Low Level Laser Therapy
Biological and Clinical Effects

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- Low Level Laser Therapy units Marketed
  - Frequencies in nm:
    - 405, 450
    - 585
    - 630, 660, 680
    - 810, 820, 850, 875, 890
    - 905, 950
How is LLLT Thought to Work?

- Naturally occurring photo receptors
- Linked to signaling pathways
  - Calcium flux
  - 3 primary pathways governing
    - Survival
    - Growth
    - Differentiation
Effects of LLLT at the Cellular Level

- 1967 – increased fibroblast growth (5x) (??)
- 1988 – increases in intra-cellular Ca+2 (??)
- 2006 – activation of ERK ½ (810nm)
- 2007 – activation of p38 and ERK 1/2 (585nm)
- Unpublished – activates CREB (810nm)
- 2002-2006 – activation of multiple genes (585-820nm)
<table>
<thead>
<tr>
<th>Response</th>
<th>Pathway</th>
<th>585nm</th>
<th>810nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>JNK</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Growth</td>
<td>ERK</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Differentiation</td>
<td>P38</td>
<td>Yes</td>
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</tr>
</tbody>
</table>
Clinical Links from Cell Biology

- LLLT frequencies:
  - 405, 450 ??
  - 585 Growth & Differentiation
  - 630, 660, 680 ??
  - 810, 820 Growth
  - 850, 875, 890 ??
  - 905, 950 ??
  - ?? Survival
Evidence for Modulation of Immune Response

- **1992** – peripheral blood monocytes
  - IL-1, IL-2, TNF, IFN, IL-2R and ICAM (632nm)

- **2002** – ischemic perfusion
  - Increases in TGF-b (660nm)

- **2006** – exposed tissue
  - Increases in IL-2 (632nm)
Evidence for Modulation of Immune Response

- **2003** – reduced inflammation in wound area
  - Number of cells and edema (670nm)

- **2005** – increased inflammation, normal tissue
  - Neutrophil, monocytes, mast cells (585nm)

- **2005** – spinal cord injury
  - Reduced IL-6 and MCP-1 (810nm)
Immune System

- Autoimmunity and Chronic Inflammation:
  - Misdirected immune to host
    - Auto-antibodies
    - Auto-reactive T lymphocytes

- Normal:
  - Resists the onslaught of invading microorganisms
    - viruses, bacteria, and parasites
  - Guide injury repair

- Cancer
  - Immune system suppressed
# LLLT on Immune Response

## Increases
- **IL-2**
  - 632nm & 820nm
  - Novoselova et.al (2006)
  - Johns et.al. unpublished
- **IL-4**
  - 585nm
  - Omi et (2005)
- **TGF-B**
  - 660nm
  - Leung et.al (2002)
- **IFN-g**
  - 632nm
  - Funk et.al (1992, 1993)

## Decreases
- **IL-6**
  - 810nm
  - Byrnes et.al. (2005)
- **IL-17**
  - 820nm
  - Johns et.al. unpublished
How Might LLLT Effect the Immune Response

- T_{H2} GATA-3 STAT-6 → IL-4
- T_{H1} T-bet STAT-4 → IFN-γ
- T_{H17} → IL-17
- T_{reg} Foxp3 → TGF-β1 (Other factors?)

IL-2

- Defence against parasitic worms
- Allergy, asthma
- Defence against intracellular pathogens
- Defence against extracellular bacteria
- Autoimmunity
- Cancer
- Immunosuppression
### Clinical Studies with LLLT

#### Increased
- Wound closure
- Chronic ulcers
- Fibroblast Growth
- Collagen production
- Vascularity

#### Immuno-suppressive
- Immune cell influx
- Snake venom
- LPS response
- However, does not appear to suppress proliferation??
- How is LLLT immuno-suppressive without inhibiting growth??

- Mechanism: enhance growth
Recommended Dosage of Low Level Laser Therapy  
Anti-Inflammatory

- World Association of Laser Therapy

- **Tendinopathies & Arthritis**
  - 1-4 points 2-8 joules/pt

- 2 Weeks - Daily treatment for 2 weeks
- 3-4 Weeks – every other day