

# Stem cells and lung injury

## Abstract

The patho-physiological pattern of acute lung injury is a complex phenomenon. The recent progress in research shows the evidence that the stem cells may exhibit their trans-differentiation in organs including lung. This development in stem cell biology related to acute lung injury has opened a lot of challenges and appreciation related to the development of therapeutic strategies for this disease. It is found that mesenchymal stem cell helps in strengthening the immune response to lessen the effect of this disease. Stem cells present within the organ found to play important role in regenerating the cells. Hence these cells have innumerable strength in curbing this disease. However very little is known about the actual molecular mechanism played by the stem cells and studies are need to be addressed before the knowing the therapeutic potential of stem cells for ALI.

**Keywords:** acute lung injury, stem cell, extracellular matrix

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**Abbreviations:** ALI, acute lung injury; AII, alveolar type ii cells; ECM, extracellular matrix; MSC, mesenchymal stem cells; BM-MSC, bone marrow derived mesenchymal stem cells; LPS, lip polysaccharide; UC-MSC, umbilical cord-mesenchymal stem cells

## Introduction

The complex underlying mechanism for repair, proliferation, differentiation and remodeling after injury is a massive phenomenon in acute lung injury and their progression.<sup>1</sup> The recent progress in research shows the evidence that the stem cells may exhibit their trans-differentiation in organs including lung. The well established archetype of lung adult stem cells explored the knowledge about transient amplification of cell progeny.<sup>2</sup> Especially the lung is consisting of persistent tissue incorporated with infrequently proliferating epithelial, interstitial and endothelial cell populations.<sup>2</sup> There is a scarcity of classical stem cell hierarchy for these kinds of essential tissues.<sup>2</sup> It is known that some differentiated mature epithelial cells and de-novo epithelial progenitors may also exhibit their role in repair mechanism.<sup>2</sup> The therapeutic target is the biggest problem to cure acute lung injury (ALI) at the molecular level, in this regards the researchers finding some important evidence to bring down the normal mechanism by treating with the stem cell therapeutics. This promising evidence may resemble their effective intervention against the progression of injury in the lung and promoting effect to develop as fibrosis. Our review explains about some important biomarkers role in lung injury and the effective stem cell therapies against the harmful biomarkers.

## Stem cell therapies for lung injury

The ALI is primarily initiated by inflammatory cell migration and their deposition in the alveolar epithelial cells, which is then, triggers the impairment of fibrinolytic system during the progression.<sup>3</sup> Studies shows that the role of pro-inflammatory and anti-inflammatory cytokines are very important for repair mechanism, but the abnormal function of this biomarkers may results in the apoptosis of alveolar epithelial cells and progressive deposition of extracellular matrix (ECM) in the lung tissues.<sup>4</sup> The recent and advanced targeting therapies have failed to regulate the progression

of this injury and mortality among those patients. The stem cell therapy is a developing area of intervention to control the disease by treating with specific stem cell markers to an individual. The in vivo experiment on mouse model showed that the administration of human umbilical cord-mesenchymal stem cells (UC-MSCs) results in the modulation of inflammatory markers for the survival of the epithelial cell.<sup>5</sup> The mesenchymal stem cells (MSCs) demonstrated the potential therapy in lung diseases.<sup>5,6</sup> These MSCs may collect from the umbilical cord (UC), adipose tissue, bone marrow, skeletal muscle and other tissues. The bone marrow derived stem cells (BM-MSCs) are capable of resolving the lipopolysaccharide (LPS)-induced lung injury.<sup>7</sup> Compared to these models, the human umbilical cord-derived mesenchymal epithelial cells are the better choice for clinical applications due to the availability, cell viability and high paracrine capability to accelerate the repair process.<sup>8-12</sup>

## Human umbilical cord-mesenchymal stem cells (uc-mscs) as a therapy to regulate the inflammatory related changes during lung injury

The illustrated models explained that the LPS-induced lung injury can be targeted through the intratracheal injection of UC-MSCs, which is involved in the reduction of inflammation in mice. The UCMSCs secretes some soluble factors, in particular, IL-6, IL-13 and PGE2 may play an important role in the therapeutic properties of UC-MSCs for ALI.<sup>13,14</sup> The mobilization of BM-MSCs in the circulation could regulate the LPS exposure, BM-MSCs has the capacity to accumulate within the inflammatory site and undergoes differentiation to generate epithelial and endothelial-like phenotype cells.<sup>13,14</sup> UC-MSCs may act on ALI through the anti-inflammatory, anti-apoptotic, immunomodulatory property and angiogenesis.<sup>15,16</sup> BM-MSCs also have the ability to attenuate the IL-10 in LPS-induced RAW264.7 cell and mice. The IL-10 plays a sequential role in the suppression of LPS-induced ALI by diminishing the induction of pro-inflammation and chemokines, which lowers the activation of NF- $\kappa$ B and mast-cell to down-regulate the pathways generating the oxidative stress to the lung cells.<sup>17</sup>

## Conclusion

Literature suggest that current treatment for ALI is only through ventilation<sup>18,19</sup> and therefore studies are required in delineating several molecular mechanism in stem cell biology thereby identifying a valuable biomarker for developing the stem cell as a therapeutic module in ALI. In the recent times most of the studies in stem cell research are concentrated on soluble factor such as anti-inflammatory cytokines and growth factors.<sup>18,19</sup> Though there are lots of limitations, the future research in the field of stem cell should continue and focus on delineating the basic mechanisms responsible for the regulation of ALI should progress and this may finally show stem cells as a future therapeutic potential.

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## Conflict of interest

The author declares no conflict of interest.

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