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Cell-tissue therapy of fetoplacental origin in recurrent implantation failure and chronic endometritis: a clinical case report

L.A. Konoplia [1, 2], A.O. Feskova [1, 2]
[1] Institute for Problems of Cryobiology and Cryomedicine of the National Academy of Sciences of Ukraine, Kharkiv, Ukraine
[2] Kharkiv National Medical University, Kharkiv, Ukraine

Chronic endometritis (CE) is a significant factor contributing to infertility and recurrent implantation failure (RIF). Conventional therapeutic approaches often demonstrate limited efficacy, particularly in treatment-resistant cases. An emerging strategy involves the use of fetoplacental-derived bioproducts, notably cryopreserved umbilical cord blood stem cells and placental homogenate, offering regenerative and immunomodulatory properties. However, existing literature provides limited insight into cryobiological aspects of these therapies, their safety, and comparative effectiveness.

A 36-year-old patient with a 4-year history of infertility, three unsuccessful IVF/ICSI cycles, and multiple transfers of euploid embryos was evaluated. Diagnostic workup revealed CD138-positive chronic endometritis (CE) and inadequate endometrial thickness (3.8 mm on day 12 of the cycle). As part of a clinical study, the patient received a therapeutic regimen comprising: a subcutaneous injection of cryopreserved umbilical cord blood concentrate (a highly purified fraction of nucleated cells with minimal plasma content) at a dose of approximately 1×10^6 cells/kg on day 1 of therapy; intramuscular injections of cryopreserved nucleated cell suspension in plasma derived from umbilical cord blood at a dose of approximately 2×10^3 cells/kg on days 5 and 7; and intramuscular administration of cryopreserved placental homogenate at a dose of 0.8 mg protein/kg on days 15, 20, and 25. The sequence and timing were based on preliminary cryobiological studies and empirical protocols aiming to sequentially stimulate immunomodulation and tissue regeneration. Therapeutic efficacy was assessed via immunohistochemical analysis of CD138 expression, serial transvaginal ultrasonography to evaluate endometrial thickness, and regular hormonal monitoring. By January 2024, histological evaluation demonstrated resolution of CE (CD138-negative status), and endometrial thickness improved to 9 mm on the 12th day of the menstrual cycle. Hormonal profiles corresponded with mid-cycle estrogen peaks, indicating a receptive endometrial state. Following double ovarian stimulation cycles in January 2024, two blastocysts were obtained, one of which was euploid (confirmed by next-generation sequencing, NGS). In August 2024, transfer of the cryopreserved euploid blastocyst resulted in a confirmed clinical pregnancy. This represented the first successful implantation after multiple years of infertility and repeated ART failures. No adverse effects were observed throughout treatment, and the therapy was well-tolerated. The administration of fetoplacental-derived cell-tissue bioproducts led to resolution of CE, improved endometrial receptivity, and successful implantation of a euploid embryo. While the observed outcome suggests potential clinical benefits of this approach, conclusions are limited by the single-case nature of the report. Further studies are warranted to evaluate safety, establish protocols, and determine comparative effectiveness *versus* standard care.

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Design of a fluidic chamber for the analysis of diffusion CPA/VA in a single cell using Raman microscopy

O.S. Hubenia [1, 2], R. Tewes [1], S. Leal-Marin [1], C. Winkler [1], A.-R. Iddi [1], B. Glasmacher [1]
[1] Institute for Multiphase Processes, Leibniz University Hannover, Garbsen, Germany
[2] Institute for Problems of Cryobiology and Cryomedicine of the National Academy of Sciences of Ukraine, Kharkiv, Ukraine

Cryopreservation is essential for safeguarding biological diversity, enabling the long-term conservation of genetic material from various species, including clinically relevant cells such as germ cells, tissue-engineered constructs, and native tissues. It plays a critical role in both biomedical research and biodiversity preservation. During cryopreservation, cryoprotectants and vitrification agents (CPA/VA) are used to protect cells and tissues from damage induced by ice formation due to the low temperature storage. Optimised storage conditions rely on precise incubation times of CPA/VA, which incorporate the diffusion rates of these CPA/VA into the target objects. Therefore, understanding the diffusion coefficient behaviour of CPA/VA under different temperatures and dynamic conditions is vital for developing effective cryopreservation strategies, offers non-invasive, label-free chemical characterisation, making it ideal for monitoring CPA concentration gradients inside living cells during equilibration.

The aim of this work was to design a fluidic chamber for real-time CPA/VA diffusion analysis in single oocytes, utilising Raman spectroscopy.

The chamber is designed to accommodate porcine and bovine oocytes, fit within the available Raman microscope's working space, focus point, and ensure stable, fixed sample positioning and maintain strict sterility throughout the experiment for consistent spectral measurements during diffusion analysis. To support this, the chamber incorporates a fully sealed, leak-proof design that prevents contamination and fluid exchange with the external environment, an essential requirement when working with sensitive biological samples and temperature-controlled reagents. Temperature regulation from –30 °C to 4 °C enables simulation of realistic cryopreservation conditions and assessment of CPA diffusion kinetics across relevant gradients. All components of the chamber are being designed using SOLIDWORKS and will be fabricated at the institute's mechanical workshop.

Once validated, this chamber will serve as a novel tool for improving the understanding of CPA kinetics in complex biological systems, paving the way for more efficient, precise cryopreservation protocols for porcine/bovine oocytes.

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