The goal of the proposed project is to develop a microvessel model in vasculature-on-a-chip systems that will enable the analysis of endothelial cells (ECs) under conditions resembling physiological/pathological conditions. The developed microvessel model will be used to study the response of endothelial cells to various stimuli that induce pathological conditions under not only static but also flow conditions similar to those in the living body.

According to statistics, cardiovascular diseases (CVDs) and cancer are now the most common causes of death. It is therefore important to learn more about the mechanisms of these diseases and to find a way of treatment. The disturbances in the function of the blood vessel network play a key role in cardiovascular diseases (CVDs). Vascular networks are lined with endothelial cells, which form a barrier between circulating blood and tissues. The role of endothelial cells is to regulate blood flow, maintain the integrity of the vessel walls, and participate in a numer of cellular processes including the inflammatory response. Damage and inflammation of the vascular endothelium are the cause of oxidative stress and resulting cellular damage. To date, mitochondria have been shown to play a key role in the regulation of many cellular processes, including calcium homeostasis, reactive oxygen species generation and nitric oxide synthesis, as well as the regulation of inflammatory responses. The standard two-dimensional cell culture was used so far for studies in this area. In comparison to *in vivo* blood vessels such an approach is widely simplified. Therefore, detailed studies on the endothelium require the development of a suitable experimental model.

Therefore, in the present project, we propose to use a new approach based on Lab-on-a-chip systems. They are a good solution used to achieve spatial cell cultures which mimic natural cel growth. The flow microsystems in which we plan to reproduce blood vessels are Vasculatureon-a-Chip (VoC) systems. They enable the creation of a three-dimensional vascular flow lumens with endothelial cells cultured on the inner walls in flow conditions. Microvessel models can thus be used to understand how microvessel networks are formed and how they respond to various external signals (e.g., biological, chemical, mechanical). In addition, the response of mitochondria exposed to pro-inflammatory factors in such a cell model can be similar to that *in vivo*.

Within this project, it will be explored how different factors, i.e., (1) structural factor - replication of different sizes of microvessels, (2) mechanical factor - simulation of shear stress condition (3) biological factor – the presence of other cells, affect microvessels formation in vasculature-on-a-chip systems. Moreover, finding the answer to the question of how different stress-inducing stimuli in endothelial cells (i.e., human umbilical vein endothelial cells (HUVECs) or human aortic endothelial cells (HAECs)) affect these cells will be crucial. First of all, cell-to-cell interactions and the architecture of the mitochondrial network will be analyzed. We hypothesize that the obtained results will differ when using cell monolayers or cells growing in developed microvascular models.

The scientific research proposed in the project on the border of chemistry, biology, medical diagnostics and microtechnology is interdisciplinary. The application of the proposed vasculature-on-a-chip approach may contribute new knowledge to understanding the mechanisms responsible for the vascular insufficiency typical of cardiovascular disease.