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 team 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:

Regular production of a define number of animals

$$F = P + BR / PI$$

Production of a batch of animals

$$F = P / (PL \times R)$$

Expected number of pups starting with a defined number of females

$$P = F \times PL \times R$$

F : number of females in breeding
P : number of pups to produce (all genotype and sex)
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 BREEDING CALCULATION

Using the formulas indicated on the top left square, it is possible to define precisely the number of breeding cages to setup for dedicated needs. This lead to safer production without excess of animals unused. Even for small production goal, it allows to make major savings both in animals produced and cages in the facility.

Here is an example, starting with a production goal of 5 animals per week.

Empirical production *

5 Trios in permanent breeding

Average weekly birth : 8,5 pups

Yearly production :
442 pups
(i.e. 182 supernumerary animals)
442 Stock cages created

Calculated production *

3 Trios in permanent breeding

Average weekly birth : 5,1 pups

Yearly production :
266 pups
(i.e. 6 supernumerary animals)
266 Stock cages created

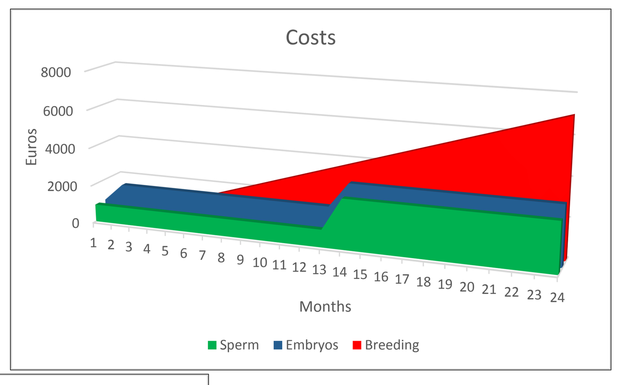
*Based on a IP of 0,85 pups/week/female and experiments performed on 8 weeks old animals

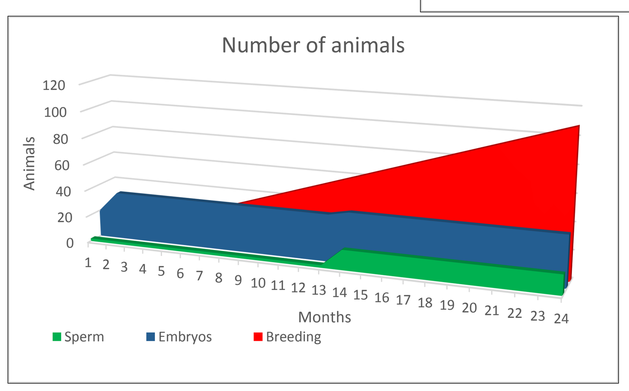
Expected gain in 1 year:

Reduction of animals - 40%
Reduction of cages - 40%

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 produced but not used for experiments. Additionally to the production of useless animals, this create costs allover the time.





Using cryopreservation to freeze all transgenic lines not use for more than 8-9 months decrease the number of animals produced and the costs.

Expected gain in 2 years:

Reduction of animals - 86%
Reduction of costs - 63%

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 induce the possibility to reduce massively the number of animals produced by breeding as breeding can be performed HOMxHOM instead of HETxHET (in order to produce HOM and WT littermates). Of course, this imply to set up an efficient genetic background drift program (for example by using cryopreservation).

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

Production HETxHET

80 pups to produce
12,5% animals of interest
16 females in breeding
72 cages in total

10 males HOM	10 females WT
10 males WT	10 females HOM
20 males HET	20 females HET

10 males HOM	10 females HOM

Production HOMxHOM

20 pups to produce
50% animals of interest
4 females in breeding
18 cages in total

Expected gain at each batch:

Reduction of animals - 75%
Reduction of cages - 75%

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 payroll)
- 400 cages/week/tech

Colony management tools	Animals saved per year	Cages reduction per week	FTE reduction per week	Cost reduction per week
Production level calculation	13200	375	0,94	3750€
Cryopreservation	3750	300	0,75	3000€
Use of congenic animals	9000	156	0,39	1558€

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 managements 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 :

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contact@3tc.fr

www.3tc.fr

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