Insight Medical Publishing

Nanoscience & Nanotechnology Research

2020

Vol.4 No.2

Nano-Carrier based Remotely Triggered Localized COX-2 Gene Interference by Near Infra Red Laser in Cancer

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Abstract

Gene silencing activity of a specific oncogene transcript to reduce expression of encoded protein by complementary base-pairing mechanism is a potential molecular therapeutic approach. Systemic delivery of therapeutic oligonucleotides (oligos) is one of the major limitations due to lack of stability, poor cellular uptake, degradation and reduced efficacy associated with RNA interference (RNAi) technology. Gene interference therapeutic strategies seek safe and efficient delivery vehicles. Hepatocellular carcinoma (HCC) is the 6th most common cancer worldwide. Abnormally elevated expression of cyclooxygenase-2 (COX-2) has been frequently observed to regulate tumor growth, invasion and metastasis in HCC. Here we have designed, a nano-therapeutic plasmonic carriers comprising gold nanorods (GNRs) which incorporate and release COX-2 interfering conjugated oligos upon illumination with near infrared (NIR) continuous wave (CW) laser (800 nm) at specific intracellular location. HepG2 cells were used to determine cellular uptake and gene silencing activity by GNRs conjugated fluorescence labeled single and double stranded oligos irradiated with NIR laser. Gene knock down was demonstrated and validated by fluorescence repression and western blot analysis. Effect of COX-2 knockdown on downstream molecular pathway was determined. Applying the optimized parameters transfection efficiencies of 78% were achieved in cells using a fluorescent labeled single and double stranded oligos while maintaining a high cell viability of >81%. Dark field microscopy, confocal microscopy and fluorescence microscopy showed significant preferential uptake of nanobiocomposite by the cells. In vitro laser triggered delivery of nanobiocomposite resulted in 81% down regulation of targeted COX-2 protein. Specific inhibition of COX-2 at translation level significantly affects downstream molecular pathway involved in cancer. Our findings emphasize that gold nanoparticle mediated laser transfection provides a potential gene interfering technique with spatial and temporal control, a novel molecular therapeutic approach for cancer treatment.

Biography:

Uzma Azeem Awan received her PhD in Biotechnology (Cancer Nanotheranostics) from University of Azad Jammu and Kashmir, Muzaffarabad, Pakistan. After completing research project as visiting research fellow at Georgia institute of Technology (USA), she was appointed as Research Associate at National Institute of Laser and Optronics (Pakistan). Now she is working as Assistant Professor in department of Biological Sciences, National University of Medical Sciences (NUMS), Pakistan since 3 years. Area of her current research interest lies at the crossroads between medical-biotechnology and advanced materials, in particular, in the fabrication and bioconjugation of metallic nanoparticles along with their biomedical applications such as gene interference, drug delivery and photothermal therapy. She has actively participated in national and international conferences.

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Euroscicon Webinar on Nanotech &Nanobiotechnology 2020 ; August 28, 2020; Webinar

Abstract Citation: Uzma Azeem Awan, *Nano-Carrier based Remotely Triggered Localized COX-2 Gene Interference by Near Infra Red Laser in Cancer*, Nanobiotech 2020, Euroscicon Webinar on Nanotech & Nanobiotechnology 2020; August 28, 2020; Webinar