AHRI ANNUAL REPORT 2018

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Forward

Like the previous years, Armauer Hansen Research Institute (AHRI) has shown tremendous progress in achieving its strategic objectives of being the best clinical and biomedical research institute in the country. In addition to its long-standing research profile, AHRI is also progressing well in the areas of non-communicable diseases research.

In 2018 alone, researchers from AHRI published 58 scientific papers in peer-reviewed journals. These publications cover a wide areas ranging from TB, leprosy, malaria, HIV and basic immunological studies. Some of the studies were published in high impact prestigious journals; one such example is the publication on Clinical Infectious Diseases about asymptomatic malaria. The study has produced data that will greatly contribute in the country's effort towards malaria elimination in selected Woredas/districts. Because of this publication and related studies, the primary author of the paper was invited to a WHO consultative meeting on malaria elimination. The bioequivalence study program has reached another milestone in 2018. We have conducted a Pivotal bioequivalence study on Ciprofloxacin (Ciproxin® 250). We have completed the clinical part of the study and submitted specimens to Regional Bioequivalence Center for bioanalysis. This study also created opportunity for training of post-graduate students. Students from CDT Africa visited our site and gained knowledge and skill about bioequivalence study. On the other hand, the establishment of HLA compatibility test facility for kidney transplantation has progressed well. Now, we have established the laboratory and have started to run samples for validation. We hope to complete the validation work and begin the actual work soon.

In addition to research, AHRI is also supporting health innovations in the country. This year, more than 100 proposals were received for funding through Grand Challenges Ethiopia initiative. Of these, 10 has been awarded for a seed grant of each 300,000.00ETB. This has increased the total awarded innovations to 24.
AHRI's support of post-graduate education has increased significantly over time. Currently, AHRI is supporting 49 PhD and 16 Masters students in different schemes. In 2018 alone, 4 PhD and 9 MSc students defended their thesis.

Our clinical research network project with five universities in Ethiopia has begun to bear fruit. We have completed several studies in the areas of antimicrobial drug resistance, hepatitis, and cancer. The success has prompted us to expand the network and included another six universities. Some of the results of the studies are accepted to be published in separate special issues in Ethiopian Medical Journal.

All these research and training activities were done while the institute was going through management transition. The Director General and Deputy Director General for Research and Innovation as well as Deputy Director General for Administration and Development were appointed since September 2018.

We look forward to having another productive year ahead.

Abebe Genetu Bayih (PhD), Director General

Vision and Mission

Mission

The mission of AHRI is to improve medical care; health and wellbeing of the public by generating and delivering scientific evidence, developing new tools and methods through biomedical, clinical and translational research, and to serve as a hub for technology transfer and capacity building in medical research and research training.

Vision

A leading medical research and training institute in Africa by 2025.

Overarching results

Leading:-

Among the top ten medical research institutes in terms of

1. Number and quality of research publications
2. State of the art lab facility
3. Number of highly skilled manpower

Executive Summary

During the year 2018 AHRI has continued to move forward with the focus of achieving its strategic objectives and ensuring the contribution towards its broader mission of improving medical care, health and well-being of the public by generating scientific evidence. The research and innovation activities have been focused primarily on addressing the identified public health priority needs of the country and in line with the plan to achieve global health sustainable development goals (SDGs). This year, a total of 66 research projects have been either completed or ongoing and 50 were published in international and local peer-reviewed journals. The institute provided research support to 51 Ph.D. and 16 MSc postgraduate students from local and international partner universities. During 2018, the institute has also played a significant role in terms of awareness creation and engaging the community on biomedical research activities.

The research conducted in Bacterial and Viral Diseases has been aimed at understanding the cause, transmission dynamics, and epidemiology of infectious diseases. Studies were also conducted to determine vaccine efficacy against infection, magnitude of antimicrobial resistance, and to develop in-house molecular assays for the detection of different viral diseases. In this regard, some of studies investigated the causes of sepsis, meningitis, severe typhoid, diarrhea, respiratory and liver diseases. Moreover, we employed genotyping techniques to understand the molecular epidemiology of pathogens and to characterize circulating strains. Translating the knowledge and evidence from those studies are believed to influence the ministry to decide and implement improved public health practices to control bacterial viral and viral diseases.

The Mycobacterial diseases are still taking big share of research conducted at AHRI. Several ongoing and newly initiated research activities investigate diagnostics, therapeutics, and characteristics of the etiologic agents including host-pathogen interactions. In the global "end TB and leprosy strategies", early detection of disease has been especially emphasized as the flagship of the division. One of the newly initiated TB research projects in 2018 is a collaborative study with the Emory University that aims at investigating immune signatures to characterize progression from latent TB Infection to active TB Disease. The other collaborative study with Queen's College, UK aimto detectingM.tuberculosisDNA in CD34 positiveblood cells from different study groups that include latently infected, active TB, contacts and HIV patients. Both projects are aiming for early TB detection.

The other newly initiated project is TBGEN, a genetic study with the aim of unraveling susceptibility to TB in four African countries, namely, Sudan, Cameroon, Eritrea and Ethiopia. Additionally, this will be a major step towards establishingbioinformatics and biorepository centers at AHRI and an increased awareness of genetic research in communities with different cultural background. The AHRI-APOPO project "Enhanced tuberculosis case detection in Addis Ababa by trained rats" envisages targeting and reaching the 60 to 70% missed cases. "ETHICOBOTS" is also a consortium project that explores ways to reduce the zoonotic impact on high-risk groups, including dairy farm workers and their families.

In this year, improved community engagement activities have been practiced using different strategies to enhance the knowledge and voluntary participation in research. Community based pulmonary TB screening and the active case detection of leprosy and contact tracing using health extension workers resulted in increased detection of undiagnosed cases. The Malaria and Neglected Tropical Diseases Research Directorate (MNTDR) is an active member of the National NTD Task Force and the Technical Working Group for the National Onchocerciasis Elimination Program. In line with this, our directorate has focused on government priority areas to provide evidence for programmatic input. Some of the evidence produced in malaria include: the utility of serology as a tool to evaluate the performance of malaria control and elimination; clustering of asymptomatic malaria infections around passively detected infections with implications regarding hotspots that potentially fuel transmission; low and patchy distribution of G6PD deficiency with implication for safe use of 8-aminoquinoline drugs such as primaquine and tafenoquine; very low performance of malaria microscopists that need attention in consolidating the gain in the fight against malaria; and a reversal of PfMDR1 mutation in P. falciparum, implicated as a prerequisite phenomenon for artemisinin-based treatment failure against P. falciparum

in sub-Saharan Africa.

The clinical trial directorate has conducted various trials that aim to shorten the duration of TB treatment for both drug-sensitive and drug-resistant TB. The result of the first phase of the STREAM trial is under review New England Journal of Medicine (NEJM) and is currently under review. Other studies investigating the adverse reaction of drugs and cost-effectiveness of traditional and new TB diagnostics are also among few of the on-going projects. Bioequivalence study on locally produced drug ciprofloxacin was also successfully conducted to determine bioavailability and assess the bioequivalence of the innovator drug against the standard products. The experience gained from this is substantial and will help us in our mission to be a renowned bioequivalence center in the region.

Ethiopia is the home for traditional healers and herbal medicine is used by different societies throughout the country. In this regard, the directorate took the initiative and has submitted a protocol for ethical review to conduct a trial on safety and efficacy of the highland herb U.simensis for the treatment of psoriasis. Conducting such studies will provide scientific evidence for the use of locally available herbs in the treatment of different health conditions. In line with this, a consultative meeting was held with stakeholders including policymakers and regulators to share ideas and discuss on the experience of different countries in this regard. As in the past, this year several students visited the clinical trial unit to observe works that are being conducted and discuss challenges and future career opportunities in clinical trials. In the future, the unit will continue to create such a platform to attract professionala to this field and fulfill the shortage of practitioners in the country.

The bioinformatics unit is a new department which works to strengthen its human and laboratory capacity. Six additional staffs were recruited in 2018 under this department and they will provide support for planned activities. The HLA laboratory, which tests compatibility for kidney transplantation for St. Paul hospital, Addis Ababa, has completed its preparation and has conducted concordance test to determine whether results are in agreement with lab results from Germany. Additional tests will be performed in the coming months and hopefully, the lab will provide compatibility tests for kidney transplantation service in Ethiopia, shortly. The directorate is working with the Ethiopian government to secure funding for different activities including for IVIg production which has many therapeutic applications in patient care. In this regard, networking activities are underway with different companies and institutes. A one-week training was also provided to various students on how to analyze Mycobacterium tuberculosis sequence data, and such training will continue to be provided regularly in the future for AHRI staffs and others interested.

The One-health Unit conducts various studies in the Somali region where communities live closely with livestock. Despite its challenges working in such remote area, the unit has conducted different studies to provide evidence on animal, human and environmental health issues facing the society. Research areas include TB diagnostics, mental health, and zoonotic diseases. In the last three years, nine postgraduate students from Haremaya and Jijiga Universities have been supported to conduct their studies. The unit is mainly supported by a grant from the Swiss government and is expected to continue for the next 9 years.

The laboratory management unit is the cornerstone of AHRI. Despite its challenges in procurement and laboratory size, the unit is striving to improve laboratory safety and create a conducive environment for students and researchers. In this regard, a laboratory manual for all major standard applications has been prepared including more than 180 standard operating procedures. The lab has provided trainings and short-term attachments for 250 students visiting the laboratory from different institutions and universities in Ethiopia. In addition, the lab has provided clinical services including histopathological and TB diagnostic tests on 2300 samples. Finally, the lab has successfully installed 40 minor and major pieces of equipment.

Grand Challenges (GC) Ethiopia has joined the global growing family of Grand Challenges programs in 2015 with an initiative to support the creation, appraisal, promotion, and scale-up of innovative ideas and concepts that are responsive to local needs. Of 14 selected innovators for the first year, 11 successfully finalized their project as per the schedule and submitted their final report. Following

the second year 2018/2019 GC announcement, more than one hundred seed grant applications were accepted and 10 innovations recommended to win the seed grant. The third-round announcement may give emphasis to adopt innovations and technological solutions that have occurred elsewhere in the world and encourage the private sectors and individual researchers to take part in the GC Ethiopia endeavor.

Clinical Research Network (CRN) has been initiated by AHRI in collaboration with five local universities aiming to build clinical research capacity and clinical laboratory diagnosis in collaborative universities on selected areas with support of the Federal Ministry of Health of Ethiopia. The topics include hepatitis, antimicrobial resistance (AMR), arboviral infections and cancer research. So far, a total of 22 postgraduate students (19 MSc and 3 Ph.D.) have been supported through the initiative. We have entered into agreement with six more Universities and thus a total of eleven institutions will take part in the network in 2019.

Knowledge Management Directorate (KMD) is the youngest directorates of all at AHRI. The scope of practices under KMD is closely connected with almost all AHRI's research, innovation and development activities to generate high-quality evidence, ensure proper documentation through advanced data management, archive and codification of the data, information and translation of the knowledge in order to retrieve and utilize the information and new knowledge that could shape health policy and implementation in Ethiopia and beyond. In the same year, we have produced two policy briefs with one already submitted to the MOH and which is currently under consideration

The Data management and Biostatistics unit has worked on different collaborative and PhD/MSc student projects, designed case record forms (CRF) and database structure, and performed double data entry, data cleaning, verification, validation, and data analysis. The unit has archived 50 various research projects which have already been published in different journals. The unit has been active in developing data management and sharing guidelines, database documentation and provision of trainings to researchers. The directorate is developinga knowledge management strategic document.

The Research Training Directorate continues to coordinate several initiatives such as Emory-Ethiopia TB Research Training (EETBRT), Biomedical Sciences Postgraduate Partnership Program (BSPP) between AHRI, AAU and various Swedish Universities, AHRI - Brighton Sussex Medical School, and AHRI - Haramaya University in improving graduate trainee research capacity. It is also working hard to improve research training through structural measures like introducing guidelines that stipulate the level of supervisors' engagement and trainee's role. In addition, in 2018, the directorate facilitated 30 lab meetings and 17 seminars which were conducted by postgraduate students, staffs, and guests. Currently, the Research Training Directorate is facilitating research training for 49 Ph.D. and 16 MSc students.

The achievements of AHRI would not have been possible without the strong support of Ministry of Health of Ethiopia, Sida and Norad. AHRI is ever in debt to its funders, its research partners, the study participants in the community for all its success. We look forward to future years with more confidence because of the encouragement and inspiration we received from our stakeholders.

2018 in a nutshell

AHRI Scientist Dr. Abebe Habte is recognized for lifetime service

AHRI participated at the 20th Federal Ministry of Health Annual review Meeting (ARM), which was held in Mekelle, Tigray region, from October, 24-26/2018.

During the meeting, a brief introduction was given to participants about AHRI and the various research activities being conducted at the Institute. At the event, Dr Abebe Habte was awarded a Lifetime Achievement Award for his professional contributions to the health sector.

Promotion of AHRI during the Mekelle annual meeting (B) Dr Abebe Habte receiving an award from Dr. Amir Aman (Minister of Health, right) and Dr. Debretsion Gebremichael (acting President of Tigray Region, left).

Ethiopia Control of Bovine Tuberculosis Strategies (ETHICOBOTS) Project Annual Review Meeting

ETHICOBOTS is a multi-partner One Health research project (2014-2019) aimed at minimizing the potential impact of bovine-tuberculosis (BTB) on poor and high-risk groups, including dairy farm workers and their families. This interdisciplinary programme addresses poverty and livelihood issues in relation to BTB in a unique manner and builds on previous studies, considering new breeds of cattle. This year, the collaborators and investigators met at AHRI from 2-5 October 2018 to evaluate progress towards project objectives.

A Community Engagement forum on HIV/AIDS in Gambella Regional State

AHRI launched a behavioural and sexually transmitted disease (STD) research focusing on women and girls at Gambella regional state with a community engagement forum. In the forum, several issues were addressed regarding STD and the research plan in general.

Media Forum established

An AHRI Media forum was established to better inform stakeholders on the Institute's strategic plan and activities. The forum aims to create a platform for consultations with the community and exchange of regular updates. More than 20 media organizations were represented at the inception meeting in Adama on research endeavor advancement and on integrating a new and improved way of research techniques with the pre-existing researches so as to enhance the community's and the country's health service in general. The media professionals had an opportunity to better inform themselves about AHRI research and desired impact on health. A consensus was reached on the need to actively work together to improve community awareness of research in Ethiopia.

Media forum held in Adama town, Ethiopia

Ethio-Norway health and higher education for development conference was held in Addis Ababa

The 3rd Conference on Ethiopia-Norway Collaboration on Health and Higher Education for Development was held on November 27, 2018 at Addis Ababa, Ethiopia. The event was organized by the Royal Norwegian Embassy in collaboration with the University of Oslo, AHRI, ALERT Hospital and Partnership for Change. Higher officials from the FMoH (HE State Minister Mrs. Sahrela Abdulahi), Norwegian Embassy in Addis Ababa (HE Ambassador Mrs. Merete Lundemo) and other distinguished guests from Ethiopia and abroad were present during the event. Dr Tore Goal, former director of AHRI, was also present at the event. At his welcome speech, Dr Abebe Genetu, AHRI Director General stated that this conference is one evidence of the strong link between AHRI and Norwegian institutions. A panel discussion was held on topics related to primary health care, trauma, surgery, paramedics and cancer.

Training on Neglected Tropical Diseases (NTDs) with a focus on podoconiosis was given to health workers from regional states

The training equipped health professionals from Amhara, Oromia and SNNP regional states with knowledge and skills on Podoconiosis treatment. Ethiopia is a pioneer in Podoconiosis care and research globally.

AHRI bids farewell to Dr. Taye Tolera and Dr. Zufan Abera

AHRI staff bid farewell to Dr. Taye Tolera (MD, MPH, PhD) and Dr. Zufan Abera (PhD). Dr. Taye served AHRI as Director General from June 2016 to September 2018 before he moved elsewhere. Dr. Zufan served AHRI as Deputy Director General from June, 08/2018 to October, 26/2018

AHRI is grateful for their contributions and unreserved service to the Institute during their leadership period and wishes them both the best in their future endeavors.

Dr. Taye Tolera and Dr. Zufan Abera during their farewell ceremony

Dr. Abebe Genetu and Dr. Alemseged Abdissa appointed as AHRI Director General and Deputy Director General, respectively

Dr. Abebe Genetu (PhD) and Dr. Alemseged Abdissa (PhD) were appointed by the Prime Minister as the new Director General and Deputy Director General of AHRI. Both are familiar with AHRI having started their research career as MSc students at the Institute several years ago and had kept close contact with AHRI ever since. Dr. Abebe Genetu holds a Master's degree from Addis Ababa University and obtained his Ph.D. degree from Calgary University, Canada. Prior to his new role as Director General of AHRI, he had served at University of Gondar, College of Medicine and health sciences at different capacities. Dr.

Abebe has tremendous experience working in leadership positions in academic and research institutions and has several publications in peer-review journals. Dr Alemseged Abdissa, Deputy Director General for Research and Innovation, holds a Master's degree from Addis Ababa University and a Ph.D. degree from the University of Southern Denmark. After finishing his Ph.D., Dr. Alemseged worked at Jimma University as Associate Professor of Microbiology. His research interests are in HIV and Microbiology.

Pictures of Dr. Abebe Genetu (left) and Dr. Alemseged Abdissa (right)

AHRI and staff contributions to charitable causes

As part of its community responsibilities, AHRI is involved in a number of charitable causes. This year's contributions included:

On the occasion of the 30th World Children Day (November 20, 2018), AHRI provided financial support to Sele Enat Mahber, a local charity that takes care of orphans and vulnerable children. During the event, His Holiness the Patriarch Abune Matiyas (Patriarch of the Ethiopian Orthodox Tewahedo Church), Her Excellency Mrs. Yalem-Tsehay Asfaw (Minister of Women, Children, and Youth) and other notable guests were present.

AHRI staff visited the Kebebe Tsehay Orphanage center (located around Sidst Killo, Addis Ababa) and provided material support worth ETB 18,000. During the program, AHRI Director General promised to continue mobilizing staff resources to support those in need.

AHRI staff provided 40 brand new foam beds (worth ETB 92580.00 /Ninety two thousand five hundred and eighty Ethiopian Birr) to Zewditu Meshesha Charity Organization. The charity provides care to children who have lost their parents. The orphanage had suffered a major fire accident last year.

The Bioequivalence Center at AHRI conducted a standard bioequivalence study on a generic ciprofloxacin product against the brand product. This round of study was particularly significant because the dossier will be presented to the WHO for pre-qualification of the Center in its bid for recognition.

I. Report from Research and Innovation

1. Bacterial and Viral Diseases Research Directorate (BVDRD)

The BVDRD Directorate conducts studies on the microbiology and epidemiology of infectious diseases with the aim of contributing to improved clinical care, disease control, and prevention. It also conducts studies to determine vaccine efficacy against infection; to determine the nature and magnitude of antimicrobial resistance, and to develop in-house molecular assays for the detection of different viral diseases.

Aetiology and molecular epidemiology of infectious diseases

Infectious diseases continue to be a fundamental impediment to human health in Ethiopia. Understanding the continually evolving trends in disease epidemiology requires regular monitoring at different sites in close collaboration with clinicians. Evidence on prevailing cause and pathogen genotype is of great importance to assist healthcare providers in the management of patients. In this regard, the BVDRD has carried out several studies to identify the prevailing causes of sepsis, meningitis, severe typhoid, diarrhea, respiratory and liver diseases in different geographical areas of the country. Increasingly, genotyping techniques are being employed to characterize circulating strains in order to better understand the molecular epidemiology of significant pathogens. Findings from such studies will help us deepen our understanding of pathogen biology that can contribute to improved diagnostic techniques, vaccines, and therapies.

In the Severe Typhoid in Africa (SETA) consortium project funded by the International Vaccine Institute (IVI) through the Bill and Melinda Gates Foundation (BMGF), we employed a combination of passive facility-based sentinel surveillance activities for febrile diseases at tertiary, secondary, and primary healthcare facilities to estimate the burden and severity of invasive salmonellosis. Clinical and microbiological data were collected prospectively from suspected typhoid and non-typhoidal salmonellosis patients in the Typhoid Surveillance in Africa Program (TSAP) conducted in 2012-2014. Only four S. typhi/paratyphi positive cases were identified from 3092 suspects investigated with blood cultures. That typhoid fever is rare in Ethiopia was a surprising finding. The frequent clinical diagnosis of typhoid fever (which is mostly based on the Widal agglutination test) is therefore false warranting recommendations to the Ministry of Health to review its guidelines on the Widal test. The implication to clinicians is that they should work on the other differential diagnoses of acute fever more thoroughly.

A research project on surveillance and serogroup distribution of meningococcal meningitis among vaccinated and non-vaccinated Ethiopians is underway to determine serogroup distribution of meningococcal meningitis among vaccinated and non-vaccinated Ethiopians. Samples are collected from nine study sites for broader representativeness than in the previous study which identified the emergence of a new serogroup (X) of N. meningitidis. It is expected that the study will identify predominant strain subtypes and clades and will provide information on waves of transmission trends in Ethiopia within the context of the African meningitis belt. As part of this meningitis study, we have initiated production of trans-isolate media (TIM) which supports the survival of strains during sample transport to a laboratory. Most bacterial causes of meningitis remain unconfirmed because of failure to grow the isolates in culture due to the distance from laboratories. Bacterial causes of meningitis such as N. meningitidis, S. pneumoniae and H. influenzae, die easily outside the host and require enriched media and body temperature to grow. TIM provides nutrients for live transportation. AHRI acquired the technology for TIM production from the Meningococcal Reference Laboratory in Oslo, Norway. The BVRD plans to provide clinicians and investigators with quality assured readymade vials for field application.

Trans-Isolate Media Production

Sterility and viability tests are proved successful in TIM produced at different batches

Invasive pneumococcal disease i(IPD) s a major cause of mortality in children. Ethiopia recently launched a pneumococcal vaccination program (PCV 10). The BVDRD has been conducting studies to measure the impact of this program on the epidemiology of the pneumococcal disease.

In a prospective observational study over a period of 12 months in children clinically suspected with IPD and acute otitis media in Addis Ababa, involving 643 children, S. aureus was found to be the predominant pathogenic species causing bacteremic pneumonia whereas S. pneumoniae and Klebsiella pneumoniae were the most common isolates causing sepsis. S. pneumoniae was still the leading cause of acute otitis media followed by S. aureus and H. influenzae. Ongoing molecular typing will inform us what proportion of the isolates are vaccine or non-vaccine variants.

The microbiology of Ethiopian traditional food is understudied. Fermentation to make injera involves hundreds of bacterial and yeast species. The composition of the microbial flora at each stage of the fermentation process has a strong impact on the nature of the injera produced at the end in terms of taste, structure, appearance and shelf life. Whether food pathogens can survive the process is also not well investigated. We have been looking into microbial fermentation dynamics in Injera to understand the diversity of fermenting microbes, their antimicrobial activity, and heavy metal tolerance. Hundreds of strains belonging to several microbial species and families were identified in short (high temperature) and long cycle (low temperature) fermentation of Injera sourdough. Most tested lactic acid bacteria inhibited the growth of enteropathogenic E. coli, Salmonella typhi and Shigella flexneri.

Hepatitis is widespread in Ethiopia and chronic liver disease contributes to the high burden of hepatocellular carcinoma, one of the most common malignancies among men in the country. Hepatitis B and C viruses both contribute to the development of hepatocellular carcinoma. Ethiopia has recently introduced vaccination against HBV. We studied the seroprevalence of hepatitis B and C virus infections in children and their mothers and HBV vaccine efficacy in children. The seroprevalence of HBV and HCV varied by study sites: 3.7% and 2.0 % in Addis Ababa, 5.7% and 2.6% in Jimma, 5.9 % and 1.1% in Harar, respectively and 3.8% HBV infection in Gondar. The overall HBsAg positivity in children ranged from 0.5% to 4.3%. The overall percentage of children with protective levels of anti-HBsAg was about 60% with a marked variation ranging from 31% in Hawassa, 32.2% in Gondar, 54.3% in Addis Ababa, 58% in Jimma to 97.5% in Haramaya. Despite the marked difference among study sites, it was evident that overall vaccine efficacy was significantly lower than the expected level of 95%. Further research

is needed to understand the reasons for the lower than desired HBV vaccine efficacy in Ethiopia. A Supplement to the Ethiopian Medical Journal specific to this problem is currently in print sponsored by AHRI.

Aetiological association of hepatitis B, C and D viruses with Hepatocellular carcinoma (HCC) and other potential causes among chronic liver diseases patients in Southern and Central Ethiopia was assessed. We found 50 % and 19% of HCC cases were HBsAg and Anti HCV positive respectively. On the other hand, we investigated the molecular epidemiology of Hepatitis B Virus genotypes, variants, and mutations among HIV co-infected and HBV mono-infected adults in selected public hospitals in Eastern Ethiopia (covering 865 HIV+ and 917 HIV-cases). HBsAg prevalence did not seem to differ much between the HIV positive (12%) and HIV negative (13.6%) individuals tested.

The BVRD is currently working on an integrated HIV bio-behavioral survey (IBBS) in Addis Ababa, Bahir Dar and Gambella among adolescent girls and young women to characterize HIV prevalence. Estimating vulnerability and risk factors for HIV in this population can guide future HIV programming. Health facility mapping, venue identification, venue verification and mapping, behavioural and biological data collection and testing have been performed in Addis Ababa. Thus far, 816 AGYW have been enrolled from Addis Ababa. All samples were tested for HIV, syphilis, and Chlamydia. Test results and treatment (if any) is being delivered to participants. We have also completed health facility mapping, venue identification, verification, and mapping in Bahir Dar, however, behavioural and biological data collection has been interrupted.

Antimicrobial Resistance

Antimicrobial resistance is an increasingly serious threat to global public health that requires action across all government sectors and society. It occurs naturally over time, usually through genetic changes, however, misuse and overuse of antimicrobials is accelerating this process and also. We are carrying out different studies to understand the magnitude of antimicrobial resistance and distribution of resistant genes in some bacterial species including S. aureus, S. pneumonia, E. coli, K. pneumoniae, N. Meningitidis among others.

We characterized bacterial profile, antibacterial susceptibility pattern and associated factors among mothers and children visiting hospitals for bacterial infections in Gondar, Dire Dawa, Hawassa, Addis Ababa and Jimma with financial support from the Ministry of Health. The proportion of drug-resistant isolates against commonly used antibiotics was in general high in all settings. S. aureus and K. pneumoniae were the most commonly isolated bacteria from cases of puerperal and neonatal sepsis. The overall prevalence of extended spectrum β-lactamase producing enteric pathogens was also high (22.1%) in a study at Jimma University Teaching Hospital. The need for effective antimicrobial stewardship programs in hospitals is apparent.

The role of environmental sources for evaluation and the spread of drug resistance in Ethiopia is unknown. We studied antimicrobial resistance genes of potentially pathogenic bacteria in Akaki river. A diverse group of bacteria including E. coli, Aeromonas species, S. enterica, V. cholerae, P. aeruginosa and other potentially pathogenic bacteria were identified. In DNA qPCR array, water samples were found to be positive for Fluoroquinolone, Aminoglycoside, β-lactamase (Class A, B, C and D), Macrolide, Multidrug resistance efflux pump, Tetracycline efflux pump, and vancomycin resistance genes. They were persistent in river water at various sampling points and site-specific genes could also be detected. Our preliminary findings indicate that Akaki River could be a potential hotspot for evolution and spread of antimicrobial resistance genes. The river drains city parts that cover hospitals, factories, and residential areas.

Assessing vaccine efficacy

Vaccines offer the most cost-effective approach to controlling infectious diseases and Ethiopia is engaged in expanding immunization services. However, very little is known about the efficacy of vaccines given to children. We are conducting different studies to estimate the efficacy of vaccines against pneumococcus, HBV, Rota, and measles in Ethiopian children (please see above).

One indicator for the detrimental effect of HIV on the immune system is the persistence of immune dysregulation despite antiretroviral treatment. We studied the humoral immune response to pneumococcal vaccination in HIV-1 infected children on ART to investigate humoral immune responses to Streptococcus pneumoniae in HIV-1 infected Ethiopian children receiving ART. Some studies suggested that early initiation of ART may limit the devastating effect of HIV on the immune system and result in an adequate humoral immune response in HIV infected individuals. The frequency of naïve and resting memory cells in ART-treated children was comparable to control subjects; exhausted memory B cells were however increased in these children. Profound homing defects were identified, with lower CXCR4 and CXCR5 expression in naïve and switched memory B cells from ART-treated children. In conclusion, homing defects of B cells to germinal center compartments may be at the basis of impaired vaccine responses during HIV-1 infection.

Development of in-house PCR assays

The cost of imported commercial kits is usually quite high and not affordable in resource-limited countries. As such, development and evaluation of a simple and cost-effective in-house PCR assay which is suitable for resource-poor settings is crucial. Currently, we are working on developing in-house assays to test HIV drug resistance, quantify HIV viral load, HBV and HPV genotypes.

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Research topics of postgraduate students supervised in the Directorate

Name	Research topic	Program	Objective	Current Status
Adugna Tsehay	Competence Assessment on Gram Stain Examination and Interpretation among Medical Laboratory Professionals working in selected Hospitals of Addis Ababa, Ethiopia	MSc	To assess the competence of laboratory technologists	Completed
Abel Abera	Phenotypic and Genotypic Characterizations of Streptococcus pneumoniae Strains from HIV + and – children in Addis Ababa, Ethiopia	PhD	To determine the prevalence of antibiotic resistance, clonal spread and genetic variability among *S. pneumonia* isolates with emphasis on macrolide and penicillin resistance	Data analysis
Tsegaye Sewnet	Epidemiology and molecular characteristics of extended spectrum beta lactamase producing Enterobacteriaceae at Jimma University Teaching Hospital, Ethiopia	PhD	To determine molecular characteristics of extended spectrum β-lactamase producing *Enterobacteriaceae*	Data analysis
Yared Hailye	Characterization of the interaction of microbiota and pathogenic enteric bacteria in an Ethiopian traditional fermented food	PhD	To understand the diversity of fermenting microbes, antimicrobial activity and heavy metal tolerance ability of fermenting Lactic acid bacteria	Data analysis
Mahlet Lemma	Humoral Immune Response to Pneumococcal Vaccination in HIV-1 infected children on ART	PhD	To understand Humoral Immune Response to Pneumococcal Vaccination in HIV-1 infected children on ART	Laboratory work
Berhanu Yitayew	Phenotypic and Molecular Characterization of Potential Pathogenic Bacteria in Akaki River and their Biological Effect on Model Organism, Ethiopia	PhD	To determine potential pathogenic bacteria in the river and its acute and chronic toxicity at the molecular level using a model organism	Laboratory work
Meron Talu	Identification of Akaki River Pollutants; Their biological effect on Livestock and Human in Addis Ababa Ethiopia	PhD	To determine Akaki river pollutants and their biological effect on Livestock and Humans	Laboratory work
Ayichew Seyoum	Molecular Epidemiology of Human Papillomavirus among women with normal and abnormal cervical cytology in Eastern Ethiopia and Development of In-House Multiplex Real-Time PCR Assay for genotyping	PhD	To determine the Molecular Epidemiology of Human Papillomavirus among women with normal and abnormal cervical cytology in Eastern Ethiopia and Development of In-House Multiplex Real-Time Polymerase Chain Reaction Assay for Genotyping	Proposal development
Abdella Gemechu	Virological Treatment Outcome, Drug Resistance Mutations and Genotyping of Human Immunodeficiency Virus among Children and Adolescents Receiving First-line Antiretroviral Therapy, Eastern Ethiopia	PhD	To determine virologic treatment outcomes, HIV drug resistance mutations and genotyping of HIV-1 in Children and adolescents in Eastern Ethiopia from January 2019 to January 2020.	Proposal development
Lopiso Desalegne	Impact of rotavirus vaccine on rotavirus prevalence, molecular genetics and immune responses: An immune-genetic comparative study	PhD	To determine virologic treatment outcomes, HIV drug resistance mutations and genotyping of HIV-1 in Children and adolescents in Eastern Ethiopia from January 2019 to January 2020.	Proposal development
Fiseha Wadilo	Viral and bacterial etiologies and biomarkers of severe acute respiratory infection among under 5 years of children in Central and Southern Ethiopia	PhD	To determine etiologies and biomarkers of severe acute respiratory infection among under 5 years of children	Proposal development

Name	Research topic	Program	Objective	Current Status
Melese Hailu	Molecular epidemiology of carbapenems and colistin resistance versus extended spectrum beta-lactamase producing *enterobacteriaceae* among septicemia suspected patients in Ethiopia.	PhD	To determine the molecular epidemiology of carbapenems and colistin resistance versus extended-spectrum beta-lactamase producing *Enterobacteriaceae* among septicemia suspected patients in Ethiopia	Ethics Review
Biruk Yeshitela	Clinical evaluation and validation of direct whole blood HIV DR assay	PhD	To validate the assay and to determine the role of whole blood HIV-1C pol genome proviral DNA amplification and sequencing assay as an alternative approaches for clinical decision in resource-limited countries with the ultimate goal of standardization and commercialization	Waiting for reagent
Henok Andualem	Cellular phenotypes of innate immune response in associated with response to hepatitis B vaccine in HIV positive and HIV negative adults at ALERT Hospital, Addis	MSc	To characterize cellular phenotypes of innate immunity associated with response to hepatitis B vaccine in HIV positive and HIV negative individuals at ALERT VCT center, Addis Ababa, Ethiopia	Waiting for reagent
Muluye Shemeles	Molecular characterization of Measles virus from confirmed Measles Outbreak in Ethiopia between 2015 and 2017	MSc	To characterize measles virus from samples collected during measles outbreaks in Ethiopia between 2015 and 2017	Waiting for reagent
Mulugeta Kiros	A relative real time HIV transmission networks: a pilot phylodynamics study for real time prevention interventions in Addis Ababa	MSc	To assess real-time phylodynamics of HIV-1 transmission networks among newly diagnosed treatment naïve patients in Addis Ababa, Ethiopia	Laboratory work
Aminu Seman	Phenotypic detection and Molecular characterization of extended-spectrum beta-lactamase genes from clinical isolates of Enterobacteriaceae in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia	MSc	To detect and characterize extended-spectrum β-lactamases genes from clinical isolates of *Enterobacteriaceae* in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia	Sample collection
Tewachew Awoke	Phenotypic and Molecular Characterization Drug Resistance in Klebsiella Pneumoniae Isolated from Patients at Tikur Anbesa Specialized Hospital	MSc	To determine phenotypic and genotypic resistant profiles of *K. pneumoniae* isolated from patients at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia	Sample collection
Shemis Sebre	Selected Microbiome and resistome assessment in Hospital environment in Addis Ababa, Ethiopia	MSc	To characterize common pathogenic bacterial strain and resistance genes(ESBL type, MRSA and VRE) in hospital environment in Addis Ababa, Ethiopia	Sample collection

2. Mycobacterial Diseases Research Directorate (MDRD)

The mission of MDRD is to generate scientific evidence in TB and leprosy that can contribute towards prevention and control of these diseases. The several ongoing and newly initiated research activities in MDRD address epidemiology, diagnostics, therapeutics, and host-pathogen interactions. In the global "End TB" and leprosy elimination strategies, early detection receives major emphasis. Hence, the directorate takes "early diagnosis of TB and leprosy" as a flagship theme.

One of the newly initiated TB research projects in 2018 is the TBRU project which is a collaborative study with Emory University that aims to identify immune signatures that characterize progression from latent TB Infection to active TB disease. Another collaborative study with Queen's College, UK, aims at testing whether MTB DNA in CD34+ cells can identify latently infected individuals. Both projects are aiming for early TB detection. Along with this, a Ph.D. student with Lund university is studying the dynamics of immune control of latent tuberculosis infection in relation to pregnancy.

Community based pulmonary TB screening using health extension workers in the Southern region has demonstrated the value of this approach in detecting undiagnosed cases. Similarly, in leprosy, active case detection and contact tracing community-based studies are being conducted in two high leprosy burden districts, Kokosa in West Arsi and Fedis in East Hararghe zones, through building the capacity of health extension workers to detect leprosy, ensure diagnosis, monitor treatment, screen household contacts and raise community awareness.

To improve TB diagnostics, the "Screen TB" consortium project funded by EDCTP has developed a multiplex lateral flow (LF) strip for simultaneous and quantitative measurement of 6 serum proteins in a single sample at Leiden University Medical College. This signature includes apolipoprotein-A1 (Apo-A1), C-reactive protein (CRP), ferritin, interferon-g induced protein 10 (IP-10), serum amyloid A (SAA) and Interleukin-6 (IL-6). The LF assay showed 86% sensitivity and 78% specificity (72% PPV and 89% NPV) when tested on Ethiopian study participants at AHRI.

The other newly initiated project is TBGEN, a genetic study with the aim of unraveling susceptibility to TB. AHRI is the lead institute and is working with partners from 3 African countries. The goals of this project include establishing a bioinformatics Center and a biorepository at AHRI. An expected outcome is also increased awareness of genetic research in communities with different cultural backgrounds.

Other basic research activities are being conducted with the aim of understanding host-pathogen interaction to eventually contribute to either diagnostics, therapeutics, vaccines or monitoring of treatment outcomes. This includes studies on intracellular signaling and T cell and APC interaction and on monocyte function in TB-HIV co-infected patients. One study measured hormones in different forms of TB and another study characterized B cells in active TB patients. Similarly, in leprosy, a study was conducted with the objective of characterizing FCgamma receptors in ENL patients and another one measured LL37 antimicrobial peptides in different forms of leprosy.

Epidemiological studies that are supported by advanced molecular typing techniques are revealing more information on transmission pathways. In-depth analysis of TB strains may also help in the clinical management of the disease. One of the Ph.D. studies focuses on characterization of Lineage 7 which is an evolutionarily ancient lineage occurring in low frequency but apparently restricted to Ethiopia. It appears to be less virulent than the dominant modern lineages and occurs in low frequency.

One of the major challenges in TB control is a low case detection rate due to technical reasons or due to the nature of or the form of the disease manifestation. The AHRI-APOPO project "Enhanced tuberculosis case detection in Addis Ababa by trained rats" envisages targeting and reaching 60 to 70% of missed cases. During the pilot phase (Mid-March to June 2018), a total of 5721 samples collected from 2946 new presumptive cases were tested. Out of this, the health facilities identified 115 smear-positive cases (3.9%) whereas the project detected 350 additional cases that were missed by microscopy at the health facilities. From July to November 2018, a total of 10,869 samples were collected from 5558 new presumptive cases in 55 clinics. Among these, health facilities found 241 smear-positive cases (4.3%)

whereas the project found 262 additional cases.

AHRI has been exploring the reasons behind the high proportion of extrapulmonary TB in Ethiopia for over a decade. Ethiopia has the largest number of cattle in Africa and bovine tuberculosis is endemic. The risk of further spread has increased in recent years due to intensive farming of exotic breed dairy cattle that are much more sensitive to TB than local zebu. ETHICOBOTS is a consortium project that aims at generating scientific evidence to inform a strategy for bovine TB control in Ethiopia. The research includes clinical and microbiological investigations among dairy farm workers to understand transmission pathways.

The "Post exposure prophylaxis for leprosy (PEP4LEP)" consortium project is a new initiative funded by EDCTP and led by the Netherlands Leprosy Relief organization, AHRI, the German Leprosy Relief Association, and the national TB and Leprosy Control Programs are consortium members and have been working since the concept note preparation with NLR and partners in Africa. The project aims to contribute towards interrupting the transmission of M. leprae by identifying the most effective and feasible method for screening of people at risk of developing leprosy and administering chemoprophylaxis (a single dose rifampicin; SDR) in Ethiopia, Mozambique, and Tanzania.

Improving clinical diagnostics of TB and leprosy using PCR based assays may help clinicians in diagnosing cases easily. Hence, PCR based M. leprae viability assay for clinical application is being assessed in collaboration with the National Hansen's Diseases Program of the USA. The assay is based on the expression of hsp18 and esxA genes, two sensitive molecular indicators that reliably detect viability of M. leprae in tissues without the need for bacterial isolation or immediate processing.

In countries like Ethiopia, it is not common to assess the cost incurred in the prevention of diseases and in the management of affected patients. Costing the delivery of tuberculosis services in Ethiopia from a health systems' perspective (VALUE-TB Ethiopia) is a new initiative by the London School of Hygiene and Tropical Medicine in collaboration with MoH and AHRI. The primary aim of the study is to estimate the cost of TB services to inform an efficient and equitable allocation of resources both to and within TB, by the Federal Ministry of Health and important stakeholders. The study is being conducted in 2 regions, SNNPR and Afar.

In 2018, relatively better community engagement activities have been conducted by most team members and focus group discussions were employed to assess knowledge and attitude to leprosy. Besides this, training was provided to health professionals to share basic knowledge and updates on TB and leprosy and creates awareness on health research.

As a result of the new collaborative projects on both TB and leprosy, we had the opportunity to increase the number of staff in the directorate and several local training opportunities were available to improve quality of research. Formal site assessments conducted by NIH and the African Academy of Sciences (AAS) approved AHRI as a site for the TBRU and TBGEN projects, respectively.

Supporting MSc and Ph.D. students has also continued and their research projects are within the priority of MDRD. Most completed research activities have been published in peer-reviewed journals. Members have also been active in networking and in applying for grants.

The instability in some regions and delay in the procurement process were the major challenges which hindered some activities.

Research Projects	PI/Co-PI	Position	Project Status	Expected completion year	Collaboration
Basic Biomedical Research in TB and leprosy					
1. Molecular Markers and mechanisms of T cell memory in tuberculosis	Meseret Habtamu	PhD	Completed. Papers published and thesis defended	2018	Oslo University
2. Monocyte function in TB, HIV and TB-HIV	Wegene Tamene	PhD	Sample collection completed and flow cytometry analysis is done.	2019	University of Leipzig
3. Dynamics of immune control of latent tuberculosis infection in relation to pregnancy	Fregenet Tesfaye	PhD	Samples collected and luminex based multi cytokine analysis completed	2020	Lund University
4. Could hormones play a role in PTB, SNPTB, EPTB and LTBI?	Yosef Tsegaye	MSc	Lab analysis is completed and thesis is in preparation	2019	Addis Ababa University
5. Antibody breadth in TB	Wassihun Admassu	MSc	Completed, defended	2019	Local
6. B cells in Tuberculosis	Tigist Girma	MSc	Completed, defended	2018	Local
7. The role of FCg receptor in ENL	Dareskedar Tsehay	MSc	Completed, defended	2018	LSHTM
8. LL37 in different forms of leprosy	Mahlet Ousman	MSc	Completed, to be defended	2018	Local
Diagnostics					
1. Evaluation of a novel microbiological test for latent tuberculosis infection in Ethiopia		NA	Ongoing	2019	Multi country
2. *M. leprae* viability assay for clinical application	Linda Adams (NHDP) Kidist Bobosha	NA	Ongoing	2018	Multi country
3. Improving the sensitivity of QFT TB Gold assay using T cell Blast and cell death inhibitory factor	Markos Abebe	NA	Completed		Norway
4. Proof of concept: Immunodiagnosis of pediatric tuberculosis using modified QuantiFERON-TB Gold In-tube test	Markos Abebe	NA	Sample collection is undergoing	2019	Local
5. Performance of Xpert MTB/RIF Assay using fecal specimens for the diagnosis of PTB in children: A systematic review and metaanalysis	Meseret Gebre	NA	Completed	2018	Local
6. Potential of Antigen-specific flow cytometry for the diagnosis of smear-negative TB and pediatric TB	Ahmed Esmael	PhD	Ongoing	2020	Local

Research Projects	PI/Co-PI	Position	Project Status	Expected completion year	Collaboration
Biomarker studies					
1. Evaluation of host biomarker-based point-of-care tests for targeted screening of active TB (Screen TB)	Adane Mihret	NA	Sample collection and lab analysis are completed.	2019	Multi country
2. Immune signatures for detection of progressors among LTBI	Liya Wassie	NA	Sample collection and lab analysis areunderway.	2021	Multi country
3. Immune response patterns among early smear converter and non-converter DOTS initiated tuberculosis patients in selected health facilities in Addis Ababa, Ethiopia	Derbie	MSc	Sample collection	2019	Local
Epidemiological studies					
1. Molecular epidemiology of tuberculosis and role of *M. bovis* in settings with high dairy development in Ethiopia (Ethicobots)	Adane Mihret	1 PhD is attached to the project	Sample collection is completed. Lab analysis is underway.	2019	Multi country
2. Epidemiology of tuberculosis in Southern Ethiopia	Yared Merid	PhD	Completed, to be defended	2019	Local
3. Molecular epidemiology, drug resistance pattern of *M. tuberculosis* and clinical outcome evaluation in Woldiya region, Ethiopia	Elena Hailu	PhD	Sample collected, molecular analysis is done and immunological analysis is underway	2019	Local
4. Genetic Diversity and Drug Resistance Pattern of Mycobacterium Species among Smear Negative Pulmonary Tuberculosis Patients	Alem Alemayehu	PhD	Sample collection is ongoing	2020	Local
5. Epidemiologic determinants of TB disease, timeliness of obtaining proper diagnostic services and related expenditure	Ezra Shimelis	PhD	Completed, to be defended	2018	Local
6. Active case detection and household tracing in Kokosa wereda	Tsehaynesh Lema	PhD	Sample collection is completed. Lab analysis and thesis preparation are underway.	2019	Multi-country
7. Mycobacterium leprae infection among Household contacts of leprosy patients in Fedis wereda (includes Ultrasound based detection of nerve enlargement as early diagnosis of leprosy)	Kedir Urgesa	PhD	Ethical approval is obtained. Community knowledge and attitude assessment are done. Preparation for sample collection is being done	2020	Local
8. An integrated approach to unraveling susceptibility to tuberculosis in Africa (TBGEN)	Abraham Aseffa	PhD students will be attached	Ethical approval from AAERC is obtained and waiting for approval from NERC.	2021	Multi Country

Research Projects	PI/Co-PI	Position	Project Status	Expected completion year	Collaboration
Operational Research					
1. Chemoprophylaxis for leprosy: comparing the effectiveness and feasibility of a skin camp intervention to a health centre based intervention. An implementation trial in Mozambique, Ethiopia, and Tanzania.	Kidist Bobosha	PhD student will be attached	Startup meeting was conducted. The proposal is being finalized for Ethical review submission.	2022	Multi country
2. MDR in EPTB	Sosina Ayalew	NA	Sample collection is underway	2019	Local
3. Occupational hazard of TB in different health facilities	Jagmar Worku	MSc	Ethical approval is obtained. Sample collection will start in Jan 2019	2019	Local
4. Enhanced case finding among presumptive TB cases attending TB clinics in Addis Ababa (routine case finding) and mass screening of inmates and prison staff in 35 prisons across Ethiopia (active case finding)	Negussie Beyene	NA	Sample collection and lab analysis are underway. The prison study has obtained ethical approval and will begin soon	2023	APOPO
5. Spatial Analysis of Tuberculosis Clustering in Dale District, Sidama Zone, Southern Ethiopia: A Population-Based Prospective Cohort Study	Markos Abebe	NA	Sample collection and lab analysis are underway.	2020	Norway
6. Value TB	Martha Minwyelet Endashaw Nadew	NA	Piloting completed. Data collection will start in Jan 2019	2019	LSHTM
7. TB in OPD	Marek Lali Kidist Bobosha Berhanu Seyoum Liya Wassie	NA	Ethical approval is obtained. Data collection will start in Feb 2019	2019	LSHTM

3. Malaria and Neglected Tropical Diseases Research Directorate (MNTDRD)

The Ethiopian Federal Ministry of Health (FMoH) has been implementing the Health Sector Development Program (HSDP) over the last two decades. This has brought tremendous gains in improving the life expectancy and quality of life of citizens. Consolidating the move, the FMoH launched the Neglected Tropical Diseases (NTDs) strategic plan and revised the malaria diagnosis and treatment guidelines with the aim to eliminate NTDs as a public health problem by 2020 and realize a malaria disease free Ethiopia by 2030. The MNTDR Directorate is an active member of the National NTD Task Force and the Technical Working Group for the National Onchocerciasis Elimination Program. In line with this, our Directorate has focused its efforts on government priority areas to provide evidence for programmatic input.

Evidence produced by the Directorate's malaria research group has demonstrated:

1. The utility of serology as a tool to evaluate the performance of malaria control and elimination and guide intervention,
    - overcomes the limitations imposed by traditional microscopy approaches
    - feels a gap in affordable tools as elimination targets are approached
    - has implications on policy or national guideline development
2. Clustering of asymptomatic malaria infections around passively detected infections with implications regarding hotspots that potentially fuel transmission
    - Contributed new knowledge on malaria transmission dynamics – hard evidence that asymptomatic infections cluster around diseased individuals
    - Has strategic relevance on identification and management of hotspots
3. Low and patchy distribution of G6PD deficiency, with implication to the safe use of 8-aminoquinoline drugs such as primaquine and tafenoquine
    - Provided data on risk levels in different geographic areas and endemicity
4. Very low performance of malaria microscopists that need attention in consolidating the gain in the fight against malaria
    - Relevant to the program alerting to the need for better education and quality control
5. A reversal of PfMDR1 mutation in P. falciparum, implicated as a prerequisite phenomenon for artemisinin-based treatment failure against P. falciparum in sub-Saharan Africa.
    - Generated data contribute to a good foundation for continued monitoring of genetic signatures of resistance which will inform malaria treatment policies.
6. The genetic implication of Low complexity region in P. vivax malaria, a new way of considering population genetics and immune escape studies.

The Directorate's research on NTDs has a direct beneficial effect to the control efforts of disease. An example is its work on improving community-based treatment or mass drug administration (MDAs). The Directorate is supporting the programmatic implementation of MDA through the provision of alternative local capacity in producing diagnostics, technical training on implementation and evaluation. For details see the ongoing and completed projects in subsequent sections.

A Completed Projects: Published/ Under Review

The epidemiology of malaria in Ethiopia differs from that in most of sub-Saharan Africa: prevalence is generally lower, highly heterogeneous, spatial and temporal characterized by frequent epidemics. Uniquely, Plasmodium vivax is endemic in most parts of Ethiopia.

Following policy change in malaria control and intervention that had begun in 1998, and intensified at the beginning of the Millennium (2004/2005), Ethiopia has achieved a substantial reduction in cases and deaths due to malaria. While most malaria-endemic countries reported a substantial increase in malaria burden in the last two years, Ethiopia is among four countries that sustained a decline in malaria burden [2]. The country is on track for a 40% reduction in incidence by 2020 [2]. In line with the global trend and motivated by these achievements, the government of Ethiopia has set an ambitious plan for shrinking malaria endemicity and achieving zero indigenous transmission in selected districts by 2030. As transmission intensity declines, finding, quantifying, and treating the sparse and heterogeneously distributed remaining infections results in operational challenges. Improved and validated tools are required to estimate levels of disease transmission (stratification), to allocate appropriate interventions, and quantify their impact and, importantly, interrupt transmission. In such a situation, traditional approaches such as parasitological and entomological measures that have played a central role in malaria control and intervention in high transmission settings will not now suffice to guide intervention in low transmission settings because numbers of positive observations (infected mosquitoes or humans) are low. These measures are also affected by environmental changes and this can vary rapidly and is affected by season. Utilization of antibody responses to malaria antigens is a low-cost alternative approach when measuring malaria transmission intensity in low-endemic settings [3]. When combined with age, seroconversion rates reflect cumulative malaria exposure in a population and can be used as a robust measure of malaria transmission intensity. Serological responses to parasite antigens are informative tools to reflect the history of malaria, monitor malaria control programmes, and have the potential to uncover heterogeneity in the effectiveness of malaria control interventions.

Transmission trends over time are critical for the understanding of drivers and for planning detection and control measures. An example is the study conducted in one of the districts chosen by the FMoH for malaria elimination, and meantime for studies into current and past burden of malaria, Babile, an endemic area located in the Eastern Oromia region. A cross-sectional survey was conducted in 14 villages of the district.

P. falciparum and P. vivax infection status were evaluated by microscopy and nested polymerase chain reaction (nPCR) to examine the current burden of malaria and history of malaria transmission.

The prevalence and density of anti-malaria apical membrane antigen-1 (AMA-1) were assessed to generate age-seroprevalence and antibody titre plots. The current infection prevalence by microscopy and nPCR was 1.4% (16/1144) and 5.0% (57/1144) for P. falciparum, and 0.4% (5/1144) and 3.6% (41/1144) for P. vivax, respectively.

Seroconversion curves showed a strong indication for a decline in exposure, 15.5 years for P. falciparum and 11.5 years for P. vivax prior to sampling. A similar rate of decline was reported by another group in another serological study, in the northwestern part of the country [4].

The current findings support evidence for a decline in malaria burden and demonstrate that malaria transmission is still ongoing in the study area, arguing in favor of continued and tailored control efforts to accelerate the stride towards elimination efforts. Whilst importation of malaria is possible, and an important source of infection in several low-endemic settings, our findings of detectable serological responses in children, often accompanied by PCR-detected infection, suggest that there is still non-negligible local transmission. Novel tools that can interrupt transmission and improved strategies on enhanced community case management to find the sparse remaining infections that plausibly maintain the infectious parasite reservoir play paramount importance in accelerating the stride towards elimination.

The striking variation in malaria indicators between villages highlights the need for better understanding of variation in the uptake of interventions and potentially tailor interventions to the local needs to accelerate elimination efforts in the region. Serology can be adapted as an alternative tool to monitor the malaria elimination effort with relatively less technical demand. The limited number of examined villages and villagers is a limitation of this study. Future larger studies might help generate high-resolution evidence on village level heterogeneity. Although AMA1 is a well-characterized marker of historical exposure at the population level [5], malaria exposure might have been missed by only measuring responses to single antigen in the present study. Further information could be generated by measuring other antigens and also short-lived antibodies to indicate recent exposure to infection across all ages [6]. In order to preserve and build on the control milestones achieved in the last two decades and accelerate the progress to elimination, the need for innovation to achieve malaria elimination is greater than ever. Above all, robust research is critical for the country to be able to build evidence-based policies and guidelines in a locally tailored manner.

The distribution of malaria infections is heterogeneous in space and time, especially in low endemic settings approaching elimination. Understanding malaria transmission patterns and approaches to identify pockets of transmission may accelerate elimination efforts. In Adama district, Ethiopia Belachew M and colleagues (Manuscript in preparation) evaluated the clustering of P. falciparum and P. vivax asymptomatic infections around passively detected malaria patients (n=18). Household members and immediate neighbors (n=498) were examined by a rapid diagnostic test, quantitative PCR (qPCR) and genotyping of 26 P. falciparum neutral microsatellite markers. A similar number of controls without malaria infection (n=18) and neighbors (n=453) were examined. Evidence for geographic clustering of infections and genetic relatedness were assessed for P. falciparum and P. vivax separately. In addition to the clinical patients, 46 P. falciparum, 16 P. vivax and 10 mixed asymptomatic infections were detected in the community by RDT. Family members who lived in households of clinical P. falciparum patients were more likely to have qPCR detected infections (20.7%, 12/58) than individuals in control households (9.5%, 41/433; OR, 2.5, 95% CI 1.2 – 5.1; P = .012). Whilst there was no evident clustering of P. vivax cases in households of clinical malaria cases (P = .837) whilst individuals who lived in households with ≥1 RDT-confirmed P. vivax infection (both symptomatic and asymptomatic) were more likely to have qPCR detected infection (25.0%, 17/68) compared to individuals in households without RDT-detected infections (11.8%, 94/795; OR, 2.5; 95% CI, 1.4–4.5; P < .0045). Infections detected in the same household showed stronger evidence for genetic relatedness compared to infections detected between households. Interestingly, there was strong evidence for genetic relatedness among clinical infections. Conclusion: The use of conventional diagnostics, supported by a detailed genotyping approach, provide evidence for a strong relatedness of infections within households and suggest that genetically related parasites are responsible for clinical P. falciparum infections recruited during the short study period. These findings may support a rational approach to reactive case detection strategies, as a plausible approach to find more infections in Ethiopia.

One of the challenges during the transition from malaria control to elimination is the capability to maintain the competency of microscopists at malaria-endemic areas. Ethiopia aimed to diagnose and treat all clinical malaria within 24 hours of fever onset in its stride to eliminate the disease by 2030. Microscopy will remain the mainstay for diagnosis at Health Center and Hospital level. Thus, continuous evaluation and performance upgrading of malaria microscopists is one of the cornerstones. Chali S and colleagues (Malaria Journal, under revision) assessed the performance of malaria microscopists compared to reference readers in diagnosing, identifying the species, and quantifying the parasitemia in Oromia region, Ethiopia. A facility based cross-sectional study was done in 86 districts from January 2017 to June 2018. Panel slides with known Plasmodium species, diagnostic blood stage and parasite density were used. Sociodemographic, educational, in service training and the routine practice of participants were captured. Sensitivity, specificity, percent agreement, and kappa score were calculated to assess the performance of professionals. A total of 174 malaria microscopists were enrolled in this study. Overall, we observed a low performance that could threaten the malaria diagnostic service; only 17% and 30% of participants correctly read all positive and negative slides respectively and 22.4% (273/1218) of the distributed slides were correctly quantified. Compared to the reference readers they had poor competence in diagnosing (74.3% Agreement and 0.45 Kappa) and species identification

(71.2% Agreement and 0.4 Kappa). Most of the study participants, 41% and 40% were graded as "in-training" with respect to species identification and identifying the diagnostic stages respectively. The performance of the malaria microscopists was poor. Therefore, in-service training/retraining and supportive supervision are needed to raise and maintain their competence.

The other challenge in elimination settings and a lesson we should learn from the previous eradication efforts is the development of resistance to antimalarial drugs as these are one of the most important tools in the fight against malaria together with vector control tools. In Ethiopia, Artemether-Lumefantrine (AL) and chloroquine are the first line treatment drugs for uncomplicated P. falciparum and P. vivax cases, respectively. P. falciparum developed resistance to most of the antimalarials over the past 50 years including against chloroquine and sulfadoxine-pyrimethamine that had spread from the hotspot (Thailand-Cambodia border) to the rest of the world (White 2004). Treatment failure to the current first-line regimens including artesunate monotherapy (Dondorp, Nosten et al. 2009) and combination therapies (Carrara, Lwin et al. 2013, Leang, Barrette et al. 2013) is spreading at the same region and history might repeat itself. Recently, evidence is emerging that selections in Pfmdr1 genes are ongoing with implications on susceptibility to the Artemisinin combination therapy in Africa. Also, more drug resistance was reported in asymptomatic infection that corroborates the evidence from experimental models which demonstrated that under low transmission settings within-host competition favors the establishment of drug resistance. Hailemeskel E and colleagues (Manuscript in preparation) assessed the prevalence of Pfcrt-K76T and Pfmdr1-N86Y among asymptomatic malaria cases under different malaria transmission settings. Community based cross-sectional surveys were conducted from October to December, 2016 in Gambella and Benishangul-Gumuz regions and from July to November, 2017 in Oromia region of Ethiopia. Dried blood spot samples (DBS) were collected from finger pricks. A total of 183 18srRNA-nPCR confirmed asymptomatic P. falciparum samples were genotyped for Pfcrt-K76T and Pfmdr1-N86Y codons using PCR-RFLP techniques. The Pfcrt-K76T and Pfmdr1-N86Y codons were successfully genotyped for 166 samples. The distribution of Pfcrt-76T mutant haplotypes was higher in Adama (96.67%) and Harar (90.0%) compared to the prevalence detected in Gambella (32.08%) and Benishangul-Gumuz (47.83%) areas. Overall, while a mixed haplotype of Pfcrt-76K/T was detected in only 13 (8%) samples; the Pfmdr1-86N wild type was fixed in Harar and Adama areas with similar higher proportions in Gambella (90.38%) and Benishangul-Gumuz (77.27%). After over two decades of the introduction of AL in Ethiopia, Pfcrt-76 K wild type was not significantly selected unlike Pfmdr1-86N wild type which was selected for across the study sites. As selection for this type has been implicated with AL drug tolerance in sub-Saharan Africa, the assessment of other Pfmdr1 codons and a country wide assessment is recommended.

One of the most important strategies in elimination settings is to reduce/block transmission from the remaining sparse human infections to mosquitoes that might potentially refuel resurgence of malaria. Among the transmission blocking strategies are vaccines and drugs that target gametocytes that are the only transmissible stages of the parasite and are not particularly affected by almost all antimalarials that are efficient in alleviating the pain and symptoms of malaria. Tadesse F and collaborators reviewed current evidence on the relevance of gametocyte sex ratio in determining infectiousness and summarized data on new markers for gametocyte quantification in one of the most reputable journals in the field of parasitology (Trends in Parasitology December 2018). A mosquito needs to ingest at least one male and one female gametocyte to become infected with malaria. The sex of P. falciparum gametocytes can be determined microscopically but recent transcriptomics studies paved the way for the development of molecular methods that allow sex-ratio assessments at much lower gametocyte densities. These sex-specific gametocyte diagnostics were recently used to examine gametocyte dynamics in controlled and natural infections as well as the impact of different antimalarial drugs. It is currently unclear to what extent sex-specific gametocyte diagnostics obviate the need for mosquito feeding assays to formally assess transmission potential. Messele A and colleagues (Malaria Journal, under review) presented their findings on P. vivax merozoite surface protein 3α (Pvmsp3α) that is one of the vaccine candidate genes which has shown strong association with immunogenicity and protectiveness. Its use is however complicated by evolutionary plasticity features which enhance immune evasion. Low complexity regions (LCRs) provide plasticity in surface proteins of Plasmodium species, but its implication in vaccine design remain unexplored. We performed population genetic, comparative phylogenetic and structural biology

analysis of the gene encoding PvMSP3α. We found three LCRs in PvMSP3α block II. Both the predicted tertiary structure of the protein and the phylogenetic trees based on this region were influenced by the presence of the LCRs. Furthermore, LCRs were mainly B cell epitopes; exclusively within or adjacent. In addition, repeat motifs mimicking one of the B cell epitopes was found within the PvMSP3a block II low complexity region. This particular B cell epitope also featured rampant alanine substitutions which might impair antibody binding. Our findings indicate that PvMSP3α blocks II possess LCRs which might confer a strong phenotypic plasticity. The phenomenon of phenotypic plasticity and implication of LCRs in malaria immunology in general and vaccine candidate genes in particular merits further exploration.

Based on preliminary data generated from completed studies, we are currently undertaking detailed evaluation of the duration of asymptomatic infections and their infectivity to mosquitoes in a longitudinal study. Host, parasite and environmental factors are also among the topics that are aimed to be investigated in detail. To generate evidence on the effect of the continued drug pressure on the parasite population in Ethiopia, we are also investigating the investment of the parasite on growth vs reproduction within the host. Previous studies had revealed that parasites start investing more on transmission than within host reproduction when under drug pressure.

4. Non-communicable Diseases Research Directorate (NCDRD)

The NCD activities at AHRI to date have principally involved cancer research, NCD risk factor screening in the context of the CEBHA international consortium, and podoconiosis via the Wellcome trust Brighton-Sussex medical school collaboration.

I. Cancer

In the field of cancer research, we have concentrated on hematologic malignancies, including acute and chronic leukemia, Non-Hodgkins (NHL) and Hodgkins Lymphoma. Collectively, these malignancies have been estimated to represent the third leading cause of death by cancer in Ethiopia. In addition, we have undertaken several studies on breast cancer, the second leading cause of cancer deaths in the country.

In the field of cancer research, much of the work at AHRI has focused on improved diagnostics and prognostics, hence our plan has been to gain research experience in modern methods of diagnosis, apply these in clinical scenarios, and wherever possible to assist in the implementation of these strategies to clinical diagnosis in clinical care centers in the country. We will thus organize the review of current activities around techniques introduced.

A. Flow Cytometry

A major emphasis has been placed on development of diagnostic capacity for leukemia immunophenotyping by flow cytometry. Although peripheral morphology together with cytogenetics—where available—has represented the traditional diagnostic focus, in recent years flow cytometry, as well as molecular biology approaches to evaluate genetic aberrations, have become important tools supplementing traditional methods for both diagnosis and prognosis. Because of AHRI's longstanding experience in flow cytometric phenotyping of the immune system, it was a logical starting point in cancer diagnosis. As MSc projects for students, we have now completed two studies, with a third nearly complete, and these have been instrumental in establishing both the usefulness and feasibility of flow cytometry in this setting. An additional PhD student, Jemal Alemu, will confirm these studies and importantly assess the impact of flow cytometric diagnosis on clinical outcomes, therapy of which may (in part) be dependent on flow results. Having completed pilot studies in flow cytometry we have catalyzed the introduction of this diagnostic modality at Tikur Anbessa Specialized Hospital, and discussions for the introduction of flow cytometry at peripheral sites in the country such as Jimma University which now are providing therapy for leukemia patients has begun.

B. Immunohistochemistry

Capacity for Immunohistochemistry (IHC) is limited in Ethiopia and increasingly demanded by pathologists for diagnosis and prognosis of solid malignancies in Ethiopia. In the NCD division we currently have one PhD project with a major focus on IHC, for the diagnosis of Hodgkin's Lymphoma (HL), and have planned two additional studies.

Hodgkin's lymphoma is a distinct type of malignancy featuring rare tumor cells of B cell origin, termed Reed Sternberg cells which comprise < 1 % of cells present in the affected lymph node. These cells occur in a background of a large heterogeneous infiltrate of reactive non-malignant cell populations. The infiltrating cells include B and T lymphocytes, plasma cells, macrophages and histiocytes, fibroblasts, mast cells and eosinophilic granulocytes. The composition of reactive cells defines the various subtypes of HL. While histological stains have classically been utilized, newer immunohistochemical approaches aid specific diagnoses. The goals of the current study are to evaluate Hodgkin's Lymphoma from

excised and fixed lymph nodes using primarily immunohistochemical and RT-PCR approaches. Thus, PhD student Makka Ali has received training in multiple histological techniques for standard H&E based diagnosis, phenotypic immunomarker analysis, and detection of Epstein Barr Virus (EBV) surface protein and cellular EBV mRNA by in situ hybridization. The identification of EBV is particularly useful as it is a common infection thought to contribute to tumorigenesis. Future work will expand sample number and included further training at Lund University to evaluate gene duplication as a mechanism of molecular overexpression of PD-1, a molecule expressed by Reed Sternberg cells which may inhibiting potentially protective cytotoxic T lymphocyte responses to the tumor.

We are planning two additional projects utilizing immunohistochemistry, for breast cancer and Non-Hodgkin's lymphoma diagnosis, but the projects are not yet finalized. In addition, as we gain familiarity with these approaches, we anticipate developing collaborations with peripheral universities in the country to transfer this technology,

C. Genetics and molecular biology

Diagnostic and prognostic tests for cancer are increasingly relying on more sophisticated molecular assays to identify genetic aberrations which may contribute to tumorigenesis as well as aiding the classification of subtypes of malignancies and predicting therapeutic responses to different drugs.

In combination with flow cytometry, PhD student Jemal Alemu will begin to examine genetic aberrations associated with acute leukemia, utilizing RT-PCR analysis as well as fluorescent-in-situ hybridization (FISH). This will project will focus on common aberrations, including the fusion transcript RUNX1-RUNXT1 common to acute myelogenous leukemia (AML) type M2, the fusion transcript PML-RAR common to AML M3, the fusion transcript CBFB-MYH11 common to AML M4,NPM1 mutations common to AML M1, and the ETV6-RUNX1 and ABL-BCR translocations common among B-cell ALL. Identification of these aberrancies solidifies the diagnosis, and also provides important prognostic information to clinicians for selection of appropriate therapy. Jemal's project has been ethically approved, he has already begun flow phenotyping, and he will soon receive FISH training at the University of Michigan.

Chronic myelogenous leukemia is associated with the pathognomonic chromosomal translocation which brings the BCR and ABL gene together forming a fusion gene, identified as the so called "Philadelphia chromosome" by cytogenetic analysis, and leading to the overexpression of a tyrosine kinase, which is the target of a class of drugs, the prototype of which is imatinib. Imatinib therapy is remarkably successful in treating CML but eventually leads to drug resistance mutations in about 10% of cases. Molecular sequencing of the ABL-BCR fusion gene to identify drug resistance mutations is the current gold standard diagnostic modality to characterize treatment failure patients and directing therapy to alternative tyrosine kinase inhibitors. The goal of PhD student Samuel Kinde, will be to characterize levels of BCR-ABL fusion products by RT-PCR to definitively identify suspect drug resistant CML, perform sequencing to identify mutations, and develop a ligation PCR approach suitable for diagnosis of drug resistance in Ethiopia. He has received training at University of Leipzig in appropriate molecular methods, has received ethical clearance, and is currently accumulating CML samples.

Considerable attention is being given to minimally invasive blood biomarker approaches for diagnostic and prognostic value. Such approaches may be particularly valuable either for early diagnosis of many cancers such as breast cancer at a stage when treatment is potentially curable, or to guide more appropriate therapy specific for a given subtype. As a first step, we have initiated a study evaluating expression of plasma miRNA among breast cancer patients compared with healthy controls. The expression level of miR-21, which inhibit phosphatases involved in down regulation of cell signaling pathways and one of the most frequently upregulated miRNA in solid tumors, and miR-195, known to target the cell signaling raf-1 gene and promote tumor cell apoptosis and decreasing breast cancer viability were significantly higher in the serum of breast cancer patients than healthy controls. Levels of two other markers previously reported to be associated with breast cancer, miR145 and miR-130b, did not different between patients and controls in our study. These results demonstrate associations with miRNA levels and breast cancer in Ethiopia and suggest further research into miRNA expression in

breast cancer is warranted in this setting.

D. Pharmacodynamics, pharmacokinetics and pharmacogenetics

Drug therapy is a cornerstone of modern medicine, but drug toxicities and inadequate biological effects can contribute to suboptimal outcomes. There are many reasons for this, not least of which is patient compliance and inadequate education, but it is well documented that drug metabolism is highly variable from patient to patient and can be influenced by many factors including overall organ function (such as by liver and kidney), as well as host genetic polymorphisms of metabolizing enzymes, in particular the cytochrome P450 system. The end result is the patients may have too low or too high levels of the drug. Although such effects impact all disciplines of medicine, patient variability in administered drug levels is particularly critical for chemotherapy drugs for cancer which typically have a very narrow therapeutic range. Significant toxicities, particularly on regenerating tissue such as bone marrow or hair, result from too high a level, and suboptimal levels can contribute to cancer relapse with drug resistance. Research into the many factors which impact chemotherapy drug levels, as well as defining simple assays or approaches which can be applied to help guide clinicians in patient treatment protocols is likely to lead to improved patient outcomes. AHRI is supporting several projects along these lines.

Hematologic toxicities related to standard breast cancer chemotherapy regimens involving 5-fluorouracil, doxorubicin and cyclophosphamide represent major complications and require frequent dose adjustments and delays in drug administration. Host drug metabolism involves many genes, including those of the highly polymorphic cytochrome P450 system, and allelic variants of the many such genes impacts drug levels and hence chemotherapy and toxic effects. As a part of the study of PhD student Jemal Hussein, key alleles of the CYP2B6, CYP3A5, CYP2C9, CYP2C19, CYP2J2 and POR genes were evaluated. We observed associations between hematological toxicity and CYP2J2*7 (CYP2J2 gene, allele 7) and POR*28 (POR gene, allele 28), and suboptimal therapy or relative dose intensity with CYP2B6*6 (CYP2B6 gene, allele 6). These indicate that some breast cancer patients' responses to chemotherapy regimens may be better predicted by CYP genotyping.

6-Mercaptopurine (6-MP) is a crucial chemotherapy drug utilized in maintenance phase therapy for acute lymphocytic leukemia (ALL). Unfortunately, its metabolites can lead substantial bone marrow toxicity. Many enzymes are involved in the metabolism of 6-MP, the most well studied being thiopurine methyltransferase (TPMT). Genetic polymorphisms in this gene lead to significantly different levels in different patients, contributing to unpredictable toxicity; hence TPMT genotype and levels are routinely evaluated in Western settings to guide dosing in patients undergoing 6-MP therapy. In the current study, PhD student Awol Mekonnen will enroll 100 ALL patients and will assess genotypes and phenotypes of TPMT as well as other enzymes and cell membrane transporters involved in 6-MP metabolism, and correlate genotypes and levels with toxicity captured from patients' charts.

A final project is directed towards Chronic Myelogenous Leukemia (CML) patients. As previously mentioned, such patients are currently receiving the tyrosine kinase inhibitor imatinib, but the drug is well known to lead to resistance in about 10% of the patients. The current study, by PhD student Yohannes Giorges, will focus on the pharmacodynamic, pharmacokinetic, and pharmacogenetic aspects of imatinib in these patients. Blood levels of the drug attained within individual patients, and identification of patient factors which impact such levels will be assessed. Such factors include compliance and concomitant use of other medications, cytochrome P450 polymorphisms, as well as renal and hepatic function. Pharmacokinetic properties will be related to the patient's biological response to therapy, including recorded drug related toxicities and reductions in the imatinib target molecule, the BCR-ABL1 fusion product. The project has received ethical approval, and patient sample collection is underway.

II. Other NCD

Diabetes, hypertension, psychiatric illness and chronic respiratory disease are many other non-communicable diseases gaining international attention due to their rapid increase in prevalence over the past two decades and their predicted impact on health care systems. Recent studies in Ethiopia have confirmed that about half of all mortality in the country is due to non-communicable diseases, of which the aforementioned diseases contribute significantly.

In approaching NCD research at AHRI we have taken two approaches. The first is through a multinational CEBHA consortium involving multiple institutions throughout Africa and focusing on NCD. The second has been to explore topics in multiple discussions with leading clinicians in the country to assist in defining priority areas for research.

CEBHA (Collaboration for Evidence-Based Healthcare and Public Health in Africa) is a consortium of multiple African partners, including Ethiopia, Malawi, Rwanda, S. Africa and Uganda, and funded by the German Ministry of Education and Research. The emphasis is on non-communicable diseases. There are multiple research tasks, two which AHRI is involved in: The first has an overall objective of establishing and monitoring a pilot intervention by community health care workers to screen community members for cardiovascular disease (CVD) risk factors. This in turn is divided into three subtasks: to pool existing STEPS data from multiple countries to evaluate the accuracy of risk definition by substituting cholesterol levels with body mass-index—as a means to reduce screening costs, 2) to explore community attitudes towards risk and chronic disease, in a qualitative study, and 3) to training community health care workers to execute and evaluate an initial screening of 1000 community members for CVD risk. The second task is to evaluate comorbidities of HIV patients including diabetes, hypertension and mental illness, and develop and evaluate improved integrated strategies to manage these problems for HIV patients. At AHRI we will only be involved in the initial evaluation of co-morbidities. PhD student Haile-Michael's thesis will be focused on these two tasks, and include as well an independent economic analysis of the cardiovascular screening approach for Ethiopia. A large part of the CEBHA funding is oriented towards capacity building and skill development in evidence-based medicine The capacity building and skills training activities within the grant are numerous, and stress importance of evidenced based medicine and public health, as well as integration of knowledge gained from research activities into policy.

Apart from CEBHA we have contacted multiple clinicians in multiple departments at Tikur Anbessa hospital to explore potential future research projects. Over the course of several meetings we probed the priorities of diabetes experts at Black Lion from a clinical care perspective, as well as to consider potential research topics of interest to them. From a clinical care perspective, high priorities were identified as patient education as well as screening efforts for diabetes. From a research perspective high priority was placed upon establishing a large prospective cohort of diabetes patients to 1) evaluate the prevalence and rate of complications of diabetes over time, and 2) as a source of patients for nested research studies aimed towards evaluating improvements in patient care (patient education, integrated care, improved therapy regimens). We are seeking funding for this. Many other smaller research projects were also identified of interest to them (outcomes of gestational diabetes, pathogenesis of malnutrition related diabetes, prevalence of non-alcoholic steatosis among diabetes, etc).

We have also had multiple discussions with member of the Pulmonary and Critical Care Department at Tikur Anbessa and have identified among chronic respiratory disease, the prevalence, risk factors and role of beta-agonists and inhaled steroids to improve outcome for wood stove related chronic obstructive pulmonary disease (COPD) as a high priority.

III. Podoconiosis

Podoconiosis or non-filarial elephantiasis is a peripheral lymphoedema associated disease thought to be related to long term exposure of bare feet to red clay soil. Recent work exploring the genetics

of podoconiosis has revealed a significant association with HLA-DRB0701 along with HLA-DQA201 and HLA-DQB201, all of which are in linkage disequilibrium. This strongly implies a T-cell mediated HLA class II restricted recognition of antigen presenting cells in the disease pathogenesis. In order to further characterize the immune system of such patients PhD student Mikias Negash plans on comparing phenotypic characteristics of T cell subsets as well as potential antigen presenting cells such as monocyte-lineage cells and dendritic cells in the blood and peripheral lesions of such patients. In addition, serum will be analyzed for cytokine and mRNA biomarkers to identify putative disease specific markers. Finally, attempts will be made to evaluate whether putative minerals known to be present in the soil are capable of selectively stimulating T cells from podoconiosis and not control patients. The proposal is under ethical review and reagents have been ordered.

Student Projects				
Project Type	PI name	Title	Status	Affiliates
PhD student	Meka Ali	Immunologic, Virologic and Genetic correlates of Hodgkin's lymphoma in Ethiopia	IRB approval, training received, most sample collected	TASH, Lund U.
PhD student	Jemal Heme	Acute Leukemia Characterization by Flow Cytometry, Cytogenetics, Molecular Markers and Its Association with Viral Infections at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia	IRB approval, overseas training soon to be initiated	TASH, U Mich
PhD student	Samuel Kinde	Gene Expression Profile of Bcr-Abl1 Fusion protein (P190,P210) versus Differential Sensitivity to Tyrosine Kinase Inhibitor Drugs' Therapy Among Ethiopian Chronic Myeloid Leukemia Patients Attending at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia.	Training received at Leibnitz, sample collection begun	TASH, Leibnitz U
PhD student	Yohannes Giorges	Pharmacodynamic, Pharmacokinetic and Pharmacogenetic Study of Tyrosine Kinase Inhibitors (TKIs) with Emphasis on Imatinib Mesylate in the treatment of the Ethiopian Chronic Myelogenous Leukemia(CML) Patients	IRB approved, midway through sample collection	TASH, AAU
MSc student	Tarik Sime	Circulating breast cancer-associated microRNA expression in serum as biomarkers for breast cancer detection	Completed, pending thesis defense	TASH
PhD student	Jemal Hussein	Pharmacokinetic and Pharmacogenetic Studies of Cyclophosphamide among Patients with Breast Cancer in Ethiopia	Thesis nearly completed, two manuscripts submitted, one published	TASH, Karolinska, AAU
PhD student	Awol Mekonnen	Genetic analysis of prognostic markers and Pharmacogenetic study of 6-Mercaptopurine in acute lymphoblastic leukemia patients in Tikur Anbessa specialized hospital, Ethiopia	IRB proposal submitted	Radboud Univ, Holland; TASH, AAU
PhD student	Mikias Negash	Host immune responses and their role in the pathogenesis of podoconiosis in Amhara Regional State, Northern Ethiopia	IRB approval, study sites identified, lab protocol optimization commenced	U. Brighton-Sussex
CEBHA	Hailemichael Getachew	Collaboration for evidenced-based health care and public health in Africa	IRB proposal submitted	PI Harriet M, Mekere Univ

5. Clinical Trial Research Directorate

The clinical trial directorate has been involved in several projects related to TB including STREAM, SIMPLICITB-008, VALUE-TB, PAVIA and others; studies on the impact of traditional medicines on psoriasis and other illnesses; and bioequivalence clinical studies.

TB Projects

Two tuberculosis clinical trials, STREAM and SIMPLICITB-008, have focused on new protocols to reduce the duration of therapy for both conventional drug sensitive TB, and drug-resistant and multi-drug resistant TB. Such shorter protocols offer the potential for greater patient compliance potentially leading to improved outcomes, as well as significant cost reductions.

The STREAM trial has been an ongoing major study since 2012 to investigate shorter duration protocols to treat MDR-TB. Together with clinical partners in S. Africa, Mongolia, Viet Nam, and within Ethiopia at St. Peter's hospital, the AHRI clinical trial team has completed the first phase, with preliminary results presented by WHO as a landmark study. A total of 454 patients, including 124 from Ethiopia, were enrolled and randomized to either the existing 20 month WHO regiment consisting of multiple injectable and oral TB drugs (regiment A), or a 9-month regiment consisting of moxifloxacin, isoniazid, clofazimine, and ethambutol for 40 weeks, supplemented by kanamycin, isoniazid and prothionamide for the first 16 weeks (regiment B). Favorable outcomes for the 9-month regiment (78%) were not inferior to the 20-month regiment (80%); both regiments experienced similar rates of adverse events. The manuscript summarizing the study is under review at the New England Journal of Medicine.

The second phase of the project is designed to evaluate the effectiveness of a 9-month regiment based on the new MDR-TB drug bedaquiline (regiment C), in comparison with the 9-month regiment B defined in phase I. In addition, regiment D, a bedaquiline based 6-month modification of regiment B will be compared with to regiment B. Since 2016, 100 patients have been pre-screened, 44 further screened leading to enrollment of 20 patients to date. 6 patients have been randomized to regiments B, C, and D. Two patients were initially randomized to regiment A, but because of the success of phase I, that cohort has no longer been continued. Of the 20 patients, 15 have completed therapy, the others continuing therapy. There has been no subject loss to follow-up or withdrawal of consent. The STREAM trials have been funded by USAID, MRC (phase I) and USAID, MRC/DFID and Janssen Research and Development (phase II).

SIMPLICITB-008 is a clinical trial evaluating a) a new 4-month treatment regimen for standard drug-sensitive smear-positive TB in comparison with the standard 6-month course, and b) the evaluation of drug resistant (DR-TB, not MDR TB) using a new 6-month regiment. The new 4-month regiment utilizes bedaquiline, pretomanid, moxifloxacin and pyrazinamide, and the new 6 month regiment the same but for 2 additional months. The study will enroll 150 subjects for each of the three cohorts, and will have 2-month, 6-month, 12-month and 24-month follow-ups. The primary outcome will be culture negativity after two months, and multiple secondary outcomes including bacteriological or clinical failure after two years. Adverse events, including bedaquiline associated electrocardiogram abnormalities and standard TB drug toxicities will be monitored. Data analysis will include a modified intention-to-treat approach for the primary outcome and per-protocol and intention-to-treat for the secondary outcomes. Ethical approval has been obtained and regulatory approval under review.

Two additional projects by the directorate are not oriented towards drug interventional trials, but rather a) evaluation of newly marketed drugs within the country for adverse effects (pharmacovigilance), and b) cost-effectiveness of traditional and newly available TB diagnostics.

The Pharmacovigilance in Africa (PAVIA) project, funded by EDCTP, aims to strengthen pharmacovigilance in four African countries: Ethiopia, Nigeria, Swaziland and Tanzania by improving their health systems readiness to effectively deliver new medical products and to monitor their post-market safety. Active collaboration between national drug agencies, public health and research institutions, as well as

local importers and local and multinational pharmaceutical manufacturers will aim to enhance drug surveillance and safety. The initial focus will be on new drugs introduced for treatment of Multidrug-Resistant Tuberculosis. International and Ethiopian PAVIA kick-off meetings have been held this past year, and initial activities in Ethiopia oriented initial assessment of the current PV system in Ethiopia, and identifying training needs which can be addressed by PAVIA.

PAVIA-PROFORMA Joint Kick-off Meeting, 30th April to 2nd May 2018, Dar es Salam

PAVIA-PROFORMA Joint in-country Kick-off Meeting, 27-31 August 2018, Addis
Project period: 2018-2021.Consortium coordinator: The Amsterdam Institute of Global Health (AIGH)

Limited research into cost effectiveness of various TB diagnostic modalities have been performed. The VALUE-TB project, sponsored by the London School of Tropical Medicine and Hygiene aims to research cost effectiveness of currently available techniques, including sputum smear and microscopy, chest x-ray, as well as new technologies Xpert MTB/RIF and loop-mediated isothermal amplification (TB-LAMP). Furthermore, the project seeks to research cost effectiveness of enhanced or active case finding. To date,

We have collected data from 14 facilities, with data from an additional 16 facilities collected in the upcoming year. This study promises to provide suitable guidance for optimal use of TB diagnostics according to national resources.

Community engagement is critical to plan and execute clinical trials. In the context of the STREAM trial, the clinical trial team at AHRI established the AHRI Community Advisory Board (CAB), with assistance

and training from our S. African STREAM study colleagues. Importantly, this board can utilize the experiences gained from STREAM to apply to other clinical trial settings. The board is comprised of 20 members from diverse community representatives including social based organizations (EDIR), district health offices, women and children affairs offices, youth and sports offices, and other institutions such as ALERT hospital and legal and public relations representatives. The board's responsibilities include creation of a platform to create community awareness using different social events, distribution of brochures, contribution to tracing patients lost to followup and patient interviews to obtain feedback on their treatment in the trial setting and suggestions for improvement. Regular meetings among the AHRI STREAM CAB members have been used to update progress, discuss ethical issues and fill knowledge gaps.

Community engagement

Community engagement

In addition to these large multi-national and institutional initiatives, the clinical trial directorate has also supervised MSc students in related topics. Netsanet Aragaw performed his thesis work on 363 MDR-TB patients, 21% of whom were HIV positive assessing outcomes with standard therapy at ALERT hospital, observing 40% cure, 36% completing therapy, 13% death and 10% loss to follow-up. Ayani Teleta plans on studying the pharmacokinetics of benzathine penicillin G in serum of 80 children with rheumatic fever and heart disease. Samples have been collected and are awaiting analysis.

Traditional Medicine Projects

Ethiopian traditional medicines have been widely used and studied, but rarely evaluated in controlled clinical trials. The clinical trial directorate has initiated multiple approaches.

The first is a safety and efficacy trial of the highland herb U.simensis in the treatment of psoriasis. Psoriasis is a common immune related chronic inflammatory dermatological condition with significant emotional, social and economic loss. Treatment is based on symptom control and relies on topical and systemic therapies such as aspirin or coal tar containing creams as well as phototherapy. This provides some improvement, but not cure and requires lifelong adherence. The planned trial will be a 6 month phase II, open label randomized control trial at the ALERT hospital to evaluate U,simensis as a topical remedy compared with existing therapies. Outcomes will be based on the Psoriasis Area and Severity Index (PASI), the usual score utilized to monitor psoriasis in clinical studies. Ethical clearances obtained from AAERC and NRERC. Clinical trial authorization is pending from EFDA.

Clinical Trial Directorate of AHRI and Directorate of Traditional and Modern Medicine of EPHI had jointly organized a consultative meeting on the Regulation and Clinical Trial of Traditional Medicine which took place at the training centre hall of Ethiopian Public Health Institute in late 2017. The meeting provided an excellent opportunity and venue for the exchange of ideas among interdisciplinary group of researchers, academicians and regulators on the national effort for traditional medicine research and development and reviewing the global, national and regional experience on the regulation and clinical trial of traditional medicine. Following this consultative meeting, AHRI and EPHI are jointly working to achieve that end and currently we are developing protocols to conduct clinical trials on two topical ointment products which are developed by EPHI TMMDR.

Bioequivalence clinical studies

The Bioequivalence team at AHRI has established a clinical facility at AHRI in 2013 with the goal of providing locally accessible and affordable bioequivalence testing. Since the conduct of the two pilot bioequivalence clinical studies in 2013 and 2014, several capacity building activities including WHO site pre-inspection have been undertaken both at the clinical site of AHRI and the bioanalytical lab of the Regional Bioequivalence Center (RBEC), which was established in 2013. The BE team at AHRI in collaboration with the RBEC has now conducted its first pivotal study on a locally produced Ciprofloxacin tablet against its innovator product. The clinical study was successfully completed during November 2018. The study was a randomized, open label, two-treatment, two-period, two-sequence crossover that was separated by 7 days of washout period. It was designed to determine the bioavailability and to assess bioequivalence of the test product and the reference product containing 500 mg ciprofloxacin HCl after a single oral dose administration under fasting conditions in healthy subjects; safety of the study subjects was monitored as well. Fifteen blood samples were drawn from each of 24 participants during the 24 hrs after drug administration for pharmacokinetic analysis at the predetermined time points. The clinical data have been compiled and the plasma samples were transferred to RBEC bioanalytical laboratory for determination of drug concentrations. The final report will be compiled as soon as the plasma bioanalysis is completed. The study dossier will be submitted to WHO for pre-qualification application.

BE Clinical study team at BE ward

QA, internal study inspection activities

Plasma separation in cold

The AHRI clinical team hosted some 20 MSc students during the conduct of its BE clinical study in November 2018. These students are studying clinical trial in College of Health Sciences, Addis Ababa University as part of the CDT-Africa postgraduate program. Their visit to our clinical site was part of their course 'Clinical trial in practice' to get an insight into the practical aspects of clinical trials. The team at AHRI used the clinical facility and the on-going BE study as platform for demonstration of good clinical and documentation practices. Development of such standard trial facilities such as the BE clinical center at AHRI can greatly contribute for postgraduate teaching in practice on top of conducting GCP compliant standard trials in the country.

Visit to the BE Clinical Center at AHRI, MSc students from CDT-Africa, AAU

6. Biotechnology and Bioinformatics Research Directorate (BTBIRD)

Following its establishment in 2017, BTBID directorate continued strengthening its case teams, biotechnology and bioinformatics case teams, in terms of funding as well as human and laboratory capacity. In 2018, the directorate has also focused on strengthening existing partnerships and establishing new partnerships that will enable or facilitate the transfer of biotechnology and bioinformatics tools and skills to AHRI.

Capacity building

Strengthening Genomics and Bioinformatics capacity

We have received funding from the FMoH and a pledge from the US Defence Threat Reduction Agency (DTRA) to acquire all the necessary equipment including, bioanalyzer, fragmenter, dedicated server, data storage and high performance computational computer to begin genomic sequencing at AHRI. In order to enhance genomics skills, two of our staff members (Meseret Habtamu and Dawit Hailu) have received training for 2 weeks in April 2018 at AGBL in Dubai on DNA sequencing. With regard to bioinformatics, 3 new staff members at different level of expertise have been recruited and an international senior bioinformatician is in the process of recruitment (shortlisting has been completed and interview has been scheduled to be conducted in February 2019). This, in addition to the existing experts we have in the directorate, will definitely strengthen the bioinformatics capacity of AHRI. The international senior bioinformatician is expected to transfer his/her skills during the limited contract period.

The new consortium project, TBGEN, is an excellent an opportunity for the directorate to strengthen its genomics and bioinformatics skills since the project has funding to purchase the necessary reagents for sequencing and to cover costs for personnel for the next 3 years. The project also has a good network with experts and labs in Europe and elsewhere to facilitate technology transfer. Considering all of this, we anticipate that DNA sequencing at AHRI will begin in the middle of April 2019. We already have several requests from local and international partners to sequence their samples from collaborative projects they have with AHRI. Once the quality of our sequence data and capacity of bioinformatics analysis is proven to be satisfactory, we will open up our facility to partner institutions.

HLA laboratory and clinical service

Kidney transplant program has been started at St. Paul's Hospital. However, all compatibility tests are still done in Germany or India. As a result, in order to get compatibility results patients have to wait a minimum of two weeks. This is unpromising for patients that are at the end stages of kidney disease. AHRI trained some of its staff on kidney compatibility test procedures and established an HLA laboratory on its ground to address this problem. Further, after several discussions with St. Paul's Hospital, memorandum of understanding (MoU) was signed to make AHRI the place where kidney transplant compatibility tests are conducted. Currently, all the reagents and equipment necessary to provide this service have been put in place and two lab technicians have been trained to work full time. AHRI has secured funding from FMOH-SDG for one year service. We have agreed to test 10 samples simultaneously with the German company and compare our results before we begin with patient service. In December 2018, 4 out of 10 samples were tested and all 4 were found to be 100% concordant with the results from the German company. We will continue this process for the remaining 6 samples before kidney transplant compatibility tests for St. Paul's Hospital patients are done at AHRI.

Networking and partnership

The FMoH assigned AHRI to work on locally producing vaccines, particularly cholera vaccine. Following this, the Biotechnology and Bioinformatics directorate at AHRI identified 3 potential institutions/ companies for collaboration i.e., IVI (Korea), EU Biologics (Korea) and Finlay Institute in Cuba. Based on further discussions and meetings involving the ministry of health, Finlay Institute was selected as the ideal partner. Business plan was developed in collaboration with Finlay and submitted to the ministry of health. However, due to the government reform the project has been put on hold for the time being. Nevertheless, Finlay and AHRI have submitted the business plan to potential international donors. Following this a high level meeting has been scheduled to be conducted in Addis Ababa involving AHRI, Finlay, ambassadors from different countries, ministers, the AU, UNICEF and other NGOs, and private companies for a thorough discussion and collaborative fund raising. This meeting is planned to be conducted in the second quarter of 2019.

Funding- MOH-SDG

The Ethiopian government has shown its interest and commitment in supporting biotechnology and bioinformatics research at AHRI by investing 1.4 million USD (38 million birr) on 5 different projects which include: (1) strengthening genomics and bioinformatics, (2) histocompatibility testing, (3) development of simple-low cost HIV-1 monitoring tools, (4) production of DAT for the diagnosis of visceral leishmaniasis, and (5) IgG purification from serum/plasma.

Intravenous immunoglobulin (IVIg) purification

Intravenous immunoglobulin (IVIg) is sterile IgG prepared by purifying human plasma pooled from large number of donors. IVIG is composed of more than 95% unmodified IgG, which has intact Fc-dependent effector functions, and trace amounts of immunoglobulin A (IgA) or immunoglobulin M (IgM). IVIg is mainly used to treat people with immunodeficiency disorders and sometimes it is co-administered with other medications for people who are fighting chronic infections. The demand for IVIg is increasing globally. Personal communication with medical doctors in Ethiopia has revealed that IVIG is also needed in this country; however, scientific studies assessing the need for IVIg in Ethiopia have not been conducted yet.

The IVIg purification project was initiated with seed money from AHRI. Following that, ministry of health of Ethiopia donated a significant amount of money from their sustainable development goals (SDG) fund to facilitate IVIg technology transfer and laboratory scale production.

In order to transition from laboratory scale to factory scale IVIg production in this country, we have reached out to several large-scale laboratories and companies. We did several email and Skype call communication with companies and labs who are engaged in plasma fractionation to get support in the process of establishing this technique in the country. From our communication, we have learned that large-scale IVIG purification is an expensive and long process .Considering the cost, we can proceed with one of two options. The first option will be to work on plasma fractionation followed by simpler purification, such as albumin purification. The second option will be purchasing crude fractionate samples followed by IVIg purification. The first option is more feasible as we already have enough raw materials to start the plasma fractionation process.

Future plan

- Conduct a pilot study to identify the need for purified blood proteins in Ethiopia
- Identify laboratories that are engaged in plasma fractionation at GMP level and willing to collaborate with us

- Identify and purchase required equipment
- Establish the technique in small scale as proof of concept at AHRI in collaboration with National blood bank

Human resource

In 2016/17, there were only 5 staff members in this directorate. In 2018, six more new staff members were recruited,of which two of them have already joined the directorate. Further, a senior bioinformatician is expected to join the directorate soon as the recruitment is almost over.)

	2017	2018	Field of expertise
1	Markos Abebe		Immunology
2	Yonas Kassahun		Bioinformatics
3	Dawit Hailu		Molecular Biology
4	Tewodros Tariku		Bioinformatics
5	Elena Hailu		Molecular Biology
6		Fiker Tadesse	Immunology
7		Melaku Tilahun- transferred from other directorates	Biotechnology, Ph. D. candidate
8		Roza Tsegaye (expected to join by the end of June)	Computer Science (AI)
9		Bethlehem Adnew	Computer Science
10		Amanuel Zewdie	Data management, Mathematics
11		Meseret Habtamu	Immunology
12		Senior bioinformatician - expected to join	

Bioinformatics training at AHRI

As part of capacity building in bioinformatics in Ethiopia, an introductory course on bioinformatics was conducted between 24- 28 December 2018 at AHRI. There were 12 participants (7 from AHRI, 1 each from EPHI, NHADIC, AAU-IBT, EBTI, and AASSTU) and 4 trainers (2 from AHRI, one from AAU-IBT and one from EBTI).

Training workshop on Mycobacterium whole genome sequence data analysis

Basic bioinformatics training workshop was conducted at AHRI. This report describes a bioinformatics training initiative started at AHRI aiming to support life science researchers and postgraduates in handling next generation sequence data.

Institutional initiatives strengthening capacity at AHRI focuses on building a bioinformatics training center, next generation sequencing (NGS) facility and computing platform to support researchers and postgraduates in Ethiopia. The faculties benefit both ongoing and new project initiatives such as

on pathogen evolution, virulence determinants and epidemiology of important pathogens, including M. tuberculosis. The workshop was aimed at delivering hands on practical introduction to NGS data analysis of Mycobacterium tuberculosis complex (MTBC) genome. Every workshop day included, 40 minutes presentation, three hours hands on practical and 20 minutes discussion. The presentation topics were on next generation sequencing technologies, examples of sequence data file formats and a stepwise description of each bioinformatics workflow during NGS data analysis.

The workshop was held at AHRI, Bioinformatics unit, 24-28 November 2018. There were 12 participants from health and biotechnology research institutes in Ethiopia.

Participants and trainers of the Workshop

Workshop participants during hands on session

The workshop participants had an opportunity to reflect on the training experience. The feedbacks highlighted the need to improve computational power of the workstations and address fluctuations of internet connectivity. The participants also expressed a satisfactory level for acquiring basic skills in handling NGS data.

In conclusion, AHRI appreciated the bioinformatics team at AHRI and the external facilitators from Addis Ababa University and the Ethiopian Biotechnology Institute for the coordination and successful workshop.

Projects initiated/facilitated by the directorate

Preparation and evaluation of in house monoclonal antibodies against commercial antibodies for clinical and research use

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Monoclonal antibodies are used clinically for diagnostics and therapeutics while they are used in research for the detection of target biological molecules.

The national biotechnology road map prepared by the Ethiopian Biotechnology Institute(EBTI)has emphasized the importance of local generation and production of monoclonal antibodies for clinical use. Accordingly, this directorate has started a project to generate monoclonal antibodies using hybridoma technology. In particular, our initial focus will be to generate anti-CD4 and anti-CD38 reagents of comparable quality to commercial products, which can be used to monitor CD4 cell count in HIV patients and tumour progression in leukemia patients, respectively. The project is meant to transfer the technology of mAb preparation and fluorescence labelling by using local expertise and international partners. We will use three different but complementary approaches to minimize the risk of the project i.e., in house generation of hybridomas or purchase hybridomas and produce monoclonal antibodies or purchase unlabeled monoclonal antibodies and make the labelling in house.

Currently, BALB/c mice are kept at NVI so they can breed in a clean and healthy environment. This was due to the transformation of AHRI's animal house into a bacteriology laboratory. THis has brought up discussions about building a new animal house at AHRI. Further, all the necessary equipment and reagents for this project are in place with the exception of CD4 and CD38 antigens, which are required for the immunization of BALB/c mice. The antigens have already been ordered but are waiting for shipping.

Funding: Federal Ministry of Innovation and Technology

7. One-Health Unit

The One-Health Unit at AHRI focuses on three major research directions, namely 1) investigation of zoonosis, 2) animal and human health systems (surveillance and health delivery) and 3) the role of the environment and wildlife in public health. These three major topics are often inter-linked within same projects (e.g. JOHI project, Brucella project).

I. One-Health in pastoral areas

The bulk of the research carried out in 2018 continued to focus on pastoral communities, particularly in the Somali Region through the JOHI and Brucellosis projects and Afar through the Brucellosis project. Pastoral communities in these two regions often live in remote areas that are faced with multiple challenges (e.g. recurrent draughts, accessibility for regular health services, pastoral movements including cross-border movements, conflicts etc.). They live closely with their livestock on which their daily livelihood depends upon. These regions, hence offer a context where One-health approaches are important and most adequate in order to improve the health of animals and people. One-Health research in pastoral communities requires long term commitment due to the unique challenges faced when working with pastoralists, such as regular seasonal migrations of people and their livestock, drought periods forcing people to move to other places, building up trust and collaboration with the communities, and traveling to remote areas (sample transport logistics, sample storage etc.). The jigjiga One-Health initiative (JOHI) that started in 2015 with Swiss Government and institutional funding is a 12-year research and development project and partnership between AHRI-Swiss TPH and Jigjiga University (JJU). The long-term commitment of this project allows collecting evidence-based data on animal, human and environmental health in selected areas in the Somali Region (SRS). These data are a prerequisite to move into small scale One-Health intervention trials, which if successful can be up-scaled further by development and government institutions. During the first 3 years, the project focused on capacity building (training of 9 post-graduate students) and operational research. The research conducted by 9 post-graduate students from Jijiga and Haramaya University has collected important baseline data on human-animal and environmental health so far, and has started identifying potentials, opportunities and gaps in health delivery systems hence setting the foundation to move in year 4 (2019) into 3 small scale intervention trials: 1) improvement of water quality and reduction of diarrhea in children, 2) piloting of an innovative mobile DOTS system for pastoralists and 3) expansion to the whole woreda of the integrated surveillance system that was piloted in year 2 and which now will also include environmental surveillance as well. The research rationale of JOHI is that each student who comes from different disciplines (e.g. social science, veterinary medicine, medicine, ecology, midwifery, nutrition, pharmacology) conducts a specific research topic but all students work together as a team in the same study area/households hence sharing unique sampling identification codes. The results are then compiled to get a unique integrated One-Health picture in the selected area. This approach also fosters grass root collaboration and integration attitude/behavior inherent to One-Health and contributes to steering Jigjiga University to become a stronghold in One-Health in the pastoral context. Discussions are held regularly with the communities on research/intervention priorities. Research and intervention protocols are shared with the local authorities and validated during yearly workshops by the communities and local authorities, while results are fed-back to the stakeholders.

In 2018 (year 3 of JOHI), the following specific research studies were carried out in Adadle woreda (SRS):

A. Drinking water quality and diarrhea in children under 5 (MSc study)

In Ethiopia, the prevalence of diarrhea in children reported was estimated to be 12%. In 2016 and 2017, SRS was hit by back to back severe draughts. A large number of pastoralist people and their livestock were forced to move long distances in search for water resulting in existing water sources becoming overloaded with people and their livestock and hence pollution of the water sources

increased. A baseline assessment of water quality, sanitation and hygiene conditions was conducted as a prerequisite to develop basic recommendations and advise potential future intervention to improve the accessibility of safe drinking water and ultimately reduce the occurrence of diarrhea, particularly in children under the age of five. A cross sectional study of 538 randomly selected households was conducted, including a questionnaire survey that also captured self-reported first and second week diarrhea prevalence and water sample collection. Water samples were also collected from sources such as rivers and wells and examined in the field for fecal contamination using a portable field kit (DelAgua). Diarrhea prevalence in the first and second week was overall 26.58% and 20.63% respectively (max 39%). Concomitant vomiting and fever was observed in 63% of the children. Only 0.9% of the children received treatment. 45% of the household drinking water contained too high coliforms/E.coli levels to be safe for drinking. Among them 16% were at very high risk of E.coli infection and required urgent water treatment. Drinking water of poor quality, inappropriate water storage condition, caregivers who were not washing hands before feeding their child, and children in the age group 12 to 24 months showed a significant association with the prevalence of diarrhea in children. Households depending on rivers and unprotected dug-well for drinking water were significantly at higher risk of having fecally contaminated water compared to those using on protected birkad. Almost all surveyed households (96%) lacked basic sanitation. The findings suggest that diarrhea morbidity could be decreased by improving water quality, promoting hand wash facilities and education about appropriate storage and hand wash practice. This research will have an intervention follow-up in 2019 where different water filtration techniques will be assessed for costs, sustainability and acceptability among communities.

B. Effect of delayed TB diagnostics in pastoralists (on-going PhD study)

The objective of this study is to assess the extent and reason of delays in diagnosis of pulmonary TB in pastoral communities, the quality of diagnosis and to estimate its association with infectiousness in selected hospitals in SRS. A mix of study designs were used with both qualitative and quantitative data collection approaches (cross-sectional, matched case-control design, comparative cross-sectional and phenomenological designs). The planned selection included: 375 pulmonary tuberculosis patients to determine the extent of delay in diagnosis; 163 paired delayed patients (cases) and timely diagnosed patients (controls) to identify the determinants of patient delay; 326 delayed and timely diagnosed patients to be screened for pulmonary cavitation and smear positivity to compare their infectiousness. Study participants were recruited prospectively as they are being diagnosed at TB care centers in 5 hospitals. Trained tuberculosis care providers interviewed patients following diagnosis using a structured questionnaire, collected 3 sputum samples, recorded smear microscopy and x-ray results, took anthropometric measurements. The three sputum samples were re-examined at AHRI for performance evaluation of smear microscopy. In-depth interviews were conducted to explore the perceptions and practices of patients, and the health system challenges. Five hospitals and 1 health center have been included in the study as well as 400+ TB suspected patients were sampled and AFB smears + chest x-rays performed. Data are currently being analyzed. This study will primarily provide comprehensive evidence on delay in diagnosis of pulmonary tuberculosis; identify its prevailing determinants and contextual features of tuberculosis medical care seeking behavior of Somali pastoralists; show the effect of diagnostic delay to infectiousness of patients; and point out the challenges of tuberculosis services provision to pastoralists. Preliminary results of this study were used to elaborate an innovative small scale intervention on the establishment of a mobile DOTS system in the study area in 2019 in close collaboration with the regional health bureau and the Mycobacteriology Directorate of AHRI.

C. Pre- and post-natal depression among pastoral women (PhD study, on-going)

Mental health remains a neglected discipline in Ethiopia at large. Information on mental health among pastoral communities is largely lacking. The aim of this study was therefore to collect data on ante- and post-natal depression among pastoral women and investigate the mental health challenges among these women in terms of causes, and support requested and received. A total of 1218 women from

15 health facilities were so far interviewed. Two interviews were conducted, one before birth and a follow-up up interview two weeks after birth. Data is currently being entered.

D. Rangeland management and soil quality (PhD study, on-going)

The environment is an inherent part in pastoralist livelihood. Degradation and droughts are factors influencing migration and health of animals and people. The objectives of this study were a) to evaluate the rangeland condition, b) to explore major land use and land cover changes, their causes and consequences in the past four decades, and c) to estimate the current livestock population and its adaptation to available food resources. Tools used were questionnaire survey, forced group discussions (FGDs), soil and vegetation sampling, Google maps and other remote sensing technology. 450 soil samples and 450 interviews were carried out. Physical and chemical analysis of the quality of soil has been undertaken in Switzerland. This data will be combined with indigenous land unit as pastoralists in the study area traditionally recognize and used for exploring the connection with forage quality. Data are currently being analyzed. In year 4 (2019), rangeland surveillance will be integrated into the animal-human surveillance system as an innovative approach for Ethiopia and Africa at large.

E. Assessment of zoonotic diseases with emphasis on Brucellosis, Q-Fever, Rift Valley Fever and Corona-Mers (PhD study, on-going)

Baseline information on various zoonotic diseases among pastoral communities in SRS are lacking. This research topic aimed at investigating important zoonotic and economic diseases in livestock, particularly camels and their owners with emphasis on Brucellosis, Q-Fever, Rift Valley fever (RVF) and Corona-Mers. A cross-sectional study with a multi-stage cluster sampling technique was conducted in 6 kebeles of Adadle woreda. Questionnaire surveys and FGDs were carried out. In total, 1050 blood samples were collected from human and animals and analyzed by commercial ELISA kits. In addition, Brucella samples were screened by Rose Bengal Plate. Overall seroprevalence of Q-fever was 41%, RVF was 14.8%, MERS was 62.2%. Brucellosis prevalence was 0.02% by RBT and 0.3% by ELISA. RVF and Q fever was highest in camels (60% and 25%, respectively) and humans (ca.50%). The univariate logistic regression analysis showed that kebeles were statistically significant for RVF seropositivity in human, whereas species, gender and age was also statistically significant. Only age was found as statistically significant for MERS seropositivity in camels. 90% of households reported abortions in the last 6 months. One important result was the very poor knowledge of zoonotic diseases among pastoralist. In year 3 (2018) further samples were collected in relation to abortion storms detected by the integrated surveillance system (see below), with results pending.

F. Integrated syndromic animal-human surveillance system (MSc research)

This research is a centerpiece of JOHI that will connect all other research fields. For the first time in Ethiopia, we attempted to set up a community-based integrated animal-human surveillance system, piloted in 19 villages that cover a population of 9730 people and 112,805 livestock. The aim of this study is to work out the communication, logistical and financial feasibility for such a system that can respond within less than 48 hours, hence contributing to improve early detection and response of human and animal diseases and syndromes. Mobile phones were distributed to the village leaders who reported when syndromes/illness occurred in humans and or in animals. Descriptive statistics will be used to see the frequency distribution of syndromes in humans and in animals, and the times taken from syndrome or disease report, to sample collection, etiological diagnosis and to interventions. The largest lag periods will be identified by a cox proportional hazard regression model. In humans, 904 cases and in livestock 671 cases were reported that would have gone unreported while using the existing channels. In people the majority of cases were gastrointestinal tract related (42.8%) followed by respiratory problems (37.8%) and febrile illnesses (15.5%). In addition, cholera cases, syphilis, TB and malaria were

reported and confirmed in humans. In livestock outbreaks, abortion storms, pox, anthrax, rabies and salmonella were reported. Rapid reporting at community level allowed fresh samples to be taken and sent to the lab. The success of this system was praised by the local authorities and will be expanded in 2019 to Woreda level in close collaboration with the local authorities. In addition to expanding, the aim will also be to decrease further the time between outbreak and response. In addition, a rangeland surveillance component will be added to the existing animal-human surveillance system and a response arm (including emergency services) gradually build- up.

The project has elaborated in 2018 an innovative One-Health training manual for Health Extension workers (HEW) and Community Animal Health Workers (CAHWs) that will be finalized for printing in 2019. The training has been given simultaneously to HEW and CAHWs for the first time as pilot in Gode, conjointly with the sector bureaus in summer 2018 and will potentially be included in the existing standard training modules of the sector bureaus as a separate module, which would have a national impact on training.

G. CDC Brucellosis project

A Brucellosis surveillance was started in 2017 funded by CDC among pastoral communities of Afar and Somali (Shinile) regions. This project complements the JOHI project in SRS in some aspects. The results of this sero-surveillance will be fed into the national Brucellosis surveillance data (CDC/FMoH). We conducted a cross sectional study with a cluster sampling design. Overall, 13 woredas (118 villages) were included in the survey and 6408 blood samples were collected from humans and livestock from same households (1196 human, 2822 goats, 974 sheep, 633 cattle and 783 camels). A semi-structured questionnaire survey was conducted in 470 households that assessed KAP, economic questions and possible risk factors of disease transmission. Serum was analyzed at AHRI by ELISA. Blood clots were stored at -20°C for future PCR analysis (Brucella strain identification). Serology is close to completion. Preliminary results suggest high Brucellosis prevalence in Afar. A second year was funded (2018-2019), during which we will finalize all the lab analysis, elaborate an animal-human transmission model and conduct an in-depth KAP survey on Brucellosis but also Anthrax in the same study sites where serum were collected. In addition, the research will help identifying current challenges of disease surveillance and identifying gaps and opportunities for improving surveillance and outbreak response in this pastoral context.

II. One-Health in the dairy sector

In the frame of the Ethicobots project, we assess the economic impacts of Bovine tuberculosis (BTB) and cost of intervention strategies on the dairy sector of Ethiopia. A longitudinal study was conducted over 3 years among 26 dairy farms in and around Addis Ababa. The farms were visited monthly and productivity parameters recorded (e.g. mortality, morbidities, fertility, trading). Over the 3 years, 1700 animals were included in the study. The results are currently being analyzed. The results of the productivity study linked with market and farm cost data will provide a baseline on which the economic impact of BTB on livestock production and costs of different interventions (e.g. test and slaughter versus vaccination) can be modeled using a dynamic livestock demographic and economic matrix.

Milk production can be affected by several factors, the main ones being nutrition and diseases. In order to put the possible role of BTB in context, we conducted 2 further research studies: 1) the potential impact of fodder quality and feeding management on milk production and 2) the mastitis prevalence in dairy cattle and isolation of pathogens that impact milk production but have also potential zoonotic risks (e.g. listeria, salmonella, streptococcus, staphylococcus, E.Coli). The study highlighted that feeding management and fodder quality was overall poor (with the exception of large commercial dairy farms), hence likely impacting on milk protein content and milk quantity. The mastitis prevalence study (core funded by AHRI) is ongoing and has suffered many long delays due particularly to the lack of reagents to be found on the local market. Lactating cows were tested for clinical and sub-clinical mastitis with

the California Milk Test (CMT). All milk samples are cultured on bacteria media. DNA from colonies is being extracted and will further be analyzed by PCR in 2019.

III. One-Health and wildlife

In the frame of the JOHI project, a small questionnaire survey was conducted among 200 pastoral households in Adadle woreda (Somali region). The aim of this study was to assess the perception pastoralists have of wildlife in their area and how these wildlife species affect the health of their livestock and people. The results are currently being analyzed.

As part of a long-term disease surveillance (post-mortem analysis) of captive wildlife in rescue centers, a particular emphasis is given to non-human primates which undergo a meticulous post-mortem analysis when found dead. In 2018, a captive olive baboon died after showing a chronic cough over many years. The lungs were severely affected and showing multiple cavities. Smears of lung tissue were ZN stain positive. Culture followed by deletion typing and spoligotyping isolated M. tuberculosis, lineage 4. The animal had been rescued from a hospital compound in Addis Ababa 6 years previously and has displayed a chronic cough since. Blood test (primagam test) came back negative.

Research projects

PI name	Project type	Project title	Status
James Wood	Ethicobots consortium	Economic assessment of BTB and intervention strategies	Field work finished, finalizing data entry
Rea Tschopp	Institutional with 3 MSc students associated from Samara University	Phase 1 (2017-2018): Sero-surveillance of brucellosis in humans and livestock in Afar and Somali region	Field work finished; serology close to completion; data entry; PCR pending
		Phase 2 (2018-2019): KAP study of Brucellosis and Anthrax in Afar and Somali region	Field data collection
Rea Tschopp	Institutional	Fodder quality and feeding management in dairy farms	Finished. Manuscript in press
		Mastitis prevalence and bacteriological milk quality	On-going; field data collection
		Wildlife zoonosis	Long term open ended research
Jakob Zinsstag	Jigjiga One Health Initiative (JOHI)	Drinking water quality and diarrhea in children under 5	Thesis finished; follow-up in 2019 as an intervention trial
		Establishment of an integrated syndromic animal-human surveillance system	Thesis finished; follow-up in 2019 as an expansion to the whole woreda
		Effect of delayed TB diagnostics in pastoralists	Data collection finished; data entry and analysis pending

PI name	Project type	Project title	Status
		Pre and post natal depression among pastoral women	Data collection finished; data entry and analysis pending
		Rangeland management and soil quality	Data collection finished; data entry and analysis pending; follow-up with integrating this arm into the animal-human surveillance system
		Assessment of zoonotic diseases with emphasis on Brucellosis, Q-Fever, Rift Valley Fever and Corona-Mers	On-going. Manuscripts in preparation
		Perception of wildlife and their threat to public and livestock health	Data collected and entered. Analysis pending
		Bovine TB	Data collected; entry and analysis pending

8. Laboratory Management Center

The Center was established in order to organize and lead the overall activities and infrastructure of the laboratory. To achieve its mission the center organized in three case teams include: Research Laboratory and Quality Assurance, Biosafety and Biosecurity and Laboratory Engineering. The Research Laboratory and Quality Assurance Case Team comprises of seven research laboratories namely clinical trial, Tuberculosis, Immunology, Molecular Biology, Bacteriology, Pathology and Parasitology Laboratories. These laboratories are equipped with high tech biomedical equipment. All the seven laboratories have their own coordinator and the whole process is led by a Laboratory Manager.

The Laboratory Engineering Case Team is primarily responsible for handling preventive, curative maintenance and calibration of the biomedical equipment. The Biosafety and Biosecurity Case team facilitate the biosafety and biosecurity issues of the institute.

The Scope of Laboratory Management Center

1. Plan, organize, direct and coordinate the laboratories operation
2. Avail reagents, laboratory equipment and manpower to effectively support execution of research projects and ensure their economic use.
3. Ensure the proper function and timely maintenance of the laboratory equipment
4. Develop and update standard laboratory operating policies and procedures
5. Provide technical support for researcher and orientation for students
6. Organize and provide laboratory training
7. Ensure biosafety and biosecurity by applying knowledge, techniques and equipment to prevent personal, laboratory and environmental exposure to potentially infectious agents or biohazards and the agents from theft and misusers.
8. Developing, implementing and reporting results of biomedical and clinical laboratory research;
9. Promoting awareness and understanding of the use of the research laboratory

New TB culture and DST Laboratory

Major achievements under Biosafety- Biosecurity case team

- Laboratory safety manual for standard application of safety procedure and practice is developed.
- Initiating of inventory for deep freezer including preparation of their box map. Jointly with senior scientists it has been started to prepare box map for isolates.
- From the waste management and disposal point of view we were working for those expired chemical and reagent and daily base waste disposal. Therefore for expired chemicals and reagents we have arranged proper deposition according to FMACA policies and waiting for the authority to receive it from us. Other infectious and noninfectious wastes are being autocad and incinerated according to the institute nation policy.
- safety audit was done for all the laboratories using minimum requirements which is indicated by WHO Biosafety manual. And improvement activities are being initiated
- The case team has kept regular meeting as well as has deliver all the possible support and assistant for all labs and projects to create safe, clean and conducive working environment.
- We identified necessary PPE for AHRI laboratory and purchasing is being processed
- We have given AHRI staff and students Vaccination for HBSAg and Yellow fever vaccination is being given for all staff who has exposure (field workers)

Major activities performed in laboratory case team

- In the implementation of GCLP and ISO 15189 requirement; the laboratory completed more than 180 standard operating procedures. And the implementation of those developed procedures is under monitoring and supervision by quality officer.
- The laboratory has been give specimen collection, processing and testing for 11 projects and for about PHD and MSc students.
- The laboratory has been monitoring off site project's performance and avail all necessary reagents, supplies, equipments and formats for Adama –wonji and wolaita sodo study sites
- The laboratory has given practical laboratory attachments for more than 250 students from different government Universities
- More than 40 minor and major equipments are installed in the fiscal year. This enhanced the laboratory performance to high level
- Supplies procured: 85 % supplies requests were procured from internal market
- Only 10 %of external purchase orders were procured
- Number of services given for patient diagnosis: 976 FNA, 728 Biopsy tests and 600 TB culture for diagnosis and follow up of MDR patients are performed
- The laboratory officially inaugurated Diagnostic service for TB culture and molecular diagnosis (negative pressure validation, equipment installation, supply the lab, renovation and personnel training performed)
- To accredit the laboratory we have performed internal audit for all laboratory units and improvement activities are initiated. In the improvement activities we identified and take actions for monitoring and controlling of Environmental conditions, measurement traceability, increase performance of EQA status, method verification & validation, insure personnel competencies. And we go half of our ways to accredit the P3 laboratory. And the application and the accreditation system will be

completed in the next fiscal year.

- Traceability of measurements was insured for 119 equipments like Freezers, Refrigerators, Autoclaves, analytical balance, micropipettes, and thermometers by calibrating in National metrology institute.
- To increase the productivity of the laboratory 10 assistant laboratory professionals are employed, oriented and start working
- We have given two short term, trainings (Biosafety-biosecurity and GCLP) for staff and students,
- Short term trainings on clinical laboratory techniques, and TB molecular diagnosis was given for 6 laboratory researchers
- We celebrated World TB day with Secondary school students by demonstrating and introducing the laboratory technologies

Major activities performed in Engineering Unit

1. New TB Culture Lab

- Maintenances and repair of the new building TB culture lab by filling the perforated walls, corners, and window and door sides with silicone paste and cement.
- Rearranging the rooms by partitioning for the best workflow and minimization of contamination to fit for the procedures of the TB culturing.
- Validating the negative/positive pressure system. Drawings of engineering, workflow of the plant is done.
- Installation of over 20 lab equipment. These are , 2 class II and 1 class I biosafety cabinets, 2 large sized CO2 incubators, Centrifuges, ultracentrifuge, mid –sized autoclave, microscope, GeneXpert, MIGITs, water distiller, deep freezers are successfully performed.
- Maintenance of 3 burned negative/positive pressure system motors, biosafety cabinet is done.

2. HLA & Biotechnology Labs on the New Building

- Preparing ante room by Aluminum partition.
- 2 new Biosafety cabinets, incubators, centrifuges, PCR device, luminex and fridges are performed.

3. Other Labs (Old Building & Clinical Trial)

- Preventive maintenance manuals and life history sheet are prepared for each of the lab devices. Daily and weekly preventive maintenance activities are undergone by the respective lab technicians for each room, which are trained by the biomedical engineering department. Monthly and annually schedules are performed by the department.
- Corrective maintenance on more than 50 devices is performed. To mention a few; deep freezers, automatic tissue processor, microscopes, autoclaves, chemistry analyzers, water deionizers, laundry machine, liquid nitrogen plant.
- Installation on 10 equipment is done. These include; automatic fluorescence microscope, the first in Africa in its kind, Elispot reader, 6 deep freezers and fridges, water distiller, thermocyclers, CO2 incubators, hematology analyzer.

- Totally over 50 lab tables, chairs, windows, doors and shelves repairing is done.
- 4 Formal and informal trainings on GCLP, fire and electrical safety and equipment operation as well as preventive maintenance is conducted.
- Training on Elispot reader maintenance and biosafety cabinet validation practical exam is taken abroad. And AHRI has got NSF certified engineer for validation of biosafety cabinets.
- Production and distribution of nitrogen had been performed until the nitrogen plant was malfunctioned
- Training was given for laboratory staff on how to perform daily and weekly preventive maintenance of their own specific equipments

Major problems

- Limited laboratory space for equipments and freezers
- Malfunction of Nitrogen plant
- Delayed procurement system

9. Grand Challenges Ethiopia

In the past few years, important initiatives have been established that encourage health innovation all around the world. One of these is the Grand Challenges (GC) program launched by Bill and Melinda Gates Foundation in 2003, with the goal of stimulating innovation in global health, an area that was starving for new ideas. A grand challenge in health is defined as "a specific critical barrier that if removed would help to solve an important public health problem." Since its launch, the Grand Challenges model has spread around the world to countries such as Brazil, Canada, India, Israel, and South Africa.

Ethiopia has joined the global growing family of Grand Challenges programs in 2015 with initiative to support the creation, appraisal, promotion, and scale-up of innovative ideas and concepts that are responsive to the defining health-related challenges and assist in the effective implementation of health sector transformation plans HSTP and contribute to achieving the sustainable development goals (SDGs) in general and to end all preventable deaths of mothers and children by 2030 in particular.

Grand Challenges Ethiopia has three principal objectives. The first principal objective is to stimulate innovations that may solve the health sector challenges and contribute to achieving SDGs in priority areas like newborn and childhood health, maternal health, antimicrobial resistance, pastoralist and other least developed regions health services. The second principal objective is to test innovation and technological solutions surfaced elsewhere but are applicable in our setting for its cost-effectiveness, social and cultural acceptability, and potential peacefulness and scalability. The third principal objective is to invest in the implementation of selected innovations at scale.

Although GC Ethiopia has been established in 2015, its first stated year of implementation was 2017/2018. The GC Ethiopia secretariat and advisory national taskforce were also established in 2017 and has developed policy and procedures documents to guide its processes. The first-year seed grant fund to stimulate innovation was announced for 2017/2018 where fourteen health innovators were selected through a competitive process. All the fourteen health innovations for testing were selected form the preset priority areas includes child health, maternal health and pastoralist community health. Among the selected fourteen, six (42.8%) innovations may improve the maternal and child health in Ethiopia. The other one (7.2%) innovation may improve pastoralist community health service and one (7.2%) innovation was cross-cutting. Of the selected innovators for 2017/2018 (first year), 11 (84.6%) successfully finalized their project as per the schedule and submitted their final report. However, two (14.3%) requested carryover for the next year and one (7.2%) has been suspended due to alleged proprietary issues.

The 2017/2018 innovation winners were from public universities and research institutes. As a result, during the implantation of first year GC Ethiopia, a platform was created for health innovators in the country that could stimulate the development and testing of new and bold ideas in the health sector. Moreover, GC Ethiopia has played significant role to encourage university scholars and researchers to engage in removing health sector challenges through innovation with the overall goal to improve the health status of the citizen.

In addition, GC Ethiopia has announced its second year seed grant for 2018/2019 and has received more than one hundred seed grant applications. However, based on the established guidelines and terms of reference GC Ethiopia has selected five innovations without any preconditions but five required revisions to accommodate comments and adjust funds appropriately. Of these 10 innovations recommended to win the seed grant for 2018/2019, one (10%) may improve maternal health, two (20%) both maternal and child health, two (2%) child health, three (30%) antimicrobial resistance and the other two (20%) are represent cross cutting themes.

Similar to the 2017/2018 year, innovators applying for seed funds for 2018/2019 are from public universities and research institutes. However, the potential contribution of private sectors and individual researchers in the health sector may be significance and justifies encouraging them as well.

Innovations and technological solutions that have occurred elsewhere in the world which are cost-effective, socially and culturally acceptable, potentially impactful and scalable are encouraged to be adapted and tested in the country. Yet this has not happened to date in both first and second year GC seed grant fund application due to lack of applications to test innovation and technological solution that have occurred elsewhere in the world. Such applications might reduce the cost and time compared to creation of new innovations.

10. Ministry of Health supported Clinical Research Network Initiative

Clinical research involves research conducted to support improvement and generation of new knowledge in the field of medicine with the goal of assisting patient care decisions and improving clinical outcomes. The Armauer Hansen Research Institute (AHRI) initiated Clinical Research Network (CRN) programme in collaboration with five local universities on selected areas with a support of the Federal Ministry of Health of Ethiopia.: hepatitis, antimicrobial resistance (AMR), arboviral infections and cancer research.

The main aim of the CRN initiative is to build clinical research capacity and clinical laboratory diagnosis in collaborative universities through the network and to address specific key health care and clinical challenges through relevant research that will provide national and local solutions and contributes to the existing knowledge.

From all collaborative universities, a total of 22 postgraduate students (19 MSc and 3 PhD) have been supported through the initiative. Moreover, the students' research on hepatitis and AMR were submitted to the Ethiopian Medical Journal to be published in its forthcoming Supplements. In order to broadly expand the CRN, AHRI has planned to increase the number of collaborators by including additional five to six local universities in 2019.

II. Development and Administration

1. Knowledge Management Directorate

Knowledge Management Directorate (KMD) is the youngest directorates of all at AHRI and comprises of four teams namely: Biostatistics and Data Management, Information Communication Technology (ICT), Research Communication and Clinical Epidemiology. However, the last two teams are in progress to be established.

The scope of practices under KMD includes but is not limited to generation of high-quality evidence, proper documentation, archive and codification of the data, information and translation of the knowledge through advanced data management system in order to retrieve and utilize the information and new knowledge that could shape health policy and implementation in Ethiopia and beyond. This includes fostering evidence-based medicine and health care through the application of clinical epidemiology, and providing updated scientific information to researchers. In addition, sharing of information and new knowledge, providing scientific support, reviewing manuscripts and facilitating the publication of completed research projects is also included in the directorate's scope. The KMD also often provides various short-term trainings to researchers in research methodology, statistical and automated software, data management and interpretation.

The directorate works further to enhance the uptake of research evidence through forums for research dissemination, preparing policy briefs, research digests, scientific and technical institutional reports and devising other research results dissemination mechanisms. It is also the greater ambition of the directorate to enhance the institutional ability to update information easily and support, guide, consult and train researchers in overall usage of current ICT technologies.

Major achievements and ongoing activities

A. Data Management and Biostatistics

The Data management and Biostatistics unit has worked on different collaborative and PhD/ MSC student projects, Case Record Form (CRF) development, design questionnaires, database structure design, double data entry, data cleaning, verification, validation and data analysis. The software and applications used for the various projects varied depending on the project. Some of the major projects included STREAM Stage 1, ETHICOBOTS, ScreenTB, TBRU, Micro-LTBI_Ethiopia, malaria and leishmaniasis studies, LED project, SETA Surveillance Study, Evaluation of the Health Extension Program (HEP) in Ethiopia, Performance Evaluation of Laboratory professionals on Malaria Microscopy in Oromia region Ethiopia, Lipid bodies-PTB-Diagnosis, Bioequivalence study of oral ciprofloxacin and multiple different MSc and PhD projects.

Apart from those activities, the unit has collected and archived properly 50 various research projects of AHRI, those have already been published in different journals during 2018.

The unit has also been active in other activities including:

- Has started and drafted to develop data management and sharing guidelines
- Establishment of a system for database documentation at AHRI
- Improvement on required generic and project specific SOPs for Data Management
- Review and advice on MSc./PhD student protocols, CRFs, Questionnaire and publications;
- Supervision of the process of some data entry and statistical analyses for some M.Sc. and PhD students.

- Provision of capacity building trainings on :

  Data management and statistical software training given to various staffs coming from different sectors including 20 staff from the Ministry of Health (MOH) and 24 staff from the Dire Dawa health bureau. In addition, 3 other staff members obtained training on data collection and analysis. The overall aim of these trainings was to develop/use the skills data management and analysis using STATA statistical software

  In general, the unit has been engaged in training activities covering skills and expertise for capacity building of the staff as well as in a project specific manner.

B. Research Communication

Even though the unit is not established yet, as part of KMD there are several activities are being accomplished. The KMD isplaying a leading role in terms of facilitating translation of researches produced by AHRI researchers to the level of health policy influence. Accordingly, in year 2018, we have produced two policy briefs with one already submitted to the MOH and which is currently under consideration. The directorate has mapped the potential partners who would be able to work closely to develop knowledge management policy and strategic documents. As part of this activity, the directorate has collected necessary documents to develop national knowledge management strategic document for biomedical research institutes.

C. Information and Communication Technology (ICT)

The ICT unit is a composition of network and system administrator, graphic designer, web management and administrator, and IT technical supporters. The unit is responsible for development, implementation and maintenance of the infrastructure, hardware, and software utilization.

Network and System administration

The team has performed the following tasks.

- Design, plan, set up, maintain and expand the network
- Administrate network security and troubleshoot network problems
- Performed data backups and disaster recovery operations
- Monitored network performance in order to determine whether adjustments need to be made, and determined where changes need to be made
- Managed servers and their operating systems
- Added users to a network and assign and update security permissions on the network

Active devices

Domain Controller Server, Edge Server, Management Server (Cisco prime), Core Switch, Access Switch, WLC (wireless Controller), Checkpoint firewall , Access points

Web Management and administration

ICT unit maintains the institute website by identifying system updates, module and plugin upgrades, security checkup and monitored web performance. The unit coordinates with all directorates to ensure that the site provides up-to-date content and functionality. The unit manages and oversees content presented on websites, and also responsible for creating, editing, posting, updating, and

occasionally cleaning up outdated content.

Other obligation were responding to website feedback and letters, and implementing changes to the site's layout and content based on website analytics and requests of directorates.

The unit monitored web traffic, performance and capacity to identify, prevent and resolve issues.

Website visitors since April 2018

Total number of site Visitor: 297,654

Unique Visitor: 49,896

December 2018, Visitor: 67,870

IT technical support

IT technical supporters were mainly responsible for the smooth running of computer systems and ensuring users get maximum benefits from them.The following are few of the tasks performed

- Install and configure computer hardware operating systems and applications
- Monitor and maintain computer systems and networks
- Maintain and administer computer networks and related computing environments, including computer hardware, systems software, applications software, and all configurations
- Troubleshoot system and network problems, diagnosing and solving hardware or software faults

Graphic Designing

The Graphic designer combines art and technology to communicate ideas through images and the layout of pdf/word documents, websites and printed pages. The team work both with images and texts. They often select the type, font, size, color, layouts, images, and line length of headlines, headings, and text. The team also decides how images and text will go together on a print or webpage, including how much space each will have to use for the printouts and web formats.

Different kinds of graphic designing were done in 2018 which includes designing policy brief, brochures, rollup banners, student guidebook, flyers and annual reports. The team used digital illustration, photo editing software, and layout software to create designs.

Additional task performed

- Intuitional email was setup using G suite
- Prepared technical specification for ICT hardware and software
- Participated on bid evaluations
- Technology and software assessment Video conference and HRM system

Ongoing activities of KMD

- Staff recruitment process
- Staff recruitment for the units of research communication and clinical epidemiology has commenced and the most relevant applicants have been shortlisted for interview.

Training

The directorate is prepared to facilitate or provide trainings on knowledge translation and management, and systematic review and meta-analysis for AHRI staff and Ph.D. Students from partners institutions. This training is expected to enhance the capacity of participants to be able to exercise and apply research synthesis, knowledge translation and policy brief to generate evidence and influence health policy.

Office set-up

A conducive working environment and office set-up contribute positively towards work productivity and outcomes. Office materials like chairs, tables, file cabinets, and shelves have been purchased. Stacks of remotely cited, often unwanted and inactive documents were sorted out and relocated to temporary storage. We are considering means to re-organize office locations to increase space needs for staff.

2. Research Training Directorate

AHRI has been engaged in postgraduate biomedical research training for over 30 years. It hosts Master's and PhD students from various universities in the country enabling them to conduct their research work through provision of supervision (by AHRI's postdoctoral researchers), laboratory facility and financial support. Recruitment of graduate students follows a publicly advertised announcement. The Research Training Directorate is responsible for the recruitment, coordination and capacity building activities related to the research training program. The directorate also facilitates several bridging courses and other capacity building activities that involve both graduate students and AHRI's researchers.

Some of these initiatives and partnerships are as follows:

Emory-Ethiopia TB Research Training (EETBRT) is TB research training program involving Emory University, AHRI, AAU and EPHI. The program is funded by the National Institutes of Health Fogarty program with the objective of providing both short and long term trainings for promising MSc, PhD and post-doctoral trainees. Fifteen fellows from the above mentioned institutes are participating in this program. Of these, three are PhD students of AHRI.

Biomedical Sciences Postgraduate Partnership Program (BSPP) is a partnership between AHRI, AAU and various Swedish Universities to train the brightest PhD students registered at AAU who could have a multiplier effect in the future. Initially, the PhD students were able to spend up to six months at their Swedish advisors laboratory. However, after taking their feedbacks and discussing the matter with the funder, Sida, their stay in Sweden has been extended up to 24 months. AHRI has recruited a new BSPP PhD student this year and currentlysupports 12 BSPP PhD students on various biomedical specializations.

Brighton-Sussex Global Health Centre is a partnership in the field of genomics of global health importance. The partnership is made between Brighton Sussex Medical School, AHRI and other African institutes and is funded by the Welcome Trust. This program has great potential for capacity building in the future. The PhD student in this program working on genomics study of Podoconiosis is finalizaing his thesis this year and we have recruited a new PhD student to work on Immunological aspects of Podoconiosis.

FMoH-AHRI clinical research collaboration is a partnership in the field of maternal and child health, hepatitis B virus and arbovirus infection and antimicrobial susceptibility profiling. The program is supported by Ministry of Health (MoH) of Ethiopia and AHRI and conducted in partnership with local PIs at Addis Ababa University, University of Gondar, Jimma University, Hawassa University and Haramaya University. This collaborative program aimed at bridging biomedical and clinical disciplines while strengthening institutional capacity. Two PhD students are currently working on hepatitis B virus and arbovirus infection under this program. This year, 19 graduate students who completed their research work under this program have graduated.

AHRI-Haramaya University joint PhD program is a a unique postgraduate program where trainees are registered at Haramaya University and receive joint supervision and courses. Currently 5 Haramaya University teaching staffs are being jointly supervised for their PhD dissertations in Medical Microbiology.

We had a review meeting of this program in 2018 with the Dean of……from Haromaya University. The success as wel as challenges were discussed and it was agreed that the program shall continue as per the existing TOR. The Research Training Directorate is currently studying this model so that AHRI can support a second university.

AHRI-Haramaya University joint PhD Program Review Meeting

Lab meetings and Seminars

The Research Training Directorate has facilitated 30 lab meetings and 17 seminars by postgraduate students, staffs and guests.

Dr. John Clemens giving a presentation on oral cholera vaccine

We have also organized the 3rd Ethiopia-Norway Conference on Health and Higher Education annual conference in collaboration with the Norway Embassy in Ethiopia, Oslo university Hospital and Partnership for change. More than 120 researchers, practitioners and other stakeholders attended the one day conference that addresses primary health care, trauma and its care, and oncology care and education in Ethiopia.

Bridging Courses

Bridging courses facilitated by the Research Training Directorate are as follows:

Bridging Coruse	Number of Participants		
	M	F	Total
Biosafety and Biosecurity	14	2	16
Proposal Development & Literature Review using EndNote	12	1	13
Grant Development and Management	6	7	13
GCP/GCLP	18	14	32
Laboratory Techniques in Molecular Biology	32	9	41
Data management and Biostatistics Using *Statistical Softwares (SPSS & STATA)*	27	3	30
Laboratory Techniques in Immunology	29	6	35
Proposal Development	12	1	13
Research Ethics	4	11	15
Introductory Bioinformatics Course	8	5	13

Congratulations to Graduates of 2018!!

In 2018, 4 PhD students and 9 MSc students defended their thesis successfully. In addition, 19 Graduate Students under the FMoH and AHRI Clinical Research Network program also graduated. Currently, 49 PhD students and 16 MSc students are working for their thesis.

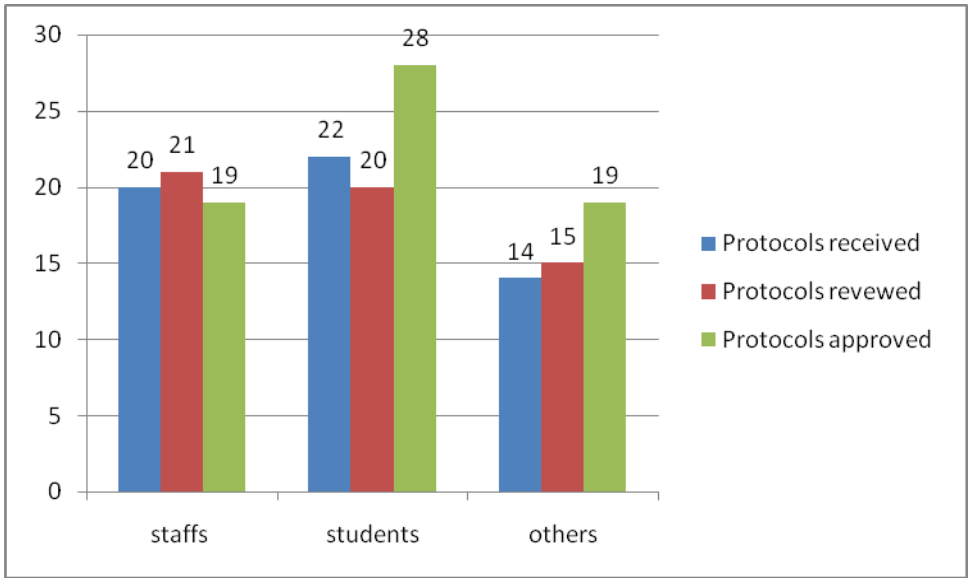
A list of 2018 graduates and their research topics

Name	Sex	Program	Thesis Title
Adugna Tsehay	M	MSc	Competency Assessment on Gram Stain examination and interpretation among medical laboratory professionals working in selected hospitals of Addis Ababa, Ethiopia.
Tigist Girma	F	MSc	Phenotypic Characterization of Peripheral B cells in Mycobacterium tuberculosis infection and disease in Addis Ababa, Ethiopia
Dareskedar Tsehay	F	MSc	The association of copy number variation of Fcgriiib Gene with the risk of Enl In Lepromatous Leprosy Patients from selected sites in Ethiopia
Migbaru Kefale	M	MSc	The role of ecological and molecular tools in evaluating performance of malaria control programs in Ethiopia

Berhanu Ayelign	M	MSc	Validation of locally produced Freeze-Dried Direct Agglutination Test Antigen for the diagnosis of Visceral Leishmaniasis at University of Gondar Hospital, North West Ethiopia
Wondimu Ashagrie	M	MSc	In vitro starvation model for assessing phenotypic drug tolerance on MTB Lineages in Ethiopia
Emawayish Andargie	F	MSc	Prevalence of Burkholderia pseudomallei and other bacterial pathogens in community acquired infections in different regions of Ethiopia
Netsanet Argaw	F	MPH	Treatment outcomes and associated factors among MDR-TB patients who were on Treatment during 2011-2016 at ALERT Hospital
Emawayish Andarige	F	MSc	Prevalence of Burkholderia pseudomallei and other bacterial pathogens in community acquired infections in different regions of Ethiopia
Geremew Tassew	M	PhD	Innate Immunity in visceral leishmaniasis
Menberework Chanyalew	F	PhD	Innate Immunity in coetaneous leishmaniasis
Marie Vanderwal	F	PhD	Evaluation of an Aloe enriched whey protein drink on measures of pediatric HIV
Yonas Bekele	M	PhD	Impaired response to HBV vaccination in HIV-1 infected chidlren: Immunopathological mechanisms

AHRI/ALERT Ethics Review Committee (AAERC)

Ethics review is the cornerstone for any biomedical research. As in the past, the AAERC has been actively working to ensure the ethical implementation of researches conducted by AHRI staff, students and other researcher who word within the premise of ALERT Center. The committee held 13 regular and two extraordinary ethical review meetings. Accordingly the committee review 56 protocols and granted approval for 66 protocols.



** The reviewed protocols are higher than the received one because of overflow from last year.*

3. Human Resources Development

Armauer Hansen Research Institute
Manpower Sorted by Gender

Gender	F	M	Total
	154	164	318

Manpower Sorted by Educational Level

Description	F	M	Total
PhD	5	13	18
MD/DVM	2	10	12
MA/MSc	21	36	57
BSc/BA	54	52	106
Diploma & Below	72	53	125
Total			**318**

4. Finance Audit Report

ARMAEUR HANSEN RESEARCH INSTITUTE (AHRI)

BALANCE SHEET

AS AT 30 JUNE 2018

Currency: Ethiopian Birr

	Notes		2017
ASSETS			
CURRENT ASSETS			
Debtors and prepayments	3	17,686,046.84	25,519,716.40
Cash and bank balance	4	42,785,417.80	18,523,932.92
		60,471,464.64	**44,043,649.32**
LIABLITES			
CURRENT LIABLITES			
Tax and other payables	5	3,013,338.52	1,855,766.17
		2,822,393.24	**1,855,766.17**
Net current assets		**57,649,071.40**	**42,187,883.15**
FUND BALANCE			
SIDA fund	6	4,282,356.21	(547,903.20)
NORAD funds	7	5,697,304.44	16,422,384.19
Other project funds	8	31,207,373.95	18,746,900.46
General fund	9	16,462,036.80	7,566,501.70
		57,649,071.40	**42,187,883.15**

ARMAEUR HANSEN RESEARCH INSTITUTE (AHRI)
INCOME AND EXPENDITURE
FOR THE YEAR ENDED 30 JUNE 2018

		Currency: Ethiopian Birr
INCOME		
Grants received and during the year	10	77,537,620.75
Less : Unutilized fund shown underfund balance		(4,392,455.29)
		73,145,165.46
Exchange rate difference related to prior year		8,917,696.13
Fund received to cover overhead costs		1,178,107.78
Government contribution		660,205.09
Exchange rate difference		5,327,435.67
Other income		9,345.85
TOTAL INCOME		**89,237,955.98**
EXPENDITURE		
SIDA and	11	23,207,572.38
NORAD		16,422,383.99
Salary and related benefits	12	17,236,216.01
Patient costs		466,221.53
Office supplies		193,790.05
Medical supplies		286,498.71
Food and food supplies		99,990.90
Fuel and lubricants		617,222.90
Research and development costs		4,260,804.56
Perdiem		5,496,188.47
Maintenance		284,510.42
Professional fee		55,846.14
Vehicle rent		248,179.88
communications		162,890.17
Training and school fee		3,102,314.36
Non-expendable assets		361,040.98
Gust accommodation		275,584.91
Bank and other charges	13	1,511,942.92
Misceanoues	14	218,791.69
		74,505,970.97
Excess of income over expenditure		**14,731,985.01**

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Training/conference/meeting participations

No	Participant	Event	Time/Duration	Place of event

1	Tsehaynesh Lema	M. leprae viability assay at National Hansen Diseases program,	May 5 to June 1, 2018	USA
2	Meseret Habtamu	Library preparation and DNA Sequencing at the ALLIANCE GLOBAL LABS (AGBL LABSs)		Dubai, United Arab Emirates
3	Liya and Kidist	Module preparation by Jhepigo organized by AHRI training Directorate		
4	Liya and Fiseha	GCP training	Nov 29-30, 2018	South Africa
5	Berhanu Seyoum	Systematic Review and Meta-analysis training organized by TB Research Advisory Committee (TRAC) of the Federal Ministry of Health.	Sept 17-21, 2018	
6	TBGEN lab team	Training on TB lab and biorepository.	August 2018	Kampala Uganda.
7	Nurses and lab technologists	Research Ethics, GCP/GCLP, Immunological assays	2801	AHRI,TBRU team
8		Kickoff meeting of the AHRI-APOPO project. Health professionals from more than 30 health facilities and delegates from Addis Ababa Health bureau attended the meeting.	January 15, 2018	Addis Ababa
	MDRD staff and students	TRAC annual conference..	March 19-23, 2018	Addis Ababa
	Adane Mihret	ScreenTB annual meeting and LFA training	12 – 14 March 2018	Gambia
9	Yonas Kassahun, Kidist Bobosha, Anteneh Getahun, Yemisrach Zewdie	H3Africa consortium meeting and new projects (TBGEN and others) inception meeting.	March 19-21, 2018.	
10	Abraham Aseffa, Kidist Bobosha, Liya Wassie, Elena hailu, Wegene Tamene, Endalamaw Gadissa	EETBRTP 4th annual conference.	July 1-3, 2018 Sept 2018.	Debrezeit Atlanta, Georgia
11	AHRI MDRD staff	APOPO consultative meeting.	Oct 11, 2018 Sept 19-21, 2018.	AHRI, Addis Ababa Kigali, Rwanda
12	Abraham Aseffa, Yonas Kassahun, Kidist Bobosha, Yemisrach Zewdie	TBGEN startup meeting.	Sept 19-21, 2018	Kigali, Rwanda,
13	Abraham Aseffa, Kidist Bobosha	PEP4LEP startup meeting	Nov 19-22, 2018	Dar Es Salaam, Tanzania
14	dal Endalamaw Gadisa	Ease Biomarkers and Precision Medicine, Serological signatures of clinical cure following successful treatment with sodium stibogluconate in Ethiopian visceral leishmaniasis	24 Oct 2018	ust Texas, USA 22-
15	G T	h a Annual conference of the American Society of Tropical Medicine and Health, Substantial household level clustering and genetic relatedness of subpatent Plasmodium falciparum and Plasmodium vivax infections in a low-endemic setting aiming for malaria elimination in Ethiopia	Nov 01, 2018	New Orleans, USA Oc
16	FitsFitsum G Tadesse	MIM Pan-African Malaria Conference, The contribution of symptomatic and asymptomatic P. vivax and P. falciparum infections to the infectious reservoir in Ethiopia Co-chaired a scientific session on Epidemiology	Apr 2018	Dakar, Senegal
17	Samuel Ayele	Data management and analysis with stata statistical software training		Bangladesh

Grants Submitted/Awarded / Rejected

Awarded / Signed

Title	Grant amount	Funder	PI	CO-PI
Genetic Susceptibility for Tuberculosis (TBGEN)	2,825,739 USD	African Academy of Science (AAS)	Abraham Aseffa (AHRI)	
EETBRTP (Ethiopia-Emory TB Research Training Program)	1,480,560 USD	D43 Fogarty (NIH)	Henry Blumberg and Abraham Aseffa ("Joint PIs")	
Improving quality of diagnostics and monitoring tools	1,400,000USD	Ministry of Health (MoH)	Markos, Andargachew, Endalamaw, Kidist and Menberework	
Validation of the visceral leishmaniasis environmental factor-based risk map:	40,000 USD	WHO	Endalamaw Gadisa (AHRI)	
Safety of the co-administration of Azithromycin, Ivermectin and Albendazole versus standard MDA regimen during Mass Drug Administration: London School of Hygiene and Tropical Medicine (LSHTM)	845,000 USD	LSHTM	Scott McPherson (LSHTM)	Endalamaw Gadisa (AHRI)
Dynamics of asymptomatic Malaria:	165,000 USD	LSHTM	Teun Busman (LSHTM)	Fitsum Girma(AHRI)
Follow up of P. vivax patients for serological correlates of relapses:	20,000 USD	LSHTM	Rick Prince	Fitsum Girma(AHRI)
KAP Brucellosis and Anthrax among pastoralists in Afar and Somali Region.	50,000 USD	CDC	Rea Tschopp (AHRI)	
Chemoprophylaxis for leprosy: comparing the effectiveness and feasibility of a skin camp intervention to a health center based intervention. An implementation trial in Mozambique, Ethiopia and Tanzania.	111,000 EURO (allocated for AHRI)	EDCTP and NLR	Liesbeth Mieras (NLR)	Kidist Bobosha (AHRI)
Stigmatizing skin diseases: co applicant (Endalamaw Gadisa) with LSHTM to NIHR (Prof lead applicant)	4,999,182 GBP	NIH (LSHTM)	Steve Walker	Endalamaw G (AHRI)
Free Professional Services to the Ministry Of Health Requested by the national Control program Evaluation of Integrated Mass Drug Administration for Neglected Tropical Diseases in Selected Districts of Ethiopia.	522,000 ETB	MOH	Sagni Challi (AHRI)	

Title	Grant amount	Funder	PI	CO-PI
Training of Trainer for coverage Evaluation on preventive chemotherapy survey tool for selected University staff.	466,766.00 ETB	MoH/SDG	Sagni Challi (AHRI)	
Technical training in podoconiosis management: Sponsored by SDG	620,482.00 ETB	MOH/SDG	Sagni Challi (AHRI)	
National ART program effectiveness study	300,000 USD	USAID	Achamyeleh Alebachew	Andargachew M (AHRI)
Enhanced detection rates of causative agent among TB patients to improvetrue zoonotic TB rate- ETHICOBOTS 2	100,000 USD	ZELS, UK	James Wood	AdaneMihret (AHRI)

Submitted / Pending Proposals

1. Evaluation of the feasibility, accuracy, and effect of a rapid point-of-care serological triage test for active TB (SeroSelectTB) in high burden, HIV-endemic African settings: a multi-centre, parallel-group, randomised controlled trial. NIPH (Carol Holms), AHRI, KCMUC, LFA laboratories; Cape Town

   Status: Pending, invited for full proposal by EDCTP

2. Modulation of C-type lectin receptor expression by helminth or HIV infection: setting the threshold for sensing of mycobacteria

   Status: invited for full proposal by DFG, Germany

   AHRI (Markos Abebe) and collaborators from National Biotechnology Development

   Agency, Nigeria and University Hospital Erlangen, Germany.

3. RD4 Swiss Gov: Migration health (800,000 CHF). Rejected. The proposal was submitted in fall 2018 (2,000,000 CHF) after revision.

   Status: pending

4. Swiss national Science Foundation: NCCR- Precision Epidemic Forecasting (PEF) as a multi country project (Guatemala, Switzerland, Ethiopia).

   Status: pending

Rejected

1. Cellulose paper based test-strip for Leishmaniasis diagnostic and follow-up in Point-of-Care: co applicant (Endalamaw Gadisa) with Instituto Superior de Engenharia do Porto to EDCTP (Felismina Moreira)

   Status: rejected

2. EDCTP: Clinical and laboratory evaluation of a fully automated multiplex PCR assay for detection of infectious agents in fereish patients and asymptomatic controls in Cote d'Ivoire and Ethiopia (2.5 mio EUR).

   Status: rejected


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Federal Democratic Republic of Ethiopia
Ministry of Health


Sida


Norad
Norwegian Agency for Development Cooperation


World Health Organization


EDCTP


ADDIS ABABA UNIVERSITY


Karolinska Institutet


EMORY UNIVERSITY


LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE


TDR
For research on diseases of poverty
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The African Academy of Sciences


giz
Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH


UiO : University of Oslo


LUND UNIVERSITY


ÖREBRO UNIVERSITY


UPPSALA UNIVERSITET


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2018 AHRI ANNUAL REPORT

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