Over the past few decades we have seen a significant increase in the average life expectancy in Poland and in the world[1]. This effect is related, inter alia, to scientific discoveries that have allowed the development of effective drugs or new therapeutic methods against the many diseases that have plagued man since the dawn of history. The increase in life expectancy is also connected with the technological progress, which has enabled to effectively protect or even replace human beings in the most dangerous areas of industry. Unfortunately, with the increase in life expectancy, the likelihood of developing neurodegenerative diseases such as Alzheimer's disease increases. So far, we have not been able to develop effective medicines that could stop or even significantly slow down the development of this disease[2].

This research project focuses on interactions on molecular level of amyloid β peptides (associated with Alzheimer disease) with human serum albumin (HSA) in the presence of human cystatin C (HCC) and selected metal cations. Our motivation based on the fact that, we still do not understand, how we can effectively stop or at least slow down the neurodegeneration processes, which of the proteins naturally occurring in the human body are able to weaken the process of amyloid β deposits formation.

The objective of this project is to characterize the role of human serum albumin in the modification (inhibition) of the kinetics of the oligomerization process of various forms of amyloid peptides in the presence of human cystatin C and other ligands and to describe the ability of HSA to bind to these peptides using a wide spectrum of the complementary research methods.

The structural analysis of the HSA complexes proposed in this project will be conducted by means of a combination of advanced spectroscopic methods (NMR spectroscopy, NMR diffusometry, Fourier transform infrared spectroscopy, circular dichroism spectroscopy, X-ray absorption spectroscopy, spectrofluorymetry), scattering techniques (small angle X-ray and neutron scattering, dynamic light scattering), microscopic studies (atomic force microscopy and transmission electron microscopy) and molecular dynamic simulations.

During the project implementation, we plan to determine the ability of human albumin to form a number of complexes with either Aβ peptides (oligomeric or monomeric forms), human cystatin C and selected ligands (metal ions, fatty acids). It is planned to use the following amyloid β peptides: **Aβ (1-40), Aβ (4-40), Aβ (1-42), Aβ (1-16) or Aβ (4-16) and their selected mutants (London variant - His6Arg or Asp7 modifications) as well as selected phosphorylated (Ser8) versions.** We would also like to investigate the effect of selected metal ions (e.g. Zn^{2+}, Cu^{+} or Cu^{2+}) and the previously mentioned HCC on the Aβ oligomerization processes. As a result, combining the results of our studies on interactions between HSA with various ligands and Aβ peptides, we expect that we will gain insight into the cooperative mechanism of the inhibition of the Aβ peptides oligomerization process by HSA.

[1] Life Expectancy Tables of Poland 2014, GUS, Warszawa.
[2] Ehret M.J., Chamberlin K.W. (2015) *Clin. Therapeutics*, **37(8)**, 1604-1616.