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Pulmonary Hypertension and Venous Thrombo-embolic Disease

APELIN-13 CO-TREATMENT WITH UMBILICAL CORD BLOOD-DERIVED MESENCHYMAL STEM CELLS IMPROVES ENGRAFTED CELL SURVIVAL AND INHIBITS MACROPHAGE ACTIVATION IN PULMONARY ARTERIAL HYPERTENSION MURINE MODEL

Poster Contributions
Poster Hall, Hall C
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Session Title: Understanding Pulmonary Vascular Disease: From Bench to Bedside
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Background: Mesenchymal stem cell (MSC)-treatment has shown clinical benefits in various diseases, however the poor viability of engrafted MSC limits therapeutic potential. Apelin-13 is a potent inotropic agent that, when administered in conjunction with MSCs treatment, improves survival and therapeutic efficacy of MSC in a murine model with peripheral arterial disease. We hypothesized that co-treatment of human umbilical cord blood-derived MSC (hUCB-MSC) with apelin-13 improves hUCB-MSC survival with a greater protective effect on PAH.

Methods: At 3 days post-injection, engrafted MSC survival in lungs was examined by measuring the mRNA level of two human MSC markers, *CD44,* and *CD90*. Two weeks after hUCB-MSC treatment, (1) RV hemodynamics was determined by echocardiography, (2) pulmonary arterial media wall thickness and fibrosis by histological assessment, and (3) genes related to macrophage activation by quantitative real-time PCR.

Results: *CD44* and *CD90* mRNA levels in lungs of co-treatment group was significantly higher than in single treatment groups. Although co-treatment did not improve the ability of hUCB-MSC to prevent RV dysfunction, arterial medial artery wall thickness, and fibrosis, it significantly decreased mRNA level of *Cd11c* and *Cd206,* markers for macrophage activation, and *Cd80*, a marker for pro-inflammatory type I macrophage (T1M). In contrast, co-treatment significantly increased mRNA level of arginase I, a marker for anti-inflammatory type 2 macrophage (T2M).

Conclusion: We report that co-treatment of apelin-13 with hUCB-MSCs improves the survival of hUCB-MSCs in lungs of PAH rat model, and also improves the ability of hUCB-MSCs to suppress macrophage activation by reduction of T1M and induction of T2M levels. Our data suggests that co-treatment of apelin-13 with hUCB-MSC protects engrafted cells from macrophage-mediated inflammation.