Chlamydial vaccine development:

Induction of humoral and cellular responses to a parapox viral-vectored antigen *in vivo*

Moredun

www.moredun.org.uk

Sean Wattegedera[1], Jackie Thomson[1], Lesley Coulter[1], Ann Wood[1], Morag Livingstone[1], Kevin Aitchison[1], Rebecca McLean[1], Javier Palarea-Albaladejo[3], Gary Entrican[1,2], David Longbottom[1], David Griffiths[1] and Colin McInnes[1]

[1]Moredun Research Institute, Scotland; [2] The Roslin Institute at The University of Edinburgh, Scotland; [3] Biomathematics and Statistics Scotland.

For further information: Sean.Wattegedera@moredun.ac.uk

1. THE BACKGROUND

- *Chlamydia abortus* is the most common cause of infectious reproductive loss in sheep in Scotland, the UK and most countries worldwide (Fig 1).

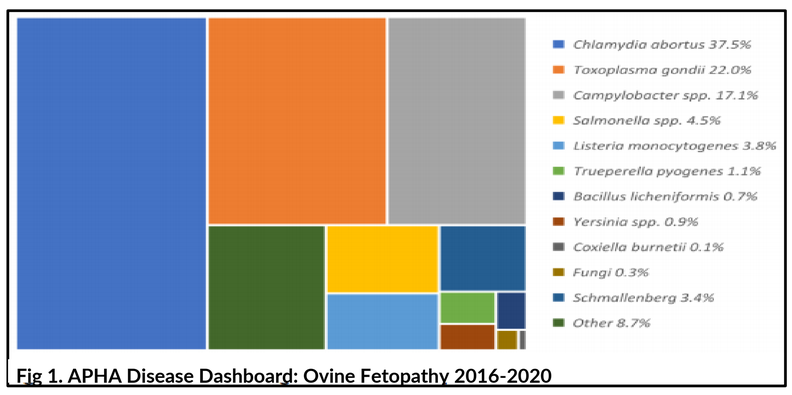

Fig 1. APHA Disease Dashboard: Ovine Fetopathy 2016-2020

- The disease (ovine enzootic abortion; OEA) can be controlled through the use of commercial inactivated and live whole organism-based vaccines.
- These vaccines are suboptimal, differing in effectiveness and having high manufacturing costs and known safety issues, and thus need replacing.
- Viral vectors are widely used in vaccines to stimulate both antibody and cellular responses for domestic food animals (1).
- Various vector-based vaccines were assessed in the 2016-22 SG SRP, including an Orf viral vector (ORFV) vaccine.
- Such vaccines have a good safety profile, while their genomes are receptive to insertion of large foreign antigen/s (2), including potential protective chlamydial antigens identified in the 2016-22 SRP.
- A modified version of sheep Orf virus (NZ2 strain) has been generated by removing the non-essential 'early gene' (Fig 2) and replacing it with chlamydial major outer membrane protein (MOMP).

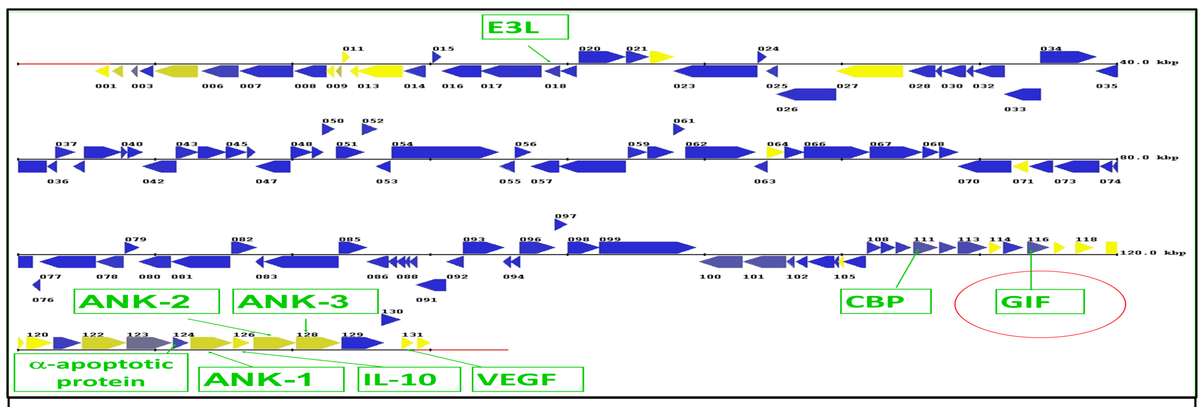

Fig 2. Genetic map of parent NZ2 strain prior to adaptation for ORFV-MOMP generation.

- T-helper-1-type cellular responses are known to be strongly associated with protection to *C. abortus* (3) and are essential in a newly developed vaccine (4).

2. AIM

To assess the immunogenicity of live and inactivated ORFV-MOMP vaccines in sheep

3. THE RESEARCH:

METHODS:

- 30 sheep free of OEA were allocated into three groups of 10. These were immunized with an intra-muscular injection of 1 x 10^7 plaque-forming units of either live or inactivated ORFV-MOMP.
- The remaining group served as unvaccinated controls. Sheep were bled regularly following both primary and booster immunisations (Fig 3).

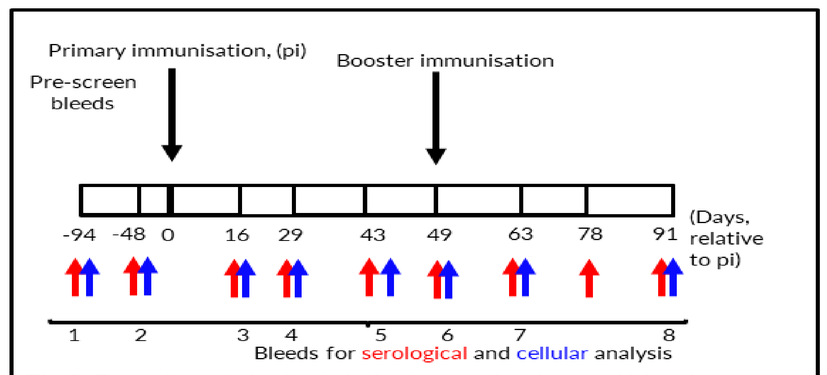

Fig 3. Experimental schedule for immunisation and blood sampling for serological and cellular analysis.

RESULTS

Primary immunisation induced MOMP-IgG in some animals from the live and the inactivated ORFV groups (bleeds 3-5) over baseline values (bleeds 1-2; $p<0.001$, Fig 4). Following booster immunisations (bleeds 6-8), a further increase of MOMP-IgG (over bleeds 3-5, $p<0.001$) was observed. The live ORFV group exhibited consistently higher responses from bleed 6 onwards. The unvaccinated group remained negative and statistically different to both vaccine groups ($p=0.0013$).

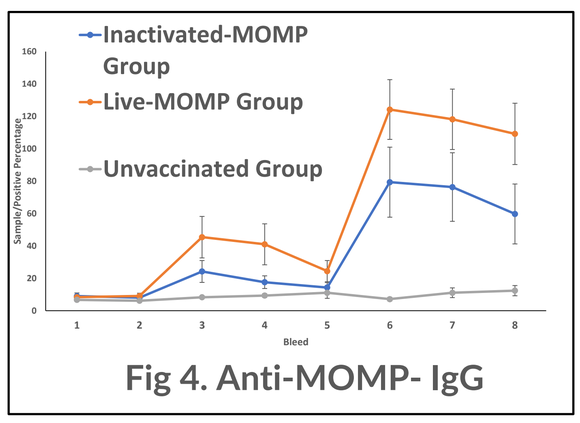

Fig 4. Anti-MOMP- IgG

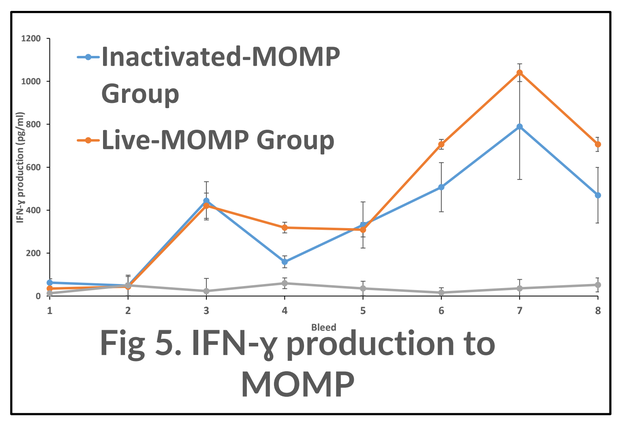

Fig 5. IFN-ɣ production to MOMP

The initial peak of the IFN-ɣ response occurred at bleed 3 for both vaccine groups following the primary immunisation (Fig 5). The post-prime responses (bleeds 3-5) were significantly greater than baseline values (bleeds 1-2, $p=0.0016$). After the booster, the magnitude of the IFN-ɣ response increased in both vaccine groups but not significantly (bleeds 3-5). Overall, the post-booster group response was greater in the live than in the inactivated ORFV-MOMP group.

4. THE OUTCOME:

CONCLUSIONS

- Humoral and cellular responses to MOMP (ORFV-MOMP groups) were significantly different to the unvaccinated group over time.
- This demonstrates vaccine-induced responses ($p<0.0001$) conferred by the ORFV vaccine system in sheep.

FUTURE WORK

- It will be important to compare the ORFV vaccines alongside other prototype vaccines in vaccine-challenge studies in this current SRP- for evaluating protective capability against experimental OEA.
- Should this vaccine platform prove successful it has the opportunity to significantly refine manufacturing processes and reduce potential production costs making future commercial exploitation a possibility.

REFERENCES
(1) Müller M., at al., *Front Immunol.* 2022. 13: 873351; (2) Rohde J., et al., PLoS One. 2013. 8(12): e83802; (3) Entrican et al., *Comp. Immunol, Micro & Inf Di*seases 2012 35: 271; (4) Livingstone M., et al., Vaccines 2021. 9: 898

Moredun Research Institute
Pentlands Science Park
Bush Loan
Penicuik
Scotland EH26 0PZ

@TheMoredunFoundation

@MoredunComms

BioSS SEFARI Scottish Government Riaghaltas na h-Alba gov.scot RESAS Rural & Environmental Science and Analytical Services