## Early protection against HPAIV H5N1 by single shot application of a live-attenuated influenza variant to mice, chickens and ferrets

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Highly pathogenic avian influenza (HPAIV) H5N1 sporadically causes severe disease in humans and involves the risk of inducing a pandemic by gaining the ability to transmit from human to human. An optimized vaccination strategy consisting of a one-shot-(oral)-vaccination protocol for birds and mammals — with a fast and strong immune response could probably be able to prevent the spread of the virus.

This study tested the NA-negative live virus variant as a prototype to induce an early onset of immunity using HPAIV challenge infection after different time points following vaccine application to prove efficacy.

9-week-old ferrets, 6-week-old mice were immunized oronasally and chickens intramuscularly with a single dose of about  $10^{4.5}\, TCID_{50}$  per animal 7, 3 and 1 day before lethal challenge infection with HPAIV H5N1. The modified live virus variant protected 100% of chickens, mice and ferrets three days after vaccination against death and severe clinical signs. Additionally, real-time RT PCR analyses of swabs, nasal washing and organ samples proved "sterile immunity" in all animals immunized 7 days before challenge infection. Furthermore, most animals developed high titers of hemagglutinin-specific antibodies after seven days, but no NA-specific reactivity; a pattern which could be used as the basis of a marker vaccine strategy.