

## Diode laser stimulation prevents Fibroblast-Myofibroblast transition reducing TRPC1 expression: new perspectives for tissue fibrosis treatment

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Fibrosis consists in a excessive and persistent formation of fibrous connective tissue that occurs frequently in different organs or tissues after an injury. The cells principally involved in the onset and progression of fibrosis, are the activated form of the fibroblasts, namely myofibroblasts. Although required for the wound healing and the reparative response to organ/tissue damage, myofibroblast persistence contributes to the increased synthesis and deposition of extracellular matrix proteins, which replace the necrotic or damaged tissue with a scar. In such perspective, identification of treatments capable of preventing myofibroblast generation and defining their molecular targets appears a key step for the design of therapeutic strategies aimed at counteracting fibrosis. On these bases, in the present study, by a morphological, biochemical and electrophysiological approach, we evaluated the effects of a diode laser treatment (635 nm) on the differentiation of NIH3T3 fibroblasts into myofibroblasts. We found that the laser stimulation was able to inhibit TGF- $\beta$ 1-induced fibroblast-myofibroblast transition and modify the myofibroblast resting membrane potential and inwardly rectifying K<sup>+</sup> currents. We also found that the treatment up-regulated metalloprotease (MMP)-2 and -9 expression and downregulated the tissue inhibitors of metalloproteinases (TIMP)1 and -2 in TGF- $\beta$ 1-treated cells. Interestingly, the effects of the laser on fibroblasts involved the Transient Receptor Potential Channel 1 (TRPC-1) functionality. In conclusion, the present study besides offering novel experimental evidence on the mechanisms of action of the diode laser, may provide a promising therapeutic perspective for the treatment of tissue fibrosis extending the potential clinical application of the low level laser therapy.

### Keywords

Diode laser, Low level Laser therapy, fibrosis, myofibroblasts, TGF- $\beta$ /Smad signaling, Transient Receptor Potential Channel 1 (TRPC-1).