Adeno-associated viral vectored delivery of monoclonal antibody genes against blood-stage malaria

Malaria remains one of the most devastating infectious diseases, resulting in the death of more than half a million individuals every year. Despite extensive efforts, the development of an efficacious vaccine has proved exceedingly difficult, and new and innovative intervention strategies are likely to be needed. Following parasite release from the liver, blood-stage vaccines aim to reduce mortality, clinical disease, and transmission, whilst potentially also allowing for natural boosting of vaccine-induced responses and the acquisition of natural immunity. However, a significant challenge in the development of a blood-stage malaria vaccine is the need to induce, and maintain, the very high levels of antibodies necessary to neutralise the parasite's rapid invasion of red blood cells. An alternative approach to obtain the required humoral immunity against blood-stage malaria is to use potent monoclonal antibodies (mAbs) as prophylactics, which would bypass the need for a vaccine to aid in current malaria elimination programmes. Vectored immuno-prophylaxis (VIP) uses viral vectors such as adeno-associated virus (AAV) to deliver mAb-expressing genes, which are expressed *in situ* following immunisation and released into the plasma. Recently, we isolated a panel of human mAbs targeting *Plasmodium* blood-stage antigens from vaccinated volunteers. In this study, we deliver novel, fully human, potently neutralising mAbs by VIP in mice, and we achieve durable and high-level serum mAb expression that is strongly inhibitory of parasite growth. This approach, combined with anti-malarial drugs and other control interventions, could provide an effective strategy towards the ambitious objective of malaria eradication.