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Deadline: February 27th, 2026

EUR CARe PhD program pre-proposal

PhD Director: Laurent Malaquin (laurent.malaquin@laas.fr)
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PhD co-Directors: Laurence Vaysse (laurence.vaysse@inserm.fr) & Jose Moran-Mirabal (mirabj@mcmaster.ca)
PhD co-Director affiliation: Restore (Toulouse, FR) & McMaster University (Canada)

Research project title: Integrated Vascularized Microphysiological System for Studying Adipose Tissue Ageing

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Research program abstract (max 500 words):

In the human body, white adipose tissue (WAT) plays a central role in energy storage by accumulating lipids. Beyond this function, WAT acts as a dynamic endocrine organ that continuously communicates with the liver, skeletal muscle, and brain to regulate appetite and whole-body energy homeostasis. Adipose tissue is among the first organs to exhibit alterations in metabolic responses and endocrine function during early ageing, contributing to chronic inflammation and systemic metabolic decline. Despite its central position, the mechanisms underlying adipose tissue functional decline during ageing remain poorly understood.

A major barrier to progress in this field is the lack of physiologically relevant human 3D adipose tissue models. To address this gap, we recently developed a modular and scalable bioengineering strategy to generate functional vascularized human white/beige adipose organoids and microtissues. This approach relies on spheroid encapsulation within GelMA hydrogels using human adult primary cells obtained from dermolipectomy procedures. To take this new engineering process a step forward notably for the development of pertinent ex-vivo microphysiological system, the present project aims to achieve controlled, standardized neovascularization of the microtissue and establish ex vivo perfusion by connecting the engineered endothelial networks to a microfluidic system via anastomosis. Our central hypothesis is that functional perfusion through engineered endothelial networks is essential to maintain tissue-scale adipose physiology, preserve cellular heterogeneity, and reveal early ageing-associated dysfunctions. The objective is to develop an engineering framework compatible with the generation of large adipose microtissues (≈1.5 cm²), enabling sustained tissue functionality—secretion, respiration, and metabolism—and supporting multimodal analyses of tissue physiology in both normal and ageing contexts.

In this context, the PhD candidate will implement a hybrid strategy combining endothelial self-organization and microfluidic engineering. First, the spatial organization and stability of endothelial networks within multispheroid adipose constructs will be investigated by using an original approach based on adaptative photopatterning of photosensitive hydrogel materials and tuning the biochemical and biomechanical properties of GelMA hydrogels [3,4]. Although GelMA has demonstrated strong potential for adipose tissue maturation, promoting robust endothelialisation, it will require further optimization of matrix properties, including crosslinking density, stiffness, and porosity. Second, the networks will be connected to a microfluidic perfusion platform, enabling controlled flow, shear stress, and long-term tissue maintenance. The resulting perfused microtissues generated in physiological and ageing conditions will support analyses of metabolic activity, oxygen consumption, adipokine secretion, and single-cell transcriptomics.

The student will benefit from LAAS-CNRS expertise in hydrogel 3D structuration, microfluidics, from collaboration with Jose Moran-Mirabal's group (McMaster University, Canada), providing access to

advanced biomaterials compatible with endothelialization strategies and from collaboration with Restore Institute for adipose tissue physiological aspects.
This interdisciplinary project integrates tissue engineering, vascular biology, microfluidics, and systems-level metabolic analysis. It will generate a unique human microphysiological system to dissect endothelial–adipocyte crosstalk, identify vascular-derived signals regulating adipose plasticity in a controlled human setting. Beyond its scientific impact, this project offers strong doctoral training value, exposing the PhD candidate to advanced biomaterials, microfabrication, live imaging, omics analyses, and translational research at the interface of biology and engineering.

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

This project directly addresses the Ageing axis by investigating mechanisms underlying adipose tissue functional decline. By developing a perfused human adipose microphysiological system, it enables analysis of ageing-associated metabolic and vascular dysfunctions. The platform also supports rejuvenation-oriented strategies and could have relevance for cancer research, where adipose–tumor interactions are critical.

2) Multidisciplinary aspect

The project integrates physics, engineering, and biology, combining biomaterials science, microfluidics, vascular biology, and adipose physiology. It bridges hydrogel design, microfabrication, endothelial self-organization, and metabolic analysis. Three complementary partners contribute expertise in biomaterials engineering, microfluidic systems, and vascular/adipose biology, ensuring strong interdisciplinary training and cross-disciplinary knowledge transfer.

3) International and/or industrial aspect(s)

The project includes an international collaboration and exchange with Jose Moran-Mirabal's group (McMaster University, Canada), providing expertise in biomaterial functionalization, hydrogel mechanics, GMP-compatible materials. This partnership strengthens technological innovation, translational potential, and exposure of the student to an internationally recognized research environment.

5 keywords in line with EUR CARe

Multidisciplinary approaches, tissue engineering, ageing, adipose tissue

5 references of the teams, highlighting the co-signatory students:

1. **Aigoin, J., Payré, B., Minvielle Moncla, J., Escudero, M.**, Goudouneche, D., Ferri-Angulo, D., Calmon, P.-F., Vaysse, L., Kemoun, P., Malaquin, L., & Foncy, J. (2025). Comparative Analysis of Electron Microscopy Techniques for Hydrogel Microarchitecture Characterization : SEM, Cryo-SEM, ESEM, and TEM. *ACS Omega, 10*(15), 14687–14698. (DOI:10.1021/acsomega.4c08096)
2. **Escudero, M**., Vaysse, L., **Eke, G.**, Peyrou, M., Villarroya, F., Bonnel, S., Jeanson, Y., **Boyer, L.**, Vieu, C., Chaput, B., **Yao, X.**, Deschaseaux, F. , Parny, M., Raymond-Letron, I., Dani, C., Carrière, A., Malaquin, L., Casteilla, L., (2023). Scalable generation of pre-vascularized and functional human beige adipose organoids. *Advanced Science, 10*(31), 2301499. (DOI :10.1002/advs.202301499)
3. **Fournié, V., Venzac, B.**, Trevisiol, E., Foncy, J., Roul, J., Assié-Souleille, S., **Escudero, M.**, Joseph, P., Reitz, A., & Malaquin, L. (2023). A microfluidics-assisted photopolymerization method for high-resolution multimaterial 3D printing. *Additive Manufacturing, 72*, 103629. (DOI:10.1016/j.addma.2023.103629)
4. **Eke, G.**, Vaysse, L., **Yao, X., Escudero, M.,** Carrière, A., Trevisiol, E., Vieu, C., Dani, C., Casteilla, L., & Malaquin, L. (2022). Cell Aggregate Assembly through Microengineering for Functional Tissue Emergence. *Cells, 11*(9), 1394**.** (DOI :10.3390/cells11091394)
5. **Babi, M., Riesco, R., Boyer, L.,** Fatona, A., **Accardo, A.,** Malaquin, L., & Moran-Mirabal, J. (2021). Tuning the Nanotopography and Chemical Functionality of 3D Printed Scaffolds through Cellulose Nanocrystal Coatings. *ACS Applied Bio Materials, 4*(12), 8443–8455. (DOI :10.1021/acsabm.1c00970)