Exploring the potential for dual vaccination against Hepatitis B virus and *Helicobacter pylori* using a recombinant virus like particle

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Hepatitis B virus (HBV) and the gastric bacterium *Helicobacter pylori* are human pathogens of global significance. Estimates suggest >50% of the world population is infected with *H. pylori*, with 10-20% developing serious sequelae. An effective vaccine for HBV is available and is composed of the small HBV envelope proteins (HBsAg) which are able to self-assemble into virus-like particles (VLPs). However, development of a *H. pylori* vaccine has been hampered by the lack of an effective delivery system and safe adjuvants. We explored co-vaccination strategies against HBV and *H. pylori* based on modified HBsAg VLPs. This approach may address *H. pylori* infections, which begin primarily in children, and the global ambition for universal vaccination of infants against HBV.

**Methods:** We inserted overlapping sequences (26-30aa) from the carboxy terminus of the *H. pylori* katA gene into the hydrophilic ‘a’ determinant region (at amino acids 127-128) of the HBsAg protein to create an expression system which guarantees surface orientation of inserted peptide sequences.

**Results:** VLPs containing KatA epitopes were produced and were able to induce KatA specific antibodies in vaccinated mice. Recombinant VLPs expressing KatA epitopes were tested in a mouse challenge model, of which three constructs induced a significant reduction in *H. pylori* bacterial load, as demonstrated by culture and histological examination of the gastric mucosa.

**Discussion:** HBsAg VLPs are highly immunogenic due to their particulate nature and repetitive sub-unit structure. We describe a novel delivery system which is also the first report of recombinant VLPs able to stimulate protective immune responses to a bacterial pathogen.