**Nanotherapy Targeting NF-κB Attenuates Acute Pain After Joint Injury**

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From the Clinical Editor:

**POTENTIAL CLINICAL SIGNIFICANCE**

Post-traumatic osteoarthritis (PTOA) results after injury to joint due to persistent inflammatory response. Patients often complain of pain, which can only be treated at present, with analgesics and anti-inflammatory drugs. The authors here studied the use of a nanoparticle (NP) comprising a peptide, p5RHH complexed to siRNA to suppress NF-κB p65 expression and studied if NF-κB suppression of NF-κB expression would reduce injury-induced joint pain in mice. They showed that p65 suppression lasted at least 21 days, with reduced pain sensitivity. The exciting findings will need to be verified in future clinical studies and hopefully would benefit a large number of suffering patients.
Abstract
Inflammation after joint injury leads to responses that result in eventual osteoarthritis development. Blockade of inflammation, by suppressing NF-kB expression, has been shown to reduce joint injury-induced chondrocyte apoptosis and reactive synovitis in vivo. Herein, we demonstrate that the suppression of NF-kB p65 expression also significantly mitigates the acute pain sensitivity induced by mechanical injury to the joint. These results suggest that early intervention with anti-NF-kB nanotherapy mitigates both structural and pain-related outcomes, which in turn may impact the progression of post-traumatic osteoarthritis.

COMMUNICATIONS

The potential utility of iron oxide nanoparticles for the prophylaxis of skin inflammation in a mouse model of psoriasis

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From the Clinical Editor:

Psoriasis is a common human skin disorder characterized by dry, inflamed and itchy skin. Although autoimmunity has been implicated, the exact mechanism is still incompletely understood. Currently the main therapeutic target has been focused on T cells. Iron oxide-based imaging agent Resovist has been showed to suppress the function of T-cells and one of their cytokines, IL-17, which is also a therapeutic target for psoriasis. In this study, the authors investigated the efficacy of topical application of Feraheme in a mouse model of chemically induced psoriasis. The results showed promise in that there was significant reduction in the total score, hyperkeratosis, and dermatitis and would suggest a potential in the clinical treatment of patients with this condition in the future.

Abstract
Several studies have demonstrated that immunosuppressive effects accompany systemic administration of some iron oxide nanoparticles (IONPs). In our earlier study, conducted using human peripheral blood mononuclear cells, we showed that therapeutic formulation of IONPs, Feraheme, approved for clinical use in the United States for the treatment of iron deficiency in chronic kidney disease, suppresses the function of activated T-cells in vitro via a mechanism involving mitochondrial damage. Here we report an in vivo study demonstrating that topical application of Feraheme prior to disease onset decreases the development of skin lesions in the mouse model of chemically induced psoriasis.

REVIEW

Precision nanomedicine in atherosclerosis therapy: how far are we from reality?

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From the Clinical Editor:

Cardiovascular diseases, mainly atherosclerosis account for nearly half of all deaths in Europe and almost 30% of global deaths. Despite the improved clinical management, cardiovascular mortality is predicted to rise in the next decades due to the increasing impact of e.g., aging, obesity, and diabetes.
Current available therapies deserve improvements and the review describes the emerging field of cardiovascular nanomedicine for selective targeting atherosclerosis and the procedure to perform clinical translation.

Abstract

Atherosclerosis, characterized by the build-up of lipids and chronic inflammation of the arterial wall, is the primary cause of cardiovascular disease and is a leading cause of death worldwide. Currently available therapies are inadequate and warrant the demand for improved technologies for more effective treatment. Although primarily the domain of antitumor therapy, recent advances have shown the considerable potential of nanomedicine to advance atherosclerosis treatment. This review details the arsenal of nanocarriers and molecules available for selective targeting in atherosclerosis and emphasize the challenges in atherosclerosis treatment.

RESEARCH ARTICLE


Simultaneous release of two drugs from polymer nano-implant inhibits recurrence in glioblastoma spheroids

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BASIC RESEARCH

Glioblastoma is the most devastating brain tumor. Despite the use of multimodal treatments, most patients relapse, often due to the highly invasive nature of gliomas. The present study describes a new polymeric brain implant capable for delivering two different drugs in recurrent glioma cells/spheroids which shows an extended duration of tumor recurrence compared to free drug combination.

Abstract

Local implant-based delivery of rationally selected combination of chemotherapeutics has some major advantages for the treatment of glioblastoma such as: (a) 100 % bio-availability locally in brain can be achieved at the tumor site (b) avoid systemic leakage and associated toxicity, and (c) simultaneous inhibition of multiple, mutually exclusive cancer mechanisms is possible. Here, we report a polymeric brain implant capable of delivering two different drugs in recurrent glioma cells. We have selected a combination of clinically used DNA alkylating agent, Temozolomide, and a DNA mismatch repair protein (Ligase IV) inhibitor, SCR-7, and delivered simultaneously into tumor spheroids formed by rat glioma cells, C6. The dual-drug loaded polymeric wafer, prepared by lyophilization method, could deliver both the drugs in a controlled fashion. To test the efficacy of this system, we have optimized an in vitro recurrent model of glioma spheroids wherein, the implant released both the drugs in a sustained fashion, thereby continuously exposing the cells to DNA methylation while inhibiting the DNA repair pathways. This leads to synergistic toxicity and inhibition of tumor recurrence for extended duration compared to free drug combination.