Studies of the specificity and immunogenicity of baculovirus-obtained recombinant binding region of *P. falciparum* EBA-181 ligand - searching for the receptor on human erythrocytes.

Malaria is a devastating disease caused by protozoans' parasites belonging to the *Plasmodium* genus. Humans can be infected by five *Plasmodium* species. The most deadly, *Plasmodium falciparum* , is responsible for severe malaria and for most deaths especially among pregnant women and children under 5 years of age in Sub-Saharan Africa. Malaria elimination remains an ambitious long-term international goal. However, the lack of an effective vaccine and the development of resistance to anti-malaria drugs and insecticides threaten the success of this program. The key task in the development of an effective vaccine is a good understanding of the complex process which allows malaria parasite to invade host erythrocytes.

During the erythrocyte stage of development, malaria parasite produces numerous proteins which are responsible for recognition of host erythrocyte and the tight junction formation. The erythrocyte binding-like (EBL) proteins play a crucial role in the attachment of merozoites to the human erythrocytes by binding to the specific receptors on the cell surface. Four functional *P. falciparum* EBL proteins were identified: the erythrocyte binding antigens EBA-175 and EBA-140 that target the glycophorin A and C receptors, respectively, the erythrocyte binding ligand EBL-1 which binds to glycophorin B, and the erythrocyte binding antigen EBA-181 whose receptor remains unknown and also is the subject of the proposed project. The presence of various EBL proteins, which target different receptors on the cell surface consistent with multiple invasion pathways, is believed to be the survival strategy of the malaria parasite.

The aim of this project is to characterize the *P. falciparum* EBA-181 ligand specificity and to identify its receptor on the human erythrocytes' surface, which takes part during the malaria parasite invasion process. The recombinant binding region (Region II) of EBA-181 ligand will be obtained in baculovirus expression system, for the first time. The receptor will be identified by binding recombinant Region II towards human erythrocytes. Moreover, the immune response raised in rabbits against the recombinant Region II will also be studied. The ability of rabbit antibodies to inhibit binding of EBA-181 ligand to human erythrocytes as well as the recognition of the recombinant Region II by human sera from the patients with history of *Plasmodium* infection, will be tested.

The proposed studies will increase the knowledge about the complex process utilized by *P. falciparum* parasite during the human erythrocytes invasion. The obtained results will allow to indicate the new receptor on the human erythrocyte surface, which is recognized by EBA-181 ligand and takes part in an alternative pathway of *P. falciparum* invasion. We also would like to show that recombinant Region II of EBAs ligand is the proper model for studying molecular mechanism of the erythrocytes invasion, without the necessity of culturing *Plasmodium* parasite in the laboratory. Furthermore, studies on immunogenicity, the inhibition of binding by rabbit antibodies, and the recognition of recombinant protein by human sera of the patients with history of *Plasmodium* infection can demonstrate that EBA-181 ligand plays an important role in the invasion of the humans. Given this, the proposed project will not only increases the knowledge about *P. falciparum* molecular mechanisms of invasion, but will also provide the necessary proof that the recombinant EBA-181 ligand should be considered as a component of the multi-valent anti-malaria vaccine.