



## Polysaccharide gene transfection agents ☆

Wahid Khan<sup>a</sup>, Hossein Hosseinkhani<sup>b</sup>, Diana Ickowicz<sup>a</sup>, Po-Da Hong<sup>b</sup>, Da-Shyong Yu<sup>c</sup>,  
Abraham J. Domb<sup>a,\*</sup>

<sup>a</sup> Institute of Drug Research, School of Pharmacy, Faculty of Medicine, Center for Nanoscience and Nanotechnology and The Alex Grass Center for Drug Design and Synthesis, The Hebrew University of Jerusalem 91120, Israel

<sup>b</sup> Graduate Institute of Biomedical Engineering, National Taiwan University of Science and Technology (TAIWAN TECH), Taipei 10607, Taiwan

<sup>c</sup> Nanomedicine Research Center, National Defense Medical Center, Taipei 10607, Taiwan

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### ABSTRACT

Gene delivery is a promising technique that involves in vitro or in vivo introduction of exogenous genes into cells for experimental and therapeutic purposes. Successful gene delivery depends on the development of effective and safe delivery vectors. Two main delivery systems, viral and non-viral gene carriers, are currently deployed for gene therapy. While most current gene therapy clinical trials are based on viral approaches, non-viral gene medicines have also emerged as potentially safe and effective for the treatment of a wide variety of genetic and acquired diseases. Non-viral technologies consist of plasmid-based expression systems containing a gene associated with the synthetic gene delivery vector. Polysaccharides compile a large family of heterogenic sequences of monomers with various applications and several advantages as gene delivery agents. This chapter, compiles the recent progress in polysaccharide based gene delivery, it also provides an overview and recent developments of polysaccharide employed for in vitro and in vivo delivery of therapeutically important nucleotides, e.g. plasmid DNA and small interfering RNA.

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## 1. Introduction

Gene therapy involves the insertion of a therapeutic gene into cells, followed by expression and the production of the required proteins. It is a promising approach for the treatment or prevention of a wide range of diseases associated with defective gene expression [1,2]. The fundamental idea is to deliver the gene to cells or tissues. This may be by activation, silencing, introduction or gene knock out and knock down, both in vitro and in vivo [3]. Successful gene therapies depend on the efficient delivery of the genetic material into the cell nucleus and its effective expression within these cells. DNA can be delivered into the cell nucleus either using physical means or by specific carriers that carry the genes into the cells. A number of techniques have been developed for DNA delivery, including direct introduction of the transgene using cell electroporation, microinjection of DNA and incorporation of the gene by vectors [4]. Successful gene therapy depends on the development of effective and secure delivery vectors [5]. The genetic material involves DNA, RNA, antisense oligonucleotide, decoy DNA and/or ribozymes. The idea underlying gene therapy is that

human disease can be treated by the transfer of genetic material into specific cells of a patient rather than by conventional drugs; however, it has yet to make its mark in medicine. Successful implementation of gene transfer in the clinic will require the coordinated development of a variety of new technologies and the establishment of unique interactions between investigators from divergent medical and basic science disciplines.

Vectors for delivering genes can be divided into two main groups: (a) viral carriers, where the DNA to be delivered is inserted into a virus, and (b) cationic molecular carriers, which form electrostatic interactions with DNA for delivering gene to cells, and include polymers and lipids [6]. Viral vectors include retroviruses, adenoviruses and adeno-associated viruses. These are effectively used for introducing genetic material into host cells, but immunogenicity, inflammatory effects and safety concerns with the use of such viruses restrict their usefulness [7]. Non-viral vectors have several advantages over viral vectors since they are chemically based materials. They do not integrate into chromosomes, have low immunogenicity, the ability to deliver large genes and no infective risk, are less expensive and easy to handle, and, most importantly, have the potential for large-scale production at a reasonable cost [8].

Recently, significant concerns have focused on non-viral vectors. Such vectors must overcome many barriers, such as low efficiency in delivery to target cells, escape from endosomes,

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\* Corresponding author. Tel.: +972 26757573; fax: +972 26757076.

E-mail address: [avid@ekmd.huji.ac.il](mailto:avid@ekmd.huji.ac.il) (A.J. Domb).