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Mesenchymal stromal cell (MSC) derived osteoprogenitors for the treatment of degenerative disc disease (DDD)

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Introduction: MSCs are easily procured from bone marrow (BM) aspirates and may be suitable for adapting successfully to the environment of the intervertebral disc (IVD) to stimulate regeneration. Through novel technology for identifying and biophysically sorting MSC subpopulations, we demonstrate that implantation of MSC derived osteoprogenitors leads to the greatest efficacy in restoring IVD matrix and function in murine models.

Methods: We studied various biophysical traits of MSCs and created microfluidic sorters that isolate an osteoprogenitor subpopulation for clinical use. IVD cells were obtained from 5 patients for analysis (L3/4, L4/5, L5/S1). We correlated pain scores with gene expression of IVD cell-produced proteins to identify biomarkers relevant to DDD. We also evaluated pre-clinically the efficacy of different MSC subpopulations in reversing degeneration in IVD cells both *in vitro* and *in vivo*.

Results: MSC osteoprogenitors are defined biophysically from other subpopulations as cells with >20µm diameter, >375Pa stiffness and <1.2% nuclear fluctuation; functionally, MSC osteoprogenitors differentiate most readily into osteo/chondro-lineages and also secrete more Aggrecan, Fgf1, Ang-1, etc, making them potentially optimal for stimulating regeneration of both IVD cells and matrix. qPCR studies of patient IVD cells show a>5 fold Aggrecan decrease with a corresponding 3 point pain increase (scale of 0-10). Stimulation of patient IVD cells with osteoprogenitors *in vitro* greatly restored production of Aggrecan (~2.5 fold improvements compared to other MSC subpopulations). Protein expression of ANG-1 was also significantly higher when IVD cells were treated with MSC osteoprogenitors *in vitro*. In murine models, the administration of osteoprogenitors most potently restored the decrease in original disc height after injury using MRI and histopathological scoring system.

Conclusion: We demonstrate a facile and clinically relevant strategy for deriving an MSC osteoprogenitor subpopulation for cell-therapy in DDD, which may potentially be more efficacious in reversing the underlying degeneration in the IVD.

Biography

Kimberley Tam graduated from The University of Adelaide 2010, PhD in Medicine (Obstetrics and Gynaecology). He had completed his postdoctoral career with Cancer Science Institute of Singapore till 2014 developing Patient-derived xenografts for drug testing. He had served in the Department of Obstetrics and Gynaecology at National University of Singapore investigating the effects of Human Wharton's Jelly Stem Cells and wound healing till 2016 and is currently based at Singapore-MIT Alliance of Research and Technology establishing pre-clinical evaluations and critical quality attributes (cQAs) for stem cell manufacturing and precision medicine. Kimberley Tam's Research and Interests include – Developing various animal models for pre-clinical evaluation, bringing bench to bedside therapies and also developing *in-vitro* diagnostic platform for stem cell cQAs..

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