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A dose-response approach using mixed dose-groups shows immune-potentiating capacity and improved efficacy in ferrets of the cationic liposomal CAF09 adjuvant in an H7N9 influenza whole inactivated virus vaccine challenge study.

Content

Background
Often contribution of an adjuvant to vaccine efficacy is shown in studies using one or up to three different doses. The suboptimal vaccine dose is determined in a prior dose finding study or based on literature. In either case, reproducibility is a problem, which affects the window to show improvement by the adjuvant. Another limitation is that these studies provide information within a limited dose range. Statistical analysis is restricted to comparing the groups, while interpolation would predict for a wider dose range. However, more doses are required for such an approach. Using multiple doses and fewer (1-2) animals per dose requires a different housing strategy. Historically, groups in challenge studies are housed separately, since non-protected placebo-animals may re-infect protected vaccinated animals. Here we tested the cationic adjuvant CAF09 in combination with a whole inactivated virus (WIV) vaccine against influenza H7N9 in a dose-response study.

Methods
20 ferrets were allocated to 4 cages of 5 ferrets. Vaccines were administered twice, three weeks apart with 5 different doses ranging from 0.94 – 15 µg HA with 2Log steps. Two cages received the H7N9 WIV only and the other two cages the CAF09 adjuvanted variant. Two weeks after last vaccination ferrets were intra-tracheally challenged with H7N9 influenza and ferrets were sacrificed after 5 days.

Results
Ferrets vaccinated with the vaccine alone show a clear dose-response on functional antibody titers clinical parameters, virus replication and pathology of the lung. The adjuvanted vaccine showed a dose-response on antibody titers after first vaccination, but all doses reached a plateau after booster vaccination. The adjuvanted-vaccine also provided near to complete protection at the lowest doses and full protection at the highest doses.

Conclusions

Thus, the dose-response approach using mixed dose-groups shows a clear dose-dependent effect of the vaccine alone and an immune potentiating effect and a strong contribution to the efficacy of the CAF09 adjuvant. However, the study design can be further improved by including a few lower doses and a placebo, such that also for the adjuvanted vaccine suboptimal effects are obtained. Moreover, re-infection of ferrets by using mixed dose-groups does not seem to play a role, since clear dose-response effects are visible for virus replication.
This study is a proof of concept of the dose-response approach, a strategy that provides results over a wider range of doses using a similar or lesser number of animals as single or multiple dose comparison studies, respectively. This allows for better investigation of adjuvant contribution and further on better clinical study design.

Choose primary session

Vaccines and antivirals

Choose secondary Session

Virus host cell interaction

Contribution Type : Paper presentation