Schizophrenia is a serious mental illness, which currently affects over 400,000 people in Poland. This psychosis is characterized by distorted perceptions of self and the surrounding world, thinking and emotions. Its symptoms are very diverse and it is often postulated that schizophrenia is not a single illness but many diseases given the collective name of schizophrenic psychoses. A variable clinical picture of this disease may suggest that its basis is complex and divergent and so far it has not been defined unequivocally, despite many years of research. This fact hinders also the choice a proper pharmacotherapy, which now is not very efficient. Therefore, the search for new potential targets for more effective pharmacotherapy based on the newest trends related to the causes of development of this disease seems important and justified.

Recently, the neurodevelopmental hypothesis, confirmed by results of population and epidemiological studies, has received a great deal of attention. These studies have indicated that functional and activity changes in the immune system of pregnant mothers can be a significant cause of schizophrenia development in the offspring. It was shown that virus and bacterial infections during pregnancy disturbed natural neurodevelopmental processes and led to malfunction in neuronal-microglial communication in the offspring. This leads, among other things, to uncontrolled microglia activation, reduced level of trophic factors, and enhanced production of pro-inflammatory cytokines, nitric oxide and excitatory amino acids which by damaging neurons, could cause psychic disturbances in adulthood (Walker & Lue, 2013; Reus ey al., 2015). Indeed, *post mortem* studies in schizophrenic patients demonstrated microglia activation in the regions engaged in the pathogenesis of this disease, while positron emission tomography revealed the increased numbers of microglia cells in the patients.
The newest trends indicate that an exceptionally significant role in the control of microglia function and activity is played by specialized protein systems, and among them fractalkine and surface antigens (clusters of differentiation, CD) including CD200 and their receptors. The significance of these proteins results mostly from the unique localization of the ligand on neuronal cells (CX3CL1, CD200) and its receptor on microglia cells (CX3CR1, CD200R). In parallel, it was demonstrated that antipsychotic drugs, especially of new generation, were efficient in normalizing not only behavioral but also biochemical disturbances, including some functions of microglia (Pagani et al., 2015; Bergon et al., 2015).

Therefore, the aim of the present project is to determine whether the changes in expression and function of the CX3CL1-CX3CR1 and CD200-CD200R neuronal-microglia protein systems are associated with development of disturbances resembling schizophrenia and to investigate their role as a target in the mechanism of action of antipsychotic drugs.

The studies will be conducted in two commonly accepted models of schizophrenia, including the neurodevelopmental models (Basta-Kaim et al., 2011a,b, 2012; Basta-Kaim et al., 2015), based on the administration of bacterial endotoxin or poly I:C virus component (Zuckerman & Weiner, 2003) to pregnant rats. The experiments will be conducted on the offspring of these dams, at different ages, at behavioral, biochemical and functional level combining *in vivo* and *in vitr*o techniques, both before and after 14-day administration of atypical antipsychotic drugs (quetiapine, risperidone, aripiprazole) and the typical reference drugs chlorpromazine.

We believe that the studies planned in the project will broaden the knowledge on neuronal-microglial communication and will explain the role of the CX3CL1-CX3CR1 and CD200-CD200R protein systems in their regulation. In addition, we will evaluate the effect of prenatal exposure to harmful factors on the development of disturbances in the mechanisms regulating these interactions in offspring which, by causing microglia dysfunction, is a key factor in the development of schizophrenia symptoms in adulthood.
We will also obtain new, pioneering data on the involvement of fractalkine and CD200 antigen and their receptors in therapeutic mechanisms of action of atypical antipsychotic drugs, which, by discovering a new target of their action, will contribute to personalization of therapy and to improvement of its efficacy especially in treatment-resistant patients.