Erbium:YAG laser-mediated oligonucleotide and DNA delivery via the skin: an animal study

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Abstract

Topical delivery of antisense oligonucleotides (ASOs) and DNA is attractive for treatment of skin disorders. However, this delivery method is limited by the low permeability of the stratum corneum (SC). The objective of this study was to enhance and optimize the skin absorption of gene-based drugs by an erbium:yttrium-aluminum-garnet (Er:YAG) laser. The animal model utilized nude mice. In the in vitro permeation study, the Er:YAG laser treatment produced a 3-30-fold increase in ASO permeation which was dependent on the laser fluence and ASO molecular mass used. The fluorescence microscopic images showed a more-significant localization of a 15-mer ASO in the epidermis and hair follicles after laser application as compared with the control. The expressions of reporter genes coding for beta-galactosidase and green fluorescent protein (GFP) in skin were assessed by X-gal staining and confocal laser scanning microscopy. The SC ablation effect and photomechanical waves produced by the Er:YAG laser resulted in DNA expression being extensively distributed from the epidermis to the subcutis. The GFP expression in 1.4 J/cm2-treated skin was 160-fold higher than that in intact skin. This non-invasive, well-controlled technique of using an Er:YAG laser for gene therapy provides an efficient strategy to deliver ASOs and DNA via the skin.