Copper is an element necessary for life of all organisms and cells breathing with oxygen. This happens as a result of a unique ability of this element to mediate (catalyze) the process of electron transfer to oxygen atoms. This results in generation of chemical energy by the organism, to support other metabolic processes. This process occurs in a protein, cytochrome c oxidase, present in mitochondria, the subcellular structures. It is very efficient, but anyway a small proportion of oxygen atoms escapes the safe path of chemical reactions, forming free oxygen radicals, which jeopardize the integrity of biomolecules. Free oxygen radicals are responsible for many pathologies, including DNA damage which can lead to the appearance of tumors. Thus, evolution developed protective mechanisms against the results of their action. Copper also participates in these processes, being present in the active center of a key protective enzyme, superoxide dismutase. Other specialized enzymes containing copper ions in their active centers exist, being responsible for synthesizing particular molecules of crucial importance for the functioning of multicellular organisms, including humans. One should mention here the biosynthesis of collagen and elastin, structural proteins of connective tissue, and production of neurotransmitters, necessary for the functioning of the brain.

Copper atoms taken up from food must be delivered in appropriate quantities to all cells of the organism, and within them to individual protein molecules. With respect to chemical properties, the copper transport inside cells is very different from the extracellular one. Inside the cells the so called reducing conditions are present, related to a low oxygen concentration. In such conditions copper forms compounds on a lower oxidation state – Cu(I), in which the copper ions are connected primarily with sulfur atoms. The intracellular transport processes are relatively well understood, They base on chaperone proteins which collect Cu(I) ions from proteins transferring them across the cell membrane and convey them to individual target enzymes. Copper on a higher oxidation state – Cu(II) is very toxic for cells. Nevertheless, copper must be transported in this form in body fluids, because of a high availability of oxygen, which immediately transforms Cu(I) into Cu(II). In spite of this, the cells take up copper as Cu(I) via the membrane receptor protein, Ctr1. Nobody knows how the copper transfer to Ctr1 occurs. Neither the site nor the mechanism of the Cu(II) reduction to Cu(I) have been established.

Albumin is the main protein of blood serum, transporting numerous metabolites, drug molecules, and metal ions, including copper, the latter as a very strong Cu(II) complex. This complex is stronger than the Cu(II) complex of Ctr1, which should prevent the transfer of copper to this receptor. In the course of our recent studies we discovered a new chemical mechanism of relaying Cu(II) by small peptide molecules, containing an X-His moiety. Two such peptides are known to be present in human blood, a tissue hormone, GHK, and a pancreas related peptide GHTD. Our initial results, which provide a starting point for this project support an idea that such peptides may mediate the transfer of copper to the Ctr1 receptor, thus playing a crucial, but hitherto unknown function of regulating the flow of copper in the organism. A demonstration and detailed elucidation of this mechanism will have an enormous impact on physiological studies, and probably also for the design of new therapies against oncological and neurodegenerative diseases, in which the impairment of copper balance has been observed. The means necessary for this aim is to perform a detailed study of albumin structure in solution, determine the sites on the surface of this large protein, where interactions with copper and the peptides occur, and explore possible mechanisms of reduction of Cu(II) to Cu(I). A clear majority of studies will be performed at the Department of Biophysics, IBB PAS. Structural studies of albumin will be performed in a collaboration with the University of Bayreuth (Germany) and NanoBioMed Centre of AMU in Poznan. Additional studies will be performed in the international and national collaboration in the University of Melbourne (Australia), University of Strasbourg (France), AMU, and in collaborating laboratories in Canada and USA.

The results of our studies will be presented to international conferences and published in the renowned scientific journals. In the course of the project we plan to arrange a collaboration with medical science institutions for a further elucidation of the studied mechanism with respect to oncological and neurodegenerative diseases.