Abstract

Chronic myeloid leukemia is malignant disease characterized by myeloproliferative clonal expansion of hematopoietic stem cell. It is causally associated with the formation of the so called Philadelphia chromosome and production of its specific product, the chimeric BCR-ABL protein. The amino acid sequence of the fusion region is unique, implying that the BCR-ABL protein carries tumor specific antigen. Currently imatinib mesylate dominates the treatment of CML. It is well tolerated and when compared to the other drugs used, it prolongs the life expectancy significantly. Unfortunately, it is not capable to cure the disease. The only potentially curative approach nowadays is the bone marrow transplantation; however, it is connected with a relatively high morbidity and mortality. Moreover, it is available only to a minority of the patients. Under these circumstances the need for the development of a relatively safe and generally available treatment is understandable. Immunotherapy could be such a treatment. Several experimental vaccines based on BCR-ABL sequence were developed and tested in mice in our institute. The DNA vaccines used were carrying sequences coding for the whole BCR-ABL protein, or for 25 amino acids long junction region (these DNA sequences were fused with adjuvant genes such as HSP70, CP, L2CP and GUS), or for fragments of BCR-ABL protein and for various mixtures of these fragments. While plasmid carrying the whole bcr-abl gene was capable of inducing protection against the challenge with the tumor cells, plasmids carrying the gene fragment coding for 25 amino acids long fusion region and plasmids carrying the gene fragments coding for portions of the BCR-ABL protein failed to do so. Some of the vaccines based on mixtures of plasmids carrying the fragments of the gene coding for the BCR-ABL protein were capable of eliciting significant protection against challenge and some were not. Based on the results obtained, we can conclude that the junction region of BCR-ABL protein is not capable of inducting protective immune response, at least in our model system. Protection against challenge induced by the whole bcr-abl gene was based on immune response against several epitopes located in ALBportion of the fusion protein.