

Answer 1:

Bibliographic Information

In vivo transdermal delivery of large molecules by pressure-mediated electroincorporation and electroporation: a novel method for drug and gene delivery. Zhang, Lei; Li, Lingna; An, Zili; Hoffman, Robert M.; Hofmann, Gunter A. Genetronics, Inc., 11199 Sorrento Valley Rd., San Diego, USA. Bioelectrochemistry and Bioenergetics (1997), 42(2), 283-292. Publisher: Elsevier, CODEN: BEBEBP ISSN: 0302-4598. Journal written in English. CAN 127:99740 AN 1997:401957 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Successful development of a noninvasive topical-based delivery system of therapeutic agents, with a handy applicator, will allow for targeted and efficient in vivo gene transfer without the potential for adverse events compared with viral methods. It also allows localized drug delivery into the skin without systemic side effects. In recent years there has been an increased interest and challenge in the delivery of macromols. through a thin outermost layer of the skin, the stratum corneum (SC). This layer acts as a significant phys. barrier to drug and gene transfer into the skin. Here the authors report the use of pressure-mediated electroincorporation (PMEI) to deliver Lupron Depot microspheres (2-20 μm) loaded with leuprolide acetate into hairless mouse skin and into human skin xenografted onto immunodeficient nude mice. The authors also demonstrate the ability to transfer the lacZ reporter gene (6.8 kb) into the hairless mouse skin by pressure-mediated electroporation (PMEP). The transfer of macromols. is achieved by pulsed elec. fields and subsequent pressure from caliper-type electrodes on topically applied microspheres or gene constructs. The ratio of efficiency to deliver Lupron Depot microspheres across the SC between pulsing and control is a factor 100 for human skin xenograft. In the case of hairless mice, the ratio is a factor 18. With elec. pulses and post-pulse pressure, the max. depth of lacZ gene expression in the dermis and transfected cells were achieved at 370 μm and 457 cells mm^{-2} , resp. Gene expression was obsd. only in the hair follicles in the case of the control. The applications of the technique could extend to peptides, proteins, oligonucleotides and genes, and open up a new perspective of topical delivery for the treatment of skin diseases.

Answer 2:

Bibliographic Information

Growth inhibition of human prostate tumor cells by an agonist of gonadotropin-releasing hormone. Loop, Stephen M.; Gorder, Christine A.; Lewis, Suzanne M.; Sainers, Joseph H.; Drivdahl, Rolf H.; Ostenson, Richard C. Research Service, Department of Veterans Affairs Medical Center, Tacoma, WA, USA. Prostate (New York, NY, United States) (1995), 26(4), 179-88. CODEN: PRSTDS ISSN: 0270-4137. Journal written in English. CAN 123:1372 AN 1995:594809 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of [D-Leu⁶,des-Gly-NH²¹0,proethylamide⁹]-GnRH, leuprolide, was detd. for the human primary prostate tumor cell line ALVA-31 by in vitro mitogenic assays. Prostate tumor cell proliferation was inhibited up to 50% by leuprolide. Inhibition was not obsd. in parallel cultures treated with other low mol. wt. bioactive peptides. The incorporation and metabolic redn. of testosterone was not affected by concns. of leuprolide that were inhibitory in the mitogenic assay. Specific high-affinity binding of ¹²⁵I-labeled leuprolide was also demonstrated on intact tumor cells with an estd. effective median dose (ED₅₀) of $<1 \times 10^{-9}\text{M}$. Inhibition of prostate tumor growth was further demonstrated in Balb/c athymic intact and castrate male mice bearing ALVA-31 tumor xenografts following chronic administration of leuprolide. These data clearly demonstrate that leuprolide can inhibit the growth of a human prostate carcinoma cell line. Studies conducted in castrate animals further suggest an alternative mechanism of growth inhibition that appears to be independent of the suppression of steroid hormone biosynthesis by LHRH analogs.