BSP ABSTRACT 2024 (2/04/2024 to 5/04/2024)

Title: Development of a whipworm vaccine using virus-like particles

Topic

- Parasite ImmunoPathology

Abstract

Trichuriasis results from infection with the intestinal dwelling parasitic nematode *T. trichiura*, colloquially known as the human whipworm. The disease affects ~465 million people worldwide and causes colitis, mucoid diarrhoea, rectal prolapse, rectal bleeding, abdominal pain/tenesmus, and iron deficiency anemia, which accumulates in ~232,000 DALYs (Disability adjusted life years) annually. Presently, Trichuriasis is treated via anthelmintic drugs as part of mass drug administration (MDA) campaigns. However, these drugs lack efficacy against *T. trichiura*. This has led to a growing interest in an anti-trichuris vaccine, which would provide long lasting immunity, staving off the potential development of drug resistance and breaking the cycle of reinfection commonly found in endemic communities. Here we describe the development of novel vaccine candidates consisting of two MHC-II T cell epitopes identified *in silico* derived from a Trichuris chitin-binding domain-containing protein (CBD) and chymotrypsin-like serine protease (CLSP). These epitopes were genetically fused to the Hepatitis B core antigen (HBcAg), a virus-like particle (VLP) that is well-documented as a vaccine carrier due to its ability to confer high levels of immunogenicity to foreign antigens. We also incorporated the universally immunogenic P2 Tetanus epitope into the vaccine candidates to further boost immunogenicity. Vaccine candidates were shown to induce the production of anti-Trichuris epitope antibodies in C57BL/6 mice. Furthermore, the inclusion of the Tetanus epitope was shown to boost the generation of parasite epitope-specific antibodies in C57BL/6 mice previously primed with the Tetanus toxoid. Despite these correlates of protection, the vaccine candidates did not induce a reduction in worm burden in C57BL/6 mice, within the first 14 days of an acute (150 eggs) *T. muris* challenge infection. Therefore, our modifications to the vaccine candidates increased the parasite-specific IgG antibody response elicited against it in certain contexts, however, this failed to translate into protection against the parasite.

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Thanks the BBSRC

JT is supported by a BBSRC DTP studentship

#Attachments? N/A

Disclosure N/A