PSEUDO-AFFINITY PURIFICATION AND FORMULATION OF A CELL-CULTURE DERIVED WHOLE INFLUENZA VIRUS VACCINE USING MAGNETIC SULFATED CELLULOSE PARTICLES

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The production of viral vaccines usually employs different unit operations where formulation and filling are the final steps of downstream processing (DSP). However, complex DSP is often hard to realize in research laboratories focusing on novel vaccine candidates. Moreover, there are no real ready-to-use tools for high-throughput DSP of whole virus particles that can speed up development. Because of these needs we developed a new platform for easy and straightforward whole virus particle purification and formulation based on magnetic sulfated cellulose particles (MSCP)1,2.

Proof of concept was carried out with an influenza A/Puerto Rico/8/34 (H1N1) whole virus vaccine for the immunization of mice. The virus particles were produced in suspension MDCK cells, clarified, inactivated, and concentrated using a standard protocol. After diafiltration to low salt buffer, the virus particles were bound to the MSCP and the virus loaded MSCP were washed and resuspended in formulation buffer.

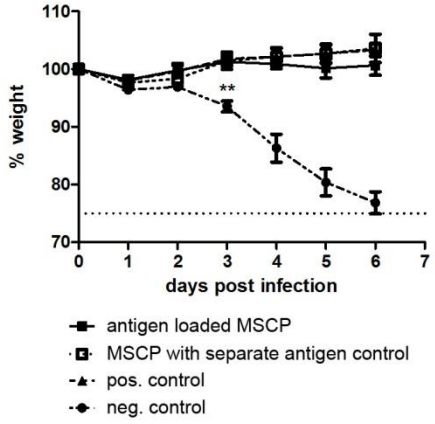

Figure 1 – Relative body weight loss after lethal virus challenge

The immunization experiment included four groups: immunization with antigen-loaded MSCP, MSCP with separate antigen control, positive control, and negative control. The injection scheme involved a first injection followed by a booster injection. After immunization, the mice were challenged with a lethal virus dose.

The results obtained showed similar high anti-influenza antibody titers in mice immunized with antigen-loaded MSCP and antigen-containing controls. All three groups did not show any weight loss after the challenge. The untreated mice showed no antibody titers and a significant weight loss after challenge (Figure 1). Additionally, the mice's lungs of the negative controls showed a 400-fold increase of influenza nucleoprotein-gene copies, indicating high virus load, when compared to mice immunized with antigen-loaded MSCP.

In summary, the use of MSCP for purification and formulation of influenza vaccines proved to be practicable and showed excellent protection after a lethal virus challenge. Besides, such a process has the potential to be implemented directly after virus production to realize a single step purification and formulation DSP2. Because of these advantages possible applications range from studies in research and development to manufacturing of veterinary vaccines. In addition, optimized MSCP systems could be of interest for future applications in the medical field including vaccine delivery and gene therapy.

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