The Rosetta Stone of lab animal models: Decoding nomenclature

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1. **Could you explain more on the line number like the "6" in BL/6?**
   When the C57BL model was created in the early 1900s, there were several different sublines being bred by C.C. Little. Nearly all mice housed in Bar Harbor, Maine were destroyed in a fire in 1947. Of the mice that were being bred at other laboratories, the sixth subline of C57BL was the most popular and was one of the models used to replenish the colonies at Bar Harbor.

2. **I thought C57BL/6N was Charles River?**
   C57BL/6NCr is the substrain carried by Charles River. Taconic carries the C57BL/6NTac and Envigo carries the C57BL/6NHsd. The “N” stands for the NIH, the institution where this model was originally housed and then distributed to all three vendors.

3. **Sometimes you see a J in C57BL/6 mice. What is it? Also the same question for the N in C57BL/10N?**
   The “J” in C57BL/6J is the lab code for Jackson Laboratories. The “N” in C57BL/10N is the lab code for the National Institutes of Health. More information on lab codes can be found at: **https://www.nationalacademies.org/ilar/lab-code-database**

4. **Why in some papers do I see 10 times backcross mentioned?**
   When creating a congenic model using traditional breeding, 10 backcrosses are required to reach a full congenic status.

5. **Do all commercial models have the whole genome sequenced of their animals to look for genetic drift?**
   No, they do not. Genetic drift is defined as a change in the frequency of an allele within a population over time. To confirm that genetic drift is happening within a colony, you would have to sequence the full genomes of every animal in that colony. This is quite expensive and would not be practical for a vendor to do on all models routinely. Genetic drift is best managed using certain breeding techniques and refreshing colonies periodically from frozen embryos.

6. **How can we consider that genetic drift is a problem in outbred strains if we want to have genetic variability?**
   Genetic drift can cause the phenotype of a colony to change over time, which can affect long term studies when using animals from that colony. Also, it can affect the phenotype of colonies at different locations of the same stock, making it difficult for investigators to source from various vendors and locations. Finally, genetic drift also includes genetic bottlenecks in outbred colonies, which can lead to health and reproductive issues.

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7. **How do you maintain a specific transgenic genotype in an outbred stock?**
   The transgene is maintained no differently than it is in an inbred model. The outbred genetic background, however, should be maintained through either specific breeding techniques or periodically refreshing with wildtype animals of the same outbred stock.

8. **How does speed congenics work?**
   Speed congenics, or selected breeding, utilizes a large panel of markers to assist in identifying the animals most genetically like the recipient strain. These animals are first identified using genetic testing techniques, and then selected to use for the breeding of the next generation. Speed congenics typically cuts the time it takes to make a congenic strain by 50%. For more information, please see**:**
   https://www.envigo.com/p/research-services/genetic-testing/speed-congenic-services/

9. **I have always been curious as to the mechanistic/genetic reason that inbred strains are less healthy. Any info on why this happens?**
   When inbred strains were first created, they went through a genetic bottleneck. Some recessive traits that had no phenotype when in heterozygous state suddenly became fixed as homozygous recessive in the new inbred model. These recessive traits are often deleterious and create health issues for the animals, such as micropthalmia in the C57BL/6 model.

10. **Does a similar nomenclature system exist for fish or Xenopus?**
    Yes. For Xenopus, the nomenclature guidelines can be found at:
    https://www.xenbase.org/gene/static/geneNomenclatureQuestions.jsp
    The nomenclature guidelines for Zebrafish can be found at:
    https://wiki.zfin.org/display/general/ZFIN+Zebrafish+Nomenclature+Conventions

11. **What are the strain codes when you are at F2, F3 or F4 generations?**
    Any breeding of a hybrid beyond F1 is no longer a hybrid model and would be considered a mixed background. The semi-colon would be used and the full nomenclature of the two inbred strains to indicate the mix. The “F” designation is also used to identify which filial generation you are at in an inbred line.

12. **Is the gene that is preserved on the new background of the congenic strain still homozygous?**
    Typically the mutation of interest is carried through the breeding process in heterozygous state. The last step of the speed congenics project is breeding the model to homozygosity for that particular gene, unless homozygous animals are not desired.

13. **What is the difference between coisogenic strain, congenic strain, insipient congenic, and conplastic strains?**
    - A *coisogenic strain* is a strain that differs from another strain at one locus only. This occurs when a mutation arises in one colony and not in another of the same strain.
    - A *congenic strain* is a strain that carries a chromosomal segment with a mutation of interest from a different strain. This is done through human intervention.
    - An *incipient congenic* is not yet completely backcrossed and is considered a mixed model.

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- A *conplastic strain* is created by backcrossing the nuclear genome from one inbred strain to the cytoplasm of another.

14. Is the nomenclature unique for hemizygous transgenic animals?
Typically Tg/0 is used in the nomenclature for animals that are hemizygous transgenics.

15. What does the + sign mean in the Lepr mutation of the congenic model?
For this type of model, the "+" indicates the wildtype allele of the leptin receptor (*Lepr*) gene.

16. Sometimes we see the alleles marked tm1.2 or tm1.3. What does it correspond to?
This nomenclature indicates that derivative alleles were used. It corresponds to different variations of what was used to create the same knockout model.

17. How about when mice get a special name, like "Goldenticket", which is Tmem173^gt? Can you explain those sorts of names?
This is called the common name. It is chosen by the inventor of the model or the vendor that is selling the model. The purpose is to make it easier to discuss the model with a shorter, less complicated name. For example, Envigo's B6;129-*Rag2*^{tm1Fwa}*Il2rg*^{tm1Rsky}/DwlHsd model has a common name of R2G2®.

18. What is Envigo's lab code?
Our lab code is Hsd, for Harlan Sprague Dawley. Envigo was created in September of 2015 through the integration of five organizations, which included Harlan Laboratories (formerly Harlan Sprague Dawley, Inc.), Huntingdon Life Sciences, GFA, NDA Analytics, and LSR associates.

19. Do lab codes ever get updated or modified?
Yes, lab codes can get updated or modified at any time on the ILAR website.

20. When you mix an inbred KO mouse (made with the cas9 technology) and an outbred mouse, what the correct nomenclature? Would it be a congenic?
Congenic recipients are inbred, so if you are mixing an inbred and an outbred mouse together and not backcrossing onto the inbred strain, it would be considered a mixed model.

21. If we create new strains in our labs, for example using the cre/lox system, should we name these properly in manuscripts and could these be checked in some way before publication?
I would encourage anyone who creates a new model to use appropriate scientific nomenclature in their publications. You can write the nomenclature guidelines committee to confirm that you have named your model correctly. The nomenclature guidelines can be found at **http://www.informatics.jax.org/mgihome/nomen/strains.shtml**

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22. Are there ever lines that can be brought back, such as the OEL strain?
If there are viable embryos stored properly, they can be brought back through cryorecovery methods.

23. What is the difference between Cre and cre? Does the capital letter mean anything?
The capital letter doesn't mean anything. These are used interchangeably depending on the preference of the investigator naming the model.

24. Do targeted knockouts through Cre/lox or CRISPR/Cas9 have a different nomenclature?
Yes. CRISPR/Cas9 is used to create an endonuclease mediated mutation and thus the nomenclature is typically reflected as em1 instead of tm1. For the cre/lox system, the targeted mutation symbol, "tm1," is used.

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