

INTRODUCTION TO PHOTOBIO-MODULATION

Juanita J. Anders, Ph.D.

**Uniformed Services University of the Health
Sciences**

Department of Anatomy, Physiology & Genetics

Don Patthoff DDS presenter



American Dental Education Association
15 March 2011

Inter Professional Contributors

- **Ronald W. Waynant,**
Ph.D. Food and Drug Administration
Center for Devices and Radiological Health
Division of Physics
- **Michael R. Hamblin, M.Sc. Ph.D.**
Associate Professor, Department of Dermatology, Harvard Medical School
Associate Chemist, Dermatology, Massachusetts General Hospital
- **Kendric Smith M.D.**
Stanford University
<http://www.photobiology.info/>
- **Donald Patthoff DDS**
General Dentist

PHOTOBIO-MODULATION – THE BEGINNING

In 1967, Endre Mester experimented with the effects of lasers on skin cancer. While applying lasers to the backs of shaven mice, he noticed that the shaved hair grew back more quickly on the treated group than the untreated group.

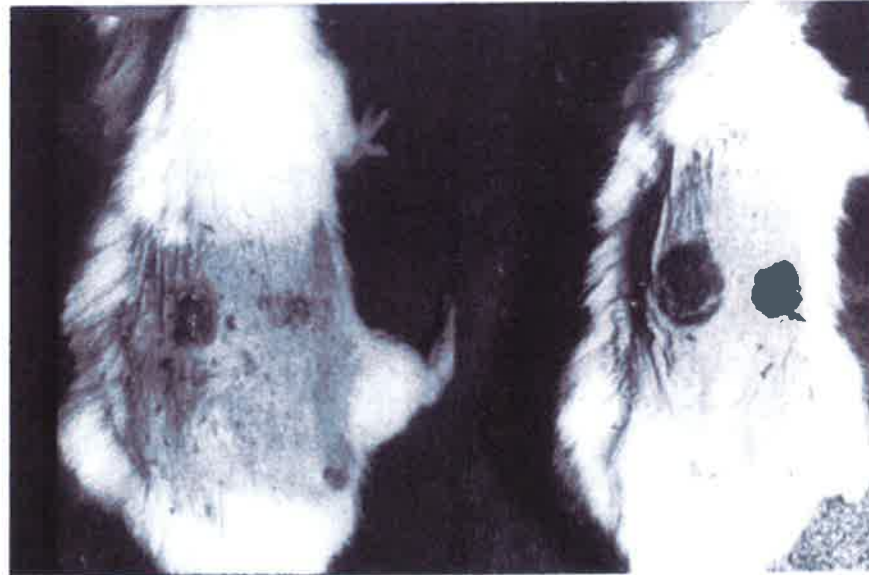
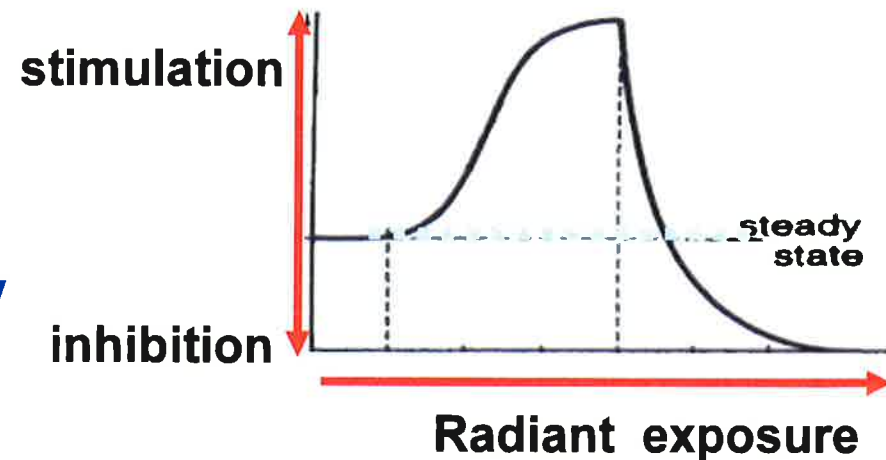


Figure 3.3 “The historic mice” II. Courtesy: Andrew Mester

PHOTOBIO-MODULATION

Also known as:
Low level light therapy
Low level laser therapy
Low power laser therapy
Light therapy or Phototherapy
Biostimulation



Photobiomodulation is an emerging medical and veterinarian application in which exposure to light (usually visible to infrared wavelengths) can stimulate or inhibit cellular function leading to beneficial clinical effects.

The "best" combination of wavelength, irradiance, radiant exposure, and treatment interval is complex and for many treatments still needs to be established.

In the US, the technology received clearance from the FDA in 2002 for hand and wrist pain associated with Carpal Tunnel Syndrome (MicroLight Corp.)



CURRENT SITUATION IN THE US

- **Most users are athletic trainers, chiropractors, and practitioners of complementary medicine**
- **For main stream medicine, LT is still unpracticed, seldom used, & thought unproven**
- **The medial and dental community needs to:**
 - 1) understand the mechanism**
 - 2) needs successful, controlled, large scale clinical trial on several Light Based Therapies**

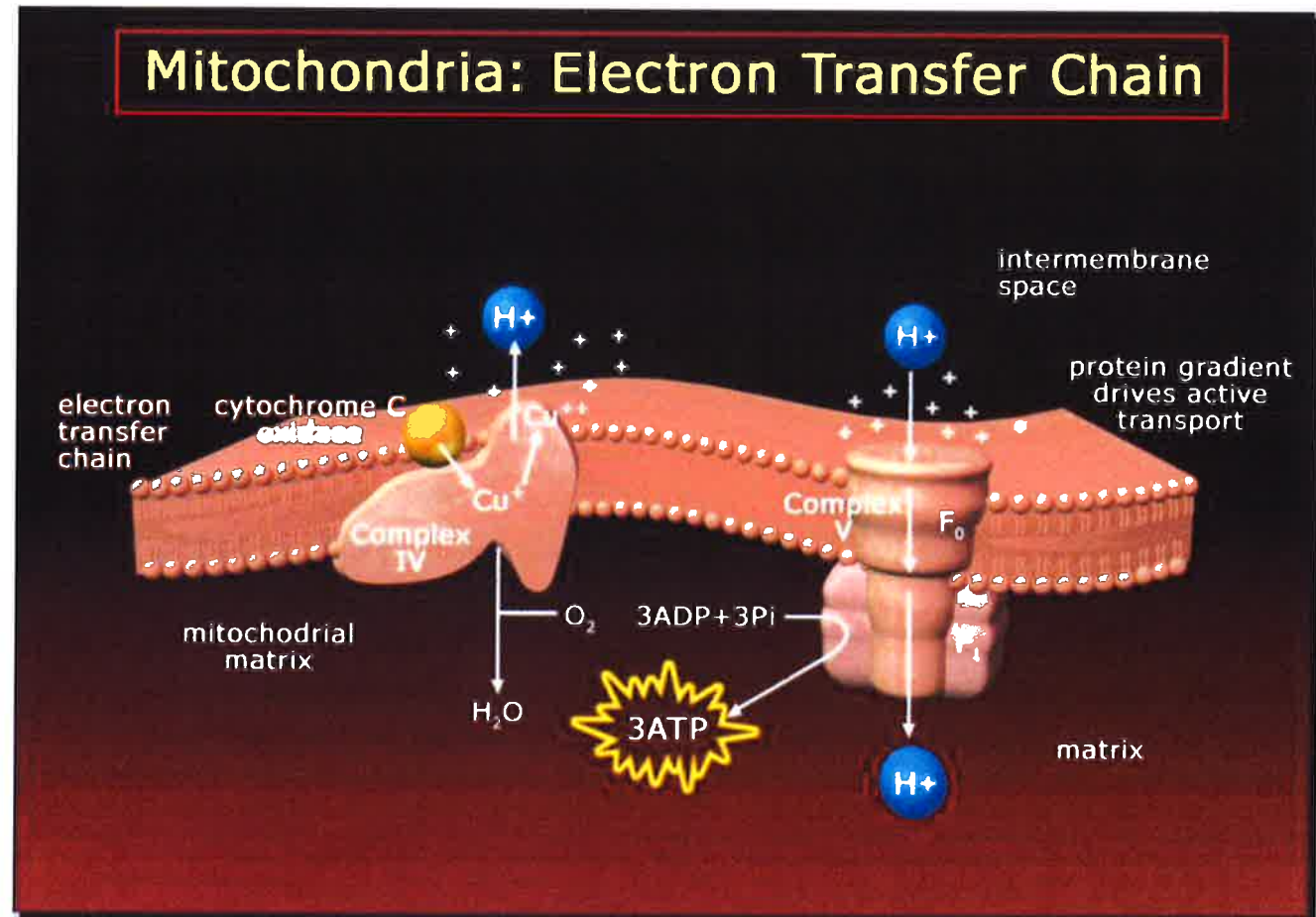
MECHANISM OF PHOTOBIO-MODULATION

- **Mitochondrial Theory**
 - **S. Passarella (1981-Present)**
 - **Tina Karu (1984-Present)**
- **Light induced low concentrations of reactive oxygen species**
- **Changes in calcium homeostasis**
 - **Rachel Lubart**
 - **Trends in Photochemistry and Photobiology 1997: 4; 277-283**
 - **Drug Development Research 2000: 50; 471-475**
 - **Moro, Greco, Marra, and Passarella**
 - **Lasers in Medical Science 2002: 17:A20**

MECHANISM OF ACTION

Red and near infrared wavelengths:

- Absorbed by Cu centers in cytochrome C oxidase
- Enhance mitochondrial viability and activity



Eells, J. T. et al. *Proceedings National Academy of Science* 2003; 100:3439-3444

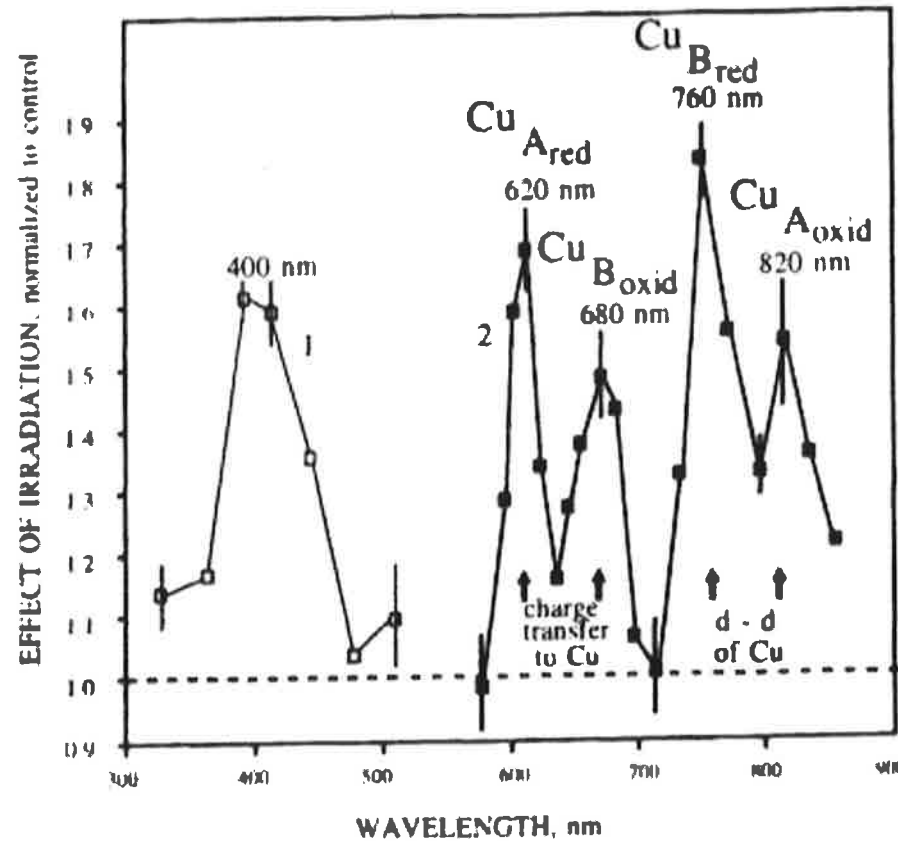
T.I. Karu "[Low power laser therapy](#)". In: *Biomedical Photonics Handbook*. Ch. 48, Editor-in-chief Tuan Vo-Dinh, Boca Raton: CRC Press. 2003.

CcOx is a photoreceptor for red and NIR

Proceedings of SPIE Vol. 4159 (2000)

MECHANISMS OF LOW-POWER LASER LIGHT ACTION ON CELLULAR LEVEL

Tina Karu



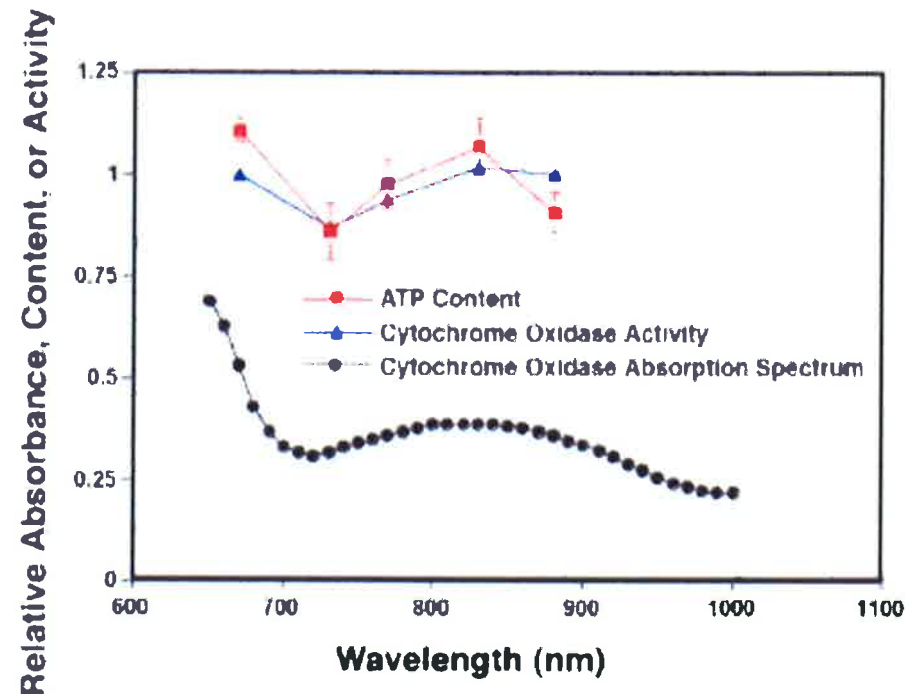
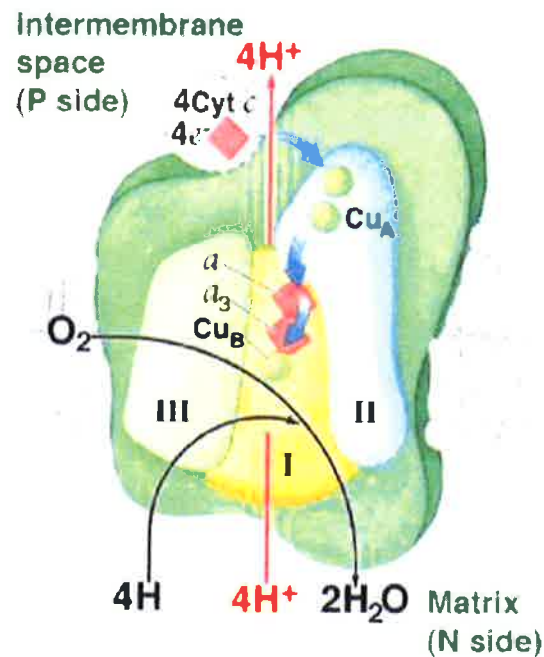
Absorption spectrum of CcOx in HeLa cells

Cytochrome c Oxidase activity increases at 810 nm

SPIE Newsroom, 2008 February 24; 2008: 1-3.

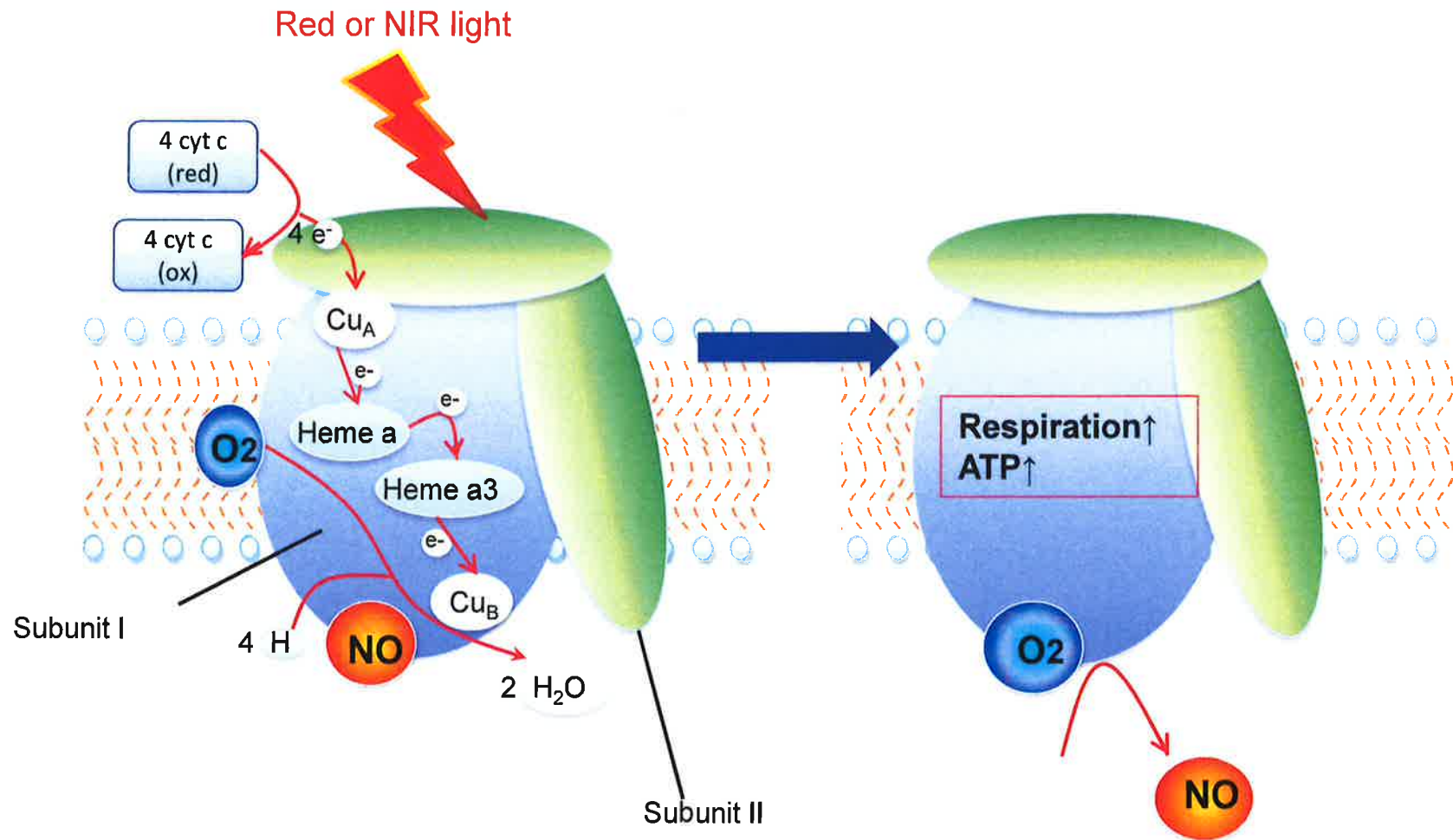
Harnessing the cell's own ability to repair and prevent neurodegenerative disease

H Whelan, K Desmet, E Buchmann, M Henry, M Wong-Riley, J Eells, and J Verhoeve



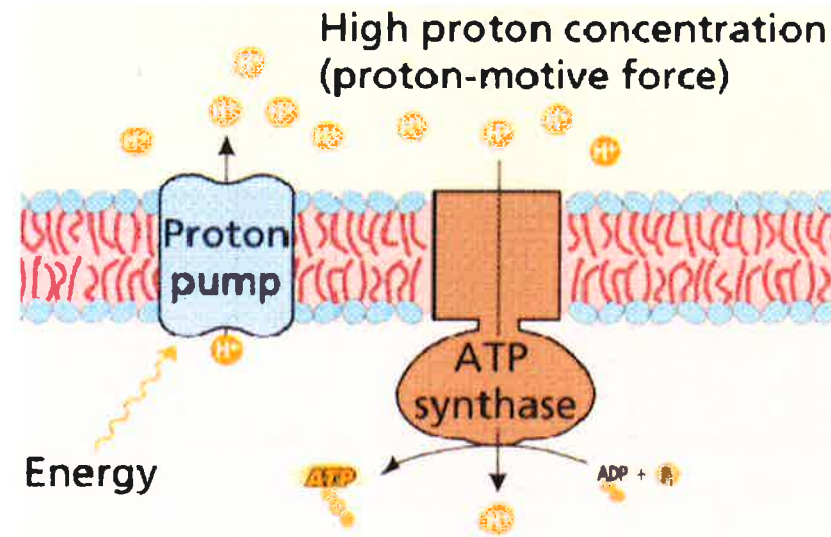
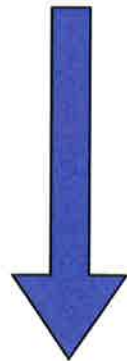
Cytochrome oxidase and the correlation between the near-IR absorption spectrum of cytochrome oxidase, ATP content, and cytochrome oxidase activity in cultured primary neuronal cells subjected to metabolic inhibition and near-IR light treatment.

Photodissociation of NO from cyt C oxidase

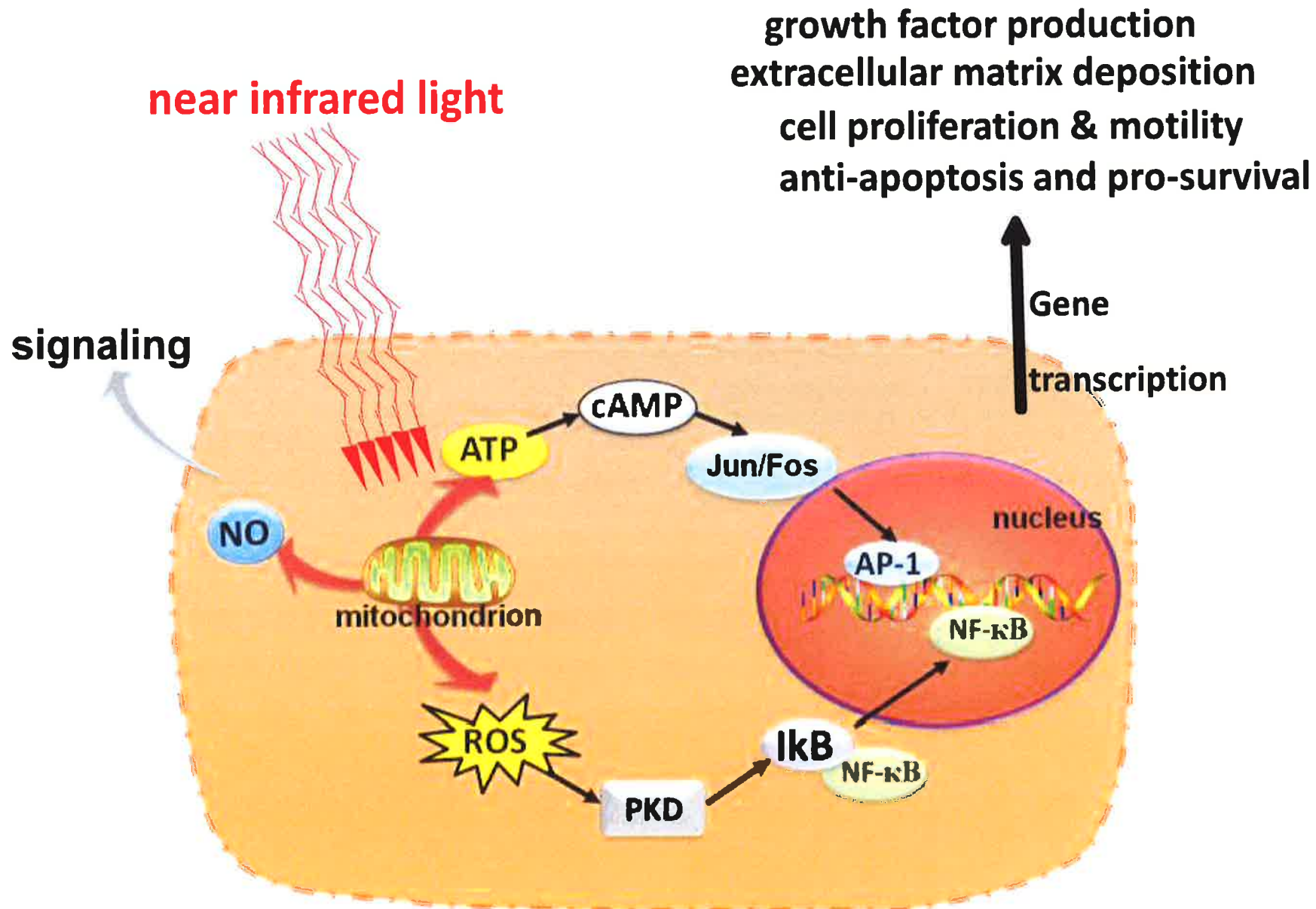


Cellular Energetics

- Increased activity CcO
- Decreased CcO binding to NO
- Increased Oxygen consumption
- Restoration of mitochondrial electrochemical gradients (PSIm)
- Increased ATP production



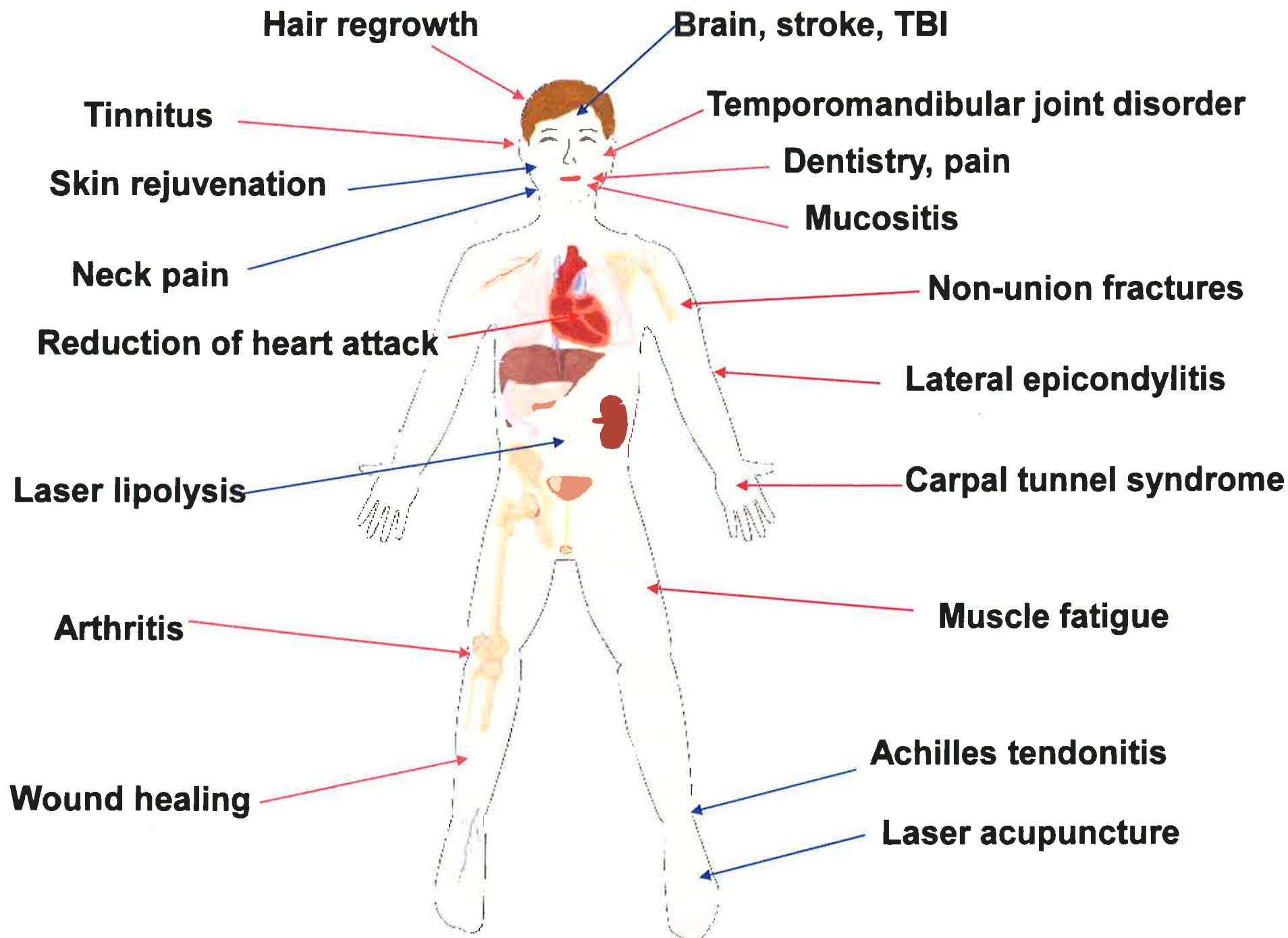
Restoration of cellular energy balance & ATP signaling

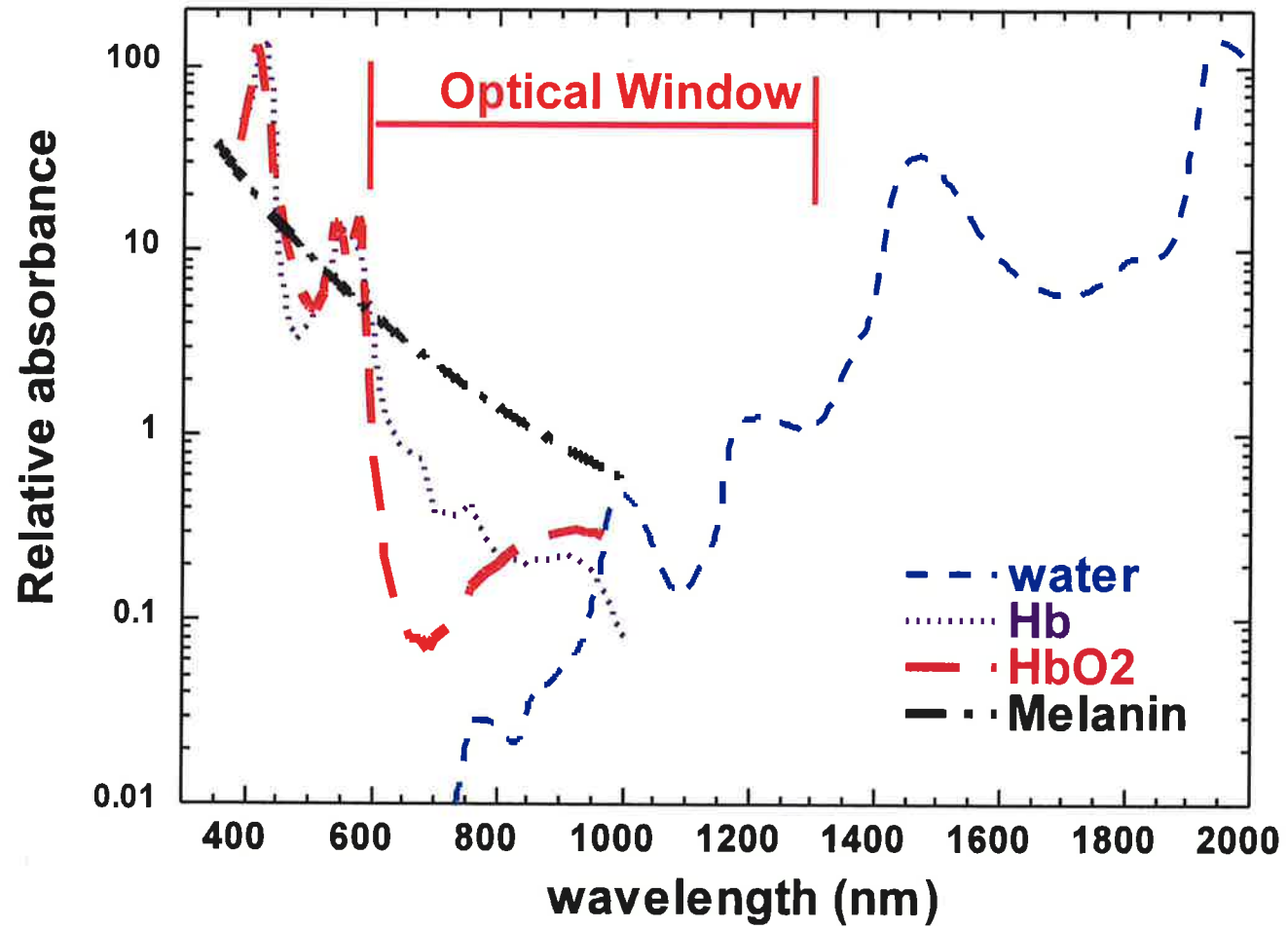


Mitochondria are also an integral part of multiple cell signaling cascades. Proteins such as GTPases, kinases and phosphatases are involved in bi-directional communication between the mitochondrial reticulum, and the rest of the cell.

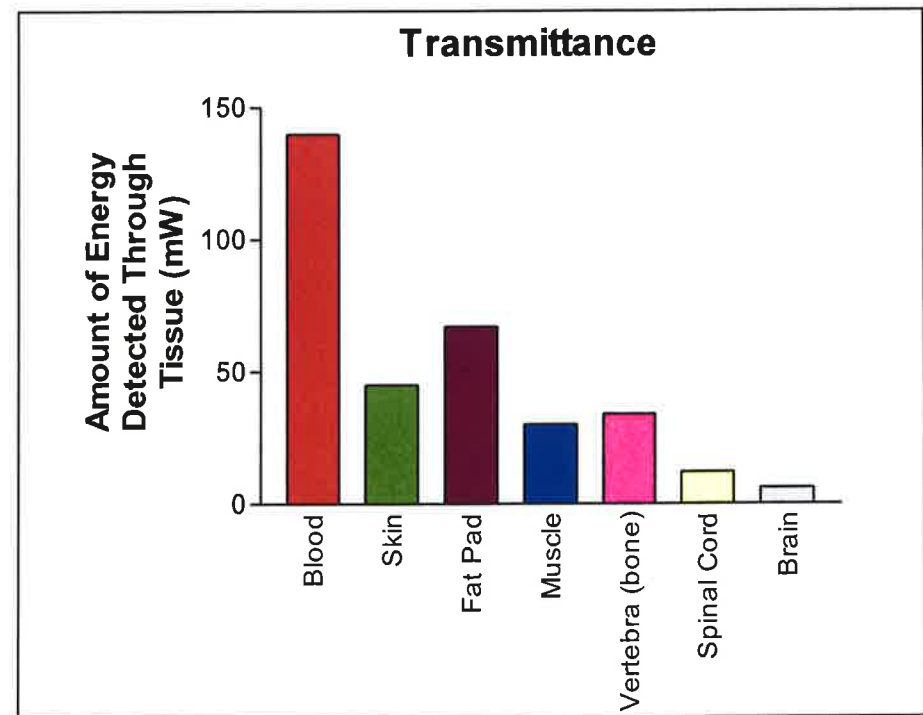
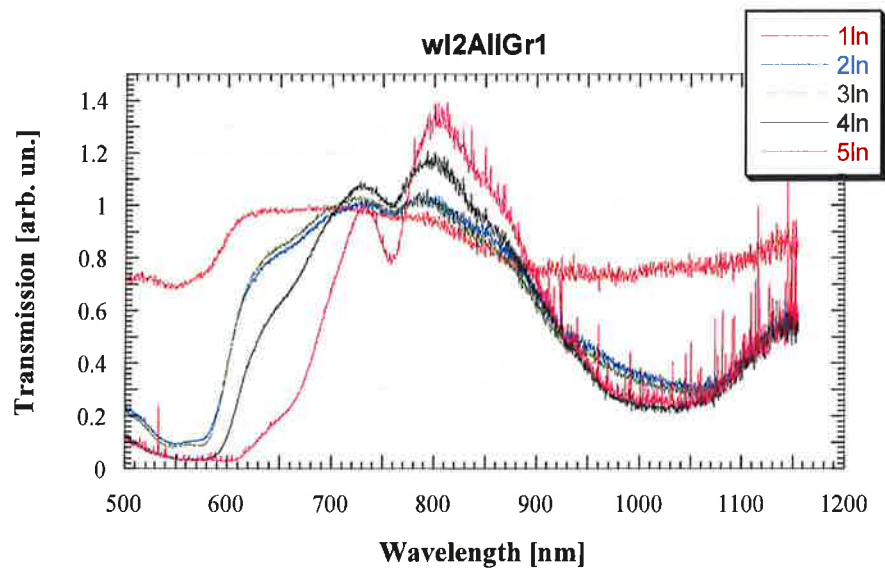
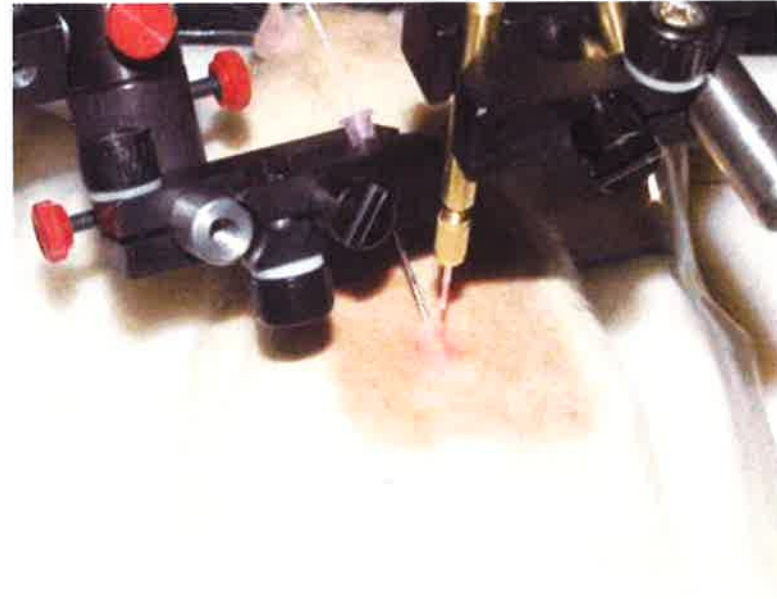
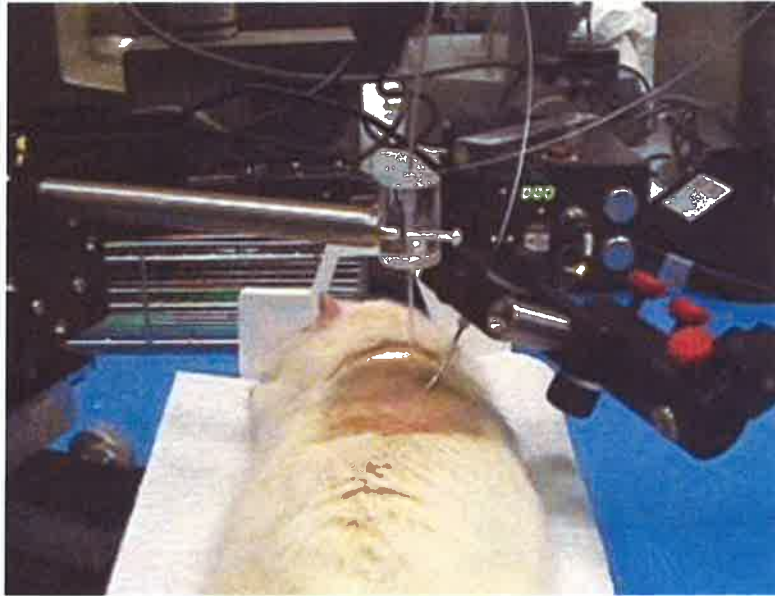
Summary of a number of experiments with different cell types, listing the different molecules that are induced by light therapy

Classification	Molecules	Biological effects of LLLT
Growth factors	BDNF, GDNF, bFGF, IGF-I, KGF, PDGF, TGF- β , VEGF	Proliferation, Differentiation, Bone nodule formation
Interleukins	IL-1 α , IL-6, IL-8, IL-2, IL-4	Proliferation, Migration, Immunological activation
Inflammatory cytokines	PGE2, COX-2, IL-1 β , TNF- α	Inhibition of inflammation
Small molecules	ATP, cGMP, ROS, Ca ²⁺ , NO	Normalization of cell function, Pain relief, Healing, Mediating cell activities, Migration, Angiogenesis

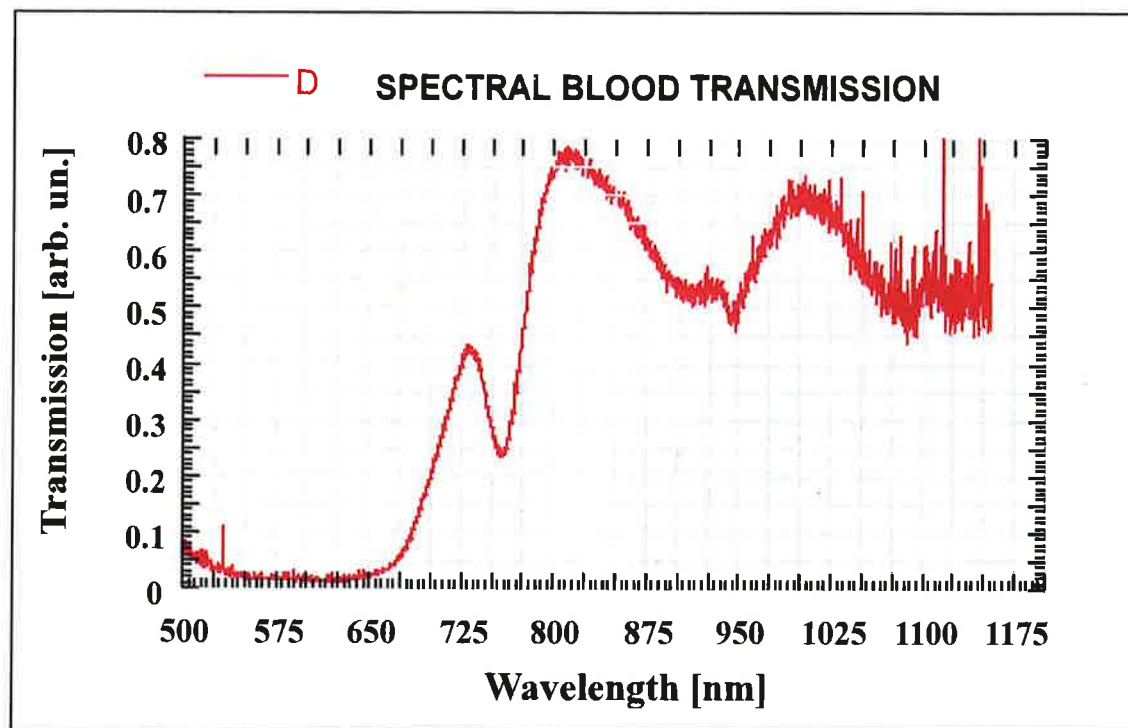
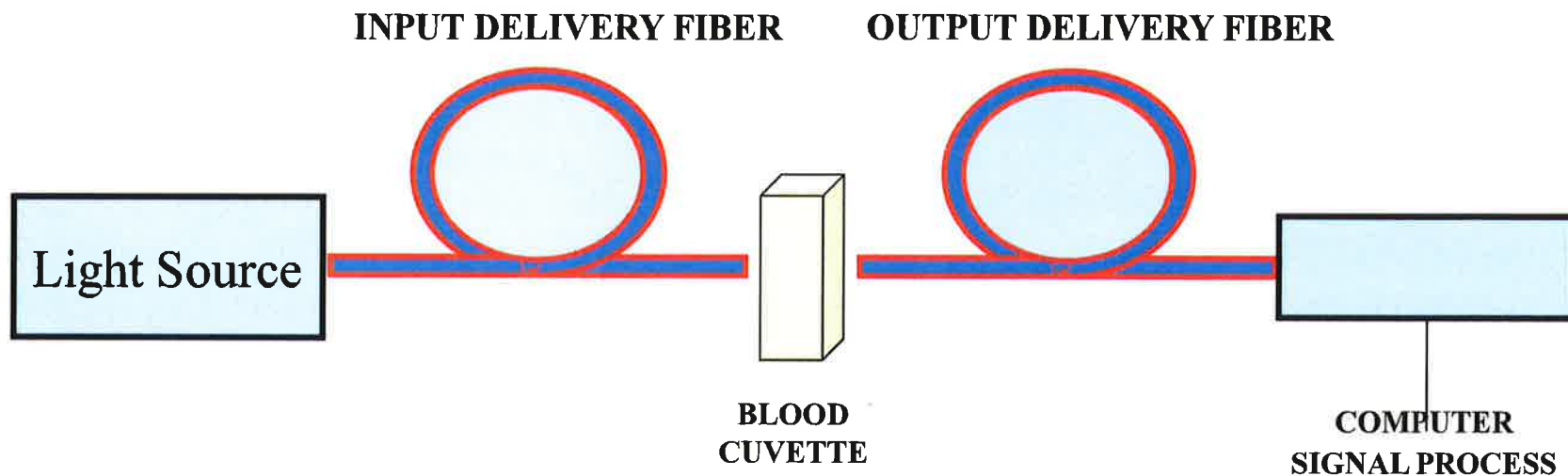




810 nm CAN PENETRATE TO THE DEPTH OF BRAIN AND SPINAL CORD: 810 nm FOUND TO HAVE HIGH ABSORPTION BY CNS TISSUE



810nm Found to Best Promote Regeneration: 810nm Has Minimal Energy Absorption by Blood and Water



MEDICAL AREAS WHERE PHOTOBIO-MODULATION CAN PLAY A MAJOR ROLE

- **Wound Healing –Tissue Repair**
- **Pain – Relief of Inflammation**
- **Central and Peripheral Nervous System –
Injury and Disease**
- **Metabolic Diseases –Diabetes**
- **Range of Dental Applications**

LIGHT ALTERS DNA/RNA EXPRESSION

Genomic analysis of spinal cord following injury and photobiomodulation

Microarray Conclusions

Expression of over 200 genes significantly altered after photobiomodulation and spinal cord injury

- Many altered genes involved in:
 - Decreasing inflammatory response
 - Decreasing glutamate receptor
 - Increasing neurotrophic factor receptor
 - Decreasing cell proliferation

INCREASING INTEREST AND ENDORSEMENT OF LIGHT THERAPY IN THE LAST 3 YEARS

Dr. Roberta Chow published in Lancet on efficacy of LT for neck pain

- intense interest in the article and reaches the Lancet Top 20 most downloaded research papers in 2010

Associations Endorsing LT:

- International Association for the Study of Pain (myofacial pain syndrome)
- The American Physical Therapy Association (achilles tendon treatment)
- BMJ sports medical journal (frozen shoulder)
- The World Health Organization (neck pain)