Final Report Summary - TOXPOX (Prevention of zoonotic tissue cyst formation in sheep using live attenuated and parapoxvirus vector based vaccines against Toxoplasma gondii)

Toxoplasma gondii is one of the most successful parasites worldwide, able to infect all warm blooded animals and people. Livestock reared for food consumption may have T. gondii cysts in their tissues which pose a risk to people consuming meat from infected animals. In the EU, most human infections are due to consumption of undercooked meat containing T. gondii cysts. Vaccination of food animals to prevent/reduce Toxoplasma tissue cyst formation would be highly effective in reducing the disease burden in humans. The only commercially available vaccine against toxoplasmosis in sheep, Toxovax, prevents congenital disease in lambs but the effect of vaccination on tissue cyst development has not been studied. An issue when using live vaccines is that there may be a risk of the vaccine strain reverting back to wild-type and causing disease in animals or humans, although it is recognized that live vaccines are effective in inducing protective Th-1 type immune responses. In this project we are interested to develop a vaccine using selected T. gondii antigens and explore the efficacy of delivering the vaccine using viral vectors. We hope that such a strategy will enable the development of a safe vaccine with the ability to stimulate specific, protective cell-mediated immune responses.

The project focussed on the development and testing of recombinant virus vectors to deliver T. gondii antigens in vivo to stimulate specific protective immune responses. Two different virus vector systems were evaluated. The project was technically rather challenging which impeded progress towards the ultimate aim which was to test the vaccine delivery strategy in sheep. Nevertheless, several important outputs were achieved within the project.

The main research outputs from the project are:

- Preparation and evaluation of transfer vectors for construction of recombinant pox viruses (ORF) containing SAG1, ROP2, GRA7 and AMA1
- Successful construction of recombinant ORFV expressing Toxoplasma gondii GRA7
- Preparation and evaluation of transfer vectors for production of recombinant lentiviruses (MVV) containing SAG1, ROP2, GRA7 and AMA1, expression has been successfully confirmed for GRA7 and AMA1
- The recombinant virus construct MVV-GRA7 has been successful in inducing a specific antibody response to T. gondii GRA7 following immunization in mice

Impacts of the project:

The project achieved the successful preparation of recombinant viral contracts using both pox viruses and lentiviruses expressing selected T. gondii antigens. Immunisation of mice with the recombinant viruses did result in induction of specific antibody responses showing that the approach had some efficacy and would be worth pursuing with the long term aim of producing a safe and effective vaccine against T. gondii tissue cysts in food animals.
The research fellow conducting the work on this project has gained many additional skills in molecular virology and immunology. These new skills, as well as working in a different country/environment has provided her with new contacts and wider recognition in the field and will enhance her career opportunities. She has been successful in securing further employment continuing research on Toxoplasma directly following on from her post-doctoral fellowship period at Moredun Research Institute.

In addition, she and collaborators at Moredun and various other European institutes have been successful in acquiring new competitive EFSA funding for further research on T. gondii in food animal. The research contacts brought together in Europe as a result of this fellowship award have enabled the development of a new European network group combining expertise in veterinary and public health to help tackle the significant problem of toxoplasmosis. The researcher also took part in a TRANSVAC training course in vaccine development; was part of a European Food safety Authority working group, attended and presented at several conferences and produced research papers during her project.

The outputs from the project have improved our understanding of the development and use of viral vectors to help deliver specific antigens to immunise animals against infectious pathogens. The new collaborations established as a result of the project have enabled the group to obtain further research funding from EFSA to help continue the work on toxoplasmosis in food animals in Europe and will help to consolidate the research partnerships formed during the TOXPOX project.

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