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ANIMAL MODEL IN PERCLINICAL RESEARCH FOR ANTI CANCER

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ABSTRACT

Cancer remains one of the major causes of death across the world, which creates a constant need for better and safer treatment options. Before any new drug is tested in humans, it must first go through detailed preclinical studies to evaluate its safety, effectiveness, pharmacokinetics, and possible toxic effects. At this stage, animal models are extremely important because they allow researchers to study tumor behavior, disease progression, and treatment responses within a living biological system. Various animal models, ranging from small rodents to larger mammals, provide valuable information about cancer development and how drugs function inside the body. Small animals such as mice and rats are widely used because they reproduce quickly, are relatively affordable to maintain, and share several genetic similarities with humans. More advanced models like genetically engineered mice, xenografts, and patient-derived xenografts have significantly improved the reliability of cancer research. Larger animals including pigs, dogs, and rabbits are also useful because their physiological characteristics often resemble those of humans, making them suitable for pharmacokinetic and translational studies. Despite these advantages, animal models also present certain limitations, mainly due to biological differences between species and ethical concerns regarding their use. To address these issues, researchers follow the 3R principles—Replacement, Reduction, and Refinement—to improve both scientific quality and animal welfare. In addition, modern technologies such as artificial intelligence, molecular imaging,

and genomic analysis are helping increase the accuracy and predictive value of animal studies. This review outlines the importance, different types, applications, advantages, and limitations of animal models in anticancer drug development, while also discussing emerging technologies that are shaping the future of preclinical cancer research.

KEYWORDS: Cancer, Animal Models, Preclinical Research, Anticancer Drugs, Xenograft, AI in Oncology.

1. INTRODUCTION

Animal models are living organisms that are used in biomedical research to simulate human diseases and biological processes. They help scientists understand how diseases develop and allow them to test new treatment strategies before moving to human clinical trials. Because many animals share physiological, genetic, and molecular similarities with humans, they provide useful insights into disease mechanisms and treatment outcomes.

These models are commonly used to study complex diseases such as cancer, diabetes, cardiovascular disorders, neurological conditions, and infectious diseases. Through carefully designed experiments, researchers can observe disease progression, identify potential therapeutic targets, and evaluate the effectiveness of new drugs in controlled environments.

In cancer research, animal models are particularly important for studying tumor initiation, growth, and metastasis, as well as the interaction between cancer cells and their surrounding microenvironment. They also help researchers evaluate drug safety, determine appropriate dosage levels, and detect possible side effects. Without preclinical testing in animals, introducing new treatments into human clinical trials would be highly unsafe.

Over time, the development of animal models has progressed significantly. Advances such as genetic engineering, patient-derived xenografts, and modern imaging technologies have made it possible to replicate human cancers more accurately. As a result, animal models have become an essential part of modern drug discovery and development.

2. Importance of Animal Models in Biomedical Research

Animal models provide several important benefits that support scientific research. They allow researchers to:

- Study disease mechanisms and biological pathways

- Evaluate drug safety and toxicity
- Test the effectiveness of potential treatments
- Understand genetic and environmental influences on disease
- Develop medical devices and therapeutic strategies

Another key advantage of animal studies is that some experiments cannot ethically or practically be conducted in humans. Animal models allow scientists to observe disease development from its early stages and study long-term treatment outcomes under controlled laboratory conditions.

Because of these advantages, animal research acts as a bridge between laboratory discoveries and clinical applications.

3. Preclinical Research

Preclinical research represents the early stage of drug development that occurs before human testing. During this phase, scientists examine the biological activity, pharmacokinetics, and safety of new compounds through laboratory experiments and animal studies.

Typically, research begins with in vitro experiments using cultured cells to identify potential therapeutic effects. However, these models cannot fully reproduce the complexity of a living organism. For this reason, animal studies are essential for understanding how a drug behaves inside the body.

Preclinical studies usually focus on several important factors

- Drug absorption
- Distribution within body tissues
- Metabolism
- Excretion
- Toxicological effects

These studies help researchers determine safe dosage levels and identify possible risks before clinical trials begin.

4. Overview of Cancer

Cancer is a group of diseases characterized by uncontrolled cell growth and the ability of abnormal cells to invade nearby tissues and spread to other parts of the body. It develops

when genetic mutations disrupt the normal processes that regulate cell growth and division.

These mutations may activate oncogenes, inactivate tumor suppressor genes, or interfere with DNA repair mechanisms. As a result, cells begin to multiply uncontrollably and eventually form tumors.

Several factors can contribute to the development of cancer, including:

- Exposure to chemical carcinogens
- Radiation
- Viral infections
- Genetic susceptibility
- Environmental pollution

Cancer remains a major global health problem and continues to be one of the leading causes of death. Although advances in diagnosis and treatment have improved survival rates, many types of cancer still require more effective therapies.

5. Classification of Anticancer Drugs

Anticancer drugs are generally classified according to their mechanisms of action against cancer cells.

5.1 Chemotherapy Drugs

Chemotherapy drugs target rapidly dividing cancer cells, although they may also affect normal cells.

Examples include

- Cyclophosphamide
- Cisplatin
- Methotrexate
- Gemcitabine
- Paclitaxel
- Vincristine
- Doxorubicin

5.2 Targeted Therapy

Targeted therapies act on specific molecules or signaling pathways involved in cancer development.

Examples include

- Imatinib
- Erlotinib
- Gefitinib
- Sorafenib
- Sunitinib

5.3 Immunotherapy

Immunotherapy enhances the body's immune system so that it can recognize and destroy cancer cells.

Examples include

- Anti-PD-1 antibodies
- Anti-PD-L1 antibodies
- Anti-CTLA-4 antibodies

5.4 Natural Compounds

Many natural substances are also being investigated for their potential anticancer effects.

Examples include:

- Curcumin
- Resveratrol
- Quercetin
- Berberine

6. Role of Animal Models in Cancer Drug Development

Animal models play a key role in studying tumor growth and evaluating how drugs affect cancer in a living system. They provide valuable information about cancer biology and treatment responses.

Major roles include

- Understanding Cancer Biology

- Researchers can observe tumor formation, metastasis, and genetic changes involved in cancer progression.
- Drug Efficacy Testing
- Animal studies help determine whether new treatments can reduce tumor growth or improve survival.
- Toxicity Evaluation
- Scientists examine whether drugs cause damage to organs such as the liver, kidneys, or heart.
- Pharmacokinetic Studies
- Animal models help determine how drugs are absorbed, distributed, metabolized, and eliminated.
- Immunotherapy Research
- Advanced animal models are used to evaluate immune-based cancer therapies.

7. Types of Animal Models Used in Anticancer Research

Animal models used in cancer research are broadly categorized into small animal models and large animal models.

8. Small Animal Models

Small animals are widely used in research because they are affordable, easy to handle, and genetically well understood.

Rodent Models (Mice and Rats)

Mice are the most commonly used animals in cancer experiments. Their genomes can be modified easily, allowing researchers to create models that closely resemble human cancers.

Advantages

- Rapid reproduction
- Low cost
- Availability of advanced genetic tools

Limitations

- Differences in immune responses and metabolism compared with humans.

9. Transplantation Models

Syngeneic Models

In these models, tumor cells from the same species are implanted into genetically similar animals.

Advantages

- Functional immune system
- Stable tumor growth

Xenograft Models

Human tumor cells are transplanted into immunodeficient mice.

Advantages

- Ability to study human tumor behavior
- Useful for drug screening

However, species differences and altered tumor characteristics may still occur.

10. Genetically Engineered Mouse Models

These models are created by modifying genes that are involved in cancer development.

Common types include

- Knockout mice
- Knock-in mice
- Transgenic mice
- Conditional gene models

These models help scientists study tumor genetics and evaluate targeted therapies.

11. Patient-Derived Xenograft Models

In this approach, tumor tissues taken directly from patients are implanted into mice.

Advantages

- Maintain tumor heterogeneity
- Preserve original genetic mutations
- Useful for personalized medicine research

However, they require surgical samples and can be costly to maintain.

12. Large Animal Models

Larger animals are sometimes used because their physiology is closer to that of humans.

- Examples include:
- Rabbits – Used in cancer therapy and drug delivery studies.
- Pigs – Share many anatomical and genetic similarities with humans.
- Dogs – Naturally occurring cancers in dogs often resemble human cancers.
- Tree Shrews – Genetically closer to primates than rodents.
- Sheep and Goats – Useful in surgical oncology and pharmacokinetic research.
- Non-Human Primates – Provide the closest similarity to humans but are subject to strict ethical regulations.

13. Applications of Animal Models in Anticancer Research

Animal models are widely used in different areas of cancer research, including:

- Tumor biology studies
- Drug screening
- Toxicity testing
- Immunotherapy development
- Personalized medicine research
- Studies on metastasis mechanisms

These studies generate valuable data that help guide human clinical trials.

14. Advantages of Animal Models

- Allow the study of complex biological systems
- Enable evaluation of drug safety and effectiveness
- Faster disease progression supports quicker research
- Possibility of genetic manipulation
- Real-time monitoring of tumor development

15. Limitations of Animal Models

Despite their importance, animal models have certain limitations:

- Biological differences between animals and humans
- Limited ability to fully predict human clinical outcomes
- Ethical concerns related to animal welfare
- High research costs

- Some models do not accurately reproduce the human tumor microenvironment

16. Ethical Considerations and the 3R Principle

- Ethical responsibility is a key aspect of animal research. Scientists follow the 3R principles:
- Replacement – Using alternative methods whenever possible
- Reduction – Minimizing the number of animals used in experiments
- Refinement – Improving experimental procedures to reduce pain and distress
- Strict institutional and international regulations ensure that animals are used responsibly in research.

17. Emerging Technologies: AI-Assisted Animal Models

Artificial intelligence is becoming increasingly important in cancer research. AI technologies can assist researchers by:

- Detecting tumors using imaging data
- Predicting responses to drugs
- Analyzing complex genomic information
- Monitoring animal behavior and disease progression

The integration of AI into preclinical research can improve accuracy and accelerate the development of new therapies.

CONCLUSION

Animal models continue to play a vital role in the development of anticancer drugs. They provide important insights into cancer biology, help evaluate new therapies, and ensure safety before human clinical trials begin. Although differences between animal and human biology present challenges, improvements in model design and technology are helping overcome these limitations.

Advances in genetic engineering, imaging methods, and artificial intelligence are transforming preclinical cancer research. When combined with ethical research practices, these innovations will contribute to the development of safer, more effective, and personalized cancer treatments.

Overall, animal models remain a crucial link between laboratory discoveries and clinical applications, playing an important role in the global effort to combat cancer.

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