

Angioplasty is a safe and effective way to unblock coronary arteries. During this procedure, a catheter is inserted into the groin or arm of the patient and guided forward through the aorta and into the coronary arteries of the heart. There, blocked arteries can be opened with a balloon positioned at the tip of the catheter. Initially, angioplasty was performed only with balloon catheters, but technical advances have been made and improved patient outcome has been achieved with the placement of small metallic spring-like devices called “stents” at the site of the blockage. The implanted stent serves as a scaffold that keeps the artery open. Despite of technological progress achieved in this area, the processes of restenosis or thrombosis remain the major limitations of invasive cardiology and are associated with a significant number reinterventions. Above mentioned processes are related to oxidative stress-mediated changes in cell signaling and involve at least two different cellular systems and their interactions: endothelial and vascular smooth muscle cells. Subsequent generations of drug-eluting stents and drug-eluting balloons are designed for a better safety profile as well as novel technologies dedicated to facilitate endothelialization are currently under investigation. In this area, the following project is focused on the ability of cell-penetrating peptides (CPPs) to delivery of CRISPR/dCas9 system designed for activation of tropomyosin-1 into primary coronary artery endothelial cells and primary coronary artery smooth muscle cells, and subsequently stabilization of their actin cytoskeleton. Interactions of cell-to-cell junctional protein complexes with the actin cytoskeleton provide proper endothelial function, the regulation of the stage of F-actin polymerization may be crucial in maintaining of endothelial barrier stability, focal adhesion and migratory potential of endothelial cells, as well as in changing their expression profile during pro-inflammatory conditions. Moreover, F-actin stabilization seem to exert dissimilar effect in vascular smooth muscle cells, so assessment of their migration and proliferation may be useful in application of the following studies in prevention against arterial vessel remodeling after mechanical injury during angioplasty. Hence, the main aim of the project is to assess the biological effect of F-actin stabilization in primary coronary artery endothelial cells and primary coronary artery smooth muscle cells exposed to tumor necrosis factor . The data obtained during realization of the following project will be important to take into consideration during projecting new generation of drug-eluting stents and balloons. Furthermore, the data acquired through this project will be used as preliminary data for other in vivo studies.