

**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:** Pathophysiological mechanisms involved in the development of mitral valve prolapse

**Summary of the internship proposal:**

Mitral valve prolapse (MVP) is a frequent cardiovascular disease with an incidence of 2.5% in the population. There is currently no medical therapy to treat this disease, the only option is to perform surgically repair or replacement of the diseased valve. We have identified the 1<sup>st</sup> causal gene (i.e. *FLNA*) associated with MVP and have generated a unique rat model KI for the *FLNA*-P637Q mutation. We confirmed the pertinence of the model which develop human-like MVP.

Relying on this unique model and the derived primary culture of mitral valve cells established in the lab, we would like to decipher the cellular and molecular mechanisms involved in the development of this disease, with the objective to identify potential therapeutic targets and develop therapeutic approaches that could be tested in our model.

We recently highlighted the main signaling pathways involved in the development of the disease. Specifically, the role of immune response and the mechanical stress imposed to the valve leaflets (as well as their interaction) appear as the main mechanisms leading to MVP. The aim of the internship project will be to elucidate the respective role of these pathways (and their interaction) on the development of MVP. Classical biochemical and molecular protocols will be used throughout the internship, as well as primary cell culture experiments and microscopy.

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