

# Enhancement of Topical Small Interfering RNA Delivery and Expression by Low -Fluence Erbium: YAG Laser Pretreatment of skin

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摘要

## Abstract

RNA interference (RNAi) is rapidly becoming an important tool that is advancing research with therapeutic aims. It is necessary to develop efficient ways of guiding small interfering RNA (siRNA) to targeted tissues to induce an RNAi effect. Herein, we report on an active method for delivering macromolecular siRNA and its plasmid vector into the skin, using erbium:YAG (Er:YAG) laser pretreatment. The amount of siRNA transported through nude mouse skin was determined with an in vitro Franz diffusion assembly. Confocal laser scanning microscopy (CLSM) was used to examine the in vivo uptake of siRNA and the vector by the skin. The stratum corneum was partially ablated with the low-fluence laser. The results of in vitro experiments indicated a significant improvement in siRNA permeation with laser exposure, which showed a 2.4- to 10.2-fold increase compared with the nontreated group depending on the fluence used (1.2–1.7J/cm<sup>2</sup>). A photomechanical wave generated by filtering the laser irradiation was sufficient to enhance siRNA permeation by 5-fold. CLSM revealed intense green fluorescence from naked siRNA within the epidermis and upper dermis after laser pretreatment, producing a 3.5-fold enhancement compared with the control. The green signal intensity in 1.7J/cm<sup>2</sup>-treated skin was 4.2-fold higher than that in intact skin after the in vivo topical application of the siRNA expression vector. The increased signal was mainly in the dermis. This noninvasive, precisely controlled technique for siRNA therapy provides an efficient way to deliver siRNA and its vector into the skin.