stem cells (iPSCs) and differentiating them into functional human cells. FCDI aims to establish a bank of HLA-matched iPSCs spanning >95% of the US population and, by extension, establish banks that match against global populations. Historical work with cord blood and solid organ transplantation indicate that a hemizygous recipient match at specific HLA loci reduces incidence of allograft rejection. Therefore, blood from individuals possessing these desirable HLA types along with additional criteria to minimize risk of rejection will be used in the manufacture of banks using FCDI's proprietary, plasmid-based reprogramming technology.

P272

Application of combined gene and cell therapy within an implantable therapeutic device for the treatment of severe haemophilia A

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New regenerative medicine approaches to treat haemophilia A require insights into cell compartments capable of producing factor VIII (FVIII). Haemaphilia A (HA) is an X-linked bleeding disease due to FVIII deficiency. We and others previously demonstrated that FVIII is produced specifically in endothelial cells. The main objective of our work is to develop the tools and technologies for a novel ex vivo cell-based therapy to treat HA that should ultimately lead to improved patient quality of life. We isolated blood outgrowth endothelial cells (BOECs) from healthy and patients' blood. BOECs were efficiently transduced by lentiviral vectors (LVs) containing the B domain deleted form of human FVIII under the Vascular Endothelial Cadherin promoter (VEC). BOECs were characterized by FACS analysis for endothelial phenotype and FVIII evaluated by APTT and ELISA. The number of integrated LV copies/cell was $\sim$3 for LV-VEC.hFVIII transduced cells. We demonstrated by FACS that FVIII was expressed by 70% of transduced cells. Ten million LV-VEC.hFVIII-BOECs were transplanted intraperitoneally in association with cytodex® 3 microcarrier beads in NOD/SCID γ-null HA (NSG-HA) mice (n = 3). BOECs survived and secreted FVIII at therapeutic levels (with a peak of 15% FVIII activity) for up to 12 weeks. As next steps, LV-transduced haemophilia patient BOECs will be transplanted into an implanted prevascularized, scalable medical device (Cell Pouch™, Sernova Corp.) and optimized for sustained secretion of FVIII in the NSG-HA mice. This is in preparation for future human clinical testing within the device in haemophilic patients by transplantation of GMP produced autologous gene corrected BOECs.

P273

The use of adipose derived stromal vascular fraction in complex non-healing wounds of soft tissues and bone defects in maxillofacial surgery in dog

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Tissue regeneration at the site of non-healing oroantral fistula with simultaneous plastic surgery reconstruction of soft tissues was carried out. Adipose tissue derived stromal vascular fraction (SVF) in combination with nickel-titanium granules (nitigran) was used as an osteoinductive material. We performed excision of the altered mucosa in the fistula. The granulations from the sinus cavity were taken out. The sinus cavity was repeatedly washed with antiseptic solutions. The bone surface was treated with milling cuts along the entire length of the fistulous course. The bottom of the defect was covered with a membrane, and the defect was filled with nickel-titanium granules saturated with SVF. The top was covered with a collagen membrane. Then the plastic surgery of the fistula with soft tissues was performed. The edges of the wound were stitched with Vicryl and additionally covered with Tissucol fibrin glue mixed with SVF. In the course of the wound healing, fibrin glue dissolved completely, releasing the cells enclosed in it, which stimulated regeneration processes. The dog was prescribed to undergo the antibiotic therapy with Maxipime at a dose of 250 mg given intramuscularly once a day for 5 days. Subsequently, dynamic X-ray examination of the animal and external examinations were carried out. As a result of the operation, the full closure of the oroantral fistula in the dog's jaw was achieved, which demonstrates the effectiveness of nitigran granules in comvination with adipose derived SVF in complex non-healing wounds of soft tissues in maxillofacial surgery.

P274

Hypoxia pre-conditioning enhances cardiac differentiation ability of human iPSCs

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Human induced pluripotent stem cells (hiPSCs) hold great promise for regenerative medicine, particularly for development of personalized therapies for human patients. One of the most common life-threatening diseases in developed countries nowadays are related to the cardiovascular system, despite available modalities. Thus, it is of immense importance to develop new treatment options for affected patients, including standardized and robust protocols for cardiomyocytes generation from patients' own samples, with or without the iPSC-stage. Knowing that reduced oxygen level (hypoxia) plays an important role in normal cardiomyogenesis *in vivo*, we hypothesized, that low oxygen condition may also influence cardiomyocytes generation from hiPSCs *in vitro*. In this study we performed cardiomyogenic differentiation from isogenic hiPS cell lines cultured continuously in hypoxia and normoxia. We found that hiPSCs cultured in hypoxia differentiated faster into mature cardiomyocytes, in comparison to their counterparts derived from normoxic cultures. The differentiation was indicated by increased levels of expression of pro-cardiomyogenic genes, including GATA4, NKX2.5 and TNNT2 and also higher mRNA levels for calcium, potassium and sodium ion channels, an indicator of mature cardiomyocytes. We conclude, that hypoxia preconditioning increases the ability of hiPSCs to differentiate into mature cardiomyocytes. Our findings might be implemented into protocols for cardiac myocytes generation in a more robust and physiological way. These data can further be exploited for preparation of drugs screening platforms and ultimately, for development of novel therapies for human patients based on iPS-derived allogeneic cardiac cells.