NASA RESEARCH FOR LED LIGHT THERAPY

Facial Rejuvenation in the Triangle of ROS (2009)

Abstract: Recently, we introduced into the conventional catalogue of biological aging a new determinant: ordered interfacial water layers. The discovery of their tunability with skin-tolerated levels of 670 nm light inspired a model, which suggested that the light, by interaction with ordered interfacial water layers in the extracellular matrix, would reverse elastin degeneration. We validated the model in a 10 month self-experiment and arrived at an effective facial rejuvenation program. Importantly, during the experimental phase we avoided extreme oxidative stressors, in particular exposure to extensive ultraviolet and infrared radiation as well as air pollution. Here we report on the adaptation of our model to the extreme oxidative stress levels prevalent in numerous polluted megacities. The results of the extension comprise a new understanding of the protective function of the skin acid mantle, new predictive insight into effects of reactive oxygen species (ROS) on interfacial water layers, and their implication in processes of biological aging, including depletion of follicular stem cell reservoirs and telomere shortening, and led to the design of an accelerated skin rejuvenation method.

Effects of Low-Level Light Therapy on Hepatic Antioxidant Defense in Acute and Chronic Diabetic Rats (2009)

Abstract: Diabetes causes oxidative stress in the liver and other tissues prone to complications. Photo-biomodulation by near infrared light (670 nm) has been shown to accelerate diabetic wound healing, improve recovery from oxidative injury in the kidney, and attenuate degeneration in retina and optic nerve. The present study tested the hypothesis that 670 nm photo-biomodulation, a low-level light therapy, would attenuate oxidative stress and enhance the antioxidant protection system in the liver of a model of type I diabetes. MaleWistar rats were made diabetic with streptozotocin (50 mg/kg, ip) then exposed to 670 nm light (9 J/cm2) once per day for 18 days (acute) or 14 weeks (chronic). Livers were harvested, flash frozen, and then assayed for markers of oxidative stress. Light treatment was ineffective as an antioxidant therapy in chronic diabetes, but light treatment for 18 days in acutely diabetic rats resulted in the normalization of hepatic glutathione reductase and superoxide dismutase activities and a significant increase in glutathione peroxidase and glutathione-S transferase activities. The results of this study suggest that 670 nm photobiomodulationmay reduce, at least in part, acute hepatic oxidative stress by enhancing the antioxidant defense system in the diabetic ratmodel.

Near infrared light protects cardiomyocytes from hypoxia and reoxygenation injury by a nitric oxide dependent mechanism (2009)

Abstract: Photo-biomodulation with near infrared light (NIR) provides cellular protection in various disease models. Previously, infrared light emitted by a low-energy laser has been shown to significantly improve recovery from ischemic injury of the canine heart. The goal of this investigation was to test the hypothesis that NIR (670 nm) from light emitting diodes produces cellular protection against hypoxia and reoxygenation-induced cardiomyocyte injury. Additionally, nitric oxide (NO) was investigated as a potential

cellular mediator of NIR. Our results demonstrate that exposure to NIR at the time of reoxygenation protects neonatal rat cardiomyocytes and HL-1 cells from injury, as assessed by lactate dehydrogenase release and MTT assay. Similarly, indices of apoptosis, including caspase 3 activity, annexin binding and the release of cytochrome c from mitochondria into the cytosol, were decreased after NIR treatment. NIR increased NO in cardiomyocytes, and the protective effect of NIR was completely reversed by the NO scavengers carboxy- PTIO and oxyhemoglobin, but only partially blocked by the NO synthase (NOS) inhibitor L-NMMA. Mitochondrial metabolism, measured by ATP synthase activity, was increased by NIR, and NO-induced inhibition of oxygen consumption with substrates for complex I or complex IV was reversed by exposure to NIR. Taken together these data provide evidence for protection against hypoxia and reoxygenation injury in cardiomyocytes by NIR in a manner that is dependent upon NO derived from NOS and non-NOS sources.

Pretreatment with near-infrared light via light-emitting diode provides added benefit against rotenone- and MPP+-induced neurotoxicity (2008)

Abstract: Parkinson's disease (PD) is a movement disorder caused by the loss of dopaminergic neurons in the substantia nigra pars compacta, leading to nigrostriatal degeneration. The inhibition of mitochondrial respiratory chain complex I and oxidative stress-induced damage have been implicated in the pathogenesis of PD. The present study used these specific mitochondrial complex I inhibitors (rotenone and 1-methyl-4-phenylpyridinium or MPP+) on striatal and cortical neurons in culture. The goal was to test our hypothesis that pretreatment with near-infrared light (NIR) via light-emitting diode (LED) had a greater beneficial effect on primary neurons grown in media with rotenone or MPP+ than those with or without LED treatment during exposure to poisons. Striatal and visual cortical neurons from newborn rats were cultured in a media with or without 200 nM of rotenone or 250 μMof MPP+ for 48 h. They were treated with NIR-LED twice a day before, during, and both before and during the exposure to the poison. Results indicate that pretreatment with NIR-LED significantly suppressed rotenone- or MPP+-induced apoptosis in both striatal and cortical neurons ($P<0.001$), and that pretreatment plus LED treatment during neurotoxin exposure was significantly better than LED treatment alone during exposure to neurotoxins. In addition, MPP+ induced a decrease in neuronal ATP levels (to 48% of control level) that was reversed significantly to 70% of control by NIR-LED pretreatment. These data suggest that LED pretreatment is an effective adjunct preventative therapy in rescuing neurons from neurotoxins linked to PD.

Modulation of rat pituitary growth hormone by 670 nm light (2008)

Abstract: In rat pituitary somatotrophs, cytochrome oxidase is co-packaged with growth hormone (GH) in some 20 storage granules. Because this enzyme is thought to be the molecular photoacceptor of red-near infrared 21 light, and because exposure of diverse tissue systems to 670 nm visible light affects their biological 22 responses (e.g., wound healing), we tested the idea that exposure of rat pituitary cells, rat hemi-pituitary 23 glands and rat pituitary homogenates to 670 nm light in vitro might alter GH storage and/or release. In 24 this report we offer evidence to show that light treatment (670 nm, 80 s, intensity 50 mW/cm2, energy 25 density 4 J/cm2) up-regulates GH release, in part

by breakdown of intracellular, oligomeric GH as deter- 26 mined by gel filtration chromatography.

NEAR-INFRARED LIGHT VIA LIGHT-EMITTING DIODE TREATMENT IS THERAPEUTIC AGAINST ROTENONE- AND 1-METHYL-4- PHENYLPYRIDINIUM ION-INDUCED NEUROTOXICITY (2008)

Abstract: Parkinson's disease is a common progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Mitochondrial dysfunction has been strongly implicated in the pathogenesis of Parkinson's disease. Thus, therapeutic approaches that improve mitochondrial function may prove to be beneficial. Previously, we have documented that near-infrared light via light-emitting diode (LED) treatment was therapeutic to neurons functionally inactivated by tetrodotoxin, potassium cyanide (KCN), or methanol intoxication, and LED pretreatment rescued neurons from KCNinduced apoptotic cell death. The current study tested our hypothesis that LED treatment can protect neurons from both rotenone- and MPP+-induced neurotoxicity. Primary cultures of postnatal rat striatal and cortical neurons served as models, and the optimal frequency of LED treatment per day was also determined. Results indicated that LED treatments twice a day significantly increased cellular adenosine triphosphate content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP+-exposed neurons as compared with untreated ones. These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson's disease by energizing the cells and increasing their viability.

Photobiomodulation for the Treatment of Retinal Injury and Retinal Degenerative Diseases (2008)

Abstract: Retinal injury and retinal degenerative diseases are a leading causes of visual impairment in the developed world. Mitochondrial dysfunction and oxidative stress play key roles in the pathogenesis of retinal injury and disease. The development and testing of strategies designed to improve mitochondrial function and attenuate oxidative stress are essential for combating retinal disease. One strategy involves the use of photobiomodulation. Photobiomodulation, low-energy photon irradiation by light in the far-red to nearinfrared (NIR) range using low energy lasers or light-emitting diode (LED) arrays, has been applied clinically in the treatment soft tissue injuries and acceleration of wound healing for more than 30 years. The therapeutic effects of photobiomodulation have been hypothesized to be mediated by intracellular signaling mechanisms triggered by the interaction of far-red to NIR photons with the mitochondrial photoacceptor molecule cytochrome oxidase which culminate in improved mitochondrial energy metabolism, increased synthesis of cytoprotective factors and cell survival.

PHOTOMODULATION OF CYTOCHROME OXIDASE (2006)

Objectives: Photobiomodulation by red to near infrared light is believed to activate mitochondrial respiratory chain components promoting cytoprotecton. Recent studies in our laboratory demonstrate that the action spectrum for stimulation of cytochrome oxidase activity and cellular ATP parallels the nearinfrared absorption spectrum of

cytochome oxidase and that 660–680 nm irradiation upregulates cytochrome oxidase activity in cultured neurons. Methanol intoxication injures the retina and optic nerve. Via formic acid, a mitochondrial toxin of cytochrome oxidase. KCN (potassium cyanide) also poisons cytochrome oxidase, and has been used to assess the efficacy of 660– 680 nm irradiation for mitochondrial neuroprotection.

Embryonic Growth and Hatching Implications of Developmental 670-nm Phototherapy and Dioxin Co-exposure (2006)

Objective: We assessed the effect of 670-nm light therapy on growth and hatching kinetics in chickens (Gallus gallus) exposed to dioxin. Background Data: Photobiomodulation has been shown to stimulate signaling pathways resulting in improved energy metabolism, antioxidant production, and cell survival. In ovo treatment with 670-nm light-emitting diode (LED) arrays improves hatching success and increases hatchling size in control chickens. Under conditions where developmental dioxin exposure is above the lethality threshold (100 ppt), phototherapy attenuates dioxin-induced early embryonic death. We hypothesized that 670-nm LED therapy would attenuate dioxin-induced developmental anomalies and increase hatching success.

Stressed Cells Survive Better with Light (2002)

Abstract: Biostimulatory effects achieved in various biosystems irradiated with light lead us to recommend photobiostimulation for the compensation of external stress stimuli in tissue engineering, as well as in cellular imaging. Bioengineered cell assemblies and tissues are exposed to extreme environmental stress states during their transfer from artificial milieus into the body and in the first phase of their implantation. Similarly, cellular imaging via optical methods could represent a major stress impact to the biosystems examined, in particular, in temporally extended investigations. In both cases, an elevated and gradually proceeding environmental stress would inhibit cellular functions and enhance cell death.

Nature Inspired Hay Fever Therapy

Abstract: The survival oriented adaptation of evolved biosystems to variations in their environment is a selective optimization process. Recognizing the optimised end product and its functionality is the classical arena of bionic engineering. In a primordial world, however, the molecular organization and functions of prebiotic systems were solely defined by formative processes in their physical and chemical environment, for instance, the interplay between interfacial water layers on surfaces and solar light. The formative potential of the interplay between light (laser light) and interfacial water layers on surfaces was recently exploited in the formation of supercubane carbon nanocrystals. In evolved biosystems the formative potential of interfacial water layers can still be activated by light. Here we report a case of hay fever, which was successfully treated in the course of a facial rejuvenation program starting in November 2007. Targeting primarily interfacial water layers on elastin fibres in the wrinkled areas, we presumably also activated mast cells in the nasal mucosa, reported to progressively decrease in the nasal mucosa of the rabbit, when frequently irradiated. Hay fever is induced by the release of mediators, especially histamine, a process associated with the degranulation of mast cells. Decrease in mast cells numbers implies a decrease in the release of

histamine. To the best of our knowledge this is the first report on the treatment of hay fever with visible light. This approach was inspired by bionic thinking, and could help ameliorating the condition of millions of people suffering from hay fever world wide.

From Microtornadoes to Facial Rejuvenation: Implication of Interfacial Water Layers

Abstract: Crystalline interfacial water layers have been observed at room temperature on both hydrophobic and hydrophilic surfaces - in air and subaquatically. Their implication in biology (and evolution) was postulated in a visionary paper in 1971 by Szent Gyo¨ rgyi. Today, they are believed to play a fundamental role in protein folding. A recent X-ray diffraction study reports on their presence on crystals in contact with their growth solution. Their subaquatic persistence on hydrophobic solids was reported in 2007. Their relevance in nanoscale phenomena is re?ected by the multidisciplinary focus in their study. In the course of a systematic exploration of interfacial water layers on solids we discovered microtornadoes, found a complementary explanation to the surface conductivity on hydrogenated diamond, and arrived at a practical method to repair elastin degeneration using light. The result was rejuvenated skin, reduced wrinkle levels, juvenile complexion, and lasting resilience.

Effects of Continuous-Wave (670-nm) Red Light on Wound Healing

Abstract: Recent work suggests that injuries can heal faster if treated by lasers emitting 670-nm red light. LED lights emitting 670-nm light are now available. This suggests that inexpensive and easyto- use 670-nm LED lights might help accelerate cutaneous wound healing. The objective was to evaluate the effect of 670-nm LED light on wound healing in SKH-1 hairless mice.

Biostimulatory Windows in Low-Intensity Laser Activation: Lasers, Scanners, and NASA's Light-Emitting Diode Array System

Abstract: The purpose of this study was to assess and to formulate physically an irreducible set of irradiation parameters that could be relevant in the achieving reproducible light-induced effects in biological systems, both in vitro and in vivo.

Clinical and Experimental Applications of NIR-LED Photobiomodulation

Abstract: This review presents current research on the use of far-red to near-infrared (NIR) light treatment in various in vitroand in vivomodels. Low-intensity light therapy, commonly referred to as "photobiomodulation," uses light in the far-red to near-infrared region of the spectrum (630–1000 nm) and modulates numerous cellular functions. Positive effects of NIR–light-emitting diode (LED) light treatment include acceleration of wound healing, improved recovery from ischemic injury of the heart, and attenuated degeneration of injured optic nerves by improving mitochondrial energy metabolism and production.

DARPA Soldier Self Care: Rapid Healing of Laser Eye Injuries with Light Emitting Diode Technology

Abstract: Photobiomodulation by light in the red to near infrared range (630-1000 nm) using low energy lasers or light- emitting diode (LED) arrays has been shown to

accelerate wound healing, improve recovery from ischemic injury and attenuate degeneration in the injured optic nerve. At the cellular level, photoirradiation at low fluences can generate significant biological effects including cellular proliferation and the release of growth factors from cells.

Dr. Harry Whelan talks about how LED might be used in hospitals around the country
NASA Video Release

Effect of NASA Light-Emitting Diode Irradiation on Molecular Changes for Wound Healing in Diabetic Mice
Abstract: The purpose of this study was to assess the changes in gene expression of near-infrared light ther- apy in a modcl of impaired wound healing. Background Data: Light-Emitting Diodes (LED), originally devel- nped fnr NASA plant grrrwth experiments in space, show promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. In this paper we present the effects of LED treat- ment on wounds in a genetically diabetic mouse model.

Effect of NASA Light-Emitting Diode Irradiation on Wound Healing
Abstract: The purpose of this study was to assess the effects of hyperbaric oxygen (HBO) and near-infrared light therapy on wound healing. Background Data: Light-emitting diodes (LED), originally developed for NASA plant growth experiments in space show promise for delivering light deep into tissues of the body to pro- mote wound healing and human tissue growth. In this paper, we review and present our new data of LED treatment on cells grown in culture, on ischemic and diabetic wounds in rat models, and on acute and chronic wounds in humans.

Effects of 670-nm Phototherapy on Development
Abstract: The objective of the present study was to assess the survival and hatching success of chickens (Gallus gallus) exposed in ovoto far-red (670-nm) LED therapy. Background Data:Photobiomodulation by light in the red to near-infrared range (630–1000 nm) using low-energy lasers orlight-emitting diode (LED) arrays has been shown to accelerate wound healing and improve recovery from ischemic injury.

Evaluation of photodynamic therapy near functional brain tissue in patients with recurrent brain tumors
Abstract: Photodynamic therapy (PDT) involves the selective retention of a photosensitizer that upon activation with light mediates tumor cell destruction via the production of singlet oxygen. This study evaluates the toxicity of PDT and a new light-delivery device based on light-emitting diode (LED) technology in selected patients with brain tumors.

Innate immunity for biodefense: A strategy whose time has come
Abstract: Defense against biothreat agents requires a broad-spectrum approach. Modulation of the innate immune system might ful?ll this requirement. Hackett’s previous review of innate immune activation as a broad-spectrum biodefense strategy

identi?ed several unresolved questions. The current article is a systematic approach to answering those questions with the focused participation of research groups developing this technology.

Light-emitting diode treatment reverses the effect of TTX on cytochrome oxidase in neurons

Abstract: Light close to and in the near-infrared range has documented benefits for promoting wound healing in human and animals. However, mechanisms of its action on cells are poorly undersottd. We hypothesied that light treatment with a light emitting diode array at 670nm (LED) is theraputic in stimulating cellular events involving increases in ctochrome oxidase activity.

Light-emitting Diodes as a Light Source for Intraoperative Photodynamic Therapy

Abstract: The development of more cost-effective light sources for photodynamic therapy of brain tumors would be of benefit for both research and clinical applications. In this study, the u se of light-emitting diode arrays for photodynamic therapy of brain tumors with Photofrin porfimer sodium was investigated.

Medical Applications of Space Light-Emitting Diode Technology - Space Station and Beyond

Abstract: Space light-emitting diode (LED) technology has provided medicine with a new tool capable of delivering light deep of the body, at wavelengths which are biologically optimal for cancer treatment and wound healing. This LED technology has already flown on Space Shuttle missions. and shows promise for wound healing applications of benefit to Space Station astronauts.

Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy

Abstract: Photobiomodulation by light in the red to near infrared range (630–1000 nm) using low energy lasers or light-emitting diode (LED) arrays has been shown to accelerate wound healing, improve recovery from ischemic injury in the heart and attenuate degeneration in the injured optic nerve. Recent evidence indicates that the therapeutic effects of red to near infrared light result, in part, from intracellular signaling mechanisms triggered by the interaction of NIR light with the mitochondrial photoacceptor molecule cytochrome c oxidase.

NASA Light Emitting Diode Medical Applications From Deep Space to Deep Sea

Abstract: LED-technology developed for NASA plant growth experiments in space shows promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. We present the results of LED-treatment of cells grown in culture and the effects of LEDs on patients' chronic and acute wounds. LED-technology is also biologically optimal for photodynamic therapy of cancer and we discuss our successes using LEDs in conjunction with light-activated chemotherapeutic drugs.

NASA Light-Emitting Diode Medical Program - Progress in Space Flight and Terrestrial Applications

Abstract: Studies on cells exposed to microgravity and hypergravity indicate that human cells need gravity to stimulate cell growth. As the gravitational force increases or decreases, the cell function responds in a linear fashion. This poses significant health risks for astronauts in long termspace flight. LED-technology developed for NASA plant growth experiments in space shows promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. This LED-technology is also biologically optomal for photodynamic therapy of cancer.

NASA Light-Emitting Diodes for the Prevention of Oral Mucositis in Pediatric Bone Marrow Transplant Patients

Abstract: The purpose of this study was to determine the effects of prophylactic near-infrared light therapy from light-emitting diodes (LEDs) in pediatric bone marrow transplant (BMT) recipients. Background Data: Oral mucositis (OM) is a frequent side effect of chemotherapy that leads to increased morbidity. Near- infrared light has been shown to produce biostimulatory effects in tissues, and previous results using near-infrared lasers have shown improvement in OM indices. However, LEDs may hold greater potential for clinical applications.

Photobiomodulation Directly Benefits Primary Neurons Functionally Inactivated by Toxins

Abstract: Far red and near infrared (NIR) light promotes wound healing, but the mechanism is poorly understood. Our previous studies using 670 nm light-emitting diode (LED) arrays suggest that cytochrome c oxidase, a pho- toacceptor in the NIR range, plays an important role in therapeutic photobiomodulation. If this is true, then an irreversible inhibitor of cytochrome c oxidase, potas- sium cyanide (KCN), should compete with LED and re- duce its beneficial effects. This hypothesis was tested on primary cultured neurons.

Photobiomodulation Partially Rescues Visual Cortical Neurons from Cyanide-induced Apoptosis

Abstract: Near-infrared light via light-emitting diode treatment has documented therapeutic effects on neurons functionally inactivated by tetrodotoxin or methanol intoxication. Light-emitting diode pretreatment also reduced potassium cyanide-induced cell death, but the mode of death via the apoptotic or necrotic pathway was unclear. The current study tested our hypothesis that light-emitting diode rescues neurons from apoptotic cell death.Possible mechanisms involve an acceleration of electron transfer in the respiratory chain and activation of photoacceptors, such as cytochrome oxidase, thus pointing to a particular role for mitochondria.

Preliminary Investigation into Light-Modulated Replication of Nanobacteria and Heart Disease

Abstract: The purpose of this preliminary study is to evaluate the effect of various wavelengths of light on nanobacteria (NB). Background Data: NB and mitochondria use light for biological processes. NB have been described as multifunctional primordial nanovesicles with the potential to utilize solar energy for replication. NB produce slime,

a pro cess common to living bacteria. Slime release is an evolutionary important stress-dependent phenomenon increasing the survival chance of individual bacteria in a colony. In the cardiovascu- lar system, stress-induced bacterial colony formation may lead to a deposition of plaque.

Therapeutic photobiomodulation for methanol-induced retinal toxicity

Abstract: Methanol intoxication produces toxic injury to the retina and optic nerve, resulting in blindness. The toxic metabolite in methanol intoxication is formic acid, a mitochondrial toxin known to inhibit the essential mitochondrial enzyme, cytochrome oxidase. Photobiomodulation by red to near-IR radiation has been demonstrated to enhance mitochondrial activity and promote cell survival in vitro by stimulation of cytochrome oxidase activity.