Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Keywords: Stem cells, Bone, Immunoregulation.

Background & Aim: Introduction: Bone regeneration is a complex process influenced by a variety of factors such as tissue interactions, inflammatory responses, and progenitor cells. NVDX3 is an allogenic/off-the-shelf product intended for use in bone voids. It is a lyophilized, terminally sterilized powder derived from a 3-D cell product containing extracellular matrix and adipose derived osteodifferentiated cells associated with hydroxyapatite/beta-tricalcium phosphate (HA/βTCP) particles. One of the main concerns in the field of allogeneic stem cell technologies is the potential induction of an unwanted immune response, whereas the low immunogenicity and potential immunosuppressive capacities of mesenchymal stem cell (MSC) are properties of major importance for MSC-based therapeutic approaches.
Methods, Results & Conclusion: Methods: NVDX3's immunoregulatory properties were evaluated through the investigation of its (i) immunogenic potential and (ii) immunoregulatory function on different populations of immune cells, including stimulated T cells and macrophages. The potential immunogenic and immunosuppressive/immunoregulatory effect of NVDX3 was investigated using in vitro bioassays. Results: NVDX3 did not induce CD3+, CD4+ and CD8+ T cell proliferation or IFN-γ production when added on unstimulated PBMCs, suggesting the absence of an immunogenic potential. In contrast, a strong immunosuppressive effect was observed in the presence of NVDX3 compounds since their addition on stimulated PBMCs completely inhibited the CD3+, CD4+ and CD8+ T cell proliferation with >98% of inhibition. The immunosuppressive properties of NVDX3 involved also immunomodulation by inhibiting the secretion of pro-inflammatory cytokines on one hand and by promoting the shift of M1 to M2 macrophages polarization on the other. The observed immunosuppression capacity of the product seems involved prostaglandin E2 (PGE2) and Indoleamine 2, 3-dioxygenase 1 (IDO) pathways. Conclusion: The primary function of NVDX3 is directed towards bone regeneration by promoting a local balance of factors essential for bone formation. The lack of immunogenicity in combination with the presence of immunomodulatory properties similar to the ones described for mesenchymal stem cells makes NVDX3 a privileged therapeutic which combines osteogenic with immunosuppressive properties.

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Mesenchymal Stem/Stromal Cells

SAFETY OF CORD TISSUE DERIVED MESENCHYMAL STROMAL CELLS IN COVID-19 RELATED ACUTE RESPIRATORY DISTRESS SYNDROME

B. Shaz[1], B. Kraft[1], J. Troy[1], E. Poehlein[1], L. Chen[1], L. Cheatham[1], R. Manyara[1], K. Hanafy[2], L. Brown[1], M. Scott[2], R. Palumbo[2], F. Vrionis[2], J. Kurtzberg[1]
[1]Duke University, Durham, NC, United States; [2]Baptist Health, Boca Raton, FL, United States.

Keywords: COVID-19, ARDS.

Background & Aim: Infection with SARS-CoV-2 results in coronavirus disease 2019 (COVID-19) and has caused a global pandemic. In severe cases, COVID-19 leads to acute respiratory distress syndrome (ARDS), due to direct lung injury and hyperinflammatory response. Treatment recommendations for COVID-related ARDS have evolved to include remdesivir, dexamethasone, and immunomodulatory drugs; however, despite these treatments, many patients still die from respiratory or multi-organ failure. Mesenchymal stromal cells (MSC) offer a novel and unique therapeutic option that might shorten time to lung injury resolution through anti-inflammatory and immune-modulatory mechanisms and by protecting the lung tissue. Thus, the aim of this study was to test the safety of human cord tissue derived MSCs (hCT-MSC) in patients with COVID-related ARDS.
Methods, Results & Conclusion: In this phase I multisite study, 10 adults with COVID- related ARDS were treated with 3 daily intravenous infusions of hCT-MSCs (post thaw 1 million cells/kg, maximum dose 100 million cells, viability ≥ 70%) (IND 19968). hCT-MSCs were manufactured at in the Robertson GMP Cell Manufacturing Laboratory at Duke. Patients were excluded if they had evidence of multi-organ failure, or were immunodeficient, receiving extracorporeal membrane oxygenation, or not expected to survive more than 24 hours. The primary endpoint was short-term safety of hCT-MSC infusions. The secondary endpoint was 28-day survival. From August to November 2020, 10 patients were enrolled (Table 1). All patients received 3 hCT-MSC doses on schedule with no infusion related reactions. There were no manufacturing failures. 28 non-serious adverse events occurred in 3 unique patients, but none were related to the study product. 8 patients also received remdesivir, 7 dexamethasone, 2 COVID convalescent plasma and 2 antibiotics. To assess HLA antibody formation, day 0 and 28 HLA antibody testing was performed and were available for 4 patients (2 died before day 28, 2 missing day 0 [1 day 28 positive, 1 day 28 negative], and 2 missing day 28): 1 patient developed HLA antibodies, and 1 patient was positive and 2 were negative pre and post infusion. Five patients died (2 before day 28, and all before day 90); none of the deaths were deemed related to the treatment. hCT-MSCs infusions are safe in patients with COVID-related ARDS. Future studies exploring their efficacy are warranted. Funded by the Marcus Foundation, Atlanta, Georgia.

Table 1 (abstract 123)
Demographics

	Participants (N=10)
Age (years)	
Mean	62.5
Range	39-19
Gender	
Female	7
Male	3
Race	
Black	2
White	6
Other	2
Ethnicity	
Hispanic or Latino	3
Not Hispanic or Latino	7
Site	
Baptist Health	2
Duke University	8

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Mesenchymal Stem/Stromal Cells

PRODUCTION OF SIZE-CONTROLLED SPHEROIDS IN A FULLY CONTROLLED LARGE-SCALE STIRRED TANK BIOREACTOR FOR CELL THERAPY AND DRUG TESTING

F. S. Petry[1], P. Czermak[1,2], D. Salzig[1]
[1]Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Gießen, Germany; [2]Faculty of Chemistry and Biology, University of Giessen, Giessen, Germany.

Keywords: Spheroids, Stirred-tank bioreactor, Shear forces.

Background & Aim: The fast-rising number of diabetics increase the focus on alternative diabetes therapies, which eliminate harmful long-term effects due to the conventional insulin application. These new therapy forms try to replace the destroyed/dysfunctional insulin-producing beta cells within the pancreas with in vitro generated highly viable und functional beta cells. The transplantation of whole pancreatic islets is strongly limited by a shortage of donor material, and the implementation of beta cells derived from induced pluripotent stem cells is hampered by difficult differentiation protocols.