NUMERICAL ASSESSMENT OF ANIMAL REDUCTION BY PROPER TRANSGENIC COLONY MANAGEMENT
Emmanuel Gomas, 3TC, France

ABSTRACT:
The workshop held in The Netherland by the end of 2013 (1) highlighted the proportion of unemployed animals in transgenic colonies. It supported the need to convince research teams and animal facility managers to properly manage their colonies in order to reduce the number of unused animals produced. To reach this goal but also to value this effort front to authorities, it's important to provide simple-to-use tools and numerical reduction data.

This study shows simple formula to evaluate number of breeding cages needed to reach a production goal. But, it also calculates animal savings made by using all colony management tools as backcross (2) or cryopreservation (3):

- Use of cryopreservation: up to 86% reduction of animals used compare to breeding over a period of 2 years
- Use of congenic or co-isogenic lines: up to 75% reduction of animals produced by using homozygote breeding compare to heterozygote breeding
- Calculation of needed breeding cages: up to 40% reduction of animals produced over a one year period compare to empirical breeding.

In the current economic situation, it’s also important to keep in mind the fact that reducing the number of unused animals is also a matter of reducing workload and costs allowing to reallocate valuable resources to research.

HOW TO CALCULATE PRODUCTION NEEDS?
One issue in transgenic animals production is to adapt the colony size to the needs. A wrong evaluation of the colony size could lead to inappropriate experimental batches (wide range of age, not enough animals, delays in experiments). Most of the time, the main trap is the definition of the initial need. But, starting with define needs, it is possible to calculate precisely production colony size to produce enough (but not too much) animals for experimental purpose.

Here is some example of calculation formula that can be used for setting up production colonies:

\[
\text{Regular production of a define number of animals} \quad F = P + \frac{BR}{Pi} \\
\text{Production of a batch of animals} \quad F = P \times (PL \times R)
\]

Expected number of pups starting with a defined number of females:

\[
P = F \times P \times (PL \times R)
\]

- F : number of females in breeding
- P : number of pups to produce (all genotypes and sexes)
- BR : number of pups needed for breeding colony renewal
- Pi : production index in pups/week/Females in breeding
- PL : average of pups per litter
- R : ratio of pregnant females expected over a define period of mating

SAVINGS MADE BY USING CRYOPRESERVATION
Up to 50% of transgenic lines housed in animal facilities are not used or only time to time. Even considering the minimum breeding colony possible, animals are still produced but not used for experiments. Additionally to the production of useless animals, this create costs all over the time.

SAVINGS MADE BY USING CONGENIC LINES
Using congenic or co-isogenic transgenic lines allows to reduce results variability and to compare data with other labs using the same genetic backgrounds. But, it also reduce the possibility to reduce massively the number of animals produced by breeding as breeding can be performed HOM/HOM instead of HET/HET (in order to produce HOM and WT intermated). Of course, this imply to set up an efficient genetic background drift program (for example by using cryopreservation).

As for the other purposes, this leads to cage savings in addition to animals savings, even for small colony as in this example of production of 10 HOM males.

IMPACT ON A FULL ANIMAL FACILITY:
Assumption:
- 300 transgenic lines
- 25% unused
- 25% with production goal of 5 animals/week
- 150 batches of 10 HOM males to produce all over the year
- Max 5 adult mice/cage
- 10€/cage/week (full cost, including payback)
- 400 cages/month/tech

<table>
<thead>
<tr>
<th>Colony management tools</th>
<th>Animals saved per year</th>
<th>Cages reduction per week</th>
<th>FTE reduction per week</th>
<th>Cost reduction per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production level calculation</td>
<td>13200</td>
<td>375</td>
<td>0,94</td>
<td>3750€</td>
</tr>
<tr>
<td>Cryopreservation</td>
<td>3750</td>
<td>300</td>
<td>0,75</td>
<td>3000€</td>
</tr>
<tr>
<td>Use of congenic animals</td>
<td>9000</td>
<td>156</td>
<td>0,39</td>
<td>1558€</td>
</tr>
</tbody>
</table>

CONCLUSION:
As shown in this poster, the savings can be important, both in animals, space and costs (cages and human resources). Knowing that reducing costs and optimizing resources will be the next challenge of most of core facilities, those examples and methods to calculate productions and costs could be highly helpful to convince research teams and facility managers to implement good practices in transgenic colony management.

In addition, it is interesting to notice that, in that case of transgenic colony management, 3R’s, results quality and resources management are all improved in the same time, by using proper strategies.

Also, the revolution of CRISPR/Cas9 will soon join those proper strategies as it will be easier and faster to produce multi-double homozygotes lines using few embryo donors and avoiding long, expensive and animal consuming breeding periods.

BIBLIOGRAPHY:
1- Workshop: "Animals bred, but not used in experiments", October 18-20, 2013, Sanpport, the Netherlands
2- The Jackson Laboratory Handbook on Genetically Standardized Mice 6th Edition
3- Strategies for managing an ever increasing mutant mouse repository. M.T. Davidson, R.A. Taft Brain Research. 2006;1091:255-257