

The aim of the project is to investigate the molecular mechanisms determining the choice between senescent or apoptotic pathway in endothelial cells. Cell response to stress and damage may range from recovery to apoptosis, which is a programmed cell death. However, an additional response may be developed by the cells experiencing damage, which is adopting a state of permanent cell-cycle arrest that is termed cellular senescence. Physiologically it is justified as a tumor-suppressing mechanism providing protection against tumorigenesis. On the dark side, however, senescence contributes to aging and age-related diseases. As endothelium is a tissue particularly exposed to adverse signals, no wonder, then, that endothelial cells may undergo senescence, becoming dysfunctional. Such premature vascular aging, which is directly linked to senescent endothelium, is associated with increased cardiovascular risk, which may manifest in coronary heart disease, myocardial infarction, stroke and peripheral artery disease.

It is not clear what determines whether cells undergo senescence or apoptosis. Understanding of those mechanisms is of basic biological interest. The knowledge on mechanisms of cellular senescence is important in respect of development of cancer and physiological aging. Research funded under this project focuses on elucidation of the detailed pathways of premature senescence and apoptotic switch in respect of two molecules: Nrf2 transcription factor and microRNA 34a, which, based on our initial data, are found to be potent modulators of these processes.