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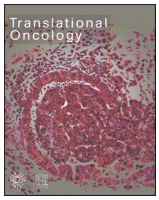

Editorial Note: Biomaterials in Cancer - From Research Breakthroughs to Clinical Implementation

Cancer remains as one of the most important health challenges worldwide, characterized by the rapid proliferation and metastasis of abnormal cells. Despite significant advancements in medical science, the pursuit of innovative solutions to diagnose, control, and treat cancer continues to be of a great importance. Researchers are increasingly exploring the potential of advanced biomaterials to address some of these challenges, leveraging their unique properties and functionalities to offer promising avenues from early diagnosis to targeted therapy. Biomaterials have emerged as pivotal tools in cancer research due to their biocompatibility, ability to be engineered for specific functions, and versatility in various biomedical applications. This class of materials, designed to interact with biological systems, are ideal for applications ranging from drug delivery systems to tissue engineering scaffolds. In addition, the multifaceted role of biomaterials in oncology is increasingly evident. The research featured in this special issue "Biomaterials in Cancer" demonstrates some of the immense potential of biomaterials to transform cancer research and therapy. By integrating advanced materials science with biomedical engineering, researchers are pioneering new strategies to combat this complex and devastating disease.

One of the main challenges in cancer treatment is delivering drugs specifically to tumor cells while minimizing harm to healthy tissues. Biomaterials can be designed to transport therapeutic agents directly to the tumor microenvironment. By modifying these materials with ligands that recognize and bind to tumor-specific markers, drugs can be released precisely where they are needed, improving treatment effectiveness and reducing systemic toxicity. This targeted approach is crucial in addressing the limitations of traditional chemotherapy, which often impacts both cancerous and healthy cells, causing severe side effects. Samaei et al. [1] evaluated the use of liposomes for treating hepatocellular carcinoma (HCC). Various therapies, including surgical resection, chemotherapy, radiotherapy, and immunotherapy, are currently used for HCC. However, this type of cancer remains difficult to cure, necessitating new treatment strategies. Conventional drugs and genes often lack the ability to specifically target tumor tissues and cells. Therefore, encapsulating drugs or genes in liposomes can enhance their accumulation at the tumor site, improving HCC suppression. Moreover, stimuli-responsive liposomes, such as those sensitive to pH, redox, and light, can deliver drugs more effectively to the tumor microenvironment, thereby increasing the therapeutic index. Since several receptors are upregulated on HCC cells, functionalizing liposomes with lactoferrin and peptides can further enhance their targeting ability. The researchers suggested that phototherapy could be enhanced by loading liposomes with photosensitizers, thereby stimulating photothermal and photodynamic ablation of HCC cells.

Advanced biomaterials are transforming imaging techniques for early cancer detection. Nanoparticles and other contrast agents enhance the sensitivity and accuracy of imaging methods such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computed Tomography (CT) scans, allowing for precise tumor localization at early stages. These innovations enable earlier intervention and improve patient outcomes. Improved imaging techniques are crucial not only for early detection but also for monitoring tumor growth and assessing treatment effectiveness, offering a comprehensive understanding of the disease. Du et al. [2] discussed the key properties of coordinated magnetic nanoparticles (MNPs), such as magnetic moment and saturation magnetization, and provided an in-depth review of mechanistic studies on doping ferrite with transition metal ions to fine-tune magnetic properties. Doping ferrite with transition metals has proven to be an effective strategy for optimizing MNPs' performance in biomedical applications. The authors also highlighted the potential mechanisms and recent progress in transition metal ion-doped MNPs (TMNPs) for bioimaging, including magnetic resonance imaging and magnetic particle imaging, and tumor therapy, such as magneto-mechanical killing, magnetothermal therapy, and drug delivery.

Luminescent nanomaterials present a cutting-edge alternative, providing a flexible platform for developing sophisticated diagnostic and therapeutic systems. Their natural ability to emit light, known as photoluminescence, allows these materials to be utilized for both diagnosing and treating diseases simultaneously. This dual functionality makes them highly valuable in medical applications, particularly in oncology. Among these innovative materials, carbon dots (CDs) and nanohydroxyapatite (nHA) have garnered significant attention for their exceptional properties and versatility as optical imaging probes. Carbon dots are tiny, carbon-based nanoparticles that exhibit excellent photoluminescence, making them ideal for high-resolution imaging. They are also biocompatible and easy to modify, which enhances their effectiveness in various medical applications. Nanohydroxyapatite, on the other hand, is a calcium phosphate material similar to human bone, which makes it highly biocompatible and suitable for medical use. Its ability to host luminescent rare-earth elements further increases its potential as a diagnostic tool. In their comprehensive review, Sengar et al. [3] delve into the different synthesis strategies and development processes for CDs and nHA-based nanomaterials. They discuss the various techniques used to produce these materials, such as chemical methods, hydrothermal processes, and sol-gel techniques, each offering unique advantages in terms of size control, surface properties, and

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luminescence efficiency. By optimizing these synthesis methods, researchers aim to enhance the performance and applicability of these nanomaterials in clinical settings. Furthermore, the review highlights the multifunctional nature of CDs and nHA, showcasing their ability to serve as both diagnostic and therapeutic agents. For instance, carbon dots can be used to visualize tumors with high precision while simultaneously delivering drugs to the affected area, thereby improving treatment efficacy and reducing side effects. Similarly, nHA can be engineered to carry therapeutic agents, providing targeted treatment to cancer cells while minimizing damage to healthy tissues. Sengar et al. also address the current challenges and future directions in the field. They emphasize the need for further research to improve the stability, biocompatibility, and targeting capabilities of these nanomaterials. By overcoming these challenges, CDs and nHA can be more effectively integrated into clinical practice, paving the way for advanced cancer treatments that are both more precise and less invasive.

The increase in the number of degenerative diseases has emerged the development of innovative biomaterials, mostly focused on reducing the adverse effects caused by current medical therapies. Theranostic materials represent an alternative to treat degenerative diseases, since they combine diagnostic properties and localized therapy spontaneously. In another research, Belman-Rodriguez et al. [4] represented the synthesis and characterization of hybrid materials designed for theranostic purposes. They suggested a composition of $LiGa_5O_8:Cr^{3+}$ (LGO) with emission lines in the near infrared (NIR), hence providing an excellent diagnostic ability. For the therapeutic aspect, they incorporated gold nanorods (AuR) with localized surface plasmon resonance (LSPR) into the hybrid nanomaterials. Upon excitation, these gold nanorods trigger plasmonic processes on their surface, raising the localized temperature and causing irreversible damage to the cells. The researchers confirmed that the hybrid nanocomposite materials could be effectively assembled using LGO and AuR, maintaining their luminescent properties and LSPR. The successful synthesis of these hybrid materials, combining NIR emission from LGO and the therapeutic capabilities of AuR, opens new possibilities for designing advanced materials with enhanced properties for medical applications.

In addition to drug delivery, biomaterials are increasingly employed in innovative therapeutic approaches. These materials can be engineered to react to specific changes in the tumor microenvironment, such as variations in pH or temperature. This capability triggers the controlled release of therapeutic substances or induces therapeutic effects like hyperthermia. This targeted precision enhances treatment efficacy while minimizing harm to surrounding healthy tissues. Furthermore, biomaterials are being investigated for their potential in combination therapies, where they can deliver multiple therapeutic agents simultaneously or synergistically enhance other treatment methods to optimize therapeutic outcomes. For instance, Kermani et al. [5] synthesized Fe-doped mesoporous 45S5-based bioactive glasses (MBGs) using the sol-gel method with Pluronic P123 as a soft template. The resulting Fe-doped MBGs maintained a glassy structure with mesoporous properties, and the inclusion of Fe_2O_3 did not significantly impair the glasses' bioactivity. Their study suggests that Fe-doped 45S5-derived glasses could be beneficial in cancer therapy by triggering Fenton's reaction and generating reactive oxygen species (ROS). While early findings are promising, further in vivo animal studies are crucial to fully explore the potential of Fe-doped MBGs in cancer therapy.

Recent advancements in biomaterials have revolutionized the landscape of immunotherapy, offering more effective treatments for cancer. One of the breakthroughs involves the use of hydrogels and other sophisticated delivery systems that can encapsulate immune cells such as CAR-T cells. This encapsulation not only protects these cells but also enhances their persistence and efficacy against tumors. By providing a supportive environment, biomaterial-based encapsulation allows CAR-T cells to retain their functionality over extended periods, facilitating sustained anti-tumor responses and potentially leading to durable remissions in cancer patients. Furthermore, biomaterials are now being harnessed to deliver immune-modulating agents that can precisely activate or suppress specific components of the immune system. This targeted modulation helps tailor immune responses to effectively combat various types of cancer. One notable study highlighted in this collection, conducted by Suraiya et al. [6], investigated an injectable gelatin-based micro-hydrogel system specifically designed for CAR-T therapy. Their findings revealed that CAR-T cells targeting TAG-72, when encapsulated in these microgels, exhibited robust viability (> 87%) even after one week of culture. This viability was comparable to cells grown under standard expansion conditions, indicating that the micro-hydrogel environment adequately supported cell survival and function. Importantly, the encapsulated CAR-T cells maintained their phenotype and demonstrated potent on-target cytotoxicity against human ovarian cancer cells both in vitro and in three-dimensional tumor spheroids. These findings underscore the potential of micro-hydrogels as versatile carrier systems capable of augmenting CAR-T immunotherapy for solid tumors, offering new avenues for improving cancer treatment outcomes.

Biomaterials play a crucial role in creating biosensors that monitor disease progression and treatment effectiveness in real time. These sensors identify specific cancer-related biomarkers, offering valuable insights for personalized medical care. By enabling continuous monitoring, biosensors assist in making timely treatment adjustments based on accurate data. Integrating biosensors with wearable devices and digital health platforms could further enhance their capabilities, providing non-invasive, real-time monitoring solutions that significantly enhance patient care and management. Terahertz (THz) technology is advancing as a non-invasive imaging method for biosensing and clinical diagnostics. Cancerous tumors exhibit higher water content and structural variations compared to healthy tissues, resulting in distinct THz absorption patterns. Recent focus in nanotechnology has explored nanoparticles as contrast agents to enhance THz imaging accuracy, sensitivity, and specificity. These multimodal agents leverage temperature-dependent THz spectra to detect changes in water molecule conformation. Sadeghi et al. [7] review advancements in THz contrast agents, aiming to improve non-invasive imaging sensitivity and specificity for translational clinical oncology. They discuss novel strategies for optimizing nanoparticle design to achieve higher sensitivity and specificity in cancer detection using THz imaging. Furthermore, their research highlights the potential of these advanced contrast agents to contribute significantly to non-invasive diagnostic practices in clinical oncology, paving the way for improved patient outcomes through early and accurate cancer detection.

Personalized medicine marks a significant shift in cancer treatment, aiming to customize medical care based on each patient's unique characteristics. This approach integrates genetic, environmental, and lifestyle factors to develop targeted therapies that are more potent and less harmful than traditional methods. In cancer care, personalized medicine involves detailed genetic profiling of tumors to pinpoint specific mutations and biomarkers targeted by precision therapies, such as inhibitors and monoclonal antibodies, which directly disrupt cancer's molecular pathways. Advanced diagnostic tools like next-generation sequencing and liquid biopsies are used to monitor treatment responses in real-time, optimizing efficacy while minimizing side effects. This strategy not only enhances treatment outcomes but also improves patient quality of life. The integration of personalized medicine into cancer care is rapidly evolving, promising highly individualized treatments that could lead to more effective disease management and potentially higher cure rates. Regarding microfluidic systems, they offer distinct advantages such as accuracy, high throughput, cost-effectiveness, parallelization capability, precise measurement, and continuous cell culture medium exchange, making them increasingly valuable in diagnosing and treating various types of cancer. For instance, Salehi et al. [8] employed a microfluidic concentration gradient device under dynamic cell culture conditions to evaluate the

anti-cancer effects of probiotic strains against breast cancer cells. Their study demonstrated that the cells proliferated for at least one day, but specific concentrations of probiotic supernatant in the system induced greater cell death signaling after two days compared to conventional static cell culture methods. Importantly, their findings underscored that optimal doses in dynamic microfluidic platforms were lower than those used in static cultures, highlighting the potential of these systems in personalized cancer therapy.

Modeling tumors accurately poses a significant challenge due to their intricate and ever-changing nature. Current models often fail to accurately replicate results obtained in controlled laboratory settings when applied to real-life scenarios, primarily because tumors exhibit different characteristics in vitro compared to in vivo environments. This discrepancy is largely influenced by the uniform nature of tumors and their surrounding microenvironments. In response to these challenges, hydrogel-based 3D bioprinting has emerged as a promising method to simulate the growth and behavior of cancer cells. This innovative approach allows researchers precise control over the size and distribution of components within the tumor microenvironment. Moreover, it enables the use of patient-specific tumor cells, rather than relying on commercially available cell lines. As such, hydrogel bioprinting is anticipated to revolutionize cancer research by providing more realistic models for studying the disease's progression and testing potential therapies. Gnatowski et al. [9] provided a comprehensive overview of cancer statistics, current modeling techniques, and their limitations. They also underscored the importance of bioprinting in cancer research, emphasizing the critical role of hydrogel selection in enhancing the accuracy of tumor models. Additionally, they explored current trends and future prospects for utilizing bioprinted models in clinical settings to advance personalized cancer treatment strategies.

The research featured in this special issue demonstrates the immense potential of biomaterials to transform cancer research and therapy. By integrating advanced materials science with biomedical engineering, researchers are pioneering new strategies to combat this complex and devastating disease. The ongoing advancements in this dynamic field promise not only to enhance our understanding of cancer biology but also to lead to more effective and personalized treatments, ultimately improving patient outcomes and quality of life. As we continue to explore the possibilities offered by biomaterials, we move closer to achieving significant breakthroughs in the fight against cancer. The synergy between biomaterials and cancer research is paving the way for innovations that were once considered unattainable. The future holds exciting prospects, where the convergence of nanotechnology, biotechnology, and material science will likely yield novel therapeutic platforms and diagnostic tools. These innovations will not only address the current challenges in cancer treatment but also anticipate and mitigate future hurdles, ensuring a sustained and progressive approach to cancer care. The contributions to this special issue highlight the diverse applications and transformative potential of biomaterials in oncology. From enhancing the precision of cancer diagnostics to improving the efficacy of therapies, biomaterials are at the forefront of a paradigm shift in cancer research. As researchers continue to push the boundaries of what is possible with biomaterials, we can anticipate a future where cancer is not just manageable but curable, ushering in an era of unprecedented medical advancement and patient care.

Declaration of Competing Interest

There is no conflict of interest to declare.

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