China Scholarship Council – University Maastricht PhD Programme

Application form

Basic information
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1. Information on prospective UM supervisors and Promotor

1a. First Supervisor/promoter:

- Title(s), initial(S), first name, surname: Dr. Berta Cillero-Pastor
- Research group: Spatial omics group for regenerative medicine, cBITE department-MERLN, Faculty Health medicine & Life Sciences

- Address for correspondence: PO Box 616, 6200 MD Maastricht
- Telephone: M +31 (0) 616208450
- E-mail: b.cilleropastor@maastrichtuniversity.nl

- Title(s), initial(S), first name, surname: Prof. Martijn van Griensven

- Research group: Molecular and Translational Regenerative Medicine

- Address for correspondence: Universiteitssingel 40, 6229 ER Maastricht/Room C3.577 PO Box 616, 6200 MD Maastricht
- Telephone: +31 6 46 70 55 65
- E-mail: M.vanGriensven@maastrichtuniversity.nl

1b. Second Supervisor/copromoter:

- Title(s), initial(S), first name, surname: Dr. Pieter J Emans
- Research group: Dept. Orthopedics, Faculty Health medicine & Life Sciences

- Address for correspondence: PO Box 616, 6200 MD Maastricht
- Telephone:
- E-mail: p.emans@maastrichtuniversity.nl

1c. Promotor (if applicable): **– see above**

2. Information on University Maastricht Faculty / Department/ Institute/ School contact person:
When the application is granted by both CSC and UU the contact person is responsible for the practical arrangements (i.e. assistance in obtaining a visa, finding accommodation, etc.) of the visit of the PhD candidate:

- Initial(S), first name, surname: Dr. Berta Cillero Pastor

- Research group: Spatial Omics for Regenerative Medicine

- Address for correspondence: PO Box 616, 6200 MD Maastricht
- Telephone: M +31 (0)616208450
- E-mail: b.cilleropastor@maastrichtuniversity.nl

- To be filled in by the applicant if already known –

1. Information on the applicant

- Initial(S), first name, surname:
- Male/female:
- Current work address:

- Telephone:
- E-mail: WeChat:
- Private address:

2. Details of applicant's home university
Note! A separate letter of recommendation by the supervisor of faculty dean of the home university is required.

- Name of home university:

- Address:

- Telephone:
- E-mail:
- Website (if available):

3. Applicant's home university supervisor of his Master Thesis:

- Title(s), initial(S), first name, surname:

- Address for correspondence:

- Telephone:
- E-mail: WeChat:

4. Research field(s)

前沿技术 / Frontier Technologies

生物技术 / Biotechnology

人类健康与疾病的生物学基础 / Biological Foundations of Human Health and Diseases

基础研究 / Basic Research

Mass spectrometry

Cell/tissue culture

Electron microscopy

5. Title of research plan for CSC-UM PhD Programme

Infrapatellar tissue phenotyping: Predictor of regenerative capacity in cartilage defect patients?

6. Short summary of research plan (max. 250 words) (A full plan has to be submitted later)

Background: Knee osteoarthritis (KOA) is one of the most prevalent chronic diseases that causes pain, loss of function and reduced quality of life. Total knee arthroplasty (TKA) is a well-established surgical intervention consisting of replacing a defective joint by an artificial joint for functional improvement. The infrapatellar fat pad (IPFP) or Hoffa's fat pad is a fatty tissue located underneath the patellar ligament, between the joint capsule and synovium. Despite the incidence of KOA, the function of the fat pad is not well studied and is debated. Traditionally, the IPFP is removed in order to facilitate surgical access to the joint. Nowadays, advanced surgery techniques allow the preservation of this tissue, however, IPFP is still partially or totally resected in around 88% of TKAs (1). Moreover, the IFP is a very heterogenous tissue, containing stem cells that could improve the regeneration capacity of cartilage in patients suffering local cartilage damage.

Study objective: The first objective of this project will consist on the characterization and design of several *in vitro* co-culture models of adipose tissue, tendon and cartilage. To better understand the role of IFP and its potential protective role in the knee, tissue biopsies obtained from patients after KOA and cartilage defect surgery will be obtained. In parallel, biopsies from racing horses suffering from cartilage pathologies will be obtained through a collaboration with the University of Perugia, Italy. Tissue explants will be stimulated with pro-inflammatory cytokines and mechanical stimuli to mimic motion and local damage. Tissue response will be evaluated using single cell spatial proteomics, secretomics and electron microscopy. Imaging mass spectrometry will be employed to

study tissue interaction while keeping the spatial location. The second objective will consist on the subclassification of these patients based on molecular markers of IFP by advance mass spectrometry, MRI and response to regenerative therapies evaluated by RNA expression and IHC.

Expected Results: We hypothesize that IFP is an essential tissue to maintain joint homeostasis by a direct cross-talk with surrounding tissues such as synovium, tendon and cartilage. Local changes in protein abundance and gene expression are expected in IFP after mechanical stimulation. More specifically, changes in the secretome and mitochondria of the IFP tissue are expected and key for joint preservation. Therefore, the potential protective of IFP tissue might be essential for cartilage regeneration. The obtained IFP molecular profiles by mass spectrometry and clinical data based on the patient response associated to different regenerative therapies, will be used for improved patient classification which will help to design better personalized medicine strategies.

Requirements: cell culture experience, chemistry/analytical chemistry background preferably in mass spectrometry

Group's performance: Publications: 306; H-Index: 67; number of citations: 16910.

7. Motivation for CSC-UM PhD application (max. 250 words)

We are currently supervising one CSC student with excellent results and received 1 CSC PhD student this year. The student is able to integrate well with the groups, the research and training expectations. Most importantly, the student is able to mature remarkably becoming new potential young leader in the scientific and industrial biomedical community.

Applicant's Curriculum Vitae (if available)
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8. Personal details

Applicant
- Title(s), initial(S), first name, surname:

CSC-UM PhD programme start 1-9-2023

- Surname:
- Nationality: Chinese
- Date of Birth:
- Country and place of birth:

9. Master's degree (if applicable)
Note: Add a copy of your Master's degree to your application
University (201 or 985 if available):
Faculty/discipline:
City and country:
Date:
Grade average:
Title Master's thesis (if applicable)
Grade for thesis:

References:

1- Zhu Z, Han W, Lu M, Lin J, Yin Z, Shang X, Weng X, Zha Z, Tian J, Lei G, Hunter DJ, Ding C. Effects of infrapatellar fat pad preservation versus resection on clinical outcomes after total knee arthroplasty in patients with knee osteoarthritis (IPAKA): study protocol for a multicentre, randomised, controlled clinical trial. BMJ Open. 2020 Oct 23;10(10):e043088. doi: 10.1136/bmjopen-2020-043088. PMID: 33099502; PMCID: PMC7590360.

Most relevant publications for this project:

1- Janssen M, Timur UT, Woike N, Welting TJ, Draaisma G, Gijbels M, van Rhijn LW, Mihov G, Thies J, Emans PJ. Celecoxib-loaded PEA microspheres as an auto regulatory drug-delivery system after intra-articular injection. J Control Release. 2016 Dec 28;244(Pt A):30-40. doi: 10.1016/j.jconrel.2016.11.003. Epub 2016 Nov 8. PMID: 27836707. Citation 49

2- Anderson JR, Chokesuwattanaskul S, Phelan MM, Welting TJM, Lian LY, Peffers MJ, Wright HL. 1H NMR Metabolomics Identifies Underlying Inflammatory Pathology in Osteoarthritis and Rheumatoid Arthritis Synovial Joints. J Proteome Res. 2018 Nov 2;17(11):3780-3790. doi: 10.1021/acs.jproteome.8b00455. Epub 2018 Oct 3. PMID: 30229649; PMCID: PMC6220363. Citation 43

3- Barre, F. P. Y., Flinders, B., Garcia, J. P., Jansen, I., Huizing, L. R. S., Porta, T., Creemers, L. B., Heeren, R. M. A., & Cillero-Pastor, B. (2016). Derivatization Strategies for the Detection of Triamcinolone Acetonide in Cartilage by Using Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry Imaging. Analytical Chemistry, 88(24), 12051-12059. https://doi.org/10.1021/acs.analchem.6b02491. Citations: 67

4- Barre, F. P. Y., Paine, M. R. L., Flinders, B., Trevitt, A. J., Kelly, P. D., Ait-Belkacem, R., Garcia, J. P., Creemers, L. B., Stauber, J., Vreeken, R. J., Cillero-Pastor, B., Ellis, S. R., & Heeren, R. M. A. (2019). Enhanced Sensitivity Using MALDI Imaging Coupled with Laser Postionization (MALDI-2) for Pharmaceutical Research. Analytical Chemistry, 91(16), 10840-10848. https://doi.org/10.1021/acs.analchem.9b02495Enhanced Sensitivity Using MALDI Imaging Coupled with Laser Postionization (MALDI-2) for Pharmaceutical Research. Citations: 65

5-Othman, Z., Pastor, B. C., van Rijt, S., & Habibovic, P. (2018). Understanding interactions between biomaterials and biological systems using proteomics. Biomaterials, 167, 191-204. https://doi.org/10.1016/j.biomaterials.2018.03.020. Citation: 65

6-Groven RVM, Nauta SP, Gruisen J, Claes BSR, Greven J, van Griensven M, Poeze M, Heeren RMA, Porta Siegel T, Cillero-Pastor B, Blokhuis TJ. Lipid Analysis of Fracture Hematoma With MALDI-MSI: Specific Lipids are Associated to Bone Fracture Healing Over Time. Front Chem. 2022 Mar 3;9:780626. doi: 10.3389/fchem.2021.780626.

7- Poh PSP, Seeliger C, Unger M, Falldorf K, Balmayor ER, van Griensven M. Osteogenic Effect and Cell Signaling Activation of Extremely Low-Frequency Pulsed Electromagnetic Fields in Adipose-Derived Mesenchymal Stromal Cells. Stem Cells Int. 2018 Jul 12;2018:5402853. doi: 10.1155/2018/5402853. Citation: 18