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*Review Article*

# Biophotonic and Electromagnetic Modulation of Stem Cell Behavior: Emerging Evidence for Environmental Optimization in Regenerative Medicine

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## Abstract

Background: Stem cell therapies have improved rapidly; however, clinical outcomes remain inconsistent. Among the factors explaining this variability, the physical environment around cells during and after transplantation has received little attention. Therefore, three lines of evidence-Ultraweak Photon Emission (UPE), Photobiomodulation (PBM) and Pulsed Electromagnetic Fields (PEMF)-point to biochemical pathways by which the electromagnetic environment influences stem cell proliferation, differentiation and migration.

Objective: This review collates current knowledge on how biophotonic signals and electromagnetic fields regulate stem cell behavior and whether deliberate optimization of the electromagnetic environment could serve as an additional technique in regenerative medicine.

Methods: We searched PubMed, Web of Science and Scopus for the following terms: "ultraweak photon emission and stem cells," "photobiomodulation and mesenchymal stem cells," and "pulsed electromagnetic field and stem cell differentiation." English-language articles published between 2004 and 2025 were examined and 58 met our inclusion criteria.

Results: UPE intensity varies with stem cell differentiation status and reflects the underlying metabolic activity. PBM at red (630-660 nm) and near-infrared (800-890 nm) wavelengths promotes Mesenchymal Stem Cell (MSC) proliferation, osteogenic commitment and migration, as evidenced by over 200 studies. Low-frequency PEMF (15-50 Hz) stimulates chondrogenic and osteogenic differentiation via calcium signaling and mammalian Target of Rapamycin (mTOR)-dependent pathways. Unexposed cell populations close to activated cells respond to photonic signals, demonstrating cell-to-cell biophotonic communication.

Conclusion: The present study clearly demonstrates that stem cells are responsive to their electromagnetic environment. Optimizing biophotonic and electromagnetic settings before, during and after stem cell operations is a viable (and testable) technique for boosting regeneration outcomes. Standardized clinical practices and prospective trials are necessary next steps.

**Keywords:** Ultraweak Photon Emission; Biophotons; Photobiomodulation; Pulsed Electromagnetic Field; Mesenchymal Stem Cells; Regenerative Medicine; Stem Cell Differentiation; Biofield Optimization

## Abbreviations

UPE: Ultraweak Photon Emission; PBM: Photobiomodulation; PEMF: Pulsed Electromagnetic Field; MSC: Mesenchymal Stem Cell; ROS: Reactive Oxygen Species; VSEL: Very Small Embryonic-Like Stem Cell; NSC: Neural Stem Cell; ADMSC: Adipose-

Derived Mesenchymal Stem Cell; BM-MSC: Bone Marrow Mesenchymal Stem Cell; hUC-MSC: Human Umbilical Cord Mesenchymal Stem Cell; VGCC: Voltage-Gated Calcium Channel; CCO: Cytochrome C Oxidase; ATP: Adenosine Triphosphate; mTOR: Mammalian Target of Rapamycin; TGF-β: Transforming Growth Factor Beta; BMP-2: Bone Morphogenetic Protein 2

## Introduction

Regenerative medicine promises to repair damaged tissue by employing the body's own or foreign stem cells. In practice, however, the scenario is more complex. Despite substantial breakthroughs in cell sources, culture and delivery techniques, outcomes differ greatly among patients [1]. This heterogeneity indicates that current practices may not account for certain aspects. The physical environment is one such factor. Cells do not function in electromagnetic silence. Every living cell produces photons at extremely low intensities, a process associated with oxidative metabolic reactions known as Ultraweak Photon Emission (UPE) [2].

Documented in bacteria, fungi, plants and animal tissues, UPE intensity correlates with cellular oxidative status and mitochondrial function [3,4]. The significance of these faint emissions is evidenced by accumulating evidence that they may participate in intercellular signaling [5,6]. Exogenous electromagnetic stimuli also influence stem cell activity. Photobiomodulation (PBM) or the use of certain wavelengths of non-thermal light, has been proven to increase cellular activity across a wide range of cell types [7]. More than 200 studies have been conducted on the effects of PBM on stem cells, with the majority indicating improvements in proliferation, differentiation and migration [8]. In addition, Pulsed Electromagnetic Fields (PEMF) alter stem cell fate via calcium signaling and downstream biochemical cascades [9,10]. The literature reveals a strong convergence. UPE, PBM and PEMF all work through similar molecular pathways, including Reactive Oxygen Species (ROS), mitochondrial membrane potential and intracellular calcium dynamics, Fig. 1 [11,12]. Can we optimize the electromagnetic environment surrounding stem cells to improve regeneration outcomes? This convergence raises a useful question that has not received much attention.

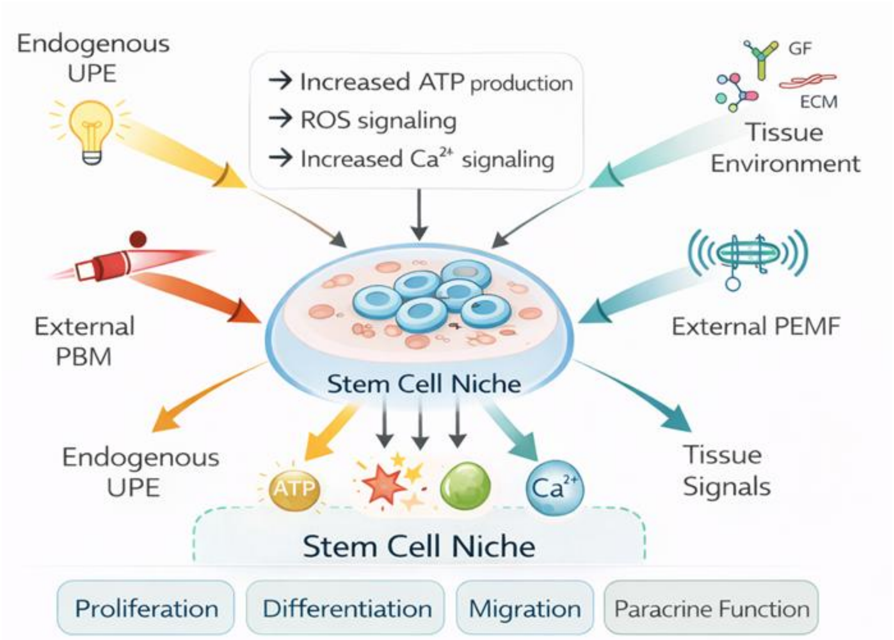

**Figure 1:** The integrated biophysical microenvironment influences stem cell fate. Endogenous ultraweak photon emission, external photobiomodulation and pulsed electromagnetic fields, as well as tissue-derived signals, all have an impact on intracellular pathways that regulate stem cell proliferation, differentiation, migration and paracrine activity.

This review includes evidence from all three domains. We investigated the distinct effects of each modality on stem cell activity, common pathways among them and potential applications of environmental electromagnetic optimization in clinical settings.

## Methodology

We searched PubMed, Web of Science and Scopus using the following terms: "ultraweak photon emission AND stem cells," "photobiomodulation AND mesenchymal stem cells," and "pulsed electromagnetic field AND stem cell differentiation." English-language peer-reviewed articles published between 2004 and 2025 were considered for inclusion. Titles and abstracts were screened for relevance to the topics of biophotonic signaling, photobiomodulation, pulsed electromagnetic fields and stem cell biology. Full texts of potentially eligible studies were retrieved and evaluated against predefined inclusion criteria: original research or systematic review articles reporting quantitative outcomes related to stem cell proliferation, differentiation, migration or paracrine function in response to photonic or electromagnetic stimuli. Case reports, conference abstracts and non-peer-reviewed sources were excluded. A total of 58 articles met the inclusion criteria and were incorporated into this review.

## Ultraweak Photon Emission and Stem Cell Biology

### *Origin and Mechanism of UPE*

UPE results from the relaxation of electrically excited species created during oxidative metabolic processes [2]. The main sources are singlet oxygen decay, excited carbonyl intermediates and lipid peroxidation products produced by mitochondria [4]. Emission intensities are exceedingly modest, ranging from a few to several hundred photons per second per square centimeter over a spectral range of approximately 200 to 800 nm [13]. The cycle of events begins with mitochondrial respiration. ROS are produced by electron transport and lead to excited molecular states. As these species return to their ground state, the energy difference is emitted as a photon [4]. Because metabolic throughput is closely linked to this process, UPE serves as a real-time readout of cellular energetics: higher metabolic rates result in more ROS, which in turn generate more photons. Stressed or diseased cells typically release at varying intensities compared to their healthy counterparts [14].

### *UPE Changes During Stem Cell Differentiation*

This issue was brought to the attention of stem cell research by a 2020 study published in Scientific Reports [15]. The authors directly detected UPE from murine neural stem cells during serial passaging and differentiation. They discovered that the ratio of neuronal differentiation to photon emission intensity changed in direct proportion to the differentiation status of the cells. It appears that closely synchronized signaling pathways produce ROS and UPE [15]. This outcome is significant for two reasons. First, it shows that UPE in stem cells is more than just metabolic noise; it not only represents but also potentially contributes to functional cellular choices. Second, it raises the question: if UPE can be regulated, would differentiation results follow? According to the same study, silver nanoparticles raised UPE intensity by 21.8-28.3% compared to controls and this increase was linked to various patterns of differentiation [15]. Research on embryo viability has provided complementary findings. A 2024 study in Scientific Reports found that UPE patterns could accurately discriminate between live and degenerated mouse embryos [16]. Using an entropy-weighted spectral fractal dimension technique, the researchers discovered that fresh and frozen embryos have unique emission characteristics. UPE contains useful information regarding cellular viability and functional status.

### *Biophotonic Cell-to-Cell Communication*

The concept that cells communicate via photons has a surprisingly lengthy history. Gurwitsch, demonstrated that cultures separated by quartz (UV-transparent) but not glass (UV-opaque) could promote each other's growth [2]. Over the next century, this insight has been duplicated and expanded in various systems. Fels, provided a beautiful illustration, demonstrating that chemically segregated Paramecium populations influenced each other's growth rates when optically connected through quartz barriers. When optical connection was prevented, the effect faded, providing strong evidence for non-chemical, light-mediated cell signaling. Levac and Dotta's proof-of-principle study introduced a new dimension [18]. B16-BL6 melanoma cells were exposed to temporally patterned blue LED stimulation, which resulted in changes in viability and photon emission frequency. Unexposed cells in close proximity (but not in direct contact) showed similar alterations. Constant blue light had no impact; only patterned stimulation caused a response. The unexposed cultures had a spectral peak of approximately 21 Hz, which matched the prominent frequency of the patterned field [18]. A 2025 iScience review expanded on this idea, stating that neural cells may have waveguiding capabilities capable of enabling optical communication pathways within the brain [19]. If verified, these findings might broaden the application of biophotonic signaling beyond cultured cells and into organized tissue systems.

### *Photobiomodulation and Stem Cell Modulation*

PBM, formerly known as Low-Level Laser Treatment (LLLT), uses non-thermal light at specified wavelengths to influence cellular activity. The field has matured rapidly. The 2025 World Association for Laser Therapy (WALT) policy document, published in the Journal of Dentistry, identified 263 articles on PBM and stem cells, of which 204 met the inclusion criteria [8]. Rastogi, Sahu and Majumder conducted a separate 2025 systematic review, cataloging studies from 2000 to 2024 using the PRISMA approach [20]. The evidence base is sufficiently strong to support consensus recommendations.

### *Effects on Stem Cell Proliferation*

PBM reliably increases stem cell proliferation and this effect is strongly wavelength dependent. Red (660 nm) and near-infrared (810 nm) light promote proliferation in adipose-derived MSCs, whereas green (540 nm) and blue (415 nm) light inhibit it [21]. This selectivity indicates that specific chromophores serve as mediators. Cytochrome C Oxidase (CCO) in the mitochondrial electron transport chain is the principal photoacceptor for red and near-infrared wavelengths [12]. When CCO absorbs PBM photons, it dissociates, inhibits nitric oxide, raises the mitochondrial membrane potential and promotes ATP synthesis [22]. The resultant surge of ROS activates downstream signaling cascades. A 2025 investigation revealed that PBM at 700-710 nm and 1064 nm with energy densities of 3-30 J/cm² increased the proliferation of meniscus-derived stem cells. The highest effect was observed at 15 J/cm² [23].

### *Effects on Stem Cell Differentiation*

PBM can control stem cell differentiation across many lineages. On the osteogenic front, Ma and colleagues found that PBM enhances osteogenic commitment in MSCs by activating the Akt signaling pathway and increasing P-Akt expression [24]. Elevated ROS levels generate mild oxidative stress, which is a known trigger for osteogenic commitment. Neural differentiation also responds. Using 635 nm and 808 nm lasers on human umbilical cord MSCs resulted in increased expression of neural markers, such as nestin and NeuN, with energy densities ranging from 0 to 10 J/cm² [25]. Adipose-derived MSCs have similar neuronal differentiation capabilities under PBM, especially when light is coupled with biological inducers (Fig. 2) [26].

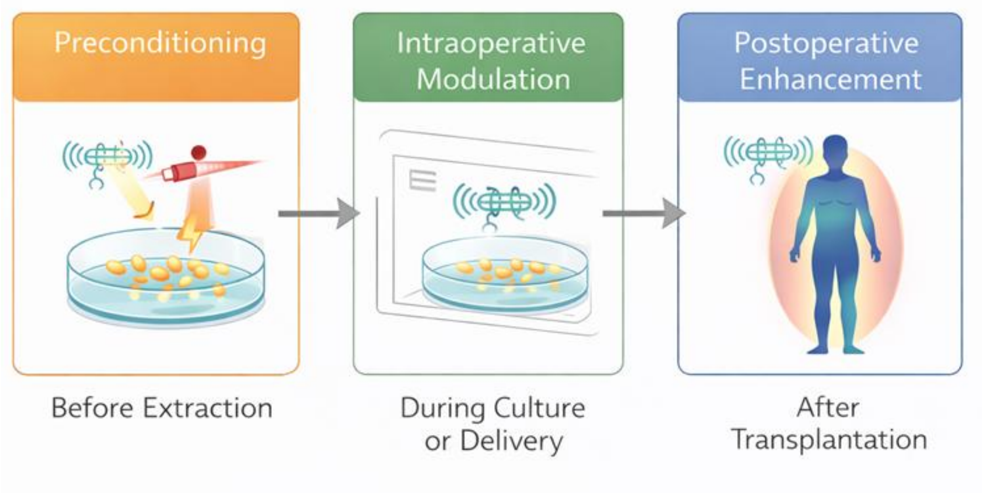

**Figure 2:** Magnetic and photonic modulation throughout the stem cell treatment workflow. Optimization methods can be used before, during and after transplantation to improve stem cell survival, integration and functional outcomes.

Chondrogenic differentiation has an intriguing twist; the impact appears to be mediated not only through direct cell stimulation but also through paracrine pathways. PBM-treated MSCs generate conditioned media that promotes chondrocyte proliferation, migration and extracellular matrix synthesis in recipient cells [27]. This secretome-mediated effect has clear clinical implications, indicating that PBM can increase the therapeutic potency of MSC-derived products without direct administration to target tissues.

### *Effects on Stem Cell Migration and Homing*

For stem cell therapies to be effective, transplanted cells must reach the site of infection. A systematic analysis of 42 studies indicated that low-power laser irradiation (780-950 nm, 10-50 J/cm²) increased MSC survival, proliferation and homing [28]. PBM-treated MSC-conditioned media also increased migration in both chondrocytes and MSCs compared to the controls [27]. Conditioning stem cells with PBM before transplantation may increase engraftment and functional integration.

## Pulsed Electromagnetic Fields and Stem Cell Fate

### *Mechanisms of PEMF Action*

PEMF therapy subjects' biological tissues to time-varying magnetic fields. The key cellular mechanism underlying this is the activation of Voltage-Gated Calcium Channels (VGCCs) in cell membranes [9]. Pall, found that VGCC blockers reduce or eliminate a wide range of EMF-induced biological effects, establishing VGCCs as direct molecular targets [9]. The resultant calcium influx triggers downstream signaling cascades that affect proliferation, differentiation and gene expression [10]. PEMF also stimulates adenosine A2A and A3 receptors, activating anti-inflammatory pathways that are directly relevant to the tissue settings in which stem cell therapies are used [29]. The mTOR signaling pathway has been identified as a key modulator of PEMF effects on osteogenic commitment. Ferroni, Gardin, Dolkart and colleagues demonstrated in Scientific Reports that PEMF exposure boosted MSC proliferation and osteogenic differentiation via activating mTOR and these effects lasted even under inflammatory circumstances [30].

### *Effects on Osteogenic Differentiation*

Exposure to PEMF at 1 mT intensity and 50 Hz frequency promotes osteogenic development in human adipose-derived MSCs [31]. After two weeks of daily exposure (2 h each day), bone-related gene expression increased significantly. After three weeks, the protein expression of osteopontin, osteocalcin and RUNX-2, established indicators of osteoblast maturation, increased [31]. A detailed 2024 review in the Frontiers in Bioengineering catalogued the effects of PEMF in numerous osteogenic studies [32]. PEMFs activate TGF-β family genes, BMP-2 and FGF-2 and increase alkaline phosphatase activity. The waveform shape, regardless of the intensity, has emerged as a significant factor influencing the outcomes.

### *Effects on Chondrogenic Differentiation*

A significant finding in chondrogenesis literature is that less can be more. Poh, et al., showed that a single ten-minute exposure to low-intensity PEMF (2 mT, 15 Hz) at the start of chondrogenic induction outperformed subsequent treatments [33]. Initial PEMF stimulation activates transient receptor potential (TRP) channels, resulting in a favorable calcium signal; however, repeated stimulation causes excessive calcium entry, reducing the chondrogenic response [33]. In addition, PEMF improves the paracrine function of MSCs during cartilage repair. Conditioned media derived from PEMF-treated MSCs enhances chondrocyte redifferentiation and extracellular matrix deposition [27]. Ten minutes of exposure was sufficient to demonstrate that brief electromagnetic conditioning can significantly increase the therapeutic potential of a stem cell preparation.

### *Effects on Immunomodulation*

The inflammatory environment is crucial for stem cell engraftment and PEMF has a beneficial dual function [34]. It reduces the release of proinflammatory cytokines (TNF-$\alpha$, IL-6, IL-8 and PGE2) while increasing the production of the anti-inflammatory cytokine IL-10 [29]. PEMF-mediated immunomodulation may aid in creating a niche that promotes stem cell survival and integration following transplantation [34].

## The ROS Mitochondria Calcium Axis

The most striking finding from the literature is that UPE, PBM and PEMF are not three distinct phenomena but rather three distinct perspectives on the same fundamental biology. All three modalities point to ROS as a major mediator [11,12]. UPE is caused by ROS-induced excited molecular species. PBM increases ROS levels via CCO-mediated mitochondrial activation. PEMF stimulates ROS generation through calcium influx and mitochondrial membrane depolarization indicated in Fig. 3. Calcium signaling represents a second point of convergence. PBM stimulates TRPV1 channels, increasing intracellular calcium levels [23]. PEMF stimulates VGCCs, with overlapping downstream effects [9]. Both stimuli activate calcium-dependent transcription factors that control stem cell fate decisions. Mitochondrial function completes the trio. UPE measures the mitochondrial metabolic state in real-time [4]. PBM directly attacks the mitochondrial CCO [12]. PEMF regulates mitochondrial membrane potential via calcium-dependent mechanisms [10].

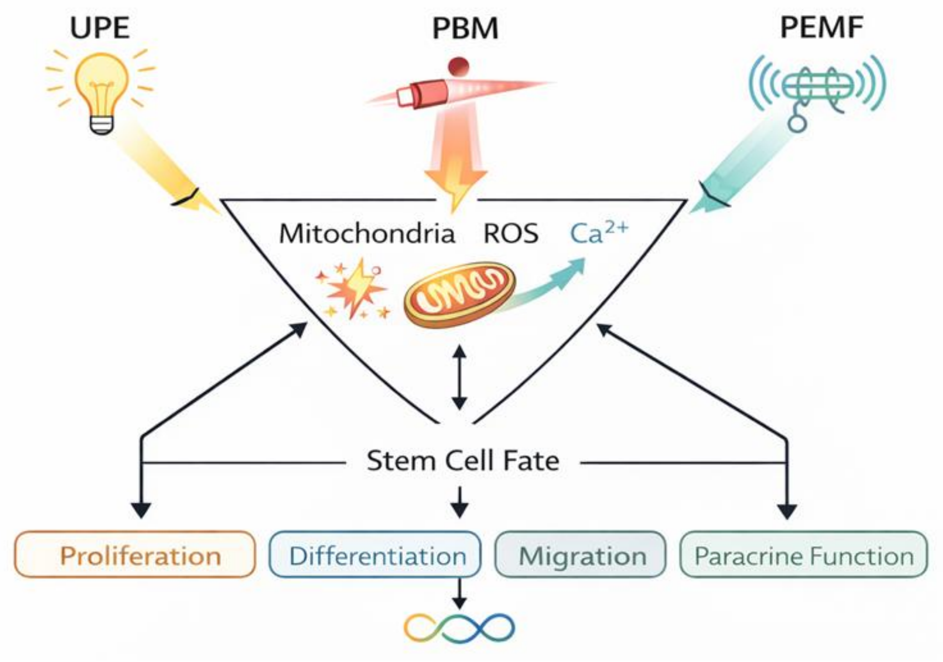

**Figure 3:** Converging molecular processes that control stem cell responses to UPE, photobiomodulation and pulsed electromagnetic fields. These stimuli regulate stem cell fate by linked effects on mitochondrial activity, reactive oxygen species production and intracellular calcium signaling, resulting in changes in proliferation, differentiation, migration and paracrine function.

Reactive oxygen species, calcium and mitochondrial activity provide a coherent framework (Table 1).

| Parameter | UPE | PBM | PEMF |
|---|---|---|---|
| ROS involvement | Source via excited molecular species | Amplified via CCO activation | Triggered via $Ca^{2+}$ influx |
| Calcium signaling | Indirect (metabolic coupling) | TRPV1 channel activation | VGCC direct activation |
| Mitochondrial target | Real-time metabolic readout | CCO (Complex IV) direct | Membrane potential via $Ca^{2+}$ |
| Proliferation effect | Correlates with differentiation | Enhanced (660-810 nm) | Enhanced (15-50 Hz) |
| Osteogenic effect | Not directly tested | Akt pathway activation | mTOR; BMP-2 upregulation |
| Paracrine effects | Cell-to-cell photonic signaling | Enhanced secretome | Enhanced secretome for cartilage |

**Table 1:** Convergence of biophotonic and electromagnetic mechanisms in stem cell biology.

## Clinical Implications for Regenerative Medicine

### *The Concept of Biofield Architecture*

The information presented here supports what we call "biofield architecture," the deliberate design of electromagnetic settings to improve stem cell preparation, distribution and post-treatment recovery. This notion is based on three well-supported principles. First, stem cells react to the electromagnetic environment. This has been supported by hundreds of PBM and PEMF investigations [8,10]. Second, stem cells communicate via biophotonic signals, with unexposed cell populations responding to photonic emissions from nearby activated cells [18]. Third, the underlying molecular mediators, reactive oxygen species, calcium and mitochondrial function, are consistent across modalities. Electromagnetic environmental optimization may be implemented at several points throughout the treatment process. PBM at 630-660 nm or 800-890 nm applied to the collected cells before injection has been shown to improve proliferative capacity and secretome quality [8,20]. A short PEMF pulse (10 min, 2 mT, 15 Hz) at the start of differentiation induction can increase chondrogenic commitment [33]. During the critical 24-72-h post-injection window, ambient electromagnetic optimization may aid engraftment. The capacity of PEMF to decrease proinflammatory cytokines while raising IL-10 may aid in the creation of a milieu more suitable for transplanted cell survival [34]. PBM conditioning of MSCs before secretome collection provides a non-pharmacological method for increasing paracrine therapeutic potency for secretome augmentation [20].

## Current Limitations

Standardization of parameters is the most important obstacle. PBM investigations employ a wide range of wavelengths, energy densities and exposure times [8]. PEMF studies vary in frequency, intensity, waveform and treatment regimen [10]. This variety makes it difficult to compare studies. The UPE-stem cell interaction is the least developed of the three domains. While UPE corresponds with the differentiation state [15], causal evidence is lacking. It is unclear whether UPE manipulation alone can have a significant impact on stem cell fate. Clinical translation data are scarce. Most evidence stems from *in-vitro* research. The 2025 WALT position paper expressly stated a significant shortage of clinical trials in all assessed domains [8]. Therefore, prospective randomized clinical trials are needed.

## Future Directions

Multi-center research should standardize PBM techniques for specific stem cell applications; the WALT 2025 recommendations provide a good starting point [8]. The significance of endogenous UPE in stem cell communication requires further investigation, especially as new ultrasensitive photon detection methods become widely available [35]. Combination studies, which examine PBM and PEMF when administered sequentially or concurrently, may indicate additive or potentiating effects. Prospective clinical trials utilizing electromagnetic environmental optimization in addition to traditional stem cell methods are required to close the translation gap Fig. 4. The burgeoning topic of quantum biology has added more theoretical frameworks [3]. If biophotonic coherence regulates cellular activity, external influences affecting photon emission and absorption patterns may significantly impact cellular behavior. This concept remains hypothetical; however, it is becoming more testable with modern technologies.

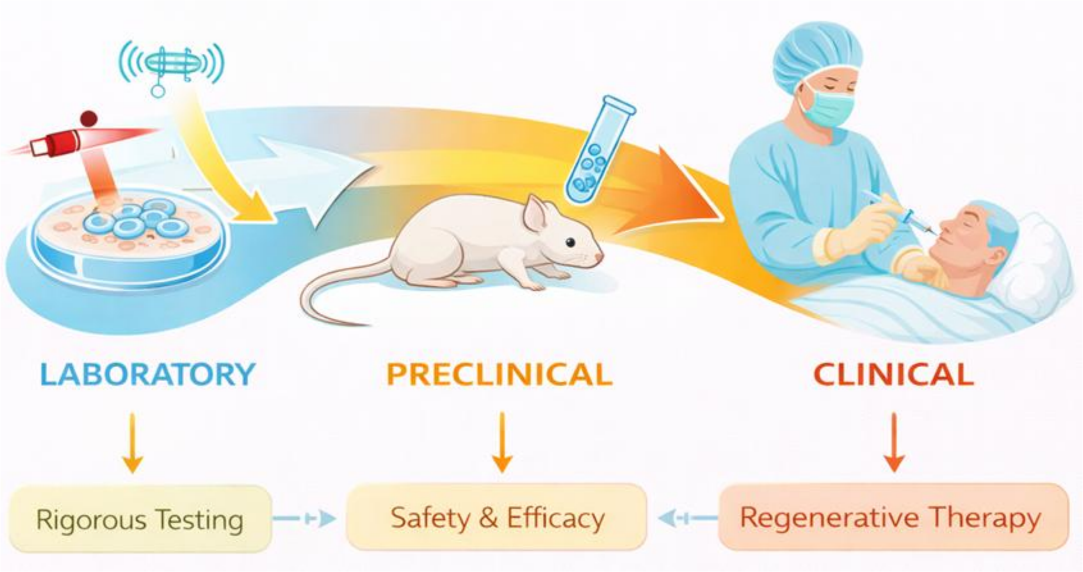

**Figure 4:** Translational framework for electromagnetic and photonic approaches to stem cell treatment. The development process moves from laboratory investigation to preclinical safety and efficacy testing, followed by clinical evaluation for regenerative therapeutic uses.

## Conclusion

Stem cells respond to their electromagnetic surroundings. This conclusion is validated by hundreds of peer-reviewed publications spanning UPE, PBM and PEMF research. The molecular foundations are becoming more well-defined, pointing to a common ROS-calcium-mitochondria signaling pathway. PBM promotes proliferation, differentiation, migration and secretome quality. PEMF influences stem cell fate and alters the inflammatory microenvironment. UPE offers a real-time view of cellular metabolic status and may participate in intercellular communication. The concept of biofield architecture, which involves improving the electromagnetic environment surrounding stem cell treatments, is a reasonable expansion rather than a replacement for existing practices. A strong preclinical basis exists; standardized procedures and prospective studies are now required to ascertain whether this strategy might improve the consistency and potency of regeneration effects.

## Conflict of Interest

The author has a commercial interest in technologies related to electromagnetic environmental optimization for regenerative medicine applications. This review was conducted independently and was not funded by any commercial entity.

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## Data Availability Statement

Not applicable.

## 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.

## Informed Consent Statement

Informed consent was taken for this study.

## Authors' Contributions

MA conceived the review, conducted the literature search and wrote the manuscript.

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