Reducing Posterior Capsule Opacification by Eliminating Myo/Nog Cells Through Targeted Drug Delivery Using 3DNA Nanocarriers and the G8 Antibody

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ABSTRACT

Purpose: Posterior Capsule Opacification (PCO) is a vision impairing disease that occurs in some adults and most children following cataract surgery. In PCO, multifocal fibroblast ingrowths into the posterior cortex and connect to form new lens capsule. In the mouse, these cells are Myo/Nog cells that express the skeletal muscle transcription factor MyoD, the BMP inhibitor Noggin and the G8 protein. As a virtue deletion of Myo/Nog cells in human lens tissue has been achieved by incubating explants with the G8 monoclonal antibody (mAb) and complement. The goal of this study was to test the specificity and efficacy of the G8 mAb compared to 3DNA nanocarriers incubated with Doxorubicin (3DNA-Dox) in explants of human lens tissue and rabbit lens undergoing cataract surgery.

Methods: Anterior human lens tissue obtained by capsulorhexis was cultured in vitro in a keratome. Lens explants were incubated with 3DNA-Dox, G8-Dox or G8-Dna-Dox. Explants were assessed for apoptosis using TUNEL. Rabbits were injected at the time of cataract surgery with either balanced salt solution (BSS) or 3DNA-Dox at doses of 0.01 or 0.14 μg. The rabbits were observed for a period of four weeks for the development of abnormal reactions, including PCO.

RESULTS: 3DNA-Dox reduced PCO compared to BSS.

3DNA-Dox significantly reduced PCO compared to BSS.

3DNA-Dox at 0.01 μg reduced PCO compared to BSS.

3DNA-Dox at 0.14 μg reduced PCO compared to BSS.

INTRODUCTION

3DNA nanocarriers are branched structures built from interconnect monomers of natural or synthetic DNA. The 3DNA monomers are composed of two DNA strands hybridized together with a double stranded “waist” and four single-stranded “arms.” 3DNA is layered by successive annealing of monomer arms. The typical 3DNA-Dox has a diameter of approximately 70nm and the payload can be regulated by the number of DNA molecules that are attached to the arms, including fluorescent reporter, aptamers, antibodies and antibodies. Dynamic cargo can be loaded into the 3DNA-Dox using antibodies. Doxorubicin can be intercalated into the double-stranded regions of the 3DNA.

The purpose of this study was to test an antibody-3DNA-Dox conjugate for specificity and toxicity in vitro and in vivo. To targeting the multifocal fibroblast, naked G8, recognizes a cell surface molecule on multifocal fibroblasts, an antibody Dirhodamine tagged G8 (D8) and an antibody tagged with MyoD factor and the Ionsomes encoymatic protein factor Noggin (Gerhart et al., 2006). G8 cells are widely distributed in the anterior and normal diseased tissues of the adult (Gerhart et al. 2006, 2007, 2012, 2014; Walker et al. 2014). Myo/Nog cells are present in the anterior and equatorial regions of the human lens, the cortex, and ciliary body (Gerhart et al., 2014). In addition to their role as regulators of BMP signaling, Myo/Nog cells develop myofibroblasts. In response to injury (Gerhart et al. 2006, 2011, 2012, 2014; Walker et al. 2015).

REFERENCES