The project aims to investigate the nature of different versions of the mutant form of the C2 protein, and then choose the best-performing ones and examine its use as a factor supporting the effect of therapeutic anti-cancer antibodies. The protein in the unmutated form is a part of the complement system, which belongs to the system of native immunity, which defends us against various pathogens. In the face of many benefits of the complement system for the general health and homeostasis of the body, one should also mention the possibility of inducing autoimmune diseases, i.e. in which the immune system attacks its own tissues and organs. This is the case when elements of the complement system (consisting of more than 30 proteins) are subject to mutations causing increased activity of one of the components. So far, the best characterised are autoimmune diseases caused by faulty regulation of the so-called alternative complement pathways - this group includes, for example, kidney diseases. The C2 protein of the complement system forms one of such complexes, the so-called classical pathway, and its role in autoimmune processes is very poorly known. Activation of the complement system is an important element of the anti-CD20 antibodies that are standard in the treatment of patients suffering from some types of leukemia and lymphomas. These antibodies, when bound to the cell's surface, activate the complement system, which then kills the target cells. One of the mechanisms of defence of cancer cells against immunotherapy is the production of complement inhibitors that destabilize the C2 protein complex. Despite the generation of several generations of new, improved antibodies, a significant proportion of patients do not respond to treatment or develop resistance over time. In the preliminary studies of our project, we analyzed the alternative pathway proteins with various mutations naturally occurring in humans and showed that they are able to improve the therapeutic effects of anti-CD20 antibodies. These mutations conditioned insensitivity to inhibitory proteins. Then we transferred some of these mutations to the analogue protein C2, and we tested the obtained proteins as a factor supporting the action of anti-CD20 antibodies. In the project we propose, we plan to create a C2 protein panel with multiple mutations that are a combination of the best-acting ones. We would like to analyze them as a supplement of anti-CD20 antibodies on various lymphoma cells. Then, by performing a test using individual inhibitors, examine the character of each of the obtained mutant C2 proteins. This will allow us to select one protein with the highest activity and resistance to all targeting them inhibitors present on the surface of tumor cells, and then test its effect as a supplement of anti-CD20 antibody therapy in an animal model obtained by injection of human lymphoma cells.