Evaluation of infectious laryngotracheitis virus recombinants as vectored live vaccines against H5N1 avian influenza virus infection of chickens

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Attenuated strains of the alphaherpesvirus causing infectious laryngotracheitis of chickens (ILTV) can be used as live vaccines which are suitable for mass application. We have further shown that hemagglutinin-expressing ILTV recombinants protect chickens against highly pathogenic avian influenza viruses (HPAIV) of the corresponding subtypes [Lüschow et al., Vaccine 19:4249-59(2001); Veits et al., J Gen Virol 84:3343-52(2003)]. However, protection against recent H5N1 HPAIV was incomplete. Therefore, a novel dUTPase-negative ILTV vector permitting rapid mutagenesis was used for insertion of the hemagglutinin or neuraminidase genes of a Vietnamese H5N1 HPAIV isolate. Compared to our previous constructs, protein expression could be considerably enhanced by addition of synthetic introns downstream of the human cytomegalovirus immediate-early promoter within the 5'-nontranslated region of the transgenes. Deletion of the viral dUTPase gene did not affect in vitro replication of the ILTV recombinants, but led to adequate attenuation in vivo. After single ocular immunization, all chickens developed H5- or N1-specific serum antibodies. Nevertheless, animals immunized with N1-ILTV died after H5N1 HPAIV challenge, although survival times were prolonged compared to nonvaccinated controls. In contrast, all chickens vaccinated with H5-ILTV, or both mutants simultaneously, survived without showing any clinical signs. Real time RT-PCR indicated limited challenge virus replication after vaccination with H5-ILTV only, but not after additional immunization with N1-ILTV. Thus, chickens can be sufficiently protected against current H5N1 HPAIV by live vaccination with an attenuated hemagglutinin-expressing ILTV mutant, and efficacy might be further increased by coadministration of a neuraminidase-expressing vector.

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