New techniques for translational tuberculosis research at Makerere

By David P. Kateete, THRiVE Post-doctoral Fellow, Makerere University and University of Oxford

THRiVE has supported the transfer of new techniques, which will strengthen translational research on tuberculosis and other infectious diseases at Makerere University. This is through the successful overseas attachment at the Sir William Dunn School of Pathology, a renowned department at the University of Oxford. Before I describe my stint, I relay my incessant memories of the Dunn School.

The Dunn School of Pathology where I trained has a very impressive history. The first textbook in Pathology (General Pathology) was written here. Other notable achievements by the department include discoveries of Acquired Immunological Tolerance, the Biochemistry behind ATP Synthesis, Flu vaccines, CD4+ cells, etc. Yet, the department is most famous for pioneering the purification of the first antibiotic Penicillin, and discovery of Cephalosporin, another terrific antibiotic. Without the successful purification of Penicillin by H.W. Florey (former faculty at the Dunn School) in 1939, Alexander Fleming’s prior discovery of Penicillin would not have benefited human kind. Penicillin purification sparked the massive

This is an “ambitious project with little funds”, this is how my supervisor Prof. David W. Dunne will always refer to my project. Confronted with deficit of funds to complete my data collection for an “ambitious project”, it was like getting a red card at the grand finale European Champions’ league match. The word of my supervisor kept clicking in my head everyday and alternatively he was reminding me to look for additional funds to support the project fieldwork. At THRiVE asking for additional funds, there was only one answer from the director “Use what you have”, in other words, the director was saying apply for funds from other sources; same lecture, different lecture rooms.

I responded to two calls for additional funds which support PhD students in Africa and in any part of the world.

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Dear Reader,

It is time to celebrate THRiVE’s first six years of existence that was made possible by the generous funding support from the Wellcome Trust. During this period we have established a THRiVE brand that is recognized and expands into many countries mainly in Africa and Europe. Efforts are ongoing to successfully complete the initiatives that were started and will lead to our realization of the full value of the already ongoing bumper harvest. We need to look into the future with new lens as we begin a new era with a renewed commitment to build a future rooted on the strong foundation laid by all partner institutions.

I was extremely delighted that during the last THRiVE Annual General Meeting (AGM) held on June 23-25, 2015 in Entebbe, Uganda participants expressed a strong sense of enthusiasm with new energy and determination to strengthen and ensure sustainability of the network. There was a palpable desire to take THRiVE to the next level as a leading Network of excellence in research and research capacity building. Mounting a successful AGM in 2016 will be a test case of our resolve and resilience as a sustainable network. The THRiVE spirit and enthusiasm will show by how we navigate the complicated landscape of research funding.

A very important aspect of our future is how we continue to mentor some of our very promising PhD and post-doctoral fellows so that they end up as research leaders of international standing. The collective expertise available across all partner institutions is a great resource that we cherish. As happens all over the globe not all those trained at this level will end up as world class researchers but will become very useful national or global citizens adding value to what they do.

production of antibiotics by the pharmaceutical industry. Interestingly, the laboratories are still intact and in use, as they were in the Florey days; the rudimentary equipment they used was left intact for obvious historical reasons. Training in the same department where the likes of Florey worked was inspiring; when I see an antibiotic, memories come to mind, of labs with meagre resources from where simple men changed the world.

My overseas supervisor was Professor Matthew Freeman, Head of Dept. Dunn School of Pathology. He discovered rhomboid proteins about three decades ago. At Makerere University, Professor Joloba’s Laboratory where I trained aims to understand the role of rhomboid proteins in bacterial pathogens. The Freeman Laboratory solely works on rhomboids and related proteins so I blended in easily. It is an international laboratory; nine Postdocs and two Ph.D. students from all over the world, with only one Briton. My research project at Oxford was modified so that I learn new skills while there, and in the end I return to Uganda with a set of techniques that are of broad value to many researchers. The techniques I learned allow quick identification of protein interactors in bacteria that are potential substrates for any enzyme; they also allow quick and efficient modification of difficult genomes such as *Mycobacterium tuberculosis*. Furthermore, a long-term collaborative relationship between the two research groups at Makerere University and Oxford University is envisaged.

Although Oxford University was the primary site for my training, frequent visits to Cambridge were arranged for me to explore other opportunities. One highlight is when I visited Professor Bentley at the Sanger Institute, Hinxton. We discussed my research interests with focus on funding issues, and acquiring genomics/bioinformatics skills as a tool to complement current research and infectious diseases in general. I also visited the MRC’s Laboratory of Molecular Biology (LMB), and established a research collaboration with structural biologist Dr. Vinoth Kumar, who will help with crystal structures of *M. tuberculosis* proteases that will be the basis for future design of inhibitors.

I enjoyed the rivalry between Oxford and Cambridge, though the former begot the latter and instilled fame to it. Sir Isaac Newton, the Cavendish Laboratory (notable for work on the DNA structure), the Wellcome Trust Sanger Institute, and MRC’s Laboratory of Molecular Biology (notable for discovery of DNA sequencing, monoclonal antibodies, etc.). All these I visited, courtesy of the Dunn School and THRiVE faculty at Cambridge.

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**MY EXPERIENCES AT THE 8TH INTERNATIONAL AIDS SOCIETY CONFERENCE IN CANADA**

By Joseph KB Matovu, THRiVE PhD Fellow

I was lucky to attend the recently concluded 8th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015) in Vancouver, Canada; thanks to the support that I received from the THRiVE Secretariat. The conference that was held at the Vancouver Convention Centre from July 19-22, 2015 attracted well over 6,000 delegates from across the globe. My poster on; “HIV risk perception and sexual risk behavior among HIV-infected married couples in Rakai, Uganda”, attracted several visitors, and I am glad that I was able to share my work...
Trained under the THRiVE Consortium is
More Than Getting a PhD

The first application was to the African Doctoral Dissertation Research Fellowships under IDRC and African Population Health Research Centre; this was unsuccessful. An army organized by a single soldier never fails; this is what I believed. I sent a 2nd application to Dan David Prize Scholarship organized by the University of Tel Aviv, Israel in the Category of Future Time Dimension in the field of Preventive Medicine and the 3rd application to Cambridge-Africa-Alborada Research Fund (waiting for results).

Reading these words of the Director of Dan David Prize scholarship, Smadar Fisher “As a member of the Dan David Prize Scholarship Committee, in addition to my position as Director of the Dan David Prize, I was extremely pleased to see the high level of your achievements and of the promise your research holds for the future”. Yes, I was very happy to receive the grant. In November, 2012, in Ghana “The winner of the best poster presentation is…..” These were the words from one member from the WELLCOME TRUST group. Winning a prize just for the little I have done, yes, little for me but for others had a different meaning. The grant and award I received will help me to complete the data collection process and will help to further develop my career. A clear message from these grants/award, was to see other people outside my world are impressed and recognizing what I do and my efforts to develop my career. Basically, these awards are telling me that “if you do one thing better, everything will come through it” and “other people outside there are recognizing your efforts”. I clearly, attribute these awards to the initial grant from THRiVE-WELLCOME TRUST; which I call “a prime grant to increase my confidence to compete with others in the world”. The grant has equipped me with strong foundation, confidence to work hard and an opportunity to interact with several seniors in the field, especially my supervisor. At THRiVE, I am not only attaining a PhD degree am also getting the knowledge on how to manage research projects (money discipline), how to network and collaborate with other researchers and to become future competitive researchers. What I have learnt so far, for the grants I won from THRiVE-WELLCOME TRUST (prime grant, equipment grant, PhD fellowship) and the ones I have submitted (as individual/in collaboration) is that “the cost of not sending a proposal in a grant call is very high as compared to dropping in an application and waiting for the verdict”

I have defended my PhD. Am currently organizing my data for four more publications, which gives me an opportunity to think of my next career development. I already see the gaps which will need me to remain in the field and in the same topic as a postdoctoral student to get clear answers for these questions. I still believe that working in a consortium as a student has more advantage than the other mode of training, so my future career development still lies within THRiVE-WELLCOME TRUST, where public health researchers are trained to standard. I hope that WELLCOME TRUST will continue to support THRiVE to raise the future stars in public health in East Africa.
HIV-infected married couples.

I said that I was lucky to attend IAS 2015 because of its overriding emphasis on HIV testing, which is my main area of research interest. Speaker after speaker presented on the opportunities that exist with HIV self-testing especially in as far as reaching people who are not reached with conventional HIV testing services is concerned. There was ample evidence to suggest that HIV self-testing – a situation where an individual obtains an HIV test kit, conducts the test and reads the HIV test results on their own – is highly acceptable, has high sensitivity and specificity and is generally non-inferior to conventional HIV testing approaches.

What was critical, though, was that many of the studies presented on HIV self-testing were done in Europe or North America and among Men who have Sex with Men (MSM), suggesting that there is still a dearth of information on the acceptability of HIV self-testing in the general, heterosexual population. I noted that there were a few studies that were presented from sub-Saharan Africa, including studies from Zimbabwe, Kenya and Malawi, but even then, these studies tended to focus more on high-risk groups (e.g. HIV-positive pregnant women) or female sex workers than the general population. Nevertheless, for those of us whose interest lies in HIV testing, the emergence of HIV self-testing provides immense opportunities to explore innovative approaches to HIV testing. Indeed, as the presentations were being made, I started wondering what role HIV self-testing can play in promoting couples’ HIV testing – an area that I am passionate about and which I explored for my doctoral research. Of course, there are issues to consider including what would happen if one of the partners was found to be HIV-positive and the other was HIV-negative, in the absence of a professional health worker to provide the necessary post-test counseling support. But, these aspects aside, HIV self-testing could be one great innovation to open windows of opportunities to improve HIV testing services uptake in populations with perennially low levels of testing including married couples. I believe that as I complete my PhD in a few months, my intention should be to focus on how to explore these emerging technological innovations much more aggressively to improve HIV testing uptake rates among at-risk and other affected populations.

I am happy that I was able to attend this conference, and I believe my attendance of this conference will not leave me the same. There are several ideas that popped up in mind as I listened to these presentations, and these should help to shape my future HIV research career post-PhD.

Research Capacity Strengthening

By Eva Muro, KCMCo

As a pharmacist I am interested in developing my skills in research methodologies and technologies applied to Pharmacokinetics and Therapeutic Drug Monitoring of Antiretroviral Medications.

My one year THRiVE Post-doc fellowship has been intense but was carefully guided and supported in several ways that makes me feel rewarded. I am intending to attend an in-depth training and hands-on use of pharmacometric tools such as the Win-Nonlin software for pharmacokinetics/pharmacodynamics (PK/PD) data analysis and physiological concepts. This knowledge will be acquired by hands-on exercises on real-life case studies by using the computer package WinNonlin in PK/PD studies in The Netherlands at Radboud University Medical College Nijmegen, Department of Clinical pharmacy. Upon completion of this training my objective is to establish a pharmacokinetic laboratory for therapeutic drug monitoring at my institution and use the validated assays for antiretroviral drugs. The Kilimanjaro Christian Medical University College is in the process of commencing a four-year Bachelor of Pharmacy degree programme. This will be one of the key laboratories for therapeutic drug monitoring in the area of HIV medication.

Through this fellowship I had an opportunity to attend an introductory course in Epidemiology and medical statistics at LSHTM. People came from all over the world with multidisciplinary educational backgrounds and we were able to share our skills, experiences and even developed networks. With the support of THRiVE award, I managed to travel to Vancouver, Canada to participate in the 8th IAS Conference on HIV Pathogenesis Treatment and Prevention as a post-doc fellow. As a researcher, I gained a better understanding on the use of new priority antiretroviral regimens for first and second line therapy in low and middle income countries in less than five years.
School Mental Health: Psychosocial competence (PSC) and mental health of young people in selected secondary schools in Northern and Central Uganda

By Catherine Abbo, Elialilia Okello, Wilson Muhwezi, Grace Akello Emilio Ovuga, Makerere University College of Health Sciences and Gulu University Faculty of Medicine

Given the more than twenty years of armed conflict in Northern Uganda, the mental health professionals in Makerere University College of Health Sciences, and Gulu University hypothesized that there would be significant differences in the psychosocial competences of the youths in Northern Uganda and those in Central Uganda. Using a mixed method preliminary study, a team of researchers from the two institutions explored understanding of psychosocial competence and mental health/illness among young people in selected secondary schools in Northern and Central Regions of Uganda. Based on the findings of the qualitative study, the team described factors that may be associated with psychosocial competence in young people with particular interest in the relationship between depression, alcohol and substance use, and perceived social support, and life events with psychosocial competence. The researchers comprised of a multidisciplinary research team of psychiatrists, social workers and medical anthropologists from Gulu and Makerere Universities. On the whole, young people from both regions have a good understanding of mental health, mental illness and most of the components of psychosocial competence. Young people of age 10 to 24 years from selected secondary schools from central region had lower levels of psychosocial competence in empathy, emotional awareness, coping with emotions and coping with stress. Northern region had low levels in the components of self efficacy, accurate self assessment and self confidence. Both regions were equally low in decision making. In general, there was a heterogeneity of factors associated with level of PSC in the two regions. Good social support was associated with accurate self assessment, self confidence and coping with emotions while moderate to severe symptoms of depression were associated with inaccurate self assessment and low self confidence. Non-use of alcohol and susceptibility to stress related illnesses had both negative and positive outcomes on different psychosocial components in these regions. The findings of the study suggest the importance of considering both positive and negative states of factors in their uniqueness in influencing the levels of psychosocial competence of young people in different contexts. Consequently, there is an urgent need for an additional implementation study that will not only provide further insights into the factors associated with different components of psychosocial competence but will set up a comprehensive intervention programme focusing on improving and/or enhancing psychosocial competence levels as well as addressing the mental health needs in terms of risk reduction of young people in secondary schools in Uganda. As a result of receiving the THRiVE Pump priming grant, the principal investigator, Catherine Abbo, was actually ‘pumped up’ clinically and she went for a two-year fellowship in Child and Adolescent Psychiatry in University of Cape Town and Red Cross Children’s Hospital in Cape Town, South Africa. Catherine has since returned to continue with research, teaching and clinical work in this sub specialty both at Makerere and Gulu Universities. The team has published one paper based on its work, made four conference presentations and has three manuscripts under review.

The Research Team met regularly in the Department of Psychiatry, Makerere University College of Health Sciences on Saturdays to discuss the progress of the project.

From left to right: Assoc Prof Willson Muhwezi, Dr Catherine Abbo, Principal Investigator, Child and Adolescent Psychiatrist, Prof Emilio Ovuga, Professor of Psychiatry overall mentor for the team, Dr Grace Akello, Medical Anthropologist with experience of qualitative research, Dr Elly Okello, Medical Anthropologist and expert in qualitative research.
To know and not to apply is not to know
2015 THRiVE Finance Management Training

By Shem Wakaindha

The 2015 THRiVE Annual General Meeting (AGM) at Imperial Resort Beach Hotel Entebbe was something of a unique experience for the finance delegation that attended. Several times such events are organized with little or no time given to finance management and donor compliance activities. Following a recent Wellcome Trust audit that was carried out on the THRiVE Consortium and the subsequent recommendations suggested for both programme and finance aspects, the programme secretariat with input from the consortium partners organized a finance management training that run concurrently with the main AGM programme activities.

A separate room was identified next to the main conference room at the AGM venue, a competent facilitator from SMART CONSULT Ltd by the names of Alfred Brian Agaba was identified and the invited grants and finance personnel were requested to attend this finance training that was majorly based on topics that could address the recommendations in the Wellcome Trust audit. Other topics important to general finance aspects were also included in this training.

A total number of 12 participants from the THRiVE consortium members turned up for this event running from 22nd to 24th June 2015 at Imperial Resort Beach Hotel in Entebbe. A majority of them expected the routine theoretical marathon discussions on finance topics such as Managing Multiple Donors, Risk Management, Foreign Exchange Management, Liquidity Management, Accounting System Selection and Implementation, Preparation for Audit, Budget Monitoring, and Internal Controls.

Initially some participants felt this was too much to deliver in the given time at the AGM. However the trainer approached the topics from the practical aspects while enabling us to relate each scenario to our daily finance and grants related activities including the use of live examples. To many participants’ surprise, a lot was learned with this approach as it simplified the much talked about theory in some of the aforementioned finance topics. In fact by the time we were done with the training most participants felt that a lot had been demystified in the shortest time possible. One participants commented as follows; “The method was practical, for instance developing the Risk Register. There was use of open-ended questions that led to discussions based on experience. Topics covered were relevant and the duration was ok. Generation of ideas from trainees was appreciated”

Throughout the course, participants were given an opportunity to record in an “Action Planner” how they would apply what they had learnt to their work to improve their performance. Many promised to implement the knowledge gained when they return to their posts. However, as the THRiVE programme approaches close-out stage, a key challenge is how to follow up on these and other crucial finance and grant related activities even in the absence of the THRiVE funding from Wellcome Trust.

London School of Hygiene and Tropical Medicine

By Jim Todd and Jenny Renju

Several activities have been conducted by the London School of Hygiene and Tropical Medicine (LSHTM) over this period, with its THRiVE African partner. A few of these are shared here.

Analysis workshop:

As part of the collaboration between the Tanzanian Ministry of Health and Social Welfare (MoHSW) through the National AIDS Control Program (NACP), LSHTM facilitated a 2 week workshop on the analysis of the care and treatment data in Tanzania. The workshop was hosted by KCMU College, and included statisticians from NIMR.
Thrive has provided me with more than just funding for doctoral training

By Bonnie Wandera, THRIVE PhD Fellow
For the last 3 years I have almost had a nearly standard to-do list of activities and they have all rotated around Alcohol and HIV. The latter is my doctoral research area generously sponsored by the THRIVE consortium with funding from the Wellcome Trust. However, in between the overt active research processes of proposal development, data collection and analysis, there are a lot of other activities that I have come to appreciate additional skills that one needs to acquire on the path to develop into a competent independent researcher. These skills happen to belong to non-science disciplines which may not have been introduced to a science-based student like myself during their undergraduate and graduate training. Some of these unwritten skills and competences, listed in no particular order, include learning to manage human resource, appreciating procurement and logistics management, financial accountability discipline and learning how to be a doctoral student. As the Principal Investigator, I had to polish my skills to negotiate with my clinical research site hosts regarding how to embed my study in a busy clinical setting without antagonizing routine clinical activities. These negotiations involved reaching a compromise with sharing staff from the clinical site as well as recruiting new research project specific staff. I had to learn how to develop job descriptions, going through recruitment processes of the temporary staff and training them on-job on how to execute their activities. In doing all these, I admit I faced a steep learning curve involving how to manage people and setting their goals. Research is a team effort and it is the responsibility of the Principal Investigator; in this case the doctoral trainee to assemble a strong team and to accordingly delegate duties to the team. I had to delegate even managerial duties to the team when I had to attend conferences and trainings both within in and out of Uganda. As I gained a foothold on personnel issues, the project needed additional finances to run which involved requesting additional money from the University. With no preapproved financial reporting template, my initial expenditure report was such a daunting task that it took me almost 5 times the time I had anticipated and furthermore it had to require a lot of assistance from my colleagues with

Hygiene and Tropical Medicine Work within the Network

Mwanza and other NGO and research institutions across Tanzania.

The workshop used the data on a central server in NACP containing more than one million HIV positive people who have attended care and treatment clinics (CTC) in Tanzania. Overall the analysis included data from over 20 million clinic visits to 748 clinics which had collected electronic data in the CTC. The teams are writing up the results into the fourth national CTC report for Tanzania, which should be available by the end of August 2015.

The workshop has proved especially useful for the current students who are studying the MSc in Epidemiology and Applied Biostatistics as they have gained insight into numerous research topics they could cover in their Masters projects. One student will spend their research attachment at NACP building stronger links for the analysis of TB incidence measured in the database. Another will build on efforts to estimate the fertility of HIV positive women in Tabora region.

ARF application:
LSHTM supported one researcher from UVRI/ MRC, Sylvia Kiwuwa, in her application for an African Research Excellent fellowship. Sylvia, who obtained her PhD from Tampere University in Finland in 2012, wants to apply her PhD findings to routinely collect Ugandan HIV data. Sylvia had analysed the adherence to ART among HIV patients in the DART trial, and the challenge is to apply the analysis from this research study into the routinely collected data, which often has issues around the quality of the data.

IBS GUGAN:
LSHTM, Makerere University and UVRI/ MRC are organising a statistics conference in Kampala on 12th and 13th November 2015. This is funded as part of the International Biometrics Society (IBS) under the Uganda Chapter (GUGAN). We expect statisticians and researchers from seven African countries and three European countries to present on topics such as Analysis.
LSHTM Work within the Network

of Routinely collected data, Abuses of Logistic regression, and Survival Analysis. The workshop will include a short course on the longitudinal data analysis (LDA) by Dr Ann Mwangi. Please go to the website (http://www.ibsgugan.com/417606674) to register for the conference, which will be held in the Mildmay complex (along the Entebbe Road).

Successful recipient of DAAD Scholarships for postgraduate studies at KCMUCo:

LSHTM worked with the newly-formed Institute of Public Health in KCMUCo to apply for DAAD funding for scholarships. The application was successful and the IPH within KCMUCo was awarded four 2-year MSc Scholarships for the LSHTM supported MSc in Epidemiology and Biostatistics and two 3-year PhD positions again for work within the remit of the IPH each year for three years (therefore a total of 12 MSc scholarships and 6 PhD scholarships). Jenny Renju (LSHTM) was assigned as the DAAD Coordinator within KCMUCo. In total 42 MSc applications were received and 8 were shortlisted and sent to DAAD for the final selection. A total of 15 PhD applications were received, 10 were submitted for internal review by KCMUCo faculty, from these 6 were requested to present to a PhD selection committee from which three were shortlisted and submitted to DAAD for the final selection. Successful candidates will begin their studies in October 2015. The DAAD scholarships are full scholarships which include various peer-to-peer support initiatives with other DAAD scholars across the region. The successful PhD students will also have the opportunity to apply for a six month research attachment at a German University to further enhance their scholarship experience.

Supporting KCMUCo to conduct a large scale evaluation on the Better Immunization Data (BID) Initiative:

The Better Immunization Data (BID) Initiative is led by PATH and funded by the Bill & Melinda Gates Foundation. They will partner with countries and global health stakeholders from the outset to develop and deploy a holistic and scalable approach that focuses on information system products, data management policies, and the practices of people that use them, in order to enable evidence-based decision-making. These components will be packaged into a replicable solution that can be easily and cost-effectively adapted by additional countries interested in using it to improve their immunization management. The group recently put out a tender to conduct an extensive evaluation of the initiative across 5 districts in Northern Tanzania. LSHTM supported KCMUCo to successfully bid for this tender. The process has ensured a collaboration of researchers both senior and junior who have come together to form an evaluation team. This is the first grant of its type to fall directly under the newly formed Institute of Public Health and provides a platform for the Institute to build its portfolio. The research will begin later in 2015 and run through till mid 2019; we are proposing that Florida Muro (THRIVE PhD fellow) and a recent graduate of the THRIVE supported MSc in epidemiology and biostatistics will manage and coordinate the field work (respectively); other postgraduate students will also be able to use part of the data for their studies.

Research Costing for Sustainability of Research Institutions and Initiatives

By Achilles Katamba, MakCHS

To ensure sustainability of Universities and Research Institutions, there is need to ensure that they accurately identify and understand the full costs of conducting research. In an effort to build research-costing capacity in THRIVE and African Research Initiative and Support – network (ARISE) partner institutions, Makerere University College of Health Sciences organized a 3-day research-costing workshop, May 19th to 21st 2015. The workshop took place at MakCHS and the content was based on the ESSENCE five keys for improving Research Costing in low- and middle-income countries that include: 1) Defining and categorizing direct and indirect costs, 2) Determining indirect cost rates, 3) Institutional management of research grants, 4) Developing relevant skills and competencies, and 5) Bridging the gap between funders and research institutions http://www.who.int/tdr/publications/non-tdrpublications/essence-framework. In addition a practical example of how to perform a full costing for research at an academic institution was done.

The workshop was facilitated by experts from Infectious Disease Institute (IDI) at Makerere University and was attended by participants from Gulu University, icipe, Kilimanjaro Christian Medical College, College of Medicine Malawi, MakCHS, National Institute of Medical Research Mwanza, University of Rwanda and Uganda Virus Research Institute. On the benefits of the information gained, participants stated that: they had a better understanding of the costs associated with implementation of research projects and they gained knowledge and skills to compute indirect costs. This enhanced their ability for proper budgeting and recovery of costs especially in settings where there are several ongoing research grants or projects. Further they pledged to advocate and work with their institutional administrative and management units to conduct a full costing for research and establish an institutional indirect cost rate.
THRiVE and MUII Partner to Equip Researchers with Next Generation Sequencing (NGS) Data Analysis Skills

By Deo Ssemwanga, John Ssemwanga, Timothy Wamala, and Jonathan Kayondo, UVRI

NGS era brings both new opportunities and challenges in the region:

Recent advances in deep sequencing resulting in massive data outputs have brought new opportunities but also myriads of data handling challenges for researchers world over. NGS platforms are currently being pioneered at select research sites across the region, Makerere and UVRI included, and it will soon be routine to sequence entire genomes of organisms (microbes, animals and plants), massively, but the resultant file outputs are enormous and their assembly daunting. Therefore, if researchers in East Africa are to benefit from these technological developments, there is a need to further strengthen their Bioinformatics sequence data analysis skills.

Collaborative training workshop involving regional, continental and international partnerships:

Towards this end, two Wellcome Trust capacity building programs; THRiVE alongside sister training program MUII jointly funded the fourth workshop of Bioinformatics in the Tropics, a course series running at the Uganda Virus Research Institute (UVRI), since 2013, as a South-South capacity development initiative to build next generation of bio-informaticians in Africa. Additionally, two other Welcome Trust centers, the Africa Center for Health and Population Studies, and KEMRI / Wellcome Trust Center at Kilifi, and other collaborating partners: the International Center of Insect Physiology and Ecology (ICIPE), H3ABioNet and the MRC/UVRI Uganda Research Unit on AIDS provided specialized technical assistance and teaching faculty.

The workshop ran from the 6th to 9th July 2015, and was designed for scientists, graduate students, postdoctoral research fellows, and exceptional undergraduates to become familiar with techniques for NGS data handling and analysis. The course attracted over 35 applicants but due to limitations of space and travel scholarships, just 25 participants from UVRI/affiliates, Makerere University and ICIPE could be sponsored. A number of successful applicants from several African countries including Uganda, Kenya, Tanzania, Ethiopia, Malawi, Cameroon, Tunisia, Morocco and South Africa were invited but couldn’t self-fund to attend. Eight (8) course teachers from Uganda, Kenya and South Africa with complementary genomics, population genetics, and bioinformatics backgrounds facilitated the course. UVRI IT

Thrive has provided me with more than just funding for doctoral training

technical knowledge on accounting. So the lesson here is that even when all the funds are used directly and correctly on the research project, the reporting has to be meticulous and detailed enough with relevant supporting information to make it easier for the auditing team. Delays in accountability eventually spill over to delays in next cycle procurements and therefore adversely affect the conduct of even a well-written and scientifically valid research project. Meanwhile as I am going through all these “new” areas I am still required to meet regularly with my supervisory team and appraise them on the doctoral training progress and submit reports as well as.

As a doctoral student with a limited budget, hiring an independent project administrator may not be feasible, therefore learning how to administer and manage my project has been a very good experience I had never anticipated I needed. Thanks to THRiVE, I have been able to appreciate and will continue to build on it going forward. The take home message is that the doctoral research training is not only about a good research idea but a lot of other fundamental tenets of research project management. I believe that not all doctoral research candidates are aware of these skills and therefore these skills should be part of the induction processes for doctoral training at Makerere University.

Photo opportunity: Dr Wandera Bonnie with his Primary Supervisor, Dr Nazarius Tumwesigye (L) after a preparatory meeting for his abstract presentation at the 2014 KBS conference on Alcohol Epidemiology in Turin, Italy.
THRiVE and MUII Partner to Equip Researchers with Next Generation Sequencing (NGS)

infrastructure; internet, analysis servers, and staff played a big role.

**Workshop flow and focus:**

The four-day workshop involved theoretical lectures and practical sessions on analysis techniques for dealing with Next Generation Sequencing (NGS) data, including an introduction to programming for the study of large data sets of HIV and other genomic data. It introduced Linux command lines for basic operations, NGS sequence data formats, QA/QC methods and Illumina sample preparation for NGS sequencing. Various topics on NGS analysis e.g. Strategies on genome assembly, read mapping, annotation, SNP calling, HIV-1 drug resistance mutation genotyping, comparative genomics, and population genetics/phylogenetics etc using command-line and graphic user interface programmes were covered (see photo below). Tools for data visualization and analysis softwares e.g. e-Biokit, Galaxy, ARTEMIS, U-gene, QUASR among others were introduced. Use of open source technologies was encouraged.

The first day of the workshop had lectures on the general introduction to NGS, its various applications, sample preparations for NGS, illumina sequencing and NGS data formats. Students were introduced to the linux command line, assembly and genome annotation and the use of Quality Assessment of Short Reads (QUASR) software. FastQC pipeline for processing, assessment and quality control of NGS data.

On the second day, the students had more practical sessions using QUASR. A keynote lecture on “Setting a genomic lab in Africa” was done by Prof. Tulio de Oliveira. The day ended with drug resistance analysis.

The third day involved the use of e-Biokit platform and genome assembly and annotation programmes such as Galaxy, ARTEMIS among others for the analysis of NGS data.

The fourth and final day had a theory on Phylogenetic analysis approaches and practical sessions on detecting HIV superinfections, HIV transmission networks and recombination using the various available free online and commercial softwares. Students at the workshop were also encouraged to utilize their own sequence data with the help of the teachers. A hot topics lecture on accurate cross-sectional incident testing was also presented. The course was concluded with a certificate award to the students [photo above] and a workshop barbeque.

The course was well received and ran smoothly. Workshop teaching and class evaluations were very encouraging with useful suggestions provided on how best to improve on future courses. The south-to-south series have been a success and we are looking forward to continue this model of collaboration possibly even in other areas. THRiVE and MUII indeed continue to help build careers of emerging researchers in the region.
Cambridge Welcomes THRiVE Post-docs and an East-West/South-South link!

After a two-year break (since the completion of the first cohort of THRiVE post-doctoral fellowships), THRiVE-Cambridge has been delighted to host THRiVE post-doctoral fellows in Cambridge again, Dr Roman Ntale from the University of Rwanda arrived in Cambridge in early June 2015 to work with Dr Jane Greatorex (from Health Public Health England and Lucy Cavendish College in Cambridge) to sequence HIV samples from MSM (men who have sex with men) networks in Rwanda. A Material Transfer Agreement between the University of Cambridge and the University of Rwanda had been signed for this. Jane is responsible for an HIV whole genome sequencing pilot project (sequencing samples from the East of England and the Midlands), and is excited to be able to increase the diversity of the expected sequencing data by including Roman’s samples from Rwanda in the study. While in Cambridge, Roman has been busy attending training on Whole Exome Sequencing and RNA-sequence data analysis. He has also been learning how to use the statistical software ‘R’ to solve biological problems. The results of his sequence analysis will elucidate HIV transmission dynamics amongst MSM. Roman is also working with Dr Simon Frost from the Department of Veterinary Medicine in Cambridge on a behavioural analysis to provide more critical information and contribute to designing more effective intervention strategies amongst this marginalised group.

Dr David Kateete from Makerere University is a THRiVE post-doctoral fellow who is being mentored by Professor Mathew Freeman at the University of Oxford. While visiting Oxford, he paid a visit to the THRiVE team in Cambridge in April 2015. It was great to hear David discuss his research on characterising the role of rhomboid proteases in virulence and drug resistance in TB. The THRiVE-Cambridge team suggested that he adds a genomics dimension to the work, and offered to introduce him to Professor Stephen Bentley at the Wellcome Trust Sanger Institute for further discussions about this. David therefore returned to Cambridge in June 2015, to meet with Stephen. They had a productive meeting about David’s work, and how to find further funding to expand the research. Stephen is now keen to see David take part in genomic analysis training run by the Sanger Institute, and will do what he can to help make this possible. The researchers also noted an overlap in their interest in a future Hospital-based maternity MRSA study that David is involved in, which they can have follow-up discussions about. Their meeting ended with David being treated to a tour of the 55 acre Sanger Genome campus!

The Cambridge attendees also had another AGM to attend in Kampala – straight after the THRiVE AGM. This was for the CAPReX initiative in Cambridge (a sister to THRiVE, also falling under the Cambridge-Africa Consortium). The Cambridge team was excited to be able to put Dr Osbourne Quaye CAPReX post-doctoral fellow from the University of Ghana, researching rotavirus in farm animals in Ghana with THRiVE PhD fellow Josephine Bwogi, who is conducting similar studies in Uganda. Both fellows have Cambridge-based mentors/collaborators and Josephine’s Cambridge mentor, Dr Ulrich Desselberger was able to go to Liverpool to meet her when she visited earlier this year. When Osbourne visited UVRI, both fellows were able to share information to mutual benefit (e.g. different sequencing techniques and various research lessons learnt). We were able to share information to mutual benefit (e.g. different sequencing techniques and various research lessons learnt) when Osbourne visited the UVRI. The UVRI visit also accorded Osbourne an opportunity to experience the much acclaimed “Kampala jam”, as his return journey from Entebbe to Kampala took almost four hours- a truly Ugandan traffic experience he will not forget any time soon!
My post-doctoral fellowship entailed training on deep sequencing and analysis of some HIV samples from Rwanda at the Addenbrookes Hospital, Cambridge (Clinical Microbiology Laboratory, Public Health England). It also involved analysing patient questionnaires to elucidate HIV transmission dynamics within hard-to-reach population networks in Rwanda. Of particular importance, we tested whether methodologies used to amplify the HIV virus from England could be applicable for the diverse world HIV viruses. We devised and tested methodologies for amplifying small sections of the virus and thereafter pooling the sections together for sequencing. We hope the methodologies we developed will be used for the sequencing of viruses derived from diverse world regions.

While at the hospital, I trained on bench at the virology laboratory at Addenbrookes hospital and went through the whole process of HIV RNA extraction, amplification, analysis and sequencing. I will be using these methodologies quite often in my present and future research.

Furthermore, as a culture, the University of Cambridge provides ongoing skills development to staff and graduates of this university, which I doubt I could have got with ease anywhere else. In order to complement laboratory training, I had to attend courses relevant to the work I was doing and it was in that context that I attended two courses; one on whole exome sequencing and RNA-sequence data analysis - this was quite important as it dealt with the real knowledge needed for handling my own HIV deep sequences. The second course was an introduction to solving biological problems with ‘R’ - while this was not enough to be able to use ‘R’ for statistical analysis, the course was an eye-opener and provided me with basic skills to further self-learn on a daily basis. A certificate of participation was provided.

The other important part of this fellowship dealt with forging a continued research relationship. We will continue to work with Dr Jane Greatorex at the University of Cambridge, who is also a senior scientist at the Addenbrookes hospital as well as Prof Simon Frost at the University of Cambridge. This is of particular importance since I expected this fellowship to provide me with an opportunity to network and collaborate with experienced researchers in order to strengthen my future research and publication capacity.

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