Red Light Interactions and Photorejuvenation

1. What is Photorejuvenation? Photorejuvenation is the process of improving the appearance of skin through the application of light. The process includes the formation of new collagen and a smoothing or evening-out of superficial pigmentation.

New collagen formation is provided by a stimulation of the collagen production of existing fibroblasts, and an increase in the number of fibroblasts (proliferation)

The results of new collagen formation are an increased skin tone and a reduction in the appearance of fine lines or wrinkles. Photoaged skin is described as skin where the collagen is damaged by breakage of collagen strands, and as a result the skin loses its elastic properties and may tend to sag. New collagen production can help to "tie" together these loose strands and reduce the sag caused by the broken collagen strands. The new collagen acts as a filler to lift the surface of the skin.

2. How does Red Light cause Photorejuvenation? The ability of red light to produce new collagen and assist in wound healing has been known since the 1980's when the properties of HeNe lasers were studied in connection with wound healing. Eventually the experiences with HeNe lasers were expanded to LED's and other incoherent light sources but the general field became known as LLLT (Low Level Light Therapy). There are hundreds of published papers of LLLT showing the benefits of increased collagen production and healing benefits of red light.

There are three main hypothesis behind the mechanisms of red light therapy. First is the PDT model which explains most of the benefits. Endogenous porphyrins in the cells absorb red light and become photoactivated. These photoactivated porphyrins create singlet oxygen which can act to signal MAPK and JNK nuclear transcription pathways. The production of reactive oxygen species (ROS) reduces the amount of glutathione in the fibroblasts and this signals the cell to produce collagen. Reduced amounts of glutathione have been shown to be the signal for collagen production as pointed out below.

The following excerpt is from "Glutathione regulates transforming growth factor-β-stimulated collagen production in fibroblasts" in *Am J Physiol Lung Cell Mol Physiol* 286: L121-L128, 2004. First published September 5, 2003; doi:10.1152/ajplung.00231.2003
1040-0605/04 (weblink to article is (**http://ajplung.physiology.org/cgi/content/full/286/1/L121**)

"In this study, we showed that TGFβ decreased the intracellular GSH content in murine embryo fibroblasts (NIH 3T3), which was followed by an increase in collagen I mRNA content and collagen protein production. Prevention of GSH depletion with N-acetylcysteine (NAC), GSH, or GSH ester abrogated TGF-β-stimulated collagen production, whereas a decrease in intracellular GSH content with L-buthionine-S,R-sulfoximine, an inhibitor of de novo GSH synthesis, enhanced TGF-β-stimulated collagen production. These results suggest that GSH depletion induced by TGF-β may mediate

TGF-β-stimulated collagen production. In addition, we showed that TGF-β stimulated superoxide production and increased release of H_2O_2 from the cells, whereas GSH ester decreased basal and TGF-β + glucose oxidase-stimulated H_2O_2 release. H_2O_2, exogenously added or continuously generated by glucose oxidase, enhanced TGF-β-stimulated collagen production, whereas suppression of superoxide production by diphenyliodonium, an NAD(P)H oxidase inhibitor, blocked TGF-β-stimulated collagen production. These data further suggest that reactive oxygen species are involved in TGF-β-stimulated collagen production and that the effect of GSH depletion on TGF-β-stimulated collagen production may be mediated by facilitating reactive oxygen species signaling."

We can see from this and other published research papers that TGF-beta, which is a powerful collagen induction molecule, works to initiate collagen production by creating ROS and depleting glutathione. We perform the similar signaling effect with red light by creating ROS by the phorpyrin photosensitization with red light, and the ROS deplete the glutathione.

Another mechanism has been set forth by Karu postulating that cytochrome oxidase in the electron transport chain absorbs the red light (610 nm –618 nm) and this absorption creates a more efficient conversion scheme for producing ATP in the cell. Increased ATP production has been linked to cellular proliferation. The mechanism may be the displacement of nitric oxide from the cytochrome oxidase. Nitric oxide (from mitochondrial nitric oxide synthase) acts as a competitive inhibitor of oxygen to the electron transport chain, and in effect blocks ATP production. Studies have shown that red light can activate the cytochrome oxidase and displace the nitric oxide leaving the electron transport chain open to oxygen coupling and increased ATP production.