mice after a lethal challenge with RVFV. The protection elicited by the MVA vaccination was related to the presence of glycoprotein specific CD8+ cells, in the absence of a consistent detection of neutralizing antibodies in vitro. To study the contribution of each glycoprotein antigen to protection a similar approach was extended to vaccines expressing only a single RVFV glycoprotein (either Gn or Gc). Our results suggest that protection of BALB/c mice upon RVFV challenge can be mediated by the activation of a strong cellular response (mainly against Gc epitopes) in the absence of a clear induction of neutralizing antibodies. However, this protection may be restricted to specific genetic backgrounds determining susceptibility to infection as shown by the lack of survival upon challenge of 129SvEv mice immunized with the same vaccines (MVAGn or MVAGc). Our data also point out that the expression of both glycoproteins enhances humoral immunogenicity perhaps explaining the higher protection rates in MVAGnGc vaccinated 129 SvEv mice. The detection of IL-2 and IL-6 supports the induction of cellular responses since both cytokines play a role in T-cell survival and activation. Thus, the identified Gc specific CD8+ T-cell population may act as a key component in the protection after challenge observed in the MVA immunized mice, contributing to the elimination of infected cells and reducing morbidity and mortality.

(PO 111)

ANALYSIS OF THE ANTIVIRAL ACTIVITY OF SILVER NANOPARTICLES AGAINST RIFT VALLEY FEVER VIRUS IN VITRO AND IN VIVO

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Rift Valley Fever virus (RVFV) is a mosquito borne pathogen causing an important disease in ruminants often transmitted to humans after epizootic outbreaks, thus becoming a very relevant pathogen for animal health due to the economic losses associated, and also for human health. Currently there is no available treatment or licensed Rift Valley fever vaccine for human use, therefore the development of new approaches able to inhibit viral replication and transmission allowing an efficient control of the disease is a must. Silver nanoparticles have been described to exert some inhibitory effect against some enveloped viruses belonging to different families. Compared to the classical antiviral approaches, the use of metal nanoparticles poses many advantages, mainly the non-emergence of resistant variants, as well as their safety and low cost.

In this work we have tested the antiviral potential against RVFV infection, both in cell culture and in animal models, of silver nanoparticles formulated as Argovit. Though the ability of silver nanoparticles to control an ongoing RVFV infection in the conditions tested seems to be limited, the incubation of virus with Argovit before the infection leads to a reduction of viral infectivity both in vitro and in vivo. Our results reveal the potential application of the microbicidal properties of silver nanoparticles to control the infectivity of this important zoonotic pathogen.

(PO 112)

ANTI-INFLAMMATORY PROPERTIES OF THE SECRET DOMAIN FROM POXVIRUS TNF RECEPTORS

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Poxviruses encode numerous proteins devoted to the control of the host's immune response, including a set of secreted, cytokine binding proteins that act mainly as competitive inhibitors of their ligands. Amongst these, a family of virally encoded TNF receptors (vTNFRs) with homology to their cellular counterparts are thought to have important roles during infection. Ectromelia virus, the causative agent of mousepox, encodes a single active vTNFR named CrmD which is known to block effectively TNFa. Additionally, CrmD contains a structurally distinct domain termed, the SECRET domain, that can bind and block the activity of a reduced set of chemokines. This domain was identified in several other poxviral secreted proteins. To address the possible concerted anti-inflammatory role of both domains, we generated recombinant ectromelia viruses lacking CrmD or expressing a truncated version that blocked TNF but not chemokine activity. We found CrmD to block the inflammatory footpad swelling reaction in vivo, with the SECRET domain contributing significantly to this activity. We next tested the ability of recombinant CrmD or a truncated version lacking the SECRET domain to block inflammation in a murine model of rheumatoid arthritis. Both approaches confirmed that the presence of a chemokine binding domain enhanced the anti-inflammatory potential of a vTNFR in vivo. Because secreted human TNFRs are currently used in the clinic for the treatment of several inflammatory conditions, we reasoned that addition of a chemokine binding domain to such a protein might enhance is activity. Therefore, we generated a set of secreted hTNFRs fused to SECRET domains derived from different viral proteins and screened them for correct TNF and chemokine inhibitory activity. One selected construct was further purified and its binding and inhibitory activity characterized in vitro and in cell culture. Finally, we determined the anti-inflammatory activity of this recombinant hTNFR-SECRET protein in vivo, showing its ability