Viral Vector Vaccines

Presentation

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Recombinant vaccinia MVA expressing E and prM/M proteins of West Nile Virus for vaccine generation

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West Nile Virus (WNV), a flavivirus, is intrinsically maintained in an enzootic cycle between mosquitos as vectors and wild birds serving as reservoir hosts. WNV can also infect and cause disease in humans and horses. The virus is widely distributed in Africa, Europe, the Middle East, Asia and the Americas and is able to cause neuroinvasive disease with the potential for severe courses especially in the elderly and immunocompromised humans. WNV infections increasingly occur in mediterranean countries with tendency to spread to central and northern Europe. Thus, safe and efficacious vaccines are urgently sought for WNV prophylaxis in humans and animals. Replication-deficient Modified Vaccinia virus Ankara (MVA) can be exploited as versatile viral vector in medical and veterinary vaccine development.

Here, we have generated and evaluated recombinant MVA delivering the WNV antigens E (envelope) and prM/M (precursor membrane/membrane) and fulfilling the requirements to undergo clinical testing in humans. The structural proteins of the WNV envelope are highly relevant vaccine antigens for the induction of WNV-specific antibody and T cell responses. Infections of human and equine cell cultures with recombinant MVA demonstrated efficient synthesis and secretion of WNV envelope proteins in mammalian cells non-permissive for MVA replication. Prime-boost immunizations in BALB/c mice induced high levels of WNV-specific antibodies. Moreover, vaccinations with recombinant MVA in HLA-A2.1-/HLA-DR1-transgenic H-2 class I-/class II-knockout mice resulted in the induction and efficient expansion of WNV-specific CD8+ T cells. Thus, results from vaccinations in two different mouse models demonstrated solid immunogenicity of MVA-WNV vector vaccines. Further evaluation in different animal models is warranted to evaluate protective efficacy against WNV and to demonstrate the potential of the recombinant MVA as candidate vaccines in humans.

Vaccines

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Lack of antibody response in pigs immunised with the transmembrane envelope protein of porcine endogenous retroviruses (PERV)

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Immunisation of different mammalian species (goats, mice, rats, rabbits, guinea pigs, hamsters) with the recombinant ectodomain of the transmembrane envelope (TM) protein p15E of the porcine endogenous retrovirus (PERV) resulted in all cases in neutralising immune sera. The sera recognised epitopes in the fusion peptide proximal region (FPPR) and in the membrane proximal external region (MPER) of p15E. Only the epitopes in the MPER are relevant for neutralisation. One epitope in the MPER shared a sequence homology with an epitope in the TM protein gp41 of HIV-1, recognised by a broadly neutralising antibody isolated from HIV-1 infected individuals (4E10).

The envelope proteins of some endogenous retroviruses (also called syncytins) in different species play an important role during formation of the syncytiotrophoblast of the placenta and have immunosuppressive properties. Interestingly, different species utilised different endogenous retroviruses in this respect. Nothing is known about the syncytins in pigs. In order to analyse whether pigs are also able to produce neutralising antibodies when immunised with p15E, and whether these antibodies can be used to study the involvement of p15E in pig placenta development, German landrace pigs were immunised with p15E of PERV. Strikingly, and in contrast to all other species, binding and neutralising antibodies were not observed in pigs as shown in three Western blot analyses and in a neutralisation assay. This indicates that pigs are tolerant to their endogenous retroviruses. In contrast, neutralising antibodies recognising the FPPR and MPER were easily induced in cats by immunisation with the feline virus p15E. In humans antibodies against the human endogenous retrovirus HERV-K were found in tumour patients and women after pregnancy. This indicates that PERV – in contrast to HERV-K and feline endogenous retroviruses – is expressed early during ontogenesis and is therefore recognised as "self-antigen". Since it was impossible to induce antibodies against p15E of PERV, other strategies should be used to identify the syncytin-like protein in pigs.