Stabilization of Plasmid DNA and Lipid-Based Therapeutics as Dehydrated Formulations

Marion dC. Molina, Nicole M. Payton and Thomas J. Anchordoquy

Introduction

Over the last decade, gene therapy has regained more attention as a promising strategy in providing opportunities for the development of novel nucleic acid-based therapeutics (e.g., DNA) for disorders that need to correct or replace the responsible defective gene(s). Indeed, the discovery of the RNA interference (RNAi) mechanism in mammalian cells revolutionized even more the field of gene therapy [1]. Since the first clinical gene-therapy trial was reported by Rosenberg and collaborators in 1990 [2], over 1900 protocols have been approved worldwide as therapeutic interventions against a wide variety of diseases [3, 4]. Diseases such as cancer, infectious diseases, muscular dystrophy, hemophilia, cystic fibrosis, and many others have been the focus of broad research and clinical activity [4–9]. In fact, private- and public-sector resources have been widely dedicated to these efforts [10–12]. There is a consensus, however, that the success of gene therapies will highly depend on the efficacy and safety of the delivery vector, of either viral or nonviral origin [13]. Significant gains in this field have principally resulted from studies involving viral vectors which are highly efficient at transferring genes (see cited reviews, [14–16]). Although the majority of clinical protocols to date involve viral vectors (~67%, [3, 4]) as major gene therapy vehicles, their use still poses significant safety concerns as a result of previous adverse events due to potent immunogenicity [17] and insertional mutagenesis [18, 19]. Based on these outcomes, viral-based gene therapy has recently seen a clear decline. For instance, the use of retroviral vectors in clinical protocols has decreased from 28% in 2004 [20] to 19.2% in 2014 [3]. The aforementioned disadvantages have prompted the emergence of nonviral alternatives. Nonviral vectors are indeed considered simpler, potentially safer for clinical use, and more amenable to large-

M. dC. Molina (✉)
Independent Pharmaceutical Consultant, 36 Cutler Drive, Ashland, 01721 MA, USA
e-mail: mdc.molina@gmail.com

N. M. Payton · T. J. Anchordoquy
School of Pharmacy, University of Colorado Denver, Aurora, 80045 CO, USA

D. Varshney, M. Singh (eds.), *Lyophilized Biologics and Vaccines,*
DOI 10.1007/978-1-4939-2383-0_10