

# WRRAIR RTS,S AND MALARIA VACCINE RESEARCH

AN HISTORICAL AND BIBLIOMETRIC  
ANALYSIS

Prepared by Gorgas Memorial Library  
October 2011



Silver Spring, Maryland



AN HISTORICAL REVIEW

# BACKGROUND



- The Walter Reed Army Institute of Research (WRAIR) and its component overseas labs, particularly those in Kenya and Thailand, have contributed significantly to vaccine development against malaria and its plasmodium host.
- WRAIR investigations through the years have provided essential foundational research leading researchers to the most recent experimental study showing that the RTS/S vaccine showed significant protection against the deadly disease. As reported in October 2011 by a frequent WRAIR collaborating organization, SmithKline, in Phase III trials, RTS/S reduced the risk of malaria infection by half in African children aged 5 to 17 months<sup>1</sup>
- This analysis examines selected fundamental papers documenting WRAIR RTS/S research and its precursor research, providing evidence of its significant influence on this research overall.

<sup>1</sup>First Results of Phase 3 Trial of RTS,S/AS01 Malaria Vaccine in African Children. N Engl J Med 2011 Oct 18. and press release <http://www.gsk.com/media/pressreleases/2011/2011-pressrelease-676305.htm> (viewed online 27 October 2011 )



- Literature reviews of the history of vaccine development were examined to identify key milestones in the development of the RTS/S vaccine and to identify groundbreaking WRAIR science on this subject. (1-5)
- A subject search of Web of Science yielded 599 citations to WRAIR papers (articles, proceedings paper, meeting abstract and reviews) related to malaria vaccine development.



# LITERATURE REVIEWS

Girard MP, Reed ZH, Friede M, Kieny MP. A review of human vaccine research and development: *Malaria. Vaccine*2007 Feb;25(9):1567-80.

Vanderberg JP. Reflections on early malaria vaccine studies, the first successful human malaria vaccination, and beyond. *Vaccine*2009 Jan;27(1):2-9.

Cohen J, Nussenzweig V, Nussenzweig R, Vekemans J, Leach A. From the circumsporozoite protein to the RTS, S/AS candidate vaccine. *Human Vaccines*2010 Jan;6(1):90-6.

Vekemans J, Ballou WR. Plasmodium falciparum malaria vaccines in development. *Expert Rev Vaccines*. [Review]. 2008 Mar;7(2):223-40.

Regules JA, Cummings JF, Ockenhouse CF. The RTS,S vaccine candidate for malaria. *Expert Rev Vaccines*. [Article]. 2011 May;10(5):589-99.



PRECURSORS

# ROOTS OF THE RTS/S VACCINE



# 1960's

Experiments on sporozite attenuation on immunization against schistosomiasis, done by WRAIR with X-irradiated Cercariae(6, 7), inspired similar studies by NYU and other researchers focused on mosquitoes

- Sadun EH. Immunization in schistosomiasis by previous exposure to homologous and heterologous Cercariae by inoculation of preparations from schistosomes and by exposure to irradiated Cercariae. *Annals of the New York Academy of Sciences*1963;113(1):418-&.
- Sadun EH, Bruce JI, Macomber PB. Parasitologic pathologic + serologic reactions to *Schistosoma mansoni* in monkeys exposed to irradiated Cercariae. *American Journal of Tropical Medicine and Hygiene*1964;13(4):548-&.



# 1970's

WRAIR studies  
the role of  
immunity in  
rodent malaria.  
(8-9)

Lourie SH. Effect of Plasmodium-berghei on immune-response in rats. *Proceedings of the Helminthological Society of Washington*. [Article]. 1972;39(NOV):477-84.

Lourie SH, Dunn MA. Effect of protective sera on course of Plasmodium-berghei in immunosuppressed rats. *Proceedings of the Helminthological Society of Washington*. [Article]. 1972;39(NOV):470-7.



# 1970's

Investigations suggest that protective antibody exerts its influence on the schizonts and/or the merozoites of malaria parasites(10)

- Diggs CL, Osler AG. Humoral Immunity in Rodent Malaria .3. Studies on Site of Antibody Action. *Journal of Immunology*. [Article]. 1975;114(4):1243-7.



NEXT STEPS

# DECODING OF THE GENES FOR CIRCUMSPOROZITE PROTEIN



# 1980's



In 1984, WRAIR entered into a Collaborative Research and Development Agreement with GlaxoSmithKline to provide a malaria vaccine using genetic engineering techniques.



- WRAIR adopted a new approach and began to focus on the development of a synthetic vaccine based on peptide constituents of Circumsporozite protein (CSP)



Early experiments involved use of monoclonal antibodies to isolate CSP and resulted in the cloning of the CSP genes of several species of the malaria parasite(11)

Weber JL, Hockmeyer WT.  
Structure of the circumsporozoite protein gene in 18 strains of *Plasmodium-falciparum*.  
*Molecular and Biochemical Parasitology* 1985;15(3):305-16.)



Work included expression of plasmodium-falciparum circumsporozoite proteins in echerichia-coli for potential use in a human malaria vaccine(12)

Young JF, Hockmeyer WT, Gross M, Ballou WR, Wirtz RA, Trosper JH, Beaudoin RL, Hollingdale MR, Miller LH, Diggs CL, Rosenberg M. Expression of Plasmodium-falciparum Circumsporozoite proteins in Escherichia-coli for potential use in a human malaria vaccine. *Science* 1985;228(4702):958-62.



Research studies in animals showed that synthesized CS proteins induced antibodies with biologic activity correlated with protection(13)

Ballou WR, Rothbard J, Wirtz RA, Gordon DM, Williams JS, Gore RW, Schneider I, Hollingdale MR, Beaudoin RL, Maloy WL, Miller LH, Hockmeyer WT. Immunogenicity of synthetic peptides from circumsporozoite protein of *Plasmodium-falciparum*. *Science*. [Article]. 1985;228(4702):996-9.



Research continued  
on the safety and  
efficacy of a  
plasmodium  
falciparum sporozite  
vaccine(14-15)

Webster HK, Boudreau EF, Pang LW, Permpnich B, Sookto P, Wirtz RA. Development of immunity in natural Plasmodium-falciparum malaria - antibodies to the falciparum sporozoite vaccine-1 antigen (R32tet32). *Journal of Clinical Microbiology*. [Article]. 1987 Jun;25(6):1002-8.

Oster CN, Hoffman SL, Plowe C, Hollingdale MR, Beier J, Mugambi M. Human-antibodies to Plasmodium-falciparum circumsporozoite protein and protection against malaria. *Clinical Research*. [Meeting Abstract]. 1987 Apr;35(3):A656-A.



INITIAL STUDIES

# RT,S/S DEVELOPMENT



# 1990's

In the early 1990's, studies in Western Kenya involved 25 adult male volunteers with prior exposure to malaria who received recombinant sporozite vaccine or placebo(16)

- Results of this study showed that response to recombinant sporozite vaccine mirrored response to mature sporozite antigen

Sherwood JA, Oster CN, Adoyoadoyo M, Beier JC, Gachihi GS, Nyakundi PM, Ballou WR, Brandlingbennett AD, Schwartz IK, Were JBO, Wirtz RA, Schneider I, Roberts CR, Young JF, Gross M, Chulay JD. Safety and immunogenicity of a *Plasmodium-falciparum* sporozoite vaccine - boosting of antibody-response in a population with prior natural exposure to malaria. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1991 May-Jun;85(3):336-40.



Paper published in the Journal of Infectious Diseases in 1995 described the production of RTS,S particles and the first phase 1 safety, immunogenicity and efficacy trial of P. falciparum sporozoite challenge of human volunteers using RTS,S/alum and RTS,S/alum/MPL(17)

Gordon DM, McGovern TW, Krzych U, Cohen JC, Schneider I, Lachance R, Heppner DG, Yuan G, Hollingdale M, Slaoui M, Hauser P, Voet P, Sadoff JC, Ballou WR. Safety, immunogenicity, and efficacy of a recombinantly produced Plasmodium-falciparum circumsporozoite-protein hepatitis-b surface-antigen subunit vaccine. *Journal of Infectious Diseases*. [Article]. 1995 Jun;171(6):1576-85.



Preliminary results of the field trial testing safety and efficacy of three formulations of recombinant circumsporozoite-protein vaccines (SBAS4, SBAS3, and SBA52) against *P. falciparum* (vaccinating a population without prior exposure to malaria) were published in 1997(18)

Stoute JA, Slaoui M, Heppner DG, Momin P, Kester KE, Desmons P, Wellde BT, Garcon N, Krzych U, Marchand M, Ballou WR, Cohen JD. A preliminary evaluation of a recombinant circumsporozoite protein vaccine against *Plasmodium falciparum* malaria. *New England Journal of Medicine* 1997 Jan;336(2):86-91.



FURTHER STRIDES

# RTS,S VACCINE AND STUDIES OF RTS,S(AS02)



# 2000's

Research on RTS,S was extremely productive in this decade (19-22) and involved numerous WRAIR researchers who presented at meetings and published papers on this topic.

Kester KE, Stoute JA, Mason C, Siangla J, Opollo M, Vigneron L, Walter M, Heppner DG, Tornieporth N, Voss G, Ballou WR, Cohen J. Safety and immunogenicity of the lyophilized RTS, S/SBAS2 malaria vaccine in a malaria-experienced adult population of western Kenya. *American Journal of Tropical Medicine and Hygiene*. [Meeting Abstract]. 2000(3 Suppl.):334.

Kester KE, Heppner DG, Ockenhouse CF, Hall BT, Voss G, De Buyl E, Van Handenhove M, Gordon DM, Krzych U, Dubois MC, Delchambre M, Tornieporth N, Vigneron L, Ballou WR, Cohen J. Double blind, randomized phase I/IIA trials of Smithkline Beecham's candidate malaria vaccines RTS, S+TRAP/SBAS2 and TRAP/SBAS2. *American Journal of Tropical Medicine and Hygiene*. [Meeting Abstract]. 2000;62(3 Suppl):201-02.

Kester KE, Cummings JF, Ockenhouse CF, Hall BT, Gordon DM, Krzych U, Holland CA, Tornieporth N, Vigneron L, Delchambre M, Cohen J, Heppner DG. Safety, immunogenicity, and preliminary efficacy of two short course schedules of GlaxoSmithKline's candidate malaria vaccine RTS,S / AS02. *American Journal of Tropical Medicine and Hygiene*. [Meeting Abstract]. 2001;65(3 Suppl):255.

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. Efficacy of recombinant circumsporozoite protein vaccine regimens against experimental *Plasmodium falciparum* malaria. *Journal of Infectious Diseases* 2001;183(4):640-7.



A key paper published in December 2001 described a randomized clinical field trial of RTS,S/AS02, a pre-erythrocytic malaria vaccine based on the circumsporozoite surface protein of *p. falciparum* fused to HBsAg and incorporating the adjuvant AS02(23)

- Conducted by WRAIR in Africa, this 1998 study of semi-immune adult men in Gambia proved the RTS,S/AS02 vaccine safe and immunogenic and established the first pre-erythrocytic vaccine that provided significant protection against *p. falciparum* infection

Bojang KA, Milligan PJM, Pinder M, Vigneron L, Allouche A, Kester KE, Ballou WR, Conway DJ, Reece WHH, Gothard P, Yamuah L, Delchambre M, Voss G, Greenwood BM, Hill A, McAdam K, Tornieporth N, Cohen JD, Doherty T, Rts SMVTT. Efficacy of RTS,S/ASO2 malaria vaccine against *Plasmodium falciparum* infection in semi-immune adult men in *The Gambia: a randomised trial. Lancet*2001 Dec;358(9297):1927-34.



A follow-up paper in 2004 showed that T cell-mediated immune responses are induced by RTS,S/AS02 in naturally exposed donors and offered a mechanism to investigate potentially protective responses in the field (24)

Pinder M, Reece WH, Plebanski M, Akinwunmi P, Flanagan KL, Lee EA, Doherty T, Milligan P, Jaye A, Tornieporth N, Ballou R, McAdam KP, Cohen J, Hill AV. Cellular immunity induced by the recombinant *Plasmodium falciparum* malaria vaccine, RTS,S/AS02, in semi-immune adults in The Gambia. *Clinical and Experimental Immunology* 2004;135(2):286-93.



WRAIR research on  
RTS,S/AS02 (25-26)  
continues to be a  
vital part of malaria  
vaccine  
development efforts

Heppner DG, Kester KE, Ockenhouse CF, Tornieporth N, Ofori O, Lyon JA, Stewart VA, Dubois P, Lanar DE, Krzych U, Moris P, Angov E, Cummings JF, Leach A, Hall BT, Dutta S, Schwenk R, Hillier C, Barbosa A, Ware LA, Nair L, Darko CA, Withers MR, Ogutu B, Polhemus ME, Fukuda M, Pichyangkul A, Gettyacamin M, Garcon N, Tucker K, Wittes J, Plowe CV, Thera MA, Duombo OK, Pau MG, Goudsmit J, Ballou WR, Cohen J. Towards an RTS,S-based, multi-stage, multi-antigen falciparum malaria: progress at the Walter Reed Army Institute of Research. *Vaccine*2005 Mar;23(17-18):2243-50.

Kester KE, McKinney DA, Tornieporth N, Ockenhouse CF, Heppner DG, Hall T, Welde BT, White K, Sun P, Schwenk R, Krzych U, Delchambre M, Voss G, Dubois MC, Gasser RA, Dowler MG, O'Brien M, Wittes J, Wirtz R, Cohen J, Ballou WR, Rts SMVEG. A phase I/IIa safety, immunogenicity, and efficacy bridging randomized study of a two-dose regimen of liquid and lyophilized formulations of the candidate malaria vaccine RTS,S/AS02A in malaria-naive adults. *Vaccine*2007 Jul;25(29):5359-66.



WRAIR research on RTS,S explores the prime boost approach(27) .

Stewart VA, McGrath SM, Dubois PM, Pau MG, Mettens P, Shott J, Cobb M, Burge JR, Larson D, Ware LA, Demoitie MA, Weverling GJ, Bayat B, Custers J, Dubois MC, Cohen J, Goudsmit J, Heppner DG. Priming with an adenovirus 35-circumsporozoite protein (CS) vaccine followed by RTS,S/AS01B boosting significantly improves immunogenicity to *Plasmodium falciparum* CS compared to that with either malaria vaccine alone. *Infect Immun*. [Article]. 2007 May;75(5):2283-90.



WRAIR research on  
RTS,S/AS01 and  
RTS,2/AS02 (28-29)  
involves field trials  
on adults in Africa.

Kester KE, Cummings JF, Ofori-Anyinam O, Ockenhouse CF, Krzych U, Moris P, Schwenk R, Nielsen RA, Debebe Z, Pinelis E, Juompan L, Williams J, Dowler M, Stewart VA, Wirtz RA, Dubois MC, Lievens M, Cohen J, Ballou WR, Heppner DG, Rts, Grp SVE. Randomized, Double-Blind, Phase 2a Trial of Falciparum Malaria Vaccines RTS,S/AS01B and RTS,S/AS02A in Malaria-Naive Adults: Safety, Efficacy, and Immunologic Associates of Protection. *Journal of Infectious Diseases* 2009 Aug;200(3):337-46.

Waitumbi JN, Anyona SB, Hunja CW, Kifude CM, Polhemus ME, Walsh DS, Ockenhouse CF, Heppner DG, Leach A, Lievens M, Ballou WR, Cohen JD, Sutherland CJ. Impact of RTS,S/AS02(A) and RTS,S/AS01(B) on Genotypes of *P. falciparum* in Adults Participating in a Malaria Vaccine Clinical Trial. *Plos One*. [Article]. 2009 Nov;4(11).



A 2011 WRAIR paper presented the examination of the immunological characteristics of RTS,S, demonstrating that in addition to TNF-alpha, IL-2 is also a significant contributing factor to RTS,S/AS vaccine induced immunity and that both T(E/EM) and T(CM) cells are major producers of IL-2(30)

Lumsden JM, Schwenk RJ, Rein LE, Moris P, Janssens M, Ofori-Anyinam O, Cohen J, Kester KE, Heppner DG, Krzych U. Protective immunity induced with the RTS,S/AS vaccine is associated with IL-2 and tnf-alpha producing effector and central memory CD4(+) T cells. *Plos One*. [Article]. 2011 Jul;6(7).



ROLE OF OVERSEAS LABS

# MALARIA VACCINE



# OVERSEAS FIELD TRIALS AND STUDIES

Results of AFRIMS field trials and research were published as early as 1980(31) and such studies continue today.(32)

Representing twelve percent (12%) of the WRAIR total, seventy-four (74) papers involving AFRIMS scientists were published on malaria vaccine research.

- Macdermott RP, Wells RA, Zolyomi S, Pavanand K, Phisphumvidhi P, Permpanich B, Gilbreath M. EXAMINATION OF PERIPHERAL-BLOOD MONONUCLEAR-CELLS AND SERA FROM THAI ADULTS NATURALLY INFECTED WITH MALARIA IN ASSAYS OF BLASTOGENIC RESPONSIVENESS TO MITOGENIC LECTINS AND ALLOGENEIC CELL-SURFACE ANTIGENS. *Infect Immun.* [Article]. 1980;30(3):781-5.
- Lumsden JM, Pichyangkul S, Srichairatanakul U, Yongvanitchit K, Limsalakpetch A, Nurmukhambetova S, Klein J, Bertholet S, Vedvick TS, Reed SG, Sattabongkot J, Bennett JW, Polhemus ME, Ockenhouse CF, Howard RF, Yadava A. Evaluation of the Safety and Immunogenicity in Rhesus Monkeys of a Recombinant Malaria Vaccine for Plasmodium vivax with a Synthetic Toll-Like Receptor 4 Agonist Formulated in an Emulsion. *Infect Immun.* [Article]. 2011 Sep;79(9):3492-500.



## USAMRU-KENYA

Similarly, work emanating from field trials in Africa and studies produced by USAMRU-Kenya were published as early as 1987 (15) and research on malaria vaccines continues to be a focal point in Africa.(33)

Representing ten percent (10%) of the WRAIR total, fifty-nine (59) papers involving USAMRU-Kenya researchers and resulting from work in Africa were published on this topic.

Oster CN, Hoffman SL, Plowe C, Hollingdale MR, Beier J, Mugambi M. HUMAN-ANTIBODIES TO PLASMODIUM-FALCIPARUM CIRCUMSPOROZOITE PROTEIN AND PROTECTION AGAINST MALARIA. Clin Res. [Meeting Abstract]. 1987 Apr;35(3):A656-A.

Waitumbi JN, Gerlach J, Afonina I, Anyona SB, Koros JN, Siangla J, Ankoudinova I, Singhal M, Watts K, Polhemus ME, Vermeulen NM, Mahoney W, Steele M, Domingo GJ. Malaria prevalence defined by microscopy, antigen detection, DNA amplification and total nucleic acid amplification in a malaria-endemic region during the peak malaria transmission season. Trop Med Int Health. [Article]. 2011 Jul;16(7):786-93.



BEYOND

# RTS,S VACCINE



## CURRENT THRUSTS

WR AIR malaria vaccine research is evolutionary and current forward-thinking initiatives include a study indicating that AMA1 might be useful in a multicomponent malaria vaccine(34) and an examination of a new technique for optical mapping of multiple malaria genomes(35).

Thera MA, Doumbo OK, Coulibaly D, Laurens MB, Ouattara A, Kone AK, Guindo AB, Traore K, Traore I, Kouriba B, Diallo DA, Diarra I, Daou M, Dolo A, Tolo Y, Sissoko MS, Niangaly A, Sissoko M, Takala-Harrison S, Lyke KE, Wu YK, Blackwelder WC, Godeaux O, Vekemans J, Dubois MC, Ballou WR, Cohen J, Thompson D, Dube T, Soisson L, Diggs CL, House B, Lanar DE, Dutta S, Heppner DG, Plowe CV. A Field Trial to Assess a Blood-Stage Malaria Vaccine. *New England Journal of Medicine*. [Article]. 2011 Sep;365(11):1004-13.

Riley MC, Kirkup BC, Johnson JD, Lesho EP, Ockenhouse CF. Rapid whole genome optical mapping of *Plasmodium falciparum*. *Malaria Journal*. [Article]. 2011 Aug;10.



IMPACT OF WRAIR MALARIA (RTS,S) VACCINE RESEARCH

# A BIBLIOMETRIC ANALYSIS



# BIBLIOMETRIC ANALYSIS PERFORMED USING WEB OF KNOWLEDGE® TOOLS

## ➤ Web of Science® (publication years 1898-2011\*)

Database of citations to the scholarly literature in the sciences, social sciences, arts, and humanities including proceedings of international conferences, symposia, seminars, colloquia, workshops, and conventions (using citations as of October 24, 2011).

## ➤ Essential Science Indicators®

Compilation of essential science performance statistics and science trend data derived from Thomson Reuters data. The chief indicators of productivity (overall influence) are journal article publication counts. Total citation counts and cites per paper are indicators of influence and impact (weighted influence). Used specifically the “Highly Cited Papers” component of this tool. Updated as of September 1, 2011 to cover a 10-year + 6-month period, January 1, 2001-June 30, 2011.

## ➤ Journal Citation Reports® 2010

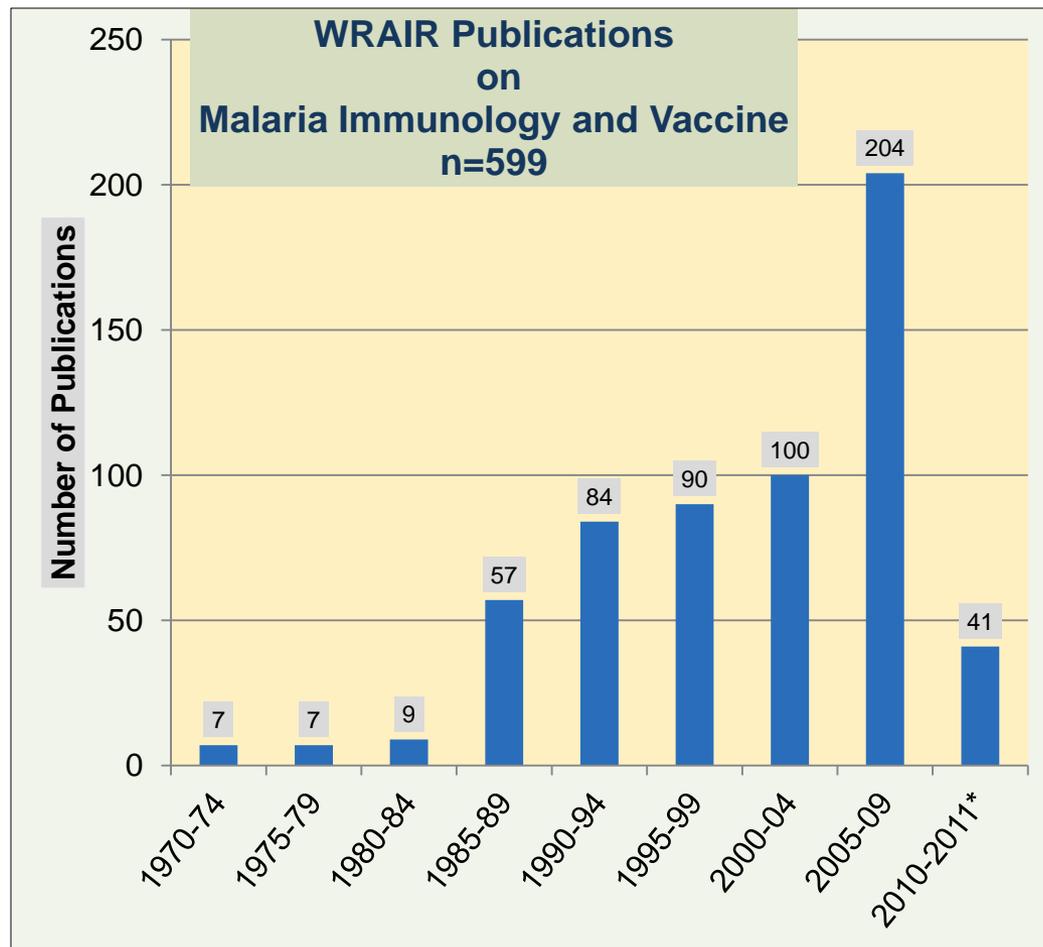
A resource tool for journal evaluation, using citation data drawn from over 11,000 journals from over 3,300 publishers in over 80 nations. Updated annually.

\*2011 represents a partial period



# PUBLICATIONS IN WEB OF SCIENCE

- WRAIR researchers published a total of 599 papers related to immunology and malaria vaccine research (i.e., articles, meeting abstracts, proceedings papers, and review) covered in Web of Science in the period 1972-2011\*
- Publishing on this subject increased to over 50 papers per year in the mid-1980's and increased regularly through the early 2000's. The number of publications published in 2005-09 more than doubled over the previous five-year period, illustrating the strength of malaria immunology and vaccine research focus at WRAIR.



\*Represents a partial period



# WRAIR RTS,S RESEARCH ON THE CONTINUUM

## Earliest Citation in Web of Science

- Presented at a meeting of the Helminthological Society of Washington, this paper is the earliest WRAIR citation identified in Web of Science on the immunology of rodent malaria, an early research focus.

Lourie SH, Dunn MA. Effect of protective sera on course of *Plasmodium-berghei* in immunosuppressed rats. *Proceedings of the Helminthological Society of Washington*. [Article]. 1972;39(NOV):470-7.

## Most Current Citation in Web of Science

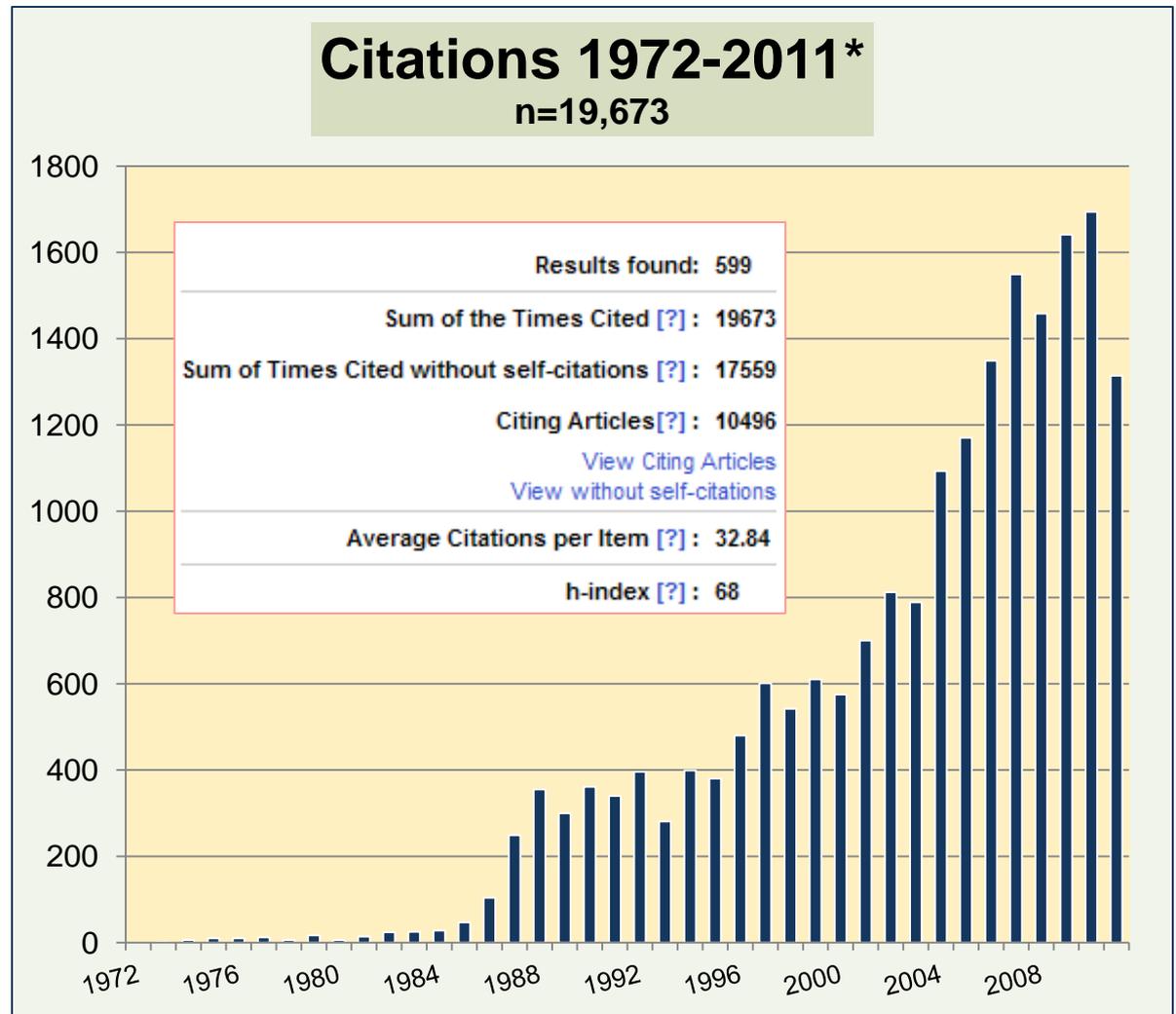
- The most current citation on malaria vaccine discusses a field trial in which 400 Malian children were immunized with either the malaria vaccine FMP2.1/AS02(A), a recombinant protein based on apical membrane antigen 1 (AMA1) or a control (rabies) vaccine and followed for 6 months. Results indicates that AMA1 might be useful in a multicomponent malaria vaccine.

Thera MA, Doumbo OK, Coulibaly D, Laurens MB, Ouattara A, Kone AK, Guindo AB, Traore K, Traore I, Kouriba B, Diallo DA, Diarra I, Daou M, Dolo A, Tolo Y, Sissoko MS, Niangaly A, Sissoko M, Takala-Harrison S, Lyke KE, Wu YK, Blackwelder WC, Godeaux O, Vekemans J, Dubois MC, Ballou WR, Cohen J, Thompson D, Dube T, Soisson L, Diggs CL, House B, Lanar DE, Dutta S, Heppner DG, Plowe CV. A Field Trial to Assess a Blood-Stage Malaria Vaccine. *New England Journal of Medicine*. [Article]. 2011 Sep;365(11):1004-13.



# CITATIONS TO WRAIR PUBLICATIONS ON MALARIA VACCINE

- Citations to WRAIR papers on malaria vaccine jumped dramatically higher in 2004 to over 1,000 citations per year and continue to rocket higher.
- Overall, WRAIR publications in this area average 32.84 citations per paper.
- WRAIR malaria vaccine publishing has a high overall h-index of 68, a level commonly associated with high honors (e.g., membership in the NAS)



\*2011 represents a partial period



# WRAIR MALARIA VACCINE PUBLICATION SOURCES

- A majority (59%) of WRAIR papers on this topic appear most commonly in these top ten (10) journal sources.

- Representing a facet of 21<sup>st</sup> century science and the importance of vaccinology and genetics in modern research, three of these journals (identified in red) have been in existence only since the 1980's and two others (noted in blue) only since the early-mid 2000's.

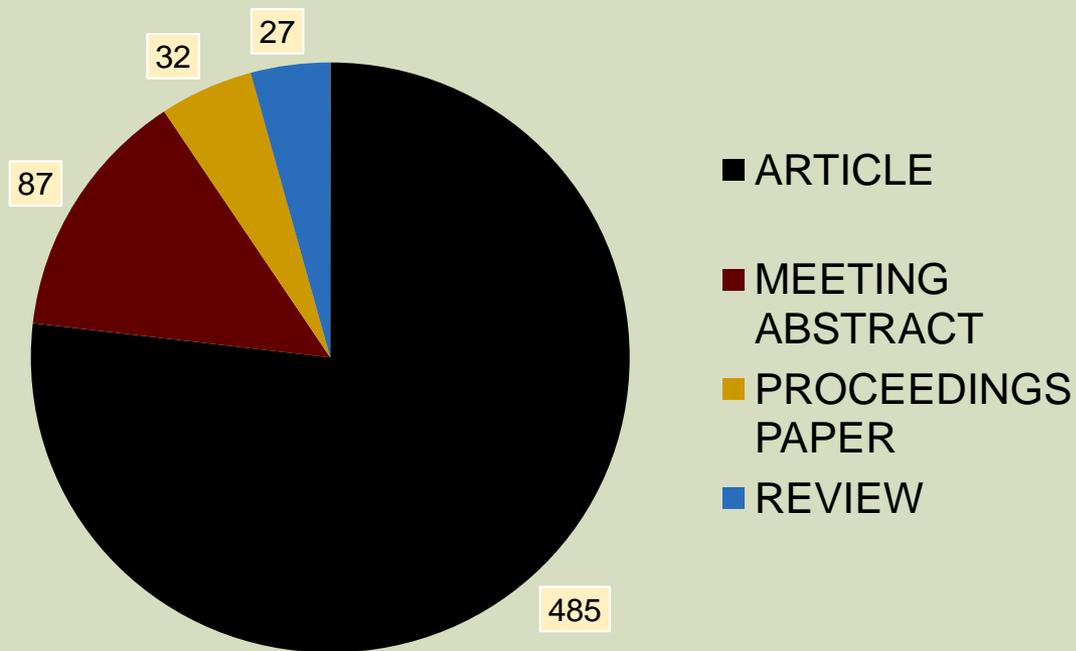
Source Titles	# of Papers	%
AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE	121	20.2
INFECTION AND IMMUNITY	56	9.349
<b>VACCINE</b>	44	7.346
JOURNAL OF INFECTIOUS DISEASES	30	5.008
JOURNAL OF IMMUNOLOGY	26	4.341
<b>MALARIA JOURNAL</b>	20	3.339
<b>PLOS ONE</b>	17	2.838
<b>EXPERIMENTAL PARASITOLOGY</b>	14	2.337
<b>MOLECULAR AND BIOCHEMICAL PARASITOLOGY</b>	14	2.337
FASEB JOURNAL	13	2.17



# WRAIR RESEARCH ON MALARIA VACCINE BY DOCUMENT TYPE

•The vast majority (81%) of WRAIR publishing on malaria vaccine appears as original research articles, illustrating its contribution to ground-breaking science.

## Number of Publications



# TOP SOURCES\* OF WRAIR MALARIA VACCINE PUBLICATIONS ANALYZED USING JOURNAL CITATION REPORTS

ISI Web of Knowledge<sup>SM</sup>

Journal Citation Reports<sup>®</sup>



Analyzed using JCR, 7 of the top 10 journal sources have an impact factor > 3 and one title, FASEB Journal, has a high impact factor of 7.201.

2010 JCR Science Edition

## MARKED JOURNAL LIST

Sorted by: Impact Factor

Abbreviated Journal Title	ISSN	2010 Total Cites	Impact Factor	5-Year Impact Factor	Immediacy Index	2010 Articles	Cited Half-life	Eigenfactor <sup>TM</sup> Score	Article Influence <sup>TM</sup> Score
FASEB J	0892-6638	38538	6.515	7.201	1.195	462	7.1	0.10353	2.521
J INFECT DIS	0022-1899	40263	6.288	6.103	1.740	535	7.7	0.11262	2.346
J IMMUNOL	0022-1767	130561	5.745	5.909	1.006	1603	7.0	0.40084	2.243
PLOS ONE	1932-6203	42799	4.411	4.610	0.515	6714	2.1	0.31957	1.941
INFECT IMMUN	0019-9567	51762	4.098	4.091	0.852	533	9.2	0.09672	1.331
VACCINE	0264-410X	26942	3.572	3.467	0.688	1105	4.5	0.08290	0.923
MALARIA J	1475-2875	4012	3.489	3.551	0.594	374	2.7	0.01855	0.999
MOL BIOCHEM PARASIT	0166-6851	7649	2.875	2.963	0.686	118	9.3	0.01483	0.985
AM J TROP MED HYG	0002-9637	16905	2.446	2.884	0.502	430	9.1	0.03423	0.910
EXP PARASITOL	0014-4894	4218	1.869	1.841	0.767	223	9.4	0.00803	0.477

[Acceptable Use Policy](#)

Copyright © 2011 Thomson Reuters.



# HIGHLY CITED PAPERS USING ESSENTIAL SCIENCE INDICATORS

ISI Web of Knowledge<sup>SM</sup>

Essential Science Indicators<sup>SM</sup>

WELCOME HELP RETURN TO MENU IN-CITES

HIGHLY CITED PAPERS FOR (MALARI\* AND VACCIN\*)

Sorted by: Citations

1 - 18 (of 18) Page 1 of 1

Total of unique papers in these searches combined = 20

ISI Web of Knowledge<sup>SM</sup>

Essential Science Indicators<sup>SM</sup>

WELCOME HELP RETURN TO MENU IN-CITES

HIGHLY CITED PAPERS FOR (PLASMOD\* AND VACCIN\*)

Sorted by: Citations

1 - 8 (of 8) Page 1 of 1



# HIGHLY CITED PAPERS USING ESSENTIAL SCIENCE INDICATORS

WRAIR researchers contributed to the most highly cited paper in ESI on this topic. It has been cited 261 times in ESI\* and 285 times in Web of Science\*.

## HIGHLY CITED PAPERS FOR (MALARI\* AND VACCIN\*)

Sorted by: Citations

1 - 18 (of 18)

Page 1 of 1

1 Citations: 261 

WEB OF SCIENCE

**Title:** EFFICACY OF RTS,S/AS02 MALARIA VACCINE AGAINST PLASMODIUM FALCIPARUM INFECTION IN SEMI-IMMUNE ADULT MEN IN THE GAMBIA: A RANDOMISED TRIAL

**Authors:** BOJANG KA; MILLIGAN PJM; PINDER M; VIGNERON L; ALLOUECHE A; **KESTER KE**; **BALLOU WR**; CONWAY DJ; REECE WHH; GOTHARD P; YAMUAH L; DELCHAMBRE M; VOSS G; [GREENWOOD BM](#); [HILL A](#); [MCADAM KPWJ](#); TORNIEPORTH N; [COHEN JD](#); DOHERTY T; RTSS MALARIA VACCINE TRIAL TEAM

**Source:** [LANCET](#) 358 (9297): 1927-1934 DEC 8 2001

**Addresses:** [MRC Labs](#), POB 273, Banjul, [Gambia](#).  
[MRC Labs](#), Banjul, [Gambia](#).  
[London Sch Hyg & Trop Med](#), London WC1, [England](#).  
[John Radcliffe Hosp](#), Inst Mol Med, Oxford OX3 9DU, [England](#).  
[Walter Reed Army Med Ctr](#), Walter Reed Army Inst Res, Washington, DC 20307 US  
[GlaxoSmithKline Biol](#), Rixensart, [Belgium](#).

**Field:** [CLINICAL MEDICINE](#)

Using ESI baselines, a paper in the field of clinical medicine published in 2001 is expected to have 195 cites to be rated in the top 1% of papers. Cited 261 times in ESI, this paper is definitively a key paper in its field. (Note: the blue hyperlinks for authors and institutions and fields indicate that these elements also are ranked in ESI).



# GLOBAL INFLUENCE OF WRAIR MALARIA VACCINE RESEARCH

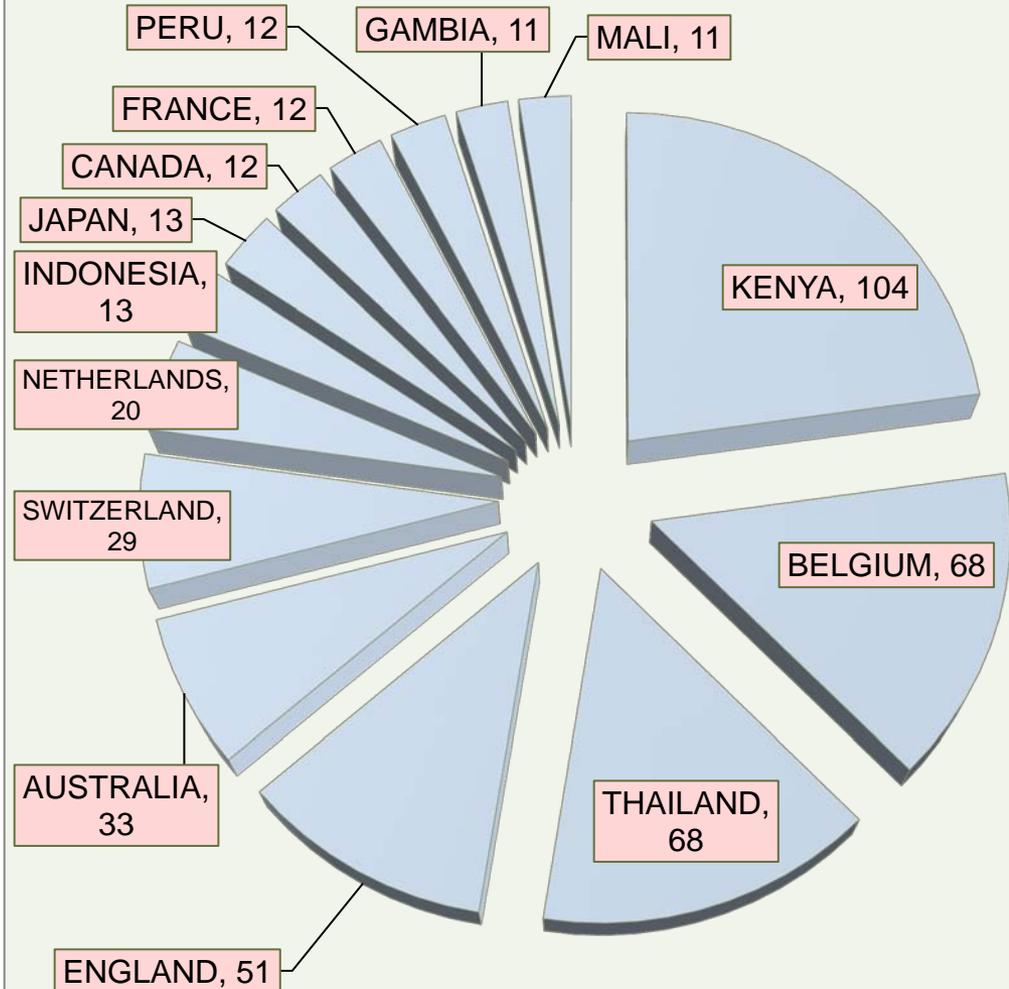


# WORLD-WIDE INFLUENCE

Understandably, scientists in the USA are the primary collaborators for WRAIR research and American scientists have worked with WRAIR on 579 of the 599 papers published.

In addition, WRAIR research on malaria vaccine and RTS,S is international in scope and has involved working with researchers in fifty-nine (59) countries. The chart shows fifteen (15) nations, other than the USA, that have worked with WRAIR more than ten (10) times, one indicator of the importance of this research to the global community.

## Collaborating Countries WRAIR Publications on Malaria Vaccine (Outside of USA)\*



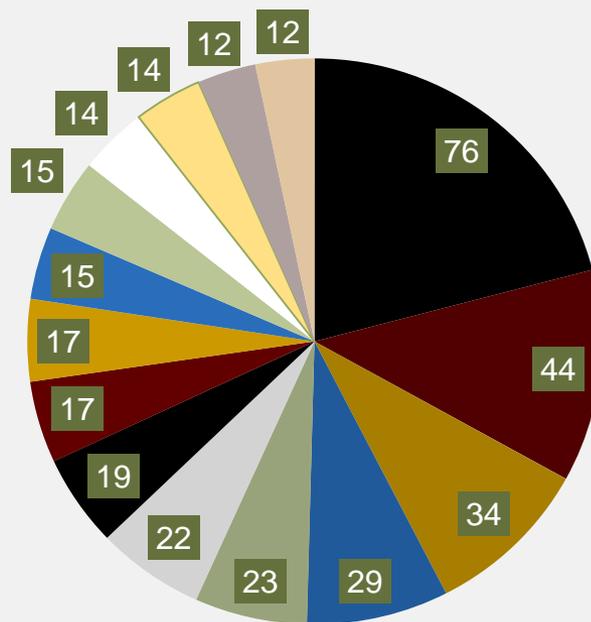
\* Chart shows only the first 15 countries



# ONE PAPER THROUGH THE GLOBAL LENS

Stoute JA, Slaoui M, Heppner DG, Momin P, Kester KE, Desmons P, Welde BT, Garcon N, Krzych U, Marchand M, Ballou WR, Cohen JD. A preliminary evaluation of a recombinant circumsporozoite protein vaccine against *Plasmodium falciparum* malaria. *New England Journal of Medicine* 1997 Jan;336(2):86-91.

## WRAIR Paper on CSP Cited by Country



This one WRAIR paper has been cited 464 times in Web of Science and 253 times by American researchers. Interestingly, researchers in eighteen (18) countries have cited this paper more than 10 times, indicating that the paper has had a global reach.



# WRAIR RTS,S AND MALARIA VACCINE RESEARCH SUMMARY

- Research on malaria vaccine, and on RTS,S in particular, has long and deep roots at WRAIR
- WRAIR researchers have contributed significantly since the 1960's, sharing their research by publishing in journals and presenting at meetings
- WRAIR research on RTS,S and malaria vaccine in general has had a critical impact on the progress of research to this point
- Field trials in Africa and Thailand and the cooperation of WRAIR overseas labs, AFRIMS and USAMRU-Kenya, have been invaluable to progress in malaria vaccine research
- Researchers worldwide rely on WRAIR research as a foundation to international endeavors on malaria vaccine

