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Regenerative medicine as a therapeutic alternative for chronic diseases and serious injuries: Advances, challenges and clinical applications

La medicina regenerativa como alternativa terapéutica para enfermedades crónicas y lesiones graves: Avances, desafíos y aplicaciones clínicas

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Summary

In recent years, regenerative medicine has experienced remarkable progress and the emergence of new applications, as well as significant challenges. This review article aims to analyze the advances, clinical applications, and challenges in regenerative medicine to drive further development and research in this field. The research adopted a qualitative approach and followed the systematic review protocol based on the PRISMA 2020 guidelines. Key advances include 3D bioprinting and cellular reprogramming, which have enabled the creation of functional tissues and organs in the laboratory, as well as the development of therapies to regenerate musculoskeletal tissue and vital organs from stem cells. Although many experimental studies on cell regeneration face challenges such as immunological compatibility and validation in aspects of safety and efficacy, these studies show great potential for more effective and less invasive treatments. According to the Regenerative Medicine 2030 Report, conducted in 2023, the regenerative medicine therapy market was valued at USD 30.43 billion worldwide; and an annual growth of 16.79% is expected from 2024 to 2030. In addition, a deeper understanding of the cellular and molecular mechanisms involved in organ and tissue regeneration has been achieved. The results demonstrate significant advances in regenerative medicine through the use of stem cells, platelet-rich plasma, organoids, and 3D printing, highlighting their application in the regeneration of bone, cartilage, neuronal, skin, and ocular tissue. Ethical and technical regulatory challenges are identified, such as the need for standardization, regulatory approval, and the development of safe and effective protocols for their clinical implementation. While regenerative medicine therapies are emerging as promising therapeutic alternatives for chronic diseases and serious injuries, continued interdisciplinary research is essential to advance their development and consolidate a future in which these conditions can be treated more efficiently and with less invasive methods, thus transforming medical practice.

Keywords: 3D bioprinting, stem cells, regenerative medicine, cell therapy, cell reprogramming.

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Abstract

In recent years, regenerative medicine has seen remarkable progress and the emergence of new applications, as well as significant challenges. This review article aims to analyze the advances, clinical applications, and challenges in regenerative medicine to drive further development and research in this field. The research adopted a qualitative approach and followed the systematic review protocol based on the PRISMA 2020 guidelines. Key advances include 3D bioprinting and cellular reprogramming, which have enabled the creation of functional tissues and organs in the laboratory, as well as the development of therapies to regenerate musculoskeletal tissues and vital organs from stem cells. Although many experimental studies on cell regeneration face challenges such as immunological compatibility and validation in terms of safety and efficacy, these studies show great potential for more effective and less invasive treatments. According to the Regenerative Medicine 2030 Report, conducted worldwide in 2023, the regenerative medicine therapy market was valued at USD 30.43 billion; and an annual growth of 16.79% is expected from 2024 to 2030. In addition, a deeper understanding of the cellular and molecular mechanisms involved in organ and tissue regeneration has been achieved. The results demonstrate significant advances in regenerative medicine through the use of stem cells, platelet-rich plasma, organoids, and 3D printing, highlighting their application in the regeneration of bone, cartilage, neuronal, skin, and ocular tissue. Ethical and technical regulatory challenges are identified, such as the need for standardization, regulatory approval, and the development of safe and effective protocols for their clinical implementation. While regenerative medicine therapies are emerging as promising therapeutic alternatives for chronic diseases and serious injuries, continued interdisciplinary research is essential to advance their development and consolidate a future in which these conditions can be treated more efficiently and with less invasive methods, thus transforming medical practice

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1. Introduction

Regenerative medicine has emerged as a promising therapeutic alternative within the field of medical sciences, as a response to the constant search to improve the quality of life of people suffering from chronic diseases and serious injuries (1). This innovative field of medicine not only offers hope, but also tangible solutions for patients with degenerative diseases, organ transplants and trauma who previously seemed incurable or were affected by limited treatments (2).

In fact, the rapid advances in regenerative medicine have completely transformed the approach to various conditions ranging from spinal cord injuries to diseases such as Parkinson's, Alzheimer's and Diabetes Mellitus. These conditions continue to be investigated for treatment through stem cell tissue regeneration (2). This branch of medical science has sparked renewed interest among the scientific community, healthcare professionals and, above all, among patients and their families.

Regenerative medicine is defined as an emerging multidisciplinary field that seeks to repair or replace injured tissues or organs through tissue engineering (3). It is divided into three main approaches: stem cells, growth factors, and extracellular matrix or scaffolding (3). Each approach has the therapeutic potential to regenerate tissues to restore their normal function, rather than simply alleviate the symptoms of diseases.

Regenerative medicine offers a number of significant benefits for patients, healthcare professionals, and society at large. These include the possibility of personalized treatment, reduced long-term dependence on medications, improved quality of life, and the potential reduction in costs associated with long-term medical care (4) .

There are several regenerative medicine techniques, such as cell therapy, tissue engineering, and genomic medicine, that have become major advances in the field of medicine. Researchers in regenerative

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medicine are exploring new ways to harness the body's regenerative potential to treat a wide range of conditions.

of pathologies. This regeneration-focused approach represents a paradigm shift in the treatment of chronic diseases and serious injuries (5).

The increasing incidence of chronic diseases and serious injuries in contemporary society demonstrates an urgent need for new therapeutic strategies. In this context, regenerative medicine, by focusing on tissue repair and regeneration, offers more lasting and less invasive solutions than conventional treatments. This represents a genuine expectation for patients facing debilitating or potentially fatal medical conditions (6).

Thus, the main objective of this study is to analyze the latest advances, challenges, and clinical applications of regenerative medicine in the treatment of chronic diseases and serious injuries. Through a comprehensive review of the scientific and clinical literature, we aim to identify current trends, clinical and ethical implications, and future opportunities in this promising and dynamic field.

Methodology

The current research was carried out from a qualitative approach, following the systematic review protocol based on the PRISMA 2020 guidelines Preferred Reporting Items for Systematic Reviews and Meta-Analyses), which led the search, selection and analysis of relevant studies (Appendix A). The research variables were advances, challenges and clinical applications in regenerative medicine.

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Search Strategy:

A systematic search was conducted in databases such as Scopus, Google Scholar, PubMed, Uptodate, Dialnet Plus, Science Direct. The use of keywords and Boolean operators allowed the publications to be specified, as follows: ("Medicine" AND "Regenerative"; "Chronic Diseases" AND NOT "Acute Diseases"; "Stem Cells" OR "Tissue Regeneration" OR "Cell Therapy" OR "Tissue Engineering").

To narrow down the search results, the following filters were applied: time limit (2017-2024), subject area (Medicine; biochemistry, genetics and molecular biology, Engineering), document types (articles, reviews, editorials, conference papers, books), keywords (regenerative medicine, stem cells, tissue regeneration, cell therapy), language (Spanish and English), and documents that are available online and do not require payment for access were included.

Eligibility Criteria:

The selected publications meet the following inclusion criteria: (1) Study types such as: scientific articles, review articles, clinical trials, books, theses, observational studies, meta-analyses; (2) Interventions related to regenerative medicine treatment, such as cell therapy, gene therapy, tissue engineering, 3D bioprinting, etc. (3) Studies published from January 2017 to February 2024; (4) Studies published in English and Spanish.

The exclusion criteria applied in the literature search are listed below: (1) Duplicate studies or those with a high risk of methodological or quality bias; (2) Studies evaluating regenerative therapies for acute or superficial diseases that are not considered within the scope of the topic;(3) Publications outside the time range of January 2017 to February 2024; (4) Studies published in languages other than English and Spanish.

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Study Selection and Data Extraction:

The researcher was responsible for filtering out publications that did not meet the inclusion criteria. Studies were selected based on keywords and a reading of their abstracts, methodology, and conclusions. A narrative synthesis of the findings of the included studies was also conducted, highlighting the advances, challenges, and clinical applications of regenerative medicine in the treatment of chronic diseases and serious injuries.

Figure 1. PRISMA diagram

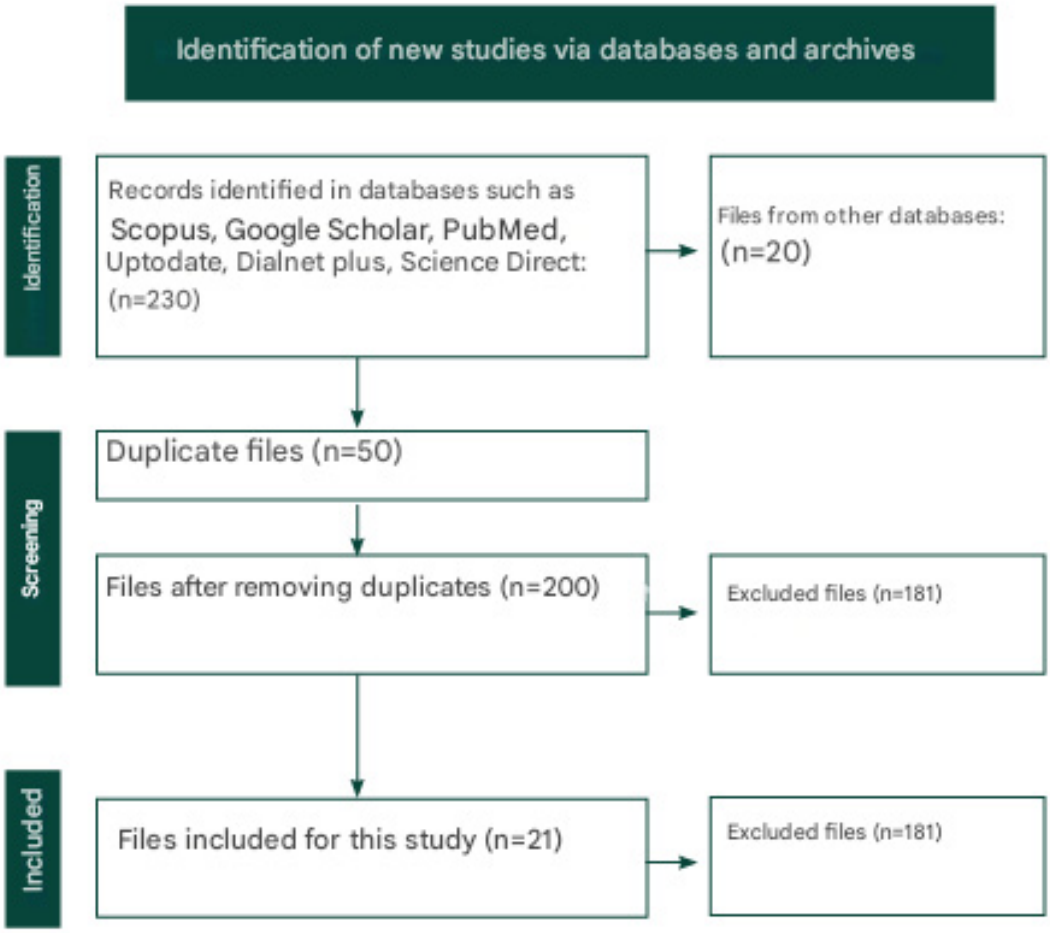

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Table 1. Results

Qualification	Authors	Year	Type of Study	Aim	Results
INTESTINAL ORGANOIDS: Present and future of biomedical research	Díaz, C.	2023	Review article	To provide an updated, literature-based overview of the applications of intestinal organoids in biomedicine and their future potential.	Intestinal organoids have proven useful in regenerative and precision medicine, as they have demonstrated the ability to model intestinal physiology and diseases, as well as epithelial damage caused by various agents. These models have allowed for in-depth studies of the molecular biology of various pathologies and the search for specific treatments. (7).
New approaches to developing safer strategies in regenerative medicine	Alkhraisat, M., Troy, M., Zalduendo, M., Anitua, E.	2019	Scientific article	Explore the advances, challenges, and clinical implications of regenerative medicine, emphasizing the use of autologous biological materials such as PRGF-Endoret for personalized tissue repair and regeneration.	PRGF-Endoret is a system that offers autologous biomaterial enriched with proteins and growth factors, capable of recreating three-dimensional matrices, providing a physical and bioactive environment for the regeneration and replication process. PRGF-Endoret has been shown to enhance the hemostatic effect, reduce the intensity of inflammation, and accelerate the proliferative and remodeling phases of bone tissue. The results also demonstrate that PRGF-Endoret is an alternative for the isolation, culture and ex vivo conservation of stem cells from different origins, without the risk of pathogen transmission or immune rejection, maintaining their phenotype and multilineage differentiation potential (4) .
Regenerative medicine: fundamentals and applications	Isaza, C., Henao, J., Aranzazu, J.	2018	Review Article	To systematically review and organize the latest information on the principles and applications of regenerative medicine.	Stem cells are special cells that can transform into other types of cells to aid tissue regeneration. Research indicates that when combined with demineralized bone and platelet-rich plasma, fracture healing is accelerated. They are also effective in the treatment of osteoarthritis, as they promote cartilage regeneration (4). In the field of eye diseases, the first commercial drug based on stem cells has already been approved for the treatment of corneal burns. Furthermore, it has been proven that the intradermal application of stem cells can prevent the formation of excessive surgical scars, preserving the normal structure and function of the skin (4) .

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Ethics in the field of Regenerative Medicine Research	Quesada, L., Barrios, C., Díaz, Z.	2021	Review Article	To examine the ethical aspects involved in research, fostering critical reflection, both cognitive and ethical, on scientific development in the field of regenerative medicine.	Regenerative medicine carries great ethical importance both in assessing the treatment of various diseases and in making responsible decisions. This includes respecting the limits of the patient's informed consent. Maintaining an appropriate ethical stance in regenerative medicine allows us to measure the impact of treatment with a responsible and humane attitude.
Ethics in regenerative medicine and platelet-rich plasma treatment	Quesada, L., León, C., Quintana, E.	2021	Review article	Analyzing regenerative medicine and platelet-rich plasma treatment from an ethical perspective	The ethical perspective linked to the use of platelet-rich plasma within regenerative medicine facilitated the analysis of scientific and technological advances, ensuring comprehensive, timely and structured medical care, supported by trained professionals and at an affordable and sustainable cost. (2) .
Background of the application of cell therapy as a health technology in medical and dental diseases.	Julia, R., Aurora, N., León, K., Riccis, S., Yolaidays, I., Naughty, N.	2023	Review article	To characterize the background of the use of cell therapy as a healthcare technology in the treatment of medical and dental diseases.	The historical study of the application of cell therapy in the treatment of medical and dental diseases has provided insight into its origin, evolution, and current status. In this context, cell therapy represents an innovative and promising option compared to conventional treatments for tissue regeneration (1) .
Neurodegenerative diseases and Cellular reprogramming: therapeutic potential and promise of rejuvenation	Lehmann, M., Mallat, M., Chiavellini, P., Brown, O., Goya, R.	2019	Book chapter	To describe emerging evidence indicating that aging is a reversible epigenetic process, along with novel reprogramming methods that would avoid the risks associated with conventional techniques requiring the generation of induced pluripotent stem cells (iPSCs).	Research into the production of neural cells, both in vitro and, to a lesser extent, in vivo, is constantly advancing. This line of research seeks to develop safe and effective protocols for obtaining patient-derived cells that can be applied in the treatment of neurological diseases such as Parkinson's, Alzheimer's, and other similar neurological pathologies. (8).

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The business of regenerative medicine and stem cells: confusion with legal implications	Cuende, N., Álvarez-Márquez, A., Díaz-Aunión, C., Castro, P., Huet, J., Pérez-Villares, J.	2021	Review article	To outline the fundamental requirements for the use of autologous biological products, with the aim of offering practical guidance for both the professionals who prescribe them and those who supervise the centers where they are administered.	The use of autologous biological products such as platelet-rich plasma (PRP) requires compliance with specific regulations, including advanced therapy manufacturing labeling, manufacturing in authorized laboratories, and compliance with regulations from the Spanish Agency for Medicines and Medical Devices (AEMPS). For experimental therapies involving cells and tissues, ethical approval and regional authorization are required. Furthermore, advanced therapy medicinal products must comply with transplant regulations regarding aspects such as donation, donor evaluation, and traceability. The Spanish National Transplant Organization (Spanish National Transplant Organization) has also issued regulations regarding medical devices used to obtain autologous cells and the classification of the resulting product as an advanced therapy medicinal product. In the case of cell and tissue transplants that are considered experimental therapies, the sponsor, in addition to submitting the study for evaluation to the corresponding research ethics committee, must request authorization from the competent authority of his autonomous community (the Autonomous Transplant Coordination) (9)

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III Congress on Tissue Engineering and Regenerative Medicine	Weinstein-Oppenheimer, C., Acevedo, C.	2023	Scientific article	To promote the exchange of ideas and cooperation within the scientific community in areas such as tissue engineering, biomaterials, regenerative medicine, and global scientific and technological advances that will influence future therapies, with the goal of contributing to the well-being and quality of life of society.	Significant progress has been made in research on Additive Biomanufacturing and its challenges in tissue replacement within Regenerative Medicine. The application of two biomanufacturing methodologies enabled the implementation of a high-resolution 3D bioprinting system capable of utilizing multiple materials and cells. Furthermore, the fabrication and validation of cellular tissues in animal models was achieved, as well as the development of a novel system for arthroscopic remarking of cartilage lesions. (7) .
Regenerative medicine, its applications and foundations	Pacios, J., Barrosos, M.	2023	Review article	To systematically compile and organize the most current information on the principles and potential uses of regenerative medicine.	The safety of regenerative medicine is supported by various investigations whose results are optimistic about the benefits of this new therapeutic strategy, and it is also assured that new treatment regimens based on regenerative medicine will continue to emerge in the coming years (10) .
Stem cells as an alternative to transvenous pacemakers	Martínez de Hoyo, K., Ortega Enciso, A., Mendoza Beltrán, F., Reynolds Pombo, J.	2020	Review article	To analyze the current development of biological pacemakers and explore future prospects for creating cardiac tissue with pacemaker function using advanced genetic technologies and tissue engineering.	Biological pacemakers, although in a preclinical stage of development, constitute an alternative to electronic devices for patients with selected cardiac diseases in the future. The main challenges faced are the difficulty in ensuring long-term engraftment and the potential risk of proarrhythmias (11) con avances en el dise˜no del cable, el tama˜no del generador, la longevidad de la batería y los algoritmos de software que se han traducido en dispositivos más peque˜nos con funcionalidad mejorada. En la actualidad existen muchos sistemas implantables de cardioestimulación capaces de reemplazar la función de los marcapasos fisiológicos (seno y nódulos aurículo-ventriculares.

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How will skin care change with research advances?	Rodriguez, P.	2018	Editorial	To analyze the efficacy of biomaterials such as umbilical cord fibrin scaffolds in the regeneration of deep wounds and their contribution to regenerative medicine.	The use of biomaterials through tissue engineering techniques allows for new treatment approaches for traditional skin wounds. A successful example is the application of fibrin scaffolds obtained from the umbilical cord for the treatment of deep wounds, which achieved homogeneous, scar-free regenerated skin. This allows us to conclude that research advances in regenerative medicine will serve as a support to current treatments to contribute to and improve tissue reconstruction (12) .
Influence of advances in tissue engineering and regenerative medicine on the progress and evolution of health	Madan Patel, G., Borah, N., Kumar, G.	2023	Review article	Examine how regenerative medicine, tissue engineering, and 3D bioprinting work together, while emphasizing advances in bioprinting technology for transplantable organs and tissues.	Tissue engineering and regenerative medicine work together to create new tissues and organs to offer an alternative to patients with deteriorating organs or debilitating diseases. Studies show that 3D bioprinting has the potential to manufacture or mimic patient-specific natural tissues from scaffolds and stem cells, where the healing and regeneration process is carefully controlled through the release of growth factors. However, improvements are needed to bring this technology to clinical application, but it remains an innovative technology for the future of medicine (5) .

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Advances in the development of organoids as study models in regenerative medicine	Aguilar, P.	2018	Thesis	To conduct a literature review to analyze current knowledge on the development of organoids as study models in the field of regenerative medicine, with a particular focus on intestinal organoids.	The study of organoids, mini organs grown in the laboratory, is booming due to their potential in regenerative medicine. The goal is to improve their development so that they better mimic real organs and optimize their transplantation to replace damaged organs. This opens the door to personalized treatment options for intestinal diseases and personalized medicine (13) se pueden crear unidades funcionales de diferentes órganos, denominados organoides, que se autoorganizan in vitro formando una estructura 3D, capaces de reproducir tanto la función como la estructura del órgano equivalente in vivo. Aunque tienen muchas más aplicaciones, son muy importantes en medicina regenerativa ya que pueden ser útiles para el tratamiento de un gran número de enfermedades donde el órgano no funciona como es debido, ya sea por un defecto genético, por un traumatismo o por otras causas. En este estudio se recogen los últimos avances en el desarrollo, así como en las diferentes formas de maduración de los organoides para su posterior trasplante en el huésped, centrándonos en los organoides intestinales y en las diferentes enfermedades que afectan a este órgano. (13.
3D printers, their innovation in the field of medicine	Alejandro, L., Rodríguez, D.	2020	Review article	Analyze the evolution of 3D printing, from its beginnings to the moment it became established as a method of innovation in medicine.	3D printing in medicine is a great innovation that guarantees more personalized and affordable care, which brings great benefits and good results to patients (7) .
Regenerative medicine for the treatment of neurodegenerative diseases	López-léón, M., Lehmann, M., Goya, R.	2017	Book section	Explore the potential of cellular reprogramming as a therapeutic strategy to restore impaired brain function, focusing on its applications in the treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's.	Mature cellular reprogramming technology will provide, in the not too distant future, effective means to functionally restore the aged brain. Two approaches have been identified: lineage reprogramming and direct reprogramming using pluripotency factors, both aimed at investigating therapeutic alternatives for degenerative diseases such as Alzheimer's and Parkinson's (6) .

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Comparative analysis of bioprinters using additive manufacturing technologies with biomaterials, with the aim of evaluating their efficiency in generating organs and tissues for the biomedical field.	Viera Valencia, L., García Giraldo, D.	2019	Thesis	To conduct a comparative study of bioprinters that use additive processes with biomaterials, with the aim of determining their effectiveness in creating organs and tissues.	Additive process technology with bioinks and biomaterials offers the possibility of manufacturing personalized models and medical supplies adapted to the specific needs of each patient (14) .
Narrative review on the use of platelet-rich plasma as an autologous therapy in regenerative medicine.	Aguilar, R., Cáceres, A.	2020	Review article	To present the theoretical foundations that support the potential use of platelet-rich plasma (PRP) and its growth factors in regenerative therapies through autologous biostimulation, especially in diseases that still lack a specific treatment.	Platelet-rich plasma (PRP) is an autologous treatment used to enhance cell regeneration and tissue healing. Although there is no standardized procedure for its use, PRP has been shown to improve vascular permeability, cell regeneration, tissue healing, and immune response. Further studies are needed to better understand its mechanism of action, but PRP could be useful in degenerative and viral diseases such as COVID-19. In this context, it could be used as a complement during asymptomatic phases, in order to modulate the immune system, promote the regeneration of damaged organs and tissues, and control the progression of multisystem biodegradation (15).

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Standardization of a 3D bioprinting protocol for creating scaffolds with potential applications in tissue engineering.	Castellanos Garzón, J., Correa Quiceno, M., Peñaranda Armbrecht, J., Holguín Ruiz, J., King Piedrahíta, A.	2023	Scientific report	To standardize a 3D bioprinting protocol for creating scaffolds with potential applications in tissue engineering. Materials such as polycaprolactone (PCL), polylactic acid (PLA) filament, flexible filament, and various bioinks were used.	Key parameters such as bed temperature, PLA filament temperature and extrusion speed were adjusted in the REGEMAT 3D bioprinter, achieving the manufacture of three scaffolds with different geometries, potentially useful in areas such as otorhinolaryngology and orthopedics (16) la medicina está siendo complementada y fortalecida con los avances en desarrollo de biomateriales y técnicas como la bioimpresión 3D para la producción de andamios y estructuras orientadas a la reparación, la regeneración o reemplazo de tejidos dañados, afectados por alguna patología o trauma, como también en la prueba de fármacos y la entrega controlada de sustancias utilizadas en el tratamiento de enfermedades, dando paso a la investigación en ingeniería de tejidos, que se define como la ciencia del diseño y fabricación de nuevos tejidos, siendo un campo multidisciplinar que requiere de los aportes de la biología para el cultivo celular, de la ingeniería de materiales y la química para el desarrollo de estructuras 3D denominadas andamios y de profesionales de la salud para su implementación en medicina regenerativa. En este sentido, la Unidad Central del Valle del Cauca incentivando la vocación científica de los estudiantes del programa de ingeniería biomédica, adquirió el equipo de bioimpresión 3D REGEMAT3D R4L que cuenta con una tecnología que ha sido optimizada para imprimir distintos tipos de tejidos como cartílago, piel, hueso y para trabajar con distintos tipos de biomateriales, colágenos, nanocelulosas, termoplásticos. Para potencializar el uso del equipo, la Universidad Central del Valle (UCEVA.

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What are the advances, challenges, and clinical applications of regenerative medicine as a therapeutic alternative for chronic diseases and serious injuries?	Hosseini S, Taghiyar L, Safari F, Baghaban Eslaminejad M.	2018	Scientific article	To explore the opportunities for using mesenchymal stem cells (MSCs), their desirable therapeutic properties in regenerative medicine, and their potential implications for clinical practice.	Regenerative medicine and tissue engineering represent the most promising therapeutic biological strategies utilizing mesenchymal stem cells (MSCs). Mesenchymal stem cells have a high capacity for self-renewal through immunomodulatory properties, making them eligible for clinical applications (21).
Applications of stem cells in regenerative medicine and disease treatment.	Mahla R.	2016	Review article	It examines a framework for the most recent advances in embryonic stem cell (ESC) transplantation and tissue engineering technologies, and the tissue-in-tissue role of hematopoietic stem cells (ESCs). It also discusses stem cells as tools for regenerative use in wildlife conservation.	Stem cells have diverse applications in tissue regeneration and disease treatments. Embryonic stem cells (ESCs) come from the inner mass of the blastocyst and are used in the treatment of neurodegenerative diseases such as spinal cord injuries and macular degeneration. Mesenchymal stem cells (MSCs) are present in bone marrow, adipose tissue, and the umbilical cord and are effective for peritoneal fibrosis and tissue regeneration. Likewise, these umbilical cord-derived cells are used to treat type 1 and 2 diabetes, improving beta cell function. Induced pluripotent stem cells (iPSCs) are adult cells reprogrammed to enhance their pluripotent characteristics. These have applications in the regeneration of damaged tissues and the restoration of neuronal functions. The aforementioned therapies are under development and require research to standardize their use and monitor results on a large scale, since they can be very useful in organ transplantation and the treatment of immunological disorders (17) . Research is focused on improving the efficacy and tolerance of stem cell transplants (17).

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Discussion

In the last two decades, regenerative medicine has made great strides in diverse fields such as molecular biology, biomedical engineering, biochemistry, physics, and ethics. One of these advances is 3D bioprinting, which would allow the generation of functional organs and tissues in the laboratory. 3D bioprinting consists of the technique of manufacturing three-dimensional tissues and organs, using living cells as raw material (18). This advance includes the design and manufacture of biological structures with biocompatible materials, based on scaffolds and stem cells, which are controlled by a computer to create complex three-dimensional models (6). This process resembles conventional 3D printing, replacing ink with biomaterials and cells.

After bioprinting, the tissue or organ is subjected to an incubation bioprocess to promote cell maturation, the use of growth factors to induce cell differentiation, as well as the implementation of perfusion techniques to promote the formation of blood vessels in organs. However, tissue vascularization and the development of new biomaterials continues to be a challenge for 3D bioprinting (14). In this regard, Castellanos-Garzón (16), in his studies, has included a bioprinting technological material, manufacturing three structures with different geometries designed for possible applications in otorhinolaryngology and orthopedics. Likewise, Aguilar (16) in his research work points out that this method of regenerative medicine is very promising to improve organ transplantation and personalized medicine.

Another significant advance found in the review articles regarding regenerative medicine is cellular reprogramming, which consists of the development of therapies based on induced stem cells for the regeneration of damaged tissues and damaged or diseased organs (8). Stem cells are the so-called stem cells that have the characteristic of self-renewing and dividing to produce new or specialized stem cells. In addition, they can

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release molecules that help repair damage caused by injury or disease and aging (10).

Stem cells serve as treatments in musculoskeletal tissues, regeneration of the heart, liver and central nervous system. Hence (8) Lehmann et al., (2018) He points out that stem cell treatments are becoming an alternative treatment for diseases such as Parkinson's and Alzheimer's, as well as therapeutic applications for injuries and grafts.

Thus, the main applications of regenerative medicine are found in tissue reproduction, to treat traumatic, degenerative or congenital injuries of the musculoskeletal system such as bone fractures, cartilage and tendon injuries, and diseases such as osteoarthritis (18). By using stem cells, biomaterials and growth factors, therapies can be developed to promote the regeneration of musculoskeletal tissues, restoring their structure and function effectively.

Another key application of regenerative medicine is the regeneration of vital organs and tissues. This area of research seeks to address chronic and degenerative diseases, as well as the shortage of organs for transplants. These regenerative therapies offer new hope for patients with terminal illnesses, providing the possibility of more effective and less invasive treatments in the future. Aguilar (15) in his experimental study demonstrated that the transplantation of epithelial organoids developed from stem cells is effective for the treatment of diseases that negatively affect the intestinal epithelium, as he experimented with mice suffering from acute colitis, achieving successful treatment. This application is quite prospective for the regenerative treatment of several human diseases.

Despite its promising applications, regenerative medicine faces several challenges that limit its full application. These include the need to overcome immunological barriers and ensure the compatibility of regenerated tissues with the recipient's immune system, especially in the case of tissue and organ transplants (18). Furthermore, the identification of suitable biomaterials and the optimization of cell culture techniques

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are essential to ensure the vascularization and functionality of tissues biofabricated through 3D printing (14).

Other challenges include generating adequate amounts of stem cells in vitro, while avoiding exposing the sample to hazards such as contamination or malignant transformation (19). Finally, according to Quesada Leyva et al. (20), the ethical, regulatory, risk and safety aspects of regenerative treatments for human application need to be considered. Ongoing research and interdisciplinary collaboration are essential to address these challenges and fully harness the potential of regenerative medicine for the benefit of human health.

Conclusions

Recent advances in regenerative medicine, such as 3D bioprinting, have shown great potential for the manufacture of anatomically functional tissues and organs in laboratories. This technique allows for the creation of complex biological structures using living cells and biomaterials, which could revolutionize medical fields such as otorhinolaryngology and orthopedics.

Cell reprogramming, another important advance in regenerative medicine, offers new hope for the treatment of a variety of diseases, as well as injuries. This strategy, which involves the development of induced stem cell-based therapies, could be key in the treatment of diverse conditions, from musculoskeletal injuries to neurodegenerative disorders such as Parkinson's and Alzheimer's.

The primary applications of regenerative medicine focus on the regeneration of musculoskeletal tissues and vital organs, such as the heart, liver, and central nervous system. These advances represent a paradigm shift in the treatment of chronic and degenerative diseases, offering new hope for patients with serious medical conditions. However, despite its promising applications, regenerative medicine faces significant

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challenges that must be addressed. These include the need to ensure the immunological compatibility of regenerated tissues, as well as ethical and willingness-based donations, regulations, and safety considerations that require rigorous attention.

The topic of regenerative medicine is exciting, as it opens the door to a future where chronic diseases and serious injuries could be treated more effectively and less invasively. However, achieving this goal requires continued research and closer interdisciplinary collaboration. More in-depth experimental research is needed to better understand the cellular and molecular mechanisms involved in tissue and organ regeneration, as well as to develop new technologies and therapeutic approaches. Furthermore, more clinical studies and trials are needed to evaluate the safety and efficacy of regenerative therapies in humans. The ethical considerations involved in this medicine must also be taken into account, which could be the subject of further research.

In conclusion, regenerative medicine represents an evolution in the approach to chronic diseases and serious injuries, offering innovative therapeutic alternatives based on the use of stem cells, biomaterials, and emerging technologies such as 3D bioprinting and organoids. While scientific advances have demonstrated high potential for tissue regeneration and personalized treatments, ethical, technical, and regulatory challenges remain that require attention to ensure safety, efficacy, and accessibility. The consolidation of this field will depend on strengthening interdisciplinary research, standardizing procedures, and establishing clear regulations that allow for its proper integration into clinical practice.

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