Université Claude Bernard Lyon 1

PhD
PEPR INSIDE

TITLE

Identification of biochemical and biomechanical biomarkers to predict osseointegration of a second-intention knee prosthesis

INTRODUCTION

Total knee arthroplasty (TKA) is the only procedure that can alleviate advanced osteoarthritis, restore mobility to patients, and significantly reduce their pain (Du et al., 2020). Between 0.72 and 1 million of such surgeries are performed each year in Europe, and projections suggest a 43% increase by 2050 (Klug et al., 2021). TKA is an increasingly well-mastered procedure, partly thanks to the use of surgical robots. According to a recent study, this has led to a decrease in patient dissatisfaction after this procedure (DeFrance and Scuderi, 2023). However, prosthesis revision remains a difficult procedure. It is characterized by a later return to physical activity after revised TKA (rTKA) than after TKA (Maugard et al., 2025), a failure rate for rTKA that has not changed significantly over the last decade (Geary et al., 2020), and a postoperative dissatisfaction rate that remains high at 34% (Winther et al., 2023), particularly in cases of persistent and unexplained pain (Rodríguez-Merchán, 2024). Pre-, per- and post-operative follow-up could be improved to better anticipate risks and adapt treatments to reduce patient dissatisfaction.

INSIDE project (dIgital twiN for post-operative monitoring of implanted-kneE) has received funding from PEPR Santé numérique. This project aims to improve patient care when planning rTKA by creating a digital twin of the implanted knee prothesis, which will be fed by a multi-scale data stream, ranging from the whole-body scale to the cellular scale. This thesis project focuses on the cellular level. Given that joint instability, aseptic loosening, and periprosthetic fractures are causes for revision, but also for re-revision of TKA (Goh et al., 2026), osseointegration of the implant is primarily concerned with the risk of surgical failure. It relies on the ability of the bone tissue to create a stable interface between the bone and the implant.

Per-operative explants (bone marrow, cortical if cut and synovium samples) will be collected and stored from 30 patients in collaboration with HCL. Blood samples will be collected at follow-ups. Given that osteoblasts and osteocytes originate from mesenchymal stromal cells and those cells are mechanosensitive cells, osseointegration is linked to biological and biomechanical aspects (Grzeskowiak et al., 2020; Vajapey et al., 2025).

OBJECTIVES

In this context, the objectives of this thesis are to (i) study the ability of mesenchymal stromal cells from patients who have undergone rTKA to differentiate into osteoblasts/osteocytes, (ii) investigate their biological responses to dynamic mechanical stimuli, and (iii) analyze bone modeling capacity.

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METHODOLOGY

To achieve this goal, the main steps will be:
- to conduct a literature review on osseointegration of orthopaedic implants
- to contribute to the assessment of the inflammatory states of the synovial fluids and the signs of chronic inflammation of bloods due to metal ions
- to define a bone differentiation protocol from mesenchymal stromal cells
- to develop a protocol of mechanical stimulation of these cells under a bio-tribo-reactor
- to apply all the methodologies to human mesenchymal stromal cells from all patients
- to analyze short-term (transcriptomics) and long-term (histology, proteomics, microarchitecture, and mechanical characterization) response of cells to mechanical stimuli
- to identify biochemical and biomechanical markers associated with the ability of cells to create bone
- to compare previous biomarkers with results from synovial fluid and blood samples to identify biomarkers that can be used in clinical settings.

CANDIDATE PROFILE

This position is open to national and international students. Candidates should have academic knowledge in cell biology and biomechanics, molecular biology, mechanics, mechanobiology. Master degree or equivalent in biomechanics or bioengineering is requested.

LABORATORIES INVOLVED

LBMC (Univ Eiffel-UCBL UMR_T 9406), Bron, https://lbmc.univ-gustave-eiffel.fr

LaMCoS (CNRS-INSA, UMR 5259), Villeurbanne, https://lamcos.insa-lyon.fr/?L=1

LYOS (INSERM-Université de Lyon UMR 1033), Lyon, https://www.lyos.fr/#

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COLLABORATIONS

This project will be performed in close collaboration with HCL including Croix-Rousse, Lyon-Sud and Edouard Herriot hospitals.

DOCTORAL SCHOOL

MEGA Doctoral School (ED 162) - Mechanics, Energy, Civil Engineering, Acoustics

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LOCALIZATION

Most of the experimental work will be carried out at LaMCoS. A working environment will also be available at LBMC and LYOS. The three laboratories are located within a 10 km radius.

APPLICATIONS

Candidates should send their application by e-mail to the supervisors, which should include a Curriculum Vitae, a letter of motivation, transcripts of Master's grades (M1 and M2) and a letter of recommendation from a previous internship. Applications will be evaluated in two stages: an evaluation of the application files and an interview.

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