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Annals of Experimental Biology, 2022, 10 (3): 50-51

(http://www.scholarsresearchlibrary.com)

ISSN:2348-1935

Gene Therapy for Acute Lung Injury Based On Non-Viral Vector Delivery

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***Received:** 10-May-022, Manuscript no. AEB-22-81450; **Editor assigned:** 12-May-2022, Pre QC no. AEB-22-81450 (PQ); **Reviewed:** 16-May-2022, QC no AEB-22- 81450 (Q); **Revised:** 20-May-2022, Manuscript no. AEB-22- 81450 (R); **Published:** 26 -May-2022*

ABSTRACT

Acute lung damage is one of the most common types of serious sickness, and despite its high death rate and rapid progression, there is presently no clinically effective treatment for it. The significance of gene therapy in acute lung injury has grown over time as our understanding of the disease's pathological mechanism has deepened. Gene therapy for acute lung injury now focuses mostly on improving alveolar fluid clearance, reducing pro-inflammatory response, and mending lung barrier. Viral and non-viral vectors are currently used as gene delivery vehicles. Though less efficient than viral vectors, non-viral delivery technologies have the advantages of being less immunogenic, more affordable, and easier to mass-produce. There has been a great deal of research into non-viral delivery systems for gene therapy, including those based on lipids, dendrimers, polymers, graphene, and other inorganic nanoparticles. Exosomes and cells have been suggested as an alternative as a possible delivery technique employed by nature to convey genes into the lungs. The review quickly covers the development of gene therapy using non-viral vectors for the treatment of acute lung damage. The difficulties and possibilities that lie ahead for putting this approach into clinical practice are examined in order to give a full view on gene therapy of acute lung damage.

Keywords: Acute Lung Injury, Vector

INTRODUCTION

Damage to the alveolar epithelial and pulmonary vascular endothelial cells known as Acute Lung Injury (ALI) is brought on by infection, trauma, shock, and exposure to toxic gases. Inflammatory cell infiltration, pro-inflammatory factor release, increased pulmonary microvascular permeability, ventilation/blood flow imbalance, and impaired lung compliance are some of the pathological characteristics of ALI. Clinical manifestations of ALI frequently include respiratory discomfort, edema in the lung parenchyma and alveoli, and refractory hypoxemia. If this illness is not properly treated, it can lead to the Development Of Multiple Organ Dysfunction Syndromes (MODS) and Acute Respiratory Distress Syndrome (ARDS), which pose a serious threat to human health and have a fatality rate of 30%-50%. Even if a patient survives ALI, lung function damage will lower their quality of life, increase the financial and emotional strain on their loved ones, and increase the overall cost of healthcare.

Over the past few decades, gene therapy has advanced significantly and developed quickly. Traditional viral vectors and conventional nonviral vectors have been replaced by biomimetic nano-delivery vectors, such as cell-based and exosome-based carriers, in the field of gene delivery. The current research shows promising results, and the developed gene delivery system can reduce pulmonary fibrosis, improve endothelial cell function, repair the damaged barrier, and inhibit the inflammatory response, among other symptoms of ALI. Gene-based therapy still faces many difficulties even though it is becoming increasingly important in the treatment of ALI.

First off, gene transfection's effectiveness is still far from ideal. The microenvironment and inflammatory response brought on by ALI may further lessen the efficacy of gene transfection. Second, the respiratory tract and alveolar surface have defense mechanisms including mucus that operate as a physiological barrier to gene delivery and gene transfection. Thirdly, the process of gene expression in vivo may be unpredictable and the delivery and transfection of genes lack selectivity. Finally, gene therapy is made

much more difficult by ALI, a complicated pathophysiological process involving multiple signaling channels.

Although there are many families and targets to pick from (inflammation, edema clearance, barrier, etc.), the optimization of the gene delivery mechanism continues to be the fundamental hurdle to effective gene therapy. Novel target genes and gene delivery vectors are essential to enhancing the clinical efficacy of gene therapy for ALI. A delivery method that expresses therapeutic levels of the related substance and has great biocompatibility and low toxicity is on the horizon. A promising treatment strategy for target genes is RNA interference (RNAi), which has the potential to stop the progression of lung disease and even undo past harm.

RNA interference therapy strategies including long double-stranded RNA (dsRNA), short-interfering RNA, micro RNA (miRNA), short hairpin RNA (shRNA), and piwi-interacting RNA (piRNA) are receiving a lot of attention since they have the potential to therapeutically silence any gene of interest. Different viral vectors and non-viral chemical/physical strategies have been developed to address some of these challenges in terms of delivery mechanism, but none have been shown to be a magic bullet resolving all of the issues. However, both the science of gene delivery and our understanding of the illness have evolved significantly in recent years. Non-viral vectors are now used to carry genes more frequently due to the immune response to viruses. Though less efficient than viral vectors, non-viral delivery technologies have the advantages of being less immunogenic, more affordable, and easier to mass-produce. Exosomes, which are nanosized delivery vehicles used by nature to carry genes into the lungs, have been proposed as an alternative. Purification techniques, however, represent a significant barrier to exosome-mediated delivery. Cell-based gene therapy is an appealing strategy because it can combine the actions of cells and genes synergistically. Cell survival after transplantation remains a significant challenge. It is hoped that ALI treatment plans will be both secure and effective.

Hybrid nanocarriers, which combine the advantages of various carriers into a single vector, seem to be the most efficient delivery method as a result. Additionally, the delivery of genes and ALI treatments may be possible using biomimetic nanoparticles made from red blood cells, white blood cells, platelets, and epithelial cells, which have been extensively studied in oncology. In conclusion, it is anticipated that future gene-based therapies for ALI will be both secure and effective.