West African Centre for Cell Biology of Infectious Pathogens

Translating Molecular Research into Healthcare Solutions for Africa

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UNIVERSITY OF GHANA

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WEST AFRICAN CENTRE FOR CELL BIOLOGY OF INFECTIOUS PATHOGENS
UNIVERSITY OF GHANA

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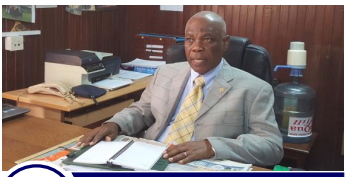

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ABOUT WACCBIP

01

Established in 2014, The West African Centre for Cell Biology of Infectious Pathogens has grown into one of the leading biomedical research & training Centres in the West African sub-region. The Centre, funded under the the World Bank's African Centres of Excellence (ACE) in Higher Education Project and the Wellcome Trust Developing Excellence in Leadership, Training and Science (DELTAS) Africa award, is led by faculty from the Department of Biochemistry, Cell and Molecular Biology (BCMB), and the Noguchi Memorial Institute for Medical Research (NMIMR) at the University of Ghana.

Our mission is to improve diagnosis, prevention, and control of tropical diseases in sub-Saharan Africa by providing advanced-level training and research excellence on the cell and molecular biology of infectious pathogens.

In our quest to foster world-class post-graduate training and disease research within the sub-region, **we aim to**:

- train high-level health professionals & biomedical scientists on cell & molecular biology of tropical diseases through short courses, MPhil, PhD & Postdoctoral programmes;
- serve as a core facility with state-of-the-art biomedical laboratories to support tropical diseases research;
- establish a Biomedical High-Performance Computing Unit to support teaching, research, and dissemination of information; and to

» increase research output & innovation by enhancing collaboration among biomedical scientists and industry partners.

OUR OPERATIONS

WACCBIP's mandate is to provide Master's, PhD, and Postdoctoral training, as well as targeted short-courses in Cell & Molecular Biology; to 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 seeks to strengthen its research output, expand its regional network beyond West Africa, train postdoctoral fellows, and provide additional PhD fellowships.

Training

Training new generations of African scientists is central to the Centre's vision. As part of our core mandate, we provide training in cell and molecular biology of tropical diseases. 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. We have put together quality training programmes targeted at different groups of seasoned and upcoming scientists. We offer:

SHORT-TERM	MASTER'S	PhD	POST-DOC
» Two-week workshops » Attachment/ internships	» One year of coursework at UG » Plus one year of research work at UG or partner institution	» One year of coursework at UG » Plus three years of research work at UG or partner institution » 6-month Student Visitor Fellowship	» Three-year research fellowship at UG or African partner institution

Research

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

The **priority pathogens** include protozoans causing diseases such as malaria and trypanosomiasis; Mycobacteria, causing tuberculosis and Buruli ulcer; other bacteria causing gastro-intestinal and blood infections; and viruses, including HIV, rotaviruses, Influenza, and Dengue. For each of the priority diseases/pathogens, research is organized into five themes:

- disease pathogenesis and immunity,
- pathogen genomics/bioinformatics,
- host genetics/genomics, host/pathogen interactions,
- molecular diagnosis, molecular epidemiology for surveillance,
- target discovery for drug and vaccine development.

There are also emerging themes in etiology of febrile illnesses in children, maternal health, and human genetics (infectious and non-communicable).

Continuously improving our research environment, WACCBIP has developed 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 provided by the Core include high-throughput multi-color flow cytometry and cell-sorting, mass spectrometry, gene expression assays, primer synthesis, and expression and purification of proteins. In addition, the WACCBIP Core operates a laboratory supplies store, and builds capacity and expertise for servicing and repair of equipment.

The WACCBIP Core facility also includes a **Biomedical High-Performance Computing Unit** (BHPCU) that provides access to cluster computing services, and scientific software for data analyses, modeling/simulation, and information dissemination.

PROJECTED OUTPUT

At the end of the four-year period of the World Bank grant, WACCBIP would have achieved the following:

- international accreditation for two new specialized graduate programs;
- enrolled 60 MPhil students, 40 PhDs and 12 post-docs, of which at least 30% would be regional and 40% female;
- trained 195 scientists and health professionals through short term courses, of which at least 30% would be regional and 40% female;
- published at least 44 peer-reviewed research publications, of which at least 50% include regional co-authors;
- attract an average of $1M per year in externally mobilized funds;
- 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; &
- developed new disease diagnostic/monitoring methods and novel drug/vaccine targets.

FUNDING & SUSTAINABILITY

WACCBIP 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. Additional proposals are also being planned for submission to the National Institutes of Health (NIH)'s Fogarty International Centre training programmes and the Gates Foundation.

We are also confident of strengthening our linkage with the private sector, which we are facilitating through the World Bank programme. There is considerable interest from Pharmaceutical companies in partnering with WACCBIP for drug discovery research, and we expect these collaborations to bring in additional funding in the next few years.

Also, with the ramping up of human genetics research, we are developing the capacity to introduce molecular testing services for genetic markers of diseases susceptibility. These services would be provided on a fee-for-service basis and coupled with a genetic counselling programme.

And, WACCBIP also operates a supplies store which procures reagents and supplies in bulk directly from manufacturers or wholesalers. The store then provides for the needs of WACCBIP faculty and students, as well as other scientists.

GOVERNANCE & STRUCTURE

WACCBIP operates as an academic unit of the College of Basic and Applied Sciences, 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 a Deputy Director, 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 international experts who directly advise the WACCBIP Director on the Centre's scientific quality and strategic research.

Faculty

WACCBIP has appointed postdoctoral Research Fellows (PhD holders), who drive the Centre's research agenda. Additional faculty are drawn from the Department of Biochemistry, Cell and Molecular Biology and the Noguchi Memorial Institute for Medical Research.

The Centre also draws on other faculty from within the College of Basic & Applied Sciences 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.

Secretariat

The WACCBIP Director is assisted by a Centre Secretariat, which has an Administrative Unit headed by a Grants Manager with qualifications equivalent to an Assistant Registrar or Faculty Research Development Officer; a Communications & Public Engagement Unit headed by a Communications Manager; an Accounts Unit headed by an Accounts Officer; and an ICT Unit headed by an ICT Officer.

Support staff and graduate interns for each unit help run the day-to-day activities of the Secretariat.

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Prof. Kwadwo A. Koram - Deputy Director

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Dr. Lydia Mosi - Logistics Coordinator

Dr. Osbourne Quaye - Head of Monitoring & Evaluation

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Prof. Dorothy Yeboah-Manu – Postdoctoral Programme Coordinator

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Dr. Anita Ghansah/Prof. Solomon Ofori-Acquah -Genetics Course Coordinators

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Ms. Ama G. Dadson - Co-Head of ICT, Physical Resources

Mr. Collins Amofah - Senior Accountant

Ms. Sika Menka - Grants Manager

Mr. Solomon Katachie - Communications Manager

Ms. Emefa Adzadu - Accounts Officer

Ms. Joyce Mwongeli Ngoi - Next-Generation Sequencing Manager

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Mrs. Constance Kocke - Procurement Officer

Ms. Marian Nanor - Accounts Officer

Ms. Kyerewaa Akuamoah Boateng - Public Engagement Officer

Mr. Theophilus Dugah - ICT Technician

Mr. Alfred Kazaresam – ICT Intern

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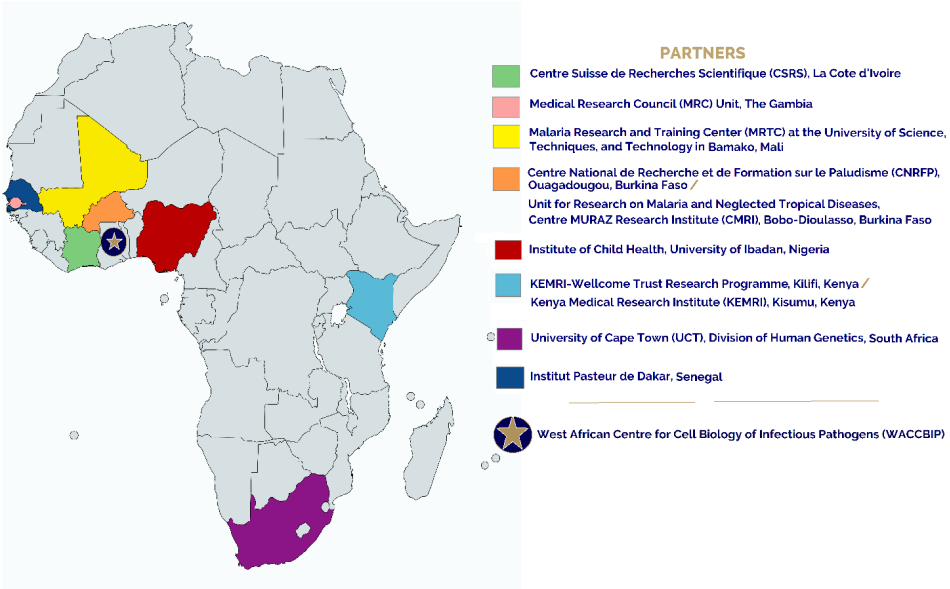
- *Kintampo Health Research Centre, Kintampo*
- *Navrongo Health Research Centre, Navrongo.*
- *La Gray Chemical Company, Nsawam*
- *Kwame Nkrumah University of Science and Technology, Kumasi*
- *University of Development Studies, Tamale*
- *LEKMA Hospital, Teshie, Accra*
- *African Research Academies 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*
- *Institut Pasteur de Dakar, Senegal*



International Partners

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- *University of Oxford, UK*
- *Oxford University, UK*
- *University of Cambridge, UK*
- *Wellcome Trust Sanger Institute, UK*
- *MalariaGEN Consortium, UK*
- *University of New Mexico, USA*
- *University of Pittsburgh, USA*
- *University of Copenhagen, Denmark*
- *University of Edinburgh, UK*
- *Francis Crick Institute, UK*
- *Imperial College, UK*
- *Queen's University, Belfast, UK*
- *University of Michigan, USA*

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2. Dr. Patrick K. Arthur
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4. Dr. Lydia Mosi
5. Dr. Theresa Manful Gwira
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56. Dr. Issa Nebie Ouedraogo

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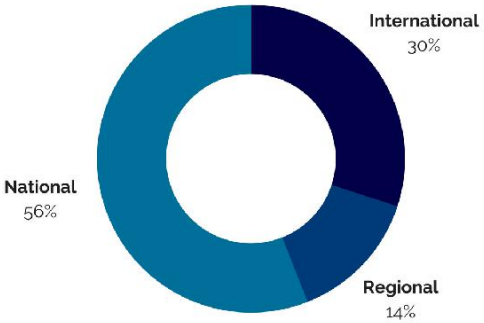


Contributing partners across 3 continents

More than 20 countries

A network of more than 1000 scientists

WACCBIP UPDATES 02

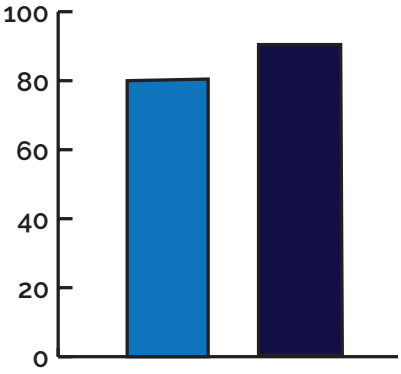
WORLD BANK ACE PROJECT

In response to the World Bank's call for proposals for their African Centres of Excellence project, faculty from the Department of Biochemistry, Cell & Molecular Biology (BCMB), and the Noguchi Memorial Institute for Medical Research (NMIMR), with support from staff of the University of Ghana Computing Systems (UGCS), proposed the establishment of WACCBIP. After two rounds of evaluation, the World Bank accepted the proposal and has subsequently committed $8 million to support WACCBIP through a financing agreement with the Government of Ghana. Funding from the World Bank enables WACCBIP to carry out, among other priorities, its training and research mandate.

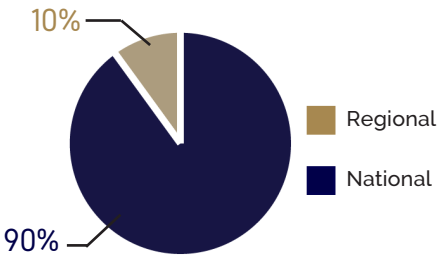
MASTER'S PROGRAMMES

WACCBIP aims to train the next generation of biomedical scientists in modern academic and professional techniques, providing the foundation for scientific research aimed at solving major national and sub-regional health challenges. Our master's programmes are research-centred and practical, setting in motion future careers in academia and in industry.

Summary of Enrolment in Master's Programmes



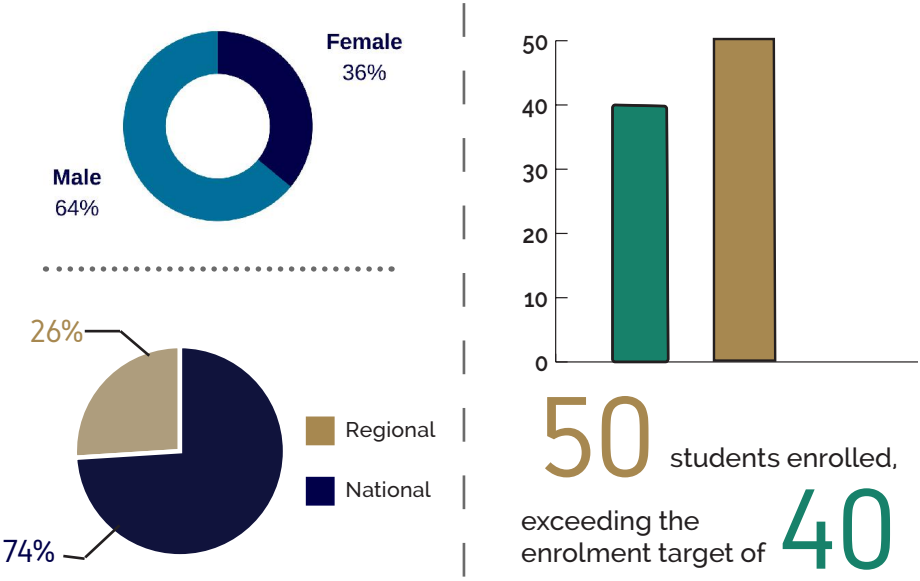
90 students enrolled, exceeding the enrolment target of **80**



PhD PROGRAMMES

WACCBIP places great value on providing high quality postgraduate training through our four-year PhD programmes. Courses are offered primarily at the Department of Biochemistry, Cell and Molecular Biology at the University of Ghana, with opportunity for short study at partner institutions worldwide. Our programmes are highly competitive and are set up to challenge and nurture talented students within a world-class environment designed to foster scientific work.

Summary of Enrolment in PhD Programmes



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Addo-Gyan K. Daniel
Amekudzi Deladem K.
Atindaana Edmond Akugbire
Bakari Soale Majeed
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Emmanuel Ayisi Manu
Joshua Kuleape
King Sandra Adelaide
Letsa Victor
Myers-Hansen James L.
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Acquah E. A. Selorm
Buatsi Esenam Dzifa
Adzadogo Senanu Richmond
Aidoo Eugene
Arhin Christian Kweku
Eke Eric Paul
Frimpong A. Dorcas
Okideran Ademola Philips

COHORT 2

Abban Lartey Raphael
Adzigbe Justice
Aflakpui Ranee
Agbemafle Sedem
Agyare Caroline Boatemaa
Ameke Selassie Louis
Anabire Nsoh Godwin
Asandem Asema Diana
Ayelazuno Felix Alexander
Badu Pheonah
Essel Charles Chess
Laryea-Akrong Elizabeth
Osei Musah
Simpson Shirley Victoria
Akyaw Priscilla Abena
Antwi Emmanuel Opoku
Kubi Ernestine
Tuffour Isaac
Languon Sylvester
Yeboah Kwasi Oduro

COHORT 3

Adjah Joshua
Antwi Achiaa Christine
Azerigyik Faustus Akankperiwen
Adjei Raymond Lovelace
Kissi-Twum Abena Adomah
Addae Charlotte Adjoa
Amisigo Cynthia Mmalebna
Asare Leonard Kwadwo
Nyarko Prince Berko
Danso Emelia Konadu
Yeboah Rebecca
Aquah Kwadwo Awudu Daniel
Carilo Isaac

COHORT 4

Ugwu Nneka
Owusu-Boateng Kwabena
Tandoh Kwesi Zandoh
Buckman Michelle Abena
Dogbe Magdalene
Owusu Adjei Rita
Ametsi Williams Godwin
Akuh Ojo-Ojogu
Ilani Philip
Adade Emmanuel Edem
Quansah Evelyn Baaba
Hodoameda Peter
Mensah Barbara
Labadah Joshua
Ayee Richmond
Opoku Grace
Asenso Samuel Ampoful
Attiku Keren Okyerebea
Ouelo Anouwouba Batabouya Elodie
Oworae Kwadwo Otieku
Yankson George Kweku Gyasi
Anyigba Claudia Adzo
Asantewaa Yvonne Yaa
Arjarquah Augustina Kwakyewaa
Ofori Ebenezer Addo
Adjahi Alda Dona
Ibrahim Abdulai Luru

WACCBIP PhD FELLOWS

COHORT 1

Abdul Rahman Ahmed R.
Amoako Nicholas
Augustina Frimpong
Ayivor-Djanie Reuben
Blessie Ethel Juliet
Dofour Aboagye Kwarteng
Matrevi Sena Adzoa
Mensah-Brown Henrietta
Obiri Dorotheah
Tagoe Emmanuel Ayitey
Van Der Puije William

COHORT 2

Abdul-Rahaman Mubarak
Abiola Isawumi
Ahorhorlu Samuel Yao
Asare Prince
Hagan Oheneba Charles Kofi
Krampa Francis Dzidefo
Lartey Belinda Naa Larteley
Luuse Arnold Togiwe
Mawuli Bernice Anane
Mensah Annie Wilhelmina
Smith Cecilia
Thiam Laty Gaye
Jagne Sheriffo

COHORT 3

Muriuki Beatrice Mukami
Niare Karamoko
Mbye Haddijatou
Nyakoe Nancy Kemuma
Hamid-Adiamoh Majidah
Gyamfi Elizabeth
Ekloh William
Acquah Festus Kojo
Kengne Ouafo Jonas Arnaud
Prah Diana Ahu
Yakass Michael Bright
Agyeman Seth
Kotey Erasmus Nikoi
Amuzu Dominic Selorm Yao
Adadey Samuel Mawuli

COHORT 4

Owusu Irene Amoakoh
Guindo Merepen Dite Agnes
Soulama Alamissa
Osei-Wusu Stephen
Domfeh Seth Agyei
Addo Samuel Ofori
Osirike Pearl Ihuoma
Morang'a Misita Collins
Sumabe Balagra Kasim
Chirawurah Jersley
Ansah Felix

WELLCOME TRUST DELTAS PROJECT

WACCBIP-DELTAS GRADUATE INTERNSHIP PROGRAMME

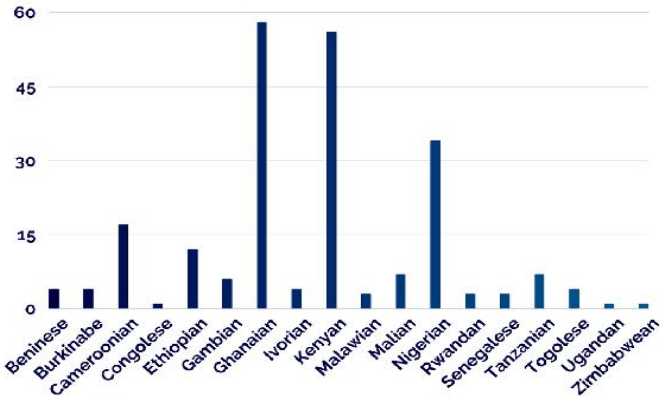
COHORT 1

Adade Emmanuel Edem
Adjei Rita Owusu
Amaning Pernell Asare
Ammah-Tagoe David
Ayee Richmond
Boateng Kyerewaa Akuamoah
Dogbe Magdalene
Mohammed Latifatu
Nanor Marian Namle
Opoku Grace
Oworae Kwadwo
Quansah Evelyn Baaba

COHORT 2

Adams Adjoa Otubea
Aklamati Diana Precious
Amakye Winifred Ruby Korang
Amaniampong Bismarck Kyei Baffour
Ampiah Milicenta Kukua Mbeaba
Appah Anna
Appiah Etwi Barimah
Aryee Ebenezer Nii Adama
Doamekpor MaryMegumi Eyram Abla
Fuseini Mohammed-Sherrif Napari
Ghartey Georgia Naa Korkoi
Mensah Isaiah Kofi Deladem
Osei Godfred Kwame
Quaye Emmanuel Kofi
Quaye Joanna Afokai
Salu Philip
Suurbaar Jonathan
Tei-Maya Frederick Mate

WACCBIP-DELTAS PhD PROGRAMME

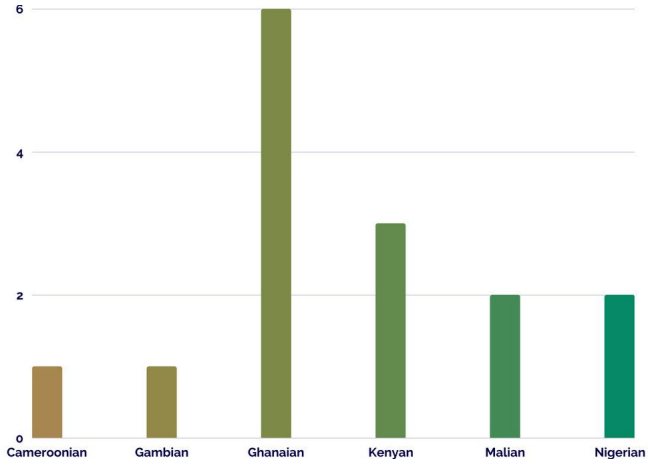


206
APPLICATIONS

18
NATIONALITIES

154(75%)

52(25%)



15
SELECTED

6
NATIONALITIES

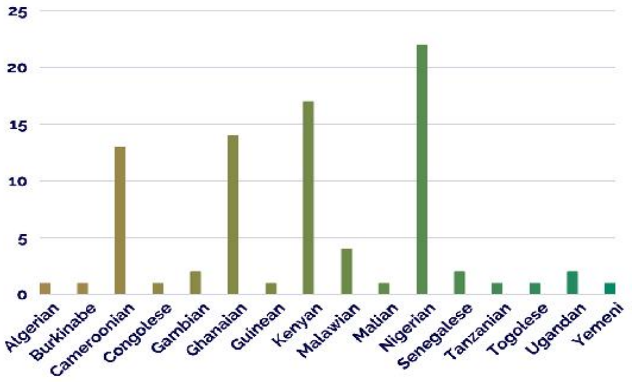
8(53%)

7(47%)

WACCBIP-DELTAS PhD FELLOWS

NAME	GENDER	NATIONALITY	HOST
Mbye Haddijatou	Female	Gambian	MRC, Gambia
Majidah Hamid-Bukola Adiamoh	Female	Nigerian	MRC, Gambia
Samuel Mawuli Adadey	Male	Ghanaian	UCT, South Africa
Dominic Selorm Yao Amuzu	Male	Ghanaian	WACCBIP, Ghana
Arnaud Jonas Kengne-Ouafo	Male	Cameroonian	WACCBIP, Ghana
Nancy Kemuma Nyakoe	Female	Kenyan	WACCBIP, Ghana
Beatrice Mukami Muriuki	Female	Kenyan	KEMRI, Kisumu, Kenya
Karamoko Niaré	Male	Malian	KEMRI, Killifi, Kenya
Collins Moranga	Male	Kenyan	WACCBIP, Ghana
Domfeh Seth Agyei	Male	Ghanaian	WACCBIP, Ghana
Chirawurah Jersley	Male	Ghanaian	WACCBIP, Ghana
Owusu Irene Amoakoh	Female	Ghanaian	WACCBIP, Ghana
Pearl Osrike	Female	Nigerian	WACCBIP, Ghana
Agnes Guindo	Female	Malian	MRTC, Mali

WACCBIP-DELTAS POSTDOCTORAL PROGRAMME

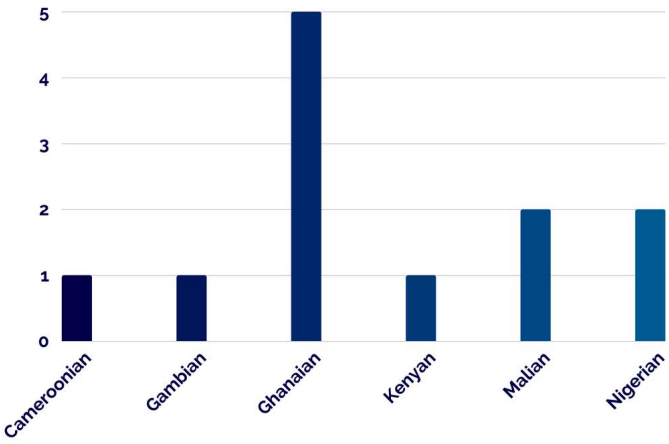


83
APPLICATIONS

16
NATIONALITIES

62(75%)

21(25%)



12
SELECTED

6
NATIONALITIES

8(67%)

4(33%)

WACCBIP-DELTAS POSTDOCTORAL FELLOWS

NAME OF FELLOW	GENDER	NATIONALITY	TRAINING INSTITUTION	DATE OF ENTRY	TITLE OF PROPOSED STUDY
Dr. Yaw Aniweh	Male	Ghanaian	WACCBIP-BCMB, University of Ghana	April 1, 2016	Unravelling the molecular players during *Plasmodium falciparum* invasion of erythrocytes
Dr. Jewelna Akorli	Female	Ghanaian	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
Dr. Adwoa Asante-Poku Wiredu	Female	Ghanaian	WACCBIP-BCMB/ NMIMR, University of Ghana	April 1, 2016	Host susceptibility to Tuberculosis (TB) in Ghana
Dr. Kolapo Oyebola	Male	Nigerian	Medical Research Unit, Fajara, the Gambia	April 1, 2016	Genetic variations and differential immunological response to malaria chemotherapy in variably exposed West African populations
Dr. Modibo Sangare	Male	Malian	MRTC at the University of Science, Techniques, and Technology, Mali	April 1, 2016	Epidemiology, clinical neurophysiology, and molecular genetic studies of Autism Spectrum Disorders in Mali
Dr. Seidina A. S. Diakite	Male	Malian	MRTC at the University of Science, Techniques, & Technology, Mali	April 1, 2016	Genomic variation in *P. falciparum* and pharmacogenomics of antimalarial drugs in Mali
Dr. Valentina Josiane Ngo Bitoungui	Female	Cameroonian	University of Cape Town, South Africa	April 1, 2016	Genetic factors associated with cardiovascular diseases in Cameroonian sickle cell disease patients
Dr. Daniel Muthui Kiboi	Male	Kenyan	Kenya Medical Research Institute, Kilifi, Kenya	May 1, 2016	Validation of candidate mutations in *Plasmodium* for resistance to the antimalarial drugs Piperaquine and Lumefantrine

NAME OF FELLOW	GEN-DER	NATION-ALITY	TRAINING INSTITUTION	DATE OF ENTRY	TITLE OF PROPOSED STUDY
Dr. Emmanuel Amlabu	Male	Nigerian	WACCBIP-BCMB, University of Ghana	Nov. 1, 2016	New Generation Malaria Vaccine Development
Dr. Lily Paemka	Female	Ghanaian	WACCBIP-BCMB, University of Ghana	July 1, 2017	Characterizing Genetic Breast Cancer Risk Factors in Ghanaian Women
Dr. Saikou Y. Bah	Male	Gambian	WACCBIP-BCMB, University of Ghana	June 1, 2017	Using bioinformatics tools to validate biosig-nature for diagnosis of childhood tuberculosis
Dr. Vincent Amarh	Male	Ghanaian	WACCBIP-BCMB, University of Ghana	January 15, 2018	Development of novel antibiotics targeting the bacterial DNA dou-ble-stand break repair pathway

DESTINATION DATA: WACCCBIP MPHIL COHORT 1 (2014-2016)

NAME OF TRAINEE	DEGREE OBTAINED	CURRENT PLACE OF EMPLOYMENT/STUDY
Stephen Osei-Wusu	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, West African Centre for Cell Biology of Infectious Pathogens , University of Ghana
Deletsu Selase	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Tokyo Medical and Dental University, Japan
Jersley D. Chirawurah	MPhil Molecular Cell Biology of Infectious Diseases	PhD student,West African Centre for Cell Biology of Infectious Pathogens, University of Ghana
Victor Letsa	MPhil Molecular Cell Biology of Infectious Diseases	
Christiana Ofori Onwona	MPhil Molecular Cell Biology of Infectious Diseases	Senior Research Assistant, Noguchi Memorial Institute for Medical Research, University of Ghana
Deladem Kofi Amekudzi	MPhil Molecular Cell Biology of Infectious Diseases	
Edmond A. Atindaana	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Department of Microbiology and Immunology, University of Michigan
Zakaria Seidu	MPhil Molecular Cell Biology of Infectious Diseases	Continous Quality Improvement (CQI) Project Manager, WorldVision Ghana, GI-WASH, Savelugu
Joshua Kuleape	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Tokyo Medical and Dental University, Japan
Ademolue Temitope Wilson	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Instituto Gulbenkian de Ciência, Portugal
James Leslie Myers-Hansen	MPhil Molecular Cell Biology of Infectious Diseases	Senior Research Assistant, Noguchi Memorial Institute for Medical Research, University of Ghana
Sandra Adelaide King	MPhil Molecular Cell Biology of Infectious Diseases	Research Assistant, West African Centre for Cell Biology of Infectious Pathogens, University of Ghana

NAME OF TRAINEE	DEGREE OBTAINED	CURRENT PLACE OF EMPLOYMENT/STUDY
Addo Ofori Samuel	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, West African Centre for Cell Biology of Infectious Pathogens , University of Ghana
Addo-Gyan K. Daniel	MPhil Molecular Cell Biology of Infectious Diseases	Senior Research Assistant, Noguchi Memorial Institute for Medical Research, University of Ghana
Abana David	MPhil Molecular Cell Biology of Infectious Diseases	Analyst, Food and Drugs Authority, Ghana
Abass Adiza	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Tokyo Medical and Dental University, Japan
Bakari Soale Majeed	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Department of Cell & Developmental Biology, University of Würzburg, Germany
Emmanuel Ayisi Manu	MPhil Molecular Cell Biology of Infectious Diseases	Coordinator, Pentecost Students Association (PENSA), Ghana
Patrick Tshibangu	MPhil Molecular Cell Biology of Infectious Diseases	
Precious Cramer	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, University of Freiburg, Germany
Buatsi Esenam Dzifa	MPhil Molecular Biology	Sales representative, Inqaba Biotec West Africa Ltd
Maame Esi Acquah	MPhil Molecular Biology	Research Assistant, Water Research Institute, Council for Scientific and Industrial Research
Frederick Ayertey	MPhil Biochemistry	Research Assistant, Centre for Plant Medicine Research, Mampong-Akwapim

DESTINATION DATA: WACCCBIP MPHIL COHORT 2 (2015-2017)

NAME OF TRAINEE	DEGREE OBTAINED	CURRENT PLACE OF EMPLOYMENT/STUDY
Isaac Tuffour	MPhil Biochemistry	Senior Research Assistant, Noguchi Memorial Institute for Medical Research, University of Ghana
Felix Alexander Ayelazuno	MPhil Molecular Cell Biology of Infectious Diseases	Research Assistant, Navrongo Health Research Centre
Ranee Aflakpui	MPhil Molecular Cell Biology of Infectious Diseases	PhD student, Albert Einstein College of Medicine NY-USA
Essel Charles-Chess	MPhil Molecular Cell Biology of Infectious Diseases	Biomedical Scientist, LEKMA Hospital, Ghana
Priscilla Abena Akyaw	MPhil Molecular Biology	Senior Research Assistant, Noguchi Memorial Institute for Medical Research, University of Ghana
Selassie Louis Ameke	MPhil Molecular Cell Biology of Infectious Diseases	Principal Biomedical Scientist and Head of Biomedical Laboratory Department, Ho Municipal Hospital, GES
Pheonah Badu	MPhil Molecular Cell Biology of Infectious Diseases	Research Assistant, Noguchi Memorial Institute for Medical Research
Ernestine Kubi	MPhil Molecular Biology	Senior Research Assistant, Noguchi Memorial Institute for Medical Research
Shirley Victoria Simpson	MPhil Molecular Cell Biology of Infectious Diseases	Senior Research Assistant, Noguchi Memorial Institute for Medical Research
Diana Asema Asandem	MPhil Molecular Cell Biology of Infectious Diseases	Research Assistant, Noguchi Memorial Institute for Medical Research, University of Ghana
Raphael Lartey Abban	MPhil Molecular Cell Biology of Infectious Diseases	University of Cape Coast

NAME OF TRAINEE	DEGREE OBTAINED	CURRENT PLACE OF EMPLOYMENT/STUDY
Justice Adzigbe	MSc. Biochemistry	Junior High School teacher , Victory Presbyterian Church
Sedem Agbemafle	MPhil Molecular Cell Biology of Infectious Diseases	Awaiting graduation
Caroline Boatemaa Agyare	MPhil Molecular Cell Biology of Infectious Diseases	University of Cape Coast
Godwin Nsoh Anabire	MPhil Molecular Cell Biology of Infectious Diseases	Research Assistant, WACCBIP/ University of Development Studies
Elizabeth Laryea-Akrong	MPhil Molecular Cell Biology of Infectious Diseases	Awaiting graduation
Musah Osei	MPhil Molecular Cell Biology of Infectious Diseases	Research Assistant, Kintampo Health Research Centre
Emmanuel Opoku Antwi	MSc Biochemistry	Awaiting graduation
Sylvester Languon	MSc Biochemistry	Research Assistant, West African Centre for Cell Biology of Infectous Pathogens
Kwasi Oduro Yeboah	MPhil Molecular Cell Biology of Infectious Diseases	G2 Medical Laboratory Services at 37 Military Hospital

NEW GRANTS WON BY FACULTY

Title	Brief Description of the Award	WACCBIP Faculty Awarded	Grant PI	Amount and Period
Hearing Impairment Genetics Studies in Africa (HI-GENES Africa)	AESA H3Africa initiative grant has been awarded to researchers to identify genes that cause non-syndromic hearing loss in African populations	Gordon Awandare	Ambroise Wonkam	$3,294,140 2017-2021
Hearing Impairment Genetics Studies in Africa (HI-GENES Africa)	National Institutes of Health (NIH) grant has been awarded to researchers to identify genes that cause non-syndromic hearing loss in African populations	Gordon Awandare	Ambroise Wonkam	$1,249,097 2017–2022
Characterization of wild trypanosome coats towards the development of an animal African trypanosomiasis vaccine	The Willowcroft Foundation has awarded a grant to the John Hopkins University, USA to characterize wild trypanosome coats towards the development of a vaccine for animal African trypanosomiasis	Theresa Manful Gwira	Monica Mugnier	$50,000 2017-2018
Accelerating the development of a malaria vaccine for Africa project	DANIDA has awarded researchers a grant to undertake phase two of a project to develop a malaria vaccine	Kwadwo Koram Gordon Awandare Michael Ofori	Lars Hviid	DKK 10,000,000 2018-2020

Title	Brief Description of the Award	WACCBIP Faculty Awarded	Grant PI	Amount and Period
NIHR Global Health Research Group on genomic surveillance of malaria in West Africa at the Wellcome Trust Sanger Institute	NIHR Global Health Research Programme has awarded a grant to establish local capacity in West Africa for genomic surveillance of malaria parasites and vectors, and to develop analytical outputs that will be of practical value to National Malaria Control Programmes (NMCPs) in planning effective interventions in the face of increasing drug and insecticide resistance.	Gordon Awandare Kwadwo Koram Lucas Amenga-Etego	Dominic Kwiatkowski	£1,999,179 2018-2021
PAMGEN: Genetic interactions between human populations and malaria parasites in different environmental settings across Africa	AESA H3Africa initiative grant has been awarded to researchers to study how genetic changes in humans and malaria parasites impact on the disease in individuals and communities in sub-Saharan Africa.	Lucas Amenga-Etego	Alfred Amambua Ngwa	$3,122,568 2018-2020

PUBLIC ENGAGEMENT ACTIVITIES

COMMUNITY TB & HEALTH SCREENING OUTREACH EVENTS

INTERNATIONAL WOMEN'S DAY 'GIRLS IN SCIENCE' PEER-MENTORING EVENT

'THE HORIZON' RADIO SHOW APPEARANCES BY WACCBIP FACULTY

TIBA COMMUNITY DURBAR, EWIM, CAPE COAST

WORLD MALARIA DAY PUBLIC FORUM, CAPE COAST

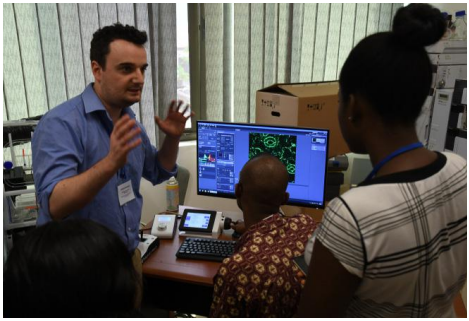
SENIOR HIGH SCHOOLS OUTREACH TOUR


NOTRE DAME SEMINARY SENIOR HIGH SCHOOL


STUDY OF MOLECULAR MODEL
WACBIP

WACCBIP EVENTS

ASCB-OXFORD WORKSHOP



WACCBIP-NCHS WORKSHOP FOR BIOMEDICAL SCIENTISTS

WACCBIP-CEM (QUEEN'S UNIVERSITY) COLLABORATIVE SYMPOSIUM

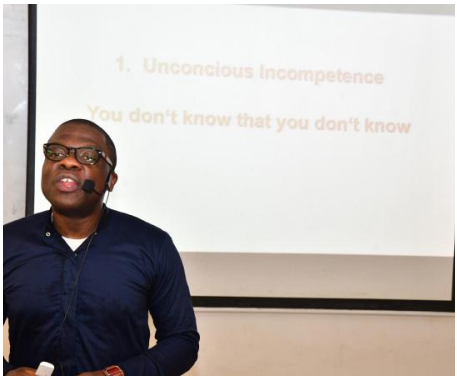
BURULI ULCER TRAINING WORKSHOP, JACOBU, ASHANTI REGION

COMMISSIONING OF NEW WACCBIP BUILDING


WACBIP


WACCBIP-Wellca
2015: Wellcome Trust DELTAS provides addition
Strengthen research
Expand regional network beyond West Africa, to inclu
Develop a post-doctoral programme for leadership
newly qualified PhDs
Provide additional PhD fellowships
Student visitor programme – students spend 6-months
WACBIP

VISITING FELLOWS LECTURES



WACCBIP RESEARCH CONFERENCE 2018 03

DIRECTOR'S MESSAGE

Prof. Gordon Awandare

Director

It is a great pleasure to welcome you to the Third Annual WACCBIP Research Conference.

In response to the feedback we received from participants of the previous two conferences, we have expanded the programme to three days to allow more time for interactions and more presentations from our fellows. This year's conference is particularly special because we are holding it in our own conference hall. This brings us great pride for how far we have come, and we are immensely grateful to our funding partners and the University Management for their support.

This new building extension was funded by the Government of Ghana through the World Bank African Centres of Excellence (ACE) project, and the furniture and information communication technology (ICT) infrastructure were provided through the Wellcome Trust/African Academy of Sciences (WT/AAS) Developing Excellence in Leadership, Training and Science (DELTAS) Africa initiative. The building provides critical facilities to complement the existing facilities in the main Biochemistry building, which was mainly designed to provide laboratories and office spaces. The new building, therefore, provides much needed classroom and conference facilities that are befitting of a Centre of Excellence.

We are also very excited that two pieces of equipment that are key to our research operations were finally installed. These are the confocal microscope (Zeiss LSM 800 with Airyscan), which is the most advanced in sub-Saharan Africa, and the 428 TB High Performance Computing unit which represents the biggest bioinformatics facility in the country. We hope that WACCBIP fellows, faculty and collaborators will make maximum use of these facilities to generate the desired impact on the scientific quality of our research.

The overall status of implementation of our training programmes are on track. Since 2014, we have enrolled 90 Master's students, 50 PhD students, and 12 Postdoctoral fellows from 10 African countries, through our WACCBIP-ACE and WACCBIP-DELTAS programmes. These are some of the best young scientists on the continent, and WACCBIP is very proud to be supporting them to develop their talents to become research leaders. This month marks a significant milestone for WACCBIP, as our first cohort of PhD students will be submitting their theses. Our first two cohorts of Master's students have completed, and the third cohort will submit their theses this month. We wish all our final year students success in completing their theses and in the oral defense that follows.

The research output of our fellows continues to increase, and they are beginning to produce publications in high impact journals. A lot of this research will be showcased in this conference through oral presentations and posters. Of particular note, we are proud of the work on malaria vaccine discovery that has resulted in the characterization of novel blood stage antigens, which have the potential to be vaccine candidates. Some of this work was published in the Journal of Infectious Diseases. Also, the investigations into the etiology of acute febrile illness have produced information that has significant public health implications. The study has reported the detection of locally transmitted dengue virus infections in children in Accra, with genomic analyses demonstrating that the virus was identical to the one reported in an outbreak in Burkina Faso. These findings have been reported to the Ministry of Health and the Ghana Health Service, and also now published in the Emerging Infectious Diseases journal. We hope the health authorities in Ghana are taking the necessary steps to increase surveillance.

So, I am very glad that all of you have taken the time to join us for this year's conference and to share in our successes as well as contribute your suggestions to help us improve further. Some of you are coming for the third time and we really appreciate your commitment and enthusiasm. We are also extremely honoured to welcome many of you for the first time, and we hope that you will be inspired by what you see and will come back again and again.

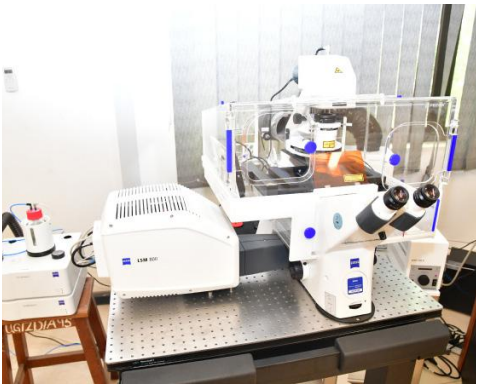
Finally, I want to thank the members of our team, which we call the 'WACCBIP Machine', consisting of our core management group and the support staff at the secretariat and beyond. These people are all superstars and the real power behind our progress.

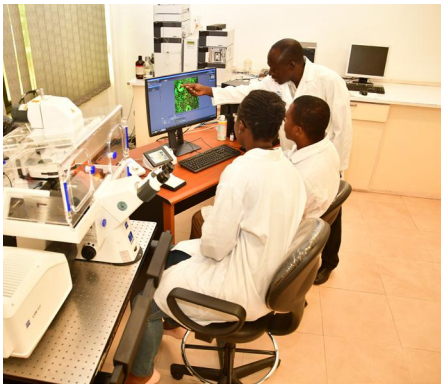
I wish you all a wonderful Science festival during these three days and beyond.

Gordon Awandare

Dell EMC High Performance Computing System

Zeiss LSM 800 Confocal Microscope with Airyscan





New WACCBIP Office Complex

Conference Chairs: Gordon Awandare, Lydia Mosi, Patrick Arthur and Kirk Deitsch

DATE	TIME	TOPICS	PRESENTER
	08.30am – 09.45am	Day 1 – Session 1: OPENING CEREMONY	
18th July	08.30am – 08.45am	• Arrival of Participants and registration • Call to order	Dr. Lydia Mosi, HOD, BCMB
	08.45am – 09.45am	• Welcome remarks and introduction of Chairman • Chairman's remarks - Pro-Vice Chancellor, Research, Innovation & Development • Brief remarks by: - Chair of WACCBIP International Advisory Board - Executive Secretary, National Council for Tertiary Education - The Country Director, World Bank, Ghana Office - President of Pharmaceutical Society of Ghana • Keynote address by Minister of Health • Official opening of conference by Minister of Education	• Prof. Gordon Awandare, Director of WACCBIP • Prof. Francis Dodoo • Prof. Keith Gull • Prof. Mohammed Salifu • Mr. Henry Kerali • Dr. Ben Botwe • Hon. Kwaku Agyeman-Manu • Hon. Matthew Opoku Prempeh
	09.45am – 10.15am	Photograph session and Coffee break	
		KEYNOTE LECTURE 1	
	10.15am – 11.00am	Towards shutting the door on malaria: red blood cell determinants of *Plasmodium* infection	• Manoj T. Duraisingh
	11:00am – 12:20am	Day 1 – Session 2: Diagnostics and Biomarker Discovery (1/1)	CHAIRS – Rachel Simmonds/ Mark Carrington
		PLENARY TALK 1	
	11.00am – 11.20pm	Mitigating the public health threat posed by emerging viruses	• Edward Wright
		FELLOWS SESSION	
	11.20am – 12.20pm	1. Pathogen and biomarker discovery among Ghanaian children presenting with acute febrile illness 2. Diversity of Emerging GII.17 Norovirus strain in pediatric acute gastroenteritis	• Nicholas Amoako • Belinda L. Lartey

		3. Development of a simple, low-cost amperometric assay for noninvasive monitoring of salivary glucose	• Francis D. Krampa
		4. Detection and molecular characterization of group A rotaviruses in a sanitary environment in the greater Accra region of Ghana	• Raymond Lovelace Adjei
	12.20pm – 01.20pm	**Lunch Break**	
	01:20pm – 03:15pm	Day 1 – Session 3: Human Genetics	CHAIRS – Theresa Gwira/ Kirk Deitsch
		PLENARY TALK 2	
	01.20pm – 01.40pm	From single-cell transcriptomics to the dynamics of differentiation	Ábel Vértesy
		FELLOWS SESSION	
	01.40pm – 02:55pm	5. IQGAP1 and pAKT are overexpressed and co-localized on tricellular junctions in invasive gastric adenocarcinoma	• Emmanuel A. Tagoe
		6. Assessing naturally acquired immune response and malaria treatment outcomes in Lagos, Nigeria	• Kolapo M. Oyebola
		7. High-throughput RFLP Assay for identification of glycophorin B deletion variants	• Dominic Selorm Yao Amuzu
		8. *GJB2* and *GJB6* mutations in non-syndromic childhood hearing impairment in Ghana.	• Samuel M. Adadey
		9. Evaluating the feasibility of Autism spectrum disorders research in Mali, West Africa	• Modibo Sangare
		PLENARY TALK 3	
	02.55pm – 03:15pm	Tantalizing dilemma in genetics causality from disease scoring statistics	• Emile R. Chimusa
	03.15pm – 03.45pm	Coffee Break	
	03.45pm – 05.25pm	Day 1 – Session 4: Drug Resistance and Drug Discovery (1/2)	CHAIRS – Alice Telesnitsky/Seth Owusu-Agyei
		PLENARY TALK 4	
	03:45pm – 04.05pm	Combinatory approaches towards useful structures of HIV integrase	Peter Kojo Quashie
		FELLOWS SESSION	•
	04.05pm – 05.05pm	10. Discovery and development of novel antifungal compounds from marine endophytic fungi sources	• Ethel Blessie

		11. Effects of iron chelators on bloodstream forms of *trypanosoma brucei*	• Cynthia Mmalebna Amisigo
		12. Analysis of antimicrobial resistance phenotypes in *Candida albicans* using modulators of *Mdr/Cdr* gene expression	• Rebecca Yeboah
		13. Molecular markers of *Plasmodium falciparum* drug resistance across two malaria endemic sites in Mali	• Seidina A. S Diakite
		PLENARY TALK 5	
	05.05pm – 05:25pm	Inhibition of gastric H^+/K^+-ATPase and *Helicobacter pylori* growth, and enhancement of mucin activity by a flavonoid-rich fraction of *Dissotis rotundifolia* plant	• Michael Buenor Adinortey
		FEATURE LECTURE 1	
	05.25pm – 05:55pm	PfEMP1-specific immunity to malaria: the current state-of-affairs	• Lars Hviid
	05.55pm – 06:55pm	Networking Cocktail	

DATE	TIME	TOPICS	PRESENTER
		KEYNOTE LECTURE 2	
19th July	09.00am – 09.45am	Mysteries of *Mycobacterium ulcerans* and Buruli Ulcer: tracking Transmission	• Pamela Small
	09.45am – 10.50am	**Day 2 – Session 1: Pathogen Biology and Discovery (1/3)**	**CHAIRS – Linda Amoah/ Julius Hafalla**
		PLENARY TALK 6	
	09.45am – 10.05am	The mechanics of *Plasmodium* merozoite invasion into the human erythrocyte: a balanced parasite-host cell contribution driving entry?	• Jake Baum
		FELLOWS SESSION	
	10.05am – 10.50am	14. Functional insights on the role of *plasmodium falciparum* claudin-like apicomplexan microneme protein (PfCLAMP): an essential gene	• Evelyn Baaba Quansah
		15. The effects of artemisinin-based combination therapy (ACT) on the dynamics of *Plasmodium falciparum, P. malariae* and *P. ovale* infections in Ghana	• Felix Ansah
		16. Transcriptome profiling of *Plasmodium falciparum* parasites from asymptomatic and symptomatic infections	• Daniel Kiboi
	10.50am – 11.20am	Coffee Break	
	11:20am – 12:45pm	Day 2 – Session 2: Pathogen Biology and Discovery (2/3)	CHAIRS – Lydia Mosi/ Sodiomon B. Sirima
		PLENARY TALK 7	
	11.20am –11.40am	Role of Mycobacterium ulcerans toxin, mycolactone, in suppression of Staphylococcus aureus virulence genes	• Heather R. Jordan
		FELLOWS SESSION	
	11:40am – 12:25pm	17. *Plasmodium falciparum* strains spontaneously switch invasion phenotype in suspension culture	• Prince B. Nyarko
		18. Blood donor variability as a modulatory factor in *Plasmodium falciparum* invasion phenotyping assays	• Laty G. Thiam

		19. The functional insight on the role of Plasmodium falciparum ABC-2 like protein on the parasites development	• Yaw Aniweh
		PLENARY TALK 8	
	12:25pm – 12:45 pm	Integrated pathogen load and dual transcriptome analysis of systemic host-pathogen interactions in severe malaria	• Aubrey Cunnington
	12:45pm – 01:45pm	Lunch Break and Poster Viewing	
	01:45pm – 03:10pm	Day 2 – Session 3: Immune Response Mechanisms and Immunogenetics (1/1)	CHAIRS – Atlanta Cook/ Asamoah Kusi
		PLENARY TALK 9	
	01.45pm - 02.05pm	A systems approach reveals immune signature associated with repeated clinical malaria episodes in children	• Yaw Bediako
		FELLOWS SESSION	
	02:05pm – 02:50pm	20. Low dose natural cryptolepine inhibits inflammation through the TLR2-NF-κb pathway 21. Characterization of T cell activation and regulation in children with asymptomatic *Plasmodium falciparum* infection 22. Binding characteristics, transcription profiles and antibody recognition patterns of *Plasmodium falciparum* selected on blood group determinants	• Ahmed Rufai Abdulrahman • Augustina Frimpong • William van der Puije
		PLENARY TALK 10	
	02.50pm - 03.10pm	Structural studies of malaria surface proteins	• Matthew Higgins
	03.10pm - 03.30pm	TURBO TALK	**CHAIRS – Patrick Arthur**
	03.30pm - 04.30pm	Coffee Break and Poster Presentation	
	04:30pm – 05.25pm	Day 2 – Session 4: Vaccine Discovery and Development (1/3)	CHAIRS – Lily Paemka/ Lars Hviid
		PLENARY TALK 11	
	04:30pm – 4.50pm	Understanding the dynamics of malaria transmission in endemic setting	Alfred Tiono
		FELLOWS SESSION	
	4.50pm – 05.05pm	23. Breadth of antibody response is associated with growth inhibitory activity of *Plasmodium falciparum* in semi-immune adults in Ghana	• Henrietta E. Mensah-Brown
		PLENARY TALK 12	
	05.05pm - 05.25pm	Research to policy in Africa: A heightened need for a changing narrative	• Collins Ouma
		FEATURE LECTURE 2	
	05.25pm - 05.55pm	Higher order genome architecture & lncRNAs permit robust transcription of immune genes	• Dr. Stephanie Fanucchi

DATE	TIME	TOPICS	PRESENTER
		KEYNOTE LECTURE 3	
20th July	09.00am – 09.45am	Controlling malaria: an evolutionary arms race	• Dominic Kwiatkowski
	09.45am – 11.15am	Day 3 – Session 1: Pathogen Biology and Discovery (3/3)	CHAIRS – Nancy Duah Quarshie/ Manoj Duraisingh
		PLENARY TALK 13	
	09.45am – 10.05am	Kintampo Health Research Centre: Hub for collaboration in scientific research and capacity building in Ghana	• Kwaku Poku Asante
		PLENARY TALK 14	
	10.05am – 10.25am	Long-distance spatiotemporal transmission patterns of Plasmodium falciparum infections across the Gambia	• Alfred Amambua-Ngwa
		FELLOWS SESSION	
	10.25am – 10.55am	24. Delineating the functions of novel *Plasmodium falciparum* merozoite antigens during erythrocyte invasion and schizont egress	• Emmanuel Amlabu
		25. Superbugs: evolving enemies from hospitals in Ghana	• Isawumi Abiola
		PLENARY TALK 15	
	10.55am – 11.15am	How HIV-1 transcription start sites dictate RNA fates	• Alice Telesnitsky
	11.15am – 11.45am	Coffee Break	
	11:45am – 12:50pm	Day 3 – Session 2: Cell Biology (1/2)	CHAIRS – Dorothy Yeboah-Manu/ Jake Baum
		PLENARY TALK 16	
	11:45am – 12:05pm	The mechanism of action of the Buruli ulcer *Mycobacterium ulcerans* exotoxin mycolactone	• Rachel E. Simmonds
		FELLOWS SESSION	
	12:05pm – 12:50pm	26. Molecular Targets of Iron Binding Phenolic Acids in *Mycobacterium smegmatis* and *Mycobacterium tuberculosis*	• Wilhelmina Anne Mensah
		27. *In vitro* effects of phenolic compounds on *Leishmania donovani*	• Christine Achiaa Antwi

		28. Effects of *Zanthoxylum zanthoxyloides* extracts on African trypanosomes	• Aboagye Kwarteng Dofuor
	12.50pm – 02:00pm	Lunch Break and Poster Viewing	
	02:00pm – 03:05pm	Day 3 – Session 3: Drug Resistance and Drug Discovery (2/2)	CHAIRS – Heather Jordan/ Neils Quarshie
		PLENARY TALK 17	
	02:00pm –02.20 pm	cAMP phosphodiesterases as drug targets in the most neglected parasitic diseases	• Harry P. De Koning
		FELLOWS SESSION	
	02:20pm – 03.05pm	29. *In vitro* mechanistic study of anti-*Leishmania* activity of novel tetracyclic iridoids isolated from *Morinda lucida*	• Faustus A. Azerigyik
		30. Artemisinin resistance associated Falcipain 2 polymorphisms in Ghanaian *Plasmodium falciparum* clinical isolates	• Sena A. Matrevi
		31. Increasing *ex-vivo* tolerance of Gambian *Plasmodium falciparum* isolates to Artemisinin-based combination therapy partner drugs	• Haddijatou Mbye
	03.05pm – 03.35pm	Coffee Break	
	03:35pm – 05.00pm	Day 3 – Session 4: Cell Biology (2/2)	CHAIRS – Pamela Small/ Solomon Ofori-Acquah
		PLENARY TALK 18	
	03.35pm – 03.55pm	Dissecting Epigenetic and Other Cellular Mechanisms at WCCB in Edinburgh	• Robin Allshire
		FELLOWS SESSION	
	03.55pm – 04.40pm	32. Cellulose modified nanocrystals and their cytotoxic effects on selected cell lines	• Nadia K. Amoateng
		33. Fine-tuning targeted therapy in ALK-addicted neuroblastoma: The case for precision medicine	• Joachim T. Siaw
		34. Development of novel antibiotics targeting the DNA double-strand break repair pathway	• Vincent Amarh
		PLENARY TALK 19	
	04.40pm – 05.00pm	In-country next-generation sequencing to support malaria surveillance networks	• Christopher Jacob
		FEATURE LECTURE 3	
	05.00pm – 05.30pm	Glutamine-HSP70: A Novel Therapeutic Target	• Douglas J. Perkins
	05.30pm – 05.40pm	• Conference Evaluation and Closing	• Prof. Gordon Awandare
	7.00pm	Dinner at the forecourt of the Biochemistry Building	

POSTER PRESENTATIONS		
NO.	TITLE	PRESENTER
35	Characterization of the mechanism of action of trypanocidal compounds	Pearl I. Osirike
36	In Silico characterization of a novel *Plasmodium falciparum* merozoite protein	Ojo-ajogu Akuh
37	Understanding resistance to anti-trypanosomal therapeutics used for trypanosome infections in cattle in southern Ghana	William Ekloh
38	Immuno-biology of *Plasmodium falciparum* STEVOR antigens: genetic diversity and gene expression	Jonas A. Kengne-Ouafo
39	Dynamics of cellular immune response over the clinical course of acute *Plasmodium falciparum* infection in children	Nancy Nyakoe
40	Evaluating the antimalarial activity of a natural product, Compound X, against laboratory Strains of *P. Falciparum*	Jersley D. Chirawurah
41	A cell-penetrating APIM peptide exerts anti-mutagenic effect on *E. Coli* MG1655 by inhibiting translesion synthesis	Balagra Kasim Sumabe
42	Investigations into the mechanisms of anti-mycobacterial drug resistance using antipsychotic compounds	Isaac Carilo
43	Interactions of Antimicrobial Compounds with selected drugs used in the Clinical Management of Sickle Cell Disease (SCD)	Leonard Asare
44	Cheminformatics-Based Drug Design Approach for Identification of Natural Product-derived HIV Entry Inhibitors based on Peptidomimetics of Broadly Neutralizing Antibody VRC01	Nneka Ugwu
45	Anti-diabetic effect of probiotics and nutraceuticals in kombucha in alloxan induced diabetic mice	Emmanuel Edem Adade
46	Characterisation of wild trypanosomes cell surface towards vaccine development	Kwadwo Oworae
47	Two Component System of Vibrio cholerae as a Potential Target against Antimicrobial Resistance (AMR)	Isaiah Kofi Mensah
48	Performance of rice and cassava extracts in the reduction of tannins from cashew apple juice	Balali Iddrisu Gadafi
49	Rational approach for inhibitor discovery targeting the energy metabolism pathway of African trypanosomes	Emmanuel Oluwadare Balogun
50	Developing prosthetic materials from reinforced CNC using cyanoacrylate (Super Glue)	Eric W. Gaba
51	Evaluation of genetic diversity and cardiovascular diseases susceptibility of sickle cell disease using single nucleotide polymorphism	Oyawoye F.O.
52	Analysis of natural antibody responses to novel *Plasmodium falciparum* Armadillo repeat proteins	Grace Opoku

POSTER PRESENTATIONS		
NO	TITLE	PRESENTER
53	Investigating the Redox Activity of Antifungal Drugs on S. *Cerevisiae* using Electrochemical Detection and Cell Viability Studies	Thomas Y A Essel
54	Drug Delivery Capabilities of Funtionalized Chitosan Using Two Dyes	Grace P Cobbold
55	Confirmation of Dengue cases during the outbreak in Burkina Faso, 2017	Amadou DICKO
56	Larvicidal activity of crude extracts of *11sterace 11sterace* less *(11steraceae)* against the *anopheles gambiae* in bobo-dioulasso, burkina faso	Aboubakar soma
57	Archaeology and medical practices of obosomase and nakpanduri practical implications	Marie-Pearl O. Seniagya
58	Norovirus culture: a review of the challenges and the prospects	Irene Amoakoh Owusu
59	Detection of Dugbe virus from ticks in Accra, Ghana	Charlotte Adwoa Addae
60	Effects of immune checkpoint molecules on disease progression, persistence and latency in HIV-infection	Darius N.K Quansah
61	Deciphering the association of a novel *Plasmodium falciparum* exported protein with parasite-induced structures	Philip Ilani
62	Investigation into intra-species indoor and outdoor resting behaviour in malaria vectors	Majidah Hamid-Adiamoh
63	Impact and Ecology of *Streptococcus infantarius* subsp. *Infantarius* in the milk value chain in Northern Côte d'Ivoire	Aimé Roland Sanhoun
64	Investigating determinants of asymptomatic *Plasmodium falciparum* infections in a high endemic area of Ghana	Mubarak Abdul-Rahman
65	PfRh2b structural polymorphism: its frequency and relation with malaria endemicity in Ghana	Jonathan Suurbaar
66	Investigating the Effect of Organic Extracts of *Dioclea reflexa* on Cancer and Normal Cells Using Electrochemical Detection and Cell viability Studies	Albert Koomson
67	Species distribution and insecticide resistance status of Anopheles mosquitoes from Cape Coast and its implication on malaria control	Andreas Kudom
68	Dynamics of *Vibrio cholerae* virulence factors associated with diarrhoea outbreaks in Ghana	Emelia Danso

KEYNOTE LECTURES & PROFILES OF SPEAKERS

KEYNOTE LECTURE 1

18th July, 2018 || 10:15 a.m. - 11:00 a.m.

Towards shutting the door on malaria: red blood cell determinants of *Plasmodium* infection

Dr. Manoj T. Duraisingh
Harvard T. H. Chan School of Public Health
mduraisi@hsph.harvard.edu

The human red blood cell is numerically the most abundant eukaryotic cell of the human body and the home of *Plasmodium* parasites during clinical malaria infections. Mutations in red blood cell hemoglobin and surface proteins have long been shown to protect against malaria infection. Genetic analysis of the host cell is challenging due to the lack of a nucleus in the highly differentiated red blood cell. Work within the Duraisingh lab has focused on identifying critical molecular determinants required by the malaria parasites, *Plasmodium falciparum* and *Plasmodium vivax*, to successfully invade and grow within red blood cells. An unbiased RNAi-based forward genetic screen of the 'RBCome' has identified numerous essential and novel red blood cell determinants that likely define different steps in the parasite invasion process of red blood cells. A comprehensive understanding of the molecular basis of *Plasmodium spp.* invasion will reveal new biology and help to inform therapeutic development.

Dr. Manoj Duraisingh

Professor, Harvard School of Public Health, Boston, USA

Associate Member, Broad Institute of MIT and Harvard

Project Leader, MESA International Center for Excellence in Malaria Research

Dr. Duraisingh has been at the Harvard School of Public Health since 2002, and is the John Laporte Given Professor in the Department of Immunology and Infectious Diseases. He is also an Associate Member at the Broad Institute. He obtained a B.A. degree in Biochemistry from the University of Oxford, and M.Sc and Ph.D. degrees in Molecular Parasitology from the London School of Hygiene and Tropical Medicine, conducting research on the molecular basis of drug-resistance in the malaria parasite.

Dr. Duraisingh then pursued postdoctoral research in molecular parasitology at the Walter and Eliza Hall Institute, Melbourne, Australia, studying fundamental parasitic processes of host cell invasion and immune evasion by malaria parasites.

Dr. Duraisingh's research programme at the HSPH focuses on the biology of host-parasite interactions in malaria. His laboratory develops and applies the latest technologies associated with *Plasmodium spp.* and red blood cell molecular genetics to study the critical interactions between the human red blood cell and the malaria parasite. Significant efforts are being made towards establishing *in vitro* blood-stage culture and genetic systems for the study and transmission of other human *Plasmodium* parasites, including *P. vivax* and *P. knowlesi*.

Dr. Duraisingh is also engaged in collaborative studies in malaria-endemic areas, particularly in India, where he has focused on the biology and pathogenesis of *P. vivax* and *P. falciparum* parasites in natural populations.

KEYNOTE LECTURE 2

19th July, 2018 || 9:00 a.m. - 9:45 a.m.

Mysteries of *Mycobacterium ulcerans* and Buruli ulcer: tracking transmission

Heather Jorden, Eric Benbow, Esai Anaganou, & Pamela L.C. Small
Mississippi State, Michigan State, Benin Buruli ulcer Control, University of Tennessee
musa.mhlanga@uct.ac.za

Environmental pathogens such as Yersinia pestis, and Clostrium tetani cause serious disease yet only accidentally infect a human host. The disappearance of the human species from the earth, would have little impact on the survival of these pathogens. Mycobacterium ulcerans, the causative agent of Buruli ulcer is such a pathogen. Although the epidemiology of Buruli ulcer in humans is reasonably well understood, the epidemiology of M. ulcerans in the environment remains a mystery. In the last ten years we have focused our research efforts on mapping and understanding the distribution of M. ulcerans in the environment in rural Benin. Results from these studies show that the presence of M. ulcerans in the environment is closely associated with human disease at the hamlet level. At small scale, M. ulcerans is highly associated with aquatic habitats. M.ulcerans DNA was detected in 51% of aquatic samples (17-100%) whereas detection from terrestrial samples taken from the same village was 5% (Range 0-18%). M.ulcerans DNA was rarely detected in samples collected within a village proper, but was abundant in agricultural spaces peripheral to a village. Finally, we found a strong association between the presence of M.ulcerans DNA in certain environments peripheral to a village where human activity was high. Thus despite the fact that human to human transmission of M.ulcerans is rare, the interaction of humans with the environment may play an important role in the ecology of M. ulcerans.

Prof. Pamela Small

Professor Emeritus, Department of Microbiology
University of Tennessee, Knoxville

Professor Pamela Small is a Professor Emeritus of Microbiology at the Department of Microbiology of the University of Tennessee in Knoxville, USA. She holds a PhD in Microbiology from Stanford University, where she also completed her postdoctoral training in 1986.

Professor Small conducts research on Buruli ulcer, with specific focus on the pathogenesis of *Mycobacterium ulcerans* infection.

Professor Pam Small and her research group are part of a 7-country consortium which has been awarded a 1 million dollars per year for three years to conduct research on Buruli Ulcer, awarded by the Optimus Foundation. In addition, the McCord Research Foundation recently announced a $25,000 grant to be awarded to Professor Small for studies on Buruli Ulcer. The title of her part of this proposal is "Transmission of Buruli ulcer from the environment to humans."

KEYNOTE LECTURE 3

20th July, 2018 || 9:00 a.m. - 9:45 a.m.

Controlling malaria: an evolutionary arms race

Dominic Kwiatkowski
Wellcome Sanger Institute and University of Oxford
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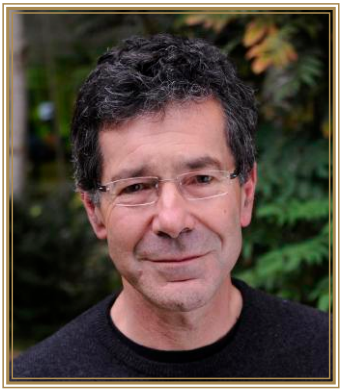
Malaria is a fight for survival involving humans, *Plasmodium* parasites and *Anopheles* mosquitoes. By integrating new genomic technologies into malaria epidemiology, we are learning about the molecular machinery of this evolutionary arms race. This talk will present recent findings on the role of structural variation in the human genome in resistance to severe malaria; on the current outbreak of multidrug resistant *P. falciparum* in Southeast Asia; and on the spread of insecticide resistance in African malaria vectors. I will discuss what needs to be done to translate this rapidly advancing area of genomic technology and evolutionary biology into powerful new surveillance tools for malaria control and elimination.



Prof. Dominic Kwiatkowski

Lead, MRC Centre for Genomics and Global Health, Oxford University

Programme Lead, Parasites and Microbes Programme, Wellcome Sanger Institute

Professor Dominic Kwiatkowski leads the Parasites and Microbes Programme at the Wellcome Sanger Institute, and the MRC Centre for Genomics and Global Health at Oxford University. The main focus of his current work is to translate genomics and computational technologies into practical tools for disease control and elimination in the developing world.

Dominic trained as a paediatrician in London and in molecular immunology in Boston before joining the MRC Labs in The Gambia in 1986. The first part of his research career focused on understanding the pathogenesis and improving the clinical management of severe malaria in African children. In 1996, he started a programme of multicentre clinical studies of malaria that have led to fundamental discoveries about the underlying biology, including the recent discovery that structural variants of host cell invasion receptors cause resistance to disease. He now leads large international collaborations to characterise the genomic diversity of parasite and mosquito populations around the world that are yielding deep insights into the evolutionary biology of drug and insecticide resistance with practical implications for disease control.

In 2005, Dominic founded MalariaGEN, a data-sharing network that has fostered productive research collaborations in over 40 malaria endemic countries, and has become a model for equitable sharing of genetic data and research capacity-building in resource-poor settings.

FEATURE LECTURES

FEATURE LECTURE 1

20th July, 2018 || 5:25 p.m. - 5:55 p.m.

PfEMP1-specific immunity to malaria: the current state-of-affairs

Lars Hviid

Centre for Medical Parasitology, University of Copenhagen and Rigshospitalet, Copenhagen, Denmark

lhviid@sund.ku.dk

The highly polymorphic protein family PfEMP1 is a key virulence factor of *Plasmodium falciparum* malaria parasites. Members of the PfEMP1 family are expressed on the surface of the infected erythrocytes, where they mediate adhesion of the infected erythrocytes in various tissues by binding to a range of host endothelial receptors. This can lead to inflammation and circulatory disturbances, which can be life-threatening. Antibody with specificity for PfEMP1 antigens is a central component of naturally acquired immunity to *P. falciparum* malaria. Recent advances in the understanding of the role of PfEMP1 and PfEMP1-specific immunity in acute and chronic infections, as well as of the molecular interactions between PfEMP1 molecules and their cognate receptors, is guiding efforts to prevent and revert key processes in malaria pathogenesis, including vaccination against specific forms of severe disease such as placental and cerebral malaria. In this presentation, I will provide an overview of the current state-of-affairs on this topic.

FEATURE LECTURE 2

20th July, 2018 || 5:00 p.m. - 5:30 p.m.

Glutamine-HSP70: a novel therapeutic target

Douglas J. Perkins
Director and Professor of Medicine, University of New Mexico, Albuquerque, New Mexico, USA
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Severe malarial anemia (SMA) is the most common life-threatening form of severe malaria in holoendemic *Plasmodium falciparum* transmission regions, and primarily occurs in children less than five years of age due to their immune-naïve status. The pathophysiological basis of SMA is multifactorial with genetic variation, parasite virulence, and environmental factors all playing important roles. Profoundly low Hb levels in SMA result from hemolysis of uninfected erythrocytes, apoptosis of non-parasitized erythrocytes, splenic retention of erythrocytes, structural and functional impairment of erythrocytes, enhanced erythrophagocytosis, and *P. falcipurum*-mediated supression of erythropoiesis. Exploration of molecular pathways through global gene expression profiling and a genome-wide association study identified heat shock protein (Hsp) 70 as an important gene in SMA pathogenesis. Hsp70 is a ubiquitous chaperone that regulates Nuclear Factor-kappa B (NF-B) signaling, and production of pro-inflammatory cytokines known to be important in malaria pathogenesis. Glutamine (Gln) is a conditionally essential amino acid that up-regulates Hsp70, prevents oxidative stress, and serves as a precursor for other amino acids that are critical during states of physiological stress. Validation experiments carried out in 1,654 Kenyan children revealed Severe malarial anemia (SMA) is the most common life-threatening form of severe malaria in holoendemic *Plasmodium falciparum* transmission regions, and primarily occurs in children less than five years of age due to their immune-naïve

status. The pathophysiological basis of SMA is multifactorial with genetic variation, parasite virulence, and environmental factors all playing important roles. Profoundly low Hb levels in SMA result from hemolysis of uninfected erythrocytes, apoptosis of non-parasitized erythrocytes, splenic retention of erythrocytes, structural and functional impairment of erythrocytes, enhanced erythrophagocytosis, and *P. falcipurum*-mediated supression of erythropoiesis. Exploration of molecular pathways through global gene expression profiling and a genome-wide association study identified heat shock protein (Hsp) 70 as an important gene in SMA pathogenesis. Hsp70 is a ubiquitous chaperone that regulates Nuclear Factor-kappa B (NF-B) signaling, and production of pro-inflammatory cytokines known to be important in malaria pathogenesis. Glutamine (Gln) is a conditionally essential amino acid that up-regulates Hsp70, prevents oxidative stress, and serves as a precursor for other amino acids that are critical during states of physiological stress. Validation experiments carried out in 1,654 Kenyan children revealed that genetic variation in Hsp70 influences susceptibility to SMA and is functionally associated with the down-regulation of Hsp70 observed in children with SMA. Moreover, measurement of circulating Gln levels showed that SMA is characterized by suppression of Gln which increases susceptibility to SMA. *In vitro* experiments revealed that Gln can dose-dependently increase malaria-induced downregulation of Hsp70. Based on these findings, supplementation of current treatment regimens with Gln may offer a viable immunotherapeutic option for reducing inflammatory-derived host damage and improving clinical outcomes in children with SMA.

FEATURE LECTURE 3

19th July, 2018 || 5:25 p.m. - 5:55 p.m.

Higher order genome architecture & lncRNAs permit robust transcription of immune genes

Stephanie Fanucchi
University of Cape Town, South Africa

LncRNAs are emerging as key intermediates that control gene regulation by coordinating 3D chromatin structure. In this study we use a combination of imaging, genome editing, genomics, and bioinformatics analysis to validate and mechanistically describe an enhancer-like lncRNA, UMLILO, which is brought in close proximity to the chemokine genes by pre-formed chromosomal contacts. Despite lacking a homolog in mice, we show that depletion of UMLILOby siRNA or CRISPR-mediated replacement with a reporter is sufficient to abrogate chemokine transcription in human cells. By acting in cis, UMLILO uses the local 3D chromatin compaction of the pre-formed chemokine TAD to direct a trimethylation complex across the chemokine promoters, facilitating their H3K4me3 activation. In this way, we reveal how pre-formed chromatin loop organization can act as a topological platform to insulate a key transcriptional pathway from gene-intrinsic noise, to achieve rapid and robust chemokine expression. As aberrant expression of these chemokines underlies multiple disease states, adjustment of chemokine levels by altering UMLILO activity may represent a valuable therapeutic strategy for chemokine driven disorders and diseases.

PLENARY SESSIONS

1

Mitigating the public health threat posed by emerging viruses

Edward Wright
Viral Pseudotype Unit, School of Life Sciences, University of Sussex,
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It is widely recognised that zoonotic viral infections represent a significant threat to global human health. An estimated 3 out of 5 emerging viral infections are zoonotic in origin and they are increasing in prevalence. They are therefore a growing public health concern, which is compounded by the fact that in nearly all cases there is a complete lack of effective diagnostic, vaccine and treatment platforms for these pathogens. One of the principal bottlenecks for working with these viruses is the paucity of high containment facilities required for most of these viruses, and where there is access to such labs, the restrictive cost of using them. This can be addressed by the use of pseudotyping technology; the generation of replication defective versions of highly pathogenic viruses bearing native viral envelope proteins (VEP), which can be employed to study early events in virus replication. Our group has spearheaded the use of pseudotyped viruses (PV) as surrogates to handling highly pathogenic viruses for virus-host interaction and sero-epidemiology studies, as well as for diagnostic assay, vaccine and therapeutic drug development. While our work has primarily focused on Lyssaviruses and Ebolaviruses, we have recently undertaken studies on Henipaviruses, Arenaviruses and Togaviruses. These studies aim to improve our understanding of the epidemiology and antigenicity of viral zoonoses, using the results to aid the development of novel intervention strategies.

2

From single-cell transcriptomics to the dynamics of differentiation

Ábel Vértesy, Javier Frias Aldeguer, Zeliha Sahin, Nicolas Rivron, Alexander van Oudenaarden & Niels Geijsen
Hubrecht Institute-KNAW (Royal Netherlands Academy of Arts and Sciences) & University Medical Center, Utrecht, The Netherlands
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A major disparity in biological research is that while most interesting questions are part of continuous processes (think of development, differentiation or disease), we are often limited to terminal, "snapshot" measurements. Recent breakthroughs in transcriptome wide profiling of single cells & in temporal reconstruction approaches allow to overcome this limitation in silico, giving a transcriptome-wide & high resolution view on the clockwork of gene regulation. A clinically and evolutionarily relevant system to study differentiation is mammalian spermatogenesis. Here, stem cells (spermatogonia) differentiate into functional gametes, but the process is not well understood. We undertook a systematic approach to delineate the events of spermatogenesis by single-cell mRNA sequencing & temporal reconstruction. Resulting temporal resolution is magnitude better than that of staging based approaches. This allowed us to systematically identify novel genes in spermatogenesis, and to delineate the regulation of meiotic sex chromosome inactivation.

3

Tantalizing dilemma in genetics causality from disease scoring statistics

Emile R. Chimusa
Division of Human Genetics, Department of Pathology, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, South Africa
Emile.chimusa@uct.ac.za

Following recent advances in Genome-Wide Association Studies (GWAS), methods of training risk prediction, detecting new risk genes, imputing untyped variants, and fine-mapping causal variants from GWAS summary statistics are playing an increasingly critical role. Several methods including polygenic risk, combined with the effect of several SNP-association at gene and pathway level computed from GWAS summary statistics, have proven valuable for predicting disease risk and understanding the genetic architecture of complex traits. In addition, the power of GWAS may significantly improve by estimating the proportion of SNP heritability attributable to various functional categories. In this talk, we will briefly present some works done and ongoing projects in both GWAS and post-GWAS. We will also discuss a basic background in disease scoring statistics, and the role of ancestry in mapping disease genes.

4

Combinatory approaches towards useful structures of HIV integrase

Peter K. Quashie & Jeffrey E. Lee
Laboratory of Structural Virology, Department of Laboratory Medicine and Pathobiology, Faculty of Medicine, University of Toronto, Toronto, Canada
peterkquashie@gmail.com

Antiretroviral therapy has greatly improved the health outcomes of infection with human immune deficiency virus (HIV), but there is still no cure. HIV integrase protein is responsible for an essential process in the HIV replication cycle-integration. Integration is the functionally-irreversible process that results in proviral DNA being covalently inserted into chromosomal DNA. Integrase is also important for many steps in the viral replication cycle: maturation, reverse transcription, nuclear import, mRNA splicing, virion assembly and viral particle maturation. Accordingly, integrase inhibitors are the most potent anti-HIV drugs ever developed. Newer integrase inhibitors; dolutegravir, cabotegravir and bictegravir are highly potent with a high genetic barrier to resistance development. However, the mechanism(s) of resistance, when it occurs, is not yet fully understood. This is due to poor amenability of HIV integrase to biochemical research and subsequently a lack of high resolution full-length/functional structures of HIV integrase. Here, we present mechanistic enzymology studies on the inhibition of HIV integrase, a hypothesis for resistance mechanisms and results from biochemical, biophysical and crystallographic studies of HIV integrase protein. We outline how our methodology can be utilized, not only for HIV integrase but for other similarly challenging viral targets.

5

Inhibition of gastric H+/K+-ATPase and *Helicobacter pylori* growth, and enhancement of mucin activity by a flavonoid-rich fraction of *Dissotis rotundifolia* plant

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Medicinal plants are commonly used in Ghanaian traditional medical practice to treat diverse kinds of diseases including gastrointestinal diseases. One such plant that is patronize by rural folks for the management of gastroduodenal ulcer is *Dissotis rotundifolia*. The flavonoid-rich fraction of *Dissotis rotundifolia* (DRF) was obtained through a sequential extraction procedure using dichloromethane and methanol as solvents. In this study, the antiulcer effect of DRF at doses of 100, 300 and 500 mg/kg bwt was investigated using aspirin, ethanol and cold stress models in rats. In vitro anti-*Helicobacter* pylori effect of DRF was also assessed using the agar well diffusion assay. Although all doses of extract showed significant gastroprotective activity as compared to negative control groups, the highest antiulcer activity was observed with 300 mg/kg bwt as confirmed by histopathological examination. In vivo activity of H+/K+ -ATPase in negative control groups in all models was found to be higher compared to normal, omeprazole and DRF treated groups ($p< 0.05$). A marked increase in glycoproteins (sialic acid, hexose, hexosamine and fucose) was observed in all the pretreated groups compared to negative control ulcer groups. There was also an increase in the total carbohydrate/protein ratio of the gastric mucosa of DRE treated rats. *In vitro Helicobacter pylori* activity denotes that plant extracts (200-800 mg/ml) and standard antibiotic drugs (amoxicillin, clarithromycin) showed antimicrobial activity against clinical isolates of *Helicobacter pylori*. The zones of inhibition ranged from 13-30 mm. Meanwhile, maximal effect was found at 400 mg/mL concentration of DRF. Implicitly it can be stated that the antiulcer effects of DRF is multifaceted. This study demonstrates that DRF performs its antiulcer effect through inhibition of H+ / K+ - ATPase, increase mucin activity and inhibition of growth of *Helicobacter pylori*.

6

The mechanics of *Plasmodium* merozoite invasion into the human erythrocyte: a balanced parasite-host cell contribution driving entry?

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Entry of the *Plasmodium* merozoite, the micron-sized cell responsible for blood-stage malaria infection, into the human erythrocyte defines establishment of malaria disease. The process is rapid yet contains a great depth of cell biology, one eukaryotic cell actively penetrating the other. Entry has long been seen as a very parasite-centric process with the merozoite literally driving its way into a passive erythrocyte. This is in marked contrast to other pathogens that utilise host-cell phagocytosis to gain entry to human cells. Has this inbalanced view been over-stated in the case of the merozoite? Recent data from several groups suggests that erythrocyte biophysical properties may also contribute to the process of merozoite entry. Here, we present our latest insights into the role of both parasite and host cell factors and how they might be contributing to lowering the energy barrier for merozoite invasion of the human red blood cell. With a particular focus on cell imaging, we present our vision of invasion being a balanced equation, where merozoite motor force and erythrocyte membrane deformability both contribute to allow the blood-stage malaria parasite to get in.

7

Role of *Mycobacterium ulcerans* toxin, mycolactone, in suppression of *Staphylococcus aureus* virulence genes

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Buruli ulcer disease (BUD) is a necrotizing skin disease caused by *Mycobacterium ulcerans* (MU). The disease is referred to as a 'mysterious disease' due to its unknown mode of transmission, ecology and pathology. BUD has been reported in over 33 countries worldwide, though highest prevalence is in West Africa. The major virulence factor of MU is mycolactone, a lipid toxin encoded by plasmid pMUM001. The toxin has been found to suppress immune cells which is responsible for BUD painless characteristic pathology. Additionally, pathogens such as *Staphylococcus aureus*, *S. epidermidis* and *Pseudomonas aeruginosa* have been isolated from BU ulcers, but without typical pathology associated with those pathogen's colonization. This raises the question whether mycolactone plays any role to provide a fitness advantage to MU in natural environments and during skin infection. The central hypothesis of our research is that mycolactone attenuates quorum sensing and virulence genes of other bacteria to outcompete those bacteria in natural environments and during skin infection. To test our hypothesis, *S. aureus* culture with mycolactone or ethanol (control) were incubated at 370C and *S. aureus* hemolytic activity and gene expression of global regulators *saer* and *agr* and virulence gene *hla* were measured at 6 hours and 22 hours of incubation. Results showed a reduction in *S. aureus* hemolytic activity with mycolactone at both timepoints compared to control. The *saer* gene was found to be significantly downregulated at 22 hours. The findings of the research will aid to understand the role of mycolactone in providing fitness to MU in polymicrobial environments. The study will also aid in determining potential BUD treatment outcomes following antibiotic treatment.

8

Integrated pathogen load and dual transcriptome analysis of systemic host-pathogen interactions in severe malaria

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The pathogenesis of infectious diseases depends on the interaction of host and pathogen. In *Plasmodium falciparum* malaria, host and parasite processes can be assessed by dual RNA-sequencing of blood from infected patients. Here we performed dual transcriptome analyses on samples from 46 malaria-infected Gambian children to reveal mechanisms driving the systemic pathophysiology of severe malaria. Integrating these transcriptomic data with estimates of parasite load and detailed clinical information allowed consideration of potentially confounding effects due to differing leukocyte proportions in blood, parasite developmental stage, and whole-body pathogen load. We report hundreds of human and parasite genes differentially expressed between severe and uncomplicated malaria, with distinct profiles associated with coma, hyperlactatemia, and thrombocytopenia. High expression of neutrophil granule-related genes was consistently associated with all severe malaria phenotypes. We observed severity-associated variation in the expression of parasite genes which determine cytoadhesion to vascular endothelium, rigidity of infected erythrocytes, and parasite growth rate. Up to 99% of human differential gene expression in severe malaria was driven by differences in parasite load, whereas parasite gene expression showed little association with parasite load. Co-expression analyses revealed interactions between human and *P. falciparum*, with prominent co-regulation of translation genes in severe malaria between host and parasite. Multivariate analyses suggested that increased expression of granulopoiesis and interferon-related genes, together with inadequate suppression of type-1 interferon signalling, best explained severity of infection. These findings provide a framework for understanding the contributions of host and parasite to the pathogenesis of severe malaria and identifying targets for adjunctive therapy.

9

A systems approach reveals immune signature associated with repeated clinical malaria episodes in children.

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Malaria is responsible for half a million deaths annually. While naturally acquired immunity provides promise of developing an effective vaccine, decades of study have yielded no definitive correlates of protection and the most advanced vaccine candidate provides only partial and short-lived protection. Given the complicated host-pathogen interactions involved it is unlikely that approaches focused on few parameters will unravel the underlying immune mechanisms responsible for immunity. We used a systems approach comprising whole blood transcriptomic, cellular and plasma analyses on a cohort of children who had been under active surveillance for malaria for several years. We developed and verified systems immunology tools capable of identifying molecular and cellular signatures of children of similar age who have experienced a "high" or "low" number of clinical malaria episodes. Transcriptomic, cellular, cytokine and active malaria surveillance were integrated to define signatures associated with malaria experience. High-episode children are distinguishable from low-episode children by enhanced expression of genes involved in immune activation and regulation, with modular analysis revealing enrichment in interferon-inducible genes. For a subset of high-episode children we also note a

distinct signature related to hemoglobin biosynthesis, which appears to correlate with clinical anaemia, and may reflect enhanced erythropoiesis in response to malaria-induced anaemia. The transcriptomic signature of enhanced immune activation in high-episode children is supported by elevated levels of pro-inflammatory cytokines (including IL-6 and TNF-), while high IL-10 and a subset of T cells distinguished high- from low-episode children. Through cellular deconvolution of the transcriptomic data, high-episode children appear to be associated with functionally altered B cells, neutrophils and CD8+ T cells and neutrophils compared to low-episode children. Whole blood analysis reveals a distinct immune signature associated with repeated episodes of clinical malaria. The implications of this signature for anti-malarial immunity are the focus of an on-going project.

10

Structural studies of malaria surface proteins

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Many of the most critical stages in the life cycle of the malaria parasite are mediated by surface proteins. These molecules are under selection pressure to bind to the molecules of the human host, as well as diversifying to avoid detection by the immune system. In this talk, I will present our stuctural studies of the *Plasmodium falciaparum* proteins involved in erythrocyte invasion and cytoadhesion, showing how they interact with critical human binding partners and how they are recognised by inhibitory antibodies.

11

Understanding the dynamics of malaria transmission in endemic setting

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In general, the dynamics of gametocyte production and infectivity, in relation to time elapsed since initial infection and malaria symptoms, is currently unknown for natural infections. To address this question, we recently conducted an observational study to examine gametocyte production and infectivity to mosquitoes in chronic malaria infections and in newly acquired infections. Two cohorts of schoolchildren were enrolled. In the first cohort (acute infection cohort), children received a curative dose of DHA-PQ to clear any preexisting infection. They were subsequently monitored weekly by PCR for incident infections. Upon first detection of infection, sampling was performed daily and monitoring continued for 42 days. Mosquito feeding assays were performed at day 0 (day of detection of infection), Day 14 and Day 35. The second cohort was identical in design but infections were not cleared. Intensive follow-up commenced once asymptomatic infections were detected for 2 consecutive months. Only 13% (7/51) of children with acute infections remained fever free after the first detection of infection by nPCR, whilst 72% (28/39) of all children with chronic infections remained asymptomatic during 42 days of intensive monitoring. Although mature gametocytes were detected at low densities, none of children with acute infections infected mosquitoes, compared to 69% (27/39) of children with chronic infections. Of the latter, some were infectious at 2 or 3 occasions during the follow-up and infected up to 98% of mosquitoes. The intensive monitoring allows the detection of symptomatic malaria before infected individuals become infectious to mosquitoes while asymptomatically-infected children are often infectious for several weeks: their identification will be key to the success of malaria elimination strategies.

12

Research to policy in Africa: A heightened need for a changing narrative

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Low uptake of research evidence in policy formulation has been associated with inadequate approaches in supply of evidence to policy makers, including inabilities of researchers to communicate effectively their research findings and knowledge for policy influence. Critical areas of focus entail carrying out research in which knowledge is produced, packaged and communicated by researchers and intermediaries who know the local context, needs and capacities of policy makers; communication and planning of research and information involving strategic thinking and appropriate timing; and involving policy makers in the initial planning stages of research projects for effective implementation of the research evidence. Advocates of evidence-informed policy making process maintain that the depth and quality of knowledge used by policy makers influence the effectiveness of policies. The uptake of research evidence in the policy making process is on the front burner of global discourses on approaches and strategies for development. Low- and middle-income countries, face challenges in using research evidence when compared with high-income nations. Given that many institutions and training providers use self-assessment as a major tool for assessing capacity, it seems likely that capacity gaps are frequently underestimated. In addition, networks and linkages, even when well developed, do not address the lack of demand of research evidence from policy makers despite the fact that these channels can help raise awareness of research amongst policy makers and serve as a conduit for knowledge flow where the demand exists. We have taken the initiative as African researchers to build capacity to improve the translation of research evidence and learning into policy and practice for effective interventions in Africa countries and beyond. The focus is to identify and maximize opportunities for policy influence for critical issues in the countries, build consensus for the issues to drive policy outreach at national and regional levels and to strengthen the capacity of Implementation Research Teams for long-term and systematic engagement with decision makers in their respective countries for more effective uptake of the evidence they generate.

13

Kintampo Health Research Centre: hub for collaboration in scientific research and capacity building in Ghana.

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Kintampo Health Research Centre (KHRC), established in 1994 is one of the three research institutions in the Ghana Health Service/Ministry of Health under the Research and Development Directorate. KHRC with its capacity has conducted several high quality biomedical and public health research with outcomes that influenced national policies in Ghana and Africa. KHRC has national and international collaborations which give platform for students, professionals and researchers to learn and share. Based on the available facilities and expertise, KHRC in the past five years has supported two (2) MPhil and three (3) PhD students in the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) program, Ghana. Again, over 100 international and local students have carried out their research work in collaboration with KHRC over the years. On maternal and child health, the Kintampo Birth Cohort Project from 2008 to 2010, archived over 20000 blood filter papers and plasma samples. The aim was to determine the risk of malaria among infants born to mothers who experienced malaria during pregnancy and followed up monthly for 2 years. Also, the Ghana Randomized Air Pollution and Health Study (GRAPHS), one of the birth cohort studies, from 2013 to 2016 looked at the impact of air pollution from cooking practices on infant health. The study archived about 1200 placental tissue blocks and slides and 1000 nasal microbiome swabs. KHRC carried out a study in the area on malaria and helminths from 2015-2016. The study has archived about 3700 blood blots, PBMCs, plasma and red cell pellets.

14

Long-distance spatiotemporal transmission patterns of *Plasmodium falciparum* infections across The Gambia

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Understanding transmission dynamics of *Plasmodium falciparum* can help focus interventions that target malaria, particularly in low transmission settings. Four hundred and eighteen *P. falciparum* isolates collected in six paired villages from western, central and eastern Gambia during the 2013 malaria transmission season were successfully genotyped for 54 single nucleotide polymorphisms (SNPs) across the genome. A linear correlation between evolutionary and genetic distance existed only within a maximum of 30% barcode difference. There was a strong spatial hierarchy between pairs of isolates within both households and villages, and between villages; but, temporal structure between pairs of isolates was less evident and relatedness declined with increasing temporal distance. Combining the temporal and genetic distance, constrained by travel data, 88 person-vector-person transmission events were identified, with more than half of these (56%) occurring within the study villages. When considering related infections between individuals living at least 70km apart, there was significantly more transmission from eastern to western Gambia, particularly at the peak (October) of the malaria transmission season. Therefore, although local transmission (i.e., within a village) remains extremely important, movement of parasites from east to west may contribute to maintain transmission in the west, where malaria transmission is already low. Based upon these findings, it is unlikely that malaria transmission in western Gambia could not be fully interrupted without intensifying malaria interventions in eastern Gambia.

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How HIV-1 transcription start sites dictate RNA fates

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HIV-1 unspliced RNAs have two broadly defined roles: to serve as the mRNAs that encode viral structural proteins or to function as genomic RNAs in progeny virions. Long-standing research has suggested that mRNA and genome fates are dictated by alternate folds of HIV-1 RNA's 5' leader region, and in recent years our collaborators have used NMR to solve 3-dimensional structures of the packageable form of this RNA. Our additional recent work has shown that HIV-1 transcription can initiate at any one of three clustered G residues, and that transcription start site (TSS) choice dictates the 5' leader region RNA's folded structure. In addition to its unspliced mRNA, HIV-1 generates many splicing products: all of which use a 5' splice site located within the 5' leader RNA. In the packageable RNA's 3-D structure, this splice site is buried in structure that appears incompatible with spliceosomal RNA association, and thus when this RNA adopts its packaging-competent conformation, the RNA seems unlikely to serve as a splicing substrate. Thus, we hypothesized that the 5' ends of spliced RNAs would represent a subset of the RNA 5' ends in cells and would be de-enriched for the preferentially-packaged TSS. Our new findings provide evidence in support of this hypothesis.

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The mechanism of action of the Buruli ulcer *Mycobacterium ulcerans* exotoxin mycolactone

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Buruli ulcer (BU) is caused by subcutaneous infection with Mycobacterium ulcerans, the third most common mycobacterial infection world-wide after TB and Leprosy. The lesions are characterised by a lack of inflammation and pain alongside tissue necrosis, which can become extensive without treatment. Unlike other mycobacteria, the virulence of BU is dominated by the function of a diffusible exotoxin, mycolactone. This lipid-like molecule is encoded by the bacteria on a single megaplasmid carrying polyketide synthase genes. In 2014 we discovered the molecular mechanism of mycolactone's function against host cells; showing that it prevents co-translocation of proteins into the endoplasmic reticulum (ER) by the Sec61 translocation machinery. Put simply, a major step in the synthesis of proteins, which will either eventually be secreted from the cell or be embedded in cell membranes, is disrupted because they cannot enter the ER's-like tube network. The knock-on effect is that proteins are made in the wrong compartment and are quickly destroyed. Not only does this mean that the affected cells can no longer make proteins vital for their normal function, but the act of manufacturing proteins in the wrong compartment is itself damaging to them. In this presentation, I will describe our research that shows how this activity explains the lack of inflammation (due to lack of cytokine secretion) and drives cell death both by apoptosis (due activation of to a cellular stress pathway driven by translational reprogramming) and coagulative necrosis (by promoting the deposition of fibrin in infected tissue).

17

cAMP phosphodiesterases as drug targets in the most neglected parasitic diseases

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There are many reasons why so few new drugs are introduced against negelected tropical disseases, including economic reasons, logistical reasons, research funding, *etc.* -- but a lack of validated drug targets is NOT the problem. Rather, we have to acrefully prioritise which drug targets we work on with the limited resources we have. And the one criterion to use must be a practical one: what has the best chance of actually making it all the way into a new drug? Should we focus on a unique target, not present in the mammalin hosts? Or, conversely, a highly conserved target for which the pharmacology has already been explored in a different context? The latter approach is called repurposing and has the enormous adavantage that much know-how in the form of assay development, structural biology, inhibitor design, toxicology and pharmacology is already available in the scientific literature and/or pharmaceutical companies. In recent years one of our drug development efforts has focussed on the enzymes that break down cAMP in the cell, the phosphodiesterases (PDEs) in a number of different parasites: *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania species*, and *Schistosoma mansoni*. PDEs are essdential in the proper functioning of cyclic nucleotide signaling and are the target of drugs for multiple human conditions. PDEs have also been validated as drug targets, especially in *Trypanosoma brucei* and *cruzi*. I will present multi-disciplinary progress in the development of new PDE inhibitors with selectivity over the homologous human enzymes. Two approaches were taken, with different fuinding mechanisms and partners. The first was with the GlaxoSmithKline Open Lab Fouondation and US partners Michael Pollastry and Robert Campbell. This involved the high-throughput screening of the entire GSK compound collection for inhibitors of *T. brucei* PDEB1. The other was EU-funded and involved the structure-based inhibitor design, and started to explore PDEs of Leishmania and Schistosoma species as drug targetrs as well.

18

Dissecting epigenetic and other cellular mechanisms at WCCB in Edinburgh

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The Wellcome Centre for Cell Biology is composed of 19 excellent research groups with state-of-the-art facilities for NGS sequencing, DNA synthesis & assembly, bioinformatics, imaging, proteomics, protein expression and structural biology. This provides us with an exceptional ability to understand key cellular mechanisms through multiple approaches. Our research attempts to understand and integrate events in pathways that have previously been studied in isolation. One major theme deals with the regulation of the flow of genetic information from the DNA in the genome into RNA and hence into cellular systems. The synthesis, maturation and degradation of RNA lies at the heart of the information processing system of all organisms. Another underlying research theme is the study of how cells establish their polarity, grow and accurately segregate their chromosomes during division. We also have a strong focus on the broad field of cellular epigenetic mechanisms, aiming to understand the interrelationship between underlying genetic alterations and their manifestation as cellular phenotypes. By bringing together the major themes of nuclear organisation, genome packaging and transmission, chromatin states and RNA biology, we aim to chart key interconnections between these processes and identify their mechanisms and regulation. I will give an overview of some of the ongoing research at WCCB. Recent research in my laboratory demonstrated that methylation on lysine 9 of histone H3 can act as a bona fide epigenetic mark allowing the transmission of information though both mitotic and meiotic divisions in fission yeast. We are now exploring the possibility that such epigenetic processes might generate phenotypic heterogeneity in genetically identical cell populations that contribute to anti-fungal resistance. In collaboration with Keith Matthews (University of Edinburgh) we are also investigating epigenetic regulation through exploring the role of proteins that are predated to install, bind or remove specific post-translational modifications on *Trypanosoma brucei* histones.

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In-country next-generation sequencing to support malaria surveillance networks.

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The use of parasite genetic information in malaria surveillance can reveal crucial information about individual malaria cases, such as markers of drug resistance, as well as information about parasite populations, including the frequency of resistance mutations, migration, diversity, and responses to interventions. To make genetic epidemiology a successful tool for malaria control and elimination, we have developed a targeted approach that allows comprehensive genotyping of important markers using high-throughput methods. This approach uses sequencing of amplicons and can be applied in any molecular laboratory with an Illumina MiSeq genomic sequencer. Sample collections are done in collaboration with both national malaria control programs and research partners, utilizing existing networks and emphasizing training in both sample collection and data interpretation. Benefits to in-country sequencing include increased training and capacity building as well as faster turn-around times. Within this system we target all known molecular markers of drug resistance, markers of co-infection with other Plasmodium species, and a molecular SNP barcode which can be used to determine the complexity of individual infections and basic population genetic statistics. A similar approach has been implemented in the Greater Mekong Subregion (GMS) and elsewhere using the Agena massArray system. Using this system, we have genotyped over 10,000 P. falciparum and P. vivax parasites in Asia as part of the GenRe-Mekong project, as well as over 5,000 more from South America and Africa. For each participating study, we provide a genetic report card "GRC" which details the genetic profile of each parasite, as well as summaries of each parasite population through maps and graphics. A website is also being designed to display results to show country and regional patterns across individual studies and will be of particular use to national malaria control programs.

FELLOWS SESSIONS

Oral Category

1

Pathogen and biomarker discovery among Ghanaian children presenting with acute febrile illness

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In the era of decreasing malaria transmission, it is imperative to characterize the etiology of acute febrile illness (AFI) in children in Ghana. Therefore, a case-control study was conducted in children aged 1-15 years at two hospitals in Accra and Kintampo. The diagnostic value of host inflammatory markers in predicting the etiology of fever was evaluated. TaqMan-based PCR and microbial cultures were employed to test blood, urine, and stool samples for various pathogens. Plasma cytokine levels were assessed by Luminex®-based magnetic bead assay. Out of 1513 blood samples analyzed, 464 (31.0%) tested positive for malaria parasites. In addition, 162 blood (65.0%) and urine (35.0%) samples had positive cultures of which 50 (31.0%) were considered pathogens. Organisms isolated were *Staphylococcus aureus* (5.5%), *Salmonella typhi* (1.2%), *Escherichia coli* (3.7%), *Streptococcus pneumonia* (0.6%), *Pseudomonas aeruginosa* (1.9 %,) *Non-typhoidal Salmonella* (2.5%), *Citrobacter freundii* (1.9%), *Enterobacter clocoae* (3.1%), *Coagulase Negative Staphylococcus* (2.5 %.). TaqMan-based PCR detections (116 blood samples) include; dengue virus (1.2%), *Coxiella burnetti* (0.6%), Rickettsia (3.1%), HIV-1 (0.6%). Febrile children had higher interleukin levels; IL1b (P =0.002), IL-6 (P <0.001), IL-10 (P =0.003), and interferon (P=0.002) compared to afebrile children. Furthermore, IL-10 was elevated in children with *Plasmodium* infections (P=0.002), while IL-2 was similarly increased in children with bacterial infections (P=0.003). Among haematological parameters evaluated, white blood cell count was the best predictor of fever (sensitivity 80.0%; specificity 60.0% and AUC of 0.70; 95% CI (0.61 to 0.80). Dengue virus and zoonotic bacteria were detected among the children, which were not clinically diagnosed. Elevated IL-1b, IL-6 and IL-10 levels were good markers of fever and elevated IL-2 was associated with bacterial infections. This report and others from Ghana and West Africa demonstrate the need for a more comprehensive approach to diagnose patients with AFI.

2

Diversity of emerging GII.17 Norovirus strain in Pediatric Acute Gastroenteritis

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Noroviruses are a highly diverse group of diarrheagenic RNA viruses and a cause of acute gastroenteritis (AGE) in all age groups with the elderly and young children usually experiencing severe clinical outcomes. The recent emergence and spread of the new GII.17 norovirus strain pose a global concern of whether it would become the new epidemic strain after the predominant GII.4 Sydney_2012 variant. This study reports the genetic diversity and phylogenetic relationship between the emerging GII.17 norovirus strains in Ghana and those elsewhere in the world. Partial polymerase and capsid gene typing was performed by Sanger sequencing of positive diarrhoeic stool specimen from children hospitalized with AGE. Genotypes were assigned with the RIVM genotyping tool while sequence and phylogenetic analysis were performed with MEGA 7 software. The GII.17 norovirus strains accounted for 6.7% of hospitalized cases within the study period. Of the six detected GII.17 strains, 3 were recombinants possessing discordant polymerase genotypes GII.Pe, GII.P13 and GII.P3. The Ghanaian GII.17 strains detected from 2008-2013 were highly diverse. The nucleotide sequence identities of their partial capsid gene ranged from 81.4%-95.9%. Even among strains detected within the same norovirus season (2013), nucleotide sequence diversity was as high as 8.7% to 17.6%. At the phylogenetic level, the 2013 strains detected in the same hospital clustered into different lineages. While some shared ancestral history with the prototype GII.17 strain C142 detected in 1978, others clustered together with contemporary GII.17 strains circulating in Cameroon, South Africa and many Asian countries. The earliest GII.17 strain detected in 2008 was distinct from any other lineage in the phylogenetic tree. The GII.17 strain emerged as far back as 2008 in Ghana but remained a minor cause of paediatric AGE in contrast to other reports. They were however highly diverse necessitating continuous monitoring and in-depth genetic analysis to better understand their evolution and implication for efforts being made towards vaccine discovery.

3

Development of a simple, low-cost amperometric assay for noninvasive monitoring of salivary glucose

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Daily continuous glucose monitoring is essential in controlling glucose levels for people with diabetes and impaired glucose tolerance. However, the inconvenience of piercing the skin to sample blood involves pain to a certain extent and may influence the compliance of frequent self-monitoring in diabetic patients or deter voluntary testing in apparently healthy individuals. In this study, we developed a simple, low-cost reagent-less electrochemical biosensor for the detection of salivary glucose in developing countries. A nanocomposite consisting of reduced graphene oxide, Mn_3O_4 nanoparticles and polyethylene glycol (PEG) was formulated and used to modify a screen-printed carbon electrode (SPCE). Glucose oxidase (GOx) was subsequently immobilized on the modified SPCE. The electroanalytical performance of the biosensor was thoroughly investigated using Faradaic electrochemical impedance spectroscopy (FEIS), cyclic voltammetry (CV) and amperometry. The presence of the Mn_3O_4 nanoparticles in the nanocomposite enhanced the electron transfer activity between the immobilized GOx and the underlying electrode surface; consequently, the biosensor showed excellent catalytic activity towards glucose. Calibration studies were done in buffer, in conjunction with amperometry and a sensitivity deemed to be satisfactory for the analysis of glucose in human saliva was found. The biosensor also exhibited excellent anti-interfering properties, good reproducibility and stability, and fast response (> 5s) during the detection of glucose. The as-prepared Graphene/Mn_3O_4/PEG nanocomposite is a promising material for the development and construction of biosensors

4

Detection and molecular characterisation of group rotaviruses in a sanitary environment in the Greater Accra Region of Ghana

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Rotavirus diarrheal related deaths was estimated to be 215,000 in 2016, with over 90% of these deaths occurring in low and middle income countries. These countries have been shown to have more uncommon genotypes of the virus. Since low and middle income countries have poor sanitation conditions, we propose that this could account for the presence of the uncommon genotypes, which contributes the higher mortality rates. The objective of this study was to determine the rotavirus genotypes circulating in the Tema Municipality (a comparatively sanitary setting) and compare to strains of a previous study that was done in Ashaiman (a comparatively less sanitary setting). IRB approval was obtained from the Noguchi Memorial Institute for Medical Research. Stool samples were collected from children below 5 years who presented with gastroenteritis in some selected hospitals within the Tema and Ashaiman Municipalities after parental consent has been sought. Questionnaires were used to obtain demographic data. The samples were tested for the presence of rotavirus using ProFlow kit. RNA was extracted from the positive samples and genotyped using reverse-transcriptase polymerase chain reaction (RT-PCR). Sanger sequencing was done to confirm the genotypes and the sequences were used for phylogenetic analysis. A total of 204 diarrheal samples were collected, out of which 8% and 13.5% were positive from Tema and Ashaiman, respectively. Three G-types (G1, G2, & G12) were found in Tema compared to five G-types (G1, G3, G9, G10 & G12) from the previous study in Ashaiman. The P-types: P[4], P[6] and P[8] were found in both settings. There were less rotavirus genotype diversity in Tema compared to Ashaiman, implying that sanitary conditions influence the diversity of rotavirus genotypes in a particular setting; hence, the need for surveillance and improved sanitation conditions.

5

IQGAP1 and pAKT are overexpressed and co-localized on tricellular junctions in invasive gastric adenocarcinoma

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Gastric adenocarcinoma (GAC) is the aggressive type of gastric cancer that originates from the epithelial cells, accounting for about 95 % of all gastric malignancies. The molecular mechanism of GAC is not clear, however, cytoskeletal rearrangement leading to epithelial mesenchymal transition (EMT) has been implicated. IQGAP1, a conserved scaffold protein mostly found in the cytoplasm interacts with F-actin and E-cadherin via the catenins to maintain cytoskeletal architecture and cell-cell contact. Altered expression and delocalization of IQGAP1 from the cytoplasm are considered critical in cytoskeletal rearrangement, cell elongation and loss of cell-cell contact. This preliminary study aimed to investigate IQGAP1 expression and subcellular localization with activated AKT in cell by cell presentation in GAC and normal biopsies. Formalin fixed paraffin embedded gastric biopsies pathologically diagnosed as GAC and normal were retrieved. Sections (3 µm) of the biopsies fixed on slides were processed for IQGAP1 and pAKT double stain immunofluorescence assay. Anti-IQGAP1 and anti-pAKT primary antibodies were incubated with the processed tissues followed by secondary antibodies conjugated with Alexa fluor 488 and 555. Slides were imaged with ZOETM Fluorescence Cell Imager, and NIH ImageJ was used to determine IQGAP1 and pAKT colocalization and subcellular (cytoplasm, bilateral and tricellular junctions) localization. Mean intensity values from at least 5 cells were used to compare subcellular localization of the proteins. Three series of 7 µm sections of biopsy in Eppendorf tubes were processed for RNA extraction, and IQGAP1 mRNA levels were quantified using RT-qPCR. IQGAP1 is overexpressed and heavily localized on the tricellular junctions in GAC, and may dock AKT for its activation. Altered expression and subcellular localization of IQGAP1 could be a potential therapeutic target.

6

Assessing naturally acquired immune response and malaria treatment outcomes in Lagos, Nigeria

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There are emerging reports of poor efficacy of artemisinin-based combination treatment (ACT). However, mutations on the Kelch-13 gene marking delayed parasite clearance have no clinically defined relationship with ACT resistance across Africa. With increasing malaria control efforts, declining acquired immunity could be responsible for varying drug response profiles that may be dependent on levels of exposure to infections. To examine antibody responses against malaria and the influence on the efficacy of artemether-lumefantrine (AL), plasma samples were collected, prior to treatment, from individuals receiving treatment for malaria. Participants were stratified into two groups: early (in 24 hours, N = 20) and late (between 48 – 72 hours, N = 30) parasite clearance after treatment, as determined by var gene acidic terminal sequence (varATS) polymerase chain reaction. Magnetic bead-based luminex assay was used to profile antibody responses specific to a panel of 21 Plasmodium falciparum sporozoite, merozoite and An. gambiae salivary antigens. Median fluorescence intensity (MFI) of the antibodies was highest against glutamate-rich protein (GLURP-R0) and lowest against merozoite surface protein (MSP2) antigen. Analysis showed a positive correlation between in expression of immunity and age of individuals (P = 0.023). However, there was no association between parasite density and antibody responses except a significant positive relationship with reticulocyte binding protein-like homologue 5 (Rh5), P = 0.047; Plasmodium exported protein (Hyp2), P = 0.037 and merozoite surface protein 11 (H103), P = 0.038. Though higher levels of antibodies against erythrocyte binding antigens (EBA 140 and 175), MSP1.19, GLURP, circumsporozoite protein (CSP) and Rh4.2 were observed in individuals who recorded early parasite clearance, there was no significant difference in antibody responses in the early and late parasitological response groups. Characterization of additional markers in larger populations is required to reveal potential immunological correlates of drug efficacy.

7

High-throughput RFLP assay for identification of Glycophorin B deletion variants

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Genetic variation in the glycophorin region of human chromosome 4 (containing GYPA, GYPB and GYPE genes) has been linked with 40% reduction in risk for severe malaria. A large structural rearrangement and hybrid variant called Dantu was identified in East African populations and linked to this signal. This region is of particular interest because glycophorins act as receptors for the erythrocyte invasion by *Plasmodium falciparum*. Apart from Dantu (absent in West Africa), other large structural variants have been identified in the glycophorin region on chromosome 4. The most common variants give rise to the deletion of the whole GYPB gene and surrounding region. In Africa, particularly West Africa, these deletions are carried by 5-15% of individuals. To investigate the effect of these deletions on malaria parasite invasion and growth in erythrocytes, it was first necessary to identify individuals carrying these variants. Here, we report the development of High-throughput Restriction Fragment Length Polymporhism assays for the two main GYPB deletion variants known as GYPB DEL1 and GYPB DEL2. The GYPB DEL1 assay is a modification of the assay reported in Leffler et al. (2017), while the GYPB DEL2 assay is novel. The investigations also resulted in the identification of the crossover/breakpoint for GYPB DEL2 variant, which was previously unknown. Using these assays, 400 samples from Southern Ghana were genotyped. The frequency of GYPB DEL1 in populations from Southern Ghana was 7% (4% Homozygous and 6% Heterozygous), while that of GYPB DEL2 was 4% (2% homozygous and 5% heterozygous). This is the first report of assays identifying specific Glycophorin B deletion types that can be used for high-throughput genotyping of populations. This allows for identification of Glycophorin B deletions for experimental work, stratification of genetic association studies, and understanding the role of this gene cluster region in malarial disease.

8

Diversity of emerging GII.17 Norovirus strain in Pediatric Acute Gastroenteritis

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Our study sought to examine the major causes of pre-lingual and post-lingual HI in Ghana as well as to investigate the role of connexin 26 and 30 gene (GJB2 and GJB6) mutations in familial and non-familial HI cases. The medical reports of 1104 students were analyzed to enroll HI patients. PCR and Sanger sequencing were used to investigate mutations within the coding region of *GJB2* and multiplex PCR and Sanger sequencing were used to analyze the prevalence of *GJB6* deletion. Results: Ninety-seven (97) families segregating HI and 19 isolated/non-familial cases where sampled. The male to female ratio was 1.49 and about 59.6% of the patients had their first comprehensive HI test between 6 to 11 years. Convulsion and cerebrospinal meningitis were major causes of post-lingual HI. Over 754 patients had pre-lingual HI of which 92.8% were congenital. Pedigree analysis of the families suggested that, over 95% possibly had autosomal recessive fashion of HI inheritance. Molecular analysis of mutations in GJB2 revealed that *GJB2-R143W* mutation, previously reported as founder a mutation in Ghana accounted for 21.6% (21/97) of familial and 10.52% (2/19) non-familial HI cases. The other 7 previously reported *GJB2* mutations in the Ghanaian population were not identified in our study. The analysis showed that, none of the study participant had *GJB6* deletion. Variants from a multiple sequence alignment of HI patients will be compared to participants with normal hearing in order to investigate other *GJB2* and GJB6 mutations in the Ghanaian population. Whole Exome Sequencing will be performed for those families that are negative for *GJB2* and *GJB6* mutations. GJB2-R143W mutation account for nearly a quarter familial non-syndromic HI cases in Ghana and should be investigated in clinical practice. Connexin 30 mutations does not account for of congenital non-syndromic HI in Ghana.

9

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.

10

Discovery and development of novel antifungal compounds from marine endophytic fungi sources

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Marine endophytic fungi (MEF) have not been explored as compared to their terrestrial counterparts in the treatment of diseases. We set out to identify and develop novel antifungal compounds from marine endophytic fungi sources using yeast genomics guided approach. Bioactive extracts were characterized by analyzing their activities against *C. albicans*, *S. cerevisiae* and a set of mutant *S. cerevisiae*. The bioactive extracts were tested under various chemical modifications to the growth media against *S. cerevisiae* and *C. albicans*. The aim was to show that the extracts to be selected possessed distinct activities and were able to maintain their activities even when the cells were under different chemical conditions. Those extracts that maintained their activities across the chemical conditions were selected as top candidates for product isolation. The 6 MEF were fermented in 20 L cultures and fractionated by Kupchan's solvent partitioning and preparative thin layer chromatography. A total of 59 active fractions were obtained from 17 out of the 21 Kupchan fractions from three of the six selected MEF after two rounds of the preparative TLCs. It is estimated that 148 active fractions could be obtained after analysis of all fractions of the 6 selected MEF. Two fractions from MEF 134 were highly active, an HPLC-HRMS full scan was performed on fractions V7 and V9. Both fractions (V7 and V9) had 2 peaks that were similar, all others were different. Preliminary structural elucidation of the compounds identified based on ms/ms spectra showed all the structures were novel. Hence, a 100 litre cultures of MEF 134 was prepared for large scale product isolation. Three other fractions from MEF 134; V1, V3 and V5 were active against *S. cerevisiae* but not the pathogenic *C. albicans*. The 3 compounds reduced HepG2 (Hepatocellular carcinoma cell line) cell proliferation.

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Effects of iron chelators on bloodstream forms of *Trypanosoma brucei*

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African trypanosomiasis still remains a lethal disease to both man and livestock. The disease still persists due to limited drug availability, emergence of drug resistance, and toxicity. Hence, there is the need to provide alternative forms of therapy. Studies have shown that the iron chelator deferoxamine exhibited anti-trypanosomal effects by inhibiting cell growth and interfering with the activity of some iron dependent enzymes. In this study, the *in vitro* effects of different phenolic acids which are known to complex iron were assessed for their trypanocidal activity against *Trypanosoma brucei brucei.* The chelators were selected based on their structures and iron-binding affinities. The IC50 values ranged from 3.3 µM to 217 µM with gallic acid being the most potent phenolic acid. A dose-dependent effect on the cell viability, morphology, mitochondrial membrane potential, cell cycle and kinetoplast synthesis of the parasite was observed with features that were similar to a standard anti-trypanosomal drug (diminazene aceturate). RT-qPCR and mRNA sequencing results show differential expression of transferrin receptor, ribonucleotide reductase and cyclin genes. The results throw more light on the possible mechanism of action on the chelators while providing alternative therapeutic approaches in the treatment of African trypanosomiasis which involves interfering with the iron metabolism of the parasite.

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Analysis of Antimicrobial Resistance Phenotypes in *Candida Albicans* Using Modulators of *Mdr/Cdr* Gene Expression

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Majority of life-threatening fungal infections in clinics are caused by *Candida albicans*. The emergence of azole resistance in fungi complicates patient management. In response to chemical stress, *C. albicans* make transient changes in the gene expression for survival. Notable among these is the upregulation of efflux pump which is known to be the main mechanism of antifungal resistance. Potent therapeutic agents targeting this resistance mechanism are urgently needed. Chemo-sensitization is postulated as one way to overcome antifungal resistance. Endophytic fungi produce bioactive metabolites which are used as chemotherapeutic agents. The aim of this study is to use modulators of *CDR* and *MDR*s as probes to study chemo-sensitization and resistance phenotypes. Also, fungal metabolites (alone and in combination with chemosensitizers) will be used to reverse antifungal resistance. On analysis of phenotypic switching of the fungal cells in the presence of efflux modulators and phenotypic modifiers, *S. cerevisiae* was more inclined to switch phenotypes as compared to *C. albicans*. In *C.albicans*, compounds PC04-23 and PC04-15 had the highest resistance breaking activity while compounds PC04-09 and PC04-14 had the most resistance-inducing activity. In *S. cerevisiae*, PC04-13 and benomyl had the highest resistance breaking activity while estradiol and 1,10-phenanthroline had the most resistance inducing activity. Levels of efflux and other stress response gene expression and activity of the protein pumps will be analysed to gain insight into resistant mechanisms. A set of 500 fungal extracts has been screened against *C. albicans* and *S. cerevisiae*, of which 40 have shown inhibitory activity. Selected bioactive extracts will be tested against *C. albicans* with efflux modulators. Chemo-sensitizing agents will also be identified from fungal metabolites via an interaction study with sub-MICs of fluconazole. It is expected at the end of the study to obtain potent antifungal or chemo-sensitizing agent from the fungal metabolites that acts on efflux pumps.

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Molecular markers of *Plasmodium falciparum* drug resistance across two malaria endemic sites in Mali

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Drug resistance is one of the greatest challenges of malaria control program in Mali. Recent advances in next-generation sequencing technologies provide a new and effective way of tracking malaria drug-resistant parasites in Africa using filter paper. We assessed the diversity in *P. falciparum* drug-resistance genes in two different endemic sites in Mali. The *crt, mdr1, dhfr, dhps* genes were analysed using targeted amplicon deep sequencing method in 270 P falciparum samples from 2 locations in Mali: Dangassa (n=214) with an intense seasonal malaria transmission and Nioro (n=56) with an unstable and short seasonal malaria transmission. Blood dried spot samples were collected from malaria patient in 2016. The Genetic diversity of *P. falciparum* were assessed using Sanger's 101 SNPs barcode method. The *crt*-CVIET chloroquine-resistance genotype was observed, respectively, in 64.4% and 45.2% of the samples, in Dangassa and Nioro (P=0.025). The prevalence of the pyrimethamine-resistance *dhfr*-IRN genotype reached 14.1% and 19.6% respectively in Dangassa and Nioro. The sulfadoxine-resistance *dhps* gene showed higher variation in Dangassa compared to Nioro (P=0.035). At least 2 variations was detected in the *dhps*-SAKAA in 17.8% of the samples in Dangassa vs 7% in Nioro. The amodiaquine-resistance *mdr1*-N86Y mutation was identified in 2 samples in Dangassa vs 1 in Nioro. The *mdr1*-Y184F mutation was found in 50.2% and 60.7% of samples respectively in Dangassa and Nioro. No piperaquine-resistance *Exo-E415G* mutation and artemisinin-resistance genetic-background were identified. A high *P. falciparum* diversity was observed; however, no clear genetic aggregation was found in the sites. Higher proportion of multiplicity of infection was observed in Dangassa either using COIL (p=0.04) or McCOIL (p=0.02) methods. Chloroquine, pyrimethamine and sulfadoxine-resistance mutations are still high in Dangassa. Our data suggest that Artemisinin and its partner drugs piperaquine are still effective in both Dangassa and Nioro.

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Functional insights on the role of *Plasmodium falciparum* Claudin-like Apicomplexan Microneme Protein (PfCLAMP); an essential gene

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Malaria is still a public health burden. With the recent reports of artemisinin resistance in *Plasmodium falciparum* coupled with the low efficacy of the available commercially approved vaccine, there is the need to continue developing new targets by functionally characterizing some of the ~60% of the parasite's genes with unknown functions. This will foster the identification of viable vaccine and possible drug targets for the development of interventions against the parasite. To this, we have studied *P. falciparum* Claudin-Like Apicomplexan Microneme Protein (PfCLAMP) (3D7_1030200) and its role during parasite development. It has been shown to be highly conserved in apicomplexans, with its orthologue in *P. falciparum* essential for parasite growth and invasion. We have confirmed the localization of CLAMP at the apical portion of merozoites using specific antibodies raised against the protein's extracellular domain. We have also demonstrated that CLAMP is differentially expressed across the different asexual stages of the parasite, with the dominant expression being in the late trophozoite and schizont stages. We have shown and validated that some clinical isolates habour multiple copies of the *CLAMP* gene. In addition, CLAMP forms complexes with other proteins, and in this study we have characterized its interacting partners. Altogether, our data demonstrates that CLAMP provides a potentially attractive target for drug and vaccine development.

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The effects of Artemisinin-based combination therapy (ACT) on the dynamics of *Plasmodium falciparum*, *P. malariae* and *P. ovale* infections in Ghana

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Artemisinin-based combination therapies (ACTs) are the first-line antimalarials recommended for the treatment of uncomplicated malaria in all endemic regions. Since the introduction of ACTs, malaria mortality has significantly reduced. However, recent reports have highlighted an increasing prevalence of the less common *Plasmodium* species, *P. malariae* and *P. ovale*. These less common *Plasmodium* species have persisted in the background and are usually detected in co-infections with *P. falciparum*. Also, the effect of ACTs on these less common *Plasmodium* species remains uncertain. Therefore, we hypothesised that ACTs are less efficacious against the less common non-*falciparum* species in cases of mixed infection and, hence, *P. malariae* and *P. ovale* mono-infections frequencies will increase following malaria treatment. To investigate this, whole blood samples were collected from a total of 500 study participants presenting with febrile illness at the participating hospitals. Individuals who tested positive for malaria were treated with ACTs and followed up on days 3, 7, 14 and 21 to assess the efficacy of ACTs on the less common malaria species. The prevalence of the non-*falciparum* species using an in-house optimized PCR protocol shows that a significantly high proportion ($P < 0.05$) of the non-*falciparum* species are undetected by the standard PCR protocol. In addition, we also demonstrated that the detection limit of the non-*falciparum* species using the conventional multiplex PCR is largely affected by the dominant *P. falciparum* in cases of mixed infection. The efficacy of ACTs on the less common non-*falciparum* species was determined based on the presence or absence of the non-*falciparum* species during the follow-up days and the results would be presented. The outcome of this study is very important for the management of malaria and for informing policy as these less common non-*falciparum* species could potentially emerge as the dominant species in the future.

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Transcriptome profiling of *Plasmodium falciparum* parasites from asymptomatic and symptomatic infections

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The human parasite *Plasmodium falciparum* can counter and evade host immune pressure by varying its genes. Despite this, individuals resident in areas of high malaria endemicity can acquire immunity against the clinical manifestations of this disease. The asymptomatic infections remain common and suggest a harmonious coexistence between the host and the parasite. Parasites in asymptomatically infected individuals are under constant immune pressure from the host. This selective pressure may drive genome reorganisation of essential parasite genes and pathways conceivably through changes in gene expression and the acquisition of mutations. We, therefore, hypothesised that the parasites in asymptomatic individuals are incubation hubs that could lead to the identification of novel vaccine candidates and drug targets. These could be identified by dissecting the genomes and transcriptomes of the parasite under direct immune pressure. In a proof-of-principle study, we used RNAseq to analyse the transcriptomes of the intraerythrocytic stage of *P. falciparum* from four asymptomatic individuals and compared them with parasites from four individuals with febrile malaria. Here, we report that a total of 1569 genes were expressed in an eight-hour window of the intraerythrocytic stage, and we found that 142 genes were differentially expressed across the two study groups. The genes identified included known vaccine candidates, proteins involved in parasite invasion and conserved *Plasmodium* proteins of unknown function. Further scrutiny of the data surprisingly revealed that the genes that were highly expressed in asymptomatic compared to symptomatic infections were components of essential metabolic pathways and the transcription machinery of the apicoplast, an indispensable organelle of the malaria parasite. These genes are thus highly plausible drugs targets. In agreement with RNAseq data, qPCR validation of four selected genes using samples from the same and a different cohort showed a similar pattern of differential gene expression.

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Plasmodium falciparum strains spontaneously switch invasion phenotype in suspension culture

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

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Blood donor variability as a modulatory factor in *Plasmodium falciparum* invasion phenotyping assays

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Plasmodium falciparum uses multiple ligand-receptor interactions to invade red blood cells (RBCs). Blood stage malaria vaccines mainly target *P. falciparum* antigens involved in RBC invasion. Thus, unraveling the nature of ligand-receptor interactions involved in invasion is crucial in malaria vaccine development. Conducting large scale *P. falciparum* phenotyping studies inevitably involves the use of blood from different donors, which could affect the outcome of *in vitro* invasion inhibitory assays. However, the effect of blood donor variability in characterizing *P. falciparum* phenotypic diversity remains unaddressed. Therefore, we are currently investigating variations in invasion efficiency/phenotype observed using different donor RBCs. RBCs were treated with different enzymes and labeled with a fluorescent dye. *P. falciparum* clinical isolates and laboratory lines were maintained *in vitro* in a gassed atmosphere and further used to conduct standard invasion assays. The percentage of invasion was determined by flow cytometry and for all assays, the parasite's invasion phenotype was adjudged by comparing invasion in untreated and enzyme-treated acceptor RBCs. Our data show that invasion efficiency of both *P. falciparum* clinical isolates and laboratory adapted strains is affected by the nature (e.g. blood group or hemoglobin genotype) of the acceptor RBCs. However, the clinical isolates tested here, in spite of all using the sialic acid independent pathway, show more diverse invasion patterns. Interestingly, our preliminary data suggest that RBC genotypes (e.g. AS hemoglobin) influence parasite invasion efficiencies in enzyme-treated RBCs. Additionally, our data show that the sensitivities of RBCs from different donors seemed to be driven by the receptor density on the donor RBC surface. This suggests that, like the parasite's genetic make-up, the intrinsic properties of the target RBCs may also play a role in the observed invasion phenotype. In conclusion, the data show that blood donor variability is a modulatory factor influencing *P. falciparum* invasion efficiency and should be an important consideration in invasion phenotyping assays.

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The functional insight on the role of *Plasmodium falciparum* ABC-2 like protein on the parasites development.

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Malaria remains a public health challenge in the world, which takes a great toll on the health and economies of low and middle-income countries. Much effort has been put in on trying to avert this challenge, yet much is needed to keep the disease under control. Over the past decades, the ABC family of proteins has been shown to have a key role in parasite survival and development. Some of the challenges faced in the deployment of drugs such as Chloroquine, Mefloquine *etc* occured because members of the ABC family of genes such as PfCRT, PfMDR1, 2, *etc.* were hampered. Mutations and copy number variations in these gene families have been linked to the cause of resistance to the drugs. To this, we have aimed at understanding the role of different ABC family of genes to which PfABC-2-like protein is one. The ABC-2-like transporters have been shown to have a role in the uptake of sugars into the cell. We have characterized the PfABC-2-like protein which is a single copy, late stage dominantly expressed gene. It is conserved across the family of Apicomplexan parasites. Sequence-wise, we have identified the gene to be highly conserved at the transmembrane domain, which is crucial for the genes function. We have shown that it is expressed in both sexual and asexual stages of the parasite. It is exported to the surface of the red blood cell. This shows a merozoites surface localization to which antibodies to the ectodomain block merozoites invasion. It is carried into the ring stage during invasion and development.

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Cryptolepine inhibits inflammation through the TLR2-NF-κB pathway

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Cryptolepine, an indoloquinoline alkaloid in *Cryptolepis sanguinolenta*, has been shown in several *in vivo* studies to have potent anti-inflammatory properties. However, its mechanisms of action are not fully understood. In this study, the anti-inflammatory effects of cryptolepine and its underlying mechanisms of action were assessed. 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-κB transcription factor, were stimulated with a TLR2 agonist (pam3CSK4) in the presence or absence of cryptolepine (0.5- 1μM). After 24-hour incubation, culture supernatants were collected and the pathway activity assessed by measuring the levels of SEAP using Quanti-Blue assay and determining the protein levels of some pro-inflammatory cytokines and chemokines (IL-1β, IL-6, TNF-α, IL-12, IL-23, CCL2, and MIP-2α) using multiplex ELISA technique. Transcript levels of the cytokines, chemokines, TLR1, TLR2, RelA and key pathway regulators including IKKβ, p105 and IκBα were also assessed by RT-qPCR. Cryptolepine significantly ($p < 0.05$) inhibited the TLR2-NF-κB pathway activity in a dose-dependent manner. Cryptolepine also suppressed the protein levels of IL-1β, IL-6, TNF-α, IL-12, IL-23, CCL2 but not MIP-2α. Transcript levels of TLR1, TLR2, RelA, IKKβ, p105, IκBα and the afore-mentioned cytokines and chemokines were all significantly decreased by cryptolepine. Suppression of the pathway activity and the levels of the target genes by cryptolepine suggests that the alkaloid exerts its anti-inflammatory activity by modulating the NF-κB signaling pathway.

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Characterization of T cell activation and regulation in children with asymptomatic *Plasmodium falciparum* infection.

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Asymptomatic *Plasmodium* infections are characterized by the absence of clinical disease and the ability to restrict parasite replication. Increasing levels of regulatory T cells (Tregs) in *Plasmodium falciparum* infections have been associated with the risk of developing clinical disease, suggesting that individuals with asymptomatic infections may have reduced Treg frequency. However, the relationship between Tregs, cellular activation, and parasite control in asymptomatic malaria remains unclear. In a cross-sectional study, we determined and compared the levels of Tregs and other T cell activation phenotypes using flow cytometry in symptomatic, asymptomatic and uninfected children before and after stimulation with infected red blood cell lysates (iRBCs). We also investigated the association between these T cell phenotypes and parasitaemia. In children with asymptomatic infections, levels of Tregs and activated T cells were comparable to those in healthy controls but significantly lower than those in symptomatic children. After iRBCs stimulation, levels of Tregs remained lower for asymptomatic vs. symptomatic children. In contrast, levels of activated T cells were higher for asymptomatic children. Strikingly, the pre-stimulation levels of two T cell activation phenotypes (CD8+CD69+ and CD8+CD25+CD69+) and the post-stimulation levels of two regulatory phenotypes (CD4+CD25+Foxp3+ and CD8+CD25+Foxp3+) were significantly positively correlated with and together explained 68% of the individual variation in parasitaemia. A machine learning model based on levels of these four phenotypes accurately distinguished between asymptomatic and symptomatic children (sensitivity=86%, specificity=94%), suggesting that these phenotypes govern the observed variation in disease status. Compared to symptomatic P. falciparum infections in children, asymptomatic infections are characterized by lower levels of Tregs and activated T cells, which are associated with lower parasitaemia. The results indicate that T cell regulatory and activation phenotypes govern both parasitaemia and disease status in paediatric malaria in the studied sub-Saharan African population.

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Binding characteristics, transcription profiles and antibody recognition patterns of *Plasmodium falciparum* selected on blood group determinants

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Variant surface antigens (VSA) expressed on *Plasmodium falciparum*-infected erythrocytes mediate binding to the vascular endothelium and uninfected erythrocytes, in part via glycan antigens of the human AB0 blood group system. This binding results in rosetting and sequestration, which are associated with malaria severity. We investigated phenotypic and molecular characteristics of P. falciparum strains selected for adhesion to blood group A or B glycans. P. falciparum strains 3D7, FMG/it and FUP/PA were repeatedly panned on A or B oligosaccharides immobilized on plastic. Adhesion assays were done using primary human endothelial cells (dermal and aorta) and BeWo cells. VSA-surface expression was measured by flow cytometry using sera from 93 Ghanaian children with malaria. The var- and rif-gene transcript levels of selected and unselected 3D7 parasites were assessed by quantitative real-time PCR. Parasites selected on blood group A or B oligosaccharide increased binding to endothelial cells 4-6 fold. Generally, serological patterns observed in parasite lines selected for binding to either blood group A or B were similar. Serum antibody reactivity to selected parasites increased relative to the isogenic non-binding parasites. Antibodies from 5-11 year-old children showed more reactivity to A/B selected parasites than those of younger children. There was no association between the blood type of the children and increased antibody reactivity to blood group A/ B binding parasites. Transcript levels of one var-gene, (3D7Pf13_0003), previously associated with blood group A rosetting, and one rif-gene, (3D7Pf13_0004), not previously associated with rosetting, were strongly associated with the A/B binding phenotype. This work demonstrates that there is increased antibody recognition of parasites selected for adhesion to blood group A and B oligosaccharides, which also have a markedly increased adhesion to endothelial cells in vitro. The selection for A/B adhesion was associated with increased transcript levels of specific genes coding for VSA.

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Breadth of antibody response is associated with growth inhibitory activity of *Plasmodium falciparum* in semi-immune adults in Ghana.

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Plasmodium falciparum causes the majority of morbidity and mortality associated with malaria. Erythrocyte invasion is a crucial step in the life cycle of the pathogen. Several antigens expressed at this stage are the targets of immunity and have been shown to be associated with protection. Antibody levels , antigen specificity and functionality of antibodies to key invasion ligands were evaluated in adults living in a holoendemic area. Antibodies against erythrocyte binding antigen (EBA) and reticulocyte-binding homologue (Rh) proteins were detected in plasma samples from adults living in a high transmission area with no recent history of clinical malaria and purified immunoglobulin G (IgG) fractions from these samples were tested in growth inhibition assays against multiple parasite lines. Different parasite isolates showed varying sensitivities to individual purified IgG fractions, ranging from 40-150% invasion efficiency compared to the uninhibited control. Breadth of antibody response was strongly asssociated with inhibitory activity. Age was not a predictor of breadth of antibody responses in our sample population. Growth inhibitory activity was significantly associated with breadth of antibody responses, suggesting that a multi-antigen approach for blood stage vaccines may offer better protection than any antigen alone. The data also demonstrate the need for careful selection of antigens to include in a potential blood stage vaccine to optimize invasion inhibition.

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Delineating the functions of novel *Plasmodium falciparum* merozoite antigens during erythrocyte invasion and schizont egress

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Erythrocyte invasion is a poorly understood molecular process that involve arrays of interaction occurring at the parasite-host cell interface. During a systematic Bioinformatics analysis, we discovered two new P. falciparum Armadillo Repeat Motif proteins (PfARM-1 and PfARM-2) that possessed structural motifs that exemplified them as surface proteins. We produced these recombinant PfARM proteins in soluble forms using bacteria expression system and confirmed the identity of the recombinant proteins by mass spectrometry. Using both human and rabbit polyclonal antibodies to these PfARM proteins, we performed time-course immunofluorescence imaging and showed stage-specific expression that was substantiated by immunoblotting of detergent-treated, 3D7 lysates from different stages. Dual immunofluorescence staining showed that these PfARM proteins and PfMSP1 are transiently localized at the parasitophorous vacuolar membrane (PVM). Although, we observed fluorescent staining predominantly on the merozoite surface, the periphery and cytoplasmic area of matured gametocytes were also stained. Since topology analysis showed that these proteins do not possess signal peptides, transmembrane domains, or GPI attachment sites, we performed cellular fractionation experiments that showed partial insolubility in both detergent and carbonate extractions. We conceptualized that these PfARM surface proteins localized at the PVM might be associated with the erythrocyte cytoskeleton and may be relevant for parasite egress. Consistent with this, protein-protein interaction assays indicated that these PfARM proteins interact with Flotillin-1, a membrane raft-associated protein that is recruited from the erythrocyte membrane to the PVM. Additionally, we showed that antibodies against these PfARM proteins inhibit parasite growth in a concentration-dependent manner. However, the precise mechanism for parasite growth inhibition remains unclear which further necessitates the need for future studies on schizont arrest and merozoite attachment assays. In summary, we describe here the discovery and characterization of two new PfARM proteins as well as an undescribed PfARM-flotillin-1 interaction that could, in different ways, mediate host cell infection.

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Superbugs: Evolving enemies from hospitals in Ghana

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The magnitude of antimicrobial resistance (AMR), especially in Gram negative bacteria associated with hospital acquired infections (HAIs) is a growing burden to public health. Members of the genus *Enterobacter*, which include various human pathogens, thrive successfully in hospital environments. As opportunistic pathogens, they have been implicated in various HAIs including sepsis, wound infections, bacteremia, UTIs, upper and lower respiratory tract infections. Here, we report for the first time, a new heteroresistant strain of *Enterobacter cloacae* complex (Ecc) with significantly high level of resistance to conventional antibiotics and last resort antibiotic peptides (polymyxin B and colistin E). This Ecc strain was highly virulent (multiplicity of infection, 103CFU/larvae) causing mortality in less than 24 hours post-infection in a Galleria infection model. The level of resistance to cationic antimicrobial peptides (CAMPs) in Galleria was also observed to be high at low concentrations of purified LPS (with polymeric o-antigen and Lipid A components). Overall, our findings demonstrate high virulence of Ecc in vivo. The extreme antimicrobial peptides resistance are driven and influenced by its membrane bound LPS profiles. This strain may be a potential 'superbug' with evolving antimicrobial resistance mechanisms, making it recalcitrant to antibiotic treatment options.

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Molecular Targets of Iron Binding Phenolic Acids in *Mycobacterium smegmatis* and *Mycobacterium tuberculosis*

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Phenolic acids (PA) found in nature which include benzoic acid and cinnamic acid derivatives have been associated with anti-tubercular properties. Though the mechanism of action of these compounds is not well understood, it is possible that due to the presence of the catecholate moiety in their structure they could act by chelating free iron in the cell. This would make iron unavailable to iron regulated genes such as IdeR which play a crucial in the survival of Mycobacterium species. In this study the potential for 13 phenolic acids to form complexes with iron (II) and iron (III) and the inhibitory effect of these compounds on the growth of *Mycobacterium smegmatis* and *Mycobacterium tuberculosis* was investigated using spectrophotometric methods. Spectral shifts observed upon addition of iron (II) and (III) were analyzed and related to their binding strength. The effect of the compounds on mycobactin levels as well as intracellular iron concentrations was also determined. The Alarma blue assay was used to establish the minimum inhibitory concentration (MIC) of the compounds. The compounds which gave MICs below 2.5 mg/ml also reduced the mycobactin and intracellular iron levels significantly. The interaction of the compounds with IdeR, MbtB,SigA and irtA *in silico* was determined using the Pyrex software. The *in silico* binding analysis revealed that rosmarinic acid, chlorogenic acid and caffeic acid interacted well with these proteins with random mean square devitions (rmsd) of between -6.2 and -8.5.

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In vitro effects of phenolic compounds on *Leishmania donovani*

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Leishmaniasis is a neglected tropical disease caused by a protozoan parasite, *Leishmania*. The disease remains a global threat to public health and requires effective chemotherapy for control and treatment. In the search for compounds that may be useful as anti-*leishmanials*, 10 phenolic compounds known to have effect on protozoan parasites were selected for investigation. The compounds were screened for their anti-*leishmanial* activities against promastigote and intracellular amastigote forms of *Leishmania donovani*. Drug dose dependent and cytotoxicity assays were conducted by the MTT method and cell cycle assay by flow cytometry. Parasite morphological and growth kinetic studies were also conducted by microscopy. Iron content analysis was done by atomic absorption spectroscopy and the level of expression of iron dependent enzymes was determined using RT-qPCR. The IC50 of the compounds ranged from 16.34 µM to 124 µM. Amongst the compounds screened, rosmarinic acid and apigenin were more effective against the promastigote and the intracellular amastigote forms with selectivity index of 15.03 and 10.45, and 17.38 and 5.2 respectively. Morphologically, rosmarinic acid treated promastigote showed a rounded morphology similar to the control (deferoxamine) treated cells. Apigenin treated promastigote had most of its cells in a more elongated form than the untreated whilst others were ruptured when viewed by fluorescence microscopy. Cell cycle analysis of promastigotes showed that rosmarinic acid and apigenin induce cell arrest in the sub G0 phase. Elevated intracellular iron levels were observed in promastigotes when cells were treated with rosmarinic acid and this correlated with the level of expression of iron dependent genes. Our data suggest that rosmarinic acid probably exerts their anti-*leishmanial* effect via iron chelation resulting in variable morphological changes and cell cycle arrest.

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*E*ffects of *Zanthoxylum zanthoxyloides* extracts on African trypanosomes

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African trypanosomiasis is a disease caused by the parasitic protozoa of the Trypanosoma genus. Despite several efforts at chemotherapeutic interventions, the disease poses serious health and economic concerns to humans and livestock of many sub-Saharan African countries. *Zanthoxylum zanthoxyloides* (*Z. zanthoxyloides*) remains an important species in the subtropical zones of the African continent. In this study, we analyzed the *in vitro* effects and mechanisms of action of *Z. zanthoxyloides* (root) fractions against *Trypanosoma brucei* (*T. brucei*) in the context of alterations in cell cycle, cell morphology and apoptosis-like cell death. Methanol, butanol and dichloromethane fractions were selectively active against *T. brucei* with respective half-maximal inhibitory concentrations of 3.89 µg/ml, 4.02 µg/ml and 7.10 µg/ml. Moreover, dichloromethane, methanol and butanol fractions significantly induced apoptosis-like cell death with remarkable alteration in the cell cycle of *T. brucei*. Dichloromethane and methanol fractions also altered the morphology and induced aggregation in most of the parasites. Overall, the results suggest that *Z. zanthoxyloides* have potential chemotherapeutic effects on African trypanosomes with implications for novel therapeutic interventions in African trypanosomiasis.

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In vitro mechanistic study of anti-*Leishmania* activity of novel tetracyclic iridoids isolated from morinda lucida

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Leishmaniasis is widely considered a neglected tropical disease, common in the tropical and subtropical regions. The disease threatens about 350 million people with approximately 12 million people suffering from the disease globally. In spite of advances in drug discovery, high toxicity, and resistance issues limits the use of current drugs available. Therefore, with current emphasizes on use of medicinal plants worldwide our group previously identified three novel tetracyclic iridoids, Molucidin, ML-2-3 and ML-F52, from a Ghanaian medicinal plant, *Morinda lucida*, to have anti-*trypanosomal* activity. The activity of tetracyclic iridiods against *Leishmania donovani* and *L. major* was studied using promastigotes and intracellular amastigotes. Infectivity and cytotoxicity were performed with RAW 264.7 macrophage cells using Amphotericin B as reference drug. The mechanisms of action were analyzed by performing Nexin Assay, Immunohistochemistry (IHC), and Cell cycle analysis. A 50% inhibitory concentration of compounds was determined by Alamar blue assay. Molucidin and ML-F52 showed significant activity against promastigote and amastigote forms of Leishmania spp. ML-F52 was shown to be more active than Molucidin and less toxic than Amphotericin B. Molucidin and ML-F52 induced apoptotic mechanism of cell death in *Leishmania donovan*i and *L. major*. No inhibition of kinetoplastid membrane protein was observed with treatment, however, iridoids inhibited cytokinesis and induced phenotypic changes in promatigotes. Molucidin induced significantly higher ''nectomonad-like'' forms (50%); non-replicating forms, and loss of kDNA. ML-F52 triggered 'cell-rounding' with loss of flagellum. In further cell cycle analysis, an enhanced peak at G2-M phase in Molucidin-treated cells was observed confirmed by accumulation of mid-mitotic forms. Iridoids induced an enhanced peak at sub-G1, also confirming the apoptotic-inducing effect of compounds. Variations in cell cycle arrest, phenotypes and cytokinesis in *Leishmania spp.* was triggered by compounds suggesting differences in effects on parasites and therefore further investigation could present potential leads against Leishmaniasis.

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Artemisinin resistance associated Falcipain 2 polymorphisms in Ghanaian *Plasmodium falciparum* clinical isolates

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Falcipain-2 gene [FP2] encodes for *Plasmodium falciparum* cysteine protease hemoglobinase, falcipian. Polymorphisms in the gene are alleged to affect artemisinin action on parasites *in vitro*. With the use of artemisinin-based combination therapy (ACT) for 13 years in Ghana, it is crucial to investigate the parasite's genome to detect any anomalies and their effect on parasite susceptibility to the drugs. This study explored the existence of *FP2* polymorphisms in clinical *P. falciparum* isolates from Ghana. The findings will serve as an early warning sign of parasite resistance in Ghana. Blood samples from 250 children aged ≤9 years with uncomplicated malaria collected between 2008 and 2016 from five sites representing three distinct ecological zones were used. Polymerase chain reaction (PCR) followed by Sanger sequencing was done on the full length of the *FP2* gene. Sequence analysis was done using Qiagen CLC main workbench version 7.9.1 software and Benchling software to determine SNPs present in the gene using the sequence of 3D7 (PF3D7_1115700) as reference. A total of 250 samples were analyzed of which 86% (215/250) had SNPs. 450 SNPs were observed with 91% (195/215) being non-synonymous. Some common SNPs observed at the various sites overtime include K31K, N32K, R60K, N133T and N163T. The observed mutation that has been associated with slow parasite clearance S69* was not observed in the analyzed samples. However, S69S was observed and other SNPs such as S68S, V70I and V70V were also observed. The detected SNPs provide invaluable information on the variability in the SNPs found at the three ecological zones with different malaria transmission patterns. The absence of the SNPs linked to ART resistance is interesting. However, some SNPs are being selected overtime. Could they be molecular markers? These SNPs will serve as baseline for the monitoring ACT efficacy in Ghana.

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Increasing *ex-vivo* tolerance of Gambian *Plasmodium falciparum* isolates to Artemisinin-based combination therapy partner drugs

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The Gambian National Malaria Control Programmes scaled up drug and vector interventions against malaria for a decade, increasing the pressure on *Plasmodium falciparum* with currently used drugs. Despite overall reduction in prevalence, malaria is still widespread in 50% of the target populations in the east, while some clinical infections in the urban west require re-treatment following the first round of first-line ACT (Artemether-Lumefantrine). Hence, it was vital to develop a phenotypic assay that can be rapidly deployed in malaria endemic settings, enabling the continuous monitoring of parasite phenotypes over the years. Additionally, we sought to determine if there are any genetic markers associated with the observed phenotypes and if such markers are under directional selection. We report on *ex-vivo* assays of samples collected from Gambian children with confirmed uncomplicated malaria; parasite survival assay (PSA) using 10 times the median IC50 of Dihydroartemisinin and Lumefantrine (n=42) and ring-stage survival assay (RSA) using 700nM of Dihydroartemisinin (n=46), to determine *ex vivo* susceptibility to artemisinins and partner drugs. We are currently performing whole genome sequencing of 100 isolates to determine candidate drug associated loci. *P. falciparum* isolates showed increasing tolerance to Lumefantrine; a key component of the first-line ACT in The Gambia. For both RSA and PSA, substantial number of isolates showed parasite growth and re-invasion following drug exposure. Increased Lumefantrine tolerance could be due to selection from Artemether-Lumefantrine; the first-line ACT in The Gambia. Previous report from The Gambia showed temporal differentiation of SNPs on chromosome 7 undergoing directional selection, which had strong associations with increasing Lumefantrine tolerance. Whole genome analysis of isolates with phenotypic profiles is currently ongoing to further affirm directional selection by Lumefantrine in Gambian parasites. Overall, parasite tolerance observed with both Dihydroartemisinin and Lumefantrine calls for robust and continuous surveillance for the efficacy of currently deployed ACTs.

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Cellulose modified nanocrystals and their cytotoxic effects on selected cell lines

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Cellulose nanocrystals (CNC), obtained from the most abundant biomass on earth, cellulose has a wide range of applications including wound-healing, targeted drug delivery and prosthetics. CNC is extensively investigated by the research community due to its mechanical, chemical and rheological properties. CNC in its unmodified form is nontoxic, however when modified with organic molecules it becomes cytotoxic. In this study we report the functionalization of CNC with polyacrylate (superglue) to explore the composite, biophysical properties and its influences on cell viability. Two separate compositions were prepared using 60mg and 100mg of CNC with 5g of polyacrylate in 16ml of dimethyl-formamide respectively labelled 60CNC and 100CNC. The resulting composite is ground and put in solution and tested on selected cell lines to investigate their cytotoxic effect. The redox potential was also measured in the presence of these nanoparticles to correlate cell viability to cell membrane disruption by the nanoparticle. The cell viability test confirmed the occurrence of high anodic peak currents in the cell electrochemistry test, recording about 15% for HeLa cells subjected to 100CNC composite and about 39% for the HeLa cells exposed to 60CNC. Expectantly, 60CNC resulted in less cells dying in both the HeLa cancer cells and the normal S.Cerevisae cells which may be an indication of the antioxidant properties yielding from the treatment of CNC with superglue curbing the redox signaling pathways of both the reactive oxygen species and the reactive nitrogen species which tends to create genomic instability with frequent uncontrolled proliferation. The combined effect of CNC and polyacrylate antioxidative properties feed on free radicals released by the cancer cells thereby decreasing cellular oxidants which has been proven to play a crucial role in carcinogenesis. This may be the explanation of the mass death of the HeLa cancer cells in the presence of 100CNC.

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Fine-tuning targeted therapy in ALK-addicted neuroblastoma: The case for precision medicine.

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Neuroblastoma is a tumour of the developing nervous system and accounts for 15% of all paediatric oncology deaths. It is a heterogeneous disease and while a subset may undergo spontaneous differentiation or regression with little or no therapy, the majority are difficult to cure with current regimes. The most common genetic features of neuroblastoma are MYCN amplification, chromosome 1p and 11q deletion, 17q gain and mutations in anaplastic lymphoma kinase (ALK). ALK mutation occurs in about 5-7% of neuroblastoma cases but this percentage increased significantly to 20-25% in the relapsed patient population. Crizotinib, the first clinically approved ALK inhibitor for the treatment of ALK-positive lung cancer has had less dramatic responses in neuroblastoma, and also exhibited differential sensitivity towards different ALK point mutations. We investigated the efficacy of a second-generation ALK inhibitor, brigatinib, in a neuroblastoma setting. Employing neuroblastoma cell lines, mouse xenograft, Drosophila melanogaster model systems expressing different constitutively active ALK variants and in biochemical assays, we showed clear and efficient inhibition of ALK activity by brigatinib. Furthermore, genomic analysis performed on tumour sample from a neuroblastoma patient identified a novel ALK-I1174T point mutation. Pharmacological inhibition profiling of this mutation in response to various ALK inhibitors showed 11-fold improved inhibition of ALK-I1174T with ceritinib when compared with crizotinib. Ceritinib was selected for use in this patient. Treatment with ceritinib was effective and resulted in tumour shrinkage. Residual tumour in the patient was surgically removed after 7.5 months of treatment. Clinical follow-up at 35 months revealed complete clinical remission. In conclusion, brigatinib and, ceritinib are effective inhibitors of ALK kinase activity in ALK-addicted neuroblastoma and should be considered respectively as potential future and viable therapeutic option for ALK-positive neuroblastoma patients alone or in combination with other treatments.

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Development of novel antibiotics targeting the DNA double-strand break repair pathways

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An unrepaired DNA double-strand break (DSB) is lethal to cells. In bacteria, DSBs are usually repaired either via an error-prone pathway which essentially ligates the two ends of the DNA break or a pathway that utilizes recombination to drive accurate repair of the DSB. Due to the lethality of an unrepaired DSB, drugs which exhibit antibacterial activity by inducing persistent DSBs have been successful in the treatment of bacterial infections. However, recurrent usage of these drugs as monotherapy has led to emergence of resistant bacterial strains which have undergone modification of the primary cellular targets of these drugs. In the present study, several diverse organic extracts from fungal sources were screened to identify candidates that exhibit antibacterial activity by either inducing persistent DSBs or inhibiting repair of a site-specific DSB that was generated in *E. coli*. The synergistic effect of the active compounds in these two categories of extracts is anticipated to exhibit robust antibacterial activity against multidrug resistant strains of bacteria. The study has also identified antibiotic-compound interactions that increase the sensitivity of *E. coli* to DSBs. These antibiotic-compound combinations would be vital for rescuing the current obsolete DSB-inducing drugs. The preliminary data from this study highlights specific cellular and molecular mechanisms that could be exploited to develop novel chemotherapy against multidrug resistant strains of bacteria. The data also indicate possible strategies for resuscitating obsolete DSB-inducing drugs.

FELLOWS SESSIONS

Poster Category

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Characterization of the mechanism of action of trypanocidal compounds

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African Trypanosomiasis is a zoonotic disease which endangers millions of human lives and has a profound negative impact on sub-Saharan agriculture. While the incidence of the human disease appears to be largely controlled now, with a marked decline in the number of reported cases, the animal disease remains a significant challenge accounting for the death of millions of livestock every year, with severe socio-economic implications. Unfortunately, there have been insufficient efforts towards the development of veterinary trypanosomiasis drugs. The few currently available drugs display unacceptable toxicity, and over-reliance has compromised their continued use as first-line therapy in the face of widespread drug resistance. Therefore, there is a need for new drugs, especially those of new compound classes with novel mechanisms of action, to avoid cross-resistance. This study aims to investigate the mechanism of action of trypanocidal compounds isolated from Nigerian medicinal plants. Compounds will be selected based on their ability to inhibit the growth of parasites. The mechanism of action of the compounds will be investigated by analysing the effect on cell cycle progression and the morphology of the trypanosomes using fluorescent microscopy, scanning electron microscope and serial block-face scanning electron microscopy. The mechanism of cell death and mitochondrial function will also be evaluated with flow cytometry. The molecular target of the compound will be investigated using an untargeted metabolomics approach as well as ribonucleic acid interference (RNAi). The data generated will provide a model mechanism of action as well as the molecular target of the selected compounds which will aid optimisation. The most promising compound would be tested in murine models and, in collaboration with GALVmed (Global Alliance for Livestock Veterinary Medicine), potentially in larger animals such as goats. This project presents a clear vision for veterinary drug development.

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In Silico characterization of a novel *Plasmodium falciparum* merozoite protein

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The completion of the *Plasmodium* genome sequence has provided the foundation for discovering new targets for the development of new intervention strategies for malaria. In this study, we have performed data-mining analysis for 3,500 genes in the genome of *P. falciparum* using published transcriptomic/proteomic data set and the prediction of protease specificity (PoPs) analysis to prioritize new invasion-related genes for functional characterization. This analysis narrowed down the number of hits to 18 top, erythrocyte invasion-type genes that included a hypothetical gene with unknown function, as well as other proteins that are already classified as malaria vaccine candidates. Furthermore, the protein sequence for this novel gene was analyzed using several Bioinformatics portals and the data suggested that the protein might play a role in erythrocyte invasion. Further experiments that could expand our current understanding of the functional role of this protein in *P. falciparum* host cell invasion are required.

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Understanding resistance to anti-trypanosomal therapeutics used for trypanosome infections in cattle in southern Ghana

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Animal African Trypanosomiasis is a major burden to livestock production in Ghana. Chemotherapy remains the most effective option for controlling the disease, however, this has led to the reports of resistance against the widely used drugs (diminazene, homidium and isometamidium). A study on the spread and mechanisms of resistance will help to maintain the effectiveness of these drugs whilst new ones are developed. The study aims to assess the presence of drug-resistant trypanosome strains in Ghana and determine the possible mechanism(s) of resistance of the anti-trypanosomal drugs. To do this we will determine the number and species of tsetse flies at our study site. Trypanosomes will be identified in the midgut, proboscis, and salivary glands of tsetse flies and blood of cattle by multiplex nested PCR. The level of parasitaemia in blood of cattle will be determined by qPCR before and after treatment with anti-trypanosomal drugs to identify drug resistant trypanosomes. Drug resistance genes will be identified in two ways i) by whole genome sequencing and ii) by their differential expression pattern determined by high throughput RNA sequencing. The molecular mechanism underlying the resistance will be investigated using RNAi technology. A preliminary experiment at the study site identified a total of 529 flies, of which 2 were Glossina tachinoides, 1 tabanus, 11 stomoxys and 515 others. Dissection of the non-teneral fly showed that it was not infective. We have identified tsetse flies, stomoxys and tabanus as possible transmitters of Animal African Trypanosomiasis.

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Immuno-biology of *Plasmodium falciparum* STEVOR antigens: genetic diversity and gene expression

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Malaria remains a serious public health problem in Africa affecting mostly children and pregnant women. A transmission blocking vaccine could be a key for malaria control and eradication. Gametocytes are the key players of transmission and antibody responses against gametocyte surface antigens (GSAs) have been demonstrated but the real targets are unknown. Based on some defined functions of STEVORs, including its involvement in roseting, sequestration of early gametocytes, and deformability of mature gametocytes, we are proposing this multifamily protein as a target of anti-gametocyte antibodies and that children with good anti-STEVOR humoral responses (plasma antibodies and memory B cells) will present with low/no gametocytaemia. As preliminary investigations, we have assessed the genetic diversity of stevor genes in field samples (Africa and South-East Asia) using genomic data collected by the MalariaGen Project and appropriate statistical algorithms. Moreover, differential stevor gene expression in the laboratory strain 3D7 (both sexual and asexual stages) was studied using single cell RNA-Seq data set available in NCBI. Phylogenetic analyses (Neighbour-joining method) revealed that stevor sequences can cluster into different clades with one of the clade having the majority (3/4) of the sequences as previously reported. The diversity was found both within and between countries. RNA-Seq analysis revealed no gametocyte-specific stevor gene expression. However, some variants (PF3D7_0832400, PF3D7_0402600, PF3D7_0617600 and PF3D7_1040200) were expressed similarly in trophozoites, schizonts and gametocytes while others (PF3D7_1149900, PF3D7_022800, PF3D7_0114600 and PF3D7_0832400) were significantly more expressed in gametocytes than asexual stages. This preliminary analysis confirmed the variable nature of the stevor genes. The variants found to be up-regulated at the gametocyte stages could be those involved in roseting and sequestration of the parasite. However, further investigations are needed to precisely validate our observations with field isolates.

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Dynamics of cellular immune response over the clinical course of acute *Plasmodium falciparum* infection in children

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Both humoral and cellular responses have been implicated in malaria immunity. However, the immunological mechanisms that induce and maintain protective immunity are still undefined. Acquisition of immunity depends on exposure but the lack of clear criteria to determine the level of exposure has complicate results interpretation. Hence, the varying nature of malaria endemicity can be exploited to explore the mechanisms of acquired immunity. Children of ages 5-14 years are currently being recruited from two regions of Ghana with distinct malaria transmission intensity (Accra (low transmission) and Kintampo (high transmission)). Blood samples are being collected from children presenting with acute Pf infection to the hospital (D0) as well as on days 7 and 21 after treatment. Sample collection is ongoing, and some preliminary analysis has been done on a proportion of the peripheral blood mononuclear cells (PBMCs) to determine predominant cell phenotypes and cell activation markers involved in cellular immune responses. Results show lower levels of T cells during infection with an increase after resolution compared to higher peripheral CD4+ T cells levels which decline after infection. Infected children had higher T-bet+, relative to Gata3+ CD4+ cells and very low levels of T regulatory FOXP3+ cells with similar patterns, but decreased proportions after disease resolution. Levels of anti-inflammatory cytokine (IL-10) were higher than the pro-inflammatory cytokines (IFN- and IL-4) during infection but overall the proportion of cytokine producing cells increased after disease resolution. Results also indicate high proportion of CD4+ T cells expressing PD-1, which decrease after disease resolution. We show persistent activation of CD4+ T cells, measured by expression of CD38, CD69 and HLA-DR even after disease resolution. These data provides preliminary insights into the kinetics of the T cells response during infection and resolution, which partly define important immune markers of protection.

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Evaluating the antimalarial activity of a natural product, Compound X, against laboratory Strains of *P. falciparum*

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The continuous emergence of drug resistant malaria parasites against almost all the replacement antimalarial drugs has been a major challenge towards malaria eradication. Artemisinin combination therapies (ACTs) have contributed immensely to the decline of malaria since their introduction. However, current reports of artemisinin resistance in South-East Asia presents a hurdle towards achieving the global agenda. Compound X has been shown to have good antimalarial activities (IC50 values ranging between 7 and 13 µM) against both chloroquine resistant and susceptible *P. falciparum* parasite strains. This compound has been proposed to target P. falciparum lactate dehydrogenase (PfLDH) enzyme. However, other studies have found a low to moderate activity of Compound X against PfLDH. The lack of concordance between these studies suggest the possible existence of other targets. Hence, the need to evaluate this natural product and identify the possible targets of this compound. The potency of compound X against six laboratory strains of *P. falciparum* (Dd2, 3D7,7G8, K1, W2mef and NF54) were evaluated using optimized in vitro growth inhibitory assays. The observed IC50 ranged between 3.83 -10.19 µM. Compound X was most active against W2mef (IC50 of 3.829 µM) and least active against NF54 (IC50 of 10.19 µM). An average IC50 of 7.75 µM was observed across the five laboratory strains.These results obtained in this study are important for obtaining the appropriate IC50 values for selecting Compound X resistant parasites. Future studies will include the screening of Compound X against clinical isolates of *P. falciparum*, selecting for resistant Compound X strains and validating the target (s) and mechanism of action of Compound X. This work will be instrumental in identifying novel targets in *P. falciparum* parasites that is crucial for the discovery of novel antimalarial compounds against drug resistant malaria parasites.

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A cell-penetrating APIM peptide exerts anti-mutagenic effect on *E. coli* MG1655 by inhibiting translesion synthesis.

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DNA damage occurs spontaneously during DNA replication. It can also be induced by endogenous and exogenous agents such as reactive oxygen species (ROS) and UV-radiation respectively. In the quest to survive and to maintain the integrity of their genomes, cells have evolved various DNA repair and DNA damage response (DDR) mechanisms to deal with these lesions. Translesion synthesis (TLS) is a DDR mechanism that involves the use of specialized polymerases to bypass a lesion, typically in an error-prone manner. TLS mechanism mostly leads to mutations, and is therefore involved in the development of antibiotic resistance in bacteria. The eukaryote DNA clamp, proliferating cell nuclear antigen (PCNA) bind to all polymerases via the PCNA via two binding motifs; the PCNA-interacting peptide box (PIP-box) and AlkB homologue-2 PCNA-interacting motif (APIM). The prokaryotic DNA clamp, the Beta-clamp, interacts with the polymerases via a broadly defines 5-6 amino acid binding motif (clamp binding motif, CBM). A cell-penetrating peptide containing APIM (APIM-peptide) is shown to interact with PCNA and to sensitize cancer cell lines to various chemotherapeutics. Interestingly the APIM–peptide has antibacterial activity. In order to determine if the APIM-peptide has any direct effect on TLS, we used the rifampicin antibiotic assay and *E. coli* MG1655 and TLS polymerase deletion strains of MG1655 as a study model. Data from the rifampicin assay show that APIM-peptide reduced the mutation frequency in the wild type (WT) but not in the deletion strains lacking the most central TLS polymerase in bacteria, PolV. The UV-induced mutations were more reduced than the spontaneous mutations. Sequencing of the rpoB gene of some rifampicin-resistant colonies reveals changes in the mutation spectra upon treatment with the APIM-peptide. Our results suggest the peptide exerts anti-mutagenic effect on the bacteria by inhibiting polV induced TLS. This demonstrates that the APIM-peptide could be of therapeutic significance in combating antibiotic resistance in combination with other antibiotics

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Investigations into the mechanisms of anti-mycobacterial drug resistance using antipsychotic compounds

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The continual emergence of drug resistant strains of *Mycobacterium tuberculosis* has caused global public health concerns. This project establishes basis for deciphering diverse resistance mechanisms in mycobacteria which would lead to the development of novel therapeutic options. Unique classes of antipsychotic compounds have been found to possess anti-mycobacterial activities against drug resistant *Mycobacterium tuberculosis*. The study seeks to use antipsychotic compounds to probe for resistance mechanisms in *Mycobacterium smegmatis*. In phenotypic based drug-drug interactions, antipsychotics in pairwise combinations with standard anti-mycobacterial drugs produced resistance breaking and resistance inducing effects. Notably two antipsychotics, flupenthixol and bromperidol, in pairwise combinations with 5-fluorouracil generated resistance breaking effects. Key resistance inducing scenarios occurred when each of two antipsychotics, trifluoperazine and bromperidol, interacted with ethionamide. The next stages of the research would involve analysing relative expression levels of target antibiotic-associated stress response genes responsible for unique phenotypic interactions. The study would also utilise phenotypic assay guided detection and isolation of novel compounds from soil borne and terrestrial endophytic fungi based on unique interactions between antipsychotics and fungal extracts or fractions. In conclusion, this study would unveil unique stress response-associated drug resistance determinants while providing novel therapeutic options to support current treatment regimens for drug resistant tuberculosis.

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Interactions of Antimicrobial Compounds with selected drugs used in the Clinical Management of Sickle Cell Disease (SCD)

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Antibiotic resistance has become a major worldwide problem, accompanied by the decline in new antibiotics production over the years. Although the spread of resistant bacteria worldwide has mainly been attributed to the injudicious use of many antibiotics, the role of other drugs used in management of pathological conditions of non-infectious diseases needs be investigated. The effects of the antibiotic-drug interactions against bacteria in SCD patients and in other chronic diseases cannot be overemphasized. This research study focuses on these interactions and their contribution to the modulation of resistance mechanisms in microbes. The findings will further be utilized to guide the isolation of novel bioactive molecules from soil-borne fungal (SBF) and terrestrial-endophytic fungal (TEF) extracts against drug-resistant bacteria. We identified mostly resistance inducing and some resistance breaking interactions between standard antibiotics and 24 phenotype modulating compounds, nine of them being SCD management drugs, against multidrug resistant strains of *S. aureus* and *E. coli*. The opioid drug, Morphine, and Deferasirox, an oral iron chelator, emerged as best resistance breaking SCD compounds. Significant resistance inducing interactions were observed with Methotrexate, compounds PC04-06 and PC04-07. Activities of standards, Amoxicillin, Gentamicin and Paramomycin were significantly altered in most interactions; with Erythromycin, Streptomycin and Moxifloxacin activities being affected in few cases. These outcomes indicate that bacterial exposure to non-antibiotic compounds may be involved in the rapid evolution of drug-resistant bacteria strains. Our analyses of microbial stress responses to these unique interactions would reveal a number of endogenous resistance-promoting genes that represent possible therapeutic targets in countering antimicrobial resistance.

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Cheminformatics-based drug design approach for identification of natural product-derived HIV entry inhibitors based on peptidomimetics of broadly neutralizing antibody VRC01

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HIV-1 infection is mediated by interaction between host cell CD4 receptor and co-receptors, with HIV Envelope protein (Env). Inhibition of HIV entry into host cell presents target for therapeutic intervention. Broadly neutralizing antibody (bNabs) are potent in neutralizing broad range of HIV strains and preventing entry into host cell. VRC01 is a CD4 binding-site class bNabs that binds to the conserved CD4 binding region of Env, however using antibodies as therapeutic agents pose challenges due to low availability and high cost. Natural products that can mimic bNabs by interacting with the conserved regions may serve as new generation of potent HIV-1 entry inhibitors. In this study, a multiconformers three-dimensional similarity search via pepMMsMIMIC was used to generate peptidomimetics of VRC01 from MMsINC® database based on the shape and pharmacophore of Fab of VRC01. Pharmacological profiling of peptidomimetics was undertaken using SwissADME and the most drug-like compounds were virtually screened against the structure of Env (PDB: 3ngb) using AutoDock Vina. LIGPLOT was used to elucidate the interactions between the compounds and the Env. Compounds that interact with the conserved amino acid residues within the binding pocket of Env were used for two-dimensional similarity query of African natural product library via JChem. A library of 120 peptidomimetics of VRC01 with the best drug-like properties was generated and used for molecular docking simulation. 45 compounds with high binding affinity with the conserved sites of the Env were identified, with 29 compounds interacting with conserved amino acid residues of HIV gp120. A total of 14 natural product compounds with similar pharmacophore fingerprint to the peptidomimetic was generated. The inhibitory activity of these 14-natural product-derived compounds will be validated using both *in vitro* and *in vivo* techniques. Identifying VRC01 mimicking natural products with high affinity for the conserved residues of HIV Env protein provide opportunity to develop a new class of HIV entry inhibitors which can prevent HIV binding to CD4.

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Anti-diabetic effect of probiotics and nutraceuticals in Kombucha in Alloxan-induced diabetic mice

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Diabetes mellitus, a metabolic disorder caused by the inability of the beta pancreatic cells to adequately produce insulin or insulin resistance of the cells. Some symptoms of diabetes include hyperglycemia, polydipsia and chronic wounds. Kombucha is a fermented tea, made by the fusion of sweetened-tea with a previous Kombucha culture. Kombucha contains a plethora of beneficial microorganisms and is also source of nutraceuticals such as flavanoids and polyphenolics. Preliminary data on the microbial ecology of the culture indicate the presence of *Paenibacillus cineris*, *Paenibacillus lactis*, *Bacillus licheniforms*, *Corynebacterium glutamic* and *Lactobacillus amylolicticus*. Kombucha tea has also demonstrated anti-diabetic potency in preliminary studies. The present study seeks to characterize novel probiotic strains associated with Kombucha, and evaluate the effect of different Kombucha treatments on the gut microbiome as well as the mode of anti-diabetic action of nutraceuticals in tea Kombucha. Appropriate mice models will be used for the animal studies and ethical clearance will be sought. Different treatments of Kombucha tea and fractionated extracts will be administered to the mice with unfermented tea and water serving as controls. Some biochemical parameters in the mice will be measured over the treatment period. Histopatholgical studies will be carried out. The effect of the treatments on the gut microbiome of the mice will also be determined by metagenomics analysis after the animal is sacrificed. Kombucha tea fractions will be assayed on β cells *in vitro*. Total DNA will be extracted from the fermented tea and sequenced for total microbial identification. Isolation, phenotypic and biochemical characterization of microorganisms will also be carried out to determine their probiotic properties. It would be expected that, novel probiotic strains would be characterized and the mode of anti-diabetic action of Kombucha would be elucidated as well as its effect on modulating the microbiome.

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Characterisation of wild trypanosomes cell surface towards vaccine development

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African Animal Trypanosomiasis (AAT) is the most predominant vector-borne disease that causes serious economic loss in cattle production. This is due to lack of effective chemotherapeutic drugs coupled with unavailability of vaccine. The main challenge to vaccine development for trypanosomes, the causative agent for AAT, is their potent antigen variation of their surface glycoprotein (VSGs) that densely covers their entire cell surface. Studies have shown that Trypanosoma vivax which is the second to *Trypanosoma brucei brucei* in prevalence expresses less dense VSGs on its surface. Preliminary data have shown that there may be other non-VSG surface proteins that are abundant on *T. vivax* and can serve as vaccine targets. The aim of this study is to identify non-VSG immunogenic surface proteins on *T. vivax* during natural infection that can serve as vaccine candidates. Two study sites (Adidome and Bolgatanga) with difference in endemicity were selected for this study. Two herds of cattle (20 each) at Adidome and Bolgatanga were selected based on their geographical location, tsetse fly density, prevalence of trypanosomiasis, age and the breed of cattle available. Blood was collected at approximately eight (8) weeks intervals. The infecting trypanosomes will be identified and characterised using a multiplex nested polymerase chain reaction targeting the trypanosome tubulin gene cluster, and sequencing. Highly expressed surface proteins will be identified through Spliced Leader RNA-sequencing. Selected non-VSG surface proteins will be expressed and their immunogenicity will be tested against sera of infected cattle using ELISA and western blotting. The data generated will identify surface proteins that may serve as potential vaccine candidates.

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Two-Component System of *Vibrio cholerae* as a potential target against Antimicrobial Resistance (AMR)

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The recent emergence of multidrug-resistant *V. cholerae* strains in endemic regions including Ghana is a major public health concern. Generally, *V. cholerae* develop antimicrobial resistance (AMR) through biofilm formation, expression of efflux pumps and membrane modifications. These resistance mechanisms have been linked to the bacterial two-component signal transduction systems. We postulate that identifying a competitive antagonist for the active site of the two component histidine kinase receptor could possibly reverse the evolution of *V. cholerae* resistance to antimicrobials. To test this hypothesis, in silico analysis was performed on the X-ray diffraction crystal structure of histidine kinase (PDB ID: 3MXQ), retrieved from the Protein Data Bank (PDB) with a resolution of 2.78 Å. The missing atoms and amino acid residues of the histidine kinase protein were incorporated into the crystal protein structure using SWISS-PDB viewer and PDB Hydro Mutation Solvation software respectively. The molecular dynamics of the solved protein structure was assessed using Gromacs. A total of 432 ligands from natural products in the AFroDb Zinc12 database were docked in silico to the energy minimized protein structure using the PyRX program. Molecular dynamics were subsequently run on the protein-ligand complexes and ligands with high protein affinity were subjected to ADME tests. The radius of gyration and root mean square deviation (RMSD) after molecular dynamics simulations demonstrated unique stability of the histidine kinase protein. Ten ligands with very low binding energies, showing high binding affinities were identified. Molecular dynamics on the protein-ligand complex indicated a slight change in protein conformation, which suggest an alteration in protein function. *In vitro* analysis of these ligands are yet to be tested on bacteria isolates in the presence of antibiotics.

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Performance of rice and caassava extracts in the reduction of tannins from cashew apple juice

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Cashew apple in spite of its high nutritional value is not consumed in its fresh apple juice form due to astringency. This study therefore aimed to optimize cashew apple juice clarification using cassava and rice extracts to reduce the astringency to enhance its wide acceptance and consumption. Cashew fruits juice were obtained by blending and filtration using microfiltration machine. Five treatments of the cashew apple juices with cassava and rice extracts concentrations (6.2ml/L and 12.4ml/L) and (10ml/L and 20ml/L) respectively were used for the clarification including one control. Each treatment was pasteurized at 750C for 15 minutes and incubated 30 minutes at 30°C. The treated juices were allowed to stay for an hour to allow the tannins to settle. The treated juices were then filtered and tested for these parameters: clarity, taste, smell, colour, swallow ability, mouth felt and general acceptability using likes and dislikes scale by forty respondents including taste experts. The study showed that 10mL/L rice extracts significantly influences the taste (78% likes) and was generally accepted (78% likes) as compared to 10mL/L of cassava extract. However, 20ml/L of rice starch and cassava starch recorded the lowest likes in almost all the parameters taken 20ml/L of rice extracts and cassava extracts recording the lowest likes could be attributed to the higher quantity of clarifier used which affected the taste of the treated juice. 10ml/L of rice extracts is therefore recommended for clarifying cashew apple juice for wide consumption.

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Rational approach for inhibitor discovery targeting the energy metabolism pathway of African trypanosomes

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The details of our efforts to obtain a novel trypanocidal compound that may be useful for the design of new class of anti-trypanosomal chemotherapy will be discussed. African trypanosomes are the pathogens of that cause sleeping sickness in human and Nagana in animals. These diseases are fatal, endemic in sub-Saharan Africa and attributed to the underdevelopment of the subregion. An estimated thousands of human lives and animals worth more than $1.5 billion are lost annually to the diseases. There is no vaccine and available therapeutic options are few and with limited efficacy, prompting the search for new drug candidates. The unique energy metabolism pathway of the parasites is considered a validated rational strategy towards the development of new drugs. Our previous results show that simultaneous inhibition of the trypanosomes' glycerol kinase (TGK) and alternative oxidase (TAO), two key enzymes for ATP synthesis in the parasites' resulted in trypanosomes death. While ascofuranone (AF) is an established TAO inhibitor, there is no known inhibitor for any TGK. The present study was aimed at the discovery of novel TGK inhibitors for co-administration with AF. Here, we utilized the combination of protein X-ray crystallography, computational medicinal chemistry and Enzyme assay approach to conduct large-scale screening of a combinatorial library. The resulting hits were of compounds possessing different structural scaffolds, which potently inhibited TGK up to submicromolar-level IC50 values. Interestingly, a number of the inhibitors caused the expected improvement in the potency of AF against trypanosome cells, causing a shift in trypanocidal activity of AF (IC50) from nanomolar to picomolar concentrations ($P<0.05$). Remarkably, one of the inhibitors proved to be a dual inhibitor of TGK and TAO.

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Developing prosthetic materials from reinforced CNC using cyanoacrylate (Super Glue).

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The last decade has witnessed over two thousand publications on topics related to cellulose (Mariano et al., 2014). Over 60% of these publications were specific to cellulose nanocrystal (CNC). The unique properties of CNC including biocompatibility, bio-degradability, high aspect ratio, light-weight, good mechanical properties and easy availability makes CNC suitable for various biomedical applications such as wound healing, bone-cartilage regeneration, dental application and prostheses (Halib et al., 2017). The rich hydroxyl groups on cellulose nanocrystal makes it possible for it to partake in the curing process of polymer nanocomposites (Xu et al., 2013). As a reinforcing agent, CNC has been used to fabricate various nanocomposites such as casting thin films of Epoxy/CNC nanocomposites (Tang & Weder, 2010) and reinforcement of stereolithic resins (Kumar et al., 2012). The current work focuses on reinforcing CNC using cyanoacrylate adhesive material; Super Glue (SG) to enhance its properties for prostheses development. The goal is to find cost-effective and mechanically robust alternative for the traditional high-cost pure Epoxy lamination resin used in fabricating prosthetic components including prosthetic socket. Different precursor molecules were used to cast six different CNC composites with varying physicochemical properties. Samples were prepared in dimethylformamide and allowed to cure at room temperature up to a week in a non-stick petri-dish. Characterization results from Fourier transform infra-red (FTIR) as well as scanning electron microscopy (SEM) revealed unique features characteristic of a porous material. Also, preliminary Brinell's test results proved the casted films to be potential composites for developing bio-interphase materials for prosthetic socket development.

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Evaluation of genetic diversity and cardiovascular diseases susceptibility of Sickle Cell Disease using single nucleotide polymorphism.

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Sickle cell disease is a genetic disorder of the red blood cell, common in sub-Saharan Africa, India and Middle East. The sickle cell individuals are susceptible to various infections like chlamydia trachoma, and other non-infectious diseases like cardiovascular diseases. In this study, the degree of manifestation of genetic variation in sickle cell cases; single nucleotide polymorphism (SNP) analysis, hematocrit values as well as lipid profile was evaluated to give an insight into the susceptibility of sickle individuals to pulmonary hypertension, haematological as well as lipid profile disorder. The preliminary study carried out among the sickle patients within Fountain University Osogbo, and their relations, revealed susceptibility to pulmonary hypertension followed a phenotype dependent pattern with those of the blood group B been more susceptible to mutational changes in GALTN 13 gene encoding polypeptide N-acetylgalactosaminyltransferase 13 and DRD2 gene encoding Dopamine receptor D2, while those of blood group O are found to be susceptible to mutational changes in PRELP gene encoding Proline and arginine rich end leucine rich repeat protein. Only 10% of the heterogeneous parents and relations were observed to exhibit the similar mutation and 60% of them were known hypertensive. Thus, in this study, the Single Nucleotide Variation with the study cohort was carried out on individuals attending sickle clinic in three tertiary hospitals in Southwest Nigeria.

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Analysis of natural antibody responses to novel *Plasmodium falciparum* Armadillo repeat proteins

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The armadillo (ARM) family of proteins are characterized by repeat motifs that are present in proteins across the eukaryotic lineage and they play diverse cellular roles in apicomplexan parasites. This study sought to identify novel targets of protective immunity or serological biomarkers for *P. falciparum* exposure. We expressed four novel *P. falciparum* ARM proteins using engineered bacteria strains for optimal production of these recombinant products in their active forms. In systematic serological screens of human antibody reactivity against these novel *Pf*ARM proteins, we observed that the dynamics of antibody acquisition varied with age and transmission intensities across the different study sites in Ghana. We affinity-purified *Pf*ARM protein-specific IgGs from the plasma of residents in malaria-endemic areas and observed that human antibodies against two of these novel *Pf*ARM proteins stained the periphery of *P. falciparum* merozoites in immunofluorescence assays. Considering the surface localization of these ARM proteins, we are currently assessing the affinity-purified human antibodies for any parasite invasion inhibitory effects.

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Investigating the redox activity of antifungal drugs on *S. Cerevisae* using electrochemical detection and cell viability studies

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The mechanism of action of most antifungal drugs involves the establishment of cellular stress sites, leading to the formation of reactive species and the transfer of unpaired electrons to vital biomolecules. In this study, antifungal drugs such as Amphotericin B, fluconazole and rifampicin were used. The cyclic voltammetry (CV) results of Amphotericin B obtained were compared to the redox activity of fluconazole and rifampicin. Amphotericin B was used as a model drug to investigate its redox activity on *S. cerevisiae* cells by targeting the plasma membrane while the remaining drugs do not have direct membrane mediated responses. The CV profiles revealed a unique correlation between the electrochemical response and cell viability, as the enhanced redox peaks corresponds to an increase in cell death. The cyclic voltammetric profiles generated, depicted the enhanced the redox activity of the *S. cerevisiae* cells by amphotericin B, through the formation of pores in the membrane. The results depict the possibility of screening new antifungal drugs that penetrate the plasma membrane, to elicit its redox activities as well as the membrane receptor target modulators. It is proposed that most plant products and other natural pools of small molecular drugs could be screened using the experimental technique developed in this work. This would also permit the identification of new molecular entities that target the plasma membrane for further biochemical characterization, since the rate of developing resistance to such classes of antimicrobial compounds is much slower than other classes of compounds.

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Drug delivery capabilities of funtionalized chitosan ssing two dyes

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Methylene Blue and Carbolfuchsin are biological dyes mostly used in biology and medicine to stain structures in biological tissues. These dyes are also used in the identification and staining of polymer structures. Over the years, researchers have been able to study the adsorption properties of Methylene Blue using chitosan composites but limited attention has been given to other dyes such as Carbolfuchsin. The present study compared adsorption and release properties of Methylene Blue and Carbolfuchsin using a one-step synthesized chitosan beads prepared by the sol-gel and cross-linking processes. The composites were characterized by Fourier Transform Infrared Spectroscopy (FTIR) and X-ray Diffraction (XRD) to ascertain their chemical identity. Adsorption studies were conducted using the two dyes at both basic and acidic pH. For Methylene Blue, all composites had comparatively lower adsorbances in acidic media after 40 hours with AA-CHI absorbing most of the dye whiles in basic Methylene Blue media, the composites recorded higher adsobance values. Carbolfuchsin on the other hand recorded negative adsorbances in the acidic medium for all the composites and positive adsorbances in the basic medium with AA-TEOS-CHI and AA-CHI adsorbing more. The release profile of these composite were fitted with an experimental model and the R-squared values indicated that the AA-CHI at pH 2.6 and AA-TEOS-CHI at pH 7.2 of Methylene Blue had steady and consistent release profile. This was same for AA-TEOS-CHI at pH 7.2 of Carbolfuchsin. The release mechanisms were analysed using Korsmeyer Peppas and Hixson-Crowell model and it was deduced that the release profile of majority of the beads were influenced by the conformational structure or surface area changes of the dyes. The results from this study supports the use of AA-TEOS-CHI as useful pH sensitive probes for various biomedical applications and the use of the two-steps synthesized beads in environmental remediation.

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Confirmation of Dengue cases during the outbreak in Burkina Faso, 2017.

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Burkina Faso is one of the countries that has been experiencing viral haemorrhagic fever epidemics in the last 5 years. The objective of this work was to describe the epidemiological situation of dengue fever in the national reference laboratory for viral haemorrhagic fever at the Centre MURAZ, Burkina Faso. Samples were collected from suspected or probable dengue patients from July to December 2017. In addition to dengue fever, other haemorrhagic fever viruses were also investigated by RT-PCR and ELISA for the detection of IgM. Positive RNA samples were tested for serotyping. There were 973 patients from twelve localities in the country with an average age of 29.31 ± 15.85 years. Of these, 677 (69.57%) were confirmed for Dengue. RNA was detected in 464 (68.53%) cases, IgM in 85 (12.55%) cases and both simultaneously in 128 (18.90%) cases. A case of dengue, West Nile and Yellow Fever co-infection has been identified. Serotyping tests on 273 RNA-positive samples showed circulation of the following serotypes: DENV1 (7.33%), DENV2 (72.53%) and DENV3 (20.14%). The national reference laboratory for viral haemorrhagic fever confirmed the circulation of three serotypes of Dengue virus with a predominance of the DENV2 serotype in 2017 in Burkina Faso. These confirmations helped to strengthen the response to the epidemic.

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Larvicidal activity of crude extracts of *Vernonia cinerea* less (*asteraceae*) against the *Anopheles gambiae* in Bobo-Dioulasso, Burkina Faso

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Mosquitoes are vectors responsible for filariasis, yellow fever, dengue fever and malaria. Among these diseases, malaria causes many deaths in children < 5 years and pregnant women. In 2017, WHO recorded 216 million cases and 445,000 associated deaths with 90% in sub-Saharan Africa. Faced with this scourge, the WHO has advocated the establishment of new control strategies such as the use of synthetic insecticides. However, some are inefficient and have adverse effects for humans and the environment. The search for new biological insecticides is necessary. *Vernonia cinerea* Less (*Asteraceae*) is widely distributed in India and the western part of Burkina Faso. It has many therapeutic uses in different traditional medicines. Our aims is to evaluate the effect of lyophilized methanolic, hydro-methanolic and aqueous extracts of *Vernonia cinerea* Less against the stage 3 and 4 *Anopheles gambiae* larvae. The plant material was collected in Banfora. The larvicidal activity of lyophilized extracts have been tested. The L3 and L4 *Anopheles gambiae* larvae were used for test. The concentrations were prepared. The larvicidal activity was tested in laboratory condition and outside laboratory. The larvae mortality was evaluated after 24h and 48h of exposure. The % of means of mortality were calculated. The data were analysis with the R version 3.0.0 software and Excel 2013. In the laboratory, methanolic extract at 100 mg/L showed 100% of mortality after 24h of exposure. In outside laboratory the same extract at 10mg/L gave 95.85 ± 1.26 % of mortality. The hydro-methanolic extracts gave LC50 of 22.27 mg / L against 3417.78 mg / L respectively in laboratory and outside laboratory. The methanolic extract is the most effective on the larvae compared to the other extracts tested. Vernonia cinerea possesses good larvicidal activity against Anopheles gambiae larvae. It may be a possible source of mosquito vector control.

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Archaeology and medical practices of Obosomase and Nakpanduri practical implications

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Archaeological artefacts have a wealth of ancient culture hidden in them. A critical analysis of these relics reveals the events that took place in the past and even the medical practices of old. Nonetheless, the use of archaeology to better understand the medical practices of most communities in Ghana are under-exploited. Plant parts and artefacts of most archaeological sites, like Obosomase, in the Eastern part of Ghana, and Nakpanduri, the Northern part of Ghana are infrequently taken into context. This paper demonstrates the analysis of artefacts; which have ancient molecules absorbed into them, to give cues into the past healing culture of these two towns. The molecules were extracted from the artefacts using methanol and ethanol, and an ultra-violet analysis performed on them. The redox activities of the extracts were analysed using cyclic voltammetry, to determine the behaviour of the absorbed molecules. The experiment revealed a high possibility of the absorbed organics present in the artefacts to be natural products, especially herbs. Thus, the absorbed molecules reveal hints into the ancient medical culture of Obosomase and Nakpanduri; the possibility of being used for several biomedical applications; and even shed light on modern ailments.

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Norovirus culture: A review of the challenges and the prospects

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Noroviruses (NV) are caliciviruses that infect the gut of their hosts and cause gastroenteritis. Different hosts, such as rodents, humans, pigs, cattle, sheep, dogs, cats and lions have been found to be infected with NV. Unlike other noroviruses, efficient cell culture systems have been established for murine noroviruses (MNV). However, some human noroviruses (HNV) have been reported to occasionally replicate at very low levels in various cell lines including 3D-cultured CaCo – 2 cells, C2BBe1, human enteroids, and human B cells. This review will analyse growth of MNVs and HNVs in various cell cultures, discuss the successes and challenges of the cell cultures, and as well identify prospects of developing robust cell culture systems for HNVs.

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Detection of Dugbe virus from ticks in Accra, Ghana

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Dugbe virus belongs to the viral family, *Nairoviridae* and genus *Orthonairo* virus. It is transmitted by tick species of three genera; *Rhipicephalus*, *Amblyomma* and *Haemaphysalis*. This study aimed to screen field collected ticks for the presence of Crimean-Congo hemorrhagic fever virus (CCHFV). Sampling was done in seven sites within Greater Accra, Northern and Upper East regions. A total of 1813 ticks were collected from cattle, dogs, sheep and goats and morphologically identified. Ticks were pooled by species, gender, study site and animal host and were homogenized. Nucleic acid was extracted and screened for CCHFV. Three of the pools tested positive for CCHFV. The positive tick species were *Rhiphicephalus sanguineus* in Navrongo, *Hyalomma rufipes* in Shai Hills, and Amblyomma variegatum in Michel Camp. Pools were further analyzed using next-generation sequencing targeted enrichment protocol. Sequencing performed on all three pools failed to confirm presence of CCHFV; however, the resulting data from one of the pools from Michel Camp, Accra showed whole genome sequence of Dugbe virus. Phylogenetic analysis of the complete sequence of the Dugbe virus using Maximum likelihood tree algorithm showed a close relationship with the Dugbe virus strain previously found in Ghana, Kenya and Nigeria. Further surveillance and characterization studies need to be conducted to determine the prevalence of the virus in Ghana.

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Effects of immune checkpoint molecules on disease progression, persistence and latency in HIV-infection

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HIV infection remains a global health challenge with no active therapy to fight HIV latency. A sub-population of HIV-infected patients, referred to as long term non-progressors (LTNPs) are known to maintain high CD4+ T cell count (usually above 500 cells/µl) even though they are not on anti-retroviral therapy (ART). The mechanism of immune interactions in these LTNPs is not well studied. Although there are host and viral factors implicated in the course of HIV disease, the role of immune checkpoint molecules (ICM) in regulating HIV progression, persistence and latency during suppressive ART is not fully understood. Immune checkpoint molecules; PD-1, CTLA-4 and TIGIT have shown strong correlations with LTNPs as well as down regulation of HIV-specific T lymphocytes. This study sought to investigate the role of ICMs on HIV persistence, progression and latency in ART-naïve and ART-exposed patients. Two groups of HIV-1 infected patients were recruited (progressors and non-progressors) and differentiated based on their CD4+ T cell count and viral load. HIV-1 negative males and females were enrolled into a control group, and CD4+ and CD8+ T lymphocytes, as well as HIV viral RNA and cytokine patterns were measured. Quantitative Viral Outgrowth Assays (QVOA) on HIV-specific T lymphocytes isolated from purified PBMCs were used to determine persistence and latency in HIV-1 infection. Plasma levels of viral RNA in non-progressors were found to be lower compared to the progressors. The cytokines measured, will give information on the immune response to inflammation. Understanding the biology of the latent reservoir and the mechanism of re-ignition of HIV-1 infection will provide a clinical rationale for blocking multiple ICMs to enhance anti-HIV immunity, as well as contribute to the development of novel therapeutic strategies targeting the persistent HIV reservoir.

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Deciphering the association of a novel *Plasmodium falciparum* exported protein with parasite-induced structures

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Plasmodium falciparum survives within host erythrocytes by devising strategies for successful export of several proteins beyond the parasitophorous vacuole. This has fostered interest in some of the membranous structures established by the parasite during protein export. We have identified a novel *P. falciparum* exported protein that harbors a canonical PEXEL variant. To functionally characterize the protein, three peptides (P1, P2, and P3) were chemically synthesized based on B-cell epitope mapping and screening for coiled-coil signatures. Stage-specific expression analysis by immunofluorescence assays (IFA) showed that the protein is expressed in late ring, trophozoite and schizont stages. Antibodies were generated against the three peptides but only anti-P3 antibody detected the full-length native parasite protein (50 kDa) in detergent-treated schizont lysates, while anti-P2 antibody detected a truncated fragment (~22 kDa) of the native protein close to the PEXEL motif and anti-P1 antibody did not detect the native protein. We also showed that the export of the protein is Brefeldin A-sensitive by comparative IFA analysis of trophozoite-infected erythrocyte ghosts, selective permeabilization of infected erythrocytes and immunoblotting. Since protein export precedes gametocytogenesis, we have shown the localization of the protein in different stages of gametocytes. Cellular fractionation experiments revealed the differences in the subcellular localization of the protein which was attributed to changes in solubility states of the protein within the parasite-host compartment. Further work on protein-protein interaction experiments is ongoing to substantiate an initial evidence suggesting that the novel *P. falciparum* exported protein (50 kDa) forms a 200 kDa multi-protein complex in trophozoite lysates. It is expected that this study may shed more insights on the association of this protein with parasite-induced membranous structures.

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Investigation into intra-species indoor and outdoor resting behaviour in malaria vectors

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Selection pressure from continued exposure to insecticides used for malaria control including indoor residual spraying (IRS) and long-lasting insecticide treated nets (LLINs) seem to be driving development of insecticide resistance and changes in resting behaviour in malaria vectors. These have been implicated to contribute significantly to the increasing residual malaria transmission in several malaria endemic settings. The aim of this study was to investigate the insecticide resistance status between indoor and outdoor-resting mosquito populations to understand their contribution to residual malaria transmission. Fed mosquitoes were collected indoors and outdoors from two communities in Ghana (Kpalsogu and Libga). These were allowed to lay eggs in the insectary and the larvae were reared to become adults. WHO insecticide susceptibility tests were carried out to determine phenotypic resistance. Sibling species identification were done by PCR. Sibling species identification were done by PCR. Biochemical and target site resistance were determined in these two groups of mosquito populations. Phenotypic resistance to deltamethrin and DDT was higher in the indoor *Anopheles gambiae* population from Kpalsogu with 24-hour post-exposure mortality of 63% (95% CI: 57.7-68.3%) compared to the outdoor mosquito population with mortality of 99% (95% CI: 98.0-100%). Mosquito populations were suspected to be resistant to bendiocarb phenotypically in both sites where the outdoor populations had mortality of 95% (95% CI: 92.6-97.4%) and 90% (95% CI: 85.4-94.6%) in the Libga indoor populations, which was higher than the outdoor population of 95% (95% CI: 92.6-97.4%). Mosquito populations were more susceptible to malathion in Libga (98-100% mortality) than in Kpalsogu (95% mortality) where there was suspected resistance. Data collection is ongoing.for the molecular insecticide resistance mechanisms and the species involved in residual malaria transmission in the two communities. The study will help to understand the contribution of insecticide resistance in residual malaria transmission.

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Impact and ecology of *Streptococcus infantarius* subsp. *Infantarius* in the milk value chain in northern Cote d'Ivoire

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Milk is an important source of income and nutrients but it is a zoonoses' transmission source due to the poor production-processing conditions. The novel *Streptococcus infantarius subsp. infantarius* (*Sii*), members of the *Streptococcus bovis/Streptococcus* equinus complex (SBSEC), are predominantly present in spontaneously fermented milk products across Africa. However, Sii has never been isolated from raw milk. SBSEC and possibly *Sii* are associated with diseases including colon cancer and infectious endocarditis. *Sii*/SBSEC prevalence data for West Africa are limited. We determined *Sii*/SBSEC prevalence in Northern Côte d'Ivoire along the cow milk supply chain during a cross-sectional study in 2014. Phenotypic and molecular analyses identified SBSEC in 27/43 (62.8%) fermented and 26/67 (38.8%) unfermented milk samples. Stratified by collection stage, fermented milk at producer and vendor level featured the highest SBSEC prevalence of 71.4% and 63.6%, respectively. Sii with 62.8% and 38.8% as well as *Streptococcus gallolyticus subsp. macedonicus* with 7.0% and 7.5% were the predominant SBSEC species identified among fermented and unfermented milk, respectively. A large variability was observed among Sii/SBSEC isolates including dairy-adapted, non-adapted and potential pathogenic *Sii*/SBSEC lineages that required detailed safety and ecology assessments. A follow-up ecological study is underway in the major milk production and consumption areas of Northern Côte d'Ivoire with the aims to determine origins of introduction of *Sii* in the milk supply chain by sampling milkers' hands, udders of cows, tongue of calves, soil, air, water, utensils and raw milk directly sampled from udders of cows. Moreover, the greater adaptation of certain *Sii* to milk metabolism, the absence of virulence factors in these *Sii* and their ability to inhibit certain food pathogens like Listeria point out potentialities of *Sii* to be an excellent starter culture. The technological properties of such *Sii* strains will also be evaluated and a *Sii*-based starter culture will be developed.

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

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Asymptomatic *Plasmodium falciparum* infection is a major obstacle for malaria elimination due to lack of clinical symptoms and challenges in diagnosing this individuals. Also the long term impact of this infection on hematological parameters in the host is not known. The aim of this study was therefore to investigate the contribution of some host factors to the establishment of asymptomatic *P. falciparum* infection and its impact on some hematological parameters. The study was conducted in Obom in the Ga South municipality of the Greater Accra Region. Three hundred and nine (309) study participants within the ages 8-50 years without any malaria related symptoms were recruited during the dry season and monitored for malaria related symptoms for six months (end of rainy season). Five milliliters (5 ml) of venous blood was obtained twice, at beginning and end of the study period, from each participant. Full blood count, Hb electrophoresis, blood group typing and screening for malaria parasites by microscopy and nested polymerase chain reaction PCR (nPCR) were done for each participant. Of the 309 study participants, 10 became symptomatic after baseline sample collection, seventy two tested positive at base line and six months and were classified as asymptomatic while 97 tested negative at base line and six month and were classified as uninfected. Age, Hb genotype, blood groups, gender and use of mosquito nets were not associated with asymptomatic infection as compared to un-infection ($P > 0.05$ in all cases). No pathological effects of asymptomatic infection were observed on hematological parameters. The results of this study suggest that some individuals can habour asymptomatic *Plasmodium falciparum* infections up to six months and the carriage of these may be submicroscopic and not alter hematological parameters.

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PfRH2b structural polymorphism: its frequency and relation with malaria endemicity in Ghana

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Plasmodium falciparum virulence is characterized by the use of surface proteins as well as organelles such as the micronemes and the rhoptries to facilitate erythrocyte invasion aimed at proliferation. The surface proteins within the multigene *Plasmodium falciparum* Reticulocyte binding protein Homologues (PfRH) family play a pivotal role in merozoites invasion. Structural polymorphism within the PfRH2b gene has been implicated in humoral immune dynamics such as, acting as a potential and potent antibodies reactivity target. More specifically, a 0.58 Kb deletion, at the C-terminus has been reported in high frequencies in Senegalese and Southeast Asian parasite populations. However, the frequency of this deletion mutation in parasite population in Ghana has not been established. We therefore hypothesized that, the observed deletion in PfRH2b is skewed towards hyper-endemic areas where humoral acquired immunity predominates due to higher parasitaemia tolerance. Here, by analyzing 740 *P. falciparum* isolates, we have successfully shown that this deletion is present within the Ghanaian population (53.5% of all isolates) and observed mainly in the Kintampo (holoendemic, 56.7%), followed by Cape Coast (mesoendemic, 52.5%) and then Accra (Hypoendemic, 50.4%). It is significant to note that, the frequencies observed concur with data published from Senegal (62.2% deleted status) and Malawi (58% deleted status). Interestingly, some parasite isolates possessed mixed PfRH2b deletion status (7.4%), indicative of multiple clonal isolates. We further sequenced the PfRH2b gene from some of the isolates from the different locations aiming to detect unreported polymorphisms emanating from immune pressure. Contrary to expectations, sequence similarities between parasites from the different locations were high. In all, we have successfully characterized the PfRH2b gene deletion region polymorphism within parasite isolates from Ghana and shown that the frequency of the deletion appears to correlate with levels of endemicity

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Investigating the effect of organic extracts of *Dioclea reflexa* on cancer and normal cells using electrochemical detection and cell viability studies.

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Dioclea reflexa is a leguminous plant that has gained much recognition over the years because of its diverse medicinal properties with impressive outcomes. Some parts of this plant -- especially, the seeds and leaves-- are known to have good antimicrobial and antioxidant activities, and has resulted in its extensive treatment of several diseases including stomach ulcer, tuberculosis, asthma and the most notable among them is cancer. However, little research has been done on how the bioactive compounds present in the extracts affect the electrochemistry (redox activity) and cell viability of normal cells of their host whiles treating oncogenic cells. The present study used different extracts of *Dioclea reflexa* from the seed and pericarp using methanol, ethanol and water to investigate their effect on different cancer cell lines (HeLa, 22RV1, DU145, and PC3). The results were compared with normal cells using electrochemical detection and cell viability studies. Gossypol is an anticancer drug and was used as a control drug for these studies. It was found that the water extracts from pericarp and seed of the *Dioclea reflexa* investigated exhibited significant increase in the anodic peak currents compared to that of Gossypol. Correspondingly, the water extracts from the pericarp recorded a cell viability of about 90% followed by the water extract from the seed with a cell viability of 45%. The results from the methanol and ethanol extracts were also investigated on all four cancer cell lines. All the results were compared to the effects of Gossypol and will be discussed in the conference.

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Species distribution and insecticide resistance status of *Anopheles* mosquitoes from Cape Coast and its implication on malaria control

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The main objectives of this study were to identify the species of *Anopheles* mosquitoes in Cape Coast, determine their insecticide resistance status and assess bio-efficacy of insecticide treated net against them. A larval survey was conducted in the entire Cape Coast between 2014 and 2017. Larvae were collected from several breeding habitats and reared to adult stage. Anopheles species were identified by both morphological and molecular techniques. The adult females were tested against eight insecticides; Permethrin 0.75%, Deltamethrin 0.05%, DDT 4%, Dieldrin 0.4%, Bendiocarb 0.1%, Propoxur 0.1%, Fenitrothion 1%, and Malathion 5%. Frequency of *Kdr* mutation and enzyme activities of the population were determined. Cone bioassay was used to assess the bio-efficacy of new ITNs and those in use in some households in Cape Coast and the surrounding towns. The major *Anopheles* species was *An. gambiae s.l,* which was dominated by *An. coluzzii.* Other species like *An. nili* and *An. hancocki* were also found. The mosquitoes were highly resistant to pyrethroid and organochlorine insecticides whiles completely susceptible to the organophosphate but slightly resistant to carbamate insecticides. The L1014F *Kdr* mutation was detected at a frequency of 87%. The mean mortality (± S.E) of mosquitoes exposed to 19 ITNs used in various households was 26.3% ± 2.5 (Figure 2). The mean duration of use was 5.6 months ± 0.7 with 1.4 ± 0.3 washes. Surprisingly, the four new ITNs also caused very low mortality (18.5% ± 6.2) to the mosquitoes. The personal protection offered by ITN undoubtedly has a positive impact on malaria control but to halt or eliminate the disease, the efficacy and adherence must be very high. It is for this reason that the insecticide resistance and reduced efficacy of ITN observed in Cape Coast are worrying and need immediate attention.

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Dynamics of *Vibrio cholerae* virulence factors associated with diarrhoea outbreaks in Ghana

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Ghana is regularly affected by Cholera outbreaks with an annual average of over 3,000 cases in two decades. In 2014, Ghana experienced an exceptionally large outbreak with over 20,000 cases. This increasing number of cases calls for investigation in a timely manner. We therefore investigated and compared clinical *V. cholerae* strains from outbreaks in Ghana with special reference to strain diversity and virulence factors acquired by these bacteria over time. A total of 219 stool samples were collected within 2012- 2015 from 9 health facilities in Ghana. Samples were cultured and obtained isolates characterised by biochemical identification, serotyping, drug susceptibility testing, phenotypic determination of extended-spectrum -lactamases (ESBLs) activity, distinct virulence genetic markers and multi-locus variable number tandem repeat analysis (MLVA). Among the 219 samples cultured, 110 (50.2%) yielded *Vibrio cholerae* O1 isolates and 109 (49.8%) were characterized as other of the 110 *V. cholerae*, 4 (3.6%) were isolated in 2012, 92 (83.6%) in 2014 and 14 (12.7%) in 2015. This study identified 75% (3/4) mono resistance to cotrimoxazole in 2012 and >87% (93/106) MDR to cotrimoxazole, nalidixic acid and ampicillin with reduced susceptibility to tetracycline, doxycycline and ciprofloxacin in both 2014 and 2015 isolates. Serotyping identified 97 (88.2%) Ogawa, 3 (2.7%) Inaba and 10 (9.1%) non-reactive. Genotypic analysis differentiated the isolates into 3 clones. MLVA is still in progress. Microbiological analysis of three cholera outbreak years illustrate newly emerging Inaba serogroup and 3 clonal complexes, which might hint to an endemic reservoir of *V. cholerae* in Ghana. Public health authorities must be vigilant and take steps to prevent cholera transmission through aquatic reservoirs. Considering the rapidly emerging MDRs among V. cholerae isolates, laboratories are encouraged to monitor antimicrobial susceptibility closely.

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