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Deadline: February 27th, 2026

EUR CARE PhD program pre-proposal

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INSERM U1301 / CNRS UMR5070 / Univ. P. Sabatier / EFS / ENVT | A geroscience and rejuvenation research center ([RESTORE](#))

PhD co-Director: *Pablo Loza Alvarez*, pablo.loza@icfo.eu

PhD co-Director affiliation: ICFO–Institut de Ciències Fotòniques, The Barcelona Institute of Science and Technology, Universitat Politècnica de Catalunya Barcelonatech

Research project title: Aging as a Scar :Mechano-Metabolic Control of Adipose Tissue Regeneration

Research program abstract (max 500 words):

Background:

Aging functions as a chronic scarring process within adipose tissue (AT). Fibrosis increases with age in human and mouse AT [[Song Y. et al., Immun Ageing \(2025\)](#)], progressively trapping mesenchymal stem cells (MSCs) in senescent, glycolytic, and pro-inflammatory states [[Ou MY. et al., Cell Death Dis \(2022\)](#)]. This maladaptive remodeling promotes systemic degeneration (sarcopenia, cancer cachexia, and metabolic syndrome) through persistent ROS-mediated inflammation [[Juanhong L. et al., Life Med \(2025\)](#); [Zhang YX. et al., Front Immunol \(2023\)](#)].

Critically, AT ages among the first tissues and, as both the primary MSC reservoir and central metabolic organ, converts from regenerative niche to pathological environment through progressive ECM stiffening **coupling mechanics to dysfunctional metabolism**.

Our inguinal subcutaneous adipose tissue (ISCAT) model recapitulates this tipping point: massive inguinal fat resection triggers collagen-rich fibrosis (NaCl control) but yields efficient adipocyte regeneration following transient BAPN-mediated cross-link relaxation [[Labit et al., Sci Rep \(2017\)](#); [Pacary et al., NPJ Regen Med \(2024\)](#); [Peurichard et al., J Theor Biol \(2019\)](#)]. This reveals a D0–D6 decision window where early mechanical softening pharmacologically reverses anti-regenerative commitment, providing a unique system to dissect the **mechanometabolic trigger of aging-like fibrosis**.

Hypothesis:

We postulate that tension within MSC/adipocyte lobules establishes, during the D0–D6 post-injury window, a short-term tensional memory that directs MSC fate through mechano-metabolic reprogramming [[Dupont et al., Nature \(2011\)](#); [Yang C. et al., Nature Materials \(2014\)](#)]. Transient relaxation of cellular/lobules contractility or matrix cross-linking is expected to decrease stiffness and fibril alignment, attenuate mechanotransductive activity, shift metabolism toward oxidative pathways, and thereby favor adipocyte regeneration over fibrotic scarring [[Koo et al., Cell Metabolism \(2018\)](#); [Nam et al., npj Biomedical Innovation \(2026\)](#); [Pacary et al., NPJ Regenerative Medicine \(2024\)](#)].

To test this hypothesis, the MECHRAMIX project will combine mechanical inference and metabolic imaging to quantitatively link local tension dynamics, lobular architecture, and metabolic state transitions to adipose tissue function during early repair.

PhD objectives :

MECHRAMIX will generate quantitative *ex vivo* maps linking lobular tension and metabolism.

1. **Tension mapping:** Mechanical tensions will be extracted from fluorescence images of adipocyte lobules using the **FOAM** mechanical inference algorithm [[Ichbiah et al., Nature Methods \(2023\)](#)], which is already implemented in our team. The method will be adapted to lobular geometry by integrating FOAM-derived surface tensions into a finite-element model and validated by comparing simulated lobular deformations with experimental uniaxial stretch curves.
2. **Mechano-metabolic registration:** Mechanical inference maps derived from fluorescence images (FOAM) will be spatially registered with Raman spectroscopic maps (cytochromes, ATP, lipids) to identify combined mechano-metabolic domains and extract robust regional features.
3. **Predictive classifier:** A machine-learning model will be trained on multimodal D0–D6 features (mechanical inference from fluorescence and Raman spectroscopic signatures) to test whether mechanical tension maps, metabolic Raman profiles, or their spatial correlation best predicts D14 outcomes (fibrosis vs adipocyte regeneration), comparing the sensitivity of each modality alone versus their combination.

Describe in 50 words max for each how this project fits the 3 defining criteria of the CARE graduate programme:

1) Relation to CARE topics of Cancer, Ageing and/or Rejuvenation

By quantifying MSCs generated tension fields and temporal pattern on adipocyte lobules, MECHRAMIX will link mechano-metabolic reprogramming to ageing-related fibrotic mechanics and enables pharmacomechanical and metabolic combinatorial interventions for ageing and rejuvenation (CARE).

2) Multidisciplinary aspect

MECHRAMIX integrates mechanobiology (tension mapping), biophysics (calibrated uniaxial stretch), tissue Raman metabolic imaging, and predictive machine learning to decode tension-driven metabolic reprogramming. The project combines imaging, computational modeling, and pharmacology to connect cellular mechanics with tissue ageing and repair outcomes.

3) International and/or industrial aspect(s)

A partnership with ICFO (Pablo Loza-Álvarez) provides advanced Raman microscopy and tissue spectroscopy expertise for mechano-metabolic analysis. This Franco-Spanish collaboration enables the multiscale technological integration and access to industrially relevant instrumentation needed to study ageing mechanics.

Keywords in line with EUR CARE

Mechano-metabolic ageing, tissue fibrosis, tension-driven rejuvenation, interdisciplinarity, multiscale integration

References of the teams, highlighting the co-signatory students:

Valappil, D. K. (2026). Digitally Scanned Light-Sheet Brillouin Microscopy and Force Inference: A Strategy Toward Quantitative Tissue Mechanics [Doctoral dissertation, Université de Toulouse]. RESTORE Laboratory, Doctoral School BSB – Biology, Health, and Biotechnology.

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Pacary, A., Peurichard, D., Vaysse, L. et al. A computational model reveals an early transient decrease in fiber cross-linking that unlocks adult regeneration. *npj Regen Med* 9, 29 (2024). <https://doi.org/10.1038/s41536-024-00373-z>

G Castro-Olvera et al., A review of label-free photonics-based techniques for cancer detection in the digestive and urinary systems 2025 *J. Phys. Photonics* 7 012002. DOI 10.1088/2515-7647/ad8613

Albert Sicre-Conesa et al., Coping with Differences in Scanned Area and Spatial Resolution for Raman/Fluorescence Images of Labeled Cells *Anal. Chem.* 2025, 97, 22, 11554–11562