We live longer and longer. Elongation of the human lifespan inevitably results in a higher incidence of diseases that do not affect, or only very rarely, young people. It is believed that the pace and effects of aging vary from person to person, which shows that the aging process is malleable. The main aim of biogerontology, the science of biology of aging, is to understand the molecular mechanisms regulating aging/senescence, with an ultimate goal to find a recipe for longevity and a way to avoid aging-related diseases. Not long ago the search for the causes of aging led to a spectacular discovery. Namely, it has been shown that removal of senescent cells from the body of old animals improves their physical condition and reduces some of the symptoms characteristic of aging. This finding reassured researchers of the importance of studying aging at the cellular level. Cellular senescence, besides contributing to organismal aging, has several important beneficial functions, including protection against proliferation of cells with damaged DNA (protection against cancer) and involvement in tissue regeneration. Senescent cells differ morphologically and biochemically from young ones. They do not divide but remain metabolically active and adopt a so-called senescence-associated secretory phenotype (SASP). Proteins secreted by senescent cells substantially impact the surrounding cells and the entire organism. Changes in the nucleus and chromatin occurring during cellular senescence are intensively studied, but little is known about alterations within the nuclear envelope (NE). The NE is responsible for the spatial separation of processes in the cellular compartments and for communication between the nucleus and the cytoplasm, in which the nuclear protein complexes (NPCs) actively participate. NPCs are composed of about 30 different proteins, nucleoporins, which are responsible for the selectivity of the transport between the cytoplasm and the nucleus, play a role in DNA repair and regulate gene expression. The composition and density of NPCs depend on cell type, physiology, differentiation and transformation. The literature reports and our preliminary results suggest that NPCs are subject to specific changes in senescent cells. Our data show that during cellular senescence, the expression of most nucleoporins is reduced. In addition, we have observed some perturbations in the nuclear transport. Nup88 is a particularly interesting nucleoporin. Its expression and level decline in senescent cells, and its localization is altered. Nup88 is found in the cytoplasmic part of NPCs but also migrates to the nuclear interior and regulates gene expression. It is found in transcriptionally inactive loci. **Our research hypothesis is that cellular senescence changes NPC composition, density, and function, disturbs the nuclear transport and allows proteins that do not usually reside there to migrate to the nucleus. We also assume that Nup88 is responsible for regulating the expression of genes essential in senescence.** The research will be carried out on young and senescent normal cells (vascular smooth muscle cells – VSMCs, fibroblasts, preadipocytes). In particular, VSMCs, the senescence of which is closely related to the development of atherosclerosis, one of the aging-related diseases (ARD), will be studied. In vitro results will be verified using cells obtained from atherosclerotic plaques (ex vivo study) to see if similar changes occur in in vivo senescence. Cells isolated from plaques are mostly senescent ones. So far, nothing is known about the role and alterations of NPCs in the process of atherosclerosis. Our research will decipher the functions, composition and density of NPCs in cellular senescence and Nup88 function in the regulation of gene expression. We will examine which genes are regulated by and which novel proteins interact with Nup88. So far, alterations in Nups content/function were suggested as a culprit of certain diseases, including Alzheimer's disease and sarcopenia, both belonging to ARD. The proposed study may help to better understand the role of NPCs alterations in senescence progression and in atherosclerosis and find new markers useful for identifying senescent cells. Understanding the mechanisms of cellular senescence can help to develop strategies used to prevent or delay this process and, in this manner, reduce the symptoms at the organismal level. The implementation of the project will provide data that will be useful in understanding and counteracting the effects of diseases caused by abnormal composition of NPCs.