



Unravelling how bi-directional cell-biomaterial interactions direct stem cell fate in 3D

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Modifiable hydrogels have revealed tremendous insight into how physical characteristics of cells' 3D environment drive stem cell lineage specification. However, in native tissues, cells do not passively receive signals from their niche. Instead they actively probe and modify their pericellular space to suit their needs, yet the dynamics of cells' reciprocal interactions with their pericellular matrix when encapsulated within hydrogels remains relatively unexplored. Here, we show that human bone marrow stromal cells (hMSC) encapsulated within hyaluronic acid-based hydrogels modify their pericellular environment through degradation and/or protein secretion, imparting them with similar pericellular stiffnesses, regardless of initial hydrogel properties. These cell-secreted pericellular matrices play a role in regulating hMSC fate, with secretion of a stiff proteinaceous pericellular matrix associated with adipogenesis, and degradation with osteogenesis. Our observations suggest that hMSC participate in a bi-directional interplay between the properties of their 3D milieu and their own secreted pericellular matrix, and that this combination of interactions drives fate.



Dr Eileen Gentleman is a Senior Research Fellow and Principal Investigator in the Centre for Craniofacial and Regenerative Biology at King's College London. She joined Imperial College London in 2005 as post-doctoral research associate (Stevens Group) after completing her PhD in Biomedical Engineering (Tulane University, USA). In 2011, she was awarded a Wellcome Trust Research Career Development Fellowship and moved to King's where her research focuses on engineering the 3D cell niche to control stem cell differentiation for tissue engineering. Her multi-disciplinary research interests also include fundamental mechanisms of biomineralisation and the role of mechano-sensing in tissue development. Her work has been published in Nature Materials, Proceedings of the National Academy of Sciences USA, and Biomaterials. Dr Gentleman has received funding awards from the Wellcome Trust, the Rosetrees Trust, the Royal Society and Orthopaedic Research UK, and is a recipient of both a Wellcome Image Award (2016) and an MIT Koch Institute Image Award (2016). The Orthopaedic Research Society named her as a finalist for their New Investigator Recognition Award (2010) and in 2013 her work in regenerative medicine was recognised with a prestigious Philip Leverhulme Prize.