The emergence of the devastating human immunodeficiency virus HIV in the human population, following cross species infection from the natural non-human primate hosts, has demonstrated the high capacity of lentiviruses to cross the species barrier, adapt to the new host and dramatically increase their pathogenic potential. Consequently, SRLV have gained research interest mainly to understand their pathogenesis, mechanisms of cross species infection, and adaptation to new hosts. Caprine arthritis encephalitis virus (CAEV) and maedi visna virus (MVV) which infect sheep and goat worldwide, belong to the *Retroviridae* family. They used to be considered species-specific viruses but molecular-epidemiological studies indicate that these viruses are capable of infecting both species and consequently, the term small ruminant lentiviruses (SRLV) is currently used. So far, SRLV strains are divided into five phylogenetic groups (A-E). Infected animals develop inflammatory diseases that affect multiple organs and are the source of infection to other animals. Serological study performed in Poland revealed that prevalence of SRLV was 44-58% in sheep and 30-72% in goats on a flock level (Olech et al., 2012, Kaba et al., 2013). Recent works established that SRLV easy and frequent transgress of species barrier and induce a persistent infection and the disease in a new hosts. Cross-species infections of SRLV occur also in sheep and goats from Poland and the new genotypes A12 and A13, which are restricted only to Poland, predominantly circulate in these animals (Olech et., 2012). In addition, recent data have clearly shown that SRLV are causing natural cross species infection in wild ungulates following contacts during the free grassing season in wilderness areas, which may generate uncontrollable reservoirs of viruses. Cross-infection of a more distant host is suggested by the report on American population consuming much raw goat milk had a high seroprevalence for CAEV and PCR amplification using CAEV-specific primers. It was also showed that the presence of functional receptor to CAEV on the surface of human cells is the only barrier that prevents CAEV molecular clone from causing productive infection in human cells (Msell-Lakhal et al., 2000).

All together these data indicate that SRLV might have a considerable potential for cross-species infection and zoonosis. It has been recently established that co-infection with SRLV of different subgroups in mixed flocks generates recombinant viruses that have a mosaic genome and probably new biological and pathogenic properties. SRLV recombination between different genetic groups and between genetic variants of the same group in goats under natural infection has been demonstrated (Pisoni et al. 2007, Ramirez et al. 2011). Resulted recombinant viruses have to be investigated to be able to correctly predict if virulent, epidemic forms of SRLV, exhibiting a modified range of target cells will arise from these cross species infections.

The hypothesis in this project is that in mixed flocks of goats/sheep and goats/sheep with domestic (cattle) or wildlife ruminants, SRLV can serve as potential reservoir of emerging viruses that following cross species infection and adaptation to new host can induce the infection in other ones. Adaptation of these viruses in cells of new host may be associated with their increased virulence, expansion of cellular and species tropism and perhaps generates recombinant viruses with new biological properties.

SRLV-infected animals from mixed flocks of goats/sheep with domestic (cattle) or wildlife ruminants will be selected by serology, using Gag and/or Env multi-epitope recombinant antigens representing subtype A1, A13, B1 and B2 of SRLV. From seropositive animals the blood for DNA isolation will be collected. For molecular study 35 selected goat/sheep (see preliminary study) and SRLV-seropositive cattle and wildlife ruminants will be used. These representative samples will be subjected for sequencing and sequence analysis in the LTR (promotor region of the virus) and envelope (*env*) gene. For virus isolation blood monocyte-derived macrophages will be cultured and cultures will be examined for viral replication (SG-PERT assay) development of syncytia (microscope observation) and virus titer in supernatants by TCID50 assay, using goat synovial membrane cells (GSM). Cell lines from domestic animals (from goat (GSM cells), sheep (PO cells), cattle (BOMac cells)) and humans (HeLa, SiHa, CasKi, HCT116, U937, and Jurkat cells) will be inoculated with selected field isolates to study *in vitro* species tropism and to investigate replication efficacy and protein profiles. The main intention is to find viruses which exhibit different tropism, replication efficacy or protein profiles. In isolates with mutations within LTR sequences LTR- promotor activity will be assessed. The proviral load in peripheral blood cells of animals infected with known, different virus genotypes will be determined by qPCR. Finally, correlation between SRLV genotype and *in vitro* biological proprieties of these isolates will be assessed.

Nowadays the emergence of new viruses, many of which are zoonotic is one of the biggest problems in public health. These findings will allow a better understanding of bio-pathology of these viruses to evaluate their potential to serve as a reservoir for emergence of viruses with heightened pathogenicity and increased tropism of species. The outcome of this project will also bring insight in the interaction between the pathogen and the new hosts that are certainly different from those seen with the natural host.