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Healing from within: Exploring the potential of Regenerative Medicines

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ABSTRACT: -
From past many researches has been conducted on the impact of Regenerative medicine (RM), which has been the subject of extensive basic study, is now starting to show promise as a treatment for a number of clinical problems, including both acute injuries and chronic illnesses. One of the most fascinating human pursuits is the study of regeneration, which has the potential to have an impact on modern human life by both presenting new medical treatments and questioning our broad conceptions of biology and evolution. Repair of tissues and organs continues to be a clinical problem. An emerging discipline called TERM is devoted for creation of alternative treatments for cells to repair. The hoped of therapeutic revolution has not yet been brought about by the sciences of TERM. RM is gaining a lot of attention from ill person, business, institution, and others. The systematic review's objective was to examine the usage of (MSC) and biomaterial in preclinical animal models. One of the top priorities that is still completely unaddressed is cartilage, Bone, spinal cord, liver, heart, nanotechnology, 3D-bioprinting, etc. regeneration (restoration/repair). The loss of organs and tissues as a result of illness and damage is what spurs the need seeking prevention that promote tissue repair and lessen the need of transplants. The area of regenerative medicine is multidisciplinary and promotes regeneration by using engineering and biological science concepts, may be able to restore both diseased and damaged tissues as well as complete organs.

Keywords: Regenerative medicine, tissue engineering, genetic engineering, stem cell, biomaterial, cell-based therapy, Scaffolds, Liver, Heart, spinal cord, bone, cartilage, nanotechnology and 3D printing.

I. INTRODUCTION:

Regenerative medicine (RM) refers as, restoring normal function involve replacing or "regenerating" human cells, organ or tissues. A number of people get benefited from regenerative medicine by avoiding back surgery, neck surgery, hip replacements, knee replacements, and various other surgical procedures to treat injuries. Instead of the present clinical approach, which mostly involves treating the symptoms, Regenerative medicine seeks to repair damaged tissue or organ systems brought on by illness, injury, or congenital issues. Regenerative medicine uses artificial organs, cellular therapy, tissue engineering, and medical technologies to accomplish these goals. The development of treatments for organs that suffer long-term damage is another goal. This approach seeks to find a cure for diseases and injuries that were previously untreatable. Combinations of these methods can replace an organ that has been damaged or enhance our body's natural healing process where it is most required. Our bodies have a natural function to repair and protect themselves when they are harmed or invaded by sickness. [1, 2]

Patients, business, academic, the medical community, and patients themselves are all interested in and hopeful about the future of regenerative medicine. The challenges to treat ailments and diseases that are unrecovered or difficult to treat catches and drives enthusiasm by most collaborate to offer answers for the present and the future. One of the crucial areas where regenerative medicine can offer an answer and fill a treatment gap is in the regeneration, restoration, or repair of damaged tissue or cartilage. Regenerative medicine is defined as the process of treating diseases by utilizing the body's natural capacity to replacing cellular or organ level, to encourage cellular translation and communication, and to rebuild organ systems, and to promote general health issue of the organism. Healing response, genetic impact or alteration, external stimulus, cellular signaling, and exogenous enhancement are examples of therapy strategies. Regeneration that might or might not include cellular transplantation will therefore be included in organ and tissue engineering but excluded from organ and tissue. In this rapidly developing profession, it's important to monitor, inform, and inspire swift discoveries in order to encourage clinical translation. The RM

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performs multidisciplinary collaboration, establishing trends through insightful commentary and vibrant discussion, and showcasing the blending of many methodologies, from fundamental adjustments in regenerative capacity to clinical applications. Studies that span multiple fields are becoming more common. [3, 4]

The main goal or objective of this is to raise the standard of the evidence more thorough investigation is required, including well planned and executed clinical studies and application to accomplish this. Clinical research is good and needs the support of study sponsors as well as a careful ethical review. Better publication practices promote the research integrity and publishing avoidance of publication bias, selective reporting of regenerative medicine results, and results of failure trials (RM) trials are additional and effective ways to increase the body of knowledge, but we are already dealing with the issues of research ethics and integrity. More and better scientific evidence must be available to patients, doctors, and regulators. It's both ethically and scientifically required to lessen uncertainty or possible to close knowledge gaps. This is necessary in order to be able to give patients and research participants a better risk-benefit analysis and more precise information. The desire for acceptable result in order to secure additional funds frequently leads to "selective" reporting or "overselling" the efficacy results. Some claim that is justified by the potential development of a safer and more effective pharmaceutical product, which is only achieved with these funding. However, recent or current experience demonstrates that the development of such a product is uncommonly prompted by an early and incompletely justified marketing authorization. [5]

Global market of Regenerative Medicine: Regenerative medicine is a $28 billion global industry is that predicted Expand at a compound annual growth rate of 23.3% to reach over $81 billion by 2023. As this technique is widely recognized on a worldwide level, India is promoting research and development in the disciplines of RM and cell-based treatment. This is done in an effort to foster domestic innovation and alliances with both national and international organizations, with the goal of achieving excellence in healthcare. Gene therapy, tissue engineering, biomaterials, 3D printing, cord blood banking, cell-based therapy, and cord blood banking are all now evolving swiftly. The use of these medicines in clinical settings is still fraught with legal and ethical difficulties. To take advantage of the expanding market for regenerative medicine, we require a strict regulatory framework. [6]

Global Strategic Market Report for Regenerative Medicine 2023: Market to Exceed $30 Billion by 2030

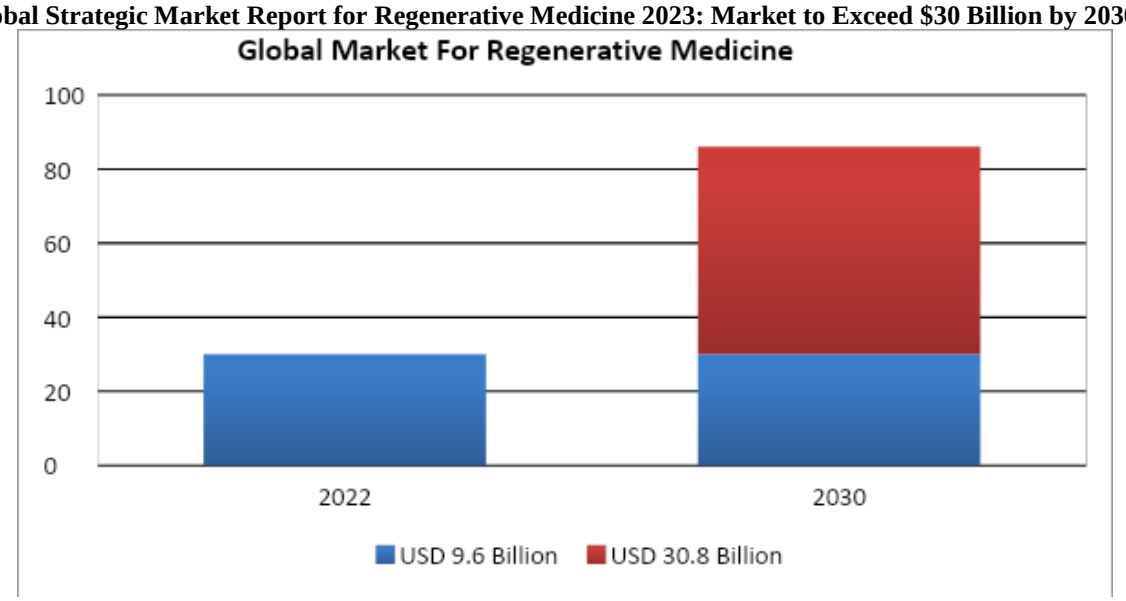

Fig 1: The global market for RM is anticipated to expand at a CAGR of 15.8% from 2022 to2030,upfromthepreviousprojectionofUS$9.6billionin2022toUS$30.8billionby2030aftertheimplementationof COVID-19.

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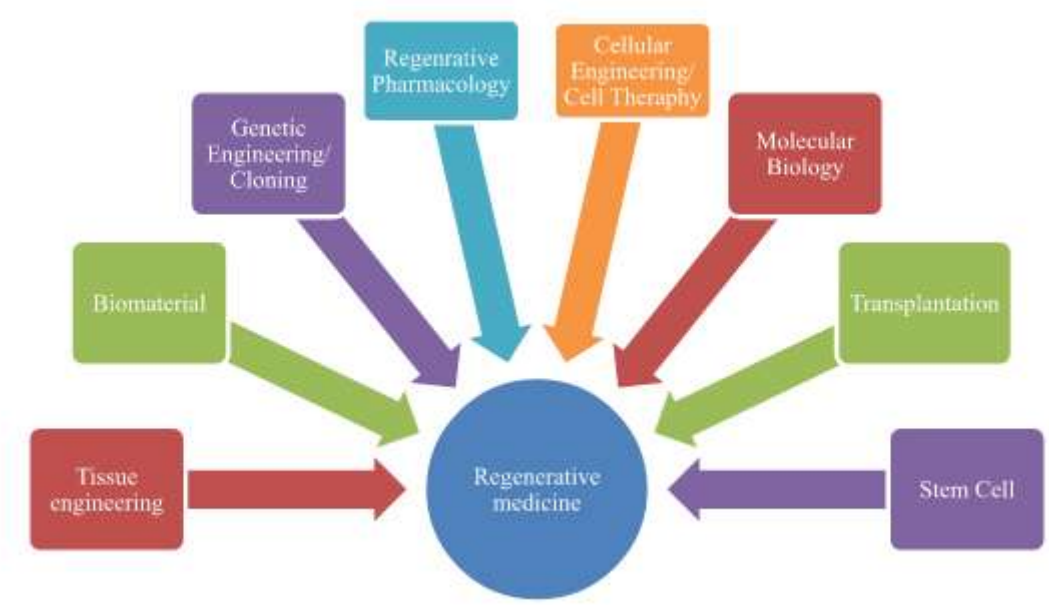
II. SCIENTIFIC PRINCIPLES OF REGENERATIVE MEDICINE



A. Tissue Engineering Regeneration

The interdisciplinary field of Cells-system based engineering, according to Langer and Vacanti in 1993, combining engineering and life science concepts to create biological substitutes that restore, maintain, or enhance tissue function or whole organ function.

There are tissues in the human body that have a limited capacity for repair or regeneration, providing a problem that is frequently challenging for clinicians to solve. Another crucial subject to take into account is the culturing environment. It is crucial to adopt proper growth conditions that resemble those seen in vivo because tissues are often 3D structures. A wide range of devices, such as spinner flasks, recirculation bioreactors, and rotating wall vessels (such as uni- and bi-axial bio-reactor rotation); have been created for this purpose. Bioreactors play a significant part in this.

The use of Tissue Engineering for tissue repair is demonstrated and explored in more detail in the below sections:

1. **Bone Tissue Engineering Regeneration:** A vascular, highly specialized type of connective tissue called bone contains between 50 and 70 percent minerals, 20 to 40 percent organics, and 10 to 15 percent water. Collagen type I makes up the majority of the organic matrix (95%) while Nano-hydroxyapatite makes up the inorganic mineral part. Since bone has a limited capacity for healing, significant bone lesions have typically been treated with auto grafts, allografts, or xenografts.

2. Cartilage Tissue Engineering Regeneration: Cartilage lacks neurons and blood vessels despite having a high-water content (75 wt %). The ECM of cartilage contains a significant amount of collagen type II and only a small percentage of chondrocytes (10 wt %) that proliferate slowly. It cannot fully repair when cartilage lesions reach a crucial size for these reasons.

3. **Osteochondral Tissue Engineering Regeneration:** OCD abnormalities may manifest as thinning of the cartilage or as the advancement of cartilage lesions into the subchondral bone. The patient's age and the severity of the lesion's requirements are also accounted for when providing care. Most OCD solutions center on evaluation and pain.

4. Meniscus Tissue Engineering Regeneration: Due of the increasing necessity to protect this tissue, there has been a lot of interest in meniscus TE over the past few years. The stability and homeostasis of the knee joint depend heavily on the meniscus, a tissue that is fibrocartilaginous is mainly made of type I collagen. Given that it has vascularized (red-red), weakly vascularized (red-white), and avascular (white-white) sections, it is a difficult tissue, as well as a known lesion site inside

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the meniscus. There is a grade of vascularization as well.

5. Intervertebral disc Tissue Engineering Regeneration: IVD degradation is a vital topic covered in TE. Between two vertebral bodies is a cartilaginous structure called the intervertebral disc. When IVD degradation advances, the avascular NP of the central region, which mostly consists of type 2 collagen and minor amounts of other collagens (such as IX, VI, and III), starts to lose its properties. This makes disc herniation more likely. Innovative therapeutics based on regenerative principles is required for the long-term management of IVD degeneration.

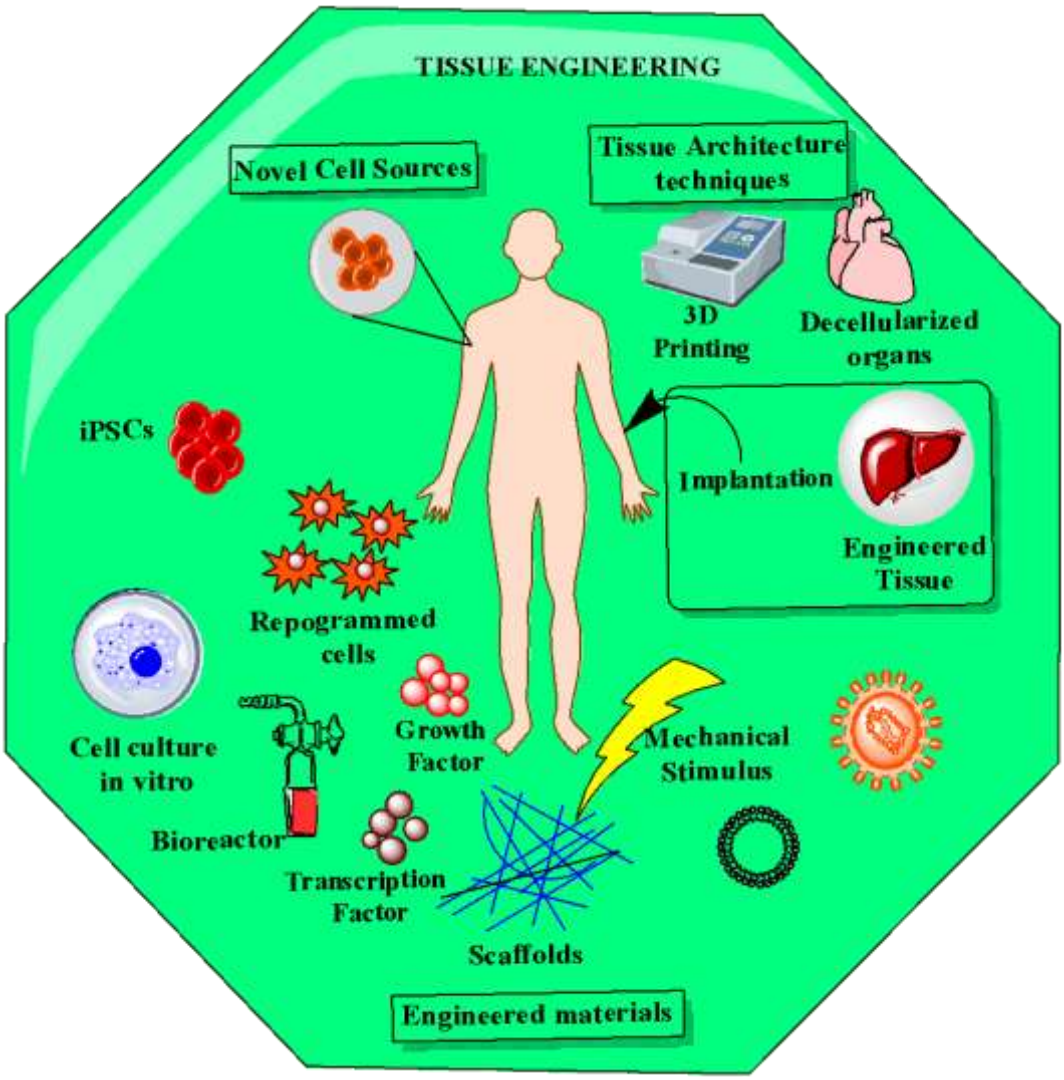

Fig -3 Novel cell sources, materials for engineering, and tissue design techniques have all led to a variety of engineered tissues during the past ten years that are better at repairing, maintaining, replacement organic tissues or enhancing.

6. Scaffolding technologies: New trends:

Scaffolds are regarded as a crucial component in the typical TE strategy as an alternative to ECM. Polymers, ceramics, and composites are some of the biomaterials that have been studied in the form of both organic and artificial 3D scaffolds. It is generally agreed that a scaffold must meet certain requirements to be utilized for TE- based applications, including:

1. Biocompatibility
2. Controlled rate of degradation
3. Porousness features an open network of holes that allow for simple 3D shape processing and

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adaptation to the therapeutic issue being treated

4. The capacity to foster cell proliferation and differentiation in tissue that has to be replaced.

6.1 FIBER BONDING: - The fiber bonding technique can be used to create micro fibrous scaffolds. Basically, a predetermined quantity of extrusion-produced microfibers is distributed at random in a specially made Teflon mold and heated under compression for a predetermined amount of time and temperature. This technique aids in maintaining the fibers spatially random arrangement so that the fiber structure does not break down. It is feasible to create scaffolds with various morphologies in terms of porosity and pore size by adjusting the compression of the bundles and the quantity and size of fibers. The creation of scaffolds with a large surface area and high porosity interconnectivity for cell attachment and quick cell and nutrient diffusion is the processing method's key benefit.

6.2 WET SPINNING: - Wet-spinning is a non-solvent-induced phase inversion method that enables the synthesis of polymer fibers using an immersion-precipitation procedure. A continuous polymer fiber is made by precipitating a polymer solution filament in a coagulation bath that contains a weak solvent (non-solvent) or a non-solvent-solvent mixture in relation to the treated polymer. Due to polymer desolubilization, which is brought on by solvent-non-solvent exchange, a homogeneous solution filament made of polymer, solvent, and maybe additives solidify.

6.3 RAPID PROTOTYPING: - The size, shape, and eventually the porosity's interconnectivity and the distribution of the pores inside the scaffold can all be controlled to a lesser extent using conventional processing methods for scaffold production. But the development of rapid prototyping and solid free form manufacturing made it possible to have the ultimate shape of an implanted device and the scaffold morphology under sufficient control.

6.4 ELECTROSPINNING: A simple, effective, affordable, and adaptable polymer process technology that makes it possible to create ultrafine fibers is electrospinning. Electrospinning fibers have exceptional qualities, including a high specific surface area because of the fibers' sub-micrometer range in diameter. The electro-spin small fibers frequently have pore sizes in the micrometer range, great interconnectivity, and porosity in a mesh-like structure. In traditional electrospinning, a droplet of polymer solution created by a syringe pump is drawn from a capillary. [8]

Biomaterials:

Definition: - Generally, it can be "any substance, if natural or artificial that amplifies, or replaces the function lost due to damage or accident"

History of biomaterials: - It has been known since prehistory that the use of "non-biological materials," now referred to as "biomaterials," has benefited human health.

Classification of biomaterials: -

Following are the three main categories into which biomaterials can be divided:

- Polymers (e.g., semi-synthetic, synthetic and natural)
- Metals (e.g., silver, platinum)
- Ceramics (e.g., Clay, glass, cement, carbon, and porcelain)

METALS: - Biomaterial is a discipline has been significantly impacted economically by metallic implants. 316L steels, f-75, silver, tantalium, cobalt, F-75, vitallium and titanium, chromium, and other alloys cobalt, among other metals, are examples of metallic implants.

POLYMERS: - Other applications in biomaterials made of polymers lie outside of regenerative-medicine or tissue regeneration. Example: -

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Name	Use
Poly-methyl methacrylate	used in mucilage bones
Poly-glycolic acid	surgical seam that breaks down
Poly-vinyl siloxane	implanted as orthodonture implants

CERAMICS: - Glass-ceramic composites, glasses, and ceramics all fall under the category of composites made out of inorganic materials. This course has demonstrated use in thermometers, diagnostic equipment, chemical ware, eyeglasses, and other items.

Properties of biomaterials: - The class to which a biomaterial belongs determines its properties. But important characteristics also include mechanical, surface, corrosion, and degradation characteristics.

1. Surface attributes: - The surface properties of an implant material are essential because connections between biomaterial and recipient cells are a surface phenomenon,
2. Corrosion: - Under physiological circumstances, corrosion occurs on metallic implants.
3. Deterioration: - Although other groups of biomaterials, such as ceramics and polymers, do not corrode, they are nevertheless prone to breakdown in physiological settings.

Example of biomaterials as regenerative medicines

1. **Hydrogels: -** A colloidal gel, a hydrogel is a dispersion media made of water. They have become crucial biomaterial scaffolds because they mimic genuine tissue. The aqueous nature of hydrogels is quite similar to that of bodily cells. They have good porosity, which enables the circulation of nutrients and waste.
2. **Cryogels :** The cryogelation process, which creates scaffolds from organic or synthetic polymers at very low temperatures without the need of inorganic solvents, produces Cryogels, which are gel matrices. [9]
3. **Placental tissue:** During pregnancy, placental tissues, also known as extra-embryonic tissues or birth tissues, promote and safeguard fetal development. They consist of the amniotic fluid, placental membrane, placental disc, and umbilical cord. [10]
4. **Albumin:** In regenerative medicine, numerous different biomaterials are utilized. Gold, platinum, titanium, steel, and other metal-based biomaterials are great due to their structural stability and inertness, but their surfaces lack bioactivity. Albumen is a protein that can withstand high temperatures since it is extremely highly soluble and fixed. The protein albumen, one of the most studied proteins, is used in many biotechnological processes, including as a medicine, Their agnostic agent, biomaterial, contrast agent, in vitro cell supplement and biosensor etc. [11]

C. Stem cell engineering: - Stem-cell engineering is a general term for similar cells have the ability to change into different cell type and to continue themselves.

The four types of stem cells are

i. **Totipotent** similar zygotes, which can give rise to extra-embryonic structures as well as any type of cell in an organism.
ii. **Pluripotent** like embryonic cells in the coating of germs.
iii. **Multipotent** if they possess the capacity to develop into several cell types.
iv. **Oligo potent** which can only divide into a certain number of different cell type.
v. **Unipotent** which results in a certain cell type.

They support tissue regeneration and maintain tissue homeostasis. They consist of the stem cells of the mesenchyme, haematological system, nervous system, and skin (as follows: MSC, HSC, NSC, and DSC).

MSCs have attracted the most research attention in the last 20 years and have the highest promise for use in regenerative medicine. In 1970, Friedenstein discovered MSCs in the spleen and bone marrow of guinea-pigs, describing them being able to develop into osteoblasts as fibroblastic cells. Eventually, it was found that MSCs may also distinguish between adipocytes and chondrocytes, which are cells derived from the mesoderm. MSCs can even differentiate into hepatocytes and neurons, which are endodermal and ectodermal origin cells. The umbilical cord, adipose tissue, bone marrow, and hair follicle, periodontal ligament, and placenta are just a few of the sites

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from which MSCs can be extracted. They must be developed and described after being isolated in order to be potentially therapeutic. [12]

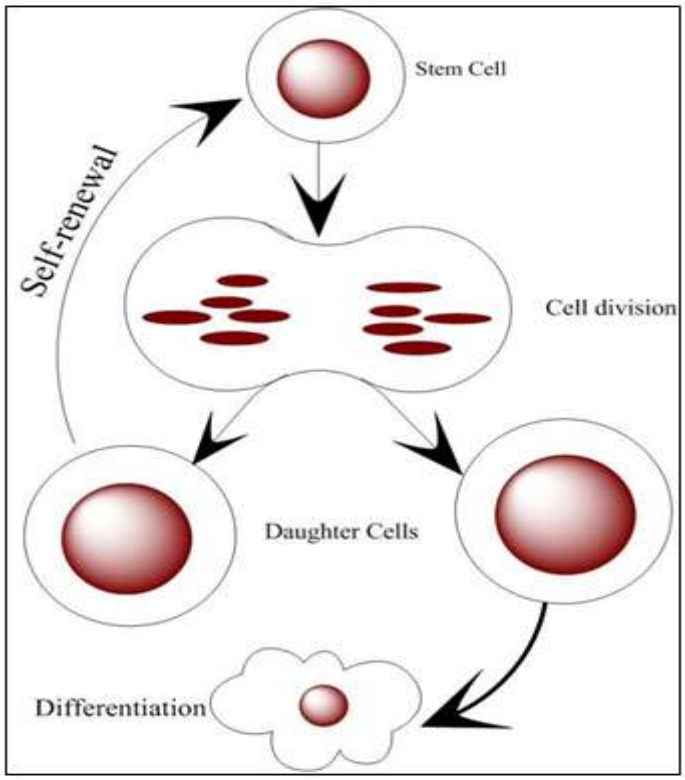

Fig.4: - Procedure involves in the use of mother cells or stem cell (RM)

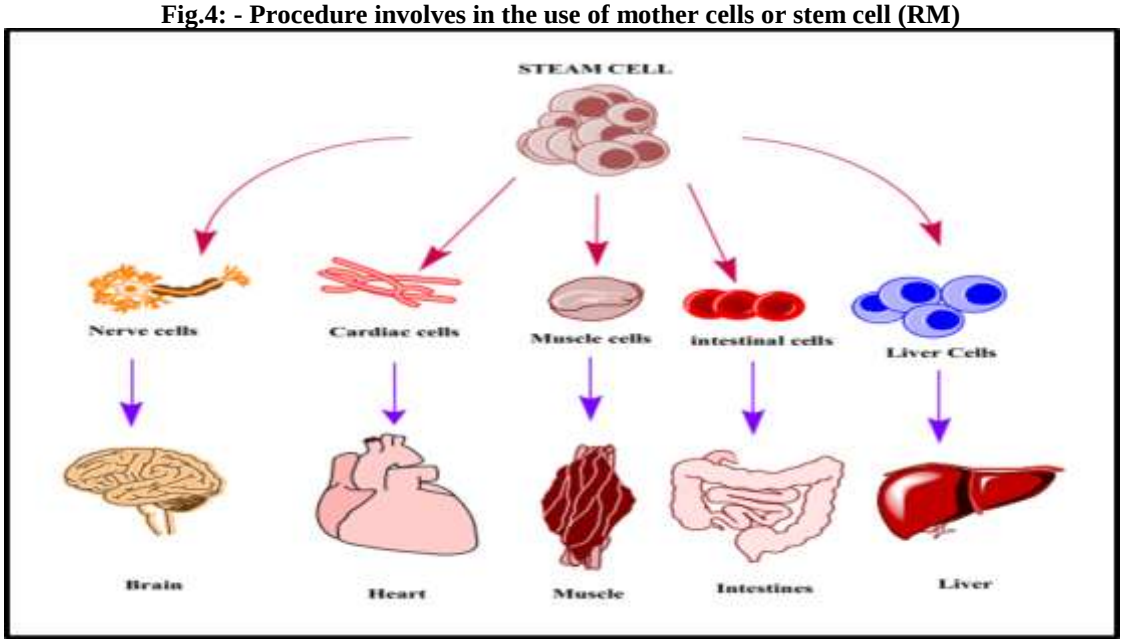

Fig: 5 The human body has a broad spectrum of motor neurons and somatic cells types. They include cells with a single function as well as specially trained cells that serve as the basis for the creation of human organ or human tissue.

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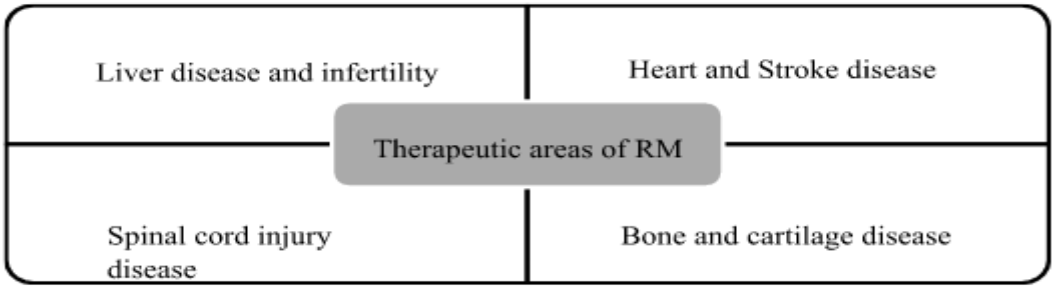
Various therapeutic areas associated with Regenerative medicine



1.Liver Regeneration Therapy

The process of liver regeneration is intricate and unusual. When a mouse liver is cut in half, the surviving liver takes about ten days to regain its original weight. Understanding the processes underlying liver regeneration could benefit patients who require extensive liver resections or transplants, as well as advance the field of regenerative medicine. Although different hepatocyte subpopulations appear to have unique proliferative capacities, every differentiated hepatocyte has the capacity to regenerate itself. Although in a laboratory context these LPCs can differentiate into hepatocytes and biliary cells, it is not known whether or how they can help in liver regeneration.

Even worse prognosis and greater fibrosis have been linked to their proliferation in chronic liver disorders. There is still debate on where these LPCs emerge from; These LPCs are derived from hepatocyte dedifferentiation. [13]

Mechanism of Liver regeneration: -

Different cell types and how they are used in liver cell-based treatments i.e. cirrhosis. On the left side of the picture are various cell types that have been isolated from individuals and are being employed in liver regeneration. Each cell type was injected, and hepatocytes, ESCs, or iPSC only through in vitro proliferation, or both through differentiation into hepatocytes, have recovered liver functions (MSCs, LSPCs).

Hepatocytes: - During liver regeneration, hepatocytes undergo three distinct and critical stages: (a) the initiating three phases: the stimulating phase, the growth phase, and the final phase.Many signaling pathways control and link these phases.

Mesenchymal stem cells (MSCs):- In-depth research is being done on mesenchymal stem cells (MSCs) for regenerative medicine because they have unique Bone marrow, Biological characteristics, umbilical cord, and adipose tissue, can all be used to harvest MSCs. In-depth research is being done on mesenchymal stem cells (MSCs) for regenerative medicine because they have unique biological characteristics. Above all be used to harvest MSCs.

Embryonic Cells (ESCs): - These are taken from the innermost mass cell of embryos in the stage of blastocyst, and are classified as pluripotency mother cell. These mother cells can continue to self-renew indefinitely, and when given the proper differentiation stimulus, they can develop into every type of cell in human body.

Induced Pluripotent Stem Cells (iPSCs): - Pluripotency factors can be used to transform somatic cells into iPSCs. They do not need embryonic material, according to Forbes et al. (2015), eliminating any ethical concerns. Additionally, because iPSCs can be created from autologous stem cells, allowing for the possibility of self-logous use and preventing immunosuppression, they have the potential to be clinically advantageous.

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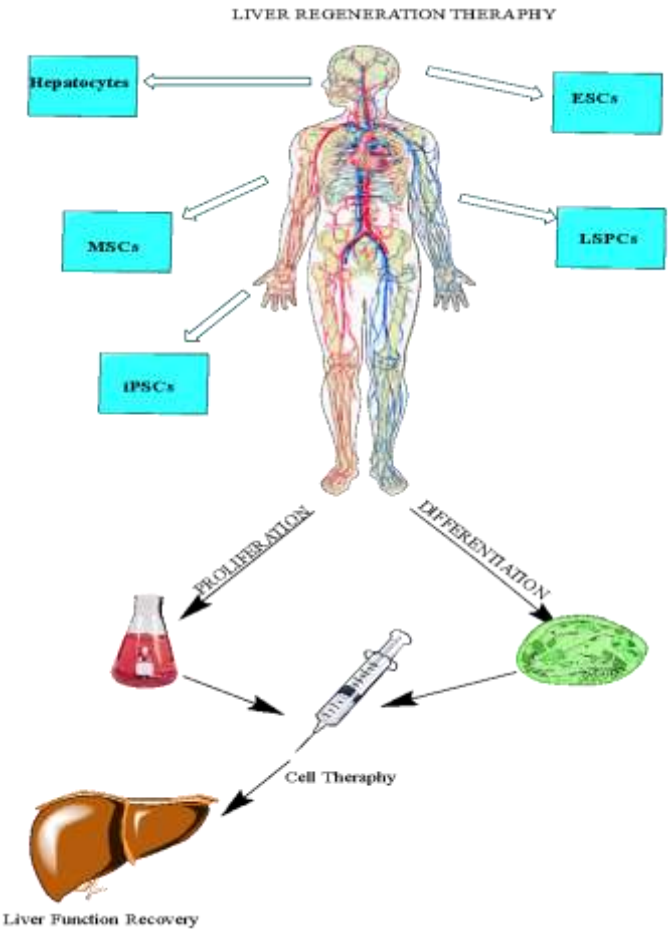

Fig.6: Various cell types and how they are used in cell-based therapies for liver cirrhosis. On the left side of the picture are several cell types that have been isolated from individuals and are being employed in liver regeneration. Each cell type has been injected and has restored liver function either through in vitro proliferation alone (hepatocytes), through differentiation into hepatocytes alone (ESCs and iPSCs), or through both (MSCs and LSPCs)

2.Heart Regeneration Therapy: - Reduced blood flow to bodily tissues is a common symptom of heart failure, and in cases of severe heart failure, this can result in significantly diminished cardiac systolic performance. Transplanting healthy regenerating cardiomyocytes into the damaged heart is an intriguing possible treatment method to increase cardiac function and mortality.

Cell replacement therapies are an additional method for heart repair. To heal and restore function, different cell types are transplanted onto or into the injured heart. Potential cell replacement procedures for heart repair are now being researched using endogenous cardiac progenitor cells (CPCs), bone marrow stem cell mobilization, and embryonic and adult stem cell transplantation. One of the cell types that have been transplanted the most successfully is ESCs, which have shown the ability to electrically integrate with host cardiac tissue, engraft, and enhance heart function following myocardial infarction. [15]

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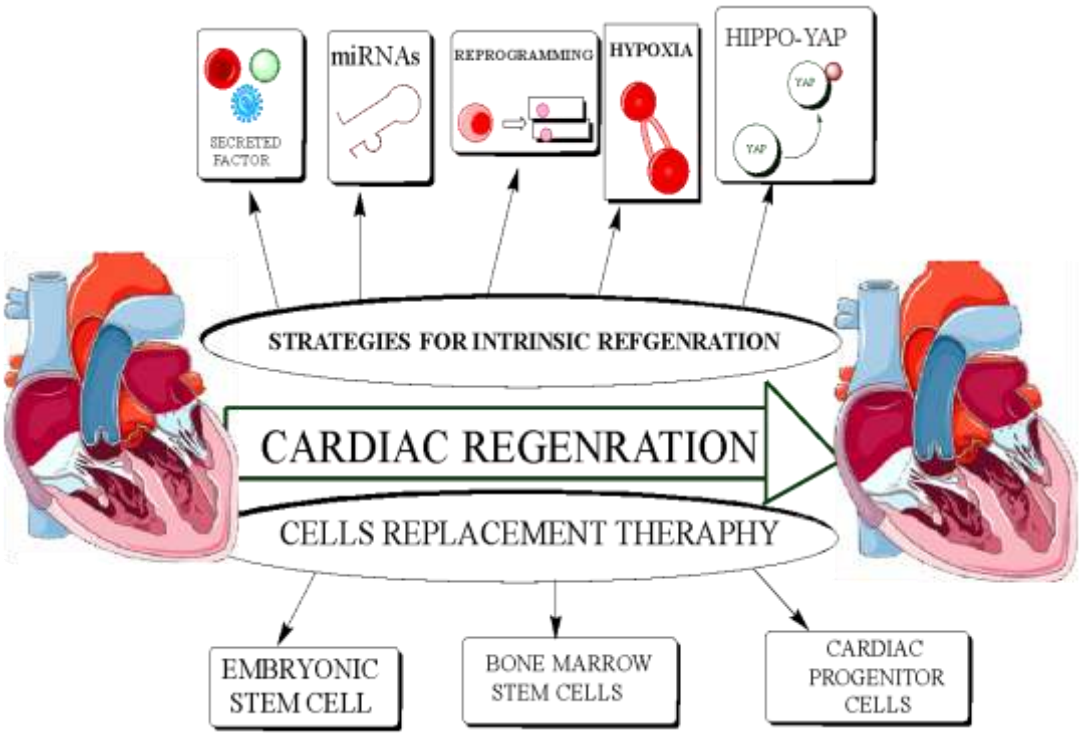

Fig.7: Intrinsic regeneration techniques (attenuation or exogenous application of secreted factors, induction of hypoxic states, cell reprogramming, manipulation of the hippo-YAP pathway, and micro-RNA interference,) and cell replacement therapies (recruiting circulating bone marrow stem cells, transplanting embryonic stem cells, and inducing cardiac progenitor cells to differentiate into new cardiomyocytes) are currently being studied to promote mammalian cardiac regeneration.

IPS Cell: - Production of IPSCs ES cell, which are derived from blastocyst embryos, are more advanced than adult stem cells, have a significant capacity for proliferation and a promising capacity for difference. But since ES cells are allogeneic, it is preferable to use robust autologous stem cells to customise cardiac regenerative medicine procedures for specific patients. According to this perspective, the effective creation of iPS cells is the most significant recent development. In order for iPS cells to be used in therapeutic settings soon, it is crucial that the outcomes of techniques for cardiomyocyte differentiation from ES cells are taken into consideration.

Brain stem cell (BM Stem): - Brain stem cells MSC, or progenitors of bone development, were first discovered in BM in 1966. 60 For a while after that, it was thought that BM-MSCs could only develop into adipocytes, connective tissues, osteoblasts, and chondroblasts. By virtue of their appearance, proliferative potential, and multipotency, BM-MSCs and BM stromal cells were initially separated 61, 62. Yet, despite all of this human research, the molecular process of BMC differentiation is still a mystery, and its discovery will enable BMC transplantation to improve its effectiveness and become a more formidable tool in the field of regenerative medicine.

Cardiac Progenitor Stem Cells: - Numerous adult organs contain stem cells, which support physiologic maintenance and pathological situations' healing mechanisms. But until recently, no one knew that stem cells could be found in the heart. More knowledge is being gained about stem cells' presence and properties in the heart. Because of recent developments in genetic engineering and methods like FAC, these stem cells' ability to develop into cardio myocytes in vivo was validated after being transplanted into a mouse myocardial infarction model, suggesting that stem cells in the heart have a tissue repair mechanism. [16]

3. Spinal cord Regeneration Therapy: - The terrible trauma of a spinal cord injury (SCI) results in permanent impairment. The therapeutic techniques are still not perfect, despite improvements in the previous ten years in the

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treatments for SCI that involve medicine, surgery, and rehabilitation. It is encouraging. The cell transplantation can be used as a therapeutic approach for the management of SCI, especially because it can concentrate on cell renewal, neuroprotection, and regeneration. There are currently few cell therapies available to treat SCI because to a number of translational barriers, including logistical and ethical issues with cell sourcing. Since iPSCs do not raise the same ethical and moral issues as other stem cells, their usage has been especially alluring. Additionally, employing iPSCs, several cell types with potential which May be created from autologous sources in the treatment of SCI. These cells can operate as replacements for missing cells or as environmental support. Other strategies, including direct reprogramming, are addressing the tumorigenicity and reprogramming therapeutically up to this point. iPSCs have recently been used in age-related macular degeneration clinical trials, its potential for translation to other disorders, like SCI, has been further demonstrated. [17]

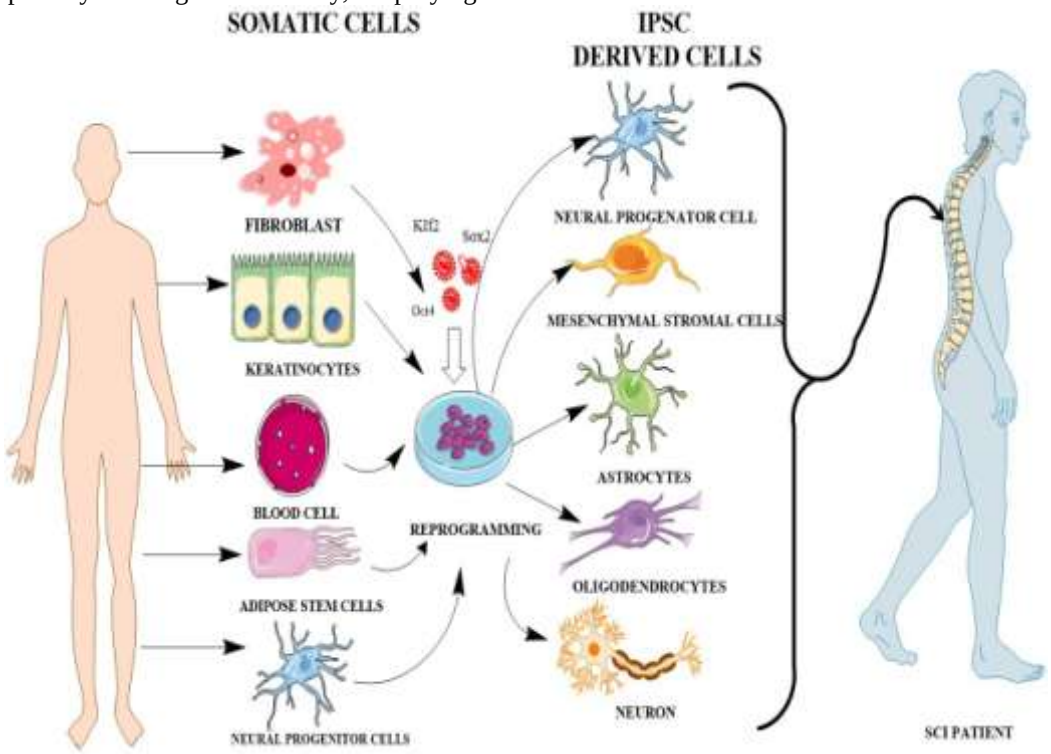

Fig 8: brain progenitor cells, Fibroblasts, keratinocytes, CD34+ cells, melanocytes, cord blood cells, and adipose stem cells are just a few of the cell types that have been utilized to create iPSCs. The process of differentiating iPSCs into the proper multipotent or differentiated cell type that may be employed for the treatment of spinal cord injury (SCI) comes after the iPSCs have been created. To present, a variety of cell types, including neurons, oligodendrocytes, astrocytes, neural crest cells, and mesenchymal stromal cells, have been effectively generated from iPSCs and transplanted into SCI animal models.

Cell Therapy for spinal cord injury:

Potential and Development: - A primer therapeutic approach for the management of Spinal Cord Injury is stem cell transplantation, which functions via a number of distinct mechanisms. Cell treatments for SCI in animals have demonstrated encouragingly positive outcomes in preclinical investigations. Some transplanted cells provide neurotrophic factors, which have therapeutic effects, which are essential for promoting neuronal survival and regeneration.

Neural progenitor's cells: - In order to replace lost or damaged neurons and glia in SCI, neural progenitor cells (NPCs) have acquired a lot of observation. In the spinal cord, rodent and human NPC transplantation has been demonstrated to enhance after traumatic spinal cord injury (SCI) in rodents, functional recovery and neuronal repair and regeneration were seen. Increased axonal regeneration, cell replacement and flexibility, remyelination and nutrient secretion, as well as immune-modulating actions, all contribute to this.

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Mesenchymal Stromal cells: - Multipotent cells called mesenchymal stromal cells (MSCs) come from the mesodermal germ layer. The effectiveness of MSCs in treating SCI has been researched in a number of labs. These findings show that MSCs primarily exert their positive effects by immunomodulating, giving trophic support, altering the environment, and providing a physical framework for expanding axons, which improves locomotor activity.

Schwann cells: - Numerous research conducted over the last two decades have shown that Schwann Cells transplantation may be effective as a treatment for SCI.

Olfactory Ensheathing Glia cells: - Myelinating cells called olfactory ensheathing glia (OEG) are formed from the olfactory mucosa. In various research using animal models of SCI, for the therapy of SCI, OEGs have also been implanted as myelinating cells. OEGs have been demonstrated to promote tissue scaffolding and remyelination, as well as to encourage the regeneration of lesioned axons.

Other cells from Embryonic Stem Cells: - It is challenging to isolate and propagate the numerous cell types outlined above, and making enough cells for SCI treatment is typically a time-consuming and exhausting task. It is critical to have enough cells available for transplantation during this window of time because this is when SCI patients should get cell therapy the most effectively.

Reprogrammed pluripotent stem cells: - Since Takahashi and Yamanaka discover Induced Pluripotent Stem Cells (iPSCs) in 2006, there have been new potential to provide Treatment of SCI patients as well as those with other diseases and injuries using pluripotent stem cells.

Keratinocytes: -Keratinocytes have attracted some interest for their possible use in reprogramming because to their simplicity in extraction from the human foreskin with minimal to no invasiveness. Keratinocytes can be reprogrammed more successfully (10 days) and quickly than fibroblasts, while having a slower rate of expansion.

Melanocytes: -Melanocytes can be reprogrammed with just the other three components because of the large quantities of endogenous Sox2 they already have.

A cord's blood cells: - The process of isolating iPSCs from cord blood is less invasive and can be cryopreserved for more than 5 years, which may be a better source of iPSCs

Adipose stem cells: - Through lipoaspiration, multipotent cells known as adipose stem cells are obtained. A 300-mL sample can yield up to 100 million cells, which can be grown for reprogramming in around 48 hours.

Making Use of iPSC-

Derived Cells to Treat SCI: - The process of treating SCI differentiates iPSCs into corresponding pluripotent or differentiated cell types. (Figure 1).

NPCs derived from iPSC: - One of the most promising cell types is NPC. SCI treatment is presently the subject of research.

Oligodendrocyte Progenitor Cells Derived from iPSC: - According to research from our group and others, the primary cause of functional recovery following NPC transplantation is myelinating oligodendrocyte progenitors generated from NPCs remyelinate host axons.

Motor Neurons derived from iPSCs: - Motor neurons (MNs) generated from stem cells are being used more frequently as cellular replacement therapies for SCI.

Neural Crest Cells derived from iPSC: - Boundary cells between the surface ectoderm and neuroectoderm are the source of neural crest cell. They are a fleeting population of cells that develop into glial cells and neurons in the periphery of the nervous system.

MSCs derived from iPSC: - A promising source of cells to treat spinal cord injury is MSCs.

4.Bone Regeneration Therapy: - Before being loaded onto constructed scaffolds made of growth factors, polymers, biomaterials, etc., mesenchymal cells from the donor patient are separated and developed in vitro into osteoblasts. After that, the scaffolds are placed on the bone to start the process of bone repair and regeneration.

1. Injured bone
2. Stem cells
3. Addition of growth factors and nanoparticle
4. Addition of polymeric Scaffolds
5. Cells grow in polymeric scaffold
6. Scaffold loaded with nanoparticles and growth factors. [19]

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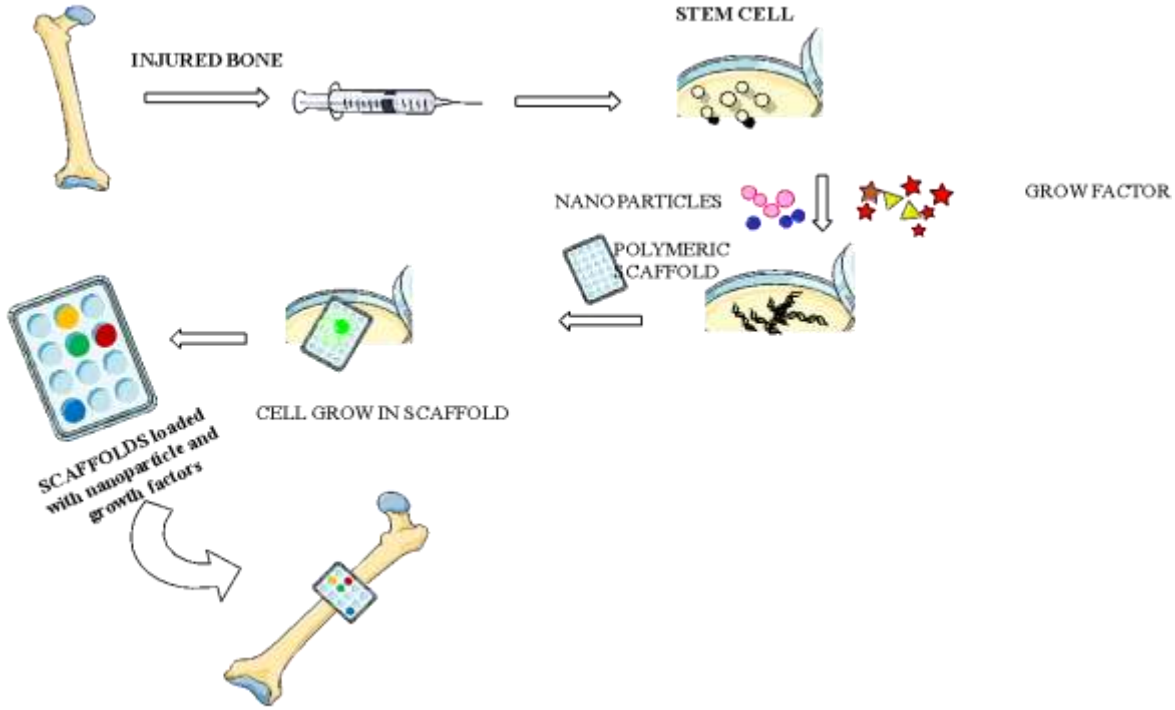

Fig.6: steps in the creation of bone tissue. Before being loaded onto constructed scaffolds made of biomaterials, polymers, growth factors, etc., mesenchymal cells from the donor patient are separated and developed in vitro into osteoblasts. After that, the scaffolds are placed on the bone to start the process of bone repair and regeneration.

5.Cartilage Regeneration Therapy

Through a number of different strategies, MSCs support cartilage repair. To replace injured cells, MSCs can multiply and develop into chondrocytes. To maintain chondrocyte morphologies, boost their proliferation, and alter the composition of the ECM, MSCs can also produce cytokines. More significantly, when exposed to inflammatory or wounded tissue, many immune cells can be affected by the immunomodulatory properties of MSCs. However, there have also been significant issues with basic and clinical trials using MSCs to repair articular cartilage damage.

The variety of MSCs has received more attention in recent years, which may be a reflection of their diversity in terms of biological traits, anatomical locations, embryonic origins, and functions. Understanding the heterogeneity of MSCs is crucial because it allows for the development of superior seed cells because heterogeneity is a significant barrier to MSC research and application. [20]

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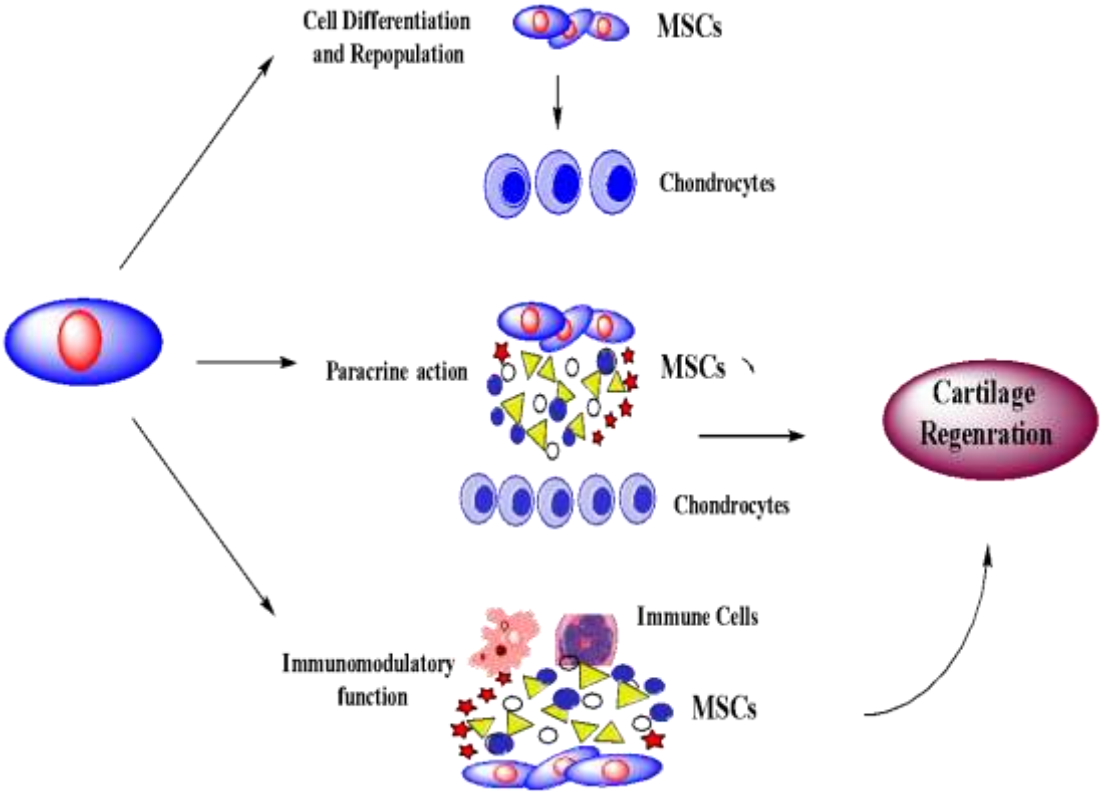

Fig7: Different mechanisms used by MSCs to encourage cartilage regeneration. MSCs have the capacity to multiply and differentiate into chondrocytes to rechange damaged cells. MSCs can also release cytokines to support chondrocyte proliferation and ECM composition, as well as to maintain chondrocyte morphologies. However, when exposed to inflammatory or injured tissue, MSCs can have immunomodulatory effects on a variety of immune cells.

D. Nanotechnology In Regenerative Medicines: - Numerous fields of medical science have seen considerable promise from nanotechnology, which has sparked improvements in medication delivery, diagnostics, and regenerative medicine. This Special Collection covers recent advances in the use of nanotechnology in modelling and treating disease, facilitating tissue regeneration, and controlling cellular differentiation.

Articles about the isolation, characterization, production, storage, and use of nanoparticles and nanofabricated materials in TERM are welcome in the collection. The growing role of extracellular vesicles, as well as the potential and difficulties we currently confront in the clinical translation of these novel medicines, will be highlighted in particular. [20]

Possible subjects could include, but are not limited to:

- Extracellular vesicles are used in regenerative medicine.
- methods for delivering nanoparticles
- nanotechnology materials
- using nano-topographies in engineering to control stem cell differentiation
- Nanotechnology for cutting-edge tissue design
- creation of in vitro diagnostic tools
- Nanoprobe creation for in-vivo imaging

E. 3D BIOPRINTING in regenerative medicines: - Bio printing's potential as a breakthrough in regenerative medicine

Although it doesn't seem like home and office printer quality has improved since the year-1990s, the world of 3D printing is full of possibilities and innovations. Bio-ink is already being tested by researchers as a method of vital organs. Medical applications of the technology currently exist in the

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form of 3D-printed prosthesis and surgical equipment.

Native tissue mimics can be produced using biomaterials and living cells using 3D printing technology. Recently, 3D bioprinting techniques have been used in regenerative medicine to produce highly specific tissue models, outperforming more traditional tissue engineering techniques. [21],[22]

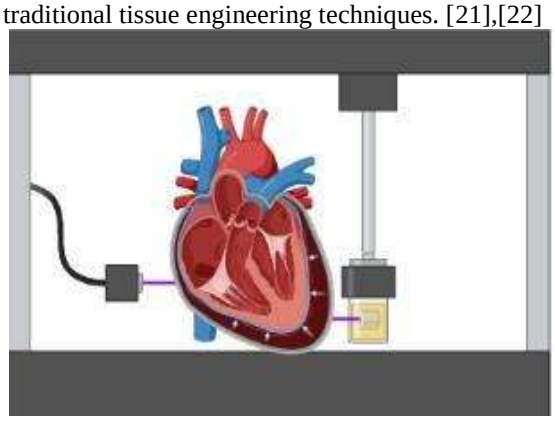

Fig.8:3D bioprinting techniques have been used in regenerative medicine to produce highly specific tissue models, outperforming more traditional tissue engineering techniques

III. CONCLUSION:

Regenerative medicine (RM) refers as in restoring normal function involve replacing or "regenerating" human cells, organ or tissues. A number of people get benefited from regenerative medicine by avoiding back surgery, neck surgery, hip replacements, knee replacements, and various other surgical procedures to treat injuries. Since it holds promise for transplantation applications that seek to recover the lost or injured tissues and organs and overcome supply constraints or immune inflammation, the last few decades have seen the growth of regenerative medicine. Here, our attention was on the most recent advancements in living materials utilized in regenerative medicine. First, we discussed the engineering approaches utilized to prepare live materials, such as 3D bioprinting, cell coating, microfluidics, and genetic engineering. The uses for these living materials were then listed, including scaffolds for tissue healing, cell therapy, tissue or organ models, etc. TERM has assumed the lead in the development of novel medicines thanks to recent advancements in domains including materials engineering, tissue/organ regeneration, and scaffold processing, nanotechnology, and stem cell basic and applied biology. In this sense, TERM's affirmation and acceptance by both the general public and the medical establishment will depend on the years to come. Many research efforts in the field of RegMed are dependent on governmental and corporate support. The recent financial crisis was the final straw in the ten-year degradation of the commercial foundations of the biotech sector. For children with congenital abnormalities, a tissue engineering and regenerative medicine (TERM) strategy may offer the ideal solution, young soldiers who were disfigured in battle, and the elderly who suffer from chronic incapacitating diseases, which are putting an increasing burden on the national economies of the world TE. Large pharmaceutical companies have been buying up some of the most important biotech startups, which might herald a new era where RegMed departs university research labs and small businesses for practical applications in the marketplace. RegMed, however, clearly entails much more than shareholder dividends. The quest for regeneration is one of humanity's oldest dreams, along with that of flight, remote communication, and moonwalking

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