

Are We Using the Most Appropriate Animals for Our Research and Are We Doing It for the Best Reasons?

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Over the last 50 years there have been demands to increase the quality of animals used for research. The numbers of animals used for individual projects have in the same period decreased, while the efforts put on the single animal to secure the highest scientific output from it have increased. Basically this is a very important part of both “refinement” and “reduction”; those two of the three R’s which, it previously has been argued, were less in focus than the last R, ‘replacement’ (Nevalainen, 2005).

Today, especially, rodents are inbred and frequently also made transgenic and hence the colonies of origin should be genetically and microbiologically screened prior to delivering the animals. This is a heavy task, and therefore the commercial breeders often seem to be better fit for the job than an in-house university or industrial supplier. To allow for reproducibility, an internationally recognized system for nomenclature is available and every breeder should have a so-called ILAR code (*International Committee on Standardized Genetic Nomenclature for Mice Rat Genome and Nomenclature Committee, 2005*).

In the years 2004 and 2005, the Scandinavian Journal of Laboratory Animal Science published 12 scientific papers in which the subjects were rats (Noorafshan *et al.*, 2005; Demir and Turkoglu, 2005; Kira *et al.*, 2005; Bentzen *et al.*, 2005; Sorensen *et al.*, 2005; Baturaite *et al.*, 2005; Ozbek *et al.*, 2004b; Gissurarson *et al.*, 2004; Hwang *et al.*, 2004; Kanter *et al.*, 2004), while in ten papers

the subjects were mice (Salimian *et al.*, 2005; Leonaviciene *et al.*, 2005; Mahmoudzadeh-Niknam, 2004; Kumar *et al.*, 2004; Stub *et al.*, 2004b; Mortensen *et al.*, 2004; Ozbek *et al.*, 2004a; Stub *et al.*, 2004a; Bizanov and Tamosiunas, 2005; Sozmen *et al.*, 2005).

Eight out of the 12 rat papers described the use of outbred rats, which were Wistar, Sprague-Dawley or TOX rats, while only four papers described the use of inbred rats, which were either Lewis or Sprague-Dawley. Actually, in two of the twelve papers it can be interpreted that the rats were either inbred or outbred, respectively, but it is not clearly stated, which of course to some extent falls back upon us as editors. Only one out of the ten mouse-based studies behind the mouse papers had been performed with outbred Swiss mice. In the remaining nine papers, the inbred mice were C57BL/6 in four papers, BALB/c in four papers, 129/Sv in two papers, while also some other, unspecific inbred strains were used (some papers used more than one strain). This difference in the use of inbred strains between rat and mouse users is highly significant in the chi-square test ($p < 0.01$).

In one mouse paper and in one rat paper the origin of the animals was not given. This again falls back upon us as editors, but it is also the responsibility of any scientist to clearly define the origin of the animals used to improve the reproducibility of the study. In five of the remaining eleven rat papers, the

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rats came from local institutional breeding, while in the other six papers the rats came from commercial or central state breeding centres. Only one of the mouse studies used two inbred strains from a commercial breeder combined with an in-house bred transgenic mouse from an inbred background. All the remaining nine mouse papers were based upon mice supplied from local institutional breeding. This difference between rats and mice is also significant ($p < 0.05$).

In five out of eleven rat papers the rats were described by internationally accepted nomenclature, while this was only the case for one of the mouse papers. Interestingly, this was the paper which had used commercially derived mice. Probably, most of the institutional breeding colonies have never been supplied with an ILAR code. The difference between rats and mice in this sense is not significant.

In the same period the journal published three papers on studies using pigs (*Nielsen and Lind, 2005; Royo et al., 2005; Lind et al., 2005*), three papers on studies using rabbits (*Ogura et al., 2004; Ritskes-Hoitinga et al., 2004; Cavallotti et al., 2004*) and one paper using the house musk shrew, *Suncus murinus* (*Hashimoto and Saito, 2005*). None of these animals were inbred, but except for one paper on rabbits, they all came from commercial breeders. One paper on rabbits as well as the paper on house musk shrews used the international nomenclature. All the pigs were clearly defined in relation to breed.

While the habit of buying animals from commercial breeders seems to be more dominant among rat users than among mouse users, the habit of using inbred strains is far more common among mouse users. The sole reason for this difference may be simply economic. It is far easier to keep a stable inbred colony in an in-house facility, as many breeding animals are needed to keep up a genetic homeostasis for an outbred colony, while outbred

animals are far cheaper than inbred animals when bought from commercial breeders. The option of in-house-breeding becomes less attractive as the species gets larger, and therefore rabbits and pigs generally are supplied from commercial sources.

Anyway, we should be aware that in the long run a larger group size and increased variation can be far more expensive than the small amount of money saved. Scientific studies should be reproducible, and we should be guided by scientific principles. For most of the studies mentioned here inbred animals would probably have been a better option and more precise information on the animals would have been preferable.

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