

## ***Abstract***

At present, chronic myeloid leukemia (CML) is one of the best understood oncological disorders at the molecular level. Its development is closely related to the translocation between chromosomes 9 and 22 that leads to the formation of the *bcr-abl* fusion gene encoding Bcr-Abl fusion protein. This gene modification results in an undesirable increase of the activity of the tyrosine kinase (TKA) encoded by the *abl* gene. After the introduction of imatinib mesylate and other tyrosine kinase inhibitors (TKI), referred to as the second generation TKI, the quality of life and the survival of patients with CML has greatly improved. Current drug treatment stops the progression of the disease and induces a remission; however, it only rarely, if ever, results in a cure. One of the main reasons is that cancer cells do not behave passively during the treatment. Frequently, the mutations of the gene lead to the selection of a clone, that is pharmacotherapy-resistant; or to an amplification of the *bcr-abl* fusion gene. Furthermore, modern drug therapy based on TKIs does not eradicate tumor stem cells, which are the source of the leukemia relapse. Currently, the only possibility of curing CML is transplantation of allogeneic hematopoietic stem cells. The weaknesses of this therapeutic approach include scarcity of suitable donors and a relatively high morbidity and mortality in the patient recipients.

At present, it is a widespread conviction among the oncologists that immunotherapy may help to solve the problems associated with the treatment of the disease, and that it could soon develop into an efficient complement of the "classical" treatments. Successful immunotherapy would also significantly reduce the cost of treatment, according to some estimates, to at least 1/3 of the current price.

The aim of the efforts of our scientific team, of which I am a member, is the development and testing of therapeutic vaccines against CML. My task was to solve some issues related to the development of the vaccine. In our experiments we are using murine (BALB/c) B210 and 12B1 cell lines transformed by the human *bcr-abl* fusion gene by means of the retroviral vectors. An integral part of our efforts is to find ways how to enhance the therapeutic effect of vaccination with other interventions.

This thesis describes the outcome of three sub-projects for which I was responsible. The first one was directed to proteomic analysis of the cell lines mentioned and aimed at explaining their different behavior *in vitro* and *in vivo*. The second concerned the development of cell vaccines directed against neoangiogenesis in CML and their testing *in vitro* and *in vivo*. The third one was an attempt to induce immunity against the SDF-1 $\alpha$  by a DNA vaccine. This chemokine plays an important role in the pathogenesis of leukemia. The studies produced a series of unexpected observations, which I tried to explain.