

Research Shows LumiPhase-R Stimulates Collagen and Improves Elastin / Fibronectin

By Bob Kronemyer, Associate Editor

The science of light emitting diode (LED) has taken a leap forward, thanks to the LumiPhase-R system from OPUSMED (Montreal, Canada). New research by the company indicates that MMP-2 (matrix metalloproteinase-2) is a formidable marker for additional dermal matrix degrading enzyme activity.

“Our research represents a new frontier for LED because we’re going beyond collagen metabolism. We are proving that with MMP-2 we can influence extracellular matrix components like elastin and fibronectin,” said Daniel Barolet, M.D., a dermatologist and the chief scientific officer at OPUSMED. “In the past, we showed that collagen type I secretion was increased by LED therapy, but now we are going a step beyond. Our strong *in vitro* model demonstrates we are able to influence other extracellular matrix compo-

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nents. Even though elastin and fibronectin are small players in the extracellular matrix compared to collagen, we now know they are positively influenced by our LED therapy.”

In addition, the LumiPhase-R restores the cellular integrity of aged and photoaged fibroblasts, enabling them to regain their full potential and basal metabolic collagen secretion level. “The goal of such a therapy is to reverse the constantly declining collagen production level over time and bring it back to basal level,” Dr. Barolet said. Patients typically schedule 12 sessions (twice a week) with the LumiPhase-R. “However, maintenance therapy is the key in keeping the best overall skin appearance,” Dr. Barolet stressed.

LumiPhase-R’s collagen-producing and anti-inflammatory effects counteract skin damage. The device’s photoinduction capability also downregulates MMP gene expression. “MMP activity plays a key role in dermal extracellular matrix turnover,” Dr. Barolet explained. “MMPs are a large family of proteolytic

enzymes, which are involved in the degradation of many different components of the extracellular matrix.” MMPs have been classified into different groups, including collagenases, gelatinases and stromelysins. “There is increasing evidence indicating that individual MMPs play an important role in aging skin,” Dr. Barolet said.

Controlled degradation of extracellular matrix is essential for the homeostasis of the dermis. “Recent evidence suggests that this homeostasis is out of balance in aging and photoaged skin,” Dr. Barolet noted. “Downregulation of MMP gene expression combined with upregulation of procollagen production is a key component for successful anti-aging photoinduction by the LumiPhase-R.”

MMP-2 or Gelatinase-A is able to degrade elastin, fibronectin, type IV collagen and gelatins, but shows no activity against laminin or interstitial collagens. “These enzymes are thought to act in conjunction with the collagenases to cause the complete degradation of interstitial collagens,” said Dr. Barolet. Gelatinase-A is widely expressed in adult tissues and is constitutively expressed in many connective tissue cells with poor regulation by growth factors.

However, induction of MMP expression by agonists requires transduction of a signal from the extracellular space to the MMP genes. “This is achieved by the agonist binding to cell membrane receptors, and in some cases to cytoplasmic receptors,” Dr. Barolet noted. “There can also be activation of cellular tyrosine kinase signal transduction cascades, transcription factor activation and induction of MMP transcription. Conversely, downregulation of MMP gene expression is triggered by LumiPhase-R treatments.”

For proof of concept on the possible mechanism of action of the LED system on MMP-2 activity,



LumiPhase-R

Photo courtesy of Daniel Barolet, M.D.

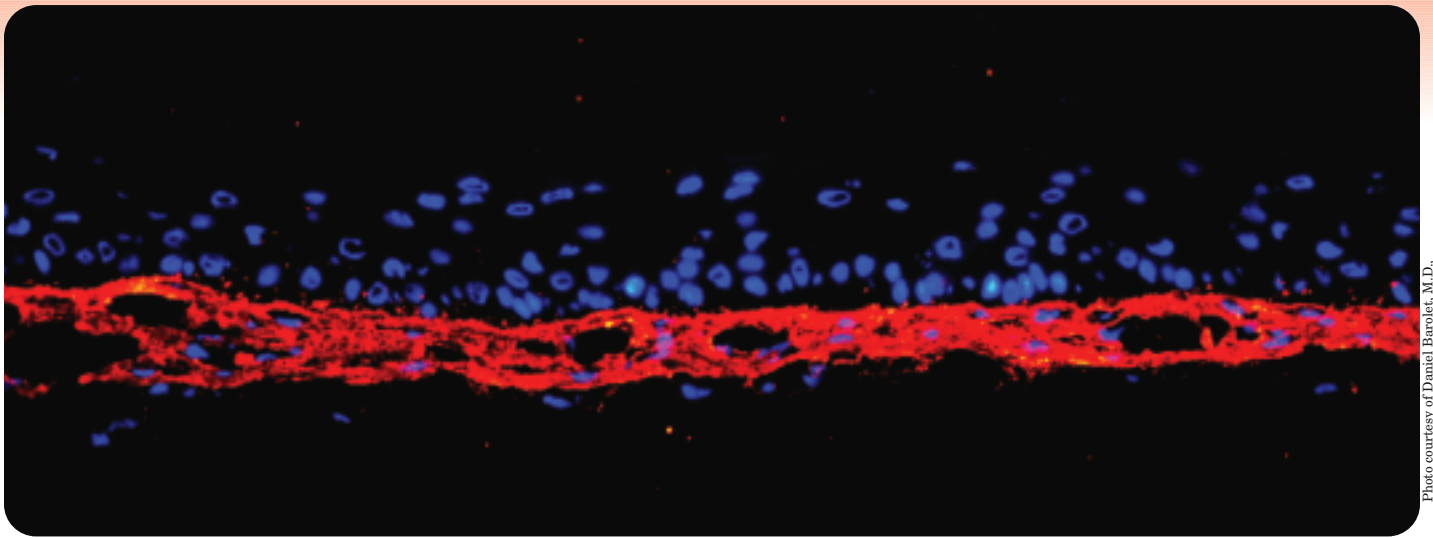


Photo courtesy of Daniel Barolet, M.D.

OPUSMED used highly sophisticated human reconstructed skin in an *in vitro* model. “This advanced technology available in our laboratory was initially developed to produce skin replacement for severely burnt patients,” Dr. Barolet conveyed. “The technology goes beyond available observations using human fibroblast-monolayers, as both human epidermis and dermis are readily available for analysis.” This innovative model also allows for periodic measurements during a one to two month treatment protocol. “Whereas procollagen production is enhanced by 40% with the model, MMP-2 is decreased proportionally as previously shown for MMP-1,” Dr. Barolet said. “These findings provide some insights on the reduced degradation of other dermal extracellular matrix components such as elastin and fibronectin.”

The role of photoinduction is another exciting aspect of the LumiPhase-R. This includes enhancement of skin appearance with or without topicals, open wound care (post-ablative treatment such as CO₂ resurfacing), useful adjunct therapy following non-

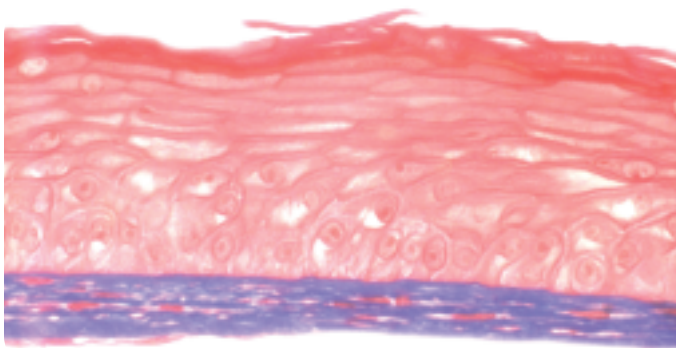


Photo courtesy of Daniel Barolet, M.D.

Human Reconstructed Skin Histopathology emphasizing procollagen type I

ablative thermal treatments, immediate post photo-damage, and wound healing (chronic leg ulcers). Photoinduction might also influence inflammatory status. “Certain skin disorders such as keratosis pilaris rubra (KPR) may improve because the LumiPhase-R also induces anti-inflammatory reactions,” Dr. Barolet said. The results of photodynamic therapy (PDT) and cosmetic PDT can also be enhanced.

The LumiPhase platform will soon offer other treatment capabilities. “A new treatment head will become available in early 2005,” Dr. Barolet said. “Using blue light at 405 nm and high power density, LumiPhase-B is intended for the treatment of inflammatory acne and superficial cosmetic PDT.”

In the near future, Dr. Barolet also expects OPUSMED to introduce ‘photoregulation.’ “This consists of combining the photoinduction of the LumiPhase-R with cosmetic PDT. The aim is to promote the non-cytotoxic or cytomodulatory effects of PDT in the epidermis while regulating extracellular matrix metabolism in the dermis in order to ultimately achieve synergistic anti-aging clinical results. It’s a two-level approach. Ours is the only LED platform that has a high enough power density to both stimulate fibroblast and act as an excellent light source for PDT.”

Dr. Barolet strongly believes that combining PDT with LumiPhase-R treatment provides a unique and extremely powerful two level skin rejuvenation strategy. “The high power LumiPhase-R pulsed-light beam can activate a previously applied photosensitizer as part of PDT, while upregulating dermal fibroblast collagen production and downregulating collagen degradation.”