To develop an infrared light-inducible lipid nanoparticle (LNP)-based mRNA gene therapy vector

研製一個紅線光控制的脂質納米體 mRNA 基因治療載體

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Research Background

Gene therapy is a novel treatment method to rescue or complement the disease phenotype caused by gene defects and abnormalities via introducing correct genetic materials (DNA for most cases) into patients' cells to produce normal gene products. Gene therapy mainly targets serious diseases without small molecule drugs and is also a kind of personalized medicine. Because of the high cost, time investment, and failure rate of gene therapy development, only a few gene therapies have been approved globally for the treatment of rare genetic diseases, and the pricy treatment expense is not affordable for ordinary people. Over time, gene therapy will fill the gap of conventional small molecule drugs and become the mainstream of human disease treatments in the future. The critical technology of gene therapy is the delivery of genetic materials to the target cell, a.k.a. the function of the vector. So far, viral and non-viral vectors are commonly used as gene therapy vectors in preclinical and clinical trials. Viral vectors are genetically engineered viruses, usually adenoviruses, adeno-associated viruses, retroviruses, lentiviruses, etc. High transfection efficiency is the common advantage of the viral vector. Viruses have evolved the characteristics of effectively invading host cells and self-replicating in large quantities. Some viral vectors also have unique advantages, such as the low immunogenicity of adenoassociated virus and the permanent transfection of hematopoietic stem cells by lentivirus. By the end of 2021, all the gene therapies that have been approved for marketing using viral vectors show that viral vectors are at the forefront of the development of gene therapy. The application of non-viral vector is later than viral vector and is still in the initial stage of development. There is no approved non-viral vector gene therapy yet, but it is believed that there will be more applications in pre-clinical and clinical settings in the future.

Research Objectives

Our previous work has focused on photoregulated chemical modification methods for the photodynamic therapy of anticancer drugs. The characteristics of the eyeball make

it an outstanding organ for photodynamic therapy. This project aims to combine photodynamic therapy and mRNA gene therapy vectors, screen for photosensitive lipids, synthesize LNPs that can be induced and released by infrared light, and test them in cells and live animals to find more effective mRNA delivery techniques. And finally, the efficacy and safety of photosensitive LNP-mRNA will be tested in models of multiple ophthalmic diseases.