Human B cell Responses to Dominant and Sub-dominant Antigens induced by a Meningococcal Outer Membrane Vesicle Vaccine in a Phase I trial

Christine S. Rollier¹, Christina Dold¹, Leanne Marsay¹, Aline Linder¹, Christopher A Green¹, Manish Sadarangani¹, Gunnstein Norheim², Jeremy P Derrick³, Ian M Feavers³, Martin C J Maiden², Andrew J Pollard¹

¹Oxford Vaccine Group, University of Oxford and the NIHR Oxford Biomedical Research Centre, Oxford, UK; ²Norwegian Institute of Public Health, Oslo, Norway. ³School of Biological Sciences, The University of Manchester, UK. ⁴National Institute for Biological Standards and Control, Potters Bar, UK. ⁵Department of Zoology, University of Oxford, UK.

1. **Introduction:** Outer membrane vesicles (OMV)
   - Vaccines and vaccine component for group B meningococcus & vaccine platform
   - Group B meningococcus: protective immune response strain specific to Porin A (PorA)
   - B cell responses to Pora (dominant) versus other (minor) antigens in OMVs?

2. **Methods:** phase I clinical trial of investigational vaccine MenPF
   - OMVs from strain genetically modified to constitutively express 8% of iron-regulated antigen FetA
   - Participants received 25 or 50 µg, three injections 8 weeks apart (weeks 0, 8 and 16)
   - Induced serum bactericidal (SBA) responses to PorA and FetA (Marsay et al., 2015)
   - Plasma and memory B cell responses to both antigens? Relation to SBA response?

3. **Results:** Plasma cell responses: induced by OMV vaccination
   - Higher response rate in participants with memory B cells at baseline
   - OMV immunization does not induce IgA plasma cell responses
     - A. PorA IgA secreting cells
     - B. FetA IgA secreting cells

4. **Results:** Memory IgG B cell responses
   - No clear increase against PorA nor FetA as compared with prior to vaccination
   - Marked increase in participants with memory B cell response prior to vaccination against PorA

5. **Results:** antibody and SBA responses
   - Higher in participants with responses prior to vaccination against all antigens
   - OMV immunization does not induce IgA plasma cell responses
     - A. SBA at week 20 (WT strain)
     - B. SBA at week 20 (PorA<sub>OMV</sub>, FetA<sub>OMV</sub>)
     - C. SBA at week 20 (PorA<sub>OMV</sub>, FetA<sub>OMV</sub>)
     - D. FetA IgG titers at week 20

6. **Conclusions**
   - OMV immunization poor inducer of memory B cell response (persistence?)
   - Stronger B cell and SBA responses in participants with pre-existing responses
   - Carriage primes responses to minor antigens, which can be boosted by OMV vaccines

Acknowledgements: Welcome Trust translational award, Innovation Schemes (082102/2/07/A and 091634/2/10/Z), and the NIHR Oxford Biomedical Research Centre, Oxford, United Kingdom, Vaccine theme.