Ad-Dawaa' Journal of Pharmaceutical Sciences
ISSN: 2654-7392, E-ISSN: 2654-6973
Vol. 6, No. 1, June 2023, p. 1 – 16
DOI: https://doi.org/10.24252/djps.v6i1.38677

Xenograft Models for Preclinical Assessment Of Anticancer Therapies: A Comprehensive Review

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Article history:
Submited: 19-6-2023
Revised: 27-6-2023
Accepted: 10-7-2023

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Cite this article: Sadaqa, E., Arsul, M.I. (2023). Xenograft models for preclinical assessment of anticancer therapies: a comprehensive review. Ad-Dawaa' J. Pharm. Sci. 6(1): 1-16.

ABSTRACT

Introduction*: Xenograft models play a pivotal role in preclinical studies for assessing the efficacy of anticancer medications. In this comprehensive review, we present an overview of current advancements and future prospects in xenograft research, focusing on their significance in guiding drug development and clinical translation.* ***Aim****: Our aim is to conduct an in-depth review of xenograft models, their utility in evaluating anticancer drug effectiveness and ultimately improve patient outcomes. Methods We conducted an in-depth literature search using databases such as ScienceDirect, Google Scholar and PubMed with keywords including "xenograft model, cancer CDX PDX." We then reviewed and analyzed relevant studies that utilized xenograft models in order to highlight key findings and contributions made through such models.* ***Results****: Our analysis showcases the essential role of xenograft models in assessing the efficacy of anticancer drugs. We discuss the benefits and limitations of these models, emphasizing their importance in guiding drug development and clinical decision-making.* ***Conclusion****: Xenograft models remain invaluable tools in preclinical cancer research despite their inherent limitations, with researchers continually striving to refine and enhance these models to ensure their reliability in an ever-evolving field of cancer therapeutics. Utilizing xenograft models allows researchers to evaluate anticancer drug activity more accurately while striving for improved patient outcomes.*

KEYWORDS*: Cancer, Anticancer therapies, Preclinical models, Cell line-derived xenografts (CDX), Patient-Derived Xenografts (PDX).*

INTRODUCTION

Cancer, which is characterized by the uncontrolled proliferation and dissemination of abnormal cells, constitutes a prominent cause of mortality on a global scale (American Cancer Society, 2018). It poses a considerable menace to public health, given the fact that millions of new cases are diagnosed annually, resulting in a significant burden on patients, their families, and healthcare systems. Cancer can manifest in various organs and tissues throughout the human body, and its onset is influenced by a multiplicity of factors, including genetic, environmental, and lifestyle determinants. Consequently, there is a pressing need for the continuous development and assessment of innovative anticancer therapies, as cancer remains a leading cause of

death worldwide. Notably, the appraisal of the effectiveness of anticancer drugs constitutes a critical element in the pursuit of efficacious cancer treatments (Institute, 2020). Antineoplastic medications have been devised to specifically target neoplastic cells and obstruct their proliferation, with the objective of diminishing tumor dimensions, thwarting metastasis, and enhancing patient outcomes (Isoldi, Visconti, & Castrucci, 2005; Zhang & Liu, 2013). However, it must be acknowledged that not all anti-neoplastic agents exhibit uniform effectiveness, and their potency may fluctuate contingent upon the cancer type and stage, in addition to the unique characteristics of the patient (Huang, Ju, Chang, Reddy, & Velmurugan, 2017; Pignatti, et al., 2022). Hence, a comprehensive and meticulous appraisal of the efficacy of anticancer drugs is imperative in order to isolate auspicious candidates that warrant further clinical development and eventual utilization in patients. Preclinical in vivo models serve a critical role in the drug development pipeline, offering insights into drug efficacy, safety, and pharmacokinetics. Among these models, xenografts have emerged as a widely adopted and valuable tool for assessing anticancer drug efficacy (Hidalgo et al., 2014).

The assessment of the effectiveness of anticancer medications requires preclinical and clinical research. Preclinical studies commonly employ in vitro cell culture assays and animal models, which consist of xenograft models such as patient-derived xenografts (PDX) and cell line-derived xenografts (CDX),which conducted to evaluate the safety and efficacy of drugs before proceeding to clinical trials. Clinical trials are conducted in human subjects to analyze the safety and efficacy of anticancer drugs in real-world circumstances. These trials typically adhere to a rigorous protocol and involve various phases, including Phase I (safety and dosage), Phase II (efficacy and side effects), and Phase III (comparative efficacy and safety) trials.

The evaluation of the effectiveness of anticancer medications is crucial in determining their possible benefits and drawbacks, as well as steering clinical decision-making (Poste, 2011; Bachelard, Coquan, du Rusquec, Paoletti, & Le Tourneau, 2021). Moreover, it facilitates the identification of drugs that exhibit the most promising outcomes for further advancement and potential employment in cancer patients (Schwaederle, et al., 2015). Furthermore, it contributes to the comprehension of the fundamental mechanisms of drug action and resistance and supports the refinement of therapeutic approaches (Zhang & Liu, 2013).

Xenograft models are a valuable tool for investigating tumor growth, microenvironment, and response to therapy in a physiologically relevant context. Such models involve the engraftment of human tumor cells or tissues into immunodeficient mice (Sharpless & DePinho, 2006). The two types of xenografts are cell line-derived xenografts (CDX) and patient-derived xenogr-

afts (PDX), each with unique advantages and limitations that researchers should consider (Tentler, et al., 2012). In this comprehensive review, we aim to elucidate the significance of utilizing the xenograft model in cancer research. Specifically, we will compare and contrast the benefits and drawbacks of CDX and PDX to provide readers with a clear understanding of which model is best suited to their research needs. Furthermore, we will showcase recent advances in the field that aim to overcome limitations and enhance the reliability and relevance of the xenograft model in preclinical cancer drug development. This review on xenograft models is expected to make significant strides forward in cancer therapeutics. By providing an in-depth examination of current state and future directions of xenograft research, this will increase researchers' comprehension of their utility in evaluating anticancer drug effectiveness. Furthermore, insights, advancements, and recommendations presented in this review are expected to spark additional studies as well as refine existing applications further, leading to groundbreaking cancer therapies with improved patient outcomes.

METHODS

Keywords xenograft model, cancer, CDX, PDX. were searched in databases such as ScienceDirect, Google Scholar, and PubMed to ensure their validity and reliable contents, and the papers had to be written in English. Xenograft models for preclinical assessment Literatures that were not relevant to xenograft and cancer were excluded. There was minimum 50 literatures from the last 10 years.

RESULTS AND DISCUSSION

Optimizing Drug Development with Xenograft Models in Cancer

Xenograft models have emerged as a highly valuable instrument in evaluating the effectiveness of anticancer medications (Jung J. , 2014). In recent times, a plethora of studies have employed these models to appraise the possibility of different compounds for the treatment of cancer. The ensuing table accentuates a few of the noteworthy investigations that have utilized xenograft models to refine drug development.

The studies presented in Table 1 collectively showcase the advantageous observations acquired from xenograft models in the advancement of innovative cancer therapeutics. These discoveries augment the increasingly expanding knowledge base directed towards tackling cancer and enhancing patient results. Nevertheless, it is crucial to acknowledge the inherent limitations of these models, and persistent research and improvement are necessary to ensure their reliability and relevance in the swiftly evolving sphere of cancer therapeutics .

Cell line-derived xenograft (CDX)

The cell line-derived xenograft (CDX) models are formulated by means of introduction already established human cancer

Table 1. Examples of Studies Utilizing Xenograft Models in Drug Development

Compound	Xenograft Model	Results
Rhodium metalloinsertor	HCT116 xenograft tumor model	Effectively inhibited tumor growth by inducing Deoxyribonucleic Acid (DNA) damage and inhibiting DNA repair mechanisms (Threatt, Synold, Wu, & Barton, 2020).
Lactoferricin B peptide	Breast cancer xenograft model	Induced apoptosis in multiple breast cancer cell lines and inhibited tumor growth in a mouse model (Rahman, et al., 2021).
Supramolecular platform for controlling and optimizing molecular architectures of siRNA targeted delivery vehicles	KB cells xenograft model	High gene silencing efficiency and tumor growth inhibition (Wen, et al., 2020).
Anti-HB-EGF antibody-modified lipid nanoparticles loaded with siRNA	Triple-negative breast cancer xenograft model	Effectively delivered Small interfering Ribonucleic Acid (siRNA)to the tumor cells resulting in significant tumor growth inhibition (Okamoto, et al., 2018).
Auraptene	4T1tumor-bearing mouse model	Inhibited tumor growth by inducing apoptosis and inhibiting angiogenesis (Shiran, et al., 2021).
Salinomycin	Primary tumor-initiating cells (TIC) isolated from human patients with colorectal liver metastasis injected into NOD/SCID mice to induce a patient-derived mouse xenograft model of colorectal cancer	This preclinical investigation using patient-derived xenografts demonstrated that salinomycin, either alone or when combined with 5-fluorouracil and oxaliplatin, showed enhanced antitumoral efficacy when compared with conventional chemotherapy regimens (Klose, et al., 2019).
Paclitaxel	A549 cancer stem cells (CSCs) Lung tumor-bearing C57BL/6 mice	In this study, it was evidenced that the antitumor effectiveness of Paclitaxel against lung cancer was significantly augmented through the process of encapsulation in liposomes, as validated via the utilization of a xenograft model (López, et al., 2021)

cell lines into immunodeficient mice (Hidalgo, et al., 2014; Kohnken, Porcu, & Mishra, 2017). As shown in Figure1. The aforementioned cell lines are generally obtained from human cancer patients and have been adapted to grow in vitro as immortalized cell lines (Hidalgo, et al., 2014). Owing to the convenience of use, reproducibility, and capacity to generate large cohorts for drug testing, the CDX models have been extensively employed in cancer research (Gao, et al., 2015). CDX models have emerged as a favored instrument for cancer exploration owing to various benefits they extend. Firstly, they are easily accessible and extensively characterized, possessing well-defined molecular and genetic traits. This renders CDX models a convenient and cost-effective alternative for preclinical investigations.

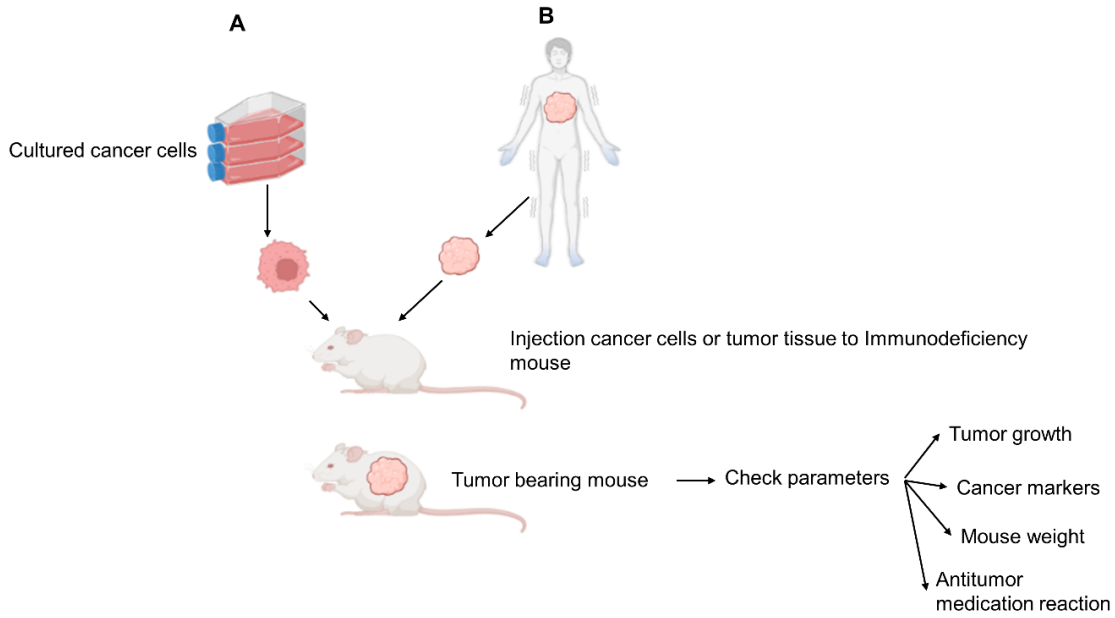

Figure 1. Schematic image that elucidates the procedural methodology employed to establish xenograft models in which A represents Cell line-derived xenograft (CDX) and B represents Patient-Derived Xenograft (PDX) for further assessment of anticancer medication by checking parameters such as tumor growth , cancer markers , mice weight and antitumor medication reaction

Secodly, CDX models can be readily propagated and maintained under controlled conditions, facilitating reproducible experiments and comparison of outcomes across diverse studies. Lastly, CDX models frequently demonstrate a high tumor take rate, as the established cancer cell lines have been optimized for in vivo tumor growth. This enables efficient generation of tumor-bearing mice for drug testing. To this end , these advantages endow CDX models with the status of a valuable tool in cancer research. Despite the advantages that CDX models offer, it is important to consider their limitations in cancer research. First and foremost, these models may not fully recapitulate the heterogeneity and complexity of human tumors, given their derivation from immortalized cell lines that may have undergone genetic and phenotypic changes during in vitro culture (Hidalgo, et al., 2014). Additionally, CDX models may not accurately represent the tumor microenvironment, as they lack the stromal components and immune cells present in human tumors. Consequently, the response to anticancer drugs that target the tumor microenvironment can be affected. Lastly, CDX models may not always predict the clinical response of patients to anticancer drugs accurately, given that they may not fully represent the variability in patient responses due to differences in genetic background, tumor heterogeneity, and patient-specific factors (Simons & Brayton, 2017). Therefore, it is crucial to consider these limitations when employing CDX models for preclinical studies

and to supplement them with other models to ensure reliable and accurate results.

Patient-Derived Xenograft (PDX)

Patient-Derived Xenograft (PDX) models are an efficacious instrument for cancer research that involve the direct implantation of unaltered tumor tissues from human patients into immunodeficient mice, without any in vitro cultivation as shown in Figure 1. The ultimate goal of this methodology is to better conserve the heterogeneity of the tumor and the microenvironment of human tumors, which consequently renders PDX models significantly more clinically relevant for drug testing (Sun, et al., 2021; Abdolahi, et al., 2022). PDX models exhibit several benefits. Firstly, they better represent the genetic and phenotypic heterogeneity of human tumors as they are directly derived from patient tumors without in vitro manipulation, thus preserving the tumor microenvironment and stromal components (Yoshida G. , 2020). Secondly, PDX models aspire to maintain the clinical relevance of patient tumors, including the histopathological characteristics, genetic mutations, and response to anticancer drugs, making them a more predictive model for clinical outcomes. Furthermore, PDX models can be implemented in personalized medicine approaches, wherein tumor tissues from individual patients can generate PDX models that can be utilized to test the efficacy of specific anticancer drugs for that particular patient, thereby allowing for personalized treatment strategies (Xie & Lin, 2020). However, it is important to recognize that PDX models are not without limitations. Firstly, establishing and maintaining PDX models can be a more arduous task compared to CDX models, as they necessitate access to fresh tumor tissues from patients, which may not be readily accessible at all times. Additionally, PDX models may exhibit limited characterization, as the molecular and genetic information of patient tumors may not always be fully available or preserved during transplantation. Secondly, PDX models may prove to be more costly and time-consuming than CDX models, necessitating specialized facilities and expertise for handling patient tumor tissues, engraftment, and maintenance of the mouse models. Finally, PDX models may present variability in experimental outcomes owing to inter- and intra-tumor heterogeneity, as well as variability in engraftment rates and growth characteristics, which can make data interpretation challenging (Byrne, et al., 2017). Overall, the employment of PDX models presents a multitude of advantages over alternative cancer models. Among these benefits, lies their capability to more accurately replicate the genetic and phenotypic heterogeneity of human tumors, in addition to their potential to more closely emulate the responses of patients to anticancer medications. These attributes render PDX models an invaluable tool for both personalized medicine and translational research. Nevertheless, it is imperative to met-

iculously examine their limitations in the context of specific research objectives.

Challenges to xenograft models

Xenograft models are significant instruments for evaluating the effectiveness of anticancer agents. However, they encounter several challenges. One of the most noteworthy obstacles is the deficiency of immunocompetence in xenograft models. When human tumors are implanted into immunodeficient mice, they fail to capture adequately the intricacy of the human immune response to cancer (Li, et al., 2021). As a result, the translatability of preclinical findings to clinical outcomes can be restricted. Additionally, xenograft models may not replicate accurately the heterogeneity of human tumors or the tumor microenvironment, both of which can influence the efficacy of anticancer drugs (Cekanova & Rathore, 2014). Another challenge is the difficulty in establishing and maintaining PDX models, which necessitate access to fresh tumor tissues from patients that may not always be readily available. PDX models may also exhibit inter- and intra-tumor heterogeneity, as well as variability in engraftment rates and growth characteristics, which can introduce variability in experimental results and make data interpretation challenging (Byrne, et al., 2017; Hidalgo, et al., 2014). Furthermore, xenograft models may not account for species-specific differences in drug metabolism, toxicity, and pharmacokinetics (Li, et al., 2021). This can limit the predictive value of xenograft models and necessitate further validation in other preclinical models, such as syngeneic models or organoids. Finally, the cost and time required for xenograft models can be higher compared to other preclinical models, which can limit their accessibility to researchers with limited resources (Cekanova & Rathore, 2014). Despite these challenges, xenograft models remain crucial tools for drug development and preclinical testing. Ongoing research and refinement of these models can help address the limitations and enhance their reliability and relevance in the rapidly evolving field of cancer therapeutics.

Recent efforts to enhance xenograft models

As previously discussed, although the advantages of xenograft models as a valuable assay for evaluating the efficacy of anticancer medication are evident, there exist several limitations that prompt researchers to improve the limitations of xenograft models. To achieve this, researchers are employing synergistic approaches that could significantly improve the accuracy of this assay, as illustrated in Table 2.

One potentially effective strategy involves the development of humanized mouse models, which integrate human immune cells or other human components to more accurately simulate the human tumor microenvironment (Jung, Seol, & Chang, 2018). Another approach entails the utilization of patient-derived xenograft (PDX) models, which entail

Table 2. Different Approaches to Enhance Xenograft Models.

Approach	Description	Cancer Type	References
Humanized mouse models	Incorporate human immune cells or other human components to model the human tumor microenvironment more accurately.	Breast cancer, Lung Cancer, Leukemia	(Siolas & Hannon, 2013; Rongvaux, et al., 2014; Park, Nedrow, Josefsson, & Sgouros, 2017; Jung, Seol, & Chang, The generation and application of patient-derived xenograft model for cancer research, 2018; Tian, Lyu, Yang, & Hu, 2020; Jacoby, Chien, & Fry, 2014)
Patient-derived xenograft (PDX) models	Involve transplanting human tumor samples directly into immunodeficient mice to better capture the genetic heterogeneity of human tumors and may be more predictive of patient response to therapy.	Breast cancer, Glioblastoma multiforme, Renal cell carcinoma, Prostate cancer, Pancreatic Cancer	(Hammers, et al., 2010; Keunen, et al., 2011; Grisanzio, et al., 2011; Siolas & Hannon, 2013; Gao, et al., 2015; Hoff, et al., 2011)
3D culture models and organoids	Can better mimic the complex three-dimensional structure of tumors and their microenvironment.	Prostate Cancer, Ovarian Cancer, Colorectal Cancer	(Lee, et al., 2013; Fujii, et al., 2016; Ho, Pek, & Soh, 2018)
Positron emission tomography (PET)	Monitor tumor growth and response to therapy in real-time	Colorectal cancer, prostate cancer, breast cancer	(Price, et al., 2002; Bokacheva, et al., 2013; Lee, et al., 2018)
Magnetic resonance imaging (MRI)	Provides high-resolution images of tumor vasculature and microenvironment, allowing for the assessment of drug delivery and efficacy in xenograft models.	Colorectal cancer, breast cancer	(Bokacheva, et al., 2013; Bollineni, Collette, & Liu, 2014; Mollard, et al., 2017; Glunde & Bhujwalla, 2011)

the transplantation of human tumor samples directly into immunodeficient mice. PDX models are believed to more effectively capture the genetic heterogeneity of human tumors and may be more predictive of patient response to therapy (Gao, et al., 2015). Numerous previous investigations have successfully employed patient-derived xenograft (PDX) models in a variety of cancer types. For example, in breast cancer, PDX models have been utilized to maintain basal-like morphology and tumor structure, as well as to evaluate the efficacy of cisplatin and ifosfamide combination therapy and trastuzumab (Derose, et al., 2011; De Plater, et al., 2010). In glioblastoma multiforme, PDX models have preserved genetic characteristics, thereby enabling the assessment of mab's efficacy in evaluating tumor angiogenesis (Wang, et al., 2009; Keunen, et al., 2011).

Moreover, PDX models in renal cell carcinoma have proven invaluable in retaining genetic and histological characteristics and evaluating the effects of sorafenib or sunitin (Hammers, et al., 2010; Grisanzio, et al., 2011). In prostate cancer, PDX models have demonstrated the differentiation and expression of androgen receptor and prostate-specific antigen (PSA), which facilitates the prediction of the efficacy of androgen ablation therapy (Wang, et al., 2005; Yoshida, et al., 2005). Finally, in pancreatic cancer, PDX models have retained the original tumor architecture, maintained a greater proportion of stromal components, and developed locoregional and distant metastases, thereby demonstrating the activity of mitomycin C and cisplatin in a patient harboring a PALB2 mutation. Notably, stromal modulation has exhibited promise in augmenting intra-tumor gemcitabine concentrations to enhance therapy efficacy (Olive, et al., 2009; Miller, Garcia, Gamblin, Vance, & Yoon, 2020).

In addition to conventional xenograft models, researchers have explored the utilization of 3D culture models and organoids, which offer a more precise representation of the intricate three-dimensional structure of tumors and their microenvironment (Lee, et al., 2013; Fujii, et al., 2016). The popularity of 3D spheroid and organoid models is on the rise due to their ability to replicate the stromal environment and multicellular structure present in vivo, providing more precise data on cell–cell interactions, tumor characteristics, Xenograft models for preclinical assessment drug discovery, and metabolic profiling of cancer cells. These models allow the replication of an in vivo-like tumor microenvironment within in vitro settings, conserving important biochemical and physical properties such as tumor hypoxia, nutrient depletion, acidosis, and heterogeneous gene expression. They create a platform to study molecular pathways linked to solid tumor malignancy and to screen and optimize pharmacological therapies in vitro. Despite certain limitations, recent advances in 3D bioprinting, "tumor-on-a-chip," and other microfabrication technologies will expedite the development of more biologically relevant in vitro tumor microenvironment (TME) models. Ultimately, tumor spheroids may become the benchmark in vitro model with high translational predictive value, decreasing the number of in vivo investigations required and accelerating the drug discovery process (Zhu, et al., 2022). Prior successful studies have employed 3D culture models and organoids to enhance the accuracy of xenograft models and evaluate the effectiveness of anticancer drugs, such as in prostate cancer, ovarian cancer, and colorectal cancer (Ho, Pek, & Soh, 2018).

The field of imaging technology has undergone significant advancements, leading to the emergence of non-invasive imaging modalities that have greatly facilitated the monitoring of tumor growth and response to therapy in real-time (Lee, Xie, & Chen, 2010; Li, et al., 2021). These modalities have been

developed through the application of advanced imaging techniques that furnish non-invasive information on drug distribution and pharmacokinetics in vivo. Positron emission tomography (PET), a medical imaging technique that employs a small amount of radioactive material to generate images of the internal body, has become increasingly indispensable in cancer research, particularly in xenograft models. PET imaging is a robust technique that enables the visualization and quantification of specific molecules in vivo, and its application has yielded valuable information on drug pharmacokinetics and biodistribution in xenograft models as well as can be used to monitor the distribution of radiolabeled anticancer drugs in xenograft models, and this has proved useful in assessing drug delivery and efficacy (Ghosh, et al., 2022) . Moreover, PET is capable of measuring changes in tumor metabolism or blood flow, thus providing critical insights into the response of tumors to treatment. This knowledge can be leveraged to optimize treatment regimens and enhance patient outcomes. PET has been utilized to great effect in breast, colorectal, and prostate cancer xenograft models, resulting in improved quality of results (Price, et al., 2002; Bokacheva, et al., 2013; Lee, et al., 2018).

Magnetic resonance imaging (MRI) is a non-invasive imaging modality that has demonstrated its utility in evaluating drug distribution and pharmacokinetics in vivo. This imaging technique has been employed to Xenograft models for preclinical assessment enhance the quality of xenograft models. By producing high-resolution images of tumor vasculature and microenvironment, MRI enables the evaluation of drug delivery and efficacy in xenograft models (Mollard, et al., 2017; Starke, et al., 023). Additionally, MRI can monitor changes in tumor size and morphology, serving as a dependable and precise approach for assessing tumor response to treatment (Bollineni, Collette, & Liu, 2014). Essentially, MRI exploits a powerful magnetic field and radio waves to capture detailed images of soft tissues within the body. This imaging technique is highly advantageous for studying xenograft models as it allows researchers to track tumor growth and progression in real-time without resorting to conventional invasive procedures. Furthermore, MRI can furnish information about the tumor microenvironment, including blood flow and oxygenation levels, which can facilitate the development of more accurate and predictive models of tumor biology and drug response. Previous investigations have underscored the significance of MRI in monitoring the growth of breast cancer over time and determining the efficacy of drug treatment (Glunde & Bhujwalla, 2011). By tracking changes in tumor size and morphology, researchers may gain valuable insights into the mechanism of action of the drug and its potential for clinical use. The utilization of sophisticated imaging methodologies such as MRI and PTE in conjunction with xenograft models harbors the

potential to enhance the dependability and pertinence of preclinical drug development studies. These methodologies can facilitate the identification of promising drug candidates and optimization of dosing regimens prior to clinical trials by furnishing non-invasive information on drug distribution and pharmacokinetics in vivo. Nonetheless, further investigation is mandatory to completely validate the employment of these techniques in preclinical drug development studies. It is imperative to continue validating and refining xenograft models to ascertain their relevancy and dependability in preclinical drug development. Standardizing experimental protocols and thoroughly characterizing the limitations of different models could enhance their predictability and applicability to clinical trials (Li, et al., 2021).

Humanized mouse models

The field of research concerning humanized mouse models is an emerging area that possesses the potential to augment the usefulness of xenograft models in the appraisal of anti-cancer drugs. By integrating human immune cells or other human components, these models more accurately emulate the human tumor microenvironment, thereby offering valuable insights into drug efficacy and toxicity (Rongvaux, et al., 2014). One of the methods employed to create humanized mouse models entails grafting human hematopoietic stem cells (HSCs) into immunodeficient mice (Shultz, Brehm, Xenograft models for preclinical assessment Martinez, & Greiner, 2012). The resultant chimeric mice possess a functional human immune system and can be utilized to examine the interplay between tumor cells and the immune system. Other approaches involve implanting human tumor tissues directly into humanized mice to create patient-derived xenograft (PDX) models (Siolas & Hannon, 2013).

Humanized mouse models have already been utilized in appraising the effectiveness of diverse anti-cancer drugs, such as immune checkpoint inhibitors (Rongvaux, et al., 2014) and antibody-drug conjugates (ADCs) (Mullard, 2013). Additionally, these models offer the potential to enhance personalized medicine approaches by enabling the appraisal of drug responses in the context of patient-derived tumors. While humanized mouse models present a promising direction for improving the utility of xenograft models, several challenges still require addressing. These challenges encompass the high cost and technical expertise required for generating and maintaining these models, as well as concerns regarding the ethical use of animals in research (Rongvaux, et al., 2014). Overall, the emergence of humanized mouse models offers an exciting opportunity to enhance the relevance and reliability of xenograft models in evaluating anti-cancer drugs. Continued research in this area has the potential to provide valuable insights into drug efficacy and toxicity, ultimately contributing to the

development of more effective cancer therapies.

CONCLUSION

After conducting a thorough evaluation of the present condition and future prospects of xenograft research in the assessment of anticancer drugs, it is evident that xenograft models have become an indispensable asset in preclinical investigations. These models offer a more realistic setting for gauging the therapeutic potential of new drugs, thereby facilitating drug development and enhancing clinical translation, ultimately leading to better patient outcomes. Despite their constraints, persistent research and refinement can ensure the dependability and relevance of xenograft models in the rapidly evolving domain of cancer therapeutics. Thus, these models persist as a pivotal tool in the battle against cancer, and their continued application and advancement are crucial for the advancement of our comprehension of cancer biology and the enhancement of the effectiveness of anticancer drugs.

ACKNOWLEDGEMENT

The authors wish to express their profound gratitude to Engineer Saad Sadaqa for his boundless guidance and resolute support.

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