



An Updated Review on Rat Genetics and Genomics: Understanding Complex Traits and Diseases

Aaravula Hemanth Babu ^a, Akula Ruchitha Sai ^a,
K Baktha Bandhavi ^a, Mopuri Jyothsna ^a,
Buddadasari Snehitha ^a, K Somasekhar Reddy ^a
and Praveen Kumar Pasala ^{a*}

^a Department of Pharmacology, Raghavendra Institute of Pharmaceutical Education and Research (RIPER) – Autonomous, KR Palli Cross, Chiyvedu (Post), Anantapur, Andhra Pradesh – 515721, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.56557/UPJOZ/2024/v45i94025

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://prh.mbimph.com/review-history/3419>

Review Article

Received: 07/02/2024

Accepted: 11/04/2024

Published: 15/04/2024

ABSTRACT

The study of the genetics and genomics of rats is essential to understanding the intricate mechanisms behind characteristics and illnesses. Rats are used by scientists to investigate a wide range of biological processes, including how the brain develops, how the immune system responds, and what goes wrong in diseases like cancer and metabolic disorders. Rats and humans are similar in physiology and genetics. This article provides a comprehensive analysis of the many advantages and applications of rat models in biomedical science, highlighting their significance in genetic and genomic research. Rat models are indispensable in research because of their many benefits.

*Corresponding author: Email: praveenpharmaco@gmail.com;

Numerous similarities between them and people make it simpler to research illnesses and test possible cures. Rats may be used to efficiently set up studies and obtain results rapidly because they breed quickly and have big litters. Furthermore, altering their DNA is not too difficult, which aids in the understanding of how genes affect complicated features and illnesses.

Rat models have been essential in the past for achieving significant breakthroughs in biomedical research. They have contributed to medical advancements by helping to elucidate fundamental biological concepts and expanding our understanding of human illnesses. Researchers may go even farther into rat genetics with the use of cutting-edge technologies like single-cell sequencing and gene editing, which will disclose more about how genes function and impact health. Rat models are quite promising, but it's important to use them responsibly. Rats must be treated humanely and research must be conducted responsibly, thus researchers must abide by tight guidelines. Issues such as genetic background variations and environmental influences must be carefully taken into account to guarantee repeatability and accuracy of research findings. In conclusion, studies on the genetics and genomics of rats offer important new perspectives on intricate biological systems and hold enormous promise for advancing our knowledge of human health and illness. We can advance farther and improve society as a whole if we keep funding this area and use technology sensibly.

Keywords: Rat genetics; rat genomics; emerging technologies; ethical considerations; genetic background effects; environmental influences.

1. INTRODUCTION

1.1 Importance of Rat Model in Genetics and Genomics

Rats are well-suited for scientific study, especially in the fields of genetics and genomics, as has long been known. They are important because of their close physiological and genetic resemblances to humans, which make them very good models for studying complex traits and illnesses. Rat models have thus been crucial in advancing our understanding of genetics, pinpointing the underlying causes of a wide range of diseases, and developing novel treatments.

Because of their genetic resemblance to humans, rats are frequently utilized in genetic and genomic research. Rats, particularly the laboratory rat species *Rattus norvegicus*, share around 85% of their genome with humans, making them an ideal model species to study genetic factors connected with human health and disease. [1]. Because of their shared genetic heritage, scientists may investigate the molecular causes of a wide range of illnesses, identify hereditary risk factors, and develop more effectively targeted therapeutics.

Rats offer several advantages as model organisms for genetic and genomic studies. Rats' larger bodies make them easier to handle, observe, and sample tissues for genetic research than mice or other smaller model animals [2]. Rats also live longer than other rodents, which

means that scientists have more time to study the causes, symptoms, and progress of genetic illnesses as well as potential treatments.

Rats also resemble humans in many ways, including their complex behaviors and physiological characteristics [3]. This trait is shared by many other organ systems, including the respiratory, cardiovascular, endocrine, and neurological systems. Rat models therefore provide researchers with a valuable new understanding of the genetic basis of many diseases and complex characteristics involving several physiological systems, such as obesity, diabetes, hypertension, and neurodegenerative disorders.

The availability of various strains with unique genetic backgrounds and phenotypic features is another benefit of using rat models in genetic and genomic research. Because of this genetic diversity, scientists may look into how genetic variation affects complex phenotypes including responsiveness to treatment, illness susceptibility, and other factors. Through the utilization of techniques like genome-wide association studies (GWAS) and quantitative trait locus mapping, scientists can pinpoint the genetic loci linked to particular traits and obtain an understanding of the biochemical mechanisms that underlie these associations.

In general, it is impossible to exaggerate the value of rat models in genetic and genomic studies. These adaptable creatures offer scientists strong resources to decipher the

genome's complexity, comprehend the genetic causes of human illnesses, and create cutting-edge treatment strategies. Researchers can quicken the rate of biomedical discovery and innovation by utilizing the physiological and genetic similarities between humans and rats, which will ultimately improve human health and well-being.

1.2 History and Significance of Rat Models in Biomedical Research

Rats have a long and storied history in biomedical research, dating back to the late 19th century when scientists recognized their potential as valuable model organisms. Over the decades, rats have become indispensable tools in various fields of biomedical research due to their physiological similarities to humans, ease of handling, and relatively short reproductive cycles. Here, we briefly discuss the historical evolution and significance of rat models in biomedical research [4].

- **Early Use in Physiology and Pharmacology:** Because of their small size, ability to adjust to conditions in laboratories, and similar physiological structure to humans, rats were first used in physiological and pharmacological research. Rats were used by scientists to investigate fundamental physiological functions like digestion, respiration, and circulation in the late 1800s and early 1900s. Rats are often used in biomedical research because of these pioneering investigations [5].
- **Research on Diabetes and Endocrinology Contributions:** The discovery of insulin in the early 20th century was one of the major advances in rat research. Insulin treatment for diabetes was developed as a result of Frederick Banting and Charles Best's 1921 discovery of insulin's function in glucose metabolism. The discovery was made possible in large part by the use of rats, as later research showed that insulin was effective in reducing blood sugar levels in diabetic rats. This discovery transformed the way diabetes is treated and demonstrated the value of using rat models in endocrinology studies [6].
- **Function in toxicity and Drug Development:** Because rats metabolize medicines similarly to humans, they are a useful tool in toxicity research and drug

development. Rats are frequently employed in chemical and pharmaceutical safety research, offering vital information on the pharmacokinetics, toxicity, and efficacy of drugs. Because of their very short lifespan, researchers are able to evaluate potential side effects and perform long-term studies on chronic drug exposure. Rats have also proved useful in the development of new medications and treatment approaches by assessing the efficacy and safety of innovative therapies prior to human clinical trials [7].

- **Developments in Genetics and Genomics:** Rats became a significant model organism for genetic study in the middle of the 20th century. Research into inheritance patterns, gene mapping, and genetic illnesses have been made easier by the creation of inbred rat strains with different genetic backgrounds. Rat models have been essential in helping to understand the genetic basis of many human diseases, such as obesity, cancer, hypertension, and neurodegenerative illnesses. Rats are now much more useful for genomic research because of the 2004 completion of the rat genome sequencing project, which gave scientists access to a complete genetic blueprint [8].
- **Contributions to Translational Research:** Rat models are still essential for bridging the gap between fundamental science findings and clinical applications in translational research. Rats are used to study the causes of disease, assess possible treatments, and create new approaches to treatment. Their close physiology and genetic resemblance to humans renders them indispensable for investigating intricate illnesses and evaluating therapies with significant potential for translation. Rats are still essential for expanding our knowledge of human health and illness, from neurological conditions to cardiovascular problems [9].

In conclusion, rat models have a rich history in biomedical research, distinguished by their diverse contributions to physiology, pharmacology, genetics, and translational medicine, among other domains. They are vital resources for scientific research and medical innovation because of their capacity to replicate human disease processes, which makes them significant model organisms. Rat models will

certainly continue to be at the vanguard of scientific inquiry as biomedical research develops, leading to improvements in human health and well-being.

2. RAT AS A MODEL ORGANISM

2.1 Rats as Model Organisms: Advantages for Genetic and Genomic Research

Rats are now considered essential model organisms in genetic and genomic research because of their many unique benefits, which make them helpful tools for examining the intricacies of the genome and how they affect human health. Here, we go over a few of the main benefits of employing rats in genetic and genomic studies:

2.1.1 Human physiological similarity

- Rats and humans have remarkably similar physiologies, especially when it comes to the shape and function of the organs. Since their neurological, endocrine, respiratory, and cardiovascular systems are so similar to human anatomy, they are excellent models for researching human diseases and physiological functions [10].
- Because of these physiological similarities, scientists can look into the genetics of human diseases in a biologically relevant setting, including obesity, diabetes, hypertension, and neurodegenerative disorders. Rat research can yield valuable insights into the mechanisms behind diseases and the development of possible human therapeutics.

2.1.2 Short generation time

- Rats have shorter generation times than other model mammalian animals such as nonhuman primates or pigs [11]. Because several generations may be observed in a very short amount of time, this short generation period speeds up genetic studies.
- Because of the quick turnover of generations, scientists can monitor inheritance patterns, carry out long-term studies, and evaluate the effects of genetic alterations on subsequent generations. Large-scale breeding studies and the study of complex traits with multifactorial inheritance patterns benefit greatly from this efficiency.

2.1.3 Large sizes of litters

- Large litter sizes are characteristic of rats; depending on the strain, the average litter size can range from 6 to 14 pups. Researchers have plenty of opportunity to create experimental cohorts with enough statistical power because of this huge litter size [1].
- Large litter sizes also make it easier to maintain a variety of genetic backgrounds within a single colony and to establish breeding colonies that are genetically uniform. Researchers are able to examine the impact of genetic variation on phenotypic features and illness susceptibility because of this genetic variety.

2.1.4 Reputable genetic resources and tools

- Rats have become more useful as model species in genetic and genomic research as a result of the substantial genetic resources and techniques that have been developed for them over time [12]. Comprehensive genomic maps, high-density genotyping arrays, and databases listing genetic variations and gene expression profiles are some of these resources.
- Moreover, the creation of inbred rat strains with unique genetic histories has made it possible for scientists to carry out accurate genetic mapping investigations, pinpoint quantitative trait loci (QTLs) linked to intricate features, and look into gene-environment interactions [13].

2.1.5 Handling and maintenance ease

- Rats are accessible model organisms for researchers of all skill levels since they are very simple to handle and care for in a laboratory setting. Their compliant demeanor, ability to adjust to captivity, and affordable housing options render them appealing options for extensive genetic and genomic research [14].
- Rats can also be subjected to a wide range of experimental treatments, such as behavioral tests, surgery, and genetic modifications like gene editing. Because of its adaptability, scientists may conduct intricate tests to look at the links between phenotype and genotype as well as gene function.

Table 1. Comparison of rats with other models

Aspect	Rats	Mice	Zebrafish
Size	Larger size compared to mice, making them suitable for surgical procedures and tissue sampling.	Smaller size, typically smaller than rats, but still larger than zebrafish	Relatively small size, ideal for high-throughput experiments
Physiological Similarity to Humans	<ol style="list-style-type: none"> 1. High degree of physiological similarity to humans, particularly in organ structure and function. 2. Insights from rat studies can directly inform our understanding of human disease mechanisms and potential therapies. 	<ol style="list-style-type: none"> 1. High degree of physiological similarity to humans, making them relevant for studying human diseases and physiological processes. 2. Insights from mouse studies can inform our understanding of disease mechanisms and potential therapies. 	<ol style="list-style-type: none"> 1. Considerable physiological similarity to humans, particularly in organ development, cardiovascular system, and immune system. 2. Zebrafish are particularly useful for studying vertebrate development due to their transparent embryos.
Genetic Tools and Resources	<ol style="list-style-type: none"> 1. Extensive genetic tools and resources available, including comprehensive genetic maps, genotyping arrays, and databases. Availability of inbred rat 2. Strains with distinct genetic backgrounds allows for precise genetic mapping studies and investigation of gene-environment interactions. 	<ol style="list-style-type: none"> 1. Extensive genetic tools and resources available, including comprehensive genetic maps, genotyping arrays, and databases. Availability of inbred mouse 2. Strains with distinct genetic backgrounds facilitates genetic mapping studies and investigation of gene-environment interactions. 	<ol style="list-style-type: none"> 1. Growing collection of genetic tools and resources, including mutant lines, transgenic lines, and gene editing techniques. 2. Zebrafish have a fully sequenced genome, facilitating genomic studies.
Ease of Handling and Maintenance	Relatively easy to handle and maintain in laboratory settings. Docile nature, adaptability to captivity, and relatively low housing costs make them attractive choices for genetic and genomic studies. Rats are also [15].	Relatively easy to handle and maintain in laboratory settings. Mice are commonly used due to their small size and ease of handling [15].	Relatively easy to handle and maintain, particularly in large numbers. Their transparent embryos also simplify observation and manipulation during development studies [16].

3. TOOLS AND RESOURCES FOR RAT GENETICS AND GENOMICS

3.1 Overview of the Genetic and Genomic Resources for Rats

The development of genetic and genomic resources for rats has advanced significantly in recent years, giving researchers essential tools to examine the genetic basis of complex features and disorders. Comprehensive genetic maps, excellent genome sequencing data, and databases listing genetic variations and gene expression profiles are some of these resources [17]. An outline of the main genetic and genomic resources for rats is given here:

3.1.1 Projects to sequence the rat genome

- A significant turning point in the study of rat genetics and genomics was reached in 2004 with the completion of the rat genome sequencing project. A thorough reference sequence for the entire rat genome was made available to researchers with the publication of the first draft of the rat genome in the journal Nature.
- The goal of further work has been to enhance the completeness and quality of the rat genome assembly. This has included identifying and annotating regulatory elements, non-coding RNAs, and genes that code for proteins. As a result of these efforts, excellent reference genome assemblies for a variety of rat strains have been created, improving the precision and dependability of genomic investigations [18].

3.1.2 Maps of genetic variations

- Because they show the relative locations of genetic markers along chromosomes, genetic maps are essential tools for genetic studies. Rat genetic maps have been created using a variety of molecular markers, such as sequence-tagged sites (STS), microsatellites, and single nucleotide polymorphisms (SNPs) [19].
- These genetic maps make it easier to uncover genomic regions linked to complex traits and disorders using genetic linkage analysis, quantitative trait locus (QTL) mapping, and fine-mapping investigations. Researchers can identify

potential genes underlying phenotypic features and explore their functional importance by using high-density genomic mapping.

3.1.3 Databases

Rat genetic and genomic data has been compiled into a number of databases, giving researchers quick access to a plethora of material for their research. Among these databases are

- **RGD (rat genome database):** Rat genetic, genomic, and phenotypic data are all integrated into one comprehensive database called RGD. It offers curated data on rat strains and genetic variants as well as genome annotations, genetic maps, QTLs, and gene expression data [20].
- **Rat mine:** Using a versatile and user-friendly interface, users may query and analyze genomic datasets using RatMine, a data warehouse that integrates genetic data from multiple sources. It gives users access to functional annotations for genes and proteins, genetic variation data, and genome annotations [21].
- **Rat genomic databases:** A number of additional databases concentrate on particular facets of the rat genome, including comparative genomics, gene expression, and epigenetics. Researchers that are interested in examining particular genetic traits or processes in rats can find useful materials in these databases [22].

3.1.4 Functional genomics resources

- Rat functional genomics research can be conducted using a number of resources, including genetic and genomic databases. These resources contain sets of transgenic rat lines, libraries of mutant rat strains, and CRISPR/Cas9 gene editing tools [23].
- By examining the biological functions of certain genes and genetic variations in vivo, functional genomics studies enable researchers to gain insight into the functional importance and possible therapeutic uses of these genetic variations. These resources allow functional validation of candidate genes and pathways found through genomic investigations, which complement genetic and genomic studies.

3.2 Common Methods in Genomics and Genetics Research in Rats

3.2.1 Mapping quantitative trait locus (QTL)

- Using a technique called QTL mapping, one can find genetic areas linked to quantitative variables like behavior, physiological characteristics, or disease susceptibility.
- By crossing two genetically distinct rat strains, scientists may examine how the progeny's phenotypic features and genetic markers separate.
- Researchers can discover genomic regions (QTLs) associated with the characteristic of interest by comparing the variance in phenotypic traits with the inheritance pattern of genetic markers [24].

3.2.2 Studies of genome-wide associations (GWAS)

- GWAS is an effective technique for locating genetic variations linked to complicated characteristics or illnesses.
- GWAS involves genotyping a large number of genetic markers throughout the genome in a population of rats that are not related and have different characteristics. After that, statistical analysis are carried out to determine whether genetic variants are substantially linked to the desired attribute.
- Rats with complex features and disorders can have new candidate genes and pathways revealed by GWAS [25].

3.2.3 Genome editing mediated by CRISPR/Cas9

- CRISPR/Cas9 technology allows for precision editing of the rat genome by introducing specific mutations, insertions, or deletion.
- Scientists create guide RNAs (gRNAs) that are complementary to particular genomic loci and introduce them into rat embryos or somatic cells along with the Cas9 enzyme.
- At the target site, the Cas9 enzyme causes double-strand breaks that are then fixed by the cell's own repair systems, frequently leading to changes such as knockout or knockin of genes.
- Rats' precise genetic alterations can be produced by CRISPR/Cas9-mediated

genome editing, which makes it easier to study the functions of individual genes and how they relate to the pathophysiology of disease [26].

4. DISEASE MODELS AND TRANSLATIONAL RESEARCH

4.1 Emphasizing the Use of Rat Models in Human Disease Research

Rat models have been essential in helping us understand human diseases in a number of areas, such as cancer, neurological disorders, metabolic disorders, and cardiovascular diseases. Their genetic richness, physiological closeness to humans, and amenability to experimental manipulations make them great instruments for translational research and disease modelling [27]. Here, we go over the important contributions that rat models have made to the understanding of several key disease categories:

4.1.1 Cardiovascular disease

- The pathogenesis of cardiovascular disorders, including hypertension, heart failure, and atherosclerosis, has been clarified in large part thanks to the use of rat models.
- The creation of antihypertensive medications and the identification of important regulatory systems involved in blood pressure management have resulted from studies on hypertension in rats [28].
- Heart failure and myocardial infarction rat models have shed light on cardiac remodeling mechanisms and heart failure treatment approaches.
- Research on atherosclerosis in rats has advanced our knowledge of the underlying molecular pathways and aided in the creation of cutting-edge treatments that target inflammation and lipid metabolism.

4.1.2 Cancer

- Numerous aspects of cancer biology, such as tumor initiation, development, metastasis, and therapeutic responses, have been studied extensively using rat models.
- The discovery of genetic and environmental variables that contribute to the development of cancer has been made

easier by the use of carcinogen-induced tumor models in rats.

- Researchers can now study tumor microenvironment interactions, oncogenic pathways, and new anticancer medicines thanks to the use of xenograft and transgenic rat models of cancer.
- Additionally useful for preclinical testing of targeted treatments, immunotherapies, and chemopreventive medicines in the treatment of cancer are rat models [29].

4.1.3 Conditions related to neurology

- Rat models have made a substantial contribution to our knowledge of neurological conditions such as epilepsy, Parkinson's disease, Alzheimer's disease, and stroke.
- Key clinical aspects of neurodegenerative illnesses have been recapitulated in transgenic rat models expressing mutant genes linked to these disorders, offering valuable insights into disease mechanisms.
- The assessment of neuroprotective tactics, stem cell therapies, and rehabilitation approaches for stroke recovery has been made possible by the use of rat models.
- Rat epilepsy research has helped produce antiepileptic medications and clarified the fundamental principles of seizure production and propagation [30].

4.1.4 Disorders of metabolism

- Numerous metabolic diseases, including obesity, diabetes, and dyslipidemia, have been studied in rat models.
- Rat models of obesity and diabetes that are produced by diet and genetics have shed light on the pathophysiology of insulin resistance, beta-cell malfunction, and metabolic problems.
- Rat models of dyslipidemia and atherosclerosis have proven invaluable in the study of lipid metabolism, cardiovascular risk factors, and dyslipidemia-specific treatment approaches.
- Rats used as bariatric surgery models have made it easier to examine the mechanisms behind metabolic surgery and the changes in metabolism linked to weight loss surgery [31].

All things considered, these instances demonstrate the effective transfer of knowledge

from rat research to clinical settings in a variety of medical specialties. Researchers have improved patient outcomes across a range of disease conditions by utilizing the physiological and genetic similarities between rats and humans to uncover novel therapeutic targets and build efficient treatment techniques. The relevance of funding preclinical research employing animal models to enhance medical science and meet unmet clinical needs is highlighted by the translational influence of rat research.

5. NEW TECHNOLOGIES AND THEIR PROSPECTS

5.1 Investigating Novel Technologies in Rat Genetics and Genomics Studies

Recent years have seen tremendous progress in the field of rat genetics and genomics research, generated by new technology.

5.1.1 Single-cell sequencing

Single-cell sequencing is a pioneering tool that enables researchers to investigate cellular diversity and gene expression patterns at unprecedented depths. Single-cell sequencing makes it possible to profile individual cells, in contrast to conventional bulk sequencing techniques that yield an average gene expression across cell populations. This discloses discrete cell kinds, conditions, and changes in intricate biological systems [32]. Single-cell sequencing is used in several biological situations in rat genetics and genomics research, including immunological responses, neurodevelopment, and cancer biology. For example, single-cell RNA sequencing (scRNA-seq) experiments conducted in rat brains have shown a variety of cell types and transcriptional states, providing insights on the diversity of neurons and the organization of circuits. In a similar vein, immune cell populations, functional states, and responses have been clarified by scRNA-seq investigations of immune cells in rat models to pathogens or therapeutic interventions.

5.1.2 Multi-omics approaches

Multi-omics techniques use data from various molecular levels, such as genomes, transcriptomics, epigenomics, proteomics, and metabolomics, to investigate biological systems in greater depth. Researchers can decipher

complex regulatory networks, find biomarkers, and clarify the molecular mechanisms behind the pathogenesis of disease by merging omics datasets. Multi-omics techniques have enormous potential in rat genetics and genomics research to analyze gene regulatory networks, find genetic modifiers of complex phenotypes, and clarify the interaction of genetic and environmental variables in disease susceptibility [33]. Combining data from genomes and epigenomics, for instance, helps clarify the epigenetic changes connected to disease states, whereas integrating data from transcriptomics and genomics can uncover gene regulatory networks underpinning complex phenotypes.

5.1.3 Technologies for gene editing

Because they allow for accurate and effective rat genome alteration, genome editing technologies, especially CRISPR/Cas9-mediated genome editing, have completely changed the area of rat genetics. Researchers can now more easily carry out functional studies of genes and their role in disease pathophysiology by introducing targeted mutations, insertions, or deletions at specified genomic loci thanks to CRISPR/Cas9 [34]. CRISPR/Cas9-mediated genome editing has been extensively employed in rat genetics and genomics research to create illness models, examine gene function, and look into potential treatment targets. For instance, CRISPR/Cas9 has been used by researchers to insert mutations linked to human diseases into rat models, which has allowed for the preclinical investigation of possible treatments and the replication of disease characteristics. Furthermore, high-throughput screening of therapeutic targets in rats and functional validation of candidate genes have been made easier by CRISPR/Cas9-mediated gene deletion and knock-in techniques.

5.2 Future Prospects: Rat Models in Precision Medicine and Personalized Therapeutics

In rat genetics and genomics research, future advancements focus on utilizing rat models for precision medicine and personalized therapeutics. This includes refining genetic resources like rat strains and genome editing tools to better model human diseases and identify new therapeutic targets. Rat models are gaining traction in precision medicine initiatives, offering a platform for testing personalized treatments and predictive biomarkers before

clinical trials. Integrating genomic data from rat models into clinical decision-making can optimize treatment strategies and improve patient outcomes. Additionally, advancements in multi-omics technologies will provide insights into disease mechanisms and personalized interventions. Overall, incorporating rat models into precision medicine holds promise for enhancing personalized therapeutics and advancing healthcare solutions.

6. ETHICAL PROBLEMS AND CHALLENGES

6.1 Ethical Considerations in Rat Genetics and Genomics Research: Animal Welfare and Gene Editing

6.1.1 Concerns regarding animal welfare

- Rats should have suitable living circumstances, which should include enough room, bedding, and environmental stimulation to enhance their wellbeing.
- Reduce suffering and agony during research processes by employing humane euthanasia, analgesia, and anesthesia [35].
- Respect the moral standards and legal frameworks set forth by institutional committees for the care and use of animals in order to guarantee that rats are treated ethically during the course of research.

6.1.2 Utilizing gene editing technologies responsibly

- When using gene editing methods, such as CRISPR/Cas9, use caution and wisdom to prevent unforeseen outcomes like off-target mutations.
- Consider the ethical consequences of changing the rat genome, such as introducing new mutations or creating genetically engineered species [36].
- Respect the legal and ethical requirements that regulate the use of gene editing technology in research settings.

6.1.3 Transparency and public engagement

- Encourage transparent information regarding research methods, such as the use of gene editing technology and rats, in order to advance public awareness and transparency.

- Assist in educating the public, legislators, and stakeholders about the moral ramifications of rat genetics and genomics research.
- Prioritize the sharing of research findings, making sure that all pertinent stakeholders are adequately informed of the advantages and disadvantages of utilizing rats in genetic and genomic research [37].

6.1.4 Institutional monitoring and adherence

- Assure adherence to institutional guidelines and policies on the use of animals in research, including procedures for ethical review and committees overseeing institutional animal care and usage.
- Put in place procedures to track and assess the welfare of research rats, such as routine health checks and the provision of necessary veterinary care.
- Encourage research organizations to adopt a culture of ethical behavior and responsible research procedures by stressing the significance of adhering to ethical principles and standards for animal welfare in all facets of rat genetics and genomics research [38].

6.2 Challenges and Limitations of Rat Models in Genetic and Genomic Research

Rat models are subject to several limits and obstacles in genetic and genomic research, which may impact the dependability and interpretation of experimental outcomes [39]. A major obstacle is the existence of genetic background effects, whereby differences between rat strains might produce inconsistent phenotypic results. Genetic heterogeneity within rat populations can make it more difficult to identify the genetic variants that cause certain traits and further confuse the link between genotype and phenotype. Environmental variables can present a big problem since they can introduce unpredictability and skew experimental results. Some examples of these factors are stress, housing circumstances, and diet. It is imperative to establish uniform environmental conditions among research institutions in order to minimize variability and enhance the reproducibility of results. Furthermore, rat genetic and genomic research is further complicated by the complexity of

phenotypes, particularly those that are influenced by several genes or environmental variables.

Finally, the development of research in this area is hampered by technological constraints, such as the time-consuming and expensive procedure of creating genetically modified rat models and the scarcity of complete genetic resources. Rat models can be made more useful in genetic and genomic research by addressing these issues by careful experimental design, managing environmental factors, using a variety of rat strains [40], and incorporating multi-omics techniques.

7. CONCLUSION

Rat genetics and genomics research are pivotal in uncovering the mechanisms of complex traits and diseases. Utilizing rat models, researchers have made significant strides across various biological processes, from neurodevelopment to metabolic disorders. Advantages like physiological similarity and genetic manipulability have led to groundbreaking discoveries in biomedicine.

Emerging technologies such as single-cell sequencing and gene editing hold promise for deeper insights into the rat genome and human health implications. However, ethical considerations, including animal welfare and responsible research, are paramount. Addressing challenges like genetic background effects requires careful experimental design.

Overall, rat genetics and genomics research offer vital insights into biological systems, with potential to advance medical science and improve human health. Continued investment, ethical awareness, and technological innovation will drive further progress in understanding complex traits and diseases.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Otto GM, Franklin CL, Clifford CB. Biology and diseases of rats. Laboratory animal medicine: Elsevier. 2015;151-207.
2. Aitman TJ, Boone C, Churchill GA, Hengartner MO, Mackay TF, Stemple DL. The future of model organisms in human

- disease research. *Nature Reviews Genetics*. 2011;12(8):575-82.
3. Sharp P, Villano JS. *The laboratory rat*: CRC press; 2012.
 4. Hedrich HJ. *History, strains and models. The Laboratory Rat*: Elsevier. 2000;3-16.
 5. Sengupta P. The laboratory rat: relating its age with human's. *International Journal of Preventive Medicine*. 2013;4(6):624.
 6. King AJ. The use of animal models in diabetes research. *British Journal of Pharmacology*. 2012;166(3):877-94.
 7. Greek R. *Animal models in drug development. New Insights into Toxicity and Drug Testing In Tech, Croatia/Europe*. 2013:123-52.
 8. Jacob HJ, Lazar J, Dwinell MR, Moreno C, Geurts AM. Gene targeting in the rat: Advances and opportunities. *Trends in Genetics*. 2010;26(12):510-8.
 9. Hashway SA, Wilding LA. *Translational potential of rats in research. The laboratory rat*: Elsevier. 2020;77-88.
 10. Treuting PM, Dintzis SM, Montine KS. *Comparative anatomy and histology: A mouse, rat, and human atlas*: Academic Press; 2017.
 11. Renner S, Dobenecker B, Blutke A, Zoels S, Wanke R, Ritzmann M, Wolf E. Comparative aspects of rodent and nonrodent animal models for mechanistic and translational diabetes research. *Theriogenology*. 2016;86(1):406-21.
 12. Chen K, Baxter T, Muir WM, Groenen MA, Schook LB. Genetic resources, genome mapping and evolutionary genomics of the pig (*Sus scrofa*). *International Journal of Biological Sciences*. 2007;3(3):153.
 13. Fu G, Dai X, Symanzik J, Bushman S. Quantitative gene–gene and gene–environment mapping for leaf shape variation using tree-based models. *New Phytologist*. 2017;213(1):455-69.
 14. Health Nlo. *Guide for the care and use of laboratory animals*: National Academies; 1985.
 15. Domínguez-Oliva A, Hernández-Ávalos I, Martínez-Burnes J, Olmos-Hernández A, Verduzco-Mendoza A, Mota-Rojas D. The importance of animal models in biomedical research: Current insights and applications. *Animals*. 2023;13 (7): 1223.
 16. Veldman MB, Lin S. Zebrafish as a developmental model organism for pediatric research. *Pediatric Research*. 2008;64(5):470-6.
 17. Shimoyama M, Smith JR, Bryda E, Kuramoto T, Saba L, Dwinell M. Rat genome and model resources. *ILAR journal*. 2017;58(1):42-58.
 18. Hermsen R, de Ligt J, Spee W, Blokzijl F, Schäfer S, Adami E, et al. Genomic landscape of rat strain and substrain variation. *BMC Genomics*. 2015;16:1-14.
 19. Jones N, Ougham H, Thomas H, Pašakinskienė I. Markers and mapping revisited: Finding your gene. *New Phytologist*. 2009;183(4):935-66.
 20. Twigger S, Lu J, Shimoyama M, Chen D, Pasko D, Long H, et al. Rat Genome Database (RGD): Mapping disease onto the genome. *Nucleic Acids Research*. 2002;30(1):125-8.
 21. Laulerkind SJ, Hayman GT, Wang S-J, Hoffman MJ, Smith JR, Bolton ER, et al. Rat genome databases, repositories, and tools. *Rat Genomics*. 2019:71-96.
 22. Shimoyama M, Hayman GT, Laulerkind SJ, Nigam R, Lowry TF, Petri V, et al. The rat genome database curators: Who, what, where, why. *PLoS computational biology*. 2009;5(11):e1000582.
 23. Galichet C, Lovell-Badge R. Applications of genome editing on laboratory animals. *Laboratory Animals*. 2022;56(1):13-25.
 24. Van Ooijen JW. Accuracy of mapping quantitative trait loci in autogamous species. *Theoretical and Applied Genetics*. 1992;84:803-11.
 25. Hayes B. Overview of statistical methods for genome-wide association studies (GWAS). *Genome-wide association studies and genomic prediction*. 2013:149-69.
 26. Xue C, Greene EC. DNA repair pathway choices in CRISPR-Cas9-mediated genome editing. *Trends in Genetics*. 2021;37(7):639-56.
 27. Szpirer C. Rat models of human diseases and related phenotypes: A systematic inventory of the causative genes. *Journal of Biomedical Science*. 2020;27(1):84.
 28. Doggrell SA, Brown L. Rat models of hypertension, cardiac hypertrophy and failure. *Cardiovascular Research*. 1998;39 (1):89-105.
 29. Talmadge JE, Singh RK, Fidler IJ, Raz A. Murine models to evaluate novel and conventional therapeutic strategies for cancer. *The American Journal of Pathology*. 2007;170(3):793-804.
 30. Cenci MA, Whishaw IQ, Schallert T. *Animal models of neurological deficits*:

- How relevant is the rat? *Nature Reviews Neuroscience*. 2002;3(7):574-9.
31. Buettner R, Schölmerich J, Bollheimer LC. High-fat diets: Modeling the metabolic disorders of human obesity in rodents. *Obesity*. 2007;15(4):798-808.
 32. Ofengeim D, Giagtzoglou N, Huh D, Zou C, Yuan J. Single-cell RNA sequencing: Unraveling the brain one cell at a time. *Trends in Molecular Medicine*. 2017;23(6):563-76.
 33. Hasin Y, Seldin M, Lusis A. Multi-omics approaches to disease. *Genome Biology*. 2017;18:1-15.
 34. Sato M, Nakamura S, Inada E, Takabayashi S. Recent advances in the production of genome-edited rats. *International Journal of Molecular Sciences*. 2022;23(5):2548.
 35. Lynch WJ, Nicholson KL, Dance ME, Morgan RW, Foley PL. Animal models of substance abuse and addiction: Implications for science, animal welfare, and society. *Comparative medicine*. 2010;60(3):177-88.
 36. Cox DBT, Platt RJ, Zhang F. Therapeutic genome editing: Prospects and challenges. *Nature Medicine*. 2015;21(2):121-31.
 37. Mitchell AS, Hartig R, Basso MA, Jarrett W, Kastner S, Poirier C. International primate neuroscience research regulation, public engagement and transparency opportunities. *Neuroimage*. 2021;229:117700.
 38. Guignet M, Campbell A, Vuong J, Whittington D, White HS. Perampanel's forgiveness factor in a variable medication adherence paradigm in a rat model of chronic epilepsy. *Journal of Translational Medicine*. 2023;21(1):642.
 39. McGonigle P, Ruggeri B. Animal models of human disease: Challenges in enabling translation. *Biochemical Pharmacology*. 2014;87(1):162-71.
 40. Padmanabhan S, Joe B. Towards precision medicine for hypertension: A review of genomic, epigenomic, and microbiomic effects on blood pressure in experimental rat models and humans. *Physiological Reviews*. 2017;97(4):1469-528.

© Copyright (2024): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<https://prh.mbimph.com/review-history/3419>