Getting closer to a vaccine against malaria

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Despite recent progress in the control of malaria in several countries, this disease still kills nearly one million young children in sub-Saharan Africa each year and it contributes significantly to poverty in many of the poorest countries in the world. The effective use of existing control tools (insecticide-impregnated bed nets, residual insecticide spraying and early case detection with effective treatment) should eliminate malaria from additional regions but global eradication of malaria is not feasible without the development of a highly effective vaccine. The most advanced malaria vaccine, known as RTS,S, is likely to be licensed for use in the next few years. The protective efficacy of RTS,S is unlikely to exceed 50% but numerous other approaches to vaccinating against malaria are showing some promise and, consequently, there are good prospects that a second-generation malaria vaccine will be much more effective.

A malaria vaccine needs to be effective against the majority of strains of Plasmodium falciparum, the cause of the most severe form of human malaria, and ideally also against Plasmodium vivax, which is a common cause of malaria in South Asia and the Western Pacific. Both these malaria parasites exhibit extensive antigenic diversity and this is a major hurdle confronting vaccine development. The complex life cycle of the malaria parasite provides many potential targets for protective immune responses induced by vaccination, but this also means there are numerous antigens that need to be evaluated for their potential as vaccine components. Although a full understanding of the adaptive immune responses that protect against malaria is still lacking, it is clear that different immune effector mechanisms operate against different parasite life cycle stages. Consequently, a major challenge has been to develop vaccines that induce high titre immune responses of the appropriate type and specificity.

An anti-P. falciparum sporozoite vaccine, RTS,S, is currently undergoing phase III clinical testing in approximately 16,000 African infants. Developed by GlaxoSmithKline in collaboration with the Walter Reed Army Institute of Research with support from the PATH Malaria Vaccine Initiative, RTS,S is likely to be registered as the first malaria vaccine, possibly within four years. However, the results of phase II trials with RTS,S suggest this vaccine is unlikely to have an efficacy greater than 50% and, therefore, a much-improved vaccine will be required before eradication of malaria could be considered feasible. The efficacy of RTS,S should be improved by combining it with one or more antigens from other parasite life cycle stages. Numerous antigens that can induce immune responses that inhibit development of the disease causing asexual blood stages of P. falciparum have been identified on the surface or in the apical organelles of merozoites, the stage of the parasite that invades host erythrocytes. Many of these antigens were initially characterised by Australian researchers and one was shown to have promise in a phase II clinical trial in Papua New Guinean children. However, support for the development of asexual blood stage antigens as vaccine components has waned recently and the focus has switched to antigens such as those on the sexual stages of the parasite, which can induce immune responses that interrupt malaria transmission. As malaria can remain endemic or cause epidemics at very low transmission intensities, carefully designed field trials will be required to assess the efficacy of this strategy.

The assessment of subunit malaria vaccines comprised of recombinant proteins formulated in adjuvants will continue but the alternative approach of delivering vaccine antigens with live viral vectors and using prime-boost strategies has also shown some promise. Other workers in the field consider that subunit vaccines are unlikely to be sufficiently efficacious and instead are investigating the use of whole parasite vaccines such as irradiation- or genetically-attenuated sporozoites. Although major scientific and logistical problems remain to be overcome before a whole parasite vaccine reaches the stage of clinical trials in an endemic setting, it is important that resources are found to fully assess whole parasite as well as subunit approaches to malaria vaccine development. The recent progress with these diverse approaches allows us to be optimistic that the goal of an effective malaria vaccine is now significantly closer.

References

Biography
Robin Anders is an Emeritus Professor in the Biochemistry Department at La Trobe University. His research interests are the development of recombinant protein subunit vaccines against malaria and the structure and function of merozoite surface proteins.