Abstract

One of the important tasks of virology and immunology is to explore the species- and cell-barriers preventing virus horizontal transmission and reveal the ways how viruses overcome these barriers and "adapt" to different species. This work is based on a well-established retroviral model – avian Rous sarcoma virus (RSV) and studies virus replication blocks in mammalian cells at both pre- and post-integration level.

Interaction of the viral envelope glycoprotein (Env) with a specific cellular receptor mediates virus entry into cells. Although mammalian orthologues of specific chicken receptors do not support RSV entry, it was observed that some RSV strains are able to enter mammalian cells. Several RSV-transformed rodent cells lines were described and analysis of provirus H20-RSV in one these cells lines (hamster H-20 tumor cell line) showed multiple mutations including two crucial amino acid substitutions in different regions of Env. Substitutions D32G and L378S confer virus transmission to hamster, human and also chicken cells lacking the appropriate receptor. Altered conformation of H20-RSV Env is similar to a receptor-primed (activated) state of Env. This observation indicates that virus can circumvent the need of original cell receptor because of spontaneous Env activation caused by single amino acid substitution.

Although RSV is occasionally able to enter and transform mammalian cells, no virus particle formation is observed. However, virus production in RSV-transformed mammalian cells can be rescued by fusion with permissive chicken cells. Analysis of this phenomenon is brought in the second part of this thesis. The RSV-transformed hamster cells produce only a marginal amount of *env* mRNA and no envelope glycoprotein. Viral genomic RNA is kept in the nucleus and cells produce only a small amount of unprocessed Gag protein. Cell fusion with chicken cells leads to an increase in *env* mRNA levels, nuclear export of genomic RNA, as well as synthesis of respective viral proteins. These results suggest that rodent cells lack some chicken-specific factor(s) required for proper processing of *env* mRNA and nuclear export of genomic RNA.