DESCRIPTION FOR THE GENERAL PUBLIC

The Bovine Leukemia Virus (BLV) together with the *Human T-cell leukaemia virus-1* (HTLV-1) belongs to the family of *Retroviridae,* is classified as a type of *Deltaretrovirus* and is the etiological factor of the enzootic bovine leucosis (EBL). Although this disease is characterized by a long incubation period, within a few hours after infection, the genetic material of the virus is integrated in the form of a provirus with the host's genome. In the course of infection, most of the animals remain clinically healthy (aleukaemic form), however, in approximately 30-70% of infected animals there occur proliferative changes in the lymphoreticular system leading to persistent lymphocytosis (leukemic form), which is mainly related to l proliferation of B (CD5+) lymphocytes. In 0,1 to 10% of infected animals tumor changes in the lymph nodes and internal organs can be observed, which is defined as tumorous form of EBL.

Once infected the animals remain virus carries lifelong. Due to lack of available vaccines the eradication of EBL based on detection of infected animals and their elimination from herds. This in turn contributes to huge economic losses caused by slaughter of infected animals, restrictions on their exports and restrictions on the sale of milk. Therefore the diagnosis of infections, by the use of serological (ELISA) and molecular methods (detection of proviral DNA by PCR) , plays a crucial role. However, the newly emerging cases of infections, recorded in already curred herds, create a significant problem. It is hypothesized that this may be caused by the presence of BLV variants with diminished replication activity which induce the infections, characterized by the delayed seroconversion and low number provirus copies. It is assumed also that in these variants lower replication may be associated with down regulated transcriptional activity that occurs as a result of mutations present in the regulatory sequences important for virus replication. Therefore, the identification of molecular mechanisms affecting virus replication is highly important, especially in the context of emerging new BLV infections and their early diagnosis.

Therefore the aim of this study is to analyze mutations in the LTR region, *tax* gene and in gene encoding microRNA of bovine leukemia provirus (BLV) isolated from the so-called newly emerging infections, noted in herds already having freedom from BLV infection, and to determine the association of these mutations with the transcriptional activity of the virus.

Detailed work plan include:

- Analysis of mutations in the LTR region and *tax* gene
- Determination of proviral load level
- Examination of transcriptional activity of selected proviruses
- Analysis of mutations in gene encoding viral miRNA and their possible impact on viral mRNA expression

The results of the research will allow assessing whether in the population of cattle naturally infected with BLV there occur genetic variants of the virus with reduced replication potential what is associated with occurrence of mutations in the regulatory regions. Assuming that the transcriptional activity of the BLV determines, in a direct way, the level of virus replication in infected cells and the number of infected cells, and also the level of induction of a humoral response, the results of examinations will be helpful in the determining the effect of mutations in regions, important for virus replication at the level of replication.

It will allow determining the role of genetic variability of BLV on the occurrence of infections characterized by a low number of copies of the provirus and the delayed seroconversion. These elements are critical to the success of diagnostics of BLV infections based on the detection of specific antibodies in blood serum and proviral DNA. An important aspect of these studies will be the possibility to refer the results of the project to the research area of infections with HTLV-1 virus at people.