Conclusion: Circulating CD16+ Mo increase in response to CLI with upregulation of leukocyte adhesion markers. These cells are preferentially retained within ischemic muscle and promote robust limb salvage in experimental HLI. Our first in man study shows that the cells remain viable in ischemic tissue. Isolation of sufficient numbers of these cells for delivery into ischemic muscle may provide a more effective cell therapy for CLI.

SINGLE-CELL MATRIX-SUPPLEMENTED HYDROGEL COCOONING OF ENDOTHELIAL PROGENITOR CELLS IMPROVES RETENTION AND THERAPEUTIC EFFICACY IN PULMONARY ARTERIAL HYPERTENSION

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Background: Late outgrowth (L) endothelial progenitor cells (EPC) represent a uniform, highly endothelial-like progenitor cell population; however, their therapeutic benefits in models of pulmonary arterial hypertension (PAH) are limited by poor cell persistence, due to rapid cell loss by apoptosis (anoikis) and redistribution to non-target organs. Temporary microencapsulation (i.e. co-cocooning) provides a portable stem cell niche, that can promote cell survival and retention in animal models of organ lung and heart injury.

Hypothesis: We hypothesize that microencapsulation of L-EPC with an agarose hydrogel supplemented with integrin-binding proteins will increase survival and retention of L-EPCs injected into the jugular vein and result in greater therapeutic benefits compared to non-cocooned L-EPCs injected into a rat monocrotaline (MCT) model of PAH.

Methods: L-EPCs were encapsulated by vortex-emulsion using various concentrations of agarose, together with fibronectin and fibrinogen, and capsule size and initial cell viability were assessed. Encapsulated and non-encapsulated L-EPCs were transduced with luciferase and administered to SD rats three days after injection of MCT. L-EPCs were tracked after injection of MCT. L-EPCs were tracked in vivo by bioluminescence imaging (BLI) to assess cell persistence and biodistribution for up to 3 weeks post cell injection. At end-study, right ventricular systolic pressure (RVSP) and right ventricular hypertrophy (RVH) were assessed for therapeutic efficacy.

Results: The initial BLI signals at 15 mins after delivery were similar in non-cocooned and cocooned L-EPCs, however, only cocooned cells could be detected by BLI after 4 and 24 hours (28 ± 12% and 12 ± 8% of baseline signal, respectively; p < 0.0001 and 0.05, n = 11), Figure 1. Microencapsulation of L-EPCs led to significant improvement in RVSP 3 weeks after delivery compared to MCT alone (56 ± 24 vs. 80 ± 7 mmHg, respectively; p < 0.05), whereas no improvement in pulmonary hemodynamics was seen with delivery of non-encapsulated cells.

Conclusions: These results demonstrate that single-cell cocooning can significantly increase retention of L-EPCs within the lungs. Furthermore, even a modest increase in L-EPC persistence over 24 hours can provide an important therapeutic benefit, not seen with non-encapsulated L-EPCs in the rat MCT model of PAH.