PhD Open Days

A novel biomimetic platform for cartilage tissue engineering and *in vitro* disease modelling

PHD Bioengineering- Cell Therapies and Regenerative Medicine

Kristin Schüler (<u>Kristin.schuler@tecnico.ulisboa.pt</u>)



Acknowledgement: This PhD project is possible thanks to the support of a INPhINIT (Incoming) fellowship from the "Ia Caixa" Foundation (ID 100010434). The fellowship code is ""LCF/BQ/DI23/11990049". This research was funded by dedicated funding from FCT-Portuguese Foundation for Science and Technology (FCT/MCTES) through projects InSilico4OCReg (PTDC/EME-SIS/0838/2021). The authors also acknowledge FCT/MTES for funding provided through iBB (UID/BIO/04565/2022) and Laboratório-Associado I4HB (LA/P/0140/2020).

Impact

) 1-2.5 % GDP



Provide the secondary diseases

Neogi, T. (2013), Leifer et al. (2021)

Problem

no nerves - late disease detection **no vascularization** – slow / no *natural regeneration*





OSTEOARTHRITIS



Fig. 1. Osteoarthritis in comparison with a healthy cartilage – (a) the composition of a healthy joint in comparison with (b) an OA diseased joint, and (c) the hierarchical structure of cartilage with collagen type II arcades

OUR SOLUTION: MULTIDISPLINARY APPROACH

Mechanical engineering

Bioreactor – design, prototyping, simulation, process finding and optimization



Advanced culture conditions with hypoxia, mechanical loading

Bio-instructive scaffold – for physiological matrix deposition

Biology

Primary human cells – patient-synovial derived mesenchymal stem cells





Bioink characterisation – rheology, mechanical

Physiological in vitro

Extra cellular matrix (ECM) – cell derived, **CRISPR** – *cell engineering for increased cartilagespecific (collagen, aggrecan) matrix production*

3D (bio) printingprinting method(extrusion, DLP printing),printing parameters

Heiden Orthopedics USA (2023):

X. Niu et al. (2022): Integrated gradient tissue-engineered osteochondral scaffolds: Challenges, current efforts and future perspectives; Joerg Eschweiler et al (2021): The Biomechanics of Cartilage—An Overview; Heiden Orthopedics USA (2023): What Is Osteoarthritis?; https://heidenortho.com/osteoarthritis/; Neogi, T. (2013): The epidemiology and impact of pain in Osteoarthritis; I. Bartolotti et al. (2021): A Roadmap of In Vitro Models in Osteoarthritis: A Focus on Their Biological Relevance in Regenerative Medicine; Leifer et al. (2021): Chapter 1: The Burden of OA-Health Services and Economics testing

Material selection for bioreactor – *translucent, biocompatible*

disease model

- High socio-economical impact
- Complex model for knowledge
 - creation

X No animal testing

used as bioink / coating

Macromolecular crowder – enhanced ECM deposition

https://icons8.com/

(Bio)-Ink development – adequate viscosity, shape fidelity, light cross-linkable, biocompatible, cell-adhesive, stable over time

Material science



Supervisor: Prof. Dr. Frederico Castelo Ferreira

Co-Supervisor: Dr. Paola Sanjuan-Alberte, Dr. João Carlos Silva

phdopendays.tecnico.ulisboa.pt