

WHO/IVR State of the Art of New Vaccines: Research and Development

References malaria

- Aguiar JC, LaBaer J, Blair PL, Shamailova VY, Koundinya M, Russell JA, Huang F, Mar W, Anthony RM, Witney A, Caruana SR, Brizuela L, Sacci JB Jr, Hoffman SL & Carucci DJ. High-throughput generation of *P. falciparum* functional molecules by recombinational cloning. *Genome Res* 2004, **14**, 2076-82.
- Alonso PL, Sacarlal J, Aponte JJ, Leach A, Macete E, Milman J, Mandomando I, Spiessens B, Guinovart C, Espasa M, Bassat Q, Aide P, Ofori-Anyinam O, Navia MM, Corachan S, Ceuppens M, Dubois MC, Demoitie MA, Dubovsky F, Menendez C, Tornieporth N & Ballou WR, Thompson R, Cohen J Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial. *Lancet* 2004, **364**, 1411-20.
- Badell E, Oeuvray C, Moreno A, Soe S, van Rooijen N, Bouzidi A & Druilhe P. Human malaria in immunocompromised mice: an *in vivo* model to study defense mechanisms against *Plasmodium falciparum*. *J Exp Med*. 2000, **192**, 1653-60.
- Ballou WR, Hoffman SL, Sherwood JA, Hollingdale MR, Neva FA, Hockmeyer WT, Gordon DM, Schneider I, Wirtz RA & Young JF. Safety and efficacy of a recombinant DNA *Plasmodium falciparum* sporozoite vaccine. *Lancet* 1987, **1**, 1277-1281.
- Banic DM, de Oliveira-Ferreira J, Pratt-Riccio LR, Conseil V, Goncalves D, Fialho RR, Gras-Masse H, Daniel-Ribeiro C & Camus C. Immune response and lack of immune response to *Plasmodium falciparum* P126 antigen and its amino-terminal repeat in malaria-infected humans. *Am J Trop Med Hyg* 1998, **58**, 768-774.
- BenMohamed L, Thomas A, Bossus M, Brahimi K, Wubben J, Gras-Masse H & Druilhe P. High immunogenicity in chimpanzees of peptides and lipopeptides derived from four new *Plasmodium falciparum* pre-erythrocytic molecules. *Vaccine* 2000, **18**, 2843-2855.
- Blackman MJ, Heidrich HG, Donachie S, McBride JS & Holder AA. A single fragment of a malaria merozoite surface protein remains on the parasite during red cell invasion and is the target of invasion-inhibiting antibodies. *J Exp Med* 1990, **172**, 379-382.
- Bojang KA, Milligan PJ, Pinder M *et al*. RTS,S Malaria Vaccine Trial Team. Efficacy of RTS,S/AS02 malaria vaccine against *Plasmodium falciparum* infection in semi-immune adult men in The Gambia: a randomised trial. *Lancet* 2001, **358**, 1927-34.
- Bonhoeffer J, Kohl K, Chen R, Duclos P, Heijbel H, Heininger U, Jefferson T & Loupi E; Brighton Collaboration. The Brighton Collaboration-enhancing vaccine safety. *Vaccine* 2004, **22**, 2046.
- Bouharoun-Tayoun H & Druilhe P. Evidence for an isotype imbalance, which may be responsible for the delayed acquisition of protective immunity. *Infect Immun* 1992, **60**, 1473-81.
- Bouharoun-Tayoun H, Attanath P, Chongsuphajaisiddhi T & Druilhe P. Antibodies which protect man against *P. falciparum* blood stages do not on their own inhibit parasite growth and invasion in vitro but act in cooperation with monocytes. *J Exp Med* 1990, **172**, 1633-41.

Brown AE, Singharaj P, Webster HK, Pipithkul J, Gordon DM & Boslego JW. Safety, immunogenicity and limited efficacy study of a recombinant *Plasmodium falciparum* circumsporozoite vaccine in Thai soldiers. *Vaccine* 1994, **12**, 102–108.

Chang SP, Case SE, Gosnell WL, Hashimoto A, Kramer KJ, Tam LQ, Hashiro CQ, Nikaido CM, Gibson HL, Lee-Ng CT, Barr PJ, Yokota BT & Hut GS. A recombinant baculovirus 42-kilodalton C-terminal fragment of Plasmodium falciparum merozoite surface protein 1 protects Aotus monkeys against malaria. *Infect Immun* 1996, **64**, 253-261.

Chen Q, Barragan A, Fernandez V, Sundstrom A, Schlichtherle M, Sahlen A, Carlson J, Datta S & Wahlgren M.. Immunization with PfEMP1-DBL1alpha generates antibodies that disrupt rosettes and protect against the sequestration of *Plasmodium falciparum*-infected erythrocytes. *Vaccine* 2004, **22**, 2701-12.

Cohen S, McGregor IA & Carrington S. Gamma globulin and acquired immunity to human malaria. *Nature* 1961, **192**, 733-7

Cortes A, Mellombo M, Mueller I, Benet A, Reeder JC & Anders RF. Geographical structure of diversity and differences between symptomatic and asymptomatic infections for *Plasmodium falciparum* vaccine candidate AMA1. *Infect Immun* 2003, **71**, 1416-1426.

Daly TM & Long CA. A recombinant 15-kilodalton carboxyl-terminal fragment of *Plasmodium yoelii yoelii* 17XL merozoite surface protein 1 induces a protective immune response in mice. *Infect Immun* 1993, **61**, 2462-2467.

Daly TM & Long,CA. Humoral response to a carboxyl-terminal region of the merozoite surface protein-1 plays a predominant role in controlling blood-stage infection in rodent malaria. *J Immunol* 1995, **155**, 236-243.

Daubersies P, Thomas AW, Millet P, Brahimi K, Langermans JA, Ollomo B, BenMohamed L, Slierendregt B, Eling W, Van Belkum A, Dubreuil G, Meis JF, Guerin-Marchand C, Cayphas S, Cohen J, Gras-Masse H & Druilhe P. Protection against *Plasmodium falciparum* malaria in chimpanzees by immunization with the conserved pre-erythrocytic liver-stage antigen 3. *Nat Med* 2000, **6**, 1258-1263.

Dodoo D, Theisen M, Kurtzhals JAL **et al.** Naturally acquired antibodies to the glutamate-rich protein are associated with protection against *Plasmodium falciparum* malaria. *J Infect Dis* 2000, **181**, 1202-5.

Doolan DL & Hoffman SL. The complexity of protective immunity against liver-stage malaria. *J Immunol.* 2000, **165**, 1453-62.

Druilhe P, Hagan P & Rook G. The importance of models of infection in the study of disease Resistance. *Trends in Microbiology* 2002, **10**, S38-46.

Duffy PE, Krzych U, Francis S & Fried M. Malaria vaccines: using models of immunity and functional genomics tools to accelerate the development of vaccines against *Plasmodium falciparum*. *Vaccine* 2005, **23**, 2235-2242

Ellis J, Ozaki LS, Gwadz RW, Cochrane AH, Nussenzweig V, Nussenzweig RS & Godson GN. Cloning and expression in *E. coli* of the malarial sporozoite surface antigen gene from *Plasmodium knowlesi*. *Nature* 1983, **302**, 536–538.

Fluck C, Smith T, Beck HP, Irion A, Betuela I, Alpers MP, Anders R, Saul A, Genton B & Felger I. Strain-specific humoral response to a polymorphic malaria vaccine. *Infect Immun* 2004, **72**, 6300-5.

Genton B, Betuela I, Felger I, Al-Yaman F, Anders RF, Saul A, Rare L, Baisor M, Lorry K, Brown GV, Pye D, Irving DO, Smith TA, Beck HP & Alpers MP. A recombinant

blood-stage malaria vaccine reduces *Plasmodium falciparum* density and exerts selective pressure on parasite populations in a phase 1-2b trial in Papua New Guinea. *J Infect Dis* 2002, **185**, 820-7.

Good M. Vaccine-induced immunity to malaria parasites and the need for novel strategies. *Trends Parasitol* 2005, **2**, 29-34.

Graves P & Gelband H. Vaccines for preventing malaria. *Cochrane Database Syst Rev*. 2000;(2):CD000129. *Cochrane Database Syst Rev*. 2003;(1):CD000129

Groux H & Gysin J. Opsonization as an effector mechanism in human protection against asexual blood stages of *Plasmodium falciparum*: functional role of IgG subclasses. *Res Immunol* 1990, **141**, 529-42.

Gruner AC, Snounou G, Brahimi K, Letourneur F, Renia L & Druilhe P. Pre-erythrocytic antigens of *Plasmodium falciparum*: from rags to riches? *Trends Parasitol*. 2003, **19**, 74-8.

Heppner DG, Cummings JF, Ockenhouse C, Kester KE, Lyon JA & Gordon DM New World monkey efficacy trials for malaria vaccine development: critical path or detour? *Trends Parasitol* 2001, **17**, 419-25.

Hermesen CC, de Vlas SJ, van Gemert GJ, Telgt DS, Verhage DF & Sauerwein RW. Testing vaccines in human experimental malaria: statistical analysis of parasitemia measured by a quantitative real-time polymerase chain reaction. *Am J Trop Med Hyg*. 2004, **71**, 196-201.

Herrington DA, Clyde DF, Losonsky G, Cortesia M, Murphy JR, Davis J, Baqar S, Felix AM, Heimer EP, Gillesen D, et al. Safety and immunogenicity in man of a synthetic peptide malaria vaccine against *Plasmodium falciparum* sporozoites. *Nature* 1987, **328**, 257-259.

Hoffman SL, Goh LML, Luke TC, Schneider I, Le TP, Doolan DL, Sacci J, de la Vega P, Dowler M, Paul C, Gordon DM, Stoute JA, Church LWP, Sedegah M, Heppner DG, Ballou WR & Richie TL. Protection of humans against malaria by immunization with radiation-attenuated *Plasmodium falciparum* sporozoites, *J Infect Dis* 2002, **185**, 1155–1164.

Inselburg J, Bathurst IC, Kansopon J, Barchfeld GL, Barr PJ & Rossan RN. Protective immunity induced in Aotus monkeys by recombinant SERA proteins of *P. falciparum*: adjuvant effects on induction of protective immunity. *Infect Immun* 1993, **61**, 2041-2047.

Inselburg J, Bathurst IC, Kansopon J, Barr PJ & Rossan R. Protective immunity induced in Aotus monkeys by recombinant SERA proteins of *P. falciparum*: further studies using SERA1 and MF75.2 adjuvant. *Infect Immun* 1993, **61**, 2048-2052

Kemp DJ, Coppel RL, Cowman AF, Saint RB, Brown GV & Anders RF, Expression of *Plasmodium falciparum* blood-stage antigens in *Escherichia coli*: detection with antibodies from immune humans, *Proc. Natl. Acad. Sci. U. S. A.* 1983, **80**, 3787–3791.

Kennedy MC et al., In vitro studies with recombinant *Plasmodium falciparum* apical membrane antigen 1 (AMA1): production and activity of an AMA1 vaccine and generation of a multiallelic response. *Infect Immun* 2002, **70**, 6948–6960.

Kester KE, McKinney DA, Tornieporth N, Ockenhouse CF, Heppner DG, Hall T, Krzych U, Delchambre M, Voss G, Dowler MG, Palensky J, Wittes J, Cohen J & Ballou WR; RTS,S Malaria Vaccine Evaluation Group. Efficacy of recombinant circumsporozoite protein vaccine regimens against experimental *Plasmodium falciparum* malaria. *J Infect Dis* 2001, **183**, 640-647.

Kilama WL. Malaria vaccines in Africa. *Acta Trop* 2003, **88**, 153-9.

Kocken, C. H., D. L. Narum, A. Massougboji, B. Ayivi, M. A. Dubbeld, A. van der Wel, D. J. Conway, A. Sanni, & A. W. Thomas. Molecular characterisation of *Plasmodium reichenowi* apical membrane antigen-1 (AMA-1), comparison with *P. falciparum* AMA-1, and antibody-mediated inhibition of red cell invasion. *Mol Biochem Parasitol* 2000, **109**, 147-156.

Li J, Mitamura T, Pang XL, Fox BA, Bzik DJ & Horii T. Differential localization of processed fragments of *Plasmodium falciparum* serine repeat antigen (SERA). *Parasitol Int* 2002, **51**, 343-352.

Ling IT, Ogun SA & Holder AA. Immunization against malaria with a recombinant protein. *Parasite Immunol* 1994, **16**, 63-67.

Luke TC & Hoffman SL. Rationale and plans for developing a non-replicating, metabolically active, radiation-attenuated *Plasmodium falciparum* sporozoite vaccine. *J Exp Biol* 2003, **206**, 3803-3808.

Lyke KE, Dicko A, Kone A, Coulibaly D, Guindo A, Cissoko Y, Traore K, Plowe CV & Doumbo O. Incidence of severe *Plasmodium falciparum* malaria as a primary endpoint for vaccine efficacy trials in Bandiagara, Mali. *Vaccine* 2004, **22**, 3169-74.

Malkin EM, Diemert DJ, McArthur JH, Perreault JR, Miles AP, Giersing BK, Mullen GE, Orcutt A, Muratova O, Awkal M, Zhou H, Wang J, Stowers A, Long CA, Mahanty S, Miller LH, Saul A & Durbin AP. Phase 1 clinical trial of apical membrane antigen 1: an asexual blood-stage vaccine for *Plasmodium falciparum* malaria. *Infect Immun* 2005, **73**, 3677-85.

Malkin EM, Durbin AP, Diemert DJ, Sattabongkot J, Wu Y, Miura K, Long CA, Lambert L, Miles AP, Wang J, Stowers A, Miller LH & Saul A. Phase 1 vaccine trial of Pvs25H: a transmission blocking vaccine for *Plasmodium vivax* malaria. *Vaccine* 2005, **23**, 3131-8.

McGregor IA. Mechanisms of acquired immunity and epidemiological patterns of epidemiological responses in malaria in man. *Bull World Health Organ* 1974; 50: 259-66

Mitchell GH, Thomas AW, Margos G, Dluzewski AR & Bannister LH. Apical membrane antigen 1, a major malaria vaccine candidate, mediates the close attachment of invasive merozoites to host red blood cells. *Infect Immun* 2004, **72**, 154-8.

Moore, Anne C. & Hill, Adrian V. S. Progress in DNA-based heterologous prime-boost immunization strategies for malaria. *Immunological Reviews* 2004, **199**, 126-143.

Moorthy VS, Imoukhuede EB, Milligan P, Bojang K, Keating S, Kaye P, Pinder M, Gilbert SC, Walraven G, Greenwood BM & Hill AS. A randomised, double-blind, controlled vaccine efficacy trial of DNA/MVA ME-TRAP against malaria infection in Gambian adults. *PLoS Med* 2004, **1**, 128-36.

Moorthy VS, Pinder M, Reece WH, Watkins K, Atabani S, Hannan C, Bojang K, McAdam KP, Schneider J, Gilbert S & Hill AV. Safety and immunogenicity of DNA/modified vaccinia virus Ankara malaria vaccination in African adults. *J Infect Dis* 2003, **188**, 1239-44.

Moree M & Ewart S. Policy challenges in malaria vaccine introduction. *Am J Trop Med Hyg.* 2004, **71**, S248-52.

Mueller AK, Labaied M, Kappe SH & Matuschewski K. Genetically modified *Plasmodium* parasites as a protective experimental malaria vaccine. *Nature* 2005, **433**, 164-167.

Nussenzweig RS, Vanderberg J, Most H & Orton C. Protective immunity produced by the injection of x-irradiated sporozoites of *Plasmodium berghei*. *Nature* 1967, **216**, 160–162.

Oeuvray C, Bouharoun-Tayoun H, Gras-Masse H, et al. Merozoite surface protein 3: a malaria protein inducing antibodies that promote *Plasmodium falciparum* killing by cooperation with blood monocytes. *Blood* 1994, **84**, 1594-602.

Oeuvray C, Theisen M, Rogier C, Trape JF, Jepsen S & Druilhe P. Cytophilic immunoglobulin responses to *Plasmodium falciparum* glutamate-rich protein are correlated with protection against clinical malaria in Dielmo, Senegal. *Infect Immun* 2000, **68**, 2617-20.

Okech B A, Nalunkuma A, Okello D, Pang XL, Suzue K, Li J, Horii T & Egwang TG. Natural human IgG subclass responses to *Plasmodium falciparum* serine repeat antigen (SERA) in Uganda. *Am J Trop Med Hyg* 2001, **65**, 912-917.

Pan W, Huang D, Zhang Q, Qu L, Zhang D, Zhang X, Xue X & Qian F. Fusion of Two Malaria Vaccine Candidate Antigens Enhances Product Yield, Immunogenicity, and Antibody-Mediated Inhibition of Parasite Growth In Vitro. *J Immunol* 2004, **172**, 6167-6174.

Pang XL & Horii, T. Complement-mediated killing of *Plasmodium falciparum* erythrocytic schizont with antibodies to the recombinant serine repeat antigen (SERA). *Vaccine* 1998, **16**, 1299-1305.

Pang XL, Mitamura T & Horii T. Antibodies reactive with the N-terminal domain of *Plasmodium falciparum* serine repeat antigen inhibit cell proliferation by agglutinating merozoites and schizonts. *Infect Immun* 1999, **67**, 1821-1827.

Patarroyo ME, Romero P, Torres ML, Clavijo P, Moreno A, Martinez A, Rodriguez R, Guzman F & Cabezas E. Induction of protective immunity against experimental infection with malaria using synthetic peptides. *Nature* 1987, **328**, 629-32.

Perlaza BL, Zapata C, Valencia AZ, Hurtado S, Quintero G, Sauzet JP, Brahimi K, Blanc C, Arevalo-Herrera M, Druilhe P & Herrera S. Immunogenicity and protective efficacy of *Plasmodium falciparum* liver-stage Ag-3 in Aotus lemurinus griseimembra monkeys. *Eur J Immunol*. 2003, **33**, 1321-7.

Pichyangkul S, Gettayacamin M, Miller RS, Lyon JA, Angov E, Tongtawe P, Ruble DL, Heppner DG Jr, Kester KE, Ballou WR, Diggs CL, Voss G, Cohen JD & Walsh DS. Pre-clinical evaluation of the malaria vaccine candidate *P. falciparum* MSP1(42) formulated with novel adjuvants. *Vaccine* 2004, **22**, 3831-24.

Polley SD & Conway DJ1. Strong diversifying selection on domains of the *Plasmodium falciparum* apical membrane antigen1 gene. *Genetics* 2001, **158**, 1505–1512.

Pombo DJ, Lawrence G, Hirunpetcharat C, Rzepczyk C, Bryden M, Cloonan N, Anderson K, Mahakunkijcharoen Y, Martin LB, Wilson D, Elliott S, Elliott S, Eisen DP, Weinberg JB, Saul A & Good MF. Immunity to malaria after administration of ultra-low doses of red cells infected with *Plasmodium falciparum*. *Lancet* 2002, **360**, 610–617.

Prato S, Maxwell T, Pinzon-Charry A, Schmidt CW, Corradin G & Lopez JA. MHC class I-restricted exogenous presentation of a synthetic 102-mer malaria vaccine polypeptide. *Eur J Immunol* 2005, **35**, 681-9.

Sabchareon A, Burnouf T, Ouattara D, Attanath P, Bouharoun-Tayoun H & Chantavanich P. Parasitologic and clinical human response to immunoglobulin administration in falciparum malaria. *Am J Trop Med Hyg* 1991, **45**, 297-308.

Scheller LF & Azad AF Maintenance of protective immunity against malaria by persistent hepatic parasites derived from irradiated sporozoites. *Proc Natl Acad Sci USA* 1995, **92**, 4066–4068.

Sherwood JA Copeland RS, Taylor KA, Abok K, Oloo AJ & Were JB. *Plasmodium falciparum* circumsporozoite vaccine immunogenicity and efficacy trial with natural challenge quantitation in an area of endemic human malaria of Kenya, *Vaccine* 1996, **14**, 817–827.

Smith JD & Deitsch KW. Pregnancy-associated malaria and the prospects for syndrome-specific antimalaria vaccines. *J Exp Med.* 2004, **200**, 1093-7.

Smith P & Milligan P. Malaria vaccine: 3 or 6 months' protection? *Lancet* 2005, **365**, 472-473.

Smith T, Schellenberg JA & Hayes R. Attributable fraction estimates and case definitions for malaria in endemic areas. *Stat Med.* 1994, **132**, 345-58.

Soe S, Singh S, Camus D, Horii T & Druilhe P. *P falciparum* SERP, a new target of monocytes dependent antibody-mediated parasite killing. *Infect Immunity* 2002, **70**, 7182-7184.

Soe S, Theisen M, Roussilhon C, Aye KS & Druilhe P. Association between protection against clinical malaria and antibodies to merozoite surface antigens in an area of hyperendemicity in Myanmar: complementarity between responses to merozoite surface protein 3 and the 220-kilodalton glutamate-rich protein. *Infect Immun* 2004, **72**, 247-52.

Stoute JA, Kester KE, Krzych U, Wellde BT, Hall T, White K, Glenn G, Ockenhouse CF, Garcon N, Schwenk R, Lanar DE, Sun P, Momin P, Wirtz RA, Golenda C, Slaoui M, Wortmann G, Holland C, Dowler M, Cohen J & Ballou WR. Long-term efficacy and immune responses following immunization with the RTS,S malaria vaccine. *J Infect Dis* 1998, **178**, 1139-1144.

Stoute JA, Slaoui M, Heppner DG, Momin P, Kester KE, Desmons P, Wellde BT, Garcon N, Krzych U & Marchand M. A preliminary evaluation of a recombinant circumsporozoite protein vaccine against *Plasmodium falciparum* malaria. RTS,S Malaria Vaccine Evaluation Group. *N Engl J Med* 1997, **336**, 86-91.

Stowers AW & Miller LH. Are trials in New World monkeys on the critical path for blood-stage malaria vaccine development? *Trends Parasitol.* 2001, **17**, 415-9.

Struik SS & Riley EM. Does malaria suffer from lack of memory? *Immunol Rev* 2004, **201**, 268-90.

Sun P, Schwenk R, White K, Stoute JA, Cohen J & Ballou WR. Protective immunity induced with malaria vaccine, RTS,S, is linked to *Plasmodium falciparum* circumsporozoite protein-specific CD4(+) and CD8(+) T cells producing IFN-gamma, *J Immunol* 2003, **171**, 6961–6967.

Suzue K, Ito M, Matsumoto Y, Tanioka Y & Horii T. Protective immunity induced in squirrel monkeys with recombinant serine repeat antigen (SERA) of *Plasmodium falciparum*. *Parasitol Int* 1997, **46**, 17–25.

Theisen M, Soe S, Jessing SG **et al.** Identification of a major B-cell epitope of the *Plasmodium falciparum* glutamate-rich protein (GLURP), targeted by human antibodies mediating parasite killing. *Vaccine* 2001, **19**, 204-12.

Theisen M, Soe S, Oeuvray C **et al.** The glutamate-rich protein (GLURP) of *Plasmodium falciparum* is a target for antibody-dependent monocyte-mediated inhibition of parasite growth *in vitro*. *Infect Immun* 1998, **66**, 11-7.

Udhayakumar V, Anyona D, Kariuki S, Shi YP, Bloland PB, Branch OH, Weiss W, Nahlen BL, Kaslow DC & Lal AA. Identification of T and B cell epitopes recognized by humans in the C-terminal 42-kDa domain of the *Plasmodium falciparum* merozoite surface protein (MSP-1). *J Immunol* 1995, **154**, 6022-30.

Verhage DF, Telgt DS, Bousema JT, Hermsen CC, van Gemert GJ, van der Meer JW & Sauerwein RW. Clinical outcome of experimental human malaria induced by *Plasmodium falciparum*-infected mosquitoes. *Neth J Med*. 2005, **63**, 52-8.

Walther M, Dunachie S, Keating S, Vuola JM, Berthoud T, Schmidt A, Maier C, Andrews L, Andersen RF, Gilbert S, Poulton I, Webster D, Dubovsky F, Tierney E, Sarpotdar P, Correa S, Huntcooke A, Butcher G, Williams J, Sinden RE, Thornton GB & Hill AV. Safety, immunogenicity and efficacy of a pre-erythrocytic malaria candidate vaccine, ICC-1132 formulated in Seppic ISA 720. *Vaccine* 2005, **23**, 857-64.

Wang R, Doolan DL, Le TP, Hedstrom RC, Coonan KM, Charoenvit Y, Jones TR, Hobart P, Margalith M, Ng J, Weiss WR, Sedegah M & de Taisne C, Norman JA, Hoffman SL. Induction of antigen-specific cytotoxic T lymphocytes in humans by a malaria DNA vaccine. *Science* 1998, **282**, 476-480.

Wang R, Epstein J, Baraceros FM, Gorak EJ, Charoenvit Y, Carucci DJ, Hedstrom RC, Rahardjo N, Gay T, Hobart P, Stout R, Jones TR, Richie TL, Parker SE, Doolan DL, Norman J & Hoffman SL. Induction of CD4(+) T cell-dependent CD8(+) type 1 responses in humans by a malaria DNA vaccine. *Proc Natl Acad Sci USA* 2001, **98**, 10817-10822.