

Review Article

# An Update on The Paradigm Shift of Regenerative Medicine

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## Abstract

Regenerative medicine, a field focused on harnessing the body's inherent healing capabilities, offers promising avenues to improve quality of life, particularly in aging populations. This study delves into the key components of regenerative medicine: triggering agents, potentiators and additives.

Triggering Agents initiate and guide the body's healing processes, exemplified by Human Growth Hormone (HGH) and synthetic bone grafts. Potentiators amplify the effectiveness of treatments, such as Hyperbaric Oxygen Therapy (HBOT) and Platelet-Rich Plasma (PRP). Additives enhance the regenerative process, including stem cell therapy and collagen.

By combining these elements through a strategy known as stacking, researchers aim to optimize regenerative outcomes. This approach involves the synergistic use of multiple therapeutic modalities to address complex biological challenges and accelerate tissue repair.

As regenerative medicine continues to evolve, the potential to mitigate the effects of aging and improve overall health and well-being becomes increasingly tangible.

**Keywords:** Regenerative Medicine; Anti-Aging; Triggering Agents; Potentiators; Additives; Stacking; Quality of Life; Life Expectancy

## Introduction

According to the WHO, quality of life is defined as a person's physical health, psychological condition, independence, relationships with others and the environment one lives in. The quality of life of humans have increased dramatically, which can be attributed to technological advancements throughout history [1]. These improvements are directly correlated with the

increase in life expectancy. Life expectancy has been increasing at a rapid rate, which can be seen with the life expectancy at birth in the EU being about 69 years in 1960 and about 80 years in 2010 [2]. Despite the increase in life expectancy, the maximal lifespan stayed consistent at 122 years [3]. Based on demographic data the limit of human life is between 115 to 126 years old [4,5].

Despite the increasing life expectancy, the quality of life in the elderly are low. This is seen in a study by Jazayeri et al., where a specific elderly (≥65 years) demographic in the Mazandaran province had their physical, mental and social health status tested. The mental and social health of the people were shown to be higher than the international standards with 41.5% and 51.8% were above the standards in mental and social health respectively. However, the physical health showed an astounding 40.7% under the standards [6].

Regenerative medicine has the potential to improve quality of life in the later stages of life. Regenerative medicine is defined as a study that treats injuries and diseases by harnessing the body's own regenerative capabilities to repair tissues and organs losing function due to disease, aging, damage or defects [7]. We believe regenerative medicines can be separated into three categories triggering agents, potentiators and additives. Triggering agents are biologics which create a response which accelerates a process. Potentiators are considered extra/adjuvant treatments to increase effectiveness. Additives are adding extra biologics which are used in the process of regeneration.

## Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

## Regeneration vs Anti-Aging

Regeneration and anti-aging are often used interchangeably, but they represent distinct approaches to counteract the effects of aging. Regeneration focuses on repairing and restoring damaged tissues, aiming to reverse the physical signs of aging [8]. It is considered a treatment approach and can involve techniques like stem cell therapy or growth factor injections to stimulate tissue growth and repair [9]. Anti-aging, on the other hand, takes a more preventative approach, focusing on slowing down the aging process itself [10]. This can involve lifestyle modifications such as diet and exercise, as well as topical treatments and medical interventions including Botox or HBOT. While both approaches have the potential to improve appearance and quality of life, regeneration offers a more targeted solution for reversing visible signs of aging, while anti-aging focuses on maintaining a youthful appearance and preventing future damage.

## Potentiators

The definition of a potentiator is a drug, herb or chemical that increases potency or effectiveness of a drug or treatment. This process can include amplifying growth factor activity, stem cells or other therapeutic factors. Potentiators can target various cellular processes, such as cell proliferation, differentiation, migration and survival [11]. By optimizing these processes, potentiators can accelerate tissue repair, improve cell engraftment and enhance overall therapeutic efficacy. This approach holds significant promise for treating a wide range of degenerative diseases and injuries, including neurological disorders, cardiovascular diseases and orthopaedic conditions [12,13].

Examples of potentiators include the Hyperbaric Oxygen Therapy (HBOT) and the use of nutrition to ensure adequate vitamins and minerals. The increase of oxygen delivery through the HBOT helps accelerate cell proliferation and angiogenesis. This can enhance the healing environment and potentiating antibiotics and wound care [14]. Nutrition, specifically vitamins and minerals, plays a crucial role in potentiating regenerative medicine. These micronutrients act as essential cofactors in various cellular processes, including cell proliferation, differentiation and tissue repair [15].

## Triggering Agents

Triggering agents in regenerative medicine are substances or stimuli that initiate and guide the body's natural healing processes to repair or regenerate damaged tissues. These agents can be chemical, biological or physical in nature and they work by activating specific cellular pathways that promote tissue growth and repair. A couple triggering agents include Human-Growth Hormone (HGH) Platelet-Rich Plasma (PRP) and synthetic bone graft. PRP injections contain a high concentration of growth factors, hence stimulating cell growth and division. PRP helps modulate inflammatory responses which is crucial in the release of pro-inflammatory cytokines attracting immune cells to the injury site [15]. HGH has shown to be a promising tool in regenerative medicine as it is crucial to stimulate cell growth and repair which can be valuable in therapeutic applications. HGH encourages the release of growth factors, which thickens and elongates bones along with growing muscle and reducing fat storages [16]. A study by Rahimzadeh et al. shows the use of HGH to help regenerate arthritis in the knee, which shows some improvements compared to the control group [17]. Synthetic bone graft is shown to be a key tool in regenerative orthopaedic cases as it can be a structural scaffold and signalling agent to stimulate bone regeneration. These grafts mimic the natural extracellular matrix of bone, providing a porous structure that encourages cell infiltration and new tissue formation [18]. By providing a conducive environment for bone cell growth and differentiation, synthetic bone grafts accelerate healing, reduce complications and improve patient outcomes in a wide range of orthopaedic and dental applications. A study by Vickers et al. shows the effectiveness of the synthetic bone graft as a triggering agent for bone regeneration in non-contained defects of the mandible [19].

## Additives

Additives consist of adding extra biologic which is in the process of the specified regeneration. These are imperative to the development of the tissue engineering scaffolds and are the framework of cells to grow and differentiate into functional tissues. Specific additives can help enhance the properties of the tissue scaffold and promote tissue regeneration.

Additives in regenerative medicine include Stem Cell therapy and Collagen. Stem cells are essential cells which can replicate themselves and can transform themselves into specialized cells like nerve, muscle or bone cells [20]. Stem cell therapy involves introducing stem cells into damaged tissues with the goal of: Regeneration (Stimulating the body's natural repair mechanisms to regenerate damaged tissue), Replacement (Replacing damaged cells with new, healthy cells derived from stem cells) and Modulation (Influencing the body's immune response to promote healing). A study completed by Mahla shows the application of stem cells in regenerative medicine and disease therapeutics [21]. Collagen is a natural protein found in the extracellular matrix, is a versatile biomaterial with significant potential in regenerative medicine. It serves as a scaffold for tissue engineering, providing a structure for cells to attach, proliferate and differentiate into new tissue [22]. Collagen has been used in topical and oral applications to accelerate hair, nail and skin growth. A study by Hwang, et al., shows the effects of fish collagen peptide in dermal papilla cells and C57BL/6 Mice Modulating Wnt/ $\beta$ -Catenin and BMP signalling Pathways [23].

### **Stacking**

Stacking is the act of combining multiple therapeutic approaches to enhance the process which is to be achieved. Regarding regenerative medicine, this can be done by combining a triggering agent with a potentiator and additive etc. Using a variety of medicines can help address different aspects of the regenerative process including inflammation reduction, tissue remodelling, combatting against bacteria etc. Stacking with different forms of regenerative medicine include using a potentiator and triggering agent, a prime example being HBOT and PRP in a study completed by Korucu et al., showing accelerated knee cartilage regeneration by stacking the two procedures [24]. An example of stacking two of the same forms of regenerative medicine is the combination of PRP and Synthetic Graft (Integran's GraftIT) for the treatment of a Pilon fracture where the PRP triggers the growth hormones, accelerating healing time and the synthetic graft acting as a triggering agent by providing a structure which encourages cell infiltration [25,26]. The ideology of stacking is a concept used by athletes, specifically body builders. These athletes use a combination of various supplements and drugs, proper dieting and a training regimen to enhance their muscular growth, strength and recovery.

### **Conclusion**

Regenerative medicine holds immense potential to revolutionize healthcare by addressing the challenges of aging and disease. By harnessing the body's inherent regenerative capabilities, this field offers innovative solutions to repair damaged tissues and organs. This study has explored the fundamental concepts of regenerative medicine, including triggering agents, potentiators and additives. The effects of these concepts can be exacerbated with the concept of stacking, the combination of multiple therapeutic procedures. By understanding these key components and their synergistic effects, we can unlock the full potential of regenerative medicine to improve human health and longevity.

### **Conflict of Interest**

Dr. Gordon Slater has a pecuniary interest in Integran a biotechnology company and Regen U clinics where he actively advises on treatment protocols and implant design.

### **Acknowledgement**

Acknowledge those who provided technical support during the study.

### **Consent to Participate**

Informed consent was obtained from each participant prior to specimen collection.

### **Financial Disclosure**

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### **Data Availability**

Data is available for the journal. Informed consents were not necessary for this paper.

### **Author's Contribution**

Dr Zadane Bachmid contributed in writing of the paper and Dr Gordon Slater contributed in Proofreading/Editing of the paper.

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