

# Laboratory Animals: Honoring the Past and Embracing Responsibility for the Future

# Laboratorijske živali: počastitev preteklosti in sprejemanje odgovornosti za prihodnost

**Key words**

mouse;  
rat;  
animal models

**Maša Čater**

University of Ljubljana, Biotechnical faculty, 1230 Domžale, Slovenia

masa.cater@bf.uni-lj.si

Accepted: 11 December 2025

Rodents, particularly mice and rats, are indispensable to life science research and have enabled major breakthroughs in understanding biology, uncovering disease mechanisms, and developing new therapies. Despite the FDA's recent plans to phase out certain mandatory animal-testing requirements and the European Commission's preparation of a "Roadmap Towards Phasing Out Animal Testing for Chemical Safety Assessments (Communication C(2023)5041)," animal models remain essential for translating basic scientific discoveries into medical advances and for improving both human and animal health. From the earliest physiological experiments that revealed the beating of the heart and the function of the nervous system, to discoveries that led to antibiotics, vaccines, and gene therapies, laboratory animals have been at the foundation of nearly every medical advance. Their contribution deserves deep appreciation and ethical reflection. The use of animals in scientific inquiry is deeply rooted in human history, from Aristotle's early dissections to the controlled experimental work of Pasteur and Lavoisier that shaped modern biomedicine [1]. With the advent of preclinical testing, drug discovery, and genetic engineering, animal models have become indispensable for studying disease mechanisms and evaluating therapeutic safety and efficacy.

Despite the goal of minimizing animal use and eventually phasing it out as soon as scientifically feasible, the

Glodavci, zlasti miši in podgane, so nepogrešljivi v znanstvenih raziskavah in so omogočili ključne preboje pri razumevanju biologije, odkrivanju mehanizmov bolezni ter razvoju novih terapij. Kljub nedavnim načrtom FDA za postopno opuščanje testiranja na živalih ter "Načrta za postopno odpravo testiranja na živalih pri oceni kemijske varnosti (Communication C(2023)5041)" s strani Evropske komisije, živalski modeli ostajajo bistveni za prenos temeljnih znanstvenih odkritij v medicinski napredek ter za izboljšanje zdravja ljudi in živali. Od najzgodnejših fizioloških poskusov, ki so razkrili utripanje srca in delovanje živčnega sistema, do odkritij, ki so vodila do antibiotikov, cepiv in genskih terapij, so laboratorijske živali temelj skoraj vsakega medicinskega napredka. Njihov prispevek si zasluži globoko spoštovanje in etični premislek. Uporaba živali v znanstvenem raziskovanju ima globoke korenine v človeški zgodovini, od Aristotelovih zgodnjih seciranj do nadzorovanih eksperimentalnih del Louisa Pasteurja in Lavoisierja, ki so oblikovala temelje sodobne biomedicine [1]. Z razvojem predkliničnega testiranja, odkrivanja zdravil in gensko-inženirskih pristopov so živalski modeli postali nepogrešljivi za preučevanje mehanizmov bolezni ter ocenjevanje varnosti in učinkovitosti terapij.

Kljub cilju zmanjševanja uporabe živali in njenega postopnega opuščanja, takoj ko bo to znanstveno izvedljivo,

complexity of biological systems cannot yet be fully replicated *in vitro*, emphasizing the value of research animals [1-3]. As Perlman (2016) noted [2], the scientific power of the mouse model arises from its shared biological foundations with humans, yet responsible use requires an understanding of the evolutionary, metabolic, and immunological differences that have emerged between species. Comparative biology has therefore been central to translational research, enabling the identification of conserved molecular and physiological mechanisms that underpin health and disease, while also highlighting where interspecies variation limits direct extrapolation. The success of an animal model depends not on its exact resemblance to humans, but on a deep understanding of where those parallels and divergences lie. Perše (2024) [3] emphasized the importance of accounting for both strain- and species-specific differences. For example, while rodents share fundamental aspects of mammalian neurobiology, metabolism, and immune function, differences in lifespan, circadian regulation, and behavioral complexity must be carefully considered when interpreting data. As Mukherjee et al. (2022) noted, appreciating this continuum of similarity strengthens the predictive power of preclinical research and prevents both overinterpretation and unnecessary repetition of studies [1].

Accordingly, studying animal biology does not only serve human medicine but also advances veterinary knowledge, contributes to conservation and welfare science, and deepens our understanding of life's diversity. By valuing both what unites and what distinguishes species, we uphold a more ethical, precise, and scientifically rigorous approach to animal research.

Traditionally, animal research relied on direct observation and handling to collect data; approaches that are often subjective, time-consuming, and can introduce stress to animals that also alters natural behavior and confounds results. Modern technology, advanced sensors, and computational methods now enable researchers to follow animals continuously and with minimal interference. Similar tools are already improving welfare monitoring in companion animals [4] and production species such as poultry [5], pigs, and cattle [6]. In laboratory animal science, this technological shift has produced an entire generation of systems for automated behavioral and physiological tracking [7]. Among these approaches, home-cage monitoring

(HCM) uniquely captures an animal's spontaneous, undisturbed behavior, important in oncology, neuroscience, and ageing studies, but also enhancing animal welfare [8, 9]. This approach is in line with the ethical and scientific framework of the 3Rs (Replacement, Reduction, and Refinement) introduced by Russell and Burch in 1959 [10]. Replacement encourages the use of alternatives such as organoids and in-silico models; Reduction seeks to obtain more information from fewer animals; and Refinement aims to minimize pain, stress, and discomfort. Further details on HCM are presented in a paper in this volume by Kaura et al. [11]. The authors conclude that integrating automated systems into daily husbandry is

zapletenosti bioloških sistemov še ni mogoče v celoti posnemati *in vitro*, kar poudarja vrednost raziskovalnih živali [1–3]. Kot je zapisal Perlman (2016) [2], znanstvena moč mišjega modela izhaja iz skupnih bioloških temeljev s človekom, vendar odgovorna uporaba zahteva razumevanje evolucijskih, presnovnih in imunoloških razlik, ki so se pojavile med vrstami. Primerjalna biologija je zato osrednja za translacijske raziskave, saj omogoča prepoznavanje ohranjenih molekularnih in fizioloških mehanizmov, ki so podlaga zdravju in bolezni, hkrati pa razkriva, kje medvrstne razlike omejujejo neposredno ekstrapolacijo.

Uspešnost živalskega modela ne temelji na njegovi popolni podobnosti človeku, temveč na poglobljenem razumevanju, kje potekajo vzporednice in kje razhajanja. Perše (2024) [3] je poudarila, da je pri uporabi živalskih modelov ključno upoštevati tako razlike med posameznimi sevi kot tudi med vrstami. Čeprav glodavci z ljudmi delijo številne osnovne značilnosti nevrobiologije, metabolizma in imunskega sistema, se razlikujejo v življenjski dobi, cirkadianih ritmih in vedenjski kompleksnosti; dejavniki, ki jih moramo pri interpretaciji rezultatov nujno vključiti. Kot navaja Mukherjee s sod. (2022), razumevanje tega kontinuuma podobnosti krepi napovedno moč predkliničnih raziskav ter preprečuje tako pretirano interpretacijo kot tudi nepotrebno ponavljanje študij [1].

V skladu s tem preučevanje biologije živali ne služi zgolj humani medicini, temveč tudi rezultira v napredujočem veterinarskem znanju, prispeva k varstvu narave in znanosti o dobrobiti ter pogloblja naše razumevanje raznolikosti življenja. S tem, ko cenimo tako tisto, kar vrste povezuje, kot tisto, kar jih razlikuje, ohranjamo bolj etičen, natančen in znanstveno strog pristop k raziskavam na živalih.

Tradicionalno so se raziskave na živalih zanašale na neposredno opazovanje in rokovanje za zbiranje podatkov. Gre za pristopa, ki sta pogosto subjektivna, zamudna in lahko povzročata stres živalim, kar spremeni njihovo naravno vedenje ter popači rezultate. Sodobna tehnologija, napredni senzori in računske metode pa danes omogočajo raziskovalcem, da živali spremljajo neprekinjeno in z minimalnim posegom. Podobna orodja se že uporabljajo za spremljanje dobrobiti pri domačih živalih [4] ter pri rejnih živalih, kot so perutnina [5], prašiči in govedo [6]. V znanosti o laboratorijskih živalih je ta tehnološki premik prinesel celotno generacijo sistemov za avtomatizirano spremljanje vedenjskih in fizioloških parametrov [7]. Med temi pristopi je spremljanje v domači kletki (angl. home cage monitoring; HCM) edinstveno, saj zajema spontano, nemoteno vedenje živali, kar je pomembno v onkologiji, nevroznanosti in raziskavah staranja, hkrati pa izboljšuje dobrobit živali [8, 9].

Ta pristop je v skladu z etičnim in znanstvenim okvirom načel 3R (zamenjava, zmanjšanje in izboljšanje), ki sta ga Russell in Burch predstavila leta 1959 [10]. Zamenjava

not merely a technical improvement but a meaningful advancement in animal welfare - and, consequently, in the quality of the science itself. Veterinarians hold a central role in this transformation. As experts in animal health, anesthesia, and welfare assessment, they ensure humane treatment and scientific validity throughout experimental processes. Their insight bridges research and ethics, from experimental design and refinement of procedures to postoperative care and welfare monitoring. Moreover, their understanding of interspecies similarities and differences allows the responsible translation of animal findings to human and veterinary medicine.

The concept of welfare has evolved beyond preventing harm to promoting positive affective states, as described by the Five Domains Model [12]. Achieving this requires moving from minimal, standardized housing toward complex, species-appropriate environments and continuous welfare assessment enabled by digital technologies. By combining veterinary expertise, behavioral science, and data-driven approaches, the field can move toward a paradigm where welfare and scientific quality are mutually reinforcing rather than competing priorities.

Researchers are actively seeking reliable and effective alternative methods, including organ-on-a-chip systems, artificial intelligence for large-scale data analysis, and 3D bioprinted tissues.

However, replacements do not yet exist for all organs, and further advances are needed to accurately replicate how organs function in coordination. This underscores the ongoing importance of humane animal research, emphasizing continuous improvements in welfare whenever alternatives are unavailable. The future of laboratory animal science lies in data-driven refinement combined with compassionate innovation. By appreciating the historic role of animals in scientific discovery and embracing technologies that respect their biology and wellbeing, researchers and veterinarians can ensure that animal research remains ethically sound, reproducible, and societally accepted. Looking ahead, our guiding principle is to honor the contributions of laboratory animals by minimizing their burden, maximizing the knowledge gained from each life, and empowering veterinarians and researchers to pursue excellence guided by empathy.

spodbuja uporabo alternativ, kot so organoidi in in silico modeli; zmanjšanje si prizadeva pridobiti več informacij z manj živalmi; izboljšanje pa stremi k zmanjšanju bolečine, stresa in neugodja. Nadaljnje podrobnosti o HCM so predstavljene v članku v tej številki, ki so ga pripravili Kaura s sodelavci [11]. V njem avtorji poudarjajo, da vključevanje avtomatiziranih sistemov v vsakodnevno oskrbo živali ni zgolj tehnična nadgradnja, temveč pomemben napredek na področju dobrobiti in posledično tudi kakovosti same znanosti. Veterinarji imajo v tej transformaciji osrednjo vlogo. Kot strokovnjaki za zdravje živali, anestezijo in oceno dobrobiti zagotavljajo humano ravnanje in znanstveno veljavnost skozi celoten eksperimentalni proces. Njihov vpogled povezuje raziskave in etiko, vse od zasnove poskusov ter izboljšanja postopkov do pooperativne oskrbe in spremljanja dobrobiti. Poleg tega jim razumevanje podobnosti in razlik med vrstami omogoča odgovorno translacijo ugotovitev iz raziskav na živalih v medicinsko in veterinarsko prakso.

Koncept dobrobiti se je razvil onkraj preprečevanja škode in vključuje spodbujanje pozitivnih afektivnih stanj, kot jih opisuje model petih domen [12]. Doseganje tega zahteva premik od minimalnih, standardiziranih bivalnih pogojev h kompleksnim, vrstno primernim okoljem ter neprekinjenemu spremljanju dobrobiti, ki ga omogočajo digitalne tehnologije. S povezovanjem veterinarske strokovnosti, vedenjskih znanosti in pristopov, temelječih na podatkih, se lahko področje premakne k paradigmi, v kateri sta dobrobit in znanstvena kakovost medsebojno podpirajoči.

Raziskovalci aktivno iščejo zanesljive in učinkovite alternativne metode, vključno s sistemi

»organ-on-a-chip«, umetno inteligenco za obsežno analizo podatkov ter 3D biotiskom tkiv. Vendar zamenjave še ne obstajajo za vse organe. Potrebne so tudi nadaljnje raziskave, da bomo znali natančno posnemati koordinirano delovanje organov. To poudarja stalni pomen humanega raziskovanja na živalih in potrebo po nenehnem izboljševanju dobrobiti, kadar alternative niso na voljo. Prihodnost znanosti o laboratorijskih živalih tako temelji na izboljšavah, ki temeljijo na podatkih, združenih z etičnim in inovativnim pristopom. S spoštovanjem zgodovinske vloge živali pri znanstvenih odkritjih in z uporabo tehnologij, ki upoštevajo njihovo biologijo in dobrobit, lahko raziskovalci in veterinarji zagotovijo, da raziskave na živalih ostanejo etične, znanstveno ponovljive in družbeno sprejete. Naše vodilo v prihodnje je torej počastiti prispevek laboratorijskih živali, zmanjševati njihovo obremenitev, maksimirati pridobljeno znanje iz vsakega življenja in opolnomočiti veterinarje in raziskovalce, da stremijo k odličnosti, vodeni z empatijo.

## References

---

1. Mukherjee P, Roy S, Ghosh D, Nandi S. Role of animal models in biomedical research: a review. *Lab Anim Res* 2022 ;38(1): 18. doi: 10.1186/s42826-022-00128-1
2. Perlman RL. Mouse models of human disease: an evolutionary perspective. *Evol Med Public Health* 2016; 2016(1): 170- 6. doi: 10.1093/emph/eow014
3. Perše M. Animal models of human pathology: revision, relevance and refinements. *Biomedicines* 2024; 12(11): 2418. doi: 10.3390/biomedicines12112418
4. Anderson N. Animal welfare and the human-animal bond in student education—how can we understand animal feelings? How do we ask for consent from a horse? *Slov Vet Res* 2025; 62(1): 5–7. doi: 10.26873/SVR-2194-2025
5. Rojs OZ, Dovč A, Hristov H, et al. Welfare assessment of commercial layers in Slovenia. *Slov Vet Res* 2020; 57(3): 133–43. doi: 10.26873/SVR-971-2020
6. Chapa JM, Maschat K, Iwersen M, Baumgartner J, Drillich M. Accelerometer systems as tools for health and welfare assessment in cattle and pigs—a review. *Behav Processes* 2020; 181: 104262. doi: 10.1016/j.beproc.2020.104262
7. Voikar V, Gaburro S. Three pillars of automated home- cage phenotyping of mice: novel findings, refinement, and reproducibility based on literature and experience. *Front Behav Neurosci* 2020; 14: 575434. doi: 10.3389/fnbeh.2020.575434
8. Terry S, Gomet C, Kerangueven A- C, et al. Activity in group-housed home cages of mice as a novel preclinical biomarker in oncology studies. *Cancers* 2023; 15(19): 4798. doi: 10.3390/cancers15194798
9. Moore JL, Kennedy J, Hassan A-A. Automated home cage monitoring of an aging colony of mice—Implications for welfare monitoring and experimentation. *Front Neurosci* 2024;18:1489308. doi: 10.3389/fnins.2024.1489308
10. Russell WMS, Burch RL. *The principles of humane experimental technique*. London: Methuen, 1959.
11. Kaura R, Hrncić D, Der vi šević A, Borbeljova V, Cevik OS, Hef fer M, et al . Smart Cages, Better Welfare: Supporting the 3Rs in Animal Research With Home-cage Monitoring and System Selection. *Slov Vet Res* 2025, 62(4): 249–58. doi: 10.26873/SVR-2247-2025
- 12 . Mellor DJ, Beausoleil NJ, Littlewood KE, McLean AN, McGreevy PD, Jones B, et al. The 2020 five domains model: Including human– animal interactions in assessments of animal welfare. *Animals (Basel)* 2020; 10(10):1870. doi: 10.3390/ani10101870