

Science and politics of malaria elimination in the Greater Mekong Subregion

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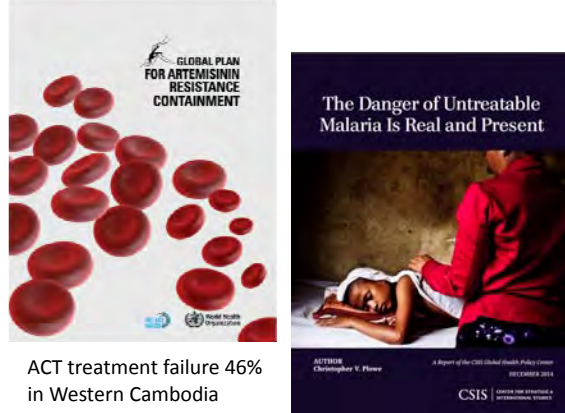
Joint International Tropical Medicine Meeting
 Bangkok
 7 December 2016

Malaria elimination will require...

...New tools

...New partnerships


...New ways of thinking



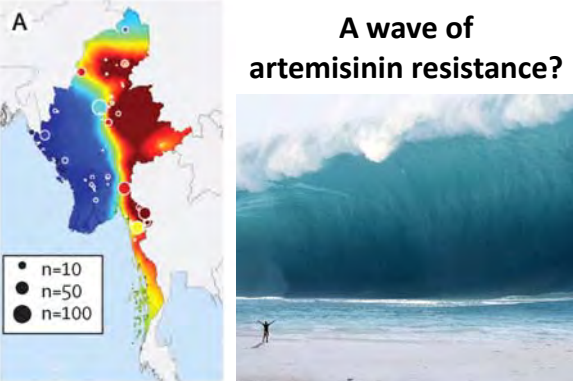
ACT treatment failure 46% in Western Cambodia

Amaratunga et al. *Lancet Inf Dis* 2016

“This artemisinin resistance—is it popping, or is it jumping?”



Professor Pe Thet Khin, former Minister of Health, Myanmar
 Nay Pyi Taw
 April 2014



A wave of artemisinin resistance?

K13 molecular marker map
 Woodrow et al. *Lancet Inf Dis* 2015

Artemisinin resistance “paternity testing” using K13 molecular marker

MAJOR ARTICLE

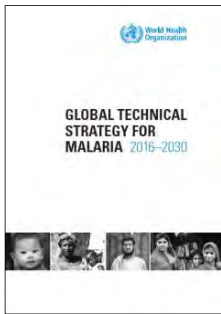
JID 2015:211 (1 March) • Takala-Harrison et al

Independent Emergence of Artemisinin Resistance Mutations Among *Plasmodium falciparum* in Southeast Asia

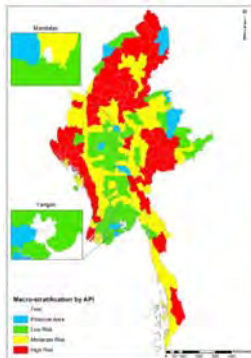
Shannon Takala-Harrison,^{1,2} Christopher G. Jacob,^{1,2} Cesar Acosta,¹ Michael P. Cummings,¹ James C. Silva,¹ Arjun M. Dondorp,¹ Mark M. Fukuda,^{1,2} Tom Toth Kien,^{1,2} Mykyro Mykyro,^{1,2} Harold Nsoh,^{1,2} Francesco Ntenda,^{1,2} Myat P. Kywe,^{1,2} Nguyen Thanh Thuy Nhat,^{1,2} Malika Inoung,¹ Orla Heffernan,¹ Fanny Ba,^{1,2} Chantira Lin,^{1,2} Stuart D. Taylor,^{1,2} David L. Saunders,¹ Frederic Ariey,¹ Gilles Mercenacq Pajulou,¹ Didier Mounoud,¹ Paul H. Newton,^{1,2} Maphoua Khamboumou,¹ Soumya Rongpanthum,¹ Peter Srengsaphan,¹ Alain-Pierre Fontem,^{1,2} Paul Sookthade,^{1,2} Worat A. Khan,¹ Amy Phee Phan,^{1,2} Myung M. Myint,¹ Myat H. Nyunt,¹ Tyler S. Brown,¹ Matthew Adams,¹ Christopher S. Pagan,¹ James Bailey,¹ John C. Tan,¹ Michael T. Forde,¹ James S. Cook,^{1,2} Elise Mottley,^{1,2} Roselyn Madlam,¹ Dennis P. Kwiatkowski,^{1,2} Richard J. White,¹ Pascal Ringwald,¹ and Christopher V. Plowe^{1,2}

K13 migration: Implications

- Many different K13 mutations arose independently on many different genetic backgrounds
- Several resistance mutations have spread between countries in the Greater Mekong Subregion (GMS)
- Based on this result, 2015 WHO recommendation:
 - **Containment is not possible**
 - **Falciparum elimination is imperative for the GMS**




Need better tools to stratify and forecast malaria risk



- Myanmar National Malaria Control Program seeks to “microstratify” malaria risk at village level
- Local transmission vs. importation?
- Sources vs. sinks of transmission?

WHO recommendations:

Mass drug administration (MDA) for GMS
...but not screen-and-treat (need better diagnostic tests)



<http://www.who.int/malaria/publications/atoz/role-of-mda-for-malaria.pdf>

Malaria Journal

Open Access

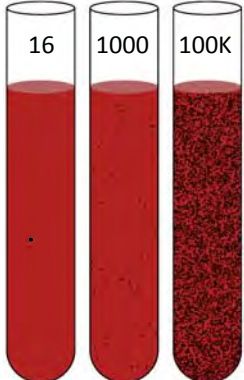
METHODOLOGY

An ultrasensitive reverse transcription polymerase chain reaction assay to detect asymptomatic low-density *Plasmodium falciparum* and *Plasmodium vivax* infections in small volume blood samples

Matthew Adams^{1†}, Sudhaanshu N. Joshi^{1†}, Gillian Mbambo¹, Amy Z. Mu¹, Shay M. Roemlich¹, Biraj Shrestha¹, Kathy A. Strauss¹, Nicole Eddington Johnson¹, Khine Zaw Oo¹, Tin Mlung Hlaing¹, Zay Yar Han¹, Kay Thwe Han¹, Si Thuza², Adam K. Richards¹, Fang Huang^{1*}, Myaing M. Nyunt¹ and Christopher V. Plowe^{1†*}

Limits of detection

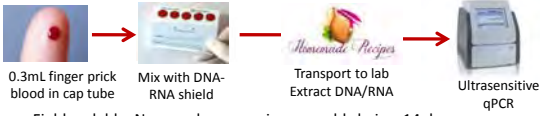
	usPCR	PCR	RDT
Parasites/mL	16	1000	100K



P. falciparum and *P. vivax* in human blood samples

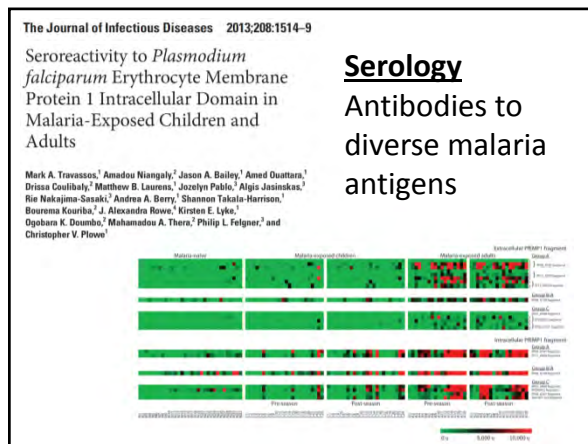
Mapping the subclinical malaria reservoir

- Ultrasensitive low-volume Reverse Transcriptase PCR
 - Sensitivity: 16 parasites/mL & can detect both Pf & Pv simultaneously



- Field scalable: No sample processing, no cold chain x 14 days
- High throughput pipeline in Yangon: >20,000 samples since 2015
- Concordant with high volume PCR from frozen venous blood
- Now achieving same lower limit of detection from dried blood spots
 - Better, cheaper, faster

Adams et al. Malaria Journal 2015
Zainabadi et al. in preparation



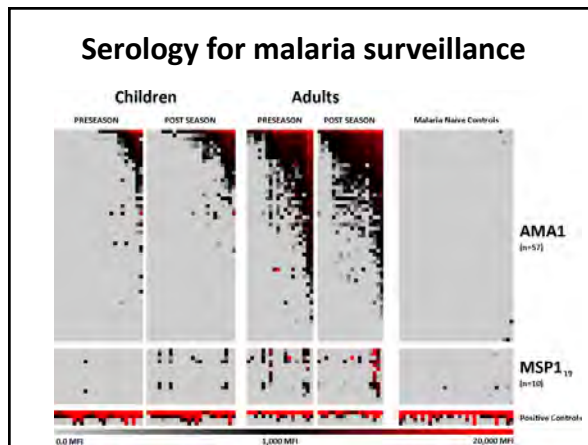
Am. J. Trop. Med. Hyg. 92(3), 2015, pp. 8-12
doi:10.4269/ajtmh.14-0148
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Short Report: Seroreactivity to a Large Panel of Field-Derived *Plasmodium falciparum* Apical Membrane Antigen 1 and Merozoite Surface Protein 1 Variants Reflects Seasonal and Lifetime Acquired Responses to Malaria

Jason A. Bailey, Jozelyn Pablo, Amadou Niangaly, Mark A. Travassos, Amed Ouattara, Drissa Coulibaly, Matthew B. Laurens, Shannon L. Takala-Harrison, Kirsten E. Lyke, Jeff Skinner, Andrea A. Berry, Algis Jasinskas, Rie Nakajima-Sasaki, Bourems Kouriba, Mahamadou A. Thera, Philip L. Felgner, Oghena K. Doumbou, and Christopher V. Plowe¹

Howard Hughes Medical Institute/Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, Maryland; Division of Infectious Diseases, Department of Medicine, University of California, Irvine, California; Laboratory of Immunogenetics, National Institute of Health, Bethesda, Maryland; Malaria Research and Training Center, Department of Epidemiology of Parasitic Diseases, University of Sciences, Techniques and Technology, Bamako, Mali

- Extremely high throughput
 - Thousands of antibody assays on a single microarray the size of a microscope slide
- Cost of equipment decreasing ten-fold



Science AAAS

THE UNLIKELY DIPLOMAT

Myaing Myaing Nyunt fled Myanmar in 1988; now she is back, forging alliances against malaria

By Leslie Roberts

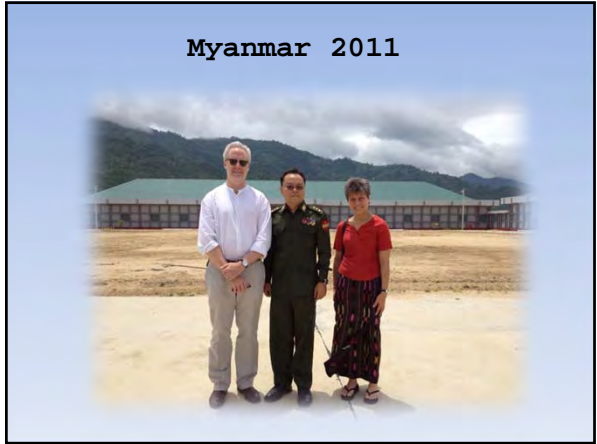
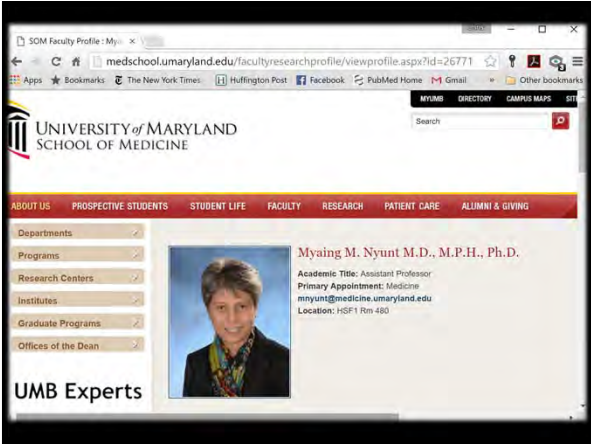
On a blistering hot October day last year, the air thick with impending rain, Myaing Myaing Nyunt and I hunched in a wooden cart toward Sa-ka-pin, a small village in the rich agricultural lowlands about 20 kilometers northeast of Mandalay, Myanmar. We grip the splintery sides of the cart as the animals plunge chest deep in the mud; when they swish their tails, mud splatters everywhere. It's 11 months before Myanmar's historic election, and with us in the back is a young doctor with "NLD," the initials of Aung San Suu Kyi's opposition party, the National League for Democracy, shaved into

his close-cropped hair. A second cart carrying township medical officers follows close behind. We stop at a wide, shallow river where a man in a dugout canoe ferries us across. Two more carts are waiting for us.

Nyunt, a malarialogist at the University of Maryland School of Medicine (UMD) in Baltimore, is visiting Sa-ka-pin to assess the extent of one of the biggest problems facing an ambitious campaign to wipe out malaria from the Mekong region (see main story, p. 28): the number of people infected with malaria who have no symptoms. It's part of a unique collaboration led by Nyunt and her husband, molecular epidemiologist and malarialogist Chris Plowe, who heads the Institute for Global Health

Myaing Myaing Nyunt

SCIENCE sciencemag.org Published by AAAS 23 APRIL 2016 • VOL. 350 ISSUE 4034 • 405



Building political will and ownership through capacity strengthening in the lab and the field



First ever NIH grant in Myanmar



BILL & MELINDA GATES foundation



MYAING MYAING NYUNT
ASST. PROFESSOR OF MEDICINE
UNIVERSITY OF MARYLAND

OPEN SOCIETY FOUNDATIONS

Malaria as a catalyst for social change



Gates Foundation Partners Meeting
Nay Pyi Taw, Myanmar
December 2014




ASTMH UNIVERSITY of MARYLAND SCHOOL OF MEDICINE CSIS | CENTER FOR STRATEGIC & INTERNATIONAL STUDIES
INSTITUTE FOR GLOBAL HEALTH

Washington DC August 2015

BILL & MELINDA GATES foundation OPEN SOCIETY FOUNDATIONS


Nay Pyi Taw 2016




DEFENCE SERVICES MEDICAL RESEARCH CENTRE
ARMY WELCOMES
GATES PARTNERS ANNUAL MEETING














Thanks to



<p>Shannon Takala-Harrison Chris Jacob Jason Bailey Andrew Pike Alexa Machikis Sonia Agarwal Andrea Berry Mark Travassos Matthew Adams Shay Roemlich Christina Shehata Cheron Jones Nicole Eddington Johnson Gillian Mbambo Braj Shrestha Sudhanshu Joshi Kayvan Zainabadi Myaing Nyunt</p> <p>Institute for Genome Sciences University of Maryland Joana Silva Amol Shetty Tim O'Connor</p> <p>Department of Geographical Sciences University of Maryland College Park Demian Nybock Kathleen Stewart Tatiana Loboda</p>	<p>Department of Medical Research Myanmar Ministry of Health Zayar Hnin Hnin Hnin Wai Lwin Kay Thwe Han Myat Phone Kyaw Kyaw Zin Thant</p> <p>Defence Services Military Academy Myanmar Ministry of Defence Khine Zaw Oo Ye Myat Kyaw Tin Maung Hlaing</p> <p>National Institute of Parasitic Diseases Chinese CDC Huang Fang Xiao-Nong Zhou</p> <p>Global Malaria Program World Health Organization Pascal Ringwald</p> <p>Community Partners International Si Thura Phyo Maung Maung Aye Aye Khaing</p> <p>Roche Innovation Technology John Tan</p>	<p>ARC3 Collaborators</p> <p>ARCE Collaborators</p> <p>TRAC Collaborators</p> <div style="margin-top: 20px;">        </div>
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