

**CMD InnoCARE (Innovation pour les maladies
CARDIOVASCULAIRES, métaboliques et RESPIRATOIRES)**
Master 2 Internship proposal (2024-2025)



Profile(s) linked to the project:

- Experimental Biology (*Recherche expérimentale*)
- Research and Biological Data Analysis (*Recherche et analyse de données biologiques*)
- Clinical Research (*Recherche clinique*)

Lab: Institut du Thorax – Inserm UMR 1087

Team: 1

Name and position of the supervisor: Capoulade Romain, CRCN, “cardiac valve diseases” group leader

Email of the supervisor: romain.capoulade@univ-nantes.fr

Candidate (if known):

Title of the internship: Study of mechanisms related to the structural bioprosthetic valve degeneration

Summary of the internship proposal:

Valvular heart diseases are frequent cardiovascular diseases. There is currently no medical therapy to treat these diseases, and the only option for the patients is to undergo valve replacement via open heart surgery. The use of biological prosthetic valves, instead of mechanical valves, is constantly growing and is currently implanted in >80% of patients. These valves provide better hemodynamic profile, but their main limitation is their durability over time. Indeed, structural bioprosthetic valve degeneration (SVD) gradually occurs post implantation, with a need for redo surgery in 10 to 12 years after initial implantation.

The pathophysiological mechanisms related to development of SVD are completely unknown. Only partial clinical data highlight potential role of lipids infiltration, inflammatory response, and implementation of fibro-calcific processes. We have recently initiated a research project focused on the understanding of the mechanisms leading to SVD, based on complementary in vitro and in vivo (rodents and large animal model) approaches. The identification of cellular and molecular mechanisms involved in the development of SVD will allow us to identify risk factors exacerbating the pathophysiological processes and develop therapeutic approaches in order to limit the incidence and progression of SVD over time.

The aim of the internship will be to elucidate the mechanisms related to SVD, with a specific focus on the recruitment and differentiation of cells repopulating the biological valve. Classical biochemical and molecular protocols, coupled with single cell-RNAseq and MRN, will be used throughout the internship, as well as primary cell culture experiments and microscopy.