

Protective antigen discovery using parasite genetics

Adrian L. Smith¹ and Damer Blake²

¹ Department of Zoology, University of Oxford, UK. ² Royal Veterinary College, London, UK.

Discovery of antigens which confer protective immunity is a major hurdle in development of sub-unit vaccines against antigenically complex pathogens. The discovery pipeline is confounded by the simple fact that host response is not exclusively targeted towards protective antigens and in complex pathogens a large proportion of the detectable response is targeted against antigens that are irrelevant for protection. Antigen discovery pipelines often focus on trying to identify “the right type of response” as a correlate of protection but whilst this strategy restricts the diversity of target antigens it does not focus on protection and false leads are commonplace. In considering this barrier to vaccine development we developed a parasite-genetics based approach for protective antigen discovery.

Previously, we reported the identification of six immune targeted loci within the genome of the important poultry parasite, *Eimeria maxima*. Here we report a major step forward in validation of the genetics led approaches in antigen discovery, having fully characterised two of these loci which included identification of two protective antigens. One of the protective antigens is a homologue of apical membrane antigen-1 (AMA-1), a gene that has a long history as a candidate for malaria vaccines. Indeed, AMA-1 homologues are protective in a wide range of apicomplexan parasites, raising the possibility of identifying conserved biological characteristics of protective antigens. The second antigen, immune-mapped protein-1 (IMP-1) confer protection represents an entirely new candidate antigen with proven protective capability. The implications of the “few protective antigens” concept in immunity to infection with antigenically complex pathogens will be considered.