

Tendon-derived cells differentially modulate proliferation of mesenchymal progenitor cells from different sources

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INTRODUCTION: Tissue engineering strategies through the use of stem cells for the repair and healing of tendon injuries are gaining prominence supported by a reduction of the clinical re-injury rates¹. However the nature of the interaction between the introduced stem cells and tendon cells is still unclear.

Hypothesis: The co-culture of mesenchymal stem cells (MSCs) with tendon derived cells influences the proliferation of MSCs and induces their differentiation towards a tendon fibroblast lineage.

METHODS: MSCs derived from equine bone marrow (BMMSCs) and tail head adipose tissue (ADMSCs), and tendon derived cells (TDCs) from the forelimb superficial digital flexor tendons were expanded in monolayer culture. 1×10^4 of test cells (BMMSCs or ADMSCs) were seeded in Multiwell Insert Systems with a microporous membrane (35mm wells with a 1 μ m pore diameter, BD Biosciences) with 5×10^5 feeder cells (ADMSCs or SDFTs). The control cells were the test cells without the feeders. The pore diameter of 1 μ m prohibits exchange of cells across the membrane. The number of test cells was counted at various days after seeding in each experimental group.

RESULTS: Feeder TDCs significantly increased ADMSC proliferation after 7 and 10 days of co-culture (Figure 1A). In contrast, BMMSC proliferation was significantly suppressed at day 8.9 but showed no significant differences compared to controls at later time points (Figure 1B). When ADMSCs were used as feeders, they did not significantly influence the growth of ADMSCs test cells except early on in co-culture (day 3). Further, the proliferation of ADMSCs was faster than BMMSCs under these co-culture conditions (Figure 1A & 1B). Both test and control cell numbers reached parity over time as they became confluent.

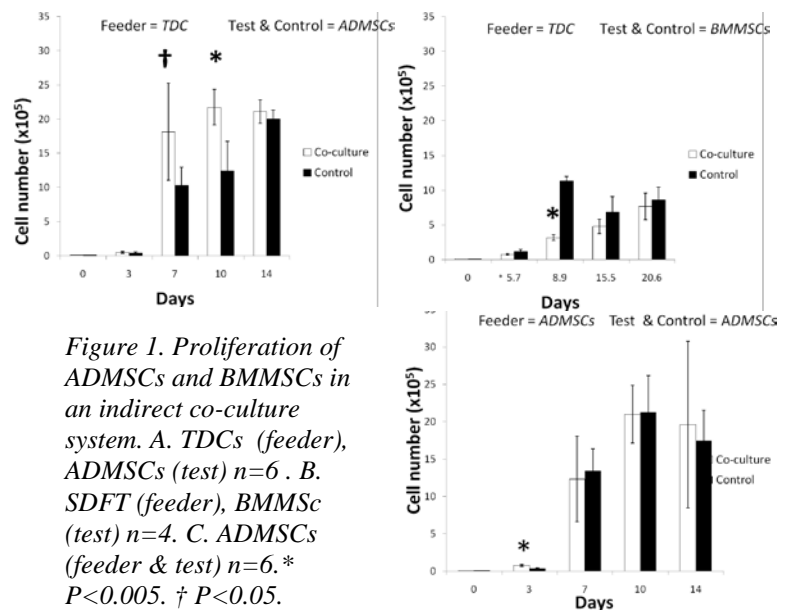


Figure 1. Proliferation of ADMSCs and BMMSCs in an indirect co-culture system. A. TDCs (feeder), ADMSCs (test) $n=6$. B. SDFT (feeder), BMMSC (test) $n=4$. C. ADMSCs (feeder & test) $n=6$. * $P < 0.005$. † $P < 0.05$.

DISCUSSION & CONCLUSIONS:

TDCs increased the proliferation rate of ADMSC but not of BMMSCs. The high rate of ADMSC proliferation in comparison with BMMSCs suggest they maybe a potentially useful alternative for therapeutic purposes as they could be expanded to greater numbers in a shorter period of time. However, as a reduced proliferation rate is the first step towards differentiation², it may be that BMMSCs with their slower proliferation are better suited at differentiating towards a tenocyte lineage than ADMSCs. To determine whether that is the case, we are currently investigating the influence of TDC feeder cells on gene expression in BMMSC and ADMSC test cells.

REFERENCES: ¹Richardson LE et al., Trends Biotechnol. 2007, 25:409-16. ²Zhu & Skoultchi. Current Opinion in Genetics & Development 2001, 10:1-97.

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