Immunotoxic characterization of a nanoparticle-based inhalable influenza vaccine in murine and human precision-cut lung slices

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Introduction

Besides the annual outbreaks of respiratory tract infections by influenza viruses, the selection pressure on circulating influenza viruses drives an antigenic drift of seasonal viruses leading to pandemics. Thus, there is a growing demand on seasonal influenza vaccines adapting to the current major virus strain. These optimal pandemic vaccines should fulfill certain requirements: 1) easy and safe administration; 2) strong and effective immune response; and 3) fast and economic way of high amount production in periods of pandemics.

In this study we tested local immunotoxicity of a new nanoparticle-based inhalable influenza vaccine in murine and human precision cut lung slices (PCLS) ex vivo.

Methods

Murine and human PCLS were treated with different concentrations of SiO2-nanoparticles, plant-derived influenza H1N1 (A/California/04/09) antigen (HAC1) only or HAC1 antigen formulated with SiO2-nanoparticles (ratio HAC1:SiO2 = 1 %). Tissue vitality was determined by WST-1 assay and live/dead staining. Cytokine secretion was measured by MSD and ELISA assays.

Results

Both, murine and human PCLS showed a trend towards attenuation of viability at high concentrations of SiO2 with and without HAC1. However, the highest doses of SiO2 are far above the intended human dosages, but were chosen to determine the limits of our test system.

The pro-inflammatory cytokine TNF-α was not induced by the different treatments. In contrast, human IL-8 and murine KC were significantly increased at high SiO2 concentrations of 1000 µg/ml. Additionally, a dose-dependent increase of IL-2 and IFN-γ was observed in human PCLS for the antigen and the combined treatment of SiO2-nanoparticles and antigen.

Summary

- We observed no cytotoxic effect of the viral protein HAC1 in living lung tissue.
- The carrier nanoparticles SiO2 was also non toxic at low concentrations in living lung. Higher concentrations showed adverse effects on viability, which was accompanied by the release of IL-8 & KC.
- IL-2 & IFN-γ are immunologically induced by HAC1

Conclusion

The low toxicity and the induced T cell specific immunoregulatory cytokine profile confirmed that the formulation of an antigen with SiO2-nanoparticles is a promising system for pandemic influenza vaccine development.

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