Immune evasion by varicelloviruses : the identification of a new family of TAP-inhibiting proteins

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The research presented in this thesis was performed in the Laboratory of Vaccine Research in the National institute of public health and the environment, Bilthoven, and in the department of Medical Microbiology, section Experimental Microbiology, at the Leiden University Medical Center, Leiden.

"The most beautiful thing we can experience is the mysterious. It is the source of all true art and science."

Albert Einstein

mojim roditeljima
to Thomas and Rebecca

Contents

Subject of this thesis

From the earliest times of their evolution, multi-cellular organisms have been defending themselves against infectious agents like nucleic acids, viruses, bacteria, fungi and parasites. Continuous selection pressure resulted in the development of sophisticated immune systems, which in their adaptive forms have exquisite specificity as well as memory for pathogen antigens. On the other hand, infectious agents developed elaborate strategies to escape from, or counteract, host defense mechanisms. Viruses are totally dependent upon host cells for replication and have developed an impressive variety of mechanisms to shield themselves from being detected by the host immune system. The subject of this thesis concerns a particular example of how viruses, specifically some members of genus *Varicellovirus*, counteract an important step in one of the acquired immunity pathways: the presentation of antigen by Major Histocompatibility Complex (MHC) class I molecules to cytotoxic T-cells. This thesis describes the discovery of a new family of proteins that inhibit the Transporter associated with Antigen Processing (TAP), and sets the first steps towards the explanation of how these inhibitors interfere with antigen transport by the MHC class I loading complex.