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Hypoxia preconditioned mesenchymal stem cells significantly ameliorate lung injury in an elastase-induced emphysema animal model

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Chronic obstructive pulmonary disease (COPD) is a progressive disease that makes patients hard to breathe. Lung emphysema is caused by inflammatory response, oxidative stress or endothelial cell apoptosis and is a smoking-related disease. Mesenchymal stem cell (MSC)-based cell therapy is a novel approach with great therapeutic potentials for the treatment of lung diseases. Despite demonstration of MSC grafting, the populations of engrafted MSCs have been shown to decrease dramatically 24 hours post-transplantation due to exposure to harsh microenvironments. Hypoxia is known to induce expression of cytoprotective genes and also secretion of anti-inflammatory, anti-apoptotic and anti-fibrotic factors. Hence, hypoxic preconditioning is thought to enhance the therapeutic potency and duration of survival of engrafted MSCs. In this study, we aimed to prolong the duration of survival of engrafted MSCs and to enhance the effectiveness of emphysema transplantation therapy by the use of hypoxia-preconditioned MSCs (HP-MSCs). Our results showed that compared to MSCs, the cyto-protective genes, such as *Bcl-2*, *CAT, HO-1, HGF* and *VEGF* in HMSCs have significant increased, the conditioned medium of HMSCs have enhanced the cell viability of elastase treated murine lung type II epithelial cells (MLE-12). Furthermore, intratracheal instillation of HP-MSCs into elastase-induced emphysema mouse model at day 14, the pulmonary respiratory function have shown significant improvement for up to 30 days of HP-MSCs treatment. Expression of inflammatory factors IL-1β, IL-6, protease, and elastin were all down-regulated in the lung tissues of the treated mice. Moreover, the histopathologic examination indicated significant amelioration of lung damages. In conclusion, we demonstrated that HP-MSCs significant improve the therapeutic effect of the emphysema. This study should improve our understanding of the protective effect of engraftment HP-MSCs in lung injury model. Furthermore, this novel approach may lead a new avenue of therapy for COPD.

Biography

Kowit-Yu Chong has completed his PhD from Southern Illinois University, School of Medicine and Post-doctoral studies from Oregan Primate Research Center. He is an Associate Professor at Chang Gung University, Taoyuan City, Taiwan. He has published more than 40 papers in reputed journals.

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