

## ECM X: Stem Cells for Musculoskeletal Regeneration. Adult and Embryonic Stem Cells for Skeletal Reconstruction

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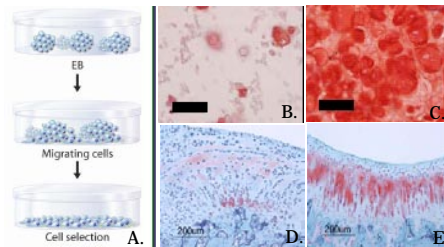
**INTRODUCTION:** Stem cells have generated significant excitement in many areas of regenerative medicine, including orthopaedics and plastic surgery. Both adult and embryonic cells have been investigated as a cell source for new cartilage tissue formation. However, their exact function or mode of action when implanted clinically in a joint environment is still unknown. Stem cells are capable of secreting molecules to modulate local host repair in addition to actually building new tissue and the respective contribution of these two modes of action in normal and diseased environment is not clear. We have been investigating these two modes of action in adult and embryonic stem cells in combination with biomaterials.

**METHODS:** We previously demonstrated the ability to encapsulate bone marrow derived stem cells (MSCs) into hydrogels and form cartilage-like tissue<sup>1</sup>. In addition, we created multilayered hydrogels to coculture different cell types together in a 3D environment<sup>2</sup>. Based on multiple clinical trials of MSCs that suggested the critical stimulatory effects of MSCs, we cocultured MSCs with chondrocytes to observe potential stimulation. In the case of embryonic stem cells, a mesenchymal progenitor population was generated to produce homogenous cartilage as previously described<sup>3</sup>.

**RESULTS:** Figures 1 and 2 demonstrate results for adult and embryonic driven cartilage formation and stimulation of cartilage formation. Adult stem cells can form cartilage but show a much more significant effect on stimulating chondrocytes to produce more tissue. Alternatively, embryonic-derived cells produce robust tissues, with fewer effects on stimulating host cells.



*Fig. 1: Chondrocytes produce matrix in hydrogels (A) which increases when cocultured with MSCs (B) however returns to control levels when MSCs differentiate to osteoblasts (C).*



*Fig. 2: A mesenchymal progenitor population was generated from embryonic stem cells as described<sup>3</sup> (A). Cells that were not exposed to chondrocyte-conditioned medium produced minimal cartilage tissue after 6 weeks of in vitro culture (B) while the cells expanded in chondrocyte-conditioned medium produced homogenous, cartilage-like tissue (C). Cells lacking chondrocyte conditioning produced a large mass of fibrous tissue in critical size athymic rat articular defects (D) while the conditioned cells re-established a normal articular tissue in a rat defect (E).*

**DISCUSSION & CONCLUSIONS:** Adult and embryonic stem cells are capable of forming cartilage tissue but their ultimate therapeutic values clinical may be different; adult cells stimulating host tissue repair and embryonic forming robust tissues. Further understanding of adult stem cell secretions and optimal differentiation states and biomaterials will be required to efficiently translate these technologies for clinical cartilage repair.

**REFERENCES:** <sup>1</sup> Williams *et al.* Tissue Eng, 2003, 9(4):679. <sup>2</sup> Sharma *et al.*, Tissue Eng, 2007 Feb;13(2):405-14. <sup>3</sup> Hwang *et al.*, PNAS, 2009, 105(52):2064.

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