ABSTRACT

Annisa Ismatul Jannah. 24020221130040. **Enhancement of Cell Regeneration with Co-Culture Therapy of Human Wharton's Jelly Mesenchymal Stem Cell in Acute Lung Injury Models.** Under the guidance of Anto Budiharjo and Wireni Ayuningtyas.

Acute Lung Injury (ALI) is a mild form of Acute Respiratory Distress Syndrome (ARDS) which is characterized by damage to the epithelial barrier that interferes with gas exchange and surfactant production. ALI has a high mortality rate, while the currently available treatments are not effective enough. This study aims to create an *in-vitro* ALI model using A549 human alveolar epithelial cells induced with lipopolysaccharide (LPS) 2.5 mg/mL and scratch treatment, as well as to evaluate the effectiveness of various therapies as candidates for new drug development for ALI. The therapies tested consisted of hWJ-MSC secretome (with or without TGF-β, PDGF, and HGF), EPC secretome (with or without atorvastatin), arterial secretome with HGF, co-culture hWJ-MSC (with or without TGF-β and PDGF), and atorvastatin. Evaluation of the effectiveness of therapy was carried out through morphological observation, proliferation assays, and measurement of inflammatory markers of IL-8 and angiogenin using flow cytometry. The ALI model is indicated by a decrease in the number and morphological changes of A549 cells, which indicates inflammation and damage to cells.. Co-culture therapy (with or without TGF-β and PDGF) showed an increase in cell number and improvement in cell morphology. Meanwhile, in the scratch model, EPC secretome therapy showed similar results, namely an increase in the number of cells and an improvement in morphology. The EPC secretome treatment also produced the highest angiogenin and the lowest IL-8 levels in both models, exhibiting regenerative and anti-inflammatory activity. This study showed that *in-vitro* ALI modeling on LPS-induced and scratch-induced A549 cells successfully presented ALI conditions. Secretome-based therapy of EPC origin, as well as co-culture (with or without TGF-β and PDGF) show significant potential for further development as a new treatment candidate for Acute Lung Injury (ALI).

Keywords: Acute Lung Injury (ALI), A549 cells, lipopolysaccharides, scratch, secretome, co-culture, IL-8, angiogenin