

The clinical study finalized after 1 year follow-up of the 15 patients treated. No serious adverse events were reported. At present, statistical analysis is being performed but all seems to indicate positive results meaning MSC administered intraarticularly could be a good option for treating mild to moderate osteoarthritis of the knee. In conclusion, the proper coordination of professionals of various disciplines (veterinarians, biotechnologists, engineers, and surgeons) facilitated the success in the development of an advanced therapy medicinal product: from proof-of-concept studies in laboratory animals to first promising results treating mild to moderate osteoarthritis of the knee in humans.

#### 48 ECM MIMETIC COLLAGEN I PEPTIDE AND FIBRONECTIN PEPTIDE - FOR CULTURE OF CELL TYPES WITH CLINICAL POTENTIAL

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Expansion of stem cells and some primary cells requires either animal-origin components in culture media or coating of the culture vessel with human or animal-derived extracellular matrix (ECM) protein, which can be source of pathogens. Growing concerns about introducing human and animal-derived pathogens into the culture necessitate the need for animal free (xeno-free and human origin components-free) culture environment.

Herein, we present ECM mimetic cultureware Collagen I peptide and Fibronectin peptide for culture of cell types requiring collagen I or fibronectin protein-coated surfaces. Mimetic cultureware are pre-coated, synthetic, animal-free, room temperature stable surface consisting of covalently-immobilized peptide presented in a functionally active manner. Collagen peptide includes GFOGER and fibronectin peptide has RGD sequence. We demonstrate expansion and functionality of several clinically relevant cell types including mesenchymal stem cells (MSCs), keratinocytes (HKN), endothelial colony forming cells (ECFCs), and cell lines for biomanufacturing (CHO and Vero) on these surfaces. In this study MSCs cultured on fibronectin peptide in defined and xeno-free media exhibited growth and morphology comparable to cells grown on human-origin matrix. Following multiple passages MSCs expressed CD90, CD105, and CD73 markers and differentiated into osteocytes and adipocytes. HKN cultured on collagen peptide exhibited growth and morphology comparable to cells grown on Collagen I. Functionality of these cells was demonstrated by *in vitro* wound healing assay. ECFCs on both the peptide surfaces showed morphology and growth comparable to natural ECM protein Collagen I or Fibronectin. Post expansion, ECFCs were able to form capillary-like structures formed by endothelial progenitor cells. CHO and Vero cells showed improved growth on ECM mimetics compared to tissue-culture surface in serum-free, low protein medium. ECM mimetic cultureware are versatile surfaces compatible with multiple media for culture of various cell types providing a ready to use alternative to ECM coating where animal-free and defined conditions are desirable.

#### 49 OVERCOMING SCALE-UP AND SCALE-OUT WITH AUTOMATION

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As the cell therapy market matures, it is becoming abundantly clear that small scale manual processes frequently utilized for early Phase trial production have difficulty achieving reasonable commercial scale cost of goods. This in turn restricts profit margins required for corporate success and effective reimbursement strategies. As a premier provider of automated cell culture systems, TAP Biosystems has built robotic platforms for the aseptic processing of roller bottle and flask cultures for over 20 years. Cellmate, launched in 1989, has been integral to the GMP production scale-up of many biologics, vaccines and tissue starting materials that remain financially successful today. Its batch processing of roller bottles can enable scale-up of allogeneic therapies with minimal process change. CellBase CT is a specialized GMP version of the CompacT series that has been effectively expanding multiple drug discovery cell lines in flasks without cross-contamination for 10+ years. With addition of UV decontamination lighting, automated particulate counting and cell imaging, autologous therapies can be safely handled according to their individual needs, with a secure audit trail of each flask interaction. Other instrumental tools: (1)

advanced microscale bioreactor, ambr, which can be used in process development for shifting from planar to stirred cultures, or in media development to reduce the requirement for costly reagents, (2) Fill-It, which can expediently decap, fill and recap cryovials to protect cell banks and cellular products from extended exposure to cryopreservation agents and (3) a collaborative effort with UCL's Julie Daniels for First-In-Man corneal replacement trials resulting in RAFT, Real Architecture for 3D Tissue.

50

#### ALLOGENIC WHARTON'S JELLY MESENCHYMAL STROMAL CELLS INTRAVENOUS INFUSION INCREASE SERUM INSULIN -LIKE GROWTH FACTOR -1 AND DEHYDROEPIANDROSTERONE IN HEALTHY VOLUNTEERS

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**Background:** The clinical effects of mesenchymal stromal cell (MSC) have been postulated to be due to its paracrine action and ability to stimulate regeneration or restore homeostasis through various growth factors. Insulin-like growth factor-1 (IGF-1) has cellular growth-promoting effects especially for neuron, skeletal muscle, liver, kidney and lungs. Dehydroepiandrosterone (DHEA) is an endogenous metabolite intermediate in the biosynthesis of the androgen and estrogen sex steroids, and is thought to be able to regulate metabolism, mood, weight and sleep. The aim of this study was to determine the effect of intravenous Wharton's Jelly-derived MSC (WJ-MSC) infusion on serum IGF-1 and DHEA levels in healthy volunteers.

**Methods:** WJ-MSC from the umbilical cord of a healthy newborn was harvested and expanded *ex vivo* after full informed consent from the parents and comprehensive health screening including genetic analysis is performed. 10 healthy volunteers were recruited (mean age 45 years; 6 men). All participants received 50 million WJ-MSC intravenously. 20 mls of venous blood were collected at baseline, 3 months and 6 months for screening.

**Results:** All participants tolerated the procedure well with no immediate allergic reactions or complications. Baseline bloods including IGF-1, DHEA, testosterone (males only), oestrogen and progesterone (females only) were within normal range. At 3 months mean levels were generally higher when compared to baseline for IGF-1 (220 vs 240 ug/L) and DHEA (4.4 vs 5.7 umol/L). At 6 months mean levels were higher than baseline for IGF-1 (220 vs 245 ug/L) and DHEA (4.4 vs 4.9 umol/L). There were no differences seen with other parameters including full blood count, fasting blood glucose levels, renal profile, liver function tests and serum tumor markers.

**Conclusions:** The paracrine effects of allogenic WJ-MSC may be mediated by IGF-1 and DHEA. Larger studies are warranted following this preliminary safety report.

51

#### CORRELATING EX VIVO AND IN VIVO OSTEOGENIC ASSAYS FOR QUALITY CONTROL OF CLINICALLY DESTINED CGMP GRADE BM-MSC

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Among diverse approaches in translational medicine, there is growing interest in use of mesenchymal stem cells (hMSC) to enhance bone regeneration. Working within a European consortium, we aimed to evaluate the osteogenic potency of primary bone marrow- (BM) hMSC cultures isolated and expanded by clinical grade procedures (cGMP). Therefore, we aimed to standardize a functional assay that was rapid, reproducible and readily applicable.

Numerous genes have been associated with the cascade of genetic changes required for osteogenic differentiation. Though expression of these genes in differentiated hMSC *ex vivo* rarely predict *in vivo* bone formation, recent studies using immortalized hMSC, have shown some correlations. We wished to explore whether such gene expression changes could also be applicable in different contexts: (1) using primary hMSC; (2) with growth medium supplemented by platelet lysate instead of fetal bovine serum and (3) at 1 week instead of 2 weeks time points.