

The vascular system consists of complex network of arteries and veins that carry blood and lymph through the body. Proper formation and organization of the vascular network is critical to permit the blood to circulate and transport nutrients, oxygen, carbon dioxide, hormones, and blood cells to and from the cells in the body to provide nourishment, help in fighting diseases and maintain homeostasis.

Development of human embryonic vasculature starts three weeks after fertilization with the formation of blood islands. Each blood island is cell aggregate consisting of the externally placed endothelial cells and hematopoietic cells placed in the middle of the island. Blood islands constitute the “seeds” of future vascular network which subsequently, coalesce into larger units and form a primitive network of tubules known as a primary capillary plexus. Newly formed primary capillary plexus continues to grow and eventually penetrate the embryo giving start to embryonic blood circulation. In the future preferential channels will form arteries and veins. The formation of the primary capillary plexus is the first and the most critical step in vascular system development. Failure to form primary capillary plexus or impairments in its development caused by genetic or environmental factors can lead to fetal death or result in abnormal vasculature formation, thus leading to inadequate oxygen supply. Unfortunately, currently available animal models to study the development of primary capillary plexus require an excessive use of vertebrate embryos. Developed recently *in vitro* models, including use of human induced pluripotent stem cells, limit the animal use in the study but lack spatial organization and rather focus on the formation of single blood island failing to resemble the architecture of the primary capillary plexus.

In the proposed research we aim to generate a model of human primary capillary plexus using microfluidics and lab on chip technology which will allow to study the initiation and development of human embryonic vasculogenesis. The technology developed in the project will provide a novel tool to study the formation of the primary capillary plexus and will overcome the limitation of currently available approaches. The blood islands-like structures will be generated with droplet microfluidics. The lab on chip technology chip will allow for precise control of architecture and spatial organization of the blood islands.

Developing a model of the primary capillary plexus is particularly important for better understanding of vasculogenesis and the impact of various genetic and environmental factors leading to abnormalities in embryonic vasculature development. A novel model the primary capillary plexus formation proposed here has high chances of having an impact on the biological and tissue engineering field. The expected results could, in the long run, contribute to establishing new treatment modalities for vascular genetic disorders and significantly advance the field of embryonic toxicology.