

The small molecule inhibitors represent an era of target-directed therapy and precision oncology used in the treatment of various malignancies. Despite the success of this therapy, they can induce side effects such as thrombosis, bleeding, and cardiovascular events. A better understanding of the pathogenesis of cardiovascular complications in patients treated with small molecule inhibitors is urgently needed to improve safety of cancer therapy. In this project we aim to characterize a possible effect of platelets on endothelial cells, to study effects of small molecule inhibitors on functionality of endothelium, and finally, to perform proof of principle, clinical study investigating whether platelets from chronic myeloid leukemia patients untreated or treated with small molecule inhibitors may have different effect on platelets compared to the healthy individuals. We will use platelets isolated from healthy humans, and patients untreated and treated with small molecule inhibitors. Platelet functionality will be assessed using light-aggregometry. The effect of small molecule inhibitors on functionality endothelial barrier integrity will be investigated. We anticipate that this research proposal will bring a novel knowledge regarding platelets and their functional effect on endothelial barrier integrity. In addition, the research proposal will provide a proof of principle, clinical study, to test whether chronic myeloid leukemia patients untreated and treated with small molecule inhibitors may have different effect on platelets and on endothelial barrier integrity.