BIOMATERIAL INCORPORATED HUMAN MESENCHYMAL STEM CELL SECRETOME FOR CARDIAC REGENERATION

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The therapeutic effect of stem cell transplants for heart disease is now attributed to the pro-regenerative microenvironment created through secreted bioactive molecules such as growth factors (GF), cytokines, and extracellular vesicles known collectively as the secretome. Mesenchymal stem cell (MSC)-derived factors have been shown to protect the heart against hypertrophy or promote synchronous contraction.[1,2] To address the short duration of secretome activity, we aimed to incorporate it into a biomaterial for sustained release and enhanced cardiac regeneration.

To produce bone marrow-derived human MSC secretome, cells were cultured for 48 hours in low serum media under three different conditions: 2D and 3D normoxia (2D and 3D), and 2D hypoxia (Hyp.). A human cytokine array was carried out to determine the cytokines and GF levels, selected factors were quantified by ELISA. The secretome activity was tested on human cardiac fibroblasts (hCFb) before encapsulation: we synthesised poly(lactic-co-glycolic acid) (PLGA) nanoparticles, using the water-oil-water emulsion method.

Several factors and cytokines such as angiogenin, VEGF, IL-6 and IL-8 were detected. ELISA analysis indicates that there was no difference in the levels of IL-6 between the secretomes, however higher levels of VEGF were detected in the secretome obtained by hypoxia. In cellular studies all three secretomes showed no cytotoxicity, the 2D and Hyp. secretomes showed the greatest proliferation of hCFbs over 7 days. Based on these results, we are currently attempting to encapsulate the secretome in PLGA nanoparticles.

References

[1] Zhu, D. et al. Nat. Commun. 12, (2021).

[2] Zou, Y. et al. ACS Appl Mater Interfaces 13, 56892–56908 (2021).

Figures

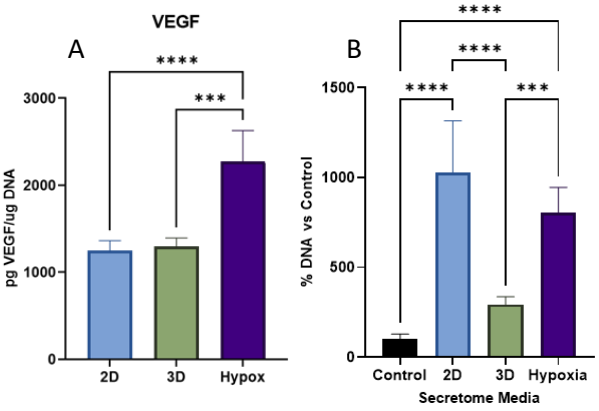

Figure 1. A) Results of the ELISA analysis of human VEGF production under different growth conditions, normalized to hMSC DNA, and **B)** Picogreen DNA analysis of the proliferation of hCFbs treated with 0.5x secretome media for 7 days.