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EXPERIMENTAL ANIMAL MODELS IN ONCOLOGY: A REVIEW OF TUMOR PROGRESSION AND THERAPY

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Abstract:

Cancer remains one of the leading causes of mortality worldwide and continues to represent a major challenge for healthcare systems due to its complex and multifactorial nature. Despite significant advancements in diagnosis and treatment, the global burden of cancer continues to rise, emphasizing the need for a deeper understanding of its underlying mechanisms and the development of more effective therapeutic strategies. Experimental models have become essential tools in cancer research, with animal models playing a particularly important role in bridging the gap between in vitro studies and clinical applications.

Animal models provide a dynamic and physiologically relevant system that allows researchers to study tumor initiation, progression, invasion, and metastasis within a living organism. These models also enable the evaluation of tumor responses to various therapeutic interventions, thereby contributing to the development of safer and more effective anticancer drugs. In addition, animal models facilitate the investigation of molecular and genetic mechanisms underlying carcinogenesis, as well as interactions between tumor cells and the host microenvironment, including immune responses and angiogenesis.

Various types of animal models are widely used in oncology research, including spontaneous tumor models, chemically induced tumor models, xenograft models, orthotopic models, patient-derived xenografts, and genetically engineered mouse models. Each of these models offers unique advantages and helps researchers explore different aspects of tumor biology, ranging from genetic alterations to treatment responses. These models have significantly advanced modern cancer therapies, including targeted therapy, immunotherapy, and gene-based treatments.

Despite certain limitations, including differences between animal and human biology, animal models remain indispensable in cancer research. They continue to provide valuable insights that support the discovery, evaluation, and optimization of novel diagnostic and therapeutic strategies. Overall, animal models play a critical role in improving our understanding of cancer and advancing the development of more effective and personalized treatment approaches.

Keywords:Animal models; Cancer research; Spontaneous tumor models; Chemically induced tumor models; Xenograft models; Orthotopic tumor models; Patient-derived xenograft (PDX); Genetically engineered mouse models (GEMM); Humanized mouse models.

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INTRODUCTION:

Health care systems are under threat as the cause of mortality spreads worldwide through a vicious disease called cancer, and it is nowhere to be found backing off, as it is the second leading cause of death throughout the planet. For instance, millions of individuals are diagnosed with cancer, and a vast number of these cases result in mortality, hence the need for advanced therapy.

Cancer is a complex disorder that has the ability to destroy the body's systems through uncontrollable cell division and tissue invasion. Here, early diagnosis is challenging, which makes the treatment hard.

This disorder differs in people based on gender and age factor. Men are commonly diagnosed with cancers like prostate, lung and bronchus, colon and rectum, and urinary bladder cancers, whereas in women, cancers like breast cancer is observed quite often, followed by lung and bronchus, uterine corpus, and thyroid. In children, cancers of the blood, brain, and lymphatic system are commonly reported.

The development of cancer occurs when a series of mutations in the genome disrupt normal functions. This process is supported by various environmental factors and chemical agents. Lung cancer is caused by exposure to carcinogenic chemicals, particularly smoking excessively.

In addition to chemical agents, biological agents like viruses and bacteria, along with physical factors like radiation, also contribute to the causation of cancer. These agents affect the genetic material, leading to abnormalities and mutations.

At the molecular level, cancer disrupts the cellular mechanisms and alter the functioning of essential genes.

Mutations in proto-oncogenes can convert them into oncogenes that promote uncontrolled cell proliferation. Similarly, the loss of tumor suppressor gene function removes essential growth control mechanisms. DNA repair systems, which normally correct genetic damage, may also become impaired, further contributing to cancer progression.

Role of animal models in cancer research

Animal models play an essential role in the development of cancer treatment. They help scientists in identifying the cause, initiation, development, and progression of tumors in the biological system. This is an important link between the lab studies and clinical trials, allowing the scientists to study the disorder in detail and evaluate it within the organism before they are tested in humans.

Furthermore, animal models are used to assess the safety and efficacy of anticancer therapies before they are introduced to human studies. These models help in optimizing treatments and reducing risks related to clinical trials.

These also help scientists understand the depth of cancer, which is the genetic basis. Animal models are used as they show very similar mutations to those of humans. Hence, the researchers are able to study cancer effectively. In addition, animal models make it possible to examine how cancer cells interact with the surrounding tumor microenvironment, including immune cells, blood vessels, and nearby tissues.

Understanding these interactions provides valuable insights into how tumors grow and respond to different treatments.

Despite their numerous advantages, animal models are not without limitations. Differences in physiology and genetic makeup between animals and humans can sometimes affect the accuracy of results. Therefore, continuous improvements in experimental techniques and model design are necessary to enhance their relevance to human disease. Nevertheless, animal models remain indispensable tools in cancer research, contributing significantly to the development of effective diagnostic and therapeutic strategies.

Types of Animal Models Used in Cancer Research

Studies cannot be directly conducted on humans because of ethical reasons hence, we take the help of animal models to understand the disease and discover its treatments. Various biomedical investigations are carried out on animals like rodents, dogs, cattle, horses, reptiles, and birds. Among these rodents like mice and rats, have a greater advantage and are widely used as they have well-characterized genetic strains, availability of standardized genetic mapping tools, extensive scientific literature, and advanced systems for genetic monitoring.

Spontaneous Tumor Models

Spontaneous Tumor Models relate to cancer that develops naturally in animals without any intervention. Here, tumors arise in natural conditions, and increase through biological interactions, hence they are highly similar to human cancer development. As a result, they are highly valuable for studying early tumor formation, disease progression, and metastasis in a realistic setting.

Tumors in cats and dogs show a resemblance to human malignancies in terms of histopathology, genetic alterations, and clinical behaviour. Due to these similarities, spontaneous tumor models provide insights to researchers to evaluate potential diagnostics and develop therapeutics.

These also have certain disadvantages. The development of cancer is unpredictable, which makes controlled studies difficult. Here, the animals in which natural tumors occur are less available, which restricts their routine use in lab research. Regardless, spontaneous tumor models remain an important component of cancer research because they provide a realistic representation of how cancer develops and progresses in living organisms.

Chemically Induced Tumor Models

Chemically Induced Tumor Models refer to cancer that is deliberately induced in animals. Here, carcinogens are administered through many routes such as oral, intravenous, nasal route, or topical application, depending on the type of tumor being studied and the target organ. These damage the DNA and induce tumors

One advantage is that this model is under control regarding dose duration, exposure, and timings. These models help in the study of different cancer stages and also help in understanding the environmental factors affecting the disease.

One disadvantage is that the tumor can take time to develop, and it may or may not resemble the tumor in humans. Plus, different animal species might respond differently to the same carcinogens. Nevertheless, they remain widely used due to their practicality and ability to provide insights into cancer mechanisms.

Genetically engineered mouse models (GEMM)

Genetically engineered mouse models are made to carry specific genes related to cancer.

These modifications may include activation of oncogenes, deletion of tumor suppressor genes, or introduction of mutations that resemble those found in human cancers. As a result, tumors develop within the animal as a direct consequence of these genetic changes.

Major advantage of this model is for identifying molecular pathways involved in cancer and for the evaluation of targeted therapies.

One limitation is that it can be time-consuming and costly. Despite this, it is a very powerful tool for studying cancer.

Xenograft Tumor Models

Here, an immunocompromised mouse is used, and tumor cells are transplanted into it. Due to a weak immune system, the mouse does not reject the foreign cells, allowing the tumors to develop and grow in the organism.

These models are particularly useful for evaluating the behavior of human cancer cells and testing the effectiveness of new anticancer drugs. Tumors can be implanted either subcutaneously, which allows easy monitoring of growth, or into the original organ site (orthotopic transplantation), which provides a more realistic environment.

These models are important as they help in preclinical testing and allow scientists to observe how tumors respond to various therapies like chemotherapy, targeted therapy, and immunotherapy. In addition, xenograft models help in studying processes such as tumor invasion, angiogenesis, and metastasis.

Although xenograft models are widely used, their limitation lies in the absence of a functional immune system, which restricts the study of immune-related responses. Nonetheless, they remain an essential component of preclinical cancer research.

Orthotopic Tumor Models

Orthotopic Tumor Models are essential in cancer research as they help in the study of how cancer behaves. Here, the tumor is induced in a particular tissue or organ, and this is the place where the tumor originates. For example, breast cancer cells may be implanted into the mammary gland of a mouse, or pancreatic cancer cells may be introduced into the pancreas. By placing the tumor in its natural anatomical location, researchers are able to study cancer growth in a more realistic biological environment.

These models are particularly valuable for studying tumor–microenvironment interactions, metastasis, and angiogenesis. Additionally, they provide better insights into drug distribution and therapeutic effectiveness compared to subcutaneous models.

Orthotopic Tumor Models are commonly used as they help scientists in identifyibg for the drug will show its action on the particular natural location where the tumor was grown and how the tumor responds towards the treatment. This helps in understanding details in a more clinically relevant setting.

However, these models have certain disadvantages. These models require specialised workers to induce the tumor at specific sites. This process can be time consuming and also costly. In addition, it can be difficult to examine the tumor as the growth is inside the body and is not easily visible, like in the case of a subcutaneous tumor. Moreover, they are still valuable in realistic research.

Patient-Derived Xenograft (PDX) Models

Patient-Derived Xenograft (PDX) Models are important, as in this model, tumor tissues are taken directly from a cancer patient and implanted into immunodeficient mice. Since the tumor sample is transferred without being extensively modified or cultured in the laboratory, it retains many of the original characteristics of the patient's cancer, including its genetic makeup, histological structure, and biological behavior.

In some cases, mice are exposed to a tumor from an individual patient, and their response to treatment is monitored to determine effective therapy for the person. PDX is used to produce individualized treatments for patients as they are known for protecting the heterogenicity of the original tumor. Tumors can develop and spread in various ways in different populations. PDX is used widely for preclinical studies.

The limitation is that it is expensive and time-consuming, and not all tumor samples successfully grow after transplantation. In addition, the mice cannot completely replicate the role of the immune system in cancer development and treatment. Despite this, PDX models are widely used in cancer research.

Humanized mouse models

Humanized mouse models are special models in which a mouse is made to mimic the human immune system. Here immunocompromised mice are administered with human immune cells . This allows the animals to develop components of a functional human immune system, enabling researchers to study interactions between human tumor cells and immune responses in a living organism. These models help overcome the limitations of traditional xenograft models, as they lack a proper immune system.

These models are especially useful for studying cancer immunology and evaluating modern immunotherapies such as immune checkpoint inhibitors, cancer vaccines, and adoptive cell therapies.

Humanized mouse models have several limitations. This process can be difficult and costly, and it may not properly replicate the human immune system. Nevertheless, humanized mouse models represent an important advancement in cancer research because they provide a more realistic platform for studying tumor–immune system interactions and evaluating emerging immunotherapies.

Advantages of Animal Models in Cancer Research

Animal models have significantly contributed in the advancement of cancer research by providing a controlled environment which shows biological mechnaisms of tumor development. In living organishms these models help the scientists in studying the complex interactions the tumor development and the reactions of it towards other surrounding cells This holistic approach enables researchers to gain a deeper understanding of critical processes such as tumor initiation, progression, invasion, and metastasisIn addition, animal models make it possible to study the genetic and molecular pathways involved in cancer development, which contributes to the identification of potential therapeutic targets.

Here, drugs are primarily used on animal models and are checked for safety and efficacy before they are tested on humansThese models allow researchers to assess drug responses, determine optimal dosages, and identify potential side effects. In addition, animal models help in the study of environmental and genetic factors affecting cancer development,

Exposure to carcinogens, dietary influences, and other external factors can be systematically studied in these models to understand their role in tumor initiation and progression. This contributes to the development of preventive strategies and public health interventions aimed at reducing cancer incidence.

Another notable advantage is their role in advancing personalized medicine. Models such as patient-derived xenografts (PDX) enable researchers to study tumors that retain the characteristics of individual patients. This allows for the evaluation of treatment responses in a patient-specific manner, helping to identify the most effective therapeutic options. As a result, animal models are increasingly being used to support individualized treatment approaches in oncology.

Finally, animal models provide a reproducible and standardized platform for scientific research. Experiments can be carefully designed and controlled, allowing for consistent and reliable results. This reproducibility is essential for validating scientific findings and ensuring that research outcomes can be translated into clinical practice.

Limitations of Animal Models in Cancer Research

Even though animal models have various advantages, there are several limitations that should be considered before reaching any conclusions of experimental outcomes. One primary drawback is that animal genes and the immune system is not the same as those of humans. Variations in genetics, metabolism, physiology, and immune system function can influence how tumors develop and respond to therapeutic interventions. As a result, findings obtained from animal studies may not always accurately predict clinical outcomes in human patients.

Another incapability of animal models is that they might not fully replicate the complexity of human cancer, thereby limiting their translational relevance. In addition, most models depend on experimental manipulation like genetic modification or tumor transplantation, which might not be the same as natural formation. This can affect the validity of the results and their applicability to real-world clinical scenarios.

The practical challenges which arise in these models are that they are costly, time consuming, may show uncertainty, are not fully under control, cannot accurately replicate a human tumor or human immune system, and also require expertise in maintenance.

Ethical considerations represent another important limitation. The use of animals in research is subject to strict regulatory guidelines to ensure humane treatment and minimize suffering. These ethical concerns can limit the extent of experimentation and require careful justification of study designs. The variability present in these model results will lead to inconsistencies in studies and complicate the interpretation of findings.
Despite these limitations, animal models play a vital role in cancer research. When used properly in combinations with other approaches, the outcome becomes more sophisticated, hence providing valuable insights into cancer biology and support the development of improved diagnostic and therapeutic strategies.

Future Perspectives of Animal Models in Cancer Research

The future of animal models in cancer research looks very promising due to continuous advancements in science and technology. Researchers are now focusing on developing more accurate and reliable models that can closely mimic human cancer. This will help in a better understanding of tumor behavior and improve the effectiveness of new treatments.

One of the major developments is the use of genetically engineered models, which allow scientists to study specific gene mutations involved in cancer. These models are expected to provide deeper insights into how cancer develops and progresses at the molecular level. In addition, patient-derived xenograft models are gaining importance as they retain the original characteristics of human tumors, making them useful for studying treatment responses.

Another important area of progress is the development of humanized models. These models include components of the human immune system, which helps researchers study immune responses and improve immunotherapy-based treatments. As immunotherapy is becoming more important in cancer treatment, such models will play a key role in future research.

Advancements in technologies such as gene editing, imaging techniques, and computational tools are also expected to improve the accuracy and efficiency of animal studies. These tools will allow researchers to analyse tumor growth and treatment responses in a more precise way.

At the same time, there is an increasing focus on reducing the use of animals in research by developing alternative methods such as cell culture techniques and computer-based models. Combining these methods with animal studies can improve research outcomes while also addressing ethical concerns.

Overall, the future of animal models in cancer research is focused on improving their accuracy, reducing limitations, and integrating modern technologies. These developments will continue to support a better understanding of cancer and help in the development of safer and more effective treatments.

CONCLUSION:

Animal models are irreplaceable tools in cancer research, helping to understand tumors and their treatments. They are used to study the initiation, progression, metastasis, and complexities between cancer cells and surrounding tissues. Researchers are able to explore this field of science through various experimental systems.

A wide range of animal models, including spontaneous tumor models, chemically induced models, genetically engineered mouse models, xenografts, orthotopic models, and patient-derived xenografts, offer diverse approaches to investigate different aspects of cancer biology. These models have played a critical role in identifying molecular pathways, understanding genetic alterations, and evaluating the safety and efficacy of novel therapeutic interventions.

In addition to improving our information about cancer, these animal models also help in preclinical testings which increases the success rate in clinical trials and contributes in the development of personalized treatment strategies and immunotherapies.

Despite various advantages, animal models have inevitable limitations as animals and humans show biological differences, and the challenges are related to cost, time, and ethical considerations. Therefore, results obtained from these models must be interpreted with caution and validated through further clinical investigations.

Nevertheless, with ongoing progress in genetic engineering, molecular biology, and experimental techniques, animal models will continue to remain an indispensable tool in cancer research. Their continued development is expected to contribute significantly to the discovery of better diagnostic methods, more effective treatments, and personalized therapeutic strategies for cancer in the future.

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