Foreword

2016 was a year of great progress for Armauer Hansen Research Institute (AHRI). In February, the Council of Ministers approved a legislation which has made AHRI an independent national research institute with substantial expansion of its mandates. Regulation 376/2016 has outlined AHRI’s national obligations to set research agendas and conduct research in biomedical technology and biotechnology, medical, clinical, genetics, bioinformatics, systems epidemiology and medical technology. Further, it has highlighted AHRI’s responsibility to develop capacity in clinical trials research and medical research training. Meanwhile, the Government of Ethiopia has shown its firm commitment to support AHRI advance its wide-range mission in these areas.

In 2016, AHRI implemented 70 research projects and reported 47 peer reviewed scientific publications. Our research projects were ethically transparent, cost efficient and were either sources of new knowledge or drivers of policy decisions. We largely focused on flagship initiatives of the Federal Ministry of Health and endeavored to develop innovative solutions. Areas of our research emphasis ranged from leprosy (the primary mission for AHRI’s establishment) to new national priorities like non-communicable diseases. With continued expansion and diversification of our research areas, we now cross the boundaries of human health and delve into zoonotic diseases that affect the health of humans and cattle. We also invested substantial amount of money and time on establishing research systems for clinical trials in the country and medical research training.

While consolidating our progress in biomedical research, we are currently charting new territories including health biotechnology and innovation in health care. We have health biotechnology roadmap in place which outlines our long-range plans of developing important diagnostics, vaccines and medicines. Likewise, we have established Grand Challenges Ethiopia aiming at stimulating, sourcing, evaluating innovations and transitioning the best ones to scale.

We have strong partnership with institutes, domestic or international, to continuously improve our performance. In particular, we are privileged to have special partnership with Sida and Norad. Our core funds principally come from these two partners. We are currently receiving generous financial support from Federal Ministry of Health. Our Scientific Advisory Board (SAB) has given us strategic guidance to improve the quality and potential impact of our research and training. Most importantly, men, women and children who willingly and continuously participate in our studies are our essential partners. I would like to sincerely thank Federal Ministry of Health, Sida, Norad, our SAB members, our study participants and all other partners for our continued collaboration for impact. I would also like to gratefully thank the vibrant AHRI team for the great work in progress.

I am confident that we will sustain this accelerated growth at AHRI and, together, we will deliver more discoveries which could potentially improve people’s daily lives.

Sincerely,

Taye Tolera Balcha, MD, MPH, PhD
Director General, Armauer Hansen Research Institute
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Executive Summary

In February 2016, the Council of Ministers re-established Armauer Hansen Research Institute (AHRI) as autonomous research arm of the Federal Ministry of Health of Ethiopia. Revisiting Ethiopia’s health research priorities and AHRI’s potential in this regard, the Council of Ministers substantially expanded the mandates of the Institute. The regulation 376/2016 has given AHRI a broad range of national mandates that include developing research agenda, conducting research by itself or through forging partnership with local or international institutes, wide dissemination of research findings and translating discoveries into policy, practice and products. Specifically, the Institute has a nationwide responsibility in research and innovations related to biomedical technology and biotechnology, medical, clinical, genetics, bioinformatics, systems epidemiology and medical technology. Further, the council approved that the Institute should play significant role in capacity building including medical research training and strengthening research systems for clinical trials in the country.

With stronger political commitment and broadened vision and mission, AHRI has conducted a diverse array of transparent health research intended to generate new knowledge and drive policy decisions. In 2016, the Institute was engaged in a total of 70 ongoing research projects, of which 20 were completed this year. During the same year, the Institute contributed 47 peer reviewed publications to science.

In tuberculosis, the Institute conducted several studies targeting pressing scientific and programmatic needs including biomarker research, diagnostic development and molecular epidemiology and mapping of the disease. Some notable ongoing projects include phenotype and functional characterization of T cell subset from lymph node lesions and peripheral blood of calves exposed to natural Mycobacterium bovis infection, evaluation of host biomarker-based point-of-care tests for targeted screening for active tuberculosis, molecular epidemiology of tuberculosis and the role of Mycobacterium bovis in settings with high dairy development, evolution of novel Mycobacterium tuberculosis genotype in East Africa and virulence trait assessment and a proof-of-concept on immunodiagnosis of paediatric tuberculosis using modified QuantiFERON-TB Gold In-Tube test. Additionally, the Institute is in the process of launching new potentially impactful studies including enhanced tuberculosis case detection by trained rats and whole genome sequencing analysis of Mycobacterium bovis isolated from cattle.

Although leprosy is eliminated nationally, scores of hot spot geographies exist. As a consequence, risk-based mapping of new leprosy cases and their household contacts is one of the Institute’s ongoing studies. As this study is integrated with Ethiopia’s novel community platform, health extension program, it is believed to enhance early case detection and minimize the rate of disability. The Institute is evaluating the diagnostic potential of Auramine O staining for leprosy and is optimizing line probe assay for detection of Mycobacterium leprae drug resistance which could be of special significance in cases of relapse. The Institute paid continued attention to the remaining uncertainties and unknowns in host-pathogen interaction in leprosy. In this regard, a research project on immunopathogenesis of erythema nodosum leprosum (ENL) was completed in 2016.

In 2016, AHRI conducted a number of basic and clinical research on bacteria and viruses aiming at improving prevention, control and detection of respiratory and related invasive bacterial pathogens; mapping antimicrobial resistance; and deeper understanding of viral oncogenes and emerging viral infections. In coherence with the health sector priorities, typhoid fever, pneumonia, meningitis and hospital acquired infections were points of research emphasis for the Institute. The impact of ten-valent pneumococcal conjugate on Streptococcus pneumoniae nasopharyngeal carriage rate, the impact of meningococcal conjugate vaccines on sero-group A transmission and systematic study of hospital acquired infections and antibiotic resistance were just few examples of research projects implemented in the area in 2016.

Similarly, the Institute conducted biomedical and clinical studies on common viruses including human immunodeficiency virus, hepatitis and influenza. In particular, a large-scale project initiated and funded by the Federal Ministry of Health is worth mentioning.
The study aimed to map arboviruses including dengue and yellow fever and to assess the overall burden of hepatitis in the country. Specific, clinically relevant works included determining serological and clinical efficacy of hepatitis B vaccination in the country, the sero-prevalence of hepatitis C and D, the burden and viral etiology of chronic hepatitis, cirrhosis, hepatocellular carcinoma among hospitalized patients, as well as the seroprevalence of Hepatitis E and its contributions to pregnancy-related hepatitis.

Guided by the Ministry’s heightened focus on zoonotic diseases, AHRI increased the depth and breadth of its One Health Initiative. Most of the research projects were conducted in the eastern part of the country where the communities are largely pastoralists. Some of the studies still underway include assessment of brucellosis, Q-fever and Rift Valley Fever among livestock and people. The Institute is also currently investigating the impact of bovine tuberculosis on diary animal productivity and exploring cost-effective strategies for the control of bovine tuberculosis among cattle.

Malaria and neglected tropical diseases studies conducted in 2016 ranged from biomedical research to operations research directly linked to national strategies to meet health sector transformation plan targets and health-related Sustainable Development Goals (SDGs). In malaria, for instance, the dynamics and implications of asymptomatic malaria as a source of malaria infection, clustering of asymptomatic malaria infections, the epidemiology of the drug resistance alleles in Plasmodium falciparum, the population genetics of Plasmodium vivax and its prevalence, and genotype of glucose-6 phosphatase dehydrogenase deficiency and in vitro drug resistance assessment techniques for different stages of Plasmodium species were notable areas of research. Further, several studies investigating important aspects of cutaneous and visceral leishmaniasis are currently underway. Another large-scale clinical research project about to be launched is intended to assess the safety of co-administered Ivermectin, Albendazole and Azithromycin. Given the high burden of the target diseases in the country, the findings of the research could potentially be a game changer in integrating elimination efforts of neglected tropical diseases with primary health care in Ethiopia and beyond.

Clinical trials are top-tier priority research methods for the Institute. While the Institute completed few clinical trials which led to consequential policy decisions, there is an ongoing multi-country trial which aims at evaluating the non-inferiority of shorter treatment regimen for multi-drug resistant tuberculosis compared with the current WHO standard. As a bioequivalence trial site, the Institute also conducted pilot clinical bioequivalence studies on two locally and regionally produced antibiotic products. Currently, it is prepared to launch the conduct of a pivotal study on a locally produced tablet product for possible WHO inspection and product pre-qualification application.

Following national priorities and community needs, the Institute widened its scope to include research in non-communicable diseases, health biotechnology and innovation in health. It has been establishing human leukocyte antigen (HLA) laboratory to support Ministry’s new initiative on renal transplantation. When completed, the HLA typing laboratory at the Institute will save considerable amount of time and cost related to renal transplantation. Further, the Institute is evaluating the clinical utility of recent global advances in diagnosis of hematologic malignancies to enhance early detection and improve treatment outcome. Currently, it uses flow cytometric methods, as well as other cellular and molecular approaches, in particular Fluorescence In Situ Hybridization (FISH) to identify pathognomonic genetic abnormalities. In health biotechnology, the Institute developed a road map with long-range plans of developing diagnostics, vaccines, medicines and treatment devices. The Institute also launched Grand Challenges Ethiopia initiative to stimulate, evaluate and transition to scale innovations that could spur the progress towards achieving SDGs and universal health coverage.

Medical research training was an integral component of AHRI’s work in 2016. The Institute supported several short-term trainings related to conduct of research including clinical trials, data analysis and reporting of research findings and research bioethics both for the staff and partner institutions. More importantly, the Institute is supporting long-term trainings including masters and doctoral studies. Overall, the Institute has supported the biomedical research training of 75 students. Of these, 45 have enrolled in doctoral studies, principally supported by the core funding.
Over the years, AHRI has established smart partnership with domestic and foreign institutes. The partnership ranges from direct financial support to co-implementation of research projects and medical research training. Norad and Sida are the major strategic partners providing the Institute’s core funding. Recently, the Government of Ethiopia began to provide the Institute with generous amount funding targeting research and development with great promises to contribute to the national targets in health. The Institute has forged essential partnership with domestic institutes including Ethiopian Public Health Institute to avoid unnecessary overlaps and to improve value for money in research and development. Further, the Institute has robust collaboration with institutes in the global south and north to facilitate cross-fertilization of transformative research ideas and transfer of technologies and solutions.

**Scientific Advisory Board**

AHRI acknowledges the invaluable contribution of the AHRI Scientific Advisory Board members to their continued advice in the development of research at the Institute. Last year’s Scientific Advisory Board meeting took place from 11-15 January 2016 at AHRI.

— Prof. Demissie Habte, Prof. Hazel Dockrell, Prof. Gunnar Bjune, Prof. Francesca Chiodi

**New SAB Members**

*Haileyesus Getahun (MD, MPH, PhD)*
Coordinator, TB/HIV and Community Engagement
WHO Global TB Programme, Geneva, Switzerland

*Prof. Tsige Gebre-Mariam*
President of the Ethiopian Academy of Sciences
Addis Ababa, Ethiopia

*Dr. Kaba Urgessa*
State Minister of Ministry of Agriculture
Addis Ababa, Ethiopia
Highlights of 2016

AHRI’s New Legislation

AHRI was formally established as a federal autonomous government office having its own legal personality through the Council of Ministers Regulation No 376/2016 issued on 19 February 2016 (Federal Negarit Gazette No. 45, p 8898-8906, Federal Democratic Republic of Ethiopia). The Institute is accountable to the Ministry of Health and will have its headquarters in Addis Ababa but may have branch offices elsewhere as may be necessary. It will have four main objectives:

1. Undertake biomedical, clinical and biotechnology research and adopt and implement scientific technologies to improve clinical care, health and well being of the public
2. Conduct clinical trials on new and improved medical diagnostic methods, vaccines and drugs to improve public health
3. Build capacity in higher education and other related institutions in the area of biomedical, clinical and medical biotechnology research and
4. Serve as a center of excellence in medical research and training in Ethiopia and Africa

Its responsibilities include developing research agenda on biomedical technology and biotechnology, medical, clinical, genetics, bioinformatics, systems epidemiology and medical technology and conduct research and evaluate impact. The Institute is mandated with the task of assessing the current capacity for clinical trials in the country, to identify potential partners and build national capacity to conduct clinical trials. It is also expected to strengthen cooperation with regions and neighboring countries in medical research and training, promote technology transfer and product development, undertake joint clinical research with international institutes, organize national fora for medical researchers and submit policy briefs to government. The Institute will have its own international advisory board appointed by the Minister of Health.

This is an historical milestone for the Institute. It formally integrates AHRI within the national health and health research system and removes barriers to access national resources and networks. It demonstrates government commitment and responds to the request of AHRI core funders to ensure sustainability of the Institute through national ownership. The legislation allows for AHRI to raise core support, grant funds, financial assistance and miscellaneous revenue from various sources to support its activities. It also allows for the Director General to establish an institutional structure that can advance innovative, translational, operational and applied research including development of a competent human workforce and an enabling working environment.

Director General appointed

Dr Taye Tolera has been appointed by H.E. Prime Minister Hailemariam Desalegn as Director General of Armauer Hansen Research Institute, effective 16 June 2016. Prior to his current assignment, he served as Special Advisor and Head of Office of the State Minister of Health. He has also served at various levels of leadership in the Oromia region, including as Deputy Head of the Regional Health Bureau, researcher and clinician. Dr.TayeTolera obtained his PhD degree in Epidemiology from Lund University, Sweden in 2015. He received Masters Degree in Public Health from the same university and Doctoral Degree in Medicine from Addis Ababa University. He has led several initiatives including country ownership and leadership of HIV programme and the establishment of Grand Challenges Ethiopia to stimulate innovations that can catalyze the progress in health sector and improve people’s daily lives. He has several publications in peer reviewed journals with particular focus on TB/HIV and health and community systems strengthening. He brings a rich experience of health service management at each level in Ethiopia.
The appointment of Dr. Taye Tolera marks the beginning of a new era for the Institute. He is very well qualified and positioned to guide the smooth transition of AHRI into a national Institute. He will build on and wisely utilize the accumulated institutional experience of AHRI that has enabled its extraordinary resilience of survival, growth and productivity through the tumultuous changes in the country over the last 45 years.

AHRI acquires new laboratory equipment

A major strength at AHRI has traditionally been its strong biomedical laboratory, “strong” not only in terms of equipment diversity and quality but also in the competence of its maintenance team. However, over the last decade, more and more pieces of equipment could not be repaired anymore because their parts were unavailable on the market. This became especially dire when the liquid nitrogen plant and both of the two main autoclaves of the Institute ceased to function. The manufacturers had long stopped producing essential components. Although AHRI could regularly replace several relatively smaller pieces of equipment through core support and competitive grants, and even purchase a FACS Canto to expand flowcytometry work through an EDCTP grant, it failed to save or acquire sufficient funds to buy larger pieces of the essentially basic large pieces that were ineligible for project support.

When it did, as for the purchase of an autoclave partially funded by EDCTP, the procurement process was too slow to complete a purchase. The autoclaves were finally installed by HEAL TB/USAID who donated two pieces to the Institute to overcome the frequent interruptions of TB laboratory work at AHRI.
Pathology laboratory Technologist on routine activity

Based on the request of AHRI and repeated recommendations of the Scientific Advisory Board, and in consultation with the Ministry of Health, specific funds were allocated by Sida for equipment and laboratory upgrade. This was further supplemented by funds from NORAD. Through the active intervention and support of the Ministry of Health, the whole procurement process was delegated to UNOPS. Although it took longer than expected, AHRI could finally manage to secure a liquid nitrogen plant, a complete set of equipment for tissue processing in the pathology lab, several biosafety cabinets, refrigerated centrifuges, deep freezers, carbon dioxide incubators and a high capacity water distiller. A second-generation Illumina sequencer is also expected to be installed in the new Biotechnology and Bioinformatics Directorate of the Institute soon. In addition, through another complementary Sida grant and the additional support of Norad, AHRI is in the process of upgrading its IT infrastructure to enable high throughput data transfer and basic performance in bioinformatics. Several new vehicles have been added to the AHRI fleet of vehicles through Norad funds. The Institute is therefore in a much stronger position in 2016 than it was earlier to face up to the new challenges of a national mandate in health research and capacity building.

Grand Challenges Ethiopia Initiative

Armauer Hansen Research Institute (AHRI), is hosting Grand Challenge Ethiopia (GCE), a new initiative of Federal ministry of Health of Ethiopia with the goal of stimulating innovation in health, an area that was starving for new ideas and to generate evidences and breakthroughs, joining a growing family of similar Grand Challenges programs across the globe. This initiative established under AHRI Director General’s Office, with its own secretariat. GCE secretariat office run by a coordinator and a program assistant to carry out the day-to-day activities of GCE. In addition, the secretariat office will be supported by a national Taskforce and an international advisory Board to provide technical support and advice for the smooth implementation of the activities included in the initiative and, on demand, short-term technical assistances from Grand Challenges Canada and Bill and Melinda Gates Foundation.

The aim of the Grand Challenges Ethiopia (GCE) is to stimulate 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 the health sector transformation plan (HSTP) and contribute to achieve the Sustainable Development Goals (SDGs). The innovations will include integrated or single application of scientific, operational or socio-cultural strategies, approaches, tools, systems and interventions.

GCE will use the following approaches to realize these ambitions:

1. Identify challenges and stimulate innovations that could solve those challenges and contribute to achieve SDGs,
2. Test innovations and technological solutions surfaced elsewhere but are applicable in our setting
3. Invest in implementation of selected innovations at scale

The main task of Grand Challenge Ethiopia secretariat includes:

- Select grand challenges and support innovations addressing these challenges by providing seed grants
- Scan for new innovations in innovation marketplace and support in-country testing of technologies and eventually invest in importing appropriate ones.
- Establish early and lasting partnership with Grand Challenges Canada and Bill and Melinda Gates Foundation to access innovations abroad.
• Select innovation for implementation at scale by using robust tools with clear metrics to measure the impact and cost of the innovation.

The following activities have been accomplished this year.

• The GCE-Secretariat has been established, the coordinator has been recruited and has started his duty
• The Annual plan has been developed
• The recruitment of Program assistant is being processed
• Terms of Reference for the task force has been developed
• The taskforce member has been selected and communicated with
• Thematic areas for this year has been selected
  • Challenge 1: Maternal health
  • Challenge 2: Newborn and childhood health
  • Challenge 3: Pastoralist and other least developed regions’ health services
• Facilitation of the test of innovations and technological solutions surfaced elsewhere
  • Support the testing of Acute Respiratory Infection Diagnostic Aid (ARIDA)
    • Support for the protocol development provided
    • The ethical approval process facilitated
**Research and Innovation**

**Mycobacterial Disease Research Directorate (MDRD)**

The History of AHRI itself begins with the study of Leprosy Immunology in the 1970s. Following the reduction in the burden of Leprosy as a result of introduction of MDT, and the increase in Tuberculosis coinciding with the onset of the HIV epidemic, the main focus of the institute shifted to tuberculosis research. Tuberculosis and Leprosy research were separately managed as two different case teams but with the new restructuring of AHRI, these two notable diseases are put under 'Mycobacterial Disease Research Directorate' with a flagship 'early diagnosis for better management'.

**Tuberculosis case team**

Although Ethiopia has made significant progress in the fight against TB, undetected TB cases among the community and the introduction of drug resistance forms of TB including MDR and XDR remain as challenges for disease control.

Multidrug resistant (MDR) and extensively drug resistant (XDR) M. tuberculosis are increasing. In line with the recognized greater effort needed to combat this problem, WHO and other stakeholders are trying to mitigate this problem through STOP TB and END TB strategies.

A comprehensive effort among researchers, pharmaceuticals, public health specialists and policy makers is necessary to meet set targets. Research should be prioritized to identify relevant research questions and conduct research that generates knowledge for development of diagnostics, vaccines and therapeutics by pharmaceuticals and used by policy makers to make evidence based decisions.

The Mycobacterial Disease Research Directorate is focused on understanding basic mechanisms of TB disease, developing methods of diagnostics, biomarkers and treatment in order to assist the national and global effort in controlling TB. The research under this directorate ranges from studying disease prevalence to understanding basic mechanisms of disease and to identifying diagnostic tools and treatment.

In 2016 there have been 23 different projects under the directorate. The figure below shows the number of new/ongoing TB projects under different categories.

A collaborative project between NIPH, AHRI and REACH Ethiopia has just launched a population based study in Dale District, Sidama Zone, Southern Ethiopia to make Spatial Analysis of Tuberculosis Clustering. Yared Merid has been studying the Molecular epidemiology and drug resistance of tuberculosis in southern region of Ethiopia. His prison study has revealed that the point prevalence of PTB was estimated to be 1748 per 100,000 persons. This rate of TB among incarcerated persons is ~16 fold higher than in the general population.
Two other studies by Elena Hailu and Solomon Yimer are looking at the molecular epidemiology of Lineage 7 and its associated drug resistance pattern and clinical manifestations. Both groups have reported that lineage 7 M. Tbis slower growing in culture compared to other lineages. Hawult Taye is studying the role of bovine TB in settings with high dairy development in Ethiopia.

With regards to diagnostics and biomarkers, the study by Markos Abebe on modified QFT-GIT for the detection of TB in HIV has been published by the European Patent Office and the study on the usefulness of this test in pediatric TB is to start in 2017. Adane Mihret is working on the development of a lateral flow based point-of-care test based on a combination of 6 biomarkers. A new version of TB diagnosis using trained rats is just launched in collaboration with APOPO. This approach has been tested in a couple of African countries and has shown promising results in increasing TB detection rate.

A collaboration with the new BioInformatics Directorate includes an Analysis of data from Whole Genome Sequencing (WGS) of Mycobacterium bovis isolated from Ethiopian cattle by Yonas Kassahun. The sequence is obtained from Animal and Plant Health Agency (APHA) in London. AHRI is expected to have its own DNA sequencer by early 2017. This project will facilitate capacity building in bioinformatics at AHRI on WGS analysis of strains from the Mycobacterium tuberculosis complex.

An immunological study conducted by Fekadu Desta on lymph node samples from cattle revealed that BCG vaccination was found to significantly reduce the microscopic granuloma score within the lymph nodes. Parallel immunohistochemistry revealed reduced numbers of macrophages and T cells but increased levels of NOS, IFN-γ and TNF-α in granulomas of BCG vaccinated compared with unvaccinated animals. Understanding the immune response during TB-HIV co-infection remains vague. Wogene Tamene is investigating the role of TB, HIV and TB/HIV co-infection on phenotypic and functional properties of subsets of peripheral blood monocytes (characterized by CD14 and CD16 expression) using selected innate immune markers such as toll like receptors (TLR2, 4, 7 & 9), chemokine receptors (CCR1, 2, 4, 5, 7 and CX3CR1) and cytokines by flow cytometry and RT-PCR.

Two projects have been conducted using a systematic review and meta-analysis approach. Liya Wassie is analyzing the usefulness of bleach digestion method on the sensitivity of smear microscopy while Mesret Gebre is analyzing the performance of Xpert MTB/RIF assay using fecal specimens for the diagnosis of pulmonary tuberculosis (TB) in children. Such approaches are new to AHRI and need to be encouraged to synthesize and generate evidence based knowledge for policy makers.

I. New projects

1. Enhanced Tuberculosis case detection in Ethiopia by trained rats (APOPO)
   Negussie Beyene¹ (PI), Christiaan Mulder¹, Cindy Fast¹, Christophe Cox¹, Markos Abebe² (CO-PI), Taye Tolera², and Ben Tegegn³
   ¹APOPO, ²AHRI, ³Addis Ababa City Administration Health Bureau

In addition to the nationwide coverage of the DOTS strategy, Ethiopia launched a complimentary approach
to reach TB patients through health extension workers. Despite all these efforts, TB still remains one of the major public health challenges in Ethiopia. With a TB prevalence of 200/100,000 of the population (WHO, 2015), Ethiopia is one of the 22 high TB burden countries. Like most Sub-Saharan African countries, the case detection rate in Ethiopia is far from the global target of 70%.

In the hope of supporting the fight against TB, APOPO (a Belgian NGO that trains rats to save life) developed a unique diagnostic technology based on the olfactory capacity of trained Giant Pouched Rats. The method can be deployed in a fast and efficient manner to evaluate large number of human sputum samples for the presence of *Mycobacterium Tuberculosis*. In Tanzania and Mozambique, APOPO has demonstrated that it can raise the detection rate of the collaborating TB clinics by more than 40%. To date, APOPO’s trained TB detection rats detected more than 10,000 TB patients that were missed by conventional microscopy.

APOPO uses operant conditioning for the training of its TB detection rats. The rats are taught to associate the scent of TB in human sputum samples with a click sound and subsequent food reinforcement. A trained rat can evaluate 40 samples in only 7 minutes. In comparison, a trained lab technician takes a full day to search for TB in the samples using microscopy with a similar or at times lower accuracy. Due to the high speed of the rat evaluation, the samples can be searched by several rats, thereby increasing the sensitivity of the method beyond that of microscopy.

Accordingly, APOPO and AHRI have signed a 5 year project agreement with the objectives of (1) contributing to the national TB control program of Ethiopia by increasing the number of identified TB patients in the short term and (2) building a local capacity of TB detection rats and personnel to create a long term impact on reducing the TB problem in Ethiopia.

**Funding:** APOPO

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**2. Spatial Analysis of Tuberculosis Clustering in Dale District, Sidama Zone, Southern Ethiopia: A Population-Based Prospective Cohort Study**

Brita Askeland Winje¹, Daniel G Datiko², Markos Abebe³, Einar Heldal¹, and Gunnstein Norheim¹

¹Norwegian Institute of Public Health, Norway; ²REACH ETHIOPIA; ³Armauer Hansen Research Institute

Geographical information systems are increasingly being used in studies on infectious diseases to identify transmission patterns and disease clusters. The objective of the study is to describe the spatial distribution of tuberculosis (TB) and identify geographic clustering of TB in the Dale District, Sidama Zone, Ethiopia and to reveal underlying socio-economic, demographic and clinical factors that may explain such clustering (WP1). The study will also determine the incidence of pulmonary tuberculosis over a 12–month period, and
assess the added value of the cluster detection techniques to routine surveillance of TB. Molecular typing of TB strains will be performed to study transmission routes.

The project conducted a kick off meeting in Hawasa on the 22\textsuperscript{nd} of August 2016.

**Current status**

By November 1\textsuperscript{st}, 2016, 4793 households have been visited, 225 individuals with presumptive TB have been identified and 156 samples have been collected. Positive sputum samples are sent to AHRI for culture.

**Funding:** NIPH, Norway

### 3. Performance of Xpert MTB/RIF assay using fecal specimens for the diagnosis of pulmonary tuberculosis (TB) in children: a systematic review and meta-analysis

Mesert Gebre\textsuperscript{1}, Lindsay Hatzenbuehler\textsuperscript{2}, Liya Wassie\textsuperscript{3}

\textsuperscript{1}All Africa Leprosy, Tuberculosis Rehabilitation and Training Center (ALERT) Hospital; \textsuperscript{2}Emory University, USA; \textsuperscript{3}Armauer Hansen Research Institute (AHRI)

Microbiological confirmation of pediatric pulmonary TB is a challenge due to several factors: the paucibacillary nature of the disease, resulting in low sensitivity of both smear microscopy and culture, the invasive nature of sample collection procedures, long culture incubation times and the need for sophisticated laboratory equipment to isolate the bacilli. The Xpert MTB/RIF assay is recommended by the WHO to overcome some of these challenges, and studies have evaluated its diagnostic capacity in children suspected of having pulmonary TB on the following specimen types: sputum, nasopharyngeal and gastric aspirates, lymph node aspirates and biopsy from different tissues. Compared to smear microscopy, geneXpert was shown to have a sensitivity of 37\% and 44\%, in expectorated induced sputum and gastric aspirate samples, respectively. In smear negative samples, its sensitivity ranged from 25-100\% in induced sputum samples and 40-100 \% in gastric fluid. More recent studies have evaluated its diagnostic use in fecal samples with a sensitivity ranging from 47\% to 84\%, as they also offer a non-invasive, easy to collect diagnostic procedure for pediatric pulmonary TB. Prior to widespread implementation of Xpert MTB/RIF assay using fecal samples, an aggregate data would provide additional information of its utility in children with pulmonary TB. In this study, we will conduct a systematic review and meta-analysis on the utility of Xpert MTB/RIF assay on fecal samples and provide a pooled sensitivity and specificity of the assay from available studies that evaluated its use as a diagnostic tool for pediatric TB.

**Funding:** NIH through the Emory-AAU-AHRI project

### II. Ongoing projects

1. **Evaluation of host biomarker-based point-of-care tests for targeted screening for active TB (Screen TB)**

Adane Mihret\textsuperscript{1}, Rawleigh Howe\textsuperscript{1} and Gerhard Walzl\textsuperscript{2}

\textsuperscript{1}Armauer Hansen Research Institute

\textsuperscript{2}Emory University, USA
Host serum protein biomarkers that indicate a high likelihood for active TB disease represent attractive targets for integration into screening tests. A promising serum host inflammatory signature was identified after investigation of more than 70 serum host inflammation markers, including acute phase proteins, T helper cell 1, T helper cell 2 and regulatory cytokines, soluble cytokine receptors and growth factors. The most promising host serum protein signature was subsequently validated on 687 people from five African countries with suspected TB, regardless of HIV infection status or ethnicity, providing the basis for the follow-up work suggested herein. The six-analyte signature of C-reactive protein (CRP), Interferon gamma (IFN-γ), pre-albumin, complement factor H (CFH), apolipoprotein A1 and inducible protein 10 (IP-10) ascertained TB disease with a sensitivity of 89% (CI 78 – 95%) and specificity of 76% (CI 68 – 83%), (positive predictive value of 61%; negative predictive value of 94%)

During the AE-TBC project, partner Leiden University Medical Centre (LUMC) developed and validated a user-friendly lateral flow assay (LFA) for simultaneous detection of multiple host TB biomarkers (cytokines and antibodies) in blood or other body fluids. These LFAs are likely to assist in rapid TB diagnosis in low-resource settings and were tested in the AE-TBC field sites. Importantly, our test formats utilize novel, nano-sized upconverting phosphor (UCP) reporter particles as read-out.

The overall objective of the study is to incorporate the six-marker signature into an UCP-LFA format, the TransDot assay, enabling fingerprick blood testing. The end-point of the study is the accuracy (sensitivity and specificity) of the UCP-LFA TransDot test on fingerprick blood for active TB and will be prospectively compared against composite gold standard diagnostic criteria of GeneXpert, MGIT, culture, TB sputum smear, CXR, TB symptom screen, response to antibiotics and response to TB treatment.

**Study Population:** A total of 200 people presenting at primary health care clinics with presumed active pulmonary tuberculosis, aged 18 to 70 years, male or female gender, will be recruited in Cape Town, South Africa, Windhoek in Namibia, Addis Ababa in Ethiopia, Banjul in The Gambia and Kampala in Uganda.

**Current status**

The project has obtained AHRI/ALERT Ethical clearance and submitted for National Ethical clearance

**Funding:** EDCTP

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2. **Molecular epidemiology and drug resistance of tuberculosis in southern region of Ethiopia**

Yared Merid¹, PI, Yimtubeznash W/amnuel³, Daniel Gemechu⁴, Tsegaye Hailu², Henery Bloomberg⁵, Markos Abebe², Abraham Aseffa²

¹Hawasa University, ²Armauer Hansen Research Institute, ³College of Health Sciences, AAU, ⁴REACH Ethiopia, Hawasa, ⁵Emory University, USA

The development and spread of drug-resistant *Mycobacterium tuberculosis* (*M. tuberculosis*) threatens
national TB control programs in several countries including that of Ethiopia. Prisons are also recognized as reservoirs for TB transmission and they are increasingly becoming ideal breeding grounds for the concentration and dissemination of TB (including MDR-TB), from which infection is transmitted to the general population. The objectives of this study is therefore to describe the molecular epidemiology and drug resistance pattern of pulmonary tuberculosis (PTB) to better understand the transmission of tuberculosis and the spread and development of MDR TB in the study settings.

The study settings include: (1) Prison, (2) Health facilities, and (3) community. Presumptive TB cases were screened for TB in Hawassa prison and new pulmonary TB cases were assessed for TB/MDR TB in health facilities. Culture and drug susceptibility testing and RD9 deletion typing is being conducted.

Data from the prison study revealed that the point prevalence of PTB was estimated to be 1748 per 100,000 persons. This rate of TB among incarcerated persons is ~16 fold higher than in the general population. This same study (titled ‘Prevalence and Molecular Epidemiology of Pulmonary Tuberculosis at Hawassa prison center, Southern Region of Ethiopia’) was presented at the 47th Union World Conference on Lung Health and highlighted as one of the top oral abstracts at the end of the conference recap session.

Current status
The data collection work for the three study settings is finalized. The laboratory tests (culture, drug susceptibility testing, RD9 deletion typing) are on progress. Spoligotyping and Whole Genome Sequencing are planned.

Funding: AHRI and NIH through Emory-AAU-AHRI project

The sample collection team for the project in Hawasa
3. Molecular Epidemiology of tuberculosis and role of *M. bovis* in settings with high dairy development in Ethiopia (ETHICOBOTS)

Hawult Taye¹, Adane Mihret¹, Yonas Kassahun¹, Abraham Aseffa¹, Stefan Berg², James Wood³

¹Armauer Hansen Research Institute, ²Animal and Plant Health Agency, ³Cambridge University

In most modern urban settings breaking of *M. bovis* transmission emphasize the need to maintain control measures for both human and bovine tuberculosis. In industrialized countries, animal TB control and elimination programs, together with milk pasteurization, have drastically reduced the incidence of disease caused by *M. bovis* in humans. In developing countries, however, animal TB is widely distributed, control measures are not applied or are applied sporadically, and pasteurization is rarely practiced.

In spite of the fact that *M. bovis* was considered as one of the neglected infectious pathogens and known to have insignificant public health importance in many developed countries; we expect higher contribution of *M. bovis*-caused TB in human from our study populations since there is rapid expansions of intensive dairy farms (with imported Holstein-Friesian and their cross breeds which are more susceptible to bovine disease) and poor awareness of the community about the transmission of the disease.

Therefore the general objective of this prospective cross-sectional study is to investigate Molecular epidemiology of tuberculosis and to determine role of *M. bovis* in humans living or working at high dairy development sites in Ethiopia.

We have been employing two means of recruitment (active case detection from the community and health facility based case findings from health sectors located around the dairy farms). In active cases finding, all individuals living or working in our study site will be screened and TB suspects who fulfill the national clinical assessment criteria will be consented for sampling. In passive case finding, all pulmonary TB patients who are coming to TB-clinics of the selected health sectors to start their treatment and cervical lymphadenitis cases who fulfill our inclusion criteria. Data collection was started in March 2016 and a total of 865 (700 sputum and 205 FNA) samples have been collected. Mycobacterium isolates will be typed (spoligotyping/deletionotyping) and those strains characterized as *M. bovis* will be further investigated through whole genome sequencing.

**Funding:** Biotechnology and Biological Sciences Research Council (BBSRC) through ETHICOBOTS project

4. Evolution of novel Mycobacterium tuberculosis genotype in East Africa and virulence trait assessment

Tone Tonjum¹, Solomon A Yimer¹, Markos A², Abraham Aseffa²

¹OUH, NIPH, ²AHRI, Amhara, Gambella and Benshangul-Gumuz Regional State Health Bureaus

Recently, a deeply rooted phylogenetic lineage of the *Mycobacterium tuberculosis* complex termed lineage 7 was discovered in Ethiopia. The EvoTB project aims at investigating the clinical and transmission relevance of *Mycobacterium tuberculosis* lineage 7 strains in Ethiopia, Sudan and South Sudan.

The study plans to collect sputum, lymph node aspirates, cerebrospinal fluid and blood samples from pulmonary TB and extra pulmonary TB (TB lymphadenitis and TB meningitis) cases from multiple sites in Ethiopia, South Sudan and Sudan.
So far sample and data have been collected from 800 patients covering 53% of the required sample size for the study. Sputum culture has been performed at Bahir Dar Regional Laboratory and AHRI. Currently, culture positive isolates, serum and plasma samples have been transferred to Oslo University hospital in Norway for advanced molecular tests. The next plan is to conduct whole genome sequencing, proteomics and lipidomics studies accordingly.

**Funding:** NIPH, OUH

5. Phenotype and Functional Characterization of T Cell Subset from Lymph Node Lesions and Peripheral Blood of Calves Exposed to Natural Mycobacterium bovis Infection

Fekadu Desta¹, PI, Gobena Ameni², Rawleigh Howe², Javier Salguero

¹Armauer Hansen Research Institute, ²Aklilu Lemma Institute of Pathobiology.

The aim of this study is to characterize properties of cells within tuberculous lymph node lesions as opposed to using peripheral blood mononuclear cells in a bovine model of tuberculosis. Our latest work has focused on characterizing the differences in the immune response in three cohorts: 1) naturally *M. bovis* infected animals, 2) BCG vaccinated, TB negative animals placed in a large reactor herd to promote infection, and 3) non-BCG vaccinated TB negative animals positioned in the same herd.

Histopathology (HE) and immunohistochemical (IHC) staining was done on a total of 45 lymph node tissue blocks (15 for each group). Five of seven evaluated monoclonal antibodies (see below) used gave a positive signal for IHC staining. BCG vaccination was found to significantly reduce microscopic granuloma score within the lymph nodes. IHC using cell surface markers revealed the number of CD68+ (macrophages) and CD3+ (T lymphocytes) to be significantly reduced in lymph node granulomas of BCG-vaccinated animals, when compared to non-vaccinated animals. IHC staining for iNOS showed a higher expression in granulomas from BCG-vaccinated animals compared to non-vaccinated animals for all stages, attaining statistical significance for stages I and IV. IHC analysis of the cytokines IFN-γ and TNF-α demonstrated significantly increased expression within the lymph node granulomas of BCG-vaccinated cattle. In the future, we plan to do additional immune phenotyping using flowcytometry, data analysis and thesis write-up.

**Funding:** AHRI

6. Characterization of innate and memory phenotypes to TB and hormone modulations in apparently healthy children and adolescents across age (TBTEA project)

Liya Wassie¹, Soren Hoff², Adane Mihret¹, Mesert Gebre³, Markos Abebe¹, Abraham Aseffa¹, Rawleigh Howe¹

¹Armauer Hansen Research Institute (AHRI); ²All Africa Leprosy, Tuberculosis Rehabilitation and Training Center (ALERT) Hospital; ³Statens Serum Institute (SSI)

In our previous study, we observed an age-dependent acquisition of TB infection among apparently healthy school-age children and adolescents. A relatively higher proportion of latent tuberculosis infection (as
assessed by IGRA test) was observed among adolescents (age above 15 yrs) compared to younger ones. Although different factors (including waning of BCG vaccination, especially considering infant immunization policies practices in the Country, or increased exposure to acquisition of infection as a result of increased age) attribute to this observed difference, in this study we aimed to investigate an alternate possibility, namely the role of puberty hormones in acquisition of latent TB infection. In this cross-sectional study, we collected blood from approximately 40 school children, aged between 11 and 20 years, recruited from primary and secondary schools in Addis Ababa and correlated levels of hormones with immune biomarkers. The phenotypes and proportions of different immune cell markers (monocytes/macrophages, T-cells, NK cells, B-cellw and Dendritic cells) were characterized from whole blood samples using flowcytometry. Plasma samples were analyzed for steroid hormones using direct ELISA. This study received ethical approval from AAERC and NRERC and was funded by EDCTP. Currently data analysis is underway.

7. Understanding Molecular Markers and Mechanisms of T- cell memory in Tuberculosis
Meseret Habtamu\textsuperscript{1,2} (PI), Markos Abebe\textsuperscript{1}, Abraham Aseffa\textsuperscript{1}, Anne Spurkland\textsuperscript{2}, Greger Abrahamsen\textsuperscript{2}
\textsuperscript{1}Armauer Hansen Research Institute, \textsuperscript{2}University of Oslo

Despite considerable advances in deciphering the immunopathogenesis of TB, our understanding of protective immunity to TB remains incomplete. In particular, relatively little is known about the expression of transcription factors by key cells of the immune system in response to TB. Using a novel Imaging Flow Cytometry approach, our objective is to measure the kinetics of NFkB nuclear translocation both in T cells and monocytes following ds-Red labelled BCG challenge. To date, 150 study participants have been recruited, which includes TB patient and endemic controls, and samples have been shipped to Oslo, Norway, for Image stream analysis. (Collaborating Institutions: AHRI, Department of Molecular Medicine, Institute of Basic Medical Sciences, University of Oslo, Norway)

8. Proof of concept: Immunodiagnosis of paediatric tuberculosis using modified QuantiFERON-TB Gold In- Tube test
Markos Abebe\textsuperscript{1}, PI, Abraham Aseffa\textsuperscript{1}, Rawleigh Howe\textsuperscript{1}, Martha Zewdie\textsuperscript{1}, Workeabeba Abebe\textsuperscript{2}, Cheryl Day\textsuperscript{3}, Carol-Holm Hansen\textsuperscript{4}
\textsuperscript{1}Armauer Hansen Research Institute, \textsuperscript{2}College of Health Science, AAU, \textsuperscript{3}Emory University, \textsuperscript{4}Norwegian Institute of Public Health

According to a CDC (2014) report, childhood TB accounts for 6% to 10% of all TB cases worldwide and as much as 40% of all new TB cases in TB endemic countries. The true burden could be much higher than thought because TB in children is difficult to diagnose.

Most of the available techniques to diagnose TB are either low in sensitivity or lack specificity or they are expensive and require standard laboratory facility and highly trained personnel. QuantiFERON TB Gold In-Tube (QFT-GIT) is a whole blood assay which has a specificity of greater than 97%. However, its sensitivity
is variable, the lowest from high TB endemic regions where such a test is most required. Moreover, the sensitivity of this test is lower in immunocompromised individuals such as HIV, cancer, pregnant mothers and children.

Recently, we have demonstrated in HIV-TB co-infected patients, that co-stimulation of whole blood with mitogen and TB antigen simultaneously (modified QFT-GIT) increases the sensitivity of the assay to detect TB in HIV co-infected patients even at low CD4 count. The significance of this modification has not been evaluated in the paediatric age group.

The aim of this study will be (1) to evaluate the performance of our modified QFT-GIT assay for the diagnosis of childhood TB and (2) characterize the type of cells that produce IFN- in the modified QFT-GIT assay.

Peripheral blood will be collected from each of the participants and IFN-\(\gamma\) sandwich ELISA will be performed according to the manufacturer’s instruction and analysed using the normalized method. We will also characterize, by flow cytometry, the cells that produce IFN-\(\gamma\) when we apply our modified QFT-GIT method.

**Funding:** AHRI, NIH through Emory-AAU-AHRI project

9. **Molecular Epidemiology, drug resistance pattern of M. tuberculosis and clinical outcome evaluation in Woldiya region, Ethiopia**

*Elena Hailu*¹, PI, *Abraham Aseffa*¹, *Markos Abebe*¹, *Tesfaye Sisay*², *Melanie Newport*⁴, *Cheryl Day*³

¹Armauer Hansen Research Institute, ²Institute of Biotechnology, AAU, ³Emory University, ⁴Brighton and Sussex, UK

Lineage 7 of *M. tuberculosis*, recently characterized at ARHI, is restricted to Ethiopia and it represents a phylogenetic branch intermediate between the ancient and modern lineages of *M. tuberculosis*. It was shown that modern lineages are generally more virulent and more globally successful, compared to other more geographically restricted lineages. Differences in immunogenicity, severity of disease, and transmission consistently indicated that Lineages 2 and 4 are more virulent than Lineages 1 and 6 but nothing is known about Lineage 7.

The aim of this study is to investigate Lineage 7 of *M. tuberculosis* experimentally and in clinical settings. The experimental focus includes the infection of THP-1 macrophage cell line and macrophages isolated from healthy donors with Lineages 1, 3, 4 and 7 of *M. tuberculosis* found and isolated in Ethiopia and comparing the profile of cytokines induced by the above mentioned lineages. This work is ongoing.

Clinical studies are being carried out in Woldiya region of Ethiopia which we found previously to have the highest prevalence of Lineage 7. Woldiya hospital and five surrounding health centers were selected for this study. All new pulmonary TB patients (smear negative and smear positive) attending the health care facility in this region are included in this study. Sputum and blood samples are taken from the patients. *M. tuberculosis* strains will be isolated from sputum samples and molecular techniques will be used for strain typing, drug resistance pattern and sequencing. Plasma is being separated from blood samples and the cytokine profile will be analyzed. Anti-coagulated blood is being stored with RNA Later solution for further RNA isolation. Sixty nine samples- sputum and blood – have been collected so far.

**Funding:** AHRI, NIH through Emory-AAU-AHRI project
10. **Monocyte Function in TB, HIV and TB HIV Co-Infected Patients**  
**Wegene Tamene (PhD student)\(^1\), Rawleigh Howe\(^1\) and Liya Wassie\(^1\)**  
\(^1\)Armauer Hansen Research Institute

People living with HIV are 20-30 times more at risk to develop active TB than HIV negative people. Cells of the monocyte-macrophage lineage are crucial cells in the pathogenesis and protection of TB disease, as well as to pathogenesis of HIV disease. Studies have suggested that HIV infected patients have reduced monocyte function and abnormal distribution of subsets of peripheral blood monocytes even after ART, which may contribute to increased susceptibility and/or progression to TB. Thus, this project aimed to investigate the role of TB, HIV and TB/HIV co-infection on phenotypic and functional properties of subsets of peripheral blood monocytes (characterized by CD14 and CD16 expression), selected innate immune markers such as toll like receptors (TLR2, 4, 7 & 9), chemokine receptors (CCR1, 2, 4, 5, 7 and CX3CR1) and cytokines in Ethiopian patients using. These markers will be evaluated by flow cytometry and RT-PCR. Currently, optimization of laboratory procedures is underway to start recruitment of study participants. This is a PhD study conducted between the University of Leipzig in Germany, EHNRI and AHRI as a sandwich program.  
**Funding:** AHRI, NIH through Emory-AAU-AHRI project

11. **Characterization of cellular and plasma biomarkers among smear negative cases of TB**  
**Ahmed Esmael (PhD student)\(^1\), Liya Wassie\(^2\), Rawleigh Howe\(^2\), Adane Mihret\(^2\) and Jyothi Rengarajan\(^3\)**  
\(^1\)Addis Ababa University; \(^2\)Armauer Hansen Research Institute (AHRI); \(^3\)Emory university, USA

The control of tuberculosis (TB) remains a huge challenge to public health. In Ethiopia and elsewhere, the majority of TB cases do not have supportive microbiological confirmation, in the form, for example of an
AFB positive sputum smear. This includes smear negative pulmonary TB, most forms of extrapulmonary TB, pediatric TB, and pulmonary TB in HIV positive subjects, and is presumed to be the case early in the smear positive TB disease course. Work up and management of these forms of TB is often far more time consuming than that of standard smear positive TB. In the absence of microbiological data, an alternate approach to explore for diagnosis of smear negative forms of TB is that of immune specificity. Recent studies have demonstrated that flowcytometric quantification of peripheral blood TB-specific T cells co-expressing activation antigens had very high capacity to distinguish patients with smear positive TB from healthy individuals with latent TB. In the present study, we would like to confirm and extend these finds to other smear negative forms of TB. In parallel to the flowcytometric approach, we plan to evaluate plasma biomarkers to determine how their levels associate with TB. Smear positive TB, smear negative pulmonary TB, control TB suspects who ultimately do not have TB (ie improve clinically without TB therapy), as well as health controls individuals with latent TB will all be evaluated in this study. Currently the student has completed developing the proposal and ready to submit for AAERC approval.

**Funding:** AHRI

**World TB day commemoration Event at AHRI**
**March 2016**

We celebrated World TB Day at AHRI with invited guests from ALERT Center [CEO, Directorates (40)], Civic society (30), High school students and their Teachers (130). The event was organized to inspire our Institution effort on averting Tuberculosis and create impression on the gatherers of the day. World TB day commemoration included debriefing on why we commemorate TB day with the motto of “End TB” in the country and beyond, This was followed by extended explanations on TB during a Poster session and visits to AHRI laboratories.

*A few pictures taken during the Poster Presentation session and the laboratory visit at AHRI*
Leprosy Case Team

The theme of the 19th international Leprosy congress which was held in Beijing in September 2016 was **Unfinished Business: stopping transmission, preventing disability, promoting inclusion**, a very comprehensive message that touches all aspects and shows the need for an integrated effort to control leprosy and reduce associated disability. Some of our team members had the opportunity to participate in the congress, present their work and discuss possible collaborations with the international scientists working on leprosy. Among the members, Dr. Edessa Negara received the best poster award from the organizers.

Among this year’s activities, the active case detection and contact tracing study in Kokosa, West Arsi zone of the Oromiya region (PhD work by Tsehaynesh Lema) was very challenging but successful. Using the existing health system, mainly Health extension workers (HEW), and the PhD student managed to cover all households in the leprosy assessment activity. Identified contacts are being assessed for any leprosy associated signs and symptoms and samples for viability and immunological assays are under collection. As part of this project, Tsehanesh organized a training on “Leprosy Diagnosis and Treatment” for health care professionals working in Kokosa Woreda, West Arsi zone, Oromiya region from April 17-23, 2016. The study is financially supported by BSPP, GLRA and TLMi Ethiopia.

The Line probe assay (LPA) technique for detection of drug resistance in *M. leprae* is now optimized to be used at AHRI for research as well as to provide support to the leprosy clinician whenever needed especially in “relapse cases”. *M. leprae* typing is the other ongoing activity in collaboration with EPHFL, Switzerland.

The presence of many uncertainties and unknowns in host-pathogen interaction in leprosy is one of the areas which need attention. One of the PhD studies completed this year (by Edessa Negera) was the dissertation “Immunopathogenesis of ENL” in collaboration with LSHTM. Other studies on viability assay establishment, investigating the role of FCγ receptor in pathogenesis of ENL and characterizing LL-37 (a cathelicidin antimicrobial peptide) in patients, contacts and healthy individuals are also among the ongoing activities.

Considering the social aspect of leprosy, a PhD study was completed and defended this year (by Daniel Taye) which aimed to explore justifications for discriminatory social relations and the inherent image of leprosy-affected people (LAP) and their families. Similarly, one MSc study (by Melese Yirga) supported by AHRI to assess the economic and biopsychosocial challenges that prohibits the rural people affected by leprosy to reintegrate to their community of origin was completed successfully.

This year, AHRI as an institution was one partner in a proposal submitted to EDCTP by KIT (The Royal Tropical Institute, the Netherlands) together with other partners focusing on chemoprophylaxis. Unfortunately, the proposal failed after the second review. Recently, a new project on a leprosy vaccine was submitted to EDCTP (Concept note) and the PI is from Erasmus University the Netherlands and other partners including AHRI were involved. This proposal also didn’t pass the first EDCT screening. Although not successful at this moment, such activities show how the scientific community is working together more than ever towards leprosy control. As a team we will continue working together with potential collaborators to eventually contribute to national and global elimination of leprosy.

The final major activity of this year was the restructuring process at AHRI, the leprosy team is now under the Mycobacterial Diseases Directorate and we hope this arrangement will help in performing better.
I. Ongoing projects

1. Application of Line Probe Assay for the Diagnosis of Drug Resistance Pattern of *M. leprae*

   Selfu Girma¹, Kidist Bobosha¹, Kassu Desta², Phillipe Busso³, Charlotte Avanzi³, Stewart Cole³ and Abraham Aseffa¹.

   ¹. Armauer Hansen Research Institute (AHRI), ². Addis Ababa University, College of Health Science, School of Allied Health Science, ³. École Polytechnique Fédérale De Lausanne (EPFL)

Reports from different leprosy endemic countries on the emergence of drug resistant strains of *M. leprae* against the widely used Multi Drug Treatment (MDT) are rising. Though there is no report on the existence of an MDT resistant strain of *M. leprae* in Ethiopia so far, there are a number of cases of intolerance to standard MDT and relapses after first administration of the treatment. Current optimal management is to place the patient on MDT for extended time or adjust the drugs within the combination without performing Drug Susceptibility Test (DST) as the test is not available. We ultimately aim to make such tests available, and are presently evaluating the Line Probe assay (LPA) to determine drug resistance patterns of *M. leprae* strains on DNA samples extracted from skin tissue. We have recruited 53 PCR positive samples and have begun optimizing the LPA. The future plan after optimizing performance will be to integrate it into routine DST of *M. leprae* in the leprosy clinic at ALERT center.

**Funding:** NORAD - SIDA Core Budget (AHRI) and Ecole Polytechnique Fédérale De Lausanne (EPFL)

2. Potential of Auramine O Staining for the Diagnosis of Leprosy.

   Selfu Girma¹, Kidist Bobosha¹, Kassu Desta², Munir Idris¹, Yohannes Tsegay¹, Phillipe Busso³, Charlotte Avanzi³, Stewart Cole³ and Abraham Aseffa¹.

   ¹. Armauer Hansen Research Institute (AHRI), ². Addis Ababa University, College of Health Science, School of Allied Health Science, ³. École Polytechnique Fédérale De Lausanne (EPFL)

The World Health Organization report of 2015 shows there were 213,899 new cases of leprosy with the detection rate of 3.81 per 100,000 populations globally in the year 2014. In Ethiopia, the trend of new case detection for the last ten consecutive years was 4200 per year on average, using the usual acid fast staining of low sensitivity. The objective of this study was to evaluate diagnostic potential of Auramine O staining for the diagnosis of leprosy using LED FM microscope. We have recruited 142 leprosy and 28 non-leprosy participants and have performed Auramine O, FF, H&E and PCR tests. The sensitivity of FF, Auramine O, H&E and PCR was 78.1%, 79%, 86.8% and 89.5%, respectively. Auramine O staining was superior compared with the routine acid fast staining. The sensitivity of PCR was much higher than all diagnostic tests in this study and we recommend Auramine O staining for the diagnosis of leprosy at low level health institutions and that of PCR diagnosis at a referral level where a PCR facility is available.

**Funding:** Norad-Sida Core Budget (AHRI) and Ecole Polytechnique Fédérale De Lausanne (EPFL)

3. Discriminatory Discourses Related To Leprosy-Affected Communities And The Underpinning Social Constructs: Addis Ababa & Kuyara In Focus

   Daniel Taye Feyisa¹,²,³, DemisseeW Beyene¹, and Animaw Anteneh²

   ¹. Armauer Hansen Research Institute (AHRI), ². Addis Ababa University, College of Health Science, School of Allied Health Science, ³. Jimma University

This study is a critical examination of discriminatory discourses and the underpinning social constructions.
about leprosy-affected people. The study is conducted to explore justifications for discriminatory social relations and the inherent image of leprosy-affected people (LAP) and their families. It was also meant to investigate the discursive manifestations and strategies of discriminations in various social affairs.

Two research sites in Ethiopia: Kuyara and Addis Ababa were selected based on convenience to the PI and the social or historical importance.

A total of 70 research participants were involved for the qualitative data. A qualitative case study research methodology was used to draw data from non-Leprosy-Affected Persons and Leprosy-Affected Persons.

The research result revealed that leprosy affected persons are referred to as unclean, weak, lame, and broken (amputated), worthless and unable to work or they are described with dehumanizing expressions and traits of low qualities. They are socially constructed as genetically contaminated ("yeqomata zer") compared with the non-LAP as the people of the ‘pure gene’. The community in general considered them as vectors of the disease, incapable, deserve punishments and they bear children of their own kind. The disease is also perceived as incurable. The LAP themselves consider the isolation/self concealment as mechanism of getting relief.

Various discriminatory discourse strategies are prevalent including self-denial or concealment, dehumanization, delegitimizing, restriction, and many others. Illogical justifications and lack of information about leprosy was deduced from the data gathered. Data from all the informants showed that the problem of explicit discrimination is not as intense as it was in the past.

The stakeholders are suggested to plan social behavioral change communication education program (SBCCEP) where the LAP play the leading role. False justifications, materialized misunderstandings, illogically explained topics in the social or medical genre and power relations (restrictions, self-concealments absence of bottom up resistance, legitimization of submissiveness) should be tackled by cumulative effort of LAP, health professionals, religious leaders, community of healthy people by means of awareness creation trainings, media campaigns, narrowing social gaps between LAP and non-LAP in general.

4. Immunopathogenesis of ENL

Edessa Negera¹,², Kidist Bobosha², Stephen Walker¹, Abraham Aseffa², Hazel M Docrell¹, Diana LoockWood¹

¹. London School of Hygiene and Tropical Medicine, ². Armauer Hansen Research Institute

Leprosy is a disease caused by Mycobacterium leprae, an acid-fast bacillus whose clinical spectrum correlates with the host immune response. Erythema nodosum leprosum (ENL) is an immune-mediated inflammatory complication causing high morbidity in affected leprosy patients. A case-control follow-up study was conducted in Ethiopia to test the hypothesis that ENL is associated with impaired immune regulation. In 46 patients with ENL and 31 lepromatous leprosy (LL) matched controls, the frequency of regulatory T-cells, memory T-cells and B-cells were analysed by flow cytometry. The in vitro pro-inflammatory cytokines production by peripheral blood mononuclear cells (PBMCs) to the response of M. leprae whole cell sonicate stimulation was determined by ELISA. Gene expression of these cytokines in the blood and skin biopsies was determined by quantitative polymerase chain reaction (qPCR) before and after treatment. Patients with ENL had lower percentages of CD4+ regulatory T-cells than LL controls at recruitment. The percentage of activated T-cells including both CD4+ and CD8+ were significantly higher in the PBMCs of patients with
ENL than in LL controls before treatment. The in vitro production and gene expression of cytokines TNF-α, IFN-γ, IL-1β, IL-6, IL-8 and IL-17A were significantly increased in untreated patients with ENL. ENL patients had a higher median percentage of tissue-like memory (TLM) and activated memory (AM) B-cells than LL controls before treatment while the median percentage of total B-cells and resting memory (RM) B-cells did not significantly differ in both groups before treatment. The level of anti-PGL-1, LAM and Ag85 antibodies were not significantly different in patients with ENL before treatment. Patients with ENL had significantly lower circulating C1q than LL controls before treatment. However, after treatment, the amount of circulating C1q was not significantly different in both groups. Our findings suggest that ENL is associated with reduced percentage of regulatory T-cells and increased CD4+/CD8+ T-cell ratio and this immune imbalance may lead to the initiation of ENL reactions in either permitting productions of antibodies critical to an immune-complex formation or as a cell-mediated immune response in patients with leprosy. Consequently, this study illuminates the role of T-cell activation in the pathogenesis of ENL reaction and challenges the long-standing dogma of immune-complexes as the sole aetiology of ENL reactions.

Funding: Homes and Hospitals of St. Gilles, London, UK

5. An assessment of the challenges of rural leprosy affected people to reintegrate within their community of origin and their coping mechanisms:
A Study in ALERT Center, Addis Ababa

Melese Yirga1,2, Tsegaye Hailu3, Zena Birhanu1
1. Armauer Hansen Research Institute(AHRI); 2. All Africa Leprosy Training and Rehabilitation Center (ALERT); 3. Armauer Hansen Research Institute (AHRI)

Leprosy affected people (PAL) from rural areas in Ethiopia have been suffering from the biological, psychological, social and economic challenges in the effort to reintegrate within the community of their origin and they have developed a variety of coping mechanisms. This study explored the challenges of rural PAL to so reintegrate and their coping mechanisms after treatment at ALERT Hospital. The study was based on an approach of qualitative inquiry with exploratory purpose, and applied the non-probability sampling method with purposive sampling. In-depth interview, key informant interview, focus group discussion and observation were employed to collect the data and thematic analysis used to analyze the data.

The finding of the study showed that rural PAL have a variety of challenges such as leprosy reactions, loss of sensation, wounds, deformities, disabilities and issues with proper treatment. They encounter psychological disorders such as anxiety and depression. Socially, they have problems with interaction, stigma, discrimination and marital relationships. Their productivity and property ownership was affected by leprosy. Finally, because of leprosy they prohibited from reintegrating within their community of origin after treatment at ALERT hospital. The study also illustrated their coping mechanisms such as hiding their health status, using traditional treatment, migration, visiting spiritual places, institutional support and begging.

The results of the study will be used for intervention programs by stakeholders to enhance the reintegration of rural PAL to their community of origin after treatment at ALERT Hospital and to increase their coping mechanisms. The study has implications for different concerned bodies to advocate andcreate awareness, for case management and stimulating further study, to improve the health access and quality of care and to have appropriate policy about the rural PAL.

6. Active case detection of new leprosy cases and household contacts in Kokosa Woreda, West Arsi zone, Oromia region, Ethiopia

Tsehaynesh Lema1,2*, Kidist Bobosha2, Edessa Negera2, Yonas Bekele2,3, Tsegaye Hailu2
Leprosy is a chronic mycobacterial disease caused by Mycobacterium leprae. The World Health Organization (WHO) reported 213,899 new cases of leprosy, 14,110 new grade two disabilities (G2D), and 1312 relapse cases globally in 2015. With the introduction of multi-drugtherapy (MDT) for leprosy, prevalence of leprosy globally decreased from >5 million cases in the mid-1980s to < 200 000 by 2015. In 2015, 3758 new cases and 482 new children cases, 384 new cases with G2D were reported from Ethiopia alarming the presence of new transmissions. In this study the main objective is to identify new leprosy cases and tracing of household contacts at risk of developing leprosy by active case detection and mapping the distribution of leprosy and assess health care facilities delivery status and outcome of leprosy treatment in one of the high leprosy burdened Woreda, Kokosa.

Knowledge, attitude and practice (KAP) of the health workers in the Woreda was assessed since it has a direct impact on the study in active case assessment, diagnosis and treating the cases. Before the main study was launched we provided training by experienced dermatologists and laboratory technologists. After an initial pilot study, the main study began in May 2016. All households in the woreda have been assessed for new leprosy cases and currently, samples are being collected from household contacts. The results from this study will provide essential information on the true burden of leprosy in the region, and contribute to better control activities for hotspot areas. As revealed by Federal Ministry of Health assessment, there are many hot spot areas in the country hence the experience and the tools from this study can be applied as a model to assess the burden in other regional states as well. Additional relevant information on active versus passive detection, household contacts tracing, circulating M. leprae strains in the region and assessment of drug resistance will provide input for control strategies. Collaborators are involved from Germany, The Netherlands and Sweden.

Funding: AHRI, GLRA, TLMiE and BSPP (Sida)

Bacterial and Viral Diseases Research Directorate (BVDRD)

Bacteriology team members: Wude Mihret, Biruk Yeshitela, Demissew Beyene, Emawayish Andargie, Mekonen Teferi, Melaku Yidnekachew

Bacteriology Case Team Website address: http://ahri.gov.et/bacteriology

The Bacteriology case team is working on clinical and applied research activities to understand the potential infectious etiology of bacterial diseases, molecular epidemiology of bacterial diseases including genetic characterization of the pathogen and diagnostics for the detection, identification, and surveillance of bacterial diseases. Last year, the team has been heavily engaged in a Clinical Research and Capacity Building Program supported by Ministry of Health involving 5 universities involved in monitoring antimicrobial sensitivity trends in neonatal, obstetric and maternity wards of University teaching hospitals. The team has previously addressed a number of research activities through molecular, immunological and biochemical research tools for detection of bacterial and related microbial etiologic agents of diseases. In this fiscal year three manuscripts were sent for publication from the research outputs of the team and were accepted for publication in local and high impact international scientific journals. Students registered for their MSc and PhD studies at different universities were recruited to use the lab facility and work in collaboration with AHRI. The students obtained research benchwork skills guided by senior researchers with specific expertise in a given research tool. As well, they use accessible reagents, chemicals and instruments required for their research activities. Students have travelled abroad to obtain laboratory training in partner institutes. Workshops were attended; research output presentations were given both at local and International research forums. The following represent brief
Bacterial Diseases Case Team

I. Completed Projects

1. Prevalence and epidemiology of meningococcal carriage in Southern Ethiopia prior to implementation of MenAfriVac, a conjugate vaccine
Demissew Beyene, Bereket Workalemahu, Guro K. Bårnes, Paul A. Kristiansen, Dominique A. Caugant and Abraham Aseffa

Bacterial conjugate vaccines have been shown to reduce transmission by blocking carriage. The epidemiology of meningococcal A carriage was investigated in Southern Ethiopia ahead of the Men A conjugate vaccine rollout in Ethiopia with the aim to conduct a postvaccination carriage study and thus determine vaccine impact. A cross-sectional meningococcal carriage study was conducted in Arba Minch, in southern Ethiopia. A total of 7479 Oropharyngeal swabs were collected from 1-29 year old volunteers and confirmed N. meningitides isolates were characterized. There was no significant difference in overall carriage between male and female participants. Highest carriage prevalence (9.80%) was found among 15-19 year olds. Carriage prevalence in females peaked at 16 years (28.26%), while prevalence in males was highest in the 23-year olds (17.14%). Serogroup W isolates were assigned to the ST-11 clonal complex and serogroup X to the ST-181 and the ST-41/44 clonal complexes. Serogroup A was not found among the carriage isolates in this area of Ethiopia but epidemic strains of serogroups W and X are circulating. The immediate public health impact of mass-vaccination with MenAfriVac is expected to be marginal in this population.

Funding: Norwegian Research Council.

2. Etiologic agents of bacterial meningitis and disease severity in Ethiopian patients (MenTAHG study)
Wude Mihret. BeyenePetros, Gunnstein Norheim, Abraham Aseffa

The aim of this study is to assess the etiologic agents of bacterial meningitis during the non-epidemic season, and to address the level of disease severity in patients clinically diagnosed to have bacterial meningitis by using biochemical, molecular and Immunologic methods. A total of 139 study participants clinically diagnosed to have bacterial meningitis were recruited from three University hospitals in Ethiopia. The cerebrospinal fluid (CSF) of forty six out of the 139 (33.1%) were diagnosed to be positive for the frequent etiologic agents N. meningitidis, S. pneumoniae and H. influenzae. Elevated levels of CSF proinflammatory cytokines, as a surrogate of disease severity, were more commonly associated with S. pneumoniae than with N. meningitidis positivity.

Funding: Norwegian Research Council, GLOBVAC grant 192477, Sponsor: NIPH, Oslo, Norway
3. The Impact of Ten-valent Pneumococcal Conjugate Vaccine (PCV10) on *Streptococcus pneumoniae* Nasopharyngeal Carriage Rate: Phenotypic and Genetic Diversity of Isolates from Addis Ababa, Ethiopia

Wondewosen Tsegaye, Yimtubezenash W/amanueal, Birgitta Henriques-Normark, Abraham Aseffa

The objectives of this project were to determine the impact of the pneumococcal PCV10 vaccine by evaluating nasopharyngeal carriage, and to analyze the phenotypic and genetic diversity of pneumococcal isolates as well as their sensitivity to currently available antibiotics. This study revealed the presence of very diverse serotypes in the country. A total of 325 nasopharyngeal pneumococcal isolates from samples at the age of six weeks and nine months were serotyped and characterized by Pulsed Field Gel Electrophoresis and Multilocus Sequence Typing. The carriage rate of *Streptococcus pneumoniae* at the age of six weeks, nine months and two years were 26.6% (210/789), 56.8% (117/206), 47.6% (95/201) respectively. A total of 61 serotypes of *Streptococcus pneumoniae* were identified from 325 typed isolates, and serotypes 6A, 11A, 15B, 23F, 15A and 19F were most commonly identified, each representing present in 3.5-4.9% of the samples. Serotypes covered by PCV10 vaccine were 20.2% (42/208) and 11.1% (13/117) for isolates collected at six weeks and nine months, respectively. Molecular typing also showed the diversity of isolates. The impact of the current vaccine was observed on a reduction of carriage of vaccine types; however, similar to other studies, non-vaccine type replacement was also demonstrated. The use of PCV13 would have an added value by increasing the coverage of additional nasopharyngeal carried isolates by at least 10% more. This work was conducted in Addis Ababa only and it is necessary to extend the investigation to other parts of the country and include clinical cases to have a complete picture of the impact of PCV on pneumococcal epidemiology.

**Funding:** AHRI Core budget.


Biruk Yeshitela

The study compared the diagnostic performance of Widal test and blood culture for diagnosis of typhoid fever in febrile patients in selected health centers of Addis Ababa. Blood cultures were done with BACTEC to isolate salmonella from patients suspected to have typhoid fever. Blood was also collected from healthy volunteers for comparison of Widal reactivity. Widal qualitative tests were done on both febrile patients and healthy controls, and the Widal quantitative test (for S. Typhi O and H antigens) was done on those with positive blood cultures. Blood culture was positive in only 2 patients whereas the widal qualitative test was positive for 93 patients. Among the 2 patients with positive blood cultures, the widal quantitative test was positive in only 1 patient. The results suggest that most of the typhoid suspects probably suffer from other illnesses, although antibiotic use could account for some negative blood cultures. A larger study (TSAP) in collaboration with several institutions across Africa had also shown that S. typhi is rarely isolated from blood cultures in Ethiopia. In this study, a substantial proportion of control healthy individuals exhibited seropositivity against O and H antigens for S. typhi. The work adds evidence to the poor performance of the widely applied Widal test as a diagnostic test for typhoid fever in Addis Ababa.
5. Severe Typhoid in Africa (SETA) Program Rapid Pilot Prospective Surveillance case control study.
Mekonnen Teferi, Biruk Yeshitela and Abraham Aseffa

The main objective of this pilot study was to assess the prevalence of invasive salmonellosis among febrile disease patients visiting selected sentinel surveillance health facilities in Ethiopia, Madagascar and Ghana. The study sites in Ethiopia were Wonji, Arba Minch, Debre Berhan, Wolaita Sodo and Addis Ababa. A total of 570 cases and 1131 controls were recruited. The cases were patients clinically diagnosed to have typhoid fever and the controls were age matched clinically healthy apparent individuals recruited from the respective community dwellers. Cases were confirmed by PCR and serological titers of anti-Salmonella spp. antibody using blood (routinely) and surgical biopsies (where applicable).

Funding: Bill and Melinda Gates Foundation.

II. Ongoing Projects

1. Systematic Study of Hospital Acquired Infections and Antibiotic Resistance: insight into the epidemiology and genetics of infection
Biruk Yeshitela, Leena Al Hassen, Abraham Aseffa

Hospital-acquired infections and antimicrobial resistance are important health issues globally. The rise in resistance is alarming, and an increasing number of countries are reporting pan-resistance to the commonly used antimicrobials in the hospital setting. The problem is particularly urgent in low- and middle-income countries where there is a lack of surveillance, reporting and infection control practices. The study aims to describe the magnitude and type of hospital acquired infections and to determine the epidemiological and genetic characteristics of Gram-negative infections and the resistance associated with them. Biochemical, molecular diagnostic tools and genetic characterization of bacterial samples will be applied.

Funding: AHRI core fund.

2. Enhanced Sentinel System for Surveillance of Bacterial Meningitides (ESBM) in Ethiopia
Biruk Yeshitela, Demissew Beyene and Abraham Aseffa

The objective of this project is to establish geographically representative sentinel sites with expanded surveillance sites, increased sample size including all age groups from different regions of Ethiopia and to evaluate the impact of MenAfriVac mass vaccination in collaboration with the Ethiopian Institute of Public Health (EPHI). Biochemical and molecular diagnostic tools were utilized. Until October 2016, a total of 873 Cerebral Spinal Fluid (CSF) samples were obtained from seven sentinel sites (Yekatit 12 hospital, Tikur Anbessa hospital, Gondar, Bahir Dar, Jimma, Arbaminch and Hawassa hospitals). Currently, Real Time (RT)-PCR analysis of these 873 CSF samples is ongoing both at AHRI and EPHI. The preliminary RT-PCR analysis of the first 532 CSF samples has identified 37 positive cases; the frequent etiologic agents are *N. meningitidis*,...
S. pneumoniae and H. influenzae. Additional CSF sample collection is ongoing in all sentinel sites.

**Funding:** Norwegian Research Council.

### 3. Melioidosis Clinical Studies to facilitate a joint research work for exploring, describing and mapping of melioidosis in Ethiopia (Research initiative)

**Emawayish Andargie, Kassu Deseta, Mekonnen Teferi, Biruk Yeshitela, Ivo Steinmenz, Abraham Aseffa**

Melioidosis is caused by soil and water dwelling bacteria, *Burkholderia pseudomallei*, and is responsible for a range of infections, most commonly pneumonia which can sometimes clinically mimic tuberculosis. While it has been traditionally identified in Southeast Asia and Australia, there is evidence of its spread worldwide. In light of the history of melioidosis in other parts of the world, and the degree to which a highly endemic situation may go undetected, there is a need to explore its possible transmission in Ethiopia. A proposal has been presented to the AHRI ethics review committee for obtaining ethical clearance prior to initiation of the study.

**Funding:** Friedrich Loeffler Institute of Medical Microbiology (FLI), University Medicine Greifswald, Germany and AHRI.

### 4. Antibiotic Resistance Monitoring project

**Biruk Yeshitila, Adane Mihret, Ebba Abate, Tefaye Kassa, Berhanu Seyoum, Tamrat Abebe, Rawleigh Howe**

Antibiotic resistance is recognized as a growing global threat. Patients with infections caused by drug-resistant bacteria are at increased risk of worse clinical outcomes and death, and consume more health-care resources than patients infected with non-resistant strains of the same bacteria. Building capacity that helps to detect and monitor antibiotic sensitivity trend in neonatal, obstetric and maternity wards of selected hospitals could be instrumental to reduce maternal and infant mortality. Currently we are working at five University teaching hospitals to build capacity that helps to determine antibiotic sensitivity pattern of bacterial isolates over time in the specific facilities. These studies are carried out mainly as part of MSc training activities, thus contributing to human resource development for health research in the regions.

### 5. Phenotypic and Genotypic Characterizations of *Streptococcus pneumoniae* Strains Isolated from HIV Seropositive (HIV +) and HIV Seronegative (HIV-) Pediatric Patients with Pneumococcal Diseases, Addis Ababa, Ethiopia

**Abel Abera, Abraham Aseffa, Daniel Asrat and Mario Vaneechoutte**

*Streptococcus pneumoniae* is the leading bacterial cause of pneumonia, sepsis, and meningitis and significant cause of morbidity in children under 5 years of age worldwide. As a result of poorer access to healthcare and due to co-morbidities, particularly of HIV infection and malnutrition, mortality rates are quite high in young children in developing countries. The aim of this study is to determine the magnitude of pneumococcal...
diseases, identify the serotypes and genotypes of invasive and non-invasive *S. pneumoniae* isolates in HIV+ and HIV- pediatrics patients with pneumococcal disease in Addis Ababa. In addition, we aim to determine the prevalence of antibiotic resistance, clonal spread and genetic variability among *S. pneumoniae* isolates with emphasis on macrolide and penicillin resistance. Ethical clearance from the National Research and Ethics committee has been obtained. Data and sample collection from three hospitals in Addis Ababa has been started beginning from August 2016 and is expected to continue until August 2017. Isolate identification and antibiotic sensitivity testing and storage of isolates are also being performed.

**Funding:** The study is supported by a PhD Training Scholarship, by VLIR UOS, Belgium

### 6. Characterization of the interaction between pathogenic enteric bacteria and normal flora during Teff fermentation

**Yared Hailaye, Solomon G-selassie, Abraham Aseffa, Jana Jass, Per-Erik Olsson**

Though normal flora involved in Teff fermentation and baking at high temperature are expected to outcompete and eliminate contaminating pathogens, the interactions between these organisms have not clearly been described and most food borne pathogens can tolerate such stresses very well. New intervention tools can be drawn by understanding such interactions. This study aims to use Teff fermentation as a model to study the interaction of normal host flora with pathogenic bacteria. Fermenting microorganisms will be isolated from household fermentations in different parts of Ethiopia using phenotypic and molecular techniques and evaluated for inhibition of pathogens enteric bacteria and binding of heavy metals. Since January 2016, the first phase of the project involving collection of samples from households and identification of microorganisms from the samples is being done in Ethiopia and Sweden.

### 7. Epidemiology and Molecular characteristics of ESBL producing gram-negative bacilli (Enterobacteriaceae and Non-fermentative) at Jimma University Teaching Hospital, Ethiopia.

**Tsegaye Sewunet, Daniel Asrat, Yimtubezinash Woldeamanuel, Abraham Aseffa, Christian Giske**

Gram-negative bacilli are common causes of morbidity and mortality in health care setting. In particular, Enterobacteriaceae have a variety of virulent factors or attributes that help them adapt to their environment. Moreover, increasing numbers of these organisms are becoming non-susceptible to commonly used antimicrobials including newer generation of β-lactam antimicrobials. These bacteria produce extended spectrum β-lactamase (ESBL) enzymes that hydrolyze the β-lactam ring of the β-lactam antimicrobials. Infections with ESBL producing bacterial strains have limited treatment options, particularly in resource limited countries. This study aims to determine molecular characteristics and epidemiology of ESBL producing gram-negative bacilli (including the Enterobacteriaceae family and non-fermentative bacilli) among patients at Jimma University Teaching Hospital (JUTH).

Currently the study is ongoing. Clinical data have been obtained from structured questionnaires. Specimens have been collected and bacterial isolates identified based on standard microbiological techniques.
Bacteriology Team Activity in Pictures

(Meningitis epidemic site (Sodo Hospital visited by AHRI MenTAHG research Team, diagnostic support was given))

Pictures from few of the field work activities of AHRI Bacteriology Team 20
Bacteriology study team of MenTAHG research project at Gondar University hospital

Bacteriology study team of MenTAHG research project at Norwegian Institute of Public Health (Norway)
Bacteriology study team of MenTAHG research project at Oslo University Hospital/Norway

AHRI Bacteriology team within the MenAfricar consortium. The Consortium conducted pilot studies of meningococcal carriage in Chad, Ethiopia, Ghana, Mali, Niger, Nigeria, and Senegal (2009-2011) and results are being published.
Viral Diseases Case Team

The name of this team evolved from HIV/STD team to viral and bacterial directorate since the new structural organization of AHRI early this year. The team has been working on HIV, hepatitis and other viral diseases of public health importance since 2000. Postgraduate students affiliated to universities in Addis Ababa and overseas are also core key players in the team, working on different aspects of viral diseases. The team consists of senior scientists, researchers, public health professionals, lab technicians and few postgraduate students affiliated to AHRI.

Overall, the team has been working on studying immune responses, seroepidemiological analyses and associated factors such as nutrition, sociodemographic and programmatic factors during these viral infections. The current report summarizes research activities and projects conducted during 2016 and briefly highlights on completed studies. All studies reported in this document received institutional (AAERC) and/or national ethical approval (NRERC).

I. Completed projects in 2016

1. Immunological Response to HBV Vaccine in Children: The Impact of HIV infection in the vaccine response in Addis Ababa, Ethiopia

PI: Desalegn (MSc student); AHRI mentors: Yonas Bekele, Dr. Rawleigh Howe and Dr. Abraham Aseffa; Karolinska Institute mentor: Prof Francesca Chiodi

This study was a collaborative study between Karolinska Institute (KI), Sweden and AHRI. The overall objective of this study was to evaluate the serological responses to HBV vaccine in HIV positive and negative children, who have no prior exposure to HBV vaccine or infection and to further assess the functional and phenotypic properties of memory B cells after HBV vaccination. About 94 % of HIV positive children responded to hepatitis B vaccine, but plasma level of antiHBsAg was significantly reduced in HIV-1 positive children (p= 0.0001). Children who were initiated in ART early after diagnosis responded with higher levels (p=0.0046). There were vaccine associated changes in subsets of memory B cells essential for sustained antibody production and these changes were reduced in HIV positive children; such memory subsets were lower prior to vaccination in HIV positive subjects. Overall, the results showed reduced plasma antibody levels and low frequency of memory B cell subsets in HIV positive children, suggesting the need for early initiation of ART and consideration for booster doses of HBV vaccine. This study is completed with financial support from KI, the Swedish Medical Research Council and AHRI; the student defended his thesis and the manuscript is under preparation.

2. Frequency of Circulating B-cell Subpopulations and Associated PD1 and CD95 Expression among HIV-1 Infected Children in Addis Ababa, Ethiopia

PI: Temesgen (MSc student); AHRI mentors: Yonas Bekele, Dr. Rawleigh Howe and Dr.
Abraham Aseffa; Karolinska Institute mentor: Prof Francesca Chiodi

HIV infection causes a wide range of adaptive immune system defects. Children may be especially prone to such defects since their immune systems are not yet completely developed. Understanding of the influence of pediatric HIV infection on circulating B cell subsets and mechanisms involved in B cell dysfunction both pre- and post-ART is incomplete. The aim of this study was to characterize B cell subpopulations including expression of PD1 and CD95 among HIV-infected children by flow cytometry. We observed that pediatric HIV infection was associated with disturbances in B cell subset composition, including increased numbers of activated and resting memory B cells with expression of markers of exhaustion and apoptosis markers. Further investigations are warranted to assess the functionality of B-cells subsets and whether change of ART drug regiments can minimize B cell dysfunction. This study was a collaborative study between Karolinska Institute (KI), Sweden and AHRI and funded by KI, Swedish Medical Research Council and AHRI. This study is completed; the student defended his thesis and the manuscript is under preparation.

PI: Meseret Abebe (MSc Student), AHRI mentors: Dr. Adane Mihret, Dr. Abraham Aseffa and Dr. Rawleigh Howe

The overall aims of this study were to survey pregnant mothers for Hepatitis E virus (HEV) and identify possible risk factors for infection. The study showed a high prevalence of circulating IgG antibodies for HEV, where age and educational status significantly correlated with infection; nearly all subjects were negative for IgM antibodies indicating prior exposure but lack of recent infection during pregnancy itself. This study is completed with support from AHRI core budget; thesis defended and manuscript is under preparation.

4. Assessment of sero-prevalence of Hepatitis B surface antigen (HBsAg) and associated factors among pregnant women at Bishoftu General Hospital, Ethiopia
PI: Zelalem Desalegn from Addis Ababa Science and Technology University, Mentors from AHRI: Dr. Liya Wassie and Dr. Adane Mihret

The objective of this cross-sectional study was to estimate the sero-prevalence of HBV surface antigen (HBsAg) and assess some risk factors among pregnant women, attending the Bishoftu General Hospital, Adama between July and September 2014. About 5% (11/202) of the study participants were positive for HBsAg and a positive response strongly correlated with a history of abortion (AOR: 6; 95% CI: 1.39-27.69), history of surgery (AOR: 5; 95% CI: 1.04-24.31) and a family history for hepatitis (AOR: 11; 95% CI: 1.63- 80.44), indicating the need for routine screening of pregnant women to alleviate the mother-to-child transmission of HBV infection. This study was funded by a grant received from Addis Ababa Science and Technology University and manuscript is already published (doi: 10.1186/s40001-016-0211-3).

5. Evaluation of the Cellular and Humoral Immune Responses to Influenza in a
Cohort of Children Living in Addis Ababa, Ethiopia
Adane Mihret, Liya Wassie, Kidist Bobosha from AHRI and the NIPH group

Despite the global burden of influenza during childhood, the seasonal impact of this disease and surveillance is not done routinely in Ethiopia. The aim of this study was to assess the humoral and cellular immune responses to influenza A and B in a cohort of children below the age of 5 years, who live in Addis Ababa. The data indicated a relatively large proportion of the population exhibited immune exposure to influenza. Serological evidence showed that 86% of the population has been exposed to the H3 influenza A virus, 51% to H1 influenza A virus and 43% to influenza B virus. These studies indicate that influenza is widely prevalent, and predicts significant morbidity and mortality among those most susceptible to either the direct effects of infection or complications from secondary bacterial infections. This study was funded by the Norwegian Institute of Public Health (NIPH) in collaboration with AHRI. The study is completed and manuscript is under preparation.

II. Ongoing PhD/MSc studies and projects

1. Nutritional status and associated risk factors in antiretroviral-naive individuals with HIV-infection and AIDS, Addis Ababa, Ethiopia: a cross-sectional study

PI: Melaku Adal (PhD student); AHRI mentor: Dr. Rawleigh Howe (AHRI) and lab assistant: Kassu Alemayehu

Malnutrition is common in people living with HIV/AIDS (PLWHA) that contributes to a reduced efficiency of anti-retroviral therapy (ART). On the other hand, individuals with high body mass index (BMI) tend to have a relatively higher prevalence of overweight and obesity, resulting in chronic metabolic abnormalities. This cross-sectional study was designed to study the association of malnutrition (BMI <18.5 kg/m2) and excess weight (BMI ≥25 kg/m2) in PLWHA. About 576 HIV-positive, ART naïve adults (71.2% women) were recruited from four hospitals in Addis Ababa between February and September 2013. Hematological parameters (CD4+ cell count and hemoglobin concentration) and total cholesterol and triacylglycerol concentrations were determined. Socio-demographic data, height, weight and WHO clinical stages of the study participants were collected using structured questionnaires. A Pearson chi-square and logistic regression was used to identify factors associated with nutritional status with HIV. The prevalence of malnutrition among the study population was 15.1% (95% CI: 7.6-22.6); whereas excess weight was observed in 22.1% (95% CI: 11.9-31.4) of the study population that includes 16.7% overweight and 5.4% obesity. The age ranges 30-39 years (AOR = 0.54; 95% CI: 0.32-0.91) and 40-79 years (AOR = 0.35; 95% CI: 0.18-0.70) in comparison to age range 18-29 years, and WHO clinical stages III/IV (AOR = 3.54; 95% CI: 1.92-6.51) were found independent predictors of malnutrition and excess weight, where excess weight was also found to be associated with total cholesterol concentration ≥200 mg/dL (AOR = 3.94; 95% CI: 2.03-7.77). A need for integration of nutritional programs as part of HIV/AIDS care is strongly recommended. This study is funded by AHRI and three manuscripts
are already submitted for publication: “Evaluation of alternative markers to predict CD4+ T-cell count in HIV disease progression and ART eligibility in resource limited settings”; “Associations of sex and serum total cholesterol with CD4+ T cell count and HIV RNA load in antiretroviral-naïve individuals in Addis Ababa” and “Under nutrition, overweight, and abnormal cholesterol and triglyceride levels in antiretroviral naïve HIV-infected adults in Addis Ababa: A cross sectional study”.

2. T cells and antibody responses to Hepatitis B virus vaccine in HIV-1 infected children and young adults

PI: Yonas Bekele PhD candidate; Karolinska Institutet, AHRI; Mentors: Prof. Francesca Chiodi and Dr. Anna Nilsson from KI; AHRI mentors: Dr. Rawleigh Howe and Dr. Abraham Aseffa

Hepatitis B Virus (HBV) causes a life-treating infection which can leads to hepatocellular carcinoma (HCC), a leading cause of death among all cancers, or cirrhosis. HBV is highly endemic in sub-Saharan Africa and East Asia with 5-10% prevalence of chronic HBV infection. The complications of HBV infection typically affect adults; much of the burden of chronic HBV is however due to childhood infection. In previous studies, HIV-1 infected individuals showed less optimal and durable serological responses to HBV vaccine. We conducted a prospective vaccination study to assess response to HBV vaccination in HIV-1 infected children receiving antiretroviral therapy (ART) (n=49) and healthy controls (n=63) to study the immunology of T follicular helper (Tfh) cells which are important for vaccine response. All children received 3 doses of recombinant DNA HBV vaccine (rDNA, Serum Institute of India, India) and at 1 month post-vaccination all children, except 4 in the HIV-1 infected group, displayed protective plasma antibody levels to HBV vaccine. Anti-HBs antibody levels were however significantly lower in HIV-1 infected children compared to healthy controls at 1 month from the last vaccination. Moreover, antibody levels decreased significantly both in HIV-1 infected individuals (P<0.0001) and healthy controls (P<0.0001) at 6 months compared to 1 month from the last vaccination dose. No significant change was measured in plasma HIV-1 viral load after vaccination compared to baseline levels. The median frequency of circulating Follicular T helper Cells (cTfh) cells prior to vaccination for healthy controls was 20.3% (range: 6.0-33.5%) and 20.8% (range: 6.7-41.2%) for HIV-1 infected children. Cytokine expression in cTfh cells was measured after 5 days of culture in presence of HBV peptide and costimulatory molecules. The expression of IFN-gamma, IL-2, IL-4 and IL-21 in cTfh cells at 1 month from vaccination was comparable in HIV-1 infected and healthy children. Plasma levels of CXCL13 were measured to assess germinal center activities. We found significantly higher levels of CXCL13 in HIV-1 infected individuals compared to healthy controls prior to and post vaccination; however, the CXCL13 levels in plasma did not correlate with antibody titers to HBV vaccine. Early initiation of ART leads to control of virus replication and maintenance of immunological functions. Collectively, these results demonstrate that the HBV vaccination response of HIV positive children is neither as strong nor as durable as HIV negative children; the finding of apparently equivalently levels of HBV specific cTfh known to be necessary for B cell induction, implies a defect in some other cellular aspect of the humoral immune response.

3. Assessment of peripheral γδ T cells: phenotypic and functional heterogeneity in mono- and co-infected HIV-TB patients in Addis Ababa,
4. Hepatitits and chronic liver disease research project

Project leaders: Dr. Rawleigh Howe and Dr. Adane Mihret together with FMoH, Ethiopia

Hepatitis B infection is a significant problem in this country, the prevalence of chronic hepatitis (HbsAg positive) is about 5-10%, and there is evidence of exposure in up to 50% of Ethiopians. Those who develop chronic disease have risks of cirrhosis, hepatic failure and hepatocellular carcinoma (HCC), and progression to these complications is increased in HIV disease. Neonates and young children are especially prone to progression to chronic hepatitis B infection, due to under developed immune systems. Vertical transmission from mother to child is the most common form of transmission in Asia, whereas in Africa, horizontal transmission predominates. The hepatitis B vaccine for children has been available for several years now, but its impact has not been well evaluated. A recent study at AHRI revealed much lower rates of protection than expected among both HIV positive and negative children, and there have been reports that failure to complete the recommended three doses is common.

Hepatitis C is also a significant problem in Ethiopia, and while the seroprevalence is much lower (1-3%), a far greater fraction of individuals develop chronic disease in comparison with Hepatitis C. Hepatitis D is a defective passenger virus, it does not encode a capsid, requiring hepatitis B virus coinfection, but such coinfected patients have greater risk of progression to the sequelae of chronic disease. Finally hepatitis E is
an acute, typically benign infection, but which for unknown reasons can lead to fulminant disease in pregnant women, and commonly occurs unpredictably in epidemics.

There are several objectives of the Hepatitis B project at AHRI. First, we would like to ascertain, in multiple sites throughout Ethiopia (Jimma, Gondor, Harrar, Hawassa and Addis Ababa), the serological efficacy of HBV vaccination (measured by anti-HBsAg titers) in the 5-8 year old child population in the country, and determine how this is effected by the number of documented doses administered. Secondly, we would like to estimate the prevalence of both chronic disease and infection, measured by HbsAg, and anti-HBc, respectively. Equal numbers (5,000 subjects) of both control unvaccinated and vaccinated individuals will be recruited for these objectives. Thirdly, we will assess HIV infection as a risk factor for reduced vaccine efficacy, and increased disease and infection prevalence. Fourthly, we will attempt to obtain a crude estimate of the degree of vertical transmission by testing mothers of chronic Hepatitis B carriers for infection and carriage, and among matched mother-child pairs, perform molecular studies of their HBV isolates to determine molecular identity of the paired strains.

Each site has involved two MSc students, and all 5 sites have commenced recruitment, one site has completed recruitment and is now performing serological analysis, one site has nearly finished recruitment, and the other three sites are not yet finished but anticipate finishing within 4 months. The first three objectives will be assessed at each site as well as among pooled data from all sites. The final objective will of necessity require detailed molecular analysis of samples gathered at all sites.

In parallel to the child hepatitis B study, seroprevalence will be determined for hepatitis C, D, and E infection at each site from randomly identified samples from 20% of the mothers collected for the child study. Such samples have been obtained, and lab analysis has begun.

A final objective will be performed on an independent adult cohort from patients with chronic hepatitis and those with hepatocellular carcinoma. Isolated hepatitis B, C, and D will be identified from patients' samples, and selected regions of each virus sequenced to determine strain and genetic diversity. We plan for these studies will be performed on a newly purchased Illumina sequencer at AHRI.

5. Evaluation of aloe and whey protein on measures of HIV enteropathy in a pediatric population.

Mary Vander Wal1,3, Meseret Gebre4, Barbara Smith1, Rawleigh Howe3


The gut associated lymphoid tissue (GALT) is the predominant site of HIV initiation which leads to rapid loss of CD4 T-cells, a significant immune response and compromise of the protective mucosal layer between the intestinal lumen and the general circulation. The compromise in epithelial integrity leads to translocation of bacterial and viral products into the general circulation leading to immune activation. A subclinical inflammatory state is established and co-morbidities develop prematurely. Immune activation markers are correlated with
poorer clinical prognosis. Strategies aimed at addressing gut integrity are needed.

The overall objective of the study is to evaluate nutritional support as an adjunct therapy to address HIV enteropathy and slow the development of co-morbid diseases. More specifically, we hypothesize that the addition of an aloe enriched whey protein drink to the diets of HIV+ children will provide nutrients to aid the body in restoring the mucosal barrier in the gut resulting in: 1) A reduction of bacterial translocation as measured by markers of enterocyte damage and bacterial translocation (Intestinal Fatty Acid Binding Protein, endotoxin, sCD14), 2) A reduction in markers of immune activation (CD38+ HLA-DR+ T Cells), and systemic inflammation (IL1β, IL-6, TNFα), 3) A reduction in oxidative stress as measured by total antioxidant capacity and total glutathione, and 4) improved immune reconstitution as measured by reduced, viral load, increased numbers of CD4 T cells and CD4 naïve subsets including putative recent thymic emigrants (CD31+) as well as cells undergoing homeostatic proliferation (Ki67).

Aloe is known to have the anti-inflammatory, anti-microbial, anti-oxidant as well as tissue healing properties. Aloe is indigenous to Ethiopia, and its use culturally congruent, economical and sustainable. Whey protein contains multiple amino acids needed for tissue healing, is a well tolerated protein source, easily absorbed, highly bioavailable, and also has anti-inflammatory and antioxidant properties.

The study is a 3 month randomized, blinded trial including children aged 4-10 from the Alert HIV Pediatric Clinic. 60 HIV+ children will be given an Aloe enriched Whey protein drink, 60 HIV+ children an isocaloric drink, and 20 HIV- children will be recruited as controls. Supplements will be given weekly along with health history forms; blood will be obtained at baseline and after trial completion.

The study has received multiple institution IRB and FMHACA approval, and recruitment has commenced.

Networking activities

Like in the previous years, the team established links with several overseas universities and institutions, in the context of proposed and ongoing projects, including the Norwegian Institute of Public Health (NIPH, Norway) and Karolinska Institute (Sweden) and Germany. In addition, some of the team members also participated in national and international meetings and training activities as part of capacity building and further networks.

The Team has long been leading networking initiatives in Ethiopia until March 2016 through the East Africa Consortium for Clinical Research (EACCR), to building capacity for clinical research and future trials in sister institutions (Butajira Hospital and Bole Health Center) in the Country.

Malarial and Neglected tropical disease Directorate

Highlights of the team’s 2016 activities

The Neglected Tropical Diseases (NTD) and Malaria case team has developed strong relationships with the federal ministry of health (FMoH) as key stakeholder. In line with the national 2020 strategic goal on eliminating the eight NTDs of public health importance, the team was requested by FMoH to do operational research
on NTD. In response, the team successfully organized national and international partners and finalized a protocol on CEM to assess the safety of Ivermectin, Albendazole and Azithromycin co-administration. As a joint clinical research capacity building initiative between AHRI and FMoH, we collaborated with Hawassa University to evaluate the prevalence of arboviral infection among acute febrile cases in the Borena, Arbaminch and Moyale areas. Moreover, we are one of the founding members of the national NTD operational research advisory committee, and member of the leishmaniasis technical working group and Onchocerciasis elimination verification task force.

The thematic areas of ongoing projects address both basic and applied questions. In the field of Malaria, the team is working on the dynamics and implication of asymptomatic malaria as source of malaria infection, the human age and/or sex dependent biting preference of mosquitoes, clustering of asymptomatic malaria infection, the epidemiology of the drug resistance alleles in \textit{P. falciparum}, the population genetics of \textit{P. vivax} and prevalence, and genotype of G6PD deficiency and \textit{in vitro} drug resistance assessment techniques for different stages of \textit{P. vivax} and \textit{P. falciparum}. In leishmaniasis, the first phase of the project studying innate immunity leishmaniasis is completed. As alluded to above, we have also project on arbovirus and a cohort event monitoring survey to assess the safety of Ivermectin, Zithromax and Albendazole co-administration. As part of our research endeavors we had 1 PhD and 6 MSc students that joined the team in the fiscal year. Of the 3 PhD students that were working with us, 2 of them are writing up their thesis and the other is expected to finish data collection in 3 months time. The team had 6 grant applications; of which 2 were initiated by the team. Of the 6; one was successful and two are in anticipation. There were 7 articles published in peer reviewed Journals, and 2 submitted and under review and 5 under write-up.

I. Completed Projects

\section*{Leishmaniasis}

The 1st funding phase of the DFG funded “Innate immunity in leishmaniasis” project is completed. Two PhD students are writing five manuscripts and preparing their thesis. One article is published, and 1 is under review. Application for the second phase of funding with DFG is pending. From this work 1 article was published, 1 is accepted for publication, 2 manuscripts have been submitted and 3 under preparation (for further information refer to 2015 annual report).

1. \textit{In vitro} permissiveness of bovine preferable mononuclear cells to \textit{Leishmania donovani} infection (\textit{Tasew et al. published})
2. Serological signatures of clinical cure following successful treatment with sodium stibogluconate in Ethiopian Visceral leishmaniasis cases (\textit{Gadisa et al. accepted})
3. Characterization of Dendritic Cell subtypes in the peripheral blood and skin biopsies of cutaneous leishmaniasis patients (\textit{Chanyalew et al., manuscripts under preparation})
4. Assessment of cytokine and chemokine production from innate immune cells in the peripheral blood of cutaneous leishmaniasis patients (\textit{Chanyalew et al., manuscripts under preparation})
5. Enhanced up regulation of CD66b expression and CD62L shedding in peripheral blood neutrophils in Cutaneous Leishmaniasis patients in response to *L. aethiopica* lysate (*Chanyalew et al.*, manuscripts under preparation)

6. Impairment of innate immune cell function during clinical visceral leishmaniasis (*Tasew et al.* manuscript submitted)


Briefly, the findings indicate:

- Bovine cells can be infected by *Leishmania donovani*, the parasite can complete its life cycle forms, yet further studies are needed to see domestic animals could serve as reservoirs.
- The serum level of certain soluble cell surface markers, chemokines and cytokines change with clinical cure indicating their potential prognostic value.
- Distinct dendritic cell subsets may be important in the response to *L. aethiopica infection*.
- High inflammatory responses by peripheral mononuclear cells were observed in cutaneous cases corroborating with its predominantly self limiting nature.
- Impaired innate inflammatory responses are associated with and may contribute to clinical progression of disease.

**Funding:** German research foundation, Armauer Hansen Research Institute

### II. Ongoing projects

**Malaria**

**Background:** The remarkable success documented in the control of malaria in the last decade and half has re-ignited efforts to achieve malaria elimination and eradication. Inline, Ethiopia aimed to achieve elimination in low transmission settings by the end of 2020, in low transmission districts. With the move towards elimination, it becomes essential to understand the contribution of asymptomatic parasite carriers to disease transmission. The prevalence of G6PD deficiency to use gametocidal drugs for sterile cure, understand the drug susceptibility pattern and genetic diversity of the circulating plasmodia species, and mosquito behavior. The ongoing projects are focused around these themes.

**Methods:** The infection dynamics is being studied, on school children, using microscopy, serology, PCR and qRT-PCR from finger prick blood samples. The infectiousness of submicroscopic malaria carriers to mosquitoes is being evaluated using membrane feeding experiments. Locally reared *A. arabiensis* colony of mosquitoes and wild mosquitoes collected from the field are being evaluated in the infectiousness experiments. Finger prick blood will also be used to determine the dynamics of infection and evaluation of submicroscopic malaria carriage as a recruitment criterion for the membrane feeding experiments. Infectiousness of carriers will be assessed using the membrane feeding assay from venous blood (5mL). The prevalence of G6PD
deficiency will be surveyed using the Fluorescent Spot Test and those with phenotypic deficiency will be genotyped. The CQ resistant alleles in *P. falciparum* will be analyzed using PCR-RFLP techniques. The biting preference of mosquitoes will be done using the DNA figure printing technique established for forensic use. The asymptomatic infection in the vicinity of a malaria case will be determined using RDTs.

**Names and specific titles of the postgraduate students are:**

1. Fitsum Tadesse (PhD student): Understanding the dynamics and infectivity of low-density asymptomatic malaria carriage in low and moderate endemic settings in Ethiopia – are they challenges for malaria elimination?
2. Addimas Tajebe (PhD student): Biological characteristics and drug resistance profile of *P. falciparum* and *P. vivax* in Ethiopia.
3. Mulualem Belachew (MSc student): Clustering of submicroscopic infections within the family and immediate neighbors of microscopically malaria confirmed cases.
4. Getaneh Tegegne (MSc student): The biting preference of the Ethiopian mosquitoes within households among the family members.
5. Getasew Shitaye (MSc student): Prevalence of G6PD in high malaria burden areas
6. Temesgen Menberu (MSc student): Prevalence of CQR Alleles in *P. falciparum*; after two Decades of Withdrawal of CQ Usage in Ethiopia

**Progress**

- **Ethical clearance has been obtained for all projects except that of Addimas Tajebe.**
- **Establishing field laboratory:** A field laboratory including rearing of mosquitoes and feeding assays was established at both sites. Intensive optimization was done at both sites on rearing, starving, feeding, and maintaining fed mosquitoes. Field mosquito collection and their maintenance at the facilities was also initiated. Many entomological and parasitological lessons have been attained.
- **Community mobilization and sample collection:** Community mobilization was done at two woredas in Jimma zone, Sekoru and Tiro Afeta. Two kebeles were included from each woreda, a total of four. For the optimization protocol and also for comparison purposes patients that had confirmed malaria (Microscopy or RDT) were enrolled in the study.
- **Results:** Samples from the two school surveys were analyzed with molecular and serology techniques. More submicroscopic infection with *P. vivax* was observed in both surveys. As compared to *P. falciparum*, the gametocyte carriage was high in *P. vivax* carriers. Most infections detected at the second survey were new, indicating the presence of infectious bites in the dry season. Moreover, the high gametocytemia in *P. vivax* might indicate submicroscopic healthy carriers are potential source of infection.

**Funding:** AHRI, Nuffic, Scholarship of Government of Singapore
Arbovirus

Background: In the modern world, despite the advances in diagnostics, therapeutics, and vaccines (re)emerging infectious diseases that affect not only the health but also the economic stability of societies are growing challenges. The public fear, global economic and societal disasters of the (re)emerging arboviral infection(s) has sent a message to the global scientific communities. Though many infected individuals are asymptomatic, clinical presentations may range from febrile illness of short duration to life threatening hemorrhagic fever or neuroinvasive disease. Also there are occasions of large seasonal epidemics, especially in regions where they were not previously detected. Arboviral infection outbreaks in previously naïve environments or their (re)emergence in endemic areas might be derived by social and/or ecological changes that demonstrate the need to better understand their epidemiology. The aim of the projects around arboviral infection(s) are: to build capacity in clinical research and virology; and produce a preliminary result on their public health significance.

Methods: Fluorescence staining based serological methods will be used to detect recent and life time exposures to arboviral infections.

1. Daniel Demissie: MSc student
   Title: Seroprevalence of Dengue virus among acute febrile cases and associated factors, in Arbaminch and Konso districts, SNNPR

2. Eshetu Negussie: MSc student
   Title: Seroprevalence of Yellow fever virus among acute febrile cases in selected health facilities and associated factors, Borena district, Oromia.

Progress: Sample collection and IgG testing completed. The exposure to dengue (25% [124/494]) and yellow fever (12% [62/505]) in the study areas is significant. Future work will include IgM testing on these samples to implicate active infection and PCR based confirmatory diagnostic tests.

Funding: Ethiopian Federal Ministry of Health

Other Neglected Tropical Diseases (NTDs)

Background: In Ethiopia, NTDs cause 873,500 Disability-Adjusted Life Year (DALYs) annually lost which is 1.9% of the total DALYs lost due to any causes in 2013. Cognizant of the problem, the Federal Ministry of Health (FMoH) aims to control or eliminate trachoma, onchocerciasis, schistosomiasis, soil transmitted helminthiasis, lymphatic filariasis, podoconiosis, leishmaniasis and dracunculiasis as a public health problem by 2020. In most NTD endemic areas, at least 5 NTDs are co-endemic. In order to accomplish the 2020 goal, the FMoH NTD operational research advisory committee identified co-administration of MDA as high priority. The aim is to assess the safety of co-administrating Ivermectin, Albendazole and Zithromax as MDA.

Method: Cohort event monitoring survey

Progress: in coordination with the FMoH NTD team and with the advice of experts from iTi, RTI, LSHTM and WHO-Geneva, the protocol write-up is being finalized.

Funding: Ethiopian Ministry of Health
Clinical Trial Directorate

The establishment of the clinical trial unit (CTU) is one of the major milestones in the history of Armauer Hansen Research Institute (AHRI). The CTU was one of several capacity building components following the first GCP/GCLP compliant clinical trial conducted in AHRI in collaboration with WHO/TDR in 2001. Since then the unit conducted a number of GCP standard clinical trials on different drugs and vaccines.

Currently the clinical trial has its own clinical trial team, its own screening and admission wards and its own laboratory. The clinical trial team has been involved in many activities in the past one year. The detailed activities carried out in each clinical trial are narrated below but to summarize them—we have two active ongoing trials: “The Evaluation of a Standardized Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB (STREAM)” and “Bioequivalence Clinical Studies.” We had also completed two: “Exploratory, phase II double blinded, randomized placebo controlled trial of shuinko ointment local application twice a day for 4 weeks in Ethiopian patients with localized cutaneous leishmaniasis” that was funded by AHRI and Nagasaki University, and “A Randomized, Placebo Controlled Trial of the Killed, Bivalent, Whole Cell Oral Cholera Vaccine in Ethiopia” that was funded by the International Vaccine Institute (IVI). The results of both projects are published in peer reviewed journals.

The clinical trial staff has also given trainings and shared their experiences in GCP and clinical trials during the trainings that were organized for researchers and PhD students. This year, sessions were delivered on research ethics, GCP and clinical trials by our staff members during February & April 2016.

The detailed clinical trial activities accomplished in each trial are described below.

The Evaluation of a Standardized Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB (STREAM)

Despite the availability of an efficacious, affordable, six-month chemotherapy regimen and having an efficient strategy to deliver treatment under direct observation to the majority of TB patients, TB control worldwide is hindered by two major issues: the emergence of multidrug resistance (MDR) and TB-HIV Co infection. The former hampered dramatically the efficacy of widely implemented standard short-course chemotherapy, thus limiting the success of efforts to fight against tuberculosis worldwide. Since 2002, at least one case of extensively drug-resistant tuberculosis (XDR-TB) has been reported from 45 countries. The existing treatment approach for MDR-TB is based largely on expert opinion and there is a lack of good evidence on optimal management. Since May 2016, WHO has recommended a short term MDR TB regimen of 9-12 month duration based on observational studies.

The primary objective of the STREAM stage I trial is to assess whether the study regimen (9 months regimen), which is based on the regimen used in Bangladesh (Van Deun et al (2010)) where relapse-free cure rate of 88% was obtained, is non-inferior to the control regimen (recommended by the WHO). The primary objective of the STREAM stage II trial is
i. To assess whether the proportion of patients with a favorable efficacy outcome at Week 76 on Regimen C (a 9 month regimen with BDQ and without injectable) is superior to that on Regimen B (a 9 month regimen with injectable/ Bangladesh regimen).

ii. To assess whether the proportion of patients with a favorable efficacy outcome at Week 76 on Regimen C is not inferior to that on Regimen B and

iii. To assess whether the proportion of patients with a favorable efficacy outcome at Week 76 on Regimen D (a 6 month regimen with BDQ and injectable) is not inferior to that on Regimen B.

The practical, program-based study design will also ensure that if the results are favorable they will be generalizable to routine program settings. In addition, health system and patient costs associated with implementation will be documented. These will be analyzed in association with the clinical outcomes of the trial using the TREAT TB Impact Assessment Framework in order to provide as much information as possible for subsequent policy and practice decision-making.

STREAM is a multi-center study which is undergone in Ethiopia, South Africa, Vietnam and Mongolia. This study was started in our site, AHRI since Feb2013. The STREAM stage I recruitment target is already met, i.e. at least 400 participants in all four participating countries. In Ethiopia, both from ALERT and St Peter’s hospitals, we achieved the recruitment target of 124 participants. All the laboratory (chemistry, hematology, sputum smear and culture), data management as well as clinical follow-up activities are proceeding smoothly. STREAM stage II was started in June of this year. So far 7 patients have been screened and 2 patients who fulfilled inclusion criteria have been randomized in the study. In parallel, follow up of STREAM stage I participants has continued. Currently 13 (out of total of 55) study participants are on follow up.

The source of fund for STREAM stage I is from USAID & MRC, whereas for STREAM stage II- it is from USAID, MRC/DFID and Janssen Research & development/LLC

Bioequivalence Clinical Studies

Establishment of an internationally recognized but locally/regionally accessible and affordable bioequivalence (BE) testing facility has recently become a necessity. A clinical testing facility was thus established at AHRI since 2013 following the establishment of the regional bioequivalence center (RBEC) as the first CRO (contract research organization) in Ethiopia. Since then the clinical trial site at AHRI in collaboration with RBEC has conducted two GCP compliant pilot clinical BE studies on two locally and regionally produced antibiotic products. The two pilot studies were on oral tablet preparations; Strox (of Universal Corporation, Kenya) in comparison to the originator Ciprobay (of Bayer HealthCare Pharmaceuticals Inc.); and COTRI (Addis Pharmaceutical Factory PLC, Ethiopia) in comparison to BACTRIM™ (Hoffmann-La Roche Inc., Germany).

As the BE clinical study requirements are harmonized and unified worldwide, such clinical studies should
fulfill international standards so that the results can be accepted and products are marketed universally. To this effect the AHRI clinical site and the RBEC have been inspected by local regulatory authority and WHO for compliance of GCP and local requirements during the conduct of the two pilot studies. In particular, the WHO visit following a pilot study was critical and considered a pre-inspection that prepares the sites for the conduct of pivotal studies for possible product prequalification application and site recognition for GCP compliance. In due course the sites have been building capacity and accumulating experience towards conducting internationally accepted studies and can become competent in the international market. Though the process has been challenging and lengthy, the sites are now prepared for the conduct of a pivotal study on a locally produced tablet product for possible WHO inspection and product pre-qualification application. The clinical study protocol is currently under its final review for regulatory approval. The source of fund for BE study is AHRI Core budget.

Community Engagement (CE) in Clinical Trial at AHRI

When Clinical Trial research is undertaken in a community, there is a need to incorporate the community structures. The research that is proposed must fulfill health related needs within the community. In addition, community members need to have some understanding of research itself, ethics and regulatory requirements. To achieve this in a meaningful way, shared and trusted structure of communication needs to be established via a community engagement (CE) plan. One approach to this effect could be establishment of a community advisory board (CAB) that continuously engaging the community in each step of a clinical research process. AHRI has been engaged in several clinical research activities particularly clinical trials needs community consultation, education and engagement at different stages. The clinical trial team at AHRI has taken the initiative to establish STREAM CAB with the support obtained from the Union through STREAM trial that could be serving beyond STREAM. To this effect a staff training and experience sharing event was held with South African colleagues in STREAM. The clinical trial team believes such move will have an impact on our experiences in CE that can also be helpful in increasing community awareness in MDRTB case detection and treatment. A stakeholder consultation meeting and CAB formation will soon be held as a first step in community engagement.
Other Activities

1. Training

Training given to clinical trial staff in 2016

<table>
<thead>
<tr>
<th>Sr</th>
<th>Title of the training</th>
<th>Period</th>
<th>Venue</th>
<th>No. of Participants</th>
<th>Organized by</th>
<th>Remark</th>
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<tr>
<td>1</td>
<td>STREAM stage 2 SIV training</td>
<td>23-25 Feb 2016</td>
<td>AHRI</td>
<td>75</td>
<td>AHRI &amp; MRC CTU</td>
<td>Staff from AHRI/ALERT &amp; St Peter’s Hosp.</td>
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<tr>
<td>2</td>
<td>STREAM TB and molecular laboratory techniques (TB culture, FDA staining, LPA &amp; more)</td>
<td>6-10 June 2016</td>
<td>AHRI</td>
<td>11</td>
<td>AHRI &amp; ITM, Belgium</td>
<td>Staff from AHRI &amp; UoG</td>
</tr>
<tr>
<td>4</td>
<td>ISO 15189 Laboratory Management System and ISO 14155 Good Clinical Practice</td>
<td>1-5 Aug 2016</td>
<td>AHRI</td>
<td>15</td>
<td>AHRI &amp; Africa Quality Consulting</td>
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<tr>
<td>5</td>
<td>Community Engagement in Clinical Research</td>
<td>21-22 Sept 2016</td>
<td>AHRI</td>
<td>8</td>
<td>AHRI &amp; The Union</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>MDRTB Management</td>
<td>24-28 Oct 2016</td>
<td>ALERT</td>
<td>4</td>
<td>Challenge TB</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>International Course on Clinical Management of MDRTB</td>
<td>April 2016</td>
<td>Jakarta, Indonesia</td>
<td>1</td>
<td>The Union</td>
<td>Sponsored by IUATLD &amp; AHRI</td>
</tr>
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</table>

The clinical trial staff have given training and shared their experiences in GCP and clinical trials during the training sessions that were organized for researchers and PhD students. This year, sessions were delivered on research ethics, GCP and clinical trials by our staff members during February & April 2016.

2. Meetings and travels

The clinical trial team has participated in the annual TRAC meeting that was held during March 2016 in Hawassa. The team leader delivered presentation on clinical trial experiences in general and STREAM trial update in particular. In addition, the team members have participated the annual STREAM investigators’ meeting which was held during July 2016 in the New York, USA.
Community Engagement in STREAM Trial & Beyond, Training & Experience Sharing event with Partners from S Africa (Sept 2016)

STREAM Stage 2 SIV Training, Staff from AHRI /ALERT & St Peter's (Feb 2016)
Non communicable Diseases Directorate

The non-communicable disease division is recently defined and at present comprises of projects related to the Ministry of Health Renal Transplantation initiative as well as projects in Cancer research.

A. HLA lab for renal transplantation initiative

Among non-communicable diseases, diabetes and hypertension are increasing in prevalence in Ethiopia as well as other resource limited countries. Long term complications of these diseases include chronic renal disease and ultimately renal failure requiring dialysis and renal transplantation. Considering the increasing burden in Ethiopia, the Government has initiated kidney transplantation program at St. Paul Hospital in close collaboration with University of Michigan (UM). In the past 2 years, the program has been able to perform kidney transplantation for more than 10 patients and was successful. HLA typing, flow cross-match and testing recipient’s serum for anti-donor antibodies are important tests in the transplantation process to choose for the right donor. Currently, these tests are being done abroad as there are no local labs performing these tests.

As part of this program, a staff member from AHRI (Kidist Bobosha) was trained in HLA typing and anti-HLA antibodies detecting techniques in the end of 2014 for 3 months at University of Michigan with the aim of establishing standard HLA lab at AHRI to support the transplantation program through providing service, to build local capacity and to support HLA associated research.

The establishment process is still ongoing where purchasing of reagents and setting up of the lab space is underway. Recently, a new agreement is signed between the Lagitre International (exclusive distributor of One lambda) and AHRI. The company have donated a Luminex machine, and also agreed to provide training and technical support to HLA team at AHRI.

As part of this capacity building process, and as part of AHRI’s tradition of providing a framework for student training, we have recruited a PhD student (Tilahun Alelign) who will be addressing the scope of HLA sensitization in chronic renal disease patients.

1. Evaluation of HLA sensitization in patients with chronic renal disease
Tilahun Alelign, Beyene Petros, Rawleigh Howe, Kidist Bobosha, and Yewondwossen Tadesse.

The Ethiopian Ministry of Health in collaboration with the University of Michigan has commenced a program in renal transplantation at St. Paul’s Hospital. Among the many factors influencing successful transplant outcome is potential for acute donor kidney rejection, and this in turn is mainly effected by the presence of pre-existing anti-HLA antibodies within the recipient which react to donor tissue. During routine pre-transplant workup, the presence of such antibodies, along with HLA compatibility, are determined by assays on donor and recipient
Within Ethiopia, there are really a limited number of potential donors for a given prospective recipient; the majority of donor kidneys have been provided by close relatives or spouses. Hence, if an individual in need of a transplant has pre-existing anti-HLA antibodies reacting with such a potential donor, he will ineligible. In Western countries, this problem has been reduced through the formation of extensive national donor registries involving thousands of potential donors and recipients, such that appropriate matching can be achieved to minimize any donor specific reactivity. However, it is unlikely that such registries will be available any time soon within Ethiopia.

This suggests that increasing eligibility in the future will require means to minimize the development of anti-HLA antibodies. Among women, such antibodies are most commonly elicited from multiple pregnancies, the host woman developing antibodies to paternally derived HLA antigens on the developing fetus. In addition, anti-HLA antibodies can be generated from blood transfusions, a particular concern among end stage chronic kidney failure patients in need of transplants, who typically require multiple blood transfusions owing to minimal renal production of erythropoetin. Within allogeneic blood, platelets and leukocytes are the principal elicitors of anti-HLA antibodies, though erythrocytes also express low levels of HLA as well, and can reactivate memory cells within previously sensitized individuals, including multiparous women. In Ethiopia, capacity exists to prefractionate blood products, and purified RBC alone would be the most preferable means of transfusion, though heavy demand often precludes convenient fractionation. Finally, anti-HLA antibodies, even if absent pre-transplantation, can eventually develop in about 25% of kidney recipients, and the presence of such antibodies is associated with higher risk of eventual organ rejection. A large number of recipients of kidney transplants performed outside the country before the current initiative at St. Paul are currently residing within Ethiopia. The extent of HLA sensitization among these kidney recipients, as well as among the chronic renal disease patients within the country potentially needing future transplants, from blood transfusions as well as multiple pregnancies is undefined.

To define the scope of this problem as well as to develop the capacity for HLA typing and cross match assays we are developing the present research study. One hundred chronic renal disease patients, either following renal transplantation, or concomitant with end stage complications such as ongoing or impending requirement for dialysis will be evaluated for sensitization to allogeneic HLA antigens, as well as risk factors for such sensitization including reception of multiple blood transfusions or a history of multiparity. Antibodies to HLA antigens as well as HLA typing will be performed by using Luminex multianalyte technology.

**B. Hematologic and solid tissue malignancies**

AHRI has commenced a collaborative venture with Tikur Anbessa hospital which aims to significantly increase local skill in more sophisticated measures needed for adequate diagnosis of leukemia and lymphoma, an approach which we hope to extend to other solid malignancies as well.

Traditionally, leukemia and lymphoma diagnosis has relied heavily on pathology evaluation of blood smears
and bone and lymph node biopsies. In recent years this approach is now supplemented with flow cytometric methods, as well as other cellular and molecular approaches, in particular Fluorescence In Situ Hybridization (FISH) to identify pathognomonic genetic abnormalities, eg rearrangements and translocations which can be either useful diagnostically or prognostically for treatment selection or followup. In general, each approach has advantages and disadvantages, with the combination of modalities considered most accurate. Indeed, the WHO diagnostic recommendations incorporate these modalities.

A total of 8 students have been recruited as part of this initiative; most projects are funded by the Ministry of Health, and others by AHRI core or other Swedish sources. Two MSc projects have or will focus exclusively on flow cytometry, utilizing 12-15 markers on peripheral blood of leukemia patients (primarily early lymphoid or myeloid markers), and disaggregated lymph node cells or bone marrow biopsy cells from lymphoma cases (utilizing markers of more mature lymphocyte subsets). A third MSc student associated with Tikur Anbessa hospital has not been principally funded by AHRI but is participating in training courses we have provided there and will be comparing flow cytometry evaluation with cytochemistry approaches. Two PhD projects will perform more extensive flow cytometric analysis (utilizing up to 24 markers), as well as FISH and cytogenetic modalities, and will more thoroughly characterize leukemia and lymphoma cases (from HIV positive and negative individuals). In addition, such projects will explore feasibility of flow and FISH techniques in diagnosis of other myeloproliferative and myelodysplastic disorders. A third PhD study will focus on chronic myelogenous leukemia, and will characterize in detail the BCL-ABL translocation, utilizing FISH, RT-PCR and sequencing approaches. The latter are currently necessary for optimal selection and efficacy monitoring of therapeutic drugs targeting the protein kinases which encode the BCL and ABL products. This study will be complemented by a fourth PhD study which will characterize the pharmacodynamics, pharmacokinetics and pharmacogenetics of such kinase inhibitors in patients receiving therapy. The final PhD student has been recently recruited and will define the role of Epstein Barr Virus infection in Hodgkin’s Lymphoma along with biomarkers associated with the malignant Reed-Steinberg cells as well as the extensive and varying inflammatory infiltrate in such lymphoma cases.

Many of the techniques planned for these studies, including FISH, cytogenetics and advanced immunohistochemistry and molecular approaches are not established in the country; hence, many of the students will have opportunities for training abroad. One student has already received training in FISH at the University of Leipzig. We have initiated collaborations with University of Toronto, MD Anderson Hospital in Texas, and the University of Lund in Sweden. The MD Anderson center has planned a year long training in cytogenetics, which, after a month long lab train course at Tikur Anbessa will be sustained with teleconferencing sessions at this hospital.

AHRI’s lab expertise in this initiative is in the realm of flow cytometry. Since this initiative has been planned ultimately for multiple locations in Ethiopia, we have selected the 4-color FACSCalibur cytometer as a platform, widely available in the country including at Tikur Anbessa referral hospital and ALERT (rather than AHRI’s more advanced 8 color FACSCanto). One of the students has finished an MSc thesis on flow cytometry evaluation of acute leukemia (see below), and we have provided multiple training sessions at Tikur
Anbessa for the other students. As well we have initiated the formation of periodic clinical rounds whereby both clinicians and lab personnel at the hospital discuss problem cases.

1. Utility of immunophenotyping by flow cytometry for diagnosis and classification of acute leukemias at Tikur Anbessa Specialized Hospital, Addis Ababa.

Metasebia Tegegn, Rawleigh Howe, Aster Tsegaye, Fatuma Hassen, Amha Gebremedhin, Abdulaziz Abuberker, Fissehatsion Tadessa, Daniel Hailu

Immunophenotypic characterization of acute leukemia is an important clinical application of flow cytometry and has become a powerful tool contributing to proper diagnosis and classification. The objective of the study was to phenotype and classify acute leukemias by flow cytometry using commonly used markers for leukemia diagnosis. 21 of 40 patients were classified as Acute Myeloblastic leukemia (AML) while 19 were identified as Acute lymphoblastic leukemia (ALL). Of all the ALL cases, 10 were B-ALL and 9 were T-ALL. Markers of immaturity HLA-DR and CD34 antigens were co expressed in 61% of AML cases, and 33% of T-ALL cases, whereas CD34 was expressed in 50% of the B-ALL cases. Myeloperoxidase and CD13 were the most commonly expressed markers of AML, whereas CD19 and cCD79a were present in all cases of B-ALL. Cytoplasmic CD3 and CD7 were the most sensitive markers for T-ALL. Discrimination of AML from ALL patients by flow cytometry was 80% concordant with traditional morphology. Notable discrepancies occurred in cases where leukemia cells expressed markers for more than one lineage. In sum, this study illustrates that immunophenotyping by flow cytometry provides useful information to confirm diagnoses of standard morphology methodology, to provide classifications where morphology is indeterminate, and to provide further lineage and maturation information for ALL not obtainable by morphology. It thus represents an important tool among many in leukemia classification and is realistic to execute in resource limited settings.

Biotechnology and Bioinformatics Directorate

The national Biotechnology Road map has outlined research initiatives to start in the area of biotechnology and bioinformatics. This includes development of infrastructure and expertise. AHRI has been assigned by Government to lead the national health biotechnology initiative. The first step in this process is to build the human resource base at the Institute. A core unit has been created in 2016 to serve as the nucleus for the eventual emergence of the Biotechnology and Bioinformatics Directorate to address the national mandate. The unit has wo main components.

1. The biotechnology component will engage in product discovery and tests for potential therapeutics, diagnostics for human and animal diseases relevant for the country, and provide capacity building training, and a research facility set up for postgraduate students.

2. The bioinformatics research facility will provide access to high-performance computing resources, data analysis and programming expertise that serve scientists at AHRI to master the informatics needs of their research. The facility will host a broad range of workshops on bioinformatics and data analysis that will provide a strong training component to successful grants.

The Biotechnology and Bioinformatics Research Initiative team currently has one postdoctoral scientist, one
MSc student and one laboratory technologist. We are planning to recruit an assistant researcher, as well as a Molecular Biology senior scientist with solid experience in both current molecular approaches as well as in bioinformatics applications. In 2016, the major research areas and research facility set up included genomics, bioinformatics lab facility set up, animal QTL polymorphism for disease and productivity study protocol development, and cattle genetics and admixture mapping proposal development.

I. Ongoing projects

1. Whole genome sequencing (WGA) analysis of *Mycobacterium bovis* isolated from Ethiopian cattle

Yonas Kassahun¹, Adane Mihret¹, Abraham Aseffa¹, Gobena Ameni², Aboma Zewdie², Stefan Berg³, Javier Nunez-Garcia³, Noel Smith³

¹Armauer Hansen Research Institute, ²Aklilu Lemma Institute of Pathobiology, ³Animal & Plant Health Agency

In a collaborative project between AHRI and APHA and other Ethiopian and international institutions, *M. bovis* strains have been collected from different settings and geographical regions in Ethiopia. Initially, a cross-sectional abattoir study, including sites in Northern, Western, Central and Southern Ethiopia was performed. A second study on surveillance of bovine TB in dairy farms in central Ethiopia isolated *M. bovis* strains which were stratified into clusters by spoligotyping and MIRU-VNTR typing. A third “Natural transmission study” was executed at the Sebeta Agro industry on 50 naïve calves exposed to a large bovine TB reactor herd for about 12 months. Post mortem evaluation of selected reactors and calves has generated a set of *M. bovis* isolates that has been spoligotyped. The current WGS study is designed based on the repository samples (*M. bovis* isolates) collected and stored at AHRI.

Focusing on subsets of the strains collected in each of the three studies described above, WGS data will be able to generate the first complete and comprehensive overview of the population structure and relationships between *M. bovis* strains/lineages in Ethiopia. The data will provide the *M. bovis* strain distribution and circulating variants at national, regional and within herd levels. As part of the ongoing project named Ethiopia Control of Bovine TB strategies (ETHICOBOTS), capacity building on molecular genetics and analysis of WGS data at AHRI and ALIPB plan will be attained by analysing the repository isolates of *M. bovis*. This project will initiate capacity building in bioinformatics at AHRI and ALIPB and specifically on WGS analysis of strains from the *Mycobacterium tuberculosis* complex.

To date, 42 isolates were successfully characterized and shipped to APHA for WGS sequencing. The sequence data will be received for the planned analysis on *M. bovis* population genetics structure. Secondly, the activity will facilitate the platform setup on capacity building and technology transfer component in the areas of pathogen genomes and bioinformatics at AHRI. AHRI is expected to have its own sequencing facility by early 2017.

Funding: Biotechnology and Biological Sciences Research Council (BBSRC) through ETHICOBOTS project

Networking:
1. Two Human Genetics projects: "Genetic diversity among 14 distinct local ethnic groups of South Omo region, Oromia region in Ethiopia" An extension of H3Africa and NIH grant projects to collaborate with ALIPB on Bioinformatics/genomics aspects of the project.

2. HIV and Gut Microbiota: A New NIH grant application submitted by Dr. Dawit Woldai (University of Mekele), to collaborate the Bioinformatics aspect of the project

**One Health Report**

*(Dr. Rea Tschopp)*

The One-Health group at AHRI is in a rapid expansion phase in terms of research studies conducted since its formal creation, and several international (OPO Foundation France, CDC Atlanta, IDRC Calgary) and national (AAU) One-Health grant proposals that have been submitted this year. Thirteen post-graduate students have been associated with the Group in 2016 coming from national Universities (Haremaya, Addis Ababa and Jigjiga) as well from Swiss Institutions (Swiss TPH, HAFL). One permanent staff (veterinarian) has been recruited. Further permanent staff will be recruited in the future as per increasing work load/projects.

The mandate of the research group includes research on integrated human-animal health services (diagnostics, health service delivery), research on zoonosis at the human-domestic animal-wildlife interface (including food-born zoonosis) and the relationship of environmental health and public health.

The group has a strong emphasis on One-Health in pastoral communities. The Jigjiga One Health Initiative (JOHI) is a 12 year long research and development program funded by the Swiss Government that aims at improving the health and well-being of pastoralists and their animals in the Ethiopian Somali Regional State (ESRS) in an integrative manner. This year has focused on operational baseline research in human and animal health but also on staff and laboratory capacity building at Jigjiga University that will serve the ESRS community in terms of diagnostics, training of community health workers and outreach as well as serving the reference hospital in Jigjiga. The research topics are in line with the priorities of the local and federal health governments and with the priorities from the communities themselves. ESRS lags behind the national statistics on most health indicators. Furthermore, there is a lack of diagnostic and therapeutic facilities in the region. Baseline information on zoonotic diseases is unknown. Many of these remote communities are not reached by the current animal and public health system in place. All research conducted will ultimately help assessing baseline status of diseases in animals and people in these communities, assessing the gaps and barriers to health service deliveries, including maternal health and provide evidence based research for a future sustainable integrated health service that can efficiently reach these mobile communities in ESRS, which will improve the prevention for instance of zoonotic diseases. The system once piloted could at a later stage be expanded cross-border.

Research conducted and or initiated this year in JOHI included the areas of nutrition, mother and child health, zoonotic diseases at the livestock-human interface, rangeland and soil management, water-born zoonosis, camel marketing and livelihood, TB care among pastoralists, and animal and human drug marketing in ESRS.
These studies are conducted in an innovative integrative way. More specifically, we assessed the micronutritional status of pastoral children (Iron, Zinc, Vitamin A), their endoparasitic burden and the analysis and impact of their gut flora on stunting. In the same households, we assessed the health behavior of mothers and their male partners and whether they seek health facilities for maternal health care in order to investigate also gaps and barriers for service utilization, we assessed among others the prevalence of brucellosis, Q-fever and Rift Valley Fever in livestock and people, we assessed the livestock herd dynamics and land use of pastoralists as well as soil quality, and we started mapping the market routes for camels.

Bovine tuberculosis (BTB) is an endemic zoonotic disease in Ethiopian cattle and is found with high prevalence in the dairy farm system in urban and peri-urban Ethiopia. Within the Ethicobots project, we are assessing the economic impact of BTB in the Ethiopian dairy sector and its impact on livelihood. Furthermore, we will assess the most cost-efficient control strategy for the country. A test-and-slaughter program including a monetary compensation for farmer for the loss of their animals as conducted in industrialized countries is not feasible in Ethiopia for economic and logistic reasons. Hence, cheaper control alternatives that are also accepted by the communities have to be found. Milk production and milk quality is a key piece of this work. BTB, besides its zoonotic potential, is known to reduce animal productivity. However, other conditions can reduce productivity as well. We therefore linked two further studies to it. We looked at the fodder quality and quantity given to dairy cattle in order to assess its impact on animal productivity and we are currently assessing mastitis prevalence in dairy cattle and do bacteriology analysis of the positive milk, focusing mainly on salmonella, streptococcus spp, staphylococcus spp, and listeria, which are important food-borne zoonosis.

Reaching beyond the science per se, the One-Health group is involved in elaborating and delivering a new One-Health curriculum for post-graduate studies together with the Federal Ministry of Education. It has been involved in the discussions on the creation of the National One Health Platform (NOHP), which declaration has been drafted and awaits ratification and is continuously expanding its One-Health network and collaboration within Ethiopia and internationally in research and education.

**Project and research studies descriptions**

1. **JOHI**

The Jigjiga One Health Initiative (JOHI) is a 12 year One Health research and development program (2015-2027) in the Ethiopian Somali Regional State (ESRS), funded by the Swiss Government, in partnership with Swiss TPH, AHRI and Jigjiga University. The project is built on 3 pillars, namely capacity building in One Health (staff and lab), operational research in One Health and health service delivery. The ultimate goal is to provide an integrated human-animal health service to reach remote pastoral communities, to improve diagnostic capacity for infectious diseases, in particular zoonotic diseases and their prevention and to improve the well-being of pastoral people and their animals.

1. **Intestinal Parasitic Infections and their Relation to Nutritional Status of Less than Five Years children, Adadleworeda Somali region, Ethiopia**

   **Students:** Khadra Ali (MSc, nutritionist) and Nathalie Guttman (MSc)

**Background:** Child undernutrition in Ethiopia is one of the highest in Africa. It ranks 6th in the world in terms
of under-5 mortality rate (Berhe and Berhane 2014). Previous studies in Ethiopia have shown that 50% of the children are malnourished and 56% of these children are infected by intestinal parasites (Worku et al 2009). The situation in ESRS is not well known.

**Objectives**: This study is assessing the prevalence and spectrum of intestinal parasites and gut microbiota in children under 5 years and its relationship to nutritional and micro-nutrient status (iron, zinc, vitamin A) and child stunting.

**Methods**: 500 children had blood and stool samples taken, coupled with anthropometry and interviews. Haemoglobin is analyzed using a commercial HaemoCue, iron and vitamin A by sandwich ELISA and zinc by absorption spectrometer. Stool samples are kept in SAF for Kato Katz analysis and dry feces is used for microbiota analysis.

**Results**: study on-going. Preliminary results show that 36% of the stool contained intestinal parasites with Giardia spp being the most frequently isolated one (17%), followed by Ascaris spp (7%), and to lesser extend Entamoeba spp, Hymenolepis spp, Entorobius spp, Taenia spp, Hookworms, Trichuris spp.

2. **Community based maternal health care service utilization and associated factors in Adadleworeda Somali regional state, Ethiopia**  
**Student: Abdurezak Adem (MSc), wid-wife**

**Background**: Approximately 23% of all deaths in Somali Region are linked to childbirth. In ESRS only 10% of women give birth with skilled birth attendant compared to the national average of 15%. Health seeking behavior of mobile pastoral women is based on individual beliefs, values and perceptions. A study conducted in Afar region in Ethiopia shows that around 90% of mothers did not seek helps unless the situation became life threatening. Male involvement in reproductive health has recently been promoted as a promising new strategy to improve maternal and child health.

**Objectives**: The study aims at assessing the maternal health seeking behavior and the importance of male partner involvement in all aspect of maternal health. It will assess the current gaps and barriers in access to maternal health care and set the premises for a long term follow up study of maternal and reproductive health.

**Methods**: Women who gave birth the last three years and their partners are interviewed (N=442). Focus Group Discussions (N=4) are being held in the communities.

**Results**: study on-going

3. **Public health and economic importance of camel diseases with the emphasis on zoonoses including brucellosis, RVF and Q-fever in Ethiopia Somali region**  
**Student: Mohammed Ibrahim (PhD), veterinarian**

**Background**: Zoonotic diseases in ESRS are not well studied and prevalences of most important diseases are not known. Pastoralists are living in close contact with their livestock and their daily livelihood depends
upon them.

**Objectives:** the study investigates the prevalence and community awareness of brucellosis, RVF and Q-fever in people and livestock in ESRS. It will determine the most important diseases that impact on camel production and marketing and will recommend cost-effective strategies to add value on the camel market chain in the region.

**Method:** 905 animal blood samples and 191 human samples have been collected. Serology will be done using commercial ELISA kits. In addition interviews have been performed.

**Results:** study on-going

### 4. Ecology and economy of rangeland and livestock population dynamics in Eastern Ethiopia: The case of the AdadleWoreda (Ethiopian Somali Regional State)

**Student:** Seid Mohammed Ali (PhD), ecologist

**Background:** Due to frequent draught and rangeland degradation, livestock productivity declined, pastoralists impoverished and pushed to increasingly depend on donors handouts. Overstocking by pastoral communities was reported to be one of the causes of rangeland degradation in Ethiopia. One of the challenges of rangeland development in Ethiopia is the lack of adequate information about rangeland resources and their dynamics. Knowledge of the current status of rangeland and livestock resources is indispensable for any pastoral development intervention in Somali region.

**Objectives:** The study explores the interaction between rangeland condition status and soil nutrient dynamics at different spatial scales (plot and landscape scales) and grazing use intensities as well as the traditional ecological knowledge of pastoralists. It will document the major land use/cover changes and the livestock population dynamics in the last 25 years and estimate the current adaptation to available feed resources and its profitability.

**Methods:** 436 soil samples were collected and 450 households interviewed for livestock population data. Focus group discussions were performed in the communities.

**Results:** study on-going

### 5. Delay in diagnosis of pulmonary tuberculosis and its association with infectiousness of adult patients in selected hospitals of ESRS

**Student:** associated PhD from Haremaya, FentabilGetnet

**Background:** Delayed TB diagnosis and care may lead to severe illness and death among patients, and increase disease transmission to close contacts. However, the general essence of delay in diagnosis and the extent to which it affects patient infectiousness that drive TB transmission in the community has not been well studied in Ethiopia and particularly in the pastoral communities of ESRS. Therefore, assessment of time delays in diagnosis and its effect on infectiousness of patients is crucial to monitor and evaluate the
effectiveness of tuberculosis control programs in controlling the disease and preventing the transmission.

**Objectives:** The study aims to determine the extent and reason of diagnostic and treatment delay in patients with pulmonary tuberculosis. It will explore disease awareness and the challenges of the health system in TB service provision to mobile pastoralist communities.

**Methods:** Pastoralists being treated for TB in health facilities will be interviewed and sputum samples collected. The samples will be re-assessed at AHRI to evaluate the quality of the smear readings in facilities in ESRS.

**Results:** field data collection pending

### II. ETHICOBOTS

The Ethicobots project is a 5 year project funded by the British Government which aims at assessing possible control programs for BTB in the dairy sector in Ethiopia. It is composed of 6 work packages distributed throughout 4 national and 3 international institutes. It will assess for instance, disease prevalence, risk factors, animal vaccine trials, and socio-economic factors. The One Health group is in charge of WP6 of the project. The study sites will include existing and emerging dairy hubs, such as greater Addis Ababa, Mekele, Hawassa and Gonder/Bahar Dar.

1. **Impact of BTB on dairy animal productivity**

**Background:** Few and out of date data from the literature show a negative economic impact of BTB on cattle productivity. However, hard data is lacking for the African setting at large.

**Objectives:** the study will assess the baseline productivity and herd structure/dynamic in intensive dairy farms as a pre-requisite for further economical modelling on the impact of BTB on the dairy sector.

**Method:** 26 intensive dairy farms (1300 animals) in and around Addis Ababa are being followed every month for a period of 3 years and data on productivity (fertility, milk, morbidity, mortality) as well as herd dynamics collected. Animals will be followed at abattoirs, carcass weight recorded and linked with the BTB status. Data will be included in an economic model.

**Results:** study on-going

2. **Analysis of Competitiveness of dairy sector and Impact of BTB on economic performances of commercial dairy farms in Ethiopia**

**Student:** Tadele Mamo, PhD (Haremaya)

**Background:** cf overall project.

**Objectives:** The study will assess the economic efficiency and competitiveness of commercial dairy farms. It will also investigate the situation of pasteurization in the country (e.g. quantity, quality, challenges), and the macro-economics of pasteurization and milk trade.

**Methods:** information will be collected through interviews and questionnaires.

**Results:** study on-going
3. **Assessment of cost-effective control strategies for BTB**

**Background:** Test-and slaughter control programs are not feasible in Ethiopia as too costly. Alternative cost-efficient and accepted control programs have to be assessed.

**Objective/Method:** Incorporation of all economic data collected by the other WPs of the project and running of mathematical and economic models.

**Results:** study on-going

### III. OTHERS

1. **Fodder situation in selected intensive dairy farms in Addis Ababa and its possible impact on animal productivity.**

Collaboration was started with the School of Agriculture, Forest and Food Science (HAFL) of Zollikofen, Switzerland. Solomon Araya did his bachelor thesis with our group, investigating the impact of nutrition in dairy cattle on productivity. He looked at the quantity and quality of fodder as well as economic aspects in 30 dairy farms in and around Addis Ababa by means of questionnaires. His results will be fed into the productivity study of ETHICOBOTS.

2. **Prevalence of mastitis and qualitative milk assessment in dairy farms in Addis Ababa**

**Background:** Cattle productivity can be severely reduced by mastitis. Sub-clinical mastitis doesn’t show any visible signs at the udder and goes undiagnosed, also posing a health threat to consumers.

**Objectives:** The study will assess the prevalence of mastitis (clinical and sub-clinical) in intensive dairy farms linked with the Ethicobots project and assess the spectrum of bacteria in the milk.

**Methods:** All milking cows in 30 dairy farms are screened for mastitis with the CMT test. Milk from CMT positive animals is collected for further bacteriological analysis at AHRI.

**Results:** study on-going. Preliminary results of 110 cows showed that mastitis prevalence was 60% with a high prevalence of Staphylococcus aureus, and Streptococcus spp; furthermore agents like Listeria spp and Salmonella spp have been identified.

3. **TB in non-human primates**

This is an on-going study over many years where we investigate the prevalence of tuberculosis in non-human primates kept as pets. This year no serology could be performed due to the Primagam test not being produced anymore. However we did several post-mortem on non-human primates and tissue culture. One Baboon showed multiple granulomas on the intestines as well as liver. The culture was TB negative. The animal had died of severe oesophagostomiasis, which is a parasitic zoonosis. The case report was published.
Steering committee JOHI in Jigjiga

Child stunting, nutritional status and parasitic burden in women and children in Adadleworeda
Serum extraction in the field (Adadleworeda) with custom made “hood” to avoid contamination with dust

Discussion with local leaders and health authority people in AdadleWoreda

Laboratory Management Center

Overview
AHRI Laboratory Management Center is structured under the Research and Innovative Directorate. The Center was established in order to organize and lead the overall activities and manage the laboratory infrastructure. To achieve its mission, the center is organized into three case teams: Research Laboratory, Biosafety and Biosecurity and Laboratory Engineering. The Research Laboratory Case Team comprises of seven research laboratories namely clinical trial, P3 Tuberculosis, Immunology, Molecular Biology, Bacteriology, Pathology and Parasitology Laboratories. These laboratories are equipped with high tech biomedical equipment. All seven laboratories have their own coordinator and the whole process is led by a Laboratory Manager. In addition to the listed laboratories, a new TB laboratory was constructed by partners to increase TB Laboratory capacity and to make AHRI a center of Excellence in TB research. To increase research capacity in emerging viral diseases the center is planning to establish a Virology Laboratory. The Laboratory Engineering Case Team is primarily responsible for handling preventive and curative maintenance, and calibration of the biomedical equipment. The Safety and Logistic Case Team is recently established as an additional case team in order to facilitate management of the biosafety and biosecurity issues of the Institute and to be able to efficiently provide common use laboratory consumables and reagents to the researchers.

The Scope of Laboratory Management Center
- Plan, organize, direct and coordinate laboratory operation
- Avail reagents, laboratory equipments and manpower to effectively support execution of research projects and ensure their economic use.
- Ensure the proper function and timely maintenance of the laboratory equipment
- Develop and update standard laboratory operating policies and procedures
- Provide technical support for researcher and orientation for students
- Organize and provide laboratory training
- Ensure biosafety by applying knowledge, techniques and equipment to prevent personal, laboratory and environmental exposure to potentially infectious agents or biohazards
- Develop, implement and report results of biomedical and clinical laboratory research;
- Promote awareness and understanding of the use of the research laboratory

Major Activities
As one of its strategic objectives, the Laboratory Management Center provides training and apprenticeship opportunities on a regular basis for postgraduate and undergraduate students coming from universities nationwide. The following Table summarizes the numbers of students and their backgrounds who attended their apprenticeshipprogram and used the lab facilities from different Universities in 2016.
The Laboratory Management Center also provides laboratory visit sessions for visitors from various universities to share AHRI experience in biomedical research. The visiting candidates are registered at their host universities in various disciplines of biomedical and health related biotechnology.

The graph below illustrates the numbers of visiting candidates and their universities in 2016.

Currently, various research activities are underway in these laboratories including research on externally funded grants, AHRI core funded student MSc and PhD student thesis research, and individual staff scientists’ research. In general, the lab team is continuously evolving to meet the challenges emanating from the increasing scope and numbers of projects, requested services and expected standards.

1. Laboratory Service

In addition to the research activity, the Laboratory Management Center provides pathology diagnostic service, primarily for the adjoining ALERT hospital. In the previous year, 1262 patient samples were evaluated in the pathology laboratory. The diagnostic service includes standard Histopathology examinations, such as with standard H&E staining and other special stainings, and collection and analysis of fine needle aspiration...
specimens. The Pathology Laboratory provides free service to all Leprosy patients and the patients declared poor by ALERT Hospital system.

2. Capacity Building, recently procured lab equipment

a. Pathology Laboratory
   - Fully Enclosed Tissue Processor (Leica)
   - Microtome (Leica)
   - Cryostat (Leica)
   - Tissue Embedding System (Leica)
   - Eppendorf Centrifuge
   - Heating Incubator

b. Immunology Laboratory
   - Bench Top Refrigerated centrifuge
   - Water Bath

c. Molecular Biology Laboratory
   - Sensitive Weight Balance
3. Networking and Trainings

Members of the Laboratory Management Center participated in several international and national workshops and training courses. This contributed to capacity building of the staff as well as improvement in quality of work done at AHRI. The following two are among the activities members were engaged in.

Melaku Tilahun and Biruk Yeshitila (Nairobi, Kenya, August 29 – September 2, 2016)

**Purpose:** Bio Risk Management Trainer Development Workshop

**Summary:** The workshop was organized by One Health Central and East Africa in collaboration with Sandia National Laboratories, USA, with the goal of capacity building for current employees with interest and appropriate background and who have been nominated by their management to become a biorisk management trainer and be a resource to their management on training needs.

Melaku Tilahun, Sosina Ayalew, Marechign Yimer, Sofia Yimam, Dawit Kebede, Wakoya Chali, Adugna Tsehay & Fikadu Zenebe (AHRI, August 1-5, 2016)

**Purpose:** In-house training on “Laboratory and Clinical Quality Management”

**Summary:** The training outlined the quality standards that are relevant to the institute's function as a clinical research institute, i.e. quality standards in laboratory and clinical trial activities. As expected the course addressed the theoretical basis and application tools of quality management standards that are relevant to the institute’s mission.
Members of Laboratory Management Center

Wash and Sterilization Room staff

Research Nurse
Development and Administration

Training

Capacity building and human resource development, particularly in the field of biomedical research is among key missions of AHRI. To this end, AHRI has been engaged in postgraduate biomedical research training for over ten years. In 2016, AHRI continued to run different programs of capacity building and human resource development by hosting students from several national universities and providing co-supervision and research support in collaboration with other partners. Postgraduate students are funded by AHRI’s core budget or by specific grants obtained for student support. A brief description of the different programs follows:

Emory-Ethiopia TB Research Training (EETBRT) is a 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. Detailed information on this program and its activities can be found in the Partnership, Planning, and Project Management section.

Biomedical Sciences Postgraduate Training Program (BSPP) is a biomedicine training partnership between AHRI, AAU and various Swedish Universities. AHRI initiated this partnership with the objective of mitigating possible quality compromises associated with the rapid expansion postgraduate training programs in the country and is funded by Sida. This program is currently supporting 10 PhD students and recruited additional three new PhD students this year.

Brighton-Sussex Global Health Centre has a postgraduate training 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.

FMoH-AHRI clinical research collaboration is a postgraduate training program in the areas of maternal and child health, hepatitis B virus, arbovirus infection, and antimicrobial susceptibility profiling. The program is supported by FMoH and AHRI and conducted in partnership with local PIs at AAU, University of Gondar, University of Jimma, Hawassa and Haromaya Universities. This collaborative program aimed at bridging biomedical and clinical disciplines while strengthening institutions capacity in the regions involved. Twenty one students, 2 PhD and 18 MSc, are involved in this collaboration. One MSc student has successfully defended his thesis this year.

AHRI-Haromaya University joint PhD program is a postgraduate program where trainees are registered at Haromaya University and receive a joint supervision. Currently 3 PhD students are enrolled in this program but the model has a potential to expand to other partner universities.

In summary, AHRI has been hosting 83 postgraduate biomedical trainees through the different training programs and its core budget support out of which 55% of the trainees were working for their PhD dissertation. From the 46 PhD level trainees, five have successfully defended their dissertation in 2016. Of the remaining
PhD students, 26 are ongoing and 15 are new. Four PhD trainees have dropped for different reasons. Likewise, six MSc students have defended their thesis leaving 24 ongoing and six new students working towards their master degrees.

**Short term training**

Short term trainings at AHRI were organized by/or in collaboration with the different directorates/offices. The following is a brief description of the trainings conducted in 2016.

- Advanced Research Ethics training- January 2016, AHRI
- Basic Research Ethics training - September 28-20, 2016, AHRI
- Clinical Trial Design and Data Analysis using SAS - October 3-10, 2016, AHRI
- Data management and analysis with R statistical software and refreshment training on EDC system (OpenClinica and RedCap) - AHRI

**List of Postgraduate Students**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name</th>
<th>Title</th>
<th>Program</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidist bobosha</td>
<td>Evaluation of M. leprae unique antigens for early detection of leprosy and cytokine profile of reactional patients</td>
<td>PhD</td>
<td>Defended</td>
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<td>2</td>
<td>Daniel Taye</td>
<td>Critical Analysis of Leprosy Discriminatory Discourse and the Underpinning Social Constructs</td>
<td>PhD</td>
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<td>3</td>
<td>Edesa Negera</td>
<td>The immunopathology of erythema nodosumleprosum</td>
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<td>Martha Zewdie</td>
<td>Analysis of immune responses and regulatory T cells in tuberculosis</td>
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<td>Defended</td>
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<td>Wubayehu Kahaliw</td>
<td>Activity test, isolation and chemical structure elucidation of anti-tuberculosis constituents from plants used in traditional medicine in Ethiopia</td>
<td>PhD</td>
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<tr>
<td>6</td>
<td>Mikias Negash</td>
<td>The role of γδ T cells heterogeneity in HIV-TB mono or dual infected patients in Addis Ababa, Ethiopia</td>
<td>MSc</td>
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<td>Tihitina Nega</td>
<td>Immunological and lipid profile among leprosy spectrum</td>
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<td>8</td>
<td>Selfu Girma</td>
<td>Comparison of Auramine O, Modified Fite-Faraco and Acid Fast Staining Techniques for the Diagnosis of Leprosy and Molecular Analyses of M.leprae</td>
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<td>Sebsib Neway</td>
<td>The biting preference of the Ethiopian mosquitoes within households among the family members.</td>
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<td>Metasebia Tegegn</td>
<td>Diagnostic Utility of Immunophenotyping by Flow Cytometry for Diagnosis and Classification of Acute Leukemias in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.</td>
<td>MSc</td>
<td>Defended</td>
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<td>11</td>
<td>Daniel Demissie</td>
<td>Prevalence, drug susceptibility pattern and associated factors of septicemia among women attending delivery in Dire Dawa, Eastern Ethiopia</td>
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<tr>
<td>#</td>
<td>Name</td>
<td>Title</td>
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<td>Status</td>
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<tr>
<td>12</td>
<td>Tsehaynesh Lema</td>
<td>Detection of new leprosy cases and tracing of household contacts at risk of developing leprosy by active case detection and assessment outcome of treatment in Kokosa Woreda, West Arsi zone, Oromia region: Clinical, molecular and immunological approach</td>
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<td>Makka Adam Ali</td>
<td>Role of EBV in Hodgkins Lymphoma</td>
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<td>New</td>
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<td>Mahlet Lemma Degefu</td>
<td>Impact of pediatric HIV infection on pneumococcal vaccination.</td>
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<td>New</td>
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<td>Tsegaye Sewenet</td>
<td>Molecular characteristics and Epidemiology of Extended Spectrum β-Lactamase (ESBL) producing gram negative bacteria (Enterobacteriacea and Non-fermentative) among human and animals at Jimma, Ethiopia</td>
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<td>Yared Hailaye</td>
<td>Molecular characterization of microbial isolates from Injera and ersho: Evaluation of the role of ersho and injera on diarrheal diseases and formulation of defined starter cultures for improved injera</td>
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<td>Ongoing</td>
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<td>Tsehayneh Kelemu</td>
<td>The impact of immune dysfunction and TB on adverse events during pregnancy</td>
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<td>Ongoing</td>
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<td>18</td>
<td>Endale Hadgua</td>
<td>Molecular and Genetic Characterization of Triple Negative Breast Cancer (TNBC) among Ethiopian Women</td>
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<td>19</td>
<td>Nigatu Tuasha</td>
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### Research Projects in Ongoing Phase

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**In 2016, Kidist Bobosha, Martha Zewdie, Wubayehu Khaliw, Daniel Taye, and Edesa Negera defended their PhD theses and Mikias Negash, Tihitina Nega, Selfu Girma, Sebsib Neway, Metasebia Tegegn, Daniel Demissie defended their MSc theses.**

**Congratulations to ALL!!!**
**Partnership, Planning and Grant Management**

**AHRI Projects monitoring activities**
The project management unit has been responsible for monitoring major projects at AHRI. This year, we managed to perform the monitoring activity for one of the quarters. In the new restructuring of AHRI, the Partnership, Policy and Grants Directorate will be responsible for project monitoring and evaluation. Currently, the Directorate is under establishment and will start functioning in early 2017.

**Norad and Sida Joint 2015 AHRI Annual Progress review Meeting**
The joint Sida-Norad AHRI annual review meeting was held on May 12, 2016 at AHRI in presence of official delegates from Sida and Norad. During the review meeting, detailed reports on research, training, financial and networking activities of 2015 were presented by Dr. Abraham Aseffa and Mr. Anteneh Getahun. The new legislation on AHRI, its expanded mandates and required restructuring were discussed. The Sida and Norad delegates appreciated the progresses made in all aspects, especially on the financial reporting. They raised several issues which were thoroughly discussed. Among the major issues was the concern on unforeseen challenges which might be faced in the near future from the high expectations of the Ethiopian government, recruitment of MSc and PhD students (too few girls!), staff turnover, brain drain, gender, financial support for big lab equipment. At the end of the meeting, the 2015 annual report was officially approved and consensus reached on several points.

**Experience sharing and capacity building for program coordinators in Sida’s bilateral research Coordination programs**
**Dr. Abraham Aseffa, Dr. Brook Lema and Dr. Kidist Bobosha**
*June 13-16, 2016, Sida Headquarters, Stockholm*

The workshop was organized by Sida aiming at experience sharing among program coordinators from Tanzania, Uganda, Rwanda, Ethiopia, Mozambique, Cambodia and Bolivia.

Our Ethiopian colleague, Prof Brook Lema from Addis Ababa University shared the experience on how they were able to expand their PhD programs and the University’s capacity to accommodate high number of PhD students using the Sida block fund which is a very successful experience. Dr. Abraham Aseffa also shared the successful experience of AHRI in communication and diffusion of results. Similarly, other program coordinators shared their best experiences of their Sida supported programs.

Other topics like gender in Science, quality assurance systems, result based management were also discussed in detail as they are very basic issues for institutes dealing with training and research and also as elements of the SDG. Similarly, thorough discussion on Good Financial Grant Practice (GFGP) and Innovation were conducted.
Ethiopia-Emory TB Research Training Program (EETB-RTP)

The Ethiopia-Emory TB Research Training Program (EETB-RTP) represents a partnership between Emory University in Atlanta (USA) and three Ethiopian institutions in Addis Ababa including AHRI, AAU, and the Ethiopian Public Health Institute (EPHI), a national public health institution that is part of the Ethiopian Federal Ministry of Health. The EETB-RTP is focused on providing didactic and mentored TB research training for promising Ethiopian investigators; the goal is to provide either short or long term training for MSc, PhD, post-doctoral trainees, clinicians and their institutions with the skills and capacity to carry out internationally relevant TB-related research (e.g., clinical and/or translational research, epidemiologic research, implementation science/operational research, behavioral/social sciences research, and laboratory based research). The EETB-RTP is funded by a Global Infectious Diseases grant from the U.S. National Institutes of Health (NIH) Fogarty International Centre. The main educational mechanism is high quality, semester long distance learning courses delivered by faculty at Emory University (Atlanta, USA) via real-time web-based video conferencing as well as through intensive short courses carried out in Ethiopia. This includes mentorship training, Biostatistics, grant writing.

In 2016, The EETB-RTP awarded 6 PhD students and 3 Mid-career researchers (post-docs) from Addis Ababa University, Armauer Hansen Research Institute and Ethiopian Public Health Institute with a fund for research and training which will last for 2 years. This is a second round award from EETB-RTP. In the first round support, 5 PhD students and one postdoctoral researcher were awarded. During the 2 years training period, trainees will get trained on Biostatistics and data management and scientific grant writing live courses. The trainees will also have the opportunity to get the expertise of potential mentors in US to support their research path in close collaboration with the mentors at their home institutes in Ethiopia.
The Ethiopia Emory TB research Training program second annual conference was held at Hawassa city in Ethiopia from June 29 to July 01 2016. Thirty five participants that include program PIs and coordinators, senior local and US mentors, the first and second round trainees attended the conference. All trainees presented their progress. Senior mentors also gave presentations on TB immunology, on how to publish, mentorship, and research ethics.
Information Tecnology and Communication

(Hilina Abraham)

AHRI is in the beginning of establishing Information and Communication Technology team.

Mission - AHRI’s ICT team mission is to provide nimble, effective, efficient, and collaborative ICT services, solutions and strategies in a timely and helpful manner that assists the institute in achieving its strategic goals.

The Information and communication Technology team has been supporting researchers, students and supporting staffs of the institute with internet connectivity, information dissemination through the website, printer sharing, networking and maintenance.

Network and Infrastructure

ICT is in its footsteps to have data center, file sharing, and enhanced network infrastructure that will make the institute use up to date technologies.

For this reason AHRI signed a contract with Ethiopian Information Network Security Agency (INSA) for

- Installation and Configuration of new servers
- Expansion of internet lines
- Intra and Inter networking
- Establishing Data Center and File sharing methodology

Website

Currently, AHRI has a website; https://ahri.gov.et. The website is used as a method of external communication and for tracking what’s happening in AHRI.
Training sessions

- **Microsoft Windows Server 2012**
  - 20410 - Installing and Configuring Windows Server 2012
  - 20411 - Administering Windows Server 2012
  - 20412 - Configuring Advanced Windows Server 2012 Services

- **Microsoft Exchange Server 2013**
  - 20341 - Core Solutions of Microsoft® Exchange Server 2013
  - 20342 - Advanced Solutions of Microsoft® Exchange Server 2013

Data management and Biostatistics

Since 2003, the data management/biostatistics unit is operating as a formal unit with proper back-up of the unit’s data, archiving, dedicated persons, and proper filing and documentation system according to acceptable practices for both general and clinical trials data management procedures.

Data management/ Biostatistics team have been working tirelessly to establish good practices and implement high quality procedures for questionnaire or CRF and database design, double data entry with good verification and validation, data analysis, output interpretation, good back-up, filing and archiving system all of which have greatly enhanced the security and confidentiality of the unit’s and collaborator’s data.

Mission and Goal

1. The mission of the Data Management/ Biostatistics Case Team is to contribute to quality data management and statistical analysis for researchers and students.
2. The goal is to provide close to 100% satisfaction for health researchers / students by providing quality data and for use in reports to help policy makers.
3. Prepare a centralized database to maximize security and quality of data; enable efficient data capture, filing and archiving. Also prepare and update Data Management SOPs
4. Identify and build capacity for Data Management/ Biostatistics and other staff who need training

Data Management and Biostatistics Team Photo

In 2016, the data management unit was engaged in and has worked on several student and collaborative projects in questionnaire or CRF development, database structure design, double data entry, data cleaning,
verification, and data analysis. The softwares and applications used for the various projects varied depending on the project. These projects included STREAM Stage 1 and Stage 2, ETHICOBOTS, Arboviruses Study, Leishmaniasis projects, LED project, SETA Rapid Pilot Surveillance Study, Task-Sharing for the Care of people with Severe Mental Disorder in a low-income country (TaSCS), and several MSc and PhD projects.

The unit has also been active in other activities including:

- Establishment of a system for Documentation of Databases in 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.
- Administration of the Off-site back-up system as well as an archiving system which we have already put in place.

**Training (capacity building)**

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

**Data management and analysis with R statistical software and refreshment training on EDC system (OpenClinica and RedCap) given to all Data Management Team**

*By Samuel Ayele and Tsegaye Hailu*

**Purpose:** The objective of the refreshment training is to develop/update the skills (OpenClinica and RedCap) database and statistical software R of staff working in AHRI Data Management, Biostatistics units and Student/Research staff.

**Modern Tools for NTD (GIS) given to Tsegaye Hailu by FMOH in collaboration with London School of Hygiene and Tropical Medicine**

**Purpose:** Epidemiology and mapping tools designed to assist in the design, implementation and evaluation of targeted and cost effective NTD control activity

**Clinical Trial design and analysis using SAS**

*Given to Samuel Ayele, Tigist Beyene and Tsegaye Hailu*

*By Addis Ababa University Statistics Department*

**Purpose:** To fill skill gaps and provide knowledge on clinical trial design and data analysis
Clinical Trial design and analysis using SAS training participant group photo

Finance and Procurement

The Institute core support in 2016 came from Sida and Norad. In 2016, for the first time, we also secured core budget from government: ETB 13,950,000.00 for recurrent budget and ETB 20,000,000.00 capital budget for the design of a new laboratory complex which together total to around USD1.5Million.
Other Project Grant

Project grants which were secured from different international organizations included:

1. ETHICOCOBOTS:- Department of Veterinary Medicine, Cambridge University five years grant from 2014 to 2018
2. Stream Stage II: extension of Stream Stage I from International Union against Tuber Clause and Lung Disease, donor USAID sub grantee to AHRI, five years grant from 2014 to 2019.
3. Screen TB: EDCTP grant from European Union 5 years grant from 2014 to 2018
4. MOH: Minister of Healthy support for clinical trial USD 500,000.00 and also MOH has signed an agreement with AHRI for grand challenge activities 1Million USD.
5. Emory University, NIPH influenza, One-health, Ministry of Science and technology project grants, Podoconiosis grant are other projects managed by the AHRI Finance Team in 2016.

Sida new agreement

In May 2016, Sida and AHRI signed a new five years agreement for the amount of SEK 49,996,906.00 granted to AHRI to support the core activities of the Institute and student support (July 2016-June 2021). AHRI received the first installment of SEK 7 Million in May 2016. The Institute has spent 35% of grant by December 2016.

Norad Support

The other core support of AHRI comes from Norad. The current agreement runs from 2014 through to June 2017 and carries a total sum of NOK 21 Million.

Procurement of Laboratory Equipment and other fixed asset

AHRI has recently (most of the final process falling into 2016) procured laboratory equipment worth around USD 1.4 Million (Norad and Sida grants for equipment) through the UNOPS procurement system. The Institute also purchased seven vehicles with Norad support, and procured a big laundry machine.

Training

Norad had allocated budget in its core support to AHRI to improve the financial performance of the Institute. Thus, the following are the title of the training courses organized locally and abroad for the finance and procurement section employees.

- EDCTP/ European and Development Countries financial management.
- Donors Rules and Regulations/Grant Financial Management/.
- Government Financial Management and IBEX Software.
- International Procurement, Custom Clearing and Logistics Process.
Financial Management Software

The other accomplishment of the Finance Team in 2016 was installing a new financial management software for the Institute. Previously, the Team had relied on Peachtree Software for its financial transaction and reporting purposes. As per government requirements, in adherence to the regulations of the Ministry of Finance and Economic Development (MOFED), the software called "Integrated Budget and Expenditure Software (IBEX)" is now installed and is being used for the government financial transaction and reporting purpose.

Financial Audit

The independent audit report of the financial accounts of AHRI submitted by the Chartered Certified Accountants (UK) Kokeb and Melkamu for the year ended Dec 31 2015 is presented below.
### Financial Statement and Audit Report (December 31, 2015)

**ARMAUER HANSEN RESEARCH INSTITUTE (AHRI)**
**BALANCE SHEET AS AT DECEMBER 2015**

**Currency: Ethiopian Birr**

<table>
<thead>
<tr>
<th><strong>ASSETS</strong></th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CURRENT ASSETS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash &amp; Bank balances</td>
<td>71,373,205.25</td>
<td>101,854,752.45</td>
</tr>
<tr>
<td>Debtors &amp; prepayments</td>
<td>12,664,274.21</td>
<td>10,892,974.26</td>
</tr>
<tr>
<td></td>
<td>84,037,479.46</td>
<td>112,747,726.71</td>
</tr>
<tr>
<td><strong>CURRENT LIABILITIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creditors &amp; Accruals</td>
<td>1,632,115.43</td>
<td>1,124,749.69</td>
</tr>
<tr>
<td><strong>FUNDS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General fund</td>
<td>10,851,403.89</td>
<td>10,453,313.41</td>
</tr>
<tr>
<td>Other Project Balance</td>
<td>14,597,601.96</td>
<td>15,801,182.37</td>
</tr>
<tr>
<td>SIDA and NORAD Balance</td>
<td>56,956,358.18</td>
<td>85,368,481.24</td>
</tr>
<tr>
<td></td>
<td>82,405,364.03</td>
<td>111,622,977.02</td>
</tr>
<tr>
<td>Total liabilities and Fund Balances</td>
<td>84,037,479.46</td>
<td>112,747,726.71</td>
</tr>
</tbody>
</table>
### ARMAUER HANSEN RESEARCH INSTITUTE (AHRI)

**STATEMENT OF INCOME AND EXPENDITURE**

FOR THE YEAR ENDED 31 DECEMBER 2015

<table>
<thead>
<tr>
<th>Recognized Income</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIDA core fund</td>
<td>12,235,723.27</td>
<td>17,551,728.44</td>
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<tr>
<td>NORAD fund</td>
<td>12,235,723.50</td>
<td>189,143.88</td>
</tr>
<tr>
<td>SIDA students fund</td>
<td>-</td>
<td>799,581.80</td>
</tr>
<tr>
<td>SIDA equipment fund</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Government contribution</td>
<td>8</td>
<td>751,002.61</td>
</tr>
<tr>
<td>Other projects funds</td>
<td>9</td>
<td>14,942,854.96</td>
</tr>
<tr>
<td>Other income</td>
<td>228,556.70</td>
<td>1,817,236.40</td>
</tr>
<tr>
<td>Exchange rate gain / loss</td>
<td>119.20</td>
<td>944.67</td>
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<tr>
<td><strong>Total receipt</strong></td>
<td><strong>38,965,596.82</strong></td>
<td><strong>35,252,910.96</strong></td>
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<table>
<thead>
<tr>
<th>EXPENDITURES</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management &amp; administration</td>
<td>2,311,126.66</td>
<td>2,591,069.37</td>
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<tr>
<td>Common support</td>
<td>9,979,663.31</td>
<td>12,134,294.09</td>
</tr>
<tr>
<td>Staff house</td>
<td>-</td>
<td>86.25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12,920,789.97</strong></td>
<td><strong>14,725,449.71</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Research units:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>2,246,746.95</td>
<td>2,123,602.09</td>
</tr>
<tr>
<td>Laboratory</td>
<td>-</td>
<td>76,579.76</td>
</tr>
<tr>
<td>Research equipment, Lab, reagents &amp; supplies</td>
<td>9,933,912.00</td>
<td>118,538.53</td>
</tr>
<tr>
<td>African fellowship / students</td>
<td>-</td>
<td>507,558.35</td>
</tr>
<tr>
<td>SIDA Student fund expenditure</td>
<td>783,164.88</td>
<td>189,143.88</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12,963,823.83</strong></td>
<td><strong>3,015,422.61</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other projects expenditures</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td><strong>13,465,885.22</strong></td>
<td><strong>14,942,854.96</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EXCESS OF INCOME OVER EXPENDITURE</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total expenditures</strong></td>
<td><strong>38,720,499.02</strong></td>
<td><strong>32,683,727.28</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FUND BALANCE brought forward</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FUND BALANCE carried forward</strong></td>
<td><strong>10,243,301.06</strong></td>
<td><strong>10,453,313.41</strong></td>
</tr>
</tbody>
</table>
Human Resource Management

Over the course of 2016, Human Resources (HR) Directorate has achieved progress in the areas of strategic workforce planning, talent attraction and retention management, recruitment, learning and development, employee engagement, and overall improved operational efficiencies.

The Directorate of Human Resources (DHR) offers in this report analysis of adopted strategies and results in the context of the Annual Work Plan (AWP), and the Medium Term Strategic Plan and evaluations completed in 2016.

The staff in Human Resources assists applicants and employees with all phases of the employment process. We oversee recruitment, interviewing, testing, background checks, selection and evaluation of administrative HF functions.

**Recruitment**

- Human Resources received and processed 1200 employment applications
- 25 employment advertisements were posted
- 22 positions were filled

As result of new system at AHRI, all non-government employees were assigned the new positions/role title based on their competence, education status, experience and others requirements listed on the guideline. Currently we have 125 employees working at AHRI and the majority (81) are scientific staff and the remaining 44 are support staff. The charts below briefly describes the employees’ educational status, gender matrix and status of contract and permanent employees.
AHRI Contract Staff by educational status:

- PHD: 211
- MSc/MBA: 165
- BSc/BA: 201737
- Diploma: 61723

(Numbers indicate number of male, female, total)

AHRI Government Staff:
- Male
- Female
- Total

Researchers job title and classification:
- Junior: 12
- Researcher: 66
- Assistant Researcher: 97
- Associate I: 51
- Associate II: 31
- Researcher I: 22
Employee engagement, retention and development

One way to engage or retain and develop the capacity of employee is to ‘buy in or built’; that is to recruit the high Caliber workforce and/or to train the existing staff. The institute intends to retain the workforce through initiating and supporting employees with respect to personal development plan. As result of this 14 employees are on the status of receiving financial support to upgrade their skills, knowledge and ability which could help the institute to meet the strategic objectives. Learning strategy is aligned to address current and emerging organizational needs while covering areas of Research Ethics, leadership, program excellence, and core learning at all levels. The base pay of almost all employees is increased as result of new systems. One important thing that works well as system is the application of on boarding as the policy. We do have strong on boarding to engage employee at any level.

Management and governance

In the process to uplift HR from a purely personnel and administrative function to a respected and value-added strategic business partnership, as per the mandate of institute, the organization established DHR. This has allowed for faster decision making and guaranteed flexibility whenever necessary. We can decide on any issue of recruitment, transfer (internal and external), promotion and discipline though these activities, limited to institute so far. Moreover in 2016 we implement the citizen charter which contributes a lot to improve the internal process of our system and enhance customer satisfaction.

Performance management

The performance management system is improved by setting goals and performance standards which are communicated to the employees so that they can be more productive, measured as a process or result. Our performance evaluation has a wholistic approach whereby the evaluation is carried out by the employees themselves (self), by peer and by supervisor. Every employee is evaluated twice a year and the feedback is communicated immediately. After performance evaluation, improvement plan is done so that the supervisor and employee work together to fill the gap. This tool is tied jointly and agreed upon on performance objective and the involvements of different parties for validity and accuracy.

Human Resource Information system

To support the HR function and to increase the efficiency, result and lower cost HRIS is one of the vital tools that has profound and cost impact. In 2016 we moved from hard paper data to more flexible simple software like excel and access to provide employees and managers with access to basic employee information.

AHRI/ALERT Ethics Review Committee

The AHRI/ALERT Ethics Review Committee (AAERC) reviews protocols of research conducted at AHRI or ALERT and/or by AHRI staff/students elsewhere in collaboration with AHRI and ALERT. The Committee has its own standard operating procedures (SOP) that helps it to function optimally with competence and consistency. In addition to the existing SOP, the Committee also developed two new SOPs on reviewing protocols involving biorepository/biobank specimens and social and behavioral studies involving human
In 2016, 37 protocols were submitted, of which 9 were reviewed through expedited procedures, 27 by full board review, and one study was exempted. The topics these covered included: Tuberculosis (6), Bacteriology (7), Leprosy (5), Neglected tropical disease (6), Clinical trials (3), and an additional 10 on various other topics including malaria, breast cancer, and Hepatitis. Nine of these protocols were PhD proposals and 9 were MSc students’ proposals.

The Committee organized and advanced research ethics training for its own members and other stakeholders from the national research ethics review committee (NRERC), Food, Medicine and Health Care Administration and Control Authority (FMHACA), IRB members from Addis Ababa University-College of Health Sciences (AAU-CHS), Haramaya University, Hawassa University, Jimma University, Bahir Dar University, Gondar University and Ethiopian Public Health Institute (EPHI). Prof. Keymanthri Moodley, from Stellenbosch University in S. Africa; Prof. Gail Davey, from Brighton and Sussex Medical School in the UK, and Dr. Adam Gilbertson, from University of North Carolina in USA gave the training on selected topics of research ethics: risk-benefit assessment, vulnerability, reviewing clinical trials, social/behavioral studies and genetic studies and on data sharing/biobanks. The training was conducted at AHRI in February 2016 and all expenses related to the training were fully funded by AHRI core budget.

The AAERC also provided short term training on research ethics for AHRI staff and students, new IRB candidates, and guests from local universities. This training was conducted from September 28-30, 2016 at AHRI.
Grant applications in 2016

1. **Title:** New Rationally Designed Vaccines against Bovine Tuberculosis  
   **Written by:** Adane Mihret  
   **Funder:** International Development Research center  
   **Status:** Rejected

2. **Title:** Development of Lateral Flow Serum Protein Biosignatures Assay for the Diagnosis of Extra pulmonary Tuberculosis  
   **Written by:** Adane Mihret  
   **Funder:** Ethiopian Ministry of Science and Technology  
   **Status:** Pending

3. **Title:** Preparation and evaluation of in house monoclonal antibodies against commercial antibodies for clinical and research use.  
   **Written By:** Markos Abebe  
   **Funder:** Ethiopian Ministry of Science and Technology  
   **Status:** Pending

4. **Title:** Post Exposure Prophylaxis with Single Dose Rifampicin for leprosy contacts while screening for common skin diseases in Nigeria, Ethiopia and Mozambique: an implementation trailChemoprophylaxis for leprosy  
   **Written by:** Erik Post (Royal Tropical Institute, KIT Health) with partners including AHRI (Kidist Bobosha)  
   **Funder:** EDCTP  
   **Status:** Failed after second review

5. **Title:** A cluster randomised trial in Ethiopia to assess the efficacy and safety of a chimeric fusion protein (LepVax), compared to standard Bacillus Calmette-Guérin (BCG Sii) to prevent leprosy and establish its potential to eradicate leprosy  
   **Written by:** Jan Hendrik Richardus (Erasmus University Medical Center) with partners including AHRI (Kidist Bobosha)  
   **Funder:** EDCTP  
   **Status:** Failed

6. **Title:** “Sustainable Food Security-Resilient and resource efficient value chains” on camel dairy technology  
   **Written by:** Rea Tschoppe (project consortium of 14 institutions from countries in the North and the South)  
   **Funder:** EU Horizon 2000 call for 5 million ERU.  
   **Status:** Rejected

7. **Title:** “The role of the gut microbiota in linear growth failure of pastoralist children five years and under in the Adadle woreda, Somali region of Ethiopia”  
   **Written by:** Rea Tschoppe (Collaboration with Pasteur Institute)  
   **Funder:** OPO Foundation on.  
   **Status:** Result Pending
8. **Title:** One Health Brucellosis in Afar and Somali Region.  
   **Written by:** Rea Tschoppe  
   **Funder:** CDC  
   **Status:** Pending  

9. **Title:** One Health rabies and brucellosis in East Shoa and Borena.  
   **Written by:** Rea Tschoppe  
   **Funder:** CDC  
   **Status:** Failed submission due to technical issues (AHRI registration with US government). Possibility of resubmitting for a later call  

10. **Title:** “Engineered Vaccines against Hemorrhagic Septicemia in Ruminants”.  
    **Written by:** Rea Tsachoppe in collaboration with University of Calgary, Canada  
    **Funder:** IDRC Livestock Vaccines Innovation Fund  
    **Status:** Result pending  

12. **Title:** Rabies prevalence in the Rift Valley  
    **Written by:** Rea Tschoppe in Collaborator with DebreZeit Faculty (AAU)  
    **Funder:**  
    **Status:** Result pending  

13. **Title:** Optimizing Ivermectin MDA to maximize its benefit to Resource-limited setting  
    **Written by:** Endalamaw Gadissa (AHRI leading collaboration with Greenwitch University)  
    **Funder:** EDCTP  
    **Status:** Failed  

14. **Title:** Dose ranging study of primaquine to evaluate its antirelapse efficacy  
    **Written by:** Oxford University in partnership with AHRI (Endalamaw Gadissa)  
    **Funder:** EDCTP  
    **Status:** Failed  

15. **Title:** Randomized controlled trial on Supervised PRimaquine Use in Ethiopia  
    **Written by:** Menzies University in partnership with AHRI (Endalamaw Gadissa)  
    **Funder:** MRC  
    **Status:** Failed  

16. **Title:** Diagnostic utility of volatile organic compounds in human breath for acute clinical malaria  
    **Written by:** Menzies University in partnership with AHRI (Endalamaw Gadissa)  
    **Funder:** MRC  
    **Status:** Failed  

17. **Title:** Developing diagnostic surveillance tools for leishmaniasis  
    **Written by:** Endalamaw Gadissa in collaboration with EPHI  
    **Funder:** Ethiopian Ministry of Science and Technology  
    **Status:** Granted
## Conference/Workshop Participation

<table>
<thead>
<tr>
<th>Participant</th>
<th>Activity</th>
<th>Conference</th>
<th>Venu</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yared Merid</td>
<td>Poster presentation</td>
<td>11th National Tuberculosis Conference</td>
<td>Dire Dawa, Ethiopia</td>
<td>March 21-23, 2016</td>
</tr>
<tr>
<td>Yared Merid</td>
<td>Participant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martha Zewdie</td>
<td>Poster presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Markos Abebe</td>
<td>Seminar presentation</td>
<td>‘Mycobacterial Disease Research at AHRI: areas for collaboration’</td>
<td>Orebro University, Sweden</td>
<td>Dec. 13-18, 2016</td>
</tr>
<tr>
<td>Tsehaynesh Lema Edessa Negera</td>
<td>Oral presentation</td>
<td>TLMi Ethiopia annual country meeting and reporting forum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsehaynesh Lema</td>
<td>Oral presentation</td>
<td>19th International Leprosy Congress (ILC)</td>
<td>Beijing, China</td>
<td>Sept 18 to 23, 2016</td>
</tr>
<tr>
<td>Liya Wassie</td>
<td>Participant</td>
<td>Global consultative meeting on “Programmatic management of latent TB infection”</td>
<td>Seoul, Republic of Korea</td>
<td>Apr. 25-May 1, 2016</td>
</tr>
<tr>
<td>Wude Mihret</td>
<td>Oral presentation</td>
<td>International pathogenic Neisseria conference (IPNC)</td>
<td>Manchester, UK</td>
<td>Sept. 4-9, 2016</td>
</tr>
<tr>
<td>Tesfamariam Mebratu</td>
<td>Oral presentation</td>
<td>Annual STREAM investigators’ meeting</td>
<td>New York, USA</td>
<td>Jul. 16, 2016</td>
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<tr>
<td>Tesfamariam Mebratu</td>
<td>Oral presentation</td>
<td>Annual TB Research Advisory Committee Meeting</td>
<td>Dire Dawa, Ethiopia</td>
<td>Mar. 21-24, 2016</td>
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<tr>
<td>Selfu Girma</td>
<td>Poster presentation</td>
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</table>
Trainings Obtained

<table>
<thead>
<tr>
<th>Name</th>
<th>Training</th>
<th>Venue</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fekadu Desta</td>
<td>Immunohistochemistry</td>
<td>University of Surrey, UK</td>
<td>Oct.31-Nov.11, 2016</td>
</tr>
<tr>
<td>Sosina Ayalew, Meseret Abebe and Adem Yesuf</td>
<td>Applied Bioinformatics for PCR and Principles of PCR Course organized by University of Gondar in collaboration with Calgary University, Canada.</td>
<td>University of Gondar, Ethiopia</td>
<td></td>
</tr>
</tbody>
</table>
Publications

Molecular typing of mycobacteria isolated from tuberculous lymphadenitis cases in Addis Ababa, Ethiopia.

Evaluation of cytokine responses against novel Mtb antigens as diagnostic markers for TB disease.

Multi-center evaluation of a user-friendly lateral flow assay to determine IP-10 and CCL4 levels in blood of TB and non-TB cases in Africa.

Diagnostic performance of a seven-marker serum protein biosignature for the diagnosis of active TB disease in African primary healthcare clinic attendees with signs and symptoms suggestive of TB.

Hepatitis B and human immunodeficiency virus co-infection among pregnant women in resource-limited high endemic setting, Addis Ababa, Ethiopia: implications for prevention and control measures.
Desalegn Z, Wassie L,Beyene HB, Mihret A, Ebstie YA.

Pharyngeal carriage of Neisseria species in the African meningitis belt.


Seroprevalence and risk factors of herpes simplex virus-2 among pregnant women attending antenatal care at health facilities in Wolaita zone, Ethiopia.
Anjulo AA, Abebe T, Hailemichael F, Mihret A.

Performance of LED Fluorescence Microscopy for the Diagnosis of Pulmonary Tuberculosis in HIV Positive Individuals in Addis Ababa, Ethiopia.
Getachew K, Abebe T, Kebede A, Mihret A, Melkamu G.

IFN-γ and IgA against non-methylated heparin-binding hemagglutinin as markers of protective immunity and latent tuberculosis: Results of a longitudinal study from an endemic setting.
Belay M, Legesse M, Mihret A, Ottenhoff TH, Franken KL, Bjune G, Abebe F.

Half of Pulmonary Tuberculosis Cases Were Left Undiagnosed in Prisons of the Tigray Region of Ethiopia: Implications for Tuberculosis Control.
Adane K, Spigt M, Ferede S, Asmelash T, Abebe M, Dinant GJ.

The socioeconomic impact of multidrug resistant tuberculosis on patients: results from Ethiopia, Indonesia and Kazakhstan.
van den Hof S, Collins D, Hafidz F, Beyene D, Tursynbayeva A, Tiemersma E.

Comparison of immune responses to a killed bivalent whole cell oral cholera vaccine between endemic and less endemic settings.

Short-course treatment for multidrug-resistant tuberculosis: the STREAM trials.
Moodley R, Godec TR; STREAM Trial Team (Conradie F, Master I, Narasimooloo R, Mebrahtu T, Kokebu DM, Lan NT, Dat PT, Tsogt B, Nyamdavaa N)
Surveillance of Bacterial Meningitis, Ethiopia, 2012-2013.

Serological signatures of clinical cure following successful treatment with sodium stibogluconate in Ethiopian visceral leishmaniasis.

Prevalence and epidemiology of meningococcal carriage in Southern Ethiopia prior to implementation of MenAfriVac, a conjugate vaccine.

Throat culture positivity rate and antibiotic susceptibility pattern of beta-hemolytic streptococci in children on secondary prophylaxis for rheumatic heart disease.
Zegeye N, Asrat D, Woldeamanuel Y, Habte A, Gedlu E, Tønjum T, Aseffa A.

Ex-vivo characterization of regulatory T cells in pulmonary tuberculosis patients, latently infected persons, and healthy endemic controls.

Household transmission of Neisseria meningitidis in the African meningitis belt: a longitudinal cohort study.

Correction: A Seroepidemiological Study of Serogroup A Meningococcal Infection in the African Meningitis Belt.

Deciphering the recent phylogenetic expansion of the originally deeply rooted Mycobacterium tuberculosis lineage 7.


In vitro permissiveness of bovine neutrophils and monocyte derived macrophages to Leishmania donovani of Ethiopian isolate.

Performance of general health workers in leprosy control activities at public health facilities in Amhara and Oromia States, Ethiopia.

Host-directed therapies for infectious diseases: current status, recent progress, and future prospects.

Patients direct costs to undergo TB diagnosis.

Bacteriological Profile and Antimicrobial Susceptibility Pattern of Blood Culture Isolates among Septicemia Suspected Children in Selected Hospitals Addis Ababa, Ethiopia.

Treatment of Cutaneous Leishmaniasis Caused by Leishmaniaaethiopica: A Systematic Review.
van Griensven J, Gadisa E, Aseffa A, Hailu A, Beshah AM, Diro E.

The Typhoid Fever Surveillance in Africa Program (TSAP): Clinical, Diagnostic, and Epidemiological Methodologies.

The Relationship Between Invasive Nontyphoidal Salmonella Disease, Other Bacterial Bloodstream Infections, and Malaria in Sub-Saharan Africa.

Tschopp R, Bekele S, Aseffa A.

Risk of tuberculous infection in adolescents and adults in a rural community in Ethiopia.
Elias D, Akuffo H, Abate E, Mekonnen Y, Aseffa A, Britton S.

Cost-effective control strategies for animal and zoonotic diseases in pastoralist populations.
Zinsstag J, Abakar MF, Ibrahim M, Tschopp R, Crump L, Bonfoh B, Schelling E.


**Patent**

Partners and Collaborators