



National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

Genetically altered mouse colonies: resources to support best practice in colony management, archiving and sharing of strains

Dr Ellen Forty – NC3Rs

‘Culture of care and responsible research’ day, The University of Jena
10 March 2022

The NC3Rs

- Independent, scientific organisation.
- Established by the UK Government in 2004
- Use the 3Rs as framework to support science, innovation and animal welfare
- Work across the bioscience sector, with research funders, industry, regulators and academia
- Budget ~ £10.6 million p.a.
- 38 staff based in London and regionally



Work with us to
advance the 3Rs
in your research
community

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www.nc3rs.org.uk

Challenges when returning to breeding mice following COVID-19 lockdown

- **Challenges, alongside opportunities to apply best practice.**
- **Expert working group to generate best practice guidance in light of challenges**



Challenges when returning to breeding mice following COVID-19 lockdown

- 1 The colony will **not be used** for research for the next six months.
- 2 Stock **animal numbers were reduced** due to pause/interruption but the colony now needs to be maintained with greater numbers, to allow for an increase in numbers for future experiments.
- 3 Stock animal numbers were reduced due to pause/interruption but the colony now needs to be expanded to breed experimental cohorts immediately.
- 4 Complex breeding is required (e.g. breeding conditional alleles, or other multi-allelic crosses) but **not all required strains are available**.
- 5 Experimental cohorts are ready, but the resources (e.g. functional, calibrated equipment, consumables or trained and competent staff) are not available.
- 6 The experiment was **only partly completed** prior to pause/interruption and the remaining part now needs to be completed.
- 7 The strain needed for a new experiment is **no longer available**.
- 8 Archiving was **incomplete** or not initiated but archiving of strain is still required.
- 9 **Rapid breeding** of animals with specific characteristics (e.g. sex or age) is required.

NC3Rs Breeding and colony management resource

Home > 3Rs resource library

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Breeding and colony management

Best practice guidance for optimising the use of animals and avoiding wastage, with an emphasis on re-establishing colonies after a pause.



> Colony management best practice

Introduction to best practices in confirming, archiving and maintaining strains.

> Colony management scenarios and strategies

Methods to address common challenges arising when re-starting breeding and animal experiments after a pause.

> Worked example of intermittent breeding

Alternative breeding strategy to avoid unnecessary wastage of animals.

> Efficient management of GA mouse colonies

NC3Rs and MRC Harwell joint webinar.

> Archiving best practice

Key considerations and timelines for cryopreserving a strain.

> Sharing & archiving of GA mice

High-level guidance highlighting opportunities for reduction and refinement.

> FAQs

Common breeding and colony management queries including a link to an email advice service.

> Email advice service

Get in touch for answers to specific questions about colony management or breeding difficult strains.

> Glossary

Definitions of key terms in breeding and colony management.



Scenario 1: The colony will not be used for the next 6 months

- A. Archive the strain**
- B. Retain holding stock but do not breed
- C. Intermittent breeding
- D. Retain holding stock with constant mating



Archiving best practice



Links to:

- Established cryopreservation protocols
- Free archiving at European Mutant Mouse Archive (EMMA)

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- **Choosing an archiving method**
 - Embryos – superovulation with natural mating or IVF, vs sperm
- **Key considerations when cryopreserving a strain**
 - Age of animals
 - Record keeping
 - When to freeze
 - Storage
 - Quality control measures
- **Timelines for archiving methods**
 - Single allele GA strain – heterozygous or homozygous
 - Multi-allelic strain – heterozygous or homozygous

www.nc3rs.org.uk/archiving-best-practice

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Intermittent breeding strategy



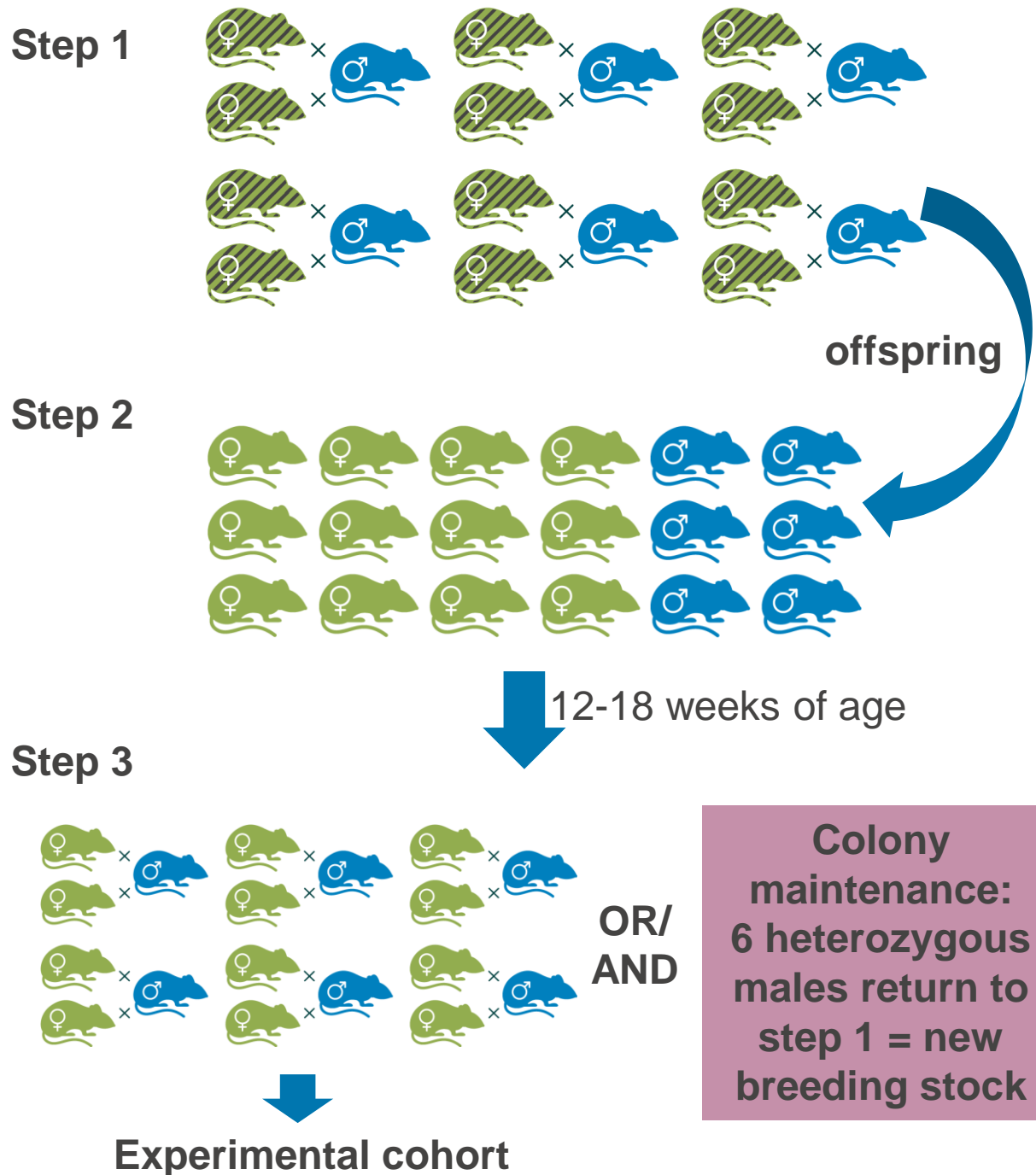
- Holding stock and only breed periodically.
- Reduces wastage to minimum, decreases cage costs, space and genotyping.
- See webinar for practical tips on implementing effective intermittent breeding in your facility.

	Tick-over colony	Intermittent breeding
Breeding strategy	Constant matings set up, frequently replacing breeding stock.	Breeding stock replaced periodically before decline in fecundity.
Matings	3 pairs at any one time, each produce litter every ~3 weeks.	6 pairs breeding only twice each per year (staggered).
Number mice/year*	300	80
Frequency genotyping	Monthly	Twice a year
Number cages/year	480 cage weeks	300 cage weeks

Worked example intermittent breeding



- Breeding stock available to produce 6 homozygous females, 6 homozygous males, 6 wild type females and 6 wild type males.
- C57BL/6N breeding stock.
- Option to also retain animals to replenish breeding stock.



Webinar recording



‘Efficient management of genetically altered mouse colonies’

Drs Sara Wells and Michelle Stewart, MRC Harwell

Recording available at www.nc3rs.org.uk/webinars

Using best practice to overcome common challenges in colony management

- Tips for maintaining efficient breeding strategies (e.g. intermittent breeding).
- How to avoid genetic drift and maintain strain integrity in closed colonies.
- How to breed from colonies reduced in size.
- How to choose an appropriate control strain.
- Breeding schemes for complex crosses.
- Tips on colony calculations and planning.

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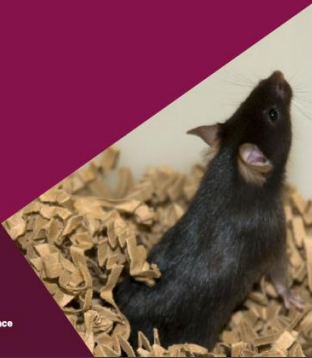
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Sharing & archiving of genetically altered mice

Opportunities for reduction
and refinement



Pioneering Better Science

- Why, what, how, when to archive
- How to share strains
- Cryopreservation checklist
- Downloadable PDF

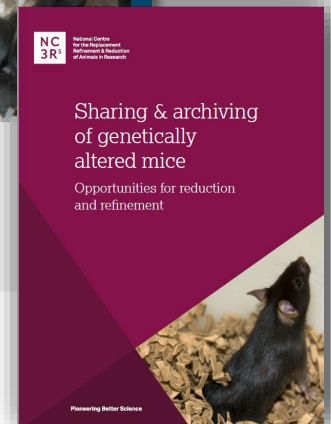
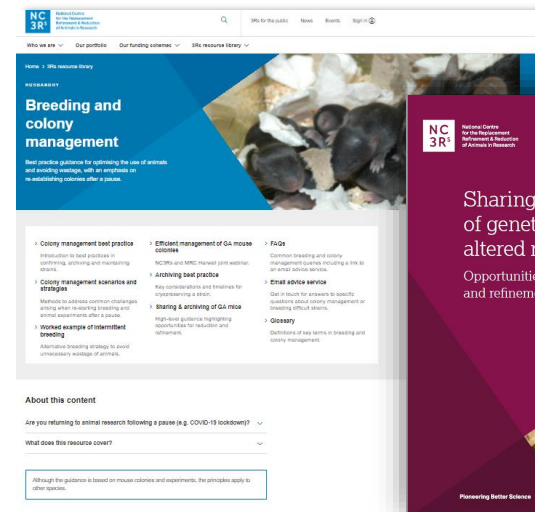
- **Updated** to reflect current best practice.
- **New** record keeping list of information required to archive/share strains.
- **New** resources for multiple species including databases, repositories and training resources for mouse, rat, *Xenopus* and zebrafish.



Summary

- The pandemic has resulted in opportunities, alongside challenges, to review and implement best practice in the management of GA mouse colonies.
- To reduce and refine the use of GA mice, all institutions should have breeding and colony management policies, including for archiving and sharing strains.
- New key resources to support best practice in colony management, archiving and sharing of strains:

- www.nc3rs.org.uk/colony-management
- www.nc3rs.org.uk/archiving-best-practice
- www.nc3rs.org.uk/sharing-archiving
- Email advice service:
colonymanagement@nc3rs.org.uk



Acknowledgements

Breeding and colony management working group

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Dr Jacqui White	The Jackson Laboratory



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Thank you!

For more information

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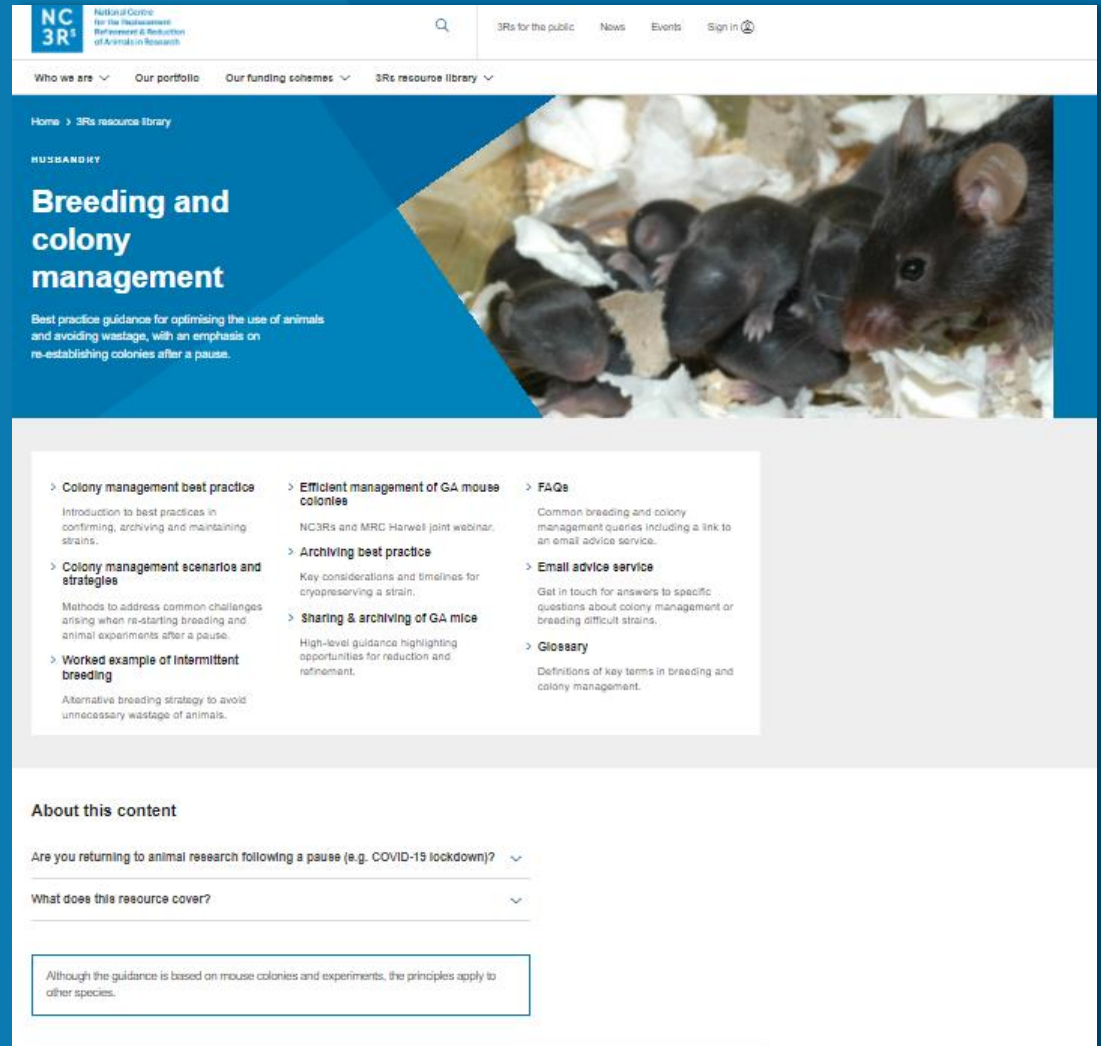
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The screenshot shows the NC3Rs website interface. At the top, there is a navigation bar with the NC3Rs logo and the text 'National Centre for the Replacement Refinement & Reduction of Animals in Research'. Below the navigation bar, there are several menu items: 'Who we are', 'Our portfolio', 'Our funding schemes', and '3Rs resource library'. The main content area features a large image of mice in a colony, with the title 'Breeding and colony management' and a subtitle 'Best practice guidance for optimising the use of animals and avoiding wastage, with an emphasis on re-establishing colonies after a pause.' Below the image, there is a grid of links to various resources, including 'Colony management best practice', 'Efficient management of GA mouse colonies', 'Archiving best practice', 'Sharing & archiving of GA mice', 'Worked example of intermittent breeding', 'FAQs', 'Email advice service', and 'Glossary'. At the bottom of the page, there is a section titled 'About this content' with two dropdown menus: 'Are you returning to animal research following a pause (e.g. COVID-19 lockdown)?' and 'What does this resource cover?'. A small text box at the bottom of the page states: 'Although the guidance is based on mouse colonies and experiments, the principles apply to other species.'

NC3Rs CRACK IT Challenge: EASE



Aim: Improve the implantation rates of early stage embryos to allow the use of non-surgical embryo transfer in the generation of transgenic mice.

www.ivfmicro.com

Webinar recording available.

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IVF micro - a novel and reliable microfluidic device that improves the developmental competence of *in vitro*-derived mouse embryos.

- The IVF Micro microfluidic system has advantages compared to standard dish culture:
 - Mimics the embryo environment *in vivo*;
 - Eliminates the use of oil, reduces nutrient stress and better supports the embryo development;
 - Reduces handling and exposure to stressors (i.e. shear stress, T and pH changes).

Why use IVF Micro?

- **Easy to use:** The system does not require specialised equipment and learning to use, a single one-hour video and half a day of on-site training is sufficient.
- **Refines protocols:** IVF Micro removes the need for surgical procedures for embryo transfer.
- **Reduces costs:** by allowing non-surgical embryo transfer, IVF Micro avoids the costs associated with surgery.