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Modifying Neisseria gonorrhoeae OMVs to promote immune responses

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Background

As Neisseria gonorrhoeae (Ng) has a remarkable ability to develop resistance to antibiotics, attention has turned towards preventative measures, including vaccines. Currently, there is no vaccine available against Ng, with the challenges faced in developing vaccines against Ng being well described, including the manipulation of host immune responses. However, there has been a resurgence of interest in vaccines as retrospective analysis revealed evidence of cross-protection against gonorrhoea after immunisation with a Neisseria meningitidis (Nm) outer membrane vesicle (OMV) vaccine. The cross-protection against Ng elicited by Nm OMVs is attributed to the similarity of cell surface proteins, suggesting that a Ng OMV vaccine could be developed. However, a key issue remains in the presence of antigens within Ng OMVs that potentially suppress immune responses.

Aim/Methods

As Ng manipulates both the innate and adaptive immune responses, we sought to abrogate this significant immunosuppression by deletion and/or replacement of genes which encode immunomodulatory factors. We generated OMVs from wild type Ng (WT OMVs) and from the modified Ng strain (modified OMVs), and mice were immunised alongside a model antigen, Nm factor H binding protein (fHbp), to determine the effect of the OMV modifications on murine immune responses.

Results

Murine antibody response generated against fHbp was significantly higher after immunisation with the modified Ng OMVs compared to WT Ng OMVs. Equally, a higher antibody titre was found against important gonococcal OMV antigens MtrE (a component of an antibiotic efflux pump) and MetQ (a methionine transporter). The ability of modified OMVs to elicit T cell proliferation was also examined via re-stimulation of splenocytes. Finally, the OMV proteomes were analysed using mass spectrometry to identify any differences in the OMVs that could contribute to the enhanced immune responses.

## Conclusions

Overall, the data demonstrate that modified Ng OMVs could be a successful vaccine platform for Ng, by circumventing the immunomodulatory effects of gonococcal proteins so that Ng antigens elicit enhanced antibody responses. N.B: Full details of the modifications made to generate immune promoting OMVs will be disclosed during the presentation.