NANOTECHNOLOGY AND TISSUE ENGINEERING: BUILDING THE FUTURE OF REGENERATIVE MEDICINE

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Abstract

Nanotechnology offers groundbreaking methods for medical diagnosis, treatment, tissue regeneration, and biomedical imaging. The small size of nanoparticles (1-100 nanometers) facilitates interaction with biological systems, improving the sensitivity and specificity of disease detection through enhanced imaging. Nanotechnology reshapes dentistry, improving diagnostics, treatment precision, and dental materials. Developing nanocomposites, nano-adhesives, and nano-bone grafts represents a significant advancement in dental materials. Nanorobots offer the potential for pain-free procedures and targeted drug delivery within the oral cavity. Nanostructured scaffolds used in tissue engineering mimic the extracellular matrix. It promotes cell growth and tissue regeneration. This technology plays a key role in improving the effective monitoring of bioelectric signals in cancer treatment using advanced sensors and electrodes. It revolutionizes surgery by enabling high-precision, minimally invasive procedures through nanorobotic technology. Organ-on-a-chip (OoC) systems offer an innovative and versatile micro-physiological platform for replicating the dynamic tissue microenvironment, enabling the study of nanotechnology-biology interactions. Researchers are using models that combine nanotechnology, microfluidics, and tissue engineering to mimic the complex dynamics of musculoskeletal tissues in a controlled manner. This allows them to effectively study disease mechanisms and assess therapeutic approaches, such as nanotechnology-based interventions. Scientists are leveraging the integration of nanotechnology with other technologies like tissue engineering to achieve targeted drug delivery, precise sensing, and versatile manipulation of cellular processes, driving a paradigm shift in research at the cellular level and early disease diagnosis and possible prognosis. Nevertheless, resolving safety and bioaccumulation issues is a prerequisite for its broader clinical translation.

Keywords: *Cancer, Dentistry, Musculoskeletal, Nanotechnology, Tissue engineering, Organs-on-a-chip*

1. Introduction

Disease and injuries caused due to multiple reasons has resulted in either tissue damage or organ loss. To prevent the tedious process of transplantation, researchers and scientists have developed innovative therapies that can regenerate the damaged tissues or organs. The novel interdisciplinary field is regenerative medicine that applies the basic principles of life sciences with engineering to regenerate and restore the normal tissues or organs from its diseased or injured state (Mao & Mooney, 2015) [Fig 1].

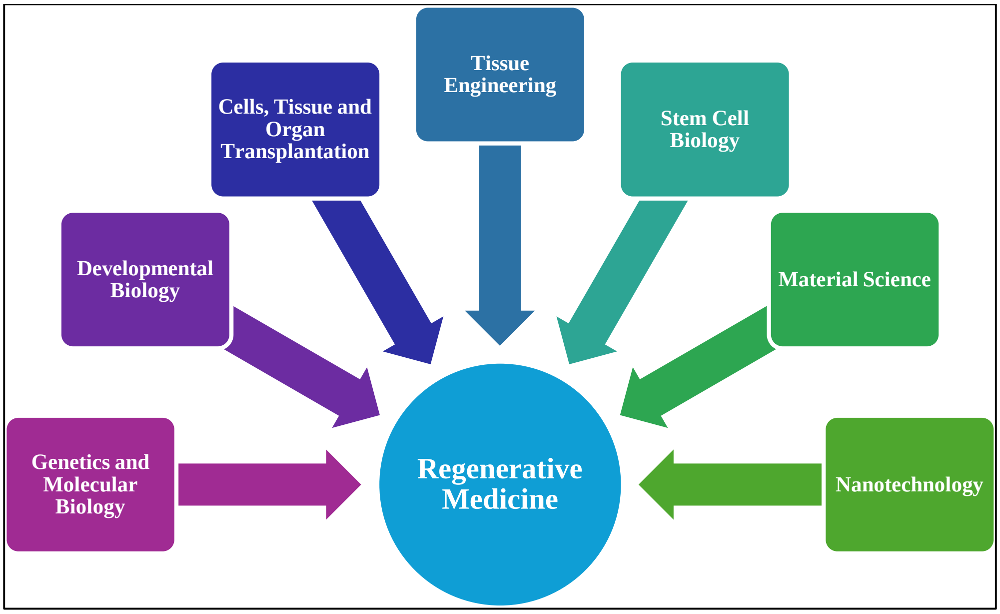

Fig 1. Interdisciplinary approach of Regenerative Medicine

Tissue engineering (TE) is focussed on growth and development of new tissue or an organ. It includes three basic requirements called as "Tissue Engineering Triad" namely cells/tissues, scaffolds and bioactive materials [Fig 2].

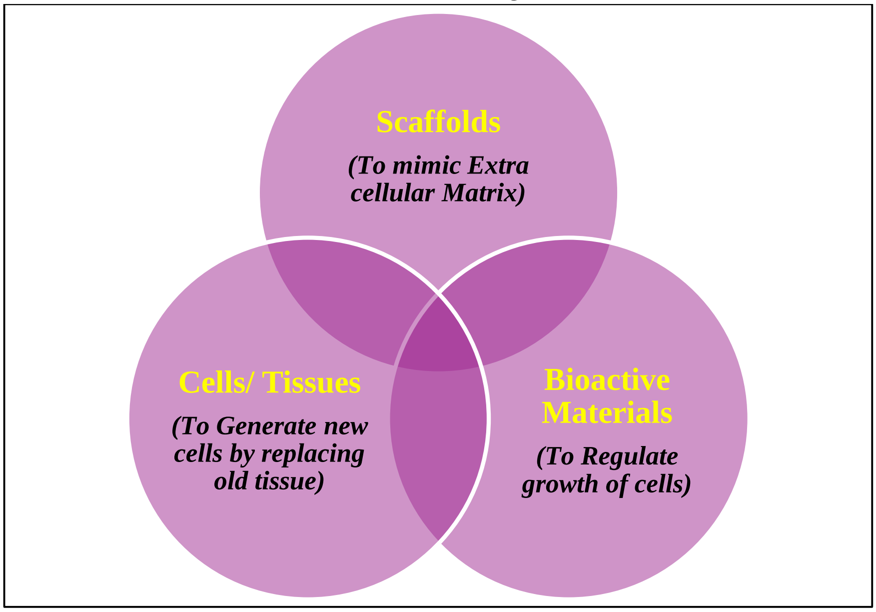

Fig 2. Tissue Engineering Triad

The prerequisites for tissue engineering includes source of cells or tissues, availability of biocompatible materials namely scaffolds, sufficient nutrients with physiological conditions for the cells or tissues to regenerate in a bioreactor and manipulating the culture requirements for cell proliferation and differentiation for the development of a respective functional tissue.

Even though, the TE Triads are available, combining them together to rebuild a tissue or an organ has become a task, as these engineered materials are not able to mimic the natural mechanisms that happens in a living cell. To overcome this limitation, one strategy is to implement the use of customized nanoparticles (NPs) engineered to solve this issue. Few reports have suggested that there is a marked improvement in biological and mechanical activities when nanoparticles were integrated with tissue engineering approach. It has been predicted that, NPs could mimic the natural extra cellular matrix efficiently and effectively due to their nano size (Hasan *et al.*, 2018).

By integrating tissue engineering along with nanotechnology, must be the future of regenerative medicine. With many preclinical and clinical trials are on their way, regenerative medicine has embarked a new strategy in developing therapies for different acute and chronic conditions like skin damages, traumas and diseases of cardiovascular system and addressing few types of cancer and more. Therefore, choosing the correct NPs with a significant property could overcome issues in tissue engineering that proves to be the future of regenerative medicine.

As nanotechnology is manipulating materials at the nanoscale (1-100 nm), it has revolutionized medicine. It offers new methods in diagnostics and therapeutics. Scientists have investigated nanotechnology in many biomedical applications, such as drug delivery, cancer therapy and dentistry (Farokhzad & Langer, 2009). Control of materials at the molecular level has dramatically enhanced treatment effectiveness and patient outcomes. This review paper gives insights into recent developments in nanotechnology and its influence on medicine, dentistry, biology, and drug delivery.

In recent years, studies on musculoskeletal (MSK) diseases, including osteoarthritis, rheumatoid arthritis, osteoporosis, and MSK cancers, have highlighted a significant and growing global health challenge. Combining nanotechnology and OoC (organ-on-a chip) technology offers a unique approach to accelerate the development of innovative and personalized therapies for MSK disorders. Despite its potential, the current utilization of nanotechnology within MSK's study of nanotechnology in OoC platforms remains notably limited. In 2023, it accounted for less than 7% of the "MSK OoCs" literature (Wang *et al.*, 2024).

Nanorobots and nanoparticles are used not only in drug delivery but also in dentistry. It has made diagnostics, treatment, and biomaterial development easier. Nanoparticles are being integrated into dental restorations, implants, and drug delivery systems, improving their strength, biocompatibility, and antibacterial properties (Bhardwaj *et al.*, 2014). Nano-filled composites increase the durability of restorations, while nanorobots hold promise for precision-based procedures such as targeted drug delivery and biofilm removal.

Furthermore, nanosensors detect oral diseases at early stages, which makes it a highly effective and minimally invasive method of dental care. Because nanotechnology makes targeted drug delivery, sophisticated imaging, and bioelectric manipulation possible, it revolutionizes the diagnosis and treatment of cancer. Nanoparticles enhance the efficacy and precision of chemotherapy, reducing damage to healthy tissues while improving drug retention and controlled release (Farokhzad & Langer, 2009).

While bio-nanoantennae have been studied to selectively induce apoptosis by manipulating cancer bioelectricity, nano-biosensors aid in early cancer detection by identifying biomarkers at the molecular level (Moreddu, 2023). These developments establish nanotechnology as an essential tool in precision oncology by bridging the gap between biology and translational medicine.

Developing drugs using nanoscale drug delivery systems improves therapeutic results, targeting effectiveness, and bioavailability. By enabling controlled drug release, nanoparticles minimize systemic side effects while guaranteeing accurate targeting of diseased tissues (Torchilin, 2014). To increase drug solubility and stability, lipid-based nanoparticles, polymeric nanocarriers, and metal-based nanosystems are employed in gene therapy, oncology, and treating infectious diseases (Bobo *et al.,* 2016). Modern pharmacology is changing due to these developments, providing individualized and incredibly successful treatment options.

The combined scientific field of biology, engineering and medicine has paved for a fascinating new branch in science that, includes nanotechnology, tissue engineering and regenerative medicine. These fields aim to overcome the shortcomings of traditional medical treatments by leveraging and enhancing the body's natural ability to heal and rebuild itself through cutting-edge technologies (Phutane *et al*., 2023). The importance of nanotechnology in association with tissue engineering approach in human health is emphasized in this review, focusing on its use in nanomedicine for imaging, screening, diagnosis, targeted drug delivery, and efficient disease treatment.

2. Methodology

- The databases used to perform this search were PubMed, Google Scholar and ScienceDirect.
- Specific keywords, such as Nanotechnology in Organ Transplantation, Nanotechnology in Medicine, Nanotechnology in Dentistry, Nanotechnology in Biology, Tissue Engineering and Regenerative medicine were used,
- This systematic search was attempted to find and analyze a wide range of research articles in nanotechnology and its various healthcare and biological applications.

3. Discussion

3.1 Cancer Therapy

Cancer has been a leading cause of death globally. Researchers have benefited from nanotechnology-based interventions in the treatment of cancer. Traditional cancer therapies, including chemotherapy and radiation, often result in severe side effects due to their non-specific nature (Liang, W *et al*., 2023). Nanoparticles have emerged as promising carriers for targeted drug delivery, allowing for selective accumulation in tumor tissues while minimizing damage to healthy cells (Liu *et al*., 2023). Nanoparticles are target-specific and have lesser systemic damage compared to traditional methods. Nanocarriers, such as liposomes, enable the controlled release of drugs and increase the therapeutic efficacy of drugs (Torchilin, 2014).

Nanotechnologies, such as bio-nanoantennae and nanoparticles, have demonstrated the ability to manipulate cancer bioelectricity, selectively inducing cancer cell apoptosis and detecting altered surface charges for diagnostic and therapeutic applications (Moreddu, R.,2023).

3.2 Drug Delivery

The use of nanotechnology in drug delivery has revolutionized the field of pharmacy. Nanocarriers enhance drugs' solubility, stability, and bioavailability, facilitating controlled and sustained release (Farokhzad & Langer, 2009). Nanotechnology in drug delivery, including targeted delivery, enhanced permeability across biological barriers, and reduced systemic toxicity were reported. Liposomes, dendrimers, and solid lipid nanoparticles are the most commonly used drug delivery vehicles. These carriers have enabled the successful development of nanomedicine-based therapeutics, such as *Doxil* (liposomal doxorubicin) for cancer treatment. Studies explore using AgNPs (silver nanoparticles) to fight multidrug-resistant bacteria. In this case, nanotechnology offers a potential solution by delivering the antimicrobial silver in a nanoparticle form, enhancing its overall effectiveness. The small size of the nanoparticles allows them to interact differently with bacterial cells compared to bulk silver (Malik *et al*., 2023). The goal is to deliver drugs precisely to diseased or damaged cells (like cancer cells) while minimizing harm to healthy tissues. This is achieved by attaching targeting molecules (ligands) to the drug delivery system (e.g., nanoparticles). These ligands bind to specific receptors present in the target cells. While targeted drug delivery is being explored for many diseases, cancer, cardiovascular, and immunological diseases are the primary focus (Farokhzad *et al*.,2006)

3.3 Dentistry

In dentistry, nanotechnology has improved dental materials, diagnostics, and treatments. According to (Mitra *et al*., 2014), Nanoparticles make dental repairs more substantial in terms of properties, growing durability and wear resistance. Nanoparticles are also applied in antimicrobial coatings and regenerative treatments. Dental Nanorobotics are tiny robots that can deliver anaesthesia, repair damaged tissues, and even perform orthodontic tooth movement.

Dental Nanomaterials are incorporated into dental materials like composites and adhesives to make them stronger, more durable, and aesthetically pleasing. Nanodiagnostics could enable early detection of oral diseases like cancer through nanosensors and other diagnostic tools.

Nanotherapeutics could improve drug delivery for oral diseases, thus making treatments more effective and reducing side effects (Bhardwaj *et al*.,2014). Overall, nanotechnology has the potential to make dental care more precise, less invasive, and more effective.

3.4 Medicine

Beyond cancer therapy, drug delivery, and dentistry, nanotechnology has significant applications in wound healing, biosensing, and tissue engineering. Nanotechnology and organ-on-a-chip (OoC) technology is used for the treatment of musculoskeletal (MSK) disorder treatment. Organs-on-a-chip, also referred to as organ-chips, micro physiological systems (MPS), or tissue-chips, are microfabricated cell culture devices that are engineered to mimic the characteristics of multicellular tissue units or functional elements of organs (Kang *et al.*,2021) [Fig 3]. Nanotechnology-based methods, such as targeted drug delivery using nanoparticles, nanostructured scaffolds for tissue regeneration, and nanoscale imaging, hold immense potential for improving MSK treatments. OoC systems provide a powerful platform to study the complex interactions between nanomaterials and MSK tissues in a controlled, micro physiological environment, mimicking the *in vivo* conditions more accurately than traditional methods. Nanomaterials can be integrated into OoC systems to create biomimetic scaffolds, enabling precise drug delivery, and facilitate advanced sensing and monitoring (Wang *et al.*, 2024).

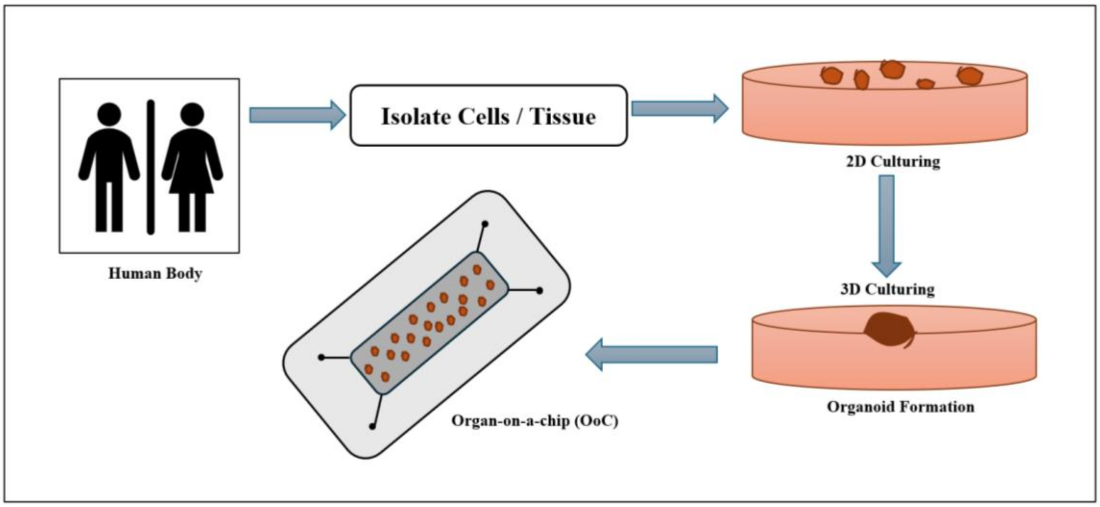

Fig 3. Model for the development of Organ-on-a-chip (OoC)

The applications of tissue engineering have been witnessed in regeneration of skin tissue, repair of cartilage, transplantation of organs, bone tissue regeneration etc.

4. Challenges in Tissue Engineering and Nanotechnology approach

Tissue engineering and nanotechnology gives an immense promise in revolutionizing advancements in medical field. Overcoming the current limitations can enable researchers, clinicians and engineers to develop personalized regenerative therapies that will improve fundamental health care in human.

The Current Challenges Include

- Biocompatibility and immunogenicity
- Vascularization and need for continuous nutrient supply

- Source of cells and its differentiation
- Maturation and appropriate integration of their function
- Reduced toxic or side effects of nanoparticles used
- Approval from regulatory board and its clinical translation

5. Conclusion

Nanotechnology and tissue engineering is the biology, transforming dentistry, medicine, organ-on-a-chip (OoC) technology, and biological research. Customized Nanomaterials in dentistry improve the biocompatibility and strength of restorative materials, enhance drug delivery for oral ailments, and contribute to antibacterial coatings for implants. In medicine, it is used for targeted drug delivery to enable effective treatments with fewer side effects and is a key enabler of advanced imaging, diagnostics, and regenerative medicine. Nanotechnology in organ-on-a-chip (OoC) systems has significantly contributed to the ability to mimic physiological conditions, and this enabled disease modelling and drug screening and reduced animal model usage.

Nanotechnology contributes significantly to advancements in biological sciences through genetic engineering, biosensing and tissue engineering. Incorporation of nanotechnology into these areas leads the way to discoveries in personalized medicine and regenerative biology. In the future, nanotechnology has vast prospects in clinical therapy, disease prevention, diagnosis and in treatment.

However, nanotechnology also presents several limitations and challenges. Toxicity and biocompatibility remain an issue, with nanoparticles accumulating in tissues, which may cause biological effects. Exorbitant costs of production and the absence of standard rules make it hard for mass clinical translation. Ethical concerns, especially in tissue engineering, genetic engineering and nanomedicine, complicate its implementation. Long-term safety information is still lacking, and more research is needed to guarantee nanotechnology's practical and responsible application in medicine. While nanotechnology in association with tissue engineering keeps raising the bar on what is possible in biology, these challenges must be overcome to incorporate it into widespread medical and biological uses.

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