

New generation vaccines: Safety aspects of nucleic acids vaccines

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Schlüsselwörter

DNA/nucleic acid vaccines, safety and efficacy, risk assessment, food producing animals, consumer protection

Problemstellung und Zielsetzung

DNA vaccination is a rapidly developing technology that offers new approaches for the development of new vaccines against emerging diseases as well as diseases for which no or only unsatisfactory vaccines exist. Parallel with novel technologies, it is essential to address safety aspects of such vaccines, which was the aim of this project. The focus was placed on application of DNA vaccines to chicken including the impact of improved vaccine formulations.

Material und Methoden

For DNA delivery a liposome formulation as well as a cationic polymer were used. Optimization of transgene expression and analysis of polymer cytotoxicity was quantified *in vitro*. For the *in vivo* studies 68 SPF chicks were injected with 100ug plasmid DNA (pDNA) *i.m.* of (i) pGL3-CMVluc; (ii) pGL3-CMVluc/liposome complexes; (iii) pGL3-CMVluc/polymer complexes. The birds were sacrificed at day 1, 7, 30 and 70 post vaccination, and blood, serum, heart, liver, stomach, spleen, lung, kidney, gonads, Fabricius bursa, brain, bone marrow, skin, muscles samples were collected for studying biodistribution of pGL3-CMVluc. After extraction of pDNA was quantified by real-time PCR, and reporter protein by luciferase activity using a luminometer.

Ergebnisse und Bedeutung

We have constructed plasmids with optimized promoter activity for chicken cells using luciferase as a sensitive reporter gene. Optimized plasmid delivery systems were identified and used *in vivo*. To study the biodistribution of pDNA, we have developed a highly sensitive and specific real-time quantitative PCR. The *in vivo* safety investigations demonstrated that pDNA was only detected at 24h post vaccination (*p.v.*) but when delivered using polymers it persisted in the muscle for up to 30 days. Surprisingly, pDNA accumulated in the skin of chicken, where it was detectable up to 30 days *p.v.* With a liposome based DNA formulation only, luciferase activity was also detected in the skin at 24h *p.v.* When a polymer-based delivery was used, pDNA was detectable in many different organs such as liver, spleen, heart and gizzard.

These results demonstrate that although the biodistribution and persistence of pDNA depends on the vaccine formulation, it can accumulate and persist several weeks in the skin of chicken. With delivery systems optimized towards improved vaccine efficacy such as polymer formulations, the pDNA can also persist at the injection site in the muscle. Although we have no evidence that the pDNA is intact, the results could pose a potential concern for the safety of DNA vaccines considering that many chicken meat products include parts of the skin.

Publikationen, Poster und Präsentationen (Formatvorlage Überschrift 2)

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