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Viral vectors for gene delivery in tissue engineering☆

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Abstract

The goal of tissue engineering is the production of functional, biocompatible tissues by seeding cells within biological or synthetic scaffolds. One tissue engineering approach involves the genetic modification of cells that are seeded onto (or into) scaffolds prior to implantation. The genetic modification is achieved through gene delivery, with can utilize viral transduction or non-viral transfection systems. Although novel non-viral systems have continued to emerge as innovative vehicles for controlled gene delivery, viruses remain the most efficient means by which exogenous genes can be introduced into and expressed by mammalian cells. Retrovirus, adenovirus, adeno-associated virus and herpes virus are widely studied viral gene transfer systems and have attracted the most attention in the field of transduction. This review thoroughly discusses the genomic structures of each virus type, along with the advantages and disadvantages of their use in tissue engineering applications.

Keywords: Tissue engineering; Gene delivery; Retrovirus; Adenovirus; Adeno-associated virus; Herpes virus; Baculovirus

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1. Introduction

Broadly defined, tissue engineering is a biotechnology that is used to develop biological materials for tissue repair, reconstruction, regeneration, or replacement [1]. The goal of tissue engineering is to create functional, biocompatible tissues, typically through the seeding of cells onto scaffolds that are of either biological or synthetic origin. Tissue engineering research holds great potential for treating trauma, burns, degenerative diseases, and other maladies that produce tissue or organ failures [2].

With the rapid development of modern gene transfer technologies, damaged cells or tissues can be repaired through somatic gene delivery and expression. Various gene-delivery strategies can be used to transfer genes of interest into damaged tissues (i.e. systemic and local delivery). Systemic delivery involves the injection of vector/DNA complexes into the bloodstream, thus distributing the complexes to tissues throughout the body. This approach is often required when the target tissue cannot be reached directly. However, this method is often characterized by a low specificity of gene expression, and a large vector concentration that is required to achieve therapeutic effects. The lack of specificity may influence and damage the function of normal healthy tissues, and the high titer of delivery complexes could carry immunologic or toxicity concerns. In addition, the lack of blood supply to various tissues (such as cartilage or meniscus) makes systemic delivery inappropriate for many musculoskeletal system injuries [1].

Local gene delivery includes in vivo, in vitro, and ex vivo strategies. In vivo methods often involve the direct injection of vector/DNA complex into the host tissue. While this method is relatively straightforward, it is associated with health risks stemming from a lack of control over the resulting gene expression. In vitro and ex vivo strategies involve growing cells in culture, during which gene delivery can take place alone or in conjunction with the delivery of growth factors, differentiation signals, or other chemical or physical alterations to the culture environment prior to transplantation into patients (in the case of ex vivo). The transplanted cells can be delivered either directly, in an encapsulated form, or as tissues comprised of cells seeded into scaffolds. Because host immune or inflammatory responses to viral particles, or toxic effects from transfection reagents, are reduced through the use of in vitro or ex vivo gene delivery, patient safety is often improved with the use of these methods [3].

One important aspect of gene therapy is the ability to deliver nucleic acids to cells of various tissues. Due to rapid clearance and nuclease degradation by the mononuclear phagocyte system, efficient “naked” DNA delivery has yielded little success and is feasible in only select tissues such as muscle [4]. Because of this limitation, the development of efficient delivery systems is critical to successful gene transfer. In general, gene delivery systems can be divided into two categories: non-viral transfection systems and viral transduction systems. Non-viral gene delivery includes chemical and