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Infection Congress 2018: Development of a chlamydial vaccine for koalas: Protection against infection as well as disease- Peter Timms- University of the Sunshine Coast

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Wild koala populations continue to experience serious declines as a result of several threatening factors including: loss of habitat, motor vehicle traum, dog attacks and, chlamydial disease. Chlamydial infections are associated with diseases ranging from ocular disease leading to blindness, as well as urinary and genital tract disease, leading to female infertility. Modeling shows that targeting chlamydial disease would have a major impact on stabilizing population decline. Our previous studies have demonstrated that koalas can be safely immunized with a vaccine containing a mixture of chlamydial major outer membrane protein (MOMP) antigens combined with a single or three-dose subcutaneous regime. Recently, large scale, field trial of the vaccine, we vaccinated 30 koalas that were outwardly clinically healthy but either chlamydia PCR negative or chlamydia PCR positive, and followed them for 1-2 years to assess the protective effect of the vaccine (compared to a control group of unvaccinated koalas). We observed strong, specific and long-lasting immune responses in the vaccinated koalas; high titer antibody responses (as measured by ELISA and also in vitro neutralization) as well as chlamydia-specific cytokine responses (interferon-gamma and IL-17 in particular). We also observed protection from progression to clinical disease in the vaccinated animals. We have also conducted a small trial to vaccinate animals which already have clinical signs of ocular disease. Instead of the normal practice of administering antibiotics (chloramphenicol, daily for 28 days, which severely disrupts the animal's gut microbiome) we vaccinated four animals with a single dose, 3-MOMP vaccine Virus detection was performed using 44 nasopharyngeal swabs. About 57% of the laboratory inspected sera remained immunoglobulin M positive, and 95% of the wipes were reverse transcriptase PCR positive. Phylogenetic analysis of sequences obtained from 30 swab samples showed circulation of two variants of genotype D8, but no genotype D4 strains as detected in 2007. For all vaccinated animals, their chlamydia PCR load decreased, often to zero, and in two animals at least, we observed a decrease in their clinical disease score. These results are promising for the future development of an effective chlamydial vaccine for use in captive as well as wild koalas.

Wild koala populations continue to have significant levels of infection with C. pecorum and as a result are suffering debilitating disease, which is threatening their long-term survival. In many populations, these levels of infection and disease are actually higher than previously reported and current treatment options are showing little to no impact on the decline in the level of infection and disease, with hospital admission records remaining stable over time. The widespread implementation of a vaccine in wild koalas could offer the protection needed to reverse this progression. To date, previous rMOMP protein vaccine trials conducted on both infected and diseased wild koala populations have been very successful. These trials have shown that a rMOMP protein vaccine stimulates the immune system and is responsible for an increase in neutralizing antibodies. Vaccinated koalas have shown a decrease in their chlamydial infectious load as well as ocular disease status, post-vaccination, and importantly, rMOMP vaccinated wild koalas have also shown a decrease in the progression to disease over a 12 month period. However, in spite of this success, there are many challenges in producing and implementing a recombinant protein format vaccine on a wider scale. A synthetic peptide based vaccine could overcome some of these challenges, assuming that it induces a strong and relevant immune response. The development of a peptide based anti-chlamydial vaccine that can elicit the same, or even stronger immune responses as the current C. pecorum MOMP vaccine, with the potential to be mass produced, would be an ideal candidate for future anti-chlamydial vaccine development. In this study, we have shown that a vaccine consisting of two relatively short peptides, derived from the full length MOMP, is capable of inducing an immune response in koalas up to 26 weeks post-vaccination. We have shown a mucosal IgA antibody response to full length rMOMP (G), in both the MOMP-peptide and MOMP-protein vaccinated koalas. Chlamydia infection and disease are endemic in free-ranging koalas. Antibiotics remain the front line treatment for Chlamydia in koalas, despite their rates of treatment failure and adverse gut dysbiosis outcomes. In more severe disease presentations that require antibiotic intervention, the effect of vaccinating during antibiotic use is not currently known. This study investigated whether a productive immune response could be induced by vaccinating koalas during antibiotic treatment for Chlamydia-induced cystitis. Plasma IgG antibody levels against the C. pecorum major outer membrane protein (MOMP) dropped during antibiotic treatment in both vaccinated and unvaccinated koalas. Post-treatment, IgG levels recovered. The IgG antibodies from naturally-infected, vaccinated koalas recognised a greater proportion of the MOMP protein compared to their naturally-infected, unvaccinated counterparts. Furthermore, peripheral blood mononuclear cell gene expression revealed an up-regulation in genes related to neutrophil degranulation in vaccinated koalas during the first month post-vaccination. These findings show that vaccination of koalas while they are being treated with antibiotics for cystitis can result in the generation of a productive immune response, in the form of increased and expanded IgG production

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