Dr. Florent ALLAGNAT
PhD; Privat Docent
Head of Research
Vascular Surgery Laboratory, Lausanne University Hospital
Rue du Bugnon 7A
CH-1005 Lausanne
Switzerland

SUR programme 2025
Florent Allagnat lab project description

Vascular diseases are major contributors to global morbidity and mortality. Advances in treatments, such as targeted drugs and regenerative therapies, have significantly improved patient outcomes. In addition, research contributes to evidence-based guidelines that optimize healthcare practices. Despite advances in medical intervention, there remains a critical need to identify preventive strategies that can effectively reduce the burden of cardiovascular diseases.

Dietary restriction (DR) has robust anti-aging effects and shows benefits against cardiovascular diseases. However, there is currently no clinical protocol leveraging the benefits of DR in vascular patients. DR comes in many forms such as calorie restriction, time restricted feeding (TRF), or macronutrient (protein, carbohydrate or lipid) restriction. The pathways involved in the benefits of DR include amino acid sensing and mTOR, the GH-IGF-1 axis, the GCN2-eIF2α-ATF4 signalling module and increased production of hydrogen sulfide (H_2S), a gasotransmitter derived from the cysteine metabolism with potent anti-inflammatory and antioxidant properties.
The Vascular Surgery Laboratory of the University Hospital of Lausanne (CHUV) is part of the Vascular Surgery Unit and is an integral part of its DNA. Over the last 15 years, the laboratory has developed various models and approaches to study vascular diseases, combining state-of-the-art preclinical models of vascular surgery in mice and large animals, precise dietary control, and comprehensive histological and molecular analysis. Below is the current research agenda.
Axis 1: Peripheral artery disease and intimal hyperplasia
Atherosclerosis in peripheral arteries leads to peripheral artery disease (PAD), where reduced blood flow to the limbs causes ischemia, which may progress to chronic limb threatening ischemia (CLTI) and associated risk of amputation. PAD patients also carry a high risk of cardiovascular event and death. Surgical revascularization is the only option for CLTI, but it is not always possible, nor effective. Moreover, even after successful revascularization, long-term patency is still plagued by re-occlusion due to the pathologic process of intimal hyperplasia (IH). IH develops in response to vessel injury, leading to the formation of neointima layer, which progressively occludes the lumen of the vessel. IH results in complex recurrent end-organ ischemia, and often leads to loss of limb, brain function, or life. Despite decades of research, PAD and IH remain poorly understood and ill-treated.
In the past 10 years, we demonstrated our expertise in the study of PAD, particularly intimal hyperplasia and neovascularisation/angiogenesis. We recently completed several studies showing that H_2S inhibit promote neovascularisation and protect against IH. The current

objective of this research line is to test various forms of DR (protein restriction and TRF), or downstream effectors of DR, to promote neovascularisation and protect against IH.

Axis 2: aortic aneurysm and dissection (AAD)

The prevalence of aortic aneurysm and dissection (AAD) continues to increase with the aging of the global population. AAD is due to degeneration/weakening of the aortic wall and affects 5% of men aged >65 years. Aortic aneurysms and dissections (AAD) can lead to aortic rupture, which has a devastating 80% mortality rate, as most aneurysms remain asymptomatic until rupture. AAD accounts for 2-3% of deaths in Western countries. Currently, there are no effective medications to prevent AAA growth and rupture, and surgery is the only option for patients with advanced AAA. Surgical repair is complicated and costly, and despite improvements, morbidity and mortality remain high.

While DR undoubtedly provides systemic health benefits in humans, there are no dietary recommendations for the management of AAD. The popularity of the TRE intervention as a viable DR regimen has increased over the past decade due to its reduced risk of malnutrition and ease of adherence. However, preclinical and clinical studies are necessary to assess the efficacy of TRF in the reduction of AAA growth and risk of rupture. If successful, TRF/TRE could provide a simple and cost-effective strategy for AAD patients beyond traditional pharmaceutical interventions.

Axis 3 Strategies to reduced peri-operative complications

Vascular surgery has one of the highest rates of perioperative events, and approximately 20% of vascular surgery patients have evidence of cardiac injury. Despite improvements in surgical techniques, grafts, and perioperative care, vascular surgery still carries a high risk of morbidity and mortality. To reduce perioperative complications in vascular patients, new prophylactic approaches to reduce patient-related risk factors before surgery are needed. DR has been proposed to provide benefits against stress, including surgical stress. Thus, DR (TRF or protein restriction) may reduce perioperative complications in vascular patients undergoing surgery.

In 2022, our department, under the leadership of Drs. A. Longchamp and Sébastien Déglise, started a prospective randomized control trial called Optimization of Diet before Surgery (OptiSurg; NCT04627688). This study aims to evaluate the feasibility and efficacy of a 2-week, 10-hour preoperative TRE in patients undergoing elective femoral endarterectomy (Fontaine stage IIb).

In parallel to our OptiSurg clinical trial, we have initiated a murine project to test the benefits of eTRF and/or low protein diet preconditioning to protect against surgical stress using various pre-clinical models.

Conclusion

Vascular surgery research is essential to the advancement of our knowledge and the improvement of outcomes in the treatment of vascular disease. It focuses on developing innovative surgical techniques, optimizing procedures, and evaluating long-term outcomes. This research enhances patient safety, minimizes complications, and contributes to evidence-based guidelines for optimal care. It also plays a critical role in training future vascular surgeons, fostering innovation and refining surgical techniques. Continued investment in vascular surgery research is essential to advancing medical knowledge, improving patient care, and achieving better outcomes for people with vascular disease.