THRIVE
TRAINING HEALTH RESEARCHERS INTO VOCATIONAL EXCELLENCE IN EAST AFRICA

News

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Insights from the Vector Ecology and Disease Workshop at International Centre of Insect Physiology and Ecology (icipe) - Thomas Odhiambo Campus – Mbita Point, Kenya

Hudson Onen, Uganda Virus Research Institute

My name is Hudson ONEN, a M.Sc. student of Makerere University and a THRIVE-2 M.Sc. fellow attached to the Entomology Division at the Uganda Virus Research Institute. At the Uganda Virus Research Institute (UVRI), I am currently involved in *Anopheles* mosquito-related research activities namely: raising colonies under insectary, field sampling of adults using pyrethrum insecticide spray catch (Psc), Human Landing Catch (HLC), aspiration using improved powered prokopack, sweep netting of male swamps, larval sampling, forced laying of gravid females, collection and morphological identification of macro invertebrates and species identification of *Anopheles gambiae* using molecular technique.

My M.Sc research focuses on the ecology of immature stages of *Anopheles* mosquitoes the principal vector of malaria in Uganda. The thesis title is "**Diversity and distribution of macro-invertebrates associated with *Anopheles gambiae* breeding habitats in selected villages along River Sezibwa, Uganda**". This study contributes to the understanding of how population of *Anopheles* mosquitoes and macro- invertebrates fluctuates in shared breeding habitats. Findings from this study may establish the role played by macro-invertebrates in reducing the mosquito vector in the fight against malaria

Hudson ONEN sampling macro-invertebrates and mosquito larvae using 350ml scooper in Kayonjo, Kayunga Uganda- July 2018

However, for a concrete conclusion to be drawn from such study, sufficiently extended base-line data should be collected which reflects both seasonal and annual variations (e.g. 3 or 4 years) in population dynamics/ fluctuations of *Anopheles* mosquitoes and macro- invertebrates in

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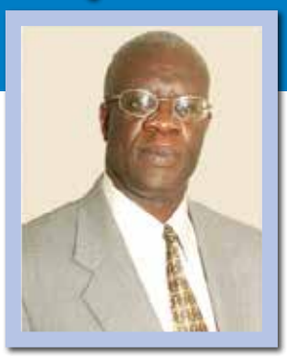
Editorial



Dear Reader,

THRiVE-2 commends its fellows for writing nearly all articles in this issue of THRiVE News. Some researchers, however, have no drive to write articles for this newsletter. Yet, sharing ideas, research findings and experiences is a key aspect of good science and it is beneficial to the researcher and the readers. The fellows' writings remind us of the statement by the philosopher Allan Bloom, "Every educational system wants to produce a certain type of human being".

What type of researcher does THRiVE-2 or DELTAS educational systems want to produce? We should also ask "What is the purpose of each student's future working and professional life? The consortium's purpose for producing doctoral graduates and the individual trainee's motivation for pursuing research training matter a great deal and help stakeholders to determine how and what the program focuses on. We need to nourish our students' spirits and to facilitate their professional and scientific careers. High quality mentorship should form a very significant component of this undertaking. Excellent mentorship by faculty should be rewarded in no less than research prowess.

The articles written by the fellows remind us of the aim in scientific writing not to lose the forest for the trees. The whole essence of scientific writing is to tell a comprehensible story arising from the available data or information. Mimi Zieger (2000) emphasised "……two good reasons why it is desirable to write clearly: first, to be sure that you yourself know what you mean, and second, to be sure that you get your message across to your readers". Clear writing helps you clarify your own thinking (Woodford, 1967). So, to all THRiVE faculty and fellows why not take advantage of the opportunity to write more articles for future issues of THRiVE News?

Insights from the Vector Ecology and Disease Workshop

shared habitats. It's upon the above background that I applied and won the THRiVE- 2 MSc supplementary research grant of 2018 for dissertation improvement.

I was privileged to be invited for a workshop on vector ecology and disease running from July 30th to August 3rd 2018 by the International Centre of Insect Physiology and Ecology (*icipe*), Kenya, Ohio State University, Training Health Researchers into Vocational Excellence (THRiVE), University of Nairobi, and Kenya Medical Research Institute (KEMRI). There were 20 attendees from different research institutions in Uganda, Kenya, Tanzania, Rwanda, Zimbabwe, Cameroon and Zambia. Facilitators were lecturers, senior researchers and staff of *icipe*.

The workshop was designed to provide a 'one-health approach which provides an overview of how vector borne diseases of animal, plants and human health are influenced by environmental conditions and how a single approach can be used to control these diseases. Topics covered included; parasite-vector interactions, vector ecology, multidisciplinary control of vectors with a focus on mosquitoes, sand flies, tsetse flies, ticks, and the latest exciting research in these areas such as gene drive technology. Among others, the training was also used as a platform for networking with researchers from other research institutions and universities across Africa and overseas in order to foster combined approach in utilization of vector's ecology and behavior to combat different vector-borne diseases such as malaria.

Since this training workshop was on Vector ecology and diseases, it was of great relevance to my career as a young scientist whose effort is geared towards understanding how the ecology of mosquitoes can be exploited in the fight malaria. I was keen to learn about various control alternatives in the pipeline of which use of symbionts was particularly fascinating.

The knowledge I gained from this training workshop has shaped and ignited my interest to enroll into Ph.D. program as soon as I defend my MSc dissertation in order to contribute towards the fight against malaria. I would like to acknowledge the sponsor of the training workshop (THRiVE-2 Project) without which I could not have the financial muscle to attend this training. In a very special way, I thank THRiVE-2 at UVRI for identifying and nominating me and for the support extended to enable me attend the training workshop at *icipe.*

Other contributors to this article are Kayondo Jonathan and E. Nyanzi.

Improving outcomes of HIV-related meningitis in sub-Saharan Africa

By David Meya, Makerere University College of Health Sciences

Over the last decade, there have been tremendous strides in improving outcomes of individuals infected with HIV, especially in terms of access to long term Antiretroviral Therapy (ART) and improved life expectancy. Although there have been rapid and significant declines in the incidence rates of opportunistic infections in the developed countries, this decline has not been as dramatic in sub-Saharan Africa.

One such infection is caused by the fungus, *Cryptococcus*, which has sadly not seen the expected dip in the number of cases even with the rapid roll out of ART across the savannah and beautiful plains of Africa, reaching the thousands and millions that continue to be infected with HIV daily.

The current global estimates of cryptococcal disease suggest a 6% prevalence of cryptococcal antigenemia among HIV-infected individuals with a CD4<100 cells/mL, translating to 278,000 patients with cryptococcal antigenemia while an estimated 223,100 incident cases of cryptococcal meningitis occur worldwide. Unfortunately, the brunt of this disease occurs in sub-Saharan Africa, which bears 73% of the disease burden with approximately 136,000 deaths annually.

Over the last 6-8 years, I have been supported through Welcome Trust (DELTAS program) to conduct research aimed at improving the grim outlook of cryptococcal disease in sub-Saharan Africa through observational, Translational science, and clinical trials.

The Cryptococcal Outcomes on ART (COAT) trial, for which I was the Ugandan Principal Investigator, was conducted in Kampala, Mbarara in Uganda and Capetown in South Africa, enrolled 177 participants with cryptococcal meningitis. We were able to demonstrate that starting ART too soon (7-11 days) after the diagnosis of cryptococcal meningitis was detrimental, with lower survival rates (55%) compared to starting 4-6 weeks after initiating antifungal therapy (survival rate 70%) - this definitive trial answered the question on the optimal timing of ART after cryptococcal meningitis and led to a policy shift in WHO guidance. Similarly, during this trial, we demonstrated that electrolyte pre-supplementation rather than waiting to replace deficiencies in electrolytes following administration the antifungal drug, amphotericin, for cryptococcal meningitis, prevented mortality during induction treatment of cryptococcal meningitis – this strategy was also adopted in the WHO guidelines. I believe implementing these two clinical strategies has prevented thousands of cryptococcal-related deaths.

More recently, during my PhD training, I explored the immunopathogenesis of immune reconstitution inflammatory syndrome, a complication of starting ART in which patients previously treated successfully for an opportunistic infection seemingly worsen after they initiate ART. I demonstrated through immunology assays using cells obtained from spinal fluid and blood that during this complication, there is a specific immunological signature and type of cell that migrates into the central nervous system, making the spinal fluid more inflammatory from the migration of these innate immune cells known as monocytes.

Over the last few years, I have also been a principal investigator on a randomised clinical trial in 17 clinics in Uganda to evaluate the screen and treat strategy for cryptococcal antigenemia (CrAg) in patients to determine the effectiveness of this intervention on decreasing mortality among the general population of HIV-infected patients with CD4<100 cells/mL.

This population was screened for presence of cryptococcal antigen in blood and those with a positive CrAg test would be treated with the antifungal drug, fluconazole, for 10 weeks. We demonstrated that this strategy is much more effective as an intervention among individuals with higher burden of cryptococcal infection, where the titer of cryptococcal antigen is >1:160. This work has led to the modification of the rapid diagnostic lateral flow assay for cryptococcal antigen to incorporate the ability to provide a semiquantitative CrAg result, however, further work is needed to determine the optimal therapy for patients who have CrAg titers greater than 1:160.

Cryptococcal disease is not the only cause of HIV-related meningitis in sub-Saharan Africa. Tuberculosis (TB) remains the etiological agent in 10-15% of HIV-associated meningitis. As part of the meningitis screening studies, we investigated the utility of newer rapid diagnostic tests including the Xpert MTB/Rif, the Xpert MTB/Rif TB Ultra (Xpert Ultra) - unique tests that employ DNA amplification techniques to determine the presence of *Mycobacterium Tuberculosis*, that causes human Tuberculosis.

Given the difficulty of confirming the diagnosis of TB meningitis, we conducted a study using the Ultra Xpert, microbiological culture and basic staining techniques using spinal fluid. We determined that the TB Ultra was much more sensitive (70%) in identifying patients with Tuberculous meningitis compared to the Xpert MTB/Rif (50-60%) and culture (60%). This work helped consolidate the Xpert Ultra as the recommended test for Tuberculous meningitis.

The DELTAS program support has been instrumental in setting the stage for building my own career, which in turn has had a multiplier effect including establishing international collaborations, mentorship of more than 50 students and fellows and I have developed a keen interest in learning how to effectively communicate science as a researcher and mentor.

FINDING THE INTERSECTION

By Dickson Muyomba, THRiVE IT Officer

Being in a network and working as a team has been one of the strategies embraced in the THRiVE consortium. This strategy has not only been implemented at the strategic level but also adopted at the operational level. I am from an Information and Communication Technology (ICT) background but have been closely working with the finance team. Initially, the connection wasn't evident until the very first finance audit for the program by Deloitte and Touche; a UK-based audit firm. It was a finance audit, I didn't expect it be ICT intense, I was wrong! To me this was an eye opener. Recently THRiVE has been conducting finance site monitoring visits to partner institutions and once a site visit program is shared including the ICT component, often times the finance officers ask the question, what have we got to do with ICT? It's during the exit meetings while sharing findings and giving recommendations that they realise the relevance and appreciate inclusion of the ICT component during the visits.

At the Secretariat, we have agreed to assess the appropriateness of IT systems at partner institutions to provide a secure and reliable ICT environment not only for finance activities but also to ensure that there is a business continuity strategy. Things like system/data backup strategies in place, password user policies and access levels, information security, risk log tracker and asset verifications are assessed alongside the finance issues.

My trip to the University of Toledo College of Medicine and Life Sciences, Toledo, Ohio USA; expanding linkages

Moses Galukande, THRiVE-2 Postdoctoral Fellow

One of my intentions and those of the architects of ***THRiVE*** is to foster sustainable, mutually beneficial collaborations beyond the doctoral and post-doctoral engagements.

This is exactly what is happening to my intentions. I made this trip to Ohio to once again meet Prof Alex Asea, see the lab he got and how to actualize the plans we agreed on of testing for HSP (Heat Shock Protein) and establish if Ugandan women over-express the HSP.

And if they do, we got an opportunity to commence anti-HSP drug trials as adjuncts to standard chemotherapy regimens and hopefully see a difference in tumor response and survival for our Ugandan women. The idea is since HSP plays a role of shielding tumor cells from therapy and/or help the injured ones mend (injured by therapy), taking it out of the equation, carries so much promise for our patients with breast cancer.

The technology set up for us to use was mass spectrometry, using a state of the art technology, replacing the option of antibody- antigen stains and identification through microscopy using a reference scale to determine the extent of staining intensity and therefore absence or presence of HSP.

Prof Asea reiterated the commitment to perform the tests at no cost to my project. However, I needed to have the samples prepped by Dr. George Mutema, who was a brilliant collaborator during my PhD studies. George is a pathologist of repute and much experience and I have been lucky to have him as part of my teams for so many years.

The Toledo campus is a place to behold. It is well-resourced and the people I met were enthusiastic about developing linkages with Makerere University College of Health Sciences. One area we explored was surgical skills training with the use of simulation technologies, of which there were no shortages.

With Prof Asea at University Prof Galukande at the Simulation of Toledo Center

Bioinformatics Training and Knowledge Transfer beyond Uganda

Gerald Mbowa, Makerere University College of Health Sciences

Bioinformatics has made a turning point in many areas of science such as Healthcare, Gene technology and Medicine. It offers innumerable applications in fields like Biotechnology, Pharmaceuticals, Medicine, etc. Having secured a THRiVE-2 PhD fellowship in July 2017 at Makerere University, I have been able to have ample protected time at Makerere University to study as required under my PhD program as well as train other students. During this period, THRiVE has funded my Bioinformatics training at the University of Cambridge, in the UK. This training experience exposed me to world class trainings at the Department of Genetics. After returning to Uganda, I have successfully been involved in Bioinformatics training in Uganda and beyond. I have carried out a Bioinformatics and Next Generation Sequencing workshop at the University of Malawi's College of Medicine in Blantyre during September, 2018.

During my fellowship at the University of Cambridge, I was delighted to work with Dr Chris Illingworth and the team at the Bioinformatics training facility at the Department of Genetics. Part of my training at Cambridge equipped me with relevant skills on how to train students in the rapidly growing field of Bioinformatics. I further got the opportunity to network with renown researchers at the Wellcome Trust Sanger Institute and the European Bioinformatics Institute (EMBL-EBI); a part of the European Molecular Biology Laboratory (EMBL). Looking at a career as a researcher at Makerere University, the networks established while in UK offered potential collaborations when applying for grants in future.

In resource-limited settings like Uganda as well as many African countries, Bioinformatics training faces specific challenges that currently need to be addressed to ensure that the new field thrives. Some of these challenges include; lack of access to local Bioinformatics expertise, access to Bioinformatics trainings, internet access, and instability and lack of Computational infrastructure. Many organisations and programs such as

Gerald Mboowa at a workshop attended by participants from EMBL and the Sanger Institute

THRiVE have explored various approaches to address some of these challenges by purchasing computational hardware and training the local Bioinformatics expertise through funding them to attend long and short face-to-face Bioinformatics training and workshops at premier institutions like University of Cambridge, the Sanger Institute and the European Bioinformatics Institute. To ensure knowledge and skills transfer, I am participating in a number of Bioinformatics capacity building programs such as;

- Computational and Molecular Epidemiology Training in TB and HIV in Uganda

https://projectreporter.nih.gov/project_info_description.cfm?aid=8897524

- Introduction to Bioinformatics and Next Generation Sequencing techniques workshop

https://news.mak.ac.ug/2018/01/bioinformatics-next-generation-sequencing-techniques-short-course

- Host pathogens interactions and basic bioinformatics a Global Infectious Diseases Research Program

http://www.bumc.bu.edu/busm-muk/program-overview/initiatives-in-uganda/

- The 3-months' online H3ABioNet – Introduction to Bioinformatics course (IBT)

https://training.h3abionet.org/IBT_2017/?page_id=2469

- Alliance for Global Health and Science and Makerere University – 2017 and 2018 Summer Workshops

http://cend.globalhealth.berkeley.edu/2018/06/12/alliance-global-health-science-makerere-university-2018-summer-workshop/

The above workshops and training opportunities iterate annually and continue to offer researchers as well as master's and doctoral students from Uganda and beyond a costless induction experience into Bioinformatics. Makerere University has now formally launched accredited master and PhD programs in Bioinformatics (https://www.breca.mak.ac.ug/), an initiative of a former THRIVE-1 Post-doctoral fellow (Dr David Kateete) who also happens to be my PhD supervisor at Makerere University.

Strengthening Governance of Grants at Gulu University

By Robert Kiduma, Charles Opira, Onen Walter Yagos and Geoffrey Tabo

THRiVE Consortium partners submit quarterly financial / accounts reports to the Secretariat by the 10th of the month following the end of the quarter. This is a detailed and robust process that not only looks at financial management and accounting, but further deals with elements such as risks assessment, information and data security etc. Some financial and accounting obstacles that impede submission of satisfactory quarterly reports include; mismatch in forecasts, difficulty in the reconciliation and balancing of accounts in different currencies (British Pounds, United States Dollars for overseas procurement and Uganda Shillings for local operations), inaccuracies in the determination of allowable and disallowable costs, inaccuracies in categorization of expenditures across the various programmatic thematic areas, among others.

A hands-on training was conducted at Gulu University from 19th to 21st September 2018 by the THRiVE-2 team from the Secretariat. The training covered specific issues that hinder submission of complete and satisfactory reports using case by case examples. In addition to addressing the financial and accounting impediments to preparation and submission of reports, the training addressed risk management, and information and data security.

Financial management was discussed and summarized as follows:

Quarterly forecasts need to be realistic. This can be achieved by reviewing and harmonizing previous quarter forecast not implemented and activities stated in the annual workplan in the subsequent quarter. In this way, the implementation teams are able to identify variations and generate the variation causal factors which are documented in the reporting template.

Budget adjustments are normal occurrences in budget implementation. There is always need to identify occurrence that may necessitate budget adjustment. These may include; low absorption/high absorption on some budget lines or over-budgeting in some budget lines. This necessitates initiation of proposals to revise the budget which is accompanied with justification.

Value for money is an important test for effective utilization of resources. Maximization of resources is hindered in circumstances where activities are duplicated by different projects operating in the same environment. It therefore implies that institutional programs need to be harmonized to maximize results. THRiVE-2 Gulu has been conducting joint activities/ workshops with Gulu University Research Ethics Committee (GUREC) and Building Stronger Universities (BSU III), a Danida funded project.

THRiVE-2 Continues To Build Capacities Of Research And Ethics Committees (Rec) To Ensure Quality Oversight On Scientific Conduct Of Research In Uganda

By Onen Walter Yagos, Robert Kiduma and Opira Charles

In order to improve the quality of scientific research reviews at Gulu University and beyond, THRiVE-2 Project at Gulu University sponsored four members of Gulu University Research Ethics Committee (GUREC) to the 10th Annual National Research Ethics Conference (ANREC) organized by Uganda National Council for Science and Technology. The ANREC which brought together delegates from within Uganda and other African countries took place between the 9th and 11th July 2018 at Serena International Conference Center in Kampala.

The goal of THRiVE in this venture is to build capacities of research ethics committees (REC) to undertake quality oversight role on scientific conduct of research in Uganda. GUREC members who benefited from the conference participation were Mr. Onen Walter Yagos, Mrs. Atim Pamela, Dr. Pancras Odongo, Ms. Julaina Obika and Mr. Robert Kiduma. The conference theme was "**Evolution of Research ethics in Uganda and the Region: Past, Present and Future**". Some of the topics presented and discussed were:

- Where is research ethics today?
- Emerging global best practices in human subjects' protection.
- Research ethics on the human-animal interface.
- Research integrity: recognizing, reporting

Accurate reconciliation and balancing of accounts in different currencies can be enhanced by use of a reliable accounting system. Finance Officers are advised to capture transactions in an accounting system and thereafter present these accounts in the reporting template.

Disbursement and Payables have to be in compliance with the grant framework. These disbursements and payables have to be tested for; allowable, allocable, reasonableness and consistency.

Risk management (RM)

RM is *the effect of uncertainty on objectives* (ISO 31000) followed by coordinated and economical application of resources to minimize, monitor, and control the possibility or impact of unfortunate events or to maximize the realization of opportunities.

During the training, risks for the quarter ending 30th September 2018 were reviewed. These included; challenges in recruiting interns, timely completion by Masters Research grant awardees and Career Development awardees. Mitigation measures were identified and discussed in detail in order to minimize the effect of the uncertainty. The importance of setting dates to close the timelines established to mitigate the risks was emphasized. It was also pointed out that a report showing details of how risks identified have been addressed and what the outcomes are, should be submitted.

Information access and data security

Physical security means protecting hard ware, while data security means protecting digital data, such as those in a database, from destructive forces and from the unwanted actions of unauthorized users, such as a cyberattack or a data breach. However, to achieve effective physical and data security, there is need to have policies that guide how this can be done.

Effective information and data sharing among members necessitates streamlining Information access. Dropbox was recommended as a depository box to archive project documents such as minutes, electronic accounting records and Newsletter articles among others. However, there is need to further explore other backup alternatives as safeguards for project information. Such alternatives should guarantee the safety of project information.

Grantsmanship

It is encouraged that the knowledge, experience and skills in grant management acquired from THRiVE-2 trainings is applied to support the activities of other projects at the University. This equally implies that individual researchers at the University who have succeeded in winning grants can be supported in areas of developing the budgets, workplan and report templates. This enables strengthening grants management at the institution and also builds confidence in the grants office.

The training addressed some of the challenges being faced by THRiVE-2 Gulu and we greatly appreciate the continued support of the Secretariat in ensuring that we comply with the THRiVE-2 standards. The recommendations from this training are going to be shared with the University Management where applicable, and especially in efforts towards having an effective grants office.

and avoiding research misconduct.

- Ethical issues with genetically-modified (GM) foods.

Important take-home messages included:

- The need to disseminate accurate and credible research data.
- The importance of proper ways of protecting research participants.
- Improving grant writing to gather research resources.
- Conducting community and public engagement (CPE) activities to share results with participants and community.
- Ethical reviews to concentrate on the science as well as ethics.
- Giving compensation that is adequate but does not amount to inducement.
- Having materials transfer agreement for research materials.
- Giving strong justifications for inclusion and exclusion criteria in research and doing risk assessment before conducting the research.

Participants from Gulu University were very appreciative of THRiVE-2 support toward building their capacities and promised to put lessons learned in practice to improve ethical conduct and standards in scientific, health research and protection of research participants. They also promised to ensure that research participants' interests, values and dignity are respected. Participants thanked THRiVE-2 for the generous support toward the conference; especially for enabling them gain more insights into issues concerning ethical conduct of scientific research and making collaborations and networking with other RECs in Uganda.

Mr. Onen Walter Yagos of Gulu University and Professor Sana Loue of Case Western Reserve University USA at the conference

Menstrual Hygiene Challenges among Tanzanian Secondary School Girls: Observations from the field

By Beatrice John; THRIVE 2 Career Development Award Recipient

The first network meeting on Menstrual Hygiene Management (MHM) of East African Researchers from MRC Uganda, KEMRI Kenya, KCMUCo, Tanzania and LSHTM was held in November 2017. The meeting aimed to bring together multi-sectoral MHM researchers and practitioners in order to develop common tools for measurement of different aspects of menstrual hygiene practices.

The meeting was an eye-opener for me as I learned different aspects on how a simple biological event (menstruation) impacts the lives of so many adolescent and young women in East Africa, and how it negatively affects attainment of their full potential because it influences their school attendance, performance as well as their mental health and social confidence.

I decided to contribute in the group that was given a task to develop tools that will assist in measuring different domains of MHM. To do this, we are conducting data collection on menstrual hygiene knowledge and practices in each of the three EA countries. We are also collecting data on psychological effects and how different school outcomes are affected among school girls; getting perspectives from both teachers and students. Statistical modelling will be done to come with up best questions that clearly measure MHM in the East African context.

At KCMUCo, a team comprising of three medical students in their 4th year, a clinical psychologist, epidemiologist/ statistician and public health specialist in adolescent health was formed. The team developed a protocol and tools for measurement and obtained ethical approval to conduct the study in one rural and one urban district in Kilimanjaro, Tanzania. Field work was done in May – July 2018. A total of 519 secondary school girls from 12 different schools participated in interviews which were followed by sessions that involved knowledge sharing in order to burst myths associated with menstruation. The sessions also involved brainstorming on how to improve the situation at each local school. Science teachers and school matrons participated in the brainstorming sessions.

Lack of pads, lack of clean toilets, lack of water, lack of places to dispose used pads, and lack of confident person/teacher to talk about issues of MHM at school were commonly voiced problems. Girls' knowledge on menstruation was low, with most believing menstrual blood to be associated with infertility for those who experience abdominal pain, eating peanuts is associated with heavy flow & painful menses and menstrual blood is unhygienic. While most did not miss school days as previously documented, their level of anxiety score was high and a sizable proportion had depression related to MHM. Improvement of physical infrastructure is not the only issue that needs to be addressed, but also a comprehensive package that addresses biology, myths and misconceptions observed, as well as a package to address psychosocial problems detected. Some of these findings will be shared in the second MHM network meeting to be held in Entebbe, Uganda in 10th to 12th October 2018.

Participants attending the menstrual hygiene management workshop in 2017

PUBLIC ENGAGEMENT FOR BETTER HEALTH: WHO SHOULD DO IT AND WHEN DOES IT START?

Rune Nathaniel Philemon, PhD Fellow KCMUCo

By Rune Nathaniel Philemon, PhD Fellow

Participants in the meeting take off time to pose for a group photo

For many, the concept of public engagement in science is a new encounter, often faced as a surprise requirement in a PhD course. Scientists being what they are, this is something new and is often feared or neglected.

Public engagement is not something new though. It is just a fancy way of saying you involve the lay community in what you are doing and how they can benefit from your work. This naturally will involve a dialogue between the expert and the non-experts; and therein lies one of the biggest dilemmas when it comes to public engagement: who is the expert? At a recent meeting of the Tanzania Medical Students Association (TAMSA) in Arusha, Tanzania, I had the pleasure of engaging with medical students from 8 medical schools. I had been asked to give a talk on the social responsibility of a medical student and this felt like the appropriate forum to gauge students' understanding of social responsibility and put a spark of community engagement in them.

Many fell into the trap of thinking that engagement is something for big time researchers and specialists. They did acknowledge, however, that in the communities they came from, understanding of basic medical concepts and facts was extremely skewed and many myths abound. I presented them with a collection of top ten myths encountered during community sessions. The myths centred on breastfeeding and prevention of mother-to-child transmission of HIV. All the participants in the group, about 200 in total, were able to easily burst all the myths. This was just a simple demonstration that every one, no matter how junior or inexperienced, has something to offer to the community and just needs an appropriate stage to offer it so as to bring about health changes in the community.

One of the key outcomes from this session was a fruitful discussion on how medical students can engage the communities around them and fulfil their social responsibility. It was agreed that there were many areas that TAMSA members were able to get involved in and one of the key ones was in educating the public as well as providing screening camps. It was resolved that the TAMSA leadership would

Question and Answer session

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PUBLIC ENGAGEMENT FOR BETTER HEALTH:

help to put together community engagement days in their calendar of activities for the coming year involving all its chapters.

Though the focus of public engagement has been mainly on research, the truth is that the community needs to be engaged even in basics that as researchers we often overlook as being common sense.

The time to engage the community, however, seems to dwindle the higher up the academic ladder you get, but there is a huge army of medical students and other higher education students that can be called upon to share with the community these basics which they have already acquired. Our role as peers in the education ladder is to help students create the stage and forums needed for public engagement.

TAMSA leadership pose for a group photo

THRIVE programme; a meeting point for inspirational Ideas

Eddie Wampande, THRiVE-2 Postdoctoral Fellow

One of the training approaches of the THRIVE program is attaching fellows in the consortia to institutions in developed countries specifically UK for scientific capacity strengthening. Under this arrangement, during the summer of 2018, I was working in the warm temperatures of Cambridge, where I was attached to Cambridge University Addenbrookes' Hospital Department of Medicine in Dr. Sergey Nejentstev (mentor) laboratory. The lab focuses on understating host (human) factors (genes) that may explain disease occurrence. While in the lab, I was exposed to various cutting-edge techniques ranging from in vitro model of macrophage infection, CRISPR-cas; an in-vitro tool used to understand human or pathogen phenotypes as well as various aspects of molecular Biology. These techniques will enrich my doctoral work. For now, my students are benefiting from the theoretical aspects of this knowledge already. While in Cambridge, I and other colleagues made a trip to the Sanger Institute; a re-known center of excellence in genome sequencing and Bioinformatics, where we met scientists interested in pathogen biology. We have continued to engage them as potential collaborators in future.

Besides the academics there were intriguing stories told over lunch time or a cup of coffee (in between lab experiments) by UK colleagues, whenever I come to think more about them I get motivated; whether the stories are true or not is another story. For instance, the story of the falling apple and the discovery of the gravitational law motivates scientists to always be observant and be critical thinkers. This can be the beginning of discoveries. Secondly, the story of the bar; "THE EAGLE" and DNA discovery, encourages one -after hectic lab work- to have time off and engage in chitchat with friends over their work. It is at such times, that discoveries are made. Lastly, many thanks to our Cambridge-THRiVE Coordinator who gave us a ride to KENTWELL House, a place rich in the natural history of England and fabulous architectural work that has stood the test of time.

Eddie Wampande and Corrina Cambridge –THRiVE Coordinator at Sanger Institute

Do hippoboscids transmit camel trypanosomiasis and zoonotic hemopathogens in northern Kenya?

Joel Bargul,
THRiVE-2 Postdoctoral Fellow

Non-tsetse transmitted camel trypanosomiasis is prevalent

Most arid and semi-arid lands (ASALs) of northern Kenya are not infested by tsetse flies (*Glossina* spp) - the only known biological vectors of African trypanosomes that cause diseases in both humans and livestock in sub-Saharan Africa. Yet our preliminary findings in a THRiVE 2-funded study show that camel trypanosomiasis is rampant in these tsetse-free zones. This is not surprising because various species of biting flies, such as Tabanids and *Stomoxys*, can mechanically transmit *Trypanosoma evansi* and *T. vivax,* and these animal trypanosomes have spread from Africa's tsetse belts into most tropical and sub-tropical areas of the world where they contribute to huge agricultural losses.

Camel trypanosomiasis is mainly caused by *T. vivax* and *T. evansi* parasites

We show through PCR-based assays that over 80% of *Hippobosca camelina* (n=400) and 48% of camels (n=531) are infected with different trypanosome species (either single or mixed infections) that include; *Trypanosoma vivax, T. evansi, T. congolense,* and *T. melophagium*. *T. vivax,* and *T. evansi* caused most of the infections.

In addition, we detected the following zoonotic pathogens both in *H. camelina* flies and in camels from which these flies were collected; *Candidatus* Anaplasma camelii (flies= 16.24%; camels= 70.28%) and *Bartonella* spp (flies= 18%; camels= 7%). *Candidatus* Ehrlichia regneryi was only detected in camels (0.4%). We observed that livestock farmers keep goats, sheep, cattle, camels, and donkeys that are often co-herded and share water troughs for drinking thus increasing the chances of disease transmission.

Hippoboscids are potential vectors of camel trypanosomiasis and zoonotic pathogens

Currently, little is known about insect vectors of animal trypanosomes in northern Kenya mostly because livestock belong to the marginalized poor nomadic pastoralists whose economic welfare is mainly neglected. Hippoboscids (commonly known as 'keds') of camels and horses were suspected, over fourty years ago, to mechanically transmit trypanosomes, but this has never been demonstrated experimentally. Our study aims to establish the role of hippoboscids, which belong to the same superfamily– *Hippoboscoidae*– with tsetse flies, in transmission of camel trypanosomiasis.

Hippobosca camelina are common ectoparasites of camels in northern Kenya and their contribution in disease transmission is not established. These exclusive blood-feeders usually infest 100% of camels throughout the year and they contribute to; anaemia, weight loss, losses in milk and meat yields, and even death-accelerating poverty. The adult fly spends its entire life on the camel's body- particularly on the underbelly where they inflict painful bites in order to access small blood vessels under the skin for bloodmeal acquisition, with some camel hosts carrying up to 100 flies at any time.

By experimentally infecting *H. camelina* following repeated feeding on *T. evansi*-infected Swiss mice, we observed that trypanosomes can survive in the fly's midgut for up to 7 hrs hence increasing chances for mechanical transmission in the next bloodmeal through regurgitation of gut contents. Our findings show that *H. camelina* and camels are infected by similar disease pathogens implying that hippoboscids could be potential vectors of animal trypanosomiasis as well as zoonotic hemopathogens they carry. A case in point is our recent finding that demonstrated for the first time the ability of *H. camelina* to transmit *Candidatus* Anaplasma cameli, an emerging zoonotic disease pathogen, from camels to laboratory mice (infection prevalence in mice= 42.1%; n= 8/19). Farmers have close association with livestock, hence are at risk of contracting zoonotic diseases and co-herding of other livestock may amplify risks.

Hippoboscids have potential use in xenodiagnosis of camel diseases

In addition, as primarily long-term camel blood-feeders, *H. camelina* may have potential in xenodiagnosis of camel pathogens that they may not transmit. This is because similar disease pathogens were detected in camels and their associated *H. camelina*.

Implications of this work

Detection of trypanosomes, *Anaplasma* spp, and *Bartonella* spp in *H. camelina* and camels is of great public health and veterinary concern. This information can guide formulation of disease control programs by animal and public health stakeholders. In addition, it can lead to less invasive xenodiagnostic approaches to identify pathogens circulating in camel herds.
Further research is ongoing to: 1) document trypanosome species associated with domestic animals co-herded with camels and their specific hippoboscids in order to study spread of the trypanosomes, 2) describe the developmental forms of trypanosomes occurring in *H. camelina*, 3) determine vectorial competence of *H. camelina* in disease transmission, and 4) identify zoonotic pathogens (arboviral, bacterial, rickettsial) in both *H. camelina* and camels.

Fibroscan an easier and accurate method to screen for liver disease

Clare Wekesa, THRiVE-2 PhD Fellow

The burden of liver disease is fast becoming a public health concern, globally. This is of more concern among persons living with HIV/AIDS in whom the progression of liver disease is accelerated. HIV-infected persons are living long enough to develop non-HIV related disease conditions such as liver disease. Liver insult from any cause manifests as liver scarring (fibrosis). Liver fibrosis is the primary lesion that can then progress to complete alteration of the liver tissue structure and/ or eventual development of liver cancer. Detection of liver fibrosis previously necessitated the use of liver biopsy, an invasive, painful procedure that carries risk of bleeding and even death. Recent developments in diagnostics encourage the use of non-invasive methods which are readily accepted by patients. These can also be done repeatedly to assess disease progression and /or response to therapy instances where fibrosis may be reversible. One such method is the use of Fibroscan, a simple scan procedure with fair accuracy.

We set out to determine and compare the proportion and predictors of liver fibrosis among HIV-infected adults in urban and rural Uganda using Fibroscan. The urban population was nested within an established urban clinic cohort and the rural population was nested within an established population cohort. We screened a total of over 2000 individuals. We recorded participant demographic information. We screened for viral hepatitis, use of tobacco, alcohol, herbal medicines and anti-retro viral therapy.

The prevalence of liver fibrosis in urban Uganda was 11% and that in rural Uganda was 15%. These proportions were statistically different. Factors associated with liver fibrosis in urban Uganda included increasing age, male gender and hepatitis B screen positivity. Whereas factors associated with liver fibrosis in rural Uganda included the use of tobacco and minimal evidence of hepatitis C screen positivity. The prevalence of liver fibrosis is high among HIV-infected persons in Uganda, being higher in rural Vs urban Uganda. There is a difference in the drivers of liver fibrosis in these two localities.

Implications of this work

The greater burden of HIV/AIDS is within sub Saharan Africa, with over 2 million people at risk of developing liver disease during their life course. There however, remains limited information on the burden of liver disease in an era of improved HIV/AIDS management. Knowledge of the current burden and drivers of disease may inform on priority areas of focus as concerns major causes of morbidity in this population at this present time.

Improving outcomes of HIV-related meningitis in sub-Saharan Africa

David Meya - THRiVE-2 Postdoctoral fellow

THRiVE's support has been instrumental in setting the stage for building my professional career over the last 8 years. My research has focused on improving the grim outlook of cryptococcal disease in sub-Saharan Africa through observational, translational science, and clinical trials. Our work has impacted policy and practice on treatment of cryptococcal meningitis and testing for TB meningitis.

Over the last decade, there have been tremendous strides in improving outcomes of individuals infected with HIV, especially in terms of access to long term Antiretroviral Therapy (ART) and improved life expectancy. Although there have been rapid and significant declines in the incidence rates of opportunistic infections in the developed countries, this decline has not been as dramatic in sub-Saharan Africa.

One such infection is caused by the fungus, *Cryptococcus*, which has sadly not seen the expected dip in the number of

cases even with the rapid roll out of ART across Africa, reaching the millions that continue to be infected with HIV.

The current global estimates of cryptococcal disease suggest a 6% prevalence of cryptococcal antigenemia among HIV-infected individuals with a CD4<100 cells/mL, translating to 278,000 patients with cryptococcal antigenemia while an estimated 223,100 incident cases of cryptococcal meningitis occur worldwide. Unfortunately, the bulk of this disease occurs in sub-Saharan Africa, which bears 73% of the disease burden with approximately 136,000 deaths annually.

The Cryptococcal Outcomes on ART (COAT) trial, for which I was the Ugandan Principal Investigator, was conducted in Kampala, Mbarara in Uganda and Cape Town in South Africa. The study enrolled 177 participants with cryptococcal meningitis and demonstrated that starting ART too soon (7-11 days) after the diagnosis of cryptococcal meningitis was detrimental, with lower survival rates (55%) compared to starting 4-6 weeks after initiating antifungal therapy (survival rate 70%). This definitive trial answered the question on the optimal timing of ART after cryptococcal meningitis and led to a policy shift in WHO guidelines. Similarly, during this trial, the team demonstrated that electrolyte pre-supplementation rather than waiting to replace deficiencies in electrolytes following administration of the antifungal drug, amphotericin, for cryptococcal meningitis, prevented mortality during induction treatment of cryptococcal meningitis – this strategy was also adopted in the WHO guidelines. Implementing these two clinical strategies has possibly prevented thousands of cryptococcal-related deaths.

During my PhD training, I explored the immunopathogenesis of immune reconstitution inflammatory syndrome, a complication of starting ART in which patients previously treated successfully for an opportunistic infection seemingly worsen after they initiate ART. We demonstrated through immunology assays using cells obtained from spinal fluid and blood that during this complication, there is a specific immunological signature and type of cell that migrates into the central nervous system, making the spinal fluid more inflammatory from the migration of these innate immune cells known as monocytes.

As Principal Investigator on a randomised clinical trial in 17 clinics in Uganda that aimed to evaluate the screen and treat strategy for cryptococcal antigenemia (CrAg) in patients, I set out to determine the effectiveness of this intervention on decreasing mortality among the general population of HIV-infected patients with CD4<100 cells/mL.

This population was screened for presence of cryptococcal antigen in blood and those with a positive CrAg test would be treated with the antifungal drug, fluconazole, for 10 weeks. We demonstrated that this strategy is much more effective as an intervention among individuals with higher burden of cryptococcal infection, where the titre of cryptococcal antigen is >1:160. This work has led to the modification of the rapid diagnostic lateral flow assay for cryptococcal antigen to incorporate the ability to provide a semiquantitative CrAg result.

Tuberculosis (TB) remains the etiological agent in 10-15% of HIV-associated meningitis. As part of the meningitis screening studies, we investigated the utility of newer rapid diagnostic tests including the Xpert MTB/Rif, the Xpert MTB/Rif TB Ultra (Xpert Ultra) - unique tests that employ DNA amplification techniques to determine the presence of *Mycobacterium Tuberculosis* that causes human Tuberculosis.

Given the difficulty of confirming the diagnosis of TB meningitis, we conducted a study using the Ultra Xpert, microbiological culture and basic staining techniques using spinal fluid. They determined that the TB Ultra was much more sensitive (70%) in identifying patients with tuberculous meningitis compared to the Xpert MTB/Rif (50-60%) and culture (60%). This work helped consolidate the Xpert Ultra as the recommended test for tuberculous meningitis.

Using pyrethroid-impregnated blankets to control malaria in humanitarian emergency situations

Jovin Kitau, THRiVE-2 Postdoctoral Fellow

Indoor-residual spraying (IRS) and insecticide-treated nets (ITNS) have been successful against malaria vectors and disease transmission in many settings. However, in emergency situations IRS and ITNs/ LLINs are complicated by the lack of preparedness coupled with inappropriate substrates for insecticide spraying and hanging nets. On the other hand, relief supplies like tents, blankets and/or sheets are often provided for warmth and

shelter as humanitarian response to displaced populations. As such, malaria and other mosquito-borne diseases may be controlled by mere impregnation of blankets provided as humanitarian response to displaced populations.

As a proof of concept, we set out to investigate the efficacy of permethrin-impregnated blankets for control of malaria in Nduta refugee camp, Kigoma; with the hypothesis that Insecticidal blankets used overnight would be effective in protecting users against malaria vectors to the extent of reducing prevalence of malaria among refugees.

Potential impact of this work

The project allows for assessment and consideration of pyrethroids-impregnated blankets for malaria control, addressing an important knowledge gap among vector control disease specialists. This will therefore provide evidence-base for replication and adaptation of findings to other settings that will further improve on malaria and mosquito-borne disease control in humanitarian emergencies. Additionally, East Africa is home to a substantial population of normadic pastoralists, who owing to their mobility malaria control through LLIN and IRS is grossly limited. The study will importantly provide evidence-base to support pyrethroid-impregnated blankets approach in malaria control in situations with limitations in LLIN use.

Using evidence of possible worm reinfection to inform the national school-based deworming programme

Stella Kepha, THRiVE-2 Postdoctoral Fellow

Currently the Kenya national school-based deworming programme recommends deworming of school children in areas where there is a possibility of infection with worms transmitted by contaminated soils. The Kenya government has been conducting the national school based deworming for a period of five years with bounce back of infection to pre-treatment levels.

As part of my PhD, we looked at what drives reinfection with worms amongst among school children who completed treatment. We had a group of 500 children who were treated with deworming drugs every 4 months for a period of 15 months. Before every treatment the children were checked for presence of worms. We found that even after four repeated (every 3 months) rounds of deworming within 15 months, some of the children had worm infection that could not clear. As currently it is only the school children who are treated, there is a possibility of transmission of worm infection from the adult untreated population. Another possibility is failure of infections to clear after treatment in some of the children. Children who had evidence of many worms before starting the cycles of treatment are the ones who seemed not to clear their worm infection. Additionally, children who were undernourished as measured by nutritional indices also had persistent worm infection despite repeated treatment.

Implications of this work

These results together with the recently completed Kenyan national school-based deworming programme show that children are still infected with worms despite having completed regular school-based deworming. This suggests that school-based deworming alone will not lead to elimination of worm infection in at risk communities. There is need to rethink the strategies the government is employing in achieving this goal. To this end the Kenya Neglected Tropical Diseases Unit is currently holding brainstorming sessions with researchers working on soil transmitted worms to develop a “breaking transmission” strategy.

Mosquito-plant interaction as a new tool for malaria control

Trizah Koyi, THRiVE-2 PhD Fellow

Malaria is an infectious disease caused by protozoan parasites of the genus *Plasmodium* and transmitted to humans by the female anopheles mosquitoes. For decades the search for new antimalarials has mainly focused on molecules that can cure humans of malaria; only recently have scientists begun to think about curing mosquitoes of the disease. This approach can reduce transmission of malaria parasite among human population and is argued to represent a promising direction for malaria elimination efforts. Through mosquito-nutrition assays, we have identified specific plants compounds that can inhibit establishment of malaria parasite (*P. falciparum*) in the mosquito. We anticipate that these bioactive compounds can serve as chemoprophylactic agents in combination with currently approved antimalarials as new treatment modalities.

High malaria transmission and emerging resistance to available antimalarials pose a major challenge to control and elimination efforts. In efforts to curb transmission the global malaria community has so far proposed the use of chemotherapeutic agents that prevent parasite spread among human populations. Previously, at icipe, we conducted a study that revealed parasitized mosquitoes (*An. gambiae*) to

feed on specific plant species. We posited that mosquitoes feed on these plants to cure themselves of malaria parasite infections and subsequently, designed an experiment to test this hypothesis. Our preliminary findings indicate that compounds from the identified mosquito host-plants can, to varying degrees, reduce the parasite burden within the mid-gut of the mosquito. These findings have opened up a new way of thinking about *An. gambiae-P. falciparum* interactions in nature and could be exploited as a new tool for malaria control.

Implications of this work

This work falls under *icipe*'s human health theme which aims to contribute towards the reduction, elimination and eradication of vector-borne diseases. The project was started over four years ago and was pioneered by Prof. Baldwyn Torto; the Head of Behavioral and Chemical Ecology Unit (BCEU). Previous findings from this study were highlighted in print and digital media and the highlights can be found on the website www.icipe.org.

THRiVE Program; a holistic model for training Researcher in Sub-Saharan Africa

Dr. Edward Wampande, Postdoc Fellow, Makerere University

Highly trained research personnel and a motivated work-force is crucial for the development of the health sector world-wide. For the last eight years, THRiVE is continuing to provide a medium and also playing a leading role in training health cadres and researchers involved in health -related research to advance their knowledge in understanding various diseases and also gain new insights in disease occurrences that might lead to novel and evidence-based approaches in detection, treatment and response. To achieve this, the program has set out to equip the scientific researchers with leadership skills, scientific tools to conduct research that addresses health issues and also acquire the knowledge of understanding community health-related issues that should be addressed rather than imposing on them exotic health interventions that are rejected most times. In a nut-shell, if all this is achieved, the program will deliver a future generation of a wholesome health workforce retooled to tackle emerging health challenges.

Think-tank of health related issues: The THRiVE fellowships are highly competitive and can only be won by equally highly competitive individuals. Needless to say, the composition of the fellows in this program is interdisciplinary where students are drawn from different reputable universities and research institutions in East Africa each bringing on board diverse (cross breeding) attributes rather than inbreeding. Therefore, this heterogeneous pool of fellows with their highly experienced supervisors (local & international) are in position to brainstorm on various aspects of health and provide workable solutions. Such a multi-disciplinary work-force can synergistically work together and this is one of the drivers of success.

PhD, Masters and Postdoc factory. Many universities in developing countries except South Africa are finding it hard to train graduate students in the context of limited resources. The available international graduate training fellowships are few and also highly competitive making them out of reach for majority of interested individuals in developing countries. Given that background, THRiVE is bridging this gap to have graduate students trained locally and internationally in a conducive research environment. For the past years this has seen over 70 doctoral students graduate from various health disciplines. Coupled with this, graduate students are exposed to various short training courses to enhance their knowledge and skills. Expert talks that inspire, especially in the field of research and leadership are also organised.

Bottom-top approaches in addressing Health issues: The paucity of public engagement philosophies among communities has far-reaching consequences in addressing health related issues. In the past this has seen excellent disease intervention approaches failing to be embraced by the recipients culminating into waste of resources and manpower. To bridge this gap, THRiVE is encouraging its fellows to engage communities in ways that can address community resistance to government health programs. The benefits of public engagement in my view are 3-fold. First, is to identify and prioritise pressing health issues within the communities which will bolster acceptability. Secondly, local people have indigenous health-related knowledge that should be tapped into. These are approaches that might be readily available and cheaper. Lastly, public engagement might be a source of research question(s) that can be tested in the laboratory or using any other appropriate tool; such unexploited innovative ideas can benefit the government in the long run.

VISIT TO RESEARCH LABORATORY INSPIRES TUMAINI SECONDARY SCHOOL STUDENTS TO TAKE ON SCIENCES

Tumaini Secondary School students and Dr Ireen Kiwelu posing for a group photo in-front of the KCRI Biotechnology Research laboratory building.

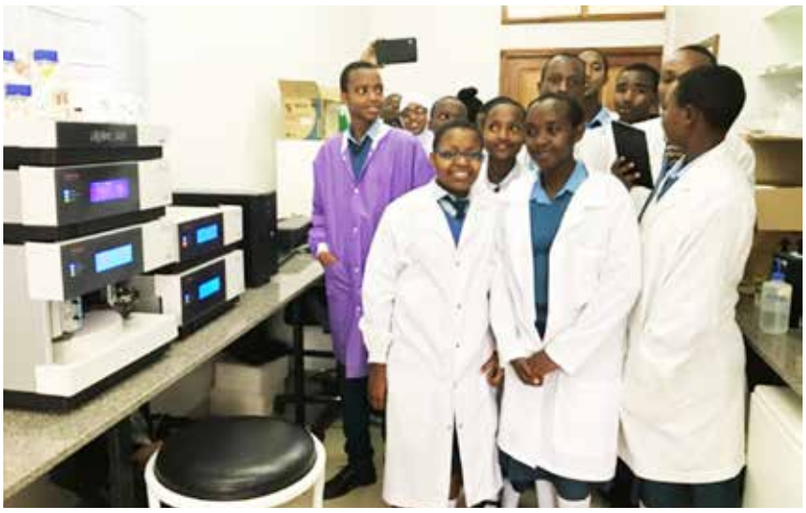
By Dr Ireen Kiwelu, THRiVE-2 Postdoctoral Fellow/Senior Lecturer Kilimanjaro Christian Medical University College

For the School engagement program, I hope to inspire school children in career development, encourage them to pursue professions in the sciences as a profession and make them aware of the importance of science and research in public health. Towards this end, I have opened up doors for school children to visit the KCRI-Biotechnology Research Laboratory so that they understand the importance of science and research as well as laboratory diagnostic tests in public health. Recently, I arranged a tour for Tumaini Senior Secondary students to the KCRI Biotechnology Research Laboratory.

Tumaini Secondary School students with their teacher (in red) and Dr. Ireen Kiwelu (with red scarf) before the laboratory tour.

During the tour at KCRI-Biotechnology Dr Ireen Kiwelu explained in detail to the students the laboratory activities and their importance, including the value of laboratory diagnostic tests in research. The students were very excited and engaged the researchers with endless questions.

The Tumaini Senior Secondary teacher was very inspired and promised to bring more students for similar tours. Conducting this kind of school engagement program in the country will inspire and attract more students to science disciplines.



Tumaini Secondary School students at Bio-analytical Unit with Dr Ireen Kiwelu showing them the HPLC machine for measuring drug levels in patients samples (pharmacokinetics).