Graduate MuSkLE - Excellence Doctoral Scholarships 2026

Laboratory: LIBM, UR7424 / Research team: Atherosclerosis, Thrombosis and Physical Activity
PhD supervision: THOMAS Amandine (amandine.thomas-zanetti@univ-lyon1.fr) / MILLON Antoine Millon (antoine.millon@chu-lyon.fr)

State of the Art. Cardiovascular diseases remain the leading cause of mortality worldwide. Atherosclerosis of the carotid arteries is a major contributor to ischemic stroke, with approximately 25% of cases resulting from the rupture of vulnerable carotid plaques. Plaque vulnerability is characterized by intense neovascularization and intraplaque hemorrhage (IPH), driven by immature and leaky micro vessels arising from the vasa vasorum. Recent advances in transcriptomics, proteomics, and single-cell RNA sequencing have improved our understanding of the molecular signatures distinguishing stable from unstable plaques. However, these discoveries have not yet translated into improved clinical management. Moreover, post-transcriptional mechanisms—particularly translational regulation and protein phosphorylation—remain largely unexplored in atherosclerosis, despite their central role in controlling protein expression and cell signaling. Regular physical activity (PA) is a well-established protective factor against cardiovascular disease. Large epidemiological studies demonstrate an inverse relationship between PA level and atherosclerotic plaque prevalence. Importantly, our previous work showed that physically active patients with asymptomatic carotid plaques exhibit a significantly lower prevalence of IPH compared to sedentary individuals. Nevertheless, the molecular mechanisms by which PA modulates plaque vulnerability remain unknown.

Hypothesis and Originality. This project is based on the hypothesis that physical activity reduces carotid plaque vulnerability by modulating translational control, phosphoprotein signaling, and systemic circulating factors. The originality of the project lies in its integrative and innovative approach, combining multi-omics analyses (proteomics, phosphoproteomics, lipidomics, metabolomics, and translatomics) with spatial and functional investigations. To our knowledge, this is the first study to address translational regulation and phosphoproteome remodeling in vulnerable atherosclerotic plaques in the context of physical activity.

Methodology and Work Plan. The project is structured around three main objectives:
1.Effect of physical activity on plaque vulnerability
Carotid plaques collected from approximately 500 patients undergoing endarterectomy will be analyzed according to individual PA levels. Multi-omics profiling will identify molecular signatures associated with plaque vulnerability. These findings will be complemented by studies in ApoE$^{-/-}$Fbn1^C1039G+/− mice, a validated model of vulnerable plaques with IPH, subjected or not to a structured exercise training protocol.
2.Translational and spatial characterization of plaques
Translational efficiency will be assessed through polysome profiling in human plaques and nascent protein labeling in mice. Candidate molecules will be spatially localized using MALDI mass spectrometry imaging and immunohistochemistry, allowing correlation with IPH-rich regions.
3.Role of circulating factors and identification of therapeutic targets
Plasma proteomic and lipidomic analyses will identify systemic mediators influenced by PA. Functional validation will be performed using ex vivo human plaque cultures, endothelial cell assays, and targeted modulation of candidate molecules in animal models.

Expected Outcomes and Impact. This project will provide unprecedented mechanistic insight into how physical activity modulates carotid plaque vulnerability. It is expected to identify novel molecular targets and systemic effectors that could be exploited for future therapeutic or preventive strategies against ischemic stroke. The PhD candidate will benefit from high-level interdisciplinary training in cardiovascular biology with strong potential for publication in high-impact international journals.

References of the research team on the topic:
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