Mouse colony management in a nutshell: Getting the most from your colonies and ensuring reproducibility

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Know your strain!

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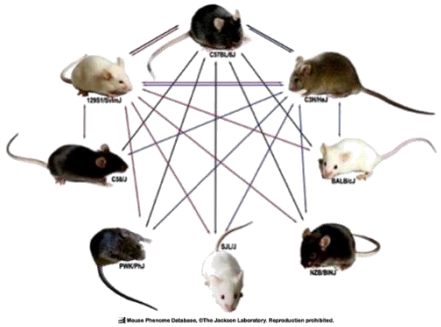
- Highly inbred = a genetically uniform experimentation group

IF PROPERLY MAINTAINED

Choosing a strain



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- Inbreds, outbreds, hybrids…
- Factors to consider will include;

Reproduction, Life-span and Spontaneous disease, cancer predisposition, drug response, immunology, specific phenotypes (e.g. pigmentation, susceptibility to disease) & availability of genomic data, what others have used.

Strain	Average weaning age (wks)	Average breeding lifespan (wks)	Average litter size (born)	Average # litters (born)	Overall tumour incidence	Specific phenotype
BALB/cJ	3	30	4.9	4.5	43%	Generation of monoclonal AB, used to study infectious disease
C57BL/6J	4	30	4.9	5.5	1-7%	Disease resistant “standard” strain
FVBN/J	4	26	5.3	8.4	50-60%	Retina degeneration, aggression in cage

Which wildtypes do you use?... What's normal for them?

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Mouse Search

Jax Employees

The Jackson Laboratory

POPULAR

C57BL/6J

Stock No: **000664** | Common Name: **B6**
Also Known As: **B6J, B6/J**

C57BL/6J is the most widely used inbred strain and the first to have its genome sequenced. Although this strain is refractory to many tumors, it is a permissive background for maximal expression of most mutations. C57BL/6J mice are resistant to audiogenic seizures, have a relatively low bone density, and develop age related hearing loss. They are also susceptible to diet-induced obesity, type 2 diabetes, and atherosclerosis. Macrophages from this strain ar...

Read More >

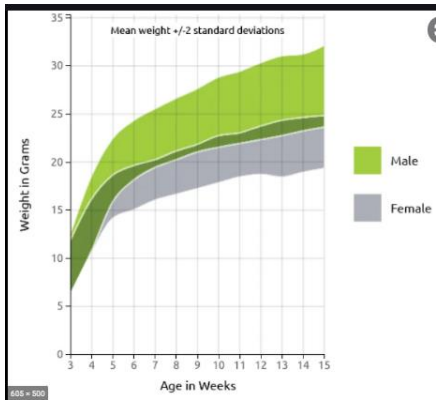
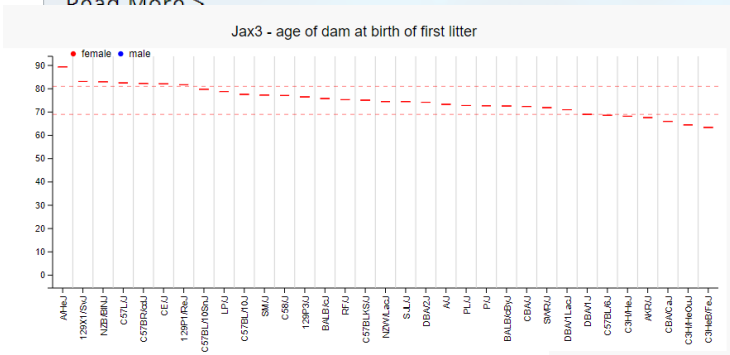
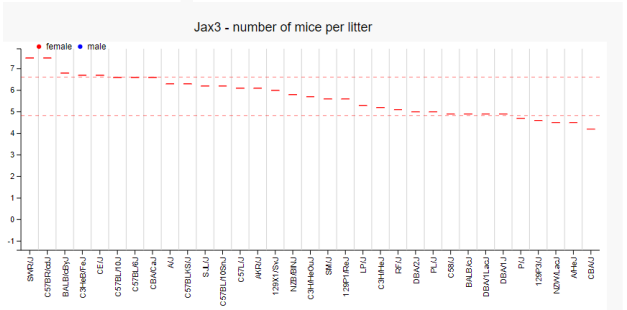


Table 1. Reproductive information for the most widely used JAX® Mice strains, readily available in large quantities.

Strain	Mean weaning age (wks)	Rotation Length† (wks)	Mean litter size (weaned)	Mean number of litters (born)	Wean:born ratio	Percent females (weaned)
BALB/cJ (000651)	3	30	5.4	4.1	0.99	50%
BALB/cByJ (001026)	3	30	5.2	3.8	0.96	56%
B6.129P2-*Apoe*^{tm1Unc}/J (002052)	4	26	4.5	3.9	0.83	44%
C3H/HeJ (000659)	3	22	5.0	3.5	0.92	44%
C57BL/6J (000664)	4	30	5.6	5.4	0.92	47%
CBA/J (000656)	3	26	4.0	5.4	0.93	48%



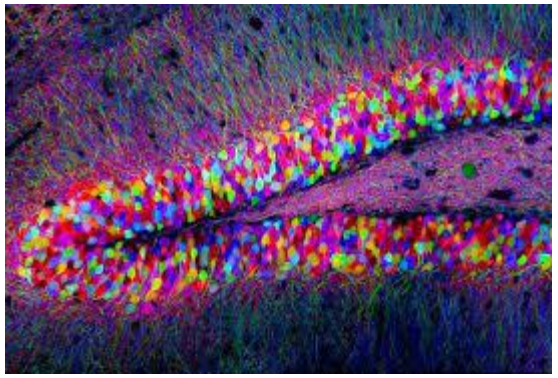


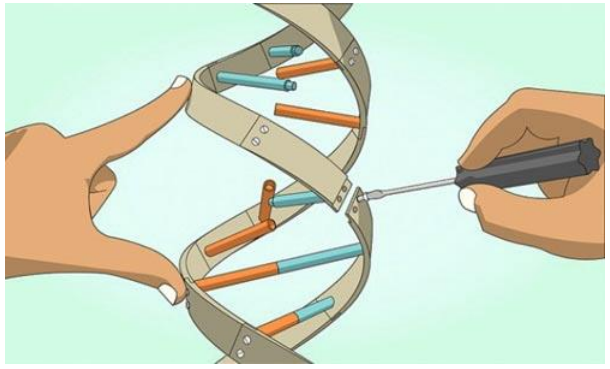
Mouse Phenome Database
at The Jackson Laboratory

Detailed Description

C57BL/6J is the most widely used inbred strain. It is commonly used as a general purpose strain and background strain for the generation of congenics carrying both spontaneous and induced mutations. Although this strain is refractory to many tumors, it is a permissive background for maximal expression of most mutations. C57BL/6J mice are used in a wide variety of research areas including cardiovascular biology, developmental biology, diabetes and obesity, genetics, immunology, neurobiology, and sensorineural research. C57BL/6J mice are also commonly used in the production of transgenic mice. Overall, C57BL/6J mice breed well, are long-lived, and have a low susceptibility to tumors. Primitive hematopoietic stem cells from C57BL/6J mice show greatly delayed senescence relative to BALB/c and DBA/2J. This is a dominant trait. Other characteristics include: 1) a high susceptibility to diet-induced obesity, type 2 diabetes, and atherosclerosis; 2) a high incidence of microphthalmia and other associated eye abnormalities; 3) resistance to audiogenic seizures; 4) low bone density; 5) hereditary hydrocephalus (early reports indicate 1 - 4 %); 6) portosystemic shunts (~5%); 7) hairloss associated with overgrooming; 8) a preference for alcohol and morphine; 9) late-onset hearing loss; 10) increased incidence of hydrocephalus and malocclusion and 11) spontaneous calcaneal luxation in 1% of aged males beginning at 6-8 months of age, resulting in ankylosing enthesopathy of that tarsal joint.

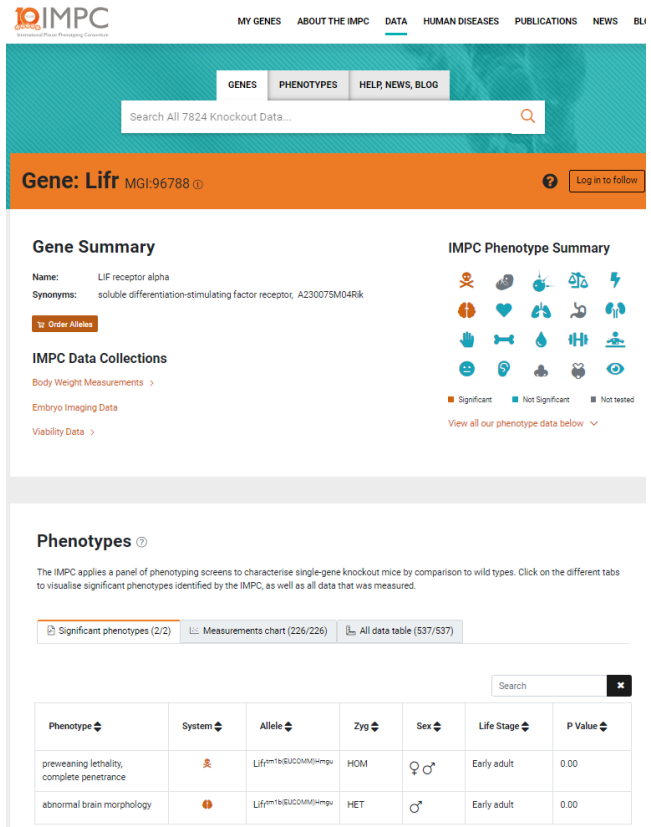
Genetically Altered (GA) animals

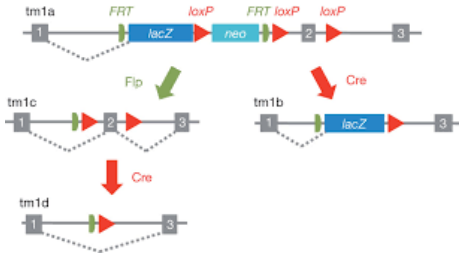


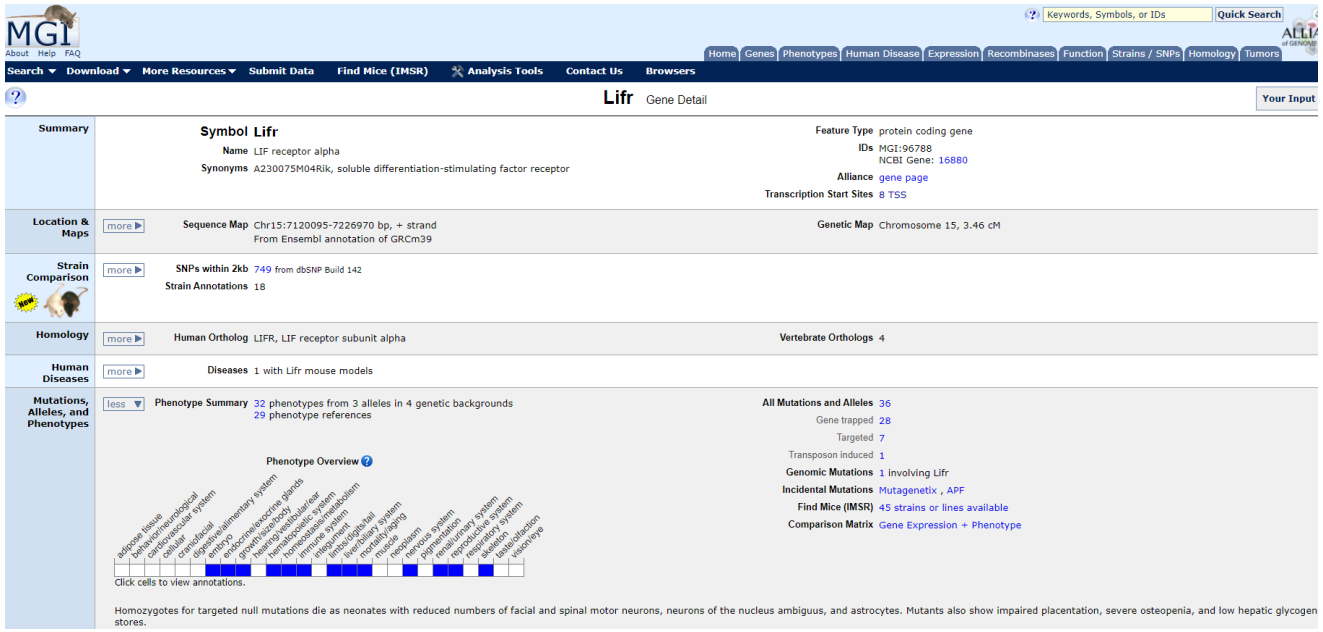


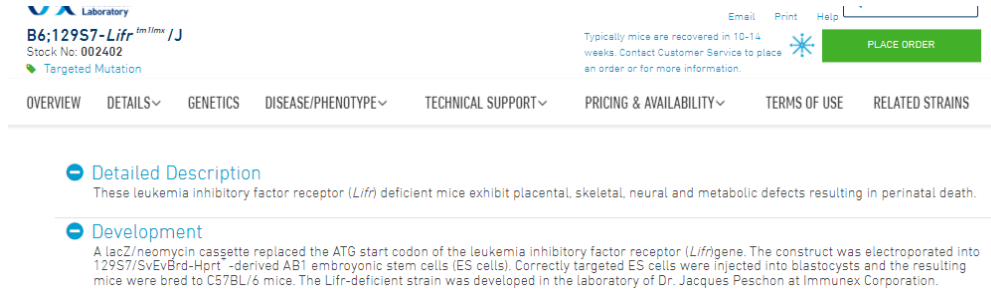
Getting the right mutation & finding out more…

Strain Name	Synonyms	States	Repository	Mutation Types	Alleles	Genes
B6/JGpt-Lifr^{em1Cd}/Gpt		sperm	GPT		Lifr^{em1Cd}/Gpt	Lifr LIF receptor alpha
B6/JGpt-Lifr^{em1Cflox}/Gpt		sperm	GPT		Lifr^{em1Cflox}/Gpt	Lifr LIF receptor alpha
Lifr$^{tm1a(EUCOMM)Hmgu}$		ES Cell	EuMMCR	targeted mutation	Lifr$^{tm1a(EUCOMM)Hmgu}$ targeted mutation 1a, Helmholtz Zentrum Muenchen GmbH	Lifr LIF receptor alpha
Lifr$^{tm1e(EUCOMM)Hmgu}$		ES Cell	EuMMCR	targeted mutation	Lifr$^{tm1e(EUCOMM)Hmgu}$ targeted mutation 1e, Helmholtz Zentrum Muenchen GmbH	Lifr LIF receptor alpha
B6NTac;B6N-Lifr$^{tm1a(EUCOMM)Hmgu}$/H	C57BL/6N-Lifr$^{tm1a(EUCOMM)Hmgu}$/H	embryo sperm	HAR Order	targeted mutation	Lifr$^{tm1a(EUCOMM)Hmgu}$ targeted mutation 1a, Helmholtz Zentrum Muenchen GmbH	Lifr LIF receptor alpha
C57BL/6N-Lifr$^{tm1a(EUCOMM)Hmgu}$/H	B6NTac;B6N-Lifr$^{tm1a(EUCOMM)Hmgu}$/H	sperm	EMMA Order	targeted mutation	Lifr$^{tm1a(EUCOMM)Hmgu}$ targeted mutation 1a, Helmholtz Zentrum Muenchen GmbH	Lifr LIF receptor alpha
C57BL/6N-Lifr$^{tm1c(EUCOMM)Hmgu}$/H	B6NTac;B6N-Lifr$^{tm1c(EUCOMM)Hmgu}$/H	sperm	EMMA Order	targeted mutation	Lifr$^{tm1c(EUCOMM)Hmgu}$ targeted mutation 1c, Helmholtz Zentrum Muenchen GmbH	Lifr LIF receptor alpha
B6NTac;B6N-Lifr$^{tm1a(EUCOMM)Hmgu}$/HTacAnuApb		sperm	APB	targeted mutation	Lifr$^{tm1a(EUCOMM)Hmgu}$ targeted mutation 1a, Helmholtz Zentrum Muenchen GmbH	Lifr LIF receptor alpha
B6;129S7-Lifr^{tm1Imx}/J		embryo	JAX Order	targeted mutation targeted mutation	Lifr^{tm1Imx} targeted mutation 1, Immunex Lifr^{tm1Imx} targeted mutation 1, Immunex	lacZ beta-galactosidase Lifr LIF receptor alpha
KOMP ES cell line Lifr$^{tm1(KOMP)Vlcg}$		ES Cell	MMRRC Order	deletion	Lifr$^{tm1(KOMP)Vlcg}$ targeted mutation 1, Velocigene	Lifr LIF receptor alpha Lifr$^{tm1(KOMP)Vlcg}$ LIF receptor alpha; targeted mutation 1, Velocige
C57BL/6N-A^{tm1Brd} Lifr$^{tm1a(EUCOMM)Hmgu}$/HMmucd	C57BL/6N-A^{tm1Brd}/a Lifr$^{tm1a(EUCOMM)Hmgu}$/HMmucd	archived sperm	MMRRC Order	targeted mutation targeted mutation	Lifr$^{tm1a(EUCOMM)Hmgu}$ targeted mutation 1a, Helmholtz Zentrum Muenchen GmbH	Lifr$^{tm1a(EUCOMM)Hmgu}$ LIF receptor alpha; targeted mutation 1a, Helmho Lifr LIF receptor alpha
B6NTac;B6N-Lifr$^{tm1c(EUCOMM)Hmgu}$/H		embryo sperm	HAR Order			Lifr LIF receptor alpha









Nomenclature

Understanding mouse strain nomenclature is critical to understand the complex strains, sub-strains, transgenics, knockouts, etc. in your care

To anticipate phenotypes and understand the importance of maintaining genetic background and good breeding records.

Common names - B6

Official Nomenclature – C57BL/6J

Nomenclature basics

Guidelines are set by the International Committee on Standardised Genetic Nomenclature for Mice.

Inbred lines – normally named for appearance and origin or occasionally phenotype

C57BL/6J

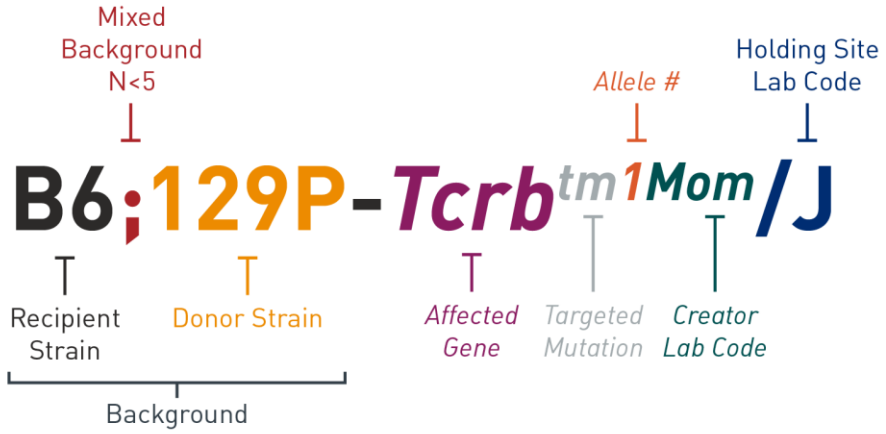
- C57BL — parent strain designation after 20 generations of brother sister mating (from CC Little, 57th female, black)
- / — separates parental strain from the sub-strain
- 6 — line number
- J — laboratory code

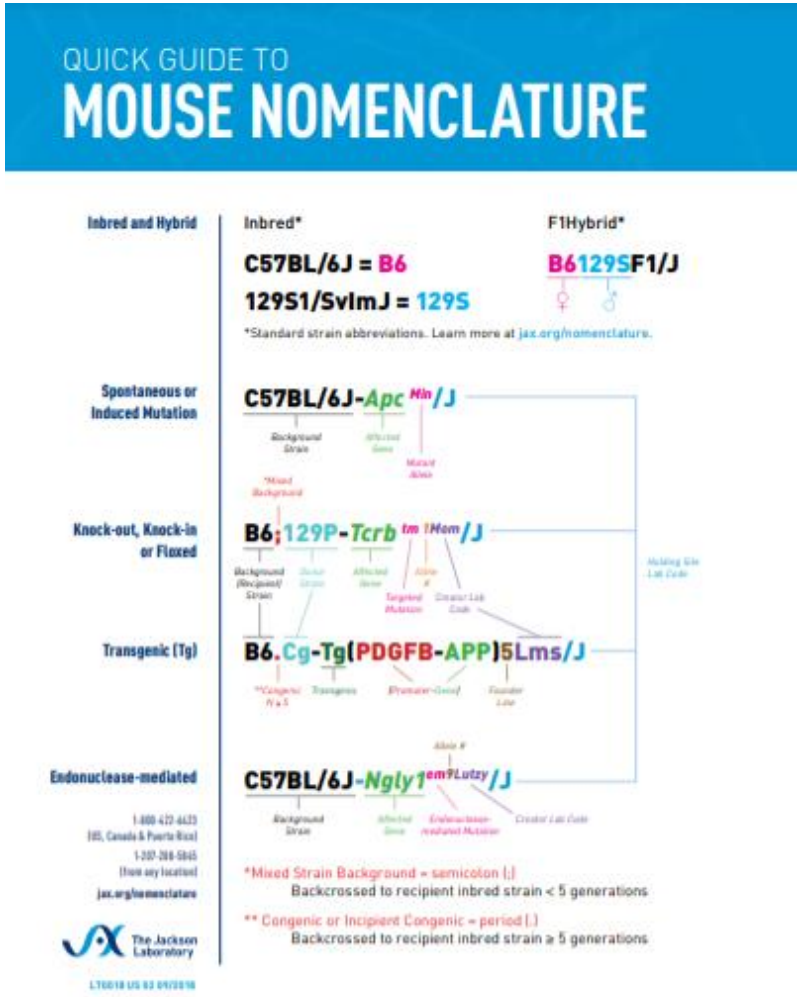
Labcode	Status	Investigator	Organization
J	active	The Jackson Laboratory	The Jackson Laboratory
Crick	active	Jan-Bas Prins	The Francis Crick Institute

Nomenclature can also tell us about how a strain has been made and bred….

And help us decide on the way forward!

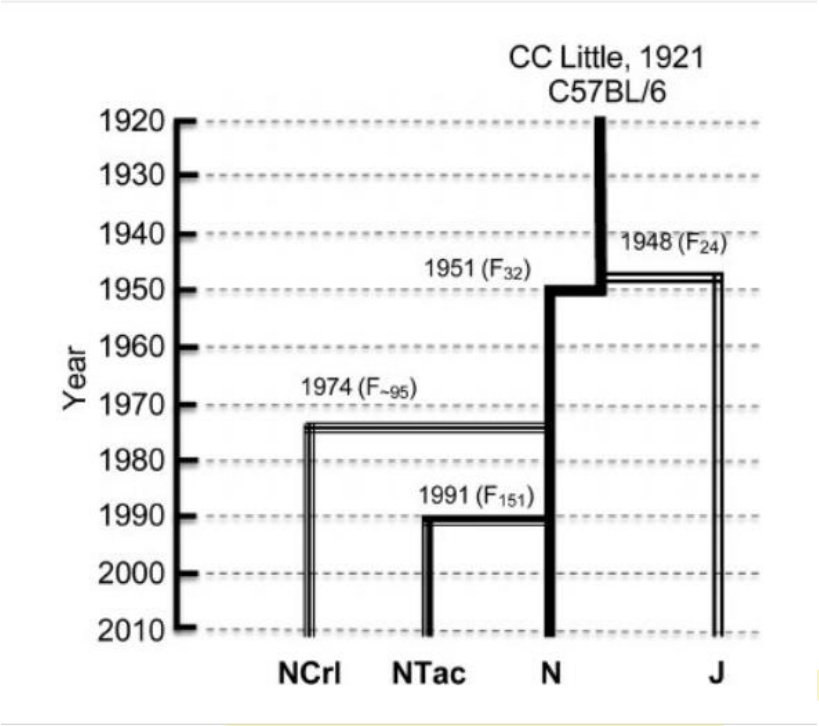
- Guide to Nomenclature & tutorial/webinars…





Genetic drift & Sub-strains

Once a colony has been separated from its parent colony by 20 generations it should be considered a new sub-strain, and named as such i.e. C57BL/6J or C57BL/6NTac



This is because of Genetic contamination & drift:

- Residual heterozygosity (Inbreds are only 99.9% similar)
- Spontaneous mutation (100 bases mutate/generation)

Genetic drift describes random fluctuations in the numbers of gene variants (alleles) in a population, and the constant tendency of genes to evolve through spontaneous mutations.

Phenotypes change on different background!!

Differing

- susceptibilities to infection
- mortality rates
- rates of tumour growth
- breeding performance
- behavioural responses

Reported phenotypes disappear…

Examples..

- IL10KO & IBD on C57BL/6J ☺ v 129Sv/Ev, BALB/c or C3H/He ☹
- APC min & intestinal polyps on C57BL/6J ☹ v AKR/J, MA/MyJ or CAST/Eij 😳
- C57BL/6J &N – difference in fear responses, cardiac function, retinal degeneration, response to high fat diet…

Slowing genetic drift & ensuring strains are on defined backgrounds

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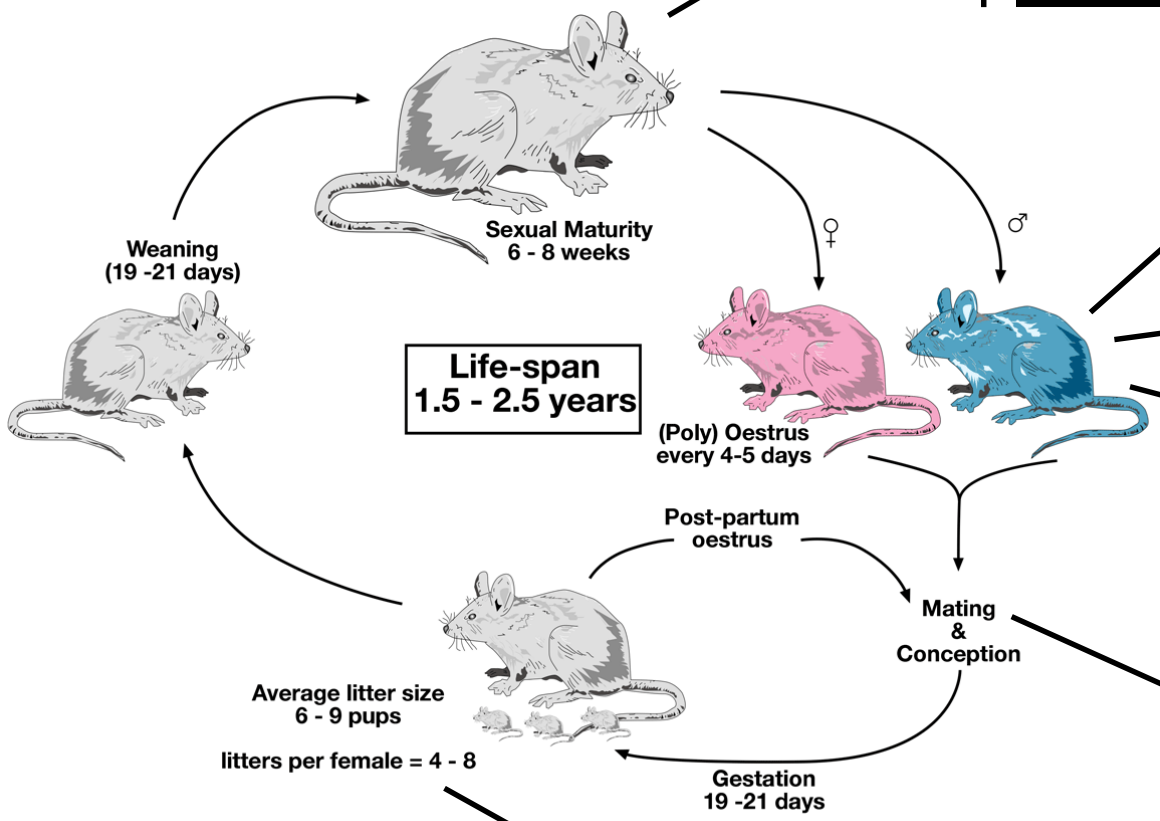
- Inbred colonies - Refresh/Replace regularly from a reliable commercial supplier every 5-10 generations.

- Genetically Altered colonies - Outcross to the wildtype (Refresh) every 5-10 generations.

- For complex GA lines (multiple alleles) - cryopreserve stock and return regularly to an earlier generation

Biology of a mouse – know your strains!!



Ensure matings are set up 6-12 weeks

Choose new breeders carefully. Best representative of the strain's characteristics.

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Replace breeders 7-8 months of age..
Strain dependent
(before performance declines)

Ensure 2-3 generations of breeders
Rotate/regular intervals

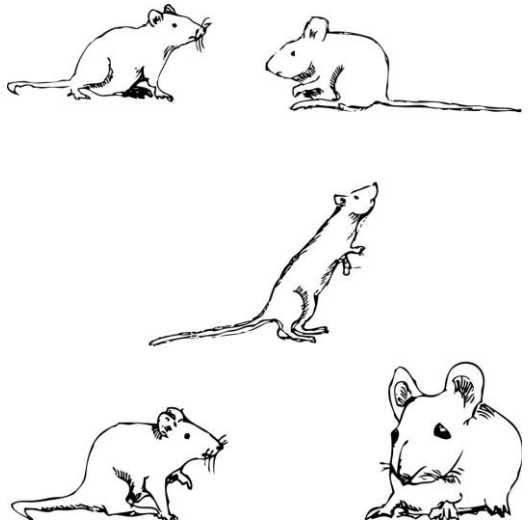
Replace non-productive breeders

Size colony based on litter size/productive breedings – but also #mice/sex/genotype/ age needed

What's normal for your strain?

- Not all strains are the same
- If working with different strains or if backcrossing to another background expect changes in performance.
- The **Mouse Phenome database** or Jax resources can give you data on the averages for each background strain which can then be compared to your GA strain

1. **Average litter size**
   (total pups/total litters)
2. **Average litter interval**
   (# litters/breeding span(wks))
3. **Production Efficiency Index (PEI)**
   (#weaned/female/week)
4. **Pre-weaning mortality**
   (#born-#weaned / #born)
5. **% Productive matings**
6. **Total litter loss**



- **Know your mice!! – good records**
  - Be informed – research your strains or other strains with similar alterations.
  - Get a full history of any new strains or characterise fully
  - Which allele are you using, how has it been made?
  - Check genotype at each generation (& check for contamination) Is your assay specific
  - Check your background – or backcross/refresh/replace from frozen stock regularly
  - Know what's normal for your background strain to spot deviation
- **Reduce waste & optimise your colonies**
  - Plan what is needed and size colony accordingly
  - Regularly review demand & use & adjust
  - Check the breeders, replace where TLL, unproductive
  - Communicate with animal care staff
  - Cryopreserve as back up/to use up spare/to remove a line
  - Look at options like intermittent breeding (Ellen to elaborate!)

Thank you for listening