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Development of an influenza vaccination protocol for use in an intervention trial to measure the effect of inulin-type fructans on immune function in humans

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Prebiotics (including inulin-type fructans) are resistant to digestion in the upper gastrointestinal tract, and so they reach the colon, where they selectively stimulate the growth and/or activity of beneficial bacteria. Through this modification of the intestinal microbiota, and by additional mechanisms, inulin-type fructans may have beneficial effects on immune function and related outcomes. Studies in laboratory animals and in humans that investigated these areas have recently been reviewed⁽¹⁾, and results indicate that inulin-type fructans are able to modulate some aspects of immune function, to improve the host's ability to respond successfully to certain intestinal infections, and to modify some inflammatory conditions. However, there are a limited number of studies investigating the effects of inulin-type fructans on immune function in healthy human adults. Although examining the immune response to vaccination has been identified as the most meaningful method to measure the response of immune system *in vivo*⁽²⁾, there are no standard protocols to follow this method. Therefore, the objectives of this work were to conduct a pilot study in healthy humans in order to establish a standardised influenza vaccination protocol to investigate the effects of a defined mixture of oligofructose and long-chain inulin on the immune response to vaccination in middle-aged subjects.

Six healthy adults aged 45–65 years completed the pilot study. They did not change their diet and were vaccinated with the 2007/2008 seasonal influenza vaccine. Fasting blood and saliva samples were taken immediately prior to vaccination and 1, 2, 4 and 6 weeks thereafter for analysis of various immune parameters, including anti-vaccine antibodies (primary outcome) and total antibody concentrations. Cell culture work was performed to establish methods for measuring *ex vivo* T-cell proliferative and cytokine responses to mitogens and the vaccine. Serum vaccine-specific and total antibody concentration profiles over 6 weeks following vaccination showed that 2 and 4 weeks post-vaccination is suitable to see the maximum antibody response: serum anti-vaccine antibody concentrations peaked at 2 weeks post-vaccination (Fig. 1), and total serum IgA, IgM and IgG and salivary sIgA concentrations had all peaked by 4 weeks post-vaccination. From cell culture work, vaccine at a 1/10 dilution was shown to induce the greatest *ex vivo* T cell responses (proliferation and cytokine production).

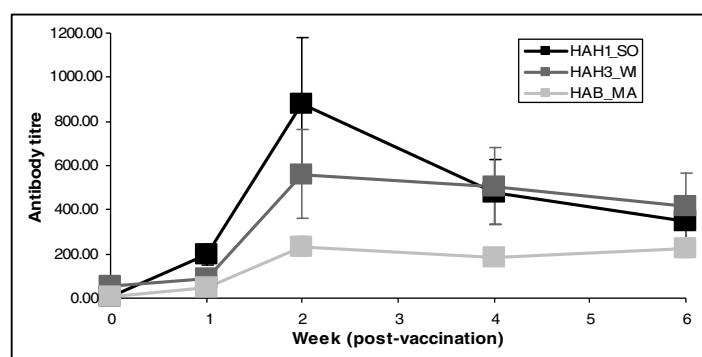


Fig. 1. Serum vaccine-specific antibody response following influenza vaccination.

In conclusion, this pilot study indicates that weeks 2 and 4 post-vaccination are considered to be the most suitable time points to analyse the effect of an oligofructose and long-chain inulin mixture on immune response to vaccination in healthy middle-aged subjects.

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1. Lomax AR & Calder PC (2009) *Brit J Nutr* **101**, 633–658.
2. Albers R, Antoine JM, Bourdet-Sicard R *et al.* (2005) *Brit J Nutr* **94**, 452–481.