Animal Research Tomorrow magazine

Issue 1 | January 2026

ART MAGAZINE

January 2026/Volume 1/Issue 1

Editorial and Production Offices

Animal Research Tomorrow

4000, Basel, Switzerland

Web: https://animalresearchtomorrow.org/en

Chief Editor: Dr. Nuno Franco

Managing Editor: Dr. Iana Buch

Personal Subscriptions Requests

Email to contact@animalresearchtomorrow.org

Advertising and Sponsorship:

Email to contact@animalresearchtomorrow.org

Editorial

Animal Research Tomorrow Magazine – a new chapter for ART

It is my pleasure to welcome you to the first issue of the ART Magazine, a new chapter for the Animal Research Tomorrow Society. This is more than just a newsletter; it is a space for ideas, perspectives, and stories that matter to everyone in our community committed to sound, relevant, transparent, and ethical animal research: scientists, veterinarians, animal welfare and ethics experts, and communicators. The motto of our magazine will be, "By scientists, for Science," highlighting the grass-roots nature of our community and our ultimate goal of improving science.

Our goal is to share credible, accessible, and thought-provoking content about biomedical research, animal welfare, and the 3Rs. The magazine will not be a peer-reviewed journal and does not aim to be one. However, we aim to soon assign each article with its own DOI, making it a permanent, searchable, and citable contribution to the public record. The magazine is introducing a Book Review section, with an interview with the main author or editor. You will also find interviews with ART Award recipients, opinion pieces from invited scientists and communicators, and news items highlighting new initiatives and resources for the community. The magazine will also share short ART publications, including our flyers, like the recent one explaining why carefully regulated severe-severity studies are still essential for progress against life-threatening diseases.

All members of the ART Society are welcome to offer their suggestions on how to improve our magazine and even submit their own short articles (e.g., a conference report, a call for action, or an opinion piece on a current topic of interest to our members).

Alongside the magazine, we are launching the Animal Research Tomorrow Series, bimonthly talks by leading researchers in biomedical science, as well as in laboratory animal welfare and the 3Rs. These seminars will be free for anyone to attend, and attending ART members will receive CPD certificates at no cost.

Together, these new initiatives reflect ART's renewed commitment to promote transparency and dialogue, as well as ethical and scientific progress for the benefit of both human and animal health.

Nuno Henrique Franco

President

Advancing Humane Science: The 3Rs Collaborative's Leadership in Refinement, Reduction, and Replacement

by Sally Thompson-Iritani

Introduction

The 3Rs Collaborative (3RsC), led by Executive Director Megan LaFollette, began as a shared vision among professionals who asked a simple but transformative question: "What are we doing for the 3Rs community beyond our organization?" [1–3]. While many had made progress improving animal welfare and scientific quality within their own programs, they saw the need for a unified, cross-sector effort. In 2015, Marilyn Brown, Deborah Curry, and Jim Foster of Charles River Laboratories turned that question into a mission. Foster, then CEO, encouraged his colleagues to lead the research world not only in innovation but also in compassion. With organizational support from Charles River, the 3Rs Collaborative launched in 2017 at the World Congress on Alternatives and Animal Use in the Life Sciences in Seattle, establishing its mission to unite scientific progress with humane responsibility [1–3].

Collaborative Innovation Across the 3Rs

The 3Rs Collaborative leads a suite of high-impact initiatives that combine innovation and ethical responsibility. The Microphysiological Systems (MPS) Initiative brings together developers, researchers, and regulators to advance in vitro tools such as organoids, spheroids, and organ-on-a-chip systems. These models serve as complementary tools to traditional animal tests, aiming to replicate key aspects of human biology. They are being evaluated for potential to enhance the relevance and reliability of data used in health research and drug development. As part of this initiative, the Drug Induced Liver Injury (DILI) project collaborates with federal partners to validate liver-specific MPS models [4].

Complementing this effort, the Artificial Intelligence (AI) Initiative explores the use of advanced computational methods, including machine learning, to improve decision making in toxicology, safety testing, and predictive modelling. This initiative helps develop advanced tools that enhance scientific accuracy while reducing reliance on animals in research [5].

The Translational Digital Biomarkers (TDBM) project works with federal partners to validate digital and in vitro systems that improve predictive toxicology. It also advances the use of digital caging solutions that enhance animal research more broadly, supporting both scientific rigor and animal welfare [6].

Building Compassionate Research Communities

The 3Rs Collaborative recognizes that humane science depends on resilient professionals. Its Culture of Care initiative provides tools for researchers, veterinarians, and caregivers to manage the emotional challenges of animal care. Through specialized institutional resources, webinars, and workshops, this initiative encourages empathy, wellness, and a strong culture of care across research organizations [7].

In parallel, the Environmental Health Monitoring (EHM) initiative replaces traditional sentinel animal use with environmental testing of cages and racks, allowing institutions to monitor health status while minimizing animal involvement. The Refinement Initiative supports improved handling, care, and enrichment strategies that promote both animal welfare and scientific rigor [8].

The 3Rs Certificate Course

Education stands as a core element of the 3RsC mission. In partnership with the CITI Program, the 3Rs

Collaborative offers the 3Rs Certificate Course, a five-hour self-paced online program composed of five modules covering the history, ethics, and modern applications of refinement, reduction, and replacement. Participants explore the integration of 3Rs principles into study design, animal care, and innovation. The course concludes with assessments that certify learners' understanding of humane science principles. It is accessible worldwide and has been incorporated into research training programs at several universities, including the University of Washington [9].

A Unified Commitment to Humane Science

Today, the 3Rs Collaborative connects more than 200 experts and over 100 U.S. organizations spanning academia, government, and industry [10]. Through initiatives such as MPS, AI, EHM, and compassion resiliency, along with its educational certificate program, the Collaborative continues to build on the founding vision of integrating better science with empathy. Each project shares one central goal: to advance both human innovation and animal welfare as inseparable parts of the same scientific mission.

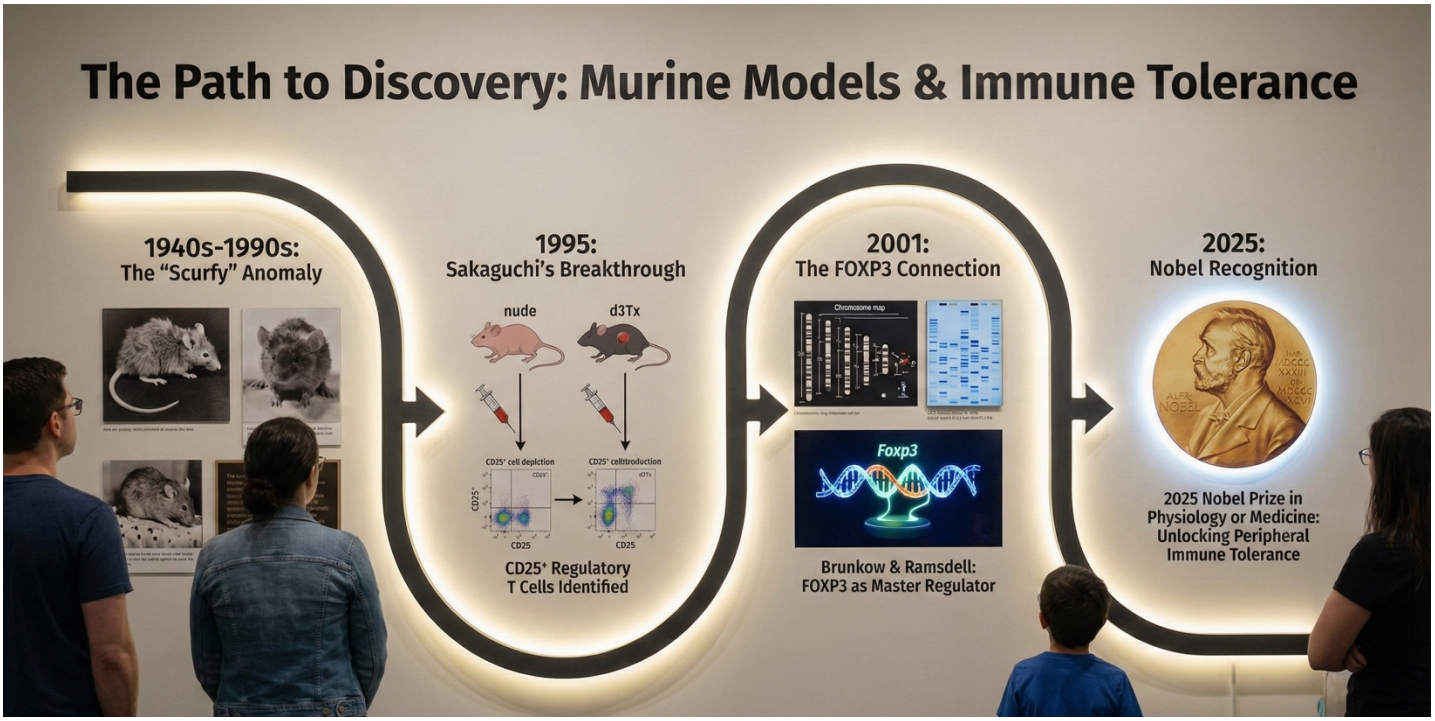
References:

1. *The 3Rs Collaborative. (2023). Strategic Plan 2023–2025. Retrieved October 28, 2025, from https://3rc.org*
2. *The 3Rs Collaborative. (n.d.). Mission Statement. Retrieved October 28, 2025, from https://3rc.org*
3. *Norecopa. (n.d.). The 3Rs Collaborative. Retrieved October 28, 2025, from https://norecopa.no*
4. *The 3Rs Collaborative. (n.d.). Microphysiological Systems Initiative; CN Bio. (n.d.). FDA DILI Project Collaboration. Retrieved October 28, 2025, from https://3rc.org/mps*
5. *The 3Rs Collaborative. (n.d.). Artificial Intelligence Initiative. Retrieved October 28, 2025, from https://3rc.org/ai*
6. *The 3Rs Collaborative. (n.d.). Translational Digital Biomarkers Initiative. Retrieved October 28, 2025, from https://3rc.org/tdb*
7. *The 3Rs Collaborative. (n.d.). Culture of Care and Compassion Fatigue Resources. Retrieved October 28, 2025, from https://3rc.org/compassion-fatigue*
8. *The 3Rs Collaborative. (n.d.). Environmental Health Monitoring and Refinement Initiatives. Retrieved October 28, 2025, from https://3rc.org/health-monitoring*
9. *CITI Program & The 3Rs Collaborative. (n.d.). 3Rs Certificate Course. Retrieved October 28, 2025, from https://about.citiprogram.org*
10. *The 3Rs Collaborative. (n.d.). Membership Information. Retrieved October 28, 2025, from https://3rc.org/membership*

Murine Models of Peripheral Immune Tolerance: The Foundational Discoveries Honored by the 2025 Nobel Prize in Physiology or Medicine

Animal Research and the 2025 Nobel Prize in Physiology or Medicine

by Stefano Gaburro



Introduction

The 2025 Nobel Prize in Physiology or Medicine was awarded jointly to Mary E. Brunkow, Fred Ramsdell, and Shimon Sakaguchi for their discoveries concerning peripheral immune tolerance. This recognition highlights one of the most significant advances in immunology over the past three decades. The pioneering work of these laureates fundamentally transformed scientific understanding of how the immune system maintains self-tolerance and prevents autoimmunity. Critically, these discoveries were made possible through meticulous research using laboratory mouse models, which provided the essential experimental platforms for identifying and characterizing regulatory T cells (Tregs) and the transcription factor FOXP3 [1, 2, 3].

The Nobel Committee emphasized that animal research was indispensable to these discoveries. As stated in the official announcement, the laureates identified the immune system's security guards, regulatory T cells, which prevent immune cells from attacking the body's own tissues. This review examines the animal models that enabled these Nobel Prize-winning discoveries, demonstrating the irreplaceable role of murine research in advancing biomedical science.

Sakaguchi's Discovery: Finding the Immune System's Peacekeepers

For decades, immunologists believed that the body prevented autoimmune disease through a single mechanism: eliminating dangerous immune cells in the thymus before they could cause harm. Shimon Sakaguchi challenged this view. Working with mice in the 1990s, he noticed something unexpected during cell transfer experiments. When he transferred certain immune cells into mice lacking a thymus, the recipients should have developed autoimmune disease, but they did not. Something was holding the immune system back.

It took Sakaguchi over a decade of research using mice to find the answer. In 1995, he identified a previously unknown class of immune cells that acted as peacekeepers, calming other immune cells and preventing them from attacking the body's own tissues. He named these regulatory T cells. When Sakaguchi removed these cells from the transferred population, recipient mice developed severe autoimmune disease affecting multiple organs. When he added them back, the disease was prevented. This elegant series of mouse experiments proved that the immune system actively polices itself through these specialized guardian cells [1, 4].

The Scurfy Mouse: An Accidental Discovery with Profound Implications

Many researchers remained skeptical of Sakaguchi's findings. More proof was needed. The crucial evidence came from an unlikely source: a mutant mouse strain that had been maintained in a laboratory for nearly half a century. The scurfy mouse first appeared in the 1940s at Oak Ridge National Laboratory in Tennessee, where scientists were studying radiation effects as part of the Manhattan Project. Male mice in this strain were born with scaly, flaky skin, massively enlarged lymph nodes, and died within weeks. Their immune systems were in open rebellion against their own bodies [2, 3].

Mary Brunkow and Fred Ramsdell, working at a biotechnology company developing treatments for autoimmune diseases, recognized that understanding what caused the scurfy mouse disease could unlock fundamental insights into autoimmunity. In an era before rapid genome sequencing, finding the responsible gene was painstaking work. The team spent years narrowing down the location, examining gene after gene, comparing healthy mice with scurfy mice. Finally, in the twentieth gene they examined, they found it: a mutation in a previously unknown gene they named FOXP3 [2, 3].

The discovery proved transformative. Brunkow and Ramsdell suspected that a rare human disease called IPEX syndrome, which causes devastating autoimmunity in young boys, might be the human equivalent of scurfy. Working with pediatricians worldwide, they confirmed that IPEX patients also carry mutations in FOXP3. The mouse model had revealed a fundamental mechanism of human disease [3, 5].

Connecting the Pieces: From Gene to Guardian Cells

The identification of FOXP3 sparked intense research activity. Two years after Brunkow and Ramsdell's publication, Sakaguchi and other researchers demonstrated that FOXP3 controls the development of the very regulatory T cells he had discovered years earlier. Mice lacking functional FOXP3 completely lacked these guardian cells, explaining why their immune systems attacked their own bodies. When scientists introduced a working copy of the FOXP3 gene into immune cells from scurfy mice, those cells regained their regulatory function [6, 7].

This convergence of discoveries, made possible entirely through mouse research, established a complete picture: FOXP3 acts as a master switch that creates regulatory T cells, and these cells continuously patrol the body to prevent autoimmune attack. Without animal models, particularly the scurfy mouse and the various immunodeficient strains used for cell transfer experiments, these connections could never have been made.

From Understanding to Treatment: Testing Therapies in Mice

The mouse models that enabled these discoveries continue to serve as essential platforms for developing treatments. Scientists demonstrated that transferring healthy regulatory T cells into scurfy mice could prevent disease, providing proof of concept for cell therapy approaches. Bone marrow transplantation studies in mice showed that even partial restoration of regulatory T cell populations could prevent fatal autoimmunity. These findings directly informed clinical approaches for IPEX syndrome, where stem cell transplantation remains the only definitive treatment [8, 9].

Clinical Impact and Ongoing Research

The discoveries honored by the 2025 Nobel Prize have profoundly influenced clinical medicine. Regulatory T cells are now recognized for their roles in modulating immune responses across multiple contexts including transplantation, cancer, infection, allergy, and pregnancy. More than 200 clinical trials investigating regulatory T cell-based interventions are currently registered, targeting cancer, asthma, inflammatory bowel disease, and even functional decline in amyotrophic lateral sclerosis (ALS) [10].

In oncology, regulatory T cells are frequently found within the tumor microenvironment, where they dampen antitumor immune responses. There is substantial interest in strategies to disable or deplete these cells in the context of cancer therapy. Conversely, enhancing regulatory T cell activity holds promise for preventing organ transplant rejection and treating autoimmune diseases. The 2025 Nobel Prize underscores the double-edged nature of immune control and invites new therapeutic strategies that modulate, rather than override, regulatory circuits [10].

Conclusion

The laboratory mouse has been indispensable in elucidating the cellular and molecular mechanisms of peripheral immune tolerance. From Sakaguchi's pioneering adoptive transfer experiments in nude and neonatally thymectomized mice to the identification of Foxp3 mutations in scurfy mice by Brunkow and Ramsdell, murine models have driven transformative advances in immunology recognized by the 2025 Nobel Prize in Physiology or Medicine. These models continue to serve as essential platforms for developing and testing novel immunotherapies aimed at restoring tolerance in autoimmune disease, preventing transplant rejection, and enhancing anti-tumor immunity.

The 2025 Nobel Prize recognition gives considerable momentum to developing therapies for transplantation and autoimmunity. As stated by the Nobel Committee, the laureates' discoveries have been decisive for understanding how the immune system functions and why autoimmune diseases do not affect everyone. The foundational discoveries made possible by animal research represent enduring contributions to biomedical science and exemplify the critical role of laboratory animal research in advancing human health.

References:

1. *Sakaguchi S, Sakaguchi N, Asano M, Itoh M, Toda M. Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). J Immunol. 1995;155:1151-1164.*
2. *Brunkow ME, Jeffery EW, Hjerrild KA, et al. Disruption of a new forkhead/winged-helix protein, scurfin, results in the fatal lymphoproliferative disorder of the scurfy mouse. Nat Genet. 2001;27:68-73.*
3. *Wildin RS, Ramsdell F, Peake J, et al. X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is the human equivalent of mouse scurfy. Nat Genet. 2001;27:18-20.*
4. *Shevach EM. Certified professionals: CD4+CD25+ suppressor T cells. J Exp Med. 2001;193:F41-F46.*
5. *Bennett CL, Christie J, Ramsdell F, et al. The immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) is caused by mutations of FOXP3. Nat Genet. 2001;27:20-21.*
6. *Hori S, Nomura T, Sakaguchi S. Control of regulatory T cell development by the transcription factor Foxp3. Science. 2003;299:1057-1061.*
7. *Fontenot JD, Gavin MA, Rudensky AY. Foxp3 programs the development and function of CD4+CD25+ regulatory T cells. Nat Immunol. 2003;4:330-336.*
8. *Bacchetta R, Barzaghi F, Roncarolo MG. From IPEX syndrome to FOXP3 mutation: a lesson on immune dysregulation. Ann N Y Acad Sci. 2018;1417:5-22.*
9. *Kim JM, Rasmussen JP, Rudensky AY. Regulatory T cells prevent catastrophic autoimmunity throughout the lifespan of mice. Nat Immunol. 2007;8:191-197.*
10. *Nobel Prize in Physiology or Medicine 2025. Press Release. The Nobel Assembly at Karolinska Institutet. October 6, 2025. https://www.nobelprize.org/prizes/medicine/2025/press-release/*

Book Review: "Rethinking the Three R's in Animal Research" by Jan Lauwereyns (Palgrave – MacMillan, 2018)

A Book Review by Augusto Vitale and Maša Čater

Some books need to be written and need to be read. These are the ones that challenge established thinking, unsettle assumptions, and push readers to reconsider what they thought they knew ("The Selfish Gene" by Richard Dawkins comes to mind). Jan Lauwereyns' "Rethinking the Three R's in Animal Research" belongs firmly in this category. As scientists who have long admired the 3Rs principles (which we consider relate more to methodology than to ethics), we found ourselves confronted by Lauwereyns' arguments. His reasoning planted a few uncomfortable – but necessary –doubts about how these principles are applied today.

Lauwereyns is a neuro-cognitive scientist with an impressive academic record and years of experience studying neuroscience in nonhuman primate (NHP) models. However, the high level of invasiveness his work required, coupled with growing doubts about the benefit of such research, ultimately led him to step away from it. This personal turning point inspired him to question the broader ethical justification for using animals, especially NHP, in laboratory research.

Lauwereyns is a sophisticated, thought-provoking writer, unafraid to challenge deeply rooted assumptions about the use of animals in science. His aim is not to dismantle animal research ethics, but to refine it. He argues that genuine progress in animal research ethics begins by deconstructing our current understanding of the Three Rs. He fully acknowledges the unquestionable legacy left by Russell and Burch but insists that the time has come to reinterpret their framework to make way for a new era of Science.

The book unfolds in four major movements. In Chapter 2, Lauwereyns traces the historical evolution of the Three R Principles, revealing what he calls a *human-centred* perspective in Russel and Burch's original vision, one aimed not so much at improving animal welfare as at making humans appear more humane. It is a rare, carefully articulated anti-speciesist interpretation of the Three Rs. While not entirely agreeing with it, it made us think. In Chapter 3, Lauwereyns draws a convincing contrast between two levels of analysis: a *micro-level*, where individual researchers earnestly strive to apply the Three Rs in daily practice, and a *macro-level*, where the broader scientific system fails to uphold these ideals, ethically, and often scientifically. Here, he makes a strong case for greater transparency and open science. Chapter 3, "The Monkey Question", delivers perhaps the book's sharpest critique. Lauwereyns questions the continued use of NHPs in neuroscience, arguing that the field still takes their necessity for granted. While the tone is occasionally harsh, his points are legitimate: one can too often overlook viable alternatives (such as rodents) and fail to ensure meaningful translational links between basic and clinical research. Most importantly, Lauwereyns reminds us that the past success in animal research does not justify its automatic continuation. Ethical standards evolve, and so must our methods. In the final chapters, Lauwereyns turns visionary. He visions a future of *collective science*, collaborative, transparent, and

ethically grounded. Only through such transformation, he argues, can the Three Rs retain their relevance and integrity.

Not every argument is equally convincing. Certain aspects, such as the limited discussion of "benefit to society" as acquisition of knowledge, feel underdeveloped. At times, Lauwereyns blurs the line between animal welfare issues and animal rights, a conceptual overlap which muddies both debates. Yet, despite – or perhaps because of – these disagreements, *Rethinking the Three R's in Animal Research* is an essential reading. It reopens a debate that urgently needs fresh air. Indeed, a book that needs to be read.

Interview with Jan Lauwereyns

What prompted you to write this book?
After working five years with monkeys in basic neuroscience, doing very 'invasive' research from 1998 to 2003, I decided to step away from it because I was disenchanted by the lack of ethical reasoning. Initially I was just curious about basic neuroscience, without questioning the validity of the research. But gradually I realized that even the best work in monkey neurophysiology did not live up to its promises. We published papers in *Nature* and *Neuron* with research that, in ethical applications, we claimed would be relevant for Parkinson's Disease. It was wishful thinking at best, or a plain lie at worst. My boss at the time said he was not an ethicist and could only focus on doing his research. I did not like that stance. Instead of keeping science and ethics separate, I thought the two perspectives should converge on good research. So, I quit the monkey work and started studying bioethics. The Three Rs seemed the optimal approach for good science and proper animal welfare, but then I noticed that my old colleagues also favoured the 3Rs, although they strongly disagreed with my criticisms. I had to figure out how come the Three Rs could seem desirable to people at opposite ends of a controversy. Probably we interpreted the Three Rs differently. I had to write the book to gain clarity in my mind and to develop and share my thinking about the Three Rs.

How do you see today the applicability of the Three Rs principles to animal science?
The Three Rs remain the best model we have for the integration of science and ethics in animal research, if we interpret them as dynamic pointers rather than static formulations. Replacement should clearly come first, with an absolute target to reduce the reliance on animals. We also have AI- and IT-driven tools for more powerful analysis and new research techniques, including, for instance, work with organoids. The good news is that the Three Rs have gained wide recognition and more momentum than ever before. The bad news is that people hear different things in them. Some hear only 'Refinement' and resist changes to research culture. Also, the Three Rs-based legislations function merely as requests, without reinforcement. The applicability is very much there, but we have more work to do, to effectively apply the Three Rs in animal research.

What future scenarios can you predict?
For me, the most exciting prospect is that the Three Rs will be used (in their updated, open-minded reinterpretation) not only for animal research, but for all types of animal use. I was always a little mystified by how passionate scientists and animal-rights activists can be about the debate on animal research, while ignoring other issues. In fact, the use of animals in research is dwarfed by other uses. The far bigger issue for human health, animal welfare and environmental sustainability is what we eat and how we produce food. The Three Rs have massive potential as principles for animal-based food production and consumption.

Meet the ART Award winners

We launched the ART awards for the 3Rs and science communication back in 2022. Our initial goal was to provide young scientists and communicators with the opportunity to realize their first innovative ideas. We did not fully realize at the time how instrumental this award would become in building the vibrant ART community. We have had some truly great projects that we are very proud of. Now is the perfect time to revisit our past winners and see what they are achieving! Meet **Miguel Gandra**, a marine scientist from the University of Algarve in Portugal, and **ART 2022 SciComm Award winner**.

Could you tell our readers a little about your current role, your main area of work, and perhaps a hobby or interest that keeps you grounded outside the professional world?

I have just submitted my PhD thesis in marine sciences at the University of the Algarve, where I have been exploring the movement ecology of sharks and other marine megafauna. My work focuses on biologging and biotelemetry — using high-resolution data to understand how these animals move, behave, and interact with their environment. Outside work, spending time in or around the water — freediving, exploring the coast, or taking photos — reminds me why I got into this in the first place. So yes, I am very much still working in the same field; if anything, I have doubled down on the very topics that the award helped me pursue.

Please give us an update on your project. Does it continue? Did some follow-up ideas and projects come out of it?

The project is still very much alive. What started as a single initiative evolved into a continuous line of work within our research group, and it has opened the door to many other ideas. We've continued producing digital content combining underwater footage and animations based on real ecological data. More recently, I also developed a demo webpage illustrating how emerging interactive tools can be used to create engaging content (https://miguelgandra.github.io/digital-scicomm/).

What were the main challenges you faced during the past years in your journey as a scientist and communicator, and what is the key accomplishment you are most proud of?

The biggest challenge has been juggling advanced data analysis, fieldwork logistics, and creative science communication — all while completing a PhD. Securing funding has also been tough; the competition is intense, and navigating applications takes a surprising amount of time and headspace. Despite these challenges, there were many rewarding moments. I am proud of the content and AR posters we created, showcased in schools and at conferences, and seeing people engage with the material was immensely gratifying.

Thinking back to when you received the award, do you feel the ART Award specifically helped you in your journey as a communicator and how?

Absolutely, the ART Award had a transformative impact on my professional journey. Beyond providing crucial financial support, it gave me the confidence to embrace science communication as a core part of my work. The award allowed me to explore new digital technologies, connect with other researchers and communicators, and opened the door to additional funding for marine conservation projects.

What is your current view on effective science communication? What is the biggest hurdle to communicating complex science to the public today? Do you think it is particularly challenging when it comes to animal research?

For me, effective science communication is about creating a genuine sense of connection and engagement. It is not just about simplifying information — it is about helping people feel why the science matters. Visual storytelling and interactivity can make a huge difference, especially in a field like marine ecology, where so much happens out of sight. As Carl Safina's quote goes, "Facts alone cannot save the world. Hearts can. Hearts must. We are working to make sure that hearts do.". In today's information-saturated world, scientific content must be accurate, engaging, and transparent — especially in animal research, where explaining the purpose, methods, and conservation value is crucial.

Is there anything we forgot to ask, or a final message, a call to action, or a thought you would like to share with our readership?

In a time when ecosystems are changing fast and misinformation is rampant, every effort to engage, educate, and inspire matters. I am grateful to ART for supporting this mission and hope it encourages more early-career researchers to explore innovative and creative ways to share their work.

A life-worth-living as an ethical justification for animal research

Opinion by Nuno Franco

In August 28th, 2023, I delivered a talk at the 12th World Congress on Alternatives and Animal Use in the Life Sciences (WC12) held in Niagara Falls, Canada, titled “Beyond harm-benefit – demanding a life worth living for laboratory animals”. Quite atypically, I felt uneasy at the start. The day before, in the opening session, the host had been unapologetically hostile towards animal-based biomedical research, and to scientists using animals. This made me, for the first time, feel unwelcome in a congress where I had first participated as a second-year PhD student (Rome, 2009) and in which I grew as a scientist and an academic, starting by presenting posters, and then moving on to deliver oral presentations, then invited talks, and then to chair sessions and organize workshops, in later editions, including in that one. So while I expected a tough crowd, as a World Congress veteran I was also sure that many would be open to different perspectives. Just in case, my opening slide had a quote attributed to Aristotle: "It is the mark of an educated mind to be able to entertain a thought without accepting it", as the thesis I was about to defend was bound to be controversial, a near-heresy, in that context. I was about to argue in favour of – at least some – animal experiments, not from the typical utilitarian harm-benefit perspective, but from the utilitarian argument that a) laboratory animals could live a life worth living; b) said life was arguably better than what most wild animals experience; c) having such a life was better than not living at all and; d) this could make the use of animals for scientific purposes ethically acceptable not because some other animal (human or otherwise) could benefit from it, but because the animals themselves being used could live a good life (or at least a life worth living).

The order by which the Three Rs were originally proposed by Russel and Burch clearly reflects a value hierarchy [1]: firstly, replace whatever is possible, then reduce whenever possible, and only after all Replacement and Reduction options are exhausted, one must refine as much as possible. Such focus on Replacement is grounded on the perception that animal research is inescapably harmful, and thus that it is against the interest of animals to be bred and used in any experiment. Animal research is nevertheless seen by most as ethically acceptable when no alternatives are available, animals are “respected”, and harms to them can be outweighed by progress in human/animal health and safety [2]. However, such benefits might be hard to predict or quantify. And quite unfortunately even the only benefit one can realistically aspire to achieve from a given study – adding to scientific knowledge [3] – is often elusive, due to poor methodological practices that render most animal studies unreproducible and unreliable (likewise, if not worse, for non-animal studies, but I will leave that for another article). Moreover, laboratory animals neither partake in research voluntarily, nor is it usually carried out to their benefit. Thus, from a utilitarian perspective, basing the ethical acceptability of animal research solely on a harm-benefit perspective carries two major problems: the first is that benefits are often speculative, unquantifiable or too indirect, and second that the animals involved do not benefit themselves, cannot consent and typically do not receive any positive outcome from the research requiring their use.

Laboratory mice can live in a complex environment with social interactions, protected from extreme weather conditions and predators, with easy access to abundant, nutritious, healthy food and clean water, and cared for a competent staff catering to their needs. In comparison, most wild mice die at a very young age, from hunger, cold, predators or disease.

It is therefore worth pondering under which circumstances the benefits to research animals could offset any harms they endure. In other words, could using animals in research be justified if they are allowed, if not a *good life*, at least a *life worth living*?

But what is a good life? Is it a stress-free life? A pain-free life? I argued in my talk that, in real life, this is never the case. One may endure transient hunger, discomfort, pain, or fear, and still have had a good life. One may suffer a serious accident, break several bones, undergo multiple surgeries, endure an arduous and painful recovery, and yet prior to and after those trying times have an otherwise happy, healthy and fulfilling life, i.e. a *good life*. Hence, what matters is the totality of one's lived experience. And even under long-term harsh conditions – e.g. chronic illness, a difficult childhood – a life can still arguably be worth living, provided it is possible to recover from the physical or psychological trauma, and thrive.

The question then becomes ascertaining whether – and if so, to what extent – laboratory animals can have a good life. While defining a good life in absolute terms may be challenging, determining whether it is a better life than that of their wild counterparts is more straightforward. For instance, most wild mice die as pups or juveniles, due to harsh weather conditions, predators, disease, malnourishment, competition with conspecifics, and other threats, including humans. Those that survive to adulthood face relentless adversity, living under constant life-threatening challenges and discomfort.

I proceeded to show to the audience a 4-tile panel that featured one of my own dogs, a picture of a couple of stray dogs in poor shape, happy laboratory beagles socially housed in an enriched environment with outdoor access, and an old picture of a sad-looking singly-housed laboratory dog in a barren cage. The pet dog – my own dog Vicky – grew up in a loving home, with plenty of social interaction, walks, play time, medical care, and freedom from fear or hunger, i.e. what can arguably be deemed to be a *good life*. Nonetheless, she did not leave her original family to join ours voluntarily nor was she consulted for major decisions that would affect her life, such as being spayed (and I still have misgivings about it). At the other extreme, stray dogs can be said to be masters of their destiny, choosing where – or whether – to roam, who to be with, what to eat and where to sleep. They are nonetheless often exposed to violence, disease, starvation, and the elements. While free to choose, often said choices are limited or non-existent. Hence, while free, their lives may not amount to *a life worth living*. The same rationale applies to laboratory dogs. While some are allowed to benefit from social housing, enrichment, human interaction, and even a life after their scientific use, others, and especially in parts of the world where regulations and standards leave much to be desired, may live confined, isolated lives with minimal stimulation. And while all will undoubtedly undergo procedures – e.g. injections, gavage, physical exams, or even more invasive interventions, such as surgery – these are likely to occupy a small part of their day, or a short period of their lives. The difference will then be in how said procedures are executed (e.g. in the attention given to adequate anaesthesia and analgesia, as well as staff competence) and in the conditions in which they spend the rest of their time, during which we have the opportunity to provide adequate food and occasional treats, warmth, comfort, company, rest, and opportunities to explore and play (for discussion on opportunities to refine the life outside of experimental procedures see Lewejohann et al. 2020 [4]).

These examples underscore a key point: quality of life reflects cumulative experience, not merely the absence of suffering always, and the presence of some adversity in human or non-human lives does not mean those lives should be defined by it. So, if we accept that under some conditions animals in research can have a genuinely good life, even with some hardship, while others clearly do not, we must reflect upon the lives we are providing to animals in science. If the answer is that these fall short of being worth living, the ethical cost is difficult to defend. Conversely, if we can secure for laboratory animals a good life, or at least a life worth living, then breeding and using them may be in and of itself ethically defensible, provided the net positive welfare experienced outweighs any discomfort or harm.

This raises both philosophical and practical challenges: from defining what counts as a life worth living to assessing positive welfare (rather than simply the absence of pain) to ensure a life in laboratories can allow more than a neutral baseline existence.

Given that my thesis assumed a utilitarian framework, there was also the problem of how to account for and weigh positive welfare gains before, during, and after research procedures against the harms they impose. One answer is to minimise – or eventually end, as proposed by the RSPCA [5] – severe suffering through refinement of husbandry, handling, procedures, early humane endpoints, and painless euthanasia, while maximizing positive welfare opportunities for as long as it is reasonable. This also means reflecting about whether the lifespan of laboratory animals is sufficiently long and of sufficient quality that one can say the aggregate is net

positive (for a discussion on welfare and longevity see [6])?

Under this framework, certain types of animal research might be harder to ethically justify, especially under regulatory frameworks that allow long-term unalleviated suffering (which is not the case of European legislation, where it is mostly forbidden). If not followed by a recovery period or meaningful post-use life, such experiments would seldom meet the "life worth living" threshold. On the other hand, studies where animals – no matter how small [7] – can recover fully and then have the potential to enjoy a long, positive, post-use life may better satisfy the utilitarian criterion of maximising net welfare.

I closed my talk by addressing the issue that adopting the "life worth living" criterion does not mean that every use of laboratory animals is ethically defensible from this perspective, though it might be from the classical (animal) harm vs. (mostly human) benefits ethical balance. It offers, however, a stronger moral foundation for those uses that unequivocally are, and which might well be the majority, while shifting the ethical focus from an anthropocentric justification to an ethics of justice towards everyone, including the sentient beings we are using.

References:

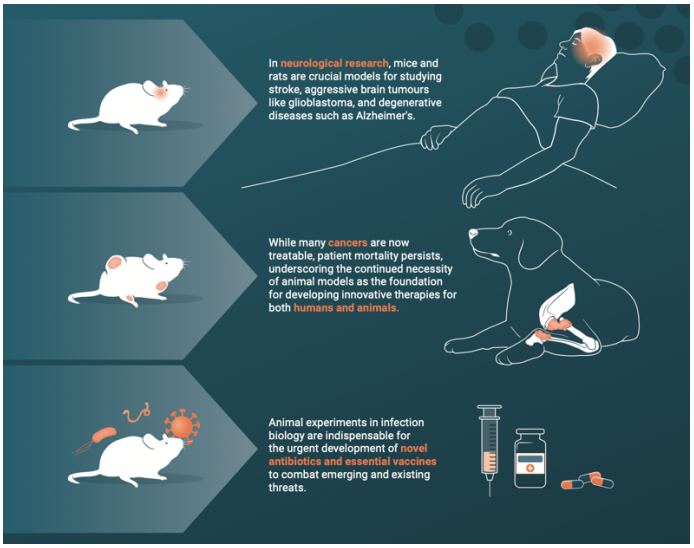
1. *Franco, N.H., P. Sandøe, and I.A.S. Olsson, Researchers' attitudes to the 3Rs—An upturned hierarchy? PLOS ONE, 2018. 13(8): p. e0200895.*
2. *Lund, T.B., J. Lassen, and P. Sandoe, Public attitude formation regarding animal research. Anthrozoos, 2012. 25(4): p. 475-490.*
3. *Grimm, H., et al., The Road to Hell Is Paved with Good Intentions: Why Harm-Benefit Analysis and Its Emphasis on Practical Benefit Jeopardizes the Credibility of Research. Animals (Basel), 2017. 7(9).*
4. *Lewejohann, L., et al., Impulse for animal welfare outside the experiment. Lab Anim, 2020. 54(2): p. 150-158.*
5. *Lilley, E., P. Hawkins, and M. Jennings, A 'Road Map' toward Ending Severe Suffering of Animals Used in Research and Testing. Alternatives to Laboratory Animals, 2014. 42(4): p. 267-272.*
6. *Franco, N.H., M. Magalhães-Sant'Ana, and I.A.S. Olsson, Welfare and quantity of life, in Dilemmas in Animal Welfare, M. Appleby, D. Weary, and P. Sandøe, Editors. 2014, CABI: Oxfordshire. p. 46-66.*
7. *Van Loo, P.L.P. and M.R.E. Janssens, Why All Healthy Laboratory Animals Should Be Rehomed, No Matter How Small. Animals (Basel), 2023. 13(17).*

ART News

New Flyer: Animal experiments with a high degree of severity

Animal experiments with a high degree of severity present a profound ethical dilemma. Despite these ethical challenges, such research is still essential to fight severe diseases in humans and animals. Animal Research Tomorrow has prepared a flyer summarizing the most important facts to support you in explaining this issue an in simple terms. Feel free to download the flyer. Currently it is available in English, more languages will follow soon. Note that you must acknowledge ART and that content cannot be altered or commercialised. If you wish the flyer translated in another language or have any requests concerning its use, please get in touch with ART.

ART is an NGO with a small budget and welcomes financial donations from individuals and institutions by either (1) joining ART as a member or by (2) making a voluntary donation to support the publication of additional flyers on topics relevant to animal research or by contacting ART.

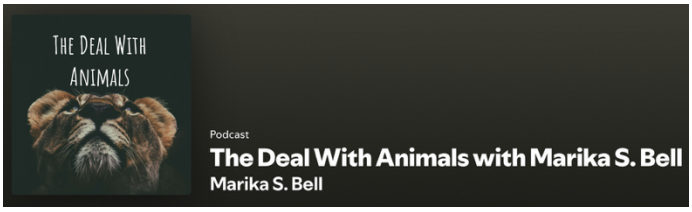


Nuno Franco at the "The Deal with Anumals Podcast" with Marika S. Bell

Words That Shape Perception: Animals in Language

Tune into this episode to explore how our choice of words impacts the lives of animals. We examine the ethical link between language and the treatment of creatures in research and domestic settings, as well as our broader moral outlook.

https://open.spotify.com/episode/7DGKwsusvy7SkVjTEb5Ki7



Facts & Figures about Animal Research Tomorrow

Members of ART

Individual Members: 276
Institutional Members: 17

Signers of the Basel Declaration

Individual Signers: 4775
Institutional Signers: 60

YouTube

Since the end of 2021 we have an Animal Research Tomorrow YouTube channel.

Become a member

We look for your support to show publicly that we are committed to the 3R principles (Replace, Reduce, Refine), i.e., plan and carry out animal testing in your area of expertise with the utmost care, and contribute to providing the public with open and transparent information about animal experiments.

We encourage scientists, veterinarians, animal caretakers and everyone with an interest in supporting the Basel Declaration principles for animal research to become a member of our society:

For individuals
€ 50
LINK

For institutions / organizations
€ 500
LINK

Or you can become a Signer, just sign the Basel Declaration free of charge
LINK

Animal
Research
Tomorrow

IMPRESSUM/CONTACT:

Animal Research Tomorrow
4000 Basel
Switzerland

www.animalresearchtomorrow.org
contact@animalresearchtomorrow.org