WACCBIP RESEARCH CONFERENCE 2017

Theme : Improving health through advanced research and training

July 6-7, 2017

CONFERENCE PROGRAMME AND ANNUAL UPDATE

West African Centre for Cell Biology of Infectious Pathogens
College of Basic and Applied Sciences
University of Ghana

www.waccbip.org

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THE ROYAL SOCIETY

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DIRECTOR'S MESSAGE

It is a great pleasure to welcome you to the Second Annual WACCBIP Research Conference. It is terrific to see that so many of you here were with us for last year's conference as well, which demonstrates the massive success and impact of the first conference. I am also excited to welcome many collaborators and friends who are visiting for the first time, I hope you would be inspired to strengthen your ties to the WACCBIP community. Based on the programme that we have put together, I am extremely confident that this year's experience would be even richer than last year's.

When we met last year, WACCBIP had achieved lift-off, and was just beginning to gain some momentum. The World Bank ACE project was in its second year, while the Wellcome Trust DELTAS programme was just beginning. This year, you would see from the quality of the science on display that WACCBIP is now in full flight. The first batch of Masters' students who were enrolled into our graduate programme have now completed their training, and will receive their degrees during the graduation ceremony on July 21. My heartiest congratulations to them for blazing the trail and setting the standard for excellence at WACCBIP. Nearly all of them have produced manuscripts from their thesis work, some of which have already been published while others are under review or being finalized for submission to various journals. We are eagerly looking forward to the completion of the first batch of WACCBIP PhD students in July 2018.

We have now completed the selection of fellows for the WACCBIP-DELTAS programme, and awarded 15 PhD and 12 Postdoctoral fellowships to young African scientists, including 11 women, from six countries across the continent. While the first batch of PhD fellows have just completed their course work and are now developing their research proposals, the Postdocs have hit the ground running. The impact of these postdocs on the quality and intensity of the science at WACCBIP has been massive, and clearly demonstrates the critical role Postdocs can play in advancing research and training in African Universities if their appointments become institutionalized.

One of our proudest achievements in the last year has been in receiving International accreditation for our graduate programmes. After more than a year of evaluation, including a site visit, the Royal Society of Biology, UK, awarded our programmes with their Advanced International Accreditation. WACCBIP thus becomes the first African institution with such accreditation, a truly remarkable endorsement of our programme as World class.

On the funding front, we have had mixed fortunes, but overall it has been net positive. Although we missed out on a few significant grants, WACCBIP faculty have won one major grant from the NIH H3Africa scheme and several collaborative grants from the UK's GCRF through joint applications with colleagues from various UK institutions. Details of these grants are provided elsewhere in this brochure. I am very grateful for the efforts that our faculty members continue to make to bring in more grants to support the training of students. My congratulations to those who were successful this year, and I hope more faculty will submit grant applications in the coming year. We have intensified our outreach to the private sector and corporate bodies. However, we are yet to see any significant acknowledgement of our efforts. We have invited more than 20 institutions to this research conference, and we are in great anticipation to see how many of them will make the time to join us.

Overall, I am incredibly proud of our achievements so far and I am very hopeful for the future. We are gradually realizing our dream of creating a hub for basic biomedical science in the sub-region. I remain highly motivated and inspired by the talent and enthusiasm of our young African scientists, either in our programme or yearning for an opportunity to join us. We see our efforts have already yielded tangible results in reducing the 'brain drain', increasing 'brain circulation', and even achieving some amount of 'brain repatriation'. I thank you for coming and I wish you a wonderful science festival during these two days and beyond.
Gordon Awandare

PROGRAMME

DATE	TIME	OPENING CEREMONY	PRESENTER
6th July	08.30am - 08.45am	Arrival of Participants and registration Call to order	MC – Mr.Ricky Kasise
	08.45am - 09.45am	Welcome remarks and introduction of Chairman Chairman's remarks Brief remarks by: -Director, Noguchi Memorial Institute for Medical Research -Provost, College of Basic and Applied Sciences -The Country Director, World Bank, Ghana Office -International Operations and Partnerships Adviser, Wellcome Trust -Executive Secretary, National Council for Tertiary Education -Minister of Health Official opening of conference by Minister of Environment, Science, Technology and Innovation	Prof. Gordon Awandare, Director of WACCBIP Prof. Francis Dodoo, Pro-Vice Chancellor, Research, Innovation and Development Prof. Kwadwo Koram Prof. Daniel K. Asiedu Mr. Henry Godfrey Rupiny Kerali Dr. Oliver Wills Prof. Salifu Mohammed Hon. Kingsley Aboagye Gyedu Prof. Kwabena Frimpong-Boateng
		KEYNOTE ADDRESS	
	09.45am - 10.15am	Progress in research capacity building in Ghana	Prof. Fred N. Binka, Founding Vice Chancellor, University of Health and Allied Sciences
	10.15am – 10.20am	Chairman's closing remarks	Prof. Francis Dodoo, Pro-Vice Chancellor, Research, Innovation and Development
	10.20am - 10.45am	**Photograph session and Coffee break**	

		PLENARY TALK 1	**CHAIRS – Prof. Dorothy Yeboah-Manu and Prof. Keith Gull**
	10.50am - 11.10pm	Adaptation and multiplication rate variation of *Plasmodium falciparum* in West Africa	Prof. David J. Conway
		FELLOWS SESSION	
	11.10am - 12.25pm	1. PfRON12 interacts with Band 3 on the erythrocyte surface	Yaw Aniweh
		2. Understanding the mechanisms of anti-inflammatory activities of cryptolepine	Ahmed Rufai Abdulrahman
		3. Acquisition of dihydropteroate synthase (*dhps*), K540E and A581G, mutations drive Copy Number Variations of *GTP Cyclohydrolase 1* (*gch1*) gene in Ghanaian *Plasmodium falciparum* field isolates	Musah Osei
		4. Evidence of altered liver function among malaria and hepatitis B co-infected pregnant women	Nsoh Godwin Anabire
		5. Probing a novel mechanism for pyrazinamide resistance in *Mycobacterium tuberculosis*	Ranee Aflakpui
		PLENARY TALK 2	
	12.25pm - 12.45pm	*Burkholderia cepacia* shows us that antibiotic resistance and inflammation are two sides of the same coin	Prof. Miguel A. Valvano
	12.45pm – 1.45pm	**Lunch Break**	
		PLENARY TALK 3	**CHAIRS – Prof. Michael Wilson and Dr. Elvis Tiburu**
	1.45pm – 2.05pm	Ecological and physiological correlates of mating in *Anopheles gambiae*	Prof. Abdoulaye Diabate
		FELLOWS SESSION	
	2.05pm – 3.20pm	6. Isolation and characterization of *Haemophilus ducreyi* strains from children with cutaneous lesions in yaws endemic regions in Ghana	Shirley Victoria Simpson
		7. Identification of specific metabolites in *Mycobacterium ulcerans* infection: exploring potential diagnostic biomarkers	Elizabeth Kai Laryea-Akrong
		8. Assessing the impact of differences in malaria transmission intensity on clinical and haematological indices in children with malaria	Henrietta Mensah-Brown

		9. Isolation and characterization of plant antitrypanosomals in African trypanosomes	Aboagye Kwarteng Dofuor
		10. *Plasmodium falciparum* Histidine Rich Protein 2 and 3 gene deletion polymorphism in Kassena-Nankana districts of Northern Ghana	Felix Alexander Ayelazuno
		PLENARY TALK 4	
	3.20pm - 3.40pm	Metabolomics and lipidomics as tools for biomarker discovery for medical research	Prof. Julian L. Griffin
	3.40pm - 4.05pm	**Coffee Break**	
		PLENARY TALK 5	**CHAIRS – Prof. Neils Quashie and Prof. Sammy Sackey**
	4:05pm – 4.25pm	Genetic determinants of diminished response of *Plasmodium falciparum* to artemether and lumefantrine in Mali	Prof Abdoulaye Djimde
		FELLOWS SESSION	
	4.25pm – 5.25pm	11. Levels and kinetics of merozoite-specific IgG in Ghanaian children with *Plasmodium falciparum* malaria	Frederica D. Partey
		12. Mutational inactivation of HIV-1 during reverse transcription is rare in a single replication cycle	Edmond Atindaana
		13. *Plasmodium falciparum* and Epstien-Barr Virus (EBV) co-infection and the expression of activation induced-cytidine deaminase in healthy primary school children in the Volta region of Ghana	Reuben Ayivor-Djanie
		14. Frameshift mutation in a conserved *Plasmodium* protein associated with piperaquine resistance in *Plasmodium berghei* ANKA	Daniel Kiboi
		PLENARY TALK 6	
	5.25pm – 5:45pm	Mechanisms of immune control and tumorigenesis of endemic Burkitt lymphoma	Prof. Ann Moormann
	5.45pm – 5.50pm	Closing	Prof. Gordon Awandare

DATE	TIME	KEYNOTE LECTURE	CHAIRS – Prof. Isabella Quakyi and Prof. Lars Hviid
7th July	09.00am - 09.30am	New frontiers in malaria vaccine development	Prof. Simon J. Draper, University of Oxford - UK
		PLENARY TALK 7	
	09.30am – 09.50am	Chronic infection and virulence: a role for the Plasmodium pir gene family?	Dr. Jean Langhorne
		FELLOWS SESSION	
	09.50am - 11.05am	15. Antibodies against the synthetic peptide of a novel *Plasmodium falciparum* Surface-Related Protein potently inhibits erythrocyte invasion	Emmanuel Amlabu
		16. *In vitro* investigation of the relationship between schistosomiasis and prostate cancer	Isaac Tuffour
		17. Molecular characterization of lifetime infections with trypanosomes in individual cattle in Ghana	Jennifer Afua Ofori
		18. Towards sensitive analyte detection: the synergistic effects of reduced graphene oxide, PEDOT:PSS, polyethylene glycol and Ionic liquid nanocomposite- modified electrodes	Francis Krampa
		19. Clinical patterns of malaria in two different epidemiological settings in Mali: Dangassa and Nioro du Sahel	Seidina Diakité
	11.05am - 11.30am	**Coffee Break**	
		PLENARY TALK 8	**CHAIRS – Prof. Douglas J Perkins and Dr. Patrick Arthur**
	11.30am -11.50am	Naturally acquired immunity to *Plasmodium falciparum* malaria: identifying targets, understanding mechanisms	Prof. Faith Osier
		TURBO-TALKS	
	11.50am - 12.10pm	Primer for posters (60 seconds each)	20 Selected Poster Presenters
		PLENARY TALK 9	
	12:10pm – 12:30pm	Genomic medicine in Africa: challenges, prospects and call for action	Prof. Ambroise Wonkam

	12.30pm – 1:30pm	**Lunch Break and Poster Presentations**	
		PLENARY TALK 10	**CHAIRS – Dr. Winfred-Peck Dorleku and Prof. Daniel Boakye**
	1:30pm – 1:50 pm	A novel mechanism of neutralizing circulating free heme that ameliorates acute complications of sickle cell disease in early development	Prof. Solomon Ofori-Acquah
		FELLOWS SESSION	
	1:50pm – 3.05pm	20. Evaluating the feasibility of Autism spectrum disorders research in Mali, West Africa	Modibo Sangare
		21. Genetic association and gene-gene interaction analysis of APOL1, MYH9 and G6PD variants in patients with chronic kidney disease	Priscilla A. Akyaw
		22. Patterns of inflammatory responses and parasite tolerance vary with malaria transmission intensity	Temitope W. Ademolue
		23. Autopsy characterization of lung microbiome of HIV-positive patients in a tertiary referral hospital in Ghana	Pheonah Badu
		24. Genetic factors associated with renal dysfunctions in adult sickle cell disease patients in Cameroon	Valentina Ngo Bitoungui Epse
		PLENARY TALK 11	
	3.05pm - 3.25pm	Exploitation of receptor-mediated endocytosis for the targeted killing of *Trypanosoma brucei* by antibody-drug conjugates	Prof. Mark Carrington
	3.25pm - 3.50pm	**Coffee Break**	
		PLENARY TALK 12	**CHAIRS – Dr. Alfred Ngwa Amambua and Dr Lucas Amenga-Etego**
	3:50pm – 4.10pm	Expanding the horizons of malaria molecular epidemiology with high-throughput sequencing in *Plasmodium falciparum*	Prof. Jeffrey A. Bailey
		FELLOWS SESSION	
	4.10pm – 5.10pm	25. Genotypic diversity of *Mycobacterium tuberculosis* complex from Southern Volta, Ghana	Selassie L. Ameke
		26. Utilizing yeast as a model organism for drug discovery against eukaryotic infections	Raphael Lartey Abban

		27 .Endothelial progenitor cells in women diagnosed with preeclampsia 28 .High-resolution melt analysis reveals a potential shift in the molecular epidemiology of antimalarial drug resistance in Nigeria	Dorotheah Obiri Kolapo M. Oyebola
		PLENARY TALK 13	
	5.10pm - 5.30pm	Serological profiling of serum antibody levels following *P. falciparum* infections in regions of contrasting endemicity in Ghana	Dr. Kevin Tetteh
	5.30pm – 5.45pm	General discussions, Conference evaluation and Closing	Prof. Gordon Awandare
	7.00pm	Dinner at the forecourt of the Biochemistry Building	

POSTER PRESENTATIONS		
NO.	**TITLE**	**PRESENTER**
29	Phenotypic changes in the T cell repertoire during *Plasmodium falciparum* malaria infections	Augustina Frimpong
30	Genetic association and interactions between APOL1, MYH9 variants and HB S and C genotypes in patients with chronic kidney disease	Ernestine Kubi
31	Prevalence of chloroquine and antifolate drug resistance point mutations in *Plasmodium falciparum* field isolates from four areas in Ghana	Felix Ansah
32	Molecular characterization of tick-borne parasites in naturally infected cattle in Ghana	Justice Adzigbe
33	Investigating the effect of blood donor variability in *Plasmodium falciparum invasion* phenotyping assays	Laty G. Thiam
34	Isolation of bacteria and yeasts associated with fruit fermentation and bioethanol extraction	Magdalene Dogbe
35	Spontaneous switching of invasion phenotypes of *Plasmodium falciparum* strains in suspension culture	Prince B. Nyarko
36	The genetics of congenital non-syndromic hearing impairment in Ghana	Samuel M. Adadey
37	*In vitro* evaluation of anticancer activities and cytotoxicities of marketed herbal products in ghana	Sylvester Languon
38	Functional characterization of *Plasmodium falciparum* PF10_0351 protein	Essel Charles-Chess
39	Asymptomatic malaria and anaemia among school children in Ho municipality, Ghana	Arnold T. Luuse
40	Molecular characterization of hepatitis B virus (HBV) in rural and semi-urban areas in three districts of the central region of Ghana	Caroline Boatemaa Agyare
41	Evaluation of Omnigene Sputum, a novel sputum transport and decontamination reagent, for microscopy, culture and DNA-based assays	Diana Asema Asandem
42	Discovery and development of novel antifungal compounds from marine endophytic fungi	Ethel Juliet Blessie
43	Characterization of *Plasmodium falciparum* SURFIN8.2 and defining its role in malaria transmission	Joshua Adjah
44	Toward identifying molecular markers of *Plasmodium falciparum* Artemisinin resistance using the CRISPR-Cas9 genome editing system	Oheneba C.K. Hagan

POSTER PRESENTATIONS		
NO.	**TITLE**	**PRESENTER**
45	K13 gene polymorphisms in *Plasmodium falciparum* isolates from ACT post treatment samples in two ecological zones in Ghana.	Sena A. Matrevi
46	*In Silico* prediction of potential natural product-derived lead compounds for the treatment of Buruli ulcer	Bismark Dankwa
47	High recent transmission rate found among *Mycobacterium tuberculosis* strains circulating in an urban setting in Ghana	Prince Asare
48	Insecticide resistant vectors and drug tolerant parasites and their Impact on malaria transmission in Ghana	Bernice Anane Mawuli
49	Genetic diversity of noroviruses in Ghanaian children hospitalized with diarrhoea in pre-rotavirus vaccination era	Belinda L. Lartey
50	Iron (II) and Iron (III) chelation by phenolic acids	Wilhelmina Annie Mensah
51	Indoor and immediate-outdoor airborne bacterial and antibiotic susceptibility profiles of a research institute	Isawumi Abiola
52	Determinants of artemisinin resistance in *Plasmodium falciparum* clinical isolates in a Ghanaian population	Samuel Yao Ahorhorlu
53	The role of malaria and tumour immunity in the pathogenesis of Endemic Burkitt's Lymphom a	Cecilia Smith
54	Investigating determinants of asymptomatic *Plasmodium falciparum* infections in a high endemic area of Ghana	Abdul-Rahman Mubarak
55	High p revalence of s ubmicroscopic *Plasmodium falciparum* i nfections in p regnant women from Bobo-Dioulasso, Burkina Faso	Alamissa Soulama

PROFILES OF KEYNOTE SPEAKERS

Professor Fred N. Binka

Fred Binka was the founding Vice-Chancellor, University of Health Allied Sciences, Ho and a Professor of Clinical Epidemiology. Until recently, he was the Coordinator for the World Health Organization (WHO) Emergency Response to Artemisinin Resistance in the Greater Mekong Sub-region in Asia. He previously held the position of Dean School of Public Health, University of Ghana and worked with the Ghana Ministry of Health for over 20 years in several capacities, including being the first Director of the Navrongo Health Research Centre. He was a member of the initial team that developed the Roll Back Malaria Initiative at WHO in Geneva. He established the Indepth-Network, an international health research NGO. His research interests are in malaria (epidemiology and control) and intervention studies (drugs and vaccines of tropical diseases). He is a recipient of the Ronald Ross medal 2010 from the London School of Hygiene and Tropical Medicine, and the first recipient of the Rudolf Geigy Medal (2000) by the Swiss Tropical Institute. Professor Binka is a strong advocate for research capacity strengthening in Africa, through support from African governments and their partners. He was awarded the EDCTP Dr Pascoal Mocumbi Prize in 2016 in recognition of his outstanding achievements in advancing health research and capacity development in Africa. Professor Binka holds a medical degree, MB. ChB (University of Ghana); MPH (Jerusalem) and PhD in Epidemiology (Basel).

Professor
Simon Draper

Simon J. Draper is a Wellcome Trust Senior Fellow, Associate Professor and Jenner Investigator at the Jenner Institute, University of Oxford, where he leads the Blood-Stage Malaria Vaccine Group. He is also a Research Prize Fellow of the Lister Institute of Preventive Medicine. His research interests include studies of vaccine-induced malaria immunity as well as the optimisation of antibody and B cell induction by subunit vaccines. His group has pioneered the use of new vectored and protein vaccine delivery platforms for antibody induction as well as for new antigen target identification. In recent years, his group has developed new vaccines targeting blood-stage antigens from the human malaria parasites Plasmodium falciparum and P. vivax, including PfRH5 and PvDBP_RII. Since 2010, his group has taken nine new vaccine candidates into proof-of-concept Phase Ia clinical trials as well as three Phase IIa controlled human malaria infection (CHMI) studies to assess vaccine efficacy. Prof Draper's work is also focusing on the isolation of human monoclonal antibodies from vaccinated volunteers in clinical trials, seeking to understand the human antibody response to key antigens and to further develop these for prophylactic or therapeutic human delivery. His talk will cover the most recent advances in the development of vaccines for malaria.

ABOUT WACCBIP

1.0 BACKGROUND

The West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) was established in 2014 with funding from the Government of Ghana under the World Bank's African Centres of Excellence (ACE) in Higher Education Project. WACCBIP is led by faculty from the Department of Biochemistry, Cell and Molecular Biology (BCMB) and the Noguchi Memorial Institute for Medical Research (NMIMR), University of Ghana. The mission of the Centre is to improve diagnosis, prevention and control of infectious diseases in sub-Saharan Africa by providing advanced level training and research excellence on the cell and molecular biology of infectious pathogens.

The Centre's mandate is to provide Masters, PhD training, and targeted short-courses in Cell & Molecular Biology, conduct applied research into biology and pathogenesis of tropical diseases and increase research output and innovation by enhancing collaboration among biomedical scientists and industry/private sector leaders in the sub-region. In addition, WACCBIP is further supported by a Wellcome Trust Developing Excellence in Leadership, Training and Science (DELTAS) Africa award to strengthen its research, expand its regional network beyond West Africa, train postdoctoral fellows and provide additional PhD fellowships.

2.0 OBJECTIVES

The key objectives of the Centre are to:

a) Train high level health professionals and biomedical scientists on cell and molecular biology of tropical diseases through MPhil, PhD and Postdoctoral programmes.

b) Serve as a hub with state-of-the art biomedical laboratories to support infectious diseases research in the sub-region.

c) Establish a Biomedical High Performance Computing Unit to provide cluster computing services to promote teaching, research, and dissemination of information among health professionals and academics in the sub-region.

d) Increase research output and innovation by serving as a focal point for enhancing collaboration among biomedical scientists and biotechnology companies in the sub-region.

3.0 OPERATIONS

Training Programmes

WACCBIP is the only African institution to have received the full five year International Advanced Degree Accreditation from the Royal Society of Biology UK (RSoB). The Centre received accreditation in November 2016 for its MPhil and PhD programmes in Molecular Cell Biology of Infectious Diseases.

Opportunities offered by the Centre include:

Short-term

- Two-week workshops
- Attachments/internships

Masters programme

- One year course work at UG
- Plus one year research at UG or partner institution

PhD programme

- One year course work at UG
- Plus three years research at UG or partner institution
- 6-month student visitor fellowship

Postdoctoral programme

- Three year research fellowship at UG or African partner institution

WACCBIP Research

The research mission of WACCBIP is to conduct cutting edge research and innovation to guide development of new approaches to disease diagnosis, prevention, and control.

Major diseases

- Protozoan Pathogens- Malaria and animal trypanosomiasis
- Mycobacteria- Tuberculosis and Buruli Ulcer
- Other bacterial infections- Gastro-intestinal and blood infections
- Viruses- HIV, Rotaviruses and Dengue

Research themes

- Diseases pathogenesis and immunity
- Molecular diagnosis
- Pathogen genomics
- Molecular epidemiology for surveillance
- Target discovery for drug and vaccine development

Emerging themes

- Etiology of febrile illnesses in children
- Maternal health
- Human genetics (Infectious and non-communicable)

Research Core facility: WACCBIP is developing a Core facility to serve as a hub for collaboration among scientists in the sub-region with access to modern research equipment for analysis of samples and other services at reasonable cost. Services to be provided by the Core include high throughput multi-color flow cytometry and cell sorting, mass spectrometry, gene expression assays, primer synthesis, DND/RNA sequencing, and expression and purification of proteins. In addition, the WACCBIP Core will operate a laboratory supplies store, and build capacity and expertise for servicing and repair of equipment.

Projected Output: At the end of the four year period of the World Bank grant, WACCBIP would have achieved the following: (i) received international accreditation for two new specialized graduate programs, (ii) enrolled 80 MPhil students, 40 PhDs, of which at least 30% would be regional and 40% female, (iii) trained 195 scientists and health professionals through short term courses, of which at least 30% would be regional and 40% female, (iv) published at least 44 peer-reviewed research publications, of which at least 50% include regional co-authors, (v) attracted an average of $1M per year in externally mobilized funds, (vi) improved research and teaching environment through building extension to provide new lecture and seminar rooms, well-equipped research core facility, established a biomedical high performance computing unit, and (vii) developed new disease diagnostic/monitoring methods and novel drug/vaccine targets.

4.0 GOVERNANCE AND STAFF

Governance: WACCBIP operates as an academic unit in the College of Basic and Applied Sciences (CBAS), under the oversight of the Provost of the College and the Pro-Vice Chancellor for Research, Innovation and Development. The Centre is led by a Director and deputy Director, and assisted by the Centre's Management Committee composed of senior academics and Industry leaders. The Management committee has sub-committees for Training and Research, Equipment/Logistics and Information Computing Technology (ICT). In addition, there is a Monitoring and Evaluation team whose head is a member of the Management committee. The Centre has an International Advisory and Scientific Review Board, comprising of international experts who directly advise the WACCBIP Director on the Centre's scientific quality and strategic research.

Secretariat: The WACCBIP Director is assisted by a Centre secretariat, with a Project Manager, an Administrator, a Research Development Officer, an Accounts

Officer, a Laboratory Technologist, and an ICT officer.

Faculty: The Centre has appointed postdoctoral Research Fellows, who drive the Centre's research agenda. Additional faculty are drawn from the BCMB, NMIMR, and other faculty from CBAS and the College of Health Sciences for teaching and supervision of students. Regional and International collaborators also support the Centre through short teaching visits and co-supervision of students, including hosting students for experiential learning.

5.0 ADDITIONAL FUNDS OUTSIDE THE WORLD BANK ACE PROJECT

In August 2015, WACCBIP was awarded one of the prestigious grants under the Wellcome Trust's Developing Excellence in Leadership, Training and Science (DELTAS) Africa Programme. The centre will receive $7,823,628.00 over five (5) years to:

1. Train 12 Postdoctoral fellows who will undertake research projects of interest, in a scientific environment that promotes the development of leadership skills and networking with other scientists in the sub- region.

2. Train 15 PhDs in Pathogen biology and Human genetics of Communicable or non-communicable diseases.

3. Offer short courses in bioethics for about 50 trainees (10 trainees annually) on responsible biomedical research conduct.

4. Offer travel fellowships for 25 trainees for six-month visits to advanced laboratories under the co-supervision of mentors in the USA and UK, to learn specialized techniques or use specialized facilities and equipment for their training and research.

5. Attract and mentor 60 newly graduated students from the major Universities in Ghana, with a keen interest in science research to work as research assistants and technicians. These interns will be mentored to choose suitable careers by joining our graduate programmes.

6.0 FUNDING AND SUSTAINABILITY

The Centre operates as a semi-autonomous unit and its activities are financed through the World Bank support, Wellcome Trust DELTAS grant and additional grants mobilized by the Centre and its faculty and collaborators. The major plan for sustainability is to continue building our faculty and placing WACCBIP in a strong position for competitive funding from donor agencies by demonstrating consistency in teaching and research

excellence. With the increased visibility and credibility that is being gained through the African Centres of Excellence Project and the Wellcome Trust DELTAS project, the Centre is well-positioned to access additional funding for its training programmes. WACCBIP is also seeking partnerships and sponsorships from individuals, private sector entities and corporate bodies who share Centre's vision of African-led research and innovation.

NEW GRANTS WON BY FACULTY

Title	Brief Description of the Award	WACCBIP faculty awarded	Grant PI	Amount and Period
Identification of specific metabolites in mycolactone producing bacteria and Buruli ulcer infection: diagnostic biomarkers through metabolomic	A Medical Research Council (MRC) grant as part of the Global Challenge Research Fund (GCRF) awarded to researchers in the UK in collaboration with researchers in developing countries to address a global problem	Dr Lydia Mosi	Prof. Julian Griffin (Cambridge) Dr. Lydia Mosi	$220,603.51 2017-2019
The Dynamics of Filovirus infections in bats in Ghana	A Medical Research Council (MRC) grant as part of the Global Challenge Research Fund (GCRF) awarded to researchers in the UK in collaboration with researchers in developing countries to address a global problem	Dr Osbourne Quaye	Prof. James Wood (Cambridge)	$742,297.62 2017-2019
Transcriptomics of African Fruit Bats in response to Ebola virus antigens	A Royal Society Challenge grant as part of the Global Challenge Research Fund (GCRF) awarded to researchers in the UK in collaboration with researchers in developing countries to address a global problem	Dr Osbourne Quaye	Dr. Olivier Restif (Cambridge)	$123,000 2017
Pocket-i-nucleic acid diagnostic (pi-NAD)	The Royal Society has awarded a grant entitled "pocket-i-nucleic acid diagnostic (pi-NAD)" under the International Collaboration Award for Research.	Prof. Gordon Awandare	Prof. Elizabeth Hall (Cambridge) Prof. Gordon Awandare	£319,385 2016-2021
Tackling Infections to Benefit Africa	The Global Health Research-Units has awarded a grant to create a new multidisciplinary Centre for Tackling Infections to Benefit Africa (the TIBA Centre).	Prof. Gordon Awandare	Prof Mark Woodhouse (Edinburgh)	£6,886,852 2017-2021
GCRF-Crick African Network	The Global Challenges Research Fund (GCRF) has awarded a collaborative grant to establish the Crick African Network (CAN), a UK-Africa collaboration, to advance high-level capacity for research in poverty-related infectious disease.	Prof. Gordon Awandare	Prof Robert Wilkinson (Crick)	£6,258,293 2017-2021
SickleGenAfrica: Sickle Cell Disease Genomics Network of Africa	The NIH has awarded a U54 H3Africa grant to support the establishment of a Centre of Excellence for Sickle Cell research at the University of Ghana	Prof. Solomon Ofori-Acquah Prof. Gordon A. Awandare	Prof. Solomon Ofori-Acquah Prof. Gordon A. Awandare Prof. Julie Makani (Muhimbili University)	$5,249,292 2017 - 2022

PICTORIAL HIGHLIGHTS OF WACCBIP EVENTS

Third Workshop on Molecular Biology, Pathogenesis and Diagnostics of Neglected Diseases, July 11-22, 2016

A group photograph of participants and faculty members

Dr. Paula MacGregor interacting with students

Participants at the workshop

Maiden Annual Research Conference, July 14-15, 2016

Group photograph of dignitaries, invited guests and WACCBIP fellows

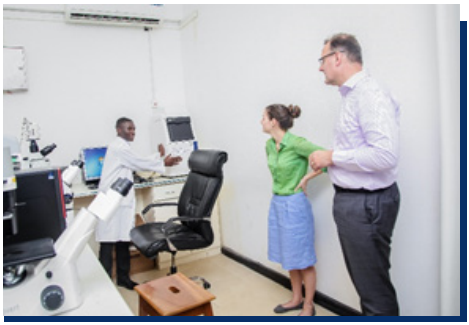
Prof. Awandare delivering his welcome address

Prof. Keith Gull delivering his keynote address

A WACCBIP fellow delivering her presentation

Site visit by Accreditation panel from the Royal Society of Biology (RSB), UK, October 13-14, 2016

Some students of WACCBIP with visiting Team



The RSB team visiting WACCBIP laboratories

Prof. Reece, Ms. Fowler and Prof. Coates - team from the RSB

Groundbreaking ceremony for the construction of the new WACCBIP Building (Biochemistry Annex), October 20, 2016

The Vice Chancellor speaking at the event

WACCBIP Director planting a tree on the site

Dignitaries at the ceremony

Artist's impression of how WACCBIP Building will fit with existing Biochemistry structure

Progress of work on the WACCBIP building project

First Bioethics Workshop, November 28 – December 2, 2016

Prof. Mahamadou Diakite and Prof. Awandare facilitating a discussion

Participants discussing topics at the workshop

Dr Angeliki Kerasidou delivering a lecture

Dr. Paulina Tindana facilitating a discussion

WACCBIP-ASCB-Oxford Workshop on Molecular Cell Biology of Protozoan Parasites, January 16-27, 2017

Workshop participants at a lecture

Visiting scientists at the opening ceremony

Participants at laboratory sessions

Sanger Experimental Genetics Malaria Course, April 30-May 5, 2017

Dignitaries at the opening ceremony

A cross-section of workshop participants

A group photograph of participants, facilitators and dignitaries

WACCBIP-WACCI Staff Retool Workshop, April 19-21, 2017

Group photo of Staff and Trainers

The Head of M&E, Dr. Osbourne Quaye, receiving his certificate of participation

WACCBIP receives Advanced International Accreditation from the Royal Society of Biology (RSoB), British House of Commons, UK, April 27, 2017

Head of Training and Research, Dr. Patrick Arthur receiving the accreditation certificate on behalf of WACCBIP at the RSoB Accreditation Ceremony, Pavilion Terrace, House of Parliament, UK

PUBLIC ENGAGEMENT ACTIVITIES

Outreach Programme to KNUST, November 17-18, 2016

A group photograph of WACCBIP outreach team and KNUST students

WACCBIP Laboratory technologist, Mr. Srinivasan Shankar giving a presentation to students

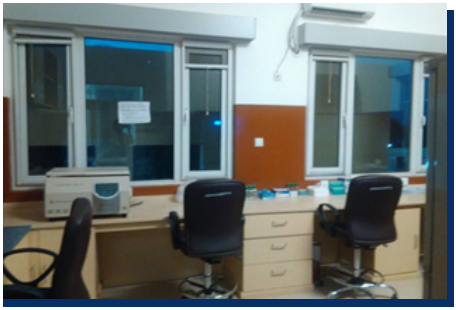
Outreach Programme to Senior High Schools, February 24 & 28, 2017

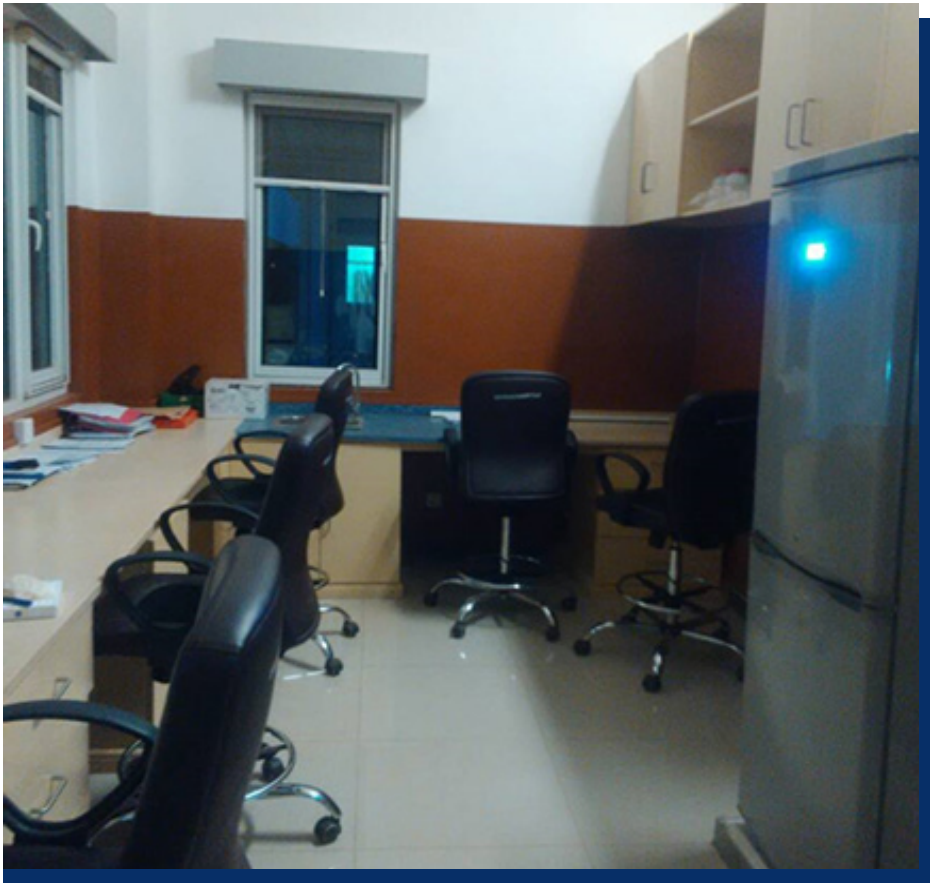
A cross section of students at the event

A group photograph of the WACCBIP team with students and staff of the secondary school

Graduate Interns delivering their presentations

Students participating in the practical session





Pictures of the research laboratory established at LEKMA

WACCBIP MANAGEMENT AND STAFF

- **Prof. Gordon A. Awandare** - Director
- **Prof. Kwadwo A. Koram** - Deputy Director
- **Dr. Patrick K. Arthur** - Head of Training & Research
- **Dr. Lydia Mosi** - Logistics Coordinator
- **Dr. Osbourne Quaye** - Head of Monitoring & Evaluation
- **Dr. Theresa Manful Gwira** - Graduate Admissions & Examinations Coordinator
- **Prof. Dorothy Yeboah-Manu** – Postdoctoral Programme Coordinator
- **Dr. Lucas Amenga-Etego/Dr. Samuel K. Kwofie** - Bioinformatics Coordinators
- **Dr. Anita Ghansah/Prof. Solomon Ofori-Acquah** -Genetics Course Coordinators
- **Mr. Barfi Adomako** - Co-Head of ICT, Electronic resources
- **Ms. Ama G. Dadson** - Co-Head of ICT, Physical resources
- **Mr. Collins Amofah** - Senior Accountant
- **Mr. Michael Somuah Nkansah** – Project Manager
- **Mr. Emmanuel Ghartey** - Research Development Officer / Centre Administrator
- **Ms. Sika Menka** - Research Development Officer / Assistant to the Director
- **Ms. Emefa Adzadu** - Accounts Officer
- **Mr. Srinivasan B. Shankar** - Laboratory Technologist
- **Mrs. Constance Kocke** - Procurement Officer
- **Mr. Vincent Appiah** - ICT Officer
- **Mr. Theophilus Dugah** - ICT Technician
- **Mr. Alfred Kazaresam** – ICT Intern

WACCBIP ADVISORY BOARD

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13.	Prof. Mahamadou Diakite	Member	Malaria Research and Training Centre, Mali
14.	Prof. K. Tanoh-Debrah	Member	Dean, School of Graduate Studies, University of Ghana
15.	Dr. Patrick Arthur	Member	Representative, Department of Biochemistry, Cell and Molecular Biology

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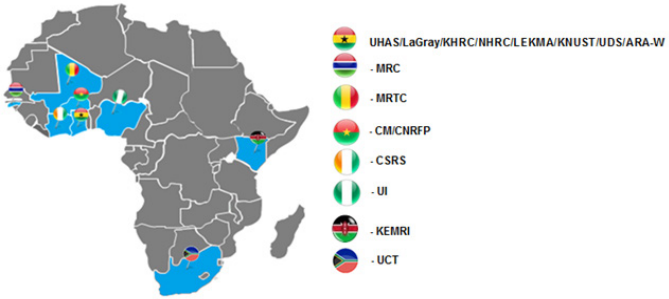
National Partners

- University of Allied Health Sciences, Ho
- Kintampo Health Research Centre, Kintampo
- Navrongo Health Research Centre, Navrongo.
- La Gray Chemical Company, Nsawam
- Kwame Nkrumah University of Science and Technology, Kumasi
- University of Development Studies, Tamale
- LEKMA Hospital, Teshie, Accra
- African Research Academies for Women, Accra

Regional Partners

- Medical Research Council (MRC) unit, the Gambia
- Malaria Research and Training Center (MRTC), University of Science, Techniques, and Technology, Bamako, Mali
- Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina Faso
- Unit for Research on Malaria and Neglected Tropical Diseases, Centre MURAZ Research Institute (CMRI), Bobo-Dioulasso, Burkina Faso
- Center Suisse de Recherche Scientifique (CSRS), La Cote d'Ivoire
- Institute of Child Health, College of Medicine, University of Ibadan, Nigeria
- Kenya Medical Research Institute, Kisumu, Kenya
- KEMRI- Wellcome Trust Research Programme, Kilifi, Kenya
- University of Cape Town (UCT), Division of Human Genetics, Faculty of Health Sciences, South Africa



WACCBIP national and regional partners

International Partners

- London School of Hygiene and Tropical Medicine, UK
- University of Cambridge, UK
- University of Oxford, UK
- Wellcome Trust Sanger Institute, UK
- MalariaGEN Consortium, UK
- University of New Mexico, USA
- University of Pittsburgh, USA
- American Society for Cell Biology, USA
- University of Copenhagen, Denmark

WACCBIP CONTRIBUTING FACULTY

Department of Biochemistry, Cell & Molecular biology, University of Ghana

1. Prof. Gordon A. Awandare
2. Dr. Patrick K. Arthur
3. Dr. Osbourne Quaye
4. Dr. Lydia Mosi
5. Dr. Theresa Manful Gwira
6. Prof. Laud Okine
7. Prof. Sammy Sackey
8. Dr. Augustine Ocloo
9. Dr. Jonathan Adjimani
10. Dr. Samuel Duodu
11. Dr. Winfred Peck-Dorleku
12. Rev. Dr. W. S. K. Gbewonyo
13. Dr. Kodzo Gbewonyo
14. Dr. Elmer Ametefe
15. Dr. Anastasia Rosebud Aikins

Noguchi Memorial Institute for Medical Research, University of Ghana

16. Prof. Kwadwo Koram
17. Dr. Kwadwo Asamoah Kusi
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20. Prof. Dorothy Yeboah-Manu
21. Prof. Daniel A. Boakye
22. Dr. Linda Eva Amoah
23. Dr. Michael Fokuo Ofori
24. Prof. Ben Gyan
25. Dr. Nancy Quashie
26. Prof. William Ampofo
27. Dr. Evelyn Bonney
28. Prof George Armah
29. Dr. Nicaise Ndam

School of Engineering, University of Ghana

30. Dr. Elvis Tiburu
31. Dr. Elsie Effah Kaufmann
32. Dr. Samuel Kwofie

College of Health Sciences, University of Ghana

33. Prof. Neils Ben Quashie
34. Prof. Julius Fobil
35. Dr. Richard H. Asmah
36. Prof. George Obeng Adjei
37. Prof. Isabella Quakyi
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39. Dr. Olayemi Edeghonghon
40. Dr. Charles Brown
41. Prof. Yaw Afrane

Navrongo Health Research Centre, Navrongo, Ghana

42. Dr. Abraham Oduro
43. Dr. Lucas Amenga-Etego
44. Dr. Paulina Tindana

Kintampo Health Research Centre, Kintampo, Ghana

45. Dr. Kwaku Poku Asante
46. Dr. Seth Owusu-Agyei

University of Health and Allied Sciences, Ho, Ghana

47. Dr. Bismarck Dinko
48. Dr. Kwabena O. Duedu

Kwame Nkrumah University of Science & Technology, Kumasi, Ghana

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University for Development Studies (UDS), Tamale, Ghana

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Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina Faso

51. Dr. Sodiomon B. Sirima
52. Dr. Issa Nebie Ouedraogo

Unit for Research on Malaria and Neglected Tropical Diseases, Centre MURAZ Research Institute (CMRI), Bobo-Dioulasso, Burkina Faso

53. Dr. Mahamodou Cisse

Center Suisse de Recherche Scientifique (CSRS), La Cote d'Ivoire

54. Prof. Bassirou Bonfoh

Kenya Medical Research Institute (KEMRI), KENYA

55. Dr. John Michael Obor Ong'echa
56. Prof. Faith Osier

University of Cape Town, South Africa

57. Prof. Ambroise Wonkam

Malaria Research and Training Centre, Bamako, Mali

58. Prof. Mahamadou Diakite
59. Prof. Seydou Doumbia

Medical Research Council, the Gambia

60. Dr. Alfred Amambua Ngwa

Harvard Malaria Initiative/Hopital Aristide Le Dantec, Dakar, Senegal

58. Dr. Amy Bei
59. Dr. Ambroise Ahouidi

University of Oxford, UK

60. Prof. Keith Gull
61. Prof. Dominic Kwiatkowski
62. Prof. Michael Parker

63. Prof. Simon Draper
64. Dr. Richard Wheeler
65. Dr. Samuel Dean

University of Cambridge, UK

66. Prof. Mark Carrington
67. Prof. Elizabeth Hall

Oxford Brookes University

68. Prof. Sue Vaughan

London School of Health and Tropical Medicine, UK

69. Prof. David Conway
70. Dr. Sam Alsford
71. Dr. Julius Hafalla
72. Dr. Kevin Tetteh
73. Dr. David A. Baker

Wellcome Trust Sanger Institute, UK

74. Dr. Oliver Billker
75. Dr. Julian Rayner

University of Pittsburgh, USA

76. Prof. Solomon Ofori-Acquah
77. Dr. David Finegold
78. Dr. Mark Gladwin

University of New Mexico School of Medicine, USA

79. Prof. Douglas Perkins

University of Heidelberg, Germany

80. Prof. Friedrich Frischknecht

Harvard University, USA

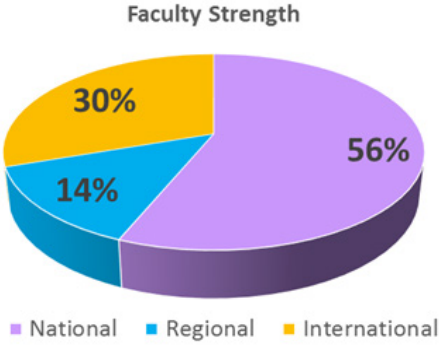
81. Prof. Manoj T. Duraisingh

University of Copenhagen, Denmark

82. Prof. Lars Hviid

American Society of Cell Biology

83. Prof. Kirk William Deitsch (Cornell University, USA)
84. Prof. John Richard McIntosh (University of Colorado, USA)
85. Dr. Martha Cyert (Stanford University, USA)
86. Prof. Joy Power (University of Colorado, USA)



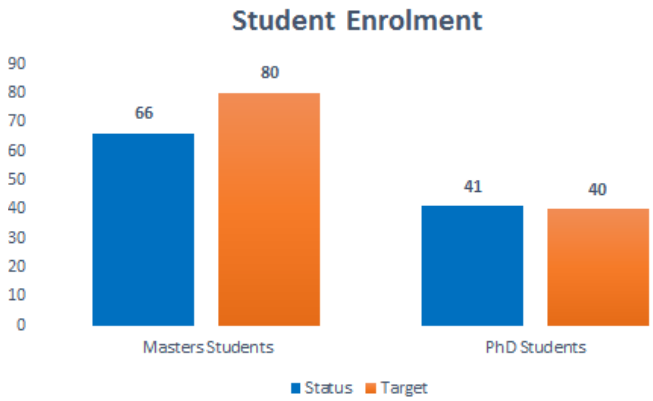
KEYNOTE SEMINAR PRESENTATIONS FROM VISITING SCIENTISTS

NAMES	INSTITUTION	TOPIC	DATE
Dr. Yaw Bediako	Crick Institute, UK	Protected or not? - The fate of naturally-acquired T cell immunity as Malaria transmission declines	May 8, 2017
Dr. Kwabena A. N. Sarpong	Washington University School of Medicine, St. Louis, USA	Unstructural Studies of the ErbB C-terminals; Probing Disorder in the Epidermal Growth Factor Receptor	April 27, 2017
Mr. Isaac Fianu	University of Göttingen, Germany	Towards structural and biochemical understanding of ssDNA deamination by AID	April 6, 2017
Dr. Prosper Kanyong	Ulster University, UK	3D Functional Cardiac Tissue Models for Regenerative Medicine	March 13, 2017
Dr. Prosper Kanyong	Ulster University, UK	Sensing and Biosensing for point-of-care biomedical applications	March 2, 2017
Dr. Lily Paemka	University of Iowa, USA	Seizures Are Regulated by Ubiquitin-specific Peptidase 9 X-linked (USP9X)	February 13, 2017
Dr. Alassane Mbengue	University of Notre Dame, USA	The ER-PI3P vesicle pathway a crucial mechanism of artemisinin resistance in *Plasmodium falciparum* malaria	December 1, 2016

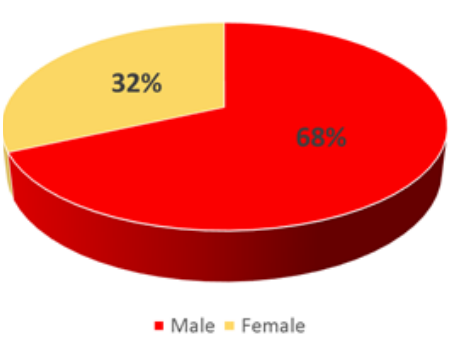
Dr. Yaw Bediako delivering his presentation

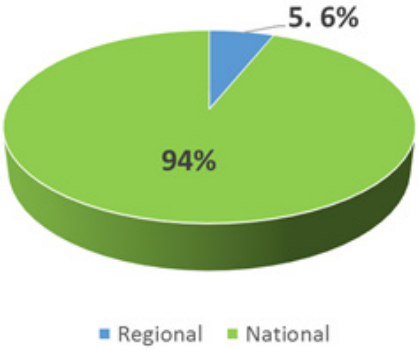
Dr Alassane Mbengue delivering his presentation

WORLD BANK AFRICAN CENTRE OF EXCELLENCE (ACE) PROJECT

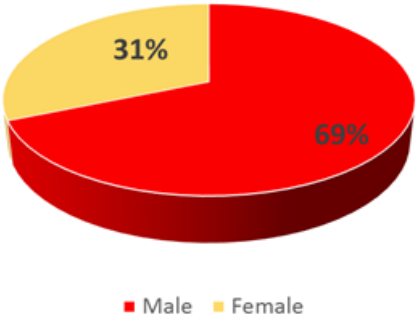


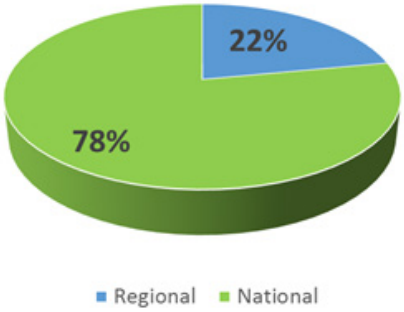
Summary of Masters Enrolment to date (N=66)





Summary of PhD Enrolment to date (N=41)

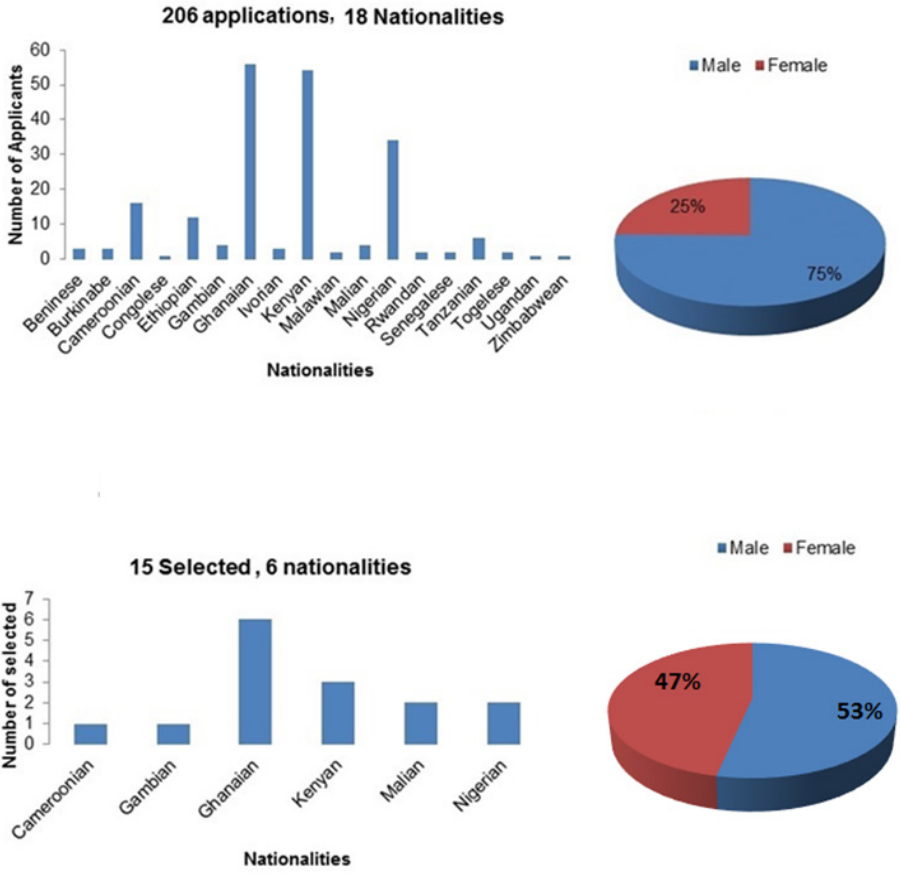




WACCBIP-DELTAS Graduate Interns

Cohort 1

1. Adade Emmanuel Edem
2. Adjei Rita Owusu
3. Amaning Pernell Asare
4. Ammah-Tagoe David
5. Ayee Richmond
6. Boateng Kyerewaa Akuamoah
7. Dogbe Magdalene
8. Mohammed Latifatu
9. Nanor Marian Namle
10. Opoku Grace
11. Oworae Kwadwo
12. Quansah Evelyn Baaba

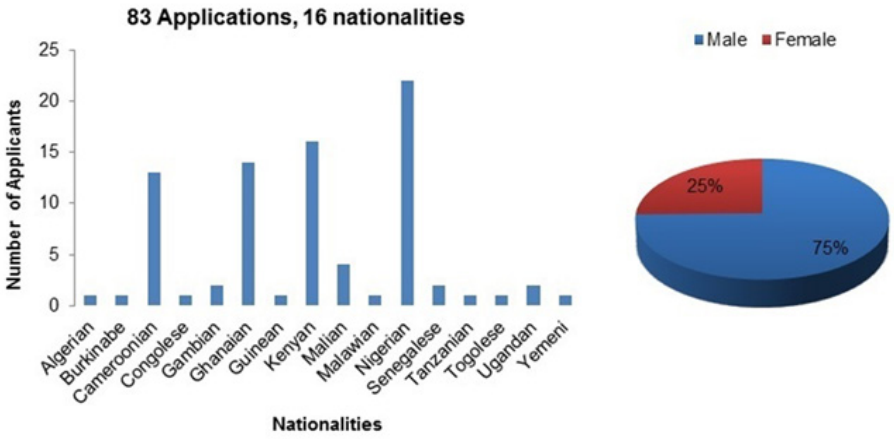


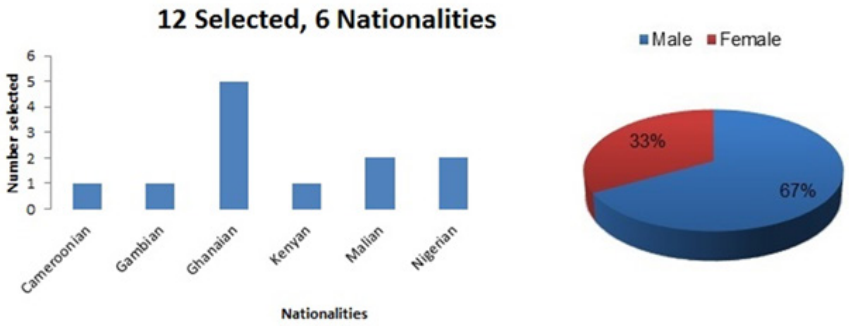
Summary of WACCBIP-DELTAS PhD fellowship applications

WACCBIP-DELTAS PhD fellows

NO.	NAME	GENDER	NATIONALITY	HOST INSTITUTION
1	Mbye Haddijatou	Female	Gambian	MRC, Gambia
2	Majidah Hamid- Bukola Adiamoh	Female	Nigerian	MRC, Gambia
3	Samuel Mawuli Adadey	Male	Ghanaian	UCT, South Africa
4	Dominic Selorm Yao Amuzu	Male	Ghanaian	WACCBIP, Ghana
5	Arnaud Jonas Kengne-Ouafo	Male	Cameroonian	WACCBIP, Ghana
6	Nancy Kemuma Nyakoe	Female	Kenyan	WACCBIP, Ghana
7	Beatrice Mukami Muriuki	Female	Kenyan	KEMRI, Kisumu-Kenya
8	Karamoko Niaré	Male	Malian	KEMRI, Killifi-Kenya
9	Collins Moranga	Male	Kenyan	WACCBIP, Ghana
10	Domfeh Seth Agyei	Male	Ghanaian	WACCBIP, Ghana
11	Chirawurah Jersley	Male	Ghanaian	WACCBIP, Ghana
12	Kuleape Joshua Agbemefa	Male	Ghanaian	WACCBIP, Ghana
13	Owusu Irene Amoakoh	Female	Ghanaian	WACCBIP, Ghana
14	Pearl Osrike	Female	Nigerian	WACCBIP, Ghana
15	Agnes Guindo	Female	Malian	MRTC, Mali

WACCBIP-DELTAS Post-doctoral fellowship programme





Summary of WACCBIP-DELTAS Postdoctoral fellowship applications

WACCBIP-DELTAS Postdoctoral fellows

NO.	NAME OF FELLOW	NATIONALITY	GENDER	TRAINING INSTITUTION	DATE OF ENTRY TO PROGRAMME	TITLE OF PROPOSED STUDY
1	Dr. Yaw Aniweh	Ghanaian	Male	WACCBIP-BCMB, University of Ghana	April 1, 2016	Unravelling the molecular players during *Plasmodium falciparum* invasion of erythrocytes
2	Dr. Jewelna Akorli	Ghanaian	Female	WACCBIP-BCMB/NMIMR, University of Ghana	April 1, 2016	The role of dominant midgut bacteria isolated from Anopheles mosquitoes in larval development and susceptibility to *Plasmodium* infection
3	Dr. Adwoa Asante-Poku Wiredu	Ghanaian	Female	WACCBIP-BCMB/NMIMR, University of Ghana	April 1, 2016	Host susceptibility to Tuberculosis (TB) in Ghana
4	Dr. Kolapo Oyebola	Nigerian	Male	Medical Research Unit, Fajara, the Gambia	April 1, 2016	Genetic variations and differential immunological response to malaria chemotherapy in variably exposed West African populations
5	Dr. Modibo Sangare	Malian	Male	Malaria Research and Training Center at the University of Science, Techniques, and Technology, Bamako, Mali	April 1, 2016	Epidemiology, clinical neurophysiology, and molecular genetic studies of Autism Spectrum Disorders in Mali.
6	Dr. Seidina A. S. Diakite	Malian	Male	Malaria Research and Training Center at the University of Science, Techniques, and Technology, Bamako, Mali	April 1, 2016	Genomic variation in *P. falciparum* and pharmacogenomics of antimalarial drugs in Mali

NO.	NAME OF FELLOW	NATIONALITY	GENDER	TRAINING INSTITUTION	DATE OF ENTRY TO PROGRAMME	TITLE OF PROPOSED STUDY
7	Dr. Valentina Josiane Ngo Bitoungui	Cameroonian	Female	University of Cape Town, South Africa	April 1, 2016	Genetic factors associated with cardiovascular diseases in Cameroonian sickle cell disease patients
8	Dr. Daniel Muthui Kiboi	K enyan	Male	Kenya Medical Research Institute, Kilifi, Kenya	May 1, 2016	Validation of candidate mutations in *Plasmodium* for resistance to the antimalarial drugs Piperaquine and Lumefantrine
9	Dr. Emmanuel Amlabu	Nigerian	M ale	WACCBIP-BCMB, University of Ghana	November 1, 2016	New Generation Malaria Vaccine Development
10	Dr. Lily Paemka	Ghanaian	Female	WACCBIP-BCMB, University of Ghana	July 1, 2017	Characterizing Genetic Breast Cancer Risk Factors in Ghanaian Women
11	Dr. Saiko Y. Bah	Gambian	M ale	WACCBIP-BCMB, University of Ghana	June 1, 2017	Using bioinformatics tools to validate biosignature for diagnosis of childhood tuberculosis
12	Dr. Ali Azeko Salifu	Ghanaian	M ale	WACCBIP-BCMB, University of Ghana	July 1, 2017	Controlled Release of a Natural Anticancer Agent from Nanoparticles for Cancer Therapeutics

Plenary Sessions

1. Adaptation and multiplication rate variation of *Plasmodium falciparum* in West Africa

David J. Conway
London School of Hygiene and Tropical Medicine, London

It is important to understand intrinsic variation in malaria parasites that affects their reproductive rates in different environments, particularly diverse areas of West Africa where there is a wide spectrum of transmission intensity and infection incidence. Different approaches will be illustrated. Firstly, genome sequence analyses of parasites at multiple sites throughout the region indicate a small number of discrete gene loci that have been under varying local selection. As well as loci encoding products known to be under immune and drug selection, results strongly implicated particular genes involved in sexual differentiation, so identifying functional and selective differences between allelic sequences is a priority. Secondly, direct measurements made of phenotypes analysed *ex vivo* show a spectrum of diversity within and between sampled populations. Asexual blood stage multiplication rates of long-term laboratory adapted *P. falciparum* clones and new clinical isolates were measured. Parasite growth of selected clones was analysed in co-culture assays with all possible heterologous pairwise combinations, which did not affect their clone-specific replication rates. Multiplication rates of new clinical isolates after a few weeks of culture showed a wide spectrum of replication rates, with the entire range being lower than for the long-term laboratory adapted clones. Multiplication rates remained stable in culture for the first few months, with the first significant increases being detected after approximately 5 months, by which stage new mutants can attain high frequencies, so experimental evolution may also identify genes affecting multiplication in different environments

2. *Burkholderia cepacia* shows us that antibiotic resistance and inflammation are two sides of the same coin

Miguel A. Valvano
The Wellcome-Wolfson Institute for Experimental Medicine, Queen's University of Belfast

The Type 6 Secretion System (T6SS) is a versatile weapon widespread among Gram-negative pathogens and symbionts. Some T6SS deliver toxins to kill or inhibit the growth of susceptible bacteria, while others have evolved to target eukaryotic cells. Macrophages infected with *B. cenocepacia,* a member of the *B. cepacia* complex of opportunistic bacteria, display dramatic alterations in their cytoskeleton architecture and undergo pyroptosis due to the activation of the pyrin inflammasome, which is mediate by a T6SS-secreted toxin called TecA. TecA is a deamidase that inactivates Rho-type GTPases. The "proinflammatory" character associated with *B. cenocepacia* infection in patients with cystic fibrosis goes hand by hand with the extreme resistance of this bacterium to nearly all classes of antimicrobials. We have found that antibiotic stress also stimulates *B. cenocepacia* to secrete molecules that counteract antimicrobials outside the bacteria cells before antibiotic can reach their targets. This represents a novel, extracellular mechanism of antimicrobial resistance. More importantly, inflammation and antibiotic resistance in chronic infection represent two sides of the same coin, which must be considered to develop novel therapies to control both infection and inflammation.

3. Ecological and physiological correlates of mating in *Anopheles gambiae*

Abdoulaye Diabate
Institut de Recherche en Sciences de la Santé/Centre MURAZ, Bobo-Dioulasso, Burkina Faso

The evolution of insecticide and drug resistance and the complexity of vectoral system have seriously challenged standard public health approaches to control malaria and to date, alternative measures are desperately needed. New control approaches envision using engineered mosquitoes to suppress or to replace existing populations. Another approach that may be effective is based on conventional sterile male release. However, availability of these tools does not necessarily guarantee ultimate success. A major concern is that presence of reproductive barriers will reduce the spread of the genes of interest between subpopulations. A second concern is the possibility that laboratory adapted mosquitoes will not be able to compete for mates in the wild. Success will depend on understanding patterns of effective mosquito reproduction that are relevant to transgene spread. Most population models assume that all individuals have the same reproductive success, which probably is not the case. The most plausible natural circumstance is variation in the competitiveness of males to acquire a mate as well as assortative mating—the tendency of certain phenotype to mate with one another—yet these phenomena have been little studied in mosquitoes. Field and large outdoor cages studies, designed to dissect the mating biology and characterize essential factors that enhance mating competitiveness in mosquitoes, are needed to provide a foundation for predicting the potential utility of genetic control. Here, some of the key practical questions that are essential to translate transgenic or sterile males technological advance into improved malaria control in the field will be addressed.

4. Metabolomics and lipidomics as tools for biomarker discovery for medical research

Julian L. Griffin
Department of Biochemistry and Cambridge Systems Biology Centre, University of Cambridge, Cambridge, CB2 1GA, UK

With recent improvements in the design and sensitivity of mass spectrometers (MS) and Nuclear Magnetic Resonance (NMR) spectrometers it is now possible to measure hundreds of metabolites in a tissue or biofluid for the price of a few dollars. Furthermore, liquid chromatography (LC)-MS is routinely used in hospitals to screen for inborn errors of metabolism and so new biomarkers generated by this metabolomics approach could be readily adopted in the clinic to screen for diseases and monitor treatment efficacy. Our laboratory at the University of Cambridge has been developing techniques to profile a wide range of metabolites for following disease either at a 'deep phenotyping level,' where the aim is to profile as many metabolites as possible to build a metabolic description of an underlying pathology, or at the epidemiological level, where a smaller number of metabolites are profiled but assays are performed on 100s-1000s of individuals. Our group has a particular interest in metabolic diseases, including non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes, and two examples will be presented to illustrate the alternative uses of metabolomics. The first example will look at how we have used lipidomics to identify biomarkers of NAFLD in a sub-group of the Fenland cohort. The second example will focus on how we have used metabolomics to increase our mechanistic understanding of mitochondrial biogenesis in white adipose tissue during the process of browning. Finally, our on-going collaborative work on Buruli ulcer infection with the University of Ghana will be discussed.

5. Genetic determinants of diminished response of *Plasmodium falciparum* to artemether and lumefantrine in Mali

Abdoulaye A. Djimde
Malaria Research and Training Center, University of Sciences, Techniques and Technology of Bamako, Mali

Artemisinin based combination therapies (ACTs) are first-line treatment for uncomplicated falciparum malaria worldwide. However, recent studies conducted in Mali showed an increased frequency of recurrent parasitemia following artemether-lumefantrine (AL) treatment. Study samples were collected during a larger clinical trial conducted by WANECAM. *Ex vivo Plasmodium falciparum* sensitivity to artemether and lumefantrine was assessed using tritiated hypoxanthine-based assay. The prevalence of molecular markers of antimalarial drug resistance (Pfcrt K76T, Pfmdr1 N86Y and K13-propeller) were measured by PCR and/or sequencing. Next generation sequencing (NGS) was performed on selected samples. GWAS was conducted using NGS data and *ex-vivo* phenotypes. Overall 61 samples were successfully analyzed in the *ex-vivo* study. Mean IC50s increased significantly between baseline and recurrent parasites for both artemether (1.6 nM versus 3.2 nM, $p < 0.001$) and lumefantrine (1.4 nM versus 3.4 nM, $p = 0.004$). Wild type Pfmdr1 N86 allele was selected after treatment (71% vs. 91%, 112 of 158 vs. 95 of 105, $p < 0.001$) but not the wild type pfcrt K76 variant (23.5% vs. 24.8%, 40 of 170 vs. 26 of 105, $p = 0.9$). Three non-synonymous K13-propeller SNPs (A522C, A578S, and G638R) were found with allele frequencies < 2%. 6462 SNPs were included in the GWAS study. Two previously un-reported new candidate loci (PF3D7_0926100 and PF3D7_0814500) were strongly associated with artemether and lumefantrine responses. Malian post-AL *P. falciparum* isolates were less susceptible to artemether and lumefantrine than baseline isolates. Associations of novel loci associated with artemether and lumefantrine responses in the field were identified. Additional ongoing studies may shed more light on the genetic determinants of diminished response to AL.

6. Mechanisms of immune control and tumorigenesis of endemic Burkitt lymphoma

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Endemic Burkitt lymphoma (eBL) is the most common childhood cancer in Sub-Saharan Africa. The survival rate for a child diagnosed with eBL in Africa is 35-45% in sharp contrast to 90% when the sporadic form (sBL) is diagnosed in the USA or Europe. The incidence of eBL (2-5 cases/100,000) is ten-fold higher compared to sBL even though both forms are indistinguishable by histology and carry the hallmark *c-MYC* translocation. It has been postulated that the increased incidence is due to a higher prevalence of transforming Epstein-Barr virus (EBV) concurrent with immune-cell altering *Plasmodium falciparum* malaria co-infections experienced by children prior to eBL diagnosis. Our studies have shown that children residing in malaria holoendemic areas who are infected with EBV early in life, experience attrition of EBV-specific IFN-y secreting aB T cell responses, and contend with more viral reactivation compared to children in non-malarious regions. However, the impact of other immune modulating parasitic co-infections, such as schistosomiasis, or the role of other mediators of viral and tumor immunosurveillance, such as natural killer (NK) cells, have not been investigated in eBL pathogenesis. Also, differences in immunity to EBV type 1 and type 2 (found at a high prevalence in Africa) have not been adequately explored. Our initial genomic investigations suggest that the somatic mutational landscape of EBV-type 2 tumors is similar to EBV-negative tumors, with more mutations in oncogenic pathways compared to EBV type 1 tumors. These findings which support our ongoing work will be discussed. A comprehensive understanding of eBL pathogenesis will not only shed light on etiologic mechanisms but will provide essential insight regarding when a prophylactic or therapeutic EBV vaccine would be effective.

7. Chronic infection and virulence: a role for the *Plasmodium* pir gene family?

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Plasmodium proteins, particularly those encoded by subtelomeric multigene families are thought to contribute to virulence and chronicity of blood-stage malaria. We study the pir (Plasmodium interspersed repeat) family, which is related to the rif/stevor gene families of *P. falciparum*. The presence of pir genes in the genomes of Plasmodium species infecting rodents allows the investigation of this gene family in vivo, with direct relevance to the majority of Plasmodium species including the important human pathogens *P. falciparum* and *P. vivax*. Mosquito transmission of *P. chabaudi* increases expression of a large subset of pir genes in acute blood-stage infection, which is associated with reduced virulence of the infection. By contrast, parasites from chronic infections or from serially blood-passaged parasites express fewer and different pirs, and are more virulent when injected into naïve mice. Our data suggest a causal link between pir expression and virulence, and with the ability of the host to establish chronic infections. The changes in pir expression in acute and chronic infections occurs in other rodent malarias and in infections in the natural host, the thicket rat, suggesting this may represent an important event for parasite survival in the blood. Mosquito-transmitted *P. chabaudi* infections elicit a very different early host response from that induced by infections initiated by serially blood-passaged parasites, which may be responsible for the reduced virulence. Our next tasks will be to elucidate the relationship between pir gene expression and virulence, and the mechanisms by which virulence is altered. Understanding the role of this Plasmodium-wide gene family is critical to the understanding of the basic biology of these infections and in engendering new research directions that could inform new interventions to combat malaria.

8. Naturally acquired immunity to *Plasmodium falciparum* malaria: identifying targets, understanding mechanisms

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Epidemiological observations, IgG passive transfer studies and experimental infections in humans all support the feasibility of developing highly effective malaria vaccines, but the precise antigens that induce protective immunity remain uncertain. The *Plasmodium falciparum* genome encodes over 5400 proteins, but less than 0.005% of these have been evaluated in clinical trials for subunit vaccines. Furthermore, although many mechanisms have been proposed as correlates of protection against malaria, only a handful have been studied in detail in multiple studies. We aim to comprehensively identify the merozoite "immunome" and the subset of these proteins that may be novel potential vaccine candidates using multi-centre cohort studies in Africa. We will also examine the relative importance of a number of antibody-dependent mechanisms of parasite clearance in mediating protection; these include the growth inhibition assay, the merozoite opsonic phagocytosis assay and the antibody-dependent neutrophil burst assay, amongst others. These data will provide a strong evidence base that could contribute to the development of the next generation of subunit vaccines against malaria.

9. Genomic medicine in Africa: challenges, prospects and call for action

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The prospects for genomic medicine in Africa have been enhanced by major initiatives that are led by international funding agencies and academics, such as the Malaria Genomic Epidemiology Network (www.malariagen.net/) and the Human Heredity and Health in Africa program (h3africa.org/), and more focus programme such as the current WACCBIP-DELTAS. There is a need for African societies to prepare for the genomics era and its consequences through education at all levels. Simple clinical applications of DNA technology could provide immediate benefit for healthcare in many African countries such as application of Genetics in prenatal diagnosis and for personalized medicine in prevalent conditions such as Down syndrome or Sickle Cell Disease (SCD). Although there is sporadic evidence of participation of Africans in researching the genomics of rare monogenic and multifactorial conditions, there is little evidence that this improved contribution of African researchers to research has an impact on genomic medicine Practice in Africa. There is therefore an urgent call to map specific mutations and variations for monogenic conditions among Africans and susceptibility to infectious and non-communicable diseases to fast track their implementation in practices. For instance, a research on congenital hearing loss among Cameroonians has revealed nearly 50% of mutations were novel and 30% of families did not have detectable mutations, auguring possibility of new genes discovery. Improved capabilities of African institutions to undertake research with: 1) the development of academic public research and partnerships among African countries themselves; 2) the development of a critical mass of expertise in bioinformatics in order to utilize the vast quantities of genomic data that are being generated; 3) Finally, all African countries need to evolve appropriate national frameworks to consider the ethical implications of genomics research and its applications in their own unique social, cultural, economic and religious context.

10. A novel mechanism of neutralizing circulating free heme that ameliorates acute complications of sickle cell disease in early development

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Intravascular hemolysis releases potentially harmful heme into the circulation. A battery of plasma proteins notably hemopexin neutralize heme by scavenging it from the circulation for degradation in the liver by heme oxygenase-1 (HO-1). The scavenging protection conferred by hemopexin is virtually exhausted in individuals and transgenic mice with sickle cell disease (SCD) because of the chronicity and severity of intravascular hemolysis. In the current study, we discovered that acute elevation of plasma heme caused lethal acute lung injury (ALI) in adult SCD mice as we have previously reported. However, nearly all the young SCD mice survived concomitant with a rapid clearance of heme by a novel mechanism independent of the known heme scavengers. We discovered that plasma contains enzymatically active HO-1 that declined with aging in both humans and mice with SCD. To determine the origin of plasma HO-1 we studied mice with targeted disruption of HO-1 expression in myeloid cells, and discovered significantly lower levels of the enzyme in these animals compared to littermates with intact murine HO-1 genes. To confirm that HO-1 is responsible for the rapid heme clearance in young SCD mice that survived in our ACS model, we treated a cohort of 3-4 weeks mice with tin protoporphyrin (SnPPIX) a potent inhibitor of HO activity. Nearly all SnPPIX-treated young SCD mice failed to clear excess heme and succumbed to ACS (n=8/9; 89%) while a majority of littermates (n=6/7; 85%) given a vehicle treatment prior to the heme infusion were protected. These data allow us to propose a new paradigm of neutralizing the danger posed by free heme, which is independent of heme scavengers, but rather involves the intravascular degradation of heme by circulating HO-1 derived primarily from PBMCs.

11. Exploitation of receptor-mediated endocytosis for the targeted killing of *Trypanosoma brucei* by antibody-drug conjugates

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Antibody-drug conjugates (ADCs) are being developed for killing of cancer cells, but not healthy cells, by combining an antibody that recognises an epitope on the cancer cell surface with a cytotoxic drug. In parallel, one of the goals in the design of therapeutics against protozoan pathogens is to destroy the invading cells without causing damage to the host. It is logical, therefore, that ADCs could provide a new class of therapeutic agents against protozoan pathogens. Further, there is clear scope for piggy-back drug development alongside anti-cancer ADCs by varying only epitope-specificity. Here, we use the African trypanosome, *Trypanosoma brucei,* as a proof-of-principle model for the use of ADCs against a protozoan parasite. This demonstrates that receptor-mediated nutrient uptake can be exploited for the delivery of a common class of anti-cancer drug into these cells, leading to specific cell killing at picomolar concentrations.

12. Expanding the horizons of malaria molecular epidemiology with high-throughput sequencing in *Plasmodium falciparum*

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High-throughput sequencing has been rapidly transforming scientific endeavors providing previously unimagined experimental scales. Our laboratory aims to drive and develop high-throughput sequencing techniques appropriate to answer both broad and focused scientific questions in infectious disease. Leveraging multiple collaborations, our work primarily aims to better understand the biology of malaria immunity and virulence as well as the evolution of malaria drug resistance with the goals of improving vaccine design and informed chemotherapy, respectively. Using whole genome sequencing we have recently examined the evolutionary context of artemisinin resistance in South East Asia suggesting that partner drug pressure may lock parasites into mutually exclusive tracks. Using amplicon deep sequencing, we have also developed methods to detect initial emergence of drug resistance within a population before lengthened parasite clearance curves become commonplace. This method is aimed at the early detection of artemisinin resistance in Africa, which we are currently trialing in Kenya and Tanzania. We have also been developing methods for highly multiplexed targeted sequencing in malaria allowing us to cost-effectively and efficiently sequence numerous loci in large numbers of infected individuals. Combined with single tube pooling of multiple individuals, these methods have the ability to push the tracking of drug resistance and parasite dynamics towards near real-time monitoring, providing rapid detailed information for public health interventions such as elimination efforts. These approaches and methods to be discussed are of general utility and also applicable to other infectious diseases or organisms of interest.

13. Serological profiling of serum antibody levels following *P. falciparum* infections in regions of contrasting endemicity in Ghana

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Antibodies are an important component of the naturally acquired immune response to malaria and are generated following repeated exposure to infection. Proteins exposed to the immune system, primarily those on the merozoite surface, the apical organelles or on the surface of the infected erythrocyte surface are targets of these antibodies. Responses to some of these targets have been associated with clinical protection from disease. Individuals living in high malaria transmission regions are likely to have developed a substantial antibody repertoire, and titre, of responses to these proteins, which can be measured using serological assays. Previously we described the expression of a large panel of novel recombinant proteins based on known and putative *Plasmodium falciparum* antigenic targets and how these reagents could be used in conjunction with the microarray platform to measure current and historical exposure to disease. The presentation will cover the screening of serum samples collected from regions of varying transmission in Ghana; Accra (n=125), Hohoe (n=24), Kintampo (n=217) and Navrongo (n=134). The preliminary data from this study will assess the antibody profile of responses to >100 purified recombinant antigens, with a particular focus on invasion-related merozoite antigens.

Fellows Sessions – Oral category

1. PfRON12 interacts with Band 3 on the erythrocyte surface

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Mentor - Gordon A. Awandare

The process of merozoites invasion is a multi-step event, involving ligands from the host as well as merozoite surface proteins. Key to the process of invasion are proteins that are resident in the micronemes as well as the rhoptries. At the neck of the rhoptries is found the rhoptry neck proteins; PfRONs. They have been implicated in mediating the formation of the tight junction complex. To this end, we sought to characterize the role of PfRON12. PfRON12 is a 36.4 kDa protein, which we have successfully purified and used to immunize mice to generate antibodies. Further experiments demonstrated that RON12 binds to an erythrocyte surface protein, and this was not abrogated by neuraminidase, trypsin and chymotrypsin treatment. However, antibodies to RON12 did not block merozoite invasion of erythrocytes. Staining with the antibodies localized RON12 as a punctuate pattern in the infected erythrocyte, consistent with published studies. Co-immunoprecipitation followed by a mass spectrometry showed that RON12 binds to the erythrocyte membrane protein Band 3. In addition, RON12 binds to erythrocyte membrane-associated proteins. Our investigations show for the first time that PfRON12 binds to Band 3 and other membrane associated proteins, but does not appear to directly be involved in erythrocyte invasion.

2. Understanding the mechanisms of anti-inflammatory activities of cryptolepine

Ahmed Rufai Abdulrahman (ahmedrufai114@gmail.com) – PhD student
Supervisors – Mohamed Mutocheluh, Jonathan Adjimani & Kwadwo Asamoah Kusi

Although inflammation plays a key role in coordinating host defense against infectious pathogens, its dysregulation results in severe pathological conditions. Dysregulated inflammatory responses come about as a result of many factors including hyperactivity of pro-inflammatory signaling pathways. Hyper-activity of the Toll like receptor (TLR) - nuclear factor kappa B (NF-kB) signaling pathway is reported to be associated with many inflammatory diseases, which makes the pathway a good therapeutic target. Although cryptolepine, an alkaloid obtained from *Cryptolepis sanguinoleta,* has been shown to have anti-inflammatory properties *in vivo,* its mechanisms of action are not fully understood. This study sought to determine the effects of cryptolepine on the pro-inflammatory signaling activity of the TLR2-NF-kB pathway. Murine macrophage cell line (Raw Blue cells) stably transfected with secreted embryonic alkaline phosphatase (SEAP) reporter gene under the control of a promoter inducible by NF-kB transcription factor, were stimulated with a TLR2 agonist (pam3CSK4) in the presence or absence of cryptolepine (0.5 - 2μM). After 24 hour incubation, culture supernatants were collected and the pathway activity assessed by measuring the levels of SEAP using Quanti-Blue assay. In the presence of the agonist alone, the TLR2-NF-kB pathway activity was increased sharply and this was significantly ($p < 0.05$) inhibited by cryptolepine in a dose-dependent manner. This study showed that cryptolepine inhibited the pro-inflammatory activity of the TLR2-NF-kB pathway as a mechanism of its anti-inflammatory property. Further studies are required to determine the possible inhibitory effect of the alkaloid on expression of the specific target genes of the NF-kB transcription factor which have significant pro-inflammatory activities.

3. Acquisition of dihydropteroate synthase (*dhps*), K540E and A581G, mutations drive copy number variations of GTP *Cyclohydrolase* 1 (*gch1*) gene in Ghanaian *Plasmodium falciparum* field isolates

Musah Osei (muskingdom1@gmail.com) – Masters Student
Supervisors - Neils B. Quashie, Gordon A. Awandare & Nancy O. Quashie

Resistance to sulfadoxine-pyrimethamine (SP) has been reported in the country and this is as a result of point mutations in the *dhps* and *dhfr* (dihydrofolate reductase) genes, the targets of the SP. There is also an evidence of amplification of GTP cyclohydrolase 1(*gch1*) gene which codes for the first enzyme in the parasite *denovo* folate pathway, amongst parasites which harbor the highest SP resistance point mutation (164L) in South East Asia. These point mutations make the parasites less fit, but the acquisition of multiple copies of the *gch1* gene may compensate for this fitness cost. Two hundred and two blood samples collected from children aged 14 years and below with uncomplicated malaria presenting at health centres from Accra, Kintampo, Cape coast, and Navrongo were used in this study. Quantitative real-time PCR (qPCR) was used to estimate the copy numbers. The *Pfdhps* and *Pfdhfr* regions were PCR amplified and directly sequenced. Ninety three percent (92.6%) and 7.4% of the parasite isolates harbored single and double copies of the *gch1* gene respectively. Duplication of *gch1* gene was independent of the different study sites (P=0.696). Point mutations at dhfr59R (P=0.026), dhfr108N (P<0.001), dhfr108T (P<0.001) and dhps43G (P=0.02) were found to be associated with the study sites. However, there were no point mutations observed at codons 164L, 50R and 163T as reported elsewhere. For correlation between the mutations and *gch1* CNV, only mutations at *dhps*540E (P=0.001), and *dhps*581G (P=0.002) were found to be significant. The findings from this study revealed that mutations at *dhps*540E and *dhps*581G strongly correlated with double *gch1* gene, implying that gch1 may compensate for the fitness cost in parasites harboring these mutations. Continuous monitoring of gch1, *dhfr* & *dhps* genes and also further studies to discover component drugs that can inhibit the *gch1* gene product are required

4. Evidence of altered liver function among malaria and hepatitis B co-infected pregnant women

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Supervisors - Gideon Kofi Helegbe, Gordon A. Awandare & Osbourne Quaye

Hepatitis B and malaria are co-endemic in Ghana. While single infections of malaria and hepatitis B among pregnant women have been extensively studied, the impact of malaria/hepatitis B co-infections on the function of the liver remains to be evaluated. We therefore evaluated the effect of malaria and hepatitis B co-infection on liver function in pregnant women in the Northern Region of Ghana. Four categories of pregnant women were recruited for this study: un-infected negative controls, singly infected with malaria, singly infected with hepatitis B virus (HBV) and co-infected with malaria and HBV. Levels of haemoglobin, malaria parasitemia and liver biochemical parameters, including alanine transferase (ALT), aspartate transferase (AST), alkaline phosphatse (ALP) and total bilirubin (Tbil) were assayed and compared across the different groups. Pregnant women recruited were between the ages of 17-41 years. Haemoglobin Levels (highest in hepatitis B [11.0 g/dL] and least in malaria single infections [9.8 g/dL]) differed significantly (P= 0.005) across the groups. Median plasmodium parasite counts were similar (P=0.3038) between malaria single infection and malaria/hepatitis B co-infected individuals. Median levels for the liver biochemical parameter were observed to be lowest in the un-infected and highest in the malaria/Hepatitis B co-infected individuals. Levels of ALT (P <0.0001), AST (P <0.0001) and Tbil (P <0.0001) all differed significantly across the groups, however, ALP levels were not significantly different among the disease categories. Our findings revealed that malaria and hepatitis B co-infection in pregnancy appeared to exacerbate the release of ALT, AST and Tbil, suggesting altered liver function. Further longitudinal studies to investigate changes in the levels of these biomarkers after the malaria infection is cleared will be important to confirm the findings of this study.

5. Probing a novel mechanism for pyrazinamide resistance in *Mycobacterium tuberculosis*

Ranee Aflakpui (ranaflap@gmail.com) - Masters Student
Supervisors - Anthony D. Baughn & Lydia Mosi

Pyrazinamide (PZA) is a cornerstone drug in the treatment regimen for tuberculosis. Inclusion of PZA contributed to reducing the treatment time from nine to six months. PZA is a pro-drug, that is converted to its active form, pyrazinoic acid (POA) by the bacterial enzyme nicotinamidase. Unlike the other TB drugs, the mechanism of action and resistance of PZA is poorly understood. Studies have identified that macrophage activation is essential for PZA efficacy. Recent studies have also shown that PZA acts by depletion of thiol active coenzyme A (CoA) levels in *M. tuberculosis.* Using *M. bovis* BCG as a model organism, we therefore sought to identify ways by which POA action can be potentiated, as well as identify novel resistance mechanisms. Using checkerboard assays, we tested the hypothesis that oxidative stress potentiates POA action by oxidizing thiol active CoA thereby reducing its abundance. We also overexpressed phosphoenolpyruvate carboxykinase (*pckA*), a key player in CoA metabolism, to ascertain if this can enhance susceptibility to POA. Also, *Himar1* mariner-based transposon mutagenesis was conducted to identify novel POA resistance conferring mutations in BCG. Synergy between POA and H_2O_2 resulted in enhanced susceptibility. Overexpression of *pckA* led to increased susceptibility of BCG to POA. From the transposon screen, it was identified that phage infection potentiates POA action through induction of cell envelope stress. Currently, ongoing Tn-seq experiments will identify novel genes that are involved in POA resistance and susceptibility in BCG. It can be concluded from this study that host derived oxidative stress experienced by *M. tuberculosis* in macrophages, is potentially associated with POA action, and importantly alterations in central metabolism that modulate CoA abundance result in modulation of POA action.

6. Isolation and characterization of *Haemophilus ducreyi* strains from children with cutaneous lesions in yaws endemic regions in Ghana

Shirley Victoria Simpson (dweeny14@gmail.com) - Masters Student
Supervisors - Kwasi K. Addo & Lydia Mosi

The epidemiology of yaws in endemic countries has further been complicated by the recent discovery of infections with H. ducreyi. Recent data suggests that cutaneous *H. ducreyi* is a major cause of chronic limb ulcerations in children aged 5 to 15 years. Yaws and *H. ducreyi* ulcers are clinically indistinguishable from each other and some other causes of skin ulcerations. Our aim was to isolate and investigate the phenotypic characteristics of cutaneous *H. ducreyi* strains. We phenotypically characterized 9 cutaneous *H. ducreyi* isolates compared to genital *H. ducreyi* strains. Symptomatic patients were screened with Dual Path Platform (DPP-RDT) Syphilis Screen & Confirm test kit (Chembio, Medford, New York) for yaws. Real-time PCR assays were used to identify *T. pallidum pertenue* DNA and *H. ducreyi* DNA from lesion exudates. We screened for azithromycin resistance markers and also amplified the 16s rRNA gene to detect the presence of other bacteria in yaws-like lesions. Patient data collected showed that 43 of 58 (74.14%) were males and 15 of 58 (25.86%) were females. The proportion of skin conditions presented by symptomatic patients was 43 of 58 (74.14%) of ulcers, 11 of 58 (18.96%) of papillomas, 2 of 58 (3.45%) of hyperkeratosis, 2 of 58 (3.45%) of macules. DPP-RDT results showed that 35 of 58 (60.34%) tested dually positive for treponemal and non-treponemal results, 21 of 58 (36.21%) were dually negative for treponemal and non-treponemal results, 2 of 58 (3.45%) were positive for treponemal and negative for non-treponemal results. Isolated cutaneous *H. ducreyi* strains by their appearance in gram-stained smears, and colony morphology and colour differed slightly compared to genital *H. ducreyi* strains. We suspect the possibility of other causes of yaws-like lesions in endemic areas.

7. Identification of specific metabolites in *Mycobacterium ulcerans* infection: exploring potential diagnostic biomarkers

Elizabeth K Laryea-Akrong (Lizzlaryea@gmail.com) - Masters Student
Supervisors - Lydia Mosi & Samuel Duodu

Buruli ulcer (BU) is a severe, slow progressing necrotizing skin infection caused by the environmental mycobacterium, *Mycobacterium ulcerans*. BU is characterized by nodule, papule and plaque formation which ultimately develops into large painless ulcers with undermined edges. In a pilot study, we sought to identify key *M. ulcerans* metabolic markers that can be found only in Buruli ulcer patients, with the ultimate aim of identifying potential targets for further development as a diagnostic tool. We also sought to determine the best sample matrix (lesion biopsy, swab or fine needle aspirate (FNA)) for the extraction and identification of metabolites using GC-MS based metabolomics. We collected tissue biopsy, swabs and FNA from 28 Buruli ulcer confirmed patients and 21 patients with other tropical ulcers. Interesting metabolites identified in both groups of patients included cadaverine, putrescine, pinitol, palmitate, naphthalene, chlopyrifos and Oxaspirol. Putrescine and pinitol metabolites are interesting because they classify all the samples as containing degenerating tissue. The fatty acid palmitate is a common metabolite present in human tissue. Pinitol and the later three identifies metabolites are chemical residues that may have been present in the treatment poultice used as unorthodox remedies by the patients. Unfortunately, due to our inability to obtain enough materials from the lesion swabs which were in the majority, we could not identify unique metabolites differentiating the Buruli ulcer patients from the control patients based on the data we obtained. We are presently performing a more detailed analysis of the metabolome of the host and mycobacterium in BU confirmed lesions. To gain more insight into the novelty of the biomarkers we identify, we have included another phase of experimentation which involves the characterization of the lipid and aqueous metabolome of *M. ulcerans* and other mycolactone producing mycobacteria including *M. pseudishottsii, M. liflandii* and *M. marinum DL*.

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

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Supervisors - David J. Conway, Ben Gyan & Gordon A. Awandare

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. A total of 567 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 analyses of parasitological, clinical, haematological and socio-economic parameters were performed. 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 ($P<0.05$). 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.

9. Isolation and characterization of plant antitrypanosomals in African Trypanosomes

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Supervisors – Laud KN Okine, Theresa Manful Gwira, Sam Alsford & Mitsuko Ohashi

African trypanosomiasis is a disease caused by the parasitic protozoa of Trypanosoma. Despite several efforts at chemotherapeutic interventions, the disease poses serious health and economic concerns to humans and animals of various sub-Saharan African countries. Commercially available drugs have reported cases of undesirable side effects, drug resistance, and difficulty in regimen application. Moreover, even though studies have reported antitrypanosomal activities of different plant extracts in several parts of the world, action and resistance mechanisms of the active compounds remain poorly understood. The isolation, identification and elucidation of mode of action of plant antitrypanosomal compounds will therefore open up new avenues for the development of antitrypanosomal chemotherapy. Blood stream forms of *Trypanosoma brucei brucei* GUTat 3.1 strains were cultivated in vitro in Iscove's Modified Dubelco's Medium (IMDM) supplemented with 10% foetal bovine serum at 5% CO2 and 37oC. Antitrypanosomal activity of extracts prepared from *Zanthoxylum zanthoxyloides* and *Bidens pilosa* were determined by cell viability, cell death and cell cycle assays. Active extracts were fractionated by bioactivity-guided column chromatography. Active antitrypanosomals were isolated by the methods of trituration and preparative TLC, followed by characterization with infrared spectroscopy (IR) and gas chromatography-mass spectrometry (GC-MS). Antitrypanosomal activities of extracts, fractions and isolates of *Zanthoxylum zanthoxyloides* and *Bidens pilosa* were exhibited via effects on cell viability, cell death (apoptosis and necrosis), and cell cycle of the parasites in a dose-dependent manner. These bioactivities originate from a limited number of antitrypanosomal compounds in the plants. The most promising antitrypanosomals were isolated from the dicholoromethane fraction of the root of *Zanthoxylum zanthoxyloides* (ZRFD) with approximate nominal masses of 224 and 282. Purification and structural elucidation of isolated antitrypanosomals by HPLC and NMR are ongoing. RNA interference target sequencing (RNAseq) will be employed to determine the mechanisms of action of antitrypanosomals in the parasite. Overall, results could have implications for potential novel therapeutic interventions in African trypanosomiasis.

10. *Plasmodium falciparum* Histidine Rich Protein 2 and 3 gene deletion polymorphism in Kassena-Nankana Districts of Northern Ghana

Felix Alexander Ayelazuno (ayelazunofelix@gmail.com) - Masters Student
Supervisors - Lucas Amenga-Etego, Linda Eva Amoah & Gordon A. Awandare

The use of pfhrp2 based RDTs to accurately diagnose malaria specific to *Plamodium falciparum* from other febrile cases reporting to health facilities in Ghana plays a vital role in the control of malaria. However, false negatives due to parasites that have deleted the pfhrp2 gene leads to the continual transmission of malaria. Determining the prevelance of parasites that have deleted the pfhrp2 gene could be of relevance to the malaria control programme. The purpose of this study was to determine the prevalence and geo-spatial distribution of *Plasmodium falciparum* histidine-rich protein 2 and 3 gene deletion polymorphism in the Kassena-Nankana Districts. Patients reporting with fever or history of fever were recruited after consenting was done. Blood spots were made on filter papers and thick and thin films were made on slides to be read by microscopy. DNA was extracted using Qiagen kit following the maufacturer's manual. The exon 1-2, exon 2 and the flanking genes of pfhrp2, the exon 2 of phrp3 were amplified using polymerase chain reaction (PCR). PCR products were resolved by agarose gel electrophoresis and viewed under UV light. The mean parasite density of the study area was found to be 1.46, prevalence of parasites that were found to have deleted the exon 1-2 of the pfhrp2 gene was 26.21% (27/103), 50.48%(52/103) had deleted the uptsream gene of pfhrp2 gene. A relatively high number of parasites were found to have deleted the exon1-2 and gene of the pfhrp2 and the upstream and downstream flankings regions. However despite the presence of these parasites the use of pfhrp2 based RDTS still remains effective in diagnosing malaria.

11. Levels and kinetics of merozoite-specific IgG in Ghanaian children with *Plasmodium falciparum* malaria

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Successful invasion of erythrocytes by *P. falciparum* merozoites requires the parasite antigen reticulocyte binding-like homologous protein 5 (PfRh5) which is specific for the host erythrocyte receptor basigin. PfRh5 forms a complex with other parasite antigen, Cysteine-rich protective antigen (PfCyRPA) and Pf113 protein. It is still unclear to what extent antibodies to these three merozoite antigens are acquired naturally following natural parasite exposure, and their contribution to clinical protection from malaria. We have used two strategies to address this issue. First, we analyzed plasma levels of PfRh5-, PfCyRPA-, and Pf113-specific antibodies in longitudinal samples from naturally infected Ghanaian children and compared with age-matched samples from healthy and asymptomatic children. Secondly, we generated human monoclonal antibodies from immune Ghanaian adults. In comparison with other well studied merozoite antigens, a relatively lower percentage of the acute patients had detectable IgG levels specific for the studied antigens which persisted six weeks after infection. There was no statistically significant difference in the median levels of IgG specific for any of the three antigens across clinical categories. Neither was there any significant correlation between asexual blood-stage parasitemia and levels of IgG specific for any of the three antigens. Taken together, these data do not suggest a protective role for any of these IgG specificities, at least not at the levels observed here. Rather, they are consistent with each of these specificities being markers of recent exposure to *P. falciparum* parasites. We have generated human monoclonal anti-PfRh5 and anti- PfCyRPA IgG antibodies from seropositive adults to investigate their ability to inhibit merozoite invasion of erythrocytes. The mode of action of the antibodies will be elucidated through their capacity to interfere with the PfRh5-basigin interaction. The findings from this study are useful in the consideration of PfRh5 as a vaccine candidate.

12. Mutational Inactivation of HIV-1 during reverse transcription is rare in a single replication cycle

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HIV-1 reverse transcriptase is estimated to be the most error-prone among retroviruses. However, the extent to which mutations during reverse transcription inactivates proviruses is not clear. We developed a system to track HIV-1 replication products and used it to quantify the extent to which mutations due to reverse transcription inactivates proviruses. Single cycle replication outcomes of first-round integrants (F1) containing 72 unique sequence tagged (zip codes) proviruses and cells that descended from them were assessed by infecting fresh HEK293T cells with the virus produced by F1. The remobilization on fresh HEK293T cells was assessed by high-throughput sequencing of zip codes in F1, F1 virus, remobilized second-round integrants (F2), and F2 virus. The presence of zip codes of F1 in the F2 was used as a marker for the fitness of proviruses in F1. Our results showed that 69 zip codes of the F1 made virus, but 8 out of the 69 in virus did not remobilize in F2. It was surprising to note that out of the 61 zip codes in F2, 59 were present in F2 virus. Since multiple cells would have been infected by virus with the same zip code, a 100% remobilization was expected. Regression analysis of the libraries revealed that, the amount of virus produced by each clonal line was different and likely reflect integration-site dependence on expression of the provirus. Even though clonal lines proliferated at different rates, with only few clones outgrow the rest. Overall, we have shown evidence suggesting that in HEK293T cells less than 10% of proviruses might have acquired inactivating mutations that rendered their virions defective, a lower estimate than what has previously been reported.

13. *Plasmodium falciparum* and Epstien-Barr virus (EBV) co-infection and the expression of activation induced-cytidine deaminase in healthy children

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Infections with *Plasmodium falciparum* and EBV are associated with the incidence of endemic Burkitt's lymphoma (eBL). EBV on one hand is ubiquitous and its genome is integrated into cells of over 96% eBL tumors. On the other hand, the association of *P. falciparum* with eBL is suggested to be only epidemiological. However, *P. falciparum* can induce the expression of Activation Induced-cytidine Deaminase (AID), which is responsible for the genetic lesion that results in the characteristic translocation in eBL. This implies that the parasite could be more involved in the events that start the cancer than is suggested. We therefore investigated *P. falciparum* and EBV co-infection in relation to the level of AID mRNA transcripts in PBMCs of healthy primary school children (ages 6-14) in a malaria endemic area in the Volta Region of Ghana. We used malaria rapid diagnostic tests (RDTs) to determine the *P. falciparum* infection status and EBV Nuclear Antigen-1 (EBNA-1) IgG/IgM ELISAs to determine the EBV infection status of the participants. Out of the 194 children, 58% tested positive for malaria RDT and 179 tested positive for EBNA-1 IgG. Forty-eight (48) were positive for EBNA-1 IgM, which suggests EBV reactivation or primary infection. Of the 113 RDT positive samples, 103 were positive for ENBA-1 IgG whiles 30 were positive for EBNA-1 IgM. Out of the 15 IgG negative samples, 10 tested positive and 5 tested negative for malaria RDT. Of the 48 EBNA-1 IgM positive samples, 30 were positive for malaria by RDT whilst 18 were malaria RDT-negative. Work is currently ongoing to compare the AID mRNA transcript levels among these subgroups.

14. Frameshift mutation in a conserved Plasmodium protein associated with piperaquine resistance in *Plasmodium berghei* ANKA

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Mentor - Faith Osier

The combination of dihydroartemisinin–piperaquine is the drug of choice for treatment of uncomplicated malaria in many African countries. In this combination, a short acting, dihydroartemisinin is partnered with long acting, piperaquine (PQ) for which resistance may emerge rapidly especially in high transmission settings. Up to date, the mechanisms of PQ resistance remains poorly understood. Here we studied mechanisms of PQ resistance using rodent parasite *Plasmodium berghei* ANKA as surrogate of *Plasmodium falciparum*. Selection of PQ-resistant *P. berghei* ANKA was accompanied by loss of sensitivity to other antimalarial drugs; lumefantrine, primaquine, artemether and chloroquine, thus may be used to study common mechanisms. Using Illumina Technology, we sequenced genomes of the PQ-resistant clones and identified nonsense mutations in PBANKA_0410500, putative transporter and frameshift mutation in a conserved *Plasmodium* protein that are potential mediators of drug action/resistance. We then used reverse genetics to validate the association of these candidate mutations with PQ resistance using two types of *PlasmoGEM* vectors; the knock out vector to mimic the nonsense mutation identified in the putative transporter and; 3HA tagging vectors to revert the mutant locus to the wild-type locus in the putative transporter or the conserved *Plasmodium* protein of the resistant clone. Transfection of transporter specific 3HA tagging vector reverted mutant locus (G1967A) to wild-type locus (A1967G) but this repair did not sensitize the parasite to PQ meaning that the transporter is not associated with PQ resistance. Interestingly, repair of the frameshift mutation in the conserved *Plasmodium* protein (G-> del 82) restored parasite sensitivity to PQ by 87% suggesting strong association with PQ sensitivity. Introduction of specific frameshift mutation in the conserved *Plasmodium* protein gene of *P. falciparum* using CRISPR/Cas9 may provide additional evidence on the role of this gene in drug resistance and guide effective design of future drugs that antagonize emergence of resistance.

15. Antibodies against the synthetic peptide of a novel *Plasmodium falciparum* Surface-Related Protein potently inhibits erythrocyte invasion

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Plasmodium falciparum erythrocyte invasion is a multi-step process that involves a large array of ligand-receptor/protein-protein interactions that are not clearly understood. To uncover the functional roles of invasion-related proteins, we employed state-of-the-art threading programs to generate 3D models that were used to predict protein-binding pockets and relevant epitopes. *In silico* approaches directed at the identification of interacting partner proteins were also employed. While a repertoire of our novel *P. falciparum* recombinant proteins are under production, we advanced our studies on PfSRP (***P****. **f****alciparum* ***S****urface **R****elated **P****rotein*), a protein whose expression has been challenging. PfSRP possesses α-helical coiled-coil structures at the regions where we designed three (3) chemically synthesized peptides and generated rabbit polyclonal antibodies (**α**-PfSRP-1, **α**-PfSRP-2 and **α**-PfSRP-3) for functional characterization. We have identified ten (10) novel hypothetical proteins with unknown functions in erythrocyte invasion. However, native PfSRP binds normal human erythrocytes suggestive of its involvement in ligand-receptor interactions. More importantly, PfSRP is processed into several proteolytic products during schizogeny prior to its secretion on the merozoite surface during invasion. Based on this, we have demonstrated a spectrin-binding function of the processed fragment of PfSRP in parasite culture supernatant that fits into an established mechanism of SUB1-processed MSP1 interaction and the spectrin network that facilitates parasite egress. Moreover, PfSRP is localized on the merozoite/gametocyte surface and time-point imaging from initial attachment to internalization of viable merozoites revealed that a fragment of PfSRP is internalized post-invasion for roles during intraerythrocytic development. Parasite growth inhibition assays show that α-PfSRP-3 antibody potently inhibits erythrocyte invasion of both laboratory strains and clinical isolates. Immuno-epidemiological studies show that malaria-exposed populations have naturally-acquired antibodies against PfSRP at varying prevalence based on transmission intensities across different endemic sites in Ghana. Our findings suggest that PfSRP is a promising target for inclusion in the current intervention strategies against blood-stage malaria.

16. *In vitro* investigation of the relationship between schistosomiasis and prostate cancer

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Schistosomiasis is a neglected tropical disease that affects 200 million people and account for 100, 000 deaths annually. In endemic geographical areas, schistosomiasis has been implicated as an etiological agent in the pathogenesis of bladder, colorectal and renal carcinoma largely due to chronic infection of tissues with *Schistosoma* eggs. Several studies have also reported cases of association between *Schistosoma* infection and prostate cancer, the most common cancer in men. The possible causal association is however poorly understood. This study therefore aimed at experimentally investigating this association and elucidating the underlying mechanism. Urine samples from individuals living in Galilea, a Schistosomiasis endemic community in the Ga South District of Ghana were collected and screened for *Schistosoma* infection via microscopy and multiplex PCR. Soluble antigens (SEA) were prepared from *Schistosoma*-egg positive urine samples and assessed for the ability to induce cancer-like phenotypes including excessive proliferation, oxidative stress (GSH depletion) and diminished apoptosis in cultured human prostate (PNT2) cells. Cell proliferative effect of SEA was evaluated by the tetrazolium-based MTS assay. Oxidative stress-inducing effect of SEA was also determined using the fluorescent probe, O-phthalaldehyde. Apoptosis-diminishing effect of SEA was evaluated via fluorescence (Hoechst) staining and flow cytometry. 14.4% (30/209) schistosomiasis prevalence was recorded. Out of 30 *Schistosoma*-infected persons, 73% (22 persons) recorded light infections whereas 27% (8 persons) were heavily infected. Microscopic and molecular analysis revealed infecting-schistosome species to be *S. haematobium* and *S. mansoni*. 63% (19 persons) were infected with *S. haematobium* only whereas 37% (11 persons) were co-infected. Prostate cell proliferation was significantly induced by 12.5µg/ml SEA (P=0.029). Also, SEA dose-dependently depleted cellular reduced glutathione (GSH). Flow cytometric analysis and fluorescence staining revealed that SEA dose-dependently and significantly diminished apoptosis in prostate cells. Schistosomiasis still remains a major health challenge. Findings of this study suggest that *schistosome*-infection may play a role in the pathogenesis of prostate cancer. In *vivo* studies are however needed to confirm this association.

17. Molecular characterization of lifetime infections with Trypanosomes in individual cattle in Ghana

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Agriculture plays a central role in the social and economic development of most developing countries. Livestock production is a key aspect in Ghana's agricultural sector because of its contribution towards food needs and revenue generation. Animal African Trypanosomiasis is the most economically important constraint to livestock productivity in sub-Saharan Africa. The disease is caused by *Trypanosoma sp.*, broad range protozoan parasites of wild and domestic animals. In Ghana, the most common trypanosome species which have been detected in cattle include; *Trypanosoma brucei brucei, T. congolense*, *T. vivax* and *T. simiae*. A cross-sectional study estimated the prevalence of the disease in cattle between 5-50%. Despite the impact of the disease, there is no study on lifetime infections with trypanosomes in cattle in Ghana. The study aimed at characterising trypanosome species throughout the natural infection cycle in cattle in Ghana over a two year period. Two herds of cattle (20 each) at Accra and Adidome were selected based on their geographical location, tsetse fly density, prevalence of trypanosomiasis and the breed of cattle available. Blood was collected at approximately five week intervals and the infecting trypanosomes were identified and characterised using a tagged multiplex nested polymerase chain reaction (PCR) targeting part of the trypanosome tubulin gene cluster and Illumina sequencing. Preliminary data show *T. brucei brucei*, *T. congolense* and *T. vivax* as the major infecting species at both study sites with *T. brucei brucei* being predominant. The data generated from this study will provide invaluable information on the biology of trypanosome infection and help inform control measures in the infected area.

18. Towards sensitive analyte detection: the synergistic effects of reduced graphene oxide, PEDOT:PSS, polyethylene glycol and Ionic liquid nanocomposite- modified electrodes

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Owing to the success of the widely used glucometer, research into biosensors for point-of-care testing has received considerable interest over the past decade. Screen printed electrodes (SPEs) used in electrochemical sensors are becoming the focus of many sensor systems as they enable easy miniaturization, inexpensive mass production and superior detection limits with small analyte volumes. In developing diagnostic tools for infectious diseases, analytical sensitivity and specificity are important parameters to consider. However, electrochemical biosensors tend to lack the surface architectures that enable optimum sensitivity and specificity to targeted analytes. To enhance conductivity of the working electrode surfaces of SPEs, doping with conjugated polymers could relatively enhance their conductivity by efficiently facilitating electron transfer. Poly (3,4-ethylenedioxythiophene):poly (styrene sulfonate) (PEDOT:PSS) which can modify SPE is a highly conductive polymer, stable and exhibits good mechanical properties. Conductivity of the PEDOT:PSS could be further improved using organic additives, ionic liquids (IL) and polyethylene glycol (PEG). Composites of reduced graphene oxide (rGO) and PEDOT:PSS also have the potential to create synergistic effect on electrical and thermal properties of electrodes. In this study, rGO, PEG, PEDOT:PSS and IL (1-ethyl-3-methylimidazolium tetrafluoroborate ([EMIM][BF4])), were used to develop high-performance rGO/PEG/IL/PEDOT:PSS nanocomposite for modifying the SPCEs. The modified electrodes were stable and highly reproducible. A composite of IL/PEDOT:PSS modified SPCE, applied in conjunction with amperometry in stirred solution could accurately detect catechol in spiked water samples. Recovery rates were over 99.0% which demonstrates the prospects of rGO, PEG, IL and PEDOT:PSS hybrid nanocomposites in enhancing the conductivity of electrodes for analyte detection.

19 Clinical patterns of malaria in two different epidemiological settings in Mali: Dangassa and Nioro du Sahel

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Despite significant reduction of the incidence and deaths related to malaria over the past decade, malaria is still a major public health problem in Mali. Investigating the specific clinical patterns of the disease in different epidemiologic settings may improve the malaria control strategy in Mali. Samples and clinical data were collected from malaria patients living in two distinct sites with different transmission settings, endemicities and length of seasonality: Dangassa, with intense and seasonal malaria transmission from June to December and Nioro du Sahel, where malaria is unstable with a short seasonal transmission from July to September. Participants were screened for malaria by rapid diagnosis test and exhaustively enrolled after confirmation by microscopy. The socio-demographic characteristics and the clinical profiles of the diseases were compared in the two sites. A total of 464 participants were enrolled, including 404 participants in Dangassa and 60 participants in Nioro. Participants in Nioro were significantly older than those in Dangassa. Patients less than 5 years old made up 27% and 6.6% of participants in Dangassa and in Nioro, respectively. All patients enrolled in Nioro had fever at enrollment, while in Dangassa, 7% did not have fever at inclusion (P = 0.02). Severe prostration was diagnosed in 13% in Nioro against 7.5% in Dangassa (P=0.07). The mean parasitemia was similar in both Nioro (20960 Pf/µL) and Dangassa (16590 pf/µL; P = 0.2). RDT test results were consistent with microscopy data (100%) in Nioro while microscopy failed to confirm malaria diagnostic in 18% of RDT positive tests in Dangassa. In Dangassa, malaria is still very high in children below 5 years, while all ages are at risk of malaria in Nioro du Sahel. RDT tests seem to be an efficient and practical tool for diagnosing malaria in Nioro du Sahel.

20. Evaluating the feasibility of Autism spectrum disorders research in Mali, West Africa

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Autism Spectrum Disorders (ASD) are characterized by impaired reciprocal social interaction and communication, with restricted repetitive and stereotyped behaviors. ASD affects 1-2% worldwide, 1 in 68 in the U.S and unknown in Africa. ASD is under-diagnosed in Mali due to stigma and limited human resources and infrastructure. This barrier can be overcome through a two-way street international collaboration. To evaluate the feasibility of collaborative genetic ASD research in Mali, we hypothesized that ASD were common in Mali. We found an ASD hospital frequency of 4.5% (105/2,343).The mean age at the first outpatient visit was 7.64 ± 3.85 years. Parents of ASD children had first degree consanguinity in 29.5% (31/105) OR= 4.37 [1.96-9.76] p=0.0001 when compared to age and sex matched controls. The landscape is favorable for ASD molecular genetics research. ASD is more frequent than expected in Mali. Bringing up the ASD awareness and training Malians in early screening and diagnosis using culturally validated standardized tools may resolve the late diagnosis issue. New genetic and environmental risk factors of ASD in Mali will improve our understanding of the ASD genetic variation in populations elsewhere. Our ASD research strategy would be applicable to other infantile neuropsychiatric disorders in Mali, West Africa.

21. Genetic association and gene-gene interaction analysis of APOL1, MYH9 and G6PD variants in patients with Chronic Kidney Disease

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Variants in the human Apolipoprotein L1 (APOL1) and the Human non-Muscle Myosin (MYH9) genes are associated with the risk of Chronic Kidney Disease (CKD) in people of West African descent, but not all individuals with the mutations develop CKD in their lifetime. We sought to determine the prevalence of G6PD variants 202 and 376 in CKD patients of unknown etiology and also determine whether G6PD variants could be a risk factor or interact with APOL1 and MYH9 gene variants in increasing the risk of developing CKD in the West African region. Two hundred blood samples from CKD patients of unknown etiology from Ghana and Nigeria were genotyped using Restriction Fragment Length Polymorphism (RFLP) following PCR amplification of the region of the G6PD gene that carries these mutations. A total of 183 samples were genotyped for G6PD variants 202 and 376. Out of this, 94 were deficient for variant 202 (69 homozygous and 25 heterozygous) representing 46.6% of the population analyzed, whilst 67 were deficient for 376 (19 homozygous and 48 heterozygous) representing 45.6%. It was also observed that 25% of the samples were heterozygous for both of the SNPs which indicates that a significant number of patients with CKD of unknown etiology may have developed the disease as a result of chronic renal failure. The prevalence rate of the G6PD variants in patients with CKD of unknown etiology was high, suggesting that G6PD deficiency may play a vital role in the risk of developing CKD of unknown etiology. Work is on-going to determine the association of G6PD variants 202 and 376 with CKD of unknown etiology and also to determine if G6PD variants interact with APOL1 and MYH9 variants in increasing the risk of CKD of unknown etiology.

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

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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, we investigated inflammatory cytokine responses in children with malaria from areas of different transmission intensities (ranging from low to high). 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. We found that 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-γ (IFN- γ), interleukin (IL)-1β, 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. 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.

23. Autopsy characterization of lung microbiome of HIV-positive patients in a tertiary referral hospital in Ghana

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Pulmonary infections are the underlying cause of high morbidity and mortality amongst HIV infected persons. Notwithstanding, there is limited data on pulmonary co-infecting pathogens and their susceptibility to commonly used antibiotics. Thus, we sought to characterize the lung microbiome of post-mortem biopsy samples of HIV/AIDS patients in Ghana. We examined 102 lung biopsies from HIV/AIDS decedents from the Korle-Bu Teaching Hospital in Ghana for mycobacteria, other bacteria, fungi and viruses. The techniques utilized included; culture, Gram/ZN staining, MALDI-TOF Mass spectrometry and PCR. The drug susceptibility pattern of Mycobacterium tuberculosis complex (MTBC) isolates and other bacteria were subsequently determined using Genotype MTBDR*plus* and disc diffusion assays respectively. We retrieved clinical data for 86 cases: 42 (48.8%) males and 42 (48.8%) females with their mean ages of 40.4 (±10.6) and 37.1 (±11.5) respectively. HIV type was defined in 39 (45.3%) cases and co-infections with TB, pneumonia, oesophageal candidiasis and/or cryptococcal disease occurred in 12 (14.3%) cases. From the mycobacterial cultures, 25 MTBC, 5 *M. abscessus* and 1 *Nocardia farcinica* were identified. Drug susceptibility testing of the MTBC isolates showed 1 isoniazid and 3 rifampicin mono-resistance. Other bacteria isolated were 217 (83.8%) with *Enterococcus species* (61), *Staphylococcus species* (35), *Escherichia coli* (28) and *Klebsiella pneumonia* (23) predominating. Of the 217, 75 Gram-negatives and 117 Gram-positives were profiled for drug sensitivity. Gram-negative isolates were most susceptible to cefoxitin and gentamicin (45.3% each) but highly resistant to cefuroxime sodium (84.0%). The Gram-positives were fairly susceptibility to levofloxacin (58.0%) but highly resistant to oxacillin (81.2%). Nine cultivable fungi; *Candida species* (6), *Cryptococcus neoformans* (1), *Pichia occidentalis* (1) and *Yarrowia lipolytica* (1) were identified whereas PCR detected 10 *Pneumocystis jiroveci*. Viruses detected in the samples included Cytomegalovirus (59), Parainfluenza-2 (1) and enterovirus (1). We showed that *Enterococcus*, *Staphylococcus*, *Mycobacteria species*, *K. pneumoniae*, *Pneumocystis jiroveci* and Cytomegalovirus are the most common co-infecting lung pathogens in HIV/AIDS patients with Gram-negative bacteria exhibiting the highest antibiotic resistance.

24. Genetic factors associated with renal dysfunctions in adult Sickle Cell Disease patients in Cameroon

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Mentor - Ambroise Wonkam

Sickle cell disease (SCD) has a high prevalence in Sub-Saharan Africa and is associated with cardiovascular diseases. Several cardiovascular phenotypes in SCD contribute to its high morbidity and mortality. Micro-albuminuria and glomerular hyper filtration are primary indicators of renal dysfunctions in SCD, with more severe manifestations previously associated with the co-inheritance of alpha-thalassemia and variants in APOL1 and HMOX1 among African Americans. The aim of this study is to identify genetic factors involved in kidney dysfunctions in SCD adult patients in Cameroon. So far we have investigated 215 patients. Clinical information, anthropometric variables, hematological indices, creatinemia, proteinuria, proteinuria-to-creatinine ratio and estimated glomerular filtration rate (eGFR) were measured. Our cohort is composed of 91% Hb SS, 6% of suspected S β thalassemia and 3% of Hb AS to be confirmed by molecular biology. The median age was 21 years [min = 5; max = 61]. 11% (n = 21) of patients had high blood pressure, and 73 % (n = 138) had a pulse of more than 80. The majority (66% n = 126) of patients had the diagnosis of SCD at more than 1 year. The median of vaso occlusive crisis occurrence was 2/year and 1 hospitalization/year. The frequency of overt stroke was 3%. Nearly 28% (n = 55) of patients have more than 10% of fetal hemoglobin. Up to 40% (n = 77) presented with micro-albuminuria, 10% (n = 19) with proteinuria. The results revealed a high proportion of micro-albuminuria and proteinuria among adult Cameroonians living with SCD in Cameroon. Further analyses will estimate glomerular hyper filtration rates and investigate various genetic associations with kidney dysfunction.

25. Genotypic diversity of *Mycobacterium tuberculosis* complex from Southern Volta, Ghana

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Due to their phylogeographical nature, data on strain diversity of Mycobacterium tuberculosis complex (MTBC) isolates in a given locality is important for inclusion of dominant strain in development of control tools. We therefore determined the phylogenetic population structure of MTBC isolates from the southern part of Volta region, which has never been done. Sputum samples were cultured and the mycobacterial isolates obtained confirmed as MTBC by PCR amplification of IS6110. The MTBCs were then genotyped by spoligotyping and their drug susceptibility profiles determined based on line probe assay using *GenoTypeMTBDRplus*. Associations between the different phylogenetic lineages of MTBC, demographic and epidemiological factors were assessed using univariate and multivariate logistic regression. Out of the 103 MTBC isolates analyzed, 73 (70.87 %), 16 (15.53 %), 7 (6.79%), 3 (2.91%), 1 (0.97 %) and 1 (0.97) were Lineage 4, Lineage 5, Lineage 6, Lineage 2, Lineage 3 and Lineage 1 respectively with 2 (1.94%) unidentified. Among the Lineage 4 isolates of *Mycobacterium tuberculosis sensu stricto* (MTBss), 49 (47.57 %) belonged to Cameroon sub-lineage. The remaining 24 Lineage 4 isolates were subdivided into 6 sub-lineages as follows: Ghana (N=18, 17.48 %), Haarlem (N=2, 1.94%), Uganda I (N=1, 0.97%), EAI (N=1, 0.97%), LAM (N=1, 0.97%), X (N=1, 0.97%) and Unidentified (N=2, 1.94%). Allowing for other demographic and epidemiological variables, we found significant geospatial localization of *Mycobacterium africanum* (Maf) within the Ho municipality compared to Ketu-South/Aflao (P-value = 0.0356, CI=0.0144 - 0.4136). The proportion of Maf (31.7%) identified from the Ho municipality was found to be higher, suggestive of Maf localization. The (OR=2.24, CI=0.11-44.91), suggests higher risk of multi drug resistance infection for MTBss than Maf. This study confirms the importance of *M. africanum* lineages in Ghana and this should be considered in the development of new diagnostics, drugs and vaccines.

26. Utilizing Yeast as a model organism for drug discovery against Eukaryotic infections

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Supervisors - Patrick K. Arthur & Jonathan Adjimani

Fungal diseases pose a serious threat to immune-compromised patients. This has resulted in high dependence on the use of antifungal agent leading to the emergence of resistant strains of pathogenic fungi such as *C. albicans*. Protozoan parasites are also responsible for several serious human diseases causing an estimate of 1.1 million combined deaths annually. This research seeks to identify bioactive molecules from wood decay fungi (WDF) extracts with activity against eukaryotic pathogens. Since *S. cerevisiae* has been extensively used as a model organism to screen for bioactive molecules, we believe this will help identify bioactive molecules from our sources. We hypothesized that bioactive molecules isolated from wood decay fungi extract will be active against *S. cerevisiae*, *C. albicans*. Also isolated antifungal molecules will be active against *P. falciparum*. 12 selected WDF cultures were extracted with ethyl acetate. The extracts were screened against *C. albicans* and *S. cerevisiae* in the presence and absence of chemical phenotypic modifiers and mutant *S. cerevisiae* by disc diffusion method. The three most active extracts were fractionated by solvent partition chromatography, size-exclusion chromatography and preparative TLC. 17% of the 12 wood decay fungi extract had antifungal activity. From the phenotypic assay, the selected (top 3 three active and 3 inactive) wood decay fungi extracts showed different responses to *C. albicans* and *S. cerevisiae*, partly due to a different cellular mechanism between the two cell types. The cumulative zones of inhibition of the 3 active extracts against the *S. cerevisiae* were higher than against *C. albicans*. Bioactivity guided fractionation showed 8 bioactive fractions from S7, 7 from G3 and 7 from R7 (A) summing up to 22 bioactive fractions. These findings stimulate the search for novel bioactive molecules from fungal sources with activity against *C. albicans* and *P. falciparum*.

27. Endothelial progenitor cells in women diagnosed with preeclampsia

Dorotheah Obiri (dorotheahos@gmail.com) – PhD student
Supervisors - Ben Gyan, Kwadwo Asamoah Kusi, Michael Fokuo Ofori & Theresa Manful Gwira

Preeclampsia is a leading cause of maternal and foetal mortality in Ghana. Although the actual cause of this condition is still unknown, it is reported that systemic inflammation results in endothelial activation and subsequent dysfunction to the endothelium. Recruitment of rare endothelial progenitor cells (EPCs) have been associated with endothelial repair in sites of endothelial damage. This study assessed and compared the levels of EPCs between women who had a healthy pregnancy and those with pregnancies complicated by preeclampsia. Women who had normal pregnancy (controls) and those who had preeclampsia after 20 weeks of gestation (cases) were sampled. EPCs were measured in whole blood by the co-expression of surface antigens (CD309, CD34, and CD133) on progenitor cells originating from the bone marrow to endothelial sites of injury. Percentage EPC levels were measured in peripheral, cord and placental blood samples from women with normal and hypertensive pregnancies. No differences in EPC levels were found between cases and controls for any of the three blood sample types. A higher number of EPCs were found in the placental blood than the cord blood among normal pregnancies. Placental and peripheral blood did not show any such significant differences. For hypertensive pregnancies, there was a higher number of EPCs in the placenta compared to periphery but not in the cord blood. The high levels of EPCs in the placental blood for both normal and hypertensive pregnancies indicate the high vascularization that occur within the placenta. Also, this site could be a potential target for EPC therapy.

28. High-resolution melt analysis reveals a potential shift in the molecular epidemiology of antimalarial drug resistance in Nigeria

Kolapo M. Oyebola (oyebolakolapo@yahoo.com) – Postdoctoral fellow
Mentor - Alfred Amambua-Ngwa

Artemisinin resistance and decline in the efficacy of first line artemisinin-based combination (ACT) drugs for malaria treatment in some endemic regions threatens the success towards global elimination of malaria. Though ACT resistance has not been confirmed in Africa, molecular survey for drug resistance alleles is vital to detect the emergence and spread of resistant strains. Here we describe the prevalence of antimalarial drug resistance markers during an ACT efficacy trial in Nigeria. Sixty-five patients were screened pre- and post-treatment with ACT on days 0, 1, 3, 7, 14, 21 and 28. Parasite clearance rates during treatment were determined by microscopy and the highly sensitive VarATS diagnostic PCR which targets multi-copy subtelomeric DNA. 18.5% of participants presented with parasitaemia 3 days post-treatment. 17% of patients presented with day 28 parasitaemia. High resolution melt analysis was carried out to amplify codons Pfcrt-76, Pfmdr1-86, Pfmdr1-184, and PfK-13 C580Y in isolates. 18.5% participants presented with parasitaemia 3 days post-treatment. 17% of patients presented with day 28 parasitaemia. The drug resistance Pfcrt-76T allele was present in 37.2% of isolates in the population. Pfmdr1-86 mutant allele was found in 12.5% of isolates. No mutant allele of the K-13 C580Y was recorded. These results indicate that withdrawal of chloroquine and use of ACTs are selecting for wildtype variants at these chloroquine resistance loci in Nigeria. However, persistence of parasitaemia in more than 10% of cases after treatment warrants further investigation of a larger population for any signs of reduced ACT efficacy in Nigeria.

Fellows Sessions – Poster category

29. Phenotypic changes in the T cell repertoire during *Plasmodium falciparum* malaria infections

Augustina Frimpong (Tinafrimp@gmail.com) - PhD Student
Supervisors - Kwadwo Asamoah Kusi, Michael Ofori & Wilfred Ndifon

Plasmodium falciparum malaria has been associated with severe morbidity and mortality in endemic areas. Acquiring natural immunity to *Plasmodium falciparum* malaria is slow and associated with repeated exposure to infection. Recent evidence suggests that the interaction between T cells (CD4+/CD8+) dictates the level of protective immunity acquired to the disease. Other studies have also demonstrated that *Plasmodium falciparum* may have the ability to modulate host immune responses through the up and down-regulation of certain immune cell surface markers. However, it remains to be elucidated the effect of *P. falciparum* infection on the T cell repertoire and how they may predict disease outcome. To address this question, blood samples were obtained from malaria infected children within the age range (1-12) years to compare their T cell profiles using flow cytometry. From the preliminary studies, we observed that T cell activation markers were highly expressed in the CD4+ T cells as compared to the CD8+ cells. CD28 was the most highly expressed for all study participants. The activation markers CD69 and CD154/CD40l were highly expressed in the asymptomatic individuals as compared to the other groups, whereas the expression of PD-1/CD279 and CTLA-4 were higher in the symptomatic subjects when compared to the asymptomatics. So far, the results suggest that *Plasmodium falciparum* malaria affects the repertoire of T cells by favouring the up-regulation and down-regulation of specific markers of interest.

30. Genetic association and interactions between *APOL1, MYH9* variants and HB S and C genotypes in patients with chronic kidney disease

Ernestine Kubi (ernestine.kubi@gmail.com) – Masters student
Supervisors - Anita Ghansah & Gordon A. Awandare

There has been a reported 4-5 times higher risk of chronic kidney disease (CKD) in African Americans and sub-Saharan Africans. This reported high risk has been associated with SNP variants in MYH9 and APOL1 genes. APOL1 and MYH9 variants explain only part of this observed high risk. Thus there is the need to identify other genetic factors involved in increasing the risk of CKD in Africa. This study sought to investigate associations between haemoglobin (HB) genotypes (S and C), APOL1 risk variants, and MYH9, and the risk of CKD and to determine any possible interactions between these genes that modify the occurrence of CKD. CKD cases and 300 healthy controls have been selected from the H3A CKD research study population for genotyping using Ligation detection reaction assay following PCR. Out of a total of 554 samples (254 cases and 300 control), 154 (27.8%) clinically tested positive for sickle cell disease. It was observed that 54 (21.25%) of the CKD cases had sickle cell nephropathy with the remaining 200 (78.7%) having CKD of unknown etiologies. The frequencies of APOL1 SNPs RS 145, RS 319 and RS 313 observed in patients with sickle cell nephropathy were 0.36, 0.30 and 0.10 respectively. MYH9 SNPs RS 481 and 487 had frequencies of 0.19 and 0.10 respectively. There was a higher frequency of APOL1 variants as compared to MYH9 amongst sickle cell nephropathy patients. However, genotyping is still ongoing to identify the associations and interactions between SNPs and the risk of CKD.

31. Prevalence of chloroquine and antifolate drug resistance point mutations in *Plasmodium falciparum* field isolates from four areas in Ghana

Felix Ansah (ansahfelix66@yaho.com) – Masters student
Supervisors – Gordon A. Awandare

The increasing prevalence of chloroquine (CQ) and antifolate drug resistant *Plasmodium falciparum* strains led to the introduction of artemisinin-based combination therapies (ACTs) as first-line drug for the treatment of uncomplicated malaria in Ghana in 2005. However, antifolate drugs are still used for intermittent preventive treatment of malaria in pregnancy and for seasonal malaria chemotherapy in infancy (IPTp/i). To investigate the prevalence of molecular markers associated with chloroquine and antifolate drug resistance in Ghana, we tested for the presence of single nucleotide polymorphisms (SNPs) in some putative genes that have been implicated in antimalarial drug resistance in clinical isolates obtained from four geographically distinct regions using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). The overall prevalence of the *pfcrt* 76T mutants was 8.8%, whereas *pfmdr1* 86**Y** and 184F polymorphisms were 10.3% and 64.7%, respectively. Majority of the isolates harboured the mutant *pfdhfr* 51I, 59R and 108N alleles at frequencies of 85.6%, 83.1% and 89.8%, respectively. *Pfdhps* 437**G** and 540**E** were also observed to be 92.2%, and 0.7%, respectively. A large proportion of the isolates harboured the $\mathbf{I}_{51}\mathbf{R}_{59}\mathbf{N}_{108}/\mathrm{G}_{437}$ quadruple point mutations (63.2%) while 4.8% only had the *pfdhfr* $\mathbf{I}_{51}\mathbf{R}_{59}\mathbf{N}_{108}$ haplotype. We observed no significant difference across the four study sites for all the SNPs ($P > 0.05$) except for *pfdhfr* 51**I** and *pfdhps* 437**G**, which were both higher in Accra and Hohoe compared to Kintampo and Navrongo. Comparison of the present results to published data shows a significant reduction in the prevalence of CQ-associated point mutations but an increase in the point mutations that mediate sulfadoxine–pyrimethamine resistance after 8 years of CQ withdrawal. The observed relatively low prevalence of the *pfcrt* 76T and *pfmdr1* 86Y genotypes may be attributable to the re-expansion of the wildtype genotype as a result of chloroquine withdrawal, whereas the high prevalence of *pfdhfr* and *pfdhps* point mutations may be due the continuous use of antifolate drugs for intermittent prevention treatment in pregnancy (IPTp) and as prophylaxis in infancy.

32. Molecular characterization of tick-borne parasites in naturally infected cattle in Ghana

Justice Adzigbe (eadzigbe@gmail.com) – Masters student
Supervisors –Theresa Manful Gwira & Winfred-Peck Dorleku

Tick-borne pathogens have significant impact on livestock production especially in cattle and results in extensive economic loses to farmers in tropical and sub-tropical areas in Africa. The most important tick-borne diseases that affect cattle in sub-Saharan Africa include babesiosis, theileriosis, heartwater and anaplasmosis. In Ghana, inadequate information exists on the species and genetic diversity of tick-borne hemoparasites and very little is known about the impact of tick-borne diseases on cattle farming. The study aimed to detect and characterize tick-borne parasites that naturally infect cattle at two different agro-ecological zones in Ghana. A total of 40 cattle, 20 from each of the study locations were sampled at four to five week intervals over a period of six months. A nested polymerase chain reaction targeting the 18S rRNA gene was used to detect the presence of tick-borne hemoparasites. Preliminary data show that most of the cattle were infected with tick-borne parasites at each time point. The species of parasites and their diversity will be determined by sequencing and phylogenetic analysis. The outcomes of this study will contribute information on the types of tick-borne parasites that infect cattle and inform control measures in the affected areas.

33. Investigating the effect of blood donor variability in *Plasmodium falciparum* invasion phenotyping assays

Laty G. Thiam (latygaye.thiam@ucad.edu.sn) - PhD Student
Supervisors - Gordon A. Awandare, Mahktar Niang, Kwadwo A. Kusi & Theresa Manful Gwira

Red blood cells (RBCs) are key components for in vitro culturing of blood stage *Plasmodium falciparum,* providing not only a substrate for asexual reproduction but also a source of nutrients for the parasite. However, conducting large scale *P. falciparum* invasion phenotyping assays necessitates the use of different blood donors, a key factor that could affect the outcome of in vitro invasion inhibitory assays (IIA). Red blood cell polymorphisms have been linked with differences in geographical locations and the global distribution of *P. falciparum* as it relates to resistance to the infection. Human RBCs of all groups are suitable for in vitro growth of *P. falciparum*, although O+ RBCs are preferred over the ABO blood groups. However, the effect of blood donor variability in characterizing *P. falciparum* phenotypic diversity remains unaddressed. Therefore, we are currently investigating variations in invasion efficiency and/or phenotype observed using different blood donors and/or blood. Our preliminary data shows that invasion efficiency of both *P. falciparum* clinical isolates and laboratory adapted strains are affected by the nature of the acceptor RBCs. The data suggest that blood donor variability is a modulatory factor influencing invasion efficiency. The study clarifies the effect of blood donor variability in *P. falciparum* phenotyping assays that would help in addressing assay to assay variations.

34. Isolation of bacteria and yeasts associated with fruit fermentation and bioethanol extraction

Magdalene Dogbe (magden2916@gmail.com) – Graduate Intern
Supervisor - Lydia Mosi

Most nations, whether economically advanced or at different stages of development are faced with the problem of disposal and treatment of wastes. In 2013, research conducted by the chefs-for-change group proved that, more than 35% of food especially fruits goes to waste in Ghana along the consequential stages of food production and supply in the country. The recycling of these fruits in terms of bioethanol production may prove more remunerative than their disposal, improving availability of bioethanol in areas where production has been largely regarded. Ethanol obtained from fermentation of renewable sources for fuel or fuel additives are known as bioethanol. In this study, fermented fruits (pineapple, orange and tomato) were differentially cultured, stained, tested using various biochemical tests and characterized molecularly using 16s rRNA and Fungal ITS 1 and 4 primers. Fermented fruits were homogenized and centrifuged and the supernatant harvested for bioethanol extraction using the rotary evaporator. A total of 18 isolates were isolated using phenotypic standard culturing techniques. From the eighteen isolates, 12 isolates were identified as bacteria using Bergey's Manual of determinative bacteriology, while 6 were confirmed as fungal isolates using lacto-phenol cotton blue stain test. An average of 39 ml, 42 ml and 32 ml of suspected ethanol was extracted from 200 ml pineapple, tomato and orange supernatant respectively. These extracts tested positive for alcohol using the Iodine/NaOH test. Bacteria and fungi were observed to be mainly associated with fruit spoilage. This work validates the necessity for bioremediation of environmental food wastes constituting nuisance or causing pollution in our community.

35. Spontaneous switching of invasion phenotypes of *Plasmodium falciparum* strains in suspension culture

Prince B. Nyarko (pbnyarko2010@gmail.com) – Masters student
Supervisor – Gordon A. Awandare

Erythrocyte invasion is an essential process for the survival of Plasmodium. To circumvent host immune response, *Plasmodium falciparum* deploys a myriad of ligands in order to successfully invade host erythrocytes. Notable among these ligands are the Reticulocyte Binding-like (RH) and Duffy Binding-like (DBL) protein families, which selectively bind specific erythrocyte surface receptors such as glycophorins, complement receptor 1 (CR1) and Basigin during invasion. Depending on the erythrocyte surface receptors used, invasion has been characterized either as sialic acid (SA) dependent or sialic acid independent (alternative pathway). Based on this, the invasion phenotypes of several laboratory-adapted and clinical isolates of *P. falciparum* have been defined. *P. falciparum* Dd2 and W2mef normally require sialated-receptors for effective invasion. However, they are able to invade and thrive when cultured continuously in neuraminidase-treated erythrocytes. We thus hypothesized that under stringent conditions Dd2 and W2mef are capable of switching invasion phenotype. To investigate this, Dd2, W2mef and 3D7 were cultivated under static and suspended culture conditions continuously for 4 months, and their invasion phenotype assessed weekly. The contribution of CR1 and Basigin to erythrocyte invasion was also ascertained with anti-CR1 antibodies (12 µg/ml) and anti-Basigin antibodies (10 µg/ml), respectively. In addition, the expression of selected invasion-mediating genes were assessed. While static Dd2 and W2mef maintained SA-dependent invasion phenotype (below 10% relative to untreated control) over the entire period, their respective suspended counterparts gradually acquired SA-independent invasion phenotype, peaking at about 70% relative to untreated control, after 12 weeks. Addition of anti-CR1 antibodies abrogated the SA-independent invasion efficiency of suspended strains. Removal of suspension conditions resulted in a gradual loss of SA-independent invasion phenotype. Our data demonstrates a novel mechanism for inducing the switching of invasion pathways in *Plasmodium falciparum* parasites and may provide clues towards a better understanding of the underlying variation in ligand expression.

36. The genetics of congenital non-syndromic hearing impairment in Ghana

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Supervisors - Goffrey K. Amedofu, Gordon A. Awandare & Ambroise Wonkam

Over 100 genes of Non-Syndromic Hearing Impairment (NSHI) have been reported, however, studies from Ghana were focused only on GJB2. The contributions of other genes in NSHI has not been well studied in Africa, and a recent report using targeted exome sequencing has indicated a high proportion of novel mutations in known genes and possibility of discovering novel genes in Africa. The study seeks to identify new genes for NSHI in Ghana. Patient's hospital records, from schools for the deaf in Ghana were examined to identify children with hearing impairment who are likely to have genetic etiology of hearing impairment (at least 25 families segregating NSHI and 100 isolated cases). Whole Exome Sequencing followed by bioinformatics analysis and Sanger sequencing will be used to identify genes and confirm the mutations and also screen control and isolated cases. Expression and functional genomics studies will be conducted to determine the effects of the novel mutations on protein function and its pathogenicity. So far, 107 out of 199 patients with pre-lingual hearing impairment of unknown cause have been identified. Eighteen (18) children from 9 families with at least two siblings living with NSHI that segregate early onset autosomal recessive NSHI were enrolled. The study results showed that majority of the patients examined were male (113) and 86 female. From the results, most of the patients (62) were diagnosed for hearing impairment between the ages of 5 to 6 years. Based on the type of hearing impairment, 176 patients had sensorineural hearing impairment. In both ears, 156 and 16 patients had profound and severe-profound hearing impairment respectively. The study will contribute to a description of the genetic architecture of NSHI in Africa, and facilitate the molecular diagnosis and follow up of affected patients and families.

37. In vitro evaluation of anticancer activities and cytotoxicities of marketed herbal products in Ghana

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Supervisors – Osbourne Quaye & Regina Appiah-Opong

There are numerous herbal products on the Ghanaian market which are purported to cure various ailments including cancer. However, scientific investigations on efficacy and toxicity of most of these products are yet to be conducted. The present study assessed the anticancer activities and cytotoxicities of herbal products on the Ghanaian market. The anti-proliferative effects of five marketed herbal products - Kantinka BA (K-BA), Kantinka Herbaltics (K-HER), Centre of Awareness (COA), a stomach (STO) and multi-cancer (MUT) product were evaluated in vitro using liver (Hep G2), breast (MCF-7), prostate (PC-3 and LNCaP) cancer and leukaemia (Jurkat) cell lines. Cytotoxicity of the medicinal products was assessed using a tetrazolium-based colorimetric assay. Total phenolic content and antioxidant activity of the products were determined using Folin-Ciocalteau and 1,1-diphenyl-2-picrylhydrazyl (DPPH) assays, respectively. Phytochemical screening was performed using standard protocols. Phytochemical screening resulted in the detection of terpenoids in most of the products (4), followed by flavonoids (3). Alkaloids were detected in only MUT, whilst tannins were absent in all the products. The highest and lowest concentrations of phenolics were recorded in MUT and K-BA, and the highest and lowest antioxidant activities were recorded in MUT and K-HER, respectively. Two products (STO and MUT) had significant activity on Hep G2 cells; and only MUT had activity on MCF-7 cells. With the exception of K-BA, all the products inhibited the proliferation of PC-3 cells, and all the products, except K-HER, inhibited the proliferation of LNCaP and Jurkat cells. The findings support the claims that the herbal products have anticancer activities. However, comprehensive animal toxicity and clinical studies must be conducted on the products to establish their safety in humans.

38. Functional characterization of *Plasmodium falciparum* PF10_0351 protein

Essel Charles-Chess (charleschess@gmail.com) - Masters Student
Supervisors - Gordon A. Awandare & Yaw Aniweh

The inadequate experimental data on the function, structure and characteristics of the *Plasmodium falciparum* genome is a limitation to current knowledge on the biology of the parasite and aetiology of malaria. Currently, about 60% of the *P. falciparum* (3D7 strain) proteins have not been characterized. Since clinical symptoms of malaria are manifested at the blood stage, proteins involved in erythrocyte invasion are important research focus for vaccine development against the backdrop of resistance to Anopheles insecticides and antimalarial drugs including ACTs. This study aimed at functionally characterizing a novel *P. falciparum* protein and validating its role during the intraerythrocytic development cycle (IDC) of the parasite. To achieve this, bioinformatic and immunoinformatic analyses were used to map out three highly antigenic epitopes for peptide synthesis and antibody production. We determined the immunogenicity of the peptides in 24 malaria-positives plasma samples from three different endemic sites. Invasion inhibition assays were also performed to test the sensitivity of antibodies to native parasite proteins. We determined the localization of the protein across the IDC. Varying recognition patterns of the peptides were observed among the study sites with Kintampo showing the highest recognition. Antibodies to the third peptide exhibited the highest level of invasion. Immunofluorescence images showed that the protein may be exported to the periphery of the RBC. We further demonstrated that the protein is expressed in the IDC of the *P. falciparum* parasite. Taken together, we can conclude that the protein may play a role in invasion.

39. Asymptomatic malaria and anaemia among school children in Ho Municipality, Ghana

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In malaria-endemic countries, a large proportion of *P. falciparum* infections are asymptomatic, and children of school going age are the most affected. Although poor nutrition, intestinal parasitic infestation and haemoglobinopathies all predispose a child to the development of anaemia, most studies suggests malaria is the single most important risk factor of anaemia among children in malaria endemic regions. Therefore, the aim of this study was to determine the prevalence of asymptomatic malaria and anaemia among school children in Ho municipality, Volta region, Ghana. The study was a cross-sectional study conducted in the Ho municipality of the Volta region. Two hundred and twenty-four (224) school children, between the ages 6-13 years were selected randomly from six primary schools. Two millilitres of venous blood samples were collected from each participant and malaria smears were prepared. The smears were examined microscopically after staining with Geimsa and haemoglobin (Hb) concentrations were determined to an accuracy of 1g/dl with the HemoCue haemoglobinometer. The prevalence of asymptomatic malaria infection among the study participants was 16.5%. Two malaria parasite species were identified, *P. falciparum* and *P. malariae*, with prevalences of 15.6 % and 0.9 % respectively among the children. The median Hb of the uninfected children was 11.2 g/dl, (range 8.1-13.2), but that of those with malaria parasites was 10.7 g/dl (range 9.7-13.2). Asymptomatic malaria is prevalent among primary school children in the Ho municipality, but comparatively lower than most parts of Ghana and Africa.

40. Molecular characterization of hepatitis B Virus (HBV) in rural and semi-urban areas in three districts of the Central Region of Ghana

Caroline Boatemaa Agyare (carolboatemaa@gmail.com) – Masters student
Supervisors – Osbourne Quaye & Samuel Duodu

Hepatitis B virus (HBV) infection is a major cause of liver inflammation accounting for 780,000 deaths annually. The introduction of HBV vaccines has significantly reduced new cases of the infection, but there are still 65 million living with the virus in sub-Saharan Africa. Currently, 10 genotypes (A-J) of HBV have been classified. Several studies have shown that the different HBV genotypes differently influence clinical presentation, progression of disease and response to treatment. In Ghana, studies on HBV circulating genotypes and their implications on epidemiology is limited, however few available data have been obtained mostly in the urban areas of the Ashanti and Greater Accra regions. This study is aimed at characterizing HBV genotypes in patients attending three District Hospitals in the Central Region of Ghana (Agona-Swedru, Effutu and Gomoa-West Districts Hospitals). Thus far, HBV DNA has been extracted from the blood of 169 HBsAg positive patients using QIAGEN DNA Blood mini kit; 70 samples from the Gomoa-West District, 51 samples from the Efutu Municipal and 48 from the Agona- West District. The extracted DNA was confirmed by amplifying the S region of the HBV genome using conventional PCR. The HBV detected in the samples were genotyped with type-specific primers using nested-multiplex PCR. The amplicons obtained will be sequenced and the nucleotide sequences will be used to determine the HBV genotypes and the relatedness of the genotypes to reference strains will be determined by phylogenetic analysis. At the end of the study, the circulating genotypes of HBV in the three Districts will be characterized. The characterization of the HBV genotypes will help understand the transmission dynamics of the virus in a rural and semi-urban setting.

41. Evaluation of Omnigene Sputum, a novel sputum transport and decontamination reagent, for microscopy, culture and DNA-based assays

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Supervisors –Dorothy Yeboah – Manu & Adwoa Asante-Poku

We evaluated the digesting and decontaminating performance of Omnigene Sputum Reagent (OMS), a recently formulated reagent, which decontaminates sputum samples while in transit and eliminates the need for cold chain, using N-Acetyl-L-Cysteine-sodium hydroxide (NALC–NaOH) as a control. Samples were decontaminated with respective methods, then smears prepared for microscopy. Mycobacterial isolation was done by culturing on Lowenstein Jensen media in duplicates after decontamination and compatibility of the OMS reagent for molecular analysis was determined by using the remaining sediments for Xpert MTB/RIF analysis. Isolated mycobacteria were identified using IS6110 PCR and hsp65 sequence analysis. The positivity, negativity and contaminating rates were then computed. Overall, 376 tubes were cultured for each of the two decontamination treatments. Prior to decontamination, 95% of the sputum samples had bacterial growth on blood agar. The main contaminants identified include Streptococcus sp. (27/94, 28.7%), Staphylococcus sp. (19/94, 20.2%) and Pseudomonas sp. (12/94, 12.7%). Subsequent blood agar cultures showed that 5/94 (5%) and 6/94 (6%) of the samples still contained contaminants after OMS and NALC – NaOH treatment respectively. Of the 94 smears made after each treatment, 82% (77) and 91% (86) were AFB positive for OMS and NALC treatment respectively. Both methods were found to agree 80% more often than expected by chance ($p<0.001$). Difference in culture positivity was not statistically significant ($p = 0.500$); 228/376 (61%) and 235/376 (62.5%) cultures were positive after OMS and NALC-NaOH decontamination respectively. The proportion of contaminated culture tubes was significantly higher ($p = 0.0000$) with NALC–NaOH decontamination 68/376 (18.1%) compared to OMS 26/376 (6.9%). All forty-five sputum-smear positive samples analyzed by Xpert MTB/RIF assay were positive after each treatment. Our findings support the use of OMS as a sputum transport and decontamination reagent in Ghana.

42. Discovery and development of novel antifungal compounds from marine endophytic fungal sources

Ethel Juliet Blessie (jeblessie@gmail.com) - PhD Student
Supervisors – Patrick Kobina Arthur, Dorcas Osei-Safo & Jonathan P. Adjimani

Discovery of new drugs have shifted from plants to microorganisms due to the enormous diversity. Terrestrial endophytic fungi have been identified as an excellent source of biologically active secondary metabolites and have become an important source of drugs for the treatment of a variety of diseases. However, marine endophytic fungi have not been explored as compared to their terrestrial counterparts in the treatment of human diseases. The aim of the study was to identify and develop novel antifungal compounds from marine endophytic fungi sources using yeast genomics guided approach. To achieve this, marine endophytic fungi were isolated from marine plant samples. Some selected pure isolated fungi (Top 6) were fermented (1-2 litres) and extracted with ethyl acetate after 4 weeks. The crude extracts were tested against *S. cerevisiae* and *C. albicans* with majority of the extracts showing activity above 10mm zone of inhibition. Characterization of the crude extracts and fractions were performed against *C. albicans*, *S. cerevisiae* and a panel of mutant *S. cerevisiae*. Also, the activities of the crude extracts were tested under various chemical conditions against *S. cerevisiae* and *C. albicans* with most of the extracts maintaining their activities across the chemical conditions. The crude extracts from the selected 6 MEF were fractionated by Kupchan's solvent partitioning and preparative thin layer chromatography (TLC). The data obtained from this study showed that the extracts possessed distinct activities and were able to maintain their activities even when the cells were under different chemical conditions. A total of 59 active fractions were obtained from the 6 selected MEF after the preparative TLC. Two of these fractions from MEF 134 produced very clear zones of inhibition between 8- 13 mm. An HPLC-HRMS full scan was performed on fractions 134FDV5V7 and 134FDV5V9 and the results show the two fractions contain similar compounds.

43. Characterization of *Plasmodium falciparum* SURFIN8.2 and its role in malaria transmission

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Supervisor – Linda Eva Amoah

The molecular mechanisms underlying the sequestration of gametocytes, preceding their release upon maturation into circulation is still an unanswered question in the biology of malaria parasites. Two present hypothesis governing gametocyte sequestration are that gametocyte infected erythrocytes (giRBC) become rigid and remain trapped in vasculature, and elasticity is regained upon maturation and then become dislodged from sequestration. The other hypothesis is that receptors on the host cell bind to ligands on the surface of the giRBC. One protein responsible for the rigidity of asexual *P. falciparum* infected erythrocytes (iRBC) is SURFIN4.2. The disruption of the SURFIN4.2 gene locus results in significant reduction of iRBC rigidity in the asexual parasite infected erythrocyte. Thus, SURFIN4.2 has been suggested to play a critical role in iRBC remodelling and subsequent pathogenesis in malaria. This research hypothesizes therefore that SURFIN8.2, a sexual stage parasite homologue of SURFIN 4.2, which is predicted to have an ectodomain exposed on the surface of giRBCs is similarly responsible for gametocyte infected erythrocyte (giRBC) sequestration, it can therefore be used as a marker for *Plasmodium falciparum* gametocyte exposure as well as a possible component of a candidate vaccine that interrupts malaria transmission.

44. Towards identifying molecular markers of *Plasmodium falciparum* artemisinin resistance using the CRISPR-Cas9 genome editing system

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Supervisors –Neils Quashie, Kwadwo Asamoah Kusi & Yaw Aniweh

The emergence of artemisinin resistant *Plasmodium falciparum* in South-Eastern Asia (SEA) poses a serious public health challenge to the malaria control programme in sub Saharan Africa. Mutations within the Kelch 13 (*k13*) gene including Y493H, C580Y, M476I, R539T and I543T have been identified and verified as molecular markers of *P. falciparum* resistance to the artemisinins in the SEA. The utility of these molecular markers for monitoring artemisinin resistance in sub Saharan Africa has not yet been ascertained. The study proposes to use the clustered regularly interspaced palindromic repeats (CRISPR) and CRISPR associated protein (Cas9) genome editing system to study the utility of these mutations as markers of artemisinin resistance and to identify novel markers of artemisinin resistance in Ghana. CRISPR-Cas9 system would be used to engineer transgenic GB4 (Ghanaian-adapted laboratory *P. falciparum* strain) bearing the individual *k13* mutations. Ring-stage assays (RSA) would be undertaken to determine the survivability compared with the parental strains. K13 genes of clinical *P. falciparum* isolates with delayed parasite clearance when patients are treated with ACT would be sequenced to identify novel mutations. CRISPR-Cas9 system would be used to replace the mutant *k13* with wild type *k13*, RSA would then be performed to determine whether the parasites will regain artemisinin sensitivity. In addition, CRISPR-Cas9 system would be used to introduce *k13* bearing Y493H, C580Y, M476I, R539T and I543T mutations into clinical artemisinin sensitive clinical *P. falciparum* strains. Survivability of the transgenic parasites would be compared with the wild type using the RSA method. It is expected that the utility of the previously known molecular markers of *P. falciparum* artemisinin resistance would be known and novel markers would be identified and verified.

45. K13 gene polymorphisms in *Plasmodium falciparum* isolates from ACT post treatment samples in two ecological zones in Ghana

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The detection of single nucleotide polymorphisms (SNPs) in the *Plasmodium falciparum* kelch propeller gene (*k13*) linked to artemisinin (ART) resistance is relevant for surveillance, as an early warning signal of emergence of resistance in artemisinin-based combination therapy (ACT). This research explored the occurrence of *k13* polymorphisms in isolates from pre- and post-treatment samples from three sites of different ecologies in Ghana. Filter paper blood blot samples from 22 uncomplicated malaria patients for both pretreatment day 0 and post treatment days 14, 21 and 28 (after the administration of amodiaquine-artesunate (AA) or artemether-lumefantrine (AL)), collected in 2014 were used. Parasite DNA was extracted from 44 samples, 32 from the forest zone (Begoro and Bekwai) and 12 from the savannah zone (Navrongo), using Qiagen DNA mini kit. Nested PCR followed by Sanger sequencing of the *k13* gene of isolates was performed. Sequence analysis with SNP detection was carried out with the software CLC Main Workbench version 7.8.1 (Qiagen). In all, 12 synonymous and 14 non-synonymous SNPs were found in 7 posttreatment samples which were novel compared to SNPs observed in Southeast Asia (SEA), Africa and Ghana. Of the 12 synonymous mutations, 8, 3 and 1 respectively for Navrongo, Begoro and Bekwai. The non-synonymous mutations were from Navrongo (7) and Begoro (7). 2 synonymous and 2 non-synonymous SNPs were observed in 4 pretreatment samples. The observation of novel synonymous and non-synonymous SNPs in *k13* gene is quite interesting for Ghana, where the cure rate of ACTs ranges between 97-100%. The detected SNPs provide a valuable information on the variability in the SNPs found at the two ecological zones with different malaria transmission patterns. The importance of the higher number of novel SNPs in the savannah than the forest zone is further discussed.

46. *In silico* prediction of potential natural product-derived lead compounds for the treatment of Buruli Ulcer

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Buruli ulcer is caused by *Mycobacterium ulcerans* and is predominant in both tropical and subtropical regions. The neglected debilitating disease is characterized by chronic necrotizing skin infections. Existing drugs such as rifampicin and streptomycin appear not to be adequately potent and efficacious against persistent infections by *Mycobacterium ulcerans*. There is the need to identify novel lead compounds which are potent and efficacious for the treatment of Buruli ulcer. The project aimed to computationally predict natural product-derived lead compounds with the potential to be developed further into potent drugs with better therapeutic efficacy than the existing ones. The 3D structure of Isocitrate lyase (ICL) of *Mycobacterium ulcerans*, a potential drug target for BU was predicted using homology modelling and further subjected to molecular dynamics simulations. A library consisting of 885 compounds derived from the AfroDb database was virtually screened against the validated ICL model using AutoDock Vina. AfroDb database is a compendium consisting of "drug-like" and structurally diverse 3D structures of natural products originating from the different geographical regions in Africa. Virtual screening is a computer-aided drug design technique composed of robust pipeline which enables the efficient docking of large compound library against drug targets for the discovery of potential inhibitors which could serve as possible lead compounds for further optimisation. Ten compounds which docked firmly within the active site pocket of the ICL receptor were assessed via in silico bioactivity assays and pharmacological profiling techniques. The potential drug leads have shown promising results pertaining to efficacy, toxicity, pharmacokinetic and safety and could be experimentally characterized for pre-clinical trials.

47. High recent transmission rate found among *Mycobacterium tuberculosis* strains circulating in an urban setting in Ghana

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Knowledge of the transmission pattern of the different circulating *Mycobacterium tuberculosis* complex (MTBC) strains which is needed for an effective TB control in Ghana, has not been critically assessed. This study therefore sought to conduct a population-based molecular epidemiological study in East Mamprusi district (Rural) and Accra Metro (Urban) using available molecular tools to assess recent TB transmission patterns. *Mycobacterium tuberculosis* isolates obtained from clinically diagnosed pulmonary TB patients within the period August 2012 to December, 2015, were confirmed as members of the MTBC using spoligotyping and/or PCR targeting IS6110. Isolates were subjected to mycobacterial interspersed repetitive unit - variable number of tandem repeat (MIRU-VNTR) typing in a stepwise manner, starting with a customized 8-MIRU loci set and followed by the remaining 7 loci of the standard MIRU-15 for clustered isolates. Molecular clustering analysis was performed with the aid of the miru-vntr*plus* online tool and bionumerics software after which recent TB transmission rates were estimated stratified by location of circulating strains. We included 2,309 TB isolates for clustering analysis and identified 1,082 (46.9%) singletons identified with each of the remaining 1,227 (53.1%) isolates belonging to one of 276 clustered cases (clustering range; 2 – 35). A greater number of cases (2,108; 91.3%) were from the urban setting as compared to the rural setting (201; 8.7%). The overall recent transmission rate across the country was estimated to be 45%. Compared to the rural setting, we found a significantly higher recent TB transmission occurring in the urban setting (Ur: 42% vs. Ru: 10% clustering, p-value < 0.001). We found that, the recently observed high TB transmission rate was significantly driven by the Cameroon, Ghana and Haarlem sub-lineages of lineage 4 (p-value <0.05). Our findings indicate possible unsuspected TB outbreaks and recommends intensified awareness.

48. Insecticide resistant vectors and drug tolerant parasites and their impact on malaria transmission in Ghana

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The global effort at controlling malaria is under threat because of the emergence and spread of both insecticide resistant vectors and drug tolerant parasites. Insecticide resistant malaria vectors have been reported in some countries in Africa, including Ghana. There have been reports of delayed parasite clearance, an indication of drug tolerant parasites, in some parts of Africa. Studies have shown that some drug tolerant parasites are transmissible within a population, while others are not. The molecular studies of the interaction between insecticide resistant malaria vectors and drug tolerant malaria parasites, as well as the tendency of these tolerant parasites to be transmitted by these resistant vectors, is therefore essential in the control of malaria. The aim of the study is to understand how resistant African malaria vectors will interact with drug tolerant malaria parasites and the effect of this interaction on malaria transmission. To achieve this aim, drug tolerant and susceptible *Plasmodium falciparum* from children with uncomplicated malaria will be cultured and fed to raised colonies of both insecticide resistant and susceptible *Anopheles gambiae*, *An. Funestus*, *An. arabiensis* and *An. coluzzii*. Parasite diversity will be determined by whole genome sequencing. Parasite infectivity of vectors will be done by sequencing sporozoites collected from infected mosquitoes. Sequence reads will be analysed using available bioinformatics tools. It is expected that knowledge about the molecular basis of the ability of insecticide resistant vectors to transmit drug tolerant malaria parasites will be gained. This information will be relevant to malaria prevention and control strategies in Ghana.

49. Genetic diversity of noroviruses in Ghanaian children hospitalized with diarrhoea in pre-rotavirus vaccination era

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Following better diagnostic techniques, global burden estimates and the research and development of prospective vaccine candidates, noroviruses have received increasing recognition as important etiological agents of severe acute gastroenteritis especially in children under five years old. This study aimed to describe the epidemiology and norovirus strain diversity pre-rotavirus vaccine era in Ghanaian children. Archived diarrhoeic stool samples collected as part of an ongoing national rotavirus surveillance from children <5 years were used. Samples were collected from sentinel sites in the Northern (Navrongo War Memorial Hospital), Middle (Komfo Anokye Teaching hospital and Agogo Presbyterian hospital) and Southern (Korle-Bu Teaching Hospital and Princess Marie Louise Children's Hospital) belts of Ghana from January 2009 to May 2012. Samples were tested for norovirus antigen by EIA, and further characterized by molecular methods including sequencing. Of the 443 diarrhoeic stool samples tested, 24.2% (107/443) of children were found to be shedding the virus. One hundred [93.5%; (100/107)] of the isolates belonged to genogroup II whiles three isolates [2.8%; (3/107)] belonged to genogroup I and 3.7% were mixed infections of both genogroups I & II. The virus was detected in all age groups of children but was predominantly found in children between the ages of 0 – 6 months. Commonly isolated genotypes pre-vaccination era included GII.4 (35.0%), GII.12 (25.0%), GII.13 (7.1%) and GII.6 (7.1%) whiles genotypes, GII.1, GII.2, GII.7 and GII.14 were less frequently observed. Phylogenetic analysis of study GII.4 strains showed them clustering with the GII.4 2006b and 2010 variants associated with global norovirus diarrhoeal epidemics. The study confirmed the significance of noroviruses as important etiological agents of childhood diarrhoeal disease. The high prevalence of recorded norovirus infection highlights the necessity for a larger study to elucidate the contribution of norovirus to the burden of gastroenteritis in Ghanaian children.

50. Iron (II) and Iron (III) chelation by phenolic acids

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Phenolic acids (PA) such as benzoic acids and cinnamic acid derivatives in natural products have been associated with anti-tubercular properties. However, their mechanism of action remains unclear. In this study, the capacity of eight phenolic acids for complex formation with iron (II) and iron (III) was investigated. A metal chelation mechanism was described by means of spectrophotometry. The UV-Vis absorption spectrophotometry showed that the absorption of the phenolic acids changes upon addition of Iron (II) and Iron (III), which resulted in several shifts in their spectra. These batochromic shifts were analysed. Furthermore, in the presence of different concentrations of EDTA (0–1 mM), a reduction of the constants was observed. However, not all of the phenolic compounds assessed here showed complex formation, those not bearing catechol or galloyl moiety like vanillic acid and ferulic acid, did not show any complex formation in our study. The ability of the phenolic compounds which chelate iron have been ranked in line with the binding constants.

51. Indoor and immediate-outdoor airborne bacterial and antibiotic susceptibility profiles of a research institute

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Bacteria are ubiquitous, the diversity and relative abundance of which have a strong public health effect. It is therefore becoming increasingly important to determine the status of bacterial contamination in indoor air, since one third of the recognized infectious diseases are transmitted through this medium. It has been shown that people spend about 80-95% of their lives in indoor and immediate-outdoor environments, inhaling air of which bacteriological profile is largely unknown. Moreover, the rising rate in the bacterial antibiotic resistance demands a research attention. The study was conducted to assess and determine the bacterial and antibiotic susceptibility profiles of indoor and immediate-outdoor air of a learning and research institute. Forty-two samples were collected from eight major sites using passive bacterial sampling techniques. Phenotypic microbiological standard procedures analysis was used to identify and characterize the isolates. Antibiotic susceptibility profiles were determined using standard disc diffusion methods and data was interpreted using protocols developed by Clinical Laboratory Institute (CLSI, 2016). Eighty-seven percent of the isolates were obtained and identified from the total samples collected. Most frequently isolated bacteria were Gram positive bacilli (41%), *Staphylococcus sp.* (24%), Gram positive cocci (15%) and Gram-negative lactose fermenting bacilli (7%). All the isolates showed resistance to at least 2-classes of the fourteen different antibiotics tested, with full resistance (100%) to ampicillin and penicillin. Resistance to flucloxacillin across the isolates was observed; highest with *Staphylococcus sp.* Seven different Anti-biotypes (Multiple Antibiotic Resistance patterns) were observed with highest susceptibility to tetracycline and gentamycin. The various air sampling sites of the institute showed the presence of bacteria, though with a low contamination rate as compared to the WHO standard; therefore, students and workers are exposed to low concentration of airborne bacteria

52. Determinants of artemisinin resistance in *Plasmodium falciparum* clinical isolates in a Ghanaian population

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Malaria chemotherapy has been one of the main stays of global malaria control. However, resistant strains of P. falciparum have evolved over time against previous effective antimalarial drugs. Though there has been a drastic global decline in malaria incidence and deaths due to Artemisinin-based Combination Therapies (ACTs) and other malaria prevention and control strategies, the emergence of artemisinin-resistant *P. falciparum,* threatens the gains made. Although complete artemisinin resistance is yet to emerge, delayed parasite clearance *in vitro* and *in vivo* has been associated with several mutations in the kelch 13 propeller domain. This study seeks to characterize determinants of artemisinin resistance in *P. falciparum* and parasite survival mechanisms in clinical isolates of Ghanaian children with uncomplicated *P. falciparum* malaria. Children aged 6 months to 14 years presenting with uncomplicated *P. falciparum* malaria will be recruited at two health facilities (Princess Marie Louise Children's Hospital and Ussher polyclinic in Accra), after obtaining written informed consent from parents. Antimalarial drug efficacy will be determined using the standard 28-day WHO *in vivo* assessment protocol and 72-hour parasite clearance dynamics. *Ex-vivo* and *in vitro* parasite susceptibility testing, and molecular assays will be done to determine parasite tolerance correlates with kelch 13 or *P. falciparum* multi-drug resistance genes (pfmdr1) and to confirm parasite origin. Mechanisms of how delayed parasite clearance phenotypes develop could be established and the possible origin of potential artemisinin resistance parasites in the local setting would be identified.

53. The role of malaria and tumour immunity in the pathogenesis of Endemic Burkitt's Lymphoma

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Endemic Burkitt's lymphoma (eBL) is a malignant B cell lymphoma in children living in sub-Saharan Africa, including Ghana. The disease is known to be associated with intense frequent exposure to *Plasmodium falciparum* malaria parasites and Epstein-Barr virus (EBV) are important co-factors in the pathogenesis. However, the molecular details of how they affect the development of eBL are only partially understood. The mechanisms of the host immune response in the pathogenesis and control of eBL are similarly unclear. It has been suggested that *P. falciparum*-specific B cells are particularly prone to malignant transformation by activated-induced cysteine deaminase (AID)-dependent *c- myc* translocation in EBV-infected B cells, and that many eBL cells therefore encode a *P. falciparum*-specific antibody. It has furthermore been proposed that auto-regulatory Vδ1+ T cells play an important role in the normal control of activated B cells, including malignant eBL cells. The physiologic role of this rather enigmatic cell subset is currently essentially unknown. The study is designed to investigate the above hypotheses by a comprehensive and advanced set of immunological and molecular methods. It is likely to provide novel information regarding the phenotypic and functional characteristics of B cells and T cells from patients with eBL, thereby enabling a deeper understanding of the molecular mechanisms of *Plasmodium falciparum* and Epstein-Barr virus involvement in endemic Burkitt's lymphoma pathogenesis, and of the host immune responses to this tumor.

54. Investigating determinants of asymptomatic *Plasmodium falciparum* infections in a high endemic area of Ghana

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The major burden of malaria in endemic areas is asymptomatic malaria, which is characterized by low parasitemia and absence of clinical symptoms. Asymptomatic carriers may continue to serve as a reservoir and source of Plasmodium infection for vector mosquitoes. The pathophysiology underlying asymptomatic infections is not fully understood. The possible hypothesis for this mechanism could include genetic predisposition, or development of partial immunity to the parasite that suppresses the symptoms. The aim of this study is to determine the mechanisms of immunity to *P. falciparum* in asymptomatic malaria in Ghanaian adults living in malaria endemic areas with different transmission intensities. The study participants were recruited from Obom in greater Accra region Ghana. A venous blood sample was collected from each study participant and screened for malaria parasites by microscopy. Logistic regression was conducted to assess the influence of mosquito nets, blood group, genotype and gender on the phenotype of malaria (symptomatic or asymptomatic). Whiles together they were found to influence malaria phenotype (R^2 = 47%, χ^2= 32.1, df= 11, N=76, P=0 .001), use of mosquito nets was found to significantly (R^2 = 28%, χ^2 = 17.5, df=1, N=76, P<0 .001) influence whether an individual was symptomatic or not. Platelet and lymphocyte counts were found to be significantly lower in the symptomatic group as compared to asymptomatic group [median (range) for platelets, 173 (78-321) versus 224 (93-485), P=0.015; and for lymphocytes 0.8 (1.3-2.1) versus 2.9 (1.2-6.0), P<0.001]. On the other hand, neutrophil counts was found to be significantly higher in the symptomatic group compared to the asymptomatic group 4.3 (1.3- 10.1), 2.2 (1.0 -5.0) P<0.001]. The use of mosquito nets was found to be a major determinant of whether infections were symptomatic or not. Furthermore, there were marked differences in immune cell counts in symptomatic individuals relative to those with asymptomatic infections.

55. High prevalence of submicroscopic *Plasmodium falciparum* infections in pregnant women from Bobo-Dioulasso, Burkina Faso

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Submicroscopic malaria infections have so far not been reported in pregnant women in Burkina Faso. The objective of this study therefore, was to assess the prevalence and the impact of sub-microscopic *Plasmodium falciparum* infections on maternal and birth outcomes.Placental blood of 176 women was collected at delivery through a cross-sectional study carried out in Bobo-Dioulasso from September to December 2010. Conventional microscopy and a real-time PCR species-specific assay were used for the detection of malaria parasites in blood smears and dried blood spots, respectively. Maternal haemoglobin concentrations and birth weights were also measured. Of the 176 women, malaria infection was detected in 19 (10.8%) by microscopy and in 167 (94.9%) by real-time PCR. The real-time PCR species-specific assay detected *P. falciparum* alone in all but one sample, which was a mixed infection with *P. falciparum* and *P. malariae*. The prevalence of submicroscopic *P. falciparum* infection was 88.6% (148/167). In addition, the prevalence of anaemia was significantly higher in pregnant women with submicroscopic parasitaemia compared to those with smear-positive parasitaemia. The prevalence of low birth weight new-borns was relatively higher among women with a submicroscopic parasitaemia (21.1%) compared to those smear-positive parasitaemia (8.8%), and aparasitaemic women (11.1%), although these differences were not statistically significant.
The prevalence of submicroscopic *P. falciparum* parasitaemia is particularly very high in this setting. This finding emphasizes the need for appropriate diagnostic methods in studies evaluating the outcome of pregnancy-associated malaria.

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