The development of angiogenesis depends on the functional state of endothelial cells, as well as on the balanced secretion of cytokines, growth factors and chemokines by endothelial cells and cells of microenvironment. Macrophages are an essential component of the microenvironment and take part in the formation of blood vessels both due to the production of cytokines and due to contact interactions with endothelial cells. One of the most important cytokines that control angiogenesis at all its stages is VEGF. Currently, the role of VEGF in the intercellular interactions of endothelial cells and macrophages is not well described.

The aim of the study was to investigate the effect of VEGF deprivation using monoclonal antibodies on angiogenesis under conditions of co-cultivation of endothelium and macrophages.

Monoclonal antibodies to VEGF-A were used for VEGF deprivation in monoculture of endothelial cells and in co-culture of endothelial cells with macrophages. The cytokines IL-1β, IL-6 and TNFα were used as inducers. When VEGF-A is removed from the medium, endothelial cells show plasticity and form longer vessels, they modify the expression of VEGF receptors. Macrophages regulate endothelial cell activity through the secretion of cytokines, including VEGF, and through contact interactions with endothelial cells. THP-1 cells increase the sensitivity of endothelial cells to VEGF by stimulating the expression of VEGFR1 and VEGFR3, this effect is VEGF-A-independent. The cytokines IL-1β, IL-6, TNFα independently stimulate non-branching angiogenesis, increasing the length of the vessels. At the same time, IL-1β increases the expression of VEGFR1 on the surface of endothelial cells. In contrast, IL-6 and TNFα decrease it, thereby regulating the sensitivity of endothelial cells to VEGF. The effects of these cytokines are not dependent on VEGF-A. Cytokines IL-1β, IL-6, TNFα promote the acquisition of anti-angiogenic properties by THP-1 cells that is independent of VEGF-A, as well as of the expression of its receptors by endothelial cells. Thus, VEGF is an important, but not the only one factor controlling angiogenesis. Under conditions of VEGF-A deficiency, either endothelial cells or microenvironment cells are able to compensate for its functional load due to the production of other growth factors.