Long noncoding RNAs in <u>R</u>ight <u>V</u>entricular <u>H</u>eart <u>F</u>ailure towards personalized healthcare.

Cardiovascular diseases have a high socio-economic burden, among which heart failure plays a major role. Both left ventricular heart failure (LVHF) and pulmonary arterial hypertension (PAH) trigger initially right ventricular hypertrophy (RVH) and eventually right ventricular heart failure (RVHF). RVHF worsens prognosis of patients and remains a poorly preventable disease, partly due to a limited knowledge of its mechanisms. In addition, there is a need for novel tools or biomarkers to predict or diagnose RVHF at an early stage of its evolution. **To cope with these unresolved medical problems, we hypothesize that long noncoding RNAs (lncRNAs) are involved in the development of RVHF and constitute an unexplored reservoir of potential therapeutic targets and biomarkers.** Therefore, **our goal is to look into the molecular mechanisms responsible for the development of RVHF, focusing on lncRNAs**. Specifically, **the project will address the following research questions**. Are lncRNAs regulated in RVHF? Do they functionally impact RVHF development? What are the mechanisms involved? Can lncRNAs be used to prevent or treat RVHF? Can they help clinicians in patient monitoring and risk stratification?

We will use two rat models of RVHF and explanted human hearts with RVHF to identify lncRNAs, using deep sequencing, that have a potential as biomarkers and therapeutic targets in RVHF. Then we will conduct a prospective biomarker study in patients at risk of RVHF. Subsequently we will use in vitro and in vivo experiments to validate that the lncRNAs selected by use can indeed be used to modify the development in RVHF in a rat model.

This is a bilateral project in which Polish partners will bring expertise in animal models of RVHF and human RVHF, while the Luxembourg partner will bring expertise in RNA work.

This project will improve our knowledge of the role lncRNAs play as possible triggers of RVHF and eventually can contribute to development of new therapies and new biomarkers of RVHF.