Characterisation of Human Bone Marrow Stromal Cell Heterogeneity for Skeletal Regeneration using a Two-Stage Colony Assay and Computational Modeling

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Introduction
Skeletal regeneration strategies rely critically on the significant expansion of stem/progenitor cell populations without the associated loss in developmental potential (i.e. the ability to induce bone/cartilage formation) [1,2]. Intrinsic or emerging heterogeneity within these cell populations impacts significantly on this expansion process. Therefore, the objective was to characterise Human Bone Marrow Stromal Cell (HBMSC) heterogeneity in terms of colony expansion potential.

Materials and Methods
A novel two stage colony (CFU-F) assay was developed in which primary (P0) single cell derived HBMSC colonies were detached and reseeded as single cells to form secondary (P1) colonies (Fig. 1a) [3]. To represent the experimental results, a simple cellular automata (CA) model was developed based on random cell movement, combined with cell division according to a hierarchically structured cell population (Fig. 1b, 2a)

Results
The experimental results clearly demonstrated that certain primary colonies were only able to form small secondary colonies, while others gave rise to a wide range of colony sizes (Fig. 2b). The model clearly demonstrated that these observations were consistent with the concept of a hierarchically structured cell population in which cells undergo senescence and stop cycling when their proliferative potential is exhausted. However, no direct correlation between primary and secondary colony size was observed in the experiment, which may be attributed to slower cell cycling times for early progenitor cells.

Discussion and Conclusions
Further characterization of HBMSC heterogeneity will be essential to design optimized cell expansion protocols to obtain significant numbers of developmentally potent cells, key to the success of skeletal regeneration strategies.

References

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