TERMIS EU 2019

termis®

Tissue Engineering Therapies:
From Concept to Clinical
Translation & Commercialisation

27-31 May 2019
Rhodes, Greece
Rodos Palace Hotel

Conference Chair:
Dimitrios I. Zeugolis, PhD

Conference Program Chair:
Maria Chatzinikolaidou, PhD

Find us at:

www.termis.org/eu2019

termis@nuigalway.ie

@termis_eu_2019

Organized by:

REMODEL
Regenerative, Modular & Developmental Engineering Laboratory

cúram

NUI Galway
OÉ Gaillimh

Laboratory of Biomaterials in Tissue Engineering
University of Crete

FORTH
Foundation for Research and Technology - Hellas

University of Crete

Organizing Secretariat:

convin

T: +30 210 6833600
E: congress@convin.gr
W: www.convin.gr

Prolonged intra-articular retention of mesenchymal stem cells by advanced microencapsulation for regenerative joint therapies

L.P. Karbaat[1], N.M. Korthagen[2], M. Baake[1], K. Warmink[3], N. Dupuis[3], S.K. Both[1], K. Coeleveld[3], B. Zoetebier[1], J. Leijten[1], H. Weinans[3], H.B.J. Kaperien[1]
Presenting Author: Lisanne Karbaat, l.p.karbaat@utwente.nl
[1]Department of Developmental BioEngineering, University of Twente, Enschede, The Netherlands
[2]University of Utrecht, The Netherlands [3]University Medical Centre Utrecht, The Netherlands.

INTRODUCTION: Intra-articular injection of mesenchymal stem cells (MSCs) show therapeutic regenerative potential for patients with osteoarthritis (OA) by restoring damaged cartilage, reducing pain, and increasing motion range in clinical studies. However, clinical efficacy is still limited, which is likely caused by the rapid clearance of MSCs from the synovial cavity. We hypothesize that prolonging the intra-articular retention of MSCs increases their therapeutic potential. Therefore, we developed an advanced micro-encapsulation technique, specifically aimed at retaining MSCs in the joint, while supporting their viability and activity. The goal herein is to assess if micro-encapsulation of MSCs prolongs their intra-articular retention and increases their therapeutic potential.

METHODS: MSCs were harvested from 12 week old Wistar rats, and labelled with a near infrared (NIR) label. An enzymatically crosslinkable polymer and a microfluidic droplet generator were used to encapsulate MSCs in microgels (eMSCs). Viability and metabolic activity were assessed. Microgels with near-infrared labelled MSCs were intra-articularly injected in healthy 12 week old Wistar rats (n=6). For four months, quantitation of the NIR signal was performed using whole animal NIR-imaging. After 8 and 16 weeks, microgels were retrieved and the presence of NIR signal and viability of the eMSCs was confirmed. Additionally, 12 week old Wistar rats (n=12), were fed a high fat diet and underwent a groove surgery to induce a mild OA phenotype. eMSCs were intra-articulary injected one week after the groove operation. Functional performance of OA rats was investigated using gait analysis. At the end point from both studies, histological analysis was performed to provide greater insight in the process and mechanism of action.

RESULTS & DISCUSSION: Microfluidic encapsulation allowed for the formation of homogenous, monodisperse microgels (diameter 100 µm, cv <5%), which contained ~13 cells/gel. In vitro, the MSCs maintained ~60% of their initial metabolic activity and survived for at least four weeks. In vivo, MSC microencapsulation increased the intra-articular retention from four weeks (signal eMSCs vs naked MSCs: 63% vs 13%) to four months (signal eMSCs vs naked MSCs: 11% vs N.A.). Microgels retrieved from the knee joint contained viable, NIR-positive MSCs, confirming that the NIR signal came from the injected cells. Gait analysis shows an improved function of osteoarthritic rats receiving eMSCs over rats receiving naked MSCs or saline controls. Histological analysis corroborated the data.

CONCLUSIONS: Our study shows that encapsulation of MSCs in microgels increases their intra-articular retention to at least four months, while protecting the MSCs against the harsh environment within the joint. Additionally, eMSCs alleviated osteoarthritic symptoms on a functional level. This approach allows for a single intra-articular injection with a significantly extended retention of therapeutic cells within the intra-articular joint cavity.

ACKNOWLEDGEMENTS: Financial support was received from the Europees Fonds voor Regionale Ontwikkeling (00392).