

In order to ensure the proper functioning of our body, each organ and each of muscle cells must be supplied with oxygen and essential nutrients such as glucose, fats, proteins, vitamins. The role of the transmitter of these molecules relies on the blood circulating in the blood vessels - veins, arteries and capillaries. The angiogenesis occurs in the first month of fetal life. Initially, blood vessels develop from stem cells in a process called vasculogenesis. As the embryo develops, new blood vessels begin to form from the existing ones in a process called angiogenesis. While the process of vasculogenesis after birth is not active, the angiogenesis can be induced also in the adult body. It can be noticed during wound healing after injuries, surgeries and cancer. In order to produce a blood vessel at a particular location, a synthesis or activation of molecules that induce the process must occur. The most important molecule involved in the process of angiogenesis is VEGF - vascular endothelial growth factor. It is responsible for the mobilization of endothelial cells, which mainly initiate creation of a new blood supply. In addition to this molecule very important role plays HGF (Hepatocyte Growth Factor) - a protein whose name comes from the first described function. Although misleading name, it also takes part in the development of blood vessels. This molecule combines with its receptor - c-Met - present on the surface of endothelial cells, and similar to VEGF stimulates them to migration and cell division. A thorough study of the mechanisms regulating the activity of the endothelial cells under HGF stimulation provides opportunities for control of angiogenesis.

A significant impact on angiogenesis appears to have the conditions in the local tissue - mainly bounded up with the insufficient supply of the oxygen. Previous studies suggest that hypoxia promotes the activation of new blood vessel formation. By observing changes in the activity of angiogenesis both the physiological and pathological, raises the question of which mechanisms are responsible for the activation or inhibition. Therefore, in this research project we will focus on understanding the mechanisms responsible for regulation of this process in cells directly creating new blood vessels and in conditions similar to those prevailing in the body - in an environment with a reduced oxygen content.

One of the main mechanisms responsible for the activation of HGF in the cell seems to be based on a molecule called HGF activator. There is a high probability that its activation runs up precisely because of hypoxia. Consequently, there is a subsequent start of the cascade of reactions leading to the formation of a new vessel. In addition, some results suggest that hypoxia may be responsible for increased levels of the early form of HGF molecule, that is produced by endothelial progenitor cells.

Another factor regulating the process of HGF activation may be microRNAs molecules. MicroRNAs are ribonucleic acid molecules of small size (22-25 nucleotides), which play an important role in regulating the levels of proteins produced by the cells. The project currently undertakes research to identify and determine the impact of a number of microRNAs that are involved in regulation of the HGF levels in vascular endothelial cells.

In the future, based on the results of our research new anti-metastases cancer therapies can be developed. These treatments will be based on inhibition of the growth of the tumour's blood supply. Moreover, the results can bring us to developing therapies that accelerate wound healing, recovering from surgical treatments and above all they give bases to the development of new methods for treatment of ischemic diseases using the principles known as regenerative medicine.