

Spectrins are structural proteins that build a cellular skeleton (the cytoskeleton) responsible for maintaining proper cell shape and elasticity while performing various cell life functions such as neurite outgrowth, lymphocyte rolling or red blood movement through narrow capillaries. The cytoskeleton is also an intracellular scaffold that facilitates transportation of cargo (eg. neurotransmitters needed to conduct neural signals) closed within endosomes or direct the proteins to the outer cell membrane, where they perform various functions like adhesion to other cells, pumping ions or transducing environmental cues to the cell interior. Among the spectrins which are 200 nm long tetramers composed of two dimers of chains  $\alpha$  and  $\beta$ , the  $\alpha$ -II chain plays a special role. In contrast to the  $\alpha$ -I chain, which is expressed only in erythrocytes,  $\alpha$ -II chain shows ubiquitous expression outside of erythrocytes. The highest expression of this chain encoded in mice by the *Spna2* gene, otherwise known as *Sptan1* (by high similarity to the human *SPTAN1* gene) occurs in the brain, cerebellum, heart, kidneys and lymphocytes. It is not surprising that the expression deficiency or mutation of this gene may be manifested in a man by cerebral ataxia or cerebral ataxia - epileptic encephalopathy (West syndrome). To understand how mutations of spectrins affect disease development, we need to create research models such as genetically modified worms - *Cenorhabditis elegans*, fly - *Drosophila melanogaster*, fish - *Danio rerio*, lab mouse - *Mus musculus*. Unfortunately, none of these animals deprived gene expression of  $\alpha$ -II chain by genetic engineering do not reach the adult form. In all these animals, this mutation is fatal at an early stage of larval or embryonic development. Hence, there is a need to search for animal models in which it will be possible to investigate the consequences of  $\alpha$ -II chain mutation of spectrin in adult subjects in which the nervous and immune systems are fully mature. In the animal house of the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences, a mouse with a spontaneous mutation appeared that showed movement coordination disorders (ataxia) and was aggressive. This mouse, named by us *Spna2mut*, has launched a new strain in which, by using the next generation sequencing of DNA, a new mutation has been discovered in the gene encoding  $\alpha$ -II chain of spectrin. The present research project aims to characterize the phenotype of this selected mouse strain. The research will focus on the nervous and immune systems and will be conducted in collaboration with scientists from the leading research center on spectrin biology of the Department of Pathology at Yale University. This research opens up a possibility of better understanding of the spectrin's roles in the development and functioning of the nervous and immune systems.