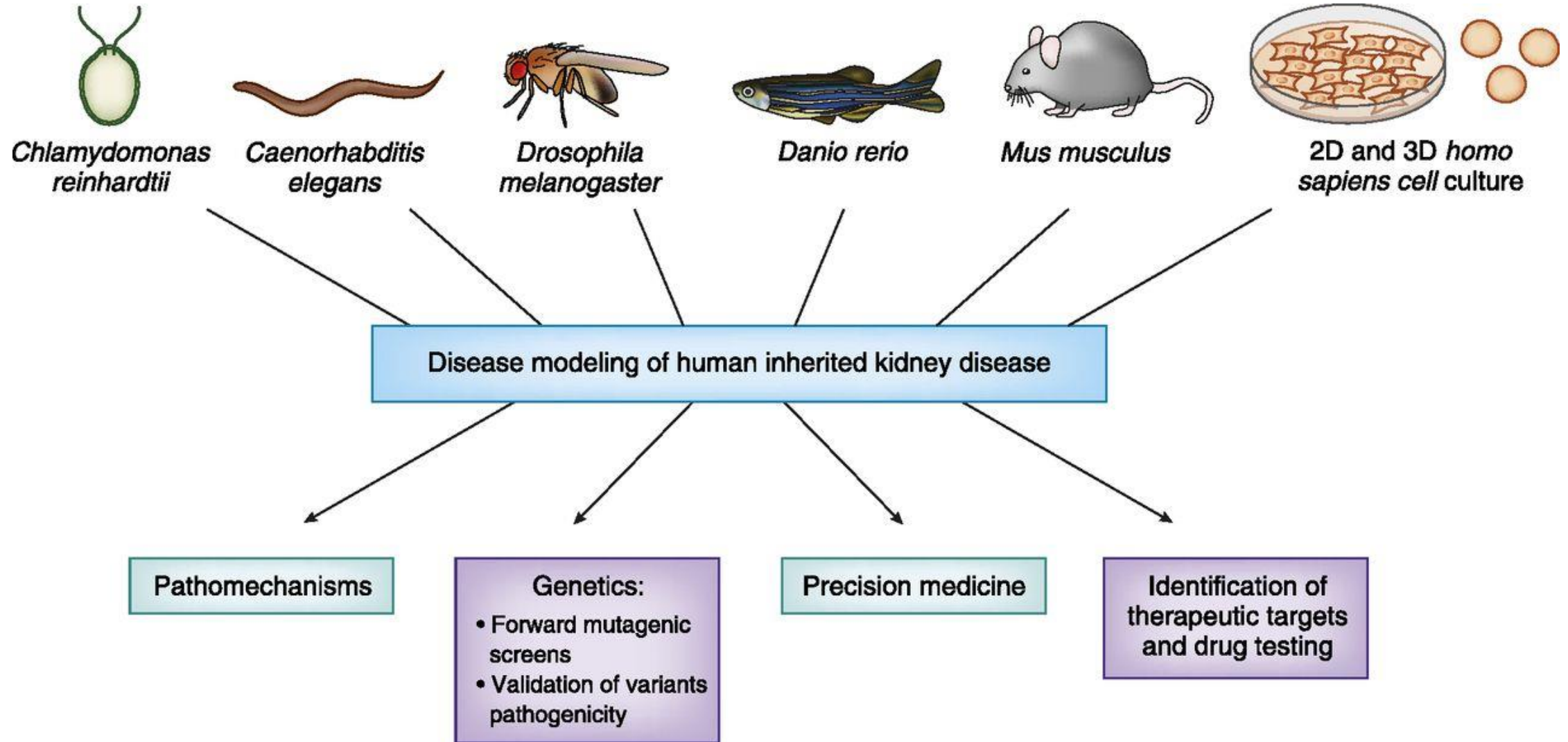
Yeast (*Saccharomyces cerevisiae*)
Fruit fly (*Drosophila melanogaster*)
Nematode worm (*Caenorhabditis elegans*)
Western clawed frog (*Xenopus tropicalis*)
Mouse (*Mus musculus*)
Zebrafish (*Danio rerio*)
Monkey (*Macaca mulatta*)



Examples of model organisms used to study genetics



Examples of model organisms used to study genetics





House mouse: Facts

- Over the past century, the house mouse (*Mus musculus*) has become the preferred mammalian model[?] for genetic research.
- In the early days of biomedical research, scientists developed mouse models by selecting and breeding specific mice to produce offspring with certain desired characteristics.
- Now scientists use mice to simulate human genetic disorders[?] in order to study their development and test new therapies.
- As a scientific tool, mice have helped to speed up the progress of research and enabled the development of important new drugs[?].
- The genome[?] sequence is approximately 3,500 million base pairs[?] in length and contains over 23,000 protein-coding genes[?] ([Ensembl](#)).



House mouse: Benefits

- Have many similarities to humans in terms of anatomy, physiology and genetics.
- Similar genome, making mouse genetic research particularly useful for the study of human diseases.
- Mice are small and cost effective: they are cheap and easy to look after.
- Multiply quickly: reproduce as often as every three weeks creating lots of offspring.
- Generation time is short, around 10 weeks: several generations can be observed at once.
- Have a short lifespan (one mouse year equals about 30 human years) which means scientists can easily measure the effects of ageing.
- Are extremely useful for studying complex diseases[?], such as atherosclerosis and hypertension, 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.



House mouse: Benefits

- 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.
- Mice are far better than flies or worms for studying complex biological systems found in humans, such as the immune, endocrine (delivers hormones? into the body), nervous, cardiovascular and skeletal systems. Like humans, mice naturally develop diseases that affect these systems, including cancer? and diabetes?.
- Immunodeficient mice (mice without a fully functioning immune system) can also be used as hosts to grow both normal and diseased human tissue. This has been a useful tool in cancer? and AIDS? research.

Examples of mouse models?



Genetically modified mouse

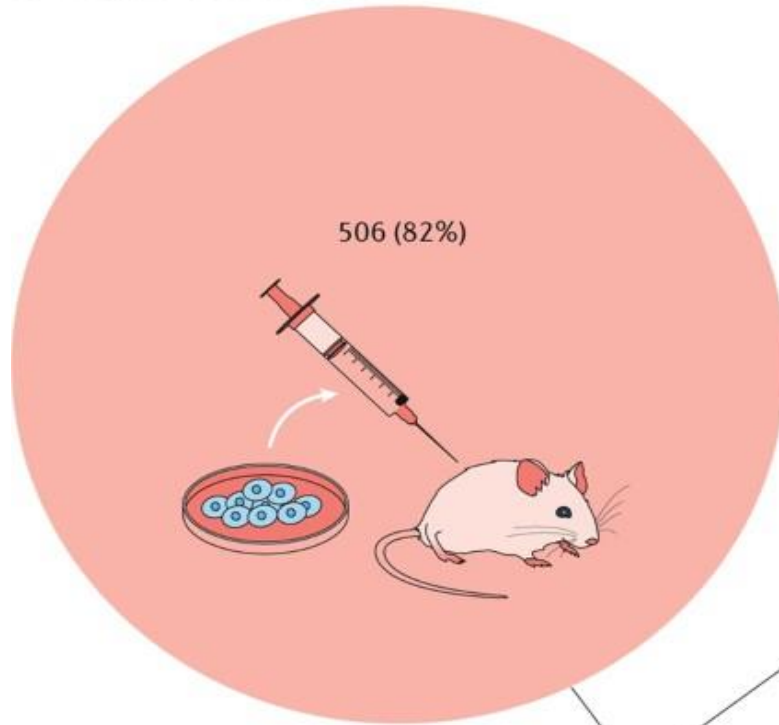
A genetically modified mouse or genetically engineered mouse model is a mouse that has had its genome altered through the use of genetic engineering techniques.

Genetically modified mice are commonly used for research or as animal models of human diseases, and are also used for research on genes.

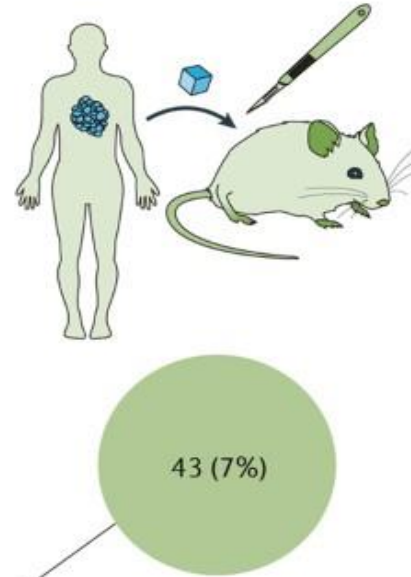
“Transgenic mouse”

Examples of mouse models

a Cell line-derived models

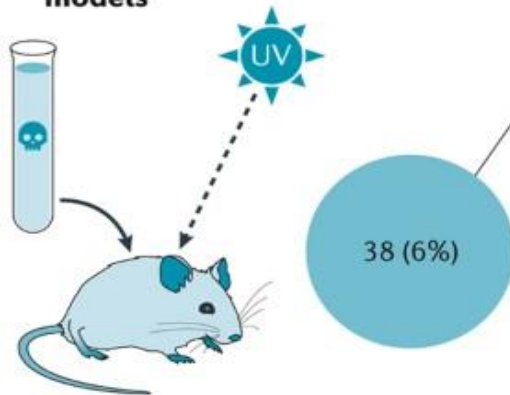


b PDX models

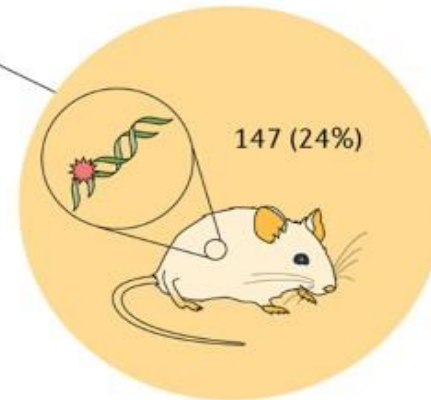


Patient derived xenografts are models of cancer where the tissue or cells from a patient's tumor are implanted into an immunodeficient or humanized mouse

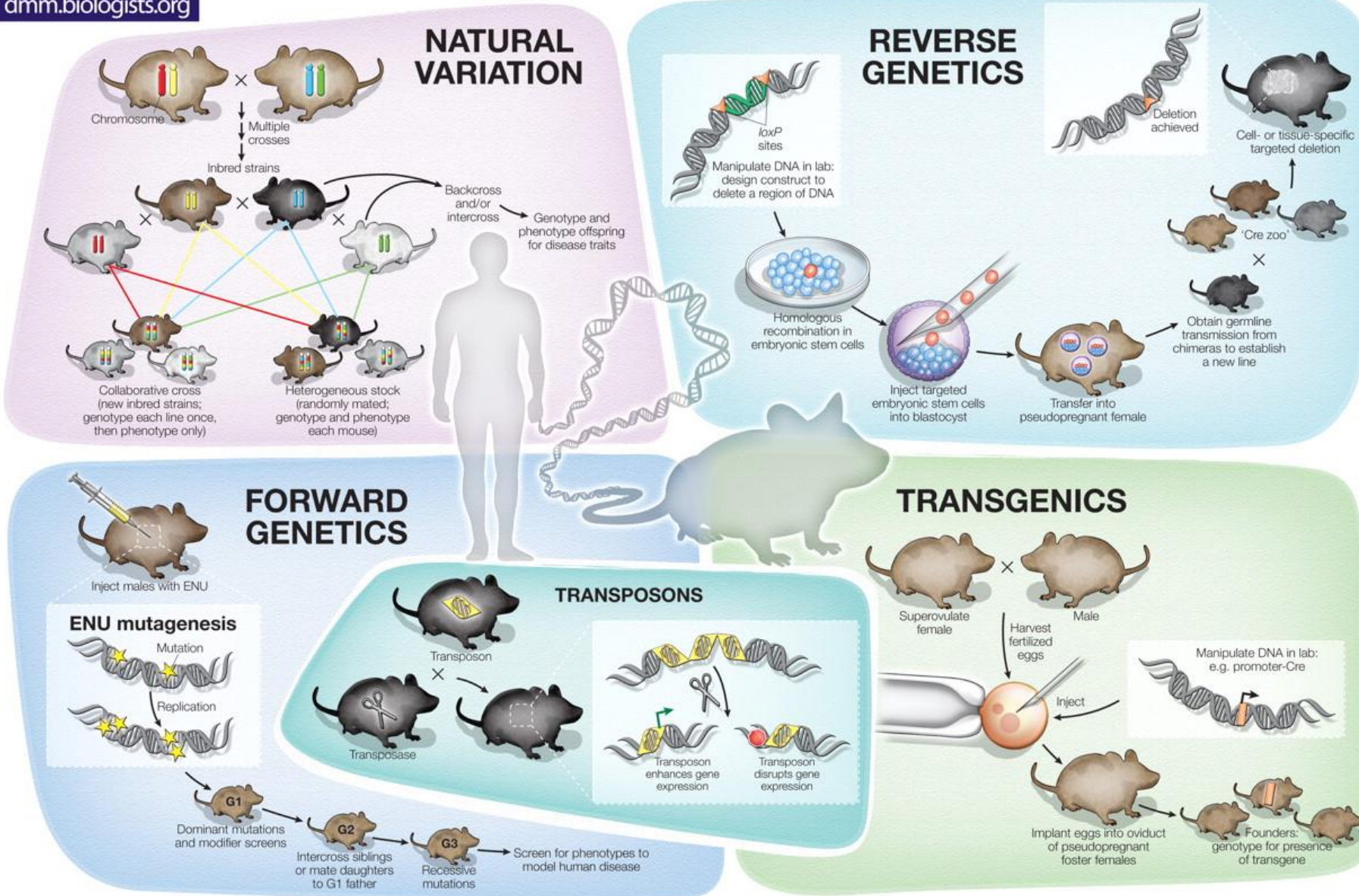
c Environmentally induced models



d GEM models



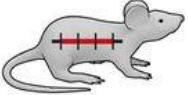

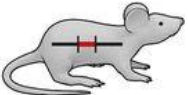

Genetically engineered mouse models

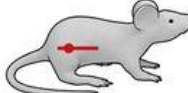





Embryonic
Stem cells

Zygotes

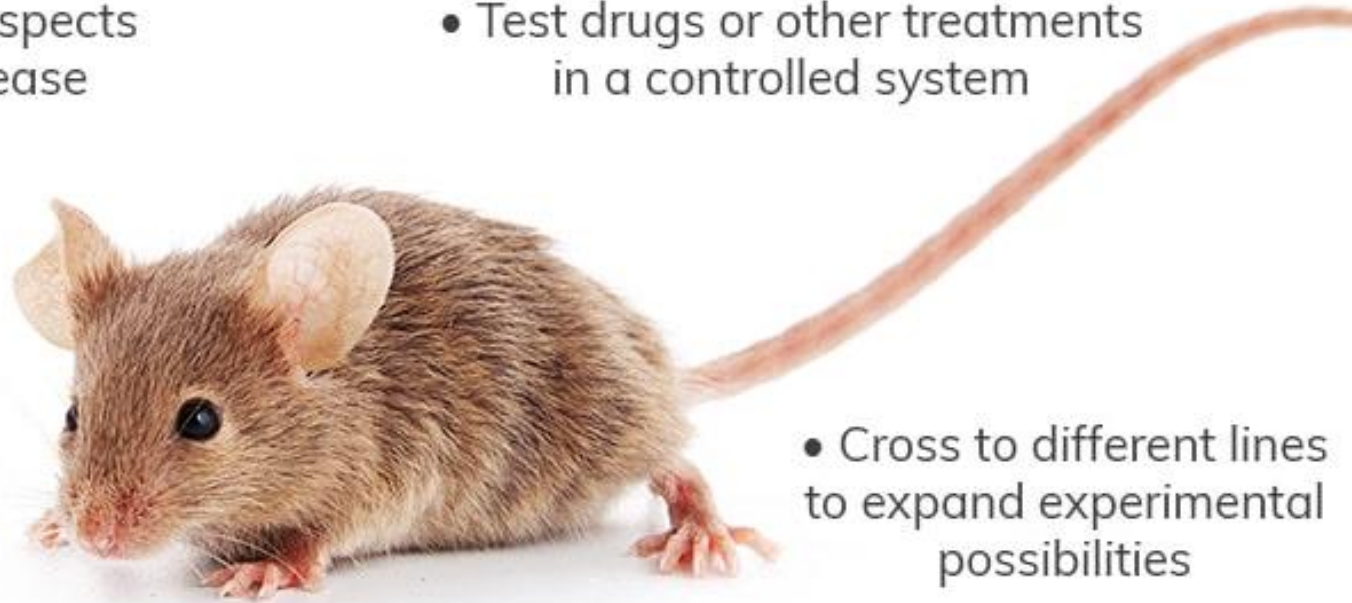
Examples of mouse models

Mouse model	Possible phenotypes	Some uses and questions
Transgenic Multiple copies of exogenous DNA 	<ul style="list-style-type: none"> • Phenotype severity often depends on transgene copy number; possible artifacts from overexpression and from insertion site of transgene 	<ul style="list-style-type: none"> • Investigating later-stage disease mechanisms • Can late-stage disease be treated?
Knockin Replace mouse sequence with another sequence expressed physiologically 	<ul style="list-style-type: none"> • Phenotype may appear in mid- and late-life; may be mild 	<ul style="list-style-type: none"> • Investigating earlier-stage disease mechanisms • When does disease start? • Can we treat prodromal/presymptomatic disease? • Can we develop biomarkers?
Genomically humanized Replace mouse sequence with the orthologous human genomic region 	<ul style="list-style-type: none"> • Phenotype may appear in mid- and late-life; may be mild 	<ul style="list-style-type: none"> • Investigating earlier-stage disease mechanisms • When does disease start? • Can we treat prodromal/presymptomatic disease? • Can we develop biomarkers? • Do human proteins behave differently from mouse proteins?
Chromosome engineered aneuploidy A chromosomal region is duplicated or deleted 	<ul style="list-style-type: none"> • Phenotype may be mild 	<ul style="list-style-type: none"> • Investigating dose-sensitive genes/mechanisms • Dose-sensitive gene mapping • Investigating disease mechanisms and biomarkers

Transchromosomal model Human chromosome added to the mouse genome 	<ul style="list-style-type: none"> • Phenotype may be mild • Expressing mouse and human genes 	<ul style="list-style-type: none"> • Investigating dose-sensitive genes/mechanisms • Dose-sensitive gene mapping • Investigating disease mechanisms and biomarkers • Investigating human genomic DNA function in a mouse cellular environment
Chimeras, mouse-mouse, and human-mouse Mice consisting of two different cell lines, e.g., mouse-mouse or mouse-human 	<ul style="list-style-type: none"> • Phenotype may be mild but depends on the cell lines used, which could be wildtype or genetically manipulated 	<ul style="list-style-type: none"> • How does pathology spread? • Is disease cell autonomous? • Do human cells behave differently from mouse cells?
Inducible and conditional Temporal or spatial control of gene expression 	<ul style="list-style-type: none"> • Phenotypes vary depending on the genetic manipulation 	<ul style="list-style-type: none"> • Investigating protein function • Investigating temporal/spatial specificity in pathogenesis • Which cell types are key to pathogenesis? • Is disease cell autonomous? • Is disease reversible?
Knockout Functionally delete a gene 	<ul style="list-style-type: none"> • Phenotypes vary but often are severe in null animals 	<ul style="list-style-type: none"> • Investigating loss of function • What are loss-of-function effects?

Why Use Transgenic Mouse Models?

- Model specific aspects of a human disease
- Test drugs or other treatments in a controlled system
- Highlight the function of your gene of interest
- Cross to different lines to expand experimental possibilities

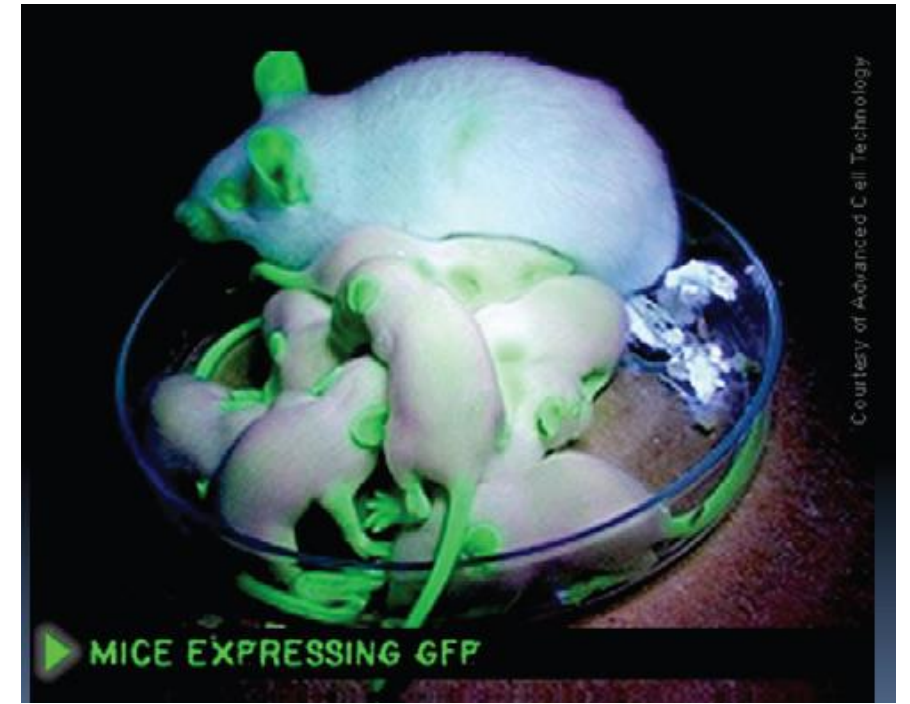


Transgenic and knockout mice



A transgenic animal is much more complex than working with cultured cells

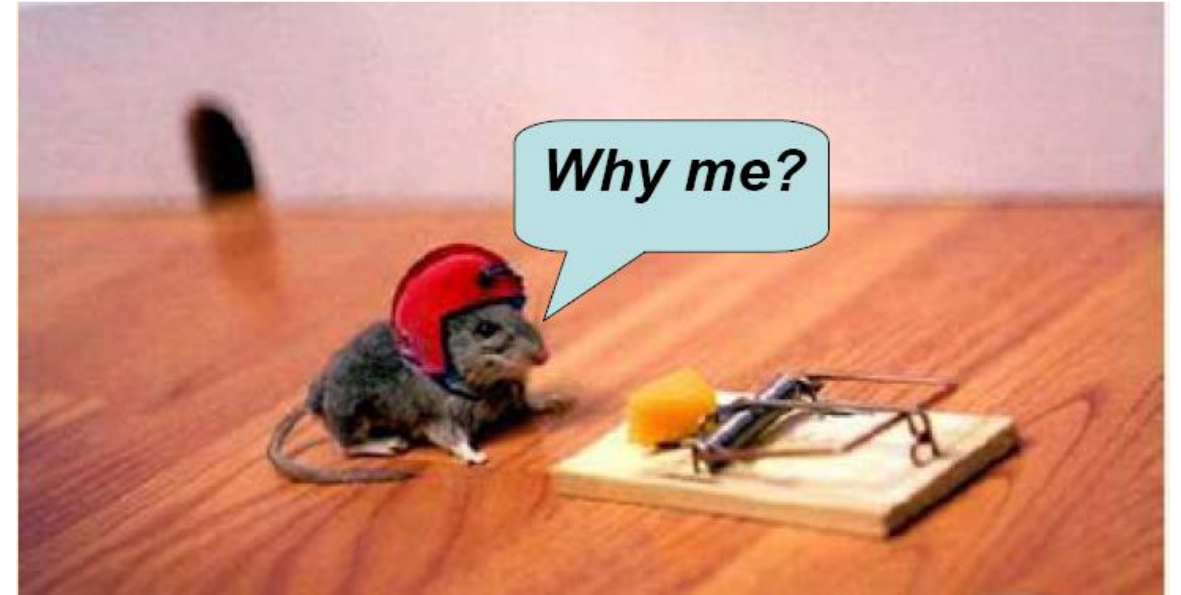
Transgenics can be used for a variety of purposes, covering both basic research and biotechnological applications



Transgenic and knockout mice

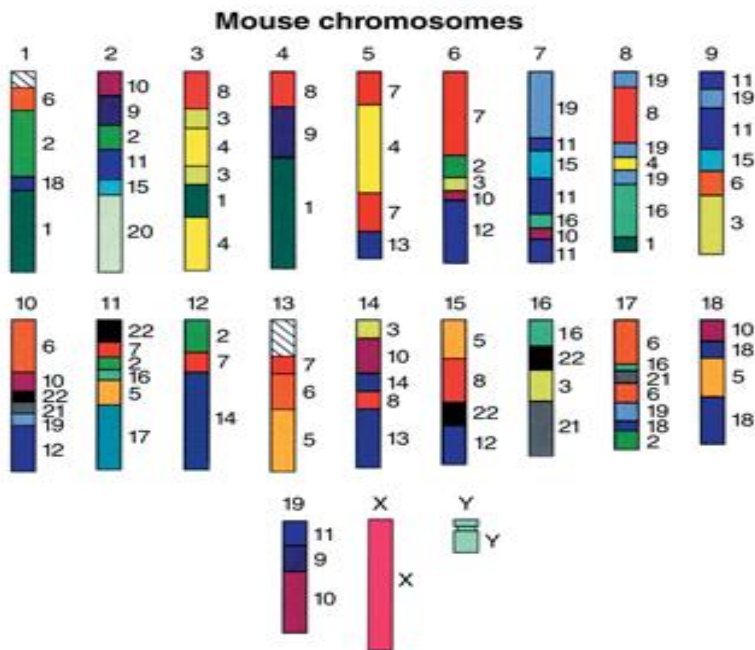
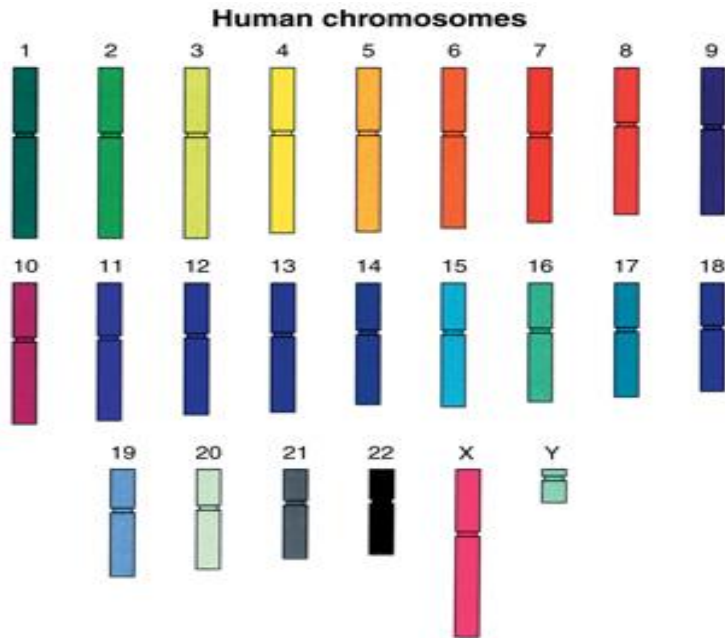
Mice have 19 autosomal chromosomes and two sex-chromosomes (X and Y), many of which contain large segments of DNA that are **highly conserved between mouse and humans**.

One of the goals of mouse transgenesis, is to use molecular genetic approaches to **create better mouse models of human diseases** that are based on known genetic lesions.



The mouse is a reliable stand-in for humans in medical research, thanks to a genome that is 85 percent identical.

Transgenic and knockout mice



Synteny: The co-localization of genes on chromosomes of related species.

Homolog: The situation where nucleic acid or protein sequences are similar because they have a common evolutionary origin. Often used loosely to indicate that sequences are very similar.

Ortholog – gene sequences are similar between species.

Paralog – gene sequences are similar within a species.

Transgenic and knockout mice

Disease Mode	Gene
Cystic Fibrosis	CFTR
Atherosclerosis	Apo E, apo (a), Apo A-II
anti-Atherosclerosis Gene Therapy	Apo AI, Apo E, LDLR
B-Thalassemia	β -globin
Sickle Cell Anemia	β^s (and variants)
Inflammatory Bowel Disease	Interleukine-2, Interleukin-10 and T-cell Receptor, β ; MHC II
Severe Combined Immunodeficiency Disease	Rag-1, Rag-2
Muscular dystrophy Gene Therapy	Dystrophin
Alzheimer's disease	β -amyloid
Amyotrophic lateral sclerosis (ALS)	neurofilament heavy chain
Insulin Dependent Diabetes Mellitus	interferon-
Cancer	many oncogenes and tumor suppressor genes



Transgenic and knockout mice

- Example: Transgenic Mice (hair gene removed)
- Used to help burn patients and others by making human facial parts (ears, nose lips, etc.)



<https://www.youtube.com/watch?v=kefoIXnLAN0>

Transgenic and knockout mice

Example

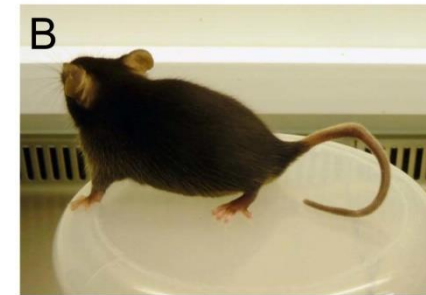
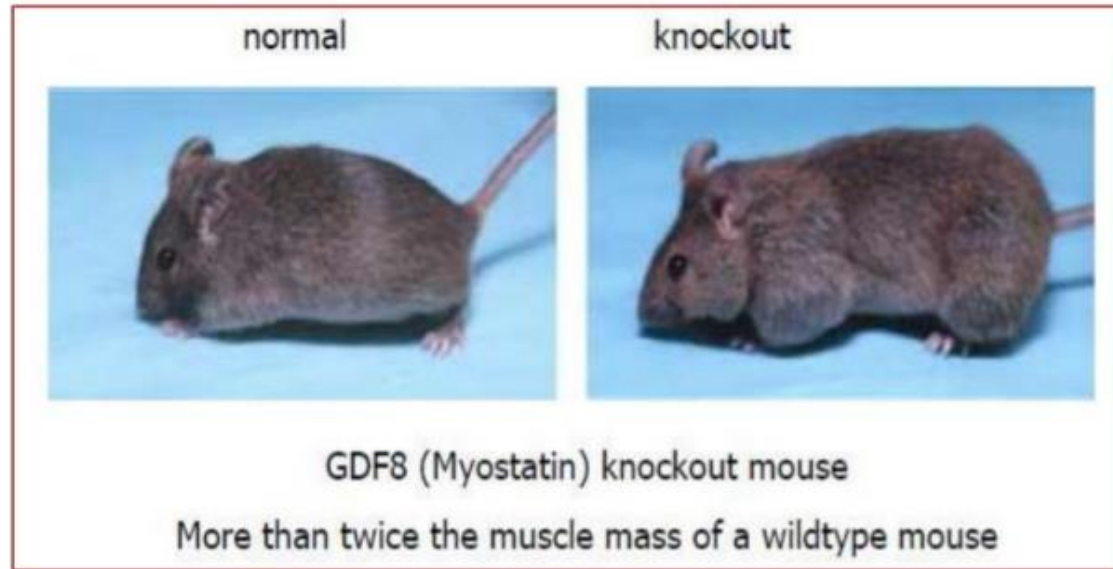
- Comparison between a transgenic mouse and a normal mouse
- The giant mouse developed from a fertilized egg transformed with a recombinant DNA molecule containing the Human Growth Hormone



- Knocking out expression of Nhlh2, a basic helix-loop helix transcription factor in mice results in adult onset obesity.



Transgenic and knockout mice



A chimeric mouse gene Targeted for the Agouti Color gene, with its offspring



Transgenic and knockout mice

- **Spontaneous Mutants**

- Occurs as the result of spontaneous mutation
- Examples:
 - db/db (Diabetic mouse)
 - nu/nu (Nude mouse)

- **Induced Mutants**

- **Transgenics**

- Overexpression
- Inducible / conditional

- **Gene targeting**

- Knock-outs
- Knock-ins

- **Mutagenic Mice:**

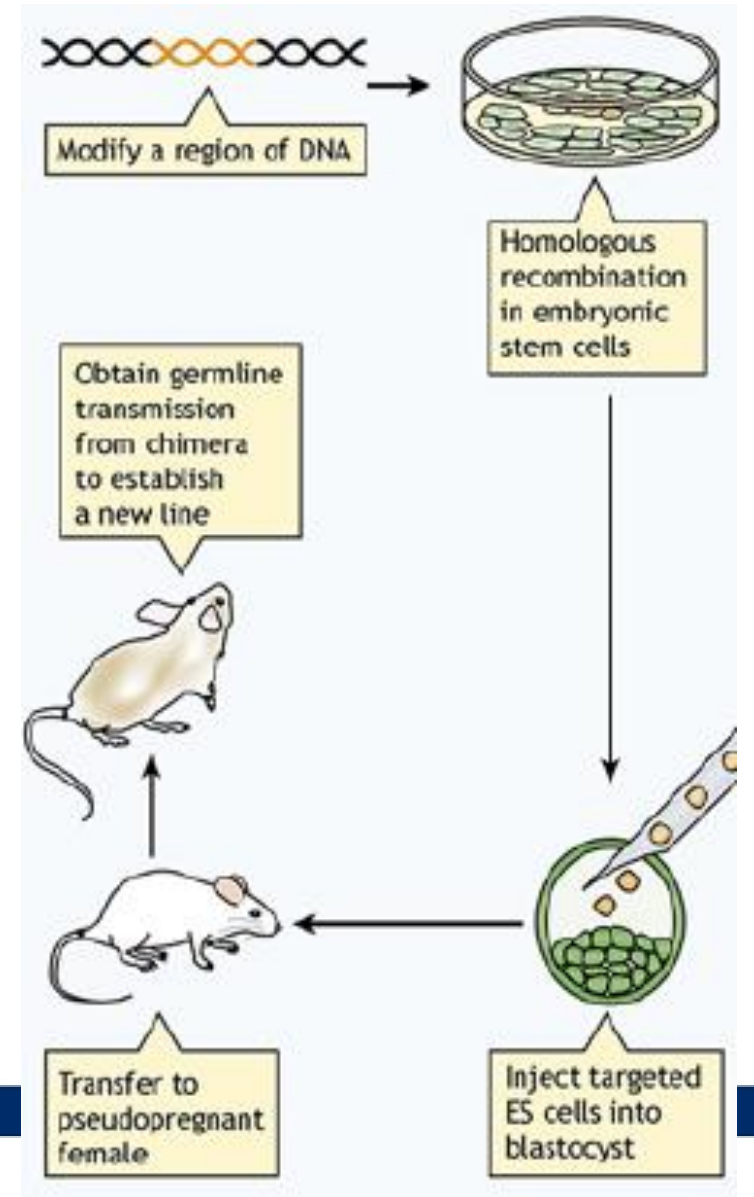
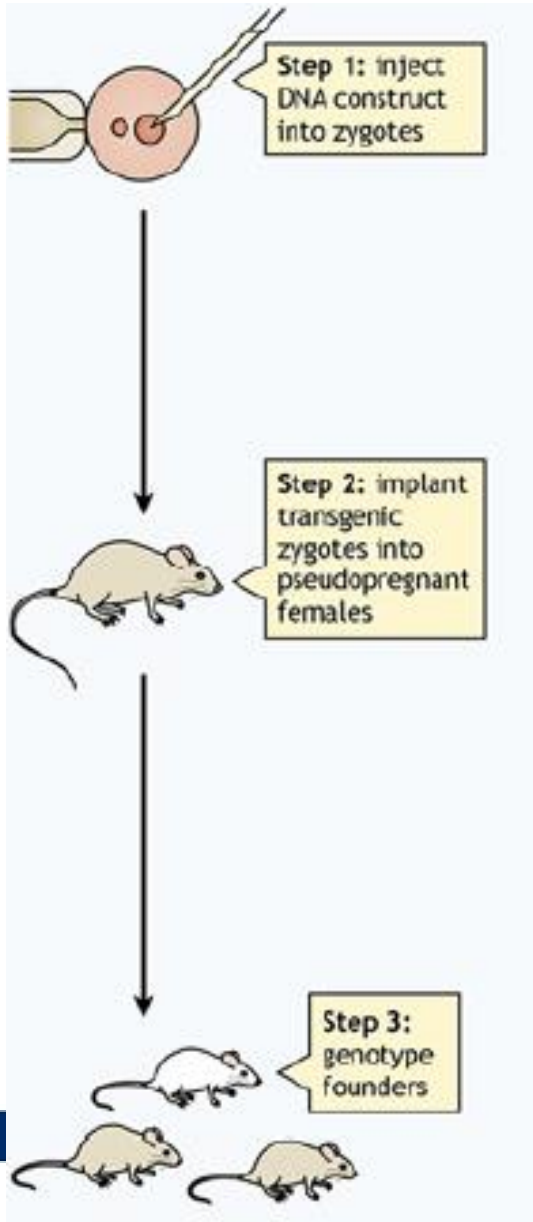
- Chemical mutagenesis of Embryonic Stem cells
- Chemical mutagenesis / Irradiation of Mice



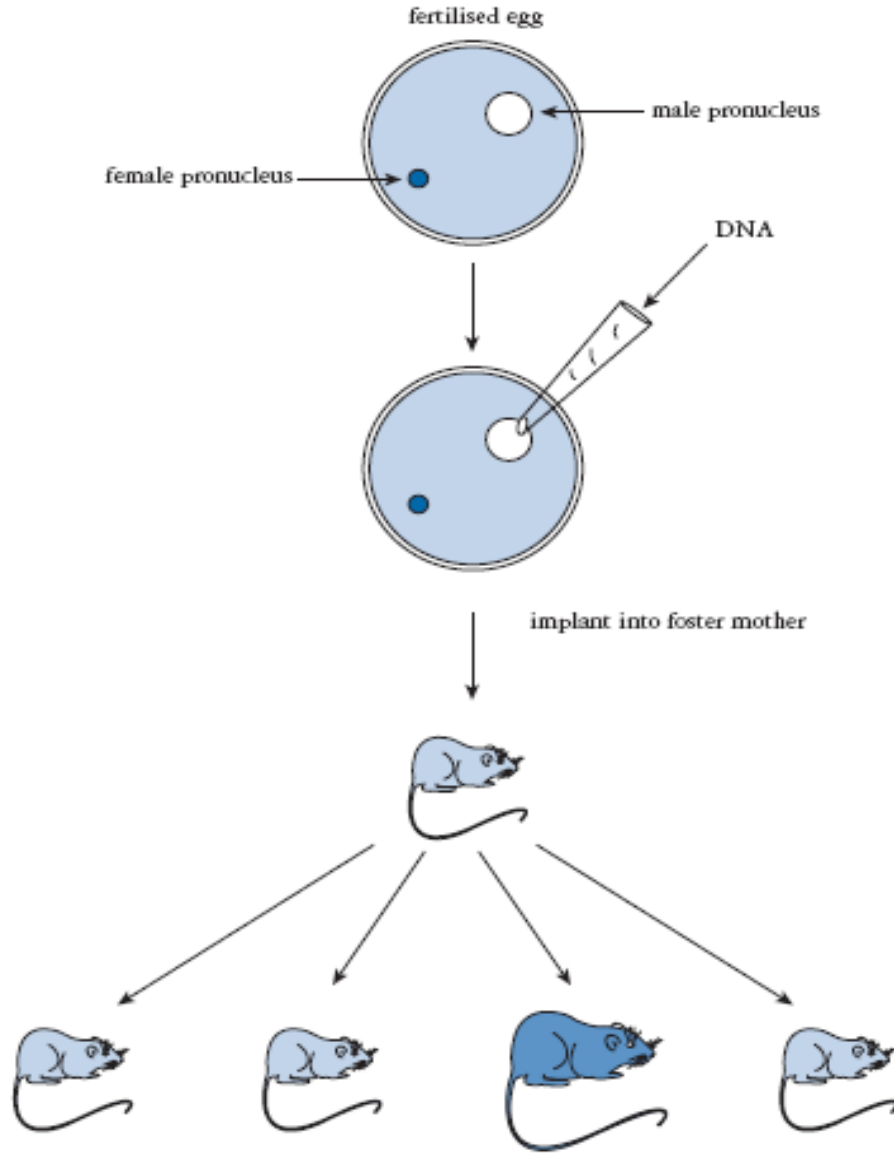
Producing Transgenic mice

Pronuclear Injection

Gene Targeting in ES Cells



Producing Transgenic mice



A **pronucleus** (plural: **pronuclei**) is the nucleus of a [sperm](#) or an [egg cell](#) during the process of [fertilization](#). The sperm cell becomes a pronucleus after the sperm enters the ovum, but before the genetic material of the sperm and egg fuse.

Aim: to alter the germ line so that the genetic change is inherited in a stable pattern

Production of transgenic mice – the construct

Transgenes should include:

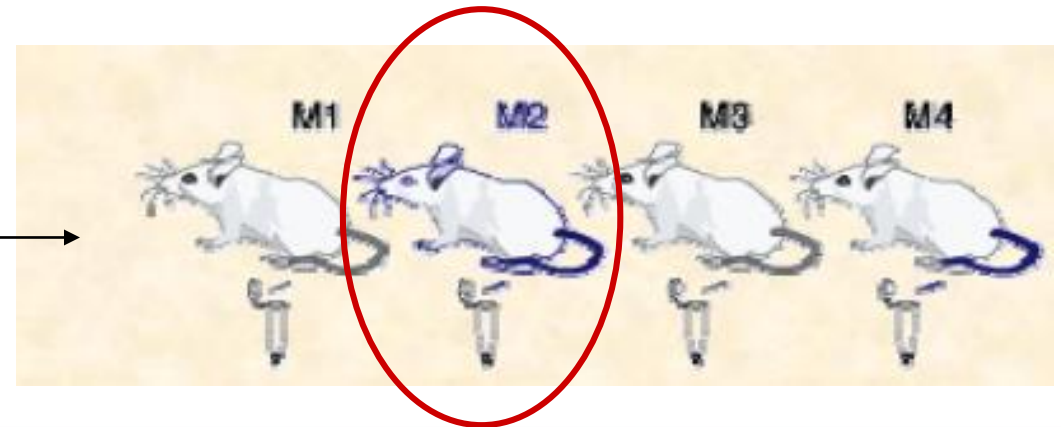
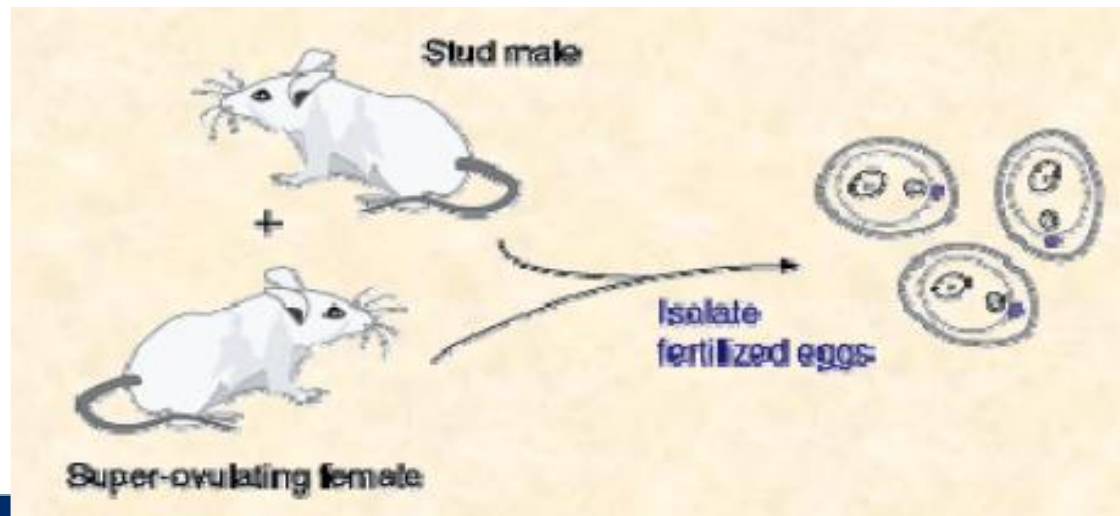
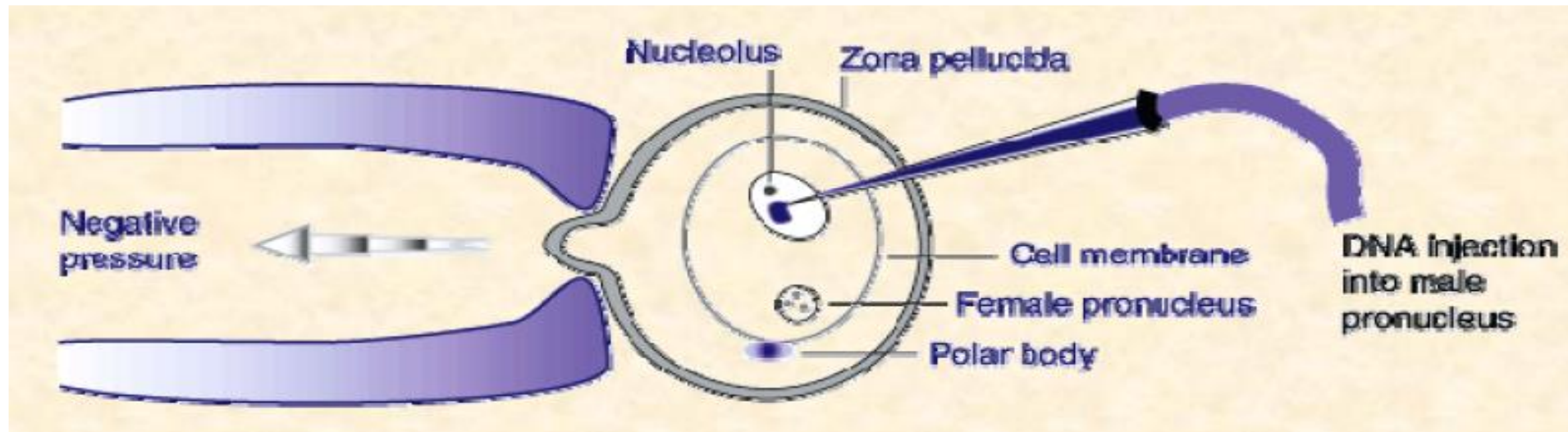


- Promoter, with or without enhancer
- Gene to be expressed, which may be a reporter gene
- Splice donor and acceptor sequences flanking an intron, these can be from another gene, e.g. beta-globin or SV40 t antigen
- Termination/polyadenylation sequences, these can be from another gene, e.g. beta-globin or SV40 t antigen
- **Transgenes must be excised from the bacterial plasmid sequences in order to be expressed in mice**
 - This is because the prokaryotic cloning vector sequences inhibit expression of eukaryotic genes introduced into the mouse genome.

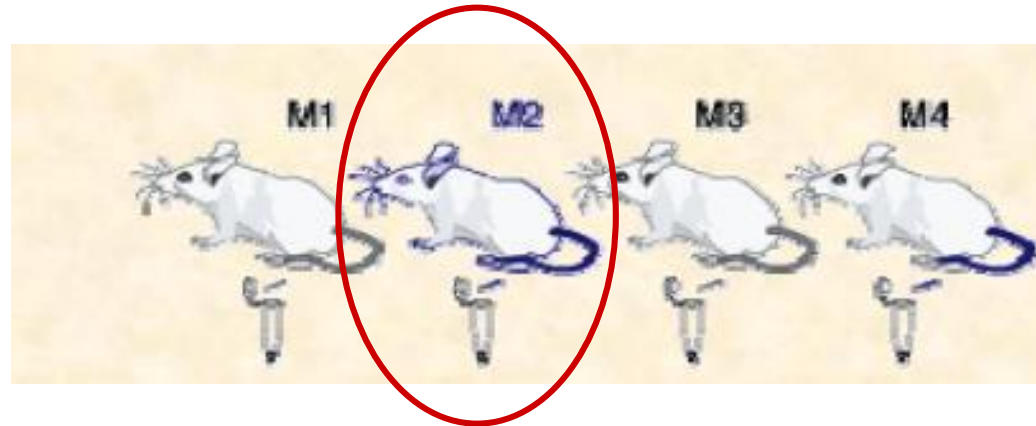
Random Integration

→ Sequences ensuring expression of the transgene

Production of transgenic mice - Introduction of genes into embryos



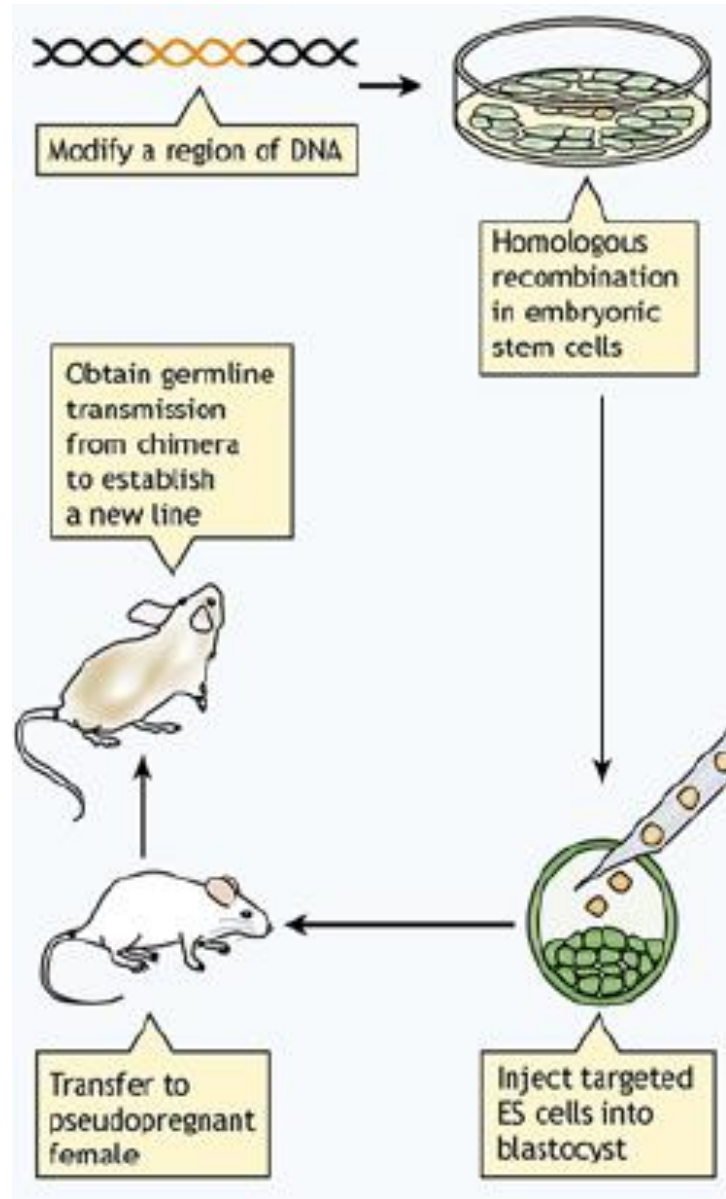
Producing Transgenic mice



M2 is backcrossed to non-transgenic mates to identify founder animals containing germline DNA integration that results in a Mendelian inheritance pattern of the transgene.

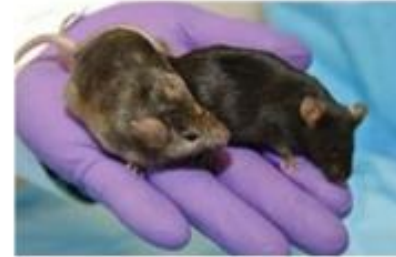


Gene Targeting in ES Cells



KO mouse

KNOCK OUT MICE



- a mouse in which a gene has been deleted/mutated (gene is inactivated)
- *specific* gene is targeted
- The loss of gene activity often causes changes in a mouse's phenotype and thus provides valuable information on the function of the gene.

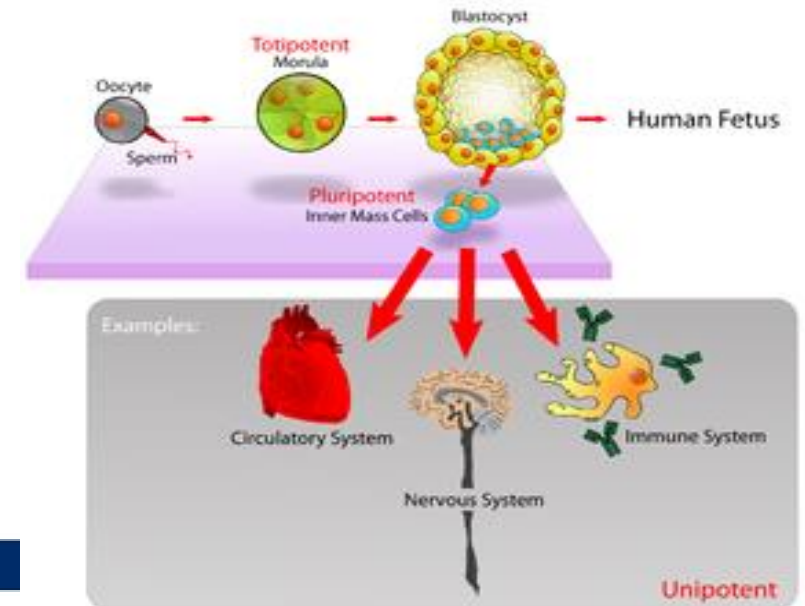
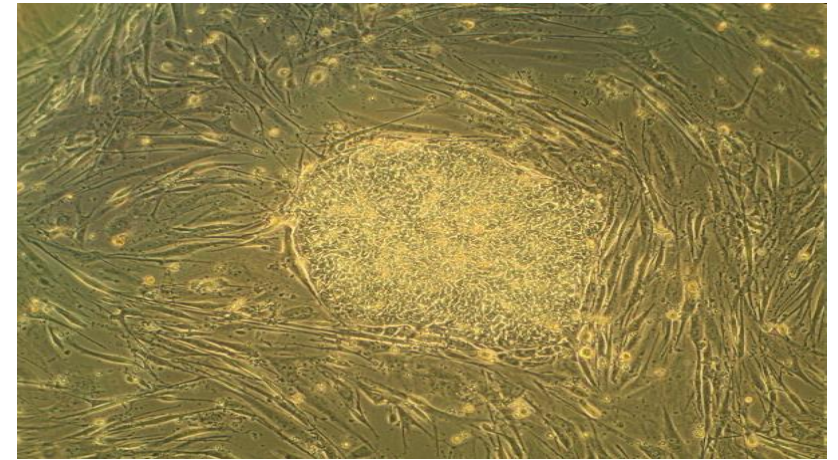
Production of transgenic mice using ES cell technology

Embryonic stem cells (ES cells) are stem cells derived from the inner cell mass of an early stage embryo known as a blastocyst.

embryos reach the blastocyst stage 4-5 days post fertilization ~they consist of 50-150 cells.

ES cells are pluripotent- are able to differentiate into all derivatives of the three primary germ layers: ectoderm, endoderm, and mesoderm.

These include each of the more than 220 cell types in the adult body



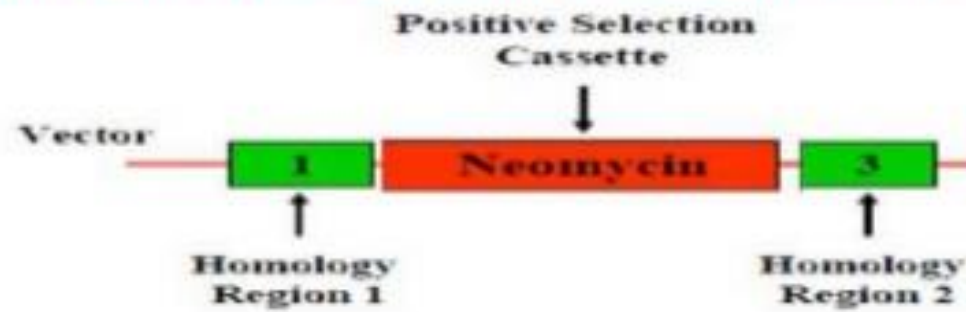
Gene Targeting in ES Cells

TARGETING CONSTRUCT FOR POSITIVE / NEGATIVE SELECTION

- To make targeting construct:
 - a positive selectable marker flanked by two "arms" of homologous sequence
 - a negative selectable marker outside one homologous arm

- **Positive selection markers**

Expression cassettes encoding antibiotic resistance genes



Gene Targeting in ES Cells

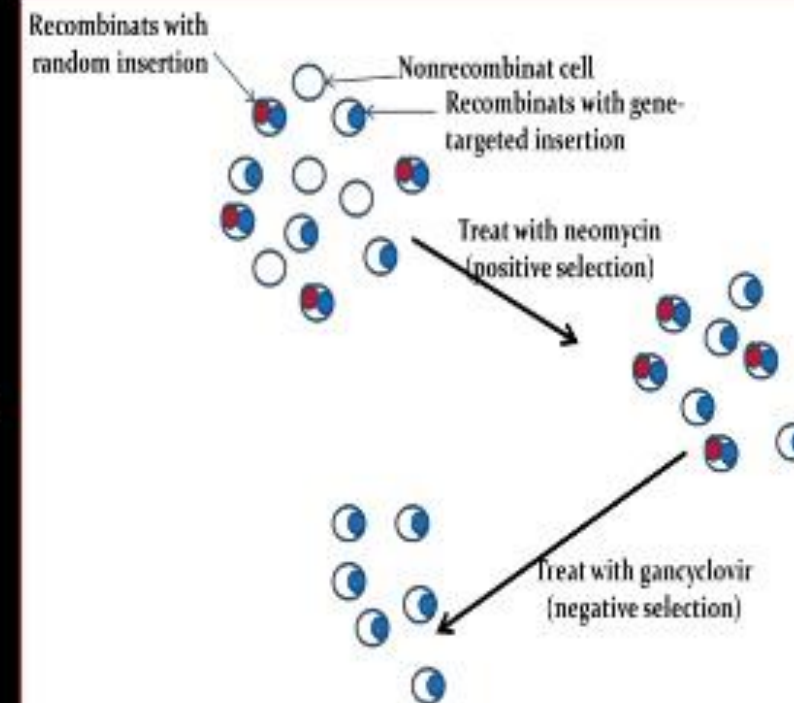
SELECTION STRATEGY

• Positive Selection

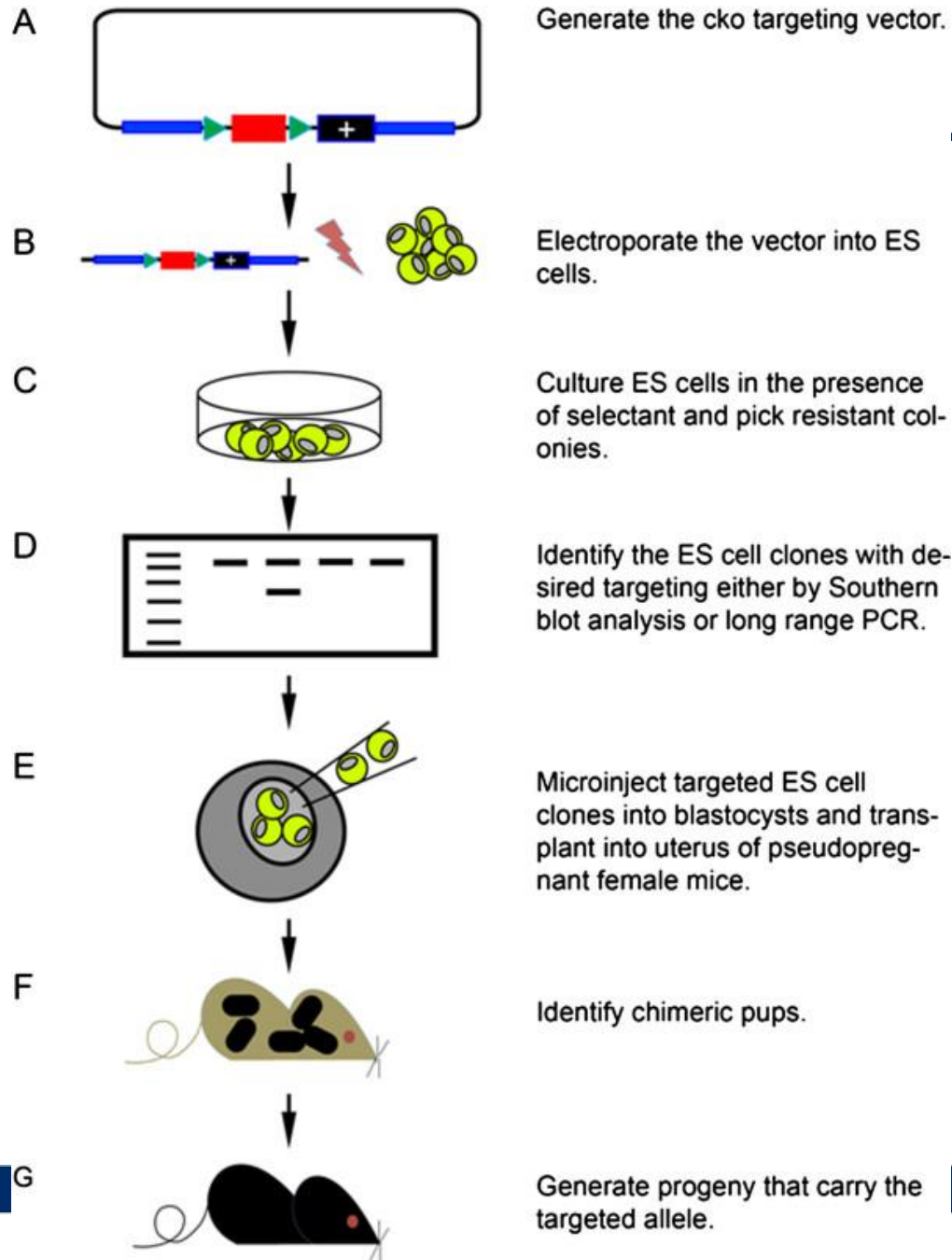
- G418
- Neomycin Resistance gene
- confers resistance to G418

• Negative Selection

- Gancyclovir
- Herpes Simplex Virus Thymidine Kinase (HSV-TK) gene.
- sensitive to gancyclovir
- selects against random integrants



Gene Targeted Mice



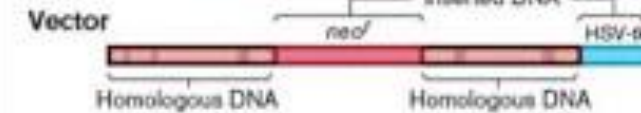
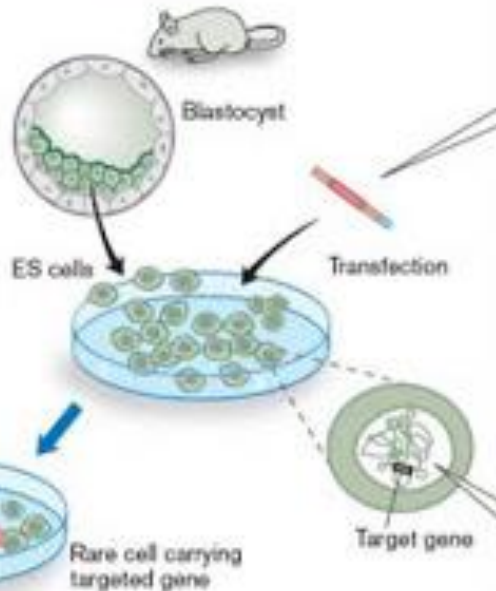
Gene Targeted Mice

--- Step 1. Gene Targeting in ES cells

Step 1 Gene targeting in ES cells

1. ES cell culture

Embryonic stem (ES) cells are cultivated from mouse pre-implantation embryos (blastocysts).

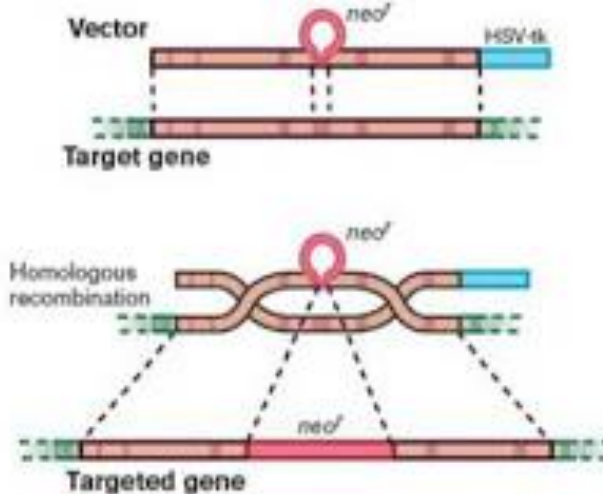


2. Construction of targeting vector

The vector contains pieces of DNA that are homologous to the target gene, as well as inserted DNA which changes the target gene and allows for positive-negative selection.

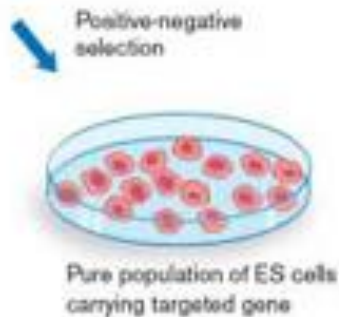
3. ES cell transfection

The cellular machinery for homologous recombination allows the targeting vector to find and recombine with the target gene.



4. Proliferation of targeted ES cell

Selection for presence of *neo^r* and absence of HSV-tk enriches targeted ES cells.

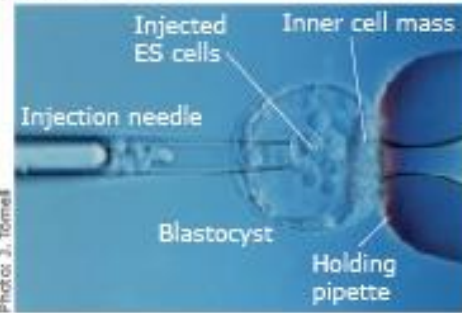


Gene Targeted Mice

Step 2. From gene targeted ES cells to gene targeted mice

6. Injection of ES cells into blastocysts

The targeted ES cells are injected into blastocysts ...



Mosaic inner cell mass

... where they mix and form a mosaic with the cells of the inner cell mass from which the embryo develops.

Photo: J. Wilbertz



Newborn chimeric mouse

8. Birth and breeding of chimeric mice

The chimeric mice mate with normal mice to produce gene targeted as well as normal offspring.



Chimeric mouse ♂

Normal mouse ♀

9. Birth of gene targeted mice

Gene targeted mice — called "knockout mice" when the targeted gene is inactivated in all cells.



Normal mice

7. Implantation of blastocysts

The injected blastocysts are implanted into a surrogate mother where they develop into chimeric embryos.



Knockout systems – a variation on the theme

1. Conditional knockouts
2. Knockin models (an additional gene function is established)

lacZ gene as a means of detecting tissue-specific gene expression

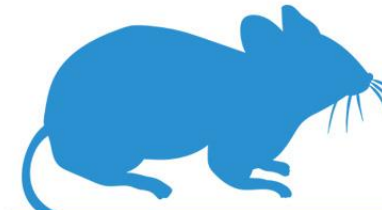
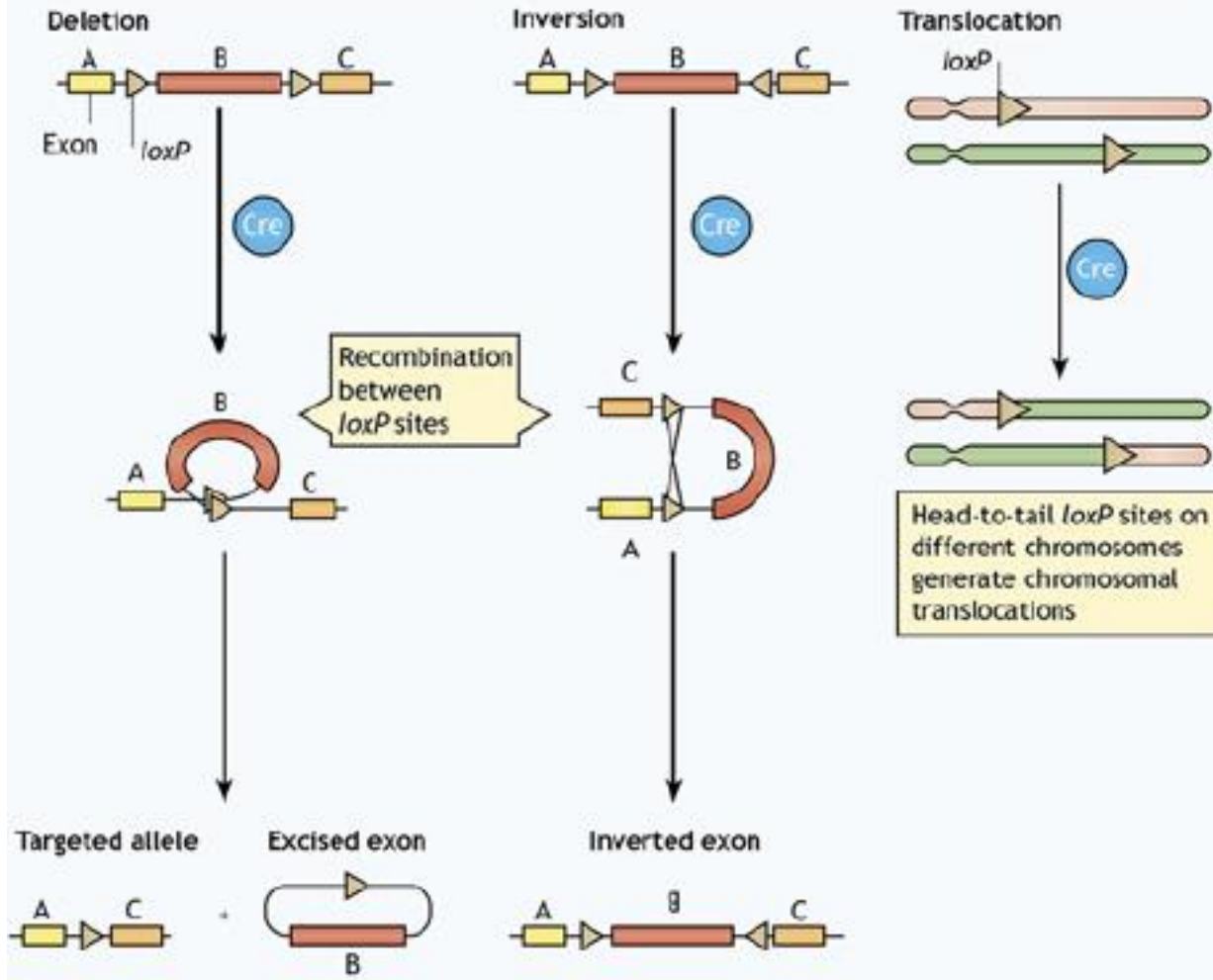
In 1995 a database was established to collate details of knockout mice. This is known as the **Mouse Knockout and Mutation Database**. There are over 5 000 entries in the Mouse Knockout and Mutation Database, which is a major resource for those interested in using the mouse as a model system for the study of gene expression, development, and disease.

MKMD can be found at [<http://research.bmn.com/mkmd>]

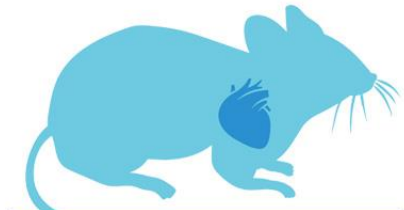


Conditional Mutagenesis

A Cre-mediated recombination events



Conventional KO
Your target gene is knocked out in all tissues at all times.



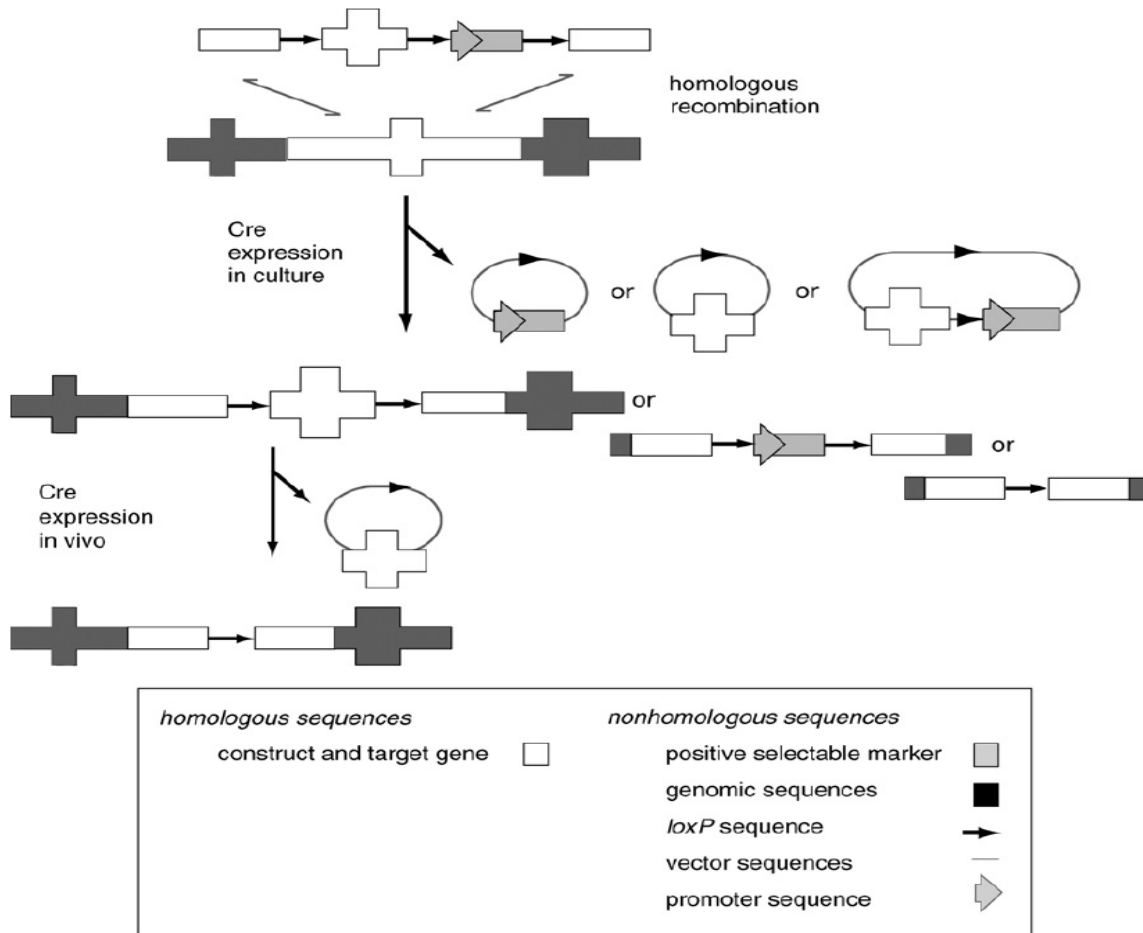
Conditional KO
You control where and when your target gene is knocked out.

Cre-Lox recombination –

The *Cre-lox* system is used as a genetic tool to control site specific recombination events in genomic DNA. This system has allowed researchers to manipulate a variety of genetically modified organisms to control gene expression, delete undesired DNA sequences and modify chromosome architecture.

Knockout systems – the variation on the theme

Conditional gene targeting using the Cre/loxP system



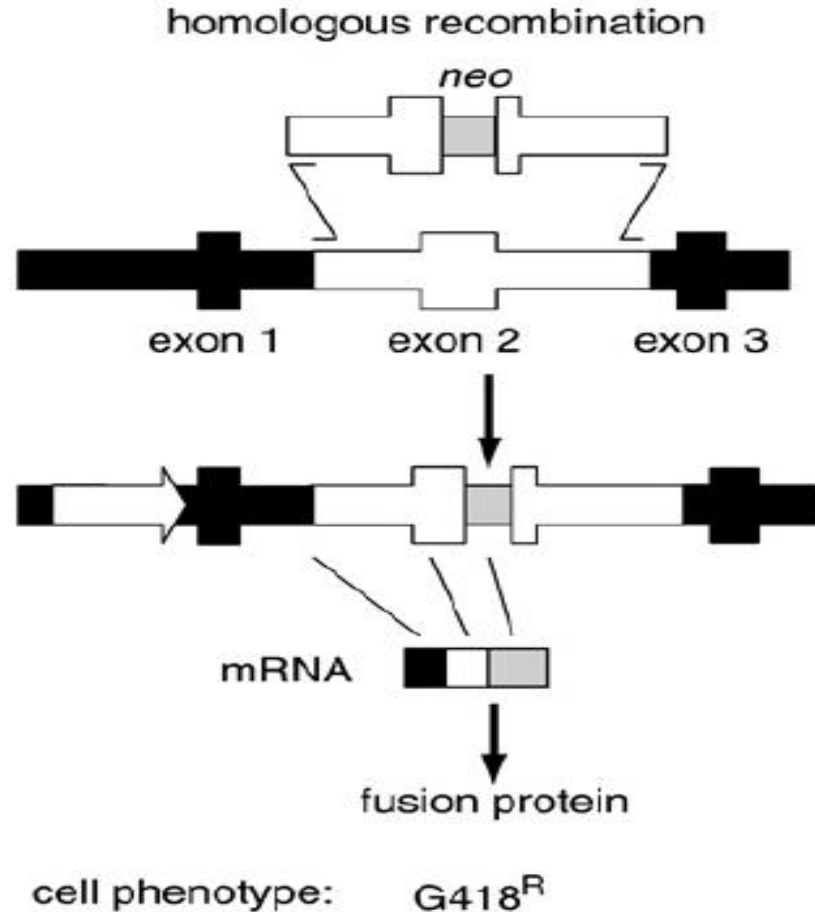
The targeting vector contains three loxP sites that flank the regions of the gene to be removed and the positive selectable marker neo.

After HR the selectable marker is excised - transient expression of Cre.

The correct recombination is identified by screening by Southern analysis or PCR.

The mutant ES cells are then used to produce mice

Using the Cre/loxP system to introduce subtle mutations



The subtle mutation is introduced along with the selectable marker in the targeting vector.

The selectable marker is then removed by transient expression of *Cre*, which leaves only the subtle mutation and the small loxP site in a silent location.

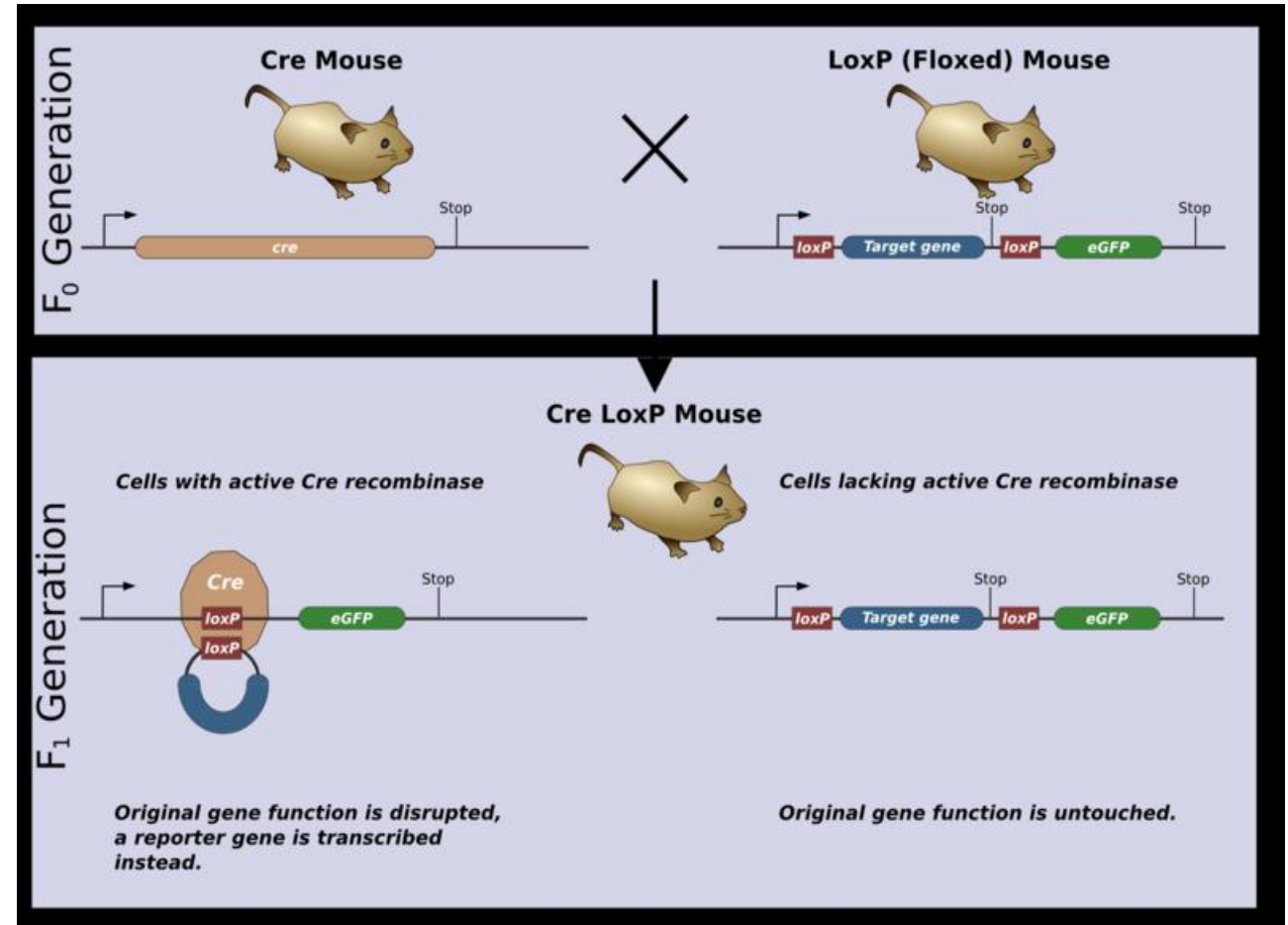
Knockout systems – the variation on the theme

Conditional gene targeting using the Cre/loxP system

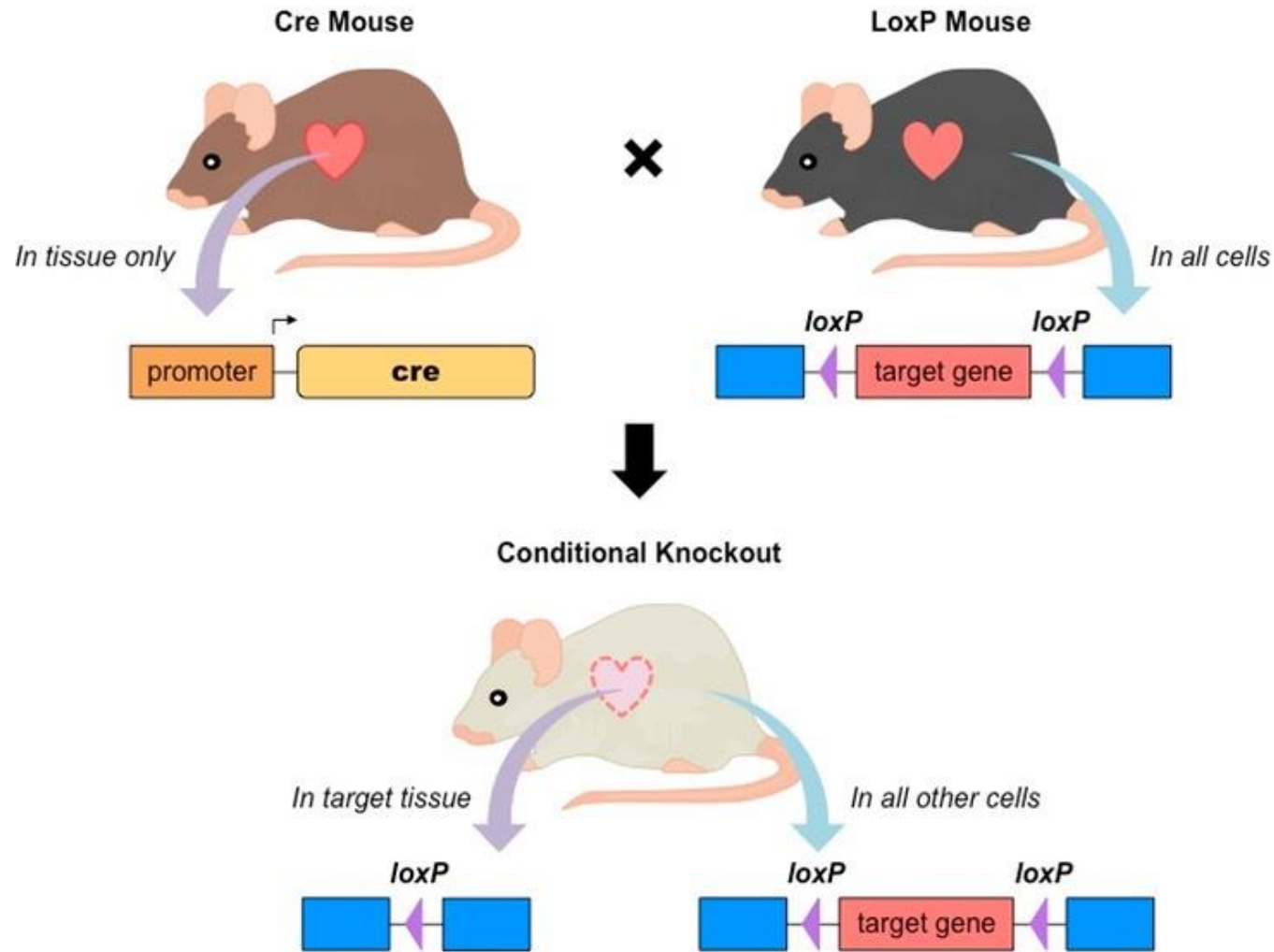
(Tissue specific knockouts/
tissue specific promoters)

a transgenic animal, which is finally bred
to an animal line expressing Cre under
either temporal or spatial control.

Cre can also be ubiquitously expressed to
obtain a knockout in all tissues, including
the germ line.

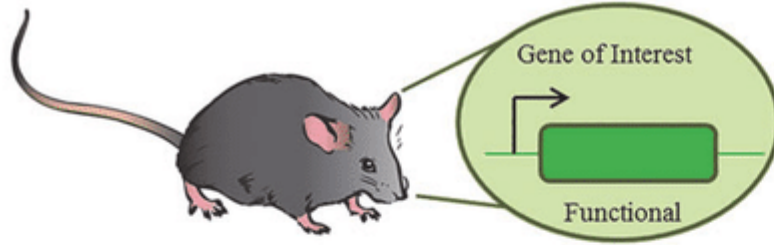


Conditional Mutagenesis

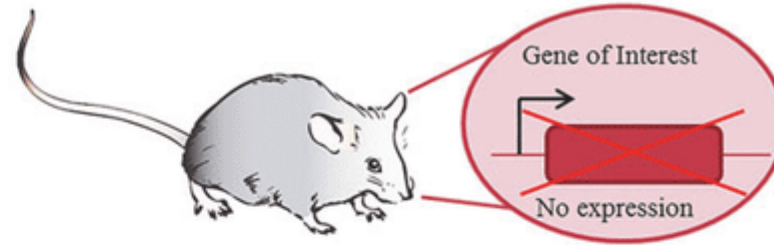


Conditional Mutagenesis

A Wild type mouse

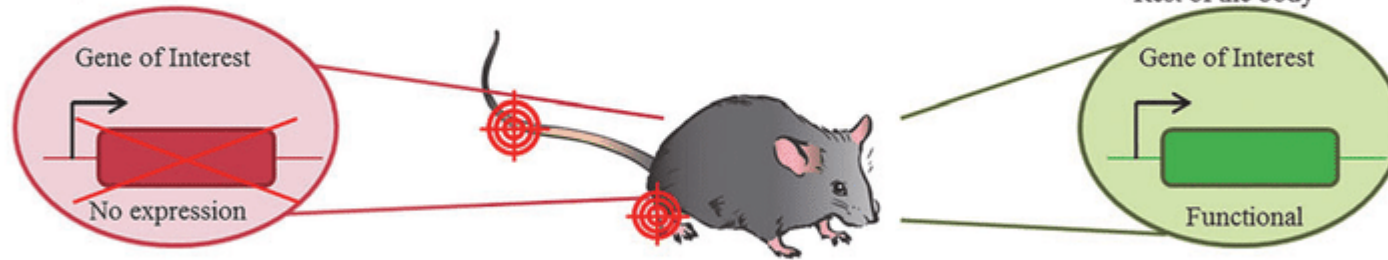


Constitutive Knockout mouse



B Tissue-specific Knockout mouse

Targeted tissue (tendons)



C Inducible Knockout mouse

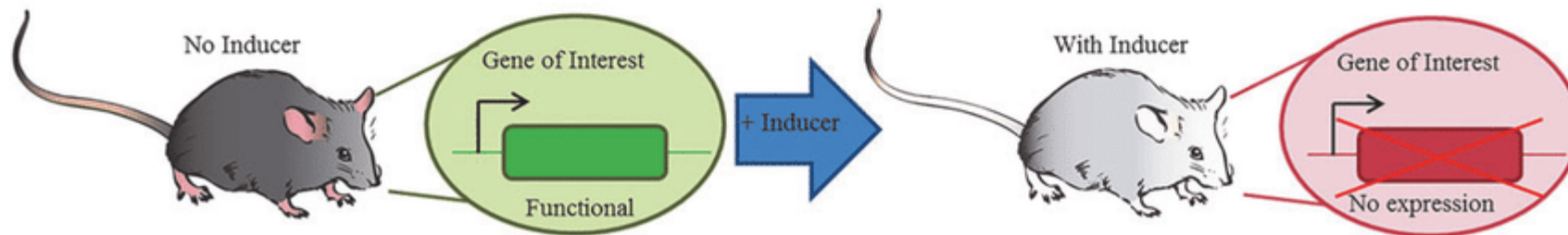
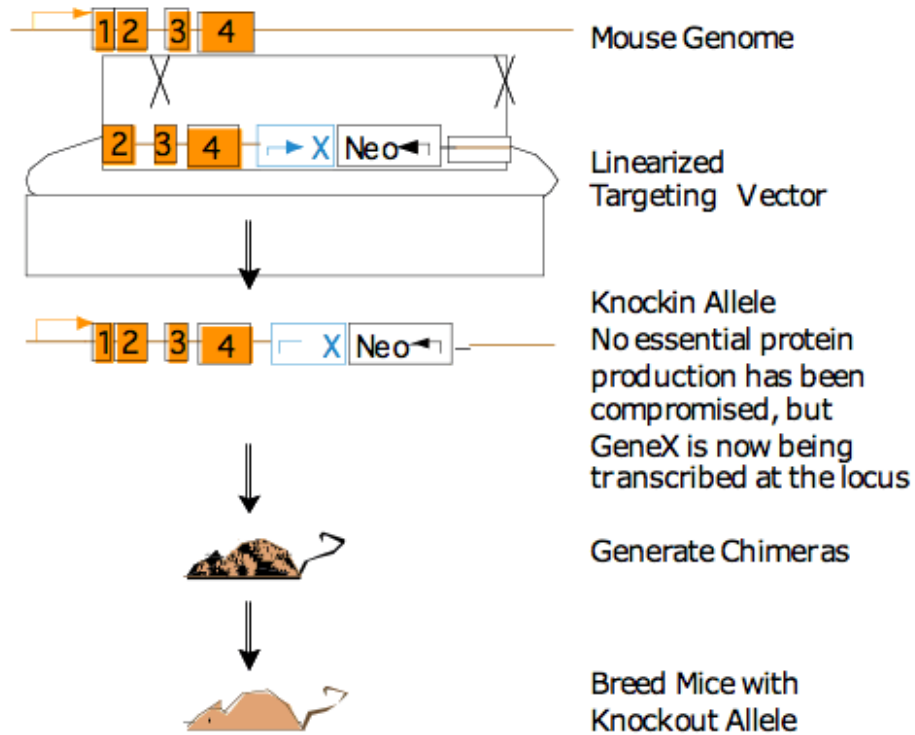


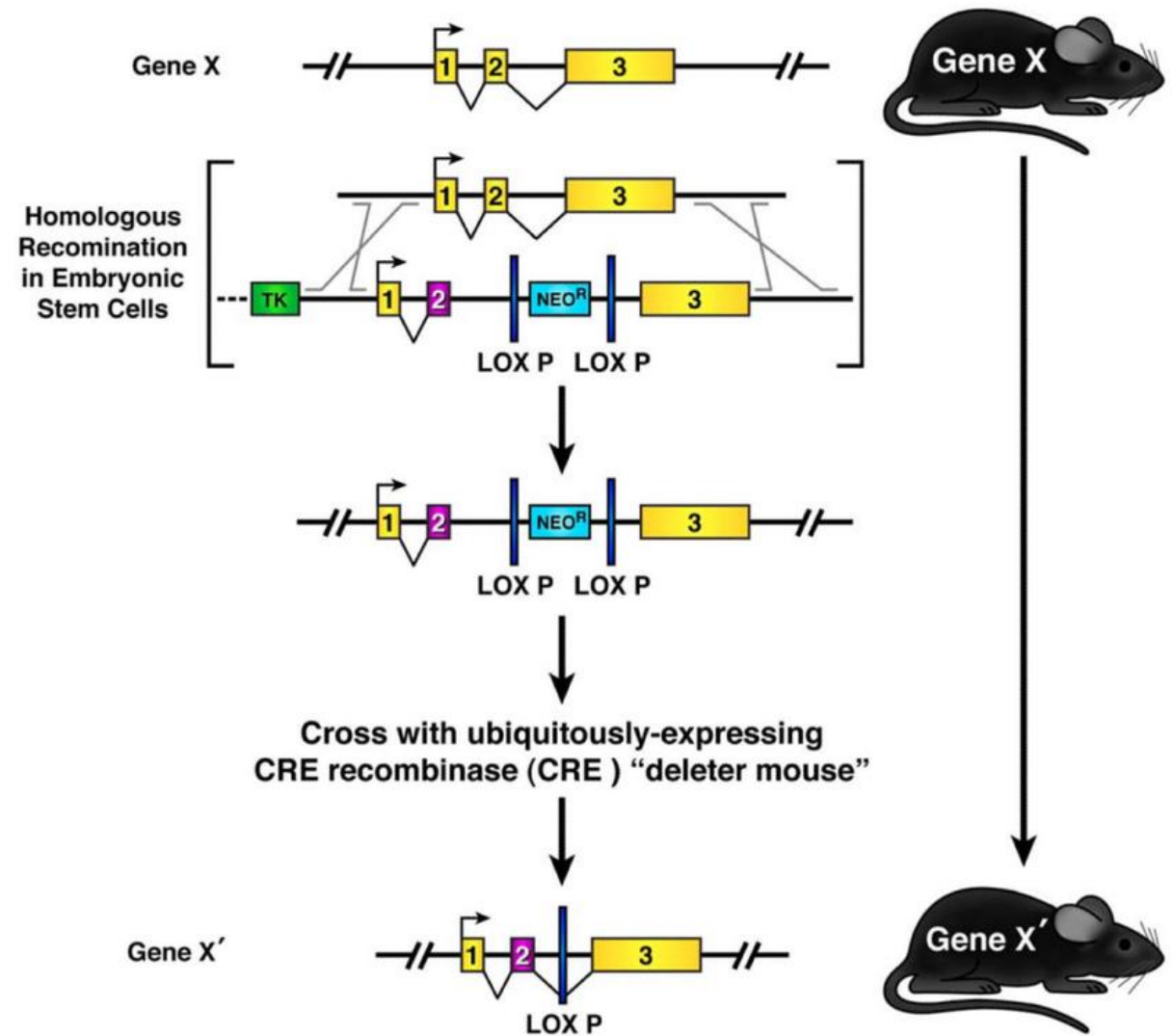
Figure 1: Gene Targeting for Knockin Mouse



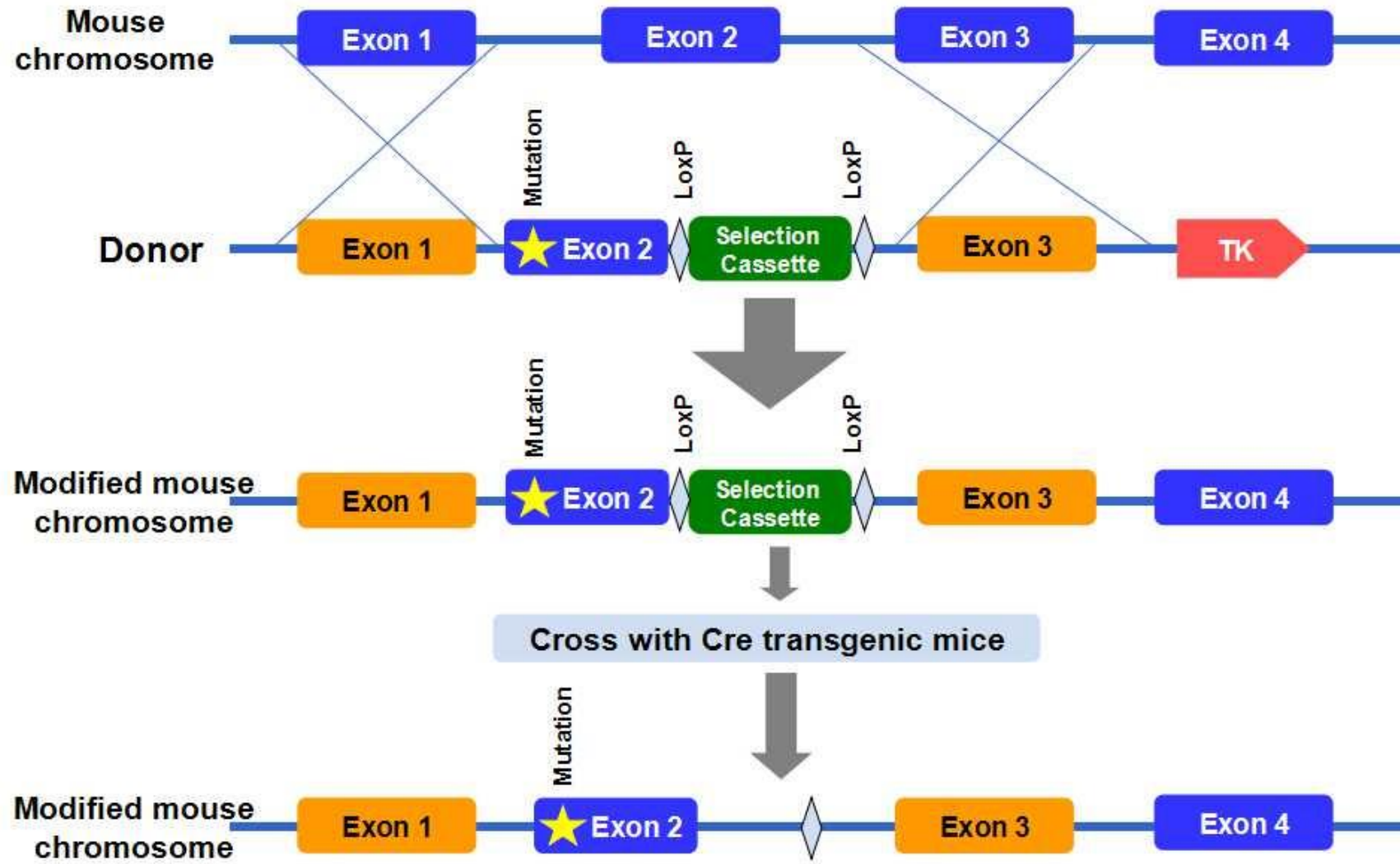
Legend

- Mouse Genomic DNA
- Non-mouse DNA
- Exons
- Promoter
- Site of Homologous Recombination
- Promoter and Gene encoding for Drug Resistance a.k.a Selection Cassette

Knock In strategy

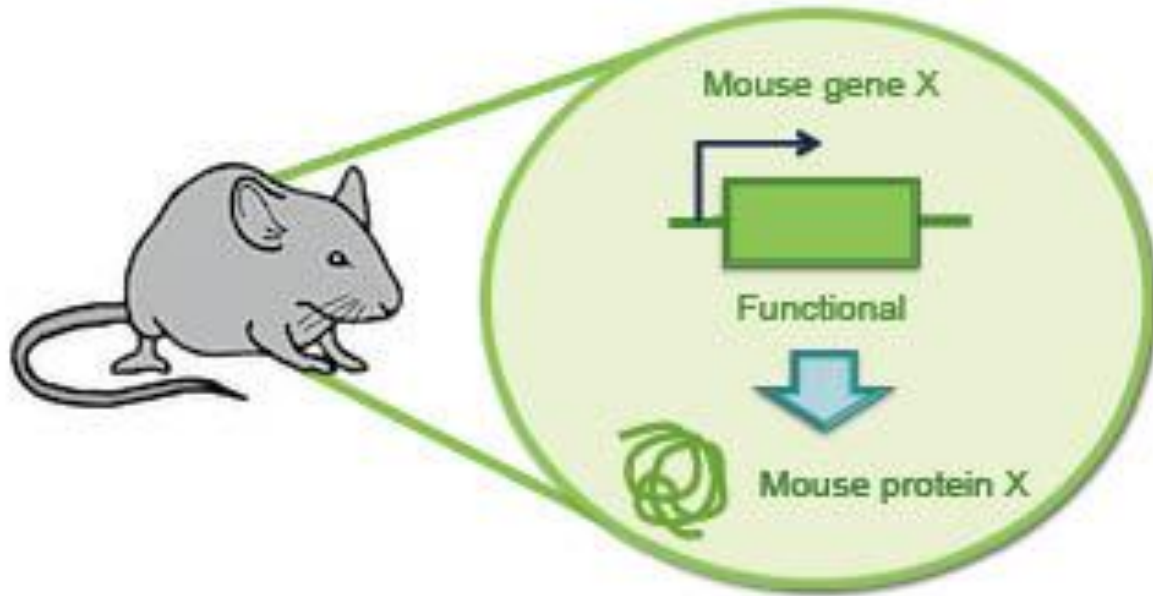


Knock In strategy: mutation

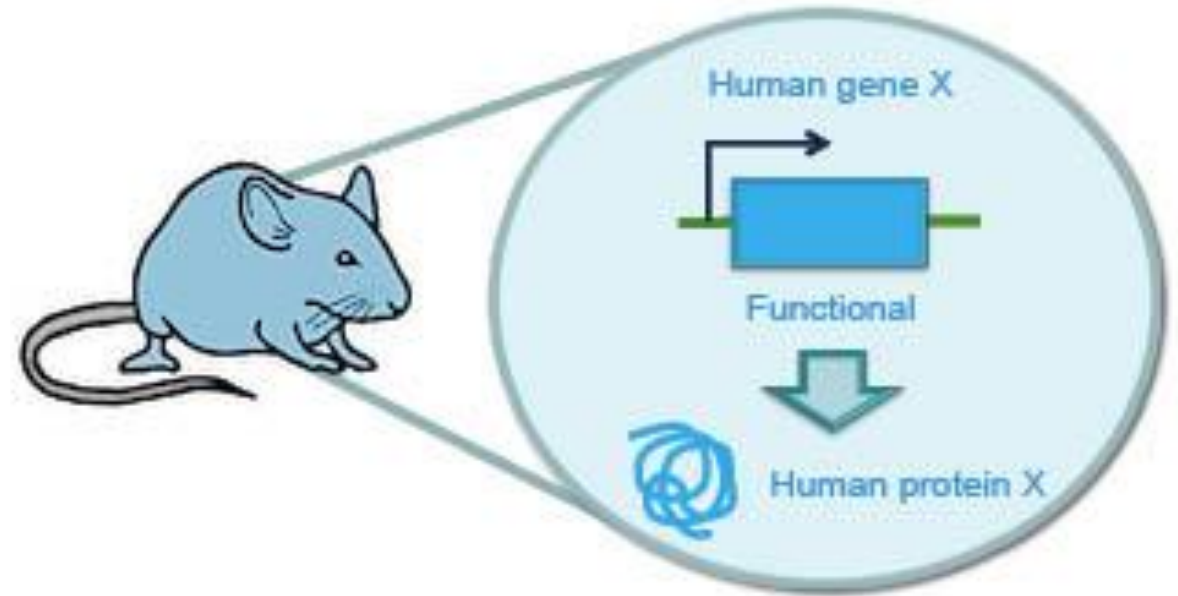


Humanized Knock In mouse

Wildtype Mouse



Humanized Knockin Mouse



Genome Editing with Programmable Endonucleases

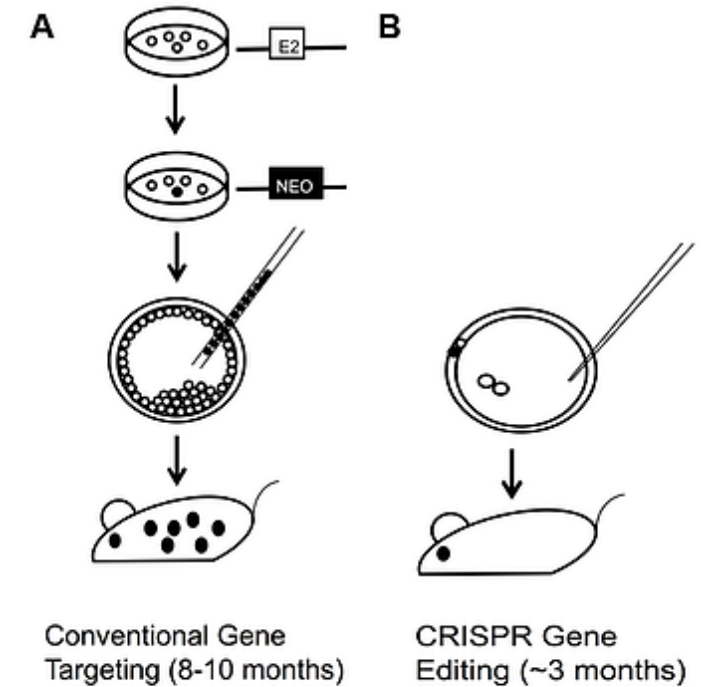
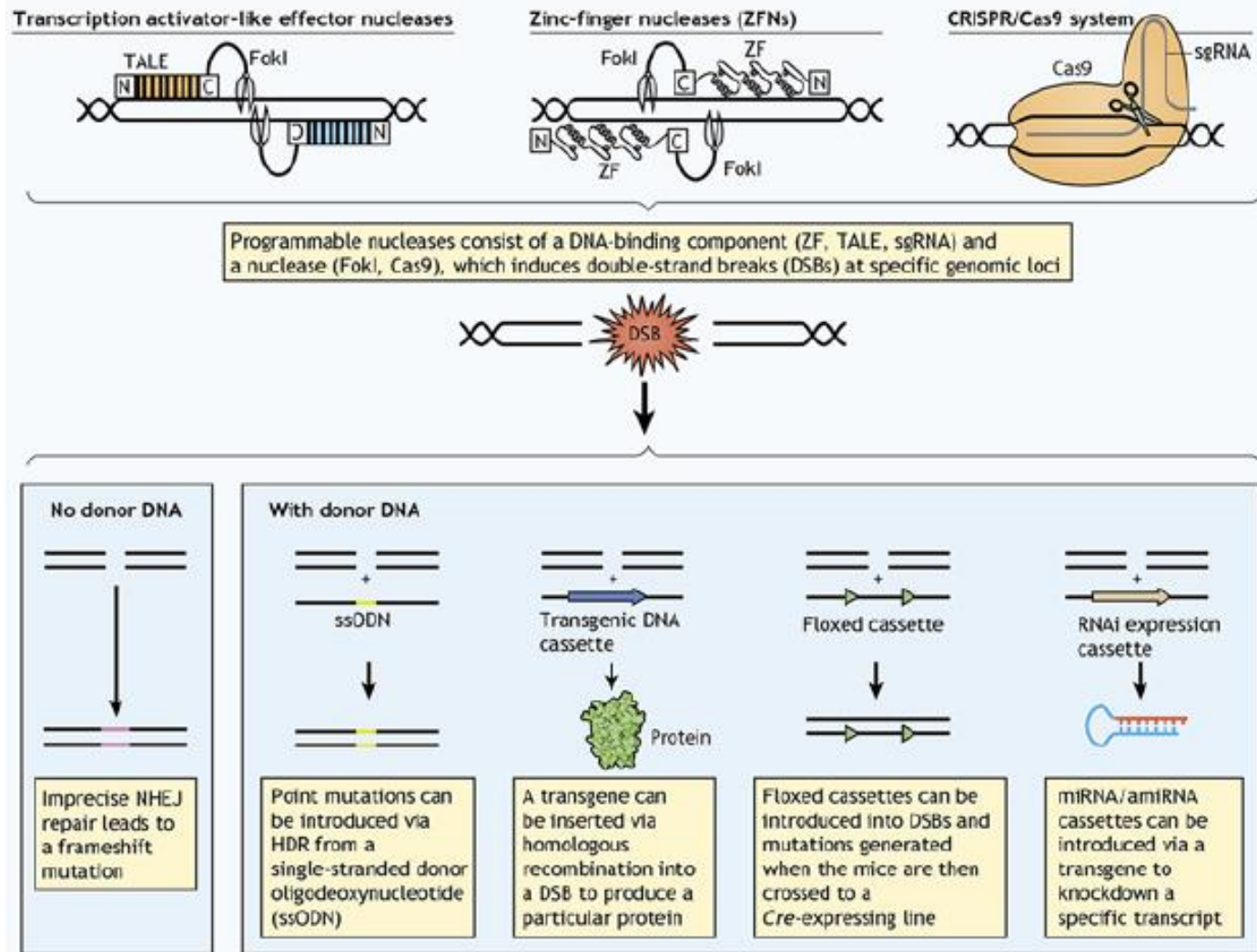
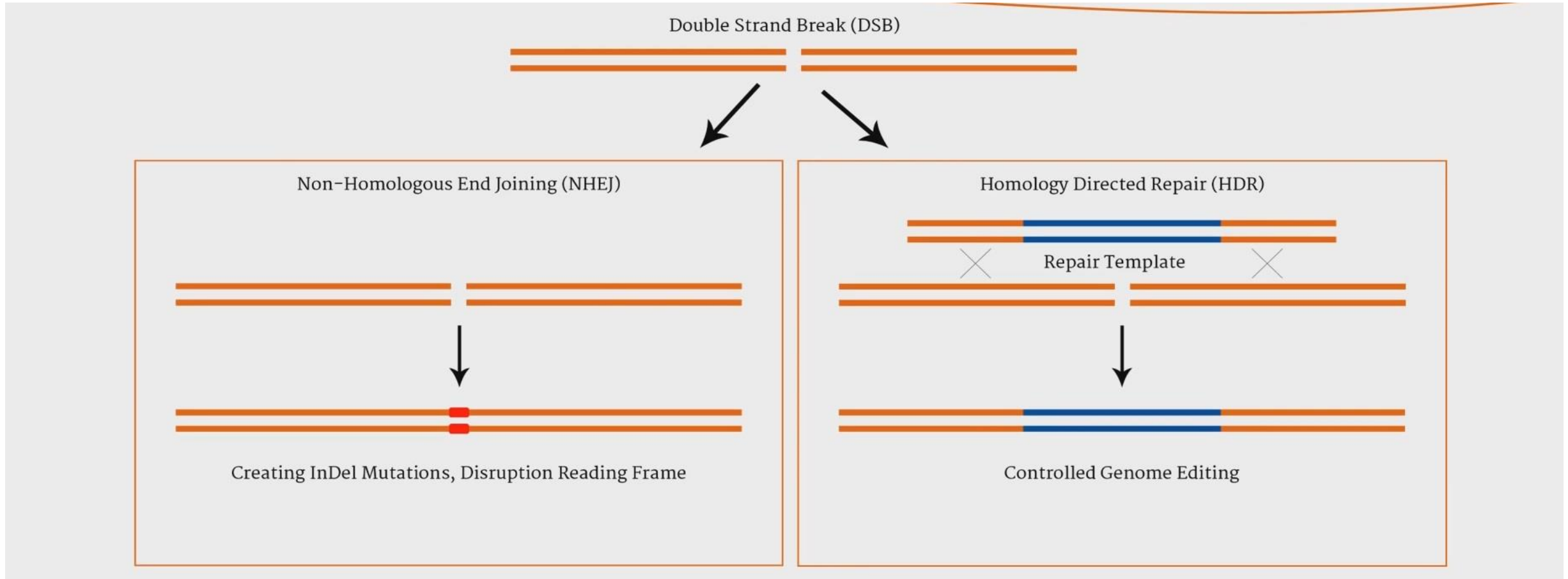
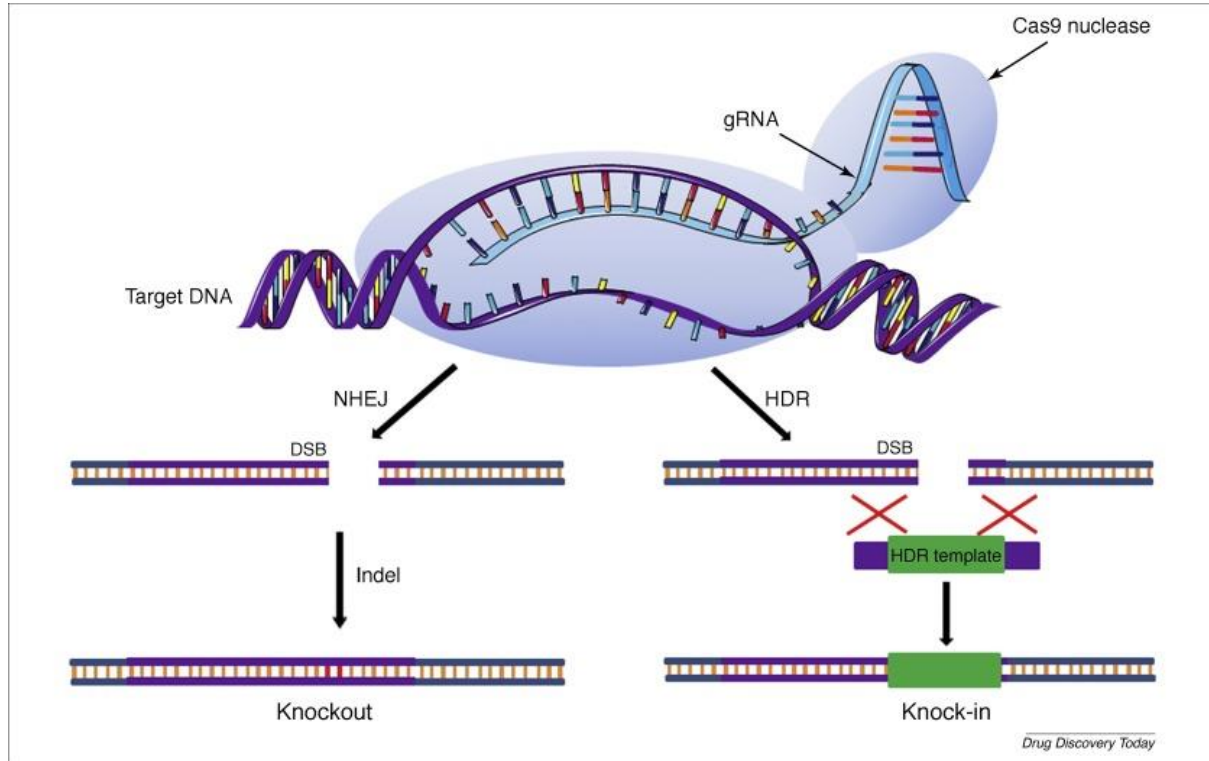


Figure 1: In conventional gene targeting (A), you must first generate your desired mutation in mouse ES cells, select for the mutation and inject the ES cells into a mouse embryo to create chimeric mice. This laborious process takes ~8-10 months. With CRISPR (B), you can inject CRISPR components directly into a zygote and obtain a knockout mouse in about 3 months. Image courtesy of Wenning Qin.

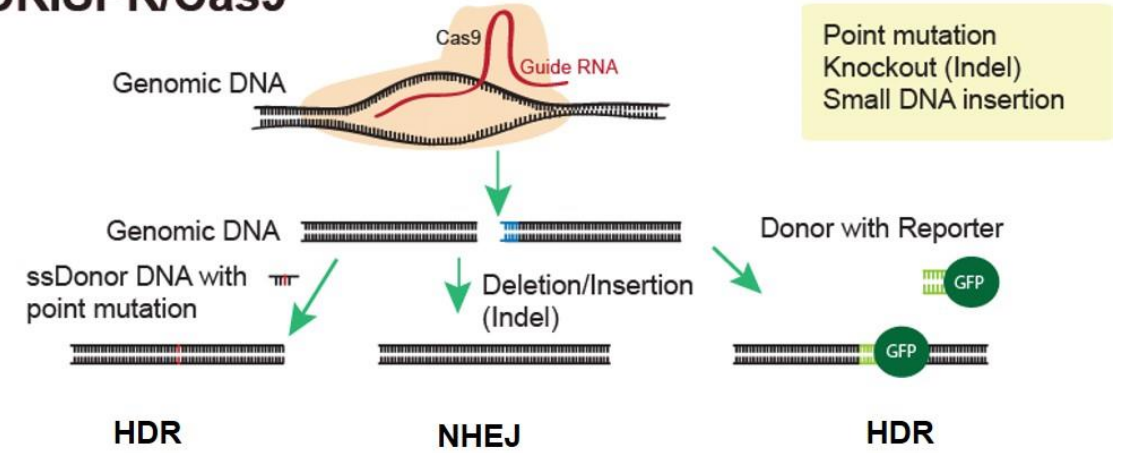
Double strand break repair



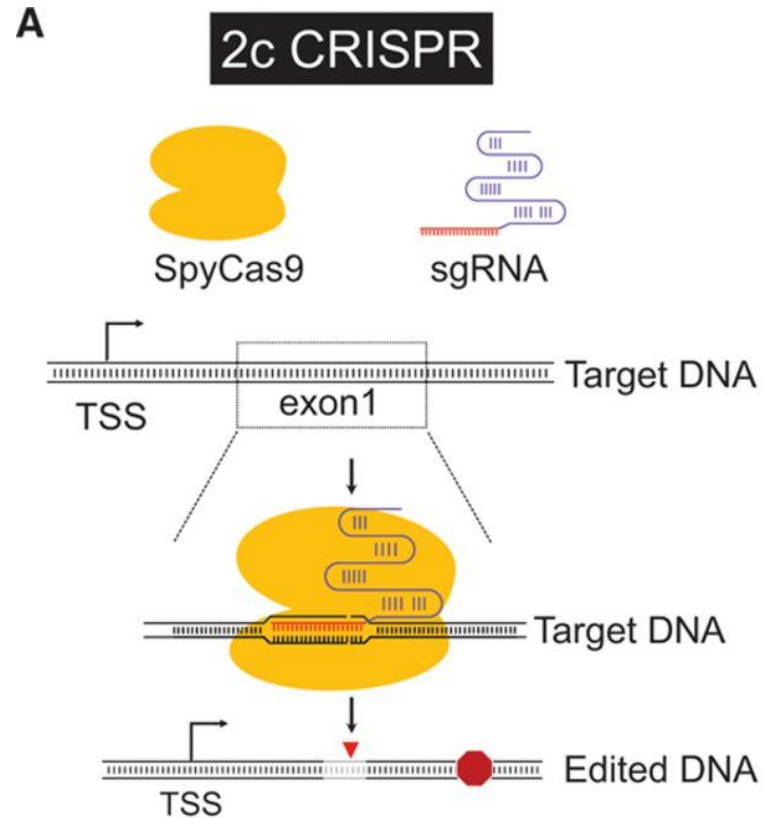
CRISPR CAS9-Mediated repair



CRISPR/Cas9

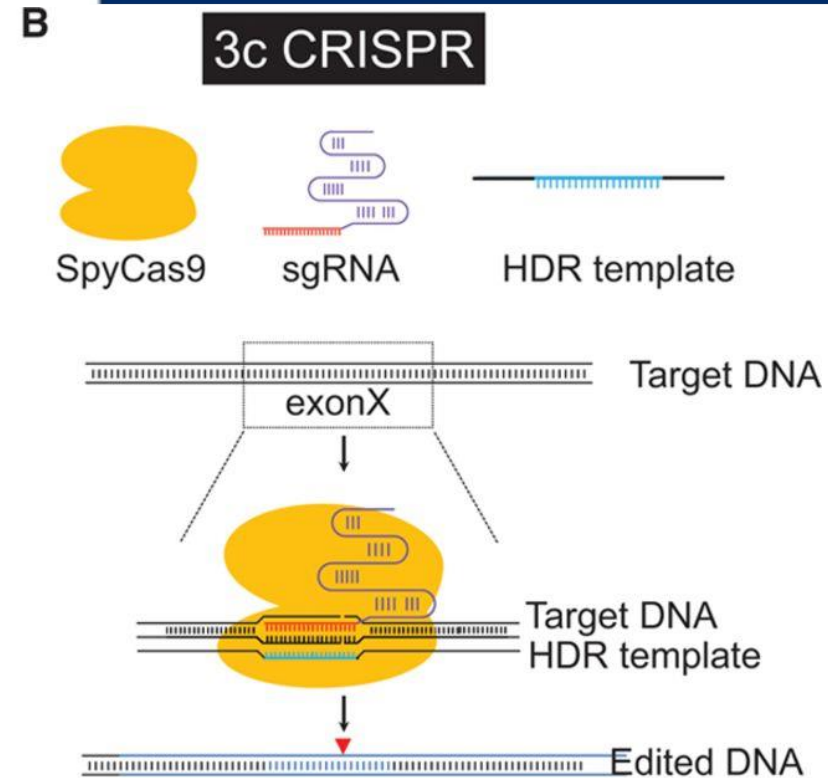


CRISPR CAS9-Mediated genome editing



Random insertion/deletion/substitution

- Frameshift
- Premature stop
- Splice disruption
- Regulatory element deletion (Promoter/enhancer/lncRNA)

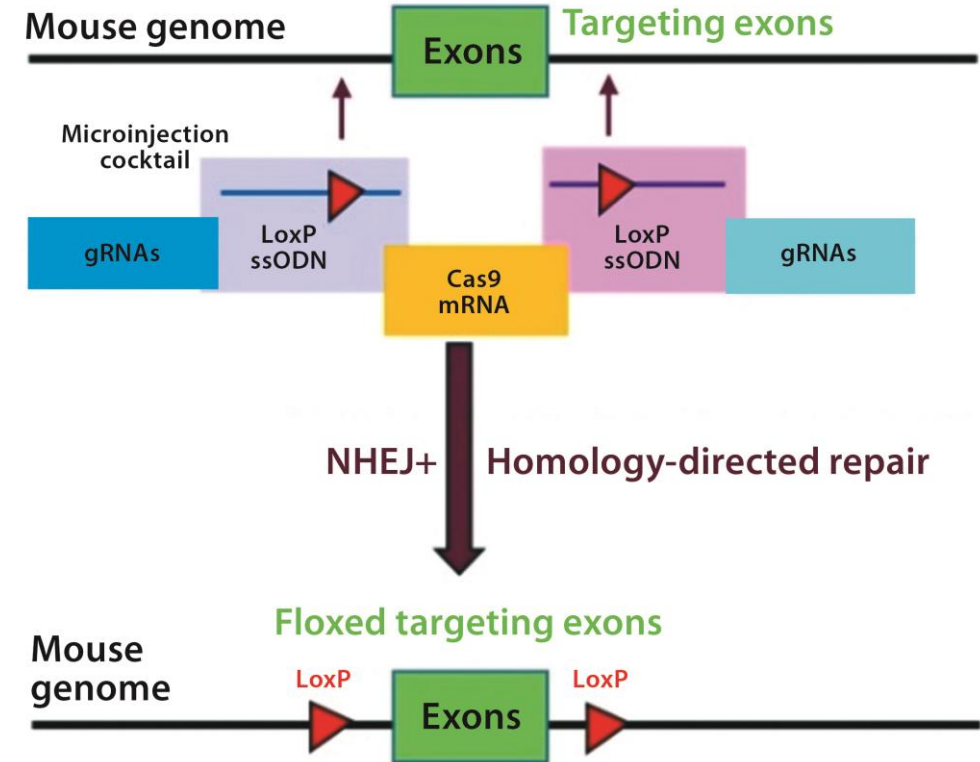
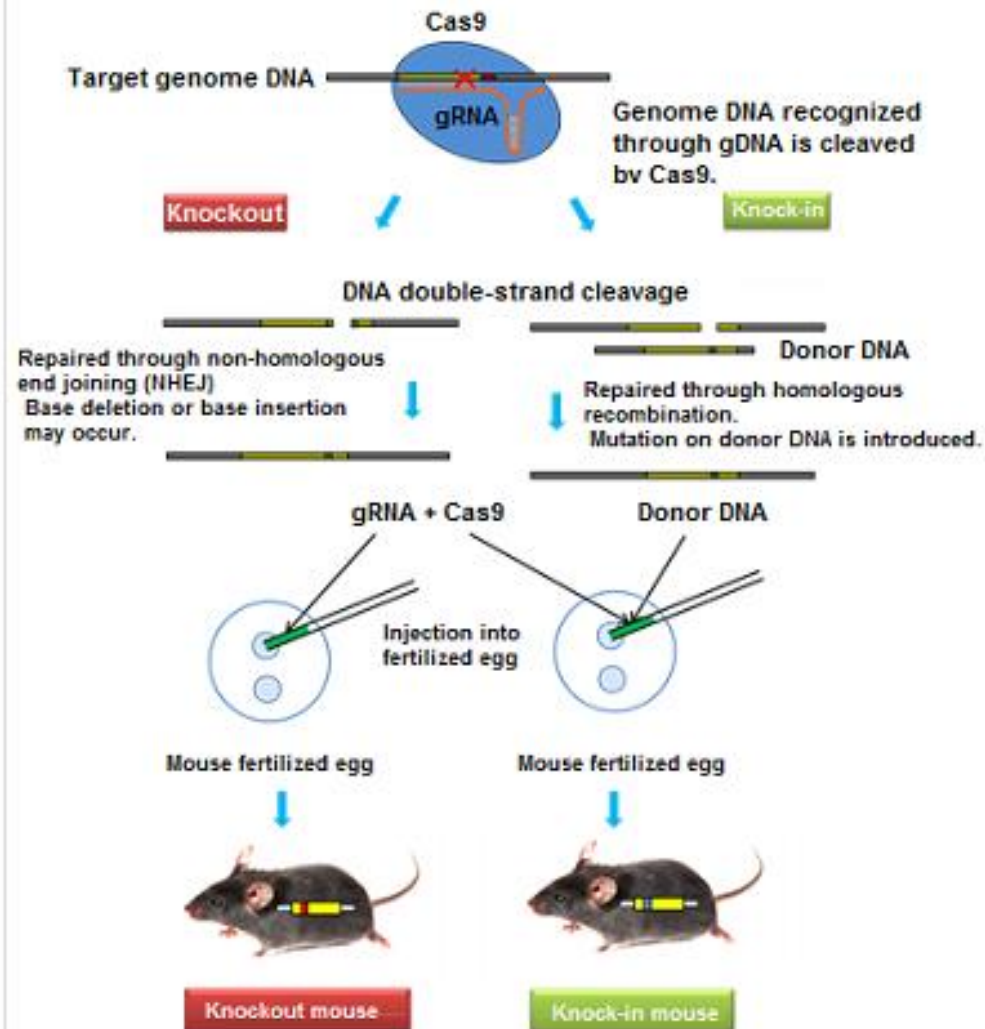


Precise genome editing

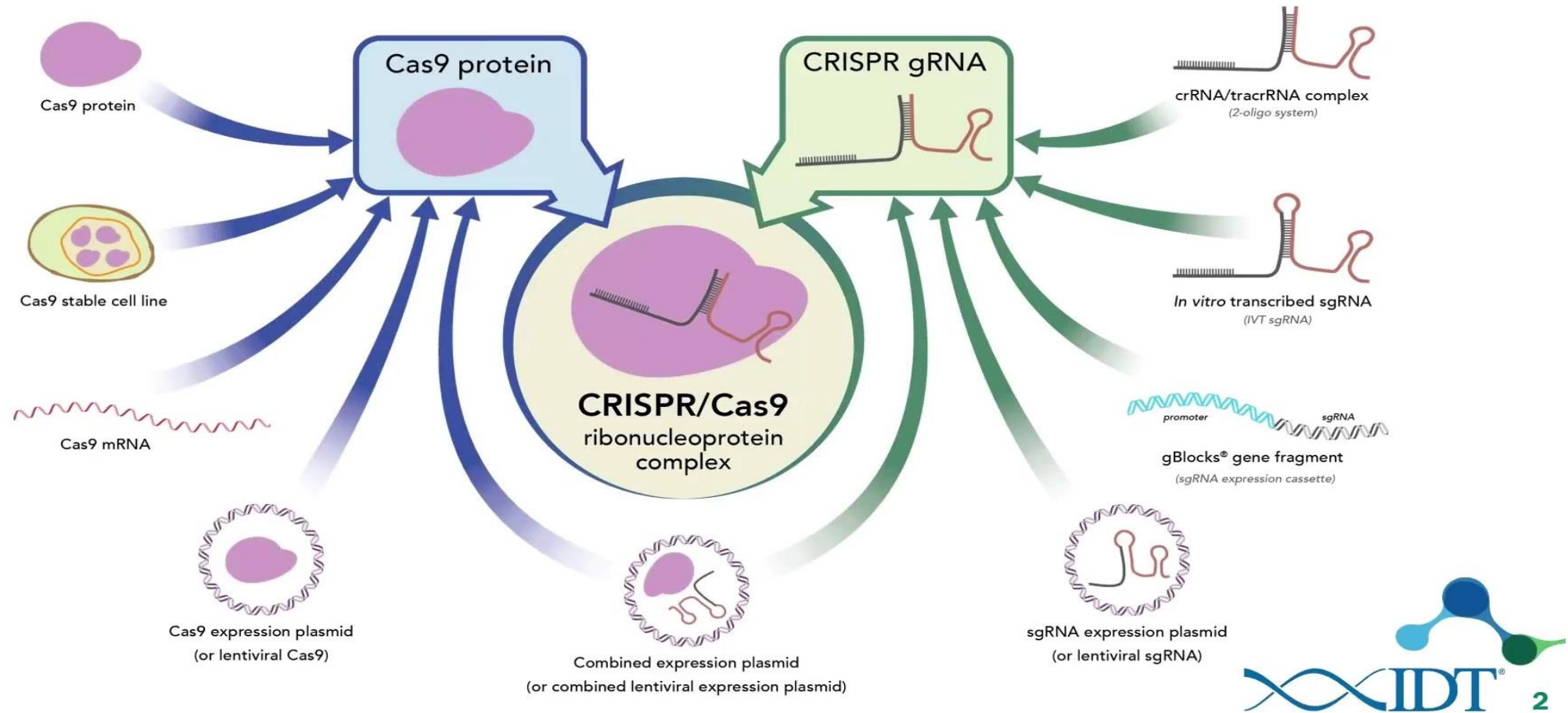
- Gene correction
- SNP modeling
- Conditional allele
- Epitope tagging
- Fine mapping regulatory element

Production of transgenic mice using CRISPR CAS9

Figure 3 Mouse production with CRISPR/Cas9

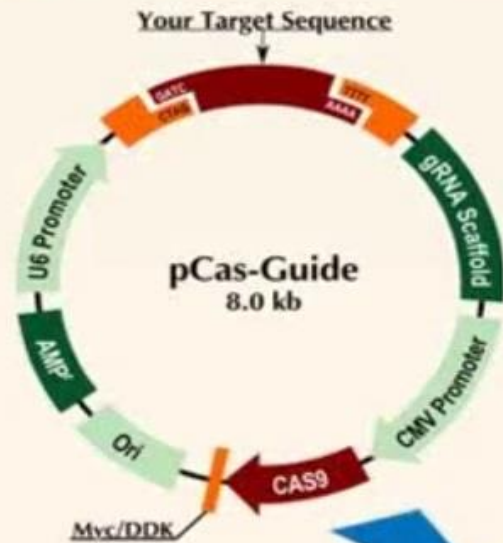


Available vector solutions

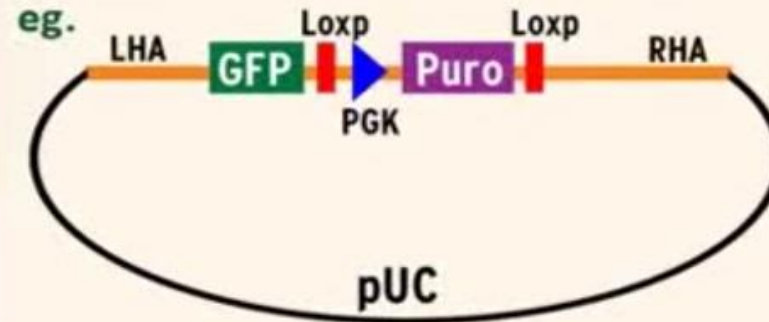


CRISPR vector systems - HR

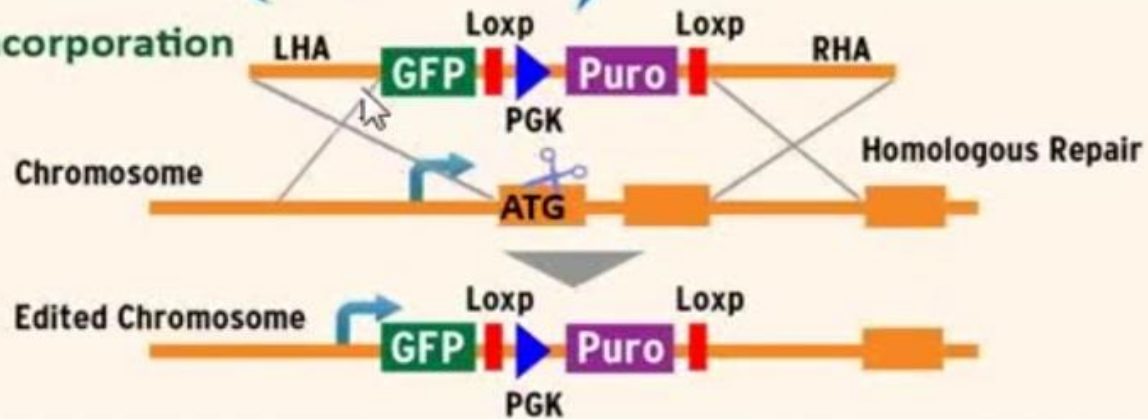
1 Target Sequence Cloned In pCas Guide Vector



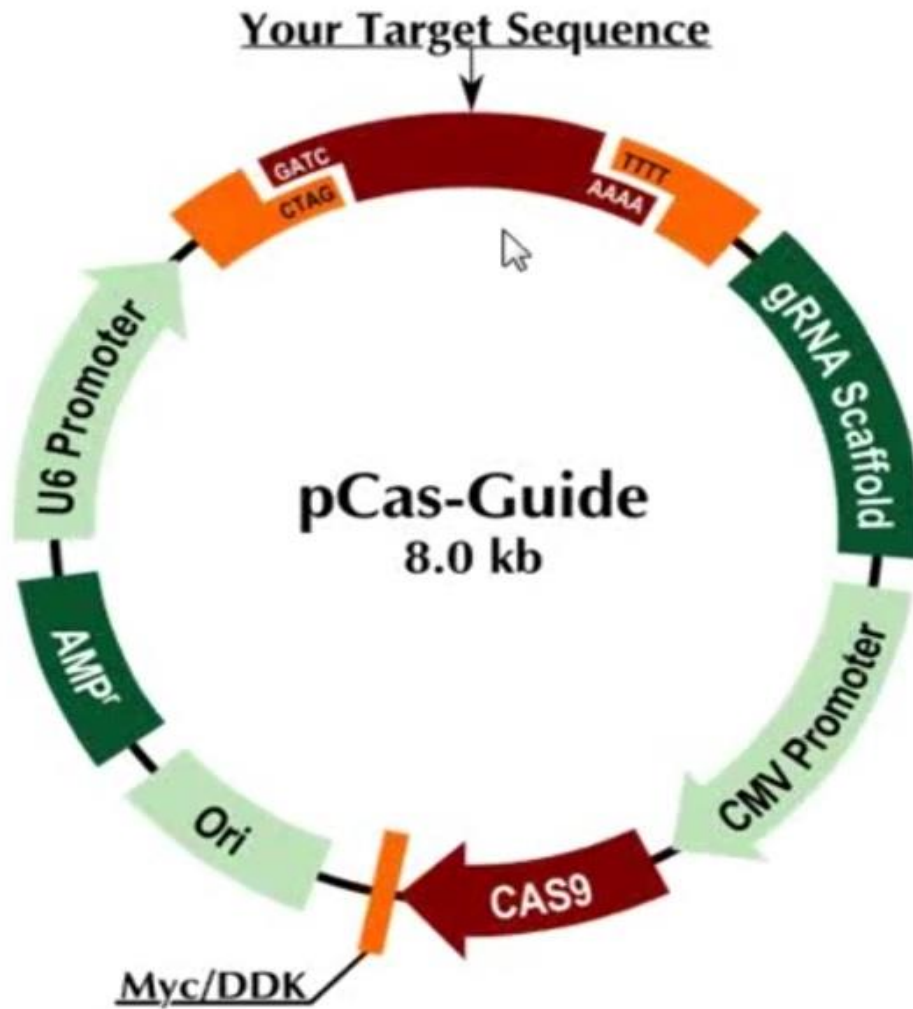
2 Donor Template DNA Containing Homologous Arms & Functional Cassette



3 Genome Incorporation



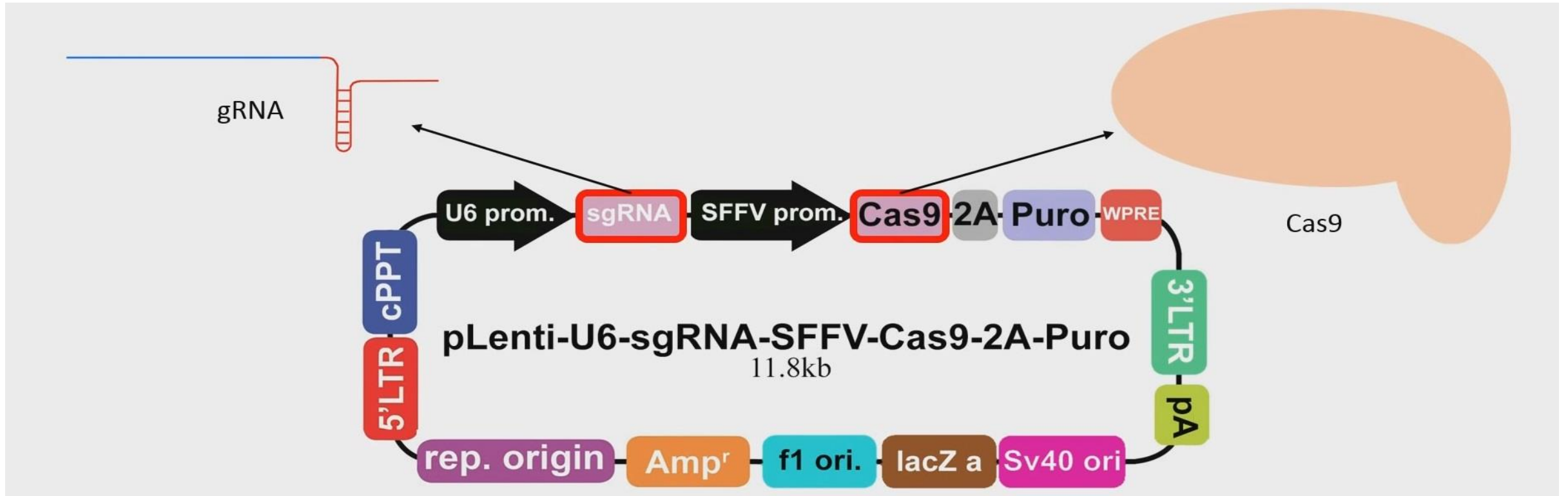
All-in vector



pCas-Guide

- Target sequence cloning
- Expresses Cas9

All-in vector

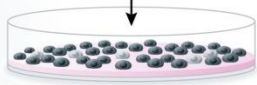


Conventional gene targeting

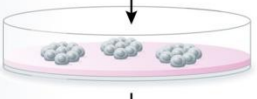
- Generation of targeting construct



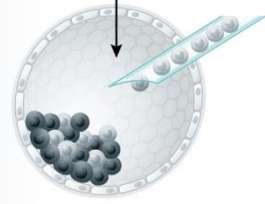
- ES cells electroporation
- Positive/negative selection



- Colony picking and expansion
- Selection and validation of targeted clones



- Injection of targeted ES cells to blastocysts
- Embryo transfer



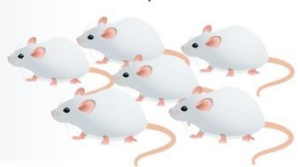
- Founder chimeric mice



- Breeding produces heterozygous mutants (N1)



- Breeding of heterozygous mice produces homozygous experimental mice

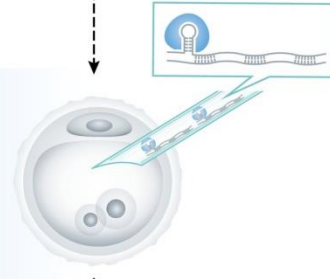


CRISPR/Cas9 gene editing

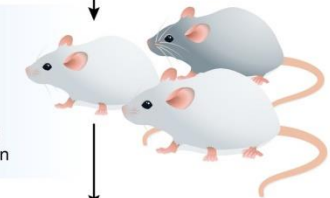
- Synthesis of targeting gRNA and Cas9



- Injection of Cas9-gRNA to zygotes
- Embryo transfer



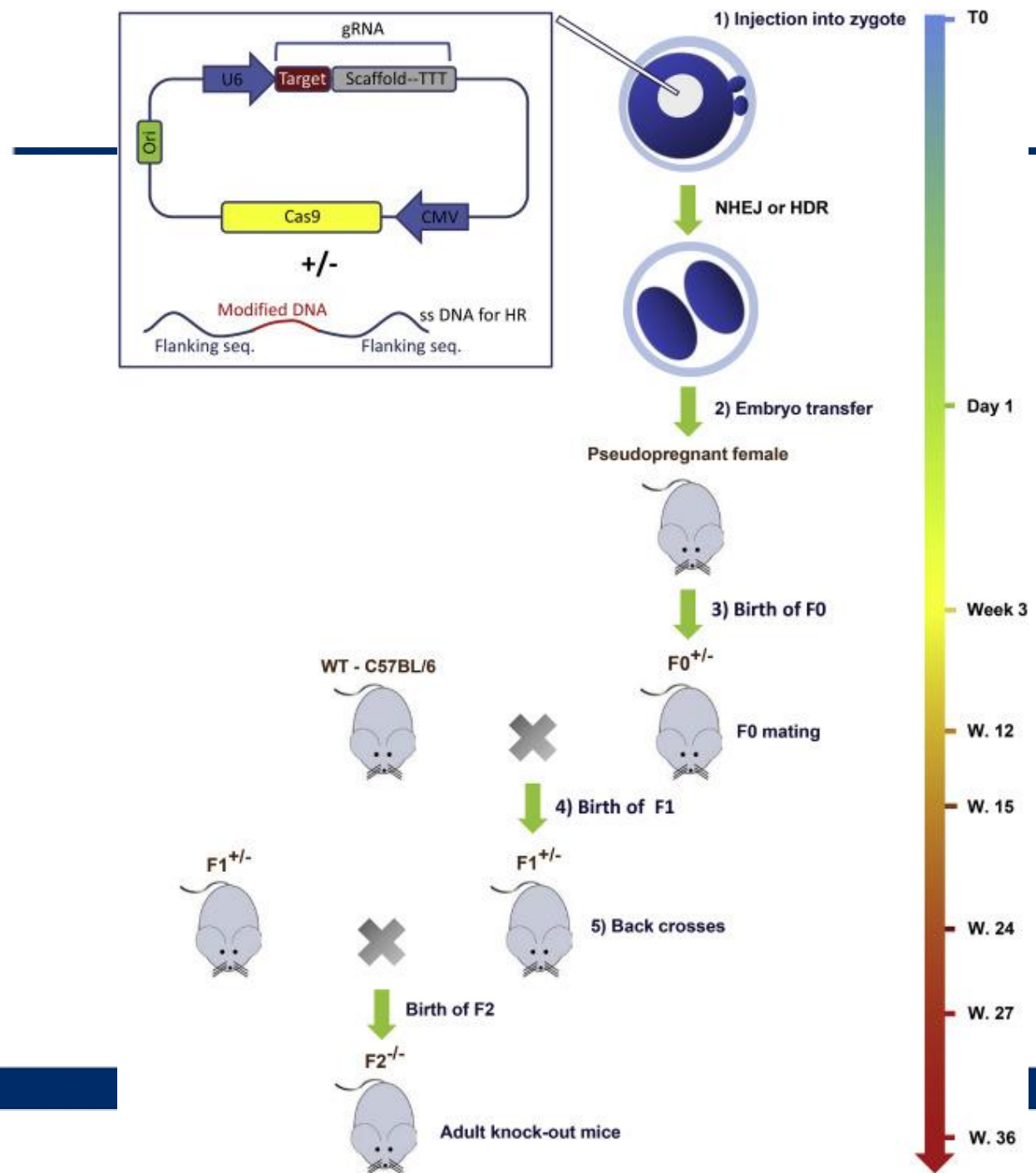
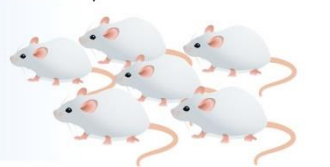
- Mosaic mice
- Heterozygous mutants
- Homozygous mutants*
- Genotyping and founder selection



- Breeding produces heterozygous mutants (N1)



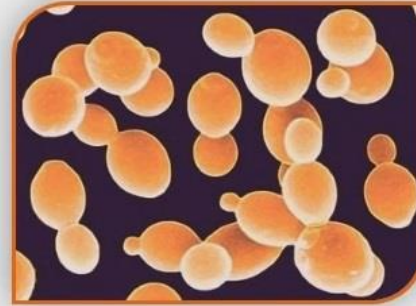
- Breeding of heterozygous mice produces homozygous experimental mice



CRISPR applications up to date



2012



Baker`s Yeast



Zebra Fish



Fruit Fly



Nematodes



Plants



Mice

Mouse strains & mouse models



The survey results indicate that mouse is the overwhelmingly preferred laboratory animal;

The most widely used mouse strains are **C57BL/6 mice** and **BALB/c mice**. Other strains, such as A/J mice, **CD1 mice**, and ICR mice, were also used.

Mouse strains & mouse models

The screenshot shows a web browser window with the following elements:

- Browser Tabs:** Join conversati, My Frontiers |, Frontiers, Informacj e p, NOS Sport - S, Manuscript —, Outline.docx, examples of tr, JAX Nomenclat X.
- Address Bar:** <https://www.jax.org/jax-mice-and-services/customer-support/tech>
- Page Header:** The Jackson Laboratory logo, a search bar with the text "Search the site & JAX® Mice", and a menu icon.
- Navigation Menu:** RESEARCH & FACULTY, EDUCATION & LEARNING, JAX® MICE & SERVICES, PERSONALIZED MEDICINE, NEWS, ABOUT US, and a yellow GIVE button.
- Breadcrumbs:** JAX Home > JAX® Mice and Services > Customer Support > Technical Support
- Main Content Area:**
 - ## NOMENCLATURE FOR MOUSE STRAINS
 - JAX® Mice are named according to the guidelines set by the International Committee on Standardized Genetic Nomenclature for Mice, and strain names are revised as necessary to conform to these guidelines.
 - Learn the highlights of mouse strain nomenclature with our short, interactive tutorial.
 - Understanding appropriate nomenclature is essential due to the complexity of strain names for substrains, transgenics, knockouts, etc. To enable broader awareness of nomenclature, The Jackson Laboratory has provided the resources below:
- Taskbar:** Windows logo, task icons for Mail, File Explorer, Edge, Firefox, Office, and PowerPoint. System tray shows the time 6:10 PM on 3/30/2021.

Mouse strains & mouse models

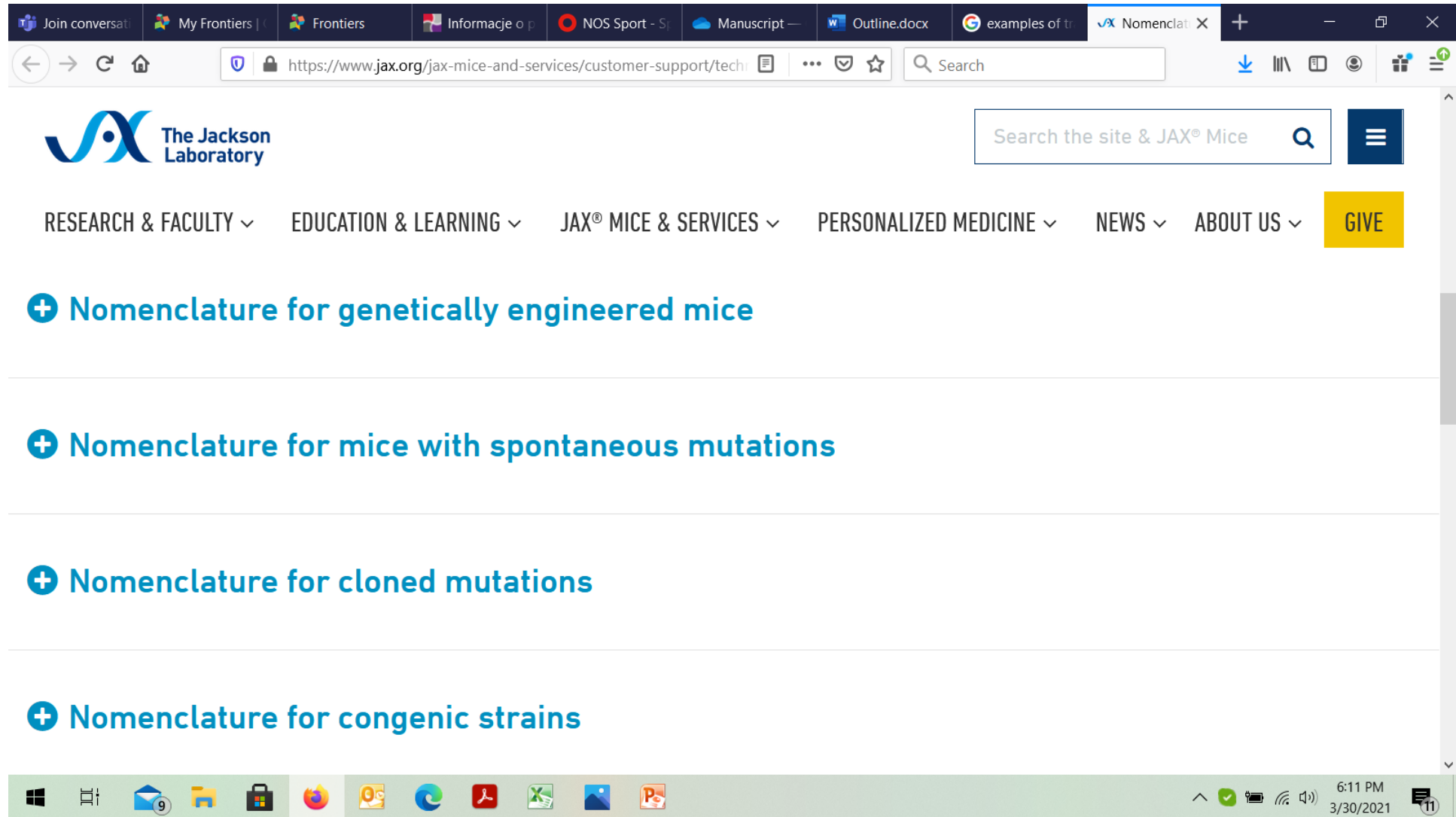
Data type	Count
Total mutant alleles (in ES cell lines and mice)	738,364
Mutant alleles in mice	24,339
Genes with mutant alleles	14,743
Genes with mutant alleles in mice	9,636
Mammalian phenotype ontology (MP) terms	8,744
Genes with phenotype annotations	8,903
Genotypes with phenotype annotations	43,335
Total MP annotations to genotypes	227,169
Human diseases with one or more genotypic mouse models	1,148
Mouse genotypes modeling human diseases	3,668
Quantitative trait loci (QTL)	4,696
Total recombinase (Cre)-expressing transgenes and alleles	1,739

^a Data as of May 5, 2012, www.informatics.jax.org. New data are added to the MGI database daily; thus, actual counts will be higher than those shown here

^b Mutant allele counts include spontaneous, induced (e.g., by ENU), and genetically engineered alleles. Transgenes, which are not part of the normal mouse genome, are not included

^c Mutants present only in ES cell lines versus those created in mice or made into mice from ES cells are distinguished in several table counts. All phenotype-related data refer to mutations present in mice

Mouse strains & mouse models



The screenshot shows a web browser window displaying the website for The Jackson Laboratory. The browser's address bar shows the URL: <https://www.jax.org/jax-mice-and-services/customer-support/tech>. The website header includes the logo for The Jackson Laboratory, a search bar with the text "Search the site & JAX® Mice", and a navigation menu with the following items: RESEARCH & FACULTY, EDUCATION & LEARNING, JAX® MICE & SERVICES, PERSONALIZED MEDICINE, NEWS, ABOUT US, and a yellow "GIVE" button.

The main content area features a list of mouse strain categories, each preceded by a blue plus sign in a circle:

- [+ Nomenclature for genetically engineered mice](#)
- [+ Nomenclature for mice with spontaneous mutations](#)
- [+ Nomenclature for cloned mutations](#)
- [+ Nomenclature for congenic strains](#)

The Windows taskbar at the bottom of the screen shows the time as 6:11 PM on 3/30/2021, along with various system icons and a notification area.

Mouse strains & mouse models

The screenshot shows a web browser window with several tabs open: "Join conversation", "My Frontiers | Ov...", "Frontiers", "Informacje o pro...", "NOS Sport - Spor...", "Manuscript — On...", "Outline.docx", and "Knockout Mo...". The address bar shows the URL: <https://www.cyagen.com/us/en/catalog-model-bank.html?gclid=E...>

The website header features the Cyagen logo with the tagline "We help you discover life". To the right of the logo is a counter displaying "78,477" and "Total Animal Models Delivered". Further right, contact information is provided: "Tel: 800-921-8930 or +1 408-969-0306 (Int'l) (8am-6pm Pacific Time)", "Email: animal-service@cyagen.com (Animal Model Services)", "animal-bank@cyagen.com (Cyagen Catalog Models)", and "cell-service@cyagen.com (Cell Products and Services)". A "My Account" link and a shopping cart icon with "0" items are also visible.

The navigation menu includes: "Custom Models", "Catalog Models", "Cell Products and Services", "Promotions", "Resources", and "About Us". A "Site Search" input field is located on the right side of the menu.

The breadcrumb trail reads: "Home > Cyagen Knockout Catalog Models".

Cyagen Knockout Catalog Models

Over **10,000** KO and cKO Mouse Models | **100%** Pure B6 Background | Delivered as Fast as **3** Months

The main content area features three promotional cards:

- Cyagen Knockout Catalog Models**: Includes a cartoon mouse wearing glasses and a "Find Your Model" button.
- Cyagen One-Minute Survey**: Promotes a survey where users can "receive \$2,000 credit" and includes a ">> Join Survey" button.
- Weekly Flash Sales for Live KO & cKO Mice**: Offers mice "As low as \$1,299" and "Shipped in just 2 weeks", with a ">> Search for Your Gene" button.

A vertical "Online Service" button is located on the right side of the page.

At the bottom, there is a search bar with the placeholder text "Search by gene name or NCBI gene ID" and a "GO" button.

The Windows taskbar at the bottom shows various application icons and the system tray with the date "3/30/2021" and time "6:51 PM".

Mouse strains & mouse models

The screenshot shows a web browser window with the Gempharmatech website. The browser's address bar displays `order.gempharmatech.com/strain/index`. The website header includes the Gempharmatech logo, navigation links for 'Products and Services', 'GPT Center', 'News', 'Marketing Activities', and 'About us', and user options for 'Register', 'The shopping cart', and 'Please log in'. The main content area is divided into a left sidebar and a main search area. The sidebar contains filter sections for 'Strain Type' (with options like Conditional knockout, Knockin, Knockout, Point mutation, and Inbred strain) and 'Research Area' (with options like Metabolic research, Developmental Biology, Tool Mice, immune system, and Tumor research). The main search area features a search bar with the placeholder text 'Please enter the strain name, gene name', a 'Hot Search' section with tags for NCG, BALB/c, nod, ace2, b6, cd3e, FVB, apoe, and BKS-DB, and a 'CDX' tag. Below the search bar, it indicates '14162 normal sales strain(s) found, 27880 strain(s) in development' and shows a pagination control. Three mouse strain entries are displayed in a list, each with a mouse icon, a name, a number, and a '+ shopping cart' button:

Name	Number
BALB/cJGpt[GF]	Number:N000296
C57BL/6JGpt[GF]	Number:N000295
ICR	Number:N000294

At the bottom of the browser window, the Windows taskbar is visible, showing various application icons and the system tray with the date and time: 6:55 PM, 3/30/2021.

Mouse strains & mouse models



The World's Largest Platform for Mouse Model Customization

- 20 years of experience
- Technical expertise in CRISPR/Cas9, TALEN, ZFN, ES cell-based HR, and Super TG
- Annual capacity of 5,000 new GEM lines
- 16,000 GEMs available for distribution and growing

Mouse strains & mouse models

◀ *Model Organisms for Biomedical Research*

Trans-NIH Mouse Initiatives



- ▶ *Deltagen and Lexicon Knockout Mice and Phenotypic Data* —New!
- ▶ *NIH Knockout Mouse Project (KOMP)* —New!
- ▶ *NIH Statement on Sharing and Distributing Mouse Resources*
- ▶ *NIH Plan for Mouse Genomics and Genetics Resources*
- ▶ *Courses & Scientific Meetings*
- ▶ *Funding Opportunities*
- ▶ *Reports & Publications*
- ▶ *Major Resources*
- ▶ *IC Contacts*

- ▶ *What's New*



Welcome to the NIH Mouse Initiatives Web site.

In March 1998, the NIH convened a group of scientists to develop priorities for mouse genomics and genetics resources. In response to the community's recommendations, the NIH has created a Trans-NIH Mouse Genomics and Genetics Resources Coordinating Group and a strategic implementation plan. For the convenience of all interested investigators, we have established this Web site as a central information resource. This site will provide information about funding opportunities; major mouse genomics and genetics resources; policies affecting resources; courses and scientific meetings related to the mouse initiative; and selected reports and publications. When appropriate, items not in response to the initiative, but which are deemed relevant to the initiative, will be posted. Posting decisions are made by a sub-committee of the Trans NIH Genomics Resources Working Group.

Suggestions for improving the Web page and for items to include are most

Mouse Genome Informatics

MGI-Mouse Genome Informatics-The international database resource for the laboratory mouse - Windows Internet Explorer

http://www.informatics.jax.org/

MGI MGI-Mouse Genome Informatics-The international dat...

Tour the MGI website

ID or symbol or name Quick Search

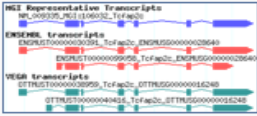
MGI Mouse Genome Informatics

About Help FAQ

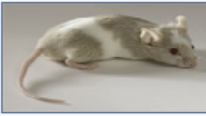
Search Download More Resources Submit Data Find Mice (IMSR) Contact Us

Explore MGI

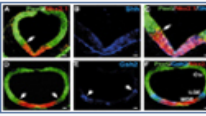
Genes




Phenotypes



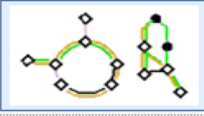
Expression



Function




Pathways



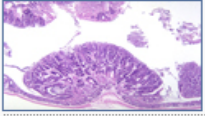
Strains / SNPs

Variation Type	DBV/2J	PfG/NU	NUJ/ELJ	Allele Summary (all strains)
SNP	G	G	A	A/G
SNP	C	C	T	C/T

Orthology



Tumors



FAQs

How do I...

- .. search for genes? [FAQ](#)
- .. find mutations for phenotypes or diseases? [FAQ](#)
- .. find expression data? [FAQ](#)
- .. view a structural genomic map? [FAQ](#)

[More FAQs](#)

News

18 September, 2008

- MGI release 4.12 features a new **Phenotype summary** section on allele detail pages, allowing easy comparisons of phenotypes across genotypes. [Read more...](#)
- The MGI 4.11 release includes enhancements related to gene expression data. [Read more...](#)
- MGI genome coordinates are now [updated](#) to NCBI Mouse Build 37 and dbSNP Build 128.

[More MGI news](#) [MGI Statistics](#)

start W:\Teaching Assignm... Microsoft PowerPoint ... PowerPoint Slide Sho... MGI-Mouse Genome I... Internet 100% 8:53 AM

Mouse Genome Informatics

Mouse Genome Informatics



Mouse Genome Database

Gene Expression Database

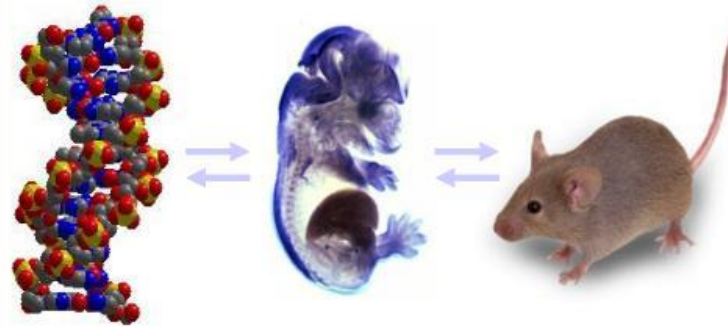
Mouse Genome Sequencing Project

Mouse Tumor Biology Database

Gene Ontology Consortium

www.informatics.jax.org

Genotype Expression Phenotype



Objective:

Facilitate the use of the mouse as a model for human biology by furthering our understanding of the relationship between genotype and phenotype.