**Title: The Up-Scale Manufacture of Chondrocytes for Allogeneic Cartilage Therapies**

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**Introduction**

Up-scaled allogeneic cellular products for cartilage therapies, along with identification of novel young donors of healthy chondrocytes, are needed to improve the cost effectiveness and wide-spread use of chondrocyte therapy.

**Materials and Methods**

Cartilage from four adult donors undergoing knee arthroplasty and two juvenile donors undergoing removal of extra digits were used to derive chondrocyte cultures in media supplemented with human platelet lysate (HPL, Stemulate®)) in the Quantum® hollow-fibre bioreactor or on tissue culture plastic (TCP) with foetal bovine serum (FBS) or HPL. Growth kinetics, flow cytometry and chondrogenesis assays were used to characterise cell products.

**Results**

The Quantum® produced higher yields of cells derived from arthroplasty patients (75±38M, in 9±1 days) cf. FBS supplemented (2.6±0.4M in 13.6±0.47 days) or HPL supplemented (6.9±3.8M in 11.0±2 days) TCP cultures. The number of population doublings for Quantum®, TCP FBS and TCP HPL being 2.82±1.18, 1.57±1.1 and 1.3±0.12, respectively. The same was seen in chondrocytes from juvenile donor digits (Quantum®: 74±37 M in 8 days; FBS supplemented TCP: 2.7±0.2M in 4±2.8 days; HPL supplemented TCP: 5.4±2.4M in 4±2.8 days). Quantum® adult donor chondrocytes displayed similar surface immunoprofiles to those grown on TCP and unlike freshly isolated cells, were immunopositive for CD90, CD73, CD105, CD166, CD151 and all integrins tested. Chondrogenic pellet analysis demonstrated that all adult donor cultures produced GAGs to varying degrees.

**Conclusion**

The data presented here represents the first use of chondrocytes in a clinical-grade expansion bioreactor. We have demonstrated that, compared to traditional cell expansion methods, the Quantum® is capable of generating higher numbers of chondrocytes. These Quantum® expanded adult chondrocytes demonstrate comparable characteristic immunoprofiles and cartilage forming capacity. The Quantum® has the potential to reduce manufacturing costs for multiple dose allogeneic chondrocyte banking. Further work will be performed to assess the potential of up-scale manufactured chondrocytes derived from juvenile digits.