It has been shown in numerous studies, that endothelial cells play a critical roles in physiologic and pathophysiologic processes such as regulation of blood fluidity, angiogenesis and tumor metastasis. Similarly to other cells, the EC cells undergo senescence process that is associated with modulations of their functions. It has been suggested that senescence of EC reduces their angiogenic capacity and contributes to the onset and progression of atherosclerosis. Additionally, despite of decreasing angiogenic function of older endothelial cells and the evidence for endothelial cell aging in vivo, surprisingly cancer incidence increases as a function of age. It is very intriguing especially concerning that angiogenesis is essential for tumor growth and metastasis. It may suggest that angiogenesis in tumors is not deficient in aged humans or it is somehow regulated but our knowledge about possible mechanisms is limited.

The aim of this project is to confirm our hypothesis about modulatory effect of tumor cells on endothelial senescent cells renewal process. We would like to determine the role of tumor secretable factors in regulating of ECs senescence and evaluate the role in this process a potentially new mechanism that involve integrin-dependent pathway. Proposed project will gain new insights into the role of tumor in modulation of senescence process in endothelium that might lead to break an barrier in tumor development and to increase tumor angiogenesis.

Experiments proposed in the project will give a new information about molecular mechanisms involved in regulation of endothelial senescence process and tumor development. It is well established that the tumor growth and metastasis depend on angiogenesis, which is impaired in older people as a consequence of endothelial senescence. On the other hand we observed that tumor microenvironment is able to renewal of endothelial senescent cells. Taking all above into consideration, understanding the mechanisms of tumor-mediated endothelial senescence reversal will be critical in determining the role of endothelial senescence in tumor growth. We truthfully believe that information that will be obtained during project realization might be a useful in the future for designing drugs and programming new strategies to anticancer therapy. Furthermore, it is known that senescent cells undergo distinct changes that may cause an impairment of endothelium function and lead to defective vascular repair, increasing prevalence of atherosclerosis or to impaired angiogenesis. Impaired angiogenesis in older people may have important clinical consequences such as impaired recovery from myocardial infarction. Thus, recognizing molecular mechanisms involved in reversing of vascular dysfunction may be helpful in developing strategies to attenuate the effect of aging in the vasculature, and help preserve the quality of life.