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THERE'S MORE TO FAT THAN STEM CELLS, CHARACTERISING FAT GRAFT MATERIALS TO UNDERSTAND THE REGENERATIVE PROPERTIES OF ADIPOSE TISSUES

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The discovery of adipose derived stromal cells (ADSCs) in 2001 led to an explosion of studies investigating their potential in a range of clinical applications. In parallel, plastic surgeons developed novel techniques following observations that fat grafting can not only restore volume but can also improve tissue repair and regeneration (1.). At present we have limited understanding of how adipose tissue processing affects biological function of injected tissues, which is urgently needed to optimise clinical fat grafting techniques. This study aimed to fully characterise lipoaspirate and formulations of adipose tissues (FAT); bridging the gap between in vitro ADSC studies and clinical fat grafting results.

Adipose tissue collected from consenting patients (NHS ethics 15/YH/0177) was processed to produce four different FAT, namely: lipoaspirate, emulsified fat (or ''nanofat''), lipocondensate (condensed SVF, with lipid removed) and cultured ADSCs. We observed lipoaspirate, emulsified fat and lipocondensate all retained some of the microstructure of adipose tissues with intact adipocytes and evidence of blood vessels. Via cytokine array analysis, adipose tissues secreted more chemokine signals compared to ADSCs while all samples secreted factors involved in extracellular matrix regulation. Functional assays demonstrated conditioned medium from adipose tissue but not cultured ADSCs were able to inhibit myofibroblast differentiation.

This study provides important data on the composition and secretory phenotype of FAT and highlights important differences between cultured ADSCs and whole tissue. It is evident the regenerative effects observed from fat grafting arise from heterogeneous tissues rather than ADSCs alone, with work ongoing to understand the mode of action.

Keywords: Liposuction

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ON-CHIP 3D CELL CULTURE PLATFORM FOR TUMOR MODELING AND DRUG SCREENING

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Three-dimensional (3D) cell culture allows cell-cell and cell-matrix interactions and provides more in vivo like models rather than 2D cell culture which cannot fully mimic native tissue. 3D cell culture on microfluidics allows formation of 3D structures that mimic the physiological and chemical microenvironment for cells[1]. These microfluidic platforms also downsize bench-top laboratory to a microchip, require miniaturized reagent, and are convenient for dynamic drug screening[2]. In this study, a microfluidic platform was designed which is housing a PLLCL scaffold fabricated by electrospinning methodology. The electrospun material resembles fibrillar structure of the extracellular matrix while favoring cell adhesion and proliferation with the help of micro-to nano-meter range fibers[3]. By combining these advantages of electrospinning technique with microfluidic system, here it was aimed to develop scaffold-based 3D tumor models and to provide a platform where drug-screening applications can be carried out easily and in a controlled manner. Developed platform has a reservoir, which allows the fabrication of free-standing electrospun PLLCL scaffold directly on top of the microfluidic chip, a channel for transporting of cell, media, and drugs, an inlet and outlet to be applicable for both static and dynamic culture. Following characterization of scaffold and microchip, 3D tumor formation was achieved on this platform by using HeLa cells, which results in high cell viability and proliferation rate. Drug screening analysis provided more in-vivo like results. These results demonstrate that this developed platform is convenient for formation of various 3D tumor models and a potential candidate for drug screening and toxicity analysis.

Keywords: 3D cell culture ; 3D tumor-on-a-chip ; Drug screening

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MICROFLUIDIC 3D HMSC POTENCY ASSAY TO RECAPITULATE COMPLEX PROTEIN REGULATION AND FEEDBACK PROCESSES OF IN VIVO PHENOTYPE

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Human mesenchymal stromal cells (hMSCs) have long been identified for their beneficial anti-inflammatory and immunomodulatory properties making them a promising cellular therapy candidate for a wide variety of disease indications. Despite almost three decades of clinical development, few hMSC products have had success making it to market.[1] While early phase hMSC clinical research progressed rapidly with promising early results, significant setbacks were faced at advanced clinical phases as clinical endpoints failed to be met.[2–6] These late stage set backs are largely attributed to the inability to accurately assess cell potency through scale up processes and across variable donor populations.[6] To address these challenges, we have engineered a perfusable microfluidic platform as a tissue-on-a-chip to predict hMSC functional performance. The system we have engineered encapsulates hMSCs in 4-arm poly(ethylene glycol)-maleimide (PEG-4MAL) hydrogel environments within a perfusable microfluidic device. We have previously demonstrated that the immunomodulatory secretion profile of hMSCs is significantly influenced by their microenvironment.[7] We have found a loss of functional utility of established potency markers IDO and PD-L1 of hMSC cultured in our microfluidic system compared to traditional 2-dimentional static culture, as well as differential protein regulation between the two platforms. Furthermore, when compared to an in vivo model, we found that the protein correlations of specific immune-relevant pathways are conserved in our microfluidic system but not 2D cultures. From these findings, we will establish a more predictive and robust hMSC potency metric.