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Critical Reviews in Oncology/Hematology 89 (2014) 352–357

CRITICAL REVIEWS IN
Oncology
Hematology
Incorporating Geriatric Oncology

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The research of nanoparticles as gene vector for tumor gene therapy

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Accepted 2 October 2013

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Abstract

With the development of molecular biology, the application of the gene therapy becomes a tendency in the development of oncotherapy. The gene therapy has been acknowledged as the major progress of modern medicine, also a focus in the oncotherapy research. Commonly vectors of the gene therapy mainly include two categories, namely, viral vectors and nonviral vectors. Nanoparticles gene vector of various different kinds of materials, which belong to non-viral carriers. It presents excellent abilities of adsorption, concentration and protection of DNA, which can be attributed as a main reason of the adsorption and operation of nano-gene vector on exogenous genes. In this article, we mainly reviewed the recent studies of the characteristics of nanoparticles, characteristics and transport mechanism of nanoparticles as gene vector, the progress on nanoparticles as gene vector in tumor gene therapy. Nano-gene vectors, as new drug and gene carriers, present characteristics such as the controlled-release, targeting, and the improvement of bioavailability. Nanoparticles for cancer imaging and therapy have evolved rapidly during the last decade and it is expected that more and more will become clinical practise. In the near future, as a new nanometer gene delivery vector will be in medical research and treatment play a bigger role.

Keywords: Nanoparticles; Gene vectors; Transfection efficiency; Tumor

1. Introduction

Nowadays, the incidence and mortality of tumors increases year by year, which seriously threatens human health. Conventional operations can remove the tumor lesion but remnants of the cancer cells still cause tumor recurrence and metastasis. Meanwhile, clinical applications of radiotherapy and chemotherapy are much limited due to serious toxic and side effect as well as their drug resistance [1]. In recent years, with the development of molecular biology, the application of the gene therapy to completely remove the lesion and to avoid the serious overall toxic and side effect becomes a tendency in the development of oncotherapy.

The gene therapy has been acknowledged as the major progress of modern medicine, also a focus in the oncotherapy research. The trigger of successful gene therapies is the gene delivery pattern. In order to distribute plasmid DNA in

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http://dx.doi.org/10.1016/j.critrevonc.2013.10.006

certain nucleuses and to insert that in specific DNA sites, it is crucial to select a proper gene delivery system. For years, numerous scholars have conducted substantial research in the gene therapy of tumors. Yet, so far, as restricted by many factors, the gene therapy did not achieve ideal effects. It will still be a difficult problem to address in the gene therapy that how the transfection efficiency of gene can be improved, so that target gene can be delivered to the target sites of the organism efficiently, targeted and showing no toxic and side effects [2]. Thus, the treatment effects from the molecular level can be achieved.

2. Types, materials and mechanism of nanoparticle gene vector

Currently, vectors of the gene therapy mainly include two categories, namely, viral vectors and nonviral vectors [3,4]. Although viral gene vectors with the representatives of retrovirus and adenoviral vector have high transfection efficiency, the preparations of these vectors are complex, showing immunogenicity, serious potential risks and failure of repeated applications in human body and other defects [5,6]. Thus, these cannot be used as satisfactory gene vectors. Meanwhile, for nonviral vectors, artificially synthesized non-bioactive materials are used to deliver nucleic acid materials into cells, which have presented advantages such as low toxicity, low immunoreactions and the excellent ability of being chemical modified. Yet, these vectors show relatively low transfection efficiency [7,8].

Nano-gene vector refers to nanocapsules or nanoparticles usually produced from biocompatible materials, which are able to form nano-vector gene complexes through wrapping or adsorbing nucleic acid molecules such as exogenous DNA. The size of nano-vector was generally between 10 and 100 nm. Due to the chemical activity produced from the huge specific surface area, it presents excellent abilities of adsorption, concentration and protection of DNA, which can be attributed as a main reason of the adsorption and operation of nano-gene vector on exogenous genes [9,10]. Materials of nano-gene vector are divided into two categories, namely, organic materials and inorganic materials. Organic materials mainly indicate polymers, including dendrimers, cationic liposomes, PLGA and chitosan; inorganic nanomaterials present advantages such as stability, good dispersion, convenient preparation, sufficiently controllable partical size, large loading capacity, no immunogenicity and insignificant cytotoxicity. Inorganic nanomaterials tend to realize the coupling of specific molecules on the surface so as to achieve targeted delivery and improve the transfection efficiency. Inorganic materials mainly include silica, iron oxide and gold nanoparticle and so on [11–15]. The advantages and disadvantages of various gene nanoparticle carrier as shown in Table 1.

Nano-gene vector can combine and concentrate DNA and RNA, effectively introducing the combined or concentrated products into a variety of cells. Through the interaction between phospholipid and glycoprotein with negative charge on the cations and cell membrane on its surface, nano-gene vector enters the cytoplasm, and a positive correlation between the amount of cations and the transfer rate of genes can be observed [16]. Nanoparticles can be integrated with DNA to form complexes. The coupling between nano-vector and DNA molecules can be integrated through static electricity and chemical bonds. The integration can effectively protect the exogenous DNA that will be combined with nanoparticles from the digestion of various enzymes [17]. Thus, the transfection efficiency will be improved. The main mechanism of the entrance of complex into cells is endocytosis. Meanwhile, specific molecules are coupled on the surface of nanoparticles such as specific antibodies or monoclonal antibodies etc., and bonded with specific receptors on the cell surface through target molecules. Under the effect of receptor-mediation, genes enter cells, and target gene transfection can be achieved safely and effectively. Nanoparticles can mediate DNA integration on chromosomal genome of nucleuses, so as to obtain the stable expression of exogenous genes.

Table 1
Type, advantages and disadvantages of gene vector.

Vector type	Advantages	Disadvantages	Representative materials
Viral vector	High transfection efficiency	The preparation of complex The immunogenicity Unable applied repeatedly	Retroviruses; adenovirus
Biological particles nanometer carrier	Biological affinity Good targeted	Low transfection efficiency Prone to immune response	Liposomes; protein
Polymer nanoparticle Carrier	Good biodegradation Good biocompatibility	Occasional cytotoxicity Low transfection efficiency Need to surface modification	PLGA; chitosan; gelatin
Magnetic metal nanoparticle carrier	The simply preparation Specific binding Small toxic and side effects Largely used	Reunion phenomenon Need surface modification Less load	Magnetic iron oxide; nano gold