Description for the general public

Objective of the project

Cardiovascular diseases (CVD), such as acute coronary syndromes (ACS), are the most common cause of morbidity and mortality worldwide. Only in 2009, the global healthcare costs for CVD were estimated at €106 billion. Each year, approximately 1,100,000 new cases of ACS are recorded in the European Union. Evidently, if we prevent ACS, we will save lives, prevent disabilities and reduce healthcare costs. ACS are caused by activation and aggregation of platelets on ruptured atherosclerotic plaque, leading to formation of a thrombus in the coronary artery and eventually to necrosis of the heart muscle. From this reason, blocking platelet activation with antagonists of the platelet P2Y12 receptor (ticagrelor or prasugrel) is the most efficient strategy to prevent recurrent ischaemic events in patients after ACS. However, even despite treatment with ticagrelor or prasugrel, recurrent ischaemic events occur in ~10% of patients within one year after the initial ACS. At present, there is not tool to predict such recurrent ischaemic events.

MicroRNAs (miRNAs) are small, non-coding RNAs which regulate the expression of 60% of human protein-encoding genes, including genes involved in the development and progression of atherosclerosis. Recently, it was observed that a major part of miRNAs is present in human platelets, and that these miRNAs are released from platelets either free or encapsulated in platelet extracellular vesicles. The profile of circulating platelet-derived microRNAs (miRNAs) changes in different pathophysiological state, such as ACS. In this project, we are going to compare the effect of ticagrelor and prasugrel on circulating platelet-derived miRNAs in patients with ACS, and to investigate whether these miRNAs can be used to predict recurrent ischaemic events over 3 years after the initial ACS.

Describe the research to be carried out

We are going to study circulating platelet-derived miRNAs in plasma samples collected from patients with ACS and randomly assigned to the group treated with ticagrelor or prasugrel as antiplatelet drug. We will isolate platelet miRNAs from plasma and from extracellular vesicles and compare the profiles of miRNAs present in the samples from selected patients who did and who did not experience recurrent ischaemic events over 3 years observation. Based on the results, we will choose the most attractive miRNAs and analyse the expression of these miRNAs in all collected samples. We believe that the identified miRNAs could be used as biomarkers of recurrent ischaemic events after ACS.

Present reasons for choosing the research topic

At present, the reasons why some patients experience recurrent ischaemic events despite optimal medical treatment after ACS remain unknown. Since miRNA profiles change after ACS, it is tempting to speculate that these changes might predict recurrent ischaemic events, including recurrent ACS. Our project is the first study to compare the effect of two strong antiplatelet drugs on circulating platelet-derived miRNAs profile in patients after ACS, as well as to evaluate whether these miRNAs can be used to stratify risk after ACS. In addition, identification of specific miRNAs which have predictive value and genes regulated by these miRNAs enables to understand the mechanisms underlying recurrent ischaemic events, essential to identify miRNA-based biomarkers and therapeutic targets in patients with ACS.