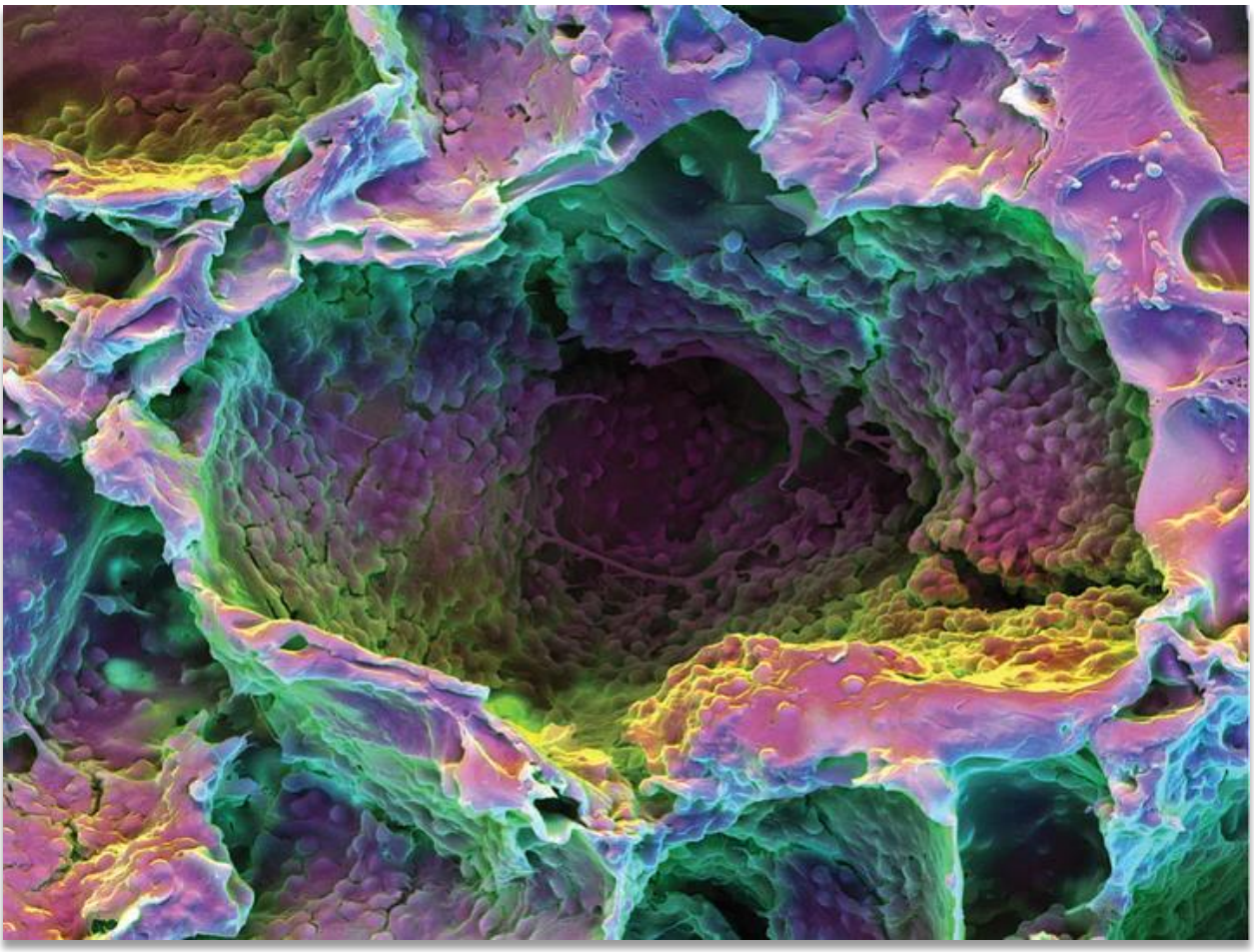

Figure 1.

## The noninvasive application of light to regrow teeth—and potentially to recover the functionality of damaged organs—is an appealing alternative to current options. Misunderstandings currently gating such treatments in no way diminish their potential.

Affecting biological change by safely exposing endogenous compounds to light is exciting for many reasons. Not only has research demonstrated the effectiveness for such noninvasive therapies, but the approaches are also low cost, thereby promising to allow treatment for individuals across the globe who traditionally have not had access to healthcare technologies.

Often called low-level light therapy (LLLT), photobiomodulation (PBM) therapy is a non-thermal process that uses non-ionizing light sources (either the coherent light of lasers or the non-coherent energy of LEDs) to trigger redox biology-chemical reactions in which the oxidation state of atoms is changed, normally through the transfer of electrons between chemical species.

PBM is being applied and investigated for a wide range of applications, including the harnessing of stem cells for tissue regeneration. Regulatory proteins called growth factors can trigger stem cells (which occur naturally in the adult body) to differentiate into a range of functional cell types. The standard method of boosting stem cell proliferation is a multi-step process that involves extracting tissue, isolating stem cells and processing them in a lab, and then returning them to the body. Recent research shows, however, that noninvasive application of light can boost the natural growth of an individual's own stem cells to enable exciting new treatments.[1]

**Stimulating organ regeneration**

When you think of organ regeneration, you may naturally think of the liver. In mammals, this organ has an inherent capacity to recover following injury—an abnormal loss of cells triggers a rapid response.

Among the studies researching the use of light to trigger for regeneration is work by Israeli scientists investigating PBM for liver tissues in the critical 48 hours following injury.[2]Researchers at Tel Aviv University and Wolfson Medical Center (Holon, Israel) built on earlier work that demonstrated 1) the ability of bone marrow-derived mesenchymal stem cells (MSCs) to naturally stimulate the formation of blood cell components in the liver, and 2) the biostimulatory effects of laser light on cells and organs—including skeletal muscle, heart, brain, and liver following injury.

Led by Uri Oron, Ph.D., at Tel Aviv University's Department of Zoology, the team excised 70% of the livers of 12 mature male rats, which they assigned randomly to two groups: a control non-laser-treated group and an experimental group. The experimental group was treated with 804 nm light from a tunable-power gallium aluminum arsenide (GaAlAs) diode laser with a 1.5-mm-diameter metal-backed glass fiber optic. The researchers applied a 2-cm-diameter beam with 5 $mW/cm^2$ power by placing the distal tip of the fiber optic to a shaved area above the surgical site 3 hours post-surgery for 60 seconds. Two days post-hepatectomy, the researchers injected both groups with 5-Bromo-2'deoxyuridine (BrdU), a synthetic nucleoside used to detect proliferating cells in living tissues.

Examining histological sections from each liver, they found a 2.6-fold increase in the number of proliferating (BrdU-positive) cells per area in the regenerating regions of livers in the laser-treated rats vs. the non-laser-treated group. Likewise, the density of newly formed blood vessels was 3.3X greater and the population of immunopositive stem cells was 2.3-fold higher, in the same area of the laser-treated livers vs. those not receiving laser treatment. The results led the researchers to conclude that PBM was helpful not only in facilitating the formation of new hepatocytes and MSCs, but also for angiogenesis.

For their next investigation, the researchers chose a more-challenging target—the mammalian heart.[2] Unlike the liver, the heart's post-injury regenerative capacity is gated by low-level cardiomyocyte proliferation and a limited number of cells expressing stem

cell marker proteins. The team tested the hypothesis that applying PBM therapy to MSCs in bone marrow at the tibia would allow the MSCs to migrate to the heart tissue damaged by myocardial infarction (MI; that is, heart attack), and thus reduce the scarring that typically occurs and interferes with normal cardiac functioning.[3]

The researchers exposed 200 rats to experimental MI. Sham-operated rats served as control, while the rest received light therapy (the researchers applied a GaAlAs diode laser, with power density of 10 mW/cm$^2$, for 100 seconds) to the bone marrow of the exposed tibia at different time intervals post-MI. At three weeks out, the researchers found that rats given laser treatment 20 minutes post-MI had significantly better outcomes compared to the untreated controls. The treated rats' infarct size was diminished 76%, ventricular dilatation was reduced 75%, and there was a 25-fold increase in cell density of MSCs in the infarcted area.

The study demonstrated a novel approach-that of applying PBM therapy to the bone marrow of infarcted rats to trigger production of the rats' own (autologous) MSCs that their systems consequently recruit to the ischemic heart. The use of autologous stem cells as therapeutic agents avoids the cumbersome practice of isolating millions of stem cells, growing them *in vitro*, and injecting them into subjects.

The study suggests clinical potential for noninvasive (or invasive, using optical fiber in the case of obese individuals) treatment of a patient's bone marrow up to 4 hours post-MI. They hope, too, that the approach can be applied to other organs damaged by ischemia or injury, or undergoing degenerative processes (i.e., neurodegenerative diseases).

Full Article

**FIGURE 1.** Arany and his colleagues researching light-facilitated dentin generation used poly-lactide-co-glycolide (PLG) scaffolding to assess three-dimensional differentiation of the subject's own stem cells. (*Used with permission from Science Translational Medicine*)

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