MASCC/ISOO 2019
ANNUAL MEETING • SAN FRANCISCO

21-23 JUNE 2019
Supportive Care Makes Excellent Cancer Care Possible #MASCC19

San Francisco,
June 21st 2019

Photobiomodulation Therapy
- A new tool in Oral Mucositis Management

Praveen R Arany BDS, MDS, MMSc, PhD
Assistant Professor,
Oral Biology & Biomedical Engineering,
School of Dental Medicine, Engineering and Applied Sciences,
University at Buffalo,
Buffalo, NY 14214

President,
World Association for photobiomoduLation Therapy (W.A.L.T.)

WALT
WORLD ASSOCIATION FOR PHOTOBIOMODULATION THERAPY

Disclosures

Company / Entity	Honoraria/ Expenses	Consulting/ Advisory Board	Funded Research	Royalties / Patent	Stock Options	Ownership/ Equity Position	Employee	Other (please specify)
Philips Research, NST Consulting, NIDCR.NIH			X					
Thor Lasers, Lumithera, Weber Medical	X							
Optimed Technology				X	X	X		
Lumitex, Roger Sciences, NeoMedLight, BioRegenTech		X						
Harvard University				X				
University at Buffalo				X			X	

President,
World **A**ssociation for **L**aser **T**herapy

Immediate Past President,
North **A**merican **A**ssociation for Photobiomodu**L**ation **T**herapy

Co-Chair, Mechanisms of Photobiomodulation
International Society for Optics and Photonics

Technical Group on Photobiomodulation
Optical **S**ociety of **A**merica (**OSA**)

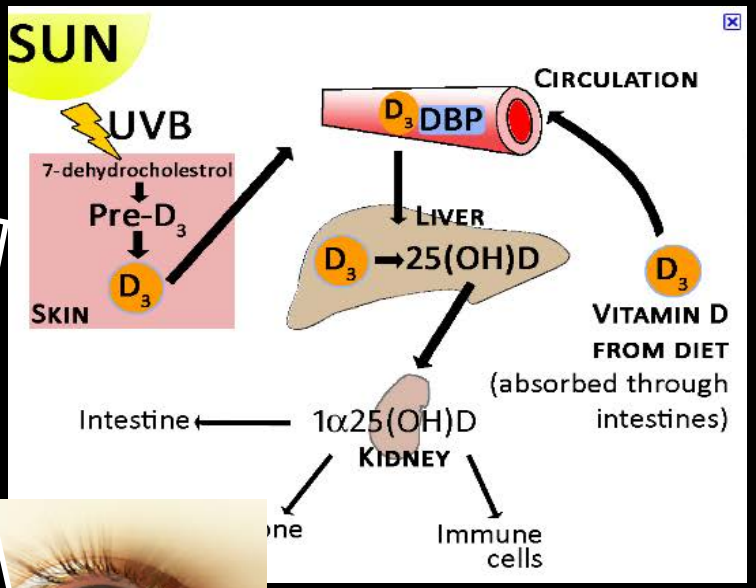
Program Chair 2019 (Symposium of Advanced Wound Care)
Wound **H**ealing **S**ociety (**WHS**)

Light Devices in Dentistry

I. Illumination	Operative lights, Fiberoptics in loupes / devices
II. Imaging	Digital imaging, Fluorescence-based diagnostics (Caries, Pre-Cancer), Optical Coherence Tomography, Multi-photon imaging, Spectroscopy
III. Manufacturing	Curing, Welding, Sintering, Milling
IV. Surgical	Hard tissue: Excavation, Bleaching, Prevent demineralization, Dentin desensitization, Bracket bonding / debonding, Photon-Induced Photoacoustic Streaming (PIPS) Soft tissue: Excisions, Photocoagulation, Field ablation, Recontouring (Esthetics, Snoring, Halitosis), Depigmentation, Curettage
V. Non-Surgical	Photodynamic therapy: Anti-microbial, Anti-tumor Photobiomodulation therapy: *Analgesia, Anti-inflammatory, Immune-modulation, Healing-Regeneration*

Arany PR **J Dent Res** 2016, 95, 9, 977

Can *light* be a *Drug*?



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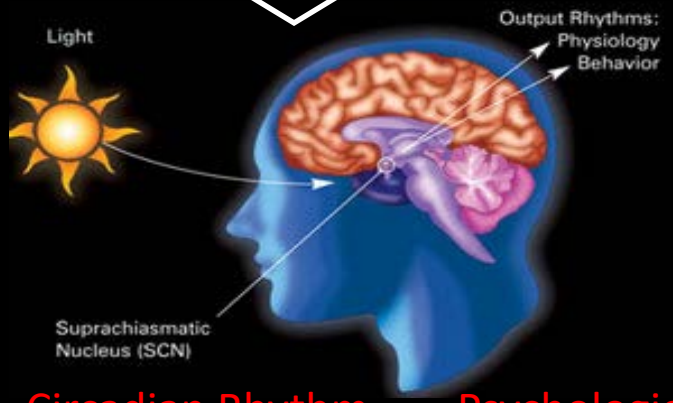
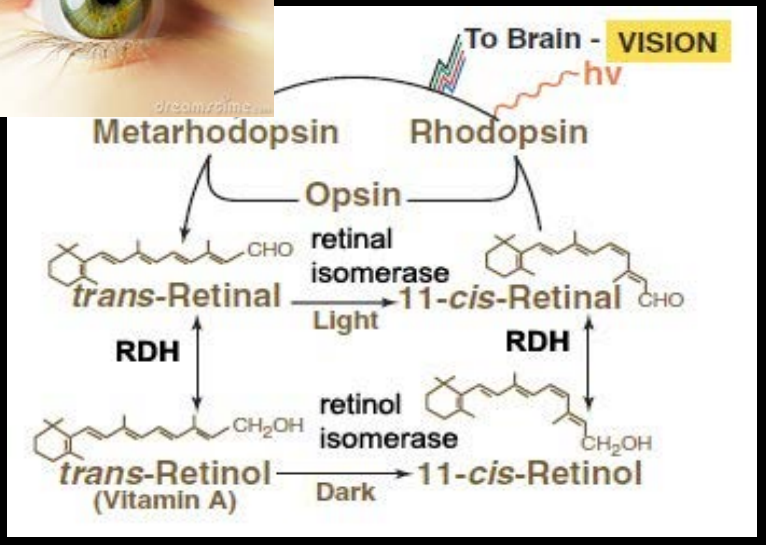


Circadian Rhythm Psychological state



A 'd*rug*' is a substance that is absorbed and alters bodily function.

Therapeutic use of *Light*

www.gemstoneuniverse.com

Niels Ryberg Finsen

Nobel Prize 1903

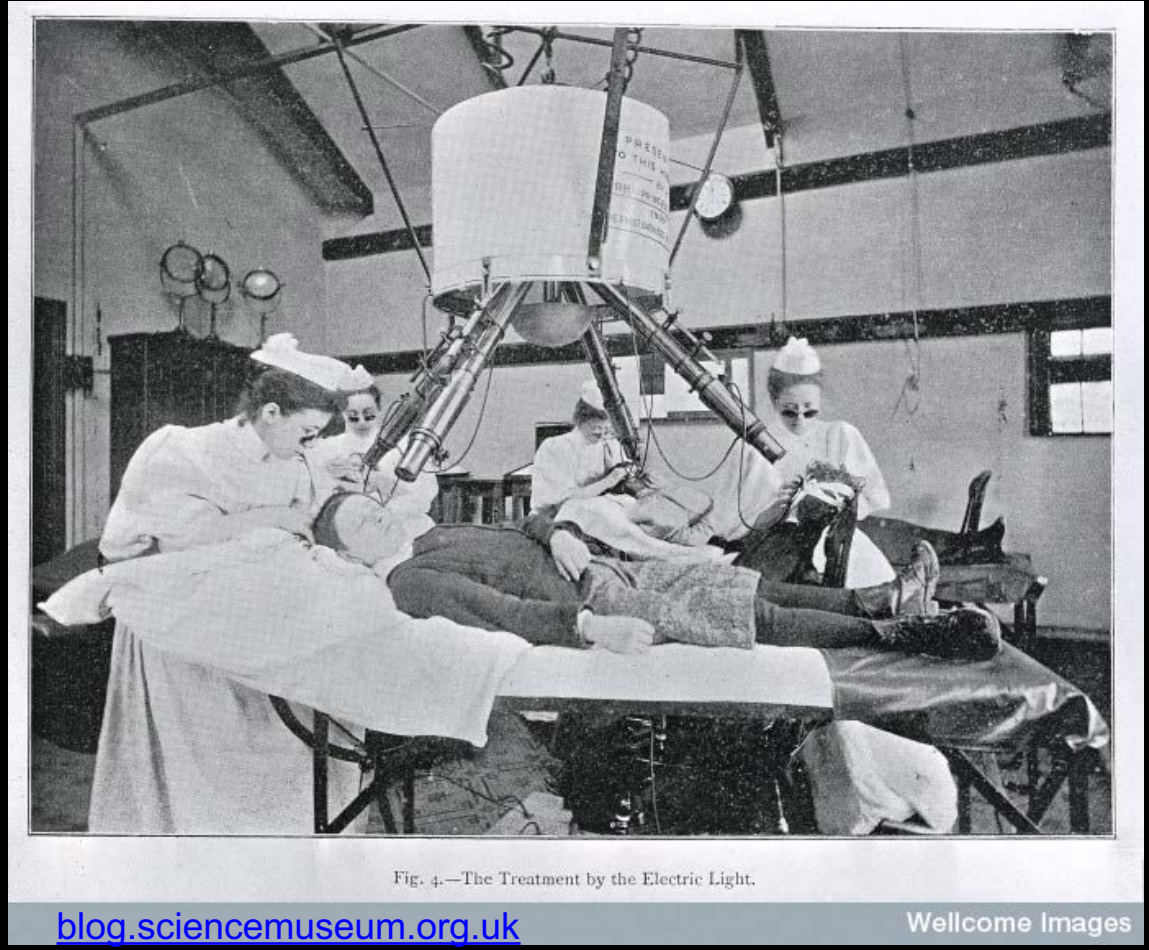
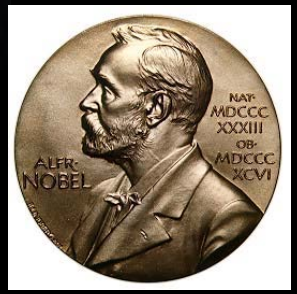


Fig. 4.—The Treatment by the Electric Light.

blog.sciencemuseum.org.uk

Wellcome Images



L.A.S.E.R.

- **Concept of L**ight **A**mplification by **S**timulated **E**mission of **R**adiation

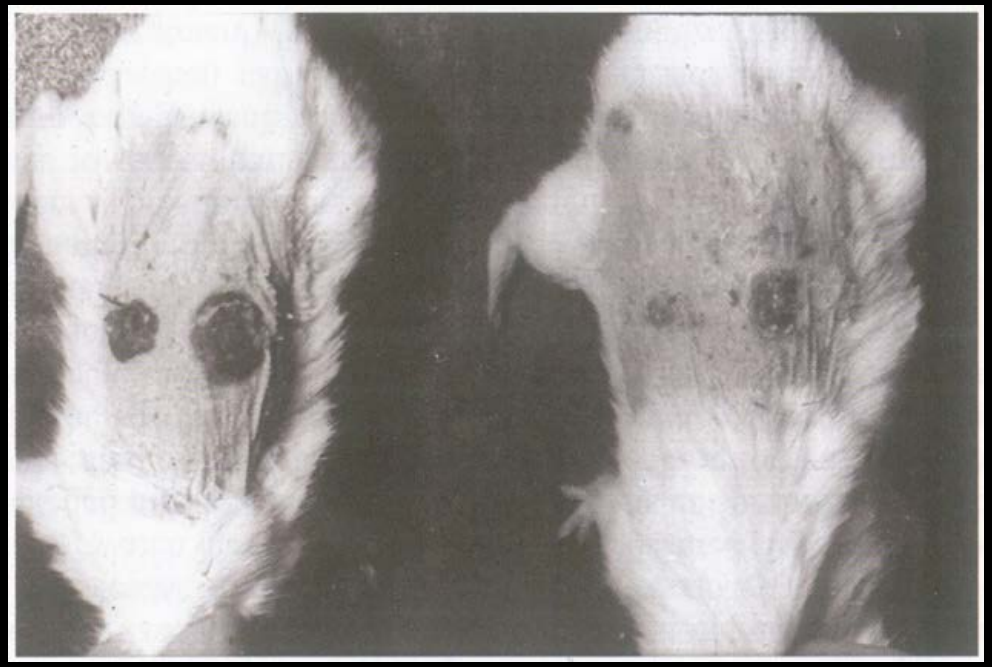
  Albert Einstein 1917

- **Construction of a *working* LASER**

  Charles Towne 1954 Theodore Maiman 1960

- Amongst the very first biological effects observed with low power lasers were *stimulation of hair growth* and *promotion of wound healing*.

  Endre Mester 1967, 1973



Photobiomodulation (PBM)Therapy

National Library of Medicine, MeSH 2015

"Use of non-ionizing source of photonic energy that generates non-thermal, therapeutic effects."

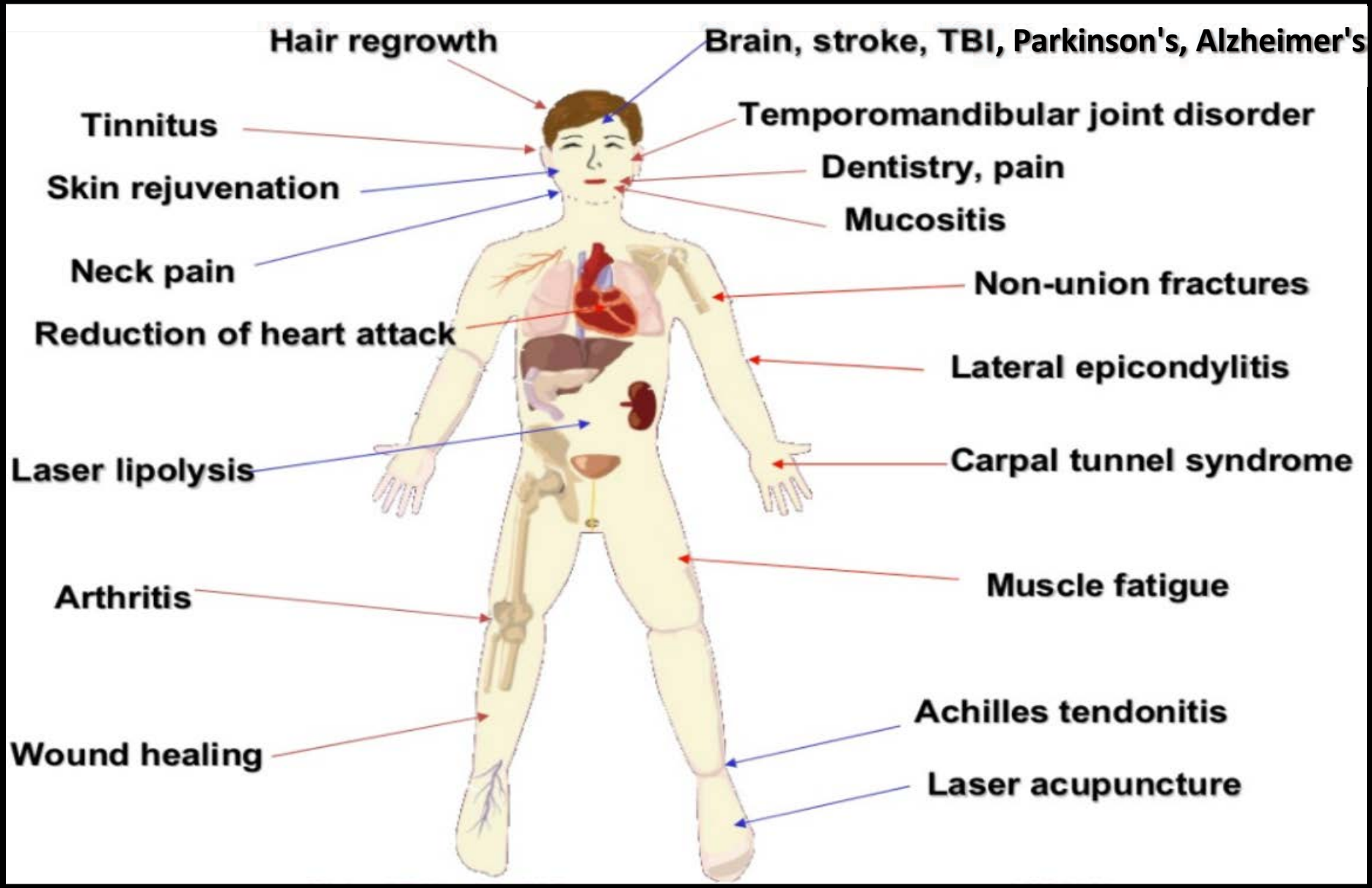
☞ ***Inhibit***: negative processes
Pain, Inflammation, aberrant immune

☞ ***Promote***: positive processes
Wound healing, Tissue regeneration, immune system

Khan I and Arany Adv Wound Care 2015

Anders JJ et al Photomed Las Surg 2015

Applications of Photobiomodulation Therapy



Slide modified from Michael Hamblin

PBM Mechanisms

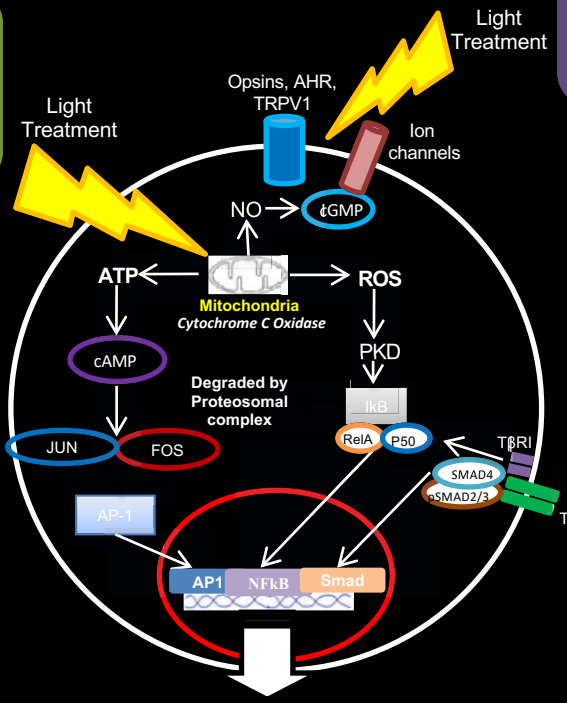
Analgesic

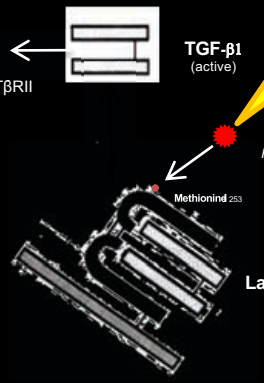
#1. Intracellular
Mitochondria
Cytochrome C Oxidase
☞ ATP, ROS incld NO

#2. Photoreceptors
Cell Membrane
Opsins, AHR, TRPV1
☞ GPCR signaling, ion flux incld Ca^{2+}

#3. Extracellular
ECM / Circulating
TGF-β1
☞ Smad, MAPK, NFkB, ATF-4

Performance





Gene Expression
Growth Factor production
Extracellular matrix deposition
Secretion of Enzymes-Hormones

Cell proliferation-Migration-Differentiation

Inhibit
Pain, Inflammation, Aberant Immune Response

Promote
Wound healing, Tissue Regeneration, immune response

Regenerative

Modified from Khan I and Arany **Adv Wound Care** 2015, 1, 4, 174

PBM mechanism 1: Intracellular

ELSEVIER

J. Photochem. Photobiol. B: Biol. 49 (1999) 1–17

Journal of Photochemistry and Photobiology B:Biology

Invited Review

Primary and secondary mechanisms of action of visible to near-IR radiation on cells

Tiina Karu *

Laser Technology Research Center of Russian Academy of Sciences, 142092 Troitsk, Moscow Region, Russia

Received 17 March 1998; accepted 9 November 1998

Lasers in Surgery and Medicine 36:307–314 (2005)

Cellular Effects of Low Power Laser Therapy Can be Mediated by Nitric Oxide

Tiina I. Karu, PhD,[1]* Ludmila V. Pyatibrat, MS,[1] and Natalia I. Afanasyeva, PhD[2]

[1]*Institute of Laser and Information Technologies of the Russian Academy of Sciences, 142190 Troitsk, Moscow, Russia*

[2]*Spectrooptical Sensing, Inc., Portland, Oregon 97205*

NEUROCHEMISTRY NEUROREPORT

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

Margaret T. T. Wong-Riley,[CA] Xuetao Bai, Ellen Buchmann[1] and Harry T. Whelan[1]

Departments of Cell Biology, Neurobiology and Anatomy, and [1]Neurology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

[CA]Corresponding Author

Received 10 July 2001; accepted 24 July 2001

AIMS Biophys. 2017 ; 4(3): 337–361. doi:10.3934/biophy.2017.3.337.

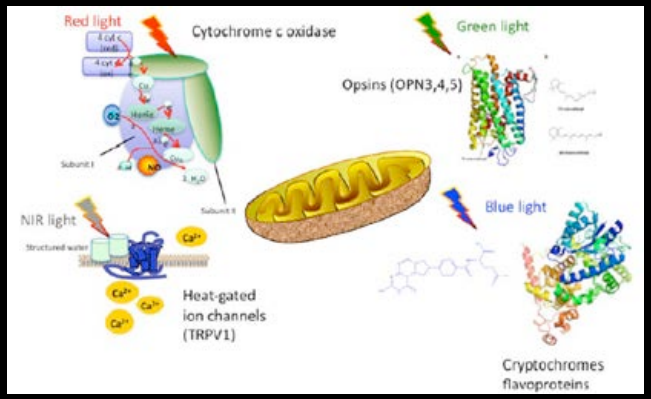
Mechanisms and applications of the anti-inflammatory effects of photobiomodulation

Michael R Hamblin[1,2,3,*]

[1]Wellman Center for Photomedicine, Massachusetts General Hospital, BAR414, 40 Blossom Street, Boston, MA 02114, USA

[2]Department of Dermatology, Harvard Medical School, Boston, MA 02115, USA

[3]Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA 02139, USA



PBM mechanism 2: Cell Membrane

SCIENTIFIC REPORTS

OPEN

Red (660 nm) or near-infrared (810 nm) photobiomodulation stimulates, while blue (415 nm), green (540 nm) light inhibits proliferation in human adipose-derived stem cells

Received: 12 January 2017
Accepted: 29 June 2017
Published online: 10 August 2017

Yuguang Wang[1,2,3,4], Ying-Ying Huang[3,4], Yong Wang[1,2], Peijun Lyu[1,2] & Michael R. Hamblin[3,4,5]

SCIENTIFIC REPORTS

OPEN

Gene expression profiling reveals aryl hydrocarbon receptor as a possible target for photobiomodulation when using blue light

Received: 10 June 2016
Accepted: 01 September 2016
Published: 27 September 2016

Anja Becker[1], Anna Klapczynski[1], Natalia Kuch[1], Fabiola Arpino[1], Katja Simon-Keller[1], Carolina De La Torre[1], Carsten Sticht[1], Frank A. van Abeelen[2], Gerrit Oversluizen[2] & Norbert Gretz[1]

PNAS

Melanopsin mediates light-dependent relaxation in blood vessels

Gautam Sikka[a], G. Patrick Hussmann[b], Deepesh Pandey[a], Suyi Cao[a], Daijiro Hori[c], Jong Taek Park[a], Jochen Steppan[a], Jae Hyung Kim[a], Viachaslau Barodka[a], Allen C. Myers[d], Lakshmi Santhanam[a,e], Daniel Nyhan[a], Marc K. Halushka[f], Raymond C. Koehler[a], Solomon H. Snyder[f,1], Larissa A. Shimoda[g], and Dan E. Berkowitz[a,e,1]

[a]Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, MD 21287; [b]Department of Neuroscience, Johns Hopkins University, Baltimore, MD 21205; [c]Department of Surgery, Johns Hopkins University, Baltimore, MD 21287; [d]Department of Allergy and Immunology, Johns Hopkins University, Baltimore, MD 21224; [e]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21205; [f]Department of Pathology, Johns Hopkins University, Baltimore, MD 21287; and [g]Division of Pulmonary Medicine, Johns Hopkins University, Baltimore, MD 21224

Contributed by Solomon H. Snyder, October 24, 2014 (sent for review June 22, 2014)

Lasers in Surgery and Medicine 49:705–718 (2017)

A New Path in Defining Light Parameters for Hair Growth: Discovery and Modulation of Photoreceptors in Human Hair Follicle

Serena Buscone, BSc,[1,2] Andrei N. Mardaryev, MD, PhD,[1] Bianca Raafs, BSc,[2] Jan W. Bikker,[3] Carsten Sticht, PhD,[4] Norbert Gretz, MD, PhD,[4] Nilofer Farjo, MD,[5] Natallia E. Uzunbajakava, PhD,[2**] and Natalia V. Botchkareva, MD, PhD[1*]

[1]*Faculty of Life Sciences, University of Bradford, Centre for Skin Sciences, Bradford, West Yorkshire BD7 1DP, United Kingdom*
[2]*Philips Research, High Tech Campus 34, Eindhoven 5656 AE, The Netherlands*
[3]*Consultants in Quantitative Methods BV, Eindhoven, The Netherlands*
[4]*Faculty Mannheim, University of Heidelberg, Center of Medical Research, Heidelberg, Germany*
[5]*Farjo Hair Institute, Manchester, United Kingdom*

Am J Physiol Lung Cell Mol Physiol 314: L93–L106, 2018.
First published September 7, 2017; doi:10.1152/ajplung.00091.2017.

RESEARCH ARTICLE

Opsin 3 and 4 mediate light-induced pulmonary vasorelaxation that is potentiated by G protein-coupled receptor kinase 2 inhibition

Sebastian Barreto Ortiz,[1]* Daijiro Hori,[1,2]* Yohei Nomura,[1,2] Xin Yun,[3] Haiyang Jiang,[3] Hwanmee Yong,[4] James Chen,[5] Sam Paek,[4] Deepesh Pandey,[1] Gautam Sikka,[1] Anil Bhatta,[1] Andrew Gillard,[1] Jochen Steppan,[1] Jae Hyung Kim,[1] Hideo Adachi,[6] Viachaslau M. Barodka,[1] Lewis Romer,[1,5,7] Steven S. An,[4] Larissa A. Shimoda,[3] Lakshmi Santhanam,[1,5] and Dan E. Berkowitz[1,5]

[1]*Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland;* [2]*Division of Cardiac Surgery, Johns Hopkins University, Baltimore, Maryland;* [3]*Division of Pulmonary and Critical Care Medicine, Johns Hopkins Asthma and Allergy Center, Johns Hopkins University, Baltimore, Maryland;* [4]*Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland;* [5]*Department of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland;* [6]*Department of Cardiovascular Surgery, Saitama Medical Center, Jichi Medical University, Shimotsuke, Japan; and* [7]*Departments of Cell Biology, Pediatrics, and the Center for Cell Dynamics, Johns Hopkins University, Baltimore, Maryland*

Submitted 28 February 2017; accepted in final form 1 September 2017

PBM mechanism 3: Extracellular

RESEARCH ARTICLE

REGENERATIVE MEDICINE

Photoactivation of Endogenous Latent Transforming Growth Factor–β1 Directs Dental Stem Cell Differentiation for Regeneration

Praveen R. Arany,[1,2,3,4,5] Andrew Cho,[5] Tristan D. Hunt,[1] Gursimran Sidhu,[1] Kyungsup Shin,[1,3] Eason Hahm,[1] George X. Huang,[1] James Weaver,[2] Aaron Chih-Hao Chen,[6] Bonnie L. Padwa,[7] Michael R. Hamblin,[6,8,9] Mary Helen Barcellos-Hoff,[10] Ashok B. Kulkarni,[5] David J. Mooney[1,2]*

Rapid advancements in the field of stem cell biology have led to many current efforts to exploit stem cells as therapeutic agents in regenerative medicine. However, current ex vivo cell manipulations common to most regenerative approaches create a variety of technical and regulatory hurdles to their clinical translation, and even simpler approaches that use exogenous factors to differentiate tissue-resident stem cells carry significant off-target side effects. We show that non-ionizing, low-power laser (LPL) treatment can instead be used as a minimally invasive tool to activate an endogenous latent growth factor complex, transforming growth factor–β1 (TGF-β1), that subsequently differentiates host stem cells to promote tissue regeneration. LPL treatment induced reactive oxygen species (ROS) in a dose-dependent manner, which, in turn, activated latent TGF-β1 (LTGF-β1) via a specific methionine residue (at position 253 on LAP). Laser-activated TGF-β1 was capable of differentiating human dental stem cells in vitro. Further, an in vivo pulp capping model in rat teeth demonstrated significant increase in dentin regeneration after LPL treatment. These in vivo effects were abrogated in TGF-β receptor II (*TGF-βRII*) conditional knockout (*DSPP*^{Cre}*TGF-βRII*$^{fl/fl}$) mice or when wild-type mice were given a TGF-βRI inhibitor. These findings indicate a pivotal role for TGF-β in mediating LPL-induced dental tissue regeneration. More broadly, this work outlines a mechanistic basis for harnessing resident stem cells with a light-activated endogenous cue for clinical regenerative applications.

Michael Hamblin, MGH
Mary-Helen Barcellos Hoff, NYU

Arany PR *et al* **Sci Transl Med** 2014, 6, 238, 1
Jobling MF *et al* **Rad Res** 2008, 166, 839

Prior 2013 Recommendation

New 2019 Recommendation

Support Care Cancer (2013) 21:333–341
DOI 10.1007/s00520-012-1605-6

SPECIAL ARTICLE

Systematic review of laser and other light therapy for the management of oral mucositis in cancer patients

Cesar Migliorati · Ian Hewson · Rajesh V. Lalla · Heliton Spindola Antunes · Cherry L. Estilo · Brian Hodgson · Nilza Nelly Fontana Lopes · Mark M. Schubert · Joanne Bowen · Sharon Elad · For the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO)

Received: 21 June 2012 / Accepted: 10 September 2012 / Published online: 22 September 2012

Abstract
Background The aim of this study was to review the available literature and define clinical practice guidelines for the use of laser and other light therapies for the prevention and treatment of oral mucositis.

Methods A systematic review was conducted by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology. The body of evidence for each intervention, in each cancer treatment setting, was assigned an evidence level. Based on

C. Migliorati (✉)
Department of Diagnostic Sciences and Oral Medicine, College of Dentistry, University of Tennessee Health Sciences Center, 875 Union Avenue, suite N231, Memphis, TN 38163, USA
e-mail: migliorati@uthsc.edu

I. Hewson
Dental Unit Royal Melbourne Hospital, Grattan Street, Parkville, Melbourne 3050, Victoria, Australia
e-mail: ihewson@bigpond.net.au

R. V. Lalla
Section of Oral Medicine, University of Connecticut Health Center, 263, Farmington Avenue, Farmington, CT 06030-1605, USA
e-mail: lalla@uchc.edu

H. S. Antunes
Department of Oral Diagnosis, School of Dentistry, Universidade do Grande Rio (UNIGRANRIO), Rio de Janeiro, Brazil
e-mail: hspindola@inca.gov.br

H. S. Antunes
Instituto Nacional de Câncer (INCA), Rua André Cavalcante, nº 37, 2º andar, Rio de Janeiro CEP:20231-050, Brazil

C. L. Estilo
Dental Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA
e-mail: estilo@MSKCC.ORG

B. Hodgson
Pediatric Dentistry, Department of Developmental Sciences, Marquette University School of Dentistry, 1801 W. Wisconsin Ave., Milwaukee, WI 53233, USA
e-mail: brian.hodgson@marquette.edu

N. N. F. Lopes
Rua Padre Priuli 11, São Paulo, São Paulo, Brazil
e-mail: nnflopes@terra.com.br

M. M. Schubert
Oral Medicine, UW School of Dentistry, Seattle Cancer Care Alliance, 825 Eastlake Avenue E, Seattle, WA 98109, USA
e-mail: mschuber@seattlecca.org

J. Bowen
School of Medical Sciences, The University of Adelaide, Frome Road, Adelaide, South Australia 5005, Australia
e-mail: joanne.bowen@adelaide.edu.au

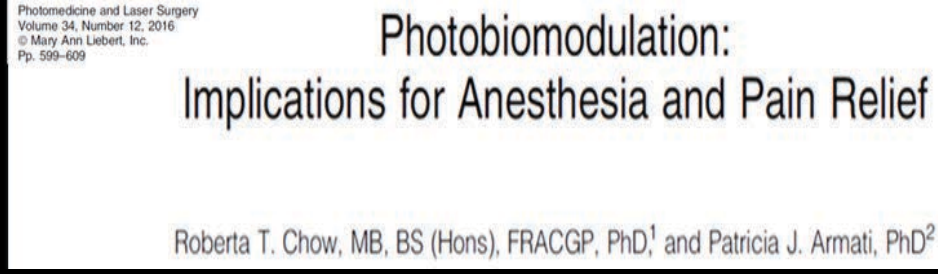
S. Elad
Division of Oral Medicine, Eastman Institute for Oral Health, University of Rochester Medical Center, 625 Elmwood Ave., Rochester, NY 14620, USA
e-mail: SElad@URMC.Rochester.edu

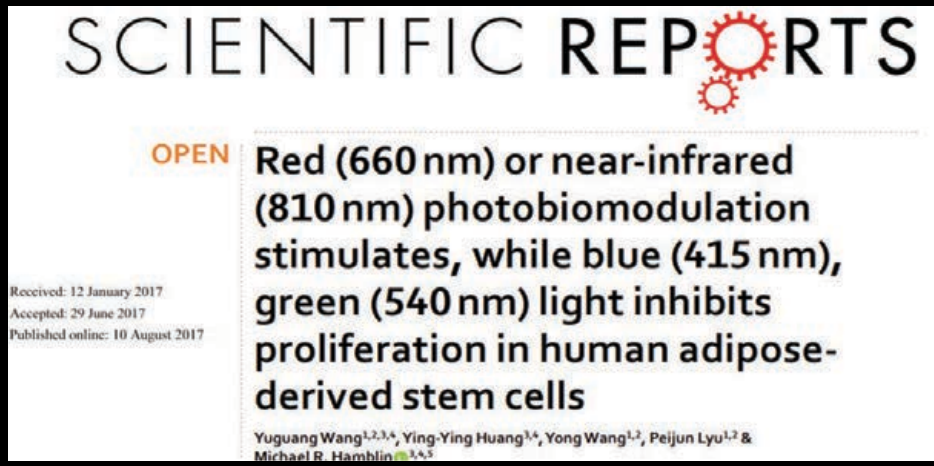
Dr. Elad's talk next.....

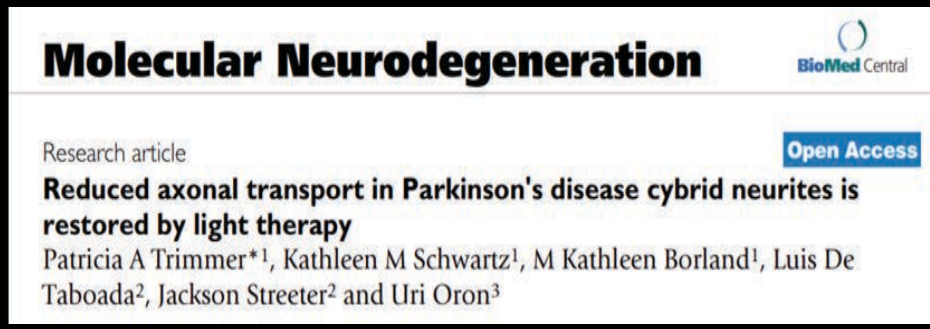
Rationale: PBM for Pain Relief in OM

- Depolarization nerve conduction
- Direct modulation of TRPV1
- Reduced axonal transport of Mitochondria in neurons

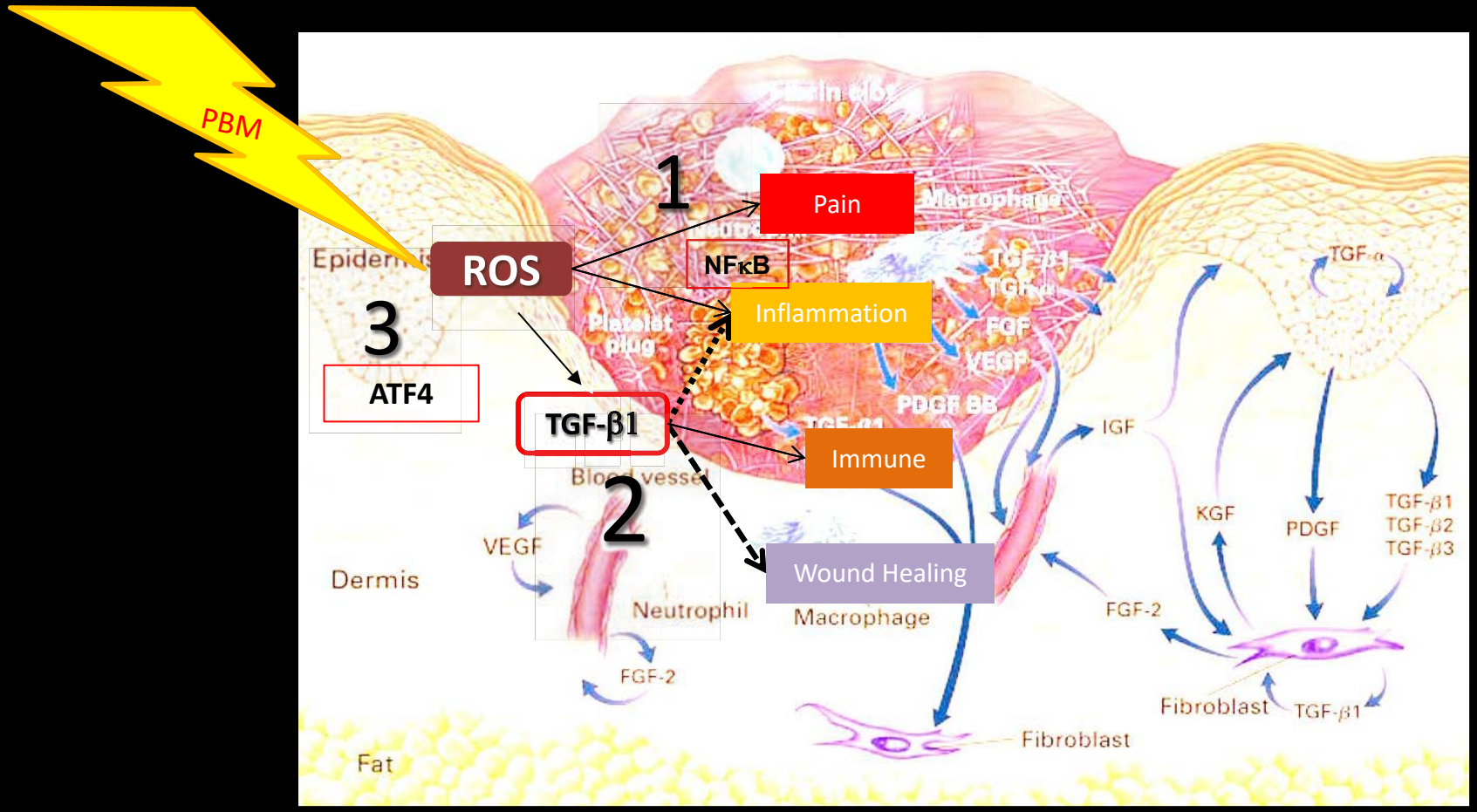
Chow R et al Lancet 2009, 374, 1897
Bjordal J et al BMC Musculsket 2008, 9:75





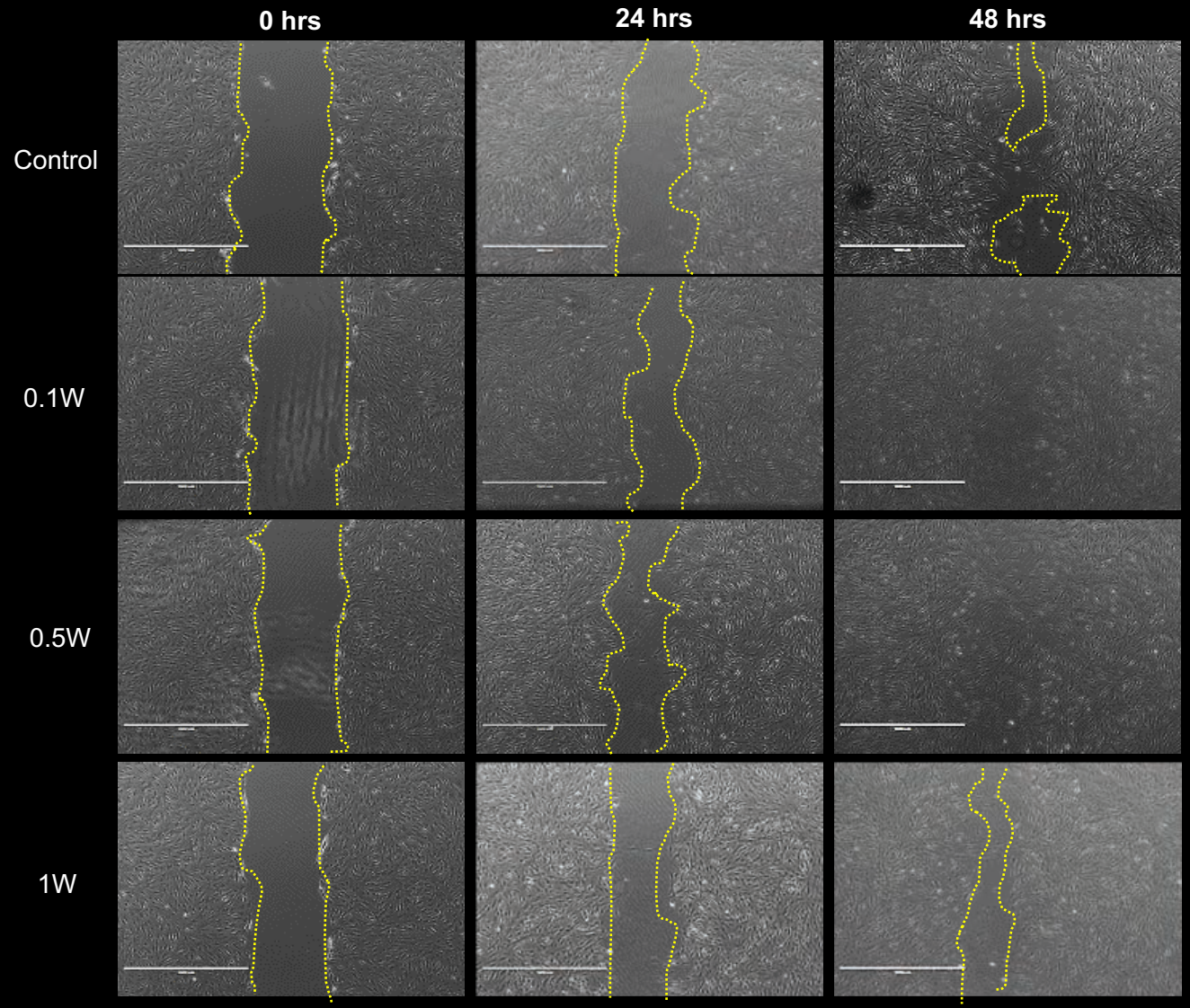


Rationale: PBM in OM for healing



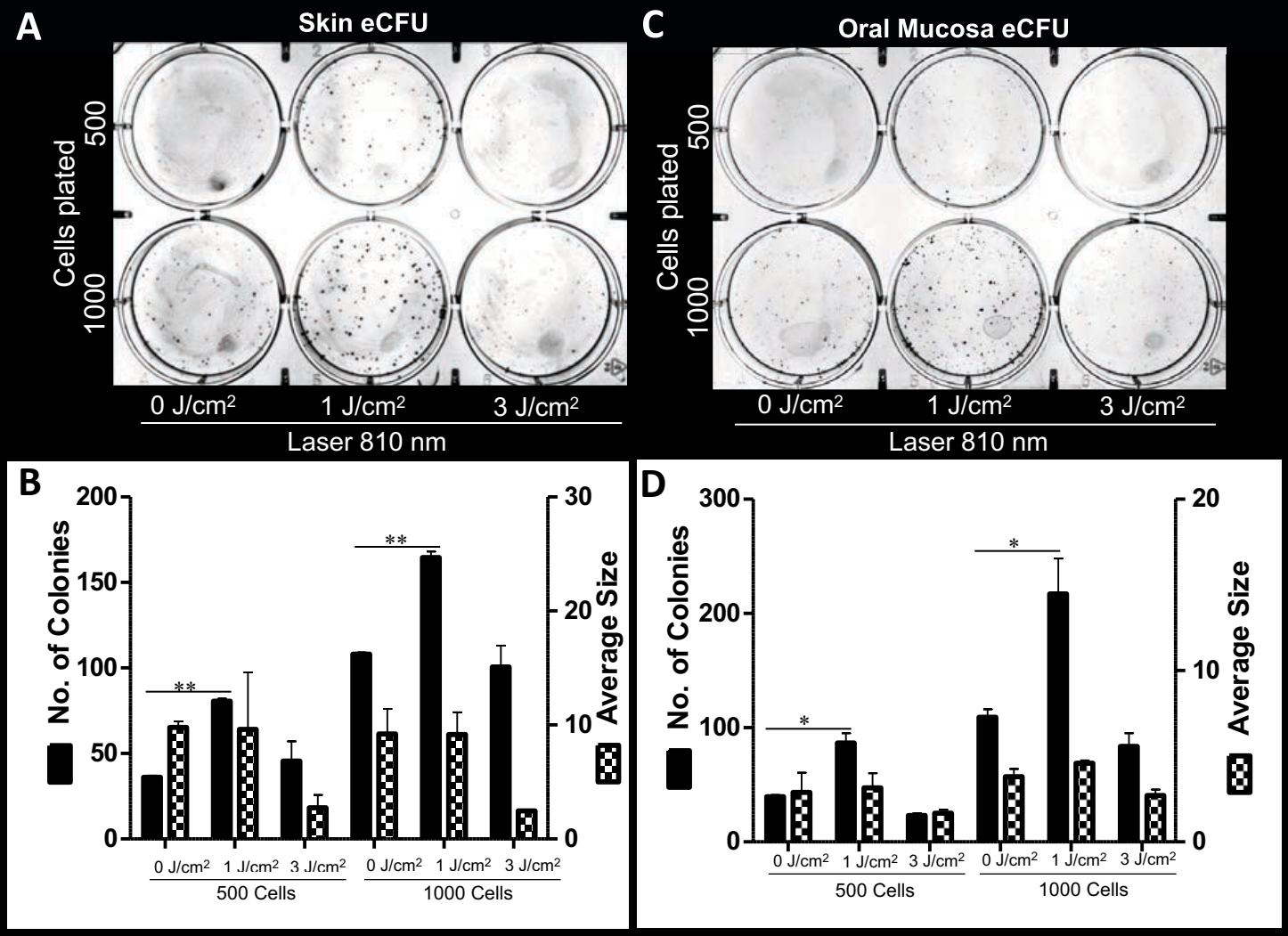
1. Arany *et al* **WRR** 2007 2. Chen*, Arany* *et al* **PLoS One** 2012 3. Arany *et al* **PMLS** 2016

PBM promotes Keratinocyte migration



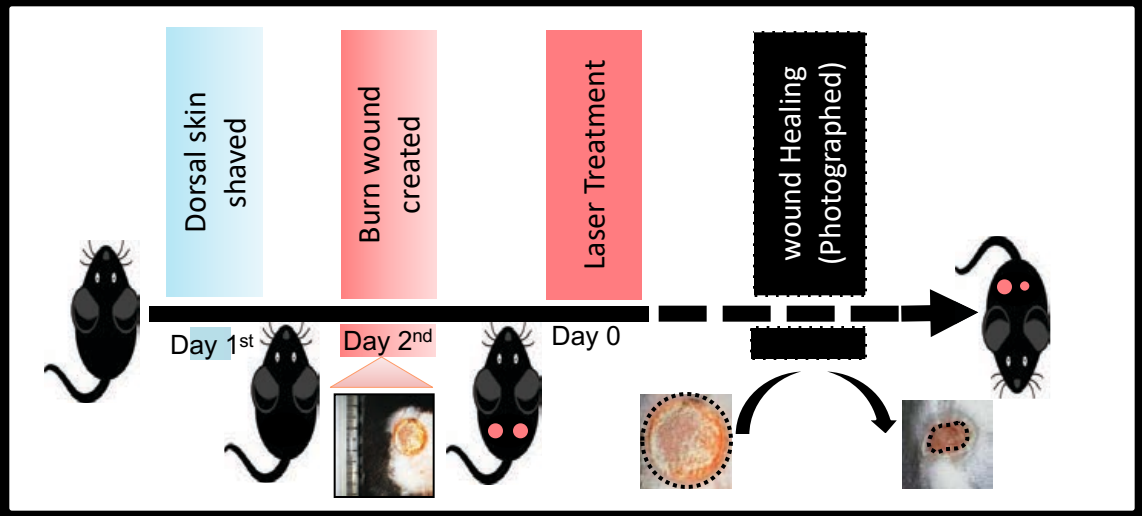
Khan et al *in preparation*

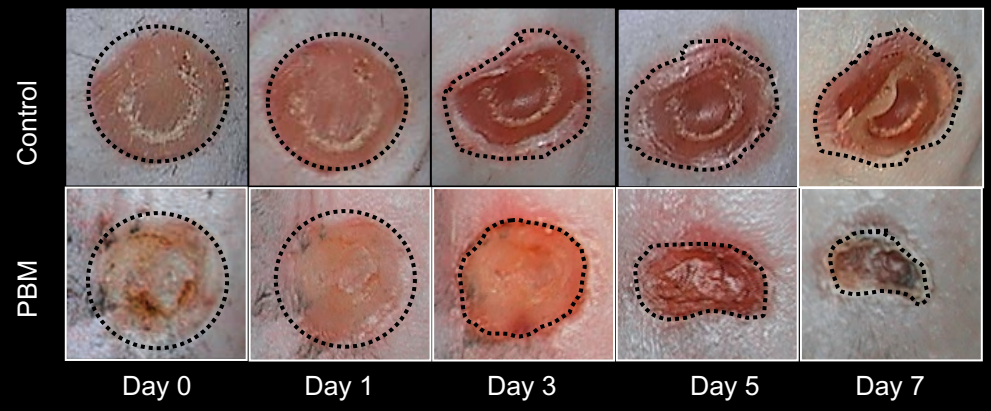
PBM increases eCFUs

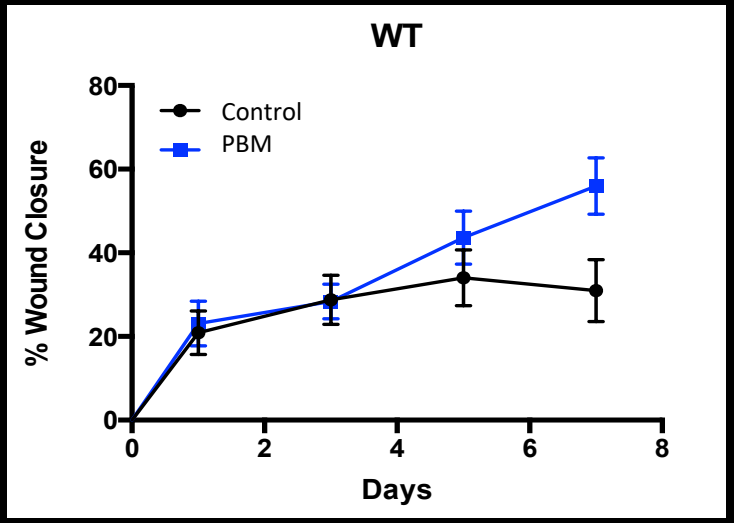


Khan and Arany Photomed Laser Surg 2016

PBM promotes Burn Wound Healing



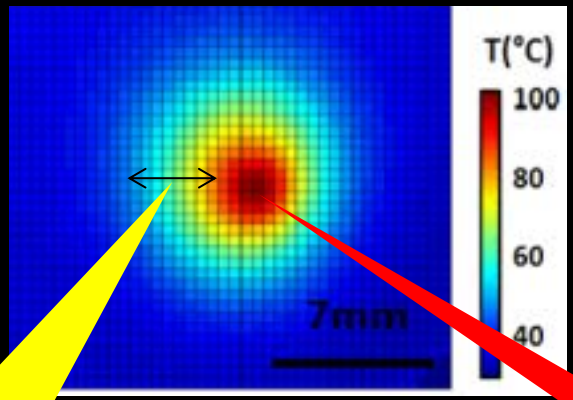




Khan et al *in preparation*

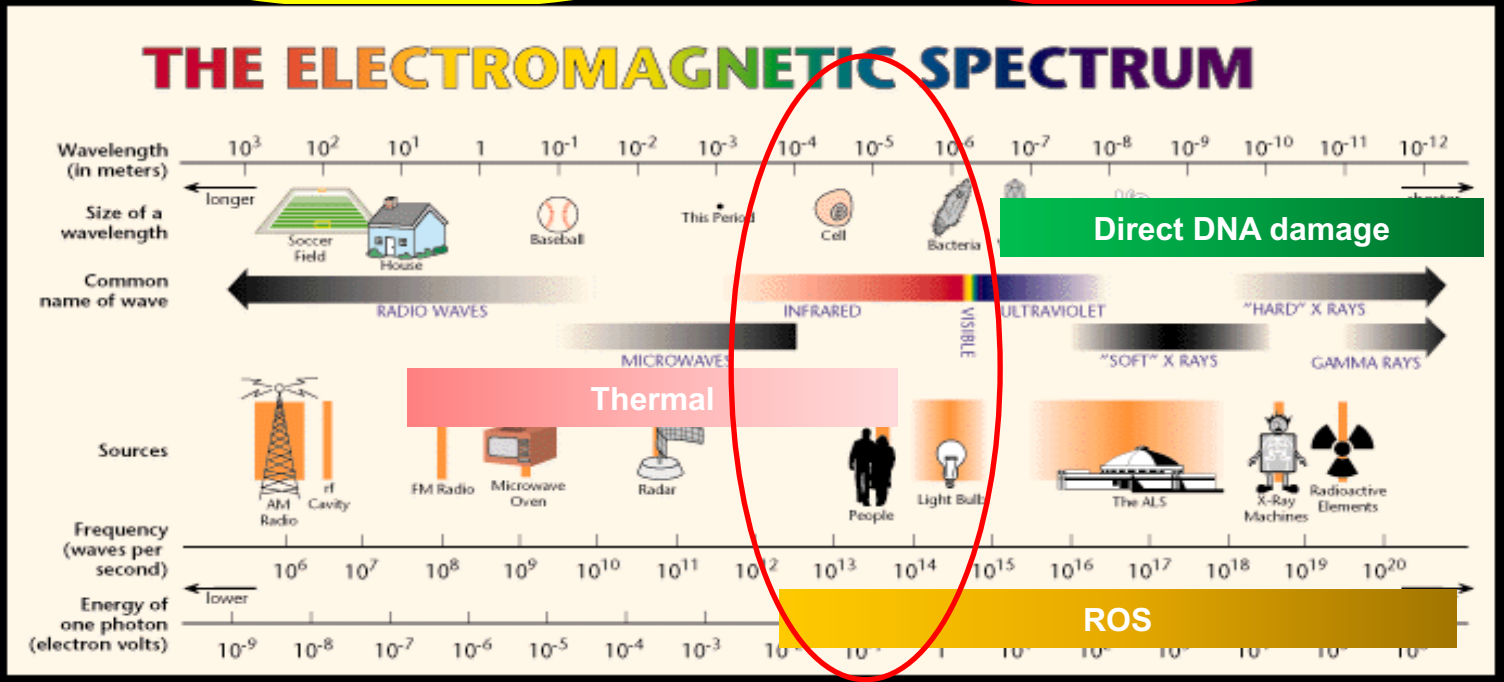
Lasers can destroy tissues.

Are they Genotoxic-Mutagenic?

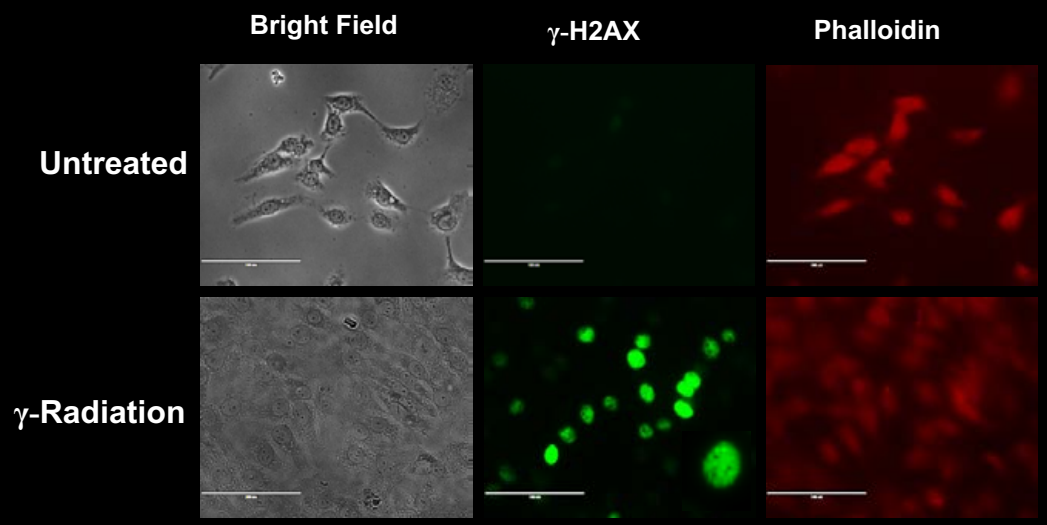


Sub-lethal

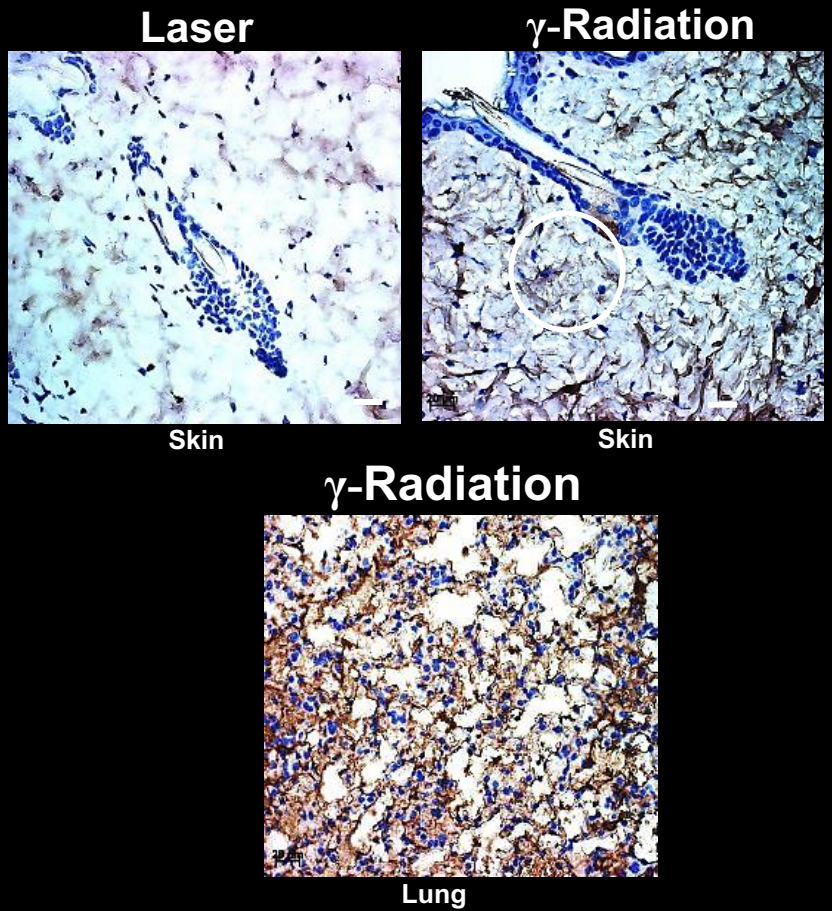
Lethal



Sub-lethal laser doses are Non-Genotoxic



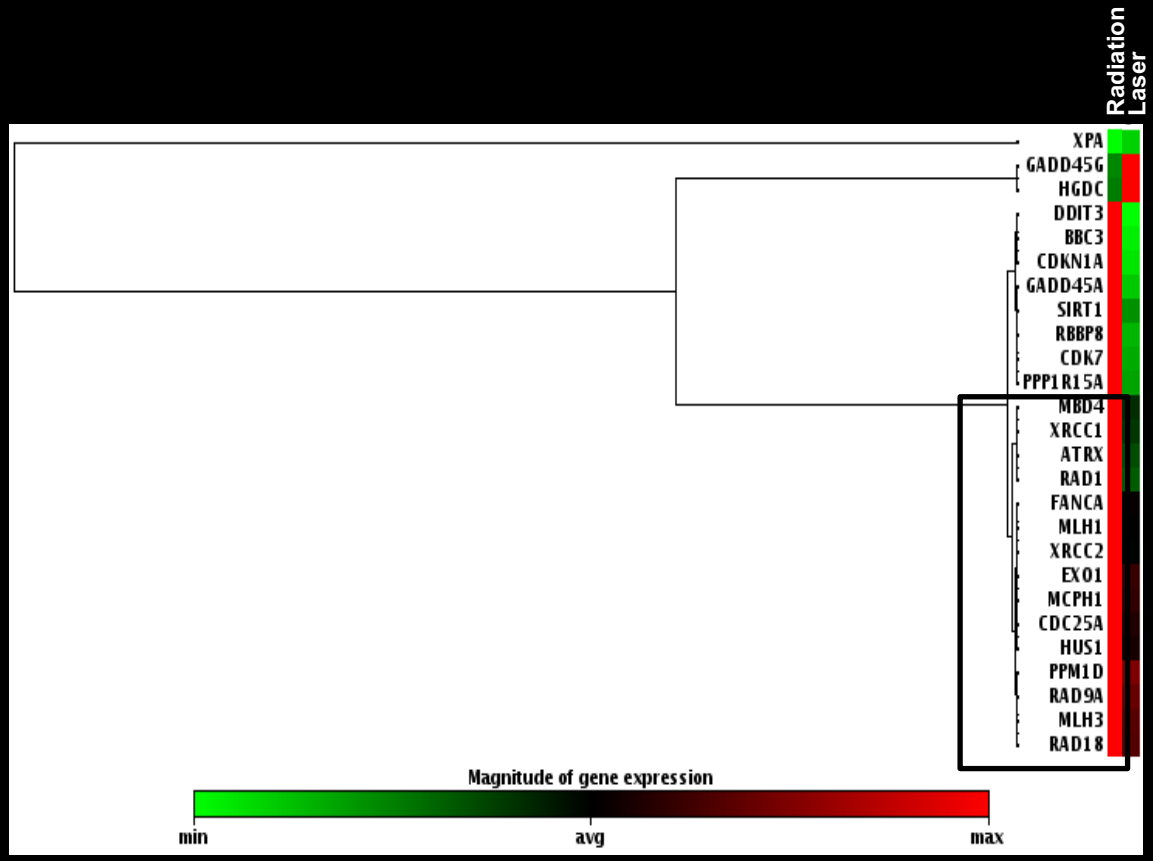
In vitro

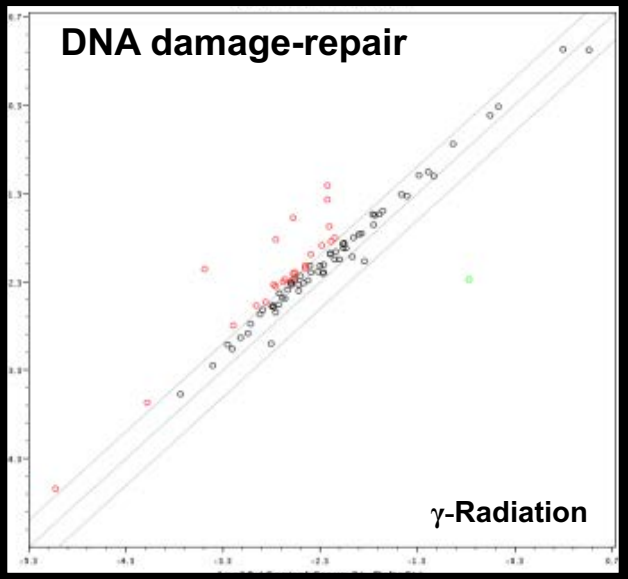


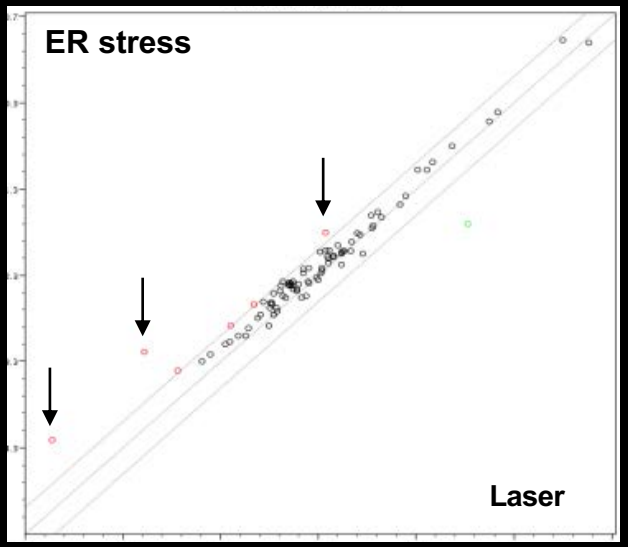
In vivo

Khan I *et al* Sci Reports 2015 , 1, 510581

Gene expression Arrays

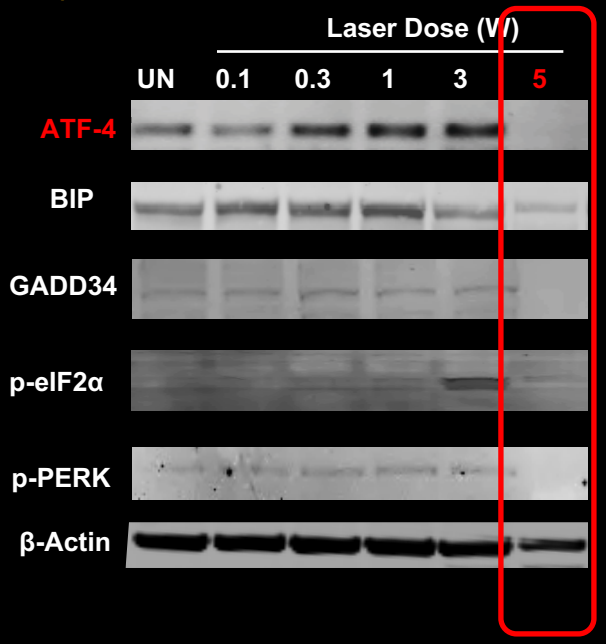


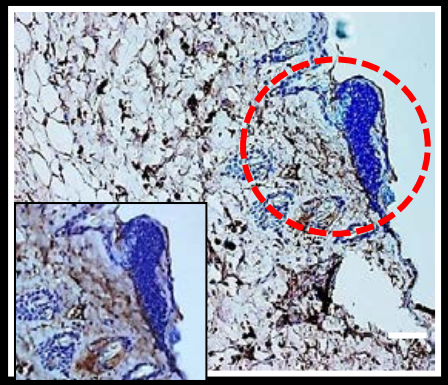


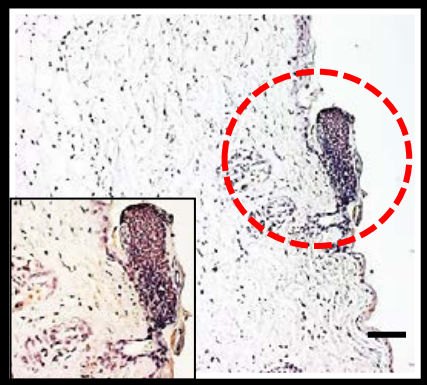


Khan I *et al* Sci Reports 2015 , 1, 510581

Cytotoxic laser dose induces ER stress

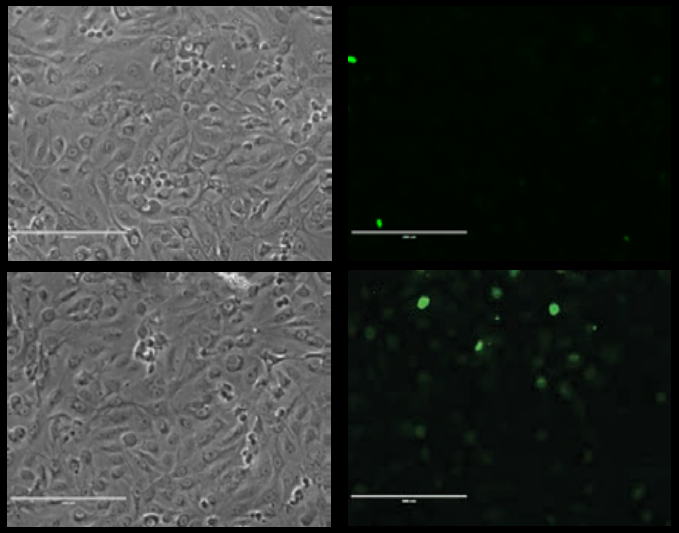




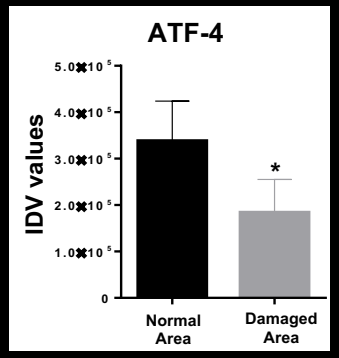


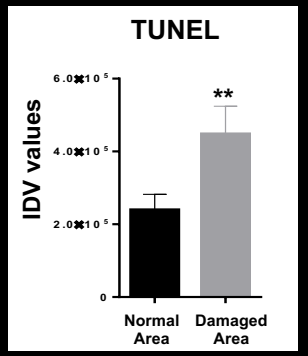
Untreated

Laser
(Sub-lethal)



Bright field ATF4





Khan and Arany Arch Tranl Med 2015

Khan I *et al* **Sci Reports** 2015 , 1, 510581

COMMITTEE ON

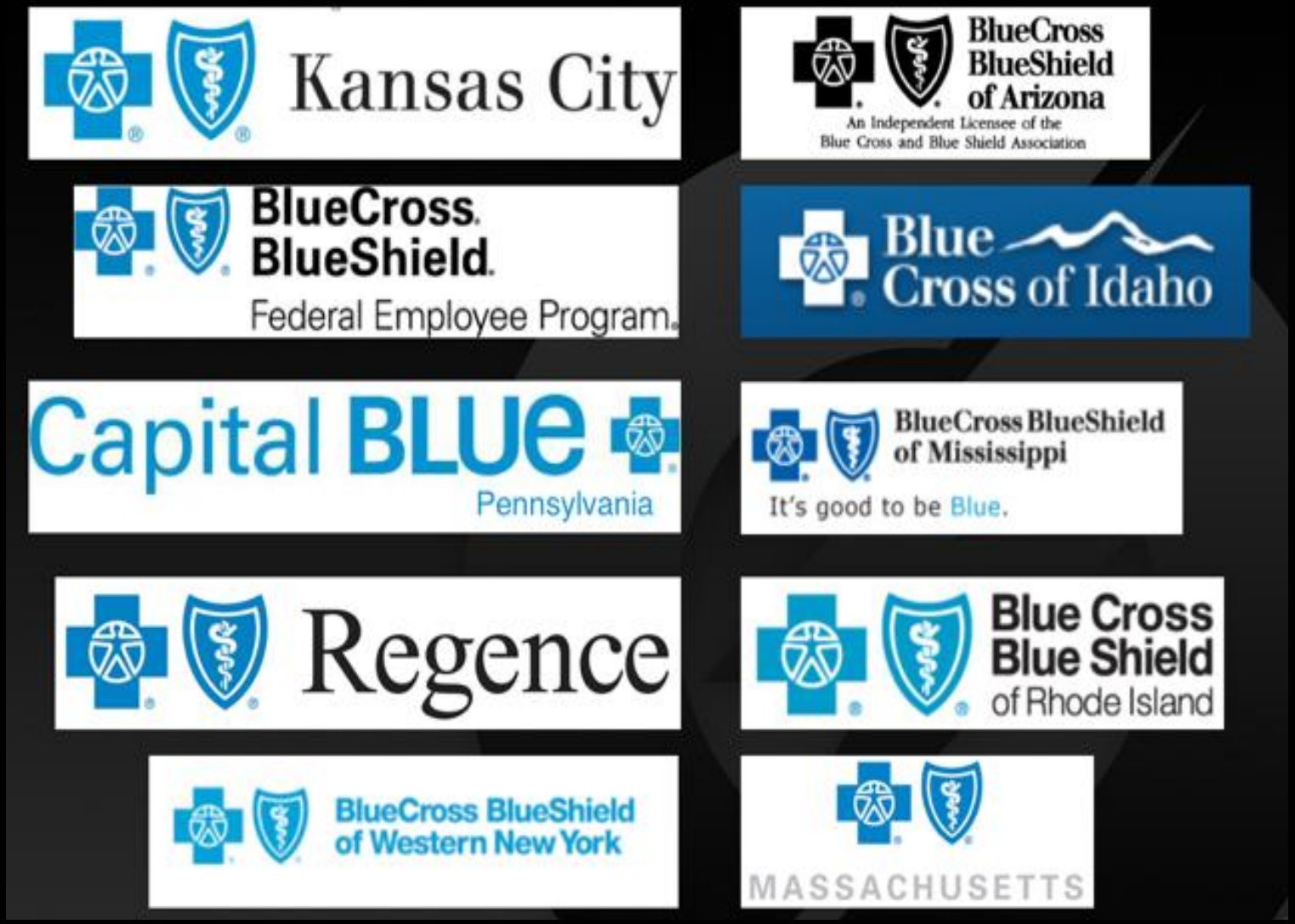
SCIENCE, SPACE, & TECHNOLOGY

Lamar Smith, Chairman

Oct 11th 2018,
Washington DC

HR6, Public Law 115-271 that mandates examination of current evidences (clinical practice guidelines, insurance), further research and funding on ***alternative pain treatments***……

Reimbursement



Billing Codes: 97026, S8948

Can light be a drug?

Yes, A *photoceutical approach for* PBM Therapy

Photokinetics *(Pharmacokinetics)*

'What body does to the light (drug)'

Photodynamics *(Pharmacodynamics)*

'What light (drug) does to the body'

praveenarany@gmail.com

Arany PR *J Dent Res* 2016