Turning fifty

Lab Animal celebrates its 50th birthday this month. This milestone anniversary presents an opportunity to reflect on how animal research has changed over the past fifty years and consider what the future might hold.

Since *Lab Animal* first launched in 1971, its mission has been to publish content that is important to the animal research community. While much has changed in animal research over the past 50 years, our mission ultimately remains unchanged: we will continue to strive to bring you cutting-edge research and knowledge that impact animal research and welfare.

In the past five decades, there has been an increasing focus on translational research that uses knowledge from an ever-growing number of model organisms to understand and treat human disease. Mice and rats have remained the mainstay of biomedical research as emerging technologies have enabled the development of newer and improved models. Notably, advances in animal transgenesis and genome editing technologies have opened new perspectives for modeling human disease. In this anniversary issue, Susan Bello, Michelle Perry and Cynthia Smith give us a brief history of making mutant mouse genetic models¹, from the generation of the first transgenic mouse and the first mouse with targeted genome modification in the 1980s, to the recent creation of more refined murine models with the advent of endonuclease-mediated gene editing.

Other innovations in the past 50 years include somatic cell nuclear transfer (SCNT), the cloning technique used to develop Dolly the sheep back in 1996. SCNT, combined with genome editing, allows quick and efficient generation of human disease models in large animals, including primates, which remain translationally relevant animal options.

In 50 years, the gene manipulation toolbox has also been expanded for flies, worms and fish; these non-mammalian models, which offer advantages of scale and speed over larger animals, have gained increased popularity for disease modeling and drug discovery. The genomes of most “traditional” model organisms (including rodents, worms and flies) were sequenced between 1998 and 2002. As sequencing technologies have advanced while costs have shrunk, scientists around the world have set ambitious goals to assemble more and more genomes. Figuring out an animal’s DNA sequences is important to analyze genome function from proteins to disease.

Along with other tools, whole-genome drafts of new species can expand the pool of model organisms available in the lab. In this issue, Monica Amorim and colleagues present the first high-quality reference genome of *Enchytraeus crypticus*², a soil invertebrate that has served as an ecotoxicology model for over 20 years. The resource could extend the use of this model to other research areas such as regeneration, immunity and aging, adding another invertebrate option for researchers.

Accelerating the development and use of invertebrate models is also a way to reduce the use of mammals in research, fulfilling one of the 3Rs. These principles of Replacement, Reduction, and Refinement were first described by W. M. S. Russell and R. L. Burch in 1959 to protect the welfare of lab animals.

Since 1971, we have moved a long way forward in regards to the protection of animals used in research. The 1980s and the 1990s witnessed considerable progress in the implementation of the 3Rs. Dedicated groups, such as the NC3Rs in the UK, have contributed the uptake of 3Rs approaches in the research community, though impactful initiatives such as the ARRIVE guidelines that we support. The 3Rs are also now embedded in several national and international laws and regulations on the use of animals for research. In the Technology Feature³ this month, we focus on Refinement and discuss efforts from researchers, veterinarians, and animal care staff over the past 30 years to refine the lives of their laboratory animals.

The implementation of the 3Rs in research facilities has also set the framework for developing a Culture of Care, which ensures those responsible for the welfare of research animals are supported as they work to provide the best care possible for their charges. In a special comment⁴ for this issue, Sally Robinson and Angela Kerton discuss objective indicators for assessing an institution’s Culture of Care and possible measures to drive improvements in the future. The authors suggest that oversight bodies such as the AWERB in the UK and IACUC in the US should reinforce their role in the promotion and maintenance of a Culture of Care within establishments. According to Penny Reynolds, IACUC could also serve as important gatekeepers

of research quality in the future by ensuring that simple reproducibility criteria are addressed in animal protocols⁵. Proper experimental design and statistical analysis of a proposed research project are key Reduction measures, as they allow the optimum number of animals to be used.

In this issue, we also feature a Q&A⁶ in which we asked a group of experts in industry and academia to discuss how the field has changed over their careers, which factors in their opinion might have contributed to the current reproducibility crisis and how they think animal research can be improved in the future. The experts highlight the need to operate meaningful changes at all levels of scientific working: in the training provided to future scientists, in the planning and conducting of the experiments, and in the analysis and reporting of the findings.

This issue also marks the return of the Protocol Review column⁷. For three decades, the column developed and written by Jerald Silverman has been an invaluable resource to increase our understanding of US animal research rules and regulations. We are very pleased that our new coordinators Lauren Danridge and Bill Greer will continue Jerry’s legacy.

Reaching this milestone is a testament to all those involved in the journal throughout the past 50 years, and we would like to thank the editorial and production staff, our authors, peer reviewers and journal advisors who have contributed to *Lab Animal* since it launched and you, our readers, for your continued interest in the journal. □

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