Novel strategies for pharmacological modulation of platelet-derived microparticles - effects on endothelium

Platelet-dependent mechanisms are involved in thrombosis, inflammation angiogenesis and contribute to vascular homeostasis. Thus, pharmacological modulation of platelet activity has become of great clinical importance carrying a new perspective for effective therapeutic strategies in many cardiovascular disorders. Currently, antiplatelet therapy plays an important role in prevention of arterial thrombosis and is thought also to be effective in preventing metastasis spread. Yet, we still have gaps in our understanding how antiplatelet agents affect cross-talk mechanisms between cells. The main intercellular communication mechanism of activated platelets involves extracellular vesicles transfer. These lipid bilayer particles carry an important cargo (in form of proteins, nucleic acids, lipids etc.) that is up taken by recipient cells. Thus, extracellular vesicles act as important messengers in health and disease. Platelet-derived extracellular vesicles (PEVs) exhibit a wide range of pro-thrombotic, pro-inflammatory properties as well as can afford endothelial barrier protection. Therefore, it seems crucial to know how applied anti-platelet treatment affects modulation of PEVs release and their properties as messengers. To date, limited studies are available considering this topic, despite the fact that the repertoire of antiplatelet agents is still increasing.

In particular, it is not known how antiplatelet agents modulate PEVs release and their effects on endothelial cells' phenotype in healthy conditions as compared with atherosclerosis. In the current project, we will take the advantage of unique methods that have been developed in JCET for comprehensive endothelial profiling in vitro and ex vivo. Combining them with methods that will be developed within the frame of this project, we aim to broaden the knowledge about effects of antiplatelet pharmacology on extracellular vesicles release and function and their cross-talk with healthy endothelium or dysfunctional endothelium in atherosclerosis.

Importantly, the research can have its continuation also in a context of different disease entities, where antiplatelet treatment effectiveness is reported biased. Proposed hypothesis and type of studies are innovative and, to our knowledge, have not been conducted yet. By complement this knowledge within the project, possibly new therapeutic avenues for many disease entities that are associated with vascular endothelial dysfunction can become opened.