

## Photoengineering of Tissue Repair in Skeletal and Cardiac Muscles

URI ORON, Ph.D.

### ABSTRACT

This review discusses the application of He-Ne laser irradiation to injured muscles at optimal power densities and optimal timing, which was found to significantly enhance (twofold) muscle regeneration in rats and, even more, in the cold-blooded toads. Multiple and frequent (daily) application of the laser in the toad model was found to be less effective than irradiation on alternate days. It was found that in the ischemia/reperfusion type of injury in the skeletal leg muscles (3 h of ischemia), infrared Ga-Al-As laser irradiation reduced muscle degeneration, increased the cytoprotective heat shock proteins (HSP-70i) content, and produced a twofold increase in total antioxidants. *In vitro* studies on myogenic satellite cells (SC) revealed that phototherapy restored their proliferation. Phototherapy induced mitogen-activated protein kinase/extracellular signal-regulated protein kinase (MAPK/ERK) phosphorylation in these cells, probably by specific receptor phosphorylation. Cell cycle entry and the accumulation of satellite cells around isolated single myofibers cultured *in vitro* was also stimulated by phototherapy. Phototherapy also had beneficial effects on mouse, rat, dog and pig ischemic heart models. In these models, it was found that phototherapy markedly and significantly reduced (50–70%) the scar tissue formed after induction of myocardial infarction (MI). The phototherapeutic effect was associated with reduction of ventricular dilatation, preservation of mitochondria and elevation of HSP-70i and ATP in the infarcted zone. It is concluded that phototherapy using the correct parameters and timing has a markedly beneficial effect on repair processes after injury or ischemia in skeletal and heart muscles. This phenomenon may have clinical applications.

### TISSUE REPAIR IN SKELETAL MUSCLE REGENERATION

#### *Preface*

**U**NDER NORMAL CIRCUMSTANCES, mammalian adult skeletal muscle is a stable tissue with very little turnover of nuclei. However, upon injury, skeletal muscle has the remarkable ability to initiate a rapid and extensive repair process, preventing the loss of muscle mass.<sup>1,2</sup> Skeletal muscle repair is a highly synchronized process involving the activation of various cellular responses. The initial phase of muscle repair is characterized by necrosis of the damaged tissue and activation of an inflammatory response. This phase is rapidly followed by activation of myogenic cells which proliferate, differentiate and fuse, leading to new myofiber formation and reconstitution of a functional contractile apparatus. Activation of adult muscle

satellite cells is a key element in this process. Muscle satellite cell activation resembles embryonic myogenesis in several ways, including the *de novo* induction of the myogenic regulatory factors. Signaling factors released during the regenerating process have been identified, but their functions remain to be fully defined. In addition, recent evidence supports the possible contribution of adult stem cells in the muscle regeneration process. In particular, bone marrow-derived and muscle-derived stem cells contribute to new myofiber formation and to the satellite cell pool after injury.

#### *Enhancement of skeletal muscle regeneration in amphibians and mammals by phototherapy*

The process of skeletal muscle regeneration after injury has been well documented in mammals and to a much lesser extent in amphibians. The effect of phototherapy on the process of