

# **2021 WACCBIP** RESEARCH CONFERENCE

Building Sustainable Research Capacity in Africa: Lessons from the Pandemic









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## Editors

Prof. Gordon Awandare Dr. Yaw Bediako

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## 01

## ABOUT WACCBIP

## WACCBIP INSPIRES

### EXCELLENCE

The West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) is a grants-funded Centre of Excellence established in 2014 to provide Master's & PhD training, as well as targeted short-courses in Cell & Molecular Biology. The Centre also has a mandate to conduct applied research into biology and pathogenesis of tropical diseases, and increase research output and innovation by enhancing collaboration biomedical among scientists and industry/private sector leaders in the sub-region. Having won two of the largest and most competitive research/training capacity funding schemes in Africa (the World Bank's African Centres of Excellence (ACE) grant and the Wellcome Trust

Developing Excellence in Leadership, Training and Science (DELTAS) Africa Initiative grant), the Centre has built a reputation for excellence across its core areas of activity in research, training, and scientific citizenship. WACCBIP's record of achievement has led to further success in winning supporting grants that are harnessed to expand and enhance its activities.

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







## OUR OPERATIONS

WACCBIP's mandate is to provide Master's, PhD, and Postdoctoral training, as well as targeted short-courses in Cell and 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. The Centre also seeks to strengthen its research output, expand its regional network beyond West Africa, and train Postdoctoral fellows.

## Research

WACCBIP's research mission is to conduct cutting-edge research to guide the development of new approaches to disease diagnosis, prevention, and control. Having established a world-class scientific research environment with wideranging technology platforms, the Centre is optimised to conduct high-quality research into an expanded range of infectious & non-communicable diseases, impacting healthcare delivery, and contributing to drug discovery and vaccine development in Africa.

Prominent among the Centre's research accomplishments are its characterization of the first locally-acquired dengue infections and the first extensive drug-resistant tuberculosis case in Ghana; its mapping of emerging malaria parasite resistance to sulphadoxine-pyrimethamine drugs, and discovery of new vaccine candidates and drug compounds for blood stage malaria; the isolation of novel compounds from herbal and fungal sources that show activity against trypanosomes and mycobacteria; its development of novel biosensor-based diagnostic tools which can be applied for detection of biomarkers of various diseases; and the identification of the specific mutation that is most associated with susceptibility to hearing impairment in Ghana.

Focusing on the COVID-19 pandemic in Ghana, researchers and fellows at WACCBIP with expertise in virology, immunology, bioinformatics, and genetics have been involved with COVID-19 related research and have aided in Ghana's response to





the pandemic. Using Next-Generation Sequencing (NGS) technology, researchers at WACCBIP have successfully sequenced over 750 genomes of the viral strains circulating in Ghana. Additionally, the Centre has completed several phases under a continuing seroprevalence study to provide critical information about SARS-CoV-2 and the spread of the disease in Ghana. This work has provided key pieces of information on the prevalence of COVID-19 and the distribution of SARS-CoV-2 variants to better inform public health interventions, including infection control measures and vaccine deployment. A total of 261 publications have been churned out of the Centre's research work since 2014.



## WRC \_\_\_\_\_ IMPACT OF WACCBIP'S RESEARCH

### HOW IT MAKES A DIFFERENCE

WACCBIP's research has covered a wide range of diseases, including infectious diseases, neglected tropical diseases and noncommunicable diseases.

### DIRECT RESEARCH TRAINING

Much of WACCBIP's research projects have been undertaken by students and postdoctoral fellows, under the supervision of faculty members. The results of these projects have greatly impacted healthcare delivery in the sub-region and identified some promising leads for drug and vaccine development. Much of the Centre's research is published with the trainees as first authors; thus, enhancing their career development and motivating them for further highquality research.

### **PANDEMIC RESPONSE**

By building world-class research capacity, WACCBIP is able to provide real-time surveillance for effective national epidemic response. Its stateof-the-art sequencing facilities, for example, were essential to tracking SARS-CoV-2 strains that were circulating in Ghana, as well as in tracing the origins of imported strains and establishing local evolution. Having high-quality sequences also



enabled the Centre to contribute to the global response to COVID-19 with submissions to GISAID, one of the first few African Centres to do so.

## CONTEXT-SPECIFIC RESEARCH

WACCBIP's solution-oriented research is directed at solving the specific healthcare challenges facing Africa. The priority diseases include malaria, trypanosomiasis, tuberculosis, Buruli ulcer, HIV, rotaviruses, influenza, and dengue, as well as non-communicable diseases such as cancers, chronic kidney disease, sickle cell disease, and diabetes. For these disease areas, it aims to find sustainable solutions that are tailored for and relevant to the African context.



## Training



WACCBIP has positioned itself as a major hub in Africa for training young African scientists. Since 2014, the Centre has provided fellowships for Master's, PhD, and postdoctoral training to more than 300 young scientists from more than 14 countries across the African continent.

The Centre also provides opportunities for career development to industry professionals through short courses. The Centre has built a pedagogic resource base comprised of local, subregional & international biomedical scientists working in world-class institutions across the globe who help facilitate specialized training programmes in Molecular Cell Biology of Infectious Diseases at the MPhil and PhD levels. These programmes are accredited by the Ghana National Accreditation Board and received the International Advanced Degree Accreditation from the United Kingdom's Royal Society of Biology in November 2016. These programmes were the first in Africa to receive endorsement from the Royal Society.

WACCBIP provides a complete pipeline of training, from Master's & PhD programmes to Graduate Internship and postdoctoral programmes, combining rigourous academic training with direct mentorship from worldclass senior scientists. A total of 377 trainees have been enrolled in longterm programmes and 892 biomedical scientists and health professionals in short courses and workshops.

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## WACCBIP'S TRAINING PIPELINE



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## WACCBIP'S TRAINING PIPELINE





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## Funding & Sustainability

The major plan of our sustainability is to continue building our faculty and placing WACCBIP in a strong psoition for competitive funding from donor agencies. We hope to do this by demonstrating consistency in teaching and reserach excellence. With the increased visibility and credibility that we have gained through the African Centres of Excellence Project and the Wellcome Trust DELTAS project, the centre is well placed to access additional funding for its training programmes. The Centre has posititioned itself as a globally competitive centre of excellence for research and training, and for that reaseon, our long-term sustainability depends on the quality of our graduates and the impact of our research.

**WACCBIP** operates as a semi-autonomous unit and its activities are financed financed through the World Bank support, Wellcome Trust DELTAS grant, and additional grants mobilized by the Centre and its faculty and collaborators.

Therefore our sustainability strategy involves four key components, with systemised strategic milestones within short-erm, medium-term, and long-term target periods.

Overall, we aim to;

- win competitive grants and research contracts;
- provide fee-for-service core facilities;
- lead innovation by leveraging patents and developing biotech spin-offs; and
- attract training contracts from industry and sectoral organisations.



## 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 subcommittees for Training and Reserach, Equipment & Logistics, and Information Communication Technology (ICT).

There is also a Monitoring and Evaluation team whose head is a member of the Management Committee. The Centre has an International Advisory & Scientific Review Board, comprising international experts who directly advise the 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 gthe Noguchi Memorial Institute for Medical Research.

The Centre also draws on other faculty from within the College of Basic and 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 experintial learning.

#### Secretariat

The WACCBIP Director is assisted by a Centre Secretariat, which has an Administration headed by a Grants Manager, a Communications & Public



Engagement Manager; an Accounts unit headed by a Senior Accounts Officer; and an ICT Unit headed by a High Performance Computing Manager.

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







## WACCBIP International Advisory Board

**WACCBIP's** International Scientific Advisory Board (ISAB) includes international experts whose mandate is to provide sound and independent scientific advice on scope of WACCBIP's scientific objectives, to guide and advice on the strategic planning and financial sustainability of the Centre, to evaluate the Centre's scientific and research outputs, and to to assess its contribution to public health at various national and international levels.

Name	Position	Institution
Prof. Keith Gull	Chairman	Sir William Dunn School of Pathology, Univ. of Oxford
Prof. Gordon Awandare	Member	Director, WACCBIP
Prof. Kirk W Deitsch	Member	Weill Cornell Medical College, Cornell University
Prof. Mark Carrington	Member	Department of Biochemistry, University of Cambridge
Prof. Eric Osei-Assibey	Member	Dean, International Pro- grammes, University of Ghana
Prof. Mahamadou Diakite	Member	Malaria Research & training center, Mali
Prof. Felix Ankomah Asante	Member	Pro-VC, ORID, University of Ghana
Prof. Kwadwo A. Koram	Member	Noguchi Memorial Institute for Medical Research, Univ. of Ghana
Dr. Abraham Oduro	Member	Ghana Health Service
Prof. Daniel K. Asiedu	Member	Provost, College of Basic and applied Sciences, Univ. of Ghana
Prof. Augustine Ocloo	member	Dean. School of Biological Sci- ences, University of Ghana
Prof. K. Tanoh-Debrah	member	Dean, School of graduate stud- ies , Univ. of Ghana



Prof. Abraham Kwabena Anang	Member	Director, Noguchi Memorial institute for Medical Research, Univ. of Ghana
Prof. Osbourne Quaye	Member	Head of Department, BCMB
Douglas J. Perkins	Member	University of New Mexico
Mr. Alex Asiedu	Member	Chief Executive Officer, STAN- LIB Ghana LTD
Mrs. Deborah M. Agyemfra	Member	Deputy Director-General Legal, Securities & Exchange Com- mision
Mr. Benjamin Kwame Botwe	Member	President, Pharmaceutical society of Ghana
Dr. Martha Gyansa-Lut- terodt	Member	Director, Technical Coordina- tion, Ministrt of Health, Ghana





# WACCBIP Management & Staff

Name	Designation
Prof. Gordon Awandare	Director / Centre Leader
Prof. Dorothy Yeboah-Manu	Deputy Director
Rev. Dr W.S.K Gbewonyo	Mentorship Coordinator
Prof. Osbourne Quaye	Head, Monitoring and Evalua- tion
Dr Lydia Mosi	Logistics Coordinator
Prof. Neils Ben Quashie	Representative for College of Health Sciences
Dr Patrick Arthur	Head, Training and Research
DrYaw Bediako	Science Ambassador and Head of Advancement
Dr Therasa Manful Gwira	Graduate Admissions and Ex- aminations Coordinator
Dr Lucas Amenga-Etego	Research Fellow
Mr Barfi-Adomako Owusu	Co-Head, ICT (Electronic Re- sources)
Mr Francis Boachie	Co-Head, ICT (Physical Re- sources)
Prof. Dorothy Yeboah-Manu	Postdoctoral Programme Coor- dinator
Prof. Daniel B. Sarpong	Representative from College of Basic and Applied Sciences
Prof. Isaac Asante	Representative for Vice Chan- cellor
Mr Anthony Hofe	Financial Manager
Dr Winfred-Peck Dorleku	Industrial Liaison
Mrs. Constance Kocke	Representative from Procure- ment Unit



Mr Collins Misita Morang'a	Representative for Graduate Students
Mr. Barfi Adomako	Co-Head of ICT, Electronic Resources
Ms. Ama G. Dadson	Co-Head of ICT, Physical Re- sources
Mr. Anthony Hofe	Finance Officer
Ms. Sika Menka	Grants Manager
Mr. Andrew M.Nantogmah	Communications Manager
Ms Emefa Adzadu	Senior Accounts Officer
Mr Vincent Appiah	High-Performance Computing Manager
Mrs Joyce Ngoi	Next-generation Sequencing Laboratory manager
Mr. Srinvasan B. Shankar	Laboratory Technologist
Mr. Felix Kyei Pepra	Administrator
Ms. Marian Nanor	Accounts Officer
Ms. Sarah Ofori Ntim	Procurement officer
Ms. Kyerewaa Akuamoah Boateng	Public Engagement Officer
Mr. Theophilus Dugah	ICT Technician
Mr. Alfred Kazaresam	ICT technician
Mr. Simon Donkoh	Administrative Assistant













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## WACCBIP UPDATES

# PUBLIC ENGAGEMENT

With a strong commitment to the principles of impactful scientific citizenship, WACCBIP places high premium on public & community engagement with numerous initiatives directed at bridging gaps in public understanding of Science. The Centre's Community/Public Engagement (CPE) activities are streamlined to foster context-specific, audience-tailored two-way communication aimed at improving community-oriented research. The Centre's focused CPE initiatives (schools engagement, community interaction programmes, outreach events) target hard-to-reach, underserved, and at-risk groups identified through community consultation in collaboration with national/district/local authorities.



## SCHOOLS ENGAGEMENT

Dedicated programmes targeted at young high school students in Ghana, aiming to inspire and encourage them to pursue careers in Science.



## COMMUNITY INTERACTION

Events & campaigns designed to create room for researchers and members of affected communities to discuss disease control, prevention & treatment.



#### **OUTREACH EVENTS**

Medical outreach events organised to provide a range of disease screening services and free medical consultation to deprived communities across Ghana.

WACBIP



annual WACCBIP's High Schools Engagement Programme is designed to inspire high school students towards collective action against common infectious diseases and to consider scientific research as a future career. either directly or in support roles. Using peer-learning strategies, postundergraduate research trainees interns) share (graduate relevant knowledge that will prepare students to become agents for disseminating best practice on prevention, control, and treatment of infectious diseases endemic to their communities, while inspiring especially female high school students to take up future careers in scientific research. Between 2017 and 2019, the programme reached more than 4000 students (see Appendix A) across more than 20 high schools across northern, western, and southern Ghana. Beneficiaries have reported

The High Schools Engagement Programme (HSEP), is a WACCBIP public engagement initiative that targets students in underresourced high schools in Ghana.

(see Appendix B) positive impacts of the programme, with students selfreporting that they were motivated to share their learnings with their communities and trainee scientists understanding the need for public engagement and developing skills towards facilitating their own public engagement activities in their future scientific careers. The programme's impact led to its selection as finalist at the 2019 Falling Walls Engage, an international platform that showcases successful science engagement projects from diverse fields.

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#### COMMUNITY INTERACTION PROGRAMMES



continuously facilitates community interaction programmes, including town hall meetings & durbars, in partnership with the Ghana Health Tuberculosis Service, National Programme, and the Ghana Education Service. These programmes are also developed and conducted in partnership with community members, advisory groups, community health workers, market associations, drama production groups, etc, with the aim of presenting vital information about infectious and non-communicable diseases to help safeguard guality of life. The Centre has established annual campaigns for malaria and breast cancer (see Appendix C), where members of vulnerable communities and highly susceptible populations are sensitised on the nature, prevention, and treatments for these diseases. The annual Breast Cancer campaign, 'Nufu (meaning 'breast') Festival', for example, reaches about 300 women each year with interactive contextspecific discussions on breast cancer and the myths surrounding the disease. The campaign also attracts significant media attention, which broadens the audience base from those reached at the physical events. The Centre has also dedicated a special campaign to address a gap in the knowledge on the genetic causes of hearing impairment across Ghana. The campaign, primarily communities targeted at with significant percentages of hearingimpaired people, uses communication strategies such as participatory rural appraisal to dispel myths surrounding the causes of the condition. Using a series of docu-dramas, translated into several local languages, the campaign aims to reach several communities across the country, explaining the genetics surrounding hearing impairment. The central message, which focuses on removing existing conceptions of witchcraft and/or infidelity as causes of hearing impairment, encourages communities to accept sufferers, thereby improving their quality of life and those of their families.

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## COMMUNITY OUTREACH ACTIVITIES







WACCBIP supports various community outreach events organised by the Centre's researchers to address identified information gaps relating to various diseases. Dedicated events for HIV/AIDS, tuberculosis, malaria/autism awareness creation, and COVID-19 (see Appendix) have been incorporated into the Centre's CPE plan. For these disease areas, the Centre aims to interact with at-risk groups/ communities to gain an understanding of their beliefs/knowledge systems, as it addresses myths/false information attached to the diseases. Medical teams also provide consultation and free screening services to members of these communities, as well as primary treatment where available. For example, the Centre funds an annual HIV/AIDS outreach event to mark World AIDS Day, where researchers speak to members of the general public about prevention and disease management. Since 2018, more than 1000 people have benefitted from this event.

Similar success has been achieved with the Centre's COVID-19 outreach events. As part of its seroprevalence research, the Centre provided free exposure screening as well as advise on disease prevention to thousands of individuals across four regions in Ghana. Researchers also dedicated significant time to speaking to local media and explaining the science behind genome sequencing and viral evolution to wider audiences across the country. The public engagement work the Centre invested in led to further collaborations with key partners such as the Rockefeller Foundation to expand the scope of COVID-19 research.



# WACCBIP'S ADVANCED SCIENTIFIC























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## WACCBIP RESEARCH CONFERENCE 2021





# MESSAGE FROM THE DIRECTOR



Dear friends,

I am so excited to welcome you to this year's WACCBIP research conference, which we usually call our annual festival of science. This would have been our sixth conference, but as you all know we had to cancel last year's conference due to the global restrictions resulting from the COVID-19 pandemic. Despite the prevailing situation we decided to proceed with this year's conference because we believe that we all have to adapt to the new normal and take advantage of the power of technology. As such we are trying out a new mixed format, which will allow our global WACCBIP community to participate in the conference while also still giving our students the opportunity to present and interact in-person with an audience in the conference room. Many of you have remained actively engaged with us throughout the difficult period since the pandemic begun, but we are excited about reconnecting with everyone again through this research conference.

While the past year has been extremely challenging for our faculty and students, we have also had the opportunity to serve our country and Africa as a whole and demonstrate the fruits of all the investments and hard work that has gone into building WACCBIP as a global centre of excellence for training and research. Both the physical and intellectual assets of WACCBIP, as well as our global network




of partners and funders have been called to action, and together we have made our community proud of the value of capacity that has been systematically built over the last seven years. WACCBIP is now a household name in Ghana because of the genome sequencing and seroprevalence studies on COVID-19 and the active engagement of our talented scientists with public health practitioners, media personnel and the general public to discuss the disease and the implications of the data we generate. I am so proud of our faculty and students who have stepped up so gallantly and applied their skills towards providing real time research data to support the pandemic control efforts.

WACCBIP's contributions to the pandemic response also clearly demonstrate the importance of sustainable funding to African research institutions. We were well positioned to respond to the crisis mainly because we are fortunate enough to have core funding from the Government of Ghana through the World Bank African Centres of Excellence project and Wellcome/African Academy of Sciences through the DELTAS Africa programme.

This commitment from these funding sources ensured that we had personnel, equipment and supplies that could be redirected immediately towards supporting the pandemic response. In addition, we received critical and timely support, such as reagents and technical assistance, from existing international networks, including the Tackling Infections to Benefit Africa (TIBA) network, ARTIC, MalariaGEN and the Crick African Network (CAN).

Indeed, the impact of our COVID-19 research efforts earned us some new funding partners, including the African Research Universities Alliance (ARUA), who have selected WACCBIP to lead the Western Africa hub of their Vaccine Development initiative, and the Rockefeller foundation which has provided us with funding to scale up our COVID-19 research nationally and into the sub-region. We are extremely grateful to our existing funders and very enthusiastic about our new partners.

Finally, based on the increased visibility that WACCBIP has gained through our research and public and community engagement work, several local and regional organizations have gladly stepped forward as sponsors for this research conference. This is a very encouraging development, and we hope that this is the beginning of a greater interest in supporting science and research in Ghana and Africa at large.

Despite all the challenges that WACCBIP and other research institutions in Africa have encountered by way of disruptions in supply chains and reduced access to laboratories, WACCBIP faculty, staff and students have strived hard to keep our systems running and nearly all research projects outside of COVID-19 have continued to tick along.





Student thesis submissions have delayed, but majority of them have already made up for the lost time and minimized the impact of the pandemic on their graduation schedule. Overall, our entire 'WACCBIP machine' has remained functional, and this is owed to our highly talented and committed faculty, staff and students. I am so honored and lucky to lead such outstanding people and look forward to greater achievements for WACCBIP in the years to come.

As usual we have a fantastic line-up of speakers for the conference this year and I wish you all an enjoyable and very fulfilling WACCBIP research conference 2021!

# GORDON AWANDARE

RC	<b>*</b>																			
PRESENTER			Lydia Mosi					-			Gordon Awandare								Francisca Mutapi	
TOPICS	OPENING CEREMONY	Arrival of participants and registration	Call to order	Welcome remarks and Introduction of Chairman	Chairman's remarks	- Prof. Felix Asante, Pro VC, RID, University of Ghana	Remarks from Stakeholder Representatives:	- Prof. Daniel Kwadwo Asiedu, Provost, CBAS, University of Ghana	- Prof. Abraham Kwabena Anang. Director, NMIMR	- Dr. Patrick Kuma-Aboagye - Director General, GHS	- Ms. Himdat Bayusuf, ACE Impact Task Team Leader	- Dr. Ahmed Jinapor, Deputy Director General, GTEC	- Emeritus Prof. Samuel Sefa-Dedeh, President, GAAS	- Prof. Tom Kariuki - Director of Programmes, AESA/AAS	Video: The WACCBIP Story	Formal Opening	- Dr. Anthony Nsiah-Asare, Presidential Adviser on Health	KEYNOTE LECTURE 1	What does Africa-led science look like during a global pandemic?	Q&A
TIME			9:30AM-10:00AM	10:00AM-10:10AM	MADC.01 MAD1.01						MAUC:UT-MAUS:UT				10:50AM-11:00AM		11:00AM-11:10AM		11:10AM-11:50AM	11:50AM-12:00PM
DATE	21ST JULY																			

12:00PM-12:10PM	Chairman's closing remarks	
12:10PM-12:30PM	Photograph break	
12:30PM-12:40PM	Presentation on the Gates Cambridge Fellowship	
Da	iy 1 -Session 2: SARS COV2 Pathogen Genomics and Host Responses	
	PLENARY TALK 1	
12:45PM-1:05pm	A chronology of COVID-19 in Ghana: What the science tells us	Peter Quashie
	FELLOWS' SESSIONS	
1:10PM-1:25PM	<ol> <li>Genomic evolution of SARS-CoV-2 variants after a year of the COVID-19 pandemic in Ghana</li> </ol>	Collins Misita
1:30PM-1:40PM	Lunch Break	
Då	y 1 -Session 3: SARS COV2 Pathogen Genomics and Host Responses	
	PLENARY TALK 2	
1:45PM-2:00PM	Emergence of novel combinations of SARS-CoV-2 spike receptor binding domain / variants in Senegal	Ambrose Ahouidi
	FELLOWS' SESSION	
2:05PM-2:20PM	2. Immune response profiling in Ghanaian COVID-19 Patients	Kesego Tapela
2:25PM-2:40PM	<ol> <li>Phylogenetic analysis of SARS-CoV-2 and structural modelling of Spike Protein in Ghanaian isolates</li> </ol>	Philip Soglo
	Day 1-Session 4: Immune Responses and Disease Pathogenesis	
	FELLOWS' SESSION	
2:45PM-3:00PM	4. PfEMP1 proteins are targets of functional antibodies acquired during severe J childhood malaria	Jennifer Suurbaar
3:05PM-3:20PM	<ol> <li>Epitope mapping and functionality of monoclonal antibodies against PfMAAP k aimed at structurally guided malaria vaccine design</li> </ol>	Kayode Shadrach

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	3:25PM-3:35PM	Coffee break		
	3:35PM-4:35PM	Poster Presentations		
	5	Day 1-Session 5: Immune Responses and Disease Pathogenesis		
		FELLOWS' SESSION		
		6. Low-levels Plasmodium falciparum parasite in asymptomatic infection does no trianer a host transcriptional resonness and only minimally affect host immune	t Diana Ahu	
	4:40PM-4:55PM	response	Prah	
		7. Serum metabolome profiles in pregnant women with malaria and chronic	Gloria	
	5:00PM-5:15PM	hepatitis B co-infection	Asantewaa	
DATE	TIME	TOPICS	RESENTER	
22ND				
JULY		KEYNOTE LECTURE 2		
	11:00AM-11:30AM	Leveraging experimental and natural genetic variation to understand host- parasite interactions and identify new malaria intervention targets	ulian Rayner	
	11:30AM-11:40AM	Q&A		
		Day 1- Session 1: Host Genetics and Pathogen Genomics		
		PLENARY TALK 3		
	11:40AM-11:55PM	The Human Cell Atlas initiative (HCA)	John Randell	
		FELLOWS' SESSIONS		
	12-00PM-12-15PM	8. GYPB deletion variants (DEL1 and DEL2) Distribution among Ghanaian		
	12:20PM-12:35PM	<ol> <li>Exploring stool microbiome patterns of paediatric acute gastroenteritis in Ghana</li> </ol>	Emmanuel Quaye	

 1:00pm-2:00pm	Lunch Break	
2:00pm-3:00pm	Poster Presentations	
3:00pm-3:05pm	Sponsor Advertisment	
	Day 2-Session 2:Drug Resisistance and Drug Discovery	
	PLENARY TALK 4	
3:05PM-3:20PM	Targeting a new microtubule-associated protein for antimalarial drug development	Emmanuel Amlabu
	FELLOWS' SESSIONS	
3:25PM-3:40PM	11. Nucleoside analogues are potent inducers of bacterial mutagenesis	Balagra Kasim Sumabe
3:45PM-4:00PM	12. Identification and cytology-based profiling of plant-derived antitrypanosomal principles from Ghanaian traditional medicines	Pearl I. Akazue
	Day 2-Session 3: Panel Discussions	
	Topic: Building sustainable scientific and technological ecosystems in Africa	
	Panelists:	
4:00PM-5:00PM	- Lucy Quist-, Managing Director, Morgan Stanley	Dr. Yaw Bediako
	- Bright Simmons- President, MPedigree	
	- Fred McBagonturi, - Inventor; President, Academic City	
	- Prof. Gordon Awandare- Director, WACCBIP	
5:00pm-5:10pm	Coffee Break	
5:10PM-5:15PM	Sponsor Advertisement	



		Day 3-Session 2: Molecular Epidemiology and Diagnostics	
		FELLOWS' SESSIONS	
		16. Development of DNA-based biosensors for ultrasensitive detection of Plasmodium falciparum, Plasmodium malariae and Plasmodium ovale in	
1	L2:40PM-12:55PM	clinical samples	Felix Ansah
1	1:00PM-1:15PM	17. Comparative genomics and stress-induced phenotypic variations among outbreak and environmental <i>Vibrio cholerae</i> isolates from Ghana	Nana Adade
1	1:20PM-1:25PM	Sponsor Advertisement	
1	L:25pm-1:30pm	Sponsor Advertisement	
1	.:30PM-1:35PM	Presentation on Ethics and community engagement on hearing impairment	Kyerewaa Akuamoah Boateng
7	1:40PM-2:40PM	Lunch Break	
N	2:40PM-3:40PM	Poster Presentations	
		Day 3-Session 2: Pathogen, Vector Biology and Vaccine Discovery	
		PLENARY TALK 7	
m	1:40PM-3:55PM	Complement C1s cleaves PfEMP1 at interdomain conserved sites inhibiting Plasmodium fatciparum cytoadherence	Yvonne Azasi
		FELLOWS' SESSIONS	
4	I:00PM-4;15PM	18. Chimeric H1 haemagglutinins induce anti-H1 HA murine antibodies that cross-react with an influenza AH5N2 strain.	Erasmus Kotey
4	I:20PM-4:35PM	19. Activation of Akt during murine norovirus infection is important at a late step in the viral life cycle	Irene Owusu
4	1:40PM-4:55PM	Coffee Break	
4	1:55PM-5:00PM	Sponsor Advertisement	
		Day 3-Session 3: Pathogen, Vector Biology and Vaccine Discovery	





	Jerry Joe Harrison		Michael Yakass	Jonathan Suurbaar		
PLENARY TALK 8	Crystal structure of a retroviral polyprotein: prototype foamy virus protease- reverse transcriptase (PR-RT)	FELLOWS' SESSIONS	20. Characterization and preliminary validation of a Yellow Fever vaccine- thymidine kinase reporter virus for bioorthogonal labelling and PET imaging	21. Characterization of the immune response to an improved malaria vaccine candidate (PfRh5.2)	Awards, Closing Remarks and Cocktail	
	5:00PM-5:15PM		5:20PM-5:35PM	5:40PM-5:55PM	6:00PM	



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PROFESSOR FRANCISCA MUTAP Co-Director for Global Health Academy and Deputy Director of Tackling Infections to Benefit Africa (TIBA) partnership, University of Edinburgh

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PROFESSOR JULIAN RAYNER Co-Director for Global Health Academy and Deputy Director of Tackling rfections to Benefit Africa (TIBA) partnership, University of Edinburgh



PROFESSOR CHRISTIAN HAPPI Director of African Center of Excellence for Genomics of Infectious Diseases (ACEGID), Redeemers University







# KEYNOTE PRESENTATIONS & **SPEAKER PROFILES**







FRANCISCA MUTAPI

# Co-Director for Global Health Academy and Deputy Director of Tackling Infections to Benefit Africa (TIBA) partnership, University of Edinburgh

Professor Francisca Mutapi is an award-winning pioneering researcher and global health leader working on infectious diseases. She is a professor in Global health Infection and Immunity at the University of Edinburgh where she is also the Deputy Director of the TIBA (Tackling Infections to Benefit Africa) Partnership, and co-Director of the Global Health Academy at the University. Her work on infectious diseases, is empowering African scientists and policymakers to tackle infectious diseases and improve epidemic preparedness prioritising local needs and solutions. She leads collaborative transformative research developing and deploying infectious disease diagnostic tools and interventions across the continent, especially in places with limited infrastructure or resources. Her tireless efforts to combat neglected tropical diseases (NTDs) have had an extraordinary impact on the control of NTDs in Africa. She has contributed to shaping national and global NTD policies by working closely with the World Health Organisation (WHO) and local governments. More recently, she has been applying her infectious disease expertise to the COVID-19 response in Africa (https://www.afro.who.int/ news/seven-things-know-about-covid-19-variants-africa).

Globally, her work on bilharzia made a major contribution to the WHO recommending screening and treatment of pre-school children for the disease enabling 50 million African children to access treatment (https://www.globalcitizen.org/en/content/the-last-milers-francisca-mutapi/). On a continental level, Prof Mutapi is co-leading the TIBA partnership represented in 9 African





countries (http://tiba-partnership.org/). TIBA is an Africa-led research programme empowering African scientists and policy makers to effectively and sustainably tackle infectious diseases and improve epidemic preparedness. On a national scale, Professor Mutapi was involved in the genesis, planning and implementation of Zimbabwe's programme treating parasitic worms in schoolchildren (~5 million), now in its 8th year.

She is helping shape research and training in Africa through independent advisory boards. She sits on several advisory bodies including the WHO Africa Regional Director's Advisory Board, the UK Government's Foreign, Commonwealth & Development Office (formerly DFID) Science Advisory Group, the UK Research and Innovation Global Challenges Research Fund Strategic Advisory Group, board of Uniting to Combat Neglected Tropical Diseases, Wellcome Trust Global Monitor External Advisory Board and Royal Society/ AAAS Fellowships steering committee and the Hideyo Noguchi Africa Prize selection committee.

She is a Fellow of the African Academy of Sciences, Royal Society of Edinburgh and the Zimbabwe Academy of Sciences. She is also a 2021 ASPEN New Voices Fellow and a TED Fellow. In 2020 she established, Mwenje Wedu Foundation (*https://www.mwenje-wedu.org/*), to support Zimbabwean children and youth. She funds her philanthropic activities via sales of her artwork (*https://www.artistsandillustrators. co.uk/francisca-mutapi*)



# What does Africa-led science look like during a global pandemic?

## Francisca Mutapi FAAS FZAS FRSE

Co-Director for Global Health Academy & Deputy Director of Tackling Infections to Benefit Africa (TIBA) partnership, University of Edinburgh

The SARS-COV-2 pandemic reached the African continent in March 2020 exposing African health systems to an additional infectious disease challenge. There were dire predictions from western scientists and media on the toll that pandemic would inflict on Africa. This has not been the case. There are several reasons for this, and in this presentation I am going to focus on one reason that has not received much attention; the contributions and expertise of African scientists to managing the pandemic. I will draw on our experiences from our Tackling Infections to Benefit Africa (TIBA) Partnership represented in 9 African countries (http://tiba-partnership.org/) of which Ghana is one. TIBA is an Africa-led research programme empowering African scientists and policy makers to effectively and sustainably tackle infectious diseases and improve epidemic preparedness. Under epidemic preparedness, our approach was to equip our partner institutions with skills and equipment that would allow research to generate evidence for policy and practise. In 2018, we trained partners in real time viral genome sequencing using a modular portable platform that can be used in low resource settings. It is not surprising then, that the TIBA partner countries have been among the few countries generating SARS CoV-2 viral sequences in Africa. I will discuss the implications of this on in-country and continental COVID-19 policy. I will also demonstrate how TIBA scientists have used our expertise in disease control, diagnostics, immunology, epidemiology and public health to inform national COVID-19 policy. I will demonstrate how our TIBA inclusive engagement policy of leaving no-one behind has allowed us to work effectively with all parties, from affected communities to national and continental stakeholders. I will end with a call for action on where we go from here?





## JULIAN RAYNER

#### Professor of Cell Biology & Director, Cambridge Institute for Medical Research, University of Cambridge

After undergraduate education in New Zealand and a PhD at the MRC Laboratory of Molecular Biology in Cambridge, Julian began working on malaria as a postdoctoral fellow in 1998 at the Centers for Disease Control and Prevention in Atlanta, where he studied how malaria parasites recognise and invade human red blood cells. In 2002 he became a faculty member at the University of Alabama at Birmingham, before returning to Cambridge in 2008 to join the Wellcome Sanger Institute as a Group Leader. In 2019, Dr. Rayner moved to the University of Cambridge, where he is Professor of Cell Biology in the School of Clinical Medicine and Director of the Cambridge Institute for Medical Research, an interdisciplinary institute that seeks to understand the molecular mechanisms of disease in order to improve human health. Julian's group is interested in the interactions that take place between malaria parasites and human red blood cells, with the goal of using biological understanding to identify and prioritise new drug and vaccine targets. Julian is also strongly committed to public engagement with research, and is Director of Wellcome Connecting Science, a learning and engagement programme on the Wellcome Genome Campus which aims to enable everyone to explore genomics and its impact on research, health and society, and delivers events to more than 30,000 scientists, healthcare professionals and members of the public every year.



# Leveraging experimental and natural genetic variation to understand host-parasite interactions and identify new malaria intervention targets

### Julian Rayner

Professor of Cell Biology & Director, Cambridge Institute for Medical Research University of Cambridge

Plasmodium parasites interact dynamically and intricately with human erythrocytes throughout the intra-erythrocytic stages of their complex life cycle, but the molecular details of many of these interactions remain unknown. This is in large part because while the first Plasmodium parasite reference genomes were completed nearly 20 years ago, roughly half of the >5,000 genes still have no clearly assigned function, due to technical difficulties in genetically manipulating the parasite genome and the large evolutionary distance from these parasites to more highly studied model eukaryotes. This unstudied half of the genome, which by definition will include unique aspects of parasite biology, is likely to be a rich source of the new intervention targets that are urgently needed to control malaria in the face of the repeated emergence and spread of drug resistance. My lab uses large-scale approaches combined with detailed cellular phenotyping to understand Plasmodium-erythrocyte interactions, and draws lessons from natural genetic variation in both humans and parasites. The presentation will incorporate lessons learned from systematic genomescale screens, and focussing on the rapid process of erythrocyte invasion, explore how new tools and methods can enhance understanding of gene function, leading to better prioritisation of new drug and vaccine targets.





# CHRISTIAN HAPPI

Director of African Center of Excellence for Genomics of Infectious Diseases (ACEGID), Redeemers University, Nigeria

Christian Happi, is a Professor of Molecular Biology and Genomics and Director of the World Bank funded African Center of Excellence for Genomics of infectious Diseases (ACEGID) in Redeemer's University, Ede, Osun State, Nigeria.

Professor Christian Happi, had his PhD from the University of Ibadan in the year 2000 and did his postdoctoral fellowship at Harvard University from 2000-2003. He subsequently worked at Harvard University as a Research Scientist (2004-2007) and became an adjunct Professor at Harvard University School of Public Health between 2007-2011.

Professor Happi in an unprecedented way, recently used next generation sequencing technology to perform the first sequence of the new SARS-CoV-2 in Africa, within 48 hours of receiving sample of the first case in Nigeria. This seminal work not only provided an insight into the detailed genetic map of the new coronavirus in Africa, not only confirm the origin of the virus, but also pave the way to the development of new countermeasures including new diagnostics, therapeutics and vaccines.

During the 2014-2016 Ebola outbreak, Professor Christian Happi and colleagues

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used advanced genomics and deep sequencing technology to rapidly develop new rapid diagnostics test (5 minutes) against Ebola Virus disease, within 4 months of the outbreak. The WHO and the US FDA approved this diagnosis. He has also worked with his collaborators to developed a novel 5 minutes rapid diagnosis test for Lassa fever. In addition to these major breakthroughs, Professor Happi discovered two new viruses (EKV-1 and EKV-2) in Ekpoma Edo State, using a new cutting-edge technology call microbial metagenomics, in 2015.

Professor Happi has received several prestigious International Awards for innovation and Health Leaderships, including the Merle Sande Africa Health Leadership in 2011 and the 2019 Human Genome Organization (HUGO) Africa Prize in recognition of his outstanding and extensive contributions in applying genomics knowledge in addressing major infectious diseases challenges in Africa, especially malaria and Lassa fever and Ebola Virus Disease and he also got the 2020 Bailey K. Ashford Medal by the American Society of Tropical Medicine and Hygiene (ASTMH).

Professor Christian Happi is a Board member of several International Organizations. His research is funded by major funding agencies and private foundations including the World Bank, the US National Institutes of Health, NIAID, Wellcome Trust, USAID, WHO, UK BBSRC, the European Union, the African Union, Illumina, the Bill and Melinda Gates Foundation, the US Department of Defense, and many others.



# Genomics characterization and surveillance of microbial threats in West Africa

### Christian Happi

Director of African Center of Excellence for Genomics of Infectious Diseases (ACEGID), Redeemers University

Identification and characterization of microbial threats such as infectious bacteria and viruses from human- tohuman or animal-to-human transmission remains crucial in public health, most especially in a globally connected world. Diseases from the most remote village in the world can spread to the most civilized city in under 48 hours because of ease in travel and doing business in the twentyfirst century. Furthermore, West African countries have been adversely affected with several infectious diseases ranging from Lassa, Ebola, Yellow fever, Dengue and the novel human coronavirus which have resulted in thousands of deaths. Here, we applied an unbiased next generation sequencing approach also known as metagenomics to detect and characterize a wide range of infectious diseases in the region from clinical samples such as blood, saliva and nasopharyngeal swabs in symptomatic and asymptomatic people during different outbreaks. Asides sequencing, we have adopted a novel and advanced diagnostic technique called CRISPR-Cas-13a (SHERLOCK) technology to develop high sensitive rapid diagnostic kits to detect SARS-CoV2, Lassa, Dengue and Ebola virus with both fluorescent and lateral flow readouts. In addition, we have also established a surveillance system in place in collaboration with health agencies in order to swiftly respond to disease outbreaks and also monitor genomic variants of viruses in real-time by using cutting edge computational tools and infrastructure at the ACEGID laboratory to study mutations and how they affect the host.



# YEMAACHI BIOTECHNOLOGY



About Us

With our research activities based in Africa, we are able to leverage access to the most genetically diverse population on the planet to build a first-of-its-kind clinical and molecular knowledgebase on cancer among African people. Ultimately, we aim to contribute towards building sustainable biomedical research and community partnerships that aid in the advancement of medicine across Africa.

We have extensive expertise in molecular biology, immunolo gy and bioinformatics and our team has decades of experience in developing and optimizing molecular testing techniques (including PCR tests) for a variety of pathogens. We recently completed setting up an advanced molecular biology research and diagnostics facility in Accra, that is our base of operations

Given the urgency of the current pandemic we have been working at the frontline of COVID control efforts through a close collaboration with the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP) - University of Ghana. We have built and released Africa's first national SARS-CoV-2 variant tracker to display the diversity of SARS-COV-2 strains sampled from around Ghana in real-time



CONTACT



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# GUEST **PANELISTS**







## LUCY QUIST

#### Managing Director, Morgan Stanley

Lucy Quist is a Managing Director at Morgan Stanley and the author of the book, 'The Bold New Normal'. She is an international business leader focused on technology, transformation and thought leadership for positive business returns. She is the first Ghanaian woman to head a multinational telecommunications company as the former CEO of Airtel Ghana. She is a co-founder of the Executive Women Network. She served as the Vice President of FIFA's normalization committee in Ghana and currently serves on the boards of INSEAD and Mercy Ships.

She is a chartered electrical and electronic engineer with a first-class honours degree from the University of East London. She holds an MBA from INSEAD in France. She has over two decades of corporate experience with blue chip companies starting at Ford Motor Company. She has held C-level positions for a decade at Tigo (Millicom), Vodafone and Airtel. Her career spans manufacturing, telecommunications, banking and automotive industries in Europe and Africa.

She is a passionate advocate who believes in harnessing Science, Technology, Engineering and Mathematics (STEM) to advance development in Africa. She also advocates for greater participation in STEM, especially for young people, across the continent.







# FRED MCBAGONLURI

### Inventor & President of Acdemic City University

Prof. Fred McBagonluri a Ghanaian Inventor and University President was born in East Legon, Accra, Ghana in 1970. He is currently the President and Provost of Academic City College, Haatso, Accra. He was the founding Dean of Engineering at Ashesi University. Prior to this appointment, he was Vice President of New Product Development at Joerns Healthcare, Arlington, TX.

He also held roles of increasing responsibilities for Fortune 500 companies in the US. He was Director of Research and Development and Director of IT at Siemens Medical. He was also World-Wide Director Research and Development, and subsequently Director of Market Development at Becton Dickinson and Co, the world largest manufacturer of injection systems.

He attended the University Staff Village Primary and Middle, Legon and St. Louis Preparatory School at Wa. He graduated from Nandom Secondary School in 1990 with a distinction and attended St. Augustine's College in Cape Coast. He earned a Head of State Award in 1991. Prof. Fred McBagonluri holds MBA from the Massachusetts Institute of Technology as Sloan Fellow and earned a Ph.D. in Materials Engineering from the University of Dayton, Dayton, OH., Masters in Engineering Science and Mechanics from Virginia Tech, Blacksburg, VA., and a Bachelor's of Science in Manufacturing Engineering (Summa cum laude) from Central State University, Wilberforce, OH.







# BRIGHT SIMONS

### President, mPedigree

Bright Simons is the President of mPedigree, a social enterprise working on three continents using innovative technologies to secure communities from the harmful effects of counterfeiting. He is honorary director of development research at IMANI, a TED and Ashoka fellow and consulted on innovation strategy by international organizations such as the World Bank, UNECA, USAID, and the Commonwealth. In 2016, Fortune Magazine named Bright in their 50 World's Greatest Leaders.













# PLENARY **SESSIONS**





## A chronology of COVID-19 in Ghana: What the science tells us

### Peter Kojo Quashie

The Coronavirus disease 2019 (COVID-19) is the worst public health crisis to hit the world in the 21st century, and likely the worst in a century. Given the scale of its impact and the time it is occurring in, this pandemic has brought about unprecedented levels of false information, pseudoscience and political massaging of scientific data. Ghana is in the second year of its COVID-19 epidemic. In the midst, WACCBIP's COVID-19 team has been busy, on many fronts. This presentation will address the changing dynamics of COVID-19 in Ghana, and how data obtained from WACCBIP's COVID-19 research activities contribute to understanding the COVID-19 situation in Ghana. Evolving scientific data coming from around the world, including on vaccines and vaccinations, will help put Ghana's experience in perspective, evaluating the impacts of variants, restrictions, free spread and immune response on the magnitude of the COVID-19 health toll in Ghana.





# Emergence of novel combinations of SARS-CoV-2 spike receptor binding domain variants in Senegal

Ambroise D Ahouidi, Mary A Rodgers, Abdou Padane, Nafissatou Leye, Ana Olivo, Moustapha Mbow, Aminata Mboup, Papa Alassane Diaw, Aminata Dia, Barbara Harris, Yacine Amet Dia Padane, Gora Lo, Todd V Meyer, Cyrille K. Diedhiou, Diabou Diagne, Ndeye Coumba Toure Kane1, Gavin Cloherty, Souleymane Mboup

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lineages that carry mutations in the spike gene are of concern for potential impact to treatment and prevention efforts. To monitor for new SARS-CoV-2 mutations, a panel of specimens were sequenced from both wave one (N=96), and wave two (N=117) of the pandemic in Senegal by whole genome next generation sequencing. Amongst these genomes, new combinations of SARS-CoV-2 spike mutations were identified, with E484K+N501T, L452R+N501Y, and L452M+S477N exclusively found in second wave specimens. These sequences are evidence of local diversification over the course of the pandemic and parallel evolution of escape mutations in different lineages.





## The Human Cell Atlas initiative (HCA)

#### John Randell

The Human Cell Atlas initiative (HCA) is an international scientific project that aims to create comprehensive reference maps of all human cells — the fundamental units of life — as a basis for understanding fundamental human biological processes and diagnosing, monitoring, and treating disease. By providing a healthy reference for disease studies, HCA will help scientists understand how genetic variants impact disease risk, define drug toxicities, discover better therapies, and advance regenerative medicine. The HCA is free and open for any scientist around the world to join, providing they agree to support its principles of transparency, ethics, equity, scientific rigor, and technological and computational innovation and excellence. This presentation will describe the scientific rationale for this project, the opportunities and challenges that this project will address, and how scientists worldwide can contribute. It will also provide updates on recent scientific and technological advances the global scientific community.



## Targeting a new microtubule-associated protein for antimalarial drug development

**Emmanuel Amlabu,** \*Ebenezer Taylor, Abdulmalik Hussein, David Amoh-Boateng, Nyarko B. Prince, Millicent Captain-Esoah, Gordon Awandare

Malaria is a global health problem that is majorly affecting the inhabitants of sub-Saharan Africa. Over the years, extensive research effort has been made towards developing an effective malaria vaccine. This decisive approach is challenged by sheer complexity of the parasite life cycle, extensive polymorphisms and poor understanding of the parasite's immunobiology. Also, the emergence of drugresistant parasites and insecticide-resistant vector are concerns that calls for new intervention strategies for malaria. Using published transcriptome data-mining analysis and protein structure predictions tools, we have identified an essential gene (PF<sub>3</sub>D7\_1449100) in the parasite that encodes a protein that harbours the CLIP associating protein (CLASP) domain, and Huntingtin, elongation factor 3, protein phosphatase 2A, and the yeast kinase TOR1 (HEAT) repeats. While the CLASP domain is known to directly engage microtubules and other microtubuleassociated proteins, the HEAT repeats function as docking sites for multi-protein complex formation. Refinement of PF3D7\_1449100 protein structure and the subsequent molecular docking studies with three pathogen box compounds (MMV688774, MMV637229 and MMV003152) that chemically disrupt microtubular assemblies exhibited binding energies within a close range. Further assessment of all three microtubule destabilizing compounds in standard blood-stage P. falciparum growth assays showed that only MMV637229 at 10µM potently inhibited parasite growth with delayed late-stage microtubule morphologies. Dual immunofluorescence labelling using specific anti-PF3D7\_1449100 rabbit polyclonal antibody and anti-tubulin acetyltransferase 1 mouse monoclonal antibody on MMV637229-treated parasites at sub-lethal concentration revealed aberrant microtubule morphologies. Altogether, our initial data suggest that PF3D7\_1449100 protein is a new molecular target of MMV637229 that inhibit blood-stage malaria. This data encourages further work on the use of chemoproteomic approaches to interrogate the function of PF3D7\_1449100 protein as a promising route to malaria control.



## Detection of a 2-host response gene expression signatures discriminating bacterial from viral infection on a microchip technology at the point-of-care.

#### Ivana Pennisi

Ivana Pennisi1,2, Jesus Rodriguez- Manzano 2,N. Moser, A. Moniri, J. Herberg1, M. Kaforou 1, M. Levin 1, P. Georgiou 2, 1Department of Infectious Disease, Imperial College London 2Department of Electrical Engineering, Imperial College London, UK.

The World Health Organization (WHO) estimates that 14.9 million of 57 million annual deaths worldwide are related directly to diseases caused by bacterial and/ or viral infections. The first crucial step in order to build a successful surveillance system is to accurately identify and diagnose the patient health conditions. We describe how to detect RNA biomarkers on our microchip technology allowing a rapid diagnosis of bacterial and viral infections in febrile children. We selected 22 clinical samples from a cohort of 455 febrile children, 11 samples from patient with bacterial infection and 11 with viral infection. We detected the 2-gene signature through the Reverse Transcription Isothermal Amplification RT-LAMP, and validated it using standard fluorescent-based gPCR instruments. We then combined the RT-LAMP assays with our semiconductor-based Lab-on-Chip platform that uses an array of chemical sensors to monitor the pH changes during nucleic-acid amplification in real-time referred to as electronic LAMP (eLAMP). In order to define a decision boundary between bacterial and viral patients on our platform we used the multivariate Logistic regression. A successful and rapid amplification on chip to detect a 2-gene signature discriminating bacterial and viral infections in paediatrics clinical samples has been demonstrated and compared with the gold standard techniques (RT-PCR) showing good sensitivity (limit of detection down to 10 copies/reaction), specificity and appropriate speed for point-of-care applications (time-to-positive reaction <20min). Observed sensitivity and specificity was 100% and AUC was 1.0 for all methods (Figure).RT-LAMP and eLAMP showed a lower limit of detection of 10 copies per reaction within 25 minutes (time-to-positive). The 2-gene signature combined with eLAMP technology provides an affordable and ultrafast diagnostic solution for discriminating bacterial from viral infection in febrile children at the Point-Of-Care.





# Diminazene resistance in Trypanosoma congolense is not caused by reduced transport capacity but associated with reduced mitochondrial membrane potential.

**Carruthers LV,** Munday JC, Ebiloma GU, Steketee P, Jayaraman S, Campagnaro GD, Ungogo MA, Donachie A, Lemgruber L, RowanTG, Peter R, Morrison LJ, Barrett MP, De Koning HP

Animal African Trypanosomiasis (AAT) is a serious illness of livestock throughout the sub-Saharan tsetse belt. The most important control measure is chemotherapy but only two treatments, diminazene and isometamidium, are available. Although resistance to both has been widely reported, the mechanisms are poorly understood. This is complicated in part because AAT is a disease complex caused by multiple trypanosome species, most importantly Trypanosoma congolense, T. vivax and T. brucei sspp. It had been assumed that the mechanisms of drug action and resistance for all three species would be similar, following the models for the only Trypanosoma species, T. b. brucei, for which this has been investigated indepth. In this species, diminazene resistance is linked to mutations in the TbAT1/P2 transporter that allows the efficient passage of the drug across the parasite's plasma membrane. However, we have previously published evidence that T. congolense does not have an equivalent of this transporter gene, which left the question of diminazene resistance still wide open. Here, we induced diminazene resistance in several independent clonal T. congolense lines and studied the phenotype. In vitro growth of the resistant lines was robust, similar to wild-type. Importantly, there was no cross-resistance with isometamidium, oxaborole trypanosomes and even most diamidines including pentamidine, only with close structural analogues of diminazene. In contrast to T. brucei, diminazene uptake in T. congolense was slow, being apparently mediated by multiple low affinity carriers including folate transporters. Expression of T. congolense folate transporters in a diminazeneresistant T. brucei line increased drug sensitivity. Flow cytometry showed that all the T. congolense diminazene-resistant lines had a reduced mitochondrial membrane potential and electron microscopy revealed that the resistant lines sustained less mitochondrial damage after incubation with diminazene. Whole genome sequencing and comparative RNAseq yielded potential adaptations in the resistant lines including mutations in vacuolar-type Ca2+-ATPases.



## Complement C1s cleaves PfEMP1 at interdomain conserved sites inhibiting Plasmodium falciparum cytoadherence

Azasi Yvonne, Low M. Leanne, Just N. Ashley, Raghavan S. R. Sai, Wang W. Christian, Valenzuela-Leon Paola, Rowe Alexandra J., Smith D. Joseph, Lavstsen Thomas, Turner Louise, Calvo Eric and Miller H. Louis.

Cytoadhesion of Plasmodium falciparum infected erythrocytes (IEs) to the endothelial lining of blood vessels protects parasites from splenic destruction, but also leads to detrimental inflammation and vessel occlusion. Surface display of the P. falciparum erythrocyte membrane protein 1 (PfEMP1) adhesion ligands exposes them to host antibodies and serum proteins. PfEMP1 are important targets of acquired immunity to malaria, and through evolution, the protein family has expanded and diversified to bind a select set of host receptors through antigenically diversified receptor-binding domains. Here, we show that complement component 15 (C1s) in serum, cleaves PfEMP1 at semi-conserved arginine motifs located at interdomain regions between the receptor-binding domains, rendering the IE incapable of binding the two main PfEMP1 receptors, CD<sub>3</sub>6 and endothelial protein C receptor (EPCR). Bioinformatic analyses of PfEMP1 protein sequences from 15 P. falciparum genomes found the C1s motif was present in most PfEMP1 variants. Prediction of C1s cleavage and loss of binding to endothelial receptors was further corroborated by testing of several different parasite lines. These observations suggest that the parasites have maintained susceptibility for cleavage by the serine protease, C1s, and provides evidence for a complex relationship between the complement system and the P. falciparum cytoadhesion virulence determinant.



## Crystal Structure of a Retroviral Polyprotein: Prototype Foamy Virus Protease-Reverse Transcriptase (PR-RT)

Harrison Jerry Joe E. K., Tuske Steve, Das Kalyan, Ruiz Francesc X., Bauman Joseph D., Boyer Paul, DeStefano Jeffrey J., Hughes Stephen H., Arnold Eddy

In most cases, proteolytic processing of the retroviral Pol portion of the Gag-Pol polyprotein precursor produces PR, RT, and IN. However, foamy viruses (FVs), express Pol separately from Gag and, when Pol is processed, only the IN domain is released. Here, we report a 2.9 Å resolution crystal structure of the mature PR-RT from prototype FV (PFV) that carries out both proteolytic processing and reverse transcription. PFV PR-RT is monomeric and the PFV PR exhibits architecture similar to one of the subunits of HIV-1 PR, which is a dimer. A C-terminal extension of PFV PR (101-145) consists of two helices adjacent to the base of the RT palm subdomain, and anchors PR next to RT. The subdomain of PFV RT - fingers, palm, thumb, and connection, and the RNase H domain -are connected by flexible linkers and their spatial arrangement is similar to the p51 subunit of HIV-1 RT. Significant spatial and conformational domain rearrangements are therefore required for nucleic acid binding. The structure of PFV PR-RT provides insights into the conformational maturation of retroviral Pol polyproteins.





## Crystal Structure of a Retroviral Polyprotein: Prototype Foamy Virus Protease-Reverse Transcriptase (PR-RT)

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# S C I E N T I F I C



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## FELLOWS SESSIONS (ORAL CATEGORY)





#### Genomic evolution of SARS-CoV-2 variants after a year of the COVID-19 pandemic in Ghana

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Globally, six or more variants of concern (VOC) have emerged that are threatening the control of COVID-19 despite the administration of more than 1.5 billion vaccine doses. Here, we present the evolution of variants in Ghana from June 2020 to May 2021 and identification of VOC. Samples (n=540) were collected from Airport (n=95/540) and several locations in Ghana (n=445/540): Accra, Tamale, Kumasi, Takoradi, and Cape-Coast. Whole viral genome sequencing and bioinformatic analysis were performed using the ARTIC protocols on MinION platform. The B.1.1.7 lineage is the most prevalent in Ghana (30 %, n=134/445), followed by the B.1.1 lineage (24 %, n=107/445). The B.1.1 lineage was detected as early as June 2020 and maintained at a high frequency peaking in November 2020 (>50 %). Subsequently the B.1 lineage surged, reaching a peak frequency of ~40 % in December. In January 2021, these lineages were overtaken by the B.1.1.7 lineage (~60 % frequency) which has sustained its transmissibility in Ghana through to March 2021 (frequency of 68 %). The B.1.525 lineage was introduced in January 2021 and has maintained a significant frequency since then. Travelers from other countries introduced the B.1.1.7, B.1.525 as well the B.1.351 lineages in December 2020. Furthermore, in March 2021, there was introduction of the B.1.617.1 variant (originally identified in India) in Ghana from travelers. Apart from the more common VOC (B.1.1.7 and B.1.525) being detected in majority of the travelers coming to Ghana in March 2021, the B.1.351 and A.23.1 VOCs were also detected (5/71). Several variants have more than 30 mutations, which indicates a higher level of genetic diversity, but the variants are not causing high levels of case fatalities as observed in other countries. It is important to continue monitoring the evolution of variants in local samples as well as detection of VOC from travelers.





#### Immune response profiling in Ghanaian COVID-19 Patients

#### Kesego Tapela, Peter K. Quashie, Yaw Bediako, Osbourne Quaye, Emmanuel Tagoe

Severe coronavirus disease 2019 (COVID-19) has been associated with the production of antibodies as an immune response and rapid increase in expression of cytokines which can lead to immune compromise, and death. COVID-19 has been less severe in Africa but no studies on immune status have yet been published. This study developed an antibody ELISA that targets Envelope, Spike and Nucleocapsid to be used to measure the concentration levels of antibodies in COVID-19 patients. Luminex<sup>™</sup> multiplex assay was used to evaluate the plasma levels of 25 cytokines from symptomatic(n=29) and asymptomatic(n=29) COVID-19 positive individuals, and negative(n=32) individuals. Samples were collected from the capitals, Cape Coast and Accra. Symptomatic patients displayed higher peak levels of IL-10, IL-2, IL-2R, IL-6, IL-8, GM-CSF, IP-10, TNF-α, IL-4, IL-5, IL-12, IFN-γ and MIP-1β compared to asymptomatic patients. Eotaxin was the only cytokine significantly higher in asymptomatic compared to symptomatic patients. Time course showed a decrease in concentration levels of 11 cytokines (IL-12, RANTES, MIP-1 $\beta$ , MCP-1, IL-1Ra, IL-2, IP-10, IL-2R, MIG, IL-4 and IL-8) up to day 14 and 21 for asymptomatic and symptomatic, respectively. All other cytokines were not detected after day 14 for both symptomatic and asymptomatic. Correlation analysis indicated different immune signatures for symptomatic and asymptomatic patients. Interestingly and somewhat baffling, Ghanaian COVID-19 uninfected samples expressed significantly higher initial levels of most cytokines compared to COVID-19 positive individuals except for key inflammation markers MIP-1 $\alpha$ , IL-7, IL-15, and IL-13. It appears that even severely sick Ghanaian COVID-19 patients may have less cytokine storm phenomena. This may be linked to a high state of immune activation in uninfected individuals, but this needs to be evaluated with a larger sample size. This report highlights the first immune profiling study of COVID-19 patients in Africa and opens new insights which can be explored further in larger studies.



#### Phylogenetic analysis of SARS-CoV-2 and structural modelling of Spike Protein in Ghanaian isolates

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The COVID-19 pandemic caused by SARS-CoV-2 is responsible for more than 169 million cases worldwide and 3 million cases in African region. Here, we show the phylogenetic relationships between isolates in Ghana. Fast5 data were assembled using ARTIC protocols to generate consensus sequences. The sequences were aligned to the reference and phylogenetic tree constructed using IQ-TREE. Nucleotide changes at internal nodes were translated to amino acids and clades were inferred. Phylogenies were constructed using Nextstrain protocols and visualized via Auspice. For all the 12074 mutational events across all isolates (n=473), the major variant class was SNPs with 52% (n=6277/12074) compared to stops, deletions, or insertions, or extragenic. The top 5 most abundant spike mutations were S:D614G, (n=446/473), S:Y145 (n=227/473), S:P681H (n=199/473), S:N501Y (n=191/473) and S:H69 (n=166/473). Phylogenetic relationships indicate that 6.7% (n=32/473) of the isolates branch to the 19B clade, while the rest of the isolates (93%, 441/473) form the 20A clade. Majority of the variants of concern branch from the 20A clade; 2/441 branch to the 21A clade, 5/441 branch to 20E (EU1), 6/441 branch to the 20H/501Y.V2, and 164/441 branch to 20I/501Y.V1. The 201/501Y.V1 variants were the most diverged with more than 30 mutations while the 19B were the least diverged with majority of the isolates having less than 30 mutations. All the 20A clade isolates contained the 614G mutation while the 19B clade had the D614 amino acid. All of the 201/501Y.V1 had the S:P681H, which was also present in 20C clade. The 20H/501Y.V2 and 20I/501Y.V1 both contain the S:N501Y, and interestingly it was present in some samples of 19B clade. Structural modelling of these mutations will reveal important characteristics of the clades. It is important to continue to monitor the abundance of these mutations because they have been associated with emergence of new phylogenies.





# PfEMP1 proteins are targets of functional antibodies acquired during severe childhood malaria

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Plasmodium falciparum malaria is an infectious disease where children less than five (5) years of age are disproportionately affected. A particular virulence factor of P. falciparum malaria is clonally variant PfEMP1 (Plasmodium falciparum erythrocyte membrane protein 1), found on the surface of infected erythrocytes (IEs). PfEMP1-mediated vascular adhesion and sequestration cause severe malaria including cerebral malaria (CM). We have linked the expression of group A PfEMP1s to the development of severe malaria and CM. A particular ICAM-1-binding group A PfEMP1 (PDF1235w DBLb3\_D4) as the target of naturally acquired immunity and its associations with exposure and immunity in children could be a useful information as a biomarker for vaccine development.We used indirect ELISA to detect antibodies (Abs) to PDF1235w DBLb3\_D4 in plasma from Beninese children less than 5 years of age and with different malaria clinical presentations (cerebral malaria, severe malaria and uncomplicated malaria). Antibodies recognizing native PfEMP1 expressed on late-stage IEs were quantified by flow cytometry. Undifferentiated THP-1 monocytic cell line were used for opsonisation-dependent phagocytosis and adhesion inhibition properties as functions of the plasma were also determined. Our results showed an increased IgG recognition to PDF1235w DBLb3\_D4, and plasma from children with uncomplicated malaria inhibited the adhesion of the domain to ICAM-1. Domain specific Abs could opsonize antigen coupled to beads and as well opsonize native proteins for phagocytosis by THP-1 monocytic cells. More so, there was an increased IgG recognition of plasma samples from children who were currently infected with P. falciparum malaria to native PFD1235w DBLb3\_D4 PfEMP1 expressed by selected 3D7-IEs compared to non-PFD1235w expressing 3D7-IEs. This support the hypothesis that there is the existence of a relatively conserved subset of PfEMP1 proteins including PDF1235w DBLb3\_D4, which is capable of adhering onto host receptors to cause severe malaria.



#### Epitope mapping and functionality of monoclonal antibodies against PfMAAP aimed at structurally guided malaria vaccine design

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The burden of malaria presents a pressing need for the development of novel antimalarial drugs and more effective vaccines. A novel protein, Plasmodium falciparum merozoite associated armadillo protein (PfMAAP), elicits protective antibody response to bloodstage infection and has been shown to correlate with a reduced risk of malaria. To commence a structurally guided understanding of PfMAAP's function, here three mouse monoclonal antibodies(mAb) were raised against PfMAAP. Epitope mapping to the N-, central repeat and C-terminal regions of the protein were carried out. mAb binding properties (endpoint and avidity) were done and correlated to their in vitro inhibition potential relative to mAbs against PfRH5. Finally, seropositivity of PfMAAP was investigated in cohort of pregnant women for further immunological insights. Our data suggested that two of the antibodies 18E6-1 and 25A6-1 had a higher binding propensity to the N-terminal than C- and central repeat regions. The 25D10-1 monoclonal recognized the wild type protein and possibly a junctional region of the protein. mAb 25A6 binds maximally and strongly to PfMAAP relative to the other mAbs. A growth inhibition assay validated the inhibition potential of all three mAbs but fell short to RH5-016 by 2 folds. Although PfMAAP was seropositive in 38% of the study participants (PfRH5 at 27%), reduce seropositivity was observed in their cord blood at delivery. Structurally, this study elucidated the binding affinity of the individually generated mAbs towards PfMAAP to inform further crystallization and structurally determination. The functionality of these mAbs has been determined, as they recognize schizont lysate and possess GIA activity. Finally, the level of seropositivity observed, places PfMAAP below seropositive and polymorphic vaccine candidates such as AMA1 and MSP1 but above PfRH5. Preclinical studies of PfMAAP would validate the observation here and how that could be translated into vaccine induced antibody functionality.





#### Low-levels Plasmodium falciparum parasite in asymptomatic infection does not trigger a host transcriptional response and only minimally affect host immune response

## **Prah A. Diana,** Cunnington Aubrey, Linda E. Amoah, Awandare A. Gordon, and Julius C. Hafalla

The Naturally acquired immunity to malaria which allows individuals to tolerate the infection without symptoms (asymptomatic) only develops after repeated exposure to the parasites. Yet, despite many years of multiple infections, sterilizing immunity is never achieved. Consequently, asymptomatic infections act as reservoirs for mosquitoes to acquire parasites and perpetuate malaria transmission. Therefore, understanding the host factors maintaining an asymptomatic state and identifying biomarkers of asymptomatic infections could inform the development of alternative clinical interventions for malaria. To this end, we investigated host factors that may contribute to differential clinical outcome during P. falciparum infection.

By combining flow-cytometric analysis of peripheral blood leukocyte subsets, whole-blood transcriptomics, plasma cytokine and antibody profiles, we show that low levels of P. falciparum parasites in the blood of asymptomatic individuals do not trigger a host transcriptional response and only minimally affect cellular immune responses. Antibodies may be the most important factor constraining parasite load below the clinical and immunological radar. We also showed that asymptomatic individuals tolerate low parasite carriage without showing symptoms because of the adequate regulation of inflammatory responses. Furthermore, symptomatic P. falciparum infection correlated with an increase in the levels of peripheral blood neutrophils, indicating a role for this cell type in disease pathogenesis.



#### Serum metabolome profiles in pregnant women with malaria and chronic hepatitis B co-infection

#### **Asantewaa Gloria,** Quaye Osbourne, Anabire Godwin, Weis, Sebastien, Helegbe K. Gideon

In the northern part of Ghana, Malaria and Chronic hepatitis B co-infection in pregnant women have been found to induce an augmented inflammatory immune response and aggravated liver damage. Despite this observed aggravated damage to the liver, there are currently no known serum metabolites characterizing malaria and HBV co-infection. This study sought to ascertain the serum metabolome of pregnant women with either malaria or hepatitis B mono-infection or a malaria and hepatitis b co-infection using a LC-MS/MS based metabolomic approach.

It was revealed that the levels of phosphatidylcholines were significantly exacerbated in the cases of malaria mono-infection. In the hepatitis B monoinfection, the concentrations of phosphatidylcholines were rather reduced. However, like in the malaria mono-infection, the level of acylcarnitine in the hepatitis B mono-infection was increased. All the important metabolites identified in the malaria/chronic hepatitis B co-infection were phosphatidylcholine acyl-alkyl (PC ae C40:5, PC ae C40:1, PC ae C42:5 and PC ae C42:3). Potential biomarkers that could be used to characterize the disease groups were also identified. The ratios PC aa C28:1/PC aa C32:0, C12-DC/Asp, and PC ae C34:1/PC ae C42:2 were observed to characterize the cases of malaria mono-infection, hepatitis B monoinfection and malaria/chronic hepatitis B co-infection respectively. In the case of malaria versus malaria/chronic hepatitis B co-infection, the potential biomarker was Met/PC ae C40:1 whiles in the case of chronic hepatitis B versus malaria/ chronic hepatitis B co-infection, the biomarker was PC ae C32:2/PC ae C34:1. These identified biomarkers could be further explored for use in diagnosis of malaria and chronic hepatitis B and distinguishing the various disease groups, which could help inform therapeutic options in such cases.



#### GYPB Deletion variants (DEL1 and DEL2) Distribution among Ghanaian Populations and relationship with Malaria

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Glycophorins play an important role in mediating the invasion of erythrocytes by Plasmodium falciparum, and thus variation in the glycophorin gene locus has implications for malaria susceptibility. In West Africa, the most common variants are deletions of the whole GYPB gene. The allele frequencies of these GYPB large deletions have been previously estimated to be between 5-15% for GYPB DEL1 and DEL2 in populations in Africa but the effect of these deletions on malaria susceptibility is still unknown. To understand this, we identified and genotyped GYPB DEL1 and DEL2 alleles to facilitate the identification of phenotypes for functional characterization of these variants and malaria disease outcomes. In this study, the distribution and the allele frequency of GYPB DEL1 and DEL2 among Ghanaian populations were determined using a high through-put assay for the identification of these deletions. We genotyped over 2000 samples from different ethnicities in Ghanaian populations. Overall, the allele frequency of GYPB deletions was observed to be 7.17% and 3.21% for GYPB DEL1 and DEL2 respectively. Within the ethnic groups, the highest allele frequencies for GYPB DEL1 and DEL2 were in the Zambrama (41.67%) and Mo (20.59%). We observed that GYPB DEL1 or DEL2 allele was associated with absence of malaria parasites and self-reported absence of malaria re-infections. This is the first comprehensive large survey on the distribution of the Glycophorin B deletion variants using a high-throughput assay to genotype different populations. This allows for further experimental work to be done using these ethnic groups with relatively high GYPB DEL1 or DEL2 variants within the Ghanaian population, and for stratification of genetic association studies to understand the role of this region in malarial disease. Also, it will pave the way for GYPB DEL1 and DEL2 surveys in other malaria endemic populations in relation to malaria susceptibility.



#### Exploring Stool Microbiome Patterns of Paediatric Acute Gastroenteritis in Ghana

#### **Emmanuel Kofi Quaye,** Adjei L. Raymond, Abiola Isawumi, Allen J. David, Caporaso Gregory, Quaye Osbourne

Acute gastroenteritis (AGE) associates with differences in the gut microbiome relative to healthy controls. Yet, how the gut microbiome differs in Ghanaian children with and without AGE remains unexplored. Here, we profile the stool microbiome of 108 Ghanaian children aged 5 years and below, comprising 58 AGE cases and 50 non-AGE healthy controls. Culture-independent bacterial and archaeal 16S rRNA gene amplicon sequence analysis reveals that AGE associates with differences in stool microbial diversity, taxonomic composition, and predicted functional pathways relative to healthy controls. AGE cases were associated with reduced microbial diversity and distinct microbial sequence profiles compared with healthy controls. AGE cases were enriched in Enterococcus and Rothia mucilaginosa and depleted in bacteria positively linked with human health. AGE cases could accurately be classified 88% and 86% of the time using a Random Forest supervised learning classifier trained on taxonomic and predicted MetaCyc pathway features, respectively. Further analysis of predicted MetaCyc pathway features identified sulfur oxidation, methanogenesis, nitrate reduction, pyruvate fermentation, and 1,4-dihydroxy-6-naphthoate biosynthesis, as some of the most enriched in AGE cases. In contrast, CMP-legionaminate,  $\beta$ -(1,4)-mannan degradation, fermentation of succinate to butanoate, biosynthesis of pyrimidine deoxyribonucleotides, and biosynthesis of UDP-N-acetylglucosamine-derived O-antigen building blocks, were most enriched in healthy controls. These findings demonstrate that in Ghana, stool microbiomes of paediatric AGE cases, compared with healthy controls, are enriched in Enterococcus and Rothia mucilaginosa, have different functional profiles and could be accurately distinguished using supervised learning.





#### Further Confirmation of the Association of SLC12A2 with Non-Syndromic Autosomal Dominant Hearing Impairment

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Background: Congenital Hearing impairment (HI) is known to be genetically heterogeneous making its genetic diagnosis challenging. Investigation of novel HI genes and variants are needed to enhance our understanding of the molecular mechanisms and to aid genetic diagnosis. Methods: Exome sequencing and analysis were performed using DNA samples obtained from affected members of two large families from Ghana and Pakistan, segregating autosomal dominant (AD) non-syndromic HI (NSHI). Using in silico approaches, we modelled and evaluated the effect of the pathogenic variant found on protein structure and functions. Results: We identified two pathogenic variants in SLC12A2, c.2935G>A: p.(E979K) and c.2939A>T: p.(E98oV), which segregate with NSHI in a Ghanaian and Pakistani family, respectively. SLC12A2 encodes an ion transporter crucial in the homeostasis of the inner ear endolymph and has recently been reported to be implicated in syndromic and non-syndromic HI. Both variants were mapped to alternatively spliced exon 21 of the SLC12A2 gene. Exon 21 encodes for 17 residues in the cytoplasmatic tail of SLC12A2, is highly conserved between species and preferentially expressed in cochlear tissues. A review of previous studies and our current data showed that out of 10 families with either AD nonsyndromic or syndromic HI, 8 (80%) had variants within the 17 amino acid residue region of exon 21 (48bp), suggesting that this alternate domain is critical to the transporter activity in the inner ear. Conclusion: The genotypic spectrum of SLC12A2 was expanded and the involvement of SLC12A2 in ADNSHI confirmed. These results also demonstrate the role that SLC12A2 plays in ADNSHI in diverse populations including sub-Saharan Africans.



#### Nucleoside Analogues are Potent Inducers of Bacterial Mutagenesis

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Drugs targeting DNA and RNA in mammalian cells or viruses can also affect bacteria present in the host and thereby induce the bacterial SOS system. This has the potential to increase mutagenesis and the development of antimicrobial resistance (AMR). Here we have examined nucleoside analogues (NAs) commonly used in anti-viral and anti-cancer therapies for potential effects on mutagenesis in Escherichia coli using the Rifampicin mutagenicity assay. To further explore the mode of action of the NAs, we applied E.coli deletion mutants, and metabolome and proteome analyses. Five out of the thirteen NAs examined, including three nucleoside reverse transcriptase inhibitors (NRTIs) and two anti-cancer drugs, increased the mutation frequency in E. coli more than 25-fold at doses that were within the reported plasma concentration range (PI.CR), but that did not affect bacterial growth. We show that the SOS response is induced and that the increase in mutation frequency is mediated by the translesion synthesis (TLS) polymerase Pol V. Quantitative mass spectrometry-based metabolite profiling did not reveal large changes in nucleoside phosphate or other central carbon metabolite pools, which suggests that the SOS induction is an effect of increased replicative stress. APIM peptide significantly reduced the stavudine-induced mutagenesis and repress SOS expression. Our results suggest that NAs/NRTIs can contribute to the development of AMR. APIM peptide can be a good drug candidate in combating AMR.



#### Identification and cytology-based profiling of plant-derived antitrypanosomal principles from Ghanaian traditional medicines

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In many parts of Africa, where orthodox treatments are not always accessible, the use of traditional medicines is a common practice. These traditional medicines are readily available and, in some cases, efficacious. The use of drugs is the most reliable method for managing human and animal African trypanosomiasis; however, the existing drugs are far from suitable with issues arising from their toxicity and lack of selectivity. Also, over-dependence and misuse of the few available drugs has driven the development and spread of drug resistance. All this highlights the need for new antitrypanosomal drugs. In this study, traditional medicines targeted against common endemic neglected tropical diseases were explored as starting points in the quest for new antitrypanosomal treatments. Using a bioassay-quided screening approach, a very promising oil (IC50: <0.0977 µg/mL) was identified, which was 1.33 times more active than diminazene aceturate (IC50: 0.13 µg/ml), one of the standard antitrypanosomal drugs. Other bioactive fractions and oils were also obtained. Surprisingly, the compounds purified from these fractions did not possess significant antitrypanosomal activity. The identified bioactive oils and fractions were not cytotoxic and were selective for trypanosomes as determined using RAW 264.7 and HEK 293 cells. Growth profiles and growth reversibility assays revealed that two of the bioactive fractions selected for mode of action studies were trypanocidal. Profiling specific cellular processes, such as cell proliferation, death, morphology, as well as mitochondrial membrane potential, the study provides insights into the distinct ways that the bioactive principles exert their trypanocidal action by targeting multiple cellular processes. It also highlights an unharnessed "gold mine" of hits and leads from traditional medicinal plants that could inform rational optimisation for the development of new antitrypanosomal drugs.



#### Multiplex PCR assay for specific detection of Infectious Spleen and Kidney Necrosis Virus (ISKNV) in cultured fish.

#### Ayiku Angela N. A., Duodu Samuel, Quashie Peter, Verner-Jeffery David, Paley Richard

Tilapia production boosts the local economy and constitutes an affordable source of animal protein for human consumption in several African countries including Ghana. Unfortunately, fish health has always been a neglected area until recently, when the aquaculture sector in Ghana experienced significantly high fish mortality and huge financial losses. Infectious Spleen and Kidney Necrosis Virus (ISKNV) was identified as a major causative agent for this mortality event, but its burden has not yet been fully assessed. Development of rapid, cost effective and reliable assays for the detection of ISKNV will facilitate surveillance, diagnosis and inform choice of control strategies. In this study, a multiplex conventional PCR assay was developed for a more sensitive molecular detection of ISKNV. The assay targeted four putative genes, namely; MCP, ATPase, VEGF and TNFR and its sensitivity was compared to a SYBR Green real time gPCR protocol using the MCP primer only. Kidney and brain tissues of symptomatic and asymptomatic moribund tilapia sampled from three (3) farms were used in field validation of the assay performance. The multiplex assay confirmed higher sensitivity and specificity for ISKNV DNA detection in fish tissues that may be applicable to use in determining the phylogeography and molecular epidemiology of ISKNV in Ghana.



# Genetic diversity and evolution of known Plasmodium falciparum drug resistance genes in Africa and Asia

#### **Frederick Mate Tei-Maya,** Collins M. Morang'a, Dominic S.Y. Amuzu, Genomics and Bioinformatics group members, Alfred Amambua-Ngwa, Gordon A. Awandare & Lucas Amenga–Etego

The inherent ability of P. falciparum to develop resistance to front line antimalarials has been a major setback in the control and eradication of malaria. Here, we sought to investigate the haplotype structure, population genetics and evolutionary pattern of drug resistance genes between Africa and Southeast Asia (SEA). Data was obtained from MalariaGEN (www.malariagen.net/) public data release (version3 and 7). The SNPs for eight resistance genes were filtered and extracted from the VCF files. The variants were used to generate a consensus sequences and analyzed using popgenome. The analysis of 2169 genomes revealed that the Pfcrt K76T mutation was proportionally different; the (T) variant was 14% (n=300/2168) in Africa and 42% (n=912/2168) in SEA. Furthermore, the Pfcrt 72-76 CVMNK Chloroquine (CQ) sensitive haplotype was highly prevalent (37%, n=801/2162) in Africa compared to SEA (1%, n=16/2162). This trend was similar for haplotypes of Pfdhfr, Pfdhps Pfmdr1 and Pfmdr2. Comparatively, two Kelch 13 (K13) mutations; A578S (unvalidated artemisinin resistance mutation) and C58oY (validated artemisinin resistance mutation) were dominant in Africa (3%, n=13/462) and SEA (52%, n=240/462) respectively. The nucleotide and haplotype diversity for majority of the drug resistance genes were significantly higher in Africa compared to SEA (Pfcrt: Pi = 11.5, Africa and 7.60 for SEA), whilst for K13 Pi = 0.51 for Africa and 0.69, SEA. Tajima D for K13 was 0.307 and 2.02 for Africa and SEA respectively, which shows high levels of balancing selection in SEA. Clonality of the samples did not influence these selection indices significantly. The data shows that drug resistance genes are more diverse in Africa than SEA. Also, that these loci are under different drug pressures in both continents to specific medicines. We observed a close relationship between P. falciparum drug resistance genes and their paralogues in gorilla P. praefalciparum and Chimpanzee P. reichenowi.



#### Development and utility of a pseudoviral assay to identify entry inhibitors of SARS- CoV-2

#### Manu A. Aaron, Oyawoye o. Fatima, Oduro-Mensah Daniel and Quashie K. Peter

The recent outbreak of coronavirus disease 2019 (COVID-19) has affected human lives and threatened our very livelihood. Very few drugs have been proven to directly target the viral cause of COVID-19, SARS-CoV-2. A combination of drugs with limited evidence have been used in management of the condition due to the severity of the pandemic. Studies have shown that the virus attaches to host cells through the interaction of SARS-CoV-2's spike glycoprotein with the angiotensinconverting enzyme 2 (ACE2) receptor on the host cells. It has subsequently been shown that preventing this interaction can be an effective infection option. This study evaluated 24 purported anti-SARS-CoV-2 herbal preparations for their ability to prevent this interaction and viral infection. These are formulations that have been marketed as potentially having antiviral activity. We utilized SARS-CoV-2 pseudovirus to infect ACE2-HEK293T. In this study, 50% (12) of the herbal drugs displayed cellular toxicity at the concentrations evaluated, 8.3% (2) showed no inhibitory property while 41.7 %( 10) showed inhibitory property. The inhibitory effect of these hits will be confirmed using live virus and will be successful preparations can be evaluated further in trials. This assay set-up is scalable and we can perform medium to high throughput screening of purported antiviral compounds/preparations.



#### Development of DNA-based biosensors for ultrasensitive detection of Plasmodium falciparum, Plasmodium malariae and Plasmodium ovale in clinical samples

#### **Felix Ansah,** Francis Krampa, Sarah Ashitei, Jacob K. Donkor, Victor E. Kornu, Jersley D. Chirawurah, Yaw Aniweh, Prosper Kanyong and Gordon A. Awandare

Accurate diagnosis of malaria is a crucial step towards disease management and health policies. However, routine diagnosis of malaria at the point-of-care (POC) primarily depend on microscopy and antigen-based Rapid Diagnostic Tests (RDTs) which lack adequate sensitivity and specificity. This study describes the first labelfree DNA-based biosensors for the rapid detection of Plasmodium falciparum, Plasmodium malariae and Plasmodium ovale. The detection mechanism is based on a change in electrochemical impedance upon interaction between the immobilized detection probe and the target DNA. The detection limits for the P. falciparum, P. malariae and P. ovale biosensors were  $11.5 \pm 1.6$  aM,  $61.7 \pm 1.2$  aM and 20.7 ± 1.1 aM, respectively. More importantly, the biosensors were validated for the direct detection of target genomic DNA in clinical samples without initial amplification. The sensitivities of the biosensors were 70.0%, 6.7% and 75.0% for P. falciparum, P. malariae and P. ovale, respectively, when compared to quantitative Polymerase Chain Reaction (qPCR). The specificities were also 100.0%, 75.0% and 100.0% for P. falciparum, P. malariae and P. ovale, respectively. The turnaround time was within 30 minutes which is comparable to the readout time for current diagnostic tools. This work represents a significant step towards accurate and rapid species-specific diagnosis of malaria at the POC.



#### Comparative genomics and stress-induced phenotypic variations among outbreak and environmental Vibrio cholerae isolates from Ghana

#### Nana Eghele Adade, Ahator D. Stephen, Mosi Lydia, Valvano Miguel, Duodu Samuel

Vibrio cholerae naturally inhabits aquatic environments and is the cause of cholera disease, a public health issue in many underdeveloped nations, including Ghana. V. cholerae must avoid a variety of stress factors in order to survive in the environment and cause disease in their hosts. Environmental strains have been found to be progenitors of clinical and outbreak strains in numerous circumstances. For a better understanding of the relationship between stress survival and virulence evolution, we looked at the genetic and phenotypic variations between environmental and outbreak strains of V. cholerae obtained in Southern Ghana. Phenotypic and genotypic traits of twelve (12) outbreak and environmental V. cholerae isolates were determined using conventional methods and whole genome sequencing (WGS). In-vitro evolution was used to investigate the impact of stress (nutrient limitation, acidic pH, high osmolarity and oxidative stress) on phenotypic evolution of virulence and antimicrobial susceptibility patterns. The results showed that the outbreak strains were toxigenic O1-serogroup, had a ST69 predominance, and multiple pathogenicity islands. The environmental strains were non-O1/O139 (non-toxigenic), with one pathogenicity island and unique MLST groupings. All strains had the hylA, rtxA, toxR, mshA, makA, als, VasX, motA, flaA, and luxS genes, but only the environmental strains had the chxA and Int1 genes. The outbreak strains harboured more antimicrobial resistance genes. Both sets of strains, showed changes in colonial morphology, antimicrobial susceptibility patterns and increased phenotypic virulence (protease, biofilm, and hemolysis). Except at acidic pH, where only environmental strains survived, both sets of strains survived the selected stress conditions. The study provided knowledge on current traits and genetic relatedness of environmental and outbreak strains of V. cholerae circulating in Southern Ghana. Further, it showed that stress can lead to the evolution of V. cholerae variants with increased virulence. These could be applied in the disease' control and management strategies.





#### Chimeric H1 haemagglutinins induce anti-H1 HA murine antibodies that cross-react with an influenza AH5N2 strain.

#### **Erasmus Nikoi Kotey,** William Kwabena Ampofo, Munir Iqbal, Osbourne Quaye

This study describes an approach that uses consensus sequence building to generate chimeric HAs: Two resultant H1 HA-based chimeras comprising of conserved sequences (within several areas spanning the head and stalk regions) of H1 and H5 or H9 HAs. These chimeric HAs, expressed in Drosophila cells (S2), were used to immunize mice. All immunized mice were protected from an infectious H1 virus challenge. Seroconverted mice sera to the H1 chimeric HA inhibited both the challenge virus and an H5 virus isolate by haemagglutination inhibition assay. These findings further emphasize that cHAs that induce broad-reactive antibodies against conserved areas of both head and stalk regions of the influenza HA hold potential for development of a universal influenza vaccine.





#### Activation of Akt during murine norovirus infection is important at a late step in the viral life cycle

#### **Owusu A. Irene,** Passalacqua D. Karla, Mirabellia Carmen, Lu Jia, Young Vivienne, Quaye Osbourne, Goodfellow Ian, Ward Vernon, and Wobus E. Christiane

Akt (Protein kinase B) is a key signaling protein in eukaryotic cells that controls many cellular processes such as glucose metabolism and cell proliferation for survival. As obligate intracellular pathogens, viruses modulate host cellular processes, including Akt signaling, for optimal replication. The mechanisms by which viruses modulate Akt and the resulting effects on infectious cycle differ widely depending on the virus. In this study, we explored the effect of Akt serine 473 phosphorylation (p-Akt) during murine norovirus (MNV) infection. p-Akt increased during infection of murine macrophages with acute MNV-1 and persistent CR3 and CR6 MNV strains. Inhibition of Akt with MK2206, an inhibitor of all three isoforms of Akt (Akt1/2/3), reduced infectious virus progeny of all three virus strains. This reduction was due to defects in virus assembly (MNV-1) or cellular egress (CR3 and CR6) in a virus strain-dependent manner. Collectively, our data demonstrate that Akt activation increases in macrophages during the late stages of the MNV infectious cycle, which may enhance viral infection in unique ways for different virus strains. The data, for the first time, indicate a role for Akt signaling in viral assembly and highlight additional phenotypic differences between closely related MNV strains.



### Characterization and preliminary validation of a Yellow Fever vaccine–thymidine kinase reporter virus for bioorthogonal labelling and PET imaging

#### **Micheal B. Yakass**

Fluorescent and luciferase bioluminescence imaging reporters have limited capabilities in tracking virus infections and tissue tropism, especially in large live animals due to low depth and sensitivity issues. Conversely, molecular imaging techniques utilizing marker gene/marker substrate with accumulation of radiolabelled metabolite in cells can be detected using positron emission tomography (PET) scanning camera in live large animals with nanoscale sensitivity. Herpes virus thymidine kinase (TK) and radiolabelled nucleoside analogues have been used as marker gene/marker substrate respectively in molecular imaging and gene therapy approaches. In this study we aimed to provide initial in vitro validation of a 17D-thymidine kinase (TK)vaccine virus intended for prospective PET imaging in live animals using established principles of TK/nucleoside systems. Applying the principle of TK/GCV-induced cell killing, here, we have demonstrated that our TK-expressing virus (17D-TK) induces significant cell death even at very low virus MOI of 0.02 and 2.5  $\mu$ M GCV. Due to preferential phosphorylation of the nucleoside analogue dF-EdU by virus-encoded TK, we also show the capability to differentially detect cells expressing virus-encoded TK (17D-TK) by bioorthogonal labelling and Click chemistryin vitro and in brains of 17D-TK infected mice pups. Taken together, we have provided initial proof and validation of a TK-expressing live attenuated vaccine virus, fit for intended purpose as PET reporter imaging in live small and large animals.



#### Characterization of the Immune Response to an Improved Malaria Vaccine Candidate (PfRh5.2)

#### Jonathan Suurbaar, Lloyd King, Sarah E. Silk, David Pulido, Jordan R. Barret, Doris Quinkert, Yaw Aniweh and Simon J. Draper

The vaccine efforts against malaria have been difficult due to the complexity of the parasite life cycle, redundancy in invasion pathways and high degrees of polymorphisms in vaccine targets. PfRh5 is a highly conserved parasite protein that forms an essential non-redundant interaction with basigin on merozoites. Antibodies that block this interaction can prevent invasion of erythrocytes and provides protection of monkeys in challenge studies. However, the plasma concentration of about 300 µg/mL polyclonal anti-PfRH5 specific antibodies needed for protection poses a new challenge. Here, we set out to design an improved PfRH5 vaccine candidate by immuno-focusing on the neutralizing kitelike structure of PfRH5 and conjugation on a Hepatitis B surface antigen (HBsAg) viral like-particle (VLP) using the SpyTag:SpyCatcher technology to improve immunogenicity. By mice and rat immunization, we characterized the immune responses to all three vaccine candidate variants - RH5.1(Wild type protein), RH5.2 (Improved antigen lacking non-neutralizing regions) and RH5.2-VLP (Improved antigen conjugated on a HBsAg VLP). At a 16 ng/mL dose, only RH5.2-VLP generated anti-RH5 specific IgG titres in the range of 104 to 105 Antibody Units. A 2 to 3-fold improvement of EC50 was observed in RH5.2 and RH5.2-VLP in Standard Growth Inhibition Assay, however no significant improvement of IgG avidity to PfRH5 was seen. IgG subclass profile was not significantly distorted by VLP conjugation, although a slight increase of IgG2b and IgG3 was observed. Our results demonstrate that, the quality and quantity of immune response can be improved with antigen immuno-focusing and VLP-conjugation respectively. Therefore, the data suggest a possible alternative route to overcoming the plasma IgG quantity challenge by a quality shift approach.





## FELLOWS SESSIONS (POSTER CATEGORY)





# Distribution and frequency of the CYP2C8\*3 and CYP2C8\*5 polymorphisms among different ethnic populations in Ghana

#### **Bright Kwabena Yemi**

Cytochrome P450 enzymes are of interest because they metabolize both endogenous and exogenous substances. As such these enzymes act on exogenous compounds such as drugs to convert them into their active compounds or break them down for excretion. CYP2C8 enzymes are of clinical importance because they metabolize antimalarial drugs. This study determined the distribution and allele frequency of CYP2C8\*3 and CYP2C8\*5 polymorphism among different ethnic populations in Ghana using allele specific-PCR and PCR RFLP. Also, a structured questionnaire was used to obtain the medical history on adverse drug reactions (ADRs) of the subjects and level of dependency on drugs metabolized by CYP2C8 enzymes. The allelic frequency for CwYP2C8\*3 and CYP2C8\*5 were observed as 0.27 and 0.43 respectively (p<0.05). There was no significant difference (p> 0.05) in the of CYP2C8\*3 and CYP2C8\*5 alleles within the ethnic groups. Also, there was no significant association between CYP2C8\*3 and CYP2C8\*5 alleles and reported ADRs (p >0.05). The high prevalence of CYP2C8\*3 and CYP2C8\*5 determined in the study population may indicate a high risk of toxicity in using drugs metabolized by CYP2C8 enzyme since CYP2C8\*3 and CYP2C8\*5 mutants have been reported to have a reduced enzymatic activity. To the best of our knowledge this is the first large genotyping survey of CYP2C8\*3 and CYP2C8\*5 polymorphisms in different ethnic groups in Ghana.



#### Caffeic Acid Exhibits Anti-Proliferation and Anti-Metastatic Effects Against Prostate Cancer Cells

#### Samuel M. Baffoe, Peggy A. Birikorang, Selorm Sabah, Jessica Kugblenu, John A. Tetteh, Osbourne Quaye, Anastasia R. Aikins

Prostate cancer is the second leading cause of cancer-related deaths among men. As a result of high toxicity of most anti-cancer drugs, there is the need to exploit highly potent extracts from natural sources whose effect are less toxic. Caffeic acid is a natural polyphenol, known to have potent anti-cancer properties. Here, we determined the effect caffeic acid has on proliferation, migration and the stemness-associated properties of prostate cancer using DU145 cell line. The anti-proliferative capacity of caffeic acid was investigated using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Flow cytometry was used for cell cycle analyses and also to determine the cancer stem cell (CSC) population after treatment with caffeic acid while wound healing assay was used to determine the effect of caffeic acid on cancer cell migration. RT-qPCR analyses was performed to determine the effect of caffeic acid on the expression of stemness and EMT-related genes. From our results, caffeic acid decreased the cell proliferation in a concentration and time-dependent manner. Flow cytometry analysis revealed that 1.25 mg/mL caffeic acid induced apoptosis at the S and G2-M phase and significantly reduced the stem cell population from about 95% to 63% and 47% at caffeic acid concentrations of 1.25 and 2.5 mg/mL respectively. Treatment of the cells with caffeic acid significantly decreased the migration of DU145 cells compared to the untreated cells. Furthermore, caffeic acid treatment of the cells resulted in the upregulation of E-cadherin (epithelial marker) and downregulation of N-cadherin (mesenchymal marker), as well as Nanog and Oct-4 which are stemness genes. In conclusion, caffeic acid exhibited significant anticancer properties against the prostate cancer cells and could be considered in the development of improved chemotherapy.



#### Drug resistance in Plasmodium malariae and Plasmodium ovale?

#### Reinhard Kobbie Danku

Although malaria remains a public health concern in sub-Saharan Africa, recent global concerted anti-malarial efforts have significantly reduced the burden. Unfortunately, the efforts are Plasmodium falciparum-focussed with the neglect of Plasmodium malariae and Plasmodium ovale. If malaria is to be eliminated and eradicated, there is the need to target all forms of human malaria-causing Plasmodium species. The true contribution of P. malariae and P. ovale to malaria worldwide is unknown mainly because they are frequently misdiagnosed; due to their characteristic low parasitemias, frequent mixed-species infection, and the subpar performance of malaria gold standard diagnostic tool. With antimalarial drug resistance posing a threat to the no malaria agenda, there is the need to periodically surveil and assess the genetic effect of drug pressure on the circulating Plasmodium species. Hence, this study seeks to analyse the genetic diversity of P. malariae and P. ovale drug resistance genes (multidrug resistance gene and Kelch-13 propeller gene) using Sanger sequencing. The resulting data will be instrumental in the development of future antimalrial drugs.





#### Phenotypic Responses of HIV Genotypes In Ghana To Novel Integrase Inhibitor-Based Antiretroviral Therapy

#### Quashie k. Peter, Quaye Osbourne, Effah N. Samuel

Data available suggests that even though all clades of HIV are susceptible to most antiretrovirals, the degree of susceptibility and resistance pathways differ, especially against newer more potent antiretrovirals (ARVs). Amongst the ARV class, integrase strand transfer inhibitors (INSTIs), like dolutegravir (DTG) have shown immense promise. This influenced its introduction, in 2019, to anchor the standard of care regimens in Ghana. Ghana, however, has CRFo2-A/G and thus DTG may not necessarily be the best drug for this virus. In this study, we sought to access the effectiveness of four (4) ARV regimens (A-D) against three HIV isolates, pNL4-3 virus (subtype B), and HIV from two Ghanaian patients (likely CRFo2-A/G). The four-drug regimens were dolutegravir/rilpivirine (A), dolutegravir/lamivudine/ efavirenz (B), tenofovir/lamivudine/efavirenz (C), and rilpivirine/emtricitabine/ tenofovir (D). All the above drugs except rilpivirine (a newer non-nucleoside reverse transcriptase inhibitor) and dolutegravir are all ARVs that have been commonly used in Ghana since 2014. Regimen B is the new standard of care in Ghana. A breakthrough resistance selection method was employed. This involved using a constant and high concentration of the drug cocktails to select highly resistant viruses within a short time. Our data initially suggested that DTG containing triple therapy (regimen B) appeared to suppress pNL4-3 better than other ARV regimens (A, C, and D). However, all ARV regimens used were not effective in suppressing patient isolates. After several weeks in culture, none of the regimens better suppressed pNL4-3 or patient isolates. In addition, all regimens selected pNL4-3 HIV with reduced susceptibility to DTG and RPV (except RPV-containing triple therapy, regimen D). One of only two patient isolates with reduced susceptibility to DTG was selected by a Non-DTG containing antiretroviral therapy (regimen C) and, only one patient isolate with reduced susceptibility to RPV was selected by Non-RPV containing therapy (regimen B).



#### Inhibition of HIV replication in vitro by three local herbal extracts

Abana Z-Y. Abana, Boateng T. Boateng, Abaidoo-Myles Araba, Quansah Darius N. K., Aboagye James O., Quaye Osbourne, Appiah-Oppong Regina, Lamptey Helena, Bonney Evelyn Y., Kyei George B

HIV continues to be a major public health threat in Africa. Although antiretroviral therapy (ART) has reduced mortality and improved lifespan, it does not provide a cure. A cure for HIV remains elusive due to the persistence of the provirus in resting CD<sub>4</sub>+T cells, which act as a reservoir to produce the virus once treatment is interrupted. Currently, various HIV cure strategies are being investigated by using novel compounds, medicinal plants, or extracts that can reactivate, inhibit and/ or block and lock the virus. We are in the process of screening a library of African herbal extracts for their ability to inhibit HIV replication or reactivate the virus from latency.

We used U87 cell lines stably transfected with CD4 and CXCR4 (U87CD4CXCR4) for the screen. Frist, the cytotoxicity levels of the extracts were determined using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay at a ten-fold dilution. The U87 CXCR4 cells were then infected with full length HIV NL4-3-luciferase in the presence of the extracts or DMSO controls. HIV replication was determined by relative luciferase activity (RLA) in the presence of luciferin. Antiretroviral drugs (Raltegravir, Zidovudine, and Darunavir) were used as control.

Three herbal extracts, at a concentration of 30ug/ml, had no toxic effect on the cells after 48 hours of treatment. Preliminary results showed that the three extracts (JJNC006SB, JJNC057SB, and JJNC064SB) at the same concentration, inhibited HIV replication in a 6, 7, and 3 fold reduction respectively.

These preliminary results indicate the inhibitory activity of the three extracts against HIV and calls for further investigation of their potential use and mechanism of action.





#### Inhibition of HIV replication in vitro by three local herbal extracts

#### Marzuq A. Ungogo, Gustavo D. Campagrano, Manal J. Natto, Ali H. Alghamdi and Harry P. de Koning

Control of African Animal Trypanosomiasis (AAT) is seriously undermined by the challenge of drug resistance. Trypanosoma brucei, one of the three species that cause AAT, has been extensively studied, and the mechanism of drug resistance in this species depend mostly on mutations in transmembrane transporters that import the drugs. However, advances in molecular parasitology have revealed enormous genetic differences between T. brucei and T. congolense. Thus, there is need to understand the genetic and molecular basis of drug resistance in T. congolense in order to aid rational drug design and development. Drug sensitivity assays showed that the EC50s of diminazene aceturate and melarsomine in T. congolense were 3 and 20 times higher than in T. brucei, respectively. In addition, T. congolense was 151 times less sensitive to pentamidine and 296 times resistant to suramin relative to T. brucei. It is hypothesised that lack of authentic orthologues of some T. brucei transporters (TbAQP2, TbAT1, and a lysosomal MFST) is responsible for low sensitivity to these drugs in T. congolense. Expression of T. brucei AQP2 (TbAQP2) in T. congolense resulted in 8-fold increase in sensitivity to pentamidine and 6-fold increase in sensitivity to melarsomine compared to wild type. The T. congolense + TbAQP2 also displayed a higher rate of uptake of [3H]pentamidine and faster lysis when exposed to melarsomine. On the other hand, T. congolense clones expressing T. brucei P2 adenosine transporter (TbAT1) show a 30-fold increased sensitivity to melarsomine and a 12-fold increase in sensitivity to diminazene, pentamidine and isometamidium. In addition, there is a higher uptake of [3H]-diminazene and [3H]-pentamidine in T. congolense clones expressing TbAT1 compared to the wild type. This indicates that differences in transporters between Trypanosoma species play important role in differential sensitivity and should be considered in the development of new drugs for AAT.



#### Insecticide Resistance Status and Mechanisms in Aedes Mosquitoes in Ghana

#### Anisa Abdulai, Attah S. Kwaku, Forson O. Akua, Afrane A. Yaw

Aedes mosquitoes are vectors of dengue and yellow fever which are major public health concerns globally. Increasing outbreaks of yellow fever and dengue fever have been reported in Africa Widespread insecticide resistance in the vectors further complicates control especially during an arboviral outbreak. Thus, prior knowledge about the mechanisms of resistance in Aedes populations in Ghana will be useful in improving pre-existing arboviral vector control measures for arboviruses in Ghana. This study was carried out in the urban sites (Accra and Tema) and suburban sites (Navrongo and Ada). Aedes larvae were collected from study sites and raised to adults in the insectary. Phenotypic resistance was determined using WHO susceptibility tests and resistant genes were detected using allelespecific PCR. Synergist assays were performed with piperonyl butoxide (PBO) to detect the involvement of oxidase enzymes in resistance. The results showed high phenotypic resistance to DDT (11.3% to 75.8%) and pyrethroids (62.5% to 88.8%) in all sites. Aedes mosquitoes in Tema were resistant to all classes of insecticides tested. Suspected resistance to carbamate and organophosphates was detected also detected in some sites. High frequency of point mutations at the voltage-gated sodium channel (F1534C and V1016I) were detected in resistant and susceptible Aedes mosquitoes from all sites suggesting that these mutations may be fixed in Aedes populations. Pre-exposure to PBO significantly enhanced the susceptibility of Aedes to some of the insecticides tested in all the sites. This may be an indicator that metabolic enzymes (oxidases) may be involved in the development of resistance in some Aedes populations. These findings shows that insecticide resistance among Aedes populations in Ghana is high and is mediated by a combination of genetic and metabolic resistance mechanisms. Therefore, regular monitoring of the resistance profile of Aedes mosquitoes is needed to inform vector control policies for arboviral diseases in Ghana.



#### Smoked Fish and Escherichia coli: The Fate of Consumers

#### Edwin Sakyi Kyei-Baffour

Diarrhea is the second largest causes of death in <5 years old children globally. In Sub-Saharan Africa including Ghana, diarrheagenic E. coli (DEC) causing food spoilage and poisoning has been associated with childhood diarrhea. Poor sanitation and unhygienic practices in this region have mitigated efforts to control the spread of diarrheagenic E. coli and this is compounded by increasing cases of antimicrobial resistance. This study profiled and characterized diarrheagenic E. coli, an important food pathogen, in smoked fish preferably consumed in Ghana. Fifty-three E. coli isolates were obtained from two-hundred and ten (210) smoked salmon fish collected from seven Ghanaian markets. Using multiplex PCR (mPCR), ten DEC-pathotypes resistant markers (virF, est1b, aafII, bfpB, ipaH, stx2, pic, daaE, stx1 and astA) were detected. Eighty-one percent (81%) of the isolates were heterogenic for more than one class of DEC-pathotypes with Entero-Invasive E. coli (EIEC) as the most common. Other pathotypes identified include ETEC (Enterotoxigenic E. coli), EAEC (Enteroaggregative E. coli), EPEC (Enteropathogenic E. coli), EHEC (Enterohemorrhagic E. coli) and DAEC (Diffusely Adherent E. coli) respectively. Out of

the eight conventional (tetracycline, amoxicillin, ciprofloxacin, amikacin, penicillin G and

ceftriaxone) and last-resort (meropenem and imipenem) antibiotics tested, all the isolates were resistant to penicillin G and 59.18%, 36.73% and 24.49% level of resistance to ceftriaxone, tetracycline and amoxicillin-clavulanate respectively. Twenty percent (20.41%) of the isolates were multidrug resistant with an average multiple antibiotic resistance index of 0.28  $\pm$  0.14 and hetero-resistance phenomenon was observed in ceftriaxone, amikacin, tetracycline, ciprofloxacin and amoxicillin-clavulanate. The study showed that smoked fish is a possible source of resistant diarrhea causing E. coli pathotypes and there is a need for proper and hygienic processing of smoked fish to prevent incidences and outbreak of severe diarrhea when consumed.



#### 'Bacteria that Travel': Sporulation and Antimicrobial Resistance

#### Eunice Ampadubea Ayerakwa, Molly Kukua Abban, Isawumi Abiola, Lydia Mosi

Bacteria have developed diverse survival mechanisms including spore formation that aids them to display resistance to antimicrobial agents. Bacillus species are known for spore formation and have been classified as 'bacteria that travel' for their diverse sporulation activities. In hospital environments where new strains of Bacillus are emerging and resistance to antibiotics is on the rise, Bacillus sporulation has been associated with hospital acquired infections including post-operative wound, sepsis, bacteremia, respiratory tract and opportunistic infections. While sporulation helps bacterial persistence in enclosed hospital Intensive Care Unit (ICU), sporulating bacteria take advantage of environmental dispersal agents such as fomites for spore propagation and distribution. These bacterial strains, beyond the spore forming phenotypes, might also have genetic factors facilitating spore formation. Using phenotypic, antibiotic and molecular assays, this study characterized sporulation markers and determined the antimicrobial resistant profiles of Bacillus species isolated from hospital ICU. Three Bacillus strains (B. subtilis, B. cereus and B. thuringiensis) identified with MALDI-TOF, 16S rRNA gene amplification and sequencing were selected for this study. The strains produced spores with malachite staining dye and showed the presence of spoVK, spoVE, sigJ, sigF, Soj, yrbC, spoJ, and yjcE sporulation markers. All the strains are multidrug resistant, as they showed resistance to at least three of the seven antibiotics tested. The highest level of resistance was to vancomycin, cloxacillin, chloramphenicol, streptomycin and trimethoprim. Overall, this study indicated that spore forming Bacillus species isolated from hospital environments harboring sporulation markers might pose serious public health risks, as they are highly resistant to antibiotics tested. There is a need for appropriate antibiotic use and appropriate disinfection practices in the ICU to mitigate spread of spore forming resistant Bacillus species.



#### Transmitted Drug Resistance of Circulating HIV-1 Sub-types in ART-naïve HIV Patients in Ghana

## **Darius N. K Quansah,** Araba Abaidoo-Myles, Seth Agyemang, Anthony T. Boateng, Peter K Quashie, George B. Kyei, Osbourne Quaye, Evelyn Y. Bonney

therapy (ART) significantly transformed Anti-retroviral has human immunodeficiency virus (HIV-1) infection from a fatal disease into a manageable chronic one. However, the emergence of drug resistance poses a challenge to the success of ART. Drug resistant strains can be either acquired by individuals as a consequence of treatment or transmitted to ART-naïve persons. The presence of drug-resistant strains can drastically reduce the effectiveness of antiretroviral therapy. While pre-treatment genotypic testing is performed routinely in high income countries, it is not done in many low middle-income countries (LMICs), including Ghana. Therefore, in Ghana, the contribution of transmitted drug resistance to treatment failure is unknown. We determined the presence of transmitted drug resistant strains in ART-naïve individuals in Ghana. Sixty-nine treatment-naive HIV-1 infected persons were enrolled from three hospitals in Accra and their clinical histories were obtained. The study participants had mean viral load and CD4 counts of 137,694 copies/ml 409 cells/µl respectively. HIV protease and reverse transcriptase genes were amplified by conventional PCR and directly sequenced. Sequences were edited and submitted to the Stanford University HIVDR database for subtype and drug resistance analysis.

We found 64% of participants with HIV-1 subtype CRFo2\_AG, 26% with subtype B and the rest with subtypes CRFo6\_cpx, A, C and G. Seven drug resistance mutations were present in nine participants. These mutations were against either non-nucleoside reverse transcriptase inhibitors (NNRTI) or protease inhibitors (PI) No nucleoside reverse transcriptase inhibitor (NRTI) mutations were found in this study. Our data confirms CRFo2\_AG as the predominant HIV-1 subtype in Ghana and indicates an increase in subtype B, which drives the HIV epidemic in Europe and America. The findings show that pre-treatment virus resistance is low among Ghanaian ART-naïve patients, which is a good promise for the country's HIV control programmes.



#### Mode of action of pathogen box compounds with potent antiinfective effect in Trypanosoma brucei

#### Temitayo S. Ademolue, Samuel K. Kwofie, Theresa M. Gwira

African trypanosomiasis remains a public health burden and a major hindrance to the growth of livestock farming in sub-Saharan Africa. Chemotherapy is threatened by widespread development of resistance, issues with toxicity and functional adaptation of the parasite to new biological niches. Target deconvolution and knowledge of mode of action of potent drugs or compounds can facilitate surveillance for the emergence of resistance, identification of off target toxicity and novel targets. Here we used computational and in vitro cellular approaches for target deconvolution and mode of action studies of 10 MMV pathogen box compounds with wide anti-infective spectrum. The growth inhibitory concentration IC50 in bloodstream form of Trypanosoma brucei brucei GuTat 3.1 cell line obtained ranged from 0.4 - 2.8  $\mu$ M. Using fluorescent dye staining of the DNA and mitochondria, we found that F11 caused cell rounding, an obvious distortion of mitochondrial integrity and increased 2N2K cell population indicating possible inhibition of cytokinesis. Using machine learning-based Open Bayesian techniques we have identified two kinases, and superoxide dismutase and trypanothione reductase as possible molecular targets for F11 and G11 respectively. Studies are underway to characterize the binding mechanism of the proposed molecular targets and also determine the effects of the compounds on the global gene expression in Trypanosoma brucei. The data generated provides promising drug candidates for development as therapeutics against African trypanosomiasis.


# Assessment of immunomodulatory and toxicological effects of two antimalarial medicinal plants in murine models

# Ayisha Mahama, Kwadwo A. Kusi, Samuel Adjei

Global health is threatened by an alarming rise in communicable and noncommunicable diseases. Increasing incidence of pathogen resistance to antibiotics and the threat of viral pandemics are contributing factors to the rise in infections. Host-directed therapies primarily boost the host immune system against a range of diseases and also eliminate drug pressure that drives the development of drug resistance. Herbal plants are a cheaper, more accessible and, multi-component alternative to synthetic drugs. However, the use of herbal formulations can also result in short-term and long-term organ damage or dysfunction to the host. There is the need for research targeted at identifying safe immunomodulatory agents to boost host immunity. In this study, fractions of Carapa procera and Alchornea cordifolia, which had previously shown anti-plasmodial activity, were investigated for their immunomodulatory and toxicological effects in murine models. To establish pre-clinical safety profiles, 14-day acute and 28-day sub-acute studies in Sprague Dawley rats and ICR mice were conducted with 1:1 chloroform fraction of Carapa procera and Alchornea cordifolia. A dosage of 2000mg/k.g p.o was administered during the acute study and 1000mg/kg p.o, 300mg/kg p.o and 100mg/kg p.o dosages during the sub-acute study. Animals showed no clinical signs of toxidromes and showed normal weight gain throughout the study. Serum biochemical analysis indicated no significant elevations in liver enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and, alkaline phosphatase (ALP). Urea (URE), creatinine (CR) also showed no significant elevations. Histopathological examinations of the liver and kidney are being carried out to confirm these findings. Immunomodulatory studies using flow cytometry will assess immune response induced by extract administration. These preliminary findings demonstrate fractions of Carapa procera and Alchornea cordifolia as safe antimalarials for the management of malaria





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

**Seth A. Domfeh,** Patrick W. Narkwa, Osbourne Quaye, Kwadwo A. Kusi, Gordon A. Awandare, Charles Ansah, Alimatu Salam and Mohamed Mutocheluh

Diverse signalling pathways are involved in carcinogenesis and one of such pathways implicated in many cancers is the interleukin 6/signal transducer and activator of transcription 3 (IL-6/STAT3) signalling pathway. Therefore, inhibition of this pathway is targeted as an anti-cancer intervention. This study aimed to establish the effect of cryptolepine, which is the main bioactive alkaloid in the medicinal plant Cryptolepis sanguinolenta, on the IL-6/STAT<sub>3</sub> signalling pathway. First, the effect of cryptolepine on the IL-6/STAT<sub>3</sub> pathway in human hepatoma cells (HepG<sub>2</sub> cells) was screened using the Cignal Finder Multi-Pathway Reporter Array. Next, to confirm the effect of cryptolepine on the IL-6/STAT<sub>3</sub> signalling pathway, the pathway was activated using 200 ng/mL IL-6 in the presence of 0.5  $- 2 \mu M$  cryptolepine. The levels of total STAT<sub>3</sub>, p-STAT<sub>3</sub> and IL-23 were assessed by ELISA. Cryptolepine downregulated 12 signalling pathways including the IL-6/STAT3 signalling pathway and upregulated 17 signalling pathways. Cryptolepine, in the presence of IL-6, decreased the levels of p-STAT3 and IL-23 in a dose-dependent fashion. Our results demonstrated that cryptolepine inhibits the IL-6/STAT<sub>3</sub> signalling pathway, and therefore cryptolepine-based remedies such as Cryptolepis sanguinolenta could potentially be used as an effective immunotherapeutic agent for hepatocellular carcinoma and other cancers.



# Antileishmanial compounds inhibit the normal cell cycle progression of promastigotes of Leishmania donovani and shows pro-oxidative potentials.

# **Emmanuel Wanday,** Cynthia M. Amisigo, Christine A. Antwi, Gordon A. Awandare, Theresa M. Gwira

In the midst of numerous setbacks that beclouds the fight against leishmaniasis; a neglected tropical disease, the search for leads for new chemotherapeutics against this disease is of outmost importance. Leishmaniasis is a disease closely associated with poverty and it is endemic in Africa, Asia, southern Europe and the Americas. It is caused by parasites of the genus Leishmania and transmitted by a sandfly vector. Fatality of the disease has increased wherever it is found. In this study, we evaluated the antileishmanial potency of eighteen pathogen box compounds and elucidated their biosafety and possible mechanisms of action against Leishmania donovani promastigotes and amastigotes in vitro. IC50s range of  $0.12\pm0.15$  to >6.25 µg/ml and  $0.13\pm0.004$  to >6.25µg/ml were observed for the promastigotes and amastigotes, respectively. We demonstrated the ability of some of the compounds to cause cytocidal effect on the parasites, induce increased production of reactive oxygen species (ROS), affect the normal parasite shape and cause the accumulation of parasites at the DNA synthesis phase of the cell cycle progression. We recommend a further in vivo study on these compounds to validate the findings.



# Evaluating the effects of Sorbitol synchronization of clinical isolates on their susceptibility to antimalarial compounds

#### Frank Obeng Addae, Adika Bridget, Chirawurah D. Jersley, Aniweh Yaw

The development of the Plasmodium parasite in the human host is highly synchronous, however, in in vitro culture, the parasite is asynchronous. Several synchronization methods including the use of 5% sorbitol, Percoll, and magnetic separation synchronization methods have been developed for synchronizing P. falciparum parasites for downstream studies. Although the effects of these synchronization methods on malaria have been demonstrated, not much is known about the effect of these synchronization methods on the response of clinical isolates with different drug susceptibilities to different antimalarials. This study evaluated the response of two clinical isolates of Plasmodium falciparum synchronized with 5% sorbitol to chloroquine, artesunate and gossypol using in vitro SYBR green-1 fluorescence-based growth inhibitory assay. The study showed varied responses in the synchronous and asynchronous cultures of clinical isolates. We found asynchronous culture of the clinical isolate A11 to be more susceptible to artesunate and gossypol, but the contrary was true for K239. Furthermore, synchronous A11 parasites were more sensitive to chloroquine compared to the asynchronous culture. But the asynchronous K239 parasites were observed to be more sensitive to chloroquine compared to the synchronous culture.

The results from this study suggests that 5% sorbitol synchronization affects the response of clinical isolates of Plasmodium falciparum to antimalarial. Therefore, synchronizing clinical isolates for downstream studies should consider variations in parasites behavior arising from the synchronization step.



# Validating the Potency of Malaria Box compounds against Plasmodium falciparum Parasites

# **Jersley D. Chirawurah,** Felix Ansah, Bridget Adika, Yaw Aniweh, Gordon A. Awandare

The emergence of drug-resistant malaria parasites to artemisinin and its partner drugs highlights the need to increase the arsenal of new antimalarials with novel mechanisms of action. We identified MMVoo6o87, MMVo85203, and MMVoo8956 from screening the Malaria Box compound library, to have high potencies against clinical isolates of P. falciparum. To further validate their potencies, we screened these compounds against five laboratory strains and twenty clinical isolates of P. falciparum using optimized in vitro growth inhibitory assays. Furthermore, we evaluated the susceptibility of the P. falciparum parasites to four standard antimalarials-Artesunate, Chloroquine, Mefloquine, and Halofantrine- and compared their potencies to the three Malaria Box compounds. On average, the laboratory strains were less susceptible (average IC50 of 162.3 nM) to the three Malaria Box compounds compared to the clinical isolates (average IC50 of 135.4 nM). MMV006087 was the most potent compound with an average IC50 of 22.13 nM compared to MMVo85203 (average IC50 of 137.90 nM) and MMVoo8956 (average IC50 of 262.30 nM). Additionally, MMV006087 exhibited higher potency in the parasites tested than Chloroquine, Mefloquine, and Halofantrine, except Artesunate. The data from this study validate the potency of MMVoo6o87 as a potential lead antimalaria drug candidate, worthy of further exploration. The differences in the response of the laboratory and clinical isolates to the three Malaria Box compounds further substantiate the need to include clinical isolates during antimalarial compound screening programs.





# Evaluating DNA damage response and repair in P. falciparum parasites

#### Bridget Adikah, Jersley D. Chirawurah, Yaw Aniweh and Gordon A. Awandare

The development of resistance to the current line of antimalarials prompts the urgent need to characterize the mechanism by which these parasites develop resistance. Knowledge of the mechanisms of resistance in malaria parasites is important for designing drugs with novel mechanisms of action. DNA damage response and repair in Plasmodium falciparum arising from reactive oxygen species (ROS) have been associated with the development of resistance in P. falciparum parasites. Gossypol is a natural product that has been shown to produce ROS in P. falciparum parasites. However, this compound has not been shown to cause DNA damage in malaria parasites. Therefore, this study sought to investigate the ability of gossypol to trigger DNA damage-repair response pathway in P. falciparum parasite. To this, we evaluated the expression levels of three BRCT-domain coding genes, PfREV, PfNLI, and PfPES associated with phospho-peptide signaling in DNA repair machinery. To achieve this, Dd2 P. falciparum strain was cultured in media containing 100µM gossypol and the parasitemia as well as the gene expression levels of PfREV, PfNLI, and PfPES were evaluated at different time points within 48 hours. From the data, we observed a decline in parasitemia over the 48 hours and this correlated with increased expression levels of PfPES and PfREV genes. Furthermore, we observed an increase in the expression level of PfNL1 at only 48 hours. Therefore, results appear to confirm that gossypol causes DNA damage response and repair in P. falciparum parasites.



# Characterizing Breast Cancer Stem cell properties in MDA-MB 231 and its anti-cancer effect by Cluoquinol

#### Jessica Eyram Kugblenu

Breast Cancer has placed an overwhelming burden on the science world today. Efforts have thus been made to employ the use of hydroxyquinolines derivatives like Cluoquinol and phenolics like gallic acid, caffeic acid and well known chemotherapeutic drugs like cisplatin in minimizing breast cancers .In this study Cluoquinol (a chloroquine analog) and antifungal drug which acts as a zinc, copper ionophore, possesses anti-angiogenesis, protesome inhibitor autophagy inhibitor has been shown to increase anti-cancer activity of chemotherapeutic drugs in cancers with an example being Nasopharyngeal Cancer Stem-cells. Recently Breast Cancer Stem cells have become a target for anti-cancer drug discovery. They make a small population in tumors which can regenerate and differentiate. They are known to be resistant to chemotherapeutic showing an important role in relapse, metastasis and tumor growth. Cancer cells gain stem- like characteristics through Epithelial to mesenchymal transition and expression of stem cell markers. In addition these cells have greater ability to form spheres. In this study, varying concentrations of Cluoquinol will be used to treat MDA-MB 231cells. The effect of the drug on cell viability will be detected with MTT assay. This will further be examined by Sphere forming assay, flow cytometry, gRT-PCR. After treatment it is expected to observe an anti- proliferative effect, sphere forming efficiency, the impact of EMT genes on the cell line.

It is expected that these effects will show potential of Cluoquinol to target chemoresistant cells in a breast tumor.

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# 'Creeping KAPE Pathogens': Phenotypic and Antimicrobial Resistance Profiles

#### Molly Kukua Abban, Isawumi Abiola, Valvano Miguel, Mosi Lydia

The global threat of antimicrobial resistance is increasing with emergence of KAPE (Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aerµginosa and Enterobacter species) pathogens from hospital environments. As opportunistic pathogens, they leverage swarm motility machineries to display resistance to antibiotics including polymyxins. Swarm motility is an adaptative response mechanisms for bacterial survival in harsh environments including the presence of antimicrobial agents or antimicrobial peptides of the innate immune systems. This study determined the swarm profiles of environmental and clinical KAPE isolates from the Intensive Care Unit of Ghanaian hospitals. Using disc diffusion assay and 0.5% nutrient agar media, AMR profiles of KAPE isolates to conventional antibiotics and swarm profile was determined. Also, the swarm potential of KAPE pathogens in the presence of varying Polymyxin B (PmB) concentrations was profiled using micro-broth dilution assays and agar diffusion. The strains showed >80% level of resistance to conventional and last-resort antibiotics tested. The MIC of the strains to PmB was between  $512 - 2048 \mu \text{g/ml}$  above the  $4 \mu \text{g/ml}$  CLSI standard for PmB resistance. It was established that 37 degree celcius was the suitable temperature for the bacterial cells to swarm with >4 cm swarm diameter, as compared to room temperature and 45 degree All the strains displayed a degree of swarm with PmB stress relative to the control; however swarming was impaired in clinical strains of K. pneumoniae and A. baumannii between 24 – 72 h. The swarm profiles at 512 µg/ml – 2048 µg/ml PmB ranges from 0.4 cm to 8.5 cm. Overall, the study established that KAPE pathogens can swarm in the presence of last-resort antibiotic PmB. While this is of great concern to public health, it also indicated that it might be difficult to control the spread of these resistant swarm bacterial cells when implicated in any infection.



# Fungopolis: Buruli ulcer and Secondary infection

#### Daisy Awuku-Asante, Elizabeth Gyamfi, Mabel Peprah, Abiola Isawumi, Lydia Mosi

Wound infections associated with post operatives, insect bites, skin abrasions and certain diseases like Buruli ulcer (BU) are becoming more of a global health concern. Buruli ulcer is a neglected tropical skin disease caused by Mycobacterium ulcerans that produces a macrolide toxin called mycolactone. The disease affects lower and upper limbs as well as the trunk. It starts as a painless nodule or plaque and further gravitates into ulcers which when not treated, can damage the parts of the body it affects. The treatment of these ulcers involves a combined therapy of rifampicin and clarithromycin or streptomycin. However, secondary infections of BU delays wound healing and encourages resistance to antibiotics. Bacteria associated with skin and wound infections has been implicated in BU secondary infections, however, there is little or no information on other microorganisms including fungi. This study aimed at profiling and characterising fungal isolates from BU lesions of patients who had undergone treatment but were still experiencing pain or delay in the healing of their wounds. Phosphate Bovine Saline (PBS) irrigated swabs samples collected from these patients were cultured directly on Sabouraud Dextrose Agar (supplemented with gentamicin) and incubated at 28 - 32 oC for 1-7 days. Twenty-seven fungal strains were isolated and identified from 20 samples cultured. Phenotypic identification and molecular characterization including morphology, nigrosine suspension mount, methylene and lactophenol cotton blue staining and amplification of the internal transcribed spacer (ITS) region showed that species of Aspergillus, Mucor, Talaromyces, Candida and Trichodema are associated with BU secondary infections in Ghana.

This study informs that microorganisms other than bacteria colonize BU lesions and might be responsible for delay in wound healing process.



# Defining the composition of PfMAAP and PfRh5 specific antibody responses using hyperimmune sera from adults living in malaria endemic areas

Nana Akua Kwayewa Boadu, Jonathan Suurbaar, Franklin Y. Nuokpem, Kayode Shadrach, Daniel Dosoo, Harry Danwonno, Kwadwo Asamoah Kusi and Yaw Aniweh.

Malaria still remains a global health concern due to the records of morbidity and mortality emerging every year. Exposure to the malaria parasite does not assure lifelong protection in adults but acquires partial immunity that protects against severe disease. Therefore, understanding the composition and mechanism of naturally acquired immunity (NAI) in adults living in endemic area, would define the endpoints of vaccine clinical trials aiming at protection above the levels acquired in adults. Here, a pooled of hyperimmune sera from 200 adults living in Ghana were obtained to characterize the composition of PfRH5 and PfMAAP specific antibody responses. Purified IgG were used to measure polyclonal IgG endpoint, avidity and subclass profile to PfRH5, N-, central repeat and C-terminal of PfMAAP. Furthermore, general seropositivity was carried with a cohort of pregnant women. Our data suggested that, PfMAAP was recognized 2-3-fold better than PfRH5 by purified IgG from the hyperimmune sera by densitometry. The purified IgG avidity to both antigens were similar, however IgG1 and IgG3 were significantly higher in PfRH5 but not in PfMAAP. Seropositivity of PfRH5 in the cohort of pregnant women was at 27% and correlated with increasing gravidae status. Seropositivity in their cord blood was lower (6.3%) and skew to multigravida women. Together, the data shows that PfMAAP and PfRH5, although recognized by hyperimmune sera, contributes minimally to naturally acquired antibody mediated immunity by composition. This reinforces the theory that, eliciting vaccine induced antibodies to otherwise less immunogenic candidates, may well accrue the needed protection above the level of naturally acquired immunity in adults living in endemic areas.



# Memory B cell Preservation and its correlation with functional antibodies in Malaria immune adults

#### Ofori Michael, Partey D. Frederica, Dowuona N.N. Jasmine

Antibodies have been repeatedly shown to be important in immunity against the blood-stage; the stage of the parasite lifecycle where symptoms occur. In the quest to develop an effective antimalarial vaccine, it is necessary to understand the maintenance of immunological memory and functional antibody responses to Plasmodium falciparum. A key question is whether the preservation of memory B cells affects the functionality of antibodies during persistent and infrequent exposures. This study therefore aims to examine the preservation of memory B cells and their correlation with functional antibodies in two regions with varying malaria transmission intensities (Accra and Cape Coast). The breadth of antibody responses and relative avidity to a panel of P.falciparum merozoite antigens was determined by ELISA in individuals living in a high malaria transmission area (Cape Coast) compared to individuals in a low transmission area (Accra). The median plasma antigen-specific IgG levels and seroprevalence were significantly higher in individuals from Cape Coast compared to Accra. The relative avidity indices of the antigen-specific IgG negatively correlated with the antigen-specific IgG levels. Peripheral B cell populations will be characterized using flow cytometry, it is expected that individuals living in Cape Coast would have elevated levels of B cells with the atypical phenotype. The in vitro functional antibody responses will be assessed using the Growth Inhibitory Activity (GIA) and phagocytosis assay. It is anticipated that individuals with a well-preserved memory B cell compartment are likely to have higher levels of functional antibodies.



# Anaplastic lymphoma kinase signalling, a therapeutic target, in neuroblastoma pathogenesis

#### **Joachim Siaw**

High-risk neuroblastomas typically display an undifferentiated or poorly differentiated morphology. Despite advances in the molecular exploration of paediatric cancers, about 50% of high-risk neuroblastoma patients lack effective treatment. It is therefore vital to understand molecular mechanisms of neuroblastoma pathogenesis, especially the mechanisms that block the differentiation process and explore new therapeutics options particularly for children with high-risk neuroblastoma. We identified an important role for oncogenic ALK-ERK1/2-SP1 signalling in the maintenance of undifferentiated neural crest-derived progenitors through the repression of DLG2, a candidate tumour suppressor gene in neuroblastoma. We showed that the restoration of DLG2 expression, via SP1 inhibition, spontaneously drives neuroblastoma cell differentiation. This highlights the importance of DLG2 in neuroblastoma cell differentiation and shows SP1 as a therapeutic target in neuroblastoma. To shed light on ALK-driven signalling processes and discover more molecular drug targets, we employed an in-vitro proximity-dependent biotinylation identification (BioID) method to identify molecules that interact with ALK. LC/MS-MS analysis identified multiple proteins, including PEAK1 and SHP2, which were validated as ALK interactors in neuroblastoma cells. Use of the SHP2 inhibitors resulted in inhibition of cell growth in ALK-driven neuroblastoma cells. In addition, we noted a strong synergistic effect of combined ALK and SHP2 inhibition that was specific to ALK-driven neuroblastoma cells, suggesting a potential therapeutic option for ALK-driven neuroblastoma.



# Extra-intestinal survival of Vibrio cholerae

## Foster Agyei Kofi, Duodu Samuel

Vibrio cholerae is the causal organism of the potentially life-threatening gastrointestinal disease cholera. The pathogen, in recent years has been found to invade intestinal layers and translocate into the bloodstream of humans. All reported toxins of V. cholerae are enterotoxins with no invasive properties. Virulent factors that enable their survival in human serum, remains unclear. In this study, we hypothesized that the ability of V. cholerae to cause extra-intestinal infections particularly bacteremia, is hinged on the presence of genes encoding invasive virulence factors. Nine (9) strains of V. cholerae; six (6) environmental strains of non-o1/0139 serogroup and three (3) clinical strains of o1 serogroup and El-Tor serotype were screened for survival in serum obtained from immunocompromised patients. Serum from immunocompetent individuals with no known underlying conditions were used as healthy controls. Three (3) environmental strains and one (1) clinical strain of V. cholerae were identified to survive the bactericidal action of serum. Whole genome sequence analysis on the survived strains identified some virulent factors possessed by the pathogen that may contribute to their survival outside the gastrointestinal tract. The cholix toxin gene (chx) present in one of the environmental strains has been known to be responsible for extra-intestinal infections. Other virulent factors identified with the potential of contributing to the invasiveness of V. cholerae were hemolysin gene (hly), repeats-in-toxin gene(rtxA), mannose sensitive hemagglutinin gene (mshA) and genes encoding for the Type VI secretion system. The results suggest that some V. cholerae isolates from Ghana exhibit serum resistance and may persist in blood to cause bacteremia. Further characterization of the serum surviving isolates to evade other innate immune response mechanisms is being currently investigated.



# An investigation into the cross-species potential of an AMA1 based malaria vaccine.

#### Franklin Y. Nuokpem, Yaw Aniweh (PhD), Kwadwo A. Kusi (PhD)

The need for an effective malaria vaccine is imperative. To achieve this, it is necessary to establish strain and species specific immune mechanisms. The Apical membrane antigen (AMA1) is an advanced malaria vaccine candidate with its vaccine potential evidenced by neutralizing antibodies. In this study, we reaffirmed high sequence and structural conservation between AMA1 proteins of P. falciparum (PfAMA1), P. malariae (PmAMA1), and P. ovale (PoAMA1) using in silico and wet-lab techniques. Results obtained suggest the possibility of designing species transcending interventions directed against the AMA1. Sequence alignment and protein homology modeling showed high similarities; PfAMA1 to PoAMA1 51.3%, and to PmAMA1 51.2%. Following successful expression of the three protein antigens using the baculovirus mediated insect cell expression system and confirmation of expressed products by mass spectrometry (TOF), cross-reactivity between the Plasmodium AMA1 antigens was determined by western blot. Of particular note is the cross-reactivity between PfAMA1 and PmAMA1 especially, and PoAMA1 when probed against purified human IgG from falciparum-dominated malaria-endemic Ghana. Also, cross-reactivity when PfAMA1 and PmAMA1 antigens were probed with falciparum generated monoclonal antibodies N3-1D7 was observed. These results suggest a good level of species AMA1 conservation in terms of sequence and structure.



# Membrane vesicles of mycobacterium ulcerans and their role in Buruli ulcer pathogenesis

## Eric Ntifo Osei, Dr. Yaw Aniweh, Dr. Lydia Mosi

Buruli ulcer remains a debilitating Neglected Tropical skin Disease (NTD) with considerable physical, economic and psychosocial consequences on affected families. The causative agent, Mycobacterium ulcerans, exists with many queries regarding its niche, mode of transmission, rapid diagnostics and pathogenesis. The release of bacterial membrane vesicles (MVs) are essential for pathogen's adaptation and virulence. The current study sought to confirm the release of MVs by M. ulcerans as a potential medium of virulence in Buruli ulcer pathogenesis. Here, we demonstrate active release of extracellular vesicles from the thick cell wall of log phase M. ulcerans (Nm 209) and M. marinum (Sa 200695) into their respective growth media. Size distributions of vesicles released by the two pathogens were similar and also did not differ from controlled vesicles from M. smegmatis. Mycolactone was not detected in both native and UV-A irradiated vesicles from M. ulcerans and neither in vesicles found in growth medium of M. marinum (Sa 200695) which also secretes mycolactone, congener F. Moreover, membrane vesicles from M. ulcerans showed persistent, concentration-dependent stimulation of RAW 264.7 cells metabolism. This eventually compromised the cells' viability via oxidative stress and after 48 hours of co-incubation, native and UV-A irradiated vesicles induced 45% and 40% cell apoptosis, respectively. Proteomic analysis on the vesicles revealed enrichment of 32 proteins mostly cell wall/ membrane localized. These included amidase amiC, aldehyde dehydrogenase, integral membrane indolylacetylinositol arabinosyltransferase EmbA/B, virulent lipoprotein LprK, maltokinase, and many conserved hypothetical proteins. Our results show that M. ulcerans (Nm 209) can actively release extracellular vesicles with some virulent protein cargoes and without mycolactone, the vesicles can trigger oxidative stress-related apoptosis in host's cells. This may contribute to early-stage apoptosis, tissue necrosis and immunosuppression in Buruli ulcer lesions and adds insight on paradoxical reactions associated with disease treatment.





# Genotypic and phenotypic diversity of Mycobacterium tuberculosis complex genotypes prevalent in West Africa

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Findings from previous comparative genomics studies of the Mycobacterium tuberculosis complex (MTBC) suggest genomic variation among the genotypes may have phenotypic implications. We investigated the diversity in the phenotypic profiles of the main prevalent MTBC genotypes in West Africa. Thirty-six whole genome sequenced drug susceptible MTBC isolates belonging to lineages 4, 5 and 6 were included in this study. The isolates were phenotypically characterized for urease activity, tween hydrolysis, Thiophen-2-Carboxylic Acid Hydrazide (TCH) susceptibility, nitric oxide production, and growth rate in both liquid (7H9) and solid media (7H11 and Löwenstein–Jensen (L-J)). Lineage 4 isolates showed the highest growth rate in both liquid (p=0.0003) and on solid (L-J) media supplemented with glycerol (p<0.001) or pyruvate (p=0.005). L6 isolates optimally utilized pyruvate compared to glycerol (p<0.001), whereas L5 isolates grew similarly on both media (p=0.05). Lineage 4 isolates showed the lowest average time to positivity (TTP) (p=0.01; Average TTP: L4=15days, L5=16.7days, L6=29.7days) and the highest logCFU/mL (p=0.04; average logCFU/mL L4=5.9, L5=5.0, L6=4.4) on 7H11 supplemented with glycerol, but there was no significant difference in growth on 7H11 supplemented with pyruvate (p=0.23). The highest release of nitrite was recorded for L<sub>5</sub> isolates, followed by L<sub>4</sub> and L<sub>6</sub> isolates. However, the reverse was observed in the urease activity for the lineages. All isolates tested were resistant to TCH except for one L6 isolate. Comparative genomic analyses revealed several mutations that might explain the diverse phenotypic profiles of these isolates. Our findings showed significant phenotypic diversity among the MTBC lineages used for this study.





# Characterization of Plasmodium malariae reticulocyte binding protein (PmRBP1a)

#### Danwonno Harry, Asamoah K. Kwadwo, Gordon Awandare, Aniweh Yaw

Regarded as the Olympic champion of persistence, Plasmodium malariae infection is more prevalent than generally perceived. Although it is considered to cause a milder form of malaria, it has been implicated in nephrotic syndrome, inflammation of the gall bladder and anaemia-related deaths. How this parasite contributes to the pathogenesis of these complications remains to be understood. Possible factors include its unique biology of a longer life cycle, typical low parasitemia and chronic-promoting factor(s) which permits its persistence in the human host. Coupled with the current neglect of P. malariae by malaria elimination programmes which can lead to its persistence prompts the need to study it. P. falciparum reticulocyte binding-like homologue 5 (PfRh5) is the leading blood-stage vaccine for Plasmodium falciparum while P. vivax reticulocyte binding protein 2b is proving to be an effective vaccine candidate for P. vivax. With the recent publication of P. malariae reference genome, Rutledge et al. (2017) also found P. malariae reticulocyte binding protein 1a (PmRBP1a) to be the most divergent among the PmRBPs suggestive of being a/the host-determining factor. A sequence homology search revealed the presence of nucleotide-binding and erythrocyte-binding domains in PmRBP1a, which indicates it might be involved in both sensing and anchorage to erythrocytes during erythrocyte invasion. The predicted tertiary structure of PmRBP1a's erythrocyte-binding domain is structurally similar to P. falciparum reticulocyte binding-like homologue 5 (PfRh5) and P. vivax reticulocyte binding homologue 2b (PvRBP2b). PmRBPs genetic analysis revealed limited genetic sequence variation in the sampled strains with evidence of the genes under purifying selection. A relatively high titre of naturally acquired antibodies specific to the N-terminus of PmRBP1a was quantified, a region that overlaps with the erythrocyte-binding domain. The measured anti-PmRBP1a was observed to positively correlate with increasing age and malaria endemicity.



# Selection and population structure of known Plasmodium falciparum vaccine candidate genes in Africa

#### Joana Ayisha Ewuntomah

Genetic variation and antigenic diversity of major vaccine candidate antigens are the main hurdles in the development of efficacious malaria vaccines. Here, we sought to determine the local temporal signatures of selection for CSP, MSP1&2, AMA-1, TRAP, and EBA175 between 2009 and 2011 in Navrongo-Ghana (n=501), and the disparities in population structure among African countries (The Gambia, Mali, Malawi, Senegal, Guinea, Ghana, and DR of Congo). Data was obtained from MalariaGEN (www.malariagen.net/) public data release (version3). RSB analysis using Rehh (ines2rsb) showed significant differentiation in chromosomes 1, 4, 7, 8 and 13. Some of the candidate markers of differentiation were found within the AMA1 gene (E405K), TRAP (T134S and K119R), and EBA175 (E592A) (P-value = 10-7). Sliding window analysis showed that the average segregating sites for AMA1 was 55.1, TRAP was 43, while EBA175 had the least with 29.4 across all African countries. Interestingly, Ghana had the lowest nucleotide diversity ( $\pi$ =11.5) for AMA1 compared to all the other African countries with an average of ( $\pi$  =21.6). The haplotype diversity for all the three genes was approximately 1 for all the African countries. Ghana had the highest Tajima D values for these vaccine antigen genes, showing balancing selection. For AMA1, Tajima D was 4.2 for Ghana while The Gambia had the least value of 1.6. For EBA175 Ghana had a Tajima's D values of 3.56 and Senegal had the least value of 1.17. The median complexity of infection (Fws) was low for all the African countries with Malawi having the lowest (Fws =0.78) and most countries ranging from (0.82-0.94). But clonality of the samples did not influence the selection indices significantly. In tandem to with previous studies, the data shows that these malaria vaccine antigens are under balancing selection with slight variation in genetic diversity across Africa.



# Provenance and Estimated Age of R143W GJB2 Founder Mutation Associated with Autosomal Recessive Non-Syndromic Hearing Impairment in Ghana

**Elvis Twumasi Aboagye,** Samuel M. Adadey, Kevin Esoh, Lucas Amenga-Etego, Gordon A. Awandare, Ambroise Wonkam

Single nucleotide variations (SNVs) account for over 80% of the genetic etiology of hearing impairment (HI) in different populations. The reported causal gene variants stem from inheriting ancestral founder mutations to germ-line de novo mutations, known to be ethnic and population specific. However, the evolutionary history, ancestral origin, age of occurrence in populations, and selection of these HI associated genetic markers remains to be extensively investigated across populations. In Ghana, the most common variant (p.R143W) accounted for as high as 25.9 % homozygous familial HI cases, and 7.9% isolated cases, and carrier frequency of 1.4% in unaffected controls. Haplotype-block analysis of exome sequence of 32 p.R143W homozygous affected non-syndromic hearing-impaired familial cases and 64 unrelated controls homozygous of the wild type were used to estimate age of the founder mutation. The Disequilibrium Mapping Likelihood Estimation (DMLE +2.3) software was used to estimate the p.R143W age in generations since the first occurrence of the reported founder mutation using seven variants in linkage disequilibrium with variant of interest. The age and origin of the most common HI causal variant (GJB2, p. Arg143Trp) reported in Ghana, was estimated to have evolved about 18,500 years ago. Despite earlier estimated 6,500 years for the same variant in Japan, this evidence suggests selection around this locus in Africa that pre-date other populations with isolated reports of the variant. The variant might also have evolved independently in these populations or might have spread by human migration.



# Detection and molecular characterization of Epstein Barr Virus (EBV) in biopsies of Ghanaian gastric cancer patients

#### **Ampofo-Asiedu Jeffery,** Tagoe A. Emmanuel, Petershie Bernard, Abrahams D. Afua, Quaye Osbourne

EBV have been implicated in the etiology of gastric cancer. This study aimed at detecting EBV genotypes and strains associated with gastric cancer (GC) cases from 55 GC biopsies (cases) and 63 non-GC biopsies (matched-controls) by polymerase chain reaction (PCR) and genomic sequencing. The samples were retrieved from the archives of the Pathology Department at Korle-Bu Teaching Hospital. Males accounted for 63.3% of the medical records retrieved and the mean age for all patients were 58.1 years. Mean age of males (57.9  $\pm$  13.83) years compared to their female counterparts ( $58.5 \pm 14.33$ ) years was not statistically significant (p-value < 0.764). There were greater odds of association with sex and qastric cancer development (odds ratio for male= 2.97; p-value < 0.0001). There were also greater odds of association with gastric adenocarcinoma and the type of gastric adenocarcinoma (odds ratio for intestinal type= 19.14; p-value< 0.0001). The frequencies of EBV positivity were 67.3% and 49.2% in the GC and non-GC biopsies respectively. The predominant genotype of the virus in the cases was EBV genotype-1 (75.7%) and in that of the controls was EBV genotype-2 (64.5%). EBV genotype-1 was significantly associated with risk of GC development ( $\chi_2$  = 20.74, p-value < 0.0001). Both cases and controls had the Mediterranean+ strain of EBV. The mean EBV load in the cases  $(3.507 \pm 0.574)$  was significantly higher than in the controls  $(2.256 \pm 0.756)$  (p < 0.0001). We conclude that EBV, especially the Mediterranean+ EBV genotype-1, is associated with GC development in Ghanaian GC patients.



# ABO Blood grouping as a potential biomarker for COVID-19 severity

#### Oyawoye O. Fatima, Peter K. Quashie, Lily Paemka

The novel coronavirus disease-2019 (COVID-19) is a pneumonia infection caused by Severe coronavirus 2. The disease has been spreading around the world rapidly and declared as a pandemic by WHO, causing an immense burden on the healthcare system around the world. The presentations of the disease include anomia, coughing, sneezing, and other non-pulmonary manifestation, which could range from mild to critical. So far, there are no definitive markers for disease prognosis. Studies have implicated the ABO blood group as a risk factor for variation in disease severity and susceptibility. However, limited investigations into the role of the ABO blood group in disease severity in Africa has been undertaken. This study therefore aims to investigate the correlation between the ABO blood grouping and disease severity in COVID-19 patients in Ghana. In this study, the blood group will be determined using a reverse blood grouping system. Disease severity amongst patient will be grouped as asymptomatic, mild/moderate and severe/critical, this data will then be correlated with the blood group using statistical tools to infer an association between the two parameters. Data from this study will give an insight into the role of the ABO blood group on disease severity and its potential use as a biomarker for prognosis.





Expression and purification of polymerases for the detection of sars-cov-2

Sarah Ashitei, Felix Ansah, Jacob K. Donkor, Victor E. Kornu, Caleb O. Appiah, Precious Opurum, Joyce Ngoi, Peter Quashie, Prosper Kanyong, Yaw Aniweh and Gordon A. Awandare

The emergence and spread of the coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2), poses a serious threat to global health. Since its outbreak in December 2019, more than 3.5 million deaths have been reported. To control the spread of this contagious virus, there is the need for a reliable and cost effective diagnostic tool for routine surveillance especially in resource limited settings. Loop-mediated isothermal amplification (LAMP) is a simple, sensitive and cost effective diagnostic tool that requires short time and minimal laboratory infrastructure making it more preferable than reverse transcription quantitative polymerase chain reaction (RT-gPCR). Therefore, in this study, the two enzymes required for RT-LAMP (Bst polymerase and reverse transcriptase) were expressed, purified and used to develop a colorimetric-based assay for the detection of SARS-CoV-2. The performance of the newly developed RT-LAMP assay was evaluated using purified RNA and crude inactivated samples from 200 cryopreserved clinical isolates. The RT-LAMP assay was based on visible color change after 35 minutes of incubation time. Compared to the gold standard RT-qPCR assay, the sensitivities of the RT-LAMP assay were 92.5% and 90.0%, on the purified RNA and crude inactivated samples, respectively. The specificity of the RT-LAMP was 100% for both the purified RNA and the crude inactivated samples. The data demonstrate the robustness of the locally developed RT-LAMP assay with a turnaround time of less than one hour. This highly sensitive and specific colorimetric assay will be instrumental towards the implementation of an accurate, affordable, and population-wide diagnostic program.



# Profiling of Bitis arietans venom composition for the identification of toxin variants that challenge snakebite therapeutics

#### Awiaga K. Collins, Awandare Gordon and Amlabu Emmanuel

Snakebite is a serious public health problem in numerous countries of the world. Bitis arietans (African puff adder) is responsible for the vast majority of envenomation in Africa due to their country-wide distribution. A major bottleneck in the development of antivenoms is large diversity of venom toxins across snake species and this could be attributed to dissimilar ecologies and diet. These factors have profound implications on the pathologies that are presented in snakebite victims. In this study, venoms were collected from Bitis arietans which were sampled from the wild in three states of northern Nigeria. We assumed that the composition of the venoms from the three states should vary since the snakes were exposed to a wide variety of ecological situations and high geographic variability for prey preference. To elucidate the possible differences in venom protein composition, SDS-PAGE and native PAGE analysis of the venom samples revealed both common and different protein composition in the venoms with varying abundance levels. While the data for Transmission Electron Microscopy and LC-MS analysis for the different venom exosomes are expected, the crude venoms were individually fractionated on analytical size exclusion chromatography (SEC) column for precise toxicity evaluation. Since B. arietans venoms are highly haemorrhagic and this unique property is mediated by proteases, all SEC fractions from the individual venom samples were subjected to enzyme-activity assays and protease-enriched fractions were identified. Using an in vivo lethality mouse model, we showed that lethality scores for the protease-enriched fractions varied significantly. The observed variation could be attributed to differential levels of specific class of protease(s) prevalent in the fractions classified using specific protease inhibitors. Thus, it is expected that our ongoing screens for small molecules with generic inhibition of specific toxin classes would be useful in circumventing challenges associated with venom variants.



# SARs-CoV-2 Sequencing: Protocol Optimization to Improve Sequencing Success Rate

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The emergence of the novel SARS-CoV2 variants poses threats against efforts being made to eradicate the virus from the globe. According to statistics, there have been over 93,775 cases of the corona virus disease 2019 (COVID-19) in Ghana, with 784 recorded deaths as of 31st May, 2021(WHO). Global case fatality rates of the disease have been related to the various strains or variants of the virus spreading within various countries. Genomic surveillance of SARs-CoV-2 plays an important role in understandwing the epidemiology and transmission of the virus. Here, we present an optimized RNA extraction protocol using over 180 COVID-19 positive samples to improve on the success rate of sequencing. Viral RNA was extracted from all samples using both QIAamp Viral RNA kit (Qiagen) and Quick-RNA Viral Kit (Zymoresearch). Sequencing of the genetic material was done using the Oxford nanopore MinION platform following an amplicon-based enrichment of the SARS-CoV-2 genome (ARTIC Protocol). In optimizing the starting material for derivation of quality amplicons for sequencing, the initial extraction and elution volumes were adjusted for both kits. This significantly improved the amplification success rate of the target SARs-CoV-2 genome. Comparison of SARS-CoV-2 genomes before and after optimization showed a significant improvement on the genome coverage with a high percentage of the genome having fewer gaps after sequence analysis which had previously precluded variant calling.



# TALKING BACTERIA': Divalent Cations and Antimicrobial Resistance

#### **Ewura-Esi Manful,** Martha A. Asare, Isawumi Abiola, Theresa Gwira, Lydia Mosi

Species of Enterobacter and Pseudomonas described as 'Global Priority Pathogens' by WHO are becoming increasingly resistant to antibiotics. Their antimicrobial resistance mechanisms have been associated with localized lipopolysaccharides (LPS) on the bacterial outer membrane. The integrity of these outer membrane-bound molecules is maintained by the strength of the negatively charged phosphate groups in the lipid A component of the LPS. However, divalent cations (Mg2+ and Ca2+) have an affinity for this phosphate ion, and this biased association can compromise the LPS for easier antibiotic penetration into the bacterial cell membrane. While the chelation of these divalent cations for bacterial cell permeabilization has been established in E. coli, there is limited information on the effects of divalent ions on antimicrobial-resistant Enterobacter and Pseudomonas isolates from Ghanaian hospital environments. This study investigated the roles of Mg2+ and Ca2+ on the growth profiles of Enterobacter and Pseudomonas species with and without antibiotics using indole quorum sensing (QS) and antimicrobial profiling assays. The strains showed 71% level of resistance to ampicillin, amoxicillin, penicillin, gentamicin, and cloxacillin, with none resistant to ceftriaxone and trimethoprim. At stock and 0.1 concentrations of Mg2+ and Ca2+, the strains maintained resistance; there was a decline in resistance to cloxacillin and penicillin. Both strains were susceptible to gentamicin at Mg2+ stock and 0.1 concentrations; penicillin-resistant Pseudomonas spp. became susceptible in the presence of Ca2+, while Enterobacter spp. was susceptible to penicillin in the presence of Mg2+. The strains were indole positive and susceptible to gentamicin with a decrease in susceptibility to ceftriaxone. Trimethoprimsensitive Enterobacter spp. became resistant to trimethoprim in the presence of indole. Overall, the study showed that QS molecules such as indole mediates bacteria susceptibility or resistance to antibiotics. It also informs that divalent cations can potentiate an increase or decrease in antibiotic effectiveness.

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