

## Mucosal vaccination: lung versus nose.

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The induction of mucosal immunity remains a holy grail in vaccine development as these immune responses have the potential to tackle the infective agent at an early stage following exposure of the host. Hence, pathogenic consequences can be prevented or severely reduced by limiting the infection prior to the disease being established.

Using a combination of vaccine delivery systems and lymphatic cannulation methods in a sheep model, the delivery of a mucosal vaccine to the lung and nose was studied in detail. Intra-nasal delivery of an influenza vaccine adjuvanted with ISCOMATRIX<sup>TM</sup> did not lead to the induction of primary immune responses in the draining lymph. Using cannulation of the lymph nodes draining the nasal area we demonstrated that the vast majority of the model antigen used did not reach the nasal mucosal lymph nodes. Indeed, bronchoscopic examination confirmed that the majority of the delivered vaccine is being channelled towards the oesophagus and swallowed. However, in animals previously immunised by subcutaneous injection, the small amount of antigen that did reach the mucosal lymph nodes was sufficient to boost a pre-established memory immune response.

Intra-lung delivery of an ISCOMATRIX<sup>TM</sup> influenza vaccine using a fibre optics bronchoscope was found to be very effective at inducing both local (i.e. lung mucosal) and systemic immune responses. Even minute amounts of influenza antigen were sufficient for the induction of immune responses leading to antibody titres able to inhibit haemagglutination, a hallmark of protective immunity against influenza. These findings were not restricted to influenza antigens but similar results were observed using two different recombinant antigens. Effective antigen-specific proliferative responses were also observed in the blood of these vaccinated animals.

By cannulating the thoracic lymph duct we were able to demonstrate the presence of a model antigen in the lymph following intra-lung delivery. This suggests that immune induction might occur in the lymph nodes draining this site. In contrast, small molecules migrated directly to the blood and were rapidly dispersed in the body of the sheep before being eliminated in the urine.

Taken together these results suggest that intra-lung vaccination might have a broad applicability for both veterinary and human vaccines, provided practical ways of pulmonary vaccine delivering can be developed.