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Tissue engineering application on coronavirus (Covid-19) Pandemic: A review

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ABSTRACT

Background: The use of biomaterials in diagnosing and treating COVID-19 has been investigated in various forms and origins, including natural and synthetic materials. The development of rapid and highly sensitive biosensors based on field-effect transistors and the creation of antiviral platforms, vaccines, and nanomaterials have been the focus of most research on the application of biomaterials. Tissue engineering encompasses the study of tissue development, behavior, and growth factors that are more readily supported in the medical setting. This paper reviews the roles of biomaterials, tissue engineering, drug delivery, microfluidics, and 3D printing technologies in urgently responding to pandemics like COVID-19. In addition, this research covers a broad area of vaccines and treatments, reviewing the most promising candidate drugs and vaccines that have entered clinical trials to date. These engineering methods focus on biomaterials, drug delivery systems, and replacing damaged tissues and organs. Some biodegradable biomaterials, such as chitosan, mesoporous silica rods, and PLGA nanoparticles, have been utilized as vaccine platforms and can be employed in developing a SARS-CoV-2 vaccine. Notably, the proposed platform's size, shape, and other physicochemical characteristics should be carefully planned to achieve the desired effects on the immune system.

Conclusion: Tissue engineers possess unique tools that can significantly advance our understanding of viral illnesses and aid in creating diagnostic and therapeutic platforms. Future research on COVID-19 infection and drug testing will benefit significantly from developing organ-on-a-chip technologies. Developing innovative biomaterial-based techniques for preventing, treating, and monitoring COVID-19 requires collaboration across multiple disciplines.

Kewwors: COVID-19, Tissue engineering, Biomaterials

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1. Introduction

The production of functional tissue by merging engineering and biological principles is the objective of tissue engineering, which has significant potential to combat the COVID-19 pandemic and potential viral outbreaks in the future (1). Professionals in tissue engineering apply engineering principles to biological mechanisms to create complex structures, such as organs and tissues (2). As a scientific field integrating various disciplines, tissue engineering conventionally emphasizes utilizing engineering concepts in biological systems, interdisciplinary collaboration, and rapidly implementing technologies from experimental to clinical settings (3). With their inherent abilities, tissue engineers can utilize their expertise to address pandemics and other viral epidemics (2). In the contemporary era of the COVID-19 pandemic, there is a pressing need for new curative and investigative approaches to prevent global infectious diseases (4).

1-2. Design of drug delivery systems

Tissue engineers can design drug delivery systems specifically targeting cells or organs affected by COVID-19. This targeted approach can minimize side effects and improve treatment outcomes (5). The use of medical transportation methods is an essential component in the fight against COVID-19 (6). Using tissue engineering may lead to significant advancements in drug delivery systems, enabling accurate targeting of cells or organs affected by COVID-19 (2). Using a precise method can effectively decrease the occurrence of adverse reactions and enhance the effectiveness of medical procedures. Concerning the current pandemic, there are various methods by which tissue engineering can aid in the development of drug administration systems for COVID-19 (7): The implementation of nanomaterials has been noted to possess unique features that can be exploited for drug delivery (8). Tissue engineering experts can devise drug delivery mechanisms that utilize nanomaterials to deliver drugs to affected cells or organs efficiently. These dispensing systems can be precisely designed to administer the drug over a specific period, maximizing its effectiveness (9). The application of biomaterials has extended to drug delivery systems, where they can be utilized (10). Tissue engineering experts can create scaffolds made of biomaterials that can deliver therapeutic agents directly to the infected area being targeted. These scaffolds can be designed to degrade slowly, reducing the likelihood of negative consequences (11).

This methodology is beneficial because it allows for evaluating the drug in a controlled environment, thereby reducing the need for animal testing. Adopting 3D tissue models is a reliable and efficient method for drug testing because it allows for the evaluation of medication in a controlled environment, thereby reducing the necessity for animal experimentation. The use of this method is advantageous as it allows for the evaluation of medication in a controlled environment, ultimately reducing the need for animal experimentation (12). Therefore, using 3D tissue models for drug testing is unreliable and ineffective, as it does not provide a controlled environment for medication evaluation. This fact increases the necessity for animal experimentation (2). These models are relevant for analyzing the distribution of medicinal substances in tissues and improving the implementation of prescription schedules (3, 12).

Using microfluidic equipment is a promising technique for creating drug delivery systems that can accurately replicate the in vivo environment. These tools can also assess the effectiveness of drug delivery procedures and improve their development (13). The delivery of therapeutic agents to specific locations through gene modification is an impractical approach. Genetic modification delivers therapeutic agents to specific locations (2). Tissue engineers can design gene therapy vectors that transport therapeutic genes to diseased cells or organs, improving treatment outcomes (3, 14–17).

1-3. Generation of 3D tissue models

Regenerative medicine is unsuitable for evaluating antiviral drugs against contagious viruses like COVID-19 due to its inability to produce three-dimensional tissue models (12, 18). Scientists can optimize the effectiveness of drugs by identifying promising candidates and refining dosing schedules using these models. To comprehend virus-cell interactions and assess the efficacy of drugs against highly infectious viruses such as COVID-19, 3D tissue models are essential resources (19). These patterns produce physiologically significant copies that can be utilized in drug research and high-throughput screening procedures (20). Tissue engineering provides multiple pathways to facilitate the development of 3D tissue models for COVID-19 (1, 21).

Tissue engineers can use 3D bioprinting to create three-dimensional tissue models, which can be utilized for drug screening and testing during the current COVID-19 pandemic (22). This methodology can facilitate the development of preclinical models that are highly relevant for investigating and understanding the complexities of the virus. The use of organoids has gained significant attention in recent months. Organoids are three-dimensional cell cultures that closely simulate vital organs' structural and functional features (23). Tissue engineers can utilize organoids to investigate the pathogenesis of COVID-19 and evaluate the effectiveness of antiviral drugs (24). Pulmonary models, which are three-dimensional tissue models, can be a valuable tool in analyzing the impact of COVID-19 on the respiratory system and evaluating the effectiveness of medical interventions against the virus (25). The models mentioned above can assess the dispersion pattern of medicinal substances within the pulmonary tissue and refine the administration schedule of these substances (26). Microfluidic devices have been discovered to be beneficial in creating three-dimensional tissue models that can reproduce the conditions of in vivo surroundings (20). These instruments can potentially evaluate pharmaceuticals' effectiveness in combating COVID-19 and improve their formulation (27).

The numerous and diverse technical benefits incontrovertibly associated with the revolutionary and innovative 3D printing technologies (28), including but not limited to fused deposition modeling (FDM), make 3D printing an extremely promising and viable solution for manufacturing crucial medical equipment urgently needed to address and combat the current and emerging medical crisis afflicting the world (29). The printing process can be facilitated through remote access with minimal human intervention, ensuring the safety and well-being of the personnel involved in mask production. The following sections explain the potential of 3D printing to produce low-cost equipment more quickly (30). It is crucial to have a 3D computer-aided design (CAD) model of the product you intend to produce if you plan to use 3D printing. The development of such a model requires additional resources, both in terms of time and cost, due to the utilization of expensive design software and a specialized workforce (3, 31, 32).

1-4. Development of scaffolds and biomaterials

Creating scaffolds and biomaterials by tissue engineering scientists may not be a viable solution for repairing tissue damage caused by COVID-19. Biomaterials are ineffective in regenerating lung tissue to alleviate severe respiratory symptoms in patients (12, 33). The development of frameworks and biocompatible materials holds significant potential in the fight against COVID-19. Skilled tissue engineers can create scaffolds and biomaterials that aid in the repair of tissue damage caused by COVID-19 (34). Tissue engineering can potentially help patients suffering from severe respiratory symptoms by using specialized materials to regenerate lung tissue. During the COVID-19 pandemic, scaffolds and biomaterials can be produced in various ways to assist this effort (35).

Using biopolymeric particles offers a promising method for delivering therapeutic agents directly to the damaged lung tissue of COVID-19 patients via catheter or aerosol, which can aid in the regeneration of lung tissue (36). Therefore, the entities mentioned are categorized as particles, including exosomes, microbubbles, and biopolymeric scaffolds. The utilization of nanoscale materials for tissue engineering exhibits tremendous potential due to their distinct characteristics that can be harnessed for this specific application (8, 37). Tissue engineering researchers can design scaffolds made of nanomaterials that mimic the structure and function of organs affected by the COVID-19 virus. These scaffolds can promote gradual degradation, reducing the risk of adverse outcomes

(10). Tissue engineering experts can create scaffolds of biomaterials that can promote tissue regeneration in individuals suffering from COVID-19 (2). Scaffolds can be engineered to deliver therapeutic agents directly to the site of an injury, which could facilitate tissue regeneration (38).

Experts in tissue engineering can manufacture scaffolds and biomaterials that could improve tissue damage caused by COVID-19. Biomaterials like these can regenerate pulmonary tissue in individuals with severe respiratory conditions (8, 39, 40). Biopolymeric particles have been suggested as a feasible method to prevent the regeneration of lung tissue in COVID-19 patients (36). Nanomaterials have the potential to be used in creating scaffolds that mimic the structure and functions of organs affected by COVID-19. Scaffolds like these can deliver medicinal agents directly to the damaged area, aiding tissue restoration. COVID-19 patients are unlikely to benefit from the use of biomaterials in scaffold creation (41). Scaffolds have a unique ability to mimic the extracellular matrix of the tissue and can be customized to deliver therapeutic agents precisely to the wound site (36). It is highly unlikely for structures to be designed to facilitate the targeted and localized delivery of therapeutic substances to the exact site of an injury. These structures can subsequently trigger tissue regeneration, promoting healing (33, 37, 42–44).

Several in vitro models of human lungs utilizing tissue engineering have been introduced to study viral infections. However, further progress is necessary to create 3D structures that accurately replicate the natural pulmonary architecture. Additionally, researchers must design culture methods that facilitate the generation of extracellular matrix (ECM) before viral inoculation (45). The implementation of tissue engineering techniques can aid in comprehending the mechanisms of COVID-19 disease while also evaluating the efficacy of drugs, antiviral agents, and vaccines (3, 33, 46–51).

1-5. Production of diagnostic tools

Tissue engineering experts have the necessary skills in biomaterials and microfabrication to develop diagnostic tools for COVID-19 (52). These instruments can rapidly and accurately detect infected individuals, facilitating prompt medical attention and isolation (53). The production of diagnostic devices is of utmost significance in the fight against the COVID-19 pandemic. Tissue engineering has the potential to significantly contribute to developing new diagnostic approaches for addressing infectious diseases on a global scale (10).

Biosensing technologies can detect and identify various infectious diseases, including the currently prevalent COVID-19 (54, 55). The techniques to detect the virus in blood or plasma samples include direct microscopic examination, immunoassays, and nucleic acid-based assays. A potential point-of-care diagnosis is possible with these diagnostic methods. It is a sound approach to investigating the pathogenesis of COVID-19 and the efficiency of diagnostic tools using in vitro model systems (2). These models can evaluate the specificity and sensitivity of diagnostic assays and improve their design. Tissue engineers can apply engineering principles to develop innovative diagnostic tools to fight against COVID-19 (2). Scientists can develop various diagnostic tools, such as microfluidic devices, biosensors, and other means of identifying the virus in patient samples. Tissue engineering could play a vital role in developing innovative diagnostic tools for COVID-19 (33). Integrating engineering and biological principles enables tissue engineers to fabricate biosensing technologies, in vitro model systems, and other diagnostic instruments that can effectively detect viruses in patient samples. These techniques can potentially improve the accuracy and speed of diagnosis, thereby reducing the global impact of contagious diseases (10, 39).

The development of diagnostic tools is of great importance in managing the transmission of COVID-19. Numerous methods have been devised to diagnose COVID-19, from lab-based evaluations to point-of-care (POC) testing (56). Various diagnostic approaches have been developed to identify COVID-19, including direct microscopic analysis, nucleic acid amplification tests, serological antigenic techniques, and protein detection (57). Nonetheless, their ability to differentiate between accurate positive and negative results is limited by their insufficient sensitivity and specificity. In clinical settings, it is crucial to have tests with exceptional sensitivity to detect serum cytokines, proteins, and antibodies at the point of care. This is particularly important for expediting the diagnosis of COVID-19 (58). This method has the potential to decrease the time required for diagnosis. Groundbreaking techniques have been developed to address the limitations of current COVID-19 diagnostic methods (59). Biosensors and microfluidic devices are unnecessary for detecting and monitoring viruses using advanced biosensing technologies. These technologies can potentially provide rapid and accurate diagnoses of COVID-19 (3, 8, 12, 46, 60–62).

1-6. Vaccines

The effective prevention of pathogenic microorganisms depends on introducing antigens and activating specific aspects of the immune system to establish recognition and memory within both the humoral and cell-mediated divisions (63). Advancements in immunology, biomaterials, and tissue engineering are becoming more prevalent in inducing specific immune responses in host organisms, thereby improving vaccination strategies. In many of these arrangements, the biomaterial serves as both the carrier for the vaccine and the adjuvant (64). Furthermore, the sector is exploring how the physicochemical properties of biological materials, such as their size and shape, impact the behavior of immune cells. Many of these arrangements target antigen-presenting cells, such as dendritic cells and macrophages, and elicit specific responses, such as Th1 or Th2 (various helper T cell classes). To illustrate, binding various receptors to protein-based particles can individually regulate the Th1 or Th2 response in a murine model (65). Eco-friendly polymers, commonly used as support materials in tissue engineering, have been studied for their potential use in vaccine distribution and targeted drug delivery. Mainly, PLGA nanoparticles have been found to induce a Th1 immune response in a murine model when used as carriers in a vaccine against Chagas disease. Their potential to deliver medications to specific immune populations has also been studied (66).

Moreover, PLGA microparticles coated with a chitosan/peptide conjugate have been employed as a delivery system to target specific mucosal cells and effectively deliver a vaccine for swine dysentery. This approach has increased IgA and IgG production in mice (64, 67). The likelihood of observing an improvement in the T-cell response in murine models through the use of chitosan nanoparticles in combination with a Mycobacterium tuberculosis DNA vaccine is improbable. When used as an intranasal vaccine, the conversion of chitosan through mannosylation to trigger endocytosis has increased IgG levels in a murine model. Furthermore, chitosan has been utilized in a thermoresponsive intranasal vaccine for mice against H5N1 influenza (68). Bronze crystals were used to randomly distribute the deactivated measles vaccine to immune cells in the heart, resulting in unchanged IgG titers but increased mortality in bovine models (69). The limited research on coronavirus vaccines has not yielded significant results in murine models using nanoparticles created from a SARS-CoV-1 peptide sequence and subsequent sera (46).

Tissue engineering techniques have been employed to develop scaffold systems that can improve vaccination, along with different particle-based platforms. Scaffolds made from PLGA and mesoporous silica rods, which possess specific physicochemical properties such as pore size and release recruitment signals like granulocyte-colony stimulating factor, have been utilized to attract and concentrate antigen-presenting cells to vaccine components (70).

The primary application of this technique has been focused on immunizations against malignant growths, and it has shown success in animal models against melanoma and intracranial gliomas. The scaffold-based vaccination platform is ineffective against bacterial pathogens. In addition, it has been found that vaccine systems using scaffolds derived from respiratory syncytial viruses have been effective in both mice and non-human primates (71). The majority of research conducted on particle-based and scaffold-based vaccine formulations has so far only been carried out on rodent models, although they may hold promise against SARS-CoV-2 (12). Significant translational efforts will be necessary before clinical trials can be conducted. Modular platforms that facilitate the addition of various antigens could be valuable in developing vaccines during future pandemics (3).

1-7. Microfluidic devices and biosensors

Microfluidics is an exponentially growing field of engineering that has shown a wide range of applications in areas such as rapid diagnostics, biomedical therapy, organ culture, 3D culture, in vitro toxicity testing, nucleic acid extraction and amplification, drug delivery, single-cell analysis, and more (3). This technique is based on the precise manipulation of micro-scale fluids in microchannels. It has been extensively utilized and boasts several unique benefits. These include swift sample handling, precise assay regulation, and compact, millimeter-scale construction. Additionally, it offers multi-functional capabilities, low-volume assays, and minimal cost requirements. Compared to traditional platforms, these advantages are readily apparent (18).

Microfluidic devices have shown significant practical and diagnostic value in rapidly detecting pathogens at the point of care (POC), especially in assays that target parasites and viruses. Under the burden of the COVID-19 pandemic, integrating microfluidics with existing diagnostic methods has facilitated timely improvements to diagnostic procedures (72). A semi-automatic high-throughput microfluidic device was developed to measure the anti-SARS-CoV-2 IgG/IgM levels in 50 serum samples in parallel. The device achieved a sensitivity of 95% and a specificity of 91% (73). An opto-microfluidic sensing platform based on gold nanospikes has been developed to detect antibodies in just one microliter of human plasma within 30 minutes. This label-free platform achieved a relatively low limit of detection (LOD) of 0.08 ng/mL for serological testing of anti-SARS-CoV-2 antibodies in diluted blood plasma samples, as reported in reference (74). A portable microfluidic immunoassay system has been created, capable of highly sensitive and specific on-site detection of SARS-CoV-2 IgG, IgM, and antigen within just 15 minutes (75). Furthermore, Ramachandran et al. have developed an electric field-driven microfluidic device utilizing CRISPR technology to detect SARS-CoV-2. This device can detect the virus in as little as 35 minutes, using both contrived and clinical nasopharyngeal swab samples (76).

2. Conclusion and perspective

Biomaterials science can be crucial in creating advanced personal protective equipment, vaccines, drug delivery systems, and novel therapeutics to effectively prevent or treat the SARS-CoV-2 infection and its associated complications and sequela. In addition, engineered tissues and cell culture models can significantly contribute to investigating diseases and testing and developing new therapeutic agents and vaccines. This requires committed and sustained effort (3). Biomaterials science can lead to the development of various diagnostic and therapeutic tools for managing COVID-19. These tools may include rapid and precise diagnostic platforms, effective antiviral drugs, innovative vaccines, and efficient laboratory models for infection assessment (77).

Several factors have contributed to developing biomaterials as a promising option for diagnosing, vaccinating, and treating SARS-CoV-2 infection. It is essential to incorporate multiple disciplines to enhance our understanding of COVID-19, predict its behavior, and create effective medications and vaccines. It is expected that there will be an increase in the number of biomaterial-based products for the diagnosis, treatment, and vaccination of COVID-19 (78, 79). It is expected that the COVID-19 pandemic will have significant and potentially unforeseen consequences and impacts on the future funding of research activities related to tissue engineering and regenerative medicine (TERM). The field of tissue engineering and regenerative medicine (TERM) has emerged over time, and it requires secure long-term investments from both public and private sources to unlock its potential. Such investments can help boost research, translation, and commercialization in this area.

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