

### **Reasons for undertaking the research topic**

Cardiovascular diseases (CVD), including acute coronary syndromes (ACS), are the leading cause of morbidity and mortality worldwide, with global healthcare costs estimated at €680 billion annually. ACS, encompassing acute myocardial infarction (AMI) and unstable angina pectoris (UAP), typically presents as severe retrosternal chest pain accompanied by dynamic ECG changes. Yet distinguishing ACS from non-cardiac chest pain (e.g., musculoskeletal pain, pulmonary embolism) remains difficult due to overlapping and non-specific early symptoms.

Despite diagnostic progress, no biomarker reliably detects myocardial infarction in its earliest stages. Cardiac troponins (cTnI/cTnT), considered the diagnostic gold standard, have significant limitations: they may remain negative in UAP and can be elevated in non-cardiac conditions such as pulmonary embolism, kidney disease, myocarditis, or sepsis.

Recently, non-coding RNAs (ncRNAs)—including microRNAs, PIWI-interacting RNAs, small nucleolar RNAs (snoRNAs), and tRNA-derived fragments (tRFs)—have emerged as promising biomarkers. These molecules are stable in biofluids, reflect disease processes, and can be analyzed using high throughput next-generation sequencing (NGS).

### **Project objective**

This project aims to determine whether circulating ncRNAs can:

- (i) distinguish ACS-related chest pain from non-cardiac causes;
- (ii) enable earlier diagnosis than cardiac troponins;
- (iii) correlate with clinical and biochemical parameters in ACS;
- (iv) predict recurrent ischemic events over a 3-year follow-up.

### **Research description**

Plasma samples from 98 patients enrolled in the LEMONADE study (34 AMI, 64 non-cardiac chest pain) will be analyzed alongside clinical data. Circulating and extracellular vesicle-associated ncRNAs will be profiled using NGS. The most promising candidates will then be validated across the entire cohort via polymerase chain reaction.

### **Expected outcomes**

The project may discover novel biomarkers enabling quicker, more accurate ACS diagnosis upon admission. Integrating ncRNA with clinical data could enhance risk prediction, supporting personalized cardiology management strategies. This will be the first comprehensive analysis of circulating ncRNAs in chest pain patients prior to diagnosis.