Angiogenic potential of adipose derived stem cells compared to the stromal vascular fraction

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INTRODUCTION: The success of tissue engineered grafts relies on a functional blood supply developing following implantation. Adipose tissue is a rich source of adipose derived stem cells (ADSC) which can be collected from patients easily and safely. Adipose tissue also contains the stromal vascular fraction (SVF), a heterogeneous mix of cells including blood cells, endothelial cells, stromal cells and ADSC. Both ADSC and SVF have been shown to improve angiogenesis however very few studies have directly compared these two cell populations. Our aim is to determine the pro-angiogenic properties of ADSC and SVF for use in tissue engineered grafts.

METHODS: SVF and ADSC were isolated from subcutaneous fat (ethics approval 15/YH/0177) using mechanical and enzymatic digestion. ADSC were purified from the SVF by adherence to plastic and both ADSC and SVF were characterised using flow cytometry markers (eBioscience). 5 x10^5 SVF cells or ADSC were cultured in 0.77mg/ml Collagen I (rat tail) gels and viability was measured by resazurin assay. Conditioned media from the gels was collected and a cytokine array was performed to quantify the release of proteins involved in angiogenesis.

RESULTS: ADSC and SVF were successfully isolated from adipose tissue. ADSC from 3 different patients were CD31-, CD34-, CD45-, CD73+, CD90+, CD105+ and CD146- while the SVF contained a heterogeneous cell population in line with previous findings (1). SVF and ADSC cultured in collagen gels remained viable for 7 day in culture. Gels containing ADSC contracted by 40% compared to control gels without cells; however contraction was not observed for gels containing SVF. After 24 hours in culture, conditioned media from gels containing ADSC and SVF showed release of pro-inflammatory cytokines including GRO, IL6, IL8, PDGF and VEGF-D (Fig 1). Gels containing SVF cells also released EGF, PLGF and VEGF-A. A similar pattern of expression was observed after 4 days in culture (Fig 2).

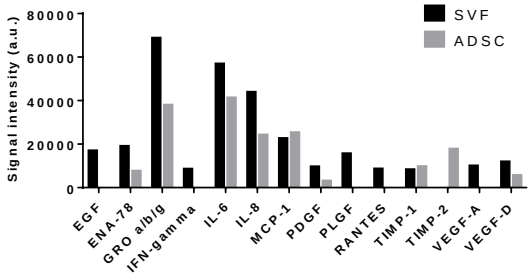

Fig. 1: Cytokine release from collagen gels containing SVF and ADSC after 24 hours in culture.

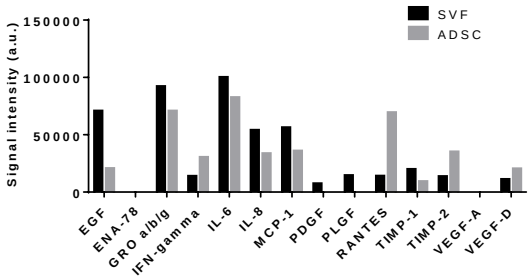

Fig 2: Cytokine release from collagen gels containing SVF and ADSC after 4 days in culture.

DISCUSSION & CONCLUSIONS: Collagen gels containing SVF cells released higher or equal levels of pro-angiogenic cytokines when compared to gels containing ADSC, with the exception of TIMP2 and RANTES. The levels of TIMP2 and RANTES may, in part, explain the increased contraction observed in these gels. In conclusion we have demonstrated SVF cells, which can be harvested with less manipulation compared to ADSC, may be an attractive alternative to ADSC for tissue engineered grafts and that both cell types are capable of sustained cytokine release.

REFERENCES: (1) P. Bourin (2013) *Cytotherapy* **15(6)**: 641–648.

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