In the aging society neurodegenerative diseases have become a major health problem. Among them, the most prevalent is Alzheimer's disease [1], and one of the risk factor is elevated level of homocysteine in the blood - hyperhomocysteinemia [2]. Activity of the homocysteine metabolism protein, Blmh [3], is reduced in the brain of Alzheimer's disease patients [4], while Blmh-KO mice lacking the Blmh protein exhibit astrogliosis, which is indicative of brain pathology [5] [6]. These Blmh-KO mice rexhibit a change of the isoelectric point of only one protein - Glod4 [7]. Because Glod4 function is not yet known, but there are suggestions of its participation in the detoxification of glyoxal, and one of the Glod4 isoforms is present only in the brain, the present project aims to clarify the Glod4 protein function in the brain in the context of Alzheimer's disease and glioksalase activity.

To elucidate molecular basis for their different isoelectric points, we will examine amino acid sequences of Glod4 protein isoforms and nucleotide sequences of Glod4 mRNA isoforms. We will check with which proteins of brain protein extract, acts Glod4 and whether it has a catalytic activity (glyoxalase).We determine if Alzheimer's disease in humans and Glod4 protein deficiency in mice significantly affect the level of mRNA and protein in the brain Glod4.

[1] Fratiglioni L., *et al.* Worldwide Prevalence and Incidence of Dementia. *Drugs Aging* 15, 365–375 (1999).
[2] Seshadri, S. *et al.* Plasma Homocysteine as a Risk Factor for Dementia and Alzheimer's Disease. *N. Engl. J. Med.* 346, 476–483 (2002).
[3] Zimny, J. *et al.* Protective Mechanisms against Homocysteine Toxicity THE ROLE OF BLEOMYCIN HYDROLASE. *J. Biol. Chem.* 281, 22485–22492 (2006).
[4] Suszynska, J. *et al.*, H. Reduced Homocysteine-Thiolactonase Activity in Alzheimer's Disease. *J. Alzheimers Dis.* 19, 1177–1183 (2010).
[5] Montoya, S. *et al.* Astrogliosis and behavioral changes in mice lacking the neutral cysteine protease bleomycin hydrolase. *Neuroscience*146, 890–900 (2007).
[6] Sofroniew, M. V. Molecular dissection of reactive astrogliosis and glial scar formation. *Trends Neurosci.* 32, 638–647 (2009).
[7] Seshadri, S. *et al.* Plasma Homocysteine as a Risk Factor for Dementia and Alzheimer's Disease. *N. Engl. J. Med.* 346, 476–483 (2002).