Nanoscale control of mesenchymal stem cells for identification of bioactive metabolites.

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Abstract

Metabolites, or biological small molecules, are usually considered in identification of biomarkers. However, they can be used to drive cellular processes, such as stem cell differentiation. Use of complex media recipes to control stem cell differentiation add artefact to metabolomics experiments and so bioengineering approaches are attractive as they can drive different stem cell fates without changing what the cells are 'fed'. We have developed metabolomics pipelines to identify bioactive metabolites that control mesenchymal stem cell (MSC) self-renewal and differentiation.

We started this research avenue using peptide hydrogels with defined stiffnesses that could control MSC chondrogenesis and osteogenesis, identifying GP18:0 and cholesterol sulphate as bioactive metabolites[1]. Next, using our nanovibrational bioreactor, the Nanokick[2], along with synthetic chemistry modification of hit metabolites, we focused on refining our putative osteospecifc metabolite candidates to tune potency and specificity identifying fludrocortisone acetate. Finally, we have used nanotopography to control MSC self-renewal[3] to identify respiration-link metabolites that drive the immunomodulatory phenotype of MSCs[4]; this is critical if we wish to grow large numbers of high quality MSCs for use as immunosuppressive therapies in transplant procedures.

Alakpa *Chem* 2016, 2) Tsimbouri *Nature BME* 2018, 3) McMurray *Nature Mat* 2011, 4) Ross *BioRxiv* 2019.

Biography

After a PhD at Queen Mary University of London on osteoblast response to bioactive composites. I moved to Glasgow to study cell-nanoscale interactions. In 2003 I became an independent researcher securing a BBSRC David Phillips Fellowship to explore mesenchymal stem cell response to nanotopography. Appointed to a lectureship in 2008 and a Readership in 2010, I became Professor of Cell Engineering at the University of Glasgow in 2014. I hold grants from EPSRC, MRC, BBSRC, Leverhulme Trust and Sir Bobby Charlton Foundation. I am director of the EPSRC-SFI lifETIME centre for doctoral training.

My research has focussed on developing insight into MSC differentiation and self-renewal using materials and mechanotransductive cues, making contributions in journals such as Nature Materials, Nature Biomedical Engineering, Advanced Materials, Chem, Science Advances etc (>180 papers). More recently I have become interested in using materials to find activity metabolites that can be used to control MSC phenotype. As well as

basic science, I am interested in translational science and have been involved in veterinary bone regeneration trials and am working now towards a human bone regeneration trail.

In 2016 I was elected a Fellow of the Royal Society of Edinburgh and have won a number of awards – most recently the Biochemical Society Industrial-Academic Collaboration Award.