

Chapter 8

Nanotechnology for Omics–Based Ocular Drug Delivery

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ABSTRACT

Millions of people suffer from ocular diseases that impair vision and can lead to blindness. Advances in genomics and proteomics have revealed a number of different molecular markers specific for different ocular diseases, thereby optimizing the processes of drug development and discovery. Nanotechnology can increase the throughput of data obtained in omics-based studies and allows for more sensitive diagnostic techniques as more efficient drug delivery systems. Biocompatible and biodegradable nanomaterials developed through omics-based research are able to target reported molecular markers for different ocular diseases and offer novel alternatives to conventional drug therapy. In this chapter, the authors review the pathophysiology, current genomic and proteomic information, and current nanomaterial-based therapies of four ocular diseases: glaucoma, uveal melanoma, age-related macular degeneration, and diabetic retinopathy. Omics-based research can be used to elucidate specific genes and proteins and develop novel nanomedicine formulations to prevent, halt, or cure ocular diseases at the transcriptional or translational level.

OCULAR DISEASE

Approximately 140 million Americans over the age of 40 suffer from a variety of ocular diseases that impair vision and may lead to blindness (NEI, 2012). The prevalence of ocular disorders will continue to increase with the worldwide aging population. Although current treatments do exist,

there is a need for better diagnostics and more efficient therapies that can arrest the progression and/or even reverse damage of ocular diseases. Currently, more information is needed to understand the pathogenesis of ocular disease as well as determining new drug targets to enhance ocular drug discovery or repositioning current drugs for more efficacious therapy.

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Limitations in Treatment for Ocular Diseases

Currently, therapies exist to delay progression of some ocular diseases; however, a better understanding of pathogenic processes is needed to find more effective treatments. Some of the common ocular diseases presented later in this chapter possess a complex interplay of genetic factors that are challenging to treat. Discovery of genes responsible for ocular disorders can aid in the development of new therapeutic agents. Clinically, we are merely treating symptoms and not targeting the actual disease mechanisms. More research needs to be completed to elucidate these mechanisms.

A number of barriers for ocular drug delivery exist, such as nasolacrimal drainage and the blood-aqueous and blood-retinal barriers. This restricts administration of potential therapeutics. Drug can be delivered by a variety of routes including topical ocular, periocular injection, intravitreal injection, and systemic administration. The topical route is a convenient method of drug delivery to the anterior segment; however, a model of transient diffusion has shown that less than 5% of a lipophilic drug and 0.5% of a hydrophilic drug penetrate the cornea (W. Zhang, Prausnitz, & Edwards, 2004), and the remainder is cleared through nasolacrimal drainage and systemic absorption (Gambhire, Bhalerao, & Singh, 2013). The amount of available drug that permeates across the sclera is reduced with cationic and lipophilic solutes and the RPE has tight intercellular junctions for hydrophilic molecules (Urtti, 2006). Additionally, the lymphatic system, blood vessels and active transporters all work to clear drugs administered through trans-scleral routes. Systemic administration of drugs requires high doses that are potentially toxic to obtain a therapeutic concentration across the blood ocular barriers (Geroski & Edelhauser, 2000; Sigurdsson, Konraethsdottir, Loftsson, & Stefansson, 2007). Intravitreal injections circumvent physiological barriers and maintain

therapeutic doses without damage to bystander tissues; however, frequent injections can lead to complications like retinal detachment, increase in ocular pressure, and hemorrhage (Peyman, Lad, & Moshfeghi, 2009). Given the presence of these physiological barriers, the development of therapies utilizing nanotechnology that efficiently deliver drugs and extend drug release to the eye would be beneficial to the progression of ocular disease treatment. Due to the lengthy pipeline in gaining FDA approval, newly repositioned drugs can be utilized to expand current disease therapy.

Omics-Based Nanotechnology

The goal of omics-based nanotechnology is to use nanoscale technology to enhance early detection, gain an understanding of pathophysiology, as well as find better treatments for eye disease. Nanogenomics refers to a new approach for medical diagnostics and therapy (Nicolini, 2006). Nanoproteomics allows us to evaluate expression of ocular proteins, identify novel therapeutic targets study the pharmacological effects of therapeutics (Steely & Clark, 2000). These new techniques can improve the current understanding of ocular diseases and aid in the discovery of therapies targeting genes responsible for ocular disease.

APPLICATION TO OCULAR DISEASES

Glaucoma

Pathophysiology

Glaucoma causes blindness in about 7 million people every year, only 10% of the people affected by glaucoma worldwide (Quigley, 1996). A number of risk factors have been identified for glaucoma, including hypertension, family history, and age, among others (Abbot F Clark & Thomas Yorio, 2003). Glaucoma is caused by progressive

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