Photobiomodulation's genetic pathways for cellular proliferation

By Lew Lim, MedicLights Research Inc., Toronto, Canada, April 1, 2013
Based on investigations by Timon CY Liu et al of South China Normal University, China.

Introduction

Prof Timon Liu (our science advisor) and his team investigated how photobiomodulation takes various genetic pathways to heal and achieve homeostasis. A large part of the findings are published in the following papers: Photobiomodulation on Stress, and Photobiomodulation-mediated Pathway Diagnostics. This article is a simplified presentation of the investigations.

In principle, our body systems seek to restore homeostasis or internal balance by "detecting" dysfunction or imbalance in the systems (more accurately described as a "negative feedback" process). Photobiomodulation - the effect of light on modifying a cellular condition - is a method that facilitates this process. More than that, the study implicates that through the expression of the genes during the photobiomodulation process, it may also enhance the health of the cells beyond their normal level.

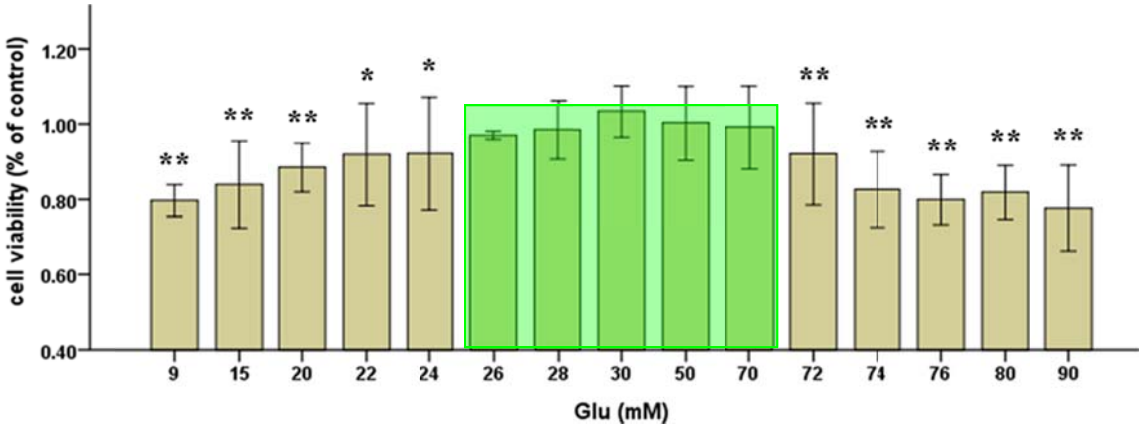
Many details (particularly the details on the study methodology) are left out; but these are available on request.

Some basics on cell proliferation and the experiments

Our body is composed of cells that constantly proliferate under a complex interplay of various genes. Even the proliferation process has to be in homeostatic condition – otherwise there could be only partial growth or on the other hand, out-of-control growth such as cancer. Healing involves cell proliferation, but this is often compromised under stress (which can be defined as an environment that causes a dysfunction). The investigations simulated this stress by subjecting the cells in high glucose solution.

In high glucose environment, the cells are found to have lower count than in a normal level glucose environment (a good case to control our sugar intake). See Figure 1 below. This suggests that under stress, the homeostatic process is only partially activated.

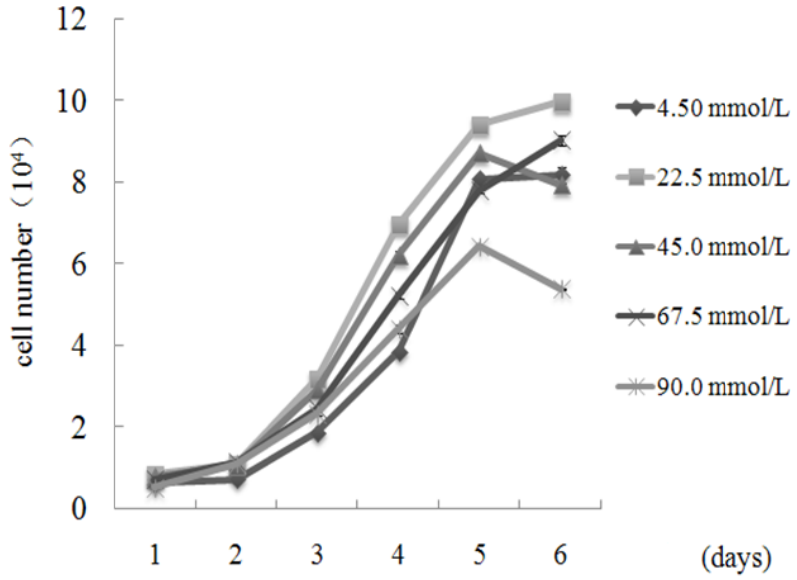
Figure 1 – Cells in different glucose levels



KY Qi. 2012. Proliferation-specific homeostasis of PC 12 cells. MS thesis, South China Normal University.

In about 3 days (72 hours) in high glucose solution, it becomes clear that cellular proliferation is significantly lower relative to normal glucose solution, although cells continue to thrive in glucose. See Figure 2 below.

Figure 2 – Glucose effect on proliferation

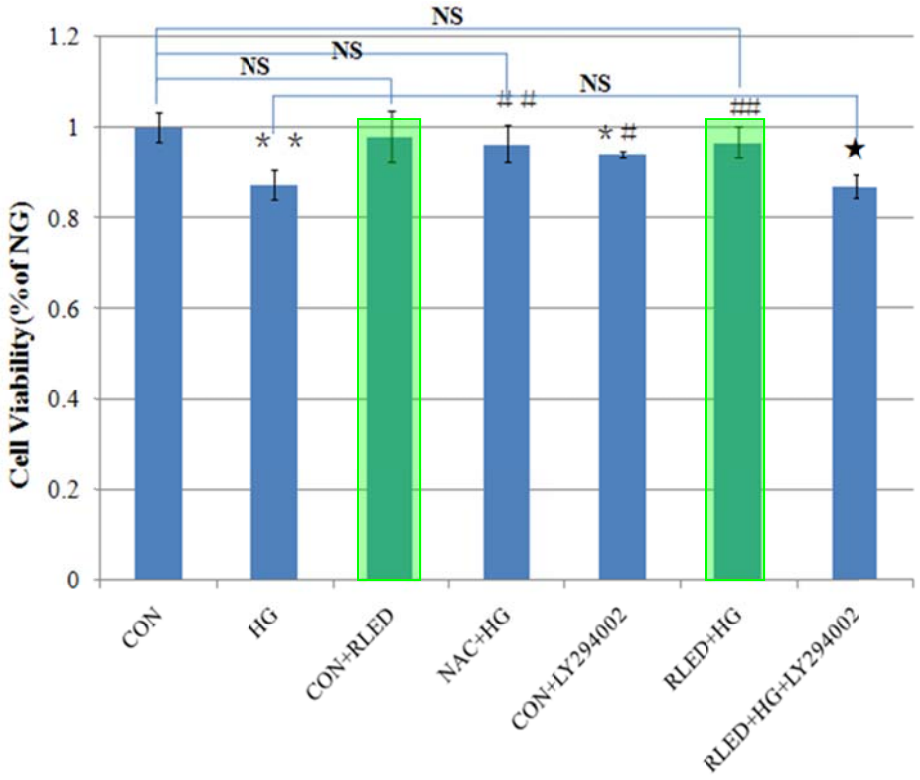


Time and concentration dependent effects of glucose on viability of C2C12 myoblasts. C2C12 myoblasts were treated with 4.5–90 mM glucose for 1–6 day. The cell viability was assessed by MTT assay. n = 3. The results are expressed as mean±SE of three independent experiments.

The effect of low intensity light

When we subject the cells under low-intensity red light, the cells in high glucose (RLED-HG) recover their proliferation level in about 3 days. See “RLED-HG” versus “HG” in Figure 3 below. “CON” in the figure stands for control (or cells in normal level glucose).

Figure 3 – RLED effects on proliferation at 72 hours



The RLED at 640 nm and 0.035 mW/cm2 on proliferation at 72 h. ＊(P < 0.05), ＊＊(P＜0.01) against nG; ＃ (P＜0.05), ＃ ＃ (P ＜0.01) against hG; NS: No significance.

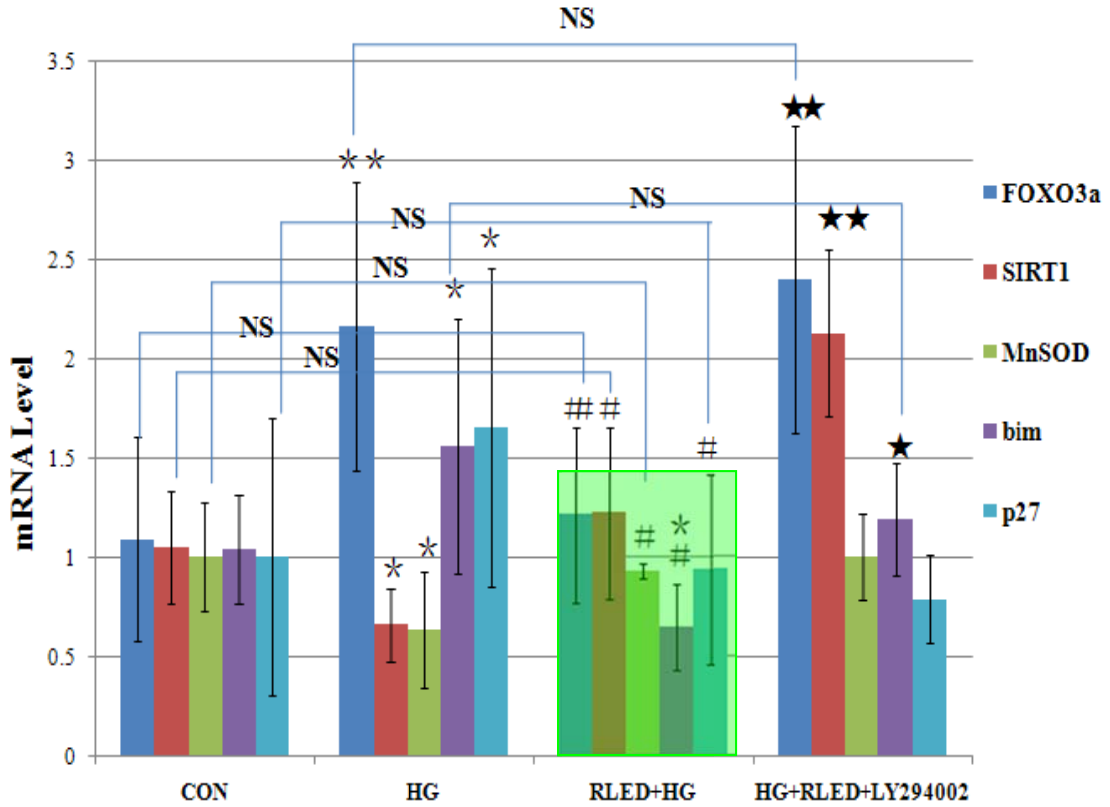
The response of stressed and dysfunctional cells

The cells in our body collectively proliferate under pre-programmed settings to restore to their desired normal functions. These “programs” would be determined by our genotype. The genes are grouped under categories that, when they work in harmony and in accordance with the programs, restore homeostatis in the targeted conditions. The groups of genes can generally categorised as **activators**, **inhibitors** and **regulators** of proliferation.

The genes are coded into working protein through messenger ribonucleic acids (mRNA). For the investigations, the research group examined the mRNA of the **activators**, manganese superoxide dismutase (MnSOD) and insulin-like growth factor 1 (IGF-1)); **inhibitors**, forkhead box O 3a (FOXO3a), B-cell lymphoma-2 interacting mediator of cell death (BIM), and p27 gene; and a **regulator**, sirtuin 1 (SIRT1). The studies found that cells that are under stress have high mRNA expressions for inhibitors and low mRNA for activators, explaining how these stressed cells have lower proliferation.

When these stressed cells (under prolonged high glucose environment), are illuminated with low intensity red light, they start to restore the levels of mRNA to recover the respective correct level of genetic activity for proliferation. See Figure 4. Thus red light of low intensity over a certain period of time has the uncanny ability to restore dysfunctional cell condition. This is reflected as a healing process, which can be recognized in the healing of wounds, alleviating pain, cellular rejuvenation, or in a more systemic sense, overcoming numerous ailments and diseases.

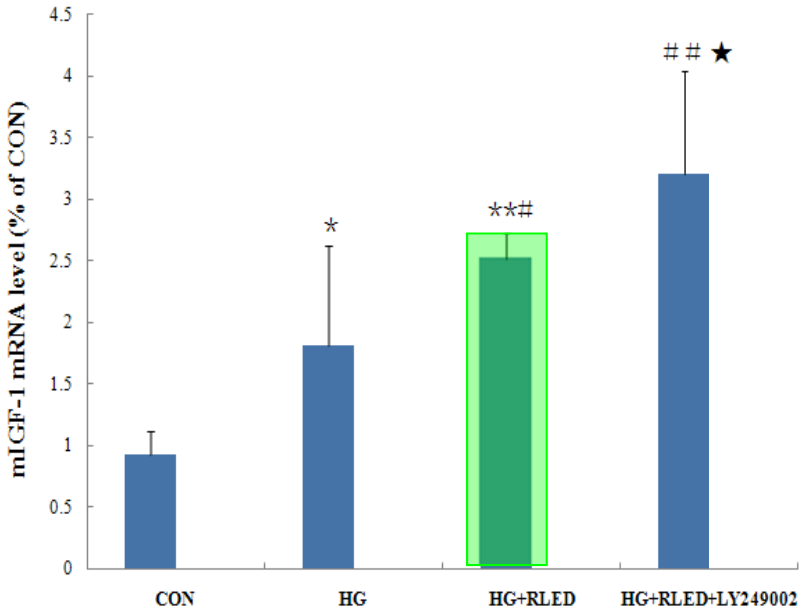
Figure 4 – RLED effects on proteins at 72 hours



The RLED at 640 nm and 0.035 mW/cm2 on protein mRNA. ＊(P < 0.05), ＊＊(P＜0.01) against nG.# (P＜0.05), # # (P＜0.01); against hG; NS: No significance.

The potent proliferation activator, IGF-1 seems to thrive in glucose and to thrive even further with the input of photobiomodulation. The infusion of a potent control inhibitor, LY294002 does not appear to have significant impact on reducing IGf-1 expression. See Figure 5.

Figure 5 – RLED effects on IGF-1 mRNA at 72 hours

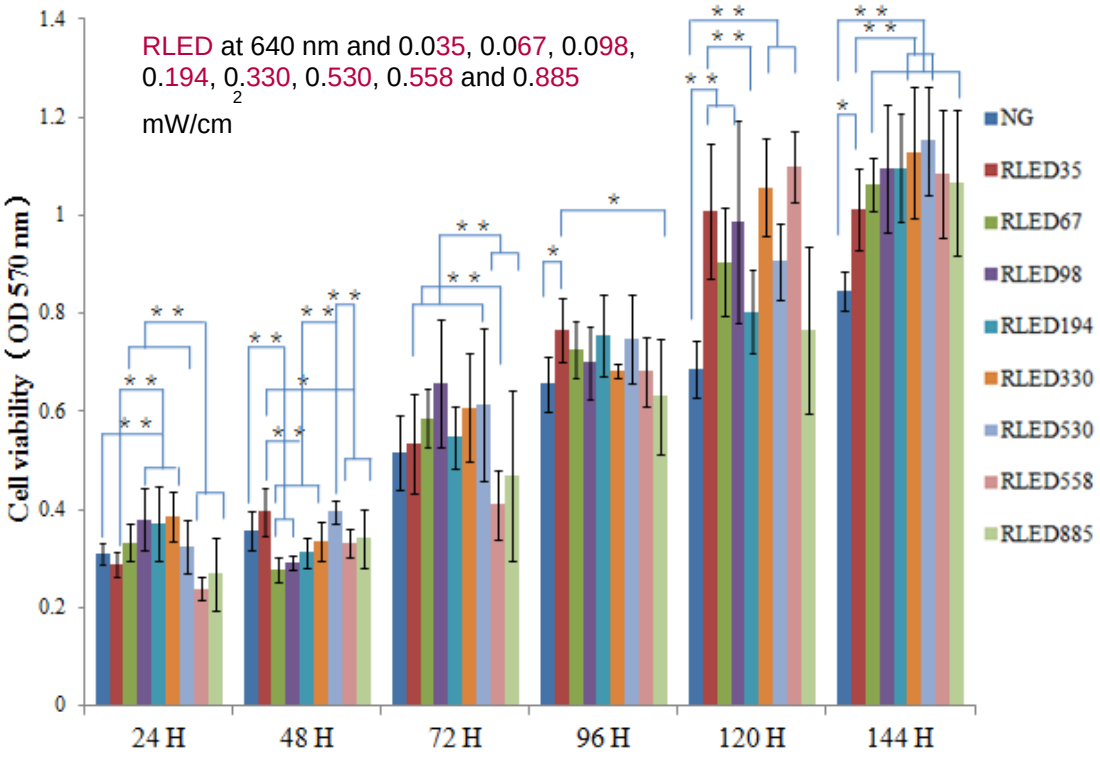


The RLED at 640 nm and 0.035 mW/cm2 on IGF-1 mRNA ＊(P < 0.05), ＊＊(P＜0.01) against nG; ＃ (P＜0.05), ＃＃ (P＜0.01) against hG

Enhancement of normal cell functions

What may be surprising is that when normal cells in normal level glucose solution are exposed to low intensity red light, the proliferation continues. It gets into the mode when homeostasis that is specific to proliferation is achieved (proliferation-specific homesostasis or “PISH”). See Figure 6. In the body there are other regulatory components to limit overactive proliferation. For example compromised inhibitor BIM needs to have mutated myc gene present to produce aggressive malignancies.

Figure 6 – RLED effects on PISH in normal glucose

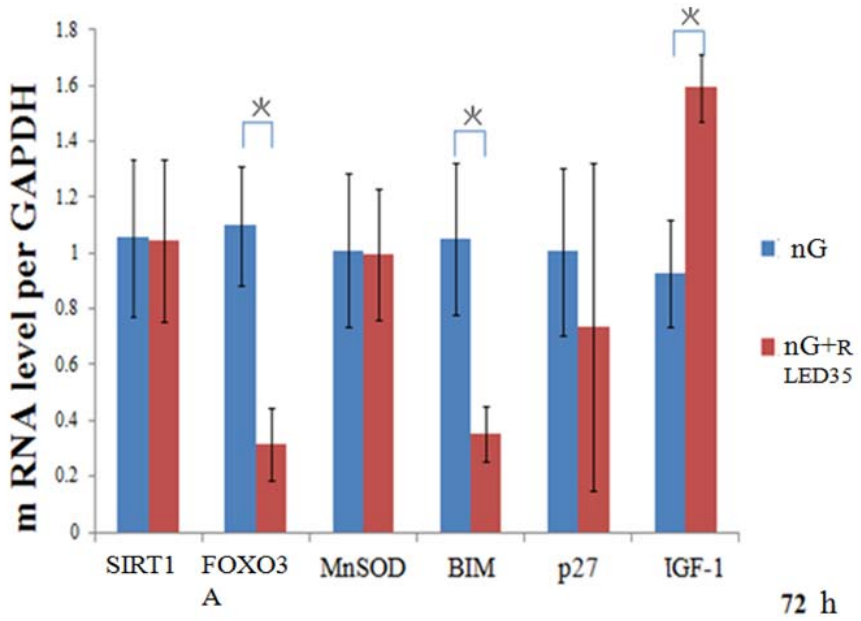


＊(P < 0.05), ＊＊(P＜0.01) against nG

Figure 7 below is telling. The mRNA of inhibitor genes for non-stressed cells in normal glucose respond to photobiomodulation in a similar manner to stressed cells. Low intesity red light limits the activity of the mRNA for inhibitor FOXO 3a, BIM and p27 genes. There were no significant change in the expression of mRNA for the activator gene mSOD as well as SIRT 1. On the other hand, activator IGF-1 responded strongly to photobiomodulation.

In layman's terms, photobiomodulation supports cellular proliferation by limiting the genetic activities that put the brakes on it. In addition, it opens the gates for the activities and put on the accelerator.

Figure 7 – Effects of RLED at 640 nm and 0.035 mW/cm2 on protein mRNA



＊(P < 0.05), ＊＊(P＜0.01) against nG

Conclusion

Assuming that the findings from the investigations, carried out on cultured cells, are largely representative of what happens inside the body, we may conclude that irradiation by low intensity red light can restore both the originall condition of stressed cells as well as enhance the functions of normal cells. This implies that photobiomodulation can be both a potent healing modality of a dysfunctional condition, and an enhancer of what may already seem to be a healthy condition. It is probably unrealistic to expect photobiomodulation to turn us all into super humans. However, there seem to be potential to use photobiomodulation to improve any exising health condition, which could eventually contribute to longevity.