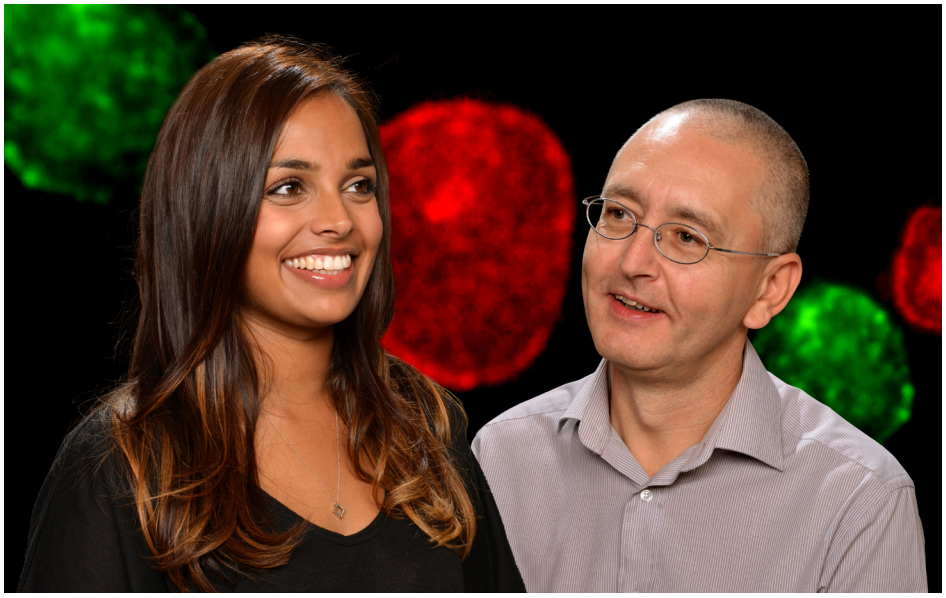
The Australian Society for Parasitology Inc.

ASP Interviews

Sejal Gohil and Brian Cooke

Sejal Gohil, Lev Kats, Torsten Seemann, Kate Fernandez, Ghizal Siddiqui and Brian Cooke (Monash University) recently published their International Journal for Parasitology article "Bioinformatic prediction of the exportome of *Babesia bovis* and identification of novel proteins in parasite-infected red blood cells". Sejal and Brian talk to Lisa Jones about their Babesia bovis research.



1. Tell us about the history of your *Babesia bovis* research and how it led to the identification and characterisation of the three novel exported parasite proteins in your recent IJP publication.

After more than a decade of research on *Plasmodium falciparum*, the Cooke laboratory also focused its interests to study a related parasite (*Babesia bovis*) that causes a disease similar to human malaria in animals – especially cattle. Sejal Gohil found out about this as an undergraduate student and joined Brian's group, first to do honours and then her PhD. 'We soon found out why no one else seemed to be doing much work on this parasite' Sejal said – 'no way to culture the parasite reliably in vitro, no way to synchronise or purify it, very few reagents to work with, no genomes, no molecular tools for genetic manipulation – I am surprised that I ever agreed to it!". Now, 4 years on, it is a completely different story. We have set up *in vitro* culture systems, developed transfection tools and protocols, generated antibodies and reagents for the study of this parasite and learned much more about its overall basic biology – but we still have a long way to go. One of the exciting discoveries (reported in this current paper) was to use bioinformatics to identify exported parasite proteins that are likely to have roles in the pathogenesis of bovine babesiosis. We think that the proteins identified using this approach would be located in appropriate places in the infected cell and have features that make them suitable as targets for the development of novel vaccines

2. What is Babesiosis and is there any cure or vaccine available to protect animals and humans from developing it?

Babesiosis is of major national and international importance. *Babesia spp*. are tick-transmitted protozoan parasites that replicate inside red blood cells (RBCs) of a number of species and cause severe disease and death in susceptible hosts, particularly cattle, horses and dogs. As many as half a billion cattle worldwide are at risk of infection by *Babesia* parasites and the economic consequences, particularly for beef and dairy industries are enormous. In Australia, *B. bovis* is the major causative agent of babesiosis in cattle. Transmission of the parasite between infected cattle by the ixodid tick *Rhipicephalus microplus* is endemic throughout the northern half of our continent and reduces the profitability of the beef and dairy cattle industry in Australia by up to $30m annually.

In the case of *B. bovis* infection, infected-RBCs sequester in post-capillary venules in a variety of organs, including the brain, for the majority of the parasites intra-erythrocytic lifecycle. For the parasite, sequestration of PRBCs is likely necessary to avoid their destruction in the spleen, but for the host, it is highly detrimental and is associated with the development of severe clinical syndromes such as cerebral babesiosis, that unless treated promptly are frequently fatal. In 2007, our laboratory showed that sequestration occurs as a result of infected-RBCs becoming abnormally adhesive for vascular endothelial

cells and significantly more rigid. Associated with these alterations is the appearance of ridge-like structures on the surface of *B. bovis*-infected RBCs that resemble the knob-like protuberances on the surface of human RBCs infected with the malaria parasite, *Plasmodium falciparum* and we have demonstrated that these *Babesia* ridges are related to the parasites ability to cause severe disease.

For almost 50 years, a chilled or frozen live attenuated vaccine has been made in Queensland at the Tick Fever Centre and deployed worldwide for the control of bovine babesiosis. We truly believe, however, that sustainable control of this disease will require the development of recombinant or subunit vaccines to eliminate the current difficulties associated with a live attenuated vaccine.

3. What impact will your results have for animals and humans at risk or suffering from Babesiosis?

Unfortunately, despite our and others significant advances in the field, we still know very little about the virulence determinants of this important pathogen at the molecular level. So much so, that the vaccine currently in use has been developed without any rational genetic basis and therefore has a number of limitations associated with the use of live attenuated parasites. We envisage that our work will significantly increase our understanding of the biology of *Babesia* parasites and will lead to the development of a better vaccine – one that could be deployed without the need for a cold chain.

4. Tell us about your supporters and how they have helped your research progress.

None of this work would ever have got off the ground without the early support and tremendous encouragement from Bob Dalgleish, Bert DeVos, Wayne Jorgensen, John Molloy, Russel Bock and numerous others from The Animal Research Institute and Tick Fever Centre (Tick Fever Research Centre as it was known then) in Queensland. With Peter Rolls now at the helm, their support remains unwavering. In addition, none of the work described in our recent paper would have been possible without the support of the ARC, who awarded us with a Discovery grant to enable this work to go forward.

5 Tell us what happens next in your Babesia bovis research?

Clearly we have learned a lot over the past few years but there is a very long way to go yet. We are currently sequencing and analysing the genomes, transcriptomes and proteomes of Australian *Babesia* isolates to increase our knowledge of this parasite and how it causes disease. In combination with our established cellular and molecular biology techniques, we are convinced that we will be able to identify suitable novel proteins as the targets for the next generation of vaccines both for *Babesia* and other important apicomplexan diseases of animals. Whether this happens of course depends on whether the lab can continue to get funding. 'Times are tough', Brian said 'and with shrinking budgets, basic research like this, particularly in the veterinary sciences, is no doubt going to suffer a bit more than our human work. We will plough on though. Given that the majority of the global burden of this disease is borne by Australia and South America, it should be our responsibility and priority to do something about it - because we can.

"Bioinformatic prediction of the exportome of Babesia bovis and identification of novel proteins in parasite-infected red blood cells" Sejal Gohil a, Lev M. Kats [a], , Torsten Seemannb, , Kate M. Fernandez [a], , Ghizal Siddiqui [a], Brian M. Cooke [a], International Journal for Parasitology 43 (2013) 409–416

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