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Application of a novel recombinant virus-like particle platform to the development of a vaccine against gonorrhoea

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Background

Gonococcal infections affect over 100 million people globally per year and are currently treated with antibiotics. Novel treatments are urgently required due to the growing rise in antibiotic resistance. No licensed gonococcal vaccines are currently available, hampered by antigenic variation and a lack of a correlate of protection following infection.

Aim/Methods

The project aims to develop a VLP-based vaccine against Neisseria gonorrhoeae and to produce it in Nicotiana tabacum plants as a low-cost expression system suitable for manufacturing vaccines in developing countries.

Results

We have developed a modified virus-like particle (VLP), derived from the core protein of the Hepatitis B virus (HBc), with the capability of binding antigens fused to antibody Fc domains (termed ‘AbBind’). Antigens are linked non-covalently to the major immuno-dominant region (MIR) of the VLP spike. Gonococcal antigen

candidates for this VLP platform were selected based on the solubility of the protein, the frequency of polymorphisms within the sequence and the degree of sequence variation between strains. Candidate antigens were fused to mouse IgG2a Fc and expressed in HEK cells by inclusion of a signal sequence, which directs the polypeptide to the endoplasmic reticulum. Immunisation studies in BALB/c female mice found high levels of antigen-specific IgG antibodies in the serum. Antigens in complex with the VLP produced higher IgG titres than antigens administered without binding to the HBc core. It was also noted that antigen-Fc fusion proteins exhibited greater stability as a result of fusion to Fc domains. The sequences encoding the modified VLPs were successfully inserted into vectors for high-yield expression in N. tabacum chloroplasts. Chloroplast transformation vectors were transformed into leaves by particle bombardment, followed by spectinomycin-based selection for transgenic cells. Following in vitro propagation of transformed leaves on spectinomycin, resistant shoots were observed after 4-6 weeks. Once the plantlet stage is reached, the expression of the VLPs will be tested before transfer to soil for scale-up.

Conclusions

The versatility of the AbBind platform to display multiple variants and a diverse range of gonococcal antigens makes it a promising technology for the development of a vaccine against gonorrhoea.