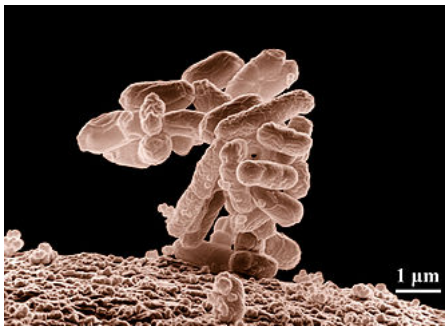
Model organism

A **model organism** (often shortened to **model**) is a non-human species that is extensively studied to understand particular biological phenomena, with the expectation that discoveries made in the model organism will provide insight into the workings of other organisms.[1][2] Model organisms are widely used to research human disease when human experimentation would be unfeasible or unethical.[3] This strategy is made possible by the common descent of all living organisms, and the conservation of metabolic and developmental pathways and genetic material over the course of evolution.[4]

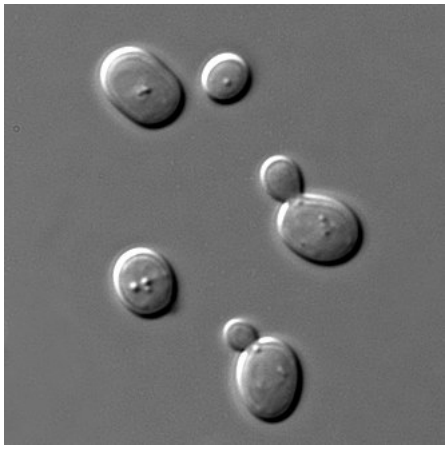
Studying model organisms can be informative, but care must be taken when generalizing from one organism to another.[5]

In researching human disease, model organisms allow for better understanding the disease process without the added risk of harming an actual human. The species chosen will usually meet a determined taxonomic equivalency to humans, so as to react to disease or its treatment in a way that resembles human physiology as needed. Although biological activity in a model organism does not ensure an effect in humans, many drugs, treatments and cures for human diseases are developed in part with the guidance of animal models.[6][7] There are three main types of disease models: homologous, isomorphic and predictive. Homologous animals have the same causes, symptoms and treatment options as would humans who have the same disease. Isomorphic animals share the same symptoms and treatments. Predictive models are similar to a particular human disease in only a couple of aspects, but are useful in isolating and making predictions about mechanisms of a set of disease features.[8]



Escherichia coli is a gram-negative prokaryotic model organism

Drosophila melanogaster, one of the most famous subjects for genetics experiments



Saccharomyces cerevisiae, one of the most intensively studied eukaryotic model organisms in molecular and cell biology

Contents

- History
- Selection
  - Phylogeny and genetic relatedness
- Use
- Disease models
- Important model organisms
  - Selected model organisms
- Limitations
  - Unintended bias
  - Alternatives
- Ethics
- See also

References
Further reading
External links

History

The use of animals in research dates back to ancient Greece, with Aristotle (384–322 BCE) and Erasistratus (304–258 BCE) among the first to perform experiments on living animals.[9] Discoveries in the 18th and 19th centuries included Antoine Lavoisier's use of a guinea pig in a calorimeter to prove that respiration was a form of combustion, and Louis Pasteur's demonstration of the germ theory of disease in the 1880s using anthrax in sheep.

Research using animal models has been central to many of the achievements of modern medicine.[10][11][12] It has contributed most of the basic knowledge in fields such as human physiology and biochemistry, and has played significant roles in fields such as neuroscience and infectious disease.[13][14] For example, the results have included the near-eradication of polio and the development of organ transplantation, and have benefited both humans and animals.[10][15] From 1910 to 1927, Thomas Hunt Morgan's work with the fruit fly *Drosophila melanogaster* identified chromosomes as the vector of inheritance for genes.[16][17] *Drosophila* became one of the first, and for some time the most widely used, model organisms,[18] and Eric Kandel wrote that Morgan's discoveries "helped transform biology into an experimental science."[19] *D. melanogaster* remains one of the most widely used eukaryotic model organisms. During the same time period, studies on mouse genetics in the laboratory of William Ernest Castle in collaboration with Abbie Lathrop led to generation of the DBA ("dilute, brown and non-agouti") inbred mouse strain and the systematic generation of other inbred strains.[20][21] The mouse has since been used extensively as a model organism and is associated with many important biological discoveries of the 20th and 21st centuries.[22]

In the late 19th century, Emil von Behring isolated the diphtheria toxin and demonstrated its effects in guinea pigs. He went on to develop an antitoxin against diphtheria in animals and then in humans, which resulted in the modern methods of immunization and largely ended diphtheria as a threatening disease.[23] The diphtheria antitoxin is famously commemorated in the Iditarod race, which is modeled after the delivery of antitoxin in the 1925 serum run to Nome. The success of animal studies in producing the diphtheria antitoxin has also been attributed as a cause for the decline of the early 20th-century opposition to animal research in the United States.[24]

Subsequent research in model organisms led to further medical advances, such as Frederick Banting's research in dogs, which determined that the isolates of pancreatic secretion could be used to treat dogs with diabetes. This led to the 1922 discovery of insulin (with John Macleod)[25] and its use in treating diabetes, which had previously meant death.[26] John Cade's research in guinea pigs discovered the anticonvulsant properties of lithium salts,[27] which revolutionized the treatment of bipolar disorder, replacing the previous treatments of lobotomy or electroconvulsive therapy. Modern general anaesthetics, such as halothane and related compounds, were also developed through studies on model organisms, and are necessary for modern, complex surgical operations.[28][29]

In the 1940s, Jonas Salk used rhesus monkey studies to isolate the most virulent forms of the polio virus,[30] which led to his creation of a polio vaccine. The vaccine, which was made publicly available in 1955, reduced the incidence of polio 15-fold in the United States over the following five years.[31] Albert Sabin improved the vaccine by passing the polio virus through animal hosts, including monkeys; the Sabin vaccine was produced for mass consumption in 1963, and had virtually eradicated polio in the United States by 1965.[32] It has been estimated that developing and producing the vaccines required the use of 100,000 rhesus monkeys, with 65 doses of vaccine

produced from each monkey. Sabin wrote in 1992, "Without the use of animals and human beings, it would have been impossible to acquire the important knowledge needed to prevent much suffering and premature death not only among humans, but also among animals."[33]

Other 20th-century medical advances and treatments that relied on research performed in animals include organ transplant techniques,[34][35][36][37] the heart-lung machine,[38] antibiotics,[39][40][41] and the whooping cough vaccine.[42] Treatments for animal diseases have also been developed, including for rabies,[43] anthrax,[43] glanders,[43] feline immunodeficiency virus (FIV),[44] tuberculosis,[43] Texas cattle fever,[43] classical swine fever (hog cholera),[43] heartworm, and other parasitic infections.[45] Animal experimentation continues to be required for biomedical research,[46] and is used with the aim of solving medical problems such as Alzheimer's disease,[47] AIDS,[48][49][50] multiple sclerosis,[51] spinal cord injury, many headaches,[52] and other conditions in which there is no useful *in vitro* model system available.

Selection

Models are those organisms with a wealth of biological data that make them attractive to study as examples for other species and/or natural phenomena that are more difficult to study directly. Continual research on these organisms focuses on a wide variety of experimental techniques and goals from many different levels of biology—from ecology, behavior and biomechanics, down to the tiny functional scale of individual tissues, organelles and proteins. Inquiries about the DNA of organisms are classed as genetic models (with short generation times, such as the fruitfly and nematode worm), experimental models, and genomic parsimony models, investigating pivotal position in the evolutionary tree.[53] Historically, model organisms include a handful of species with extensive genomic research data, such as the NIH model organisms.[54]

Often, model organisms are chosen on the basis that they are amenable to experimental manipulation. This usually will include characteristics such as short life-cycle, techniques for genetic manipulation (inbred strains, stem cell lines, and methods of transformation) and non-specialist living requirements. Sometimes, the genome arrangement facilitates the sequencing of the model organism's genome, for example, by being very compact or having a low proportion of junk DNA (e.g. yeast, arabidopsis, or pufferfish).

When researchers look for an organism to use in their studies, they look for several traits. Among these are size, generation time, accessibility, manipulation, genetics, conservation of mechanisms, and potential economic benefit. As comparative molecular biology has become more common, some researchers have sought model organisms from a wider assortment of lineages on the tree of life.

Phylogeny and genetic relatedness

The primary reason for the use of model organisms in research is the evolutionary principle that all organisms share some degree of relatedness and genetic similarity due to common ancestry. The study of taxonomic human relatives, then, can provide a great deal of information about mechanism and disease within the human body that can be useful in medicine.

Various phylogenetic trees for vertebrates have been constructed using comparative proteomics, genetics, genomics as well as the geochemical and fossil record.[55] These estimations tell us that humans and chimpanzees last shared a common ancestor about 6 million years ago (mya). As our closest relatives, chimpanzees have a lot of potential to tell us about mechanisms of disease (and what genes may be responsible for human intelligence). However, chimpanzees are rarely used in research and are protected from highly invasive procedures. Rodents are the most common animal models. Phylogenetic trees estimate that humans and rodents last shared a common ancestor ~80-

100mya.[56][57] Despite this distant split, humans and rodents have far more similarities than they do differences. This is due to the relative stability of large portions of the genome, making the use of vertebrate animals particularly productive.

Genomic data is used to make close comparisons between species and determine relatedness. As humans, we share about 99% of our genome with chimpanzees[58][59] (98.7% with bonobos)[60] and over 90% with the mouse.[57] With so much of the genome conserved across species, it is relatively impressive that the differences between humans and mice can be accounted for in approximately six thousand genes (of ~30,000 total). Scientists have been able to take advantage of these similarities in generating experimental and predictive models of human disease.

Use

There are many model organisms. One of the first model systems for molecular biology was the bacterium *Escherichia coli*, a common constituent of the human digestive system. Several of the bacterial viruses (bacteriophage) that infect *E. coli* also have been very useful for the study of gene structure and gene regulation (e.g. phages Lambda and T4). However, it is debated whether bacteriophages should be classified as organisms, because they lack metabolism and depend on functions of the host cells for propagation.[61]

In eukaryotes, several yeasts, particularly *Saccharomyces cerevisiae* ("baker's" or "budding" yeast), have been widely used in genetics and cell biology, largely because they are quick and easy to grow. The cell cycle in a simple yeast is very similar to the cell cycle in humans and is regulated by homologous proteins. The fruit fly *Drosophila melanogaster* is studied, again, because it is easy to grow for an animal, has various visible congenital traits and has a polytene (giant) chromosome in its salivary glands that can be examined under a light microscope. The roundworm *Caenorhabditis elegans* is studied because it has very defined development patterns involving fixed numbers of cells, and it can be rapidly assayed for abnormalities.

Disease models

Animal models serving in research may have an existing, inbred or induced disease or injury that is similar to a human condition. These test conditions are often termed as **animal models of disease**. The use of animal models allows researchers to investigate disease states in ways which would be inaccessible in a human patient, performing procedures on the non-human animal that imply a level of harm that would not be considered ethical to inflict on a human.

The best models of disease are similar in etiology (mechanism of cause) and phenotype (signs and symptoms) to the human equivalent. However complex human diseases can often be better understood in a simplified system in which individual parts of the disease process are isolated and examined. For instance, behavioral analogues of anxiety or pain in laboratory animals can be used to screen and test new drugs for the treatment of these conditions in humans. A 2000 study found that animal models concorded (coincided on true positives and false negatives) with human toxicity in 71% of cases, with 63% for nonrodents alone and 43% for rodents alone.[62]

In 1987, Davidson et al. suggested that selection of an animal model for research be based on nine considerations. These include "1) appropriateness as an analog, 2) transferability of information, 3) genetic uniformity of organisms, where applicable, 4) background knowledge of biological properties, 5) cost and availability, 6) generalizability of the results, 7) ease of and adaptability to experimental manipulation, 8) ecological consequences, and 9) ethical implications."[63]

Animal models can be classified as homologous, isomorphic or predictive. Animal models can also be more broadly classified into four categories: 1) experimental, 2) spontaneous, 3) negative, 4) orphan.[64]

Experimental models are most common. These refer to models of disease that resemble human conditions in phenotype or response to treatment but are induced artificially in the laboratory. Some examples include:

- The use of metrazol (pentylenetetrazol) as an animal model of epilepsy[65]
- Induction of mechanical brain injury as an animal model of post-traumatic epilepsy[66]
- Injection of the neurotoxin 6-hydroxydopamine to dopaminergic parts of the basal ganglia as an animal model of Parkinson's disease.[67]
- Immunisation with an auto-antigen to induce an immune response to model autoimmune diseases such as Experimental autoimmune encephalomyelitis[68]
- Occlusion of the middle cerebral artery as an animal model of ischemic stroke[69]
- Injection of blood in the basal ganglia of mice as a model for hemorrhagic stroke[70][71]
- Sepsis and septic shock induction by impairing the integrity of barrier tissues, administering live pathogens or toxins[72]
- Infecting animals with pathogens to reproduce human infectious diseases
- Injecting animals with agonists or antagonists of various neurotransmitters to reproduce human mental disorders
- Using ionizing radiation to cause tumors
- Using gene transfer to cause tumors[73][74]
- Implanting animals with tumors to test and develop treatments using ionizing radiation
- Genetically selected (such as in diabetic mice also known as NOD mice)[75]
- Various animal models for screening of drugs for the treatment of glaucoma
- The use of the ovariectomized rat in osteoporosis research
- Use of *Plasmodium yoelii* as a model of human malaria[76][77][78]

Spontaneous models refer to diseases that are analogous to human conditions that occur naturally in the animal being studied. These models are rare, but informative. Negative models essentially refer to control animals, which are useful for validating an experimental result. Orphan models refer to diseases for which there is no human analog and occur exclusively in the species studied.[64]

The increase in knowledge of the genomes of non-human primates and other mammals that are genetically close to humans is allowing the production of genetically engineered animal tissues, organs and even animal species which express human diseases, providing a more robust model of human diseases in an animal model.

Animal models observed in the sciences of psychology and sociology are often termed **animal models of behavior**. It is difficult to build an animal model that perfectly reproduces the symptoms of depression in patients. Depression, as other mental disorders, consists of endophenotypes[79] that can be reproduced independently and evaluated in animals. An ideal animal model offers an opportunity to understand molecular, genetic and epigenetic factors that may lead to depression. By using animal models, the underlying molecular alterations and the causal relationship between genetic or environmental alterations and depression can be examined, which would afford a better insight into pathology of depression. In addition, animal models of depression are indispensable for identifying novel therapies for depression.[80][81]

Important model organisms

Model organisms are drawn from all three domains of life, as well as viruses. The most widely studied prokaryotic model organism is *Escherichia coli* (*E. coli*), which has been intensively investigated for over 60 years. It is a common, gram-negative gut bacterium which can be grown and cultured easily

and inexpensively in a laboratory setting. It is the most widely used organism in molecular genetics, and is an important species in the fields of biotechnology and microbiology, where it has served as the host organism for the majority of work with recombinant DNA.[82]

Simple model eukaryotes include baker's yeast (*Saccharomyces cerevisiae*) and fission yeast (*Schizosaccharomyces pombe*), both of which share many characters with higher cells, including those of humans. For instance, many cell division genes that are critical for the development of cancer have been discovered in yeast. *Chlamydomonas reinhardtii*, a unicellular green alga with well-studied genetics, is used to study photosynthesis and motility. *C. reinhardtii* has many known and mapped mutants and expressed sequence tags, and there are advanced methods for genetic transformation and selection of genes.[83] *Dictyostelium discoideum* is used in molecular biology and genetics, and is studied as an example of cell communication, differentiation, and programmed cell death.

Among invertebrates, the fruit fly *Drosophila melanogaster* is famous as the subject of genetics experiments by Thomas Hunt Morgan and others. They are easily raised in the lab, with rapid generations, high fecundity, few chromosomes, and easily induced observable mutations.[84] The nematode *Caenorhabditis elegans* is used for understanding the genetic control of development and physiology. It was first proposed as a model for neuronal development by Sydney Brenner in 1963, and has been extensively used in many different contexts since then.[85][86] *C. elegans* was the first multicellular organism whose genome was completely sequenced, and as of 2012, the only organism to have its connectome (neuronal "wiring diagram") completed.[87][88]

Laboratory mice, widely used in medical research

Arabidopsis thaliana is currently the most popular model plant. Its small stature and short generation time facilitates rapid genetic studies,[89] and many phenotypic and biochemical mutants have been mapped.[89] *A. thaliana* was the first plant to have its genome sequenced.[89]

Among vertebrates, guinea pigs (*Cavia porcellus*) were used by Robert Koch and other early bacteriologists as a host for bacterial infections, becoming a byword for "laboratory animal," but are less commonly used today. The classic model vertebrate is currently the mouse (*Mus musculus*). Many inbred strains exist, as well as lines selected for particular traits, often of medical interest, e.g. body size, obesity, muscularity, and voluntary wheel-running behavior.[90] The rat (*Rattus norvegicus*) is particularly useful as a toxicology model, and as a neurological model and source of primary cell cultures, owing to the larger size of organs and suborganellar structures relative to the mouse, while eggs and embryos from *Xenopus tropicalis* and *Xenopus laevis* (African clawed frog) are used in developmental biology, cell biology, toxicology, and neuroscience.[91][92] Likewise, the zebrafish (*Danio rerio*) has a nearly transparent body during early development, which provides unique visual access to the animal's internal anatomy during this time period. Zebrafish are used to study development, toxicology and toxicopathology,[93] specific gene function and roles of signaling pathways.

Other important model organisms and some of their uses include: T4 phage (viral infection), *Tetrahymena thermophila* (intracellular processes), maize (transposons), *hydras* (regeneration and morphogenesis),[94] cats (neurophysiology), chickens (development), dogs (respiratory and cardiovascular systems), *Nothobranchius furzeri* (aging),[95] and non-human primates such as the rhesus macaque and chimpanzee (hepatitis, HIV, Parkinson's disease, cognition, and vaccines).

Selected model organisms

The organisms below have become model organisms because they facilitate the study of certain characters or because of their genetic accessibility. For example, *E. coli* was one of the first organisms for which genetic techniques such as transformation or genetic manipulation has been developed.

The genomes of all model species have been sequenced, including their mitochondrial/chloroplast genomes. Model organism databases exist to provide researchers with a portal from which to download sequences (DNA, RNA, or protein) or to access functional information on specific genes, for example the sub-cellular localization of the gene product or its physiological role.

	Model Organism	Common name	Informal classification	Usage (examples)
Virus	Phi X 174	ΦX174	Virus	evolution[96]
Prokaryote	*Escherichia coli*	E. Coli	Bacteria	bacterial genetics, metabolism
Eukaryote, unicellular	*Dictyostelium discoideum*		Amoeba	immunology, host–pathogen interactions[97]
	Saccharomyces cerevisiae	Brewer's yeast Baker's yeast	Yeast	cell division, organelles, etc.
	Schizosaccharomyces pombe	Fission yeast	Yeast	cell cycle, cytokinesis, chromosome biology, telomeres, DNA metabolism, cytoskeleton organization, industrial applications[98][99]
	Chlamydomonas reinhardtii		Algae	hydrogen production[100]
	Tetrahymena thermophila, *T. pyriformis*		Ciliate	education,[101] biomedical research[102]
	Emiliania huxleyi		Plankton	surface sea temperature[103]
Plant	*Arabidopsis thaliana*	Thale cress	Flowering plant	population genetics[104]
	Physcomitrella patens	Spreading earthmoss	Moss	molecular farming[105]
	Populus trichocarpa	Balsam popular	Tree	drought tolerance, lignin biosynthesis, wood formation, plant biology, morphology, genetics, and ecology[106]
Animal, nonvertebrate	*Caenorhabditis elegans*	Nematode, Roundworm	Worm	differentiation, development
	Drosophila melanogaster	Fruit fly	Insect	developmental biology, human brain degenerative disease[107][108]
	Callosobruchus maculatus	Cowpea Weevil	Insect	developmental biology
Animal, vertebrate	*Danio rerio*	Zebrafish	Fish	embryonic development
	Fundulus heteroclitus	Mummichog	Fish	effect of hormones on behavior[109]
	Nothobranchius furzeri	Turquoise killifish	Fish	aging, disease, evolution
	Oryzias latipes	Japanese rice fish	Fish	fish biology, sex determination[110]
	Anolis carolinensis	Carolina anole	Reptile	reptile biology, evolution
	Mus musculus	House mouse	Mammal	disease model for humans
	Gallus gallus	Red junglefowl	Bird	embryological development and organogenesis
	Taeniopygia guttata	Zebra finch	Bird	vocal learning, neurobiology[111]
	Xenopus laevis *Xenopus tropicalis*[112]	African clawed frog Western clawed frog	Amphibian	embryonic development

Limitations

Many animal models serving as test subjects in biomedical research, such as rats and mice, may be selectively sedentary, obese and glucose intolerant. This may confound their use to model human metabolic processes and diseases as these can be affected by dietary energy intake and exercise.[113] Similarly, there are differences between the immune systems of model organisms and humans that lead to significantly altered responses to stimuli,[114][115][116] although the underlying principles of genome function may be the same.[116] The impoverished environments inside standard laboratory cages deny research animals of the mental and physical challenges are necessary for healthy emotional development.[117] Without day-to-day variety, risks and rewards, and complex environments, some have argued that animal models are irrelevant models of human experience.[118]

Mice differ from humans in several immune properties: mice are more resistant to some toxins than humans; have a lower total neutrophil fraction in the blood, a lower neutrophil enzymatic capacity, lower activity of the complement system, and a different set of pentraxins involved in the inflammatory process; and lack genes for important components of the immune system, such as IL-8, IL-37, TLR10, ICAM-3, etc.[119] Laboratory mice reared in specific-pathogen-free (SPF) conditions usually have a rather immature immune system with a deficit of memory T cells. These mice may have limited diversity of the microbiota, which directly affects the immune system and the development of pathological conditions. Moreover, persistent virus infections (for example, herpesviruses) are activated in humans, but not in SPF mice, with septic complications and may change the resistance to bacterial coinfections. “Dirty” mice are possibly better suitable for mimicking human pathologies. In addition, inbred mouse strains are used in the overwhelming majority of studies, while the human population is heterogeneous, pointing to the importance of studies in interstrain hybrid, outbred, and nonlinear mice.[120]

Unintended bias

Some studies suggests that inadequate published data in animal testing may result in irreproducible research, with missing details about how experiments are done omitted from published papers or differences in testing that may introduce bias. Examples of hidden bias include a 2014 study from McGill University in Montreal, Canada which suggests that mice handled by men rather than women showed higher stress levels.[121][122][123] Another study in 2016 suggested that gut microbiomes in mice may have an impact upon scientific research.[124]

Alternatives

Ethical concerns, as well as the cost, maintenance and relative inefficiency of animal research has encouraged development of alternative methods for the study of disease. Cell culture, or *in vitro* studies, provide an alternative that preserves the physiology of the living cell, but does not require the sacrifice of an animal for mechanistic studies. Human, inducible pluripotent stem cells can also elucidate new mechanisms for understanding cancer and cell regeneration. Imaging studies (such as MRI or PET scans) enable non-invasive study of human subjects. Recent advances in genetics and genomics can identify disease-associated genes, which can be targeted for therapies.

Many biomedical researchers argue that there is no substitute for a living organism when studying complex interactions in disease pathology or treatments.[125][126]

Ethics

Debate about the ethical use of animals in research dates at least as far back as 1822 when the British Parliament under pressure from British and Indian intellectuals enacted the first law for animal protection preventing cruelty to cattle.[127] This was followed by the Cruelty to Animals Act of 1835 and 1849, which criminalized ill-treating, over-driving, and torturing animals. In 1876, under pressure from the National Anti-Vivisection Society, the Cruelty to Animals Act was amended to include regulations governing the use of animals in research. This new act stipulated that 1) experiments must be proven absolutely necessary for instruction, or to save or prolong human life; 2) animals must be properly anesthetized; and 3) animals must be killed as soon as the experiment is over. Today, these three principles are central to the laws and guidelines governing the use of animals and research. In the U.S., the Animal Welfare Act of 1970 (see also Laboratory Animal Welfare Act) set standards for animal use and care in research. This law is enforced by APHIS's Animal Care program.[128]

In academic settings in which NIH funding is used for animal research, institutions are governed by the NIH Office of Laboratory Animal Welfare (OLAW). At each site, OLAW guidelines and standards are upheld by a local review board called the Institutional Animal Care and Use Committee (IACUC). All laboratory experiments involving living animals are reviewed and approved by this committee. In addition to proving the potential for benefit to human health, minimization of pain and distress, and timely and humane euthanasia, experimenters must justify their protocols based on the principles of Replacement, Reduction and Refinement.[129]

"Replacement" refers to efforts to engage alternatives to animal use. This includes the use of computer models, non-living tissues and cells, and replacement of “higher-order” animals (primates and mammals) with “lower” order animals (e.g. cold-blooded animals, invertebrates, bacteria) wherever possible.[130]

"Reduction" refers to efforts to minimize number of animals used during the course of an experiment, as well as prevention of unnecessary replication of previous experiments. To satisfy this requirement, mathematical calculations of statistical power are employed to determine the minimum number of animals that can be used to get a statistically significant experimental result.

"Refinement" refers to efforts to make experimental design as painless and efficient as possible in order to minimize the suffering of each animal subject.

See also

- Animals in space
- Animal testing
- Animal testing on invertebrates
- Animal testing on rodents
- Cellular model (numerical), e.g., *Mycoplasma genitalium*.
- Ensembl genome database of model organisms
- Generic Model Organism Database
- Genome project
- History of animal testing
- History of model organisms
- Mouse models of breast cancer metastasis
- Mouse models of colorectal and intestinal cancer
- RefSeq - the Reference Sequence database

References

1. Fields, S.; Johnston, M (2005-03-25). "CELL BIOLOGY: Whither Model Organism Research?".

Science. **307** (5717): 1885–1886. doi:10.1126/science.1108872 (https://doi.org/10.1126%2Fscience.1108872). PMID 15790833 (https://pubmed.ncbi.nlm.nih.gov/15790833). S2CID 82519062 (https://api.semanticscholar.org/CorpusID:82519062).

2. Griffiths, E. C. (2010) What is a model? (http://www.emily-griffiths.postgrad.shef.ac.uk/models.pdf) Archived (https://web.archive.org/web/20120312220527/http://www.emily-griffiths.postgrad.shef.ac.uk/models.pdf) March 12, 2012, at the Wayback Machine
3. Fox, Michael Allen (1986). *The Case for Animal Experimention: An Evolutionary and Ethical Perspective* (https://books.google.com/books?id=yTfNH3cScKAC). Berkeley and Los Angeles, California: University of California Press. ISBN 978-0-520-05501-8. OCLC 11754940 (https://www.worldcat.org/oclc/11754940) – via Google Books.
4. Allmon, Warren D.; Ross, Robert M. (December 2018). "Evolutionary remnants as widely accessible evidence for evolution: the structure of the argument for application to evolution education" (https://doi.org/10.1186%2Fs12052-017-0075-1). *Evolution: Education and Outreach*. **11** (1): 1. doi:10.1186/s12052-017-0075-1 (https://doi.org/10.1186%2Fs12052-017-0075-1). S2CID 29281160 (https://api.semanticscholar.org/CorpusID:29281160).
5. Slack, Jonathan M. W. (2013). *Essential Developmental Biology*. Oxford: Wiley-Blackwell. OCLC 785558800 (https://www.worldcat.org/oclc/785558800).
6. Chakraborty, Chiranjib; Hsu, Chi; Wen, Zhi; Lin, Chang; Agoramoorthy, Govindasamy (2009-02-01). "Zebrafish: A Complete Animal Model for In Vivo Drug Discovery and Development". *Current Drug Metabolism*. **10** (2): 116–124. doi:10.2174/138920009787522197 (https://doi.org/10.2174%2F138920009787522197). PMID 19275547 (https://pubmed.ncbi.nlm.nih.gov/19275547).
7. Kari, G; Rodeck, U; Dicker, A P (July 2007). "Zebrafish: An Emerging Model System for Human Disease and Drug Discovery". *Clinical Pharmacology & Therapeutics*. **82** (1): 70–80. doi:10.1038/sj.clpt.6100223 (https://doi.org/10.1038%2Fsj.clpt.6100223). PMID 17495877 (https://pubmed.ncbi.nlm.nih.gov/17495877). S2CID 41443542 (https://api.semanticscholar.org/CorpusID:41443542).
8. "Pinel Chapter 6 - Human Brain Damage & Animal Models" (https://web.archive.org/web/20141013041340/http://academic.uprm.edu/~ephoebus/id85.htm). Academic.uprm.edu. Archived from the original (http://academic.uprm.edu/~ephoebus/id85.htm) on 2014-10-13. Retrieved 2014-01-10.
9. Cohen BJ, Loew FM. (1984) Laboratory Animal Medicine: Historical Perspectives in Laboratory Animal Medicine Academic Press, Inc: Orlando, FL, USA; Fox JG, Cohen BJ, Loew FM (eds)
10. Royal Society of Medicine (13 May 2015). "Statement of the Royal Society's position on the use of animals in research" (https://royalsociety.org/topics-policy/publications/2015/animals-in-research/).
11. National Research Council and Institute of Medicine (1988). *Use of Laboratory Animals in Biomedical and Behavioral Research* (https://books.google.com/books?id=EzorAAAAYAAJ). National Academies Press. p. 37. ISBN 9780309038393. NAP:13195.
12. Lieschke, Graham J.; Currie, Peter D. (May 2007). "Animal models of human disease: zebrafish swim into view". *Nature Reviews Genetics*. **8** (5): 353–367. doi:10.1038/nrg2091 (https://doi.org/10.1038%2Fnrg2091). PMID 17440532 (https://pubmed.ncbi.nlm.nih.gov/17440532). S2CID 13857842 (https://api.semanticscholar.org/CorpusID:13857842).
13. National Research Council and Institute of Medicine (1988). *Use of Laboratory Animals in Biomedical and Behavioral Research* (https://books.google.com/books?id=EzorAAAAYAAJ). National Academies Press. p. 27. ISBN 9780309038393. NAP:13195.
14. Hau and Shapiro 2011:
    - Jann Hau; Steven J. Schapiro (2011). *Handbook of Laboratory Animal Science, Volume I, Third Edition: Essential Principles and Practices* (https://books.google.com/books?id=D-IHAaggi_4C). CRC Press. p. 2. ISBN 978-1-4200-8456-6.
    - Jann Hau; Steven J. Schapiro (2011). *Handbook of Laboratory Animal Science, Volume II, Third Edition: Animal Models* (https://books.google.com/books?id=yk7TFvsFCBcC). CRC Press. p. 1. ISBN 978-1-4200-8458-0.

15. Institute of Medicine (1991). *Science, Medicine, and Animals* (https://archive.org/details/sciencemedicinea00comm). National Academies Press. p. 3 (https://archive.org/details/sciencemedicinea00comm/page/3). ISBN 978-0-309-56994-1.
16. "The Nobel Prize in Physiology or Medicine 1933" (http://nobelprize.org/nobel_prizes/medicine/laureates/1933/index.html). Nobel Web AB. Retrieved 2015-06-20.
17. "Thomas Hunt Morgan and his Legacy" (https://www.nobelprize.org/nobel_prizes/medicine/laureates/1933/morgan-article.html). Nobel Web AB. Retrieved 2015-06-20.
18. Kohler, *Lords of the Fly*, chapter 5
19. Kandel, Eric. 1999. "Genes, Chromosomes, and the Origins of Modern Biology" (http://www.columbia.edu/cu/alumni/Magazine/Legacies/Morgan/), *Columbia Magazine*
20. Steensma, David P.; Kyle Robert A.; Shampo Marc A. (November 2010). "Abbie Lathrop, the "Mouse Woman of Granby": Rodent Fancier and Accidental Genetics Pioneer" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2966381). *Mayo Clinic Proceedings*. **85** (11): e83. doi:10.4065/mcp.2010.0647 (https://doi.org/10.4065%2Fmcp.2010.0647). PMC 2966381 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2966381). PMID 21061734 (https://pubmed.ncbi.nlm.nih.gov/21061734).
21. Pillai, Shiv. "History of Immunology at Harvard" (https://web.archive.org/web/20131220022416/https://immunology.hms.harvard.edu/about-us/history). *Harvard Medical School:About us*. Harvard Medical School. Archived from the original (https://immunology.hms.harvard.edu/about-us/history) on 20 December 2013. Retrieved 19 December 2013.
22. Hedrich, Hans, ed. (2004-08-21). "The house mouse as a laboratory model: a historical perspective". *The Laboratory Mouse*. Elsevier Science. ISBN 9780080542539.
23. Bering Nobel Biography (http://nobelprize.org/nobel_prizes/medicine/laureates/1901/behring-bio.html)
24. Walter B. Cannon Papers, American Philosophical Society (http://www.amphilsoc.org/library/mole/c/cannon.htm) Archived (https://web.archive.org/web/20090814184304/http://www.amphilsoc.org/library/mole/c/cannon.htm) August 14, 2009, at the Wayback Machine
25. Discovery of Insulin (http://www.mta.ca/faculty/arts/canadian_studies/english/about/study_guide/doctors/insulin.html) Archived (https://web.archive.org/web/20090930142937/http://www.mta.ca/faculty/arts/canadian_studies/english/about/study_guide/doctors/insulin.html) September 30, 2009, at the Wayback Machine
26. Thompson bio ref (http://www.dlife.com/dLife/do/ShowContent/inspiration_expert_advice/famous_people/leonard_thompson.html) Archived (https://web.archive.org/web/20090210030429/http://www.dlife.com/dLife/do/ShowContent/inspiration_expert_advice/famous_people/leonard_thompson.html) 2009-02-10 at the Wayback Machine
27. [1] (http://www.adb.online.anu.edu.au/biogs/A130374b.htm) John Cade and Lithium
28. Raventos J (1956) *Br J Pharmacol* 11, 394
29. Whalen FX, Bacon DR & Smith HM (2005) *Best Pract Res Clin Anaesthesiol* 19, 323
30. "Archived copy" (https://web.archive.org/web/20100311191427/http://www.post-gazette.com/pg/05093/481117.stm). Archived from the original (http://www.post-gazette.com/pg/05093/481117.stm) on 2010-03-11. Retrieved 2015-06-20. Virus-typing of polio by Salk
31. "Archived copy" (https://web.archive.org/web/20080905022100/http://www.post-gazette.com/pg/05094/482468.stm). Archived from the original (http://www.post-gazette.com/pg/05094/482468.stm) on 2008-09-05. Retrieved 2008-08-23. Salk polio virus
32. [2] (http://americanhistory.si.edu/polio/virusvaccine/vacraces2.htm) History of polio vaccine
33. "the work on [polio] prevention was long delayed by... misleading experimental models of the disease in monkeys" | ari.info (http://www.animalresearch.info/en/resources/163/-the-work-on-polio-prevention-was-long-dela/)
34. Carrel A (1912) *Surg. Gynec. Obst.* 14: p. 246
35. Williamson C (1926) *J. Urol.* 16: p. 231
36. Woodruff H & Burg R (1986) in *Discoveries in Pharmacology* vol 3, ed Parnham & Bruinvels, Elsevier, Amsterdam
37. Moore F (1964) *Give and Take: the Development of Tissue Transplantation*. Saunders, New York

38. Gibbon JH (1937) *Arch. Surg.* 34, 1105
39. [3] (http://www.rawbw.com/~hinshaw/cgi-bin/id?1375) Hinshaw obituary
40. [4] (http://www.discoveriesinmedicine.com/Ra-Thy/Streptomycin.html) Streptomycin
41. Fleming A (1929) *Br J Exp Path* 10, 226
42. Medical Research Council (1956) *Br. Med. J.* 2: p. 454
43. *A reference handbook of the medical sciences*. William Wood and Co., 1904, Edited by Albert H. Buck.
44. Pu, Ruiyu; Coleman, James; Coisman, James; Sato, Eiji; Tanabe, Taishi; Arai, Maki; Yamamoto, Janet K (February 2005). "Dual-subtype FIV vaccine (Fel-O-Vax® FIV) protection against a heterologous subtype B FIV isolate". *Journal of Feline Medicine and Surgery*. **7** (1): 65–70. doi:10.1016/j.jfms.2004.08.005 (https://doi.org/10.1016%2Fj.jfms.2004.08.005). PMID 15686976 (https://pubmed.ncbi.nlm.nih.gov/15686976). S2CID 26525327 (https://api.semanticscholar.org/CorpusID:26525327).
45. Dryden, MW; Payne, PA (2005). "Preventing parasites in cats". *Veterinary Therapeutics*. **6** (3): 260–7. PMID 16299672 (https://pubmed.ncbi.nlm.nih.gov/16299672).
46. Sources:
    - P. Michael Conn (29 May 2013). *Animal Models for the Study of Human Disease* (https://books.google.com/books?id=dVLVLIV8rD0C). Academic Press. p. 37. ISBN 978-0-12-415912-9.
    - Lieschke, Graham J.; Currie, Peter D. (May 2007). "Animal models of human disease: zebrafish swim into view". *Nature Reviews Genetics*. **8** (5): 353–367. doi:10.1038/nrg2091 (https://doi.org/10.1038%2Fnrg2091). PMID 17440532 (https://pubmed.ncbi.nlm.nih.gov/17440532). S2CID 13857842 (https://api.semanticscholar.org/CorpusID:13857842).
    - Pierce K. H. Chow; Robert T. H. Ng; Bryan E. Ogden (2008). *Using Animal Models in Biomedical Research: A Primer for the Investigator* (https://books.google.com/books?id=NtWM8gD9Z2MC). World Scientific. pp. 1–2. ISBN 978-981-281-202-5.
    - Jann Hau; Steven J. Schapiro (2011). "The contribution of laboratory animals to medical progress" (https://books.google.com/books?id=D-IHAaggi_4C). *Handbook of Laboratory Animal Science, Volume I, Third Edition: Essential Principles and Practices*. CRC Press. ISBN 978-1-4200-8456-6.
47. Guela, Changiz; Wu, Chuang-Kuo; Saroff, Daniel; Lorenzo, Alfredo; Yuan, Menglan; Yankner, Bruce A. (July 1998). "Aging renders the brain vulnerable to amyloid β-protein neurotoxicity". *Nature Medicine*. **4** (7): 827–831. doi:10.1038/nm0798-827 (https://doi.org/10.1038%2Fnm0798-827). PMID 9662375 (https://pubmed.ncbi.nlm.nih.gov/9662375). S2CID 45108486 (https://api.semanticscholar.org/CorpusID:45108486).
48. AIDS Reviews 2005;7:67-83 Antiretroviral Drug Studies in Nonhuman Primates: a Valid Animal Model for Innovative Drug Efficacy and Pathogenesis Experiments (http://www.aidsreviews.com/files/2005_7_2_67_83.pdf) Archived (https://web.archive.org/web/20081217131711/http://www.aidsreviews.com/files/2005_7_2_67_83.pdf) December 17, 2008, at the Wayback Machine
49. PMPA blocks SIV in monkeys (http://www.thebody.com/cdc/tb165.html)
50. PMPA is tenofovir (http://www.thebody.com/bp/dec99/medical.html)
51. Jameson, Bradford A.; McDonnell, James M.; Marini, Joseph C.; Korngold, Robert (April 1994). "A rationally designed CD4 analogue inhibits experimental allergic encephalomyelitis". *Nature*. **368** (6473): 744–746. Bibcode:1994Natur.368..744J (https://ui.adsabs.harvard.edu/abs/1994Natur.368..744J). doi:10.1038/368744a0 (https://doi.org/10.1038%2F368744a0). PMID 8152486 (https://pubmed.ncbi.nlm.nih.gov/8152486). S2CID 4370797 (https://api.semanticscholar.org/CorpusID:4370797).
52. Lyuksyutova, AL; Lu C-C, Milanesio N; Milanesio, N; King, LA; Guo, N; Wang, Y; Nathans, J; Tessier-Lavigne, M; et al. (2003). "Anterior-posterior guidance of commissural axons by Wnt-Frizzled signaling". *Science*. **302** (5652): 1984–8. Bibcode:2003Sci...302.1984L (https://ui.adsabs.harvard.edu/abs/2003Sci...302.1984L). doi:10.1126/science.1089610 (https://doi.org/10.1126%2Fscience.1089610). PMID 14671310 (https://pubmed.ncbi.nlm.nih.gov/14671310). S2CID 39309990 (https://api.semanticscholar.org/CorpusID:39309990).

53. What are model organisms? (http://genome.wellcome.ac.uk/doc_WTD020803.html) Archived (https://web.archive.org/web/20061028072001/http://genome.wellcome.ac.uk/doc_WTD020803.html) October 28, 2006, at the Wayback Machine
54. NIH model organisms (http://www.nih.gov/science/models/) Archived (https://web.archive.org/web/20070822041956/http://www.nih.gov/science/models/) August 22, 2007, at the Wayback Machine
55. Hedges, S. Blair (November 2002). "The origin and evolution of model organisms". *Nature Reviews Genetics*. **3** (11): 838–849. doi:10.1038/nrg929 (https://doi.org/10.1038%2Fnrg929). PMID 12415314 (https://pubmed.ncbi.nlm.nih.gov/12415314). S2CID 10956647 (https://api.semanticscholar.org/CorpusID:10956647).
56. Bejerano, G.; Pheasant, M.; Makunin, I.; Stephen, S.; Kent, W. J.; Mattick, J. S.; Haussler, D. (2004). "Ultraconserved Elements in the Human Genome" (http://www.bx.psu.edu/~ross/ComparGeno/BejeranoUCEsSci.pdf) (PDF). *Science*. **304** (5675): 1321–1325. Bibcode:2004Sci...304.1321B (https://ui.adsabs.harvard.edu/abs/2004Sci...304.1321B). CiteSeerX 10.1.1.380.9305 (https://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.380.9305). doi:10.1126/science.1098119 (https://doi.org/10.1126%2Fscience.1098119). PMID 15131266 (https://pubmed.ncbi.nlm.nih.gov/15131266). S2CID 2790337 (https://api.semanticscholar.org/CorpusID:2790337).
57. Chinwalla, A. T.; Waterston, L. L.; Lindblad-Toh, K. D.; Birney, G. A.; Rogers, L. A.; Abril, R. S.; Agarwal, T. A.; Agarwala, L. W.; Ainscough, E. R.; Alexandersson, J. D.; An, T. L.; Antonarakis, W. E.; Attwood, J. O.; Baertsch, M. N.; Bailey, K. H.; Barlow, C. S.; Beck, T. C.; Berry, B.; Birren, J.; Bloom, E.; Bork, R. H.; Botcherby, M. C.; Bray, R. K.; Brent, S. P.; Brown, P.; Brown, E.; Bult, B.; Burton, T.; Butler, D. G.; et al. (2002). "Initial sequencing and comparative analysis of the mouse genome" (https://doi.org/10.1038%2Fnature01262). *Nature*. **420** (6915): 520–562. Bibcode:2002Natur.420..520W (https://ui.adsabs.harvard.edu/abs/2002Natur.420..520W). doi:10.1038/nature01262 (https://doi.org/10.1038%2Fnature01262). PMID 12466850 (https://pubmed.ncbi.nlm.nih.gov/12466850).
58. Kehrer-Sawatzki, H.; Cooper, D. N. (2007). "Understanding the recent evolution of the human genome: Insights from human-chimpanzee genome comparisons". *Human Mutation*. **28** (2): 99–130. doi:10.1002/humu.20420 (https://doi.org/10.1002%2Fhumu.20420). PMID 17024666 (https://pubmed.ncbi.nlm.nih.gov/17024666). S2CID 42037159 (https://api.semanticscholar.org/CorpusID:42037159).
59. Kehrer-Sawatzki, Hildegard; Cooper, David N. (2007-01-18). "Structural divergence between the human and chimpanzee genomes". *Human Genetics*. **120** (6): 759–778. doi:10.1007/s00439-006-0270-6 (https://doi.org/10.1007%2Fs00439-006-0270-6). PMID 17066299 (https://pubmed.ncbi.nlm.nih.gov/17066299). S2CID 6484568 (https://api.semanticscholar.org/CorpusID:6484568).
60. Prüfer, K.; Munch, K.; Hellmann, I.; Akagi, K.; Miller, J. R.; Walenz, B.; Koren, S.; Sutton, G.; Kodira, C.; Winer, R.; Knight, J. R.; Mullikin, J. C.; Meader, S. J.; Ponting, C. P.; Lunter, G.; Higashino, S.; Hobolth, A.; Dutheil, J.; Karakoç, E.; Alkan, C.; Sajjadian, S.; Catacchio, C. R.; Ventura, M.; Marques-Bonet, T.; Eichler, E. E.; André, C.; Atencia, R.; Mugisha, L.; Junhold, J. R.; Patterson, N. (2012). "The bonobo genome compared with the chimpanzee and human genomes" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3498939). *Nature*. **486** (7404): 527–531. Bibcode:2012Natur.486..527P (https://ui.adsabs.harvard.edu/abs/2012Natur.486..527P). doi:10.1038/nature11128 (https://doi.org/10.1038%2Fnature11128). PMC 3498939 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3498939). PMID 22722832 (https://pubmed.ncbi.nlm.nih.gov/22722832).
61. Grada, Ayman; Mervis, Joshua; Falanga, Vincent (October 2018). "Research Techniques Made Simple: Animal Models of Wound Healing" (https://doi.org/10.1016%2Fj.jid.2018.08.005). *Journal of Investigative Dermatology*. **138** (10): 2095–2105.e1. doi:10.1016/j.jid.2018.08.005 (https://doi.org/10.1016%2Fj.jid.2018.08.005). PMID 30244718 (https://pubmed.ncbi.nlm.nih.gov/30244718).

62. Olson, Harry; Betton, Graham; Robinson, Denise; Thomas, Karluss; Monro, Alastair; Kolaja, Gerald; Lilly, Patrick; Sanders, James; Sipes, Glenn; Bracken, William; Dorato, Michael; Van Deun, Koen; Smith, Peter; Berger, Bruce; Heller, Allen (August 2000). "Concordance of the Toxicity of Pharmaceuticals in Humans and in Animals". *Regulatory Toxicology and Pharmacology*. **32** (1): 56–67. doi:10.1006/rtph.2000.1399 (https://doi.org/10.1006%2Frtph.2000.1399). PMID 11029269 (https://pubmed.ncbi.nlm.nih.gov/11029269).
63. Davidson, M. K.; Lindsey, J. R.; Davis, J. K. (1987). "Requirements and selection of an animal model". *Israel Journal of Medical Sciences*. **23** (6): 551–555. PMID 3312096 (https://pubmed.ncbi.nlm.nih.gov/3312096).
64. Hughes, H. C.; Lang, C. (1978). "Basic Principles in Selecting Animal Species for Research Projects". *Clinical Toxicology*. **13** (5): 611–621. doi:10.3109/15563657808988266 (https://doi.org/10.3109%2F15563657808988266). PMID 750165 (https://pubmed.ncbi.nlm.nih.gov/750165).
65. White HS (1997). "Clinical significance of animal seizure models and mechanism of action studies of potential antiepileptic drugs" (https://doi.org/10.1111%2Fj.1528-1157.1997.tb04523.x). *Epilepsia*. 38 Suppl 1 (s1): S9–17. doi:10.1111/j.1528-1157.1997.tb04523.x (https://doi.org/10.1111%2Fj.1528-1157.1997.tb04523.x). PMID 9092952 (https://pubmed.ncbi.nlm.nih.gov/9092952). S2CID 46126941 (https://api.semanticscholar.org/CorpusID:46126941).
66. Glushakov, Alexander V.; Glushakova, Olena Y.; Doré, Sylvain; Carney, Paul R.; Hayes, Ronald L. (2016). "Animal Models of Posttraumatic Seizures and Epilepsy". *Injury Models of the Central Nervous System*. Methods in Molecular Biology. **1462**. pp. 481–519. doi:10.1007/978-1-4939-3816-2_27 (https://doi.org/10.1007%2F978-1-4939-3816-2_27). ISBN 978-1-4939-3814-8. PMC 6036905 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6036905). PMID 27604735 (https://pubmed.ncbi.nlm.nih.gov/27604735).
67. Halje P, Tamtè M, Richter U, Mohammed M, Cenci MA, Petersson P (2012). "Levodopa-induced dyskinesia is strongly associated with resonant cortical oscillations" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6621755). *Journal of Neuroscience*. **32** (47): 16541–51. doi:10.1523/JNEUROSCI.3047-12.2012 (https://doi.org/10.1523%2FJNEUROSCI.3047-12.2012). PMC 6621755 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6621755). PMID 23175810 (https://pubmed.ncbi.nlm.nih.gov/23175810).
68. Bolton, C. (October 2007). "The translation of drug efficacy from in vivo models to human disease with special reference to experimental autoimmune encephalomyelitis and multiple sclerosis". *Inflammopharmacology*. **15** (5): 183–187. doi:10.1007/s10787-007-1607-z (https://doi.org/10.1007%2Fs10787-007-1607-z). PMID 17943249 (https://pubmed.ncbi.nlm.nih.gov/17943249). S2CID 8366509 (https://api.semanticscholar.org/CorpusID:8366509).
69. Leker, R. R.; Constantini, S. (2002). "Experimental Models in Focal Cerebral Ischemia: Are we there yet?". *Research and Publishing in Neurosurgery*. Acta Neurochirurgica. Supplement. **83**. pp. 55–59. doi:10.1007/978-3-7091-6743-4_10 (https://doi.org/10.1007%2F978-3-7091-6743-4_10). ISBN 978-3-7091-7399-2. PMID 12442622 (https://pubmed.ncbi.nlm.nih.gov/12442622).
70. Wang J, Fields J, Doré S (2008). "The development of an improved preclinical mouse model of intracerebral hemorrhage using double infusion of autologous whole blood" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4725309). *Brain Res*. **1222**: 214–21. doi:10.1016/j.brainres.2008.05.058 (https://doi.org/10.1016%2Fj.brainres.2008.05.058). PMC 4725309 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4725309). PMID 18586227 (https://pubmed.ncbi.nlm.nih.gov/18586227).
71. Rynkowski, Michal A; Kim, Grace H; Komotar, Ricardo J; Otten, Marc L; Ducruet, Andrew F; Zacharia, Brad E; Kellner, Christopher P; Hahn, David K; Merkow, Maxwell B; Garrett, Matthew C; Starke, Robert M; Cho, Byung-Moon; Sosunov, Sergei A; Connolly, E Sander (January 2008). "A mouse model of intracerebral hemorrhage using autologous blood infusion". *Nature Protocols*. **3** (1): 122–128. doi:10.1038/nprot.2007.513 (https://doi.org/10.1038%2Fnprot.2007.513). PMID 18193028 (https://pubmed.ncbi.nlm.nih.gov/18193028). S2CID 22553744 (https://api.semanticscholar.org/CorpusID:22553744).
72. Korneev, K. V. (18 October 2019). "Mouse Models of Sepsis and Septic Shock" (https://doi.org/10.1134%2FS0026893319050108). *Molecular Biology*. **53** (5): 704–717. doi:10.1134/S0026893319050108 (https://doi.org/10.1134%2FS0026893319050108). PMID 31661479 (https://pubmed.ncbi.nlm.nih.gov/31661479).

73. Eibl RH, Kleihues P, Jat PS, Wiestler OD (1994). "A model for primitive neuroectodermal tumors in transgenic neural transplants harboring the SV40 large T antigen" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1887088). *Am J Pathol*. **144** (3): 556–564. PMC 1887088 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1887088). PMID 8129041 (https://pubmed.ncbi.nlm.nih.gov/8129041).
74. Radner H, El-Shabrawi Y, Eibl RH, Brüstle O, Kenner L, Kleihues P, Wiestler OD (1993). "Tumor induction by ras and myc oncogenes in fetal and neonatal brain: modulating effects of developmental stage and retroviral dose". *Acta Neuropathologica*. **86** (5): 456–465. doi:10.1007/bf00228580 (https://doi.org/10.1007%2Fbf00228580). PMID 8310796 (https://pubmed.ncbi.nlm.nih.gov/8310796). S2CID 2972931 (https://api.semanticscholar.org/CorpusID:2972931).
75. Homo-Delarche F, Drexhage HA (2004). "Immune cells, pancreas development, regeneration and type 1 diabetes". *Trends Immunol*. **25** (5): 222–9. doi:10.1016/j.it.2004.02.012 (https://doi.org/10.1016%2Fj.it.2004.02.012). PMID 15099561 (https://pubmed.ncbi.nlm.nih.gov/15099561).
76. Hisaeda, Hajime; Maekawa, Yoichi; Iwakawa, Daiji; Okada, Hiroko; Himeno, Kunisuke; Kishihara, Kenji; Tsukumo, Shin-ichi; Yasutomo, Koji (January 2004). "Escape of malaria parasites from host immunity requires CD4+CD25+ regulatory T cells". *Nature Medicine*. **10** (1): 29–30. doi:10.1038/nm975 (https://doi.org/10.1038%2Fnm975). PMID 14702631 (https://pubmed.ncbi.nlm.nih.gov/14702631). S2CID 2111178 (https://api.semanticscholar.org/CorpusID:2111178).
77. Coppi A, Cabinian M, Mirelman D, Sinnis P (2006). "Antimalarial activity of allicin, a biologically active compound from garlic cloves" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472199). *Antimicrob. Agents Chemother*. **50** (5): 1731–7. doi:10.1128/AAC.50.5.1731-1737.2006 (https://doi.org/10.1128%2FAAC.50.5.1731-1737.2006). PMC 1472199 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472199). PMID 16641443 (https://pubmed.ncbi.nlm.nih.gov/16641443).
78. Frischknecht F, Martin B, Thiery I, Bourgouin C, Menard R (2006). "Using green fluorescent malaria parasites to screen for permissive vector mosquitoes" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1450296). *Malar. J.* **5** (1): 23. doi:10.1186/1475-2875-5-23 (https://doi.org/10.1186%2F1475-2875-5-23). PMC 1450296 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1450296). PMID 16569221 (https://pubmed.ncbi.nlm.nih.gov/16569221).
79. Hasler, G. (2004). "Discovering endophenotypes for major depression" (https://doi.org/10.1038%2Fsj.npp.1300506). *Neuropsychopharmacology*. **29** (10): 1765–1781. doi:10.1038/sj.npp.1300506 (https://doi.org/10.1038%2Fsj.npp.1300506). PMID 15213704 (https://pubmed.ncbi.nlm.nih.gov/15213704).
80. Krishnan, Vaishnav; Nestler, Eric J. (2011). "Animal Models of Depression: Molecular Perspectives". *Molecular and Functional Models in Neuropsychiatry*. Current Topics in Behavioral Neurosciences. **7**. pp. 121–147. doi:10.1007/7854_2010_108 (https://doi.org/10.1007%2F7854_2010_108). ISBN 978-3-642-19702-4. PMC 3270071 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3270071). PMID 21225412 (https://pubmed.ncbi.nlm.nih.gov/21225412).
81. Wang, Qingzhong; Timberlake, Matthew A.; Prall, Kevin; Dwivedi, Yogesh (July 2017). "The recent progress in animal models of depression" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5605906). *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. **77**: 99–109. doi:10.1016/j.pnpbp.2017.04.008 (https://doi.org/10.1016%2Fj.pnpbp.2017.04.008). PMC 5605906 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5605906). PMID 28396255 (https://pubmed.ncbi.nlm.nih.gov/28396255).
82. "Bacteria" (http://www.microbiologyonline.org.uk/about-microbiology/introducing-microbes/bacteria). Microbiologyonline. Retrieved 27 February 2014.
83. "Chlamydomonas reinhardtii resources at the Joint Genome Institute" (https://web.archive.org/web/20080723150730/http://genome.jgi-psf.org/chlamy/). Archived from the original (http://genome.jgi-psf.org/chlamy) on 2008-07-23. Retrieved 2007-10-23.
84. James H. Sang (2001). "Drosophila melanogaster: The Fruit Fly" (https://books.google.com/books?id=JjLWYKqehRsC&q=drosophila+eggs+day+lifetime&pg=PA157). In Eric C. R. Reeve (ed.). *Encyclopedia of genetics*. USA: Fitzroy Dearborn Publishers, I. p. 157. ISBN 978-1-884964-34-3. Retrieved 2009-07-01.

85. Riddle, Donald L. (1997). *C. elegans II* (https://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowTOC&rid=ce2.TOC). Plainview, N.Y: Cold Spring Harbor Laboratory Press. ISBN 978-0-87969-532-3.
86. Brenner, S (1974). "The Genetics of *Caenorhabditis elegans*" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1213120). *Genetics*. **77** (1): 71–94. doi:10.1093/genetics/77.1.71 (https://doi.org/10.1093%2Fgenetics%2F77.1.71). PMC 1213120 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1213120). PMID 4366476 (https://pubmed.ncbi.nlm.nih.gov/4366476).
87. White, J; et al. (1986). "The structure of the nervous system of the nematode Caenorhabditis elegans" (https://doi.org/10.1098%2Frstb.1986.0056). *Philos. Trans. R. Soc. Lond. B Biol. Sci*. **314** (1165): 1–340. Bibcode:1986RSPTB.314....1W (https://ui.adsabs.harvard.edu/abs/1986RSPTB.314....1W). doi:10.1098/rstb.1986.0056 (https://doi.org/10.1098%2Frstb.1986.0056). PMID 22462104 (https://pubmed.ncbi.nlm.nih.gov/22462104). S2CID 5006466 (https://api.semanticscholar.org/CorpusID:5006466).
88. Jabr, Ferris (2012-10-02). "The Connectome Debate: Is Mapping the Mind of a Worm Worth It?" (http://www.scientificamerican.com/article.cfm?id=c-elegans-connectome). *Scientific American*. Retrieved 2014-01-18.
89. About Arabidopsis on The Arabidopsis Information Resource page (http://www.arabidopsis.org/portals/education/aboutarabidopsis.jsp#hist) (TAIR)
90. Kolb, E. M.; Rezende, E. L.; Holness, L.; Radtke, A.; Lee, S. K.; Obenaus, A.; Garland Jr, T. (2013). "Mice selectively bred for high voluntary wheel running have larger midbrains: support for the mosaic model of brain evolution". *Journal of Experimental Biology*. **216** (3): 515–523. doi:10.1242/jeb.076000 (https://doi.org/10.1242%2Fjeb.076000). PMID 23325861 (https://pubmed.ncbi.nlm.nih.gov/23325861).
91. Wallingford, J.; Liu, K.; Zheng, Y. (2010). "MISSING" (https://doi.org/10.1016%2Fj.cub.2010.01.012). *Current Biology*. **20** (6): R263–4. doi:10.1016/j.cub.2010.01.012 (https://doi.org/10.1016%2Fj.cub.2010.01.012). PMID 20334828 (https://pubmed.ncbi.nlm.nih.gov/20334828). S2CID 235311984 (https://api.semanticscholar.org/CorpusID:235311984).
92. Harland, R.M.; Grainger, R.M. (2011). "MISSING" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3601910). *Trends in Genetics*. **27** (12): 507–15. doi:10.1016/j.tig.2011.08.003 (https://doi.org/10.1016%2Fj.tig.2011.08.003). PMC 3601910 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3601910). PMID 21963197 (https://pubmed.ncbi.nlm.nih.gov/21963197).
93. Spitsbergen JM, Kent ML (2003). "The state of the art of the zebrafish model for toxicology and toxicologic pathology research—advantages and current limitations" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1909756). *Toxicol Pathol*. **31** (Suppl): 62–87. doi:10.1080/01926230390174959 (https://doi.org/10.1080%2F01926230390174959). PMC 1909756 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1909756). PMID 12597434 (https://pubmed.ncbi.nlm.nih.gov/12597434).
94. Chapman, J. A.; Kirkness, E. F.; Simakov, O.; Hampson, S. E.; Mitros, T.; Weinmaier, T.; Rattei, T.; Balasubramanian, P. G.; Borman, J.; Busam, D.; Disbennett, K.; Pfannkoch, C.; Sumin, N.; Sutton, G. G.; Viswanathan, L. D.; Walenz, B.; Goodstein, D. M.; Hellsten, U.; Kawashima, T.; Prochnik, S. E.; Putnam, N. H.; Shu, S.; Blumberg, B.; Dana, C. E.; Gee, L.; Kibler, D. F.; Law, L.; Lindgens, D.; Martinez, D. E.; et al. (2010). "The dynamic genome of Hydra" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4479502). *Nature*. **464** (7288): 592–596. Bibcode:2010Natur.464..592C (https://ui.adsabs.harvard.edu/abs/2010Natur.464..592C). doi:10.1038/nature08830 (https://doi.org/10.1038%2Fnature08830). PMC 4479502 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4479502). PMID 20228792 (https://pubmed.ncbi.nlm.nih.gov/20228792).
95. Harel, I.; Benayoun, B. R. N. A.; Machado, B.; Singh, P. P.; Hu, C. K.; Pech, M. F.; Valenzano, D. R.; Zhang, E.; Sharp, S. C.; Artandi, S. E.; Brunet, A. (2015). "A Platform for Rapid Exploration of Aging and Diseases in a Naturally Short-Lived Vertebrate" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344913). *Cell*. **160** (5): 1013–26. doi:10.1016/j.cell.2015.01.038 (https://doi.org/10.1016%2Fj.cell.2015.01.038). PMC 4344913 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344913). PMID 25684364 (https://pubmed.ncbi.nlm.nih.gov/25684364).

96. Wichman, Holly A.; Brown, Celeste J. (2010-08-27). "Experimental evolution of viruses: Microviridae as a model system" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2935103). *Philosophical Transactions of the Royal Society B: Biological Sciences*. **365** (1552): 2495–2501. doi:10.1098/rstb.2010.0053 (https://doi.org/10.1098%2Frstb.2010.0053). PMC 2935103 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2935103). PMID 20643739 (https://pubmed.ncbi.nlm.nih.gov/20643739).
97. Dunn, Joe Dan; Bosmani, Cristina; Barisch, Caroline; Raykov, Lyudmil; Lefrançois, Louise H.; Cardenal-Muñoz, Elena; López-Jiménez, Ana Teresa; Soldati, Thierry (2018-01-04). "Eat Prey, Live: Dictyostelium discoideum As a Model for Cell-Autonomous Defenses" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5758549). *Frontiers in Immunology*. **8**: 1906. doi:10.3389/fimmu.2017.01906 (https://doi.org/10.3389%2Ffimmu.2017.01906). PMC 5758549 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5758549). PMID 29354124 (https://pubmed.ncbi.nlm.nih.gov/29354124).
98. Fission Yeast GO slim terms | PomBase (http://www.pombase.org/browse-curation/fission-yeast-go-slim-terms)
99. Lock, A; Rutherford, K; Harris, MA; Hayles, J; Oliver, SG; Bähler, J; Wood, V (13 October 2018). "PomBase 2018: user-driven reimplementation of the fission yeast database provides rapid and intuitive access to diverse, interconnected information" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6324063). *Nucleic Acids Research*. **47** (D1): D821–D827. doi:10.1093/nar/gky961 (https://doi.org/10.1093%2Fnar%2Fgky961). PMC 6324063 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6324063). PMID 30321395 (https://pubmed.ncbi.nlm.nih.gov/30321395).
00. Batyrova, Khorcheska; Hallenbeck, Patrick C. (2017-03-16). "Hydrogen Production by a Chlamydomonas reinhardtii Strain with Inducible Expression of Photosystem II" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5372659). *International Journal of Molecular Sciences*. **18** (3): 647. doi:10.3390/ijms18030647 (https://doi.org/10.3390%2Fijms18030647). PMC 5372659 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5372659). PMID 28300765 (https://pubmed.ncbi.nlm.nih.gov/28300765).
01. Smith, Joshua J.; Wiley, Emily A.; Cassidy-Hanley, Donna M. (2012). "Tetrahymena in the Classroom". *Tetrahymena Thermophila*. Methods in Cell Biology. **109**. pp. 411–430. doi:10.1016/B978-0-12-385967-9.00016-5 (https://doi.org/10.1016%2FB978-0-12-385967-9.00016-5). ISBN 9780123859679. PMC 3587665 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3587665). PMID 22444155 (https://pubmed.ncbi.nlm.nih.gov/22444155).
02. Stefanidou, Maria (2014). "The use of the protozoan Tetrahymena as a cell model". In Castillo, Victor; Harris, Rodney (eds.). *Protozoa: Biology, Classification and Role in Disease*. Nova Science Publishers. pp. 69–88. ISBN 978-1-62417-073-7.
03. Fielding, Samuel R. (March 2013). "Emiliania huxleyi specific growth rate dependence on temperature" (https://doi.org/10.4319%2Flo.2013.58.2.0663). *Limnology and Oceanography*. **58** (2): 663–666. Bibcode:2013LimOc..58..663F (https://ui.adsabs.harvard.edu/abs/2013LimOc..58..663F). doi:10.4319/lo.2013.58.2.0663 (https://doi.org/10.4319%2Flo.2013.58.2.0663).
04. Platt, Alexander; Horton, Matthew; Huang, Yu S.; Li, Yan; Anastasio, Alison E.; Mulyati, Ni Wayan; Ågren, Jon; Bossdorf, Oliver; Byers, Diane; Donohue, Kathleen; Dunning, Megan; Holub, Eric B.; Hudson, Andrew; Le Corre, Valérie; Loudet, Olivier; Roux, Fabrice; Warthmann, Norman; Weigel, Detlef; Rivero, Luz; Scholl, Randy; Nordborg, Magnus; Bergelson, Joy; Borevitz, Justin O. (2010-02-12). "The Scale of Population Structure in Arabidopsis thaliana" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2820523). *PLOS Genetics*. **6** (2): e1000843. doi:10.1371/journal.pgen.1000843 (https://doi.org/10.1371%2Fjournal.pgen.1000843). PMC 2820523 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2820523). PMID 20169178 (https://pubmed.ncbi.nlm.nih.gov/20169178).
05. Bohlender, Lennard L.; Parsons, Juliana; Hoernstein, Sebastian N. W.; Rempfer, Christine; Ruiz-Molina, Natalia; Lorenz, Timo; Rodríguez Jahnke, Fernando; Figl, Rudolf; Fode, Benjamin; Altmann, Friedrich; Reski, Ralf; Decker, Eva L. (2020-12-18). "Stable Protein Sialylation in Physcomitrella" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7775405). *Frontiers in Plant Science*. **11**: 610032. doi:10.3389/fpls.2020.610032 (https://doi.org/10.3389%2Ffpls.2020.610032). PMC 7775405 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7775405). PMID 33391325 (https://pubmed.ncbi.nlm.nih.gov/33391325).

06. https://academic.oup.com/treephys/article/33/4/357/1716508
07. Lindquist, Susan L.; Bonini, Nancy M. (22 Jun 2006). "Parkinson's Disease Mechanism Discovered" (https://www.hhmi.org/news/parkinsons-disease-mechanism-discovered). *Science Express*. Howard Hughes Medical Institute. Retrieved 11 Jul 2019.
08. Kim, H; Raphayel, A; LaDow, E; McGurk, L; Weber, R; Trojanowski, J; Lee, V; Finkbeiner, S; Gitler, A; Bonini, N (2014). "Therapeutic modulation of eIF2α-phosphorylation rescues TDP-43 toxicity in amyotrophic lateral sclerosis disease models" (http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC3934366&blobtype=pdf). *Nature Genetics*. **46** (2): 152–60. doi:10.1038/ng.2853 (https://doi.org/10.1038%2Fng.2853). PMC 3934366 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3934366). PMID 24336168 (https://pubmed.ncbi.nlm.nih.gov/24336168). Retrieved 11 Jul 2019.
09. Non-Mammalian Hormone-Behavior Systems https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/fundulus-heteroclitus
10. Siegfried, K.R. (2017). "Molecular and Chromosomal Aspects of Sex Determination". *Reference Module in Life Sciences*. doi:10.1016/B978-0-12-809633-8.03245-3 (https://doi.org/10.1016%2FB978-0-12-809633-8.03245-3). ISBN 978-0-12-809633-8.
11. Mello, Claudio V. (2014). "The Zebra Finch, Taeniopygia guttata: An Avian Model for Investigating the Neurobiological Basis of Vocal Learning" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4571486). *Cold Spring Harbor Protocols*. **2014** (12): 1237–1242. doi:10.1101/pdb.emo084574 (https://doi.org/10.1101%2Fpdb.emo084574). PMC 4571486 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4571486). PMID 25342070 (https://pubmed.ncbi.nlm.nih.gov/25342070).
12. "JGI-Led Team Sequences Frog Genome" (https://web.archive.org/web/20110807211657/http://www.genomeweb.com//node/939634?hq_e=el&hq_m=701632&hq_l=1&hq_v=2de76155bb). *GenomeWeb.com*. Genome Web. 29 April 2010. Archived from the original (http://www.genomeweb.com//node/939634?hq_e=el&hq_m=701632&hq_l=1&hq_v=2de76155bb) on August 7, 2011. Retrieved 30 April 2010.
13. Martin B, Ji S, Maudsley S, Mattson MP (2010). " "Control" laboratory rodents are metabolically morbid: Why it matters" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2852022). *Proceedings of the National Academy of Sciences*. **107** (14): 6127–6133. Bibcode:2010PNAS..107.6127M (https://ui.adsabs.harvard.edu/abs/2010PNAS..107.6127M). doi:10.1073/pnas.0912955107 (https://doi.org/10.1073%2Fpnas.0912955107). PMC 2852022 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2852022). PMID 20194732 (https://pubmed.ncbi.nlm.nih.gov/20194732).
14. Mestas, Javier; Hughes, Christopher C. W. (March 2004). "Of Mice and Not Men: Differences between Mouse and Human Immunology" (https://doi.org/10.4049%2Fjimmunol.172.5.2731). *The Journal of Immunology*. **172** (5): 2731–2738. doi:10.4049/jimmunol.172.5.2731 (https://doi.org/10.4049%2Fjimmunol.172.5.2731). PMID 14978070 (https://pubmed.ncbi.nlm.nih.gov/14978070). S2CID 10536403 (https://api.semanticscholar.org/CorpusID:10536403).
15. Seok, Junhee; Warren, H. Shaw; Cuenca, Alex G.; Mindrinos, Michael N.; Baker, Henry V.; Xu, Weihong; Richards, Daniel R.; McDonald-Smith, Grace P.; Gao, Hong; Hennessy, Laura; Finnerty, Celeste C.; López, Cecilia M.; Honari, Shari; Moore, Ernest E.; Minei, Joseph P.; Cuschieri, Joseph; Bankey, Paul E.; Johnson, Jeffrey L.; Sperry, Jason; Nathens, Avery B.; Billiar, Timothy R.; West, Michael A.; Jeschke, Marc G.; Klein, Matthew B.; Gamelli, Richard L.; Gibran, Nicole S.; Brownstein, Bernard H.; Miller-Graziano, Carol; Calvano, Steve E.; Mason, Philip H.; Cobb, J. Perren; Rahme, Laurence G.; Lowry, Stephen F.; Maier, Ronald V.; Moldawer, Lyle L.; Herndon, David N.; Davis, Ronald W.; Xiao, Wenzhong; Tompkins, Ronald G.; Abouhamze, Amer; Balis, Ulysses G. J.; Camp, David G.; De, Asit K.; Harbrecht, Brian G.; Hayden, Douglas L.; Kaushal, Amit; O'Keefe, Grant E.; Kotz, Kenneth T.; Qian, Weijun; Schoenfeld, David A.; Shapiro, Michael B.; Silver, Geoffrey M.; Smith, Richard D.; Storey, John D.; Tibshirani, Robert; Toner, Mehmet; Wilhelmy, Julie; Wispelwey, Bram; Wong, Wing H (2013-02-26). "Genomic responses in mouse models poorly mimic human inflammatory diseases" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3587220). *Proceedings of the National Academy of Sciences of the United States of America*. **110** (9): 3507–3512. Bibcode:2013PNAS..110.3507S (https://ui.adsabs.harvard.edu/abs/2013PNAS..110.3507S). doi:10.1073/pnas.1222878110 (https://doi.org/10.1073%2Fpnas.1222878110). PMC 3587220 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3587220). PMID 23401516 (https://pubmed.ncbi.nlm.nih.gov/23401516).

16. Jubb, Alasdair W; Young, Robert S; Hume, David A; Bickmore, Wendy A (15 January 2016). "Enhancer turnover is associated with a divergent transcriptional response to glucocorticoid in mouse and human macrophages" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707550). *Journal of Immunology*. **196** (2): 813–822. doi:10.4049/jimmunol.1502009 (https://doi.org/10.4049%2Fjimmunol.1502009). PMC 4707550 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707550). PMID 26663721 (https://pubmed.ncbi.nlm.nih.gov/26663721).
17. Lahvis, Garet, *The inescapable problem of lab animal restraint* (https://www.ted.com/talks/garet_lahvis_the_inescapable_problem_of_lab_animal_restraint), retrieved 2020-10-26
18. Lahvis, Garet P (2017). "Unbridle biomedical research from the laboratory cage" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5503508). *eLife*. **6**: e27438. doi:10.7554/eLife.27438 (https://doi.org/10.7554%2FeLife.27438). PMC 5503508 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5503508). PMID 28661398 (https://pubmed.ncbi.nlm.nih.gov/28661398).
19. Korneev, K. V. (18 October 2019). "Mouse Models of Sepsis and Septic Shock" (https://doi.org/10.1134%2FS0026893319050108). *Molecular Biology*. **53** (5): 704–717. doi:10.1134/S0026893319050108 (https://doi.org/10.1134%2FS0026893319050108). PMID 31661479 (https://pubmed.ncbi.nlm.nih.gov/31661479).
20. Korneev, K. V. (18 October 2019). "Mouse Models of Sepsis and Septic Shock" (https://doi.org/10.1134%2FS0026893319050108). *Molecular Biology*. **53** (5): 704–717. doi:10.1134/S0026893319050108 (https://doi.org/10.1134%2FS0026893319050108). PMID 31661479 (https://pubmed.ncbi.nlm.nih.gov/31661479).
21. "The world's favourite lab animal has been found wanting, but there are new twists in the mouse's tale" (https://www.economist.com/news/christmas-specials/21712058-evolution-scientific-mainstay-worlds-favourite-lab-animal-has-been-found). *The Economist*. Retrieved 2017-01-10.
22. Katsnelson, Alla (2014-04-28). "Male researchers stress out rodents". *Nature*: nature.2014.15106. doi:10.1038/nature.2014.15106 (https://doi.org/10.1038%2Fnature.2014.15106). S2CID 87534627 (https://api.semanticscholar.org/CorpusID:87534627).
23. "Male Scent May Compromise Biomedical Research" (http://www.sciencemag.org/news/2014/04/male-scent-may-compromise-biomedical-research). *Science* | *AAAS*. 2014-04-28. Retrieved 2017-01-10.
24. "Mouse microbes may make scientific studies harder to replicate" (http://www.sciencemag.org/news/2016/08/mouse-microbes-may-make-scientific-studies-harder-replicate). *Science* | *AAAS*. 2016-08-15. Retrieved 2017-01-10.
25. "FDA: Why are animals used for testing medical products?" (https://www.fda.gov/AboutFDA/Transparency/Basics/ucm194932.htm). *FDA*. 2019-06-18.
26. "Society Of Toxicology: Advancing valid alternatives" (https://web.archive.org/web/20130105120605/http://www.toxicology.org/ms/air4.asp). Archived from the original (http://www.toxicology.org/ms/air4.asp) on 2013-01-05.
27. British animal protection legislation (https://web.archive.org/web/20061214034848/http://homepage.tinet.ie/~pnowlan/Chapter-77.htm).
28. AWA policies (http://awic.nal.usda.gov/government-and-professional-resources/federal-laws/animal-welfare-act).
29. NIH need-to-know (http://grants.nih.gov/grants/olaw/investigatorsneed2know.pdf)
30. list of common model organisms approved for use by the NIH (https://web.archive.org/web/20000815070936/http://www.nih.gov/science/models/))

Further reading

- Marx, Vivien (June 2014). "Models: stretching the skills of cell lines and mice" (https://doi.org/10.1038%2Fnmeth.2966). *Nature Methods*. **11** (6): 617–620. doi:10.1038/nmeth.2966 (https://doi.org/10.1038%2Fnmeth.2966). PMID 24874573 (https://pubmed.ncbi.nlm.nih.gov/24874573). S2CID 11798233 (https://api.semanticscholar.org/CorpusID:11798233).
- Goldstein, Bob; King, Nicole (November 2016). "The Future of Cell Biology: Emerging Model Organisms" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5077642). *Trends in Cell Biology*. **26**

(11): 818–824. doi:10.1016/j.tcb.2016.08.005 (https://doi.org/10.1016%2Fj.tcb.2016.08.005). PMC 5077642 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5077642). PMID 27639630 (https://pubmed.ncbi.nlm.nih.gov/27639630).

- Lloyd, Kent; Franklin, Craig; Lutz, Cat; Magnuson, Terry (June 2015). "Reproducibility: Use mouse biobanks or lose them" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4636083). *Nature*. **522** (7555): 151–153. Bibcode:2015Natur.522..151L (https://ui.adsabs.harvard.edu/abs/2015Natur.522..151L). doi:10.1038/522151a (https://doi.org/10.1038%2F522151a). PMC 4636083 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4636083). PMID 26062496 (https://pubmed.ncbi.nlm.nih.gov/26062496).

External links

- Wellcome Trust description of model organisms
- National Institutes of Health Comparative Medicine Program Vertebrate Models (https://orip.nih.gov/comparative-medicine/programs/vertebrate-models/)
- NIH Using Model Organisms to Study Human Disease (https://www.nigms.nih.gov/Education/Pages/modelorg_factsheet.aspx/)
- National Institutes of Health Model Organism Sharing Policy (https://grants.nih.gov/grants/policy/model_organism/)
- Why are Animals Used in NIH Research (https://grants.nih.gov/grants/policy/air/why_are_animals.htm/)
- Disease Animal Models – BSRC Alexander Fleming (http://www.fleming.gr/)
- Emice (http://emice.nci.nih.gov/) – National Cancer Institute
- Knock Out Mouse Project – KOMP (https://www.komp.org/)
- Mouse Biology Program (https://mbp.mousebiology.org/)
- Mutant Mouse Resource & Research Centers, National Institutes of Health, supported Mouse Repository (https://www.mmrrc.org/)
- Rat Resource & Research Center (http://www.rrrc.us/) – National Institutes of Health, supported Rat Repository
- NIH Model Organism Research Reproducibility and Rigor (https://www.mmrrc.org/about/reproducibility.php/)