

Inhibition of intracellular Co-Factors for HCMV Replication - New strategy for antiviral therapy

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Human cytomegalovirus (HCMV), one of eight human herpesviruses, can cause serious, life threatening diseases in newborns and immunocompromised patients, i.e. organ transplant recipients and patients with AIDS. The current available drugs caused multiple problems including resistances. This, in turn, would necessitate the characterisation of new targets supporting different modes of action.

To this end, an active interference with cellular proteins as co-factors of the viral replication may offer viable alternatives. Viral maturation involves capsid assembly, DNA packaging and nuclear egress or release of nucleocapsids. The capsids are released into the cytoplasm by a budding process through the inner (INM) and outer nuclear membranes (ONM) and get their final envelope by budding at cytoplasmic cisternae.

In this project cellular candidates involved in the budding steps will be screened using the yeast two hybrid system with our cellular gene bank and viral DNA packaging proteins (e.g. HCMV terminase, pUL77). Interactions will next be verified by *in vitro* and *in vivo* binding analysis, GST-pull down assays with *in vitro* expressed proteins and GST-fusion proteins and co-immunoprecipitations of infected cells. The next step is computer aided drug design analysis of the identified host factor, followed by chemical synthesis of the proposed inhibitor. The synthesized compounds will then analysed concerning their antiviral activity by using different approaches including plaque assays, electron microscopy. In addition, the effect of the compound on the time course of infection will be analyzed using life cell imaging

Interlinkage

Andreas Hermann's group concerning life cell imaging will be helpful for this project.