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The study of localization of beta-amyloid peptide monomers in cells by fluorescence microscopy

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Motivation and Aim: Alzheimer's disease (AD) is the most common form of dementia in the elderly (60–80 % of all known dementia) and one of the socially significant age-related diseases. Currently, this neurodegenerative disease affects more than 50 million people worldwide and is the fifth most common cause of death for people over 65 in developed countries. This number is expected to triple by 2050 unless significant progress is made in research for early diagnosis and new effective therapies [1]. In Russia, the number of people who sufferer from Alzheimer's disease was estimated at more than 1 million people, the majority of patients are women (80 %), about 85 % of patients were aged 70–89 years. Previously, a significant increase in cases of Alzheimer's disease was predicted to 1.3 million people by 2020 [2] only due to an increase in the average age of Russian citizens. However, complications caused by viral diseases and stress will definitely lead to an additional increase in cases of neurodegeneration, since modern studies show an unambiguous effect of viral diseases on the risk of neurodegeneration due to the involvement of common molecular immunological mechanisms [3, 4]. At the same time, at the moment, the proportion of official mortality of Russian citizens from neurodegenerative (mainly Alzheimer's) diseases is significantly less than in other countries. Russian researchers explain this by the presence of a significant number of not diagnosed cases, due to the clear age dependence of neurodegeneration and the similarity of the age-and-sex pyramids of Russia and other countries. Researchers also pay attention to the lack of modern domestic approaches to diagnosis [5]. It is important that the indicators of the lost years of life of citizens at an economically active age are socially and economically significant [6]. Patients initially require general assistance at home, then there is a need for qualified assistance, nursing care and nurse services, as well as the placement of the patient in a hospital. This involves a significant amount of resources of citizens and the state. Improving the diagnosis of Alzheimer's disease at an early stage, the emergence of new diagnostic approaches, the use of new cost-effective drugs will reduce the social and economical burden imposed on relatives of patients and the healthcare system [5].

Despite the enormous progress in science and medicine, there are no effective methods of therapy and early diagnosis – more than 100 years after the disease was first described as a form of progressive, neurodegenerative and behavioral disorder by Alois Alzheimer in Germany [7]. From this fact, it can be concluded that the lack of a detailed description of the molecular and cellular mechanisms involved in the pathogenesis of Alzheimer's disease, and neurodegeneration in general, does not allow the development of effective

pharmacological drugs and early diagnosis. Increasing evidence indicates an important role that Aβ peptides play in AD progression [8]. Despite extensive research in this area, there exists controversial uncertainty in aspects of Aβ toxicity, mechanisms of Aβ internalization and interaction with cell lipid membranes [9]. At the same time, it is worth paying attention to the presence of a small number of perfect new promising modern developments at the highest level of development of physico-chemical, including structural, methods [10–13]. Experimental information obtained in physiologically relevant conditions is required for understanding molecular mechanisms in detail, create therapeutic potential, and, further, for the rational development of new biologically active compounds and screening of existing ones to obtain the most effective candidates for medicines, as well as the development of methods of early diagnosis.

Results: The modern development of optical fluorescence microscopy methods allow us to use of the modern a state of the art to understand the molecular mechanisms of intracellular transport and the localization of proteins and peptides in simulated pathophysiological processes occurring in the human body.

Conclusion: The time-dependent interaction of physiologically justified low concentration Aβ with human neuroblastoma SH-SY5Y was studied. By means of confocal microscopy we showed that externally applied fluorescently labeled Aβ primarily localized to cellular membrane, this is followed by the internalization of Aβ, depending on the cells differentiation state. The colocalization with acidic vesicles such as endosomes and lysosomes produces measurable toxic effects on mitochondria.

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