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Review

Stem cell therapy for lung diseases: From fundamental aspects to clinical applications

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Abstract: The respiratory system is a complex group of organs in the human body, all of which are necessary in breathing. Due to its special anatomy and composition, after exposure to various damaging factors such as micro particles, carbon granules and toxic gases, the respiratory system can be affected by a variety of damage without return to its original state. Currently, the prevalence of lung diseases, including asthma, and chronic obstructive pulmonary diseases, such as emphysema, has increased remarkably. New therapeutic approaches are desperately needed to discover regenerative medicine approaches, especially cell therapy. This review summarizes the recent advances in stem cell treatments and the research efforts conducted through the application of stem cell therapy for respiratory system diseases. In particular, researchers have used animal models to gather data about treating lung injury by stem cell transplantation. This review concentrated on the findings about route, timing and adjustment of cell transplantation dose, optimum stem cell type selection and potency marker of cells as therapeutic agents. These factors are essential subjects for approval and clinical transplantation. The current clinical trials aiming at treatment of lung diseases by stem cells are mentioned and discussed.

Key words: Stem cell Therapy; Lung diseases; Respiratory system.

Introduction

Respiratory disease is a medical term that covers pathological conditions affecting the tissues and organs responsible for gas exchange in the body, and involves conditions of the nose, nasal cavity, pharynx, larynx, trachea, lungs, bronchi, bronchioles, alveoli and the nerves and muscles of breathing (1). Respiratory diseases range from mild and insignificant diseases, such as the common cold, to dangerous diseases, such as bacterial pneumonia, pulmonary embolism and, in their final stages, more complex illnesses such as acute asthma or lung cancer (2). Respiratory diseases impose a remarkable global healthcare burden. Current data show that 235 million people have asthma, at least 200 million suffer from chronic obstructive pulmonary disease (COPD), 65 million struggle with moderate-to-severe COPD, and more than 50 million people endure occupational lung diseases. At least 1 billion people suffer from chronic respiratory conditions and more than 2 billion people are threatened by toxic effects of biomass fuel consumption. In addition, 1 billion are living in outdoor polluted air and 1 billion have contact with tobacco smoke. Four million people die annually from chronic respiratory disease before reaching mature ages. COPD is the fourth leading cause of death worldwide. Lung cancer

is considered the most deadly cancer in the world, causing death in more than 1.4 million people annually, and the number of cases is growing (3). Epidemiological data on respiratory diseases are very limited in the WHO's Eastern Mediterranean Region, including Iran. Both acute and chronic lung injuries involve different kinds of symptoms, ranging from mild and reversible changes, such as allergies, to severe and irreversible problems, such as asthma, fibrosis and chronic obstructive diseases. In most diseases affecting the airways, the epithelial linings of the airway are found to be at risk of irreversible damages that cannot naturally be repaired. Currently, lung transplantation and surgery are the standard treatment approaches (4,5). In many type of dysfunctions, the prolonged use of bronchodilators is effective, if the terminal airways or bronchioles have malfunctioned or are damaged. Long-term bronchodilator therapy can lead to major problems and safety concerns regarding these patients, and there is an urgent demand for a new therapeutic strategy to overcome these issues (6). Transplantation is hindered by a shortage of organ donors and severe surgical, technical and immunological complications, which urge innovative therapeutic approaches (7). One approach is grafting cell populations capable to regenerate and replace damaged lung and airway epithelia. Recently, the use of cell therapy to