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Research interests

Our group studies specific aspects of the molecular biology and immunology of flaviviruses. These are small enveloped viruses comprising a number of important human pathogens, such as yellow fever, dengue, Japanese encephalitis, West Nile, and tick-borne encephalitis viruses. A major focus of our research is directed towards the elucidation of structure-function relationships of flavivirus envelope glycoproteins that mediate receptor-binding and membrane fusion activity and are the targets for protective antibody responses. In the area of molecular antigenic structure, we are interested in the structural basis of antibody-mediated virus neutralization and the immunodominance of B- and T-cell responses after natural infections and vaccinations.

Thesis projects

Flaviviruses constitute a group of about 70 different but antigenically related viruses, most of which are transmitted to humans by mosquitoes or ticks, including important human pathogens such as yellow fever, dengue, West Nile, Japanese encephalitis, and tick-borne encephalitis viruses. Protection against flavivirus infections is mediated by antibodies that bind to the major viral envelope protein (E). The atomic structure of this protein from several flaviviruses has been determined by X-ray crystallography, and cryo-electron microscopy has provided a detailed molecular picture of the overall protein organization at the surface of virus particles. The functional activity of antibodies can therefore be studied at a structural level.

The following questions will be addressed in our projects

1. What is the fine-specificity and functional activity of antibody responses to flavivirus antigens in the course of natural infections and immunizations?
2. What is the epitope-specificity of CD4 T cells after immunization with the 17D Yellow Fever live vaccine?

The projects include the cloning and expression of flavivirus antigens in pro- and eukaryotic systems and the application of in vitro and in vivo assays that allow the analysis of the fine specificity and functional activity of B- and T-cell responses on the basis of the known atomic structures.

Selected publications

Kiermayr, S., Stiasny, K. & Heinz, F. X. (2009). Impact of quaternary organization on the antigenic structure of the tick-borne encephalitis virus envelope glycoprotein E. J. Virol. 83, 8482-91.

Fritz, R., Stiasny, K. & Heinz, F. X. (2008). Identification of specific histidines as pH sensors in flavivirus membrane fusion. J. Cell Biol. 183, 353-61.

Stiasny, K., Kiermayr, S., Holzmann, H. & Heinz, F. X. (2006). Cryptic properties of a cluster of dominant flavivirus cross-reactive antigenic sites. J. Virol. 80, 9557-9568.

Bressanelli, S., Stiasny, K., Allison, S. L., Stura, E. A., Duquerroy, S., Lescar, J., Heinz, F. X. & Rey, F. A. (2004). Structure of a flavivirus envelope glycoprotein in its low-pH-induced membrane fusion conformation. Embo J. 23, 728-38.