

A COMPENDIUM OF SCHOLARLY WORKS

by

Prof. Gordon A. Awandare

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A Compilation of Scholarly Works of Professor Gordon A. Awandare

Compilation

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A compilation of scholarly works

Profile of Professor Gordon Akanzuwine Awandare

Gordon Akanzuwine Awandare is a Professor of Biochemistry, Cell and Molecular Biology and the Pro Vice-Chancellor responsible for Academic and Students Affairs (Pro VC ASA) at University of Ghana. He is also the Founding Director of the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP), University of Ghana, and a visiting Professor at the Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, UK.

Education

Gordon Awandare completed his O'level in 1991 at Notre Dame Seminary Secondary School, Navrongo and A'level in 1993 at Presbyterian Boys Secondary School, Legon. He then obtained his Bsc Biochemistry in 1998 and MPhil Biochemistry in 2002 at the University of Ghana, Legon. Subsequently he obtained a PhD in Infectious Diseases and Microbiology from the University of Pittsburgh, Pennsylvania, USA in 2007.

Career

While studying for his Master's degree from 1999 – 2002, Gordon Awandare worked as a Research Assistant at the Immunology Unit of the Noguchi Memorial Institute for Medical Research (NMIMR), University of Ghana and at the Unité d'Immunologie Moléculaire des Parasites, Institut Pasteur, Paris. After obtaining his Master's degree, he was appointed Lecturer at the Department of Biochemistry, University of Ghana in 2002, where he worked for one year before leaving to the United States of America for his PhD studies in 2003.

After obtaining his PhD in 2007, Professor Awandare worked as a Scientist at the Division of Malaria Vaccine Development of the Walter Reed Army Institute of Research, Silver Spring, Maryland until 2010 when he returned to the University of Ghana to establish his research group. He was promoted to Senior Lecturer in 2011, Associate Professor in 2015 and Professor in 2018. He was Head of Department of Biochemistry, Cell and Molecular Biology from 2013 to 2017. In 2014, he led the establishment of the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) after winning one of the World Bank's African Centres of Excellence grants and became the Founding Director of the Centre.

He was appointed Pro Vice-Chancellor for Academic and Student Affairs, University of Ghana in December 2021 and assumed office in January 2022.

Teaching, Research and Mentorship

Gordon Awandare has expertise in Cell and Molecular Biology, Immunology and Genetics. His research works encompass both infectious diseases and non-communicable diseases, with a focus on understanding pathogen biology and disease mechanisms to generate knowledge for development of diagnostics, vaccines and drugs. The majority of his research output is on malaria, including investigating mechanisms of red cell invasion, innate and adaptive immune responses, and the role of human genetic variation in influencing disease pathogenesis. He played a leading role in the discovery of complement receptor 1 as a major receptor used by malaria parasites to invade red blood cells. His other works on malaria have covered parasite population genetics, genomic surveillance for drug resistance, and the impact of transmission intensity on immunity to malaria. Gordon Awandare has also done significant research on the genetics of hearing impairment, where his team identified the genetic mutations that predispose individuals to developing the condition in Ghana. During the COVID-19 pandemic, Gordon Awandare's team played a leading role in Ghana's response by providing research data on seroprevalence and genomic diversity of circulating SARS-CoV-2 viruses. He has more than 150 peer-reviewed journal publications in a wide range of journals, including some of the leading infectious diseases and immunology journals. He has supervised 14 postdoctoral fellows, 20 PhD students and 23 Master's students, and mentored many young scientists in Ghana and across Africa.

Grants and Capacity-building

Gordon Awandare has an outstanding record of winning grants and building research partnerships across the world. He has successfully managed several large multinational and multidisciplinary training and research projects, involving many high-level academics and multi-million-dollar budgets. Since 2011, he has directly attracted over 40m USD in grant funds to the University of Ghana, including winning highly competitive grants including two World Bank African Centres of Excellence grants valued at 14.5m USD and two Wellcome Trust DELTAS awards amounting to 11.5m USD. He has also won grants from the National Institute for Health and Care Research (NIHR), UK; National Institutes of Health (NIH),

USA; Royal Society, UK; UK's Foreign Commonwealth and Development Office (FCDO); UK Research and Innovation (UKRI); Rockefeller Foundation; and African Research Universities Alliance (ARUA). These grants have provided advanced scientific equipment, infrastructure, and fellowships to more than 350 African scientists for Masters, Doctoral and Postdoctoral training at the University of Ghana.

Leadership and membership of boards and committees

Within the University of Ghana, Gordon Awandare is currently the Board Chairman for the University of Ghana Enterprises Limited (UGEL). He Chairs the Implementation Committee for the Vice-Chancellor's Classroom Modernization Project, as well as nine (9) statutory Boards and Committees. He has been a member of the Academic Board and served on the Business and Executive Committee for many years. He has also been Chairman, Centre Management Committee for WACCBI, and member of Management committees/boards for many units, including, Office of Research Innovation and Development (ORID), Noguchi Memorial Institute for Medical Research, School of Pharmacy, Legon Centre for International Affairs and Diplomacy, School of Biological Sciences, and School of Nuclear and Allied Sciences, Ghana Atomic Energy Commission. Prof Awandare has also Chaired or served on numerous Adhoc committees at the University of Ghana, including the Search Committee for Vice Chancellor in 2020/2021.

At the National level, Gordon Awandare is currently the Foundation Chairman of the Governing Council of the CK Tedam University of Technology and Applied Sciences in Navrongo, where he is also Chairman of the University's Finance Committee. He has previously served on the Governing Council of the University of Development Studies, Tamale, where he was also the Chairman of the University's Audit Report Implementing Committee. Gordon Awandare is a member of the Advisory Board of Yemaachi Biotech, a biotechnology company in Accra which was founded by one of his mentees. He was recently appointed as a member of the Foundation Governing Board of the National Vaccine Institute of Ghana.

Gordon Awandare serves on numerous prestigious international boards and committees, including, Chairman, West African Network of Infectious Disease ACEs (WANIDA), a World Bank/French Government funded collaborative network for training and research; Member, Expert Advisory Board, Wellcome Trust Centre for Infectious Diseases Research in Africa (CIDRI), University of Cape Town, South Africa; Deputy Director and Member of Steering Committee, Crick African Network, Francis Crick Institute, UK; Member; Steering Committee, National Institute of Health Research Global Research Unit on Tackling Infections to Benefit Africa (TIBA), University of Edinburgh, UK; Member, International Scientific Advisory Board of the Malawi Liverpool Wellcome Trust Programme, Malawi; Technical Consultant, Science Engagement to support Evidence Informed Policy Responses to COVID-19 in Africa, Africa Academy of Sciences, Nairobi, Kenya; Member, Lancet COVID-19 Commission, Africa task Force; Member, Editorial Board, Parasitology; Member, MalariaGEN Governance Committee, Wellcome Sanger Institute, UK; Member of Council, Society for Experimental Biology and

Medicine; Member, Advisory Board, AAS Open Research, African Academy of Sciences; Member, Wellcome Sanger Institute Advanced Courses and Scientific Conferences Steering Group, UK.

Awards and Honors

Prof Awandare was a recipient of the Royal Society Pfizer award for 2015 for achievements in molecular and cellular studies of malaria, and science capacity building in Africa. At the University of Ghana, he received the Distinguished Award for Meritorious Service in 2014, Citation of Honor in recognition of contributions to science development in the College of Basic and Applied Sciences in particular, and University of Ghana in general in 2020 and Meritorious Award in Recognition of Outstanding Service, College of Basic and Applied Sciences in 2021.

He is a Fellow of the Ghana Academy of Arts and Sciences and the Royal Society of Biology of the UK. In 2019, he was appointed the first Global Editor for Africa for Experimental Biology and Medicine, the journal of the Society for Experimental Biology and Medicine. He has been profiled in some prestigious global media, including The Scientist Magazine in recognition of his impact on science capacity building in Africa and Kenya Airways' Msafiri Magazine as one of Africa's Brilliant Minds.

Family

Gordon Awandare hails from Kandiga, in the Upper East region. He was born in Bolgatanga in November 1974 to Mr. Joseph Atoriyah and Mrs Immaculate Atoriyah, who were both Teachers. He is the first of four children of his parents, and his siblings are Eunice Awandare, Jerome Awandare and Flavia Awandare. Gordon is married to Mrs Massah Awandare and they have three children, Marie, Gabrielle and Jeremy. Gordon is from a big extended family and has many close aunts, uncles, nieces and nephews.

POSTDOCTORAL FELLOWS & GRADUATE STUDENTS SUPERVISED



Postdoctoral Fellows Supervised

#	Name	Research area	Period
1.	Dr. Daniel Muthui Kiboi	Malaria parasite experimental genetics	2016-2018
2.	Dr. Seidina A. S. Diakite	Malaria parasite genomics and pharmacogenomics	2016-2019
3.	Dr. Modibo Sangare	Genetics of autism spectrum disorder	2016-2019
4.	Dr. Kolapo Muiyiwa Oyebola	Malaria parasite drug resistance	2016-2019
5.	Dr. Yaw Aniwah	Malaria parasite biology	2016-2021
6.	Dr. Emmanuel Amlabu	Malaria vaccine discovery	2016-2021
7.	Dr. Lily Paemka	Genetics of triple-negative breast cancer	2017-2020
8.	Dr. Yaw Bediako	Malaria immunology	2019-2021
9.	Dr. Peter Quashie	HIV and COVID-19 molecular epidemiology	2019-2021
10.	Dr. Alassane Mbengue	Development of resistance to anti-malarial drugs	2019-2021
11.	Dr. Joe Mutungi	Malaria vaccine development	2019-2021
12.	Dr. Gloria Amegatcher	Development of peptide array for fever diagnosis	2019-2021
13.	Dr. Henrietta Mensah-Brown	Rosetting and severe malarial pathogenesis	2019-2021
14.	Dr. Kanny Diallo	Meningitis pathogenesis	2020-date
15.	Dr. Shameka Thomas	Sickle Cell Disease and Prenatal Care	2022-date
16.	Dr. Frederica Partey	COVID-19 Vaccine responses in Ghana	2022-date
17.	Dr. Stephen Amoah	Impact of Cocoa on Diabetes Mellitus	2022-date
18.	Dr. Jerry Joe Harrison	Characterization of HIV-2 proteins	2022-date

Graduate Students Supervised

#	Name	Project Title	Level	Period of Study	Role
1.	James Abugri	<i>Plasmodium falciparum</i> population genomics and molecular epidemiology of antimalarial drug resistant genes in Ghana.	PhD	2012 - 2016	Main Supervisor
2.	Jennifer Ofori	Characterization of trypanosomes and determination of corresponding antibody production in cattle in Ghana.	PhD	2013 - 2018	Co-Supervisor
3.	Frederica Dedo Partey	Assessing the PfPRh5 role in naturally acquired immunity and its potential as a vaccine candidate	PhD	2013 - 2018	Main Supervisor
4.	Henrietta Mensah-Brown	Targets and patterns of erythrocyte invasion inhibitory antibody responses in malaria.	PhD	2014 -2018	Main Supervisor
5.	Nicholas Amoako	Investigating the etiology of febrile illnesses in Ghana.	PhD	2014 - 2019	Main Supervisor
6.	William van der Puije	The identification of <i>Plasmodium falciparum</i> parasite molecules involved in severe malarial anemia	PhD	2014 -2019	Main Supervisor
7.	Reuben Ayivor-Djanie	Regulation of Activation Induced Cytidine Deaminase (AID) in response to <i>P. falciparum</i> infection.	PhD	2014 - 2019	Main Supervisor
8.	Emmanuel A. Tagoe	<i>Helicobacter pylori</i> infection and manipulation of host system to induce gastric cancer	PhD	2014- 2019	Co-Supervisor
9.	Sena Matrevi	Artemisinin resistance associated Falcipain 2 polymorphisms in Ghanaian <i>Plasmodium falciparum</i> clinical isolates	PhD	2014- 2020	Co-Supervisor
10.	Francis D. Krampa	Towards sensitive analyte detection: the synergistic effects of reduced graphene oxide, PEDOT:PSS, polyethylene glycol and ionic liquid nanocomposite-modified electrodes	PhD	2015- 2019	Main Supervisor
11.	Laty Gaye Thiam	Investigating the effect of blood donor variability in <i>Plasmodium falciparum</i> invasion phenotyping assays	PhD	2015-2019	Main Supervisor
12.	Bernice E. Mawuli	Insecticide resistant vectors and drug tolerant parasites and their impact on malaria transmission in Ghana	PhD	2015-2021	Co-Supervisor
13.	Mubarak Abdul Rahman	Investigating determinants of asymptomatic <i>Plasmodium falciparum</i> infections in a high endemic area of Ghana	PhD	2015-2021	Co-Supervisor
14.	Arnold Luuse Togiwe	Maternal and Fetal T-cell responses to the placental malaria-associated antigen "VAR2CSA"	PhD	2015-2020	Co-Supervisor
15.	Collins Misita Morang'a	Investigation of host and parasite genetic factors mediating parasite tolerance during <i>Plasmodium falciparum</i> infections	PhD	2015-2021	Co-Supervisor
16.	Dominic Amuzu	Investigating Glycophorin variants and mechanisms conferring resistance to severe malaria in Ghanaian population	PhD	2016-2021	Main Supervisor
17.	Nancy Kemuma Nyakoe	Mapping cellular and humoral immune responses over the clinical course of acute <i>Plasmodium falciparum</i> infection in children to identify signatures associated with immunity	PhD	2016-2021	Main Supervisor
18.	Jersley O. Chirawurah	The role of Rh proteins in <i>P. falciparum</i> invasion of erythrocytes	PhD	2017- date	Main Supervisor
19.	Felix Ansah	Assessing the effect of antimalarial drug resistance polymorphisms on malaria parasite gametocytogenesis	PhD	2017 - 2021	Main Supervisor
20.	Elvis Twumasi Aboagye	Investigating genetic markers of autosomal recessive non-syndromic hearing impairment in Ghana	PhD	2018 - date	Co-Supervisor
21.	Henrietta Mensah-Brown	Investigating erythrocyte invasion mechanisms of <i>P. falciparum</i> clinical isolates from Ghanaian children.	MPhil	2011 -2013	Main Supervisor
22.	David Osei Obuobi	Role of Complement Receptor 1 (CR1) in <i>Plasmodium falciparum</i> invasion of erythrocytes in Ghanaian children	MPhil	2011 -2014	Main Supervisor
23.	Rupert Delimini	Investigation on the dengue virus; exposure and infection in Ghanaian children with malaria	MPhil	2012 - 2014	Main Supervisor
24.	Richard Nortey-Mensah	Determination of the role of carotenoid biosynthesis in the intraerythrocytic stages of <i>P. falciparum</i>	MPhil	2013 - 2015	Co-Supervisor
25.	Andrea Twumwaa Arku	The effect and mechanism of action of <i>Cryptosporidium parvum</i> on gametocyte development and viability.	MPhil	2013 -2015	Co-Supervisor
26.	Jersley O. Chirawurah	The role of Rh proteins in <i>P. falciparum</i> invasion of erythrocytes	MPhil	2014 - 2016	Main Supervisor
27.	Atindaana Edmond Akugbire	Molecular characterization of inactivated HIV-1 after a single replication cycle	MPhil	2014 - 2016	Co-Supervisor
28.	Christiana O. Onwona	<i>Plasmodium falciparum</i> drug resistant alleles and clonal diversity in asymptomatic carriers in Northern Ghana	MPhil	2014-2016	Co-Supervisor

29.	James L. Myers-Hansen	Impact of vector control interventions on the population structure of <i>P. falciparum</i> in Ghana	MPhil	2014-2016	Co-Supervisor
30.	Temitope W. Ademolue	Investigation of how the Sickie Cell trait condition protects against severe forms of Malaria disease	MPhil	2014-2016	Main Supervisor
31.	Patrick Tshibangu	<i>Plasmodium falciparum</i> drug resistance genes and population genetics	MPhil	2014-2016	Co-Supervisor
32.	Musah Osei	Copy Number Variation of GTP Cyclohydrolase 1 (GCH1) gene and its impact on antifolate drug resistance of <i>Plasmodium falciparum</i> in Ghana	MPhil	2015-2017	Co-Supervisor
33.	Charles-Chess Essel	Functional Characterization of Pf10_0351 during <i>Plasmodium falciparum</i> Development	MPhil	2015- 2017	Main Supervisor
34.	Nsoh Godwin Anabire	Malaria and Hepatitis B co-infection in pregnant women in Northern Ghana- characterization of Liver function, immune response and HBV Genotypes	MPhil	2015- 2017	Co-Supervisor
35.	Priscilla Abena Akyaw	Genetic association and gene-gene interaction analysis of APOL1, MYH9 and G6PD variants in patients with chronic kidney disease	MPhil	2015-2017	Co-Supervisor
36.	Ernestine Kubi	Association of APOL1 risk variants, MYH9 and Hemoglobin genotypes S and C in Chronic Kidney Disease	MPhil	2015- 2017	Co-Supervisor
37.	Prince Berko Nyarko	Deconstructing invasion phenotype switching in <i>Plasmodium falciparum</i>	MPhil	2016 -2018	Main Supervisor
38.	Daniel K. A. Aquah	Characterization of <i>Plasmodium falciparum</i> Novel Gene, Pfc0355c (PF3D7_0308300)	MPhil	2016 -present	Main Supervisor
39.	Akuh Ojo-Ojogu	Molecular characterization of a <i>Plasmodium falciparum</i> merozoite protein.	MPhil	2017-2019	Co-Supervisor
40.	Ilani Philip	Elucidating the molecular mechanism(s) underlying the membrane association of a novel <i>Plasmodium falciparum</i> protein	MPhil	2017-2019	Co-Supervisor
41.	Opoku Grace	Biophysical and immunological characterization of a <i>Plasmodium falciparum</i> merozoite protein	MPhil	2017-2020	Co-Supervisor
42.	Barbara Mensah	Gene-environment interaction between APOL1 renal risk variants and JC and BK polyoma virus in patients with HIVAN	MPhil	2017-2019	Co-Supervisor
43.	Frederick Tei-Maya	Analysis of antimalarial drug resistance genes from a population-based study in Ghana	MPhil	2018-2021	Main Supervisor



RESEARCH AND TRAINING GRANTS

Research Grants with at least \$20,000 to University of Ghana

#	Project Title	Role	Awarding Body	Amount	Grant period
1.	WACCIP-DELTAS programme II	Project Director	Wellcome/ Science for Africa Foundation	\$4,400,000	03/04/2023 – 31/03/2027
2.	West Africa, West Indies, West London: Mechanisms driving heterogeneity in immunity to SARS- CoV-2 variants	Co-Director	Wellcome	£3,058,019 (Sub-award £701,290)	02/01/2023 – 31/12/2026
3.	IMPAVES: Integration of malaria parasite and vector surveillance in Ghana	Co-investigator Grant holder: Lucas Amenga- Etego	Bill & Melinda Gates Foundation	\$1,503,325	01/03/2022 -28/02/2026
4.	NIHR Global Health Research Group on Establishing Regional Hubs for Genomic Surveillance in West Africa, at the Wellcome Sanger Institute	Co-investigator Grant holder: Sonia Goncalves (Wellcome Sanger Institute)	National Institute for Health and Care Research, UK	£2,981,004 (Sub-award £1,082,929)	01/09/2022- 31/08/2025
5.	NIHR Global Health Research Group on Digital Diagnostics for African Health Systems	Co-investigator Grant holder: Aubrey Cunnington, Imperial College London, UK	National Institute for Health and Care Research, UK	£2,999,952 (Sub-award £473,100)	01/08/2022- 31/07/2026
6.	Public Engagement to strengthen COVID-19 genomics research in Africa	Co-investigator Grant holder: Ian Goodfellow, University of Cambridge, UK	Wellcome Trust, UK	£110,536 (Sub-award £99,801.00)	01/05/2022- 30/04/2024
7.	Public Understanding of Big data in Genomics Medicine in Africa (PUBGEM-Africa)	Co-investigator (Principal Investigator for Ghana site) Grant holder: Ambroise Wonkam, University of Cape Town	National Institutes of Health, USA	\$1,853,796 (Sub-award \$245,376)	20/09/2021 - 31/07/2026
8.	Comprehensive national surveillance for COVID-19 and building laboratory capacity for sustainable disease control in Ghana	Principal Investigator	Foreign, Commonwealth & Development Office	£1,000,000	27/10/2021- 30/04/2023
9.	Using antibody technology to decipher the immunological impact of SARS- CoV-2 variants on pandemic control	Co-Investigator Grant holder: Peter Quashie Co-applicant (Principal Investigator for Africa component)	Bill & Melinda Gates Foundation	\$998,736	26/10/2021- 31/08/2025
10.	Expansion and support of SARS-CoV- 2 sequencing in West and Central Africa to support the COVID-19 pandemic response	Co-applicant (Principal Investigator for Africa component) Grant holder: Ian Goodfellow, University of Cambridge, UK	Foreign, Commonwealth & Development Office/ Wellcome	£2,284,586 (Sub-award £519,840)	01/09/2021 – 28/02/2023
11.	Cellular dissection of Plasmodium falciparum erythrocyte invasion	Co-applicant Grant holder: Julian Rayner, University of Cambridge, UK	Wellcome Trust	£2,214,779 (Sub-award £189,628)	01/01/2021- 31/12/2025
12.	Tracking COVID-19 infection in West Africa to guide public health interventions Grant ref: 2021 HTH 006	Principal Investigator	Rockefeller Foundation	\$799,627	01/04/2021- 31/03/2022
13.	Building Capacity for Vaccine Development in Africa: Strengthening Capacity to Support Innovative Research Grant ref: OR2020-75206	Principal Investigator	Open Society Foundation (OSF)/African Research Universities Alliance (ARUA)	\$500,000	01/12/2020- 30/11/2022
14.	Do epigenetic processes promote drug resistance in the malaria parasite, <i>Plasmodium falciparum</i> ?	Co-investigator (Principal Investigator for Ghana site) Grant holders: Robin Allshire & Gordon Awandare	The Royal Society, UK	£220,504.00 (Sub-award £154,353)	01/12/2020 – 30/11/2023

15.	Digital Diagnostics for Africa Network	Co-investigator (Principal Investigator for Ghana site) Grant holder: Aubrey Cunningham, Imperial College, UK	Engineering and Physical Sciences Research Council (EPSRC), UK	£135,412 (Sub-award budget - £50,875)	01/05/2020-30/04/2021
16.	West African Network of Infectious Diseases ACEs (WANIDA)	Principal Investigator (Network Leader)	French Development Agency (AFD)	€1,500,000	05/06/2020-04/06/2024
17.	Novel rapid malaria diagnostic linking detection and surveillance	Co-investigator (Principal Investigator for Ghana site) Grant holder: Jake Baum, Imperial College, UK	Global Challenges Research Fund, UK	£144,482 (Sub-award budget - £29,325)	01/08/2019-31/07/2020
18.	African advanced bioinformatics training network	Co-applicant (Principal Investigator for Ghana site) Grant holder: Thomas Otto, University of Glasgow, UK	Global Challenges Research Fund, UK	£33,643 (Sub-award budget - £25,000)	01/08/2019-30/06/2020
19.	Contract research for image analysis of <i>Plasmodium malariae</i> and <i>Plasmodium ovale</i> and machine learning for differentiating the <i>Plasmodium</i> species using nou's mLab® in Ghana	Principal Investigator for Ghana site Grant holder: Yanis Ben Amor, Columbia University	Columbia University, USA	Sub-award budget - \$64,860	01/04/2019-31/03/2020
20.	West African Centre for Cell Biology of Infectious and non-communicable diseases (WACCBIP+NCDs)	Principal Investigator (Centre Leader)	World Bank, USA	\$5,500,000	01/01/2019 - 31/12/2024
21.	WACCBIP-Wellcome Trust DELTAS Programme', Research Enrichment, Public	Principal Investigator (Programme Director)	Wellcome Trust, UK/ African Academy of Sciences/Alliance for Accelerating Excellence in Science in Africa (AESA)	\$189,130	01/10/2018-31/08/2020
22.	Engagement Contract research for analysis of malaria parasites for drug-resistance mutations	Principal Investigator	Health Strategy and Delivery Foundation, Nigeria	\$26,200	01/09/2018-31/08/2019
23.	NIHR Global Health Research Group on genomic surveillance of malaria in West Africa	Co-applicant (Principal Investigator for Ghana site) Grant holder: Dominic Kwiatkowski, University of Oxford	National Institute for Health Research, UK	£2,000,000 (Sub-award budget - £734,440)	01/04/2018-31/03/2021
24.	Training and Research on Severe Malarial Anemia	Co-applicant (Principal Investigator for Ghana site) Grant holder: Douglas J Perkins, University of New Mexico, USA	National Institutes of Health, USA	\$1,341,641	03/01/2017 - 02/01/2022
25.	Hearing Impairment Genetics Studies in Africa (HI-GENES Africa)	Co-investigator (Principal Investigator for Ghana site) Grant holder: Ambroise Wonkam, University of Cape Town	Wellcome Trust-AESA H3Africa	\$3,294,140 (Sub-award budget - \$68,971)	01/11/2017-31/10/2021
26.	SickleGenAfrica: Sickle Cell Disease Genomics Network of Africa Grant ref: 1U54HL141011	Co-Principal Investigator (Multiple PI) Grant holders: Solomon Fiifi Ofori-Acquah, Gordon A. Awandare, and Julie Makani	National Institutes of Health (NIH/NHLBI), USA	\$5,547,803	18/09/2017 – 30/06/2022
27.	Hearing Impairment Genetics Studies in Africa (HI-GENES Africa) Grant ref: 1U01HG009716	Co-investigator (Principal Investigator for Ghana site) Grant holder: Ambroise Wonkam, University of Cape Town	National Institutes of Health (NIH/NHGRI), USA	\$1,249,097 (Sub-award budget - \$114,772)	15/09/2017 – 30/06/2022

28.	GCRF-Crick African Network	Co-investigator (Principal Investigator for Ghana site) Grant holder: Prof Robert Wilkinson, Francis Crick Institute, UK	Research Councils UK (RCUK), Global Challenges Research Fund (GCRF)	£6,336,136 (Sub-award budget - £2,011,087)	01/07/2017-30/06/2021
29.	Tackling Infections to Benefit Africa (TIBA)	Co-investigator (Principal Investigator for Ghana site) Grant holder: Mark Woolhouse, University of Edinburgh, UK Co-Principal investigator	National Institutes of Health Research (NIHR), UK	£6,886,852 (Sub-award budget - £639,571)	01/04/2017-31/03/2021
30.	Pocket-i-nucleic acid diagnostic (pi-NAD) Grant Ref: IC160089	Grant holders: Elizabeth Hall (University of Cambridge) and Gordon A. Awandare	The Royal Society, UK	£319,385	01/12/2016 – 30/11/2021
31.	Immuno-biology of sexual stage antigens of <i>Plasmodium falciparum</i> parasites Grant ref: 110090/Z/15/Z	Co-investigator Grant holder: Bismarck Dinko, University of Health and Allied Sciences	Wellcome Trust, UK	£163,540	01/11/2016 – 01/11/2019
32.	WACCBIP-Wellcome Trust DELTAS Programme Grant ref: 107755/Z/15/Z	Principal Investigator (Programme Director)	Wellcome Trust, UK	\$ 7,809,000	01/09/2015 – 31/08/2020
33.	West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) Grant ref: ACE:002	Principal Investigator (Centre Leader)	World Bank, USA	\$8,000,000	01/02/2014 - 31/12/2019
34.	Targets and patterns of erythrocyte invasion inhibitory antibody responses in malaria Grant ref: AA130127	Co-Principal Investigator Grant holders: David Conway (London School of Hygiene and Tropical Medicine) and Gordon A. Awandare	Leverhulme-Royal Society, UK	£179,200	01/09/2014 – 31/08/2017
35.	Characterization of trypanosome infections over the lifetime of cattle in Ghana Grant ref: AA130045	Role: Co-Investigator Grant holders: Theresa Manful (University of Ghana) and Mark Carrington (University of Cambridge)	Leverhulme-Royal Society, UK	£160,300	06/08/2013 – 31/07/2016
36.	Role of complement receptor 1 in erythrocyte invasion by <i>P. falciparum</i> in semi-immune Ghanaians Grant ref: R01A1102848	Principal Investigator	National Institutes of Health (NIH/NIAD), USA	\$249,958	08/03/2012 - 28/02/2017
37.	Parasite population genomics and functional studies towards development of a blood stage malaria vaccine Grant ref: ERC-AdG-294428	Co-Investigator (Principal Investigator for Ghana site) Grant holders: David Conway (London School of Hygiene and Tropical Medicine)	European Research Council	€2,948,083	01/07/2012 - 30/06/2015
38.	Alternative molecular mechanisms for erythrocyte invasion by <i>Plasmodium falciparum</i> in Ghana Grant ref: AA110050	Co-Principal Investigator Grant holders: David Conway (London School of Hygiene and Tropical Medicine) and Gordon A. Awandare	Leverhulme-Royal Society, UK	£147,985	01/09/2011 - 31/08/2014



INAUGURAL LECTURE ABSTRACT

How our immune system acquires tolerance to malaria and helped us survive COVID-19

Malaria and COVID-19 are two of the most devastating infectious diseases that have impacted public health globally. While they are caused by two entirely different pathogens, their clinical manifestations overlap significantly, and these similarities mirror the immunological mechanisms that determine disease outcomes. In this lecture, the biology of the two pathogens, as well as the human immune responses to infections by these pathogens will be discussed. In addition, the lecture will discuss science capacity building in Africa, and the impact of the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) in developing science leadership on the continent.

One of the most remarkable phenomena observed during the COVID-19 pandemic was the relatively low mortality in sub-Saharan Africa, despite various ominous predictions of devastation of the continent. Data will be presented to demonstrate how frequent exposure to malaria trained the human immune system to tolerate further infections. Furthermore, the data will show that the malaria-induced reprogramming of the immune system was beneficial to people living in malaria endemic areas during the COVID-19 pandemic by protecting them from severe disease and death.

Malaria is caused by a parasite known as Plasmodium, and the specific type that causes the most disease and death in humans is called Plasmodium falciparum. This parasite is transmitted from one human to another through the bite of an infected Anopheles mosquito. Although the parasites go to the liver first, they eventually enter the blood where they repeatedly invade, grow and burst out of red blood cells. During each cycle, when the parasites burst out, large quantities of parasite products are released into the blood, which stimulate the immune system, and cause symptoms such as fever. The immediate reaction of the immune system is an inflammatory response, characterized by the release of mediators including cytokines such as interleukin-12 (IL-12), Tumor necrosis factor alpha (TNF-alpha) and reactive nitrogen and oxygen species, which help kill the parasites. However, excessive production of these pro-inflammatory mediators can be deleterious to human tissues and organs, and therefore needs to be carefully regulated to prevent exacerbation of disease pathogenesis.

In individuals living in malaria-endemic countries such as Ghana and the rest of sub-Saharan Africa, exposure to malaria begins early in childhood, with immunity (resistance) being acquired after repeated infections by Plasmodium. This acquired resistance to malaria appears to be two-fold: anti-parasite immunity and anti-disease immunity. While anti-parasite immunity is mediated by the development of specific antibodies targeting P. falciparum, which act to suppress parasite multiplication, our data demonstrate that anti-disease immunity is mediated by controlling excessive inflammation and thereby minimizing clinical symptoms without necessarily clearing the parasites. In that sense, anti-disease immunity is essen-

tially clinical immunity, which can be achieved by 'tolerating' the parasites. Recent research indicates that the blunting of inflammatory responses that confers tolerance to malaria parasites is mediated by epigenetic (on-top-of genetics) mechanisms, which involve reprogramming of immune cells to prevent them from responding to inflammatory stimuli. Therefore, the anti-disease effects of malaria-induced tolerance appears to extend beyond Plasmodium stimulation to other inflammatory stimuli, including other pro-inflammatory pathogens such as certain bacteria and viruses.

COVID-19 is caused by the Novel Coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which is highly contagious and transmitted through the oral and nasopharyngeal routes. Although SARS-CoV-2 is a much smaller and less complex pathogen than Plasmodium, COVID-19 shares several symptoms with malaria, including fever/chills, headaches, malaise, vomiting etc. As observed in malaria, COVID-19 pathogenesis is characterized by the increased release of pro-inflammatory cytokines, the so-called 'cytokine storm', which if unchecked could cause multi-organ damage in the patients. Furthermore, the majority of SARS-CoV-2 infections are asymptomatic (without clinical symptoms), which mirrors the situation in malaria-endemic areas, where the majority of Plasmodium-infected individuals show no symptoms of disease. Given these curious similarities between COVID-19 and Malaria, and the general trend of less COVID-19 severity in sub-Saharan Africa, it was of interest to investigate the possible interactions between the two diseases. Therefore, we investigated the production of cytokines in SARS-CoV-2-infected individuals in Ghana who were either asymptomatic or had mild to severe symptoms of COVID-19. Our data show clearly that asymptomatic infections were associated with a distinct lack of inflammatory responses while individuals showing symptoms had significantly increased levels of pro-inflammatory cytokines in their blood. Of significant interest, we also observed that evidence of high previous exposure to malaria was associated with a blunted inflammatory response and protection from clinical disease following a SARS-CoV-2 infection, indicating the impact of malaria-induced tolerance to inflammatory stimuli.

Taken together, the evidence from our research establishes that our immune system learnt how to tolerate malaria parasites after repeated infections by inhibiting our cells from responding to further stimulation. Further, our work extended to COVID-19 and showed that the immune cell reprogramming that was acquired from living in a malaria-endemic area protected us against development of severe disease during infections by SARS-CoV-2. These findings contribute to a better understanding of the global dynamics of COVID-19 infections and mortality.

DIAGNOSTICS AND INNOVATION



Sensitive detection of symptomatic and asymptomatic malaria with seven novel parasite-specific LAMP assays and translation for use at point-of-care

Malpartida-Cardenas K, Moser N, Ansah F, Pennisi I, Ahu Prah D, Amoah LE, **Awandare G**, Hafalla JCR, Cunningham A, Baum J, Rodriguez-Manzano J, & Georgiou P (2023)

[Microbiology spectrum](#) (2023 Impact Factor: 9.043)

Abstract

Human malaria is a life-threatening parasitic disease with high impact in the sub-Saharan Africa region, where 95% of global cases occurred in 2021. While most malaria diagnostic tools are focused on *Plasmodium falciparum*, there is a current lack of testing non-*P. falciparum* cases, which may be underreported and, if undiagnosed or untreated, may lead to severe consequences. In this work, seven species-specific loop-mediated isothermal amplification (LAMP) assays were designed and evaluated against TaqMan quantitative PCR (qPCR), microscopy, and enzyme-linked immunosorbent assays (ELISAs). Their clinical performance was assessed with a cohort of 164 samples of symptomatic and asymptomatic patients from Ghana. All asymptomatic samples with a parasite load above 80 genomic DNA (gDNA) copies per μL of extracted sample were detected with the *Plasmodium falciparum* LAMP assay, reporting 95.6% (95% confidence interval [95% CI] of 89.9 to 98.5) sensitivity and 100% (95% CI of 87.2 to 100) specificity. This assay showed higher sensitivity than microscopy and ELISA, which were 52.7% (95% CI of 39.7 to 67%) and 67.3% (95% CI of 53.3 to 79.3%), respectively. Nine samples were positive for *P. malariae*, indicating coinfections with *P. falciparum*, which represented 5.5% of the tested population. No samples were detected as positive for *P. vivax*, *P. ovale*, *P. knowlesi*, or *P. cynomolgi* by any method. Furthermore, translation to the point-of-care was demonstrated with a subcohort of 18 samples tested locally in Ghana using our handheld lab-on-chip platform, Lacewing, showing comparable results to a conventional fluorescence-based instrument. The developed molecular diagnostic test could detect asymptomatic malaria cases, including submicroscopic parasitemia, and it has the potential to be used for point-of-care applications.

Importance

The spread of *Plasmodium falciparum* parasites with *Pfhrp2/3* gene deletions presents a major threat to reliable point-of-care diagnosis with current rapid diagnostic tests (RDTs). Novel

molecular diagnostics based on nucleic acid amplification are needed to address this liability. In this work, we overcome this challenge by developing sensitive tools for the detection of *Plasmodium falciparum* and non-*P. falciparum* species. Furthermore, we evaluate these tools with a cohort of symptomatic and asymptomatic malaria patients and test a subcohort locally in Ghana. The findings of this work could lead to the implementation of DNA-based diagnostics to fight against the spread of malaria and provide reliable, sensitive, and specific diagnostics at the point of care.

2

Global Distribution of Founder Variants Associated with Non-Syndromic Hearing Impairment

Aboagye ET, Adadey SM, Wonkam-Tingang E, Amenga-Etego L, **Awandare GA**, Wonkam A (2023)

[Genes](#) (2023 Impact Factor: 4.141)

Abstract

The genetic etiology of non-syndromic hearing impairment (NSHI) is highly heterogeneous with over 124 distinct genes identified. The wide spectrum of implicated genes has challenged the implementation of molecular diagnosis with equal clinical validity in all settings. Differential frequencies of allelic variants in the most common NSHI causal gene, gap junction beta 2 (*GJB2*), has been described as stemming from the segregation of a founder variant and/or spontaneous germline variant hot spots. We aimed to systematically review the global distribution and provenance of founder variants associated with NSHI. The study protocol was registered on PROSPERO, the International Prospective Register of Systematic Reviews, with the registration number “CRD42020198573”. Data from 52 reports, involving 27,959 study participants from 24 countries, reporting 56 founder pathogenic or likely pathogenic (P/LP) variants in 14 genes (*GJB2*, *GJB6*, *GSDME*, *TMC1*, *TMIE*, *TM-PRSS3*, *KCNQ4*, *PJVK*, *OTOF*, *EYA4*, *MYO15A*, *PDZD7*, *CLDN14*, and *CDH23*), were reviewed. Varied number short tandem repeats (STRs) and single nucleotide polymorphisms (SNPs) were used for haplotype analysis to identify the shared ancestral informative markers in a linkage disequilibrium and variants’ origins, age estimates, and common ancestry computations in the reviewed reports. Asia recorded the highest number of NSHI founder variants (85.7%; 48/56), with variants in all 14 genes, followed by Europe (16.1%; 9/56). *GJB2* had the highest number of ethnic-specific P/LP founder variants. This review reports on the global distribution of NSHI founder variants and relates their evolution to population migration history, bottleneck events, and demographic changes in populations linked with the early evolution of deleterious founder alleles. International migration and regional and cultural intermarriage, coupled to

rapid population growth, may have contributed to re-shaping the genetic architecture and structural dynamics of populations segregating these pathogenic founder variants. We have highlighted and showed the paucity of data on hearing impairment (HI) variants in Africa, establishing unexplored opportunities in genetic traits.

Keywords: [hearing impairment](#); [non-syndromic](#); [genetics](#); [founder variant](#); [gab junction beta 2 \(GJB2\)](#); [global populations](#)

3

Analysis and validation of silica-immobilised BST polymerase in loop-mediated isothermal amplification (LAMP) for malaria diagnosis

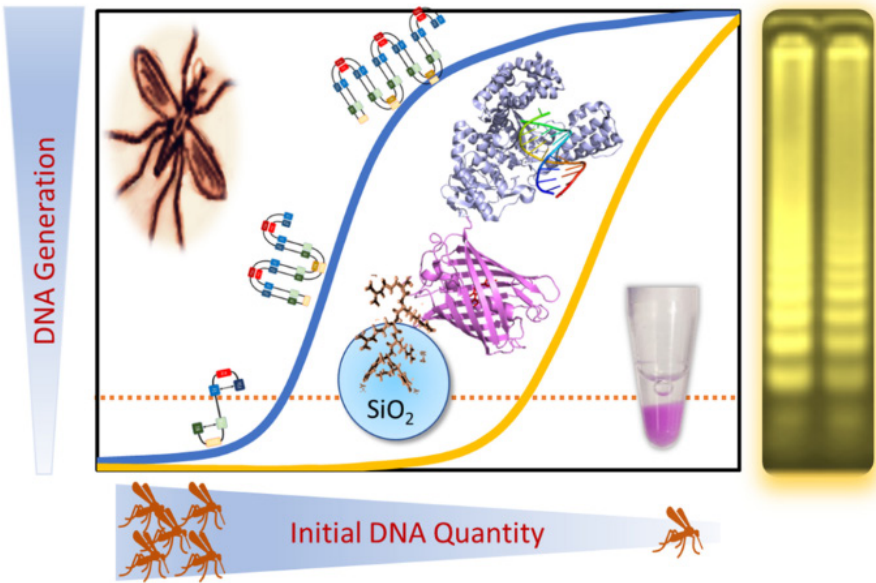
Seevaratnam D, Ansah F, Aniweh Y, **Awandare GA**, & Hall EAH (2022)

[Analytical and Bioanalytical Chemistry](#) (2023 Impact Factor: 4478)

Abstract

Bacillus stearothermophilus large fragment (BST_{LF}) DNA polymerase is reported, isolated on silica via a fused R5 silica-affinity peptide and used in nucleic acid diagnostics. mCherry (mCh), included in the fusion construct, was shown as an efficient fluorescent label to follow the workflow from gene to diagnostic. The R5 immobilisation on silica from cell lysate was consistent with cooperative R5-specific binding of R5₂-mCh-FL-BST_{LF} or R5₂-mCh-H10-BST_{LF} fusion proteins followed by non-specific protein binding (including *E. coli* native proteins). Higher R5-binding could be achieved in the presence of phosphate, but phosphate residue reduced loop-mediated isothermal amplification (LAMP) performance, possibly blocking sites on the BST_{LF} for binding of Beta- and Gamma-phosphates of the dNTPs. Quantitative assessment showed that cations (Mg²⁺ and Mn²⁺) that complex the PPi product optimised enzyme activity. In malaria testing, the limit of detection depended on *Plasmodium* species and primer set. For example, 1000 copies of *P. knowlesi* 18S rRNA could be detected with the P.KNO-LAU primer set with Si-R5₂-mCh-FL-BST_{LF}, but 10 copies of *P. ovale* 18S rRNA could be detected with the POVA-HAN primer set using the same enzyme. The Si-immobilised BST_{LF} outperformed the commercial enzyme for four of the nine *Plasmodium* LAMP primer sets tested. Si-R5₂-mCh-FL-BST_{LF} production was transferred from Cambridge to Accra and set up de novo for a trial with clinical samples. Different detection limits were found, targeting the mitochondrial DNA or the 18S rRNA gene for *P. falciparum*. The results are discussed in comparison with qPCR and sampling protocol and show that the Si-BST_{LF} polymerase can be optimised to meet the WHO recommended guidelines.

Graphical abstract



Ultrasensitive electrochemical genosensors for species-specific diagnosis of malaria

Ansah F, Krampa F, Donkor JK, Owusu-Appiah C, Ashitei S, Kornu VE, Danku RK, Chirawurah JD, **Awandare GA**, Aniweh Y, Kanyong P (2022)

[Electrochimica Acta](#) (2023 Impact Factor: 7.336)

Abstract

The absence of reliable species-specific diagnostic tools for malaria at point-of-care (POC) remains a major setback towards effective disease management. This is partly due to the limited sensitivity and specificity of the current malaria POC diagnostic kits especially in cases of low-density parasitaemia and mixed species infections. In this study, we describe the first label-free DNA-based genosensors based on electrochemical impedance spectroscopy (EIS) for species-specific detection of *P. falciparum*, *P. malariae* and *P. ovale*. The limits of detection (LOD) for the three species-specific genosensors were down in attomolar concentrations ranging from 18.7 aM to 43.6 aM, which is below the detection limits of previously reported malaria genosensors. More importantly, the diagnostic performance of the three genosensors were compared to quantitative real-time polymerase chain reaction (qPCR) assays using purified genomic DNA and the paired whole blood lysates from clinical samples. Remarkably, all the qPCR-positive purified genomic DNA samples were correctly identified by the genosensors indicating 100% sensitivity for each of the three malaria species. The specificities of the three genosensors ranged from 66.7% to 100.0% with a Therapeutic Turnaround Time (TTAT) within 30 min, which is comparable to the TTAT of current POC diagnostic tools for malaria. This work represents a significant step towards the development of accurate and rapid species-specific nucleic acid-based toolkits for the diagnosis of malaria at the POC.

Keywords: Genosensor Electrochemical impedance spectroscopy (EIS) Malaria Plasmodium species Deoxyribonucleic acid (DNA)

5

Development of Cooperative Primer-Based Real-Time PCR Assays for the detection of *Plasmodium malariae* and *Plasmodium ovale*

Ansah F, Suurbaar J, Darko D, Anabire NG, Blankson SO, Domson BKS, Soulama A, Kpasra P, Chirawurah JD, Amenga-Etego L, Kanyong P, **Awandare GA**, Aniweh Y (2021)

[Journal of Molecular Diagnostics](#) (2023 Impact Factor: 5.341)

Abstract

Plasmodium malariae and *Plasmodium ovale* are increasingly gaining public health attention as the global transmission of [falciparum malaria](#) is decreasing. However, the absence of reliable *Plasmodium* species-specific detection tools has hampered accurate diagnosis of these minor *Plasmodium* species. In this study, SYBR Green-based real-time PCR assays were developed for the detection of *P. malariae* and *P. ovale* using cooperative primers that significantly limit the formation and propagation of primers-dimers. Both the *P. malariae* and *P. ovale* cooperative primer-based assays had at least 10-fold lower detection limit compared with the corresponding conventional primer-based assays. More important, the cooperative primer-based assays were evaluated in a cross-sectional study using 560 samples obtained from two health facilities in Ghana. The prevalence rates of *P. malariae* and *P. ovale* among the combined study population were 18.6% (104/560) and 5.5% (31/560), respectively. Among the *Plasmodium*-positive cases, *P. malariae* and *P. ovale* mono-infections were 3.6% (18/499) and 1.0% (5/499), respectively, with the remaining being co-infections with *Plasmodium falciparum*. The study demonstrates the public health importance of including detection tools with lower detection limits in routine diagnosis and surveillance of nonfalciparum species. This will be necessary for comprehensively assessing the effectiveness of malaria interventions and control measures aimed toward global malaria elimination.

6

Machine learning approaches classify clinical malaria outcomes based on haematological parameters

Morang'a CM, Amenga-Etego L, Bah SY, Appiah V, Amuzu D, Amoako N, Abugri J, Cunningham AJ, **Awandare GA** & Otto TD (2020)

[BMC Medicine](#) (2023 Impact Factor: 11.15)

Abstract

Background

Malaria is still a major global health burden, with more than 3.2 billion people in 91 countries remaining at risk of the disease. Accurately distinguishing malaria from other diseases, especially uncomplicated malaria (UM) from non-malarial infections (nMI), remains a challenge. Furthermore, the success of rapid diagnostic tests (RDTs) is threatened by *Pfhrp2/3* deletions and decreased sensitivity at low parasitaemia. Analysis of haematological indices can be used to support the identification of possible malaria cases for further diagnosis, especially in travellers returning from endemic areas. As a new application for precision medicine, we aimed to evaluate machine learning (ML) approaches that can accurately classify nMI, UM, and severe malaria (SM) using haematological parameters.

Methods

We obtained haematological data from 2,207 participants collected in Ghana: nMI ($n = 978$), SM ($n = 526$), and UM ($n = 703$). Six different ML approaches were tested, to select the best approach. An artificial neural network (ANN) with three hidden layers was used for multi-classification of UM, SM, and uMI. Binary classifiers were developed to further identify the parameters that can distinguish UM or SM from nMI. Local interpretable model-agnostic explanations (LIME) were used to explain the binary classifiers.

Results

The multi-classification model had greater than 85% training and testing accuracy to distinguish clinical malaria from nMI. To distinguish UM from nMI, our approach identified platelet counts, red blood cell (RBC) counts, lymphocyte counts, and percentages as the top classifiers of UM with 0.801 test accuracy (AUC=0.866 and F1 score=0.747). To distinguish SM from nMI, the classifier had a test accuracy of 0.96 (AUC=0.983 and F1 score=0.944) with mean platelet volume and mean cell volume being the unique classifiers of SM. Random forest was used to confirm the classifications, and it showed that platelet and RBC counts were the major classifiers of UM, regardless of possible confounders such as patient age and sampling location.

Conclusion

The study provides proof of concept methods that classify UM and SM from nMI, showing that the ML approach is a feasible tool for clinical decision support. In the future, ML approaches could be incorporated into clinical decision-support algorithms for the diagnosis of acute febrile illness and monitoring response to acute SM treatment particularly in endemic settings.

Cell trace far-red is a suitable erythrocyte dye for multi-color *Plasmodium falciparum* invasion phenotyping assays

Thiam, L. G, Aniweh Y, Quansah, E. B, Donkor, J. K, Gwira, T. M, Kusi, KA, Niang M, & **Awandare G. A** (2020)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

Plasmodium falciparum erythrocyte invasion phenotyping assays are a very useful tool for assessing parasite diversity and virulence, and for characterizing the formation of ligand–receptor interactions. However, such assays need to be highly sensitive and reproducible, and the selection of labeling dyes for differentiating donor and acceptor erythrocytes is a critical factor. We investigated the suitability of cell trace far-red (CTFR) as a dye for *P. falciparum* invasion phenotyping assays. Using the dyes carboxyfluorescein diacetate succinimidyl ester (CFDA-SE) and dichloro dimethyl acridin one succinimidyl ester (DDAO-SE) as comparators, we used a dye-dilution approach to assess the limitations and specific staining procedures for the applicability of CTFR in *P. falciparum* invasion phenotyping assays. Our data show that CTFR effectively labels acceptor erythrocytes and provides a stable fluorescent intensity at relatively low concentrations. CTFR also yielded a higher fluorescence intensity relative to DDAO-SE and with a more stable fluorescence intensity over time. Furthermore, CTFR did not affect merozoites invasion of erythrocytes and was not toxic to the parasite's intraerythrocytic development. Additionally, CTFR offers flexibility in the choice of combinations with several other DNA dyes, which broaden its usage for *P. falciparum* erythrocyte invasion assays, considering a wider range of flow cytometers with various laser settings.

8

Recent advances in the development of biosensors for malaria diagnosis

Krampa, F. D., Aniweh, Y., Kanyong, P., & **Awandare, G. A** (2020)

[Sensors](#) (2023 Impact Factor: 3.847)

Abstract

The impact of malaria on global health has continually prompted the need to develop more effective diagnostic strategies that could overcome deficiencies in accurate and early detection. In this review, we examine the various biosensor-based methods for malaria diagnostic biomarkers, namely; *Plasmodium falciparum* histidine-rich protein 2 (PfHRP-2), parasite lactate dehydrogenase (pLDH), aldolase, glutamate dehydrogenase (GDH), and the biocrystal hemozoin. The models that demonstrate a potential for field application have been discussed, looking at the fabrication and analytical performance characteristics, including (but not exclusively limited to): response time, sensitivity, detection limit, linear range, and storage stability, which are first summarized in a tabular form and then described in detail. The conclusion summarizes the state-of-the-art technologies applied in the field, the current challenges and the emerging prospects for malaria biosensors.

Keywords: [malaria biomarkers](#); [biosensors](#); [clinical diagnosis](#); [medical devices](#); [biosensing](#)

Highlights on the Application of Genomics and Bioinformatics in the Fight Against Infectious Diseases: Challenges and Opportunities in Africa

Bah, S. Y., Morang'a, C. M., Kengne-Ouafo, J. A., Amenga-Etego, L., & **Awandare, G. A.** (2018)

[Frontiers in Genetics](#) (2023 Impact Factor: 4.772)

Abstract

Genomics and bioinformatics are increasingly contributing to our understanding of infectious diseases caused by bacterial pathogens such as *Mycobacterium tuberculosis* and parasites such as *Plasmodium falciparum*. This ranges from investigations of disease outbreaks and pathogenesis, host and pathogen genomic variation, and host immune evasion mechanisms to identification of potential diagnostic markers and vaccine targets. High throughput genomics data generated from pathogens and animal models can be combined with host genomics and patients' health records to give advice on treatment options as well as potential drug and vaccine interactions. However, despite accounting for the highest burden of infectious diseases, Africa has the lowest research output on infectious disease genomics. Here we review the contributions of genomics and bioinformatics to the management of infectious diseases of serious public health concern in Africa including tuberculosis (TB), dengue fever, malaria and filariasis. Furthermore, we discuss how genomics and bioinformatics can be applied to identify drug and vaccine targets. We conclude by identifying challenges to genomics research in Africa and highlighting how these can be overcome where possible.

Keywords: antimicrobial resistant; bioinformatics; diagnosis; genomics; infectious diseases.

Multi-population genomic analysis of malaria parasites indicates local selection and differentiation at the *gdv1* locus regulating sexual development

Duffy, C. W., Amambua-Ngwa, A., Ahouidi, A. D., Diakite, M., **Awandare, G. A.**, Ba, H., Tarr, S. J., Murray, L., Stewart, L. B., D'Allessandro, U., Otto, T. D., Kwiatkowski, D. P., & Conway, D. J. (2018)

[Scientific Report](#) (2023 Impact Factor: 4.996)

Abstract

Parasites infect hosts in widely varying environments, encountering diverse challenges for adaptation. To identify malaria parasite genes under locally divergent selection across a large endemic region with a wide spectrum of transmission intensity, genome sequences were obtained from 284 clinical *Plasmodium falciparum* infections from four newly sampled locations in Senegal, The Gambia, Mali and Guinea. Combining these with previous data from seven other sites in West Africa enabled a multi-population analysis to identify discrete loci under varying local selection. A genome-wide scan showed the most exceptional geographical divergence to be at the early gametocyte gene locus *gdv1* which is essential for parasite sexual development and transmission. We identified a major structural dimorphism with alternative 1.5 kb and 1.0 kb sequence deletions at different positions of the 3'-intergenic region, in tight linkage disequilibrium with the most highly differentiated single nucleotide polymorphism, one of the alleles being very frequent in Senegal and The Gambia but rare in the other locations. Long non-coding RNA transcripts were previously shown to include the entire antisense of the *gdv1* coding sequence and the portion of the intergenic region with allelic deletions, suggesting adaptive regulation of parasite sexual development and transmission in response to local conditions.

Genomics and epigenomics of congenital heart defects: expert review and lessons learned in Africa

[OMICS: A Journal of Integrative Biology](#) (2023 Impact Factor: 3.978)

Thomford, N. E., Dzobo, K., Yao N. A., Chimusa, E., Evans, J., Okai, E., Kruszka, P., Muenke, M., **Awandare, G.**, Wonkam, A., & Dandara, C (2018)

Abstract

Congenital heart defects (CHD) are structural malformations found at birth with a prevalence of 1%. The clinical trajectory of CHD is highly variable and thus in need of robust diagnostics and therapeutics. Major surgical interventions are often required for most CHDs. In Africa, despite advances in life sciences infrastructure and improving education of medical scholars, the limited clinical data suggest that CHD detection and correction are still not at par with the rest of the world. But the toll and genetics of CHDs in Africa has seldom been systematically investigated. We present an expert review on CHD with lessons learned on Africa. We found variable CHD phenotype prevalence in Africa across countries and populations. There are important gaps and paucity in genomic studies of CHD in African populations. Among the available genomic studies, the key findings in Africa were variants in *GATA4* (P193H), *MTHFR* 677TT, and *MTHFR* 1298CC that were associated with atrial septal defect, ventricular septal defect (VSD), Tetralogy of Fallot (TOF), and patent ductus arteriosus phenotypes and 22q.11 deletion, which is associated with TOF. There were no data on epigenomic association of CHD in Africa, however, other studies have shown an altered expression of *miR-421* and *miR-1233-3p* to be associated with TOF and hypermethylation of CpG islands in the promoter of *SCO2* gene also been associated with TOF and VSD in children with non-syndromic CHD. These findings signal the urgent need to develop and implement genetic and genomic research on CHD to identify the hereditary and genome–environment

interactions contributing to CHD. These projected studies would also offer comparisons on CHD pathophysiology between African and other populations worldwide. Genomic research on CHD in Africa should be developed in parallel with next generation technology policy research and responsible innovation frameworks that examine the social and political factors that shape the emergence and societal embedding of new technologies.

12

Local diagnostics kits for Africa being developed in Ghana

Yaw, A., Prosper, K., Krampa, F. & **Awandare, G. A** (2018). Local diagnostics kits for Africa being developed in Ghana

[Nature](#) (2023 Impact Factor: 69.504)

Correspondence

In our view, building local capacity in diagnostics could help Africa to tackle diseases such as malaria, HIV/AIDS and tuberculosis. We have set up a unit to design and develop diagnostic kits at the University of Ghana's West African Centre for Cell Biology of Infectious

Pathogens (WACCBIP: <http://www.waccbip.org>).

A robust service to monitor public health and deliver treatment depends on reliable early diagnosis of medical conditions. Africa is generally very limited in its development and deployment of diagnostics systems, however, so these are mostly brought in at high cost from the developed world.

Furthermore, the stability and usability of such sensing systems are hampered by poor storage conditions and inadequately trained personnel. Using local platforms such as ours for developing diagnostic sensors and instrumentation will help to meet the continent's growing demand for them. The hope is that ill health will no longer impede the economic prospects of the continent.

Polydopamine-functionalized graphene nanoplatelet smart conducting electrode for bio-sensing applications

Kanyong, P., Krampa, F., Aniweh, Y. & **Awandare, G.** (2018)

[Arabian Journal of Chemistry](#) (2023 Impact Factor: 6.212)

Abstract

The development of a novel polydopamine (PDA)-functionalized graphene [nanoplatelets](#) (GNPs)-based disposable sensor is described. The sensor was fabricated by drop-coating PDA@GNPs in [polyethylene glycol](#) (PEG) and poly(3,4-ethylenedioxythiophene (PEDOT):poly(styrenesulfonate) (PSS) aqueous suspension onto the working area of a screen-printed electrode (SPE). The final sensor, designated as PDA@GNPs/PPP/SPE, was characterized by scanning electron microscopy (SEM), Raman spectroscopy, Faradaic electrochemical impedance spectroscopy (FEIS) and [cyclic voltammetry](#) (CV). Mediated detection of hydrogen peroxide (H_2O_2) via the redox properties of PDA was achieved. It showed excellent [selectivity](#) and sensitivity towards H_2O_2 with a limit of detection and sensitivity of $0.55 \mu\text{M}$ ($\text{S/N} = 3$) and $3.0 \mu\text{A mM}^{-1} \text{cm}^{-2}$, respectively. Thereafter, [glucose oxidase](#) (GOx) was immobilized onto the electrode to develop GOx/PDA@GNPs/PPP/SPE sensor. The glucose biosensor exhibited a limit of detection of $0.25 \mu\text{M}$ ($\text{S/N} = 3$) and a sensitivity of $0.51 \mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$; thus, proving its potential suitability for bio-sensing applications.

Enzyme-based amperometric galactose biosensors: A review

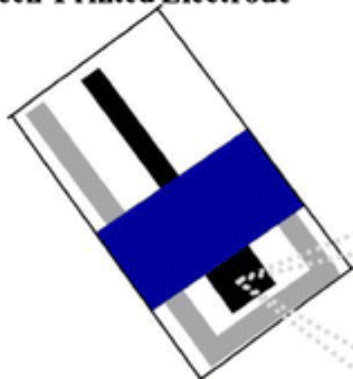
Kanyong, P., Krampa, F. D., Aniweh, Y. & **Awandare, G. A.** (2017)

[Microchimica Acta](#) (2023 Impact Factor: 6.408)

Abstract

This review (with 35 references) summarizes the various strategies used in biosensors for galactose, and their analytical performance. A brief comparison of the enzyme immobilization methods employed and the analytical performance characteristics of a range of galactose biosensors are first summarized in tabular form and then described in detail. Selected examples have been included to demonstrate the various applications of these biosensors to real samples. Following an introduction into the field that covers the significance of sensing galactose in various fields, the review covers biosensors based on the use of galactose oxidase, with a discussion of methods for their immobilization (via cross-linking, adsorption, covalent bonding and entrapment). This is followed by a short section on biosensors based on the use of galactose dehydrogenase. The conclusion section summarizes the state of the art and addresses current challenges.

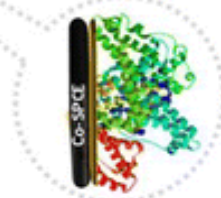
a Screen-Printed Electrode



b Galactose Biosensor



c Dummy Biosensor



Fabrication of a disposable screen-printed (a) electrochemical galactose biosensor (b) for real sample analysis and a dummy biosensor (c) for compensating the effect of interferences

Recent Progress in the Development of Diagnostic Tests for Malaria

Krampa, D. F., Aniweh, Y., **Awandare, G. A.**, & Kanyong P. (2017)

[Diagnostics](#) (2023 Impact Factor: 3.992)

Abstract

The impact of malaria on global health has continually prompted the need to develop effective diagnostic strategies. In malaria endemic regions, routine diagnosis is hampered by technical and infrastructural challenges to laboratories. These laboratories lack standard facilities, expertise or diagnostic supplies; thus, therapy is administered based on clinical or self-diagnosis. There is the need for accurate diagnosis of malaria due to the continuous increase in the cost of medication, and the emergence and spread of drug resistant strains. However, the widely utilized Giemsa-stained microscopy and immunochromatographic tests for malaria are liable to several drawbacks, including inadequate sensitivity and false-positive outcomes. Alternative methods that offer improvements in performance are either expensive, have longer turnaround time or require a level of expertise that makes them unsuitable for point-of-care (POC) applications. These gaps necessitate exploration of more efficient detection techniques with the potential of POC applications, especially in resource-limited settings. This minireview discusses some of the recent trends and new approaches that are seeking to improve the clinical diagnosis of malaria.

Keywords: rapid diagnostic tests (RDT), biosensing, lateral flow assays, *Plasmodium* spp., multiplex biomarker detection, histidine-rich protein 2 (HRP2), lactate dehydrogenase (LDH), aldolase, point-of-care tests (POCT), disposal medical devices, infectious diseases.

Disposable Amperometric Sensor Based on High-Performance PEDOT:PSS/Ionic Liquid Nanocomposite Thin Film-Modified Screen-Printed Electrode for the Analysis of Catechol in Natural Water Samples

Krampa, D. F., Aniweh, Y., **Awandare, G. A.**, & Kanyong P. (2017)

[Sensors](#) (2023 Impact Factor: 3.847)

Abstract

A conducting polymer-based composite material of poly(3,4-ethylenedioxythiophene) (PEDOT): poly(4-styrenesulfonate) (PSS) doped with different percentages of a room temperature ionic liquid (IL), 1-ethyl-3-methylimidazolium tetrafluoroborate ([EMIM][BF₄]), was prepared and a very small amount of the composite (2.0 μL) was drop-coated on the working area of a screen-printed carbon electrode (SPCE). The SPCE, modified with PEDOT:PSS/IL composite thin-film, was characterized by cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), scanning electron microscopy (SEM), profilometry and sessile contact angle measurements. The prepared PEDOT:PSS/IL composite thin-film exhibited a nanoporous microstructure and was found to be highly stable and conductive with enhanced electrocatalytic properties towards catechol, a priority pollutant. The linear working range for catechol was found to be 0.1 μM –330.0 μM with a sensitivity of 18.2 $\text{mA}\cdot\text{mM}\cdot\text{cm}^{-2}$ and a calculated limit of detection (based on $3\times$ the baseline noise) of 23.7 μM . When the PEDOT:PSS/IL/SPCE sensor was used in conjunction with amperometry in stirred solution for the analysis of natural water samples, the precision values obtained on spiked samples (20.0 μM catechol added) ($n = 3$) were 0.18% and 0.32%, respectively, with recovery values that were well over 99.0%.

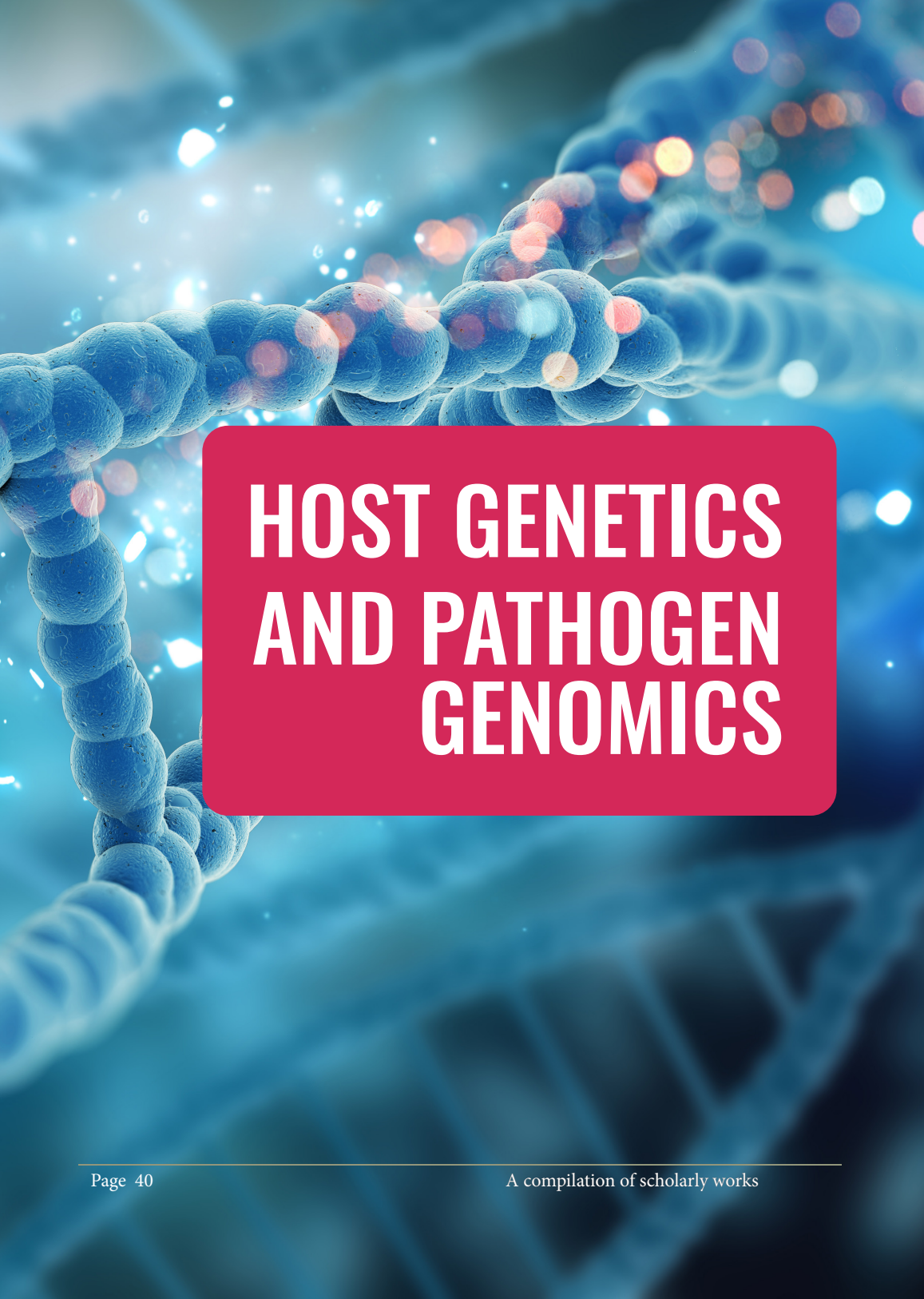
Investigating the Influence of Temperature on the Kaolinite-Base Synthesis of Zeolite and Urease Immobilization for the Potential Fabrication of Electrochemical Urea Biosensors

Anderson, D. E., Balapangu, S., Fleischer, H. N. A., Viade, R. A., Krampa, F. D., Kanyong, P., **Awandare, G. A.**, & Tiburu, E. K. (2017)

[Sensors](#) (2023 Impact Factor: 3.847)

Abstract

Temperature-dependent zeolite synthesis has revealed a unique surface morphology, surface area and pore size which influence the immobilization of urease on gold electrode supports for biosensor fabrication. XRD characterization has identified zeolite X (Na) at all crystallization temperatures tested. However, N₂ adsorption and desorption results showed a pore size and pore volume of zeolite X (Na) 60 °C, zeolite X (Na) 70 °C and zeolite X (Na) 90 °C to range from 1.92 nm to 245 nm and 0.012 cm³/g to 0.061 cm³/g, respectively, with no significant differences. The specific surface area of zeolite X (Na) at 60, 70 and 90 °C was 64 m²/g, 67 m²/g and 113 m²/g, respectively. The pore size, specific surface area and pore volumes of zeolite X (Na) 80 °C and zeolite X (Na) 100 °C were dramatically increased to 4.21 nm, 295 m²/g, 0.762 cm³/g and 4.92 nm, 389 m²/g, 0.837 cm³/g, in that order. The analytical performance of adsorbed urease on zeolite X (Na) surface was also investigated using cyclic voltammetry measurements, and the results showed distinct cathodic and anodic peaks by zeolite X (Na) 80 °C and zeolite X (Na) 100 °C. These zeolites' molar conductance was measured as a function of urea concentration and gave an average polynomial regression fit of 0.948. The findings in this study suggest that certain physicochemical properties, such as crystallization temperature and pH, are critical parameters for improving the morphological properties of zeolites synthesized from natural sources for various biomedical applications.



HOST GENETICS AND PATHOGEN GENOMICS

A genetic Study of the Ghanaian Population Using 15 Autosomal STR Loci

Kofi AE, Agyemang DA, Ghansah A, **Awandare GA**, Hakim HM, Khan HO, Nur Haslindawaty AR, Aziz MY, Chambers GK, Edinur HA (2023).

[Biochemical Genetics \(2023\)](#) Impact Factor: 2.22)

Abstract

Autosomal short tandem repeat (STR) population data collected from a well characterized population are needed to correctly assigning the weight of DNA profiles in the courtroom and widely used for ancestral analyses. In this study, allele frequencies for the 15 autosomal short tandem repeat (STR) loci included in the AmpF/STR® Identifier® plus kit (D8S1179, D21S11, D7S820, CSF1P0, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, VWA, TPOX, D18S51, D5S818, FGA) were obtained by genotyping 332 unrelated individuals of Ghanaian origin. Statistical tests on STR genotype data showed no significant departure from Hardy–Weinberg equilibrium (HWE). The overall match probability, combined power of exclusion and combined power of discrimination for these loci were 1 in 3.85×10^{17} , 0.99999893 and 0.99999998, respectively. Polymorphic information content (PIC) greater than 0.70 was observed for all loci except TH01 and D13S317. These statistical parameters confirm that this combination of loci is valuable for forensic identification and parentage analysis. Our results were also compared with those for 20 other human populations analyzed for the same set of markers. We observed that the Ghanaian population grouped with other African populations in two-dimensional principal coordinate (PCO) and a neighbor-joining (N-J) data mapping and placed closest to Nigerians. This observation reflects cultural similarities and geographical factors, coupled with the long history of migration and trading activities between Ghana and Nigeria. Our report provides what we believe to be the first

published autosomal STR data for the general Ghanaian population using 15 loci genotyped using the AmpF/STR® Identifiler® plus kit methodology. Our data show that the loci tested have sufficient power to be used reliably for DNA profiling in forensic casework and help to elucidate the genetic history of people living in the country.

Variants of LRP2, encoding a multifunctional cell-surface endocytic receptor, associated with hearing loss and retinal dystrophy

Faridi R, Yousaf R, Gu S, Inagaki S, Turriff AE, Pelstring K, Guan B, Naik A, Griffith AJ, Adadey SM, Aboagye ET, **Awandare GA**, Morell RJ, Tsilou E, Noyes AG, Sulmonte LAG, Wonkam A, Schrauwen I, Leal SM, Azaiez H, Brewer CC, Riazuddin S, Hufnagel RB, Hoa M, Zein WM, de Dios JK, Friedman TB (2023)

[Clinical Genetics](#) (2023 Impact Factor: 4.296)

Abstract

Hereditary deafness and retinal dystrophy are each genetically heterogenous and clinically variable. Three small unrelated families segregating the combination of deafness and retinal dystrophy were studied by exome sequencing (ES). The proband of Family 1 was found to be compound heterozygous for NM_004525.3: *LRP2*: c.5005A>G, p.(Asn1669Asp) and c.149C>G, p.(Thr50Ser). In Family 2, two sisters were found to be compound heterozygous for *LRP2* variants, p.(Tyr393Cys) and an experimentally confirmed c.7715+3A>T consensus splice-altering variant. In Family 3, the proband is compound heterozygous for a consensus donor splice site variant *LRP2*: c.8452_8452+1del and p.(Cys3150Tyr). In mouse cochlea, *Lrp2* is expressed abundantly in the stria vascularis marginal cells demonstrated by smFISH, single-cell and single-nucleus RNAseq, suggesting that a deficiency of LRP2 may compromise the endocochlear potential, which is required for hearing. *LRP2* variants have been associated with Donnai–Barrow syndrome and other multisystem pleiotropic phenotypes different from the phenotypes of the four cases reported herein. Our data expand the phenotypic spectrum associated with pathogenic variants in *LRP2* warranting their consideration in individuals with a combination of hereditary hearing loss and retinal dystrophy.

A novel autosomal dominant GREB1L variant associated with non-syndromic hearing impairment in Ghana

Adadey SM, Aboagye ET, Esoh K, Acharya A, Bharadwaj T, Lin NS, Amenga-Etego L, **Awandare GA**, Schrauwen I, Leal SM, Wonkam A (2022)

[BMC Medical Genomics](#) (2023 Impact Factor: 3.622)

Abstract

Background: Childhood hearing impairment (HI) is genetically heterogeneous with many implicated genes, however, only a few of these genes are reported in African populations.

Methods: This study used exome and Sanger sequencing to resolve the possible genetic cause of non-syndromic HI in a Ghanaian family.

Results: We identified a novel variant c.3041G>A: p.(Gly1014Glu) in *GREB1L* (DFNA80) in the index case. The *GREB1L*: p.(Gly1014Glu) variant had a CADD score of 26.5 and was absent from human genomic databases such as TopMed and gnomAD. *In silico* homology protein modeling approaches displayed major structural differences between the wildtype and mutant proteins. Additionally, the variant was predicted to probably affect the secondary protein structure that may impact its function. Publicly available expression data shows a higher expression of *Greb1L* in the inner ear of mice during development and a reduced expression in adulthood, underscoring its importance in the development of the inner ear structures.

Conclusion: This report on an African individual supports the association of *GREB1L* variant with non-syndromic HI and extended the evidence of the implication of *GREB1L* variants in HI in diverse populations.

Exome sequencing of families from Ghana reveals known and candidate hearing impairment genes

Wonkam A, Adadey SM, Schrauwen I, Aboagye ET, Wonkam-Tingang E, Esoh K, Popel K, Manyisa N, Jonas M, deKock C, Nembaware V, Cornejo Sanchez DM, Bharadwaj T, Nasir A, Everard JL, Kadlubowska MK, Nouel-Saied LM, Acharya A, Quaye O, Amedofu GK, **Awandare GA**, & Leal SM (2022)

[Communications Biology](#) (2023 Impact Factor: 6.548)

Abstract

We investigated hearing impairment (HI) in 51 families from Ghana with at least two affected members that were negative for *GJB2* pathogenic variants. DNA samples from 184 family members underwent whole-exome sequencing (WES). Variants were found in 14 known non-syndromic HI (NSHI) genes [26/51 (51.0%) families], five genes that can underlie either syndromic HI or NSHI [13/51 (25.5%)], and one syndromic HI gene [1/51 (2.0%)]. Variants in *CDH23* and *MYO15A* contributed the most to HI [314% (16/51 families)]. For *DSPP*, an autosomal recessive mode of inheritance was detected. Post-lingual expression was observed for a family segregating a *MARVELD2* variant. To our knowledge, seven novel candidate HI genes were identified (13.7%), with six associated with NSHI (*INPP4B*, *CCDC141*, *MYO19*, *DNAH11*, *POTEL*, and *SOX9*); and one (*PAX8*) with Waardenburg syndrome. *MYO19* and *DNAH11* were replicated in unrelated Ghanaian probands. Six of the novel genes were expressed in mouse inner ear. It is known that *Pax8*^{-/-} mice do not respond to sound, and depletion of *Sox9* resulted in defective vestibular structures and abnormal utricle development. Most variants (48/60; 80.0%) have not previously been associated with HI. Identifying seven candidate genes in this study emphasizes the potential of novel HI genes discovery in Africa.

Age Estimate of GJB2-p.(Arg143Trp) Founder Variant in Hearing Impairment in Ghana, Suggests Multiple Independent Origins across Populations

Aboagye ET, Adadey SM, Esoh K, Jonas M, de Kock C, Amenga-Etego L, **Awandare GA**, & Wonkam A (2022)

[Biology](#) (2023 Impact Factor: 5.168)

Abstract

Gap junction protein beta 2 (*GJB2*) (connexin 26) variants are commonly implicated in non-syndromic hearing impairment (NSHI). In Ghana, the *GJB2* variant p.(Arg143Trp) is the largest contributor to NSHI and has a reported prevalence of 25.9% in affected multiplex families. To date, in the African continent, *GJB2*-p.(Arg143Trp) has only been reported in Ghana. Using whole-exome sequencing data from 32 individuals from 16 families segregating NSHI, and 38 unrelated hearing controls with the same ethnolinguistic background, we investigated the date and origin of p.(Arg143Trp) in Ghana using linked markers. With a Bayesian linkage disequilibrium gene mapping method, we estimated *GJB2*-p.(Arg143Trp) to have originated about 9625 years (385 generations) ago in Ghana. A haplotype analysis comparing data extracted from Ghanaians and those from the 1000 Genomes project revealed that *GJB2*-p.(Arg143Trp) is carried on different haplotype backgrounds in Ghanaian and Japanese populations, as well as among populations of European ancestry, lending further support to the multiple independent origins of the variant. In addition, we found substantial haplotype conservation in the genetic background of Ghanaian individuals with biallelic *GJB2*-p.(Arg143Trp) compared to the *GJB2*-p.(Arg143Trp)-negative group with normal hearing from Ghana, suggesting a strong evolutionary constraint in this genomic region in Ghanaian populations that are homozygous for *GJB2*-p.(Arg143Trp). The present study evaluates the age of *GJB2*-p.(Arg143Trp) at 9625 years and supports the multiple independent origins of this variant in the global population.

Cell-based analysis of CLIC5A and SLC12A2 variants associated with hearing impairment in two African families

Adadey SM, Wonkam-Tingang E, Alves de Souza Rios L, Aboagye ET, Esoh K, Manyisa N, De Kock C, **Awandare GA**, Mowla S, Wonkam A (2022)

[Frontiers in Genetics](#) (2023 Impact Factor: 4.772)

Abstract

We have previously reported CLIC5A and SLC12A2 variants in two families from Cameroon and Ghana, segregating non-syndromic hearing impairment (NSHI). In this study, biological assays were performed to further functionally investigate the pathogenicity of CLIC5 [c.224T>C; p.(L75P)] and SCL12A2 [c.2935G>A: p.(E979K)] variants. Ectopic expression of the proteins in a cell model shows that compared to wild-type, both the CLIC5A and SLC12A2 variants were overexpressed. The mutant CLIC5A protein appears as aggregated perinuclear bodies while the wild-type protein was evenly distributed in the cytoplasm. Furthermore, cells transfected with the wild-type CLIC5A formed thin membrane filopodia-like protrusions which were absent in the CLIC5A mutant expressing and control cells. On the other hand, the wild-type SLC12A2 expressing cells had an axon-like morphology which was not observed in the mutant expressing and control cells. A network analysis revealed that CLIC5A can interact with at least eight proteins at the base of the stereocilia. This study has generated novel biological data associated with the pathogenicity of targeted variants in CLIC5A and SLC12A2, found in two African families, and therefore expands our understanding of their pathobiology in hearing impairment.

Hearing loss in Africa: current genetic profile

Adadey SM, Wonkam-Tingang E, Aboagye ET, Quaye O, **Awandare GA**, Wonkam A (2021)

[Human Genetics](#) (2023 Impact Factor: 3.767)

Abstract

Hearing impairment (HI) is highly heterogeneous with over 123 associated genes reported to date, mostly from studies among Europeans and Asians. Here, we performed a systematic review of literature on the genetic profile of HI in Africa. The study protocol was registered on PROSPERO, International Prospective Register of Systematic Reviews with the registration number "CRD42021240852". Literature search was conducted on PubMed, Scopus, Africa-Wide Information, and Web of Science databases. A total of 89 full-text records was selected and retrieved for data extraction and analyses. We found reports from only 17/54 (31.5%) African countries. The majority (61/89; 68.5%) of articles were from North Africa, with few reports found from sub-Saharan Africa. The most common method used in these publications was targeted gene sequencing ($n = 66/111$; 59.5%), and only 13.5% ($n = 15/111$) used whole-exome sequencing. More than half of the studies were performed in families segregating HI ($n = 51/89$). *GJB2* was the most investigated gene, with *GJB2*: p.(R143W) founder variant only reported in Ghana, while *GJB2*: c.35delG was common in North African countries. Variants in *MYO15A* were the second frequently reported in both North and Central Africa, followed by *ATP6V1B1* only reported from North Africa. Usher syndrome was the main syndromic HI molecularly investigated, with variants in five genes reported: *USH2A*, *USH1G*, *USH1C*, *MYO7A*, and *PCDH15*. *MYO7A*: p.(P1780S) founder variant was reported as the common Usher syndrome variant among Black South Africans. This review provides the most comprehensive data on HI gene variants in the largely under-investigated African populations. Future exomes studies particularly in multiplex families will likely provide opportunities for the discovery of the next sets of novel HI genes, and well as unreported variants in known genes to further our understanding of HI pathobiology, globally.

Further confirmation of the association of SLC12A2 with non-syndromic autosomal-dominant hearing impairment

Adadey SM, Schrauwen I, Aboagye ET, Bharadwaj T, Esoh KK, Basit S, Acharya A, Nouel-Saied LM, Liaqat K, Wonkam-Tingang E, Mowla S, **Awandare GA**, Ahmad W, Leal SM, Wonkam A (2021)

[Journal of Human Genetics](#) (2023 Impact Factor: 3.767)

Abstract

Congenital hearing impairment (HI) is genetically heterogeneous making its genetic diagnosis challenging. Investigation of novel HI genes and variants will enhance our understanding of the molecular mechanisms and to aid genetic diagnosis. We performed exome sequencing and analysis using DNA samples from affected members of two large families from Ghana and Pakistan, segregating autosomal-dominant (AD) non-syndromic HI (NSHI). Using in silico approaches, we modeled and evaluated the effect of the likely pathogenic variants on protein structure and function. We identified two likely pathogenic variants in *SLC12A2*, c.2935G>A:p.(E979K) and c.2939A>T:p.(E980V), which segregate with NSHI in a Ghanaian and Pakistani family, respectively. *SLC12A2* encodes an ion transporter crucial in the homeostasis of the inner ear endolymph and has recently been reported to be implicated in syndromic and non-syndromic HI. Both variants were mapped to alternatively spliced exon 21 of the *SLC12A2* gene. Exon 21 encodes for 17 residues in the cytoplasmatic tail of SLC12A2, is highly conserved between species, and preferentially expressed in cochlear tissues. A review of previous studies and our current data showed that out of ten families with either AD non-syndromic or syndromic HI, eight (80%) had variants within the 17 amino acid residue region of exon 21 (48 bp), suggesting that this alternate domain is critical to the transporter activity in the inner ear. The genotypic spectrum of *SLC12A2* was expanded and the involvement of *SLC12A2* in ADNSHI was confirmed. These results also demonstrate the role that *SLC12A2* plays in ADNSHI in diverse populations including sub-Saharan Africans.

Investigations of Kidney Dysfunction-Related Gene Variants in Sickle Cell Disease Patients in Cameroon (Sub-Saharan Africa)

Ngo-Bitoungui, VJ, Belinga, S, Mnika, K, Masekoameng, T, Nembaware, V, Essomba, RG, Ngo-Sack, F, **Awandare, GA**, Mazandu, GK and Wonkam, A (2021)

[Frontiers in Genetics](#) (2023 Impact Factor: 4.772)

Abstract

Background: Renal dysfunctions are associated with increased morbidity and mortality in sickle cell disease (SCD). Early detection and subsequent management of SCD patients at risk for renal failure and dysfunctions are essential, however, predictors that can identify patients at risk of developing renal dysfunction are not fully understood.

Methods: In this study, we have investigated the association of 31 known kidney dysfunctions-related variants detected in African Americans from multi-ethnic genome wide studies (GWAS) meta-analysis, to kidney-dysfunctions in a group of 413 Cameroonian patients with SCD. Systems level bioinformatics analyses were performed, employing protein-protein interaction networks to further interrogate the putative associations.

Results: Up to 61% of these patients had micro-albuminuria, 24% proteinuria, 71% glomerular hyperfiltration, and 5.9% had renal failure. Six variants are significantly associated with the two quantifiable phenotypes of kidney dysfunction (eGFR and crude-albuminuria): *AICF-rs10994860* ($P = 0.02020$), *SYPL2-rs12136063* ($P = 0.04208$), and *APOL1 (G1)-rs73885319* ($P = 0.04610$) are associated with eGFR; and *WNT7A-rs6795744* ($P = 0.03730$), *TMEM60-rs6465825* ($P = 0.02340$), and *APOL1 (G2)-rs71785313* ($P = 0.03803$) observed to be protective against micro-albuminuria. We identified a protein-protein interaction sub-network containing three of these gene variants: *APOL1*, *SYPL2*, and *WNT7A*,

connected to the Nuclear factor NF-kappa-B p105 subunit (NFKB1), revealed to be essential and might indirectly influence extreme phenotypes. Interestingly, clinical variables, including body mass index (BMI), systolic blood pressure, vaso-occlusive crisis (VOC), and haemoglobin (Hb), explain better the kidney phenotypic variations in this SCD population.

Conclusion: This study highlights a strong contribution of haematological indices (Hb level), anthropometric variables (BMI, blood pressure), and clinical events (i.e., vaso-occlusive crisis) to kidney dysfunctions in SCD, rather than known genetic factors. Only 6/31 characterised gene-variants are associated with kidney dysfunction phenotypes in SCD samples from Cameroon. The data reveal and emphasise the urgent need to extend GWAS studies in populations of African ancestries living in Africa, and particularly for kidney dysfunctions in SCD.

Blood donor variability is a modulatory factor for *P. falciparum* invasion phenotyping assays

Thiam LG, Nyarko PB, Kusi KA, Niang M, Aniweh Y, and **Awandare GA** (2021)

[Scientific Reports](#) (2023 Impact Factor: 4.996)

Abstract

Human erythrocytes are indispensable for *Plasmodium falciparum* development. Unlike other eukaryotic cells, there is no existing erythroid cell line capable of supporting long-term *P. falciparum* in vitro experiments. Consequently, invasion phenotyping experiments rely on erythrocytes of different individuals. However, the contribution of the erythrocytes variation in influencing invasion rates remains unknown, which represents a challenge for conducting large-scale comparative studies. Here, we used erythrocytes of different blood groups harboring different hemoglobin genotypes to assess the relative contribution of blood donor variability in *P. falciparum* invasion phenotyping assays. For each donor, we investigated the relationship between parasite invasion phenotypes and erythrocyte phenotypic characteristics, including the expression levels of surface receptors (e.g. the human glycophorins A and C, the complement receptor 1 and decay accelerating factor), blood groups (e.g. ABO/Rh system), and hemoglobin genotypes (e.g. AA, AS and AC). Across all donors, there were significant differences in invasion efficiency following treatment with either neuraminidase, trypsin or chymotrypsin relative to the control erythrocytes. Primarily, we showed that the levels of key erythrocyte surface receptors and their sensitivity to enzyme treatment significantly differed across donors. However, invasion efficiency did not correlate with susceptibility to enzyme treatment or with the levels of the selected erythrocyte surface receptors. Furthermore, we found no relationship between *P. falciparum* invasion phenotype and blood group or hemoglobin genotype. Altogether, our findings demonstrate the need to consider erythrocyte donor uniformity and anticipate challenges associated with blood donor variability in early stages of large-scale study design.

HIV Viremia Is Associated With APOL1 Variants and Reduced JC-Viruria

Kruzel-Davila E, Sankofi BM, Kubi Amos-Abanyie E, Ghansah A, Nyarko A, Agyemang S, **Awandare GA**, Szwarcwort-Cohen M, Reiner-Benaim A, Hijazi B, Ulasi I, Raji YR, Boima V, Osafo C, May Adabayeri V, Matekole M, Olanrewaju TO, Ajayi S, Mamven M, Antwi S, Ademola AD, Plange-Rhule J, Arogundade F, Akyaw PA, Winkler CA, Salako BL, Ojo A, Skorecki K, Adu D (2021)

[Frontiers of Medicine](#) (2023 Impact Factor: 9.927)

Abstract

Variants in the *Apolipoprotein L1* (*APOL1*) gene (G1-rs60910145, rs73885319, G2-rs71785313) are common in Africans and in individuals of recent African ancestry and are associated with an increased risk of non-diabetic chronic kidney disease (CKD) and in particular of HIV associated nephropathy (HIVAN). In light of the significantly increased risk of HIVAN in carriers of two *APOL1* risk alleles, a role in HIV infectivity has been postulated in the mechanism of *APOL1* associated kidney disease. Herein, we aim to explore the association between HIV viremia and *APOL1* genotype. In addition, we investigated interaction between BK and JC viruria, CKD and HIV viremia. A total of 199 persons living with HIV/AIDS (comprising 82 CKD cases and 117 controls) from among the participants in the ongoing Human Heredity and Health in Africa (H3Africa) Kidney Disease Research Network case control study have been recruited. The two *APOL1* renal risk alleles (RRA) genotypes were associated with a higher risk of CKD (OR 12.6, 95% CI 3.89-40.8, $p < 0.0001$). Even a single *APOL1* RRA was associated with CKD risk (OR 4.42, 95% CI 1.49-13.15, $p = 0.007$). The 2 *APOL1* RRA genotypes were associated with an increased probability of having HIV viremia (OR 2.37 95% CI 1.0-5.63, $p = 0.05$). HIV viremia was associated with increased CKD risk (OR 7.45, 95% CI 1.66-33.35, $P = 0.009$) and with a significant reduction of JC virus urine shedding (OR 0.35, 95% CI 0.12-

0.98, $p = 0.046$). In contrast to prior studies, JC viruria was not associated with CKD but was restricted in patients with HIV viremia, regardless of CKD status. These findings suggest a role of *APOL1* variants in HIV infectivity and emphasize that JC viruria can serve as biomarker for innate immune system activation.

Keywords: APOL1; BK viruria; HIV viremia; JC viruria; innate immune; kidney disease.

Sickle Cell Disease Genomics of Africa (SickleGenAfrica) Network: ethical framework and initial qualitative findings from community engagement in Ghana, Nigeria and Tanzania

Anie KA, Olayemi E, Paintsil V, Owusu-Dabo E, Adeyemo TA, Sani MU, Galadanci NA, Nnodu O, Tluway F, Adjei DN, Mensah P, Sarfo-Antwi J, Nwokobia H, Gambo A, Benjamin A, Salim A, Osae-Larbi JA, Ofori-Acquah SF; **SickleGenAfrica Network** (2021)

[BMJ Open](#) (2023 Impact Factor: 3.006)

Abstract

Objectives: To provide lay information about genetics and sickle cell disease (SCD) and to identify and address ethical issues concerning the Sickle Cell Disease Genomics of Africa Network covering autonomy and research decision-making, risk of SCD complications and organ damage, returning of genomic findings, biorepository, data sharing, and healthcare provision for patients with SCD.

Design: Focus groups using qualitative methods.

Setting: Six cities in Ghana, Nigeria and Tanzania within communities and secondary care.

Participants: Patients, parents/caregivers, healthcare professionals, community leaders and government healthcare representatives.

Results: Results from 112 participants revealed similar sensitivities and aspirations around genomic research, an inclination towards autonomous decision-making for research, concerns about biobanking, anonymity in data sharing, and a preference for receiving

individual genomic results. Furthermore, inadequate healthcare for patients with SCD was emphasised.

Conclusions: Our findings revealed the eagerness of patients and parents/caregivers to participate in genomics research in Africa, with advice from community leaders and reassurance from health professionals and policy-makers, despite their apprehensions regarding healthcare systems.

Breast cancer in sub-Saharan Africa: The current state and uncertain future

Anyigba CA, **Awandare GA**, & Paemka L (2021)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

Breast cancer is the commonest cause of global cancer-related deaths in women and a public health burden in sub-Saharan Africa (SSA). Although the disease incidence in SSA seems lower, mortality rates are disproportionately high in comparison to high-income countries. The global disease burden is growing, with SSA reporting the majority of cases; however, the dearth of information results in insufficient data which is barely representative of the actual disease burden in this population. Future incidence predictions assign the subregion with a majority of the cases and associated deaths. Breast cancer presents with racial and ethnic variations, and available evidence suggests geographical diversity and persistent risk factors that have barely been explored in SSA. Breast cancer is a complex genetic disease, but the genetic risk factors in the extant African population, which is the most genetically diverse population, is scant and of low quality. This review focuses on the burden, prevalence, detection, treatment, survival, biology, as well as risk factors, and reinforces the need for breast cancer-associated risk factor investigation and population-specific studies in SSA.

Analysis of *Plasmodium falciparum* Rh2b deletion polymorphism across different transmission areas

Aniweh, Y., Suurbaar, J., Morang'a, C. M., Nyarko, P. B., Wright, K. E., Kusi, K. A., Ansah, F., Kyei-Baafour, E., Quansah, E., Asante, J., Thiam, L. G., Higgins, M. K., & **Awandare, G. A** (2020)

[Scientific Reports](#) (2023 Impact Factor: 4.996)

Abstract

Despite significant progress in controlling malaria, the disease remains a global health burden. The intricate interactions the parasite *Plasmodium falciparum* has with its host allows it to grow and multiply in human erythrocytes. The mechanism by which *P. falciparum* merozoites invade human erythrocytes is complex, involving merozoite proteins as well as erythrocyte surface proteins. Members of the *P. falciparum* reticulocyte binding-like protein homolog (PfRh) family of proteins play a pivotal role in merozoite invasion and hence are important targets of immune responses. Domains within the PfRh2b protein have been implicated in its ability to stimulate natural protective antibodies in patients. More specifically, a 0.58 kbp deletion, at the C-terminus has been reported in high frequencies in Senegalese and Southeast Asian parasite populations, suggesting a possible role in immune evasion. We analysed 1218 *P. falciparum* clinical isolates, and the results show that this deletion is present in Ghanaian parasite populations (48.5% of all isolates), with Kintampo (hyper-endemic, 53.2%), followed by Accra (Hypo-endemic, 50.3%), Cape Coast (meso-endemic, 47.9%) and Sogakope (meso-endemic, 43.15%). Further analysis of parasite genomes stored in the MalariaGEN database revealed that the deletion variant was common across transmission areas globally, with an overall frequency of about 27.1%. Interestingly, some parasite isolates possessed mixed PfRh2b deletion and full-length alleles. We further showed that levels of antibodies to the domain of PfRh2 protein were similar to antibody levels of PfRh5, indicating it is less recognized by the immune system.

GJB4 and GJC3 variants in non-syndromic hearing impairment in Ghana

Adadey SM, Esoh KK, Quaye O, Amedofu GK, **Awandare GA** & Wonkam A (2020)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

The contribution of *GJB4* and *GJC3* gene variants to hearing impairment in Africa has not yet been studied. Here, we investigated the contribution of these genes to autosomal recessive non-syndromic hearing impairment in Ghanaian children. Hearing-impaired children from 141 simplex and 59 multiplex families were enrolled from 11 schools for the deaf in Ghana. The coding regions of *GJB4* and *GJC3* were amplified, sequenced, and analyzed for the study participants previously found to be negative for *GJB2* and *GJB6* variants. Seven *GJB4* and one *GJC3* variants were identified. One out of the seven *GJB4* variants was classified as likely pathogenic, while the others were either benign or synonymous. The likely pathogenic variant (p.Asn119Thr/rs190460237) was predicted to be likely associated with hearing impairment. We modeled the wild-type and mutant proteins of this variant (p.Asn119Thr) to evaluate the effect of the mutation on protein structure and ligand-binding properties. The mutant and not the wild type had the potential to bind N-Ethyl-5'-Carboxamido Adenosine (DB03719) which was due to a slight structural change that was observed. No clinically relevant variant was identified in the *GJC3* gene. We report for the first time a likely pathogenic *GJB4* variant that may be associated with non-syndromic hearing impairment in Ghana; the finding will add to the body of evidence of the contribution of *GJB4* to hearing impairment cases around the world.

Enhancing Genetic Medicine: Rapid and Cost-Effective Molecular Diagnosis for a GJB2 Founder Mutation for Hearing Impairment in Ghana

Adadey, S.M., Tingang Wonkam, E., Twumasi Aboagye, E., Quansah, D., Asante-Poku, A., Quaye, O., Amedofu, G.K., **Awandare, G.A.**, Wonkam, A (2020)

[Genes](#) (2023 Impact Factor: 4.141)

Abstract

In Ghana, gap-junction protein Beta 2 (*GJB2*) variants account for about 25.9% of familial hearing impairment (HI) cases. The *GJB2*-p.Arg143Trp (NM_004004.6:c427C>T/OMIM: 121011.0009/rs80338948) variant remains the most frequent variant associated with congenital HI in Ghana, but has not yet been investigated in clinical practice. We therefore sought to design a rapid and cost-effective test to detect this variant. We sampled 20 hearing-impaired and 10 normal hearing family members from 8 families segregating autosomal recessive non syndromic HI. In addition, a total of 111 unrelated isolated individuals with HI were selected, as well as 50 normal hearing control participants. A restriction fragment length polymorphism (RFLP) test was designed, using the restriction enzyme NciI optimized and validated with Sanger sequencing, for rapid genotyping of the common *GJB2*-p.Arg143Trp variant. All hearing-impaired participants from 7/8 families were homozygous positive for the *GJB2*-p.Arg143Trp mutation using the NciI-RFLP test, which was confirmed with Sanger sequencing. The investigation of 111 individuals with isolated non-syndromic HI that were previously Sanger sequenced found that the sensitivity of the *GJB2*-p.Arg143Trp NciI-RFLP testing was 100%. All the 50 control subjects with normal hearing were found to be negative for the variant. Although the test is extremely valuable, it is not 100% specific because it cannot differentiate between other mutations at the recognition site of the restriction

enzyme. The *GJB2*-p.Arg143Trp NciI-RFLP-based diagnostic test had a high sensitivity for genotyping the most common *GJB2* pathogenic and founder variant (p.Arg143Trp) within the Ghanaian populations. We recommend the adoption and implementation of this test for hearing impairment genetic clinical investigations to complement the newborn hearing screening program in Ghana. The present study is a practical case scenario of enhancing genetic medicine in Africa.

Keywords: GJB2-p.R143W; Ghana; NciI-RFLP; hearing impairment; rapid diagnostic test.

Connexin Genes Variants Associated with Non-Syndromic Hearing Impairment: A Systematic Review of the Global Burden

Adadey SM, Wonkam-Tingang E, Twumasi Aboagye E, Nayo-Gyan DW, Boatemaa Ansong M, Quaye O, **Awandare GA**, & Wonkam A. (2020)

[Life \(Basel\)](#) (2023 Impact Factor: 3.251).

Abstract

Mutations in connexins are the most common causes of hearing impairment (HI) in many populations. Our aim was to review the global burden of pathogenic and likely pathogenic (PLP) variants in connexin genes associated with HI. We conducted a systematic review of the literature based on targeted inclusion/exclusion criteria of publications from 1997 to 2020. The databases used were PubMed, Scopus, Africa-Wide Information, and Web of Science. The protocol was registered on PROSPERO, the International Prospective Register of Systematic Reviews, with the registration number "CRD42020169697". The data extracted were analyzed using Microsoft Excel and SPSS version 25 (IBM, Armonk, New York, United States). A total of 571 independent studies were retrieved and considered for data extraction with the majority of studies (47.8% ($n = 289$)) done in Asia. Targeted sequencing was found to be the most common technique used in investigating connexin gene mutations. We identified seven connexin genes that were associated with HI, and *GJB2* (520/571 publications) was the most studied among the seven. Excluding PLP in *GJB2*, *GJB6*, and *GJA1* the other connexin gene variants (thus *GJB3*, *GJB4*, *GJC3*, and *GJC1* variants) had conflicting association with HI.

Biallelic *GJB2* PLP variants were the most common and widespread variants associated with non-syndromic hearing impairment (NSHI) in different global populations but absent in most African populations. The most common *GJB2* alleles found to be predominant in specific populations include; p.Gly12ValfsTer2 in Europeans, North Africans, Brazilians, and Americans; p.V37I and p.L79Cfs in Asians; p.W24X in Indians; p.L56Rfs in Americans; and the founder mutation p.R143W in Africans from Ghana, or with putative Ghanaian ancestry. The present review suggests that only *GJB2* and *GJB3* are recognized and validated HI genes. The findings call for an extensive investigation of the other connexin genes in many populations to elucidate their contributions to HI, in order to improve gene-disease pair curations, globally.

Keywords: [connexin](#); [gap junction protein](#); [gene variant](#); ***GJB2***; [systematic review](#)

Screening for GJB2-R143W-Associated Hearing Impairment: Implications for Health Policy and Practice in Ghana

Samuel M Adadey, Osbourne Quaye, Geoffrey K Amedofu , Gordon A Awandare, Ambroise Wonkam (2020)

[Public Health Genomics](#) (2023 Impact Factor: 2.132)

Abstract

Genetic factors significantly contribute to the burden of hearing impairment (HI) in Ghana as there is a high carrier frequency (1.5%) of the connexin 26 gene founder variant *GJB2*-R143W in the healthy Ghanaian population. *GJB2*-R143W mutation accounts for nearly 26% of causes in families segregating congenital non-syndromic HI. With HI associated with high genetic fitness, this indicates that Ghana will likely sustain an increase in the number of individuals living with inheritable HI. There is a universal newborn hearing screening (UNHS) program in Ghana. However, this program does not include genetic testing. Adding genetic testing of *GJB2*-R143W mutation for the population, prenatal and neonatal stages may lead to guiding genetic counseling for individual and couples, early detection of HI for at-risk infants, and improvement of medical management, including speech therapy and audiologic intervention, as well as provision of the needed social service to enhance parenting and education for children with HI. Based on published research on the genetics of HI in Ghana, we recommend that the UNHS program should include genetic screening for the *GJB2*-R143W gene variant for newborns who did not pass the initial UNHS tests. This will require an upgrade and resourcing of public health infrastructures to implement the rapid and cost-effective *GJB2*-R143W testing, followed by appropriate genetic and anticipatory guidance for medical care.

Keywords: [Health policy](#), [GJB2-R143W founder mutation](#), [Hearing impairment](#), [Newborn screening](#), [Ghana](#)

GJB2 and GJB6 Mutations in Non-Syndromic Childhood Hearing Impairment in Ghana

Adadey, S. M., Manyisa, N., Mnika, K., De Kock, C., Nembaware, V., Quaye, S., Amedofu, G. K., **Awandare, G.** & Wonkam, A (2019)

[Frontiers in Genetics](#) (2023 Impact Factor: 4.772)

Abstract

Our study aimed to investigate *GJB2* (connexin 26) and *GJB6* (connexin 30) mutations associated with non-syndromic childhood hearing impairment (HI) as well as the environmental causes of HI in Ghana. Medical reports of 1,104 students attending schools for the deaf were analyzed. Families segregating HI, as well as isolated cases of HI of putative genetic origin were recruited. DNA was extracted from peripheral blood followed by Sanger sequencing of the entire coding region of *GJB2*. Multiplex PCR and Sanger sequencing were used to analyze the prevalence of *GJB6*-D3S1830 deletion. Ninety-seven families segregating HI were identified, with 235 affected individuals; and a total of 166 isolated cases of putative genetic causes, were sampled from 11 schools for the deaf in Ghana. The environmental factors, particularly meningitis, remain a major cause of HI impairment in Ghana. The male/female ratio was 149. Only 59.6% of the patients had their first comprehensive HI test between 6 to 11 years of age. Nearly all the participants had sensorineural HI (99.5%; $n = 639$). The majority had pre-lingual HI (68.3%, $n = 754$), of which 92.8% were congenital. Pedigree analysis suggested autosomal recessive inheritance in 96.9% of the familial cases. *GJB2*-R143W mutation, previously reported as founder a mutation in Ghana accounted for 25.9% (21/81) in the homozygous state in familial cases, and in 7.9% (11/140) of non-familial non-syndromic congenital HI cases, of putative genetic origin. In a control population without HI, we found a prevalent of *GJB2*-R143W carriers of 14% (2/145), in the heterozygous state. No *GJB6*-D3S1830 deletion was identified in any of the HI patients. *GJB2*-R143W mutation accounted

for over a quarter of familial non-syndromic HI in Ghana and should be investigated in clinical practice. The large connexin 30 gene deletion (GJB6-D3S1830 deletion) does not account for of congenital non-syndromic HI in Ghana. There is a need to employ next generation sequencing approaches and functional genomics studies to identify the other genes involved in most families and isolated cases of HI in Ghana.

Keywords: Africa; *GJB2* and *GJB6*; Ghana; genetics; hearing impairment.

Validation of two parent-reported autism spectrum disorders screening tools M-CHAT-R and SCQ in Bamako, Mali

Sangare M, Toure HB, Toure A, Karembé A, Dolo H, Coulibaly YI, Kouyate M, Traore K, Diakité SA, Coulibaly S, Togora A, Guinto CO, **Awandare GA**, Doumbia S, Diakite M, Geschwind DH (2019)

[eNeurologicalSci](#) (2023 Impact Factor: 0.571)

Abstract

Background

Early screening is crucial for early [autism spectrum disorders](#) (ASD) diagnosis and intervention. ASD screening tools have mostly been constructed based on the Western cultural context. We hypothesized that their use in Mali may require a prior validation.

Objective

To validate the modified checklist for autism in toddlers-Revised (M-CHAT-R) and the social communication questionnaire (SCQ) in the Malian sociocultural context for ASD screening.

Study design

We administered M-CHAT-R and SCQ in 947 toddlers aged 16–30 months old at the district and community health centers in Bamako and 120 patients (60 autistic and 60 age and sex matched controls) aged ≥ 4 years old at the psychiatry department in Bamako. Toddlers at moderate to high risk of ASD underwent M-CHAT-R/F and clinical evaluation by an ASD multidisciplinary team. M-CHAT-R and SCQ were evaluated for cultural appropriateness by Malian anthropologists. The sensitivity, specificity, PPV, NPV were determined for both M-CHAT-R and SCQ. Health professionals have been trained during ASD seminary on how to use M-CHAT-R and SCQ for ASD screening in Bamako.

Results

We found for the M-CHAT-R a sensitivity of 50%, a specificity of 100%, a PPV of 100% and a NPV of 87%. The SCQ had a sensitivity of 71%, a specificity of 72%, a PPV of 73% and a NPV of 70%. We have found four out of 20 items on the M-CHAT-R that were culturally inappropriate in the Malian context.

Discussion

M-CHAT-R and SCQ can be used for early autism screening in Mali. In the future, we plan to train a descent number of Malian physicians in chief and pediatricians at the district hospitals across the country to integrate the early ASD screening into the national health system.

Conclusion

M-CHAT-R has a perfect specificity and SCQ a fair diagnostic accuracy for ASD in Mali.

SMIM1 at a glance; discovery, genetic basis, recent progress and perspectives

Aniweh Y, Nyarko PB, Quansah E, Thiam LG, **Awandare GA** (2019)

[Parasite Epidemiol Control](#) (2023 Impact Factor: 0.625)

Abstract

Recent elucidation of the genetic basis of the Vel blood group system has offered the field of [blood transfusion](#) medicine an additional consideration in determining the causes of hemolytic reactions after a patient is transfused. The identification of the [SMIM1](#) gene to be responsible for the Vel blood group allows molecular based tools to be developed to further dissect the function of this antigen. Genetic signatures such as the homozygous 17 bp deletion and the heterozygous 17 bp deletion in combination with other [single nucleotide polymorphisms](#) (SNPs) and [insertion sequences](#) regulate the expression level of the gene. With this knowledge, it is now possible to study this antigen in-depth.

Comparison of genomic signatures of selection on *Plasmodium falciparum* between different regions of a country with high malaria endemicity

Duffy, C. W., Assefa, S. A., MacInnis, B., Abugri, J., Amoako, N., Owusu-Agyei, S., Anyorigiya, T., Kwiatkowski, D. P., Conway, D. J. & **Awandare, G. A.** (2015)

[BMC Genomics](#) (2023 Impact Factor: 4.558)

Abstract

Background

Genome wide sequence analyses of malaria parasites from widely separated areas of the world have identified contrasting population structures and signatures of selection. To compare relatively closely situated but ecologically contrasting regions within an endemic African country, population samples of *Plasmodium falciparum* clinical isolates were collected in Ghana from Kintampo in the central forest-savannah area, and Navrongo in a drier savannah area ~350 km to the north with more seasonally-restricted transmission. Parasite DNA was sequenced and paired-end reads mapped to the *P. falciparum* reference genome.

Results

High coverage genome wide sequence data for 85 different clinical isolates enabled analysis of 121,712 single nucleotide polymorphisms (SNPs). The local populations had similar proportions of mixed genotype infections, similar SNP allele frequency distributions, and eleven chromosomal regions had elevated integrated haplotype scores (iHS) in both. A between-population Rsb metric comparing extended haplotype homozygosity indicated a stronger signal within Kintampo for one of these regions (on chromosome 14) and in Navrongo

for two of these regions (on chromosomes 10 and 13). At least one gene in each of these identified regions is a potential target of locally varying selection. The candidates include genes involved in parasite development in mosquitoes, members of variant-expressed multigene families, and a leading vaccine-candidate target of immunity.

Conclusions

Against a background of very similar population structure and selection signatures in the *P. falciparum* populations of Ghana, three narrow genomic regions showed evidence indicating local differences in historical timing or intensity of selection. Sampling of closely situated populations across heterogeneous environments has potential to refine the mapping of important loci under temporally or spatially varying selection.

Macrophage migration inhibitory factor (MIF) promoter polymorphisms and susceptibility to severe malarial anemia

Awandare, G. A., Martinson, J. J., Were, T., Ouma, T., Davenport, G. C., Ong'echa, J. M., Wang, W. K., Leng, L., Ferrell, R. E., Bucala, R., & Perkins, D. J. (2009)

[Journal of Infectious Diseases](#) (2022 Impact Factor: 7.759)

Abstract

Background

Severe malarial anemia (SMA) resulting from *Plasmodium falciparum* infection is one of the leading causes of childhood mortality in sub-Saharan Africa. The innate immune mediator macrophage migration inhibitory factor (MIF) plays a critical role in the pathogenesis of SMA

Methods

To investigate the influence of MIF genetic variation on susceptibility to SMA, haplotypes of the *MIF* -173G/C and -794CATT₅₋₈ polymorphisms were examined in a cohort of Kenyan children

Results

A statistically significant relationship between increasing frequencies of longer CATT repeats at -794 and increasing severity of malarial anemia was observed. In addition, there was a strong association between lower MIF concentrations and longer CATT repeats. Multivariate logistic regression analyses demonstrated that the 6G haplotype (ie, *MIF* -794CATT₆/-173G) was associated with protection against SMA, whereas carriers of the 7C or 8C haplotype

had increased risk of developing SMA. Furthermore, carriers of the 7C or 8C haplotype had reduced plasma MIF levels during acute disease

Conclusions

The findings demonstrate that variation in the MIF promoter influences susceptibility to SMA and peripheral MIF production. However, the *MIF* –173 and –794 polymorphisms appear to have both independent and interactive effects on different measures of disease severity, suggesting that MIF plays a complex role in malarial pathogenesis

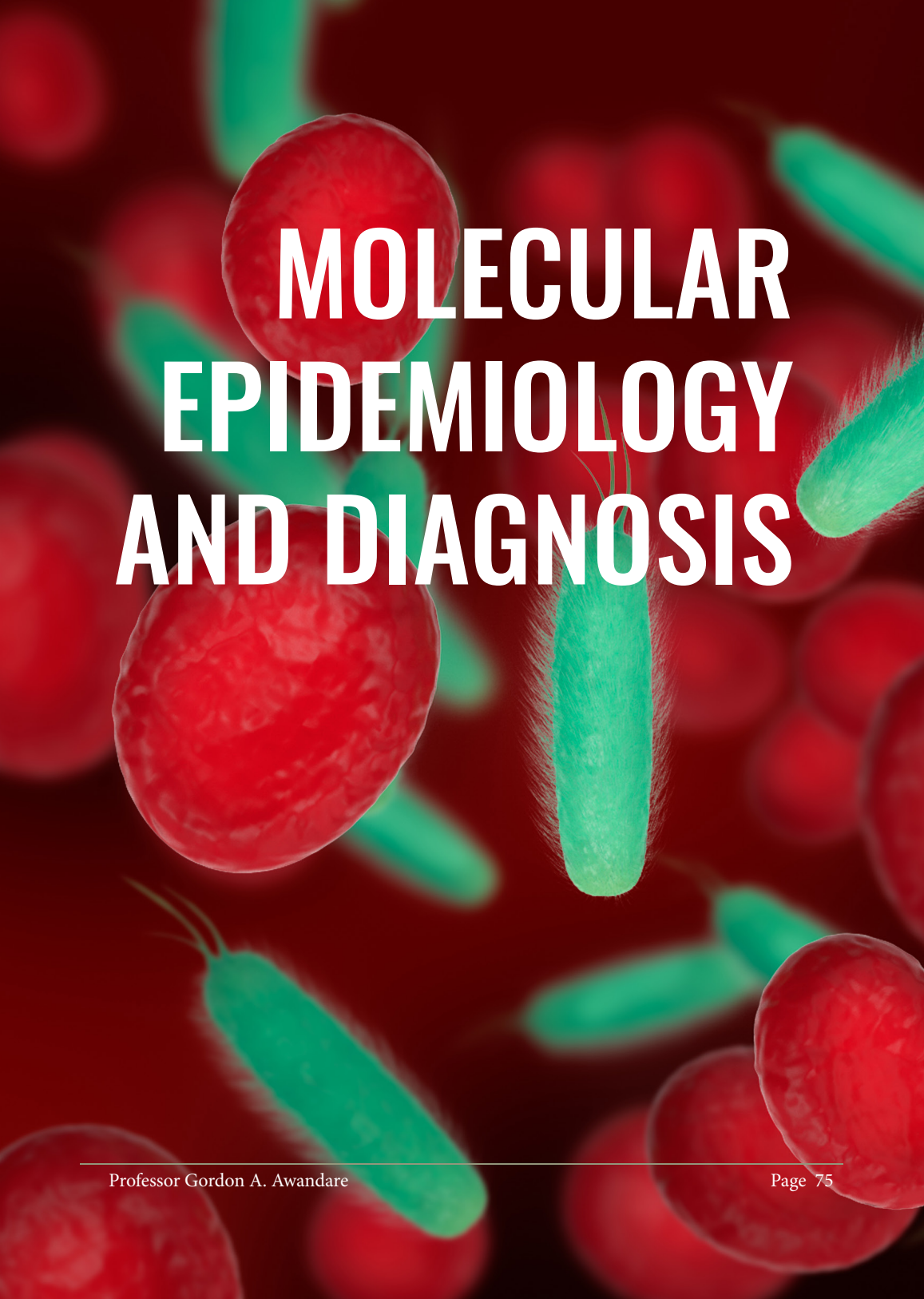
Polymorphic Variability in the Interleukin (IL)-1beta Promoter Conditions Susceptibility to Severe Malarial Anemia and Functional Changes in IL-1beta Production

Ouma, C., Davenport, G. C., **Awandare, G. A.**, Keller, C. C., Were, T., Otieno, M. F., Vulule, J. M., Martinson, J., Ong'echa, J. M., Ferrell, R. E., & Perkins, D. J. (2008)

[Journal of Infectious Diseases](#) (2022 Impact Factor: 7.759)

Abstract

Interleukin (IL)-1 Beta is a cytokine released as part of the innate immune response to *Plasmodium falciparum*. Because the role played by IL-1 Beta polymorphic variability in conditioning the immunopathogenesis of severe malarial anemia (SMA) remains undefined, relationships between IL-1 Beta promoter variants (-31C/T and -511A/G), SMA (hemoglobin [Hb] level <6.0 g/dL), and circulating IL-1 Beta levels were investigated in children with parasitemia ($n = 566$) from western Kenya. The IL-1 Beta promoter haplotype -31C/-511A (CA) was associated with increased risk of SMA (Hb level <6.0 g/dL; odds ratio [OR], 1.98 [95% confidence interval {CI}, 1.55–2.27]; $P < .05$) and reduced circulating IL-1 Beta levels ($P < .05$). The TA (-31T/-511A) haplotype was nonsignificantly associated with protection against SMA (OR, 0.52 [95% CI, 0.18–1.16]; $P < .11$) and elevated IL-1 Beta production ($P < .05$). Compared with the non-SMA group, children with SMA had significantly lower IL-1 Beta levels and nonsignificant elevations in both IL-1 receptor antagonist (IL-1Ra) and the ratio of IL-1Ra to IL-1 Beta. The results presented demonstrate that variation in IL-1 Beta promoter conditions susceptibility to SMA and functional changes in circulating IL-1 Beta levels.

The background of the slide is a dark red color, overlaid with numerous microscopic images of bacteria. There are two primary types of bacteria visible: red, spherical (cocci) and green, rod-shaped (bacilli). Some of the green rods have fine, hair-like structures (flagella) extending from them. The bacteria are scattered across the frame, with some in sharp focus and others blurred, creating a sense of depth. The title text is centered over this background.

MOLECULAR EPIDEMIOLOGY AND DIAGNOSIS

Pf7: an open dataset of *Plasmodium falciparum* genome variation in 20,000 worldwide samples

MalariaGEN; Abdel Hamid MM, Abdelraheem MH, Acheampong DO, Ahoudi A, Ali M, Almagro-Garcia J, Amambua-Ngwa A, Amaratunga C, Amenga-Etego L, Andagalu B, Anderson T, Andrianaranjaka V, Aniebo I, Aninagyei E, Ansah F, Ansah PO, Apinjoh T, Arnaldo P, Ashley E, Auburn S, **Awandare GA**, Ba H, Baraka V, Barry A, Bejon P, Bertin GI, Boni MF, Borrmann S, Bousema, Mandara CI, Marfurt J, Marsh K, Maude RJ, Mayxay M... (2023)

[Wellcome Open Research](#) (2023 Impact Factor: 1.777)

Abstract

We describe the MalariaGEN Pf7 data resource, the seventh release of *Plasmodium falciparum* genome variation data from the MalariaGEN network. It comprises over 20,000 samples from 82 partner studies in 33 countries, including several malaria endemic regions that were previously underrepresented. For the first time we include dried blood spot samples that were sequenced after selective whole genome amplification, necessitating new methods to genotype copy number variations. We identify a large number of newly emerging *crt* mutations in parts of Southeast Asia, and show examples of heterogeneities in patterns of drug resistance within Africa and within the Indian subcontinent. We describe the profile of variations in the C-terminal of the *csp* gene and relate this to the sequence used in the RTS,S and R21 malaria vaccines. Pf7 provides high-quality data on genotype calls for 6 million SNPs and short indels, analysis of large deletions that cause failure of rapid diagnostic tests, and systematic characterisation of six major drug resistance loci, all of which can be freely downloaded from the MalariaGEN website.

Keywords: data resource; genomic epidemiology; genomics; malaria; plasmodium falciparum.

Phenotypic characterization of Ghanaian *P. falciparum* clinical isolates reveals a homogenous parasite population

Thiam LG, Nyarko PB, Ansah F, Niang M, **Awandare GA**, Aniweh Y (2022)

[Frontiers in Immunology](#) (2023 Impact Factor: 8.786)

Abstract

Background: Erythrocyte invasion by *P. falciparum* involves functionally overlapping interactions between the parasite's ligands and the erythrocyte surface receptors. While some *P. falciparum* isolates necessarily engage the sialic acid (SA) moieties of the erythrocytes during the invasion, others use ligands whose binding is independent of SA for successful invasion. Deciphering the major pathway used by *P. falciparum* clinical isolates represent a key step toward developing an efficient blood stage malaria vaccine.

Methods: We collected a total of 156 malaria-infected samples from Ghanaian children aged 2 to 14 years and used a two-color flow cytometry-based invasion assay to assess the invasion phenotype diversity of Ghanaian *P. falciparum* clinical isolates. Anti-human CR1 antibodies were used to determine the relative contribution of the PfRh4-CR1 interaction in the parasites invasion phenotype and RT-qPCR was used to assess the expression levels of key invasion-related ligands.

Results: Our findings show no clear association between demographic or clinical data and existing reports on the malaria transmission intensity. The complete invasion data obtained for 156 isolates, showed the predominance of SA-independent pathways in Ghanaian clinical isolates. Isolates from Hohoe and Navrongo had the highest diversity in invasion profile. Our data also confirmed that the PfRh4-CR1 mediated alternative pathway is important in Ghanaian clinical isolates. Furthermore, the transcript levels of ten invasion-related genes obtained in the study showed little variations in gene expression profiles within and between parasite populations across sites.

Conclusion: Our data suggest a low level of phenotypic diversity in Ghanaian clinical isolates across areas of varying endemicity and further highlight its importance in the quest for new intervention strategies, such as the investigation of blood-stage vaccine targets, particularly those targeting specific pathways and able to trigger the stimulation of broadly neutralizing invasion antibodies.

A longitudinal two-year survey of the prevalence of trypanosomes in domestic cattle in Ghana by massively parallel sequencing of barcoded amplicons

Ofori JA, Bakari SM, Bah S, Kolugu MK, Aning GK, **Awandare GA**, Carrington M, & Gwira TM (2022)

[PLoS Neglected Tropical Diseases](#) (2022 Impact Factor: 4.781)

Abstract

Background

Animal African Trypanosomiasis (AAT) is one of the most economically important diseases affecting livestock productivity in sub-Saharan Africa. The disease is caused by a broad range of *Trypanosoma* spp., infecting both wild and domesticated animals through cyclical and mechanical transmission. This study aimed to characterize trypanosomes present in cattle at regular intervals over two years in an AAT endemic and a non-endemic region of Ghana.

Methodology/Principal findings

Groups of cattle at Accra and Adidome were selected based on their geographical location, tsetse fly density, prevalence of trypanosomiasis and the breed of cattle available. Blood for DNA extraction was collected at approximately four to five-week intervals over a two-year period. Trypanosome DNA were detected by a sensitive nested PCR targeting the tubulin gene array and massively parallel sequencing of barcoded amplicons. Analysis of the data was a semi-quantitative estimation of infection levels using read counts obtained from the sequencing as a proxy for infection levels. Majority of the cattle were infected with multiple species most of the time [190/259 (73%) at Adidome and 191/324 (59%) at Accra], with *T. vivax* being the most abundant. The level of infection and in particular *T. vivax*, was higher in Adidome, the location with a high density of tsetse flies. The infection level varied

over the time course, the timings of this variation were not consistent and in Adidome it appeared to be independent of prophylactic treatment for trypanosome infection. Effect of gender or breed on infection levels was insignificant.

Conclusions/Significance

Most cattle were infected with low levels of several trypanosome species at both study sites, with *T. vivax* being the most abundant. The measurements of infection over time provided insight to the importance of the approach in identifying cattle that could suppress trypanosome infection over an extended time and may serve as reservoir.

***Helicobacter Pylori* Variants with ABC-Type Tyrosine Phosphorylation Motif in Gastric Biopsies of Ghanaian Patients**

Tagoe EA, **Awandare GA**, Quaye O, Asmah RH, Archampong TN, Osman MA, & Brown CA (2021)

[BioMed Research International](#) (2023 Impact Factor: 3.246)

Abstract

Background: *Helicobacter pylori* pathogenicity and disease severity are determined by the tyrosine phosphorylation motifs of CagA protein. This study is aimed at detecting the presence of *H. pylori* and identifying the CagA tyrosine phosphorylation motifs in Ghanaian patients. **Material and Methods.** A total of 94 archival genomic DNA samples from gastric biopsies were used for the study, and *H. pylori* was detected by amplifying the 16S rRNA gene. The 3-end variable region of the *cagA* gene was amplified, and the entire 3-end was sequenced and translated into amino acids. **Results.** *H. pylori* was detected in 53.2% (50/94) of the samples, and all the detected bacteria harboured the *cagA* gene. Two variants of the bacteria were identified based on the size of the amplified *cagA* gene: 207 bp and 285 bp. The 207 bp and 285 bp variants accounted for 74% and 22%, respectively, and 4% showed both fragments. Translated amino acid sequence of the *cagA* gene showed EPIYA-A, EPIYA-B, and EPIYA-C (ABC type) motifs, indicating the Western variant. The CagA protein C-terminal showed insertion of amino acids in the sequence flanking the EPIYA-A motif at the N-terminal and a complete deletion of the EPIYA-CC and EPIYA-CCC motifs together with the flanking sequences. **Conclusions.** *H. pylori* identified were Western variant (ABC type) with unique amino acid insertions, suggesting unique variants in Ghanaian patients. Further investigation is however required to understand the role of the molecular diversity of the variant in gastric disease outcome.

An open dataset of *Plasmodium falciparum* genome variation in 7,000 worldwide samples

Ahoudi, A, Ali, M, Almagro-Garcia, J, Amambua-Ngwa, A, Amaratunga, C, Amato, R, Amenga-Etego, L, Andagalu, B, Anderson, TJC, Andrianaranjaka, V, Apinjoh, T, Ariani, C, Ashley, EA, Auburn, S, **Awandare, G** et al. (2021)

[Wellcome Open Research](#) (2023 Impact Factor: 1.777)

Abstract

MalariaGEN is a data-sharing network that enables groups around the world to work together on the genomic epidemiology of malaria. Here we describe a new release of curated genome variation data on 7,000 *Plasmodium falciparum* samples from MalariaGEN partner studies in 28 malaria-endemic countries. High-quality genotype calls on 3 million single nucleotide polymorphisms (SNPs) and short indels were produced using a standardised analysis pipeline. Copy number variants associated with drug resistance and structural variants that cause failure of rapid diagnostic tests were also analysed. Almost all samples showed genetic evidence of resistance to at least one antimalarial drug, and some samples from Southeast Asia carried markers of resistance to six commonly-used drugs. Genes expressed during the mosquito stage of the parasite life-cycle are prominent among loci that show strong geographic differentiation. By continuing to enlarge this open data resource we aim to facilitate research into the evolutionary processes affecting malaria control and to accelerate development of the surveillance toolkit required for malaria elimination.

Intrinsic multiplication rate variation and plasticity of human blood stage malaria parasites

Stewart LB, Diaz-Ingelmo O, Claessens A, Abugri J, Pearson RD, Goncalves S, Drury E, Kwiatkowski DP, **Awandare GA** & Conway DJ. (2020)

[Communications Biology](#) (2023 Impact Factor: 6.548)

Abstract

Pathogen multiplication rate is theoretically an important determinant of virulence, although often poorly understood and difficult to measure accurately. We show intrinsic asexual blood stage multiplication rate variation of the major human malaria parasite *Plasmodium falciparum* to be associated with blood-stage infection intensity in patients. A panel of clinical isolates from a highly endemic West African population was analysed repeatedly during five months of continuous laboratory culture, showing a range of exponential multiplication rates at all timepoints tested, mean rates increasing over time. All isolates had different genome sequences, many containing within-isolate diversity that decreased over time in culture, but increases in multiplication rates were not primarily attributable to genomic selection. New mutants, including premature stop codons emerging in a few isolates, did not attain sufficiently high frequencies to substantially affect overall multiplication rates. Significantly, multiplication rate variation among the isolates at each of the assayed culture timepoints robustly correlated with parasite levels seen in patients at clinical presentation, indicating innate parasite control of multiplication rate that contributes to virulence.

High-throughput genotyping assays for identification of glyophorin B deletion variants in population studies

Amuzu DSY, Rockett KA, Leffler EM, Ansah F, Amoako N, Morang'a CM, Hubbart C, Rowlands K, Jeffreys AE, Amenga-Etego LN, Kwiatkowski DP & **Awandare GA** (2020)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

Glycophorins are the most abundant sialoglycoproteins on the surface of human erythrocyte membranes. Genetic variation in glycophorin region of human chromosome 4 (containing *GYP A*, *GYP B*, and *GYP E* genes) is of interest because the gene products serve as receptors for pathogens of major public health interest, including *Plasmodium sp.*, *Babesia sp.*, Influenza virus, *Vibrio cholerae* El Tor Hemolysin, and *Escherichia coli*. A large structural rearrangement and hybrid glycophorin variant, known as *Dantu*, which was identified in East African populations, has been linked with a 40% reduction in risk for severe malaria. Apart from *Dantu*, other large structural variants exist, with the most common being deletion of the whole *GYP B* gene and its surrounding region, resulting in multiple different deletion forms. In West Africa particularly, these deletions are estimated to account for between 5 and 15% of the variation in different populations, mostly attributed to the forms known as DEL1 and DEL2. Due to the lack of specific variant assays, little is known of the distribution of these variants. Here, we report a modification of a previous *GYP B* DEL1 assay and the development of a novel *GYP B* DEL2 assay as high-throughput PCR-RFLP assays, as well as the identification of the crossover/breakpoint for *GYP B* DEL2. Using 393 samples from three study sites in Ghana as well as samples from HapMap and 1000 G projects for validation, we show that our assays are sensitive and reliable for genotyping *GYP B* DEL1 and DEL2. To the best of our knowledge, this is the first report of such high-throughput genotyping assays by PCR-RFLP for identifying specific *GYP B* deletion types in populations. These assays will enable better identification of *GYP B* deletions for large genetic association studies and functional experiments to understand the role of this gene cluster region in susceptibility to malaria and other diseases.

High cases of submicroscopic *Plasmodium falciparum* infections in a suburban population of Lagos, Nigeria

Umunnakwe, F. A, Idowu, E. T, Ajibaye, O, Etoketim, B, Akindele, S, Shokunbi A. O, Otubanjo O. A, **Awandare G. A**, Amambua-Ngwa A, & Oyebola KM (2019)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Asymptomatic malaria parasites are significant sources of infections for onward malaria transmission. Conventional tools for malaria diagnosis such as microscopy and rapid diagnostic test kits (RDT) have relatively low sensitivity, hence the need for alternative tools for active screening of such low-density infections.

Methods

This study tested *var* acidic terminal sequence-based (*var*ATS) quantitative polymerase chain reaction (qPCR) for screening asymptomatic *Plasmodium falciparum* infections among dwellers of a sub-urban community in Lagos, Nigeria. Clinically healthy participants were screened for malaria using microscopy, RDT and *var*ATS qPCR techniques. Participants were stratified into three age groups: 1–5, 6–14 and > 14 years old.

Results

Of the 316 participants screened for asymptomatic malaria infection, 78 (24.68%) were positive by microscopy, 99 (31.33%) were positive by RDT and 112 (35.44%) by *var*ATS qPCR. Participants aged 6–14 years had the highest prevalence of asymptomatic malaria, with geometric means of ~116 parasites/μL and ~6689 parasites/μL as detected by microscopy and *var*ATS, respectively.

Conclusion

This study has revealed high prevalence of asymptomatic malaria in the study population, with *varATS* detecting additional sub-microscopic infections. The highest concentration of asymptomatic malaria was observed among school-age children between 6 and 14 years old. A large-scale screening to identify other potential hotspots of asymptomatic parasites in the country is recommended.

Prevalence of malaria and hepatitis B among pregnant women in Northern Ghana: Comparing RDTs with PCR

Anabire, N. G., Aryee, P. A., Abdul-Karim, A., Abdulai, I. B., Quaye, O., **Awandare, G. A.**, & Helegbe, G. K.

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

Background

High prevalence of malaria and hepatitis B has been reported among pregnant women in Ghana. In endemic areas, the diagnoses of malaria and hepatitis B among pregnant women on antenatal visits are done using histidine-rich protein 2 (HRP2) and hepatitis B surface antigen (HBsAg) rapid diagnostic tests (RDTs), respectively, which are, however, reported to give some false positive results. Also, socio-economic determinants have been drawn from these RDTs results which may have questionable implications. Thus, this study was aimed at evaluating the prevalence of malaria and hepatitis B by comparing RDTs with polymerase chain reaction (PCR) outcomes, and relating the PCR prevalence with socio-economic status among pregnant women in Northern Ghana.

Methods

We screened 2071 pregnant women on their first antenatal visit for *Plasmodium falciparum* and hepatitis B virus (HBV) using HRP2 and HBsAg RDTs, and confirming the infections with PCR. Socio-economic and obstetric information were collected using a pre-tested questionnaire, and associations with the infections were determined using Pearson's chi-square and multinomial logistic regression analyses at a significance level of $p < 0.05$.

Results

The prevalence of the infections by RDTs/PCR was: 14.1%/134% for *P. falciparum* mono-infection, 7.9%/7.5% for HBV mono-infection, and 1.9%/1.7% for *P. falciparum*/HBV co-infection.

No statistical difference in prevalence rates were observed between the RDTs and PCRs ($\chi^2 = 0.119$, $p = 0.73$ for malaria and $\chi^2 = 0.139$, $p = 0.709$ for hepatitis B). Compared with PCRs, the sensitivity/specificity of the RDTs was 97.5%/99.1% and 97.9%/99.4% for HRP2 and HBsAg respectively. Socio-economic status was observed not to influence HBV mono-infection among the pregnant women (educational status: AOR = 0.78, 95% CI = 0.52–1.16, $p = 0.222$; economic status: AOR = 1.07, 95% CI = 0.72–1.56, $p = 0.739$; financial status: AOR = 0.66, 95% CI = 0.44–1.00, $p = 0.052$). However, pregnant women with formal education were at a lower risk for *P. falciparum* mono-infection (AOR = 0.48, 95% CI = 0.32–0.71, $p < 0.001$) and *P. falciparum*/HBV co-infection (AOR = 0.27, 95% CI = 0.11–0.67, $p = 0.005$). Also those with good financial status were also at a lower risk for *P. falciparum* mono-infection (AOR = 0.52, 95% CI = 0.36–0.74, $p < 0.001$).

Conclusion

Our data has shown that, the RDTs are comparable to PCR and can give a representative picture of the prevalence of malaria and hepatitis B in endemic countries. Also, our results support the facts that improving socio-economic status is paramount in eliminating malaria in endemic settings. However, socio-economic status did not influence the prevalence of HBV mono-infection among pregnant women in Northern Ghana.

Detection of dengue virus among children with suspected malaria, Accra, Ghana. *Emerging Infectious Diseases*

Amoako, N., Duodu, S., Dennis, F. E., Bonney, J. H. K., Asante, K. P., Ameh, J., Mosi, L., Hayashi, T., Agbosu, E. E., Pratt, D., Operario, D. J., Fields, B., Liu, J., Houpt, E. R., Armah, G. E., Stoler, J. and **Awandare, G. A.** (2018)

[Emerging Infectious Diseases](#) (2023 Impact Factor: 16.126)

Abstract

We report new molecular evidence of locally acquired dengue virus infections in Ghana. We detected dengue viral RNA among children with suspected malaria by using a multipathogen real-time PCR. Subsequent sequence analysis revealed a close relationship with dengue virus serotype 2, which was implicated in a 2016 outbreak in Burkina Faso.

The accurate diagnosis of nonmalarial febrile illnesses remains a large challenge in many malaria-endemic countries (1). The etiologic agents in this context are often not identified because of nonspecific clinical symptoms and diagnostic limitations (2); for example, of 457 patients in Nigeria who were presumptively treated for malaria, only 3.9% tested positive (3). Because of the decline in malaria transmission over the past decade in many endemic areas, including Ghana, there is a critical need for a comprehensive characterization of the etiology of acute febrile illness (AFI) (4). Dengue virus infections cause symptoms that are similar to those of malaria, and considering the increasing reports of dengue outbreaks in countries neighboring Ghana (5–8), there is an increased need for dengue surveillance.

Evaluation of hematological indices of childhood illnesses in Tamale Metropolis of Ghana

Anabire, N. G, Aryee, P. A., Addo, F., Anaba, F., Kanwugu, O. N., Ankrah, J., **Awandare, G. A.** & Helegbe, G. K. (2018)

[Journal of Clinical and Laboratory Analysis](#) (2023 Impact Factor: 3.124)

Abstract

Background

Although hematological indices cannot in entirety be used to diagnose diseases or defects, the appropriate interpretation of these indices could complement diagnostics such as microscopy and serology for numerous illnesses in children. This study sought to evaluate distinct hematological indices characterizing different childhood illnesses.

Methods

Full blood counts from 150 children (age range from 1 to 15 year) presenting different disease conditions at the Tamale Central Hospital were assessed. The hematological indices were compared between disease categories, and relationships between disease indicators were determined.

Results

The prevalence of the diagnosed childhood illness were: 50.7% malaria, 20.0% diarrhea, 13.3% typhoid fever, 10.0% Sickle Cell Disease (SCD), and 6.0% malaria-typhoid co-infection. Fever was diagnosed in a majority (66.0%) of the children, but was independent of each disease group, ($\chi^2 = 9.18$, $P = .057$). Of the 24 hematological indices analyzed, eight; red blood cell (RBC) ($P < .001$), hemoglobin (Hb) ($P < .001$), mean cell volume (MCV) ($P = .002$), mean cell hemoglobin (MCH) ($P < .001$; lowest and below normal range for SCD), red cell distribution

width (RDW_CV) ($P < .001$), eosinophil percentage [EOS (%)] ($P = .001$), eosinophil number [EOS#] ($P = .002$), and platelets (PLT) ($P = .001$; lowest for malaria) differed significantly across the different disease groups. Levels of Hb and/or MCV were below the normal reference ranges for most of the diagnosed diseases. In addition, low PLT and MCH were respectively distinct for children with malaria and SCD.

Conclusion

Hematological indices including Hb, MCV and PLT, or MCH may be useful indices that could incite further diagnostic tests for malaria or SCD among children in Ghana.

***Plasmodium falciparum* malaria cases detected for prompt treatment by rapid diagnostic tests in the Ho Teaching Hospital of the Volta Region of Ghana**

Dinko, B., Amakpa, E., Kweku, M., Amoah, P., Tampuori, J., Adjuik, M., **Awandare, G. A.**, & Deitsch, K. W (2018)

[Parasite Epidemiology and Control](#) (2023 Impact Factor: 0.625)

Abstract

Background

Prompt diagnosis and effective treatment of malaria cases with efficacious drugs is an important strategy in the management and control of malaria in endemic populations. As part of a study investigating the factors modulating the development of *Plasmodium falciparum* gametocytes in the human host, we assessed the rate of RDT positivity of patients in different departments of the Ho Teaching Hospital and the relation with age and anaemia.

Materials and methods

Eight-hundred and ten individuals attending clinic at various departments within the Ho Teaching Hospital were screened for malaria antigenaemia using RDT as a point-of-entry investigation. RDT positive individuals were immediately treated for malaria whereas RDT negative individuals were treated for other ailments. Haematological analyses were performed for 69 of these patients and the relationship between RDT results and [haemoglobin levels](#) were investigated.

Results

The overall RDT positivity rate was 19.8% (160/810) of all individuals screened. There was no significant difference in the haemoglobin levels of RDT-positive and RDT-negative individuals (p value = 0.272). The highest number of attendees screened was children in the paediatric outpatient department and paediatric ward, 62% (507/810), with RDT positivity rate of 17% (91/507). We found the highest RDT positivity rate of 51% (19/37) in the male medical ward.

Conclusions

This study shows that RDT is a useful tool in promoting prompt diagnosis and management of malaria and though children form a majority of hospital attendees and malaria infections, the frequency of malaria detection may be higher in adults as compared to children.

Assessing the impact of differences in malaria transmission intensity on clinical and haematological indices in children with malaria

Mensah-Brown, H. E., Abugri, J., Asante, K. P., Dwomoh, D., Dosoo, D., Atuguba, F., Conway, D. J. and **Awandare, G. A** (2017)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Malaria control interventions have led to a decline in transmission intensity in many endemic areas, and resulted in elimination in some areas. This decline, however, will lead to delayed acquisition of protective immunity and thus impact disease manifestation and outcomes. Therefore, the variation in clinical and haematological parameters in children with malaria was assessed across three areas in Ghana with varying transmission intensities.

Methods

A total of 568 children between the ages of 2 and 14 years with confirmed malaria were recruited in hospitals in three areas with varying transmission intensities (Kintampo > Navrongo > Accra) and a comprehensive analysis of parasitological, clinical, haematological and socio-economic parameters was performed.

Results

Areas of lower malaria transmission tended to have lower disease severity in children with malaria, characterized by lower parasitaemias and higher haemoglobin levels. In addition, total white cell counts and percent lymphocytes decreased with decreasing transmission intensity. The heterozygous sickle haemoglobin genotype was protective against disease

severity in Kintampo ($P = 0.016$), although this was not significant in Accra and Navrongo. Parasitaemia levels were not a significant predictor of haemoglobin level after controlling for age and gender. However, higher haemoglobin levels in children were associated with certain socioeconomic factors, such as having fathers who had any type of employment ($P < 0.05$) and mothers who were teachers ($P < 0.05$).

Conclusions

The findings demonstrate significant differences in the haematological presentation and severity of malaria among areas with different transmission intensity in Ghana, indicating that these factors need to be considered in planning the management of the disease as the endemicity is expected to decline after control interventions.

Comparison of malaria diagnostic methods in four hospitals in the Volta region of Ghana

Dinko, B., Ayivor-Djanie, R., Abugri, J., Agboli, E., Kye-Duodu, G., Tagboto, S., Tampuori, J., Adzaku, F., Binka, F. N., & **Awandare, G. A (2016)**

[Malaria World Journal](#) (2023 Impact Factor: 3469)

Abstract

Background. Rapid diagnostic tests (RDTs) and microscopy are routinely used for the diagnosis of malaria in Ghana. DNA-based polymerase chain reaction (PCR) is not yet used routinely. We compared diagnostic methods and tested the sensitivities of different malaria diagnostic methods against PCR. Materials and methods. Study participants from four hospitals with a suspicion of malaria donated finger -prick blood for RDT and blood film examination. In addition, a blood spot was collected for PCR analysis, prior to treatment. Retrospective species-specific PCR was performed on all samples collected. Results. Using PCR we found an overall malaria prevalence of 39% among the 211 evaluable blood spots (83/211) and this ranged between 6-61% across the four hospitals. Of the 164 participants with RDT data, malaria prevalence was 57% (94/164), ranging from 3-100% from the four hospitals. Microscopy was the least sensitive with a parasite prevalence of 21% (25/119) of the evaluable 119 participants, varying from 9 to 35% across three health facilities. By comparison, we found the sensitivities and specificities of RDT results when compared to PCR to be slightly higher than microscopy compared to PCR. These were 56.4% versus 41.7% and 90% versus 81.9%, respectively, but generally lower than expected. Ninety-five percent of the PCR-detected infections were *P. falciparum*, while 4% were mixed species infections of *P. falciparum* and *P. malariae*, with the remaining being a mono-infection of *P. malariae*. Conclusions. While using PCR as a gold standard, we found RDT to be more reliable in diagnosing malaria than microscopy. In addition, a majority of malaria-treated cases were not supported by PCR diagnosis, leading to possible overtreatment. Pragmatic strategies are needed to ensure suspected malaria cases are accurately diagnosed before treatment.

Association of placental *Plasmodium falciparum* parasitaemia with maternal and newborn outcomes in the periurban area of Bobo-Dioulasso, Burkina Faso

Cisse, M., Diallo, H. A., Some, A. D., Poda, A., **Awandare, G. A.**, & Guiguemde, R. T (2016)

[Parasitology Open](#) (2023 Impact Factor: 3.243)

Abstract

The prevalence of placental malaria and its impact on maternal and newborn outcomes have been poorly documented in periurban settings of Burkina Faso. Peripheral and placental blood from 320 mothers, and cord blood from their newborns were collected through a cross-sectional study and used to prepare thick and thin blood films. Maternal haemoglobin concentration and birthweight were also measured. The overall malaria parasitaemia prevalence in peripheral, placental and cord blood was of 17.2, 9.1 and 0.9%, respectively. *Plasmodium falciparum* was the sole species found in all cases and the mean parasite density in placental blood was 4.5 ± 0.8 parasites μL^{-1} . Primigravida (aOR: 3.5; 95% CI (1.1–11.2)) and women who did not use a bed net (aOR: 2.6; 95% CI (1.1–6.3)), were at higher odds of placental malaria infection. Women with placental parasitaemia were at increased odds of maternal anaemia (aOR: 3.1; 95% CI (1.3–7.4)). There was no odds difference for LBW between mothers with placental parasitaemia and those without. Placental malaria parasitaemia resulted in a significant mean birthweight reduction of 200 g. Placental malaria infection is higher in primigravida. Use of insecticide-treated bed nets should be therefore emphasized for primigravida during the first antenatal care visit.

Evidence of Recent Dengue Exposure Among Malaria Parasite-Positive Children in Three Urban Centers in Ghana

Stoler, J., Delimini, R. K., Bonney, K. J.H., Oduro, A. R., Owusu-Agyei, S., Fobil, J. N., & **Awandare, G. A.** (2015)

[American Journal of Tropical Medicine and Hygiene](#) (2023 Impact Factor: 3.707)

Abstract

Blood samples of 218 children ages 2–14 years old with confirmed malaria in hospitals across Ghana were tested for dengue virus exposure. We detected dengue-specific immunoglobulin M (IgM) antibodies in 3.2% of the children, indicating possible coinfection, and IgG antibodies in 21.6% of them, which suggests previous exposure. Correlates of exposure are discussed.



DRUG RESPONSE MECHANISMS AND RESISTANCE

Parasite clearance dynamics in children hospitalised with severe malaria in the Ho Teaching Hospital, Volta Region, Ghana

Paris L, Tackie RG, Beshir KB, Tampuori J, **Awandare GA**, Binka FN, Urban BC, Dinko B, Sutherland CJ (2022).

[Parasite Epidemiology and Control](#) (2023 Impact Factor: 0.625)

Abstract

Background: Over 90% of severe malaria (SM) cases occur in African children. Parenteral [artesunate](#) is currently the recommended treatment for SM. Studies of [parasite clearance](#) in paediatric SM cases are needed for assessment of therapeutic outcomes but are lacking in Africa.

Methods: Severe malaria patients were recruited in the children's emergency ward at Ho Teaching Hospital, Ghana, in 2018. Blood samples were taken upon admission, every 24 h for 3 days and 1 week after treatment, and DNA extracted. Parasitaemia and parasite densities were performed by microscopy at enrolment and the follow-up days wherever possible. Relative parasite density was measured at each timepoint by duplex qPCR and parameters of parasite clearance estimated.

Results: Of 25 evaluable SM patients, clearance of qPCR-detectable parasites occurred within 48 h for 17 patients, but three out of the remaining eight were still qPCR-positive on day 3. Increased time to parasite clearance was seen in children ≥ 5 years old, those with lower [haemoglobin levels](#) and those with a high number of previous malaria diagnoses, but these associations were not statistically significant.

Conclusion: We examined parasite clearance dynamics among paediatric cases of SM. Our observations suggest that daily sampling for qPCR estimation of *P. falciparum* peripheral density is a useful method for assessing treatment response in hospitalised SM cases. The study demonstrated varied parasite clearance response, thus illuminating the complex nature of the mechanism in this important patient group, and further investigations utilizing larger sample sizes are needed to confirm our findings.

***Plasmodium malariae* and *Plasmodium falciparum* comparative susceptibility to antimalarial drugs in Mali**

Dembele L, Aniwah Y, Diallo N, Sogore F, Sangare CPD, Haidara AS, Traore A, Diakité SAS, Diakite M, Campo B, **Awandare GA**, & Djimde AA (2021)

[Journal of Antimicrobial Chemotherapy](#) (2023 Impact Factor: 5.758)

Abstract

Objectives

To evaluate *Plasmodium malariae* susceptibility to current and lead candidate antimalarial drugs.

Methods

We conducted cross-sectional screening and detection of all *Plasmodium* species malaria cases, which were nested within a longitudinal prospective study, and an *ex vivo* assessment of efficacy of a panel of antimalarials against *P. malariae* and *Plasmodium falciparum*, both PCR-confirmed mono-infections. Reference compounds tested included chloroquine, lumefantrine, artemether and piperaquine, while candidate antimalarials included the imidazolopiperazine GNF179, a close analogue of KAF156, and the *Plasmodium* phosphatidylinositol-4-OH kinase (PI4K)-specific inhibitor KDU691.

Results

We report a high frequency (3%–15%) of *P. malariae* infections with a significant reduction in *ex vivo* susceptibility to chloroquine, lumefantrine and artemether, which are the current frontline drugs against *P. malariae* infections. Unlike these compounds, potent inhibition of *P. malariae* and *P. falciparum* was observed with piperaquine exposure. Furthermore, we evaluated advanced lead antimalarial compounds. In this regard, we identified strong inhibition of *P.*

malariae using GNF179, a close analogue of KAF156 imidazolopiperazines, which is a novel class of antimalarial drug currently in clinical Phase IIb testing. Finally, in addition to GNF179, we demonstrated that the *Plasmodium* PI4K-specific inhibitor KDU691 is highly inhibitory against *P. malariae* and *P. falciparum*.

Conclusions

Our data indicated that chloroquine, lumefantrine and artemether may not be suitable for the treatment of *P. malariae* infections and the potential of piperaquine, as well as new antimalarials imidazolopiperazines and PI4K-specific inhibitor, for *P. malariae* cure.

***Ex Vivo Plasmodium malariae* Culture Method for Antimalarial Drugs Screen in the Field**

Dembele L, Diallo N, Sogore F, Diarra B, Ballo FI, Daou A, Diakite O, Bare Y, Sangare CPO, Haidara AS, Diakite SAS, Niangaly A, Diakite M, Campo B, **Awandare GA**, Aniweh Y, Djimde AA (2021)

[ACS Infectious Diseases](#) (2023 Impact Factor: 5.578)

Abstract

In vitro and *ex vivo* cultivation of *Plasmodium (P) falciparum* has facilitated active research into the malaria parasite toward the quest for basic knowledge and the discovery of effective drug treatments. Such a drug discovery program is currently difficult for *P. malariae* simply because of the absence of *in vitro* and *ex vivo* cultivation system for its asexual blood stages supporting antimalarial evaluation. Despite availability of artemisinin combination therapies effective on *P. falciparum*, *P. malariae* is being increasingly detected in malaria endemic countries. *P. malariae* is responsible for chronic infections and is associated with a high burden of anemia and morbidity. Here, we optimized and adapted *ex vivo* conditions under which *P. malariae* can be cultured and used for screening antimalarial drugs. Subsequently, this enabled us to test compounds such as artemether, chloroquine, lumefantrine, and quinine for *ex vivo* antimalarial activity against *P. malariae*.

Keywords: *Plasmodium malariae*; drug discovery; *ex vivo* culture; malaria; nonfalciparum.

A year of genomic surveillance reveals how the SARS-CoV-2 pandemic unfolded in Africa

Wilkinson E, Giovanetti M, Tegally H, San JE, Lessells R, Cuadros D, Martin DP, Rasmussen DA, Zekri AN, Sangare AK, Ouedraogo AS, Sesay AK, Priscilla A, Kemi AS, ... **Awandare GA**, Schubert G, ...Tessema SK, Happi C, Nkengasong J, de Oliveira T (2021)

[Science](#) (2023 Impact Factor: 63.832)

Abstract

The progression of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in Africa has so far been heterogeneous, and the full impact is not yet well understood. In this study, we describe the genomic epidemiology using a dataset of 8746 genomes from 33 African countries and two overseas territories. We show that the epidemics in most countries were initiated by importations predominantly from Europe, which diminished after the early introduction of international travel restrictions. As the pandemic progressed, ongoing transmission in many countries and increasing mobility led to the emergence and spread within the continent of many variants of concern and interest, such as B.1.351, B.1.525, A.23.1, and C.1.1. Although distorted by low sampling numbers and blind spots, the findings highlight that Africa must not be left behind in the global pandemic response, otherwise it could become a source for new variants.

Cryptolepine inhibits hepatocellular carcinoma growth through inhibiting interleukin-6/STAT3 signalling

Domfeh SA, Narkwa PW, Quaye O, Kusi KA, **Awandare GA**, Ansah C, Salam A, & Mutocheluh M (2021)

[BMC Complementary Medicine and Therapies](#) (2023 Impact Factor: 2.838)

Abstract

Background

Diverse signalling pathways are involved in carcinogenesis and one of such pathways implicated in many cancers is the interleukin 6/signal transducer and activator of transcription 3 (IL-6/STAT3) signalling pathway. Therefore, inhibition of this pathway is targeted as an anti-cancer intervention. This study aimed to establish the effect of cryptolepine, which is the main bioactive alkaloid in the medicinal plant *Cryptolepis sanguinolenta*, on the IL-6/STAT3 signalling pathway.

Methods

First, the effect of cryptolepine on the IL-6/STAT3 pathway in human hepatoma cells (HepG2 cells) was screened using the Cignal Finder Multi-Pathway Reporter Array. Next, to confirm the effect of cryptolepine on the IL-6/STAT3 signalling pathway, the pathway was activated using 200 ng/mL IL-6 in the presence of 0.5–2 μ M cryptolepine. The levels of total STAT3, p-STAT3 and IL-23 were assessed by ELISA.

Results

Cryptolepine downregulated 12 signalling pathways including the IL-6/STAT3 signalling pathway and upregulated 17 signalling pathways. Cryptolepine, in the presence of IL-6, decreased the levels of p-STAT3 and IL-23 in a dose-dependent fashion.

Conclusion

Our results demonstrated that cryptolepine inhibits the IL-6/STAT3 signalling pathway, and therefore cryptolepine-based remedies such as *Cryptolepis sanguinolenta* could potentially be used as an effective immunotherapeutic agent for hepatocellular carcinoma and other cancers.

Temporal evolution of sulfadoxine-pyrimethamine resistance genotypes and genetic diversity in response to a decade of increased interventions against *Plasmodium falciparum* in northern Ghana

Amenga-Etego LN, Asoala V, Agongo G, Jacob C, Goncalves S, **Awandare GA**, Rockett KA, Kwiatkowski D (2021)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Anti-malarial drug resistance remains a key concern for the global fight against malaria. In Ghana sulfadoxine-pyrimethamine (SP) is used for intermittent preventive treatment of malaria in pregnancy and combined with amodiaquine for Seasonal Malaria Chemoprevention (SMC) during the high malaria season. Thus, surveillance of molecular markers of SP resistance is important to guide decision-making for these interventions in Ghana.

Methods

A total of 4469 samples from uncomplicated malaria patients collected from 2009 to 2018 was submitted to the Wellcome Trust Sanger Institute, UK for DNA sequencing using MiSeq. Genotypes were successfully translated into haplotypes in 2694 and 846 mono infections respectively for *pfdhfr* and *pfdhps* genes and the combined *pfhdfr/pfdhps* genes across all years.

Results

At the *pfdhfr* locus, a consistently high (> 60%) prevalence of parasites carrying triple mutants (IRNI) were detected from 2009 to 2018. Two double mutant haplotypes (NRNI and ICNI) were found, with haplotype NRNI having a much higher prevalence (average 13.8%) than ICNI (average 3.2%) across all years. Six *pfdhps* haplotypes were detected. Of these, prevalence of

five fluctuated in a downward trend over time from 2009 to 2018, except a *pf dhps* double mutant (**AGKAA**), which increased consistently from 2.5% in 2009 to 78.2% in 2018. Across both genes, *pf dhfr/pf dhps* combined triple (**NRNI+AAKAA**) mutants were only detected in 2009, 2014, 2015 and 2018, prevalence of which fluctuated between 3.5 and 5.5%. The combined quadruple (**IRNI+AAKAA**) genotype increased in prevalence from 19.3% in 2009 to 87.5% in 2011 before fluctuating downwards to 19.6% in 2018 with an average prevalence of 37.4% within the nine years. Prevalence of parasites carrying the quintuple (**IRNI+AGKAA** or **SGEAA**) mutant haplotypes, which are highly refractory to SP increased over time from 14.0% in 2009 to 89.0% in 2016 before decreasing to 78.9 and 76.6% in 2017 and 2018 respectively. Though quintuple mutants are rising in prevalence in both malaria seasons, together these combined genotypes vary significantly within season but not between seasons.

Conclusions

Despite high prevalence of *pf dhfr* triple mutants and combined *pf dhfr/pf dhps* quadruple and quintuple mutants in this setting SP may still be efficacious. These findings are significant as they highlight the need to continuously monitor SP resistance, particularly using deep targeted sequencing to ascertain changing resistance patterns.

***Plasmodium falciparum* Malaria Parasites in Ghana Show Signatures of Balancing Selection at Artemisinin Resistance Predisposing Background Genes**

Tandoh, KZ, Amenga-Etego, L, Quashie, NB, **Awandare, G**, Wilson, M & Duah-Quashie, NO (2021)

[Evolutionary Bioinformatics](#) (2023 Impact Factor: 2.031)

Abstract

Sub-Saharan Africa is courting the risk of artemisinin resistance (ARTr) emerging in *Plasmodium falciparum* malaria parasites. Current molecular surveillance efforts for ARTr have been built on the utility of *P. falciparum* kelch13 (*pfk13*) validated molecular markers. However, whether these molecular markers will serve the purpose of early detection of artemisinin-resistant parasites in Ghana is hinged on a *pfk13* dependent evolution. Here, we tested the hypothesis that the background *pfk13* genome may be present before the *pfk13* ARTr-conferring variant(s) is selected and that signatures of balancing selection on these genomic loci may serve as an early warning signal of ARTr. We analyzed 12 198 single nucleotide polymorphisms (SNPs) in Ghanaian clinical isolates in the Pf3K MalariaGEN dataset that passed a stringent filtering regimen. We identified signatures of balancing selection in 2 genes (phosphatidylinositol 4-kinase and chloroquine resistance transporter) previously reported as background loci for ARTr. These genes showed statistically significant and high positive values for Tajima's D, Fu and Li's F_s and Fu and Li's D. This indicates that the biodiversity required to establish a *pfk13* background genome may have been primed in clinical isolates of *P. falciparum* from Ghana as of 2010. Despite the absence of ARTr in Ghana to date, our finding supports the current use of *pfk13* for molecular surveillance of ARTr in Ghana and highlights the potential utility of monitoring malaria parasite populations for balancing selection in ARTr precursor background genes as early warning molecular signatures for the emergence of ARTr.

Elucidating the possible mechanism of action of some pathogen box compounds against *Leishmania donovani*

Amlabu WE, Antwi CA, **Awandare G**, Gwira TM (2020)

[PLoS Neglected Tropical Diseases](#) (2022 Impact Factor: 4.781)

Abstract

Leishmaniasis is one of the Neglected Tropical Diseases (NTDs) which is closely associated with poverty and has gained much relevance recently due to its opportunistic coinfection with HIV. It is a protozoan zoonotic disease transmitted by a dipteran *Phlebotomus*, *Lutzomyia*/ *Sergentomyia* sandfly; during blood meals on its vertebrate intermediate hosts. It is a four-faceted disease with its visceral form being more deadly if left untreated. It is endemic across the tropics and sub-tropical regions of the world. It can be considered the third most important NTD after malaria and lymphatic filariasis. Currently, there are numerous drawbacks on the fight against leishmaniasis which includes: non-availability of vaccines, limited availability of drugs, high cost of mainstay drugs and parasite resistance to current treatments. In this study, we screened the antileishmanial activity, selectivity, morphological alterations, cell cycle progression and apoptotic potentials of six Pathogen box compounds from Medicine for Malaria Venture (MMV) against *Leishmania donovani* promastigotes and amastigotes. From this study, five of the compounds showed great promise as lead chemotherapeutics based on their high selectivity against the *Leishmania donovani* parasite when tested against the murine mammalian macrophage RAW 264.7 cell line (with a therapeutic index ranging between 19–914 (promastigotes) and 1–453 (amastigotes)). The cell cycle progression showed growth arrest at the G0-G1 phase of mitotic division, with an indication of apoptosis induced by two (2) of the pathogen box compounds tested. Our findings present useful information on the therapeutic potential of these compounds in leishmaniasis. We recommend further *in vivo* studies on these compounds to substantiate observations made in the *in vitro* study.

Assessment of antimalarial drug resistant markers in asymptomatic *Plasmodium falciparum* infections after 4 years of indoor residual spraying in Northern Ghana

Myers-Hansen JL, Abuaku B, Oyebola MK, Mensah BA, Ahorlu C, Wilson MD, **Awandare G**, Koram KA, Ngwa AA, & Ghansah A (2020)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

Background

Drug resistance remains a concern for malaria control and elimination. The effect of interventions on its prevalence needs to be monitored to pre-empt further selection. We assessed the prevalence of *Plasmodium falciparum* gene mutations associated with resistance to the antimalarial drugs: sulfadoxine-pyrimethamine (SP), chloroquine (CQ) and artemisinin combination therapy (ACTs) after the scale-up of a vector control activity that reduced transmission.

Methods

A total of 400 *P. falciparum* isolates from children under five years were genotyped for seventeen single nucleotide polymorphisms (SNPs) in *pfprt*, *pfmdr1*, *pfdhfr*, *pfdhps* and *pfk13* genes using polymerase chain reaction (PCR) and high resolution melting (HRM) analysis. These included 80 isolates, each randomly selected from cross-sectional surveys of asymptomatic infections across 2010 (baseline), 2011, 2012, 2013 (midline: post-IRS) and 2014 (endline: post-IRS) during the peak transmission season, when IRS intervention was rolled out in Bunkpurugu Yunyoo (BY) District, Ghana. The proportions of isolates with drug resistant alleles were assessed over this period.

Results

There were significant decreases in the prevalence of *pfdhfr*-I₅₁R₅₉N₁₀₈ haplotype from 2010 to 2014, while the decline in *pfdhfr/pfdhps*-I₅₁R₅₉N₁₀₈G₄₃₇ during the same period was not significant. The prevalence of lumefantrine (LM), mefloquine (MQ) and amodiaquine (AQ) resistance-associated haplotypes *pfmdr1*-N₈₆F₁₈₄D₁₂₄₆ and *pfmdr1*-Y₈₆Y₁₈₄Y₁₂₄₆ showed decreasing trends ($z = -2.86$, $P = 0.004$ and $z = -2.71$, $P = 0.007$, respectively). Each of *pfcr*-T76 and *pfmdr1*-Y86 mutant alleles also showed a declining trend in the asymptomatic reservoir, after the IRS rollout in 2014 ($z = -2.87$, $P = 0.004$ and $z = -2.65$, $P = 0.008$, respectively). Similarly, Pyrimethamine resistance mediating polymorphisms *pfdhfr*-N108, *pfdhfr*-I51 and *pfdhfr*-R59 also declined ($z = -2.03$, $P = 0.042$, $z = -3.54$, $P < 0.001$ and $z = -4.63$, $P < 0.001$, respectively), but not the sulphadoxine resistance mediating *pfdhps*-G437 and *pfdhps*-F436 ($z = -0.36$, $P = 0.715$ and $z = 0.41$, $P = 0.684$, respectively). No mutant *pfk13*-Y580 were detected during the study period.

Conclusion

The study demonstrated declining trends in the prevalence of drug resistant mutations in asymptomatic *P. falciparum* infections following transmission reduction after an enhanced IRS intervention in Northern Ghana.

High resistance to reverse transcriptase inhibitors among persons infected with human immunodeficiency virus type 1 subtype circulating recombinant form 02_AG in Ghana and on antiretroviral therapy

Deletsu, S. D., Maina, E. K., Quaye, O., Ampofo, W. K., and **Awandare, G. A.**, & Bonney EY (2020).

[Medicine](#) (2023 Impact Factor: 1.817)

Abstract

This study sought to determine the dominant circulating human immunodeficiency virus type 1 (HIV-1) subtype and associated drug resistance mutations in Ghana.

This cross-sectional study was conducted with archived samples collected from patients who received care at 2 hospitals in Ghana from 2014 to 2016. Blood samples were earlier processed into plasma and peripheral blood mononuclear cells and stored at -80°C . Ribonucleic acid (RNA) was extracted from the archived plasma. Two HIV-1 genes; protease and reverse transcriptase, were amplified, sequenced using gene-specific primers and analyzed for subtype and drug resistance mutations using the Stanford HIV Database.

Of 16 patient samples successfully sequenced, we identified the predominance of HIV-1 subtype *CRF02_AG* (11/16, 68%). Subtypes *G* (2/16, 13%), dual *CRF02_AG/G* (2/16, 13%), and *CRF01_AE* (1/16, 6%) were also observed. Major nucleoside reverse transcriptase inhibitor (NRTI) resistance mutations, *M184I/V*, *D67N*, *T215F*, and *K70R/E* were found. Non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance mutations, *K103N*, *Y181C*, *V90I*, *F227L*, and *V106A* were also prevalent. Additionally, and at a lower level, protease inhibitor (PI)-resistance mutations, *M46I*, *I54 V*, *V82A*, *L90 M*, and *I471 V*, were also present in the sequences from antiretroviral therapy (ART)-experienced individuals. Two NRTI-associated

drug resistance mutations (DRMs) (*D67N* and *T69N*) were present in sequences from 1 ART-naive individual.

HIV-1 subtype CRF02_AG was most frequently detected in this study thus confirming earlier reports of dominance of this subtype in the West-African sub-region and Ghana in particular. The detection of these drug resistance mutations in individuals on first-line regimen composed of NRTI and NNRTI is an indication of prolonged drug exposure without viral load monitoring. Routine viral load monitoring is necessary for early detection of virologic failure and drug resistance testing will inform appropriate choice of regimens for such patients.

Insecticide resistance in indoor and outdoor-resting *Anopheles gambiae* in Northern Ghana

Hamid-Adiamoh M, Ngwa AA, Nwakanma D, D'Alessandro U, **Awandare GA**, Afrane YA (2020)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Selection pressure from continued exposure to insecticides drives development of insecticide resistance and changes in resting behaviour of malaria vectors. There is need to understand how resistance drives changes in resting behaviour within vector species. The association between insecticide resistance and resting behaviour of *Anopheles gambiae* sensu lato (*s.l.*) in Northern Ghana was examined.

Methods

F₁ progenies from adult mosquitoes collected indoors and outdoors were exposed to DDT, deltamethrin, malathion and bendiocarb using WHO insecticide susceptibility tests. Insecticide resistance markers including voltage-gated sodium channel (*Vgsc*)-1014F, *Vgsc*-1014S, *Vgsc*-1575Y, glutathione-S-transferase epsilon 2 (*GSTe2*)-114T and acetylcholinesterase (*Ace1*)-119S, as well as blood meal sources were investigated using PCR methods. Activities of metabolic enzymes, acetylcholine esterase (AChE), non-specific Beta-esterases, glutathione-S-transferase (GST) and monooxygenases were measured from unexposed F₁ progenies using microplate assays.

Results

Susceptibility of *Anopheles coluzzii* to deltamethrin 24 h post-exposure was significantly higher in indoor (mortality = 5%) than outdoor (mortality = 2.5%) populations ($P = 0.02$). Mosquitoes were fully susceptible to malathion (mortality: indoor = 98%, outdoor = 100%). Susceptibility

to DDT was significantly higher in outdoor (mortality=9%) than indoor (mortality=0%) mosquitoes ($P = 0.006$). Mosquitoes were also found with suspected resistance to bendiocarb but mortality was not statistically different (mortality: indoor = 90%, outdoor = 95%. $P = 0.30$). Frequencies of all resistance alleles were higher in F_1 outdoor (0.11–0.85) than indoor (0.04–0.65) mosquito populations, while *Vgsc-1014F* in F_0 *An. gambiae sensu stricto* (s.s) was significantly associated with outdoor-resting behaviour ($P = 0.01$). Activities of non-specific Beta-esterase enzymes were significantly higher in outdoor than indoor mosquitoes (Mean enzyme activity: Outdoor = 1.70/mg protein; Indoor = 1.35/mg protein. $P < 0.0001$). AChE activity was also more elevated in outdoor (0.62/mg protein) than indoor (0.57/mg protein) mosquitoes but this was not significant ($P = 0.08$). Human blood index (HBI) was predominantly detected in indoor (18%) than outdoor mosquito populations (3%).

Conclusions

The overall results did not establish that there was a significant preference of resistant malaria vectors to solely rest indoors or outdoors, but varied depending on the resistant alleles present. Phenotypic resistance was higher in indoor than outdoor-resting mosquitoes, but genotypic and metabolic resistance levels were higher in outdoor than the indoor populations. Continued monitoring of changes in resting behaviour within *An. gambiae s.l.* populations is recommended.

A comprehensive analysis of drug resistance molecular markers and *Plasmodium falciparum* genetic diversity in two malaria endemic sites in Mali

Diakité S. A. S, Traoré K, Sanogo I, Clark TG, Campino S, Sangaré M, Dabita D, Dara A, Konaté D. S, Doucouré F, Cissé A, Keita B, Doumbouya M, Guindo M. A, Toure M. B, Sogoba N, Doumbia S, **Awandare G. A**, Diakité M (2019)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Drug resistance is one of the greatest challenges of malaria control programme in Mali. Recent advances in next-generation sequencing (NGS) technologies provide new and effective ways of tracking drug-resistant malaria parasites in Africa. The diversity and the prevalence of *Plasmodium falciparum* drug-resistance molecular markers were assessed in Dangassa and Nioro-du-Sahel in Mali, two sites with distinct malaria transmission patterns. Dangassa has an intense seasonal malaria transmission, whereas Nioro-du-Sahel has an unstable and short seasonal malaria transmission.

Methods

Up to 270 dried blood spot samples (214 in Dangassa and 56 in Nioro-du-Sahel) were collected from *P. falciparum* positive patients in 2016. Samples were analysed on the Agena MassARRAY® iPLEX platform. Specific codons were targeted in *Pfcr*, *Pfmdr1*, *Pfdhfr*, and *Pfdhps*, *Pfprps10*, *Pfferredoxin*, *Pfexonuclease* and *Pfmdr2* genes. The Sanger's 101-SNPs-barcode method was used to assess the genetic diversity of *P. falciparum* and to determine the parasite species.

Results

The *Pfcr*_T_76I chloroquine-resistance genotype was found at a rate of 64.4% in Dangassa and 45.2% in Nioro-du-Sahel ($p=0.025$). The *Pfdhfr*_51I-59R-108N pyrimethamine-resistance genotype was 14.1% and 19.6%, respectively in Dangassa and Nioro-du-Sahel. Mutations in the *Pfdhps*_S436-A437-K540-A581-613A sulfadoxine-resistance gene was significantly more prevalent in Dangassa as compared to Nioro-du-Sahel ($p=0.035$). Up to 17.8% of the isolates from Dangassa vs 7% from Nioro-du-Sahel harboured at least two codon substitutions in this haplotype. The amodiaquine-resistance *Pfmdr1*_N86Y mutation was identified in only three samples (two in Dangassa and one in Nioro-du-Sahel). The lumefantrine-reduced susceptibility *Pfmdr1*_Y184F mutation was found in 39.9% and 48.2% of samples in Dangassa and Nioro-du-Sahel, respectively. One piperaquine-resistance *Exo*_E415G mutation was found in Dangassa, while no artemisinin resistance genetic-background were identified. A high *P. falciparum* diversity was observed, but no clear genetic aggregation was found at either study sites. Higher multiplicity of infection was observed in Dangassa with both COIL ($p=0.04$) and Real McCOIL ($p=0.02$) methods relative to Nioro-du-Sahel.

Conclusions

This study reveals high prevalence of chloroquine and pyrimethamine-resistance markers as well as high codon substitution rate in the sulfadoxine-resistance gene. High genetic diversity of *P. falciparum* was observed. These observations suggest that the use of artemisinins is relevant in both Dangassa and Nioro-du-Sahel.

Prevalence of chloroquine and antifolate drug resistance alleles in *Plasmodium falciparum* clinical isolates from three areas in Ghana

Abugri, J., Ansah, F., Asante, K. P., Opoku, C. N., Amenga-Etego, L. A. & **Awandare, G. A.** (2018)

[AAS Open Research](#) (2023 Impact Factor: 1.8)

Abstract

Background: The emergence and spread of resistance in *Plasmodium falciparum* to chloroquine (CQ) necessitated the change from CQ to artemisinin-based combination therapies (ACTs) as first-line drug for the management of uncomplicated malaria in Ghana in 2005. Sulphadoxine-pyrimethamine (SP) which was the second line antimalarial drug in Ghana, was now adopted for intermittent preventive treatment of malaria in pregnancy (IPTp).

Methods: To examine the prevalence of molecular markers associated with CQ and antifolate drug resistance in Ghana, we employed restriction fragment length polymorphism polymerase chain reaction to genotype and compare single nucleotide polymorphisms (SNPs) in the *P. falciparum* chloroquine resistance transporter (*pfcr*t, PF3D7_0709000), multidrug resistance (*pfmdr*1, PF3D7_0523000), bifunctional dihydrofolate reductase-thymidylate synthase (*pfdhfr*, PF3D7_0417200) and dihydropteroate synthase (*pfdhps*, PF3D7_0810800) genes. Parasites were collected from children with malaria reporting to hospitals in three different epidemiological areas of Ghana (Accra, Kintampo and Navrongo) in 2012-2013 and 2016-2017.

Results: The overall prevalence of the CQ resistance-associated *pfcr*t 76T allele was 8%, whereas *pfmdr*1 86Y and 184F alleles were present in 10.2% and 65.1% of infections, respectively. The majority of the isolates harboured the antifolate resistance-associated *pfdhfr* alleles 51I (834%), 59R (85.9 %) and 108N (90.5%). *Pfdhps* 437G and

540E were detected in 90.6% and 0.7% of infections, respectively. We observed no significant difference across the three study sites for all the polymorphisms except for *pfdhps* 437G, which was more common in Accra compared to Kintampo for the 2016-2017 isolates. Across both *pfdhfr* and *pfdhps* genes, a large proportion (61%) of the isolates harboured the quadruple mutant combination (I₅₁ R₅₉ N₁₀₈/ G₄₃₇). CQ resistance alleles decreased during the 12 years after CQ withdrawal, but an mediate SP resistance alleles increased.

Conclusion: Surveillance of the prevalence of resistance alleles is necessary in monitoring the efficacy of antimalarial drugs.

A barcode of multilocus nuclear DNA identifies genetic relatedness in pre- and post-Artemether/Lumefantrine treated *Plasmodium falciparum* in Nigeria

Oyebola, K. M., Aina, O. O., Idowu, E. T., Olukosi, Y. A., Ajibaye, O. S., Otubanjo, O. A., Awolola, T. S., **Awandare, G. A.**, & Amambua-**Ngwa, A.** (2018)

[BMC Infectious Diseases](#) (2023 Impact Factor: 3.669)

Abstract

Background

The decline in the efficacy of artemisinin-based combination treatment (ACT) in some endemic regions threatens the progress towards global elimination of malaria. Molecular surveillance of drug resistance in malaria-endemic regions is vital to detect the emergence and spread of mutant strains.

Methods

We observed 89 malaria patients for the efficacy of artemether-lumefantrine for the treatment of uncomplicated *Plasmodium falciparum* infections in Lagos, Nigeria and determined the prevalence of drug resistant strains in the population. Parasite clearance rates were determined by microscopy and the highly sensitive *var* gene acidic terminal sequence (*varATS*) polymerase chain reaction for 65 patients with samples on days 0, 1, 3, 7, 14, 21 and 28 after commencement of treatment. The genomic finger print of parasite DNA from pre- and post-treatment samples were determined using 24 nuclear single nucleotide polymorphisms (SNP) barcode for *P. falciparum*. Drug resistance associated alleles in chloroquine resistance transporter gene (*crt-76*), multidrug resistance genes (*mdr1*–86 and *mdr1*–184), dihydropteroate synthase (*dhps*-540), dihydrofolate reductase (*dhfr*-108) and kelch domain (*K*-13580) were genotyped by high resolution melt analysis of polymerase

chain reaction (PCR) fragments.

Results

By varATS qPCR, 12 (18.5%) of the participants had detectable parasite DNA in their blood three days after treatment, while eight (12.3%) individuals presented with genotypable day 28 parasitaemia. Complexity of infection (Col) was 1.30 on day 0 and 1.34 on day 28, the mean expected heterozygosity (H_e) values across all barcodes were 0.50 ± 0.05 and 0.56 ± 0.05 on days 0 and 28 respectively. Barcode (π) pairwise comparisons showed high genetic relatedness of day 0 and day 28 parasite isolates in three (37.5%) of the eight individuals who presented with re-appearing infections. *Crt*-76 mutant allele was present in 38 (58.5%) isolates. The *mdr1*-86 mutant allele was found in 56 (86.2%) isolates. No mutation in the *K*-13580 was observed.

Conclusions

Persistence of DNA-detectable parasitaemia in more than 18% of cases after treatment and indications of genetic relatedness between pre- and post-treatment infections warrants further investigation of a larger population for signs of reduced ACT efficacy in Nigeria.

Prevalence of chloroquine and antifolate drug resistance mutations in *Plasmodium falciparum* field isolates from two areas in Ghana

James Abugri, Felix Ansah, Nicholas Amoako, Felix Ansah, Lucas Amenga-Etego, David J. Conway, and **Gordon A. Awandare** (2018)

[Open Research Africa](#)

Abstract

Background: The emergence and spread of resistance in *Plasmodium falciparum* to chloroquine (CQ) necessitated the change from CQ to artemisinin-based combination therapies (ACTs) as first-line drug for the management of uncomplicated malaria in Ghana in 2005. Sulphadoxine-pyrimethamine (SP) which was the second line antimalarial drug in Ghana, was now adopted for intermittent preventive treatment of malaria in pregnancy (IPTp).

Methods: To examine the prevalence of molecular markers associated with CQ and antifolate drug resistance in Ghana, we employed restriction fragment length polymorphism polymerase chain reaction to genotype and compare single nucleotide polymorphisms (SNPs) in the *P. falciparum* chloroquine resistance transporter (*pfcr*t, PF3D7_0709000), multidrug resistance (*pfmdr*1, PF3D7_0523000), bifunctional dihydrofolate reductase-thymidylate synthase (*pfdhfr*, PF3D7_0417200) and dihydropteroate synthase (*pfdhps*, PF3D7_0810800) genes. Parasites were collected from children with malaria reporting to hospitals in three different epidemiological areas of Ghana (Accra, Kintampo and Navrongo) in 2012-2013 and 2016-2017.

Results: The overall prevalence of the CQ resistance-associated *pfcr*t 76T allele was 8%, whereas *pfmdr*1 86Y and 184F alleles were present in 10.2% and 65.1% of infections, respectively. The majority of the isolates harboured the antifolate resistance-associated *pfdhfr* alleles 51I (83.4%), 59R (85.9 %) and 108N (90.5%). *Pfdhps* 437G and 540E were detected in 90.6% and 0.7% of infections, respectively. We observed no significant difference across the three study sites for all the polymorphisms except

for *pfdhps* 437G, which was more common in Accra compared to Kintampo for the 2016-2017 isolates. Across both *pfdhfr* and *pfdhps* genes, a large proportion (61%) of the isolates harboured the quadruple mutant combination (I₅₁ R₅₉ N₁₀₈/ G₄₃₇). CQ resistance alleles decreased during the 12 years after CQ withdrawal, but an mediate SP resistance alleles increased.

Conclusion: Surveillance of the prevalence of resistance alleles is necessary in monitoring the efficacy of antimalarial drugs.

High concordance of *Pfdhfr* and *Pfdhps* genotypes between matched peripheral and placental isolates of delivered women in Bobo-Dioulasso, Burkina Faso

Cissé, M., **Awandare, G. A.**, Somé, F. A., Hayette, M., & Guiguemde, R. T. (2017)

[Annals of Parasitology](#) (2023 Impact Factor: 0.228)

Abstract

Whether maternal peripheral parasites constitute a representative sample of the overall population infecting the individual, remains unknown in Burkina Faso. We therefore compared *Pfdhfr* and *Pfdhps* genotypes between matched peripheral and placental isolates. PCR-restriction fragment length polymorphism (PCR-RFLP) analysis of polymorphic codons of the *Pfdhfr* gene (51, 59, 108 and 164) and the *Pfdhps* gene (437 and 540) was performed in 18 matched peripheral and placental dried blood spots of delivered women in Bobo-Dioulasso. Both *Pfdhfr* and *Pfdhps* genes were successfully genotyped in 944% (17/18) of the matched samples. Only 8.8% (3/34) of genotypes were of the wild type, while 20.6% (7/34), 20.6% (7/34), 23.5% (8/34) and 26.5% (9/34) comprised one, two, three and four mutations, respectively. None of the samples carried both *Pfdhfr* I164L and *Pfdhps* K540E mutations. A concordance of 824% was observed in matched samples for both the *Pfdhfr* and *Pfdhps* genes. Setting placental alleles as the reference, a concordance of 100% was obtained with *Pfdhfr* mutation S108N, *Pfdhfr* mutation C59R+S108N, and *Pfdhfr* mutation N51I+C59R+S108N, respectively. Likewise, a concordance of 85.7% was observed with the *Pfdhps* mutation A437G. For epidemiological purposes, peripheral blood *Pfdhfr* and *Pfdhps* genotyping is sufficient for monitoring SP resistant molecular markers in pregnant women.

Recent uptake of intermittent preventive treatment during pregnancy with sulfadoxine–pyrimethamine is associated with increased prevalence of *Pfdhfr* mutations in Bobo-Dioulasso, Burkina Faso

Cisse, M., **Awandare, G. A.**, Soulama, A., Tinto, H., Hayette, M. P., & Guiguemdé R. T. (2017)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

The impact of sulfadoxine–pyrimethamine (SP) used as intermittent preventive treatment during pregnancy (IPTp-SP) on mutant parasite selection has been poorly documented in Burkina Faso. This study sought first to explore the relationship between IPTp-SP and the presence of mutant parasites. Second, to assess the relationship between the mutant parasites and adverse pregnancy outcomes.

Methods

From September to December 2010, dried blood spots (DBS) were collected during antenatal care visits and at delivery from 109 pregnant women with microscopically confirmed *falciparum* malaria infection. DBS were analysed by PCR–restriction fragment length polymorphism (PCR–RFLP) for the polymorphisms at codons 51, 59, 108, and 164 of the *Pfdhfr* gene and codons 437 and 540 in the *Pfdhps* gene.

Results

Both the *Pfdhfr* and *Pfdhps* genes were successfully genotyped in 92.7% (101/109) of the samples. The prevalence of *Pfdhfr* mutations N51I, C59R and S108N was 71.3, 42.6 and 64.4%, respectively. Overall, 80.2% (81/101) of samples carried the *Pfdhps* A437G mutation. None of the samples had the *Pfdhfr* I164L and the *Pfdhps* K540E mutations. The prevalence of the triple

mutation N51I + C59R + S108N was 25.7% (26/101). The use of IPTp-SP was associated with a threefold increased odds of *Pf dhfr* C59R mutation [crude OR 3.29; 95% CI (1.44–7.50)]. Pregnant women with *recent* uptake of IPTp-SP were at higher odds of both the *Pf dhfr* C59R mutation [adjusted OR 4.26; 95% CI (1.64–11.07)] and the *Pf dhfr* intermediate-to-high resistance, i.e., ≥ 2 *Pf dhfr* mutations [adjusted OR 3.45; 95% CI (1.18–10.07)]. There was no statistically significant association between the presence of the *Pf dhfr* intermediate-to-high resistance and parasite densities or both maternal haemoglobin level and anaemia.

Conclusion

The data indicate that despite the possibility that IPTp-SP contributes to the selection of resistant parasites, it did not potentiate pregnancy-associated malaria morbidity, suggesting the continuation of SP use as IPTp in Burkina Faso.

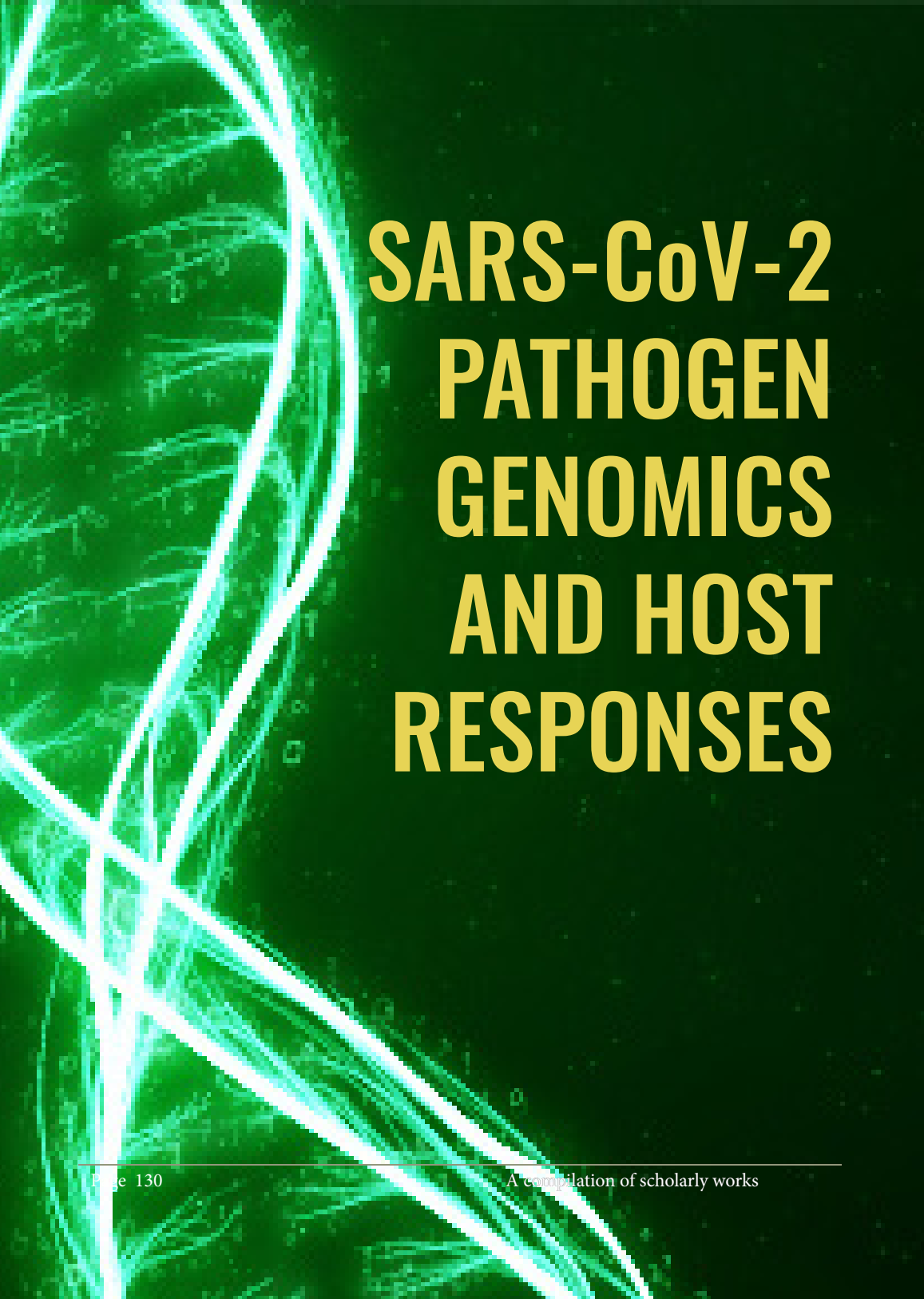
Genomic epidemiology of artemisinin resistant malaria

MalariaGEN *Plasmodium falciparum* Community Project (2016)

[eLife](#) (2023 Impact Factor: 8.713)

Abstract

The current epidemic of artemisinin resistant *Plasmodium falciparum* in Southeast Asia is the result of a soft selective sweep involving at least 20 independent *kelch13* mutations. In a large global survey, we find that *kelch13* mutations which cause resistance in Southeast Asia are present at low frequency in Africa. We show that African *kelch13* mutations have originated locally, and that *kelch13* shows a normal variation pattern relative to other genes in Africa, whereas in Southeast Asia there is a great excess of non-synonymous mutations, many of which cause radical amino-acid changes. Thus, *kelch13* is not currently undergoing strong selection in Africa, despite a deep reservoir of variations that could potentially allow resistance to emerge rapidly. The practical implications are that public health surveillance for artemisinin resistance should not rely on *kelch13* data alone, and interventions to prevent resistance must account for local evolutionary conditions, shown by genomic epidemiology to differ greatly between geographical regions.



SARS-CoV-2 PATHOGEN GENOMICS AND HOST RESPONSES

The COVID-19, tuberculosis and HIV/AIDS: Ménage à Trois

Udoakang AJ, Djomkam Zune AL, Tapela K, Nganyewo NN, Olisaka FN, Anyigba CA, Tawiah-Eshun S, Owusu IA, Paemka L, **Awandare GA**, Quashie PK (2023)

[Frontiers in Immunology](#) (2023 Impact Factor: 8.786)

Abstracts

In December 2019, a novel pneumonic condition, Coronavirus disease 2019 (COVID- 19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), broke out in China and spread globally. The presentation of COVID-19 is more severe in persons with underlying medical conditions such as Tuberculosis (TB), Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome (HIV/AIDS) and other pneumonic conditions. All three diseases are of global concern and can significantly affect the lungs with characteristic cytokine storm, immunosuppression, and respiratory failure. Co-infections of SARS-CoV-2 with HIV and *Mycobacterium tuberculosis* (Mtb) have been reported, which may influence their pathogenesis and disease progression. Pulmonary TB and HIV/AIDS patients could be more susceptible to SARS-CoV-2 infection leading to lethal synergy and disease severity. Therefore, the biological and epidemiological interactions of COVID-19, HIV/AIDS, and TB need to be understood holistically. While data is needed to predict the impact of the COVID-19 pandemic on these existing diseases, it is necessary to review the implications of the evolving COVID-19 management on HIV/AIDS and TB control, including therapy and funding. Also, the impact of long COVID on patients, who may have this co-infection. Thus, this review highlights the implications of COVID-19, HIV/AIDS, and TB co-infection compares disease mechanisms, addresses growing concerns, and suggests a direction for improved diagnosis and general management.

Conflicting COVID-19 excess mortality estimates

Moeti M, Makubalo L, Gueye AS, Balde T, Karamagi H, **Awandare G**, Thumbi SM, Zhang F, Mutapi F, Woolhouse M (2023)

[The Lancet](#) (2023 Impact Factor: 202.731)

Abstract

A study¹ by the COVID-19 Excess Mortality Collaborators estimates more than 18 million COVID-19 deaths globally by the end of 2021—three times those reported. The COVID-19 Excess Mortality Collaborators claim that under-ascertainment is especially severe in sub-Saharan Africa, with actual deaths 14 times higher than the 150 000 reported—more than 2 million excess deaths across the region in 2020–21.

Although we welcome efforts to quantify the burden of the pandemic, we consider this level of under-reporting of deaths implausible. There is no evidence of such a huge death toll and COVID-19 particularly affected large cities where spikes in the mortality rate would be readily visible.² We note the modelling approach in the study¹ assumes a homogeneous Africa, well represented by a few, atypical locations, leading to unreliable out-of-sample extrapolations. For example, the estimates for Kenya equate to an increase of more than 50% from a baseline of 280 000 deaths annually and imply that a country with alert health services and a mandatory death registration system identified only 3% of COVID-19-related deaths.

The evolving SARS-CoV-2 epidemic in Africa: Insights from rapidly expanding genomic surveillance

Tegally H, San JE,, **Awandare GA**,Tessema SK, de Oliveira T, Happi C, Lessells R, Nkengasong J, Wilkinson E (2022)

[Science](#) (2023 Impact Factor: 63.832)

Abstract

Introduction: Investment in Africa over the past year with regard to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) sequencing has led to a massive increase in the number of sequences, which, to date, exceeds 100,000 sequences generated to track the pandemic on the continent. These sequences have profoundly affected how public health officials in Africa have navigated the COVID-19 pandemic.

Rationale: We demonstrate how the first 100,000 SARS-CoV-2 sequences from Africa have helped monitor the epidemic on the continent, how genomic surveillance expanded over the course of the pandemic, and how we adapted our sequencing methods to deal with an evolving virus. Finally, we also examine how viral lineages have spread across the continent in a phylogeographic framework to gain insights into the underlying temporal and spatial transmission dynamics for several variants of concern (VOCs).

Results: Our results indicate that the number of countries in Africa that can sequence the virus within their own borders is growing and that this is coupled with a shorter turnaround time from the time of sampling to sequence submission. Ongoing evolution necessitated the continual updating of primer sets, and, as a result, eight primer sets were designed in tandem with viral evolution and used to ensure effective sequencing of the virus. The pandemic unfolded through multiple waves of infection that were each driven by distinct genetic lineages, with B.1-like ancestral strains associated with the first pandemic wave of

infections in 2020. Successive waves on the continent were fueled by different VOCs, with Alpha and Beta cocirculating in distinct spatial patterns during the second wave and Delta and Omicron affecting the whole continent during the third and fourth waves, respectively. Phylogeographic reconstruction points toward distinct differences in viral importation and exportation patterns associated with the Alpha, Beta, Delta, and Omicron variants and subvariants, when considering both Africa versus the rest of the world and viral dissemination within the continent. Our epidemiological and phylogenetic inferences therefore underscore the heterogeneous nature of the pandemic on the continent and highlight key insights and challenges, for instance, recognizing the limitations of low testing proportions. We also highlight the early warning capacity that genomic surveillance in Africa has had for the rest of the world with the detection of new lineages and variants, the most recent being the characterization of various Omicron subvariants.

Conclusion: Sustained investment for diagnostics and genomic surveillance in Africa is needed as the virus continues to evolve. This is important not only to help combat SARS-CoV-2 on the continent but also because it can be used as a platform to help address the many emerging and reemerging infectious disease threats in Africa. In particular, capacity building for local sequencing within countries or within the continent should be prioritized because this is generally associated with shorter turnaround times, providing the most benefit to local public health authorities tasked with pandemic response and mitigation and allowing for the fastest reaction to localized outbreaks. These investments are crucial for pandemic preparedness and response and will serve the health of the continent well into the 21st century.

Probing SARS-CoV-2-positive plasma to identify potential factors correlating with mild COVID-19 in Ghana, West Africa

Tapela K, Oyawoye FO, Olwal CO, Oporum PC, Amponsah JA, Segbedzi KAL, Tetteh B, Kumi-Ansah F, Mutungi JK, Obodai E, Amoako E, Agyemang S, Ndam NT, Ampofo WK, Rayner JC, **Awandare GA**, Paemka L, Bediako Y, Quashie PK (2022)

[BMC Medicine](#) (2023 Impact Factor: 11.15)

Abstract

Background: West Africa has recorded a relatively higher proportion of asymptomatic coronavirus disease 2019 (COVID-19) cases than the rest of the world, and West Africa-specific host factors could play a role in this discrepancy. Here, we assessed the association between COVID-19 severity among Ghanaians with their immune profiles and ABO blood groups.

Methods: Plasma samples were obtained from Ghanaians PCR-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive individuals. The participants were categorized into symptomatic and asymptomatic cases. Cytokine profiling and antibody quantification were performed using Luminex™ multiplex assay whereas antigen-driven agglutination assay was used to assess the ABO blood groups. Immune profile levels between symptomatic and asymptomatic groups were compared using the two-tailed Mann-Whitney *U* test. Multiple comparisons of cytokine levels among and between days were tested using Kruskal-Wallis with Dunn's post hoc test. Correlations within ABO blood grouping (O's and non-O's) and between cytokines were determined using Spearman correlations. Logistic regression analysis was performed to assess the association of various cytokines with asymptomatic phenotype.

Results: There was a trend linking blood group O to reduced disease severity, but this association was not statistically significant. Generally, symptomatic patients displayed significantly ($p < 0.05$) higher cytokine levels compared to asymptomatic cases with exception of Eotaxin, which was positively associated with asymptomatic cases. There were also significant ($p < 0.05$) associations between other immune markers (IL-6, IL-8 and IL-1Ra) and disease severity. Cytokines' clustering patterns differ between symptomatic and asymptomatic cases. We observed a steady decrease in the concentration of most cytokines over time, while anti-SARS-CoV-2 antibody levels were stable for at least a month, regardless of the COVID-19 status.

Conclusions: The findings suggest that genetic background and pre-existing immune response patterns may in part shape the nature of the symptomatic response against COVID-19 in a West African population. This study offers clear directions to be explored further in larger studies.

Detection of SARS-CoV-2 intra-host recombination during superinfection with Alpha and Epsilon variants in New York City

Wertheim JO, Wang JC, Leelawong M, Martin DP, Havens JL, Chowdhury MA, Pekar JE, Amin H, Arroyo A, **Awandare GA**, Chow HY, Gonzalez E, Luoma E, Morang'a CM, Nekrutenko A, Shank SD, Silver S, Quashie PK, Rakeman JL, Ruiz V, Torian LV, Vasylyeva TI, Kosakovsky Pond SL, Hughes S (2022)

[Nature Communications](#) (2023 Impact Factor: 17.694)

Abstract

Recombination is an evolutionary process by which many pathogens generate diversity and acquire novel functions. Although a common occurrence during coronavirus replication, detection of recombination is only feasible when genetically distinct viruses contemporaneously infect the same host. Here, we identify an instance of SARS-CoV-2 superinfection, whereby an individual was infected with two distinct viral variants: Alpha (B.1.1.7) and Epsilon (B.1429). This superinfection was first noted when an Alpha genome sequence failed to exhibit the classic S gene target failure behavior used to track this variant. Full genome sequencing from four independent extracts reveals that Alpha variant alleles comprise around 75% of the genomes, whereas the Epsilon variant alleles comprise around 20% of the sample. Further investigation reveals the presence of numerous recombinant haplotypes spanning the genome, specifically in the spike, nucleocapsid, and ORF 8 coding regions. These findings support the potential for recombination to reshape SARS-CoV-2 genetic diversity.

Genetic diversity of SARS-CoV-2 infections in Ghana from 2020-2021

Morang'a CM, Ngoi JM, Gyamfi J, Amuzu DSY, Nuertey BD, Soglo PM, Appiah V, Asante IA, Owusu-Oduro P, Armoo S, Adu-Gyasi D, Amoako N, Oliver-Commey J, Owusu M, Sylverken A, Fenteng ED, M'cormack VV, Tei-Maya F, Quansah EB, Ayivor-Djanie R, Amoako EK, Ogbe IT, Yemi BK, Osei-Wusu I, Mettle DNA, Saiid S, Tapela K, Dzabeng F, Magnussen V, Quaye J, Oporum PC, Carr RA, Ababio PT, Abass AK, Akoriyea SK, Amoako E, Kumi-Ansah F, Boakye OD, Mibut DK, Odoom T, Ofori-Boadu L, Allegye-Cudjoe E, Dassah S, Asoala V, Asante KP, Phillips RO, Osei-Atweneboana MY, Gyapong JO, Kuma-Aboagye P, Ampofo WK, Duedu KO, Ndam NT, Bediako Y, Quashie PK, Amenga-Etego LN, & **Awandare GA** (2022).

[Nature Communications](#) (2023 Impact Factor: 17.694)

Abstract

The COVID-19 pandemic is one of the fastest evolving pandemics in recent history. As such, the SARS-CoV-2 viral evolution needs to be continuously tracked. This study sequenced 1123 SARS-CoV-2 genomes from patient isolates (121 from arriving travellers and 1002 from communities) to track the molecular evolution and spatio-temporal dynamics of the SARS-CoV-2 variants in Ghana. The data show that initial local transmission was dominated by B.1.1 lineage, but the second wave was overwhelmingly driven by the Alpha variant. Subsequently, an unheralded variant under monitoring, B.1.1.318, dominated transmission from April to June 2021 before being displaced by Delta variants, which were introduced into community transmission in May 2021. Mutational analysis indicated that variants that took hold in Ghana harboured transmission enhancing and immune escape spike substitutions. The observed rapid viral evolution demonstrates the potential for emergence of novel variants with greater mutational fitness as observed in other parts of the world.

Trends of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody prevalence in selected regions across Ghana

Quashie PQ, Mutungi JK, Dzabeng F, Oduro-Mensah D, Oporum PC, Tapela K, Udoakang A, WACCBIP COVID-19 Team, Asante I, Paemka L, Kumi-Ansah F, Quaye O, Amoako E, Armah R, Kilba C, Boateng NA, Ofori M, Kyei GB, Bediako Y, Ndam N, Abugri J, Ansah P, Ampofo WK, Mutapi F & **Awandare GA** (2021)

[Wellcome Open Research](#) (2023 Impact Factor: 1.777)

Abstract

Background: We set out to estimate the community-level exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Ghana.

Methods: Phased seroprevalence studies of 2729 participants at selected locations across Ghana were conducted. Phase I (August 2020) sampled 1305 individuals at major markets/lorry stations, shopping malls, hospitals and research institutions involved in coronavirus disease 2019 (COVID-19) work. The study utilized a lateral flow rapid diagnostic test (RDT) which detected IgM and IgG antibodies against SARS-CoV-2 nucleocapsid protein.

Results: During Phase I, 252/1305 (19%) tested positive for IgM or IgG or both. Exposure was significantly higher at markets/lorry stations (26.9%) compared to malls (9.4%), with 41–60-year group demonstrating highest seropositivity (27.2%). Exposure was higher in participants with no formal education (26.2%) than those with tertiary education (13.1%); and higher in informally employed workers (24.0%) than those in the formal sector (15.0%). Results from phases II and III, in October and December 2020 respectively, implied either reduced transmissions or loss of antibody expression in some participants. The Upper East region showed the lowest seropositivity (2%). Phase IV, in February 2021, showed doubled seropositivity in the upper income bracket (26.2%) since August 2020, reflective of Ghana's

second wave of symptomatic COVID-19 cases. This suggested that high transmission rates had overcome the initial socioeconomic stratification of exposure risk. Reflective of second wave hospitalisation trends, the 21-40 age group demonstrated modal seropositivity (24.9) in Phase IV whilst 40-60 years and 60+ previously demonstrated highest prevalence.

Conclusions: Overall, the data indicates higher COVID-19 seroprevalence than officially acknowledged, likely implying a considerably lower-case fatality rate than the current national figure of 0.84%. The data also suggests that COVID-19 is predominantly asymptomatic COVID-19 in Ghana. The observed trends mimic clinical trends of infection and imply that the methodology used was appropriate.

A SARS-CoV-2 nucleocapsid ELISA represents a low-cost alternative to lateral flow testing for community screening in LMI countries

Humbert MV, Oporum PC, Brendish NJ, Poole S, He P, Katis I, Quaye J, Bediako Y, Duriez PJ, Eason RW, Sones C, Quaye O, **Awandare GA**, Christodoulides M, Clark TW, Quashie PK, McCormick CJ (2021)

[Journal of Infection](#) (2023 Impact Factor: 38.637)

Abstract

Background Controlling the spread of SARS-CoV-2 is problematic because of transmission driven by asymptomatic and pre-symptomatic individuals. Community screening can help identify these individuals but is often too expensive for countries with limited health care resources. Low-cost ELISA assays may address this problem, but their use has not yet been widely reported. **Methods** We developed a SARS-CoV-2 nucleocapsid ELISA and assessed its diagnostic performance on nose and throat swab samples from UK hospitalised patients and sputum samples from patients in Ghana. **Results** The ELISA had a limit of detection of 84 pg/ml antigen and 16 pfu/ml virus. When tested on UK samples (128 positive and 10 negative patients), sensitivity was 58.6% (49.6-67.2) rising to 78.3% (66.7-87.3) if real-time PCR Ct values > 30 were excluded, while specificity was 100% (69.2-100). In a second trial using the Ghanaian samples (121 positive, 96 negative), sensitivity was 52% (42.8-61.2) rising to 72.6% (61.8-81.2) when a > 30 Ct cut-off was applied, while specificity was 100% (96.2-100). **Conclusions:** Our data show that nucleocapsid ELISAs can test a variety of patient sample types while achieving levels of sensitivity and specificity required for effective community screening. Further investigations into the opportunities that this provides are warranted.

Keywords: Diagnosis; ELISA; Nucleocapsid; SARS-cov-2; Test.

Genomic analysis of SARS-CoV-2 reveals local viral evolution in Ghana

Ngoi JM, Quashie PK, Morang'a CM, Bonney JHK, Amuzu DSY, Kumordjie S, Asante IA, Bonney EY, Eshun M, Boatemaa L, Magnussen V, Kotey EN, Ndam NT, Tei-Maya F, Arjarquah AK, Mutungi JK, Obodai E, Otchere ID, Bediako Y, Amenga-Etego LN, Odoom JK, Anang AK, Kyei GB, Adu B, Ampofo WK & **Awandare GA** (2020)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

The confirmed case fatality rate for the coronavirus disease 2019 (COVID-19) in Ghana has dropped from a peak of 2% in March to be consistently below 1% since May 2020. Globally, case fatality rates have been linked to the strains/clades of circulating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) within a specific country. Here we present 46 whole genomes of SARS-CoV-2 circulating in Ghana, from two separate sequencing batches: 15 isolates from the early epidemic (March 12–April 1 2020) and 31 from later time-points (25–27 May 2020). Sequencing was carried out on an Illumina MiSeq system following an amplicon-based enrichment for SARS-CoV-2 cDNA. After genome assembly and quality control processes, phylogenetic analysis showed that the first batch of 15 genomes clustered into five clades: 19A, 19B, 20A, 20B, and 20C, whereas the second batch of 31 genomes clustered to only three clades 19B, 20A, and 20B. The imported cases (6/46) mapped to circulating viruses in their countries of origin, namely, India, Hungary, Norway, the United Kingdom, and the United States of America. All genomes mapped to the original Wuhan strain with high similarity (99.5–99.8%). All imported strains mapped to the European superclade A, whereas 5/9 locally infected individuals harbored the B4 clade, from the East Asian superclade B. Ghana appears to have 19B and 20B as the two largest circulating clades based on our sequence analyses. In line with global reports, the D614G linked viruses seem

to be predominating. Comparison of Ghanaian SARS-CoV-2 genomes with global genomes indicates that Ghanaian strains have not diverged significantly from circulating strains commonly imported into Africa. The low level of diversity in our genomes may indicate lower levels of transmission, even for D614G viruses, which is consistent with the relatively low levels of infection reported in Ghana.

COVID-19: Time for precision epidemiology

Koks S, Williams RW, Quinn J, Farzaneh F, Conran N, Tsai SJ, **Awandare G**, & Goodman SR (2020)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

The global COVID-19 (SARS-CoV2, COVID-19) tsunami caused by SARSCoV2 is inundating and often-overwhelming health care systems in most countries and regions. Numbers of infected people and the death toll are increasing, with the fortunate exception of the first hit or the best prepared regions of East Asia. While some governments have had success in containing the spread of the virus, the global situation is constantly changing, usually for the worse, and the measures applied by different countries have often been ineffective.

Are we responding too slowly or are our measures too mild or too generic to contain the virus? It is clear that we are missing something, as most of our attempts have been unable to stop the spread of infection. SARS-CoV2 is a new virus and we are missing much key information that is vital to develop and implement fast and appropriate interventions.

Data-driven action is needed to improve the effectiveness and efficiency of interventions at all phases of this pandemic. The present commentary addresses a few of the key—(and we sincerely hope), obvious issues to blunt the trajectory of COVID-19—not just in this early phase of the pandemic, but also during the subsequent more pervasive and quiescent phases of spread and viral mutation.



IMMUNE RESPONSES AND DISEASE PATHOGENESIS



High Plasma Levels of Neopterin Are Associated with Increased Mortality among Children with Severe Malaria in Benin

Blankson SO, Rietmeyer L, Tettey P, Dikroh L, Torniyigah B, Adamou R, Moussiliou A, Padounou C, Amoussou A, Mensah BA, Alao MJ, **Awandare G**, Ndam NT, Roussilhon C, Tahar R (2023)

[Diagnostics](#) (2023 Impact Factor: 3.992)

Abstract

Among the barriers to accessing adequate treatment and high-level monitoring for malaria febrile patients is the lack of effective prognostic markers. Neopterin, which is a marker of monocyte/macrophage activation, was found have increased during severe malaria. In this study, we used quantitative ELISA in order to assess the levels of plasma soluble neopterin in 151 patients from a cohort of Beninese children with severe malaria. We evaluated the prognostic accuracy of this molecule in order to predict the outcome of the disease. Our results show that neopterin levels were not significantly different between patients with different forms of severe malaria, including severe non-cerebral malaria (SNCM) and cerebral malaria (CM). However, the levels of this molecule were found to be higher in patients with severe malarial anemia (SMA) among both CM and SNCM cases (p -value = 0.02). Additionally, the levels of this molecule were found to be higher in patients who died from these pathologies compared to those who survived among the two clinical groups (p -value < 0.0001) and within the same group (p -value < 0.0001 for the CM group, p -value = 0.0046 for the SNCM group). The AUC-ROC for fatality among all the severe cases was 0.77 with a 95%CI of (0.69–0.85). These results suggest that plasma neopterin levels constitute a potential biomarker for predicting fatality among severe falciparum malaria patients.

Keywords: [neopterin](#); [severe malaria](#); [cerebral malaria](#); [anemia](#); *[Plasmodium falciparum](#)*; [Benin](#)

***Plasmodium falciparum* Sexual Commitment Rate Variation among Clinical Isolates and Diverse Laboratory-Adapted Lines**

Stewart LB, Freville A, Voss TS, Baker DA, **Awandare GA**, Conway DJ (2022)

[Microbiology Spectrum](#) (2023 Impact Factor: 9.043)

Abstract

Asexual blood-stage malaria parasites must produce sexual progeny to infect mosquitoes. It is important to understand the scope and causes of intraspecific variation in sexual commitment rates, particularly for the major human parasite *P. falciparum*. First, two alternative assay methods of measuring sexual commitment were compared to test a genetically modified *P. falciparum* line with elevated commitment rates inducible by overexpression of GDV1. The methods yielded correlated measurements with higher sensitivity and precision being achieved by one employing detection of the early gametocyte differentiation marker Pfs16. Thus, this was used to survey a diverse range of parasite lines and test each in multiple biological replicate assays in a serum-free medium supplemented with Albumax. There were differences among six recent clinical isolates from Ghana in their mean rates of sexual commitment per cycle, ranging from 3.3% to 12.2%. Among 13 diverse long-term laboratory-adapted lines, mean sexual commitment rates for most ranged from 4.7% to 134%, a few had lower rates with means from 0.3 to 1.6%, and one with a nonfunctional *ap2-g* gene always showed zero commitment. Among a subset of lines tested for the effects of exogenous choline to suppress commitment, there were significant differences. As expected, there was no effect in a line that had lost the *gdl* gene and that had generally low commitment, whereas the others showed quantitatively variable but significant responses to choline, suggesting potential trait variation. The results indicated the value of performing multiple replicate assays for understanding the variation of this key reproductive trait that likely

affects transmission.

Importance: Only sexual-stage malaria parasites are transmitted from human blood to mosquitoes. Thus, it is vital to understand variations in sexual commitment rates because these may be modifiable or susceptible to blocking. Two different methods of commitment rate measurement were first compared, demonstrating higher sensitivity and precision by the detection of an early differentiation marker, which was subsequently used to survey diverse lines. Clinical isolates from Ghana showed significant variation in mean per-cycle commitment rates and variation among biological replicates. Laboratory-adapted lines of diverse origins had a wider range with most being within the range observed for the clinical isolates, while a minority consistently had lower or zero rates. There was quantitative variation in the effects when adding choline to suppress commitment, indicating differing responsiveness of parasites to this environmental modification. Performing multiple assay replicates and comparisons of diverse isolates was important to understand this trait and its potential effects on transmission.

Population-based sero-epidemiological investigation of the dynamics of SARS-CoV-2 infections in the Greater Accra Region of Ghana

Mensah BA, Ndong IC, Quashie PK, Guichet E, Abuaku B, Effah-Baafi Y, Tapela K, Asiedu K, Appiedu-Addo SNA, Obheng LB, Amponsah JA, Kusi KA, Ofori M, Ayoub A, Courtin D, Tahar R, Delaporte E, **Awandare G**, Ndam NT (2022)

[Scientific Reports](#) (2023 Impact Factor: 4.996)

Abstract

The coronavirus disease 2019 (COVID-19) pandemic devastated countries worldwide, and resulted in a global shutdown. Not all infections are symptomatic and hence the extent of SARS-CoV-2 infection in the community is unknown. The paper presents the dynamics of the SARS-CoV-2 epidemic in the Greater Accra Metropolis, describing the evolution of seroprevalence through time and by age group. Three repeated independent population-based surveys at 6-week intervals were conducted in from November 2020 to July 2021. The global and by age-groups weighted seroprevalences were estimated and the risk factors for SARS-CoV-2 antibody seropositivity were assessed using logistic regression. The overall age-standardized SARS-CoV-2 antibody seroprevalence for both spike and nucleocapsid increased from 13.8% (95% CI 11.9, 16.1) in November 2020 to 39.6% (95% CI 34.8, 44.6) in July 2021. After controlling for gender, marital status, education level, and occupation, the older age group over 40 years had a higher odds of seropositivity than the younger age group (OR 3.0 [95% CI 1.1–8.5]) in the final survey. Pupils or students had 3.3-fold increased odds of seropositivity (OR 3.2 [95% CI 1.1–8.5]) compared to the unemployed. This study reinforces that, SARS-CoV-2 infections have been significantly higher than reported.

Molecular Characterization and Immuno-Reactivity Patterns of a Novel *Plasmodium falciparum* Armadillo-Type Repeat Protein, PfATRP

Amlabu E, Ilani P, Opoku G, Nyarko PB, Quansah E, Thiam LG, Anim M, Ayivor-Djanie R, Akuh OA, Mensah-Brown H, Rayner JC, & **Awandare GA** (2020)

[Frontiers in Cellular and Infection Microbiology](#) (2023 Impact Factor: 6.073)

Abstract

Nearly half of the genes in the *Plasmodium falciparum* genome have not yet been functionally investigated. We used homology-based structural modeling to identify multiple copies of Armadillo repeats within one uncharacterized gene expressed during the intraerythrocytic stages, PF3D7_0410600, subsequently referred to as *P. falciparum* Armadillo-Type Repeat Protein (PfATRP). Soluble recombinant PfATRP was expressed in a bacterial expression system, purified to apparent homogeneity and the identity of the recombinant PfATRP was confirmed by mass spectrometry. Affinity-purified α -PfATRP rabbit antibodies specifically recognized the recombinant protein. Immunofluorescence assays revealed that α -PfATRP rabbit antibodies reacted with *P. falciparum* schizonts. Anti-PfATRP antibody exhibited peripheral staining patterns around the merozoites. Given the localization of PfATRP in merozoites, we tested for an egress phenotype during schizont arrest assays and demonstrated that native PfATRP is inaccessible on the surface of merozoites in intact schizonts. Dual immunofluorescence assays with markers for the inner membrane complex (IMC) and microtubules suggest partial colocalization in both asexual and sexual stage parasites. Using the soluble recombinant PfATRP in a screen of plasma samples revealed that malaria-infected children have naturally acquired PfATRP-specific antibodies.

Keywords: PfATRP; immunolocalization; immunoreactivity; recombinant protein; serosurveillance.

Comparison of leucocyte profiles between healthy children and those with asymptomatic and symptomatic *Plasmodium falciparum* infections

Prah DA, Amoah LE, Gibbins MP, Bediako Y, Cunningham AJ, **Awandare GA** & Hafalla JCR. (2020)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

The immune mechanisms that determine whether a *Plasmodium falciparum* infection would be symptomatic or asymptomatic are not fully understood. Several studies have been carried out to characterize the associations between disease outcomes and leucocyte numbers. However, the majority of these studies have been conducted in adults with acute uncomplicated malaria, despite children being the most vulnerable group.

Methods

Peripheral blood leucocyte subpopulations were characterized in children with acute uncomplicated (symptomatic; n = 25) or asymptomatic (n = 67) *P. falciparum* malaria, as well as malaria-free (uninfected) children (n = 16) from Obom, a sub-district of Accra, Ghana. Leucocyte subpopulations were enumerated by flow cytometry and correlated with two measures of parasite load: (a) plasma levels of *P. falciparum* histidine-rich protein 2 (PfHRP2) as a proxy for parasite biomass and (b) peripheral blood parasite densities determined by microscopy.

Results

In children with symptomatic *P. falciparum* infections, the proportions and absolute cell counts of total (CD3+) T cells, CD4+T cells, CD8+T cells, CD19+B cells and CD11c+dendritic cells (DCs) were significantly lower as compared to asymptomatic *P. falciparum*-infected and

uninfected children. Notably, CD15 + neutrophil proportions and cell counts were significantly increased in symptomatic children. There was no significant difference in the proportions and absolute counts of CD14 + monocytes amongst the three study groups. As expected, measures of parasite load were significantly higher in symptomatic cases. Remarkably, *Pf*HRP2 levels and parasite densities negatively correlated with both the proportions and absolute numbers of peripheral leucocyte subsets: CD3 + T, CD4 + T, CD8 + T, CD19 + B, CD56 + NK, $\gamma\delta$ + T and CD11c + cells. In contrast, both *Pf*HRP2 levels and parasite densities positively correlated with the proportions and absolute numbers of CD15 + cells.

Conclusions

Symptomatic *P. falciparum* infection is correlated with an increase in the levels of peripheral blood neutrophils, indicating a role for this cell type in disease pathogenesis. Parasite load is a key determinant of peripheral cell numbers during malaria infections.

Immune Responses to the Sexual Stages of *Plasmodium falciparum* Parasites

Kengne-Quafo, J. A., Sutherland, C. J., Binka, F. N., **Awandare, G. A.**, Urban, B. C., & Dinko, B. (2019)

[Frontiers in Immunology](#) (2023 Impact Factor: 8.787)

Abstract

Malaria infections remain a serious global health problem in the world, particularly among children and pregnant women in Sub-Saharan Africa. Moreover, malaria control and elimination is hampered by rapid development of resistance by the parasite and the vector to commonly used antimalarial drugs and insecticides, respectively. Therefore, vaccine-based strategies are sorely needed, including those designed to interrupt disease transmission. However, a prerequisite for such a vaccine strategy is the understanding of both the human and vector immune responses to parasite developmental stages involved in parasite transmission in both man and mosquito. Here, we review the naturally acquired humoral and cellular responses to sexual stages of the parasite while in the human host and the *Anopheles* vector. In addition, updates on current anti-gametocyte, anti-gamete, and anti-mosquito transmission blocking vaccines are given. We conclude with our views on some important future directions of research into *P. falciparum* sexual stage immunity relevant to the search for the most appropriate transmission-blocking vaccine.

Antibody Reactivity to Merozoite Antigens in Ghanaian Adults Correlates With Growth Inhibitory Activity Against *Plasmodium falciparum* in Culture

Mensah-Brown, H. E., Aspelting-Jones, H., Delimini, R. K., Asante, K. P., Amlabu, E., Bah, S. Y., Beeson, J. G., Wright, G. J., Conway, D. J., & **Awandare, G. A** (2019)

[Open Forum Infectious Diseases](#) (2023 Impact Factor: 4433.)

Abstract

Background

Plasmodium falciparum uses a repertoire of merozoite-stage proteins for invasion of erythrocytes. Antibodies against some of these proteins halt the replication cycle of the parasite by preventing erythrocyte invasion and are implicated as contributors to protective immunity against malaria.

Methods

We assayed antibody reactivity against a panel of 9 recombinant antigens based on erythrocyte-binding antigen (EBA) and reticulocyte-like homolog (Rh) proteins in plasma from children with malaria and healthy adults residing in 3 endemic areas in Ghana using enzyme-linked immunosorbent assay. Purified immunoglobulin (Ig)G from adult plasma samples was also tested for invasion inhibition against 7 different *P falciparum* culture lines, including clinical isolates.

Results

Antibodies against the antigens increased in an age-dependent manner in children. Breadth of reactivity to the different antigens was strongly associated with in vitro parasite growth inhibitory activity of IgG purified from the adults. The strongest predictors of breadth of

antibody reactivity were age and transmission intensity, and a combination of reactivities to Rh2, Rh4, and Rh5 correlated strongly with invasion inhibition.

Conclusions

Growth inhibitory activity was significantly associated with breadth of antibody reactivity to merozoite antigens, encouraging the prospect of a multicomponent blood-stage vaccine.

Keywords: falciparum malaria, growth inhibitory activity, humoral immunity, invasion, vaccine development

Impact of malaria and hepatitis B co-infection on clinical and cytokine profiles among pregnant women

Anabire NG, Aryee PA, Abdul-Karim A, Quaye O, **Awandare GA**, Helegbe GK (2019)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

Background

The overlap of malaria and chronic hepatitis B (CHB) is common in endemic regions, however, it is not known if this co-infection could adversely influence clinical and immunological responses. This study investigated these interactions in pregnant women reporting to antenatal clinics in Ghana.

Methods

Clinical parameters (hemoglobin, liver function biomarker, peripheral malaria parasitemia, and hepatitis B viremia) and cytokine profiles were assayed and compared across four categories of pregnant women: un-infected, mono-infected with *Plasmodium falciparum* (*Malaria group*), mono-infected with chronic hepatitis B virus (*CHB group*) and co-infected (*Malaria+CHB group*).

Results

Women with *Malaria+CHB* maintained appreciably normal hemoglobin levels (mean $\pm$ SEM = 10.3 $\pm$ 0.3 g/dL). That notwithstanding, Liver function test showed significantly elevated levels of alanine aminotransferase, aspartate aminotransferase and total bilirubin [$P < 0.001$ for all comparisons]. Similarly, the *Malaria+CHB group* had significantly elevated pro-inflammatory cytokines, including tumour necrosis factor alpha (TNF- α), interleukin (IL)-1 β , and IL-6 [$P < 0.05$ for all comparisons]. In women with *Malaria+CHB*, correlation analysis showed significant negative association of the pro-inflammatory cytokines responses with malaria parasitemia [IL-1 β ($P < 0.001$; $r = -0.645$), IL-6 ($P = 0.046$; $r = -0.394$) and IL-12 ($P = 0.011$; $r = -0.49$)]. On the other hand, the

pro-inflammatory cytokine levels positively correlated with HBV viremia [$TNF-\alpha$ ($P = 0.004$; $r = 0.549$), $IL-1\beta$ ($P < 0.001$; $r = 0.920$), $IL-6$ ($P < 0.001$; $r = 0.777$), $IFN-\gamma$ ($P = 0.002$; $r = 0.579$), $IL-2$ ($P = 0.008$; $r = 0.512$) and $IL-12$ ($P < 0.001$; $r = 0.655$)]. Also, for women in the *Malaria+CHB* group, parasitemia was observed to diminish HBV viremia [$P = 0.003$, $r = -0.489$].

Conclusion

Put together the findings suggests that *Malaria+CHB* could exacerbate inflammatory cytokine responses and increase susceptibility to liver injury among pregnant women in endemic settings.

Serum biochemical parameters and cytokine profiles associated with natural African trypanosome infections in cattle

Bakari, S. M., Ofori, J. A. Kusi, K. A., Aning, G. K., **Awandare , G. A.**, Carrington, M., & Gwira, M. T. (2017)

[Parasites & Vectors](#) (2023 Impact Factor: 4.052)

Abstract

Background

Animal African trypanosomiasis (AAT) greatly affects livestock production in sub-Saharan Africa. In Ghana prevalence of AAT is estimated to range between 5 and 50%. Studies have reported serum biochemical aberrations and variability in cytokine profiles in animals during infection. However, information regarding the biochemical parameters and cytokine profiles associated with natural infections are limited. This study was therefore aimed at investigating changes in the levels of serum biochemical parameters and inflammatory cytokines during a natural infection.

Methods

Nested internal transcribed spacer (ITS)-based PCR and sequencing were used to characterise trypanosome infection in cattle at two areas in Ghana (Adidome and Accra) of different endemicities. The cattle were sampled at four to five-week intervals over a period of six months. Levels of serum biochemical parameters, including creatinine, cholesterol, alkaline phosphatase (ALP), alanine aminotransferase (ALT), total bilirubin and total protein and cytokines (interleukin 10, interleukin 4, interleukin 12, interferon gamma and tumor necrosis factor alpha) were measured in serum samples and then compared between infected cattle and uninfected controls.

Results

The predominant trypanosome species detected in Accra (non-endemic) and Adidome (endemic) were *Trypanosoma theileri* and *Trypanosoma vivax*, respectively. Serum biochemical parameters were similar between infected and uninfected cattle in Accra. Infected cattle at Adidome however, had significantly higher levels of ALP, creatinine, total protein and total bilirubin ($P < 0.05$) and significantly lower levels of cholesterol ($P < 0.05$) at specific time points. At basal levels and during infection, significantly higher pro-inflammatory to anti-inflammatory (Th1/Th2) cytokine ratios were observed in cattle at Adidome compared to Accra ($P < 0.05$), indicating a shift towards Th1 immune response in Adidome. Levels of IL-10 were, however, significantly elevated in infected cattle in Accra ($P < 0.05$), suggesting high anti-inflammatory cytokine response in Accra.

Conclusion

These results suggests that cattle in an endemic area repeatedly infected with trypanosomes of different species or different antigenic types demonstrate high pro-inflammatory (Th1) immune response and biochemical alterations whereas cattle in a non-endemic area with predominantly chronic *T. theileri* infections demonstrate high anti-inflammatory response and no biochemical alterations.

Sickle cell trait is associated with controlled levels of heme and mild pro-inflammatory response during acute malaria infection

Ademolue, T., Amodu, O., & **Awandare, G. A.** (2017)

[Clinical & Experimental Immunology](#) (2023 Impact Factor: 5.732)

Abstract

The controlled induction of haemoxygenase-1 (HO-1), an enzyme that catabolizes haem, has been shown to reduce haem, preventing pathologies associated with haem toxicity. The hemoglobin genotype HbAS confers reduced susceptibility to severe complications of malaria by a mechanism that is not well understood. Using a longitudinal approach, we investigated the effect of baseline concentrations of HO-1 on the accumulation of haem during acute *Plasmodium falciparum* malaria in HbAS and HbAA genotypes. Plasma concentrations of haem, HO-1 and cytokines were quantified in venous blood obtained from children (9 months–5 years of age) during malaria infection, and at convalescence (baseline levels). Parasitaemia was determined during malaria infection. In patients with the HbAA genotype, there was a significant elevation in the plasma concentration of haem ($P=0.002$), and a consequent increased induction of HO-1 ($P<0.001$) during *falciparum* malaria compared with levels at convalescence. Contrary to HbAA, plasma concentration of haem did not change in the HbAS genotypical group ($P=0.110$), and the induction of HO-1 was reduced during malaria compared with levels at convalescence ($P=0.006$). Higher plasma levels of haem were observed in HbAS compared with HbAA at convalescence ($P=0.010$), but this difference did not affect the levels of HO-1 within each genotype ($P=0.450$). Relatively milder proinflammatory responses were observed in HbAS children during malaria infection compared to HbAA children. Our findings suggest that a mechanism of reduced susceptibility to severe malaria pathologies by the HbAS genotype may involve the control of haem, leading to controlled levels of HO-1 and milder proinflammatory responses during acute malaria.

Patterns of inflammatory responses and parasite tolerance vary with malaria transmission intensity

Ademolue, T.W., Aniweh, Y., Kusi, K. A. & **Awandare, G.A.** (2017)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

In individuals living in malaria-endemic regions, parasitaemia thresholds for the onset of clinical symptoms vary with transmission intensity. The mechanisms that mediate this relationship are however, unclear. Since inflammatory responses to parasite infection contribute to the clinical manifestation of malaria, this study investigated inflammatory cytokine responses in children with malaria from areas of different transmission intensities (ranging from low to high).

Methods

Blood samples were obtained from children confirmed with malaria at community hospitals in three areas with differing transmission intensities. Cytokine levels were assessed using the Luminex®-based magnetic bead array system, and levels were compared across sites using appropriate statistical tests. The relative contributions of age, gender, parasitaemia and transmission intensity on cytokine levels were investigated using multivariate regression analysis.

Results

Parasite density increased with increasing transmission intensity in children presenting to hospital with symptomatic malaria, indicating that the parasitaemia threshold for clinical malaria increases with increasing transmission intensity. Furthermore, levels of pro-inflammatory cytokines, including tumour necrosis factor alpha (TNF- α), interferon-gamma (IFN- γ), interleukin (IL)-1 β , IL-2, IL-6, IL-8, and IL-12, decreased with increasing transmission

intensity, and correlated significantly with parasitaemia levels in the low transmission area but not in high transmission areas. Similarly, levels of anti-inflammatory cytokines, including IL-4, IL-7, IL-10 and IL-13, decreased with increasing transmission intensity, with IL-10 showing strong correlation with parasitaemia levels in the low transmission area. Multiple linear regression analyses revealed that transmission intensity was a stronger predictor of cytokine levels than age, gender and parasitaemia.

Conclusion

Taken together, the data demonstrate a strong relationship between the prevailing transmission intensity, parasitaemia levels and the magnitude of inflammatory responses induced during clinical malaria.

Analysis of Erythrocyte Invasion Mechanisms of *Plasmodium falciparum* Clinical Isolates Across 3 Malaria- Endemic Areas in Ghana

Mensah-Brown, H. E., Amoako, N., Abugri, J., Stewart, L. B., Agongo, G., Dickson, E. K., Ofori, M. F., Stoute, J. A., Conway, D. J., & **Awandare, G. A.** (2015)

[Journal of Infectious Diseases](#) (2022 Impact Factor: 7.759)

Abstract

Background: *Plasmodium falciparum* invades human erythrocytes by using an array of ligands that interact with several receptors, including sialic acid (SA), complement receptor 1 (CR1), and basigin. We hypothesized that in malaria-endemic areas, parasites vary invasion pathways under immune pressure. Therefore, invasion mechanisms of clinical isolates collected from 3 zones of Ghana with different levels of endemicity (from lowest to highest, Accra, Navrongo, and Kintampo) were compared using standardized methods.

Methods: Blood samples were collected from children aged 2-14 years in whom malaria was diagnosed, and erythrocyte invasion phenotypes were determined using the enzymes neuraminidase, chymotrypsin, and trypsin, which differentially cleave receptors from the erythrocyte surface. In addition, antibodies against CR1 and basigin were used to determine the contributions of these receptors to invasion. Gene expression levels of *P. falciparum* invasion ligands were also examined.

Results: The parasites generally expressed SA-independent invasion phenotypes across the malaria-endemic areas, with parasites from Kintampo showing the highest invasion rates in neuraminidase-treated erythrocytes. CR1 was a major mediator of SA-independent invasion, while basigin was essential for both SA-dependent and SA-independent invasion

mechanisms. Furthermore, expression of the basigin ligand PfRh5 was the best predictor of donor parasitemia.

Conclusions: Erythrocyte invasion phenotypes expressed by *P. falciparum* are influenced by endemicity levels, and the PfRh5-basigin pathway is a potential vaccine target.

Keywords: *Plasmodium falciparum*; basigin; complement receptor 1; endemicity; erythrocyte invasion; ligand gene expression; malaria.

Innate Immune response to malaria: the role of cytokine genes

Awandare, G. A., & Perkins, D. J. (2014)

Molecular approaches to understanding life and disease: a reader from Department of Biochemistry, Cell and Molecular Biology University of Ghana

Abstract

Malaria remains the leading cause of mortality in children under five years old in Africa. Although the determinants of malaria disease outcomes are not completely known, it is clear that intensity and breadth of the innate immune response to the infection is a major factor that influences the pathogenesis of malaria in children. Therefore, a major pillar of malaria research at the Department of Biochemistry, Cell and Molecular Biology has been the investigation of the natural immune response elicited by the presence of the malaria parasite in blood, as well as the relationship between this immune response and manifestations of severe life-threatening complications of the disease. Working with collaborators at the Noguchi Memorial Institute for Medical Research, Legon, and the University of Pittsburgh, Pennsylvania, we have examined the production of inflammatory mediators, including cytokines, chemokines and effector molecules in children with various forms of malaria. In addition, we investigated the relationships of genetic variation of these immune mediators with susceptibility to severe malaria. Significantly, our results demonstrate that the innate immune regulatory cytokine known as macrophage migration inhibitory factor (MIF) plays

a critical role in determining whether the innate immune response induced in children with malaria leads to protection or enhance pathogenesis.

Insights into deregulated TNF and IL-10 production in malaria: implications for understanding severe malarial anaemia

Boeuf, P. S., Loizon, S., **Awandare, G. A.**, Tetteh, J. K., Addae, M. M., Adjei, G. O., Goka, B., Kurtzhals, J. A., Puijalon, O., Hviid, L., Akanmori, B. D., & Behr, C. (2012)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Severe malarial anaemia (SMA) is a major life-threatening complication of paediatric malaria. Protracted production of pro-inflammatory cytokines promoting erythrophagocytosis and depressing erythropoiesis is thought to play an important role in SMA, which is characterized by a high TNF/IL-10 ratio. Whether this TNF/IL-10 imbalance results from an intrinsic incapacity of SMA patients to produce IL-10 or from an IL-10 unresponsiveness to infection is unknown. Monocytes and T cells are recognized as the main sources of TNF and IL-10 *in vivo*, but little is known about the activation status of those cells in SMA patients.

Methods

The IL-10 and TNF production capacity and the activation phenotype of monocytes and T cells were compared in samples collected from 332 Ghanaian children with non-overlapping SMA (n=108), cerebral malaria (CM) (n=144) or uncomplicated malaria (UM) (n=80) syndromes. Activation status of monocytes and T cells was ascertained by measuring HLA-DR⁺ and/or CD69⁺ surface expression by flow cytometry. The TNF and IL-10 production was assessed in a whole-blood assay after or not stimulation with lipopolysaccharide (LPS) or

phytohaemagglutinin (PHA) used as surrogate of unspecific monocyte and T cell stimulant. The number of circulating pigmented monocytes was also determined.

Results

Monocytes and T cells from SMA and CM patients showed similar activation profiles with a comparable decreased HLA-DR expression on monocytes and increased frequency of CD69⁺ and HLA-DR⁺ T cells. In contrast, the acute-phase IL-10 production was markedly decreased in SMA compared to CM ($P = .003$) and UM ($P = .004$). Although in SMA the IL-10 response to LPS-stimulation was larger in amplitude than in CM ($P = .0082$), the absolute levels of IL-10 reached were lower ($P = .013$). Both the amplitude and levels of TNF produced in response to LPS-stimulation were larger in SMA than CM ($P = .019$). In response to PHA-stimulation, absolute levels of IL-10 produced in SMA were lower than in CM ($P = .005$) contrasting with TNF levels, which were higher ($P = .001$).

Conclusions

These data reveal that SMA patients have the potential to mount efficient IL-10 responses and that the TNF/IL-10 imbalance may reflect a specific monocyte and T cell programming/polarization pattern in response to infection.

Mechanisms of erythropoiesis inhibition by malarial pigment and malaria-induced proinflammatory mediators in an in vitro model

Awandare, G. A., Kempaiah, P., Ochiel, D. O., Piazza, P., Christopher, C.K., & Perkins, D. J. (2011)

[American Journal of Hematology](#) (2023 Impact Factor: 13.268)

Abstract

One of the commonest complications of *Plasmodium falciparum* malaria is the development of severe malarial anemia (SMA), which is, at least in part, due to malaria-induced suppression of erythropoiesis. Factors associated with suppression of erythropoiesis and development of SMA include accumulation of malarial pigment (hemozoin, *PfHz*) in bone marrow and altered production of inflammatory mediators, such as tumor necrosis factor (TNF)- α , and nitric oxide (NO). However, studies investigating the specific mechanisms responsible for inhibition of red blood cell development have been hampered by difficulties in obtaining bone marrow aspirates from infants and young children, and the lack of reliable models for examining erythroid development. As such, an in vitro model of erythropoiesis was developed using CD34+ stem cells derived from peripheral blood to examine the effects of *PfHz*, *PfHz*-stimulated peripheral blood mononuclear cell (PBMC)-conditioned media (CM-*PfHz*), TNF- α , and NO on erythroid cell development. *PfHz* only slightly suppressed erythroid cell proliferation and maturation marked by decreased expression of glycophorin A (GPA). On the other hand, CM-*PfHz*, TNF- α , and NO significantly inhibited erythroid cell proliferation. Furthermore, decreased proliferation in cells treated with CM-*PfHz* and NO was accompanied by increased apoptosis of erythropoietin-stimulated CD34+ cells. In addition, NO significantly inhibited erythroid cell maturation, whereas TNF- α did not appear to be detrimental to maturation. Collectively, our results demonstrate that *PfHz* suppresses erythropoiesis by acting both directly on erythroid cells, and indirectly via inflammatory mediators produced from *PfHz*-stimulated PBMC, including TNF- α and NO.

Naturally acquired hemozoin by monocytes promotes suppression of RANTES in children with malarial anemia through an IL-10-dependent mechanism

Were, T., Davenport, G. C., Ouma, Y. E., Hittner, B. J., **Awandare, G. A.**, Otieno, M. F., Ouma, C., Orago, A. S., Vulule, J. M., Ong'echa, J. M., & Perkins, D. J. (2009)

[Microbes and Infection](#) (2022 Impact Factor: 9.570)

Abstract

Regulated upon activation, normal T-cell expressed, and secreted (RANTES, CCL-5) is an important immunoregulatory mediator that is suppressed in children with malarial anemia (MA). Although pro-inflammatory (e.g., TNF- α , IL-1 β and IFN- γ) and anti-inflammatory (e.g., IL-4, IL-10 and IL-13) cytokines regulate RANTES production, their effect on RANTES in children with MA has not been determined. Since intraleukocytic malarial pigment, hemozoin (Hz), causes dysregulation in chemokine and cytokine production, the impact of naturally acquired Hz (*pfHz*) on RANTES and RANTES-regulatory cytokines (TNF- α , IFN- γ , IL-1 β , IL-4, IL-10, and IL-13) was examined. Circulating RANTES levels progressively declined with increasing levels of pigment-containing monocytes (PCM) ($P = 0.035$). Additional experiments in cultured peripheral blood mononuclear cells (PBMC) showed that monocytic acquisition of *pfHz* (*in vivo*) was associated with suppression of RANTES under baseline ($P = 0.001$) and stimulated conditions ($P = 0.072$). Although high PCM levels were associated with decreased circulating IFN- γ ($P = 0.003$) and IL-10 ($P = 0.010$), multivariate modeling revealed that only PCM ($P = 0.048$, $\beta = -0.171$) and IL-10 ($P < 0.0001$, $\beta = -0.476$) were independently associated with RANTES production. Subsequent *in vitro* experiments revealed that blockade of endogenous IL-10 significantly increased RANTES production ($P = 0.028$) in PBMC from children with naturally acquired Hz. Results here demonstrate that monocytic acquisition of Hz suppresses RANTES production in children with MA through an IL-10-dependent mechanism.

Keywords: Malaria; Hemozoin; Monocytes; RANTES; IL-10

Suppression of a novel hematopoietic mediator in children with severe malarial anemia

Keller, C. C., Ouma, C., Ouma, Y., **Awandare, G. A.**, Davenport, G. C., Were, T., Hittner, J. B., Vulule, J. M., Ong'echa, J. M., & Perkins, D. J. (2009)

[Infection and Immunity](#) (2022 Impact Factor: 3.609)

Abstract

In areas of holoendemic *Plasmodium falciparum* transmission, severe malarial anemia (SMA) is a leading cause of pediatric morbidity and mortality. Although many soluble mediators regulate erythropoiesis, it is unclear how these factors contribute to development of SMA. Investigation of novel genes dysregulated in response to malarial pigment (hemozoin [PfHz]) revealed that stem cell growth factor (SCGF; also called C-type lectin domain family member 11A [CLEC11A]), a hematopoietic growth factor important for development of erythroid and myeloid progenitors, was one of the most differentially expressed genes. Additional experiments with cultured peripheral blood mononuclear cells (PBMCs) demonstrated that PfHz decreased SCGF/CLEC11A transcriptional expression in a time-dependent manner. Circulating SCGF levels were then determined for Kenyan children (n = 90; aged 3 to 36 months) presenting at a rural hospital with various severities of malarial anemia. SCGF levels in circulation (P = 0.001) and in cultured PBMCs (P = 0.004) were suppressed in children with SMA. Circulating SCGF also correlated positively with hemoglobin levels (r = 0.241; P = 0.022) and the reticulocyte production index (RPI) (r = 0.280; P = 0.029). In addition, SCGF was decreased in children with reduced erythropoiesis (RPI of < 0.001) and in children with elevated levels of naturally acquired monocytic PfHz (P = 0.019). Thus, phagocytosis of PfHz promotes a decrease in SCGF gene products, which may contribute to reduced erythropoiesis in children with SMA.

Increased circulating interleukin (IL)-23 in children with malarial anemia: in vivo and in vitro relationship with co-regulatory cytokines IL-12 and IL-10

Ong'echa, J. M, Remo, A. M., Kristoff, J, Hittner, J. B., Were, T., Ouma, C., Otieno, R. O., Vulule, J. M, Keller, C. C., **Awandare, G. A.** & Perkins, D. J. (2008)

[Clinical Immunology](#) (2023 Impact Factor: 10.19)

Abstract

Severe malarial anemia (SMA) is a leading cause of mortality among children in sub-Saharan Africa. Although the novel cytokine, interleukin (IL)-23, promotes anemia in chronic inflammatory diseases, the role of IL-23 in SMA remains undefined. Since IL-23 and IL-12 share the IL-12p40 subunit and IL-12R β 1 receptor, and are down-regulated by IL-10, relationships among these cytokines were explored in Kenyan children with varying severities of malarial anemia. Children with malarial anemia had increased circulating IL-23 and IL-10 and decreased IL-12 relative to healthy controls. Enhanced anemia severity and elevated parasitemia were associated with increased IL-10 relative to IL-23 and IL-12. Further exploration of the relationships among the cytokines using an in vitro model in which peripheral blood mononuclear cells were treated with synthetic hemozoin (sHz, malarial pigment) revealed that IL-12p35 and IL-23p19 transcripts had a sustained induction over 72 h, while IL-12p40 and IL-10 message peaked at 24 h, and rapidly declined thereafter. Taken together, results here show that IL-23 is elevated in children with malarial anemia, and that IL-10 and IL-12 appear to have important regulatory effects on IL-23 production during childhood malaria.

Keywords: *Plasmodium falciparum*; Malarial anemia; Hemozoin; Cytokines; IL-23; IL-12; IL-10

150. Complement activation in Ghanaian children with Severe *Plasmodium falciparum* malaria

Helegbe, G. K., Goka, B. Q., Kurtzhals, J. A. L., Addae, M. M., Ollaga, E., Tetteh, J. K. A., Dodoo, D., Ofori, M., Hirayama, K., **Awandare, G. A.**, & Akanmori, B. D. (2007)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Severe anaemia (SA), intravascular haemolysis (IVH) and respiratory distress (RD) are severe forms of *Plasmodium falciparum* malaria, with RD reported to be of prognostic importance in African children with malarial anaemia. Complement factors have been implicated in the mechanism leading to excess anaemia in acute *P. falciparum* infection.

Methods

The direct Coombs test (DCT) and flow cytometry were used to investigate the mean levels of RBC-bound complement fragments (C3d and C3bαβ) and the regulatory proteins [complement receptor 1 (CD35) and decay accelerating factor (CD55)] in children with discrete clinical forms of *P. falciparum* malaria. The relationship between the findings and clinical parameters including coma, haemoglobin (Hb) levels and RD were investigated.

Results

Of the 484 samples tested, 131(27%) were positive in DCT, out of which 115/131 (87.8%) were positive for C3d alone while 16/131 (12.2%) were positive for either IgG alone or both. 674% of the study population were below 5 years of age and DCT positivity was more common in this age group relative to children who were 5 years or older (Odds ratio, OR = 3.8; 95%CI, 2.2–6.7, $p < 0.001$). DCT correlated significantly with RD ($\beta = -304$, $p = 0.006$), but multiple regression analysis revealed that, Hb ($\beta = -0.341$, $p = 0.012$) and coma ($\beta = -0.256$,

$p = 0.034$) were stronger predictors of RD than DCT ($\beta = 0.228$, $p = 0.061$). DCT was also not associated with IVH, $p = 0.19$, while spleen size was inversely correlated with Hb ($r = -0.402$, $p = 0.001$). Flow cytometry showed similar mean fluorescent intensity (MFI) values of CD35, CD55 and C3b $\alpha\beta$ levels on the surfaces of RBC in patients and asymptomatic controls (AC). However, binding of C3b $\alpha\beta$ correlated significantly with CD35 or CD55 ($p < 0.001$).

Conclusion

These results suggest that complement activation contributed to anaemia in acute childhood *P. falciparum* malaria, possibly through induction of erythrophagocytosis and haemolysis. In contrast to other studies, this study did not find association between levels of the complement regulatory proteins, CD35 and CD55 and malarial anaemia. These findings suggest that complement activation could also be involved in the pathogenesis of RD but larger studies are needed to confirm this finding.

Higher production of peripheral blood macrophage migration inhibitory factor in healthy children with a history of mild malaria relative to children with a history of severe malaria

Awandare, G. A., Kremsner, P. G., Hittner, J. B., Keller, C. C., Clark, I. A., Weinberg, J. B., & Perkins, D. J. (2007)

[*American Journal of Tropical Medicine and Hygiene*](#) (2023 Impact Factor: 3.707)

Abstract

Plasmodium falciparum malaria is one of the leading causes of childhood morbidity and mortality in sub-Saharan Africa. The host immune response to *P. falciparum* is a critical determinant of malarial pathogenesis and disease outcomes. Macrophage migration inhibitory factor (MIF) is a central regulator of innate immune responses to bacterial and parasitic infections. Our recent investigations demonstrated that peripheral blood MIF production was suppressed in children with severe malaria. Because examination of MIF production in children with active disease does not account for the inherent ability of the host to generate MIF, basal circulating MIF and peripheral blood mononuclear cell (PBMC) MIF transcript levels were determined in healthy children with a history of either mild or severe malaria. Children with prior mild malaria had higher plasma MIF levels and PBMC MIF transcripts than children with an identical number of previous episodes of severe malaria. These results suggest that increased basal MIF production may be important in generating immune responses that protect against the development of severe malaria.

Role of monocyte-acquired hemozoin in suppression of macrophage migration inhibitory factor in children with severe malarial anemia

Awandare, G. A., Ouma, Y., Ouma, C., Were, T., Otieno, R., Keller, C. C., Davenport, G. C., Hittner, J. B., Vulule, J., Ferrell, R., Ong'echa, J. M., & Perkins, D. J. (2007)

[Infection and immunity](#) (2022 Impact Factor: 3.609)

Abstract

Severe malarial anemia (SMA), caused by *Plasmodium falciparum* infections, is one of the leading causes of childhood mortality in sub-Saharan Africa. Although the molecular determinants of SMA are largely undefined, dysregulation in host-derived inflammatory mediators influences disease severity. Macrophage migration inhibitory factor (MIF) is an important regulator of innate inflammatory responses that has recently been shown to suppress erythropoiesis and promote pathogenesis of SMA in murine models. To examine the role of MIF in the development of childhood SMA, peripheral blood MIF production was examined in Kenyan children (aged <3 years, n = 357) with *P. falciparum* malarial anemia. All children in the study were free from bacteremia and human immunodeficiency virus type 1. Since deposition of malarial pigment (hemozoin [Hz]) contributes to suppression of erythropoiesis, the relationship between MIF concentrations and monocytic acquisition of Hz was also examined in vivo and in vitro. Circulating MIF concentrations declined with increasing severity of anemia and significantly correlated with peripheral blood leukocyte MIF transcripts. However, MIF concentrations in peripheral blood were not significantly associated with reticulocyte production. Multivariate regression analyses, controlling for age, gender, and parasitemia, further revealed that elevated levels of pigment-containing monocytes (PCM) was associated with SMA and decreased MIF production. In addition, PCM levels were a better predictor of hemoglobin and MIF concentrations than parasite density. Additional experiments in malaria-naïve individuals demonstrated that hemozoin caused

both increased and decreased MIF production in cultured peripheral blood mononuclear cells (PBMC) in a donor-specific manner, independent of apoptosis. However, PBMC MIF production in children with acute malaria progressively declined with increasing anemia severity. Results presented here demonstrate that acquisition of hemozoin by monocytes is associated with suppression of peripheral blood MIF production and enhanced severity of anemia in childhood malaria.

Increased levels of inflammatory mediators in children with severe *Plasmodium falciparum* malaria with respiratory distress

Awandare, G. A., Goka, B., Boeuf, P., Tetteh, J. K. A., Kurtzhals, J. A. L., Behr, C., & Akanmori, B. D. (2006)

[Journal of Infectious Diseases](#) (2022 Impact Factor: 7.759)

Abstract

Background: Respiratory distress (RD), a symptom of underlying metabolic acidosis, has been identified as a major risk factor for mortality in children with severe malaria in Africa, yet the molecular mediators involved in the pathogenesis of RD have not been identified

Methods: We studied circulating levels of mediators of inflammation—including the cytokines tumor necrosis factor (TNF)-alpha and interleukin (IL)-10; the chemokines macrophage inflammatory protein (MIP)-1alpha, MIP-1Beta, and IL-8; and the immune activation marker neopterin—in children with RD, severe malarial anemia (SMA), cerebral malaria (CM), and uncomplicated malaria (UM)

Results: Children with RD had significantly higher plasma levels of TNF-alpha, IL-10, and neopterin and a significantly higher TNF-alpha:IL-10 ratio than those without RD. In addition, the results demonstrated that, relative to UM, CM was associated with increased levels of TNF-alpha and decreased levels of MIP-1alpha, whereas SMA was associated with decreased levels of IL-10. Circulating levels of neopterin were inversely correlated with hemoglobin, whereas levels of MIP-1Beta were positively correlated with parasitemia

Conclusions: We conclude that distinct clinical presentations of severe malaria are associated with specific patterns of inflammatory mediators. In particular, we show, to our knowledge for the first time, that patients with malaria and RD have a strong and unbalanced proinflammatory response that may be involved in the pathogenesis of the underlying metabolic acidosis.

A macrophage migration inhibitory factor promoter polymorphism is associated with high-density parasitemia in children with malaria

Awandare, G. A., Ouma, C., Keller, C. C., Were, T., Otieno, R., Ouma, Y., Davenport, D. C., Hittner, J. B., Vulule, Ong'echa, J. M., Ferrell, R., & Perkins, D. J. (2006)

[Genes and Immunity](#) (2023 Impact Factor: 4.248)

Abstract

Macrophage migration inhibitory factor (MIF) is a pleiotropic cytokine that regulates innate and adaptive immune responses to bacterial and parasitic infections. Functional promoter variants in the MIF gene influence susceptibility to inflammatory diseases in Caucasians. As the role of genetic variation in the MIF gene in conditioning malaria disease outcomes is largely unexplored, the relationship between a G to C transition at MIF –173 and susceptibility to high-density parasitemia (HDP) and severe malarial anemia (SMA) was examined in Kenyan children (aged 3–36 months; $n=477$) in a holoendemic *Plasmodium falciparum* transmission region. In a multivariate model, controlling for age, gender, HIV-1 status, and sickle-cell trait, MIF –173CC was associated with an increased risk of HDP compared to MIF –173GG. No significant associations were found between MIF –173 genotypic variants and susceptibility to SMA. Additional studies demonstrated that homozygous G alleles were associated with lower basal circulating MIF levels relative to the GC group. However, stimulation of cultured peripheral blood mononuclear cells with malarial pigment (hemozoin) increased MIF production in the GG group and decreased MIF production in the GC group. Thus, variability at MIF –173 is associated with functional changes in MIF production and susceptibility to HDP in children with malaria.

Decreased circulating macrophage migration inhibitory factor (MIF) protein and blood mononuclear cell MIF transcripts in children with *Plasmodium falciparum* malaria

Awandare, G. A., Hittner, J. B., Kreamsner, P. G., Ochiel, D. O., Keller, C. C., Weinberg, J. B., Clark, I. A., & Perkins, D. J. (2006)

[Clinical Immunology](#) (2022 Impact Factor: 10.19)

Abstract

Plasmodium falciparum malaria remains one of the most frequently lethal diseases affecting children in sub-Saharan Africa, yet the immune mediators that regulate pathogenesis are only partially defined. Since macrophage migration inhibitory factor (MIF) is important for regulating innate immunity in bacterial and parasitic infections, circulating MIF and peripheral blood mononuclear cell (PBMC) MIF transcripts were investigated in children with acute falciparum malaria. Peripheral blood levels of MIF-regulatory cytokines and effector molecules, including interferon (IFN)- γ , tumor necrosis factor (TNF)- α , interleukin (IL)-12, IL-10, transforming growth factor (TGF)- β 1, bicyclo-prostaglandin (PG) E_2 , and nitric oxide synthase activity were also determined. Circulating MIF and PBMC MIF mRNA were significantly lower in children with acute malaria relative to healthy, malaria-exposed children. Peripheral blood MIF levels showed no association with either parasitemia or hemoglobin concentrations. Circulating MIF was, however, significantly associated with IL-12 and TGF- β 1. Multiple regression analyses revealed that IFN- γ was the most significant predictor of peripheral blood MIF concentrations. These findings suggest that reduced MIF production may promote enhanced disease severity in children with falciparum malaria.

Keywords: Macrophage migration inhibitory factor (MIF); *Plasmodium falciparum*; Malaria; Anemia; Immunity; Cytokines.

Differential regulation of beta-chemokines in children with *Plasmodium falciparum* malaria

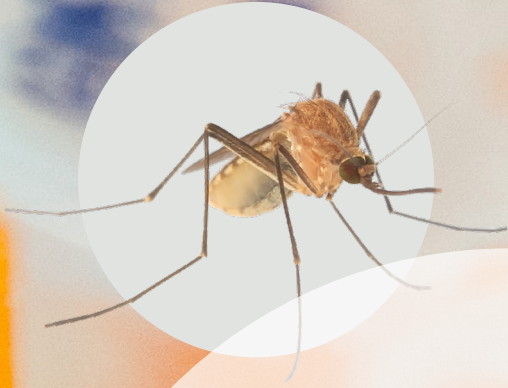
Ochiel, D. O., **Awandare, G. A.**, Keller, C. C., Hittner, J. B., Kremsner, P. J., Weinberg, J. B., & Perkins, D. J. (2005)

[Infection and Immunity](#) (2022 Impact Factor: 3.609)

Abstract

Chemokines regulate the host immune response to a variety of infectious pathogens. Since the role of chemokines in regulating host immunity in children with *Plasmodium falciparum* malaria has not previously been reported, circulating levels of beta-chemokines (MIP-1alpha, MIP-1beta, and RANTES) and their respective transcriptional profiles in ex vivo peripheral blood mononuclear cells (PBMCs) were investigated. Peripheral blood MIP-1alpha and MIP-1beta levels were significantly elevated in mild and severe malaria, while RANTES levels decreased with increasing disease severity. Beta-chemokine gene expression profiles in blood mononuclear cells closely matched those of circulating beta-chemokines, illustrating that PBMCs are a primary source for the observed pattern of beta-chemokine production during acute malaria. Statistical modeling revealed that none of the chemokines was significantly associated with either parasitemia or anemia. Additional investigations in healthy children with a known history of malaria showed that children with prior severe malaria had significantly lower baseline RANTES production than children with a history of mild malaria, suggesting inherent differences in the ability to produce RANTES in these two groups. Baseline MIP-1alpha and MIP-1beta did not significantly differ between children with prior severe malaria and those with mild malaria. Additional in vitro experiments in PBMCs from healthy, malaria-naïve donors revealed that *P. falciparum*-derived hemozoin (Hz; malarial pigment) and synthetic Hz (beta-hematin) promote a similar pattern of beta-chemokine gene expression. Taken together, the results presented here demonstrate that children with severe

malaria have a distinct profile of beta-chemokines characterized by increased circulating levels of MIP-1alpha and MIP-1beta and decreased RANTES. Altered patterns of circulating beta-chemokines result, at least in part, from Hz-induced changes in beta-chemokine gene expression in blood mononuclear cells.



PATHOGEN VECTOR BIOLOGY & VACCINE DISCOVERY



Characterization of a novel *Plasmodium falciparum* merozoite surface antigen and potential vaccine target

Niaré K, Chege T, Rosenkranz M, Mwai K, Saßmannshausen Z, Odera D, Nyamako L, Tuju J, Alfred T, Waitumbi JN, Ogutu B, Sirima SB, **Awandare G**, Kouriba B, Rayner JC, & Osier FHA (2023)

[Frontiers in Immunology \(2023\)](#) Impact Factor: 8.787)

Abstract

Introduction: Detailed analyses of genetic diversity, antigenic variability, protein localization and immunological responses are vital for the prioritization of novel malaria vaccine candidates. Comprehensive approaches to determine the most appropriate antigen variants needed to provide broad protection are challenging and consequently rarely undertaken.

Methods: Here, we characterized PF3D7_1136200, which we named Asparagine-Rich Merozoite Antigen (ARMA) based on the analysis of its sequence, localization and immunogenicity. We analyzed IgG and IgM responses against the common variants of ARMA in independent prospective cohort studies in Burkina Faso (N = 228), Kenya (N = 252) and Mali (N = 195) using a custom microarray, Div-KILCHIP.

Results: We found a marked population structure between parasites from Africa and Asia. African isolates shared 34 common haplotypes, including a dominant pair although the overall selection pressure was directional (Tajima's D = -2.57; Fu and Li's F = -9.69; P < 0.02). ARMA was localized to the merozoite surface, IgG antibodies induced Fc-mediated degranulation of natural killer cells and strongly inhibited parasite growth in vitro. We found profound serological diversity, but IgG and IgM responses were highly correlated and a hierarchical clustering analysis identified only three major serogroups. Protective IgG and

IgM antibodies appeared to target both cross-reactive and distinct epitopes across variants. However, combinations of IgG and IgM antibodies against selected variants were associated with complete protection against clinical episodes of malaria.

Discussion: Our systematic strategy exploits genomic data to deduce the handful of antigen variants with the strongest potential to induce broad protection and may be broadly applicable to other complex pathogens for which effective vaccines remain elusive.

Short-term cryopreservation and thawing have minimal effects on *Plasmodium falciparum* ex vivo invasion profile

Thiam LG, Ansah F, Niang M, **Awandare GA**, Aniweh Y (2022)

[Frontiers in Cellular and Infection Microbiology](#) (2023 Impact Factor: 6.073)

Abstract

Ex vivo phenotyping of *P. falciparum* erythrocyte invasion diversity is important in the identification and down selection of potential malaria vaccine targets. However, due to the lack of appropriate laboratory facilities in remote areas of endemic countries, direct processing of *P. falciparum* clinical isolates is usually not feasible. Here, we investigated the combined effect of short-term cryopreservation and thawing processes on the ex vivo invasion phenotypes of *P. falciparum* isolates. Ex-vivo or in vitro invasion phenotyping assays were performed with *P. falciparum* clinical isolates prior to or following culture adaptation, respectively. All isolates were genotyped at Day 0 for parasite clonality. Subsequently, isolates that were successfully culture-adapted were genotyped again at Days 7, 15, 21, and 28-post adaptation. Invasion phenotyping assays were performed in isogenic isolates revived at different time points (3, 6, and 12 months) post-cryopreservation and the resulting data were compared to that from ex-vivo invasion data of matched isogenic parental isolates. We also show that short-term culture adaptation selects for parasite clonality and could be a driving force for variation in invasion phenotypes as compared to ex vivo data where almost all parasite clones of a given isolate are present. Interestingly, our data show little variation in the parasites' invasion phenotype following short-term cryopreservation. Altogether, our data suggest that short-term cryopreservation of uncultured *P. falciparum* clinical isolates is a reliable mechanism for storing parasites for future use.

Highly Variable Expression of Merozoite Surface Protein MSPDBL2 in Diverse *Plasmodium falciparum* Clinical Isolates and Transcriptome Scans for Correlating Genes

Hocking SE, Stewart LB, Freville A, Reid AJ, Tarr SJ, Tetteh KKA, Flueck C, Ahouidi AD, Amambua-Ngwa A, Diakite M, **Awandare GA**, Conway DJ (2022)

[mBio](#) (2023 Impact Factor: 7.786)

Abstract

The merozoite surface protein MSPDBL2 of *Plasmodium falciparum* is under strong balancing selection and is a target of naturally acquired antibodies. Remarkably, MSPDBL2 is expressed in only a minority of mature schizonts of any cultured parasite line, and *mispdbl2* gene transcription increases in response to overexpression of the gametocyte development inducer GDV1, so it is important to understand its natural expression. Here, MSPDBL2 in mature schizonts was analyzed in the first *ex vivo* culture cycle of 96 clinical isolates from 4 populations with various levels of infection endemicity in different West African countries, by immunofluorescence microscopy with antibodies against a conserved region of the protein. In most isolates, less than 1% of mature schizonts were positive for MSPDBL2, but the frequency distribution was highly skewed, as nine isolates had more than 3% schizonts positive and one had 73% positive. To investigate whether the expression of other gene loci correlated with MSPDBL2 expression, whole-transcriptome sequencing was performed on schizont-enriched material from 17 of the isolates with a wide range of proportions of schizonts positive. Transcripts of particular genes were highly significantly positively correlated with MSPDBL2 positivity in schizonts as well as with *mispdbl2* gene transcript levels, showing overrepresentation of genes implicated previously as involved in gametocytogenesis but not including the gametocytogenesis master regulator *ap2-g*. Single-cell transcriptome analysis

of a laboratory-adapted clone showed that most individual parasites expressing *mspdbl2* did not express *ap2-g*, consistent with MSPDBL2 marking a developmental subpopulation that is distinct but likely to co-occur alongside sexual commitment.

Importance: These findings contribute to understanding malaria parasite antigenic and developmental variation, focusing on the merozoite surface protein encoded by the single locus under strongest balancing selection. Analyzing the initial *ex vivo* generation of parasites grown from a wide sample of clinical infections, we show a unique and highly skewed pattern of natural expression frequencies of MSPDBL2, distinct from that of any other antigen. Bulk transcriptome analysis of a range of clinical isolates showed significant overrepresentation of sexual development genes among those positively correlated with MSPDBL2 protein and *mspdbl2* gene expression, indicating the MSPDBL2-positive subpopulation to be often coincident with parasites developing sexually in preparation for transmission. Single-cell transcriptome data confirm the absence of a direct correlation with the *ap2-g* master regulator of sexual development, indicating that the MSPDBL2-positive subpopulation has a separate function in asexual survival and replication under conditions that promote terminal sexual differentiation.

Investigating a *Plasmodium falciparum* erythrocyte invasion phenotype switch at the whole transcriptome level

Nyarko, P.B., Tarr, S.J., Aniweh, Y. Stewart, L. B., Conway, D. J. & **Awandare, G. A.** (2020)

[Scientific Reports](#) (2023 Impact Factor: 4.996)

Abstract

The central role that erythrocyte invasion plays in *Plasmodium falciparum* survival and reproduction makes this process an attractive target for therapeutic or vaccine development. However, multiple invasion-related genes with complementary and overlapping functions afford the parasite the plasticity to vary ligands used for invasion, leading to phenotypic variation and immune evasion. Overcoming the challenge posed by redundant ligands requires a deeper understanding of conditions that select for variant phenotypes and the molecular mediators. While host factors including receptor heterogeneity and acquired immune responses may drive parasite phenotypic variation, we have previously shown that host-independent changes in invasion phenotype can be achieved by continuous culturing of the W2mef and Dd2 *P. falciparum* strains in moving suspension as opposed to static conditions. Here, we have used a highly biologically replicated whole transcriptome sequencing approach to identify the molecular signatures of variation associated with the phenotype switch. The data show increased expression of particular invasion-related genes in switched parasites, as well as a large number of genes encoding proteins that are either exported or form part of the export machinery. The genes with most markedly increased expression included members of the erythrocyte binding antigens (*EBA*), reticulocyte binding homologues (*RH*), surface associated interspersed proteins (*SURFIN*), exported protein family 1 (*EPFI*) and *Plasmodium* Helical Interspersed Sub-Telomeric (*PHIST*) gene families. The data indicate changes in expression of a repertoire of genes not previously associated with erythrocyte invasion phenotypes, suggesting the possibility that moving suspension culture may also select for other traits.

***Plasmodium falciparum* Merozoite Associated Armadillo Protein (PfMAAP) Is Apically Localized in Free Merozoites and Antibodies Are Associated With Reduced Risk of Malaria**

Aniweh Y, Nyarko PB, Charles-Chess E, Ansah F, Osier FHA, Quansah E, Thiam LG, Kamuyu G, Marsh K, Conway DJ, Tetteh KKA, & **Awandare GA** (2020)

[Frontiers in Immunology](#) (2023 Impact Factor: 8.787)

Abstract

Understanding the functional role of proteins expressed by *Plasmodium falciparum* is an important step toward unlocking potential targets for the development of therapeutic or diagnostic interventions. The armadillo (ARM) repeat protein superfamily is associated with varied functions across the eukaryotes. Therefore, it is important to understand the role of members of this protein family in *Plasmodium* biology. The *Plasmodium falciparum* armadillo repeats only (PfARO; Pf3D7_0414900) and *P. falciparum* merozoite organizing proteins (PfMOP; Pf3D7_0917000) are armadillo-repeat containing proteins previously characterized in *P. falciparum*. Here, we describe the characterization of another ARM repeat-containing protein in *P. falciparum*, which we have named the *P. falciparum* Merozoites-Associated Armadillo repeats protein (PfMAAP). Antibodies raised to three different synthetic peptides of PfMAAP show apical staining of free merozoites and those within the mature infected schizont. We also demonstrate that the antibodies raised to the PfMAAP peptides inhibited invasion of erythrocytes by merozoites from different parasite isolates. In addition, naturally acquired human antibodies to the N- and C- termini of PfMAAP are associated with a reduced risk of malaria in a prospective cohort analysis.

Keywords: Malaria; antibodies; antigen; armadillo; invasion; merozoites; recombinant protein.

Localization and function of a *Plasmodium falciparum* protein (PF3D7_1459400) during erythrocyte invasion

Amlabu E, Nyarko PB, Opoku G, Ibrahim-Dey D, Ilani P, Mensah-Brown H, Akporh GA, Akuh OA, Ayugane EA, Amoh-Boateng D, Kusi KA, **Awandare GA** (2020)

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Abstract

Nearly 60% of *Plasmodium falciparum* proteins are still uncharacterized and their functions are unknown. In this report, we carried out the functional characterization of a 45 kDa protein (PF3D7_1459400) and showed its potential as a target for blood stage malaria vaccine development. Analysis of protein subcellular localization, native protein expression profile, and erythrocyte invasion inhibition of both clinical and laboratory parasite strains by peptide antibodies suggest a functional role of PF3D7_1459400 protein during erythrocyte invasion. Also, immunoreactivity screens using synthetic peptides of the protein showed that adults resident in malaria endemic regions in Ghana have naturally acquired plasma antibodies against PF3D7_1459400 protein. Altogether, this study presents PF3D7_1459400 protein as a potential target for the development of peptide-based vaccine for blood-stage malaria.

Impact statement

Plasmodium falciparum malaria is a global health problem. Erythrocyte invasion by *P. falciparum* merozoites appears to be a promising target to curb malaria. We have identified and characterized a novel protein that is involved in erythrocyte invasion. Our data on protein subcellular localization, stage-specific protein expression pattern, and merozoite invasion inhibition by α -peptide antibodies suggest a role for PF3D7_1459400 protein during *P. falciparum* erythrocyte invasion. Even more, the human immunoepidemiology data present PF3D7_1459400 protein as an immunogenic antigen which could be further exploited for the development of new anti-infective therapy against malaria.

Comparative analysis of asexual and sexual stage *Plasmodium falciparum* development in different red blood cell types

Amoah LE, Acquah FK, Nyarko PB, Cudjoe E, Donu D, Ayanful-Torgby R, Sey F, Williamson KC & Awandare GA (2020)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Red blood cell (RBC) polymorphisms are suggested to influence the course of *Plasmodium falciparum* malaria. Whereas some variants have been found to be protective, others have been found to enhance parasite development. This study evaluated the effect of variant haemoglobin (Hb) and ABO blood groups on *P. falciparum* merozoite invasion, multiplication rates as well as gametocyte development.

Methods

Approximately 2.5 mL of venous blood was collected from each participant. Flow cytometry was used to determine the in vitro merozoite invasion rates of NF54 parasites into the blood of 66 non-parasitaemic individuals with variant Hb genotypes (HbSS, HbSC) and blood groups (A, B, O), which were then compared with invasion into HbAA blood. The ex vivo asexual parasite multiplication and gametocyte production rates of parasites from 79 uncomplicated malaria patients with varying Hb genotypes (HbAS, HbAC and HbAA) were also estimated using microscopy.

Results

Merozoite invasion rates were significantly reduced by about 50% in RBCs containing HbSS and HbSC relative to HbAA cells. The presence of blood group O and B reduced the invasion

rates of HbSS by about 50% and 60%, respectively, relative to HbSC but the presence of blood group A removed the inhibitory effect of HbSS. The initial parasite densities in uncomplicated malaria patients with Hb genotypes HbAS and HbAC cells were similar but significantly lower than those with genotype HbAA. The ex vivo parasite multiplication rate, gametocytaemia and gametocyte conversion rates followed a similar trend but did not reach statistical significance ($p > 0.05$).

Conclusions

Parasite invasion rate into erythrocytes is dependent on both erythrocyte blood group antigen and haemoglobin genotype as blood group O and B provided protection via reduced merozoite invasion in RBCs containing HbSS relative to HbSC. Regardless of haemoglobin type, greater than 70% malaria patients had circulating ring stage parasites that differentiated into stage II gametocytes in 4 days.

Schizont transcriptome variation among clinical isolates and laboratory-adapted clones of the malaria parasite *Plasmodium falciparum*

Tarr, S. J., Diaz-Ingelmo, O., Stewart, L. B., Hocking, S. E., Murray, L., Duffy, C. W., **Otto, T. D.**, Chappel, L., Rayner, J. C., **Awandare, G. A.**, & **Conway, D. J.** (2018)

[BMC Genomics](#) (2023 Impact Factor: 4.558)

Abstract

Background

Malaria parasites are genetically polymorphic and phenotypically plastic. In studying transcriptome variation among parasites from different infections, it is challenging to overcome potentially confounding technical and biological variation between samples. We investigate variation in the major human parasite *Plasmodium falciparum*, generating RNA-seq data on multiple independent replicate sample preparations of merozoite-containing intra-erythrocytic schizonts from a panel of clinical isolates and from long-term laboratory-adapted clones, with a goal of robustly identifying differentially expressed genes.

Results

Analysis of biological sample replicates shows that increased numbers improve the true discovery rate of differentially expressed genes, and that six independent replicates of each parasite line allowed identification of most differences that could be detected with larger numbers. For highly expressed genes, focusing on the top quartile at schizont stages, there was more power to detect differences. Comparing cultured clinical isolates and laboratory-adapted clones, genes more highly expressed in the laboratory-adapted clones include those encoding an AP2 transcription factor (PF3D7_0420300), a ubiquitin-binding protein and two

putative methyl transferases. In contrast, higher expression in clinical isolates was seen for the merozoite surface protein gene *dblmsp2*, proposed to be a marker of schizonts forming merozoites committed to sexual differentiation. Variable expression was extremely strongly, but not exclusively, associated with genes known to be targeted by Heterochromatin Protein 1. Clinical isolates show variable expression of several known merozoite invasion ligands, as well as other genes for which new RT-qPCR assays validate the quantitation and allow characterisation in samples with more limited material. Expression levels of these genes vary among schizont preparations of different clinical isolates in the first ex vivo cycle in patient erythrocytes, but mean levels are similar to those in continuously cultured clinical isolates.

Conclusions

Analysis of multiple biological sample replicates greatly improves identification of genes variably expressed between different cultured parasite lines. Clinical isolates recently established in culture show differences from long-term adapted clones in transcript levels of particular genes, and are suitable for analyses requiring biological replicates to understand parasite phenotypes and variable expression likely to be relevant in nature.

Functional characterization of *Plasmodium falciparum* surface related Antigen (PfSRA) as a potential blood-stage vaccine target

Amlabu, E., Mensah-Brown, H., Nyarko, P. B., Akuha, O., Opoku, G., Ilani P., Oyagbenro, R., Asiedu K., Aniweh, Y. & **Awandare, G. A.** (2018)

[Journal of Infectious Diseases](#) (2022 Impact Factor: 7.759)

Abstract

Plasmodium falciparum erythrocyte invasion is a multistep process that involves a spectrum of interactions that are not well characterized. We have characterized a 113-kDa immunogenic protein, PF3D7_1431400 (PF14_0293), that possesses coiled-coil structures. The protein is localized on the surfaces of both merozoites and gametocytes, hence the name *Plasmodium falciparum* surface-related antigen (PfSRA). The processed 32-kDa fragment of PfSRA binds normal human erythrocytes with different sensitivities to enzyme treatments. Temporal imaging from initial attachment to internalization of viable merozoites revealed that a fragment of PfSRA, along with PfMSP1₁₉, is internalized after invasion. Moreover, parasite growth inhibition assays showed that PfSRA P1 antibodies potently inhibited erythrocyte invasion of both sialic acid-dependent and -independent parasite strains. Also, immunoepidemiological studies show that malaria-infected populations have naturally acquired antibodies against PfSRA. Overall, the results demonstrate that PfSRA has the structural and functional characteristics of a very promising target for vaccine development.

Keywords: *Plasmodium falciparum*, malaria vaccine, erythrocyte invasion, novel antigens, naturally acquired immunity.

***Plasmodium falciparum* strains spontaneously switch invasion phenotype in suspension culture**

Awandare, G.A., Nyarko, P. B., Aniweh, Y., Ayivor-Djanie, R., & Stoute, J. A. (2018)

[Scientific Reports](#) (2023 Impact Factor: 4.996)

Abstract

The extensive redundancy in the use of invasion ligands by *Plasmodium falciparum*, and its unique ability to switch between invasion pathways have hampered vaccine development. *P. falciparum* strains Dd2 and W2mef have been shown to change from sialic acid (SA)-dependent to SA-independent phenotypes when selected on neuraminidase-treated erythrocytes. Following an observation of increasing ability of Dd2 to invade neuraminidase-treated cells when cultured for several weeks, we systematically investigated this phenomenon by comparing invasion phenotypes of Dd2, W2mef and 3D7 strains of *P. falciparum* that were cultured with gentle shaking (*Suspended*) or under static (*Static*) conditions. While *Static* Dd2 and W2mef remained SA-dependent for the entire duration of the investigation, *Suspended* parasites spontaneously and progressively switched to SA-independent phenotype from week 2 onwards. Furthermore, returning *Suspended* cultures to *Static* conditions led to a gradual reversal to SA-dependent phenotype. The switch to SA-independent phenotype was accompanied by upregulation of the key invasion ligand, reticulocyte-binding homologue 4 (RH4), and the increased invasion was inhibited by antibodies to the RH4 receptor, CR1. Our data demonstrates a novel mechanism for inducing the switching of invasion pathways in *P. falciparum* parasites and may provide clues for understanding the mechanisms involved.

Evaluating anti-disease immunity to malaria and implications for vaccine design

Ademolue, T.W. & **Awandare, G.A.** (2018)

[Immunology](#) (2023 Impact Factor: 7.215)

Abstract

Immunity to malaria could be categorized broadly as antiparasite or antidisease immunity. While most vaccine research efforts have focused on antiparasite immunity, the evidence from endemic populations suggest that antidisease immunity is an important component of natural immunity to malaria. The processes that mediate antidisease immunity have, however, attracted little to no attention, and most interests have been directed towards the antibody responses. This review evaluates the evidence for antidisease immunity in endemic areas and discusses the possible mechanisms responsible for it. Given the key role that inflammation plays in the pathogenesis of malaria, regulation of the inflammatory response appears to be a major mechanism for antidisease immunity in naturally exposed individuals.

Kinetics of antibody responses to PfRH5-complex antigens in Ghanaian children with *Plasmodium falciparum* malaria

Partey, F. D., Castberg, F. C., Sarbah, E. W., Silk, S. E., **Awandare, G. A.**, Draper, S. J., Opoku, N., Kweku, M., Ofori, M. F., Hviid, L., & Barfod, L. (2018)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

Plasmodium falciparum PfRH5 protein binds Ripr, CyRPA and Pf113 to form a complex that is essential for merozoite invasion of erythrocytes. The inter-genomic conservation of the PfRH5 complex proteins makes them attractive blood stage vaccine candidates. However, little is known about how antibodies to PfRH5, CyRPA and Pf113 are acquired and maintained in naturally exposed populations, and the role of PfRH5 complex proteins in naturally acquired immunity. To provide such data, we studied 206 Ghanaian children between the ages of 1–12 years, who were symptomatic, asymptomatic or aparasitemic and healthy. Plasma levels of antigen-specific IgG and IgG subclasses were measured by ELISA at several time points during acute disease and convalescence. On the day of admission with acute *P. falciparum* malaria, the prevalence of antibodies to PfRH5-complex proteins was low compared to other merozoite antigens (EBA175, GLURP-R0 and GLURP-R2). At convalescence, the levels of RH5-complex-specific IgG were reduced, with the decay of PfRH5-specific IgG being slower than the decay of IgG specific for CyRPA and Pf113. No correlation between IgG levels and protection against *P. falciparum* malaria was observed for any of the PfRH5 complex proteins. From this we conclude that specific IgG was induced against proteins from the PfRH5-complex during acute *P. falciparum* malaria, but the prevalence was low and the IgG levels decayed rapidly after treatment. These data indicate that the levels of IgG specific for PfRH5-complex proteins in natural infections in Ghanaian children were markers of recent exposure only.

Gametocyte development and carriage in Ghanaian individuals with uncomplicated *Plasmodium falciparum* malaria

Dinko, B., Ansah, F., Agyare-Kwabi, C., Tagboto, S., Amoah, L., Urban, B., Sutherland, C., Williamson, K., **Awandare, G.**, Binka, F., & Deitsch, K. (2018)

[American Journal of Tropical Medicine and Hygiene](#) (2023 Impact Factor: 3.707)

Abstract

Plasmodium falciparum gametocytes develop over 9–12 days while sequestered in deep tissues. On emergence into the bloodstream, they circulate for varied amounts of time during which certain host factors might influence their further development. We aimed to evaluate the potential association of patient clinical parameters with gametocyte development and carriage via in vivo methods. Seventy-two patients were enrolled from three hospitals in the Volta region of Ghana in 2016. Clinical parameters were documented for all patients, and gametocyte prevalence by microscopy was estimated at 12.5%. By measuring RNA transcripts representing two distinct gametocyte developmental stages using reverse transcriptase quantitative polymerase chain reaction (RT-qPCR), we obtained a more precise estimate of gametocyte carriage while also inferring gametocyte maturation. Fifty-three percent of the study participants harbored parasites expressing transcripts of the immature gametocyte-specific gene (*PF3D7_1477700*), whereas 36% harbored *PF3D7_1438800* RNA-positive parasites, which is enriched in mid and mature gametocytes, suggesting the presence of more immature stages. Linear logistic regression showed that patients older than 5 years but less than 16 years were more likely to carry gametocytes expressing both *PF3D7_1477700* and *PF3D7_1438800* compared with younger participants, and gametocytemia was more likely in mildly anemic individuals compared with those with severe/moderate anemia. These data provide further evidence that a greater number of malaria patients harbor gametocytes than typically estimated by microscopy and suggest a possible association between age, fever, anemia, and gametocytemia.

Variations in the quality of malaria-specific antibodies with transmission intensity in a seasonal malaria transmission area of Northern Ghana

Kusi K. A., Manu E. A., Manful Gwira T., Kyei-Baafour E., Dickson E. K., Amponsah J. A., Remarque E. J., Faber B. W., Kocken C. H. M., Dodoo D., Gyan B. A., **Awandare G. A.**, Atuguba F, Oduro A. R., Koram K. A. (2017)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

Introduction

Plasmodium falciparum induced antibodies are key components of anti-malarial immunity in malaria endemic areas, but their antigen targets can be polymorphic. Induction of a high proportion of strain-specific antibodies will limit the recognition of a broad diversity of parasite strains by these responses. There are indications that circulating parasite diversity varies with malaria transmission intensity, and this may affect the specificity of elicited anti-malarial antibodies. This study therefore assessed the effect of varying malaria transmission patterns on the specificity of elicited antibody responses and to identify possible antibody correlates of naturally acquired immunity to malaria in children in an area of Ghana with seasonal malaria transmission.

Methods

This retrospective study utilized plasma samples collected longitudinally at six time points from children aged one to five years. Multiplex assays were used to measure antibody levels against four *P. falciparum* AMA 1 variants (from the 3D7, FV0, HB3 and CAMP parasite strains) and the 3D7 variant of the EBA 175 region II antigen and the levels compared between symptomatic and asymptomatic children. The relative proportions of cross-reactive and strain-specific antibodies against the four AMA 1 variants per sampling time point were

assessed by Bland-Altman plots. The levels of antibodies against allelic AMA1 variants, measured by singleplex and multiplex luminex assays, were also compared.

Results

The data show that increased transmission intensity is associated with higher levels of cross-reactive antibody responses, most likely a result of a greater proportion of multiple parasite clone infections during the high transmission period. Anti-AMA1 antibodies were however associated with a history of infection rather than protection in this age group.

Conclusion

The data contribute to understanding the underlying mechanism of the acquisition of strain-transcending antibody immunity following repeated exposure to diverse parasite strains.

Malaria Vaccine Development: Focusing Field Erythrocyte Invasion Studies on Phenotypic Diversity

The West African Merozoite Invasion Network (WAMIN): (in alphabetical order): Ahoudi A. D., Amambua-Ngwa A., **Awandare, G. A.**, Bei A. K., Conway D. J., Diakite M., Duraisingh M. T., Rayner J. C., Zenonos Z. A (2016)

[Trends Parasitology](#) (2023 Impact Factor: 10.528)

Abstract

Erythrocyte invasion by *Plasmodium falciparum* merozoites is an essential step for parasite survival and proliferation. Invasion is mediated by multiple ligands, which could be promising vaccine targets. The usage and sequence of these ligands differs between parasites, yet most studies of them have been carried out in only a few laboratory-adapted lines. To understand the true extent of natural variation in invasion phenotypes and prioritize vaccine candidates on a relevant evidence base, we need to develop and apply standardized assays to large numbers of field isolates. The West African Merozoite Invasion Network (WAMIN) has been formed to meet these goals, expand training in *Plasmodium* phenotyping, and perform large-scale field phenotyping studies in order to prioritize blood stage vaccine candidates.

Keywords

Malaria; merozoite; invasion; alternative receptors; antibody inhibition assays; vaccine

Variation in *Plasmodium falciparum* Erythrocyte Invasion Phenotypes and Merozoite Ligand Gene Expression across Different Populations in Areas of Malaria Endemicity

Bowyer, P. W., Stewart, L. B., Aspeling-Jones, H., Mensah-Brown, H. E., Ahouidi, A. D., Amambua-Ngwa, A., **Awandare, G. A.**, & Conway, D. J. (2015)

[Infection and Immunity](#) (2022 Impact Factor: 3.609)

Abstract

Plasmodium falciparum merozoites use diverse alternative erythrocyte receptors for invasion and variably express cognate ligands encoded by the erythrocyte binding antigen (*eba*) and reticulocyte binding-like homologue (*Rh*) gene families. Previous analyses conducted on parasites from single populations in areas of endemicity revealed a wide spectrum of invasion phenotypes and expression profiles, although comparisons across studies have been limited by the use of different protocols. For direct comparisons within and among populations, clinical isolates from three different West African sites of endemicity (in Ghana, Guinea, and Senegal) were cryopreserved and cultured *ex vivo* after thawing in a single laboratory to assay invasion of target erythrocytes pretreated with enzymes affecting receptor subsets. Complete invasion assay data from 67 isolates showed no differences among the populations in the broad range of phenotypes measured by neuraminidase treatment (overall mean, 40.6% inhibition) or trypsin treatment (overall mean, 83.3% inhibition). The effects of chymotrypsin treatment (overall mean, 79.2% inhibition) showed heterogeneity across populations (Kruskal-Wallis $P = 0.023$), although the full phenotypic range was seen in each. Schizont-stage transcript data for a panel of 8 invasion ligand genes (*eba175*, *eba140*, *eba181*, *Rh1*, *Rh2a*, *Rh2b*, *Rh4*, and *Rh5*) were obtained for 37 isolates, showing

similar ranges of variation in each population except that *eba175* levels tended to be higher in parasites from Ghana than in those from Senegal (whereas levels of *eba181* and *Rh2b* were lower in parasites from Ghana). The broad diversity in invasion phenotypes and gene expression seen within each local population, with minimal differences among them, is consistent with a hypothesis of immune selection maintaining parasite variation.

Malaria parasites in blood red cell invasion mechanisms

Awandare, G. A., & Stoute, J. A. (2014)

Molecular approaches to understanding life and disease: a reader from Department of Biochemistry, Cell and Molecular Biology University of Ghana

Abstract

Abstract

As a result of concerted efforts towards malaria control, the incidence of severe life-threatening malaria has reduced significantly in Ghana over the last decade. However, the development of an effective deployable vaccine remains the optimal strategy for solving the menace of malaria. Although the parasites initially infect liver cells, clinical symptoms of malaria are caused only after the parasites has moved into the blood and invaded red blood cells. Therefore, targeting the invasion process is a logical approach for the design of vaccines for preventing malaria. A major part of the research at the Department of Biochemistry, Cell and Molecular Biology over recent years has focused on gaining a thorough understanding of the molecular mechanisms through which the malaria parasite infects and propagates itself in red blood cells. This overview describes the highlights of some of the most significant research findings resulting from work conducted in collaboration with partners locally and internationally, including the Noguchi Memorial Institute for Medical Research, Legon, and the Walter Reed Army Institute of Research, Maryland. One of the most significant findings of these studies was the elucidation of a novel role for complement receptor 1 (CR1) as a major receptor used by *Plasmodium falciparum* for invading red blood cells.

Erythrocyte invasion receptor preferences of *Plasmodium falciparum* isolates in Ghanaian children

Henrietta Mensah-Brown, Nicholas Amoako, James Abugri, Godfred Agongo, Emmanuel K. Dickson, Jose A. Stoute, David J. Conway, **Gordon A. Awandare** (2013)

[Abstract](#)

Clinical manifestations of *Plasmodium falciparum* infection are caused by invasion of erythrocytes by the malaria parasite, a process which is mediated by multiple receptor-ligand interactions. Antibodies against some parasite ligands have been shown to significantly inhibit parasite growth in vitro, demonstrating that these interactions may be good targets for the development of an effective blood stage vaccine. This study was aimed at investigating the erythrocyte receptors used by *P. falciparum* isolates in Ghana. *P. falciparum* isolates were collected from children aged 2-14 years attending hospitals in three ecologically distinct zones in Ghana: Accra, Kintampo and Navrongo. Erythrocyte invasion assays were performed to test the ability of the parasites to invade erythrocytes treated with neuraminidase, trypsin and chymotrypsin, which selectively remove receptors from the erythrocyte surface. In addition, antibodies against two recently identified receptors, basigin and complement receptor 1 (CR1) were used to determine the dependence of the isolates on these pathways. Two to four assays were performed on each isolate. All 16 field isolates tested so far were capable of invading neuraminidase-treated erythrocytes, with invasion efficiencies of 40-80% relative to untreated erythrocytes, indicating that these parasites had sialic acid-independent invasion phenotypes. Invasion of trypsin or chymotrypsin-treated erythrocytes varied between 20-60% relative to untreated erythrocytes representing the contributions of glycophorins A, B, and C. Furthermore, for nearly all the parasites tested, anti-CR1 antibodies significantly inhibited invasion of neuraminidase-treated erythrocytes, confirming the role of CR1 as the major sialic acid-independent receptor for *P. falciparum*. Additional isolates are being tested and results from about 50 parasites will be presented.

Examining selection on *Plasmodium falciparum* at different endemic sites within Ghana

Craig Duffy, Samuel Assefa, James Abugri, Nicholas Amoako, Thomas Ayorigiya, Bronwyn MacInnis, Dominic Kwiatkowski, David Conway, **Gordon Awandare** (2014)

Abstract

Plasmodium falciparum uses a variety of alternative ligand-receptor interactions in order to invade red blood cells. The diversity of these pathways has traditionally been investigated by assessing the ability of parasite isolates to invade red blood cells that have been enzyme treated to selectively remove receptors. To date a variety of assay formats have been reported in different studies, but a standardised assay has not been applied to compare across population samples from diverse locations. Here we investigate *P. falciparum* invasion phenotypes from clinical isolates sampled in three sites on a gradient of transmission intensity in West Africa, using a single assay format. This is the first large-scale comparative analysis of erythrocyte invasion by clinical isolates from different endemic countries assayed in a single laboratory. Assays were performed on over 100 *P. falciparum* isolates from Ghana, Guinea and Senegal, that were cryopreserved at source and thawed so that the laboratory operator of the invasion assay was blinded to the sample source. These isolates were phenotyped for their ability to invade erythrocytes treated with neuraminidase, trypsin, chymotrypsin or a combination of these enzymes, in the first round of invasion following thawing but prior to adaption to culture. RNA was isolated for qRT-PCR from the schizont stage of a subset of these ex vivo cultured isolates in order to determine the relative expression levels of parasite invasion ligand genes. The data are analysed to explore the hypothesis that particular invasion pathways are selected in areas of high infection endemicity where there is strong acquired immunity against the parasite ligands, compared with areas of lower endemicity where immune selection.

***Plasmodium falciparum* field isolates use complement receptor 1 (CR1) as a receptor for invasion of erythrocytes**

Awandare, G. A., Spadafora, C., Moch, K. J., Dutta, S., Haynes, J. D., & Stoute, J. A. (2011)

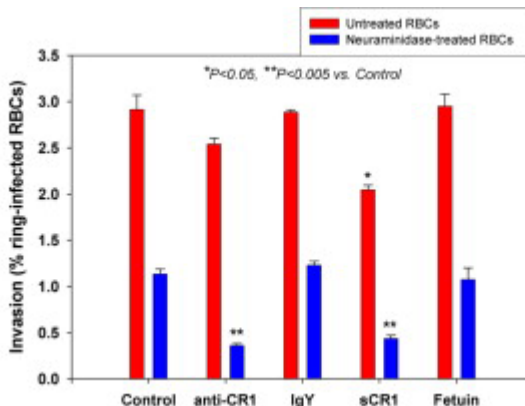
[Molecular and Biochemical Parasitology](#) (2023 Impact Factor: 1.845)

Abstract

A majority of *Plasmodium falciparum* strains invade erythrocytes through interactions with sialic acid (SA) on glycoporphins. However, we recently reported that complement receptor 1 (CR1) is a SA-independent invasion receptor of many laboratory strains of *P. falciparum*. To determine the role of CR1 in erythrocyte invasion among *P. falciparum* field isolates, we tested eight isolates obtained from children in Kenya. All the parasites examined were capable of invading in a SA-independent manner, and invasion of neuraminidase-treated erythrocytes was nearly completely blocked by anti-CR1 and soluble CR1 (sCR1). In addition, anti-CR1 and sCR1 partially inhibited invasion of intact erythrocytes in a majority of isolates tested. Sequencing of the hypervariable region of *P. falciparum* AMA-1 showed considerable diversity among all the isolates. These data demonstrate that CR1 mediates SA-independent erythrocyte invasion in *P. falciparum* field isolates.

Graphical abstract

Invasion of erythrocytes by *Plasmodium falciparum* field isolates is inhibited by CR1 antagonists suggesting that CR1 is used as a receptor by these parasites.



Complement receptor 1 is a sialic acid independent erythrocyte receptor of *Plasmodium falciparum*

Spadafora, C., **Awandare, G. A.**, Kopydlowski, K. M., Czege, J., Moch, K. J., Finberg, W. R., Tsokos, G. C. & Stoute, J. A. (2010)

[PLoS Pathogens](#) (2023 Impact Factor: 7464)

Abstract

Plasmodium falciparum is a highly lethal malaria parasite of humans. A major portion of its life cycle is dedicated to invading and multiplying inside erythrocytes. The molecular mechanisms of erythrocyte invasion are incompletely understood. *P. falciparum* depends heavily on sialic acid present on glycophorins to invade erythrocytes. However, a significant proportion of laboratory and field isolates are also able to invade erythrocytes in a sialic acid-independent manner. The identity of the erythrocyte sialic acid-independent receptor has been a mystery for decades. We report here that the complement receptor 1 (CR1) is a sialic acid-independent receptor for the invasion of erythrocytes by *P. falciparum*. We show that soluble CR1 (sCR1) as well as polyclonal and monoclonal antibodies against CR1 inhibit sialic acid-independent invasion in a variety of laboratory strains and wild isolates, and that merozoites interact directly with CR1 on the erythrocyte surface and with sCR1-coated microspheres. Also, the invasion of neuraminidase-treated erythrocytes correlates with the level of CR1 expression. Finally, both sialic acid-independent and dependent strains invade CR1 transgenic mouse erythrocytes preferentially over wild-type erythrocytes but invasion by the latter is more sensitive to neuraminidase. These results suggest that both sialic acid-dependent and independent strains interact with CR1 in the normal red cell during the invasion process. However, only sialic acid-independent strains can do so without the presence of glycophorin sialic acid. Our results close a longstanding and important gap in the understanding of the mechanism of erythrocyte invasion by *P. falciparum* that will eventually make possible the development of an effective blood stage vaccine.



DRUG DISCOVERY

Comparative susceptibility of *Plasmodium ovale* and *Plasmodium falciparum* field Isolates to reference and lead candidate antimalarial drugs in Ghana

Aniweh Y, Soulama A, Chirawurah J, Ansah F, Danwonno HA, Sogore F, Rouillier M, Campo B, Amenga-Etego L, Djimde AA, **Awandare GA**, & Demebele L (2023)

[Microbiology spectrum \(2023\)](#) Impact Factor: 9.043)

Abstract

Malaria treatments resulted in the decline of the deadliest *Plasmodium falciparum* globally while species, such as *P. ovale*, infections have been increasingly detected across sub-Saharan Africa. Currently, no experimental drug sensitivity data are available to guide effective treatment and management of *P. ovale* infections, which is necessary for effective malaria elimination. We conducted a prospective study to evaluate *P. ovale* epidemiology over 1 year and determined *ex vivo* susceptibility of the field isolates to existing and lead advanced discovery antimalarial drugs. We report that while *P. falciparum* dominated both symptomatic and asymptomatic malaria cases, *P. ovale* in mono or co-infections caused 7.16% of symptomatic malaria. Frontline antimalarials artesunate and lumefantrine inhibited *P. ovale* as potently as *P. falciparum*. Chloroquine, which has been withdrawn in Ghana, was also highly inhibitory against both *P. ovale* and *P. falciparum*. In addition, *P. ovale* and *P. falciparum* displayed high susceptibility to quinine, comparable to levels observed with chloroquine. Pyrimethamine, which is a major drug for disease massive prevention, also showed great inhibition of *P. ovale*, comparable to effects on *P. falciparum*. Furthermore, we identified strong inhibition of *P. ovale* using GNF179, a close analogue of KAF156 imidazolopiperazines, which is a novel class of antimalarial drugs currently in clinical phase II testing. We further demonstrated that the *Plasmodium* phosphatidylinositol-4-OH kinase (PI4K)-specific inhibitor, KDU691, is highly inhibitory against *P. ovale* and *P. falciparum* field isolates. Our data indicated that existing and lead advanced discovery antimalarial drugs are suitable for the treatment of *P. ovale* infections in Ghana.

Importance: Current malaria control and elimination tools such as drug treatments are not specifically targeting *P. ovale*. *P. ovale* can form hypnozoite and cause relapsing malaria. *P. ovale* is the third most dominant species in Africa and requires radical cure treatment given that it can form liver dormant forms called hypnozoites that escape all safe treatments. The

inappropriate treatment of *P. ovale* would sustain its transmission in Africa where the medical need is the greatest. This is a hurdle for successful malaria control and elimination. Here, we provided experiment data that were lacking to guide *P. ovale* treatment and disease control policy makers using reference antimalarial drugs. We also provided key experimental data for 2 clinical candidate drugs that can be used for prioritization selection of lead candidate's identification for clinical development.

Reconsidering the incubation period of Marburg virus disease

Schneider KA, Bonney JHK, Kubio C, **Awandare GA**, Eichner M (2022)

[Lancet Infectious Diseases](#) (2023 Impact Factor: 71.421)

Abstract

Several outbreaks of [Marburg virus disease](#) (MVD) with a total of 475 cases have been reported globally so far. Although some of these cases were [zoonotic](#), two larger outbreaks with human-to-human transmission occurred in the Democratic Republic of the Congo (154 cases) and in Angola (252 cases).¹

In August 2022, Ghana announced that the country can again be regarded to be free of [MVD](#).^{2, 3} The control of such outbreaks crucially depends on knowing the [incubation period](#): it establishes which contacts of known cases should be traced, how long they need to be quarantined, and when a country can be declared free of MVD; and it also helps to identify [zoonotic](#) reservoirs. Although the onset of the disease is easily recognised, the time of infection (which is needed to calculate the incubation period) can only be established for patients with very short exposure windows. Especially for newly emerging and rare infections, initial outbreak investigations are caught in a vicious circle: some previous knowledge should be used to establish when and from whom new patients might have acquired their infection.

Estimates on the MVD [incubation period](#) have, thus, been highly influenced by the original outbreak in Marburg, Germany, in 1967, where laboratory workers were exposed to infected monkey organs for several weeks.⁴ The time of infection could be narrowed down in only four of 21 cases, and was argued to be 5–7 days. All these patients had direct contact with blood; those with a short incubation period were infected by contaminated broken glass or needles, suggesting an initial [viral load](#) that might have been much higher than found after human-to-human transmission.

At the same time, six more MVD cases occurred in Frankfurt, Germany, after contact with the blood from infected monkeys; in this outbreak, the incubation period was narrowed down to 7–9 days.⁵ This interval coincided with that of patients from Kenya, where the infection occurred in the hospital or at a funeral and patients had either skin contact with infected blood or got infected from highly contagious cases or corpses.⁶ Based on the original outbreak and on information that has been gathered during subsequent outbreaks, the incubation period of MVD is believed to last for 5–10 days (range, 3–21), yet newer evidence from Angola and from the latest outbreak in Ghana shows that this range has been underestimated.^{7, 8}

One of the reasons for this might be that historic estimates ignore the route of transmission and the infecting [viral load](#), which might influence the duration of the incubation period.¹ Two patients from Angola who were infected by human-to-human transmission had an incubation period of at least 23 and 26 days,⁷ contradicting the previous upper limit of 21 days.

Observations: from the latest outbreak in Ghana provide further evidence of a longer incubation period. The index patient of the Ghana outbreak developed MVD on June 24, 2022, two days after returning from travel to the western region of Ghana, where he had entered abandoned mines (such places had previously been associated with zoonotic MVD reservoirs).⁹ His son and wife had contact with him from his return to their home on June 22, until his burial on June 27. After completing a 21-day quarantine period and daily monitoring, they developed symptoms on July 17 (for the son) and July 21 (for the wife), and were diagnosed with MVD.^{2, 8, 10} Because the wife became symptomatic only 4 days after her son, it is highly unlikely that he infected her. Hence, the incubation period of the son was 21–24 days, and that of his mother was 25–28 days. These two secondary infections provide further evidence for an extended incubation period after human-to-human transmission.

Together with the two documented patients infected by household transmission in Angola who had an incubation period of 21 or more days, the recent outbreak in Ghana shows that new estimates of the incubation period of MVD that account for the route of infection are urgently needed. A thorough study of the clinical records of all previous outbreaks, which is less biased towards the assumption of a short incubation period of 5–9 days, would be necessary to obtain adequate estimates and to inform [public health policy](#).

The Pharmacologically Active Alkaloid Cryptolepine Activates a Type 1 Interferon Response That Is Independent of MAVS and STING Pathways

Domfeh SA, Narkwa PW, Quaye O, Kusi KA, Addy BS, Lant S, Sumner RP, Maluquer de Motes C, **Awandare GA**, Ansah C, Mutocheluh M (2022)

[Journal of Immunology Research](#) (2023 Impact Factor: 4493)

Abstract

Type 1 interferons (IFN-1) are pleiotropic cytokines with well-established anticancer and antiviral properties, particularly in mucosal tissues. Hence, natural IFN-1-inducing treatments are highly sought after in the clinic. Here, we report for the first time that cryptolepine, a pharmacoactive alkaloid in the medicinal plant *Cryptolepis sanguinolenta*, is a potent IFN-1 pathway inducer. Cryptolepine increased the transcript levels of *JAK1*, *TYK2*, *STAT1*, *STAT2*, *IRF9*, and *OAS3*, as well as increased the accumulation of STAT1 and OAS3 proteins, similar to recombinant human IFN- γ . Cryptolepine effects were observed in multiple cell types including a model of human macrophages. This response was maintained in MAVS and STING-deficient cell lines, suggesting that cryptolepine effects are not mediated by nucleic acids released upon nuclear or organelle damage. In agreement, cryptolepine did not affect cell viability in concentrations that triggered potent IFN-1 activation. In addition, we observed no differences in the presence of a pharmacological inhibitor of TBK1, a pleiotropic kinase that is a converging point for Toll-like receptors (TLRs) and nucleic acid sensors. Together, our results demonstrate that cryptolepine is a strong inducer of IFN-1 response and suggest that cryptolepine-based medications such as *C. sanguinolenta* extract could be potentially tested in resource-limited regions of the world for the management of chronic viral infections as well as cancers.

Some novel antileishmanial compounds inhibit normal cell cycle progression of *Leishmania donovani* promastigotes and exhibits pro-oxidative potential

Amlabu WE, Amisigo CM, Antwi CA, **Awandare GA**, Gwira TM (2021)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

In the midst of numerous setbacks that beclouds the fight against leishmaniasis; a neglected tropical disease, the search for new chemotherapeutics against this disease is of utmost importance. Leishmaniasis is a disease closely associated with poverty and endemic in Africa, Asia, southern Europe and the Americas. It is caused by parasites of the genus *Leishmania* and transmitted by a sandfly vector. In this study, we evaluated the antileishmanial potency of eighteen pathogen box compounds and elucidated their biosafety and possible mechanisms of action against *Leishmania donovani* promastigotes and amastigotes *in vitro*. IC₅₀s range of 0.12±0.15 to >6.25 µg/ml and 0.13±0.004 to >6.25µg/ml were observed for the promastigotes and amastigotes, respectively. We demonstrated the ability of some of the compounds to cause cytocidal effect on the parasites, induce increased production of reactive oxygen species (ROS), disrupt the normal parasite morphology and cause the accumulation of parasites at the DNA synthesis phase of the cell cycle. We recommend a further *in vivo* study on these compounds to validate the findings.

Epilepsy Research in Mali: A Pilot Pharmacokinetics Study on First-Line Antiepileptic Drug Treatment

Sangare M, Doumbia F, Sidibe O, Oumar AA, Bah S, Kouyate M, Diakite SS, Traore K, Karembe A, Haidara MS, Coulibaly SP, Coulibaly S, Togora A, Dolo H, Traore D, Doumbia S, Diakite M, Maiga Y, Diawara A, Kuate C, Kim HG, **Awandare GA** (2020)

[Journal of Epilepsy Research](#) (2023 Impact Factor: 2.991)

Abstract

Background and Purpose

The indication and benefit of plasma level of antiepileptic (AEDs) has been debating in the monitoring of people living with epilepsy and the epilepsy treatment gap has largely been documented in developed countries. This study was aimed to highlight the epilepsy treatment gap between rural and urban Mali.

Methods

We conducted a pilot study on AEDs treatment from September 2016 to May 2019. For 6 months, 120 children and young adults living with epilepsy (rural site, 90; urban site, 30) received phenobarbital, valproic acid and/or carbamazepine. At our rural study site, we determined the AED plasma levels, monitored the frequency, severity and the duration of seizure, and administered monthly the McGill quality of life questionnaire. At our urban study site, each patient underwent an electroencephalogram and brain computed tomography scan without close monitoring.

Results

At the rural study site, patients were mostly on monotherapy; AED levels at 1 month (M1) (n=90) and at 3 months (M3) (n=27) after inclusion were normal in 50% at M1 versus

55.6% at M3, low in 42.2% at M1 versus 33.3% at M3 and high in 7.8% at M1 versus 11.1% at M3. AED levels at M1 and at M3 were significantly different $p<0.0001$. By M3, seizures (n=90) were <1/month in 26.7%, and lasted less than 1 minute in 16.7%. After a yearlong follow up, all 90 patients reported a good or excellent quality of life. At our urban study site, patients (n=30) were on carbamazepine and valproic acid in 66.67% and monotherapy (carbamazepine) in 33.33%. By November 2018, only six out 30 patients (on bi-therapy) were still taking their medications.

Conclusions

Epilepsy diagnostic and treatment are a real concern in Mali. Our data showed appropriate AED treatment with close follow up resulted in a better quality of life of patients in rural Mali. We will promote the approach of personalized medicine in AED treatment in Mali.

Key words: [Epilepsy](#), [Carbamazepine](#), [Quality of life](#), [Phenobarbital](#), [Valproic acid](#), [Mali](#)

Investigating the conformation of S100-Beta protein under physiological parameters using computational modeling: A clue for rational drug design

Tiburu, E. K., Issah, I., Darko, M., Armah-Sekum, R. E., Gyampo, S. O. A., Amoateng, N. K., Kwofie, S. K. & **Awandare, G** (2018)

[Open Biomedical Engineering Journal](#) (2023 Impact Factor: 0.178)

Abstract

Background:

Physiochemical factors such as temperature, pH and cofactors are well known parameters that confer conformational changes in a protein structure. With S100- Beta protein being a metal binding brain-specific receptor for both extracellular and intracellular functions, a change in conformation due to the above-mentioned factors, can compromise their cellular functions and therefore result in several pathological conditions such as Alzheimer's disease, Ischemic stroke, as well as Myocardial Infarction.

Objective:

The studies conducted sought to elucidate the effect of these physiological factors on the conformational dynamics of S100 Beta protein using computational modeling approaches.

Method:

Temperature-dependent and protein-cofactor complexes molecular dynamics simulations were conducted by varying the temperature from 100 to 400K using GROMACS 5.0.3. Additionally, the conformational dynamics of the protein was studied by varying the pH at 5.0, 7.4 and 9.0 using Ambertools17. This was done by preparing the protein molecule, solvating and minimizing its energy level as well as heating it to the required temperature, equilibrating and simulating under desired conditions (NVT and NPT ensembles).

Results:

The results show that the protein misfolds as a function of increasing temperature with alpha helical content at 100K and 400K being 57.8% and 43.3%, respectively. However, the binding sites of the protein were not appreciably affected by temperature variations. The protein displayed high conformational instability in acidic medium (pH ~5.0). The binding sites of Ca^{2+} , Mg^{2+} and Zn^{2+} were identified and each exhibited different groupings of the secondary structural elements (binding motifs). The secondary structure analysis revealed different conformational changes with the characteristic appearance of two beta hairpins in the presence of Zn^{2+} and Mg^{2+} .

Conclusion:

High temperatures, different cofactors and acidic pH confer conformational changes to the S100 Beta structure and these results may indicate the design of novel drugs against the protein.

Antimalarial activity of Malaria Box Compounds against *Plasmodium falciparum* clinical isolates

Chirawurah, D. J., Ansah, F., Nyarko, P. B., Duodu, S., Aniweh, Y., & **Awandare, G. A.** (2017)

[International Journal for Parasitology](#) (2023 Impact Factor: 4.33)

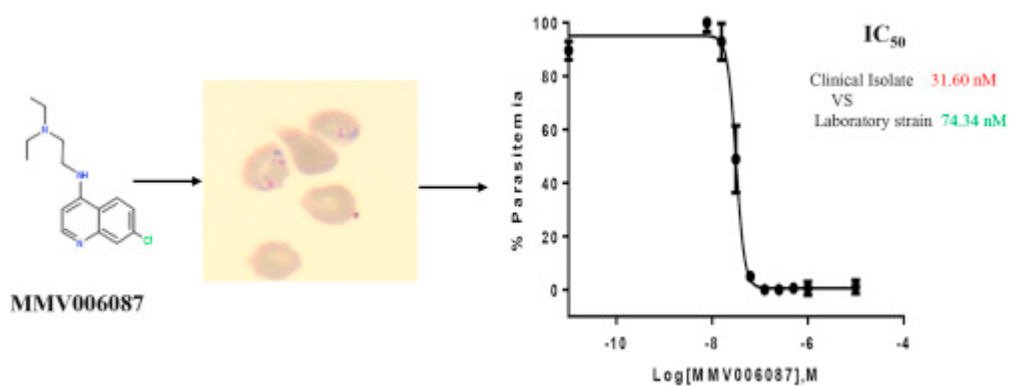
Abstract

Malaria remains a major cause of childhood deaths in resource-limited settings. In the absence of an effective vaccine, drugs and other interventions have played very significant roles in combating the scourge of malaria. The recent reports of resistance to [artemisinin](#) necessitate the need for new [antimalarial drugs](#) with novel mechanisms of action. Towards the development of new, affordable and easily accessible antimalarial drugs for endemic regions, the Medicines for Malaria Venture (MMV) assembled a total of 400 active antimalarial compounds called the Malaria Box. The potency and the efficacy of the Malaria Box Compounds have been determined mainly using laboratory strains of *P. falciparum*.

This study investigated the potency of twenty compounds from the Malaria Box against four clinical isolates from Ghana, using optimized *in vitro* growth inhibitory assays. Seven out of the 20 compounds screened had 50% inhibitory concentration (IC_{50}) below 500 nM. The most active among the selected compounds was MMV006087 (average IC_{50} of 30.79 nM). Variations in the potency of the Malaria Box Compounds were observed between *P. falciparum* clinical isolates and Dd2 strain. We also investigated the sensitivity of the clinical isolates to [chloroquine](#) and [artesunate](#). The N093 clinical isolate was found to be resistant to chloroquine but showed high sensitivity to artesunate.

The results underscore the importance of including clinical isolates with different drug-resistant backgrounds, in addition to laboratory strains, in validating potential compounds during antimalarial compound screening programs.

Graphical abstract



Keywords: Plasmodium Malaria box Clinical isolates Potency Erythrocytes Compounds

Experimental demonstration of the possible role of *Acanthamoeba polyphaga* in the Infection and disease progression in Buruli ulcer (BU) using ICR Mice

Azumah, B. K., Addo, P. G., Dodoo, A., **Awandare, G.**, Mosi, L., Boakye, D. A., Wilson, M. D. (2017)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

The transmission of Buruli ulcer (BU), caused by *Mycobacterium ulcerans* (*MU*), remains puzzling although a number of hypothesis including through bites of infected aquatic insects have been proposed. We report the results of experiments using ICR mice that give credence to our hypothesis that *Acanthamoeba* species may play a role in BU transmission. We cocultured *MU* N2 and *MU* 1615 which expresses red fluorescent protein (RFP) and *Acanthamoeba polyphaga* (*AP*), and confirmed infected *AP* by Ziehl-Neelsen (ZN) staining. We tested for viability of *MU* inside *AP* and observed strong RFP signals inside both trophozoites and cysts after 3 and 42 days of coculturing respectively. ICR mice were topically treated, either on shaved intact or shaved pinpricked rumps, with one of the following; *MU* N2 only (2.25×10^6 colony forming units [CFU] / ml), *MU* N2:*AP* coculture (2.96×10^4 CFU: 1.6×10^6 cells/ml), *AP* only (1.6×10^6 cells/ml), PYG medium and sterile distilled water. Both *MU* N2 only and *MU* N2:*AP* elicited reddening on day (D) 31; edema on D 45 and D 44 respectively, and ulcers on D 49 at pinpricked sites only. To ascertain infectivity and pathogenicity of *MU* N2 only and *MU* N2:*AP*, and compare their virulence, the standard mouse footpad inoculation method was used. *MU* N2:*AP* elicited reddening in footpads by D 3 compared to D 14 with *MU* N2 only of the same dose of *MU* N2 (2.96×10^4 CFU). ZN-stained *MU* were observed in both thin sectioned and homogenized lesions, and aspirates from infected sites. Viable *MU* N2 were recovered from cultures of the homogenates and aspirates. This study demonstrates in ICR mice *MU* transmission via passive infection, and shows that punctures in the skin are prerequisite for infection, and that coculturing of *MU* with *AP* enhances pathogenesis.

Antifungal and anti-proliferative effects of Zeolites A and X on Yeast pathogenic and cancer cells in vitro

Tiburu E. K., Mutocheluh, M., Arthur, P. K., Narkwa, P. W., Salifu, A. A., Agyei, M. A., Yeboah, R., Fleischer, H. N. A., Zhuang, J. and **Awandare, G.** (2017)

[Journal of Biomaterials and Tissue Engineering](#) (2023 Impact Factor: 0.144)

Abstract

Efficient radiation and radiochemotherapy without interruption is a major challenge for developing cancer treatment with clinical relevance. Here, we synthesized low silica zeolite X and zeolite A, and characterized them using methods including, Nitrogen Adsorption and Desorption and X-ray diffraction. Porosity measurements revealed external surface areas of 27.10 and 19.18 m²/g, and volumes of 0.016 and 0.012 cm³/g respectively. The zeolite X nanoparticles with the larger external surface area prevented cancer cells growth but zeolite A which had smaller surface area had opposite effect on the cancer cell lines. We observed inhibitory effects of 52% in HeLa cervical and 97% in both Vero and RAW 264.7 cancer cells respectively in the presence of zeolite X nanoparticles. We also observed 17% inhibition in *C. albicans* growth at zeolite X concentrations up to 10 ng/μL contrary to the enhancement of *C. albicans* cell growth in the presence of zeolite A at the same concentrations. The current work showed the selective inhibition of cancer cells using two zeolites of different external surface areas, pore volumes and configuration but the same chemical composition.

Expression, Purification, and Monitoring of Conformational Changes of hCB2 TMH67H8 in Different Membrane-Mimetic Lipid Mixtures Using Circular Dichroism and NMR Techniques

Tiburu E. K., Zhuang J., Fleischer H. N., Arthur P. K., **Awandare G. A** (2017)

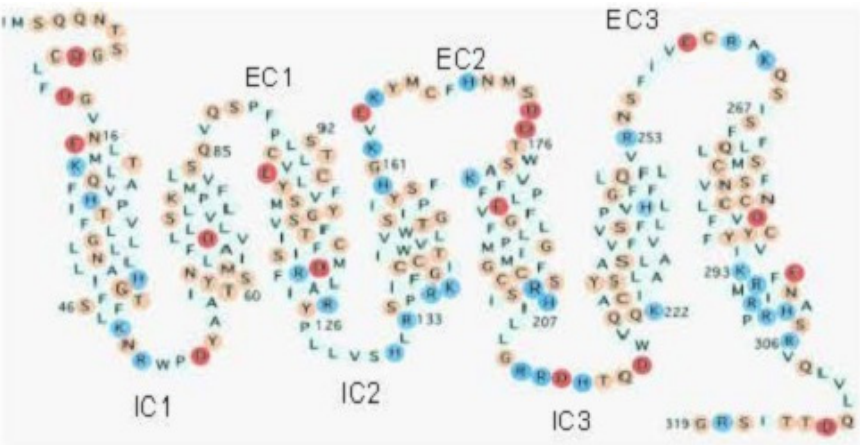
[Membranes](#) (2023 Impact Factor: 4.562)

Abstract

This work was intended to develop self-assembly lipids for incorporating G-protein coupled receptors (GPCRs) in order to improve the success rate for nuclear magnetic resonance spectroscopy (NMR) structural elucidation. We hereby report the expression and purification of uniformly ^{15}N -labeled human cannabinoid receptor-2 domain in insect cell media. The domain was refolded by screening several membrane mimetic environments. Different q ratios of isotropic bicelles were screened for solubilizing transmembrane helix 6, 7 and 8 (TMH67H8). As the concentration of dimyristoylphosphocholine (DMPC) was increased such that the q ratio was between 0.16 and 0.42, there was less crowding in the cross peaks with increasing q ratio. In bicelles of $q = 0.42$, the maximum number of cross peaks were obtained and the cross peaks were uniformly dispersed. The receptor domain in bicelles beyond $q = 0.42$ resulted in peak crowding. These studies demonstrate that GPCRs folding especially in bicelles is protein-specific and requires the right mix of the longer chain and shorter chain lipids to provide the right environment for proper folding. These findings will allow further development of novel membrane mimetics to provide greater diversity of lipid mixtures than those currently being employed for GPCR stability and folding, which are critical for both X-ray and NMR studies of GPCRs.

Keywords: [selective and uniform labeling](#); [insect cells](#); [bicelles](#); [NMR](#)

Graphical Abstracts



The background of the page is a close-up, slightly blurred image of a stack of rolled-up newspapers. The papers are stacked in a way that shows the edges of many pages, creating a textured, layered appearance. A bright green rounded rectangle is centered on the page, containing the title in white text. The title is in a bold, sans-serif font, with 'PUBLIC HEALTH' on the first line and 'AND POLICY' on the second line.

PUBLIC HEALTH AND POLICY

Predictors of COVID-19 epidemics in countries of the World Health Organization African Region

Zhang F, Karamagi H, Nsenga N, Nanyunja M, Karinja M, Amanfo S, Chase-Topping M, Calder-Gerver G, McGibbon M, Huber A, Wagner-Gamble T, Guo CG, Haynes S, Morrison A, Ferguson M, **Awandare GA**, Mutapi F, Yoti Z, Cabore J, Moeti MR, Woolhouse MEJ (2021)

[Nature Medicine](#) (2023 Impact Factor: 87.244)

Abstract

Countries of the World Health Organization (WHO) African Region have experienced a wide range of coronavirus disease 2019 (COVID-19) epidemics. This study aimed to identify predictors of the timing of the first COVID-19 case and the per capita mortality in WHO African Region countries during the first and second pandemic waves and to test for associations with the preparedness of health systems and government pandemic responses. Using a region-wide, country-based observational study, we found that the first case was detected earlier in countries with more urban populations, higher international connectivity and greater COVID-19 test capacity but later in island nations. Predictors of a high first wave per capita mortality rate included a more urban population, higher pre-pandemic international connectivity and a higher prevalence of HIV. Countries rated as better prepared and having more resilient health systems were worst affected by the disease, the imposition of restrictions or both, making any benefit of more stringent countermeasures difficult to detect. Predictors for the second wave were similar to the first. Second wave per capita mortality could be predicted from that of the first wave. The COVID-19 pandemic highlights unanticipated vulnerabilities to infectious disease in Africa that should be taken into account in future pandemic preparedness planning.

Appreciating the complexity of localized malaria risk in Ghana: Spatial data challenges and solutions

Bempah, S., Curtis, **Awandare, G** & Ajayakumarb, J. (2020)

[Health & Place](#) (2023 Impact Factor: 4.931)

Abstract

Various factors have been associated with the ongoing high prevalence of malaria in Ghana. Among these are poor sanitation, low socioeconomic status (SES), building construction and other proximate micro environmental risks, and individual behaviors. What makes the curbing of malaria more challenging, is that for many of the most impacted areas there is little data for modeling or predictions, which are needed, as risk is not homogenous at the sub-neighborhood scale. In this study we use available local surveillance data combined with novel on-the-ground fine scale environmental data collection, to gain an initial understanding of malaria risk for the Teshie township of Accra, Ghana. Mapped environmental risk factors include open drains, stagnant water and trash. Overlaid onto these were clinical data of reported malaria cases collected between 2012 and 2016 at LEKMA hospital. We then enrich these maps with local context using a new method for malaria research, spatial video geonarratives (SVGs). These SVGs provide insights into the underlying spatial-social patterns of risks, to reveal where traditional data collection is lacking, and how and where to develop local intervention strategies.

Science advisers around the world on 2020

Awandare G, André E, Corrales-Aguilar E, Chen CJ, Mostajo-Radji MA, Jancoriene L, & Nemer M (2020)

[Nature](#) (2023 Impact Factor: 69.504)

Abstract

In Ghana, the pandemic has not been severe, and deaths have been very low compared with those in other parts of the world. Our group was among the first to sequence SARS-CoV-2 in Africa. We achieved this because we are building capacity for next-generation sequencing for other research purposes, including malaria-parasite genomics.

When the pandemic hit, we quickly redirected those resources and personnel to work on sequencing the virus because we felt it was important to be able to track the transmission and evolution of the virus locally. This was challenging because we did not have all the necessary reagents and had to improvise. We also had to obtain some reagent components from various collaborators in the United Kingdom. Many exciting projects have had to be put on hold. Students' research has been delayed, and they've been unable to complete their PhD or master's programmes on schedule.

In responding to pandemics, leadership has to be decisive. For example, masks should have been mandated early on. And lockdowns would have worked better had they been targeted, imposed quickly and enforced strictly.

In the big picture, African governments need to build scientific capacity sustainably rather than resorting to firefighting only when a pandemic hits. We should be preparing for the next pandemic as soon as this one ends.

Enhancing science preparedness for health emergencies in Africa through research capacity building

Kinyanjui S, Fonn S, Kyobutungi C, Vicente-Crespo M, Bonfoh B, Ndungu T, Sewankambo NK, Djimde AA, Gaye O, Chirwa T, Musenge E, Elliot A, Nakanjako D, Chibanda D & **Awandare G (2020)**

[BMJ Global Health](#) (2023 Impact Factor: 8.056)

Abstract

With more than 9.3 million cases and 480 000 deaths recorded to date,¹ COVID-19 pandemic has put global emergency preparedness and the capacity of national health systems to predict and respond to major emergencies under a sharp scrutiny. The response to the pandemic is focused on testing, case management and control measures such as personal hygiene, quarantine and social distancing. However, in most African countries, as elsewhere, these measures are not backed by reliable context-specific data. Instead, they are largely dependent on epidemic curves from China and Europe which appear to differ from those in sub-Saharan Africa. Given the massive economic and social disruptions occasioned by the control measures, governments and other stakeholders are desperate for accurate real-time data on the pandemic's progress and to inform intervention strategies. Furthermore, scarcity of medical and laboratory resources due to increased demand globally coupled with international travel restrictions has forced countries to look inwards for local innovations and adaptations in COVID-19 testing options and interventions, as well as personal protective equipment (PPE).

Current and Novel Approaches in Influenza Management

Kotey, E., Lukosaityte, D., Quaye, O., Ampofo, W., **Awandare, G.**, & Iqbal, M (2019)

[Vaccines](#) (2023 Impact Factor: 4.961)

Abstract

Influenza is a disease that poses a significant health burden worldwide. Vaccination is the best way to prevent influenza virus infections. However, conventional vaccines are only effective for a short period of time due to the propensity of influenza viruses to undergo antigenic drift and antigenic shift. The efficacy of these vaccines is uncertain from year-to-year due to potential mismatch between the circulating viruses and vaccine strains, and mutations arising due to egg adaptation. Subsequently, the inability to store these vaccines long-term and vaccine shortages are challenges that need to be overcome. Conventional vaccines also have variable efficacies for certain populations, including the young, old, and immunocompromised. This warrants for diverse efficacious vaccine developmental approaches, involving both active and passive immunization. As opposed to active immunization platforms (requiring the use of whole or portions of pathogens as vaccines), the rapidly developing passive immunization involves administration of either pathogen-specific or broadly acting antibodies against a kind or class of pathogens as a treatment to corresponding acute infection. Several antibodies with broadly acting capacities have been discovered that may serve as means to suppress influenza viral infection and allow the process of natural immunity to engage opsonized pathogens whilst boosting immune system by antibody-dependent mechanisms that bridge the innate and adaptive arms. By that; passive immunotherapeutics approach assumes a robust tool that could aid control of influenza viruses. In this review, we comment on some improvements in influenza management and promising vaccine development platforms with an emphasis on the protective capacity of passive immunotherapeutics especially when coupled with the use of antivirals in the management of influenza infection.

Keywords: [Influenza virus](#); [vaccines](#); [passive immunization](#); [immunotherapeutics](#)

EBM and SEBM Inaugurates its African Global Editor and Office

Goodman, S. R., & **Awandare, G. A.**

[Experimental Biology and Medicine](#) (2023 Impact Factor: 4.088)

Comments from the EBM Editor-in-Chief

When I was interviewed to become the Editor-in-Chief of EBM in 2006, I told the SEBM Council of my plans to globalize Experimental Biology and Medicine, and by virtue of doing so would globalize the Society of Experimental Biology and Medicine. Thankfully the SEBM Council was supportive of this plan, and we began our expansion beyond the borders of the United States. We opened our first EBM/SEBM Global Office at the National Cheng Kung University in Taiwan in January 2008 with Dr. Huan-Yao Lei as our initial Asian Global Editor and Dr. Sean Tsai as the current Editor. In July 2008, we established our European EBM/SEBM Office at Kings College London, with Dr. Farzin Farzaneh as our European Global Editor. SEBM/EBM opened a China Outreach Office in 2013, at Shanghai Jiao Tong University. In 2015, that Office was moved to Sichuan University, West China Hospital and Dr. James Kang became our Executive Director of that Office. Our first Latin America EBM/SEBM Global Office was established in Brazil at the University of Campinas (UNICAMP) in June 2018. Dr. Nicola Conran became our first EBM Latin America Global Editor.

I was very excited as I boarded my flight headed to Ghana, West Africa, in July 2019. I was traveling to open our first EBM/SEBM Africa Global Office at the University of Ghana and to inaugurate our first EBM Africa Global Editor: Prof. Gordon Awandare. Gordon is a Professor in the Department of Biochemistry, Cell and Molecular Biology at University of Ghana. He became the Founding Director of the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) at University of Ghana in 2014. Gordon established a WACCBIP Research Conference on Infectious Diseases which attracts speakers from across Africa,

as well as Global experts in this field. I had the great pleasure to attend this three day Research Conference where I presented a talk on SEBM and EBM, followed by an Inauguration Ceremony for our EBM Africa Global Editor. I witnessed many outstanding presentations and learned a great deal about Infectious Diseases that impact the globe. For me the highlight of the Conference was the oral and poster presentations by the WACCBIP graduate students and post-doctoral fellows. Since 2014 Gordon and his colleagues have trained and mentored more than 200 African graduate students and post-doctoral fellows.

Environmental health risks and benefits of the use of mosquito coils as malaria prevention and control strategy

Hogarh, J. N., Agyekum, T. P., Bempah, C. K., Owusu-Ansah, E. D. J., Avicor, S. W., **Awandare, G. A.**, Fobil, J. N., & Obiri-Danso, K (2018)

[Malaria Journal](#) (2023 Impact Factor: 3.122)

Abstract

Background

Malaria is an infectious disease that causes many deaths in sub-Saharan Africa. In resource-poor malaria endemic communities, mosquito coils are commonly applied in households to repel the vector mosquito that transmits malaria parasites. In applying these coils, users have mainly been interested in the environmental health benefits potentially derived from repelling the mosquito, while oblivious of the environmental health risks that may be associated with exposure to emissions from the use of mosquito coil. This study evaluated the effectiveness of the mosquito coil, ascertained and/or estimated the toxic emissions that may emanate from the coil, and determined its overall appropriateness by conducting a risk–benefit analysis of the use of this strategy in malaria prevention at household levels.

Methods

The repellent ability of mosquito coils was tested by conducting a mosquito knockdown/mortality test in experimental chambers synonymous of local room spaces and conditions. The gaseous and particulate emissions from the mosquito coil were also analysed. Additional scenarios were generated with the Monte Carlo technique and a risk–benefit analysis was conducted applying @Risk software.

Results

Mosquito mortality arising from the application of various mosquito coils averagely ranged between 24 and 64%, which might not provide adequate repellency effect. Emissions from the mosquito coil were also found to contain CO, VOCs, SO₂, NO₂, PM_{2.5} and PM₁₀. The Hazard Index of the respective pollutants characterized over a lifetime exposure scenario was low (<1 for each pollutant), which suggests that the concentrations of the specific chemicals and particulate matter emitted from the mosquito coil may not constitute adverse environmental health risk.

Conclusion

Although the risk of morbidity from the use of the mosquito coil was low, the coil yielded limited protection as a mosquito avoidance method. It may, therefore, have a reduced benefit in controlling malaria and should be applied sparingly in a highly regulated manner only when traditionally proven effective vector control strategies are not available or too expensive for resource-poor malaria endemic regions.

Public Health Burden of Hearing Impairment and the Promise of Genomics and Environmental Research: A Case Study in Ghana, Africa

Adadey, S. M., **Awandare, G.**, Amedofu, G. K., & Wonkam, A. (2017)

[OMICS: A Journal of Integrative Biology](#) (2023 Impact Factor: 3.978)

Abstract

Hearing impairment (HI) is one of the most disabling conditions of major global health burden that contributes adversely to the social and economic development of a country, if not managed properly. A proper assessment of the nationwide burden and etiology of HI is instrumental in the prevention, treatment, and management of the condition. This article sought to perform an expert review of HI in Ghana to determine the present knowledge of its burden and possible causes of the condition. A literature search was conducted in PubMed using the following keywords: "hearing loss" OR "hearing impairment" OR "deafness" AND "Ghana." The literature was scanned until July 20, 2017, with specific inclusion of targeted landmark and background articles on HI. From the search, 18 of out 5869 articles were selected and considered for the review. The results of the search indicated that there were no extensive studies to determine the national burden of HI in Ghana. However, the few studies assessed suggested that the disease is either acquired or inherited. The burden of acquired HI was higher in adults than children, women than men, and people working in a noisy environment. Regarding the genetic cause, specific founder mutations in *GJB2* gene (R143W, L79P, V178A, R184Q, A197S, I203K, and L214P) was the only identified genetic cause of HI in Ghana, but the other HI genes were not investigated. There has been some modest effort to study HI in Ghana, but comprehensive studies on the genetic and environmental etiologies (using the "multi-OMICS" approaches), classification, and burden of HI on Ghana are needed.

Building Sustainable Local Capacity for Global Health Research in West Africa

Sam-Agudu N. A., Paintsil, E., Aliyu, M. H., Kwara, A., Ogunsola, F., Afrane, Y. A., Onoka, C., **Awandare, G. A.**, Amponsah, G., Cornelius, L. J., Mendy, G., Sturke, R., Ghansah, A., Siberry, G. K., Ezeanolue E. E. (2016)

[Annals of Global Health](#) (2023 Impact Factor: 3.64)

Abstract

Background

Global health research in resource-limited countries has been largely sponsored and led by foreign institutions. Thus, these countries' training capacity and productivity in global health research is limited. Local participation at all levels of global health knowledge generation promotes equitable access to evidence-based solutions. Additionally, leadership inclusive of competent local professionals promotes best outcomes for local contextualization and implementation of successful global health solutions. Among the sub-Saharan African regions, West Africa in particular lags in research infrastructure, productivity, and impact in global health research.

Objective

In this paper, experts discuss strategies for scaling up West Africa's participation in global health evidence generation using examples from Ghana and Nigeria.

Methods

We conducted an online and professional network search to identify grants awarded for global health research and research education in Ghana and Nigeria. Principal investigators, global health educators, and representatives of funding institutions were invited to add their knowledge and expertise with regard to strengthening research capacity in West Africa.

Findings

While there has been some progress in obtaining foreign funding, foreign institutions still dominate local research. Local research funding opportunities in the 2 countries were found to be insufficient, disjointed, poorly sustained, and inadequately publicized, indicating weak infrastructure. As a result, research training programs produce graduates who ultimately fail to launch independent investigator careers because of lack of mentoring and poor infrastructural support.

Conclusions

Research funding and training opportunities in Ghana and Nigeria remain inadequate.

Recommendations

We recommend systems-level changes in mentoring, collaboration, and funding to drive the global health research agenda in these countries. Additionally, research training programs should be evaluated not only by numbers of individuals graduated but also by numbers of independent investigators and grants funded. Through equitable collaborations, infrastructure, and mentoring, West Africa can match the rest of Africa in impactful global health research.

Keywords: [western Africa](#)[capacity-building](#)[financial support](#)[global health](#)[research](#)

Febrile illness diagnostics and the malaria-industrial complex: a socio-environmental perspective

Stoler J. & **Awandare G. A** (2016)

[BMC Infectious Diseases](#) (2023 Impact Factor: 3.669)

Abstract

Background

Global prioritization of single-disease eradication programs over improvements to basic diagnostic capacity in the Global South have left the world unprepared for epidemics of chikungunya, Ebola, Zika, and whatever lies on the horizon. The medical establishment is slowly realizing that in many parts of sub-Saharan Africa (SSA), particularly urban areas, up to a third of patients suffering from acute fever do not receive a correct diagnosis of their infection.

Main body

Malaria is the most common diagnosis for febrile patients in low-resource health care settings, and malaria misdiagnosis has soared due to the institutionalization of malaria as the primary febrile illness of SSA by international development organizations and national malaria control programs. This has inadvertently created a “malaria-industrial complex” and historically obstructed our complete understanding of the continent’s complex communicable disease epidemiology, which is currently dominated by a mélange of undiagnosed febrile illnesses. We synthesize interdisciplinary literature from Ghana to highlight the complexity of communicable disease care in SSA from biomedical, social, and environmental perspectives, and suggest a way forward.

Conclusion

A socio-environmental approach to acute febrile illness etiology, diagnostics, and management would lead to substantial health gains in Africa, including more efficient malaria control.

Such an approach would also improve global preparedness for future epidemics of emerging pathogens such as chikungunya, Ebola, and Zika, all of which originated in SSA with limited baseline understanding of their epidemiology despite clinical recognition of these viruses for many decades. Impending ACT resistance, new vaccine delays, and climate change all beckon our attention to proper diagnosis of fevers in order to maximize limited health care resources.

Associations between Red Cell Polymorphisms and *Plasmodium falciparum* Infection in the Middle Belt of Ghana

Amoako, N., Asante, K. P., Adjei, G., **Awandare, G. A.**, Bimi, L., & Owusu-Agyei, S. (2014)

[PLoS One](#) (2023 Impact Factor: 3.752)

Abstract

Background

Red blood cell (RBC) polymorphisms are common in malaria endemic regions and are known to protect against severe forms of the disease. Therefore, it is important to screen for these polymorphisms in drugs or vaccines efficacy trials. This study was undertaken to evaluate associations between clinical malaria and RBC polymorphisms to assess biological interactions that may be necessary for consideration when designing clinical trials.

Method

In a cross-sectional study of 341 febrile children less than five years of age, associations between clinical malaria and common RBC polymorphisms including the sickle cell gene and G6PD deficiency was evaluated between November 2008 and June 2009 in the middle belt of Ghana, Kintampo. G6PD deficiency was determined by quantitative methods while haemoglobin variants were determined by haemoglobin titan gel electrophoresis. Blood smears were stained with Giemsa and parasite densities were determined microscopically.

Results

The prevalence of clinical malarial among the enrolled children was 31.9%. The frequency of G6PD deficiency was 19.0% and that for the haemoglobin variants were 74.7%, 14.7%, 9.1%, 0.9% respectively for HbAA, HbAC, HbAS and HbSS. In Multivariate regression analysis, children with the HbAS genotype had 79% lower risk of malaria infection compared to those with the HbAA genotypes (OR=0.21, 95% CI: 0.06–0.73, $p=0.01$). HbAC genotype was not

significantly associated with malaria infection relative to the HbAA genotype (OR=0.70, 95% CI: 0.35–1.42, $p=0.33$). G6PD deficient subgroup had a marginally increased risk of malaria infection compared to the G6PD normal subgroup (OR=1.76, 95% CI: 0.98–3.16, $p=0.06$).

Conclusion

These results confirm previous findings showing a protective effect of sickle cell trait on clinical malaria infection. However, G6PD deficiency was associated with a marginal increase in susceptibility to clinical malaria compared to children without G6PD deficiency.

Deconstructing "malaria": West Africa as the next front for dengue fever surveillance and control

Stoler, J., Dashti, R. A., Anto, F., Fobil, J. N., & **Awandare, G. A.** (2014)

[Acta Tropica](#) (2023 Impact Factor: 3.222)

Abstract

Presumptive treatment of febrile illness patients for malaria remains the norm in endemic areas of West Africa, and "malaria" remains the top source of health facility outpatient visits in many West African nations. Many other febrile illnesses, including bacterial, viral, and fungal infections, share a similar symptomatology as malaria and are routinely misdiagnosed as such; yet growing evidence suggests that much of the burden of febrile illness is often *not* attributable to malaria. Dengue fever is one of several viral diseases with symptoms similar to malaria, and the combination of rapid globalization, the long-standing presence of *Aedes* mosquitoes, case reports from travelers, and recent seroprevalence surveys all implicate West Africa as an emerging front for dengue surveillance and control. This paper integrates recent vector ecology, public health, and clinical medicine literature about dengue in West Africa across community, regional, and global geographic scales. We present a holistic argument for greater attention to dengue fever surveillance in West Africa and renew the call for improving differential diagnosis of febrile illness patients in the region.

Graphical abstract

Community	Regional	Global
Limited public and vector control program awareness of dengue or the <i>Aedes</i> vector	Rapid population growth and intensifying globalization	Economic burden of misdiagnosis for both patients and health care systems
Urban ecology supports prime breeding environment for vector species	<i>Mesquite</i> vector presence established in entomology literature	Climate change implications for geographic changes to vector distributions
Inefficient consumption of health services due to over-diagnosis of clinical malaria	Etiology of febrile illness established in seroprevalence surveys	Potential for emergence of ACT-resistant <i>Plasmodium</i> beyond Southeast Asia
Unfamiliarity with dengue among local medical establishment, and ambiguity of field diagnostics	Local dengue acquisition established in international traveler case reports	Slow progress in development of vaccines against malaria and dengue



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