Breeding systems and Genetically Altered Animals

Standardisation of laboratory animals in research produces more accurate results. Less variation between animals reduces the number of animals needed, reduces inter-experiment variation, increases reproducibility and comparability of results, and also saves time and money. Therefore, it is important to standardise animals for their genetic characteristics, the environmental conditions, their nutrition, and their microbiological status.

Breeding systems aim to produce animals with a defined set of desired characteristics. Different systems may be employed in order to produce different results.
Different methods employed depending on what is to be achieved, e.g. inbreeding, outbreeding, backcrossing.

Inbred
Inbred strains are produced by 20 generations of brother x sister matings. They are almost completely homozygous, and are genetically stable. Lists of mouse strains can be found on the website of the Jackson Lab *www.jax.org*

Outbred
Outbred stocks are random bred, or mated to maximise outbreeding. They are heterozygous so animals are not uniform. They are genetically unstable, so characteristics can change over time. They are considered by some to be closer to a 'natural' population.

Backcrossing
This system is used to transfer a desired genetic characteristic from one background strain to another. E.g. Strain 1 carries mutation/genetic alteration of interest, which is to be transferred to animal of strain 2. Mate a strain 1 animal with a strain 2 animal, then select offspring carrying the gene of interest (strain 1/2 hybrids). Mate these offspring back to strain 2 animals. Then repeat the process of selection of offspring and crossing back to the desired parental strain 5-10 times.

Congenic strains differ in a single length of chromosome.

Coisogenic strains differ at a <u>single</u> locus (often arise by mutation in an inbred strain)

F1 – this notation is used for the first generation offspring from a cross between two strains.
F2 – this is used for offspring produced by mating F1 animals

Genetically Altered Animals (GAA) have an (artificially) induced change in their DNA. These may be spontaneous mutants, produced by selective breeding of animals with particular characteristics; animals produced by mutagenesis, where the rate of mutation of DNA is increased by exposure to chemicals or radiation; or transgenics, produced by manipulation of germ cells or embryos to add or delete genetic material. Use of GAA is increasing, and this is likely to continue. The sophistication of techniques for genetic manipulation is increasing. Use of GAA is controlled by the Genetically Modified Organisms (Contained Use) Regulations 2005.

Transgenic animals may be produced by a variety of techniques, including pronuclear microinjection, embryonic stem cell manipulation, use of viral vectors, and many other methods. There may be welfare implications for creation of GAA, either from the procedures used in their generation or from the effects of genetic modification, and therefore the ASPA provides them with additional protection from the moment of creation.

Genotyping

Many methods can be used to determine the genotype of GAA. Generally these rely on analysis of DNA. Traditionally this has been achieved by taking a (large) piece of tissue and analysing the DNA. Tissue samples can be taken from the tail, or ear. Modern techniques for amplification of segments of DNA such as PCR allow this analysis to be done on a very small sample, e.g. blood, hair or check cells. The least severity procedure should be used.

Identification

It is important to be able to identify GAA having determined their genetic status. Sometimes they can be identified by coat colour. Alternatively, they can be identified by ear notching, microchips, use of pens to mark fur or tails, tattooing, or ear tags.

Mouse passports

GAA should ideally come with a 'passport', giving details of the effects of the modification and any special care needed, in comparison with their non-GA counterparts. However there is often very little data on non-GA animals! The NC3Rs set up a working party, which recommended structured welfare assessments of GAA (www.nc3rs.org.uk/GAmice). The suggestion is that assessments are made of neonates, and repeated at weaning, and when adulthood is reached. A simple check sheet is used to record the proportion with compromised welfare. The aim is to develop a welfare profile to aid in management for each strain.