Research seminar: Cradle of TB

January 29th, 2015 – February 13th, 2015
Bahir Dar, Ethiopia
Network for molecular epidemiology of *Mycobacterium tuberculosis* in Ethiopia, Sudan and South Sudan: the cradle of the new lineage 7
January 29th-31st, 2015: Research workshop, Bahir Dar, Amhara Region, Ethiopia

February 9th-13th, 2015: Laboratory course in techniques for detection of tuberculosis, AHRI laboratory, Addis Ababa, Ethiopia

February 9th-11th, 2015: Bioinformatics course focused on whole genome analysis of *Mycobacterium tuberculosis*, AHRI, Addis Ababa, Ethiopia

Organized by
Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia
Norwegian Institute of Public Health (NIPH), Oslo, Norway
Oslo University Hospital (OUS), Oslo, Norway
Amhara Regional State Health Burea, Bahir Dar, Ethiopia

Sponsored by:

[The Research Council of Norway](#)
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1 Practical information for participants

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Seminar committee
AHRI  Dr. Markos Abebe, PhD, post-doctoral scientist AHRI, Ethiopia
ARSHB  Zebideru Zewdie, MPH, Depty Bureau Head, ARSHB, Bahir Dar, Ethiopia
        Endalkachew Desalegne, MPH, ARSHB, Bahir Dar, Ethiopia
NIPH  Dr. Gunnstein Norheim, scientist, NIPH, Norway
        Dr. Brita Askeland Winje, PhD, Senior Advisor, NIPH, Norway
OUS  Dr. Solomon Yimer, PhD, Post-doctoral researcher; OUS, Norway

Advisors
Dr. Abraham Aseffa, Director, AHRI, Ethiopia
Prof. Dominique A. Caugant, NIPH, Norway
Prof. Tone Tønjum, OUS, Norway

Location of conference venue
Homeland Hotel
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Accommodation and refund of travel expenses
Accommodation for participants and travel expenses for participants will be covered by grants from the Norwegian Research Council and the NIPH. Please contact Markos Abebe, AHRI for further details.
Global tuberculosis situation
Tuberculosis incidence and mortality has been declining in all WHO regions since 2001, and treatment success rates have been maintained at 85% or more since 2007. Yet, tuberculosis is still a significant public health problem with considerable disease burden and mortality. Tuberculosis (TB) is the major public health threat in many developing countries. It is estimated that one third of the global population is infected with TB. In 2013, an estimated 9 million people developed TB and 1.5 million died from the disease, 360,000 of whom were HIV-positive. Africa has the highest cases and deaths of TB per capita and contributes significant proportion to the global TB burden (WHO 2014).

The world has been united to control the TB pandemic since 2000 and global commitments have been made by the international community. Reversing incidence and 50% reduction of prevalence and mortality from TB (compared with 1990) have been targeted under the Millennium Development Goal (MDG) Six by 2015. The World Health Organization (WHO) plans to eliminate TB by 2050 and the Stop TB strategy was implemented in 2006 to achieve these targets. The end of 2015 marks a transition from the MDGs to a post-2015 strategy (the End TB Strategy) with 2035 targets of a 95% reduction in TB deaths and 90% reduction in TB incidence compared to 2015. Case notification remains a challenge and in 2013 it is estimated that 3 million cases were either not diagnosed or diagnosed but not reported to national TB programs (NTPs).

Overall, TB mortality has decreased by 45% since 1990 and the prevalence rate fell by 41% during the same period (WHO 2014). Despite the encouraging results achieved by the Stop TB strategy however, the global targets are still not fully achieved in most high TB burden countries. Globally in 2013, 3.5% of new and 20.5% of previously treated cases were estimated to have had MDR-TB, translating into 480,000 people. On average, 9% of these had XDR-TB. There has been a three-fold increase in the number of patients started on MDR-TB treatment, yet there is an increasing gap between people diagnosed with MDR-TB and those who have access to MDR-TB treatment. MDR treatment outcomes are poor in some areas with a global success rate at 48%.

Seventy percent of the TB patients known to be living with HIV in 2013 were started on antiretroviral therapy (ART). In Africa, 41% tested were HIV positive (global co-infection rate: 18%) (WHO 2014). The majority of TB cases do not know their HIV status. Because of these challenges, it is anticipated that the goals for reduction of TB incidence, prevalence and mortality may not be met in most sub-Saharan African countries according to the milestone set in the Global Plan.

The epidemiology of TB has changed in the last two decades due to emergence of HIV and drug resistant TB. Understanding the challenges of TB control is crucial to achieve the global targets for TB control and elimination. Country specific epidemiological and operational research are warranted to investigate the challenges and forward evidence based recommendations for policy action. Besides this, basic and clinical research is
needed to better understand the pathogenesis and immunology of TB, and to identify targets for diagnostics, drugs and vaccines.

Ethiopia, Sudan and South Sudan are three neighboring countries in sub Saharan Africa that share a long distance border. These countries have had long time relationship as a result of cross border population movements (e.g. trade and migration). This has implications to cross-border transmission of TB. There is a very high TB burden in Ethiopia, Sudan and South Sudan. The WHO recommended directly observed treatment short course strategy (DOTS) has been implemented in Ethiopia and Sudan since the last two decades. Despite the continued TB control efforts however, the number of TB cases is still very high.

**TB in Ethiopia, Sudan and South Sudan**

Ethiopia is one of the least developed countries in the world with an estimated population of 85 million. The country is currently among the top three in Africa and eighth among the 22 high TB burden countries worldwide. The prevalence and incidence of TB in the country is estimated at 211/100 000 and 224/100 000 population, respectively (WHO 2014). 11% of the TB cases in Ethiopia are infected with HIV (WHO 2014). The smear-positive case detection rate is low compared to the 70% case detection target as set by WHO. According to recent evidence from a rural area in Ethiopia, two-third of the infectious TB patients are not detected (Tadesse et. al., 2011). MDR-TB is on the rise in recent years. A recent study of M. tuberculosis isolates (Mtb) among pulmonary tuberculosis patients in the Amhara Region of Ethiopia showed the presence of high level of diversity of strains among the 237 Mtb isolates (Yimer et al., 2013). The most exciting finding in this study was the identification of a very high proportion Spoligo-International-Type (SIT) 910 and SIT 1729 belonging to a new Mtb lineage called lineage 7. Mtb lineage 7 strains are thought to have emerged approximately 70,000 years ago, near the time at which modern humans migrated out of Africa (Comas et al., 2013). This suggests an urgent need of conducting further epidemiological studies to investigate the reasons driving the TB epidemic in Ethiopia. Among others a study focusing on the molecular epidemiology of TB is important to understand the diversity of emerging strains and their associations with severity of illness and transmissibility of TB infection. This will help to propose appropriate strategies to control the TB epidemic and ultimately achieve the global targets in Ethiopia.

The Republic of Sudan is the largest country in the African continent and has an estimated population of 37 million. The country has been severely affected by war, famine and flood in recent decades and has a large population of internally displaced persons (El- Sony et. al., 2002). TB is a major public health problem in Sudan. The prevalence and incidence of TB in the country was estimated at 207/100000 population and 114/100000 population, respectively (WHO 2013). The proportion of undetected TB amounts 56% and eight percent of the TB patients are HIV infected. MDR-TB is estimated at 1.8% among
Background

new and 19% among retreatment cases, respectively. Tuberculosis care and treatment is provided by the National Tuberculosis Control Program of the Ministry of Health and by a number of non-governmental organizations (NGOs) that provide care to displaced persons, including those living in refugee camps. The private sector is involved the provision of TB control. Challenges in TB control in Sudan include: increase in drug resistance, unregulated TB control activities in the private sector, poor surveillance and supervision activities.

South Sudan is a new nation in Africa with a population of eight million. The country is one of the poorest countries in the world with half of its population living on less than 1 US$ per day. The prevalence and incidence of TB is estimated at 257/100,000 population and 146/100,000 population, respectively. Twelve percent of TB patients are infected with HIV (WHO 2013). The health infrastructure in South Sudan is not well developed. Currently, TB treatment and prevention activities are provided by multi-lateral and non-governmental organizations in collaboration with government. The country has achieved 53% case notification rate and 70% treatment success rate for smear positive TB (WHO 2013). The key challenges facing TB control program include: high number of undetected infectious TB cases, low DOTS coverage, inadequate number of health staff and health infrastructure, lack of a reference laboratory, inadequate community involvement in TB control and care, inadequate implementation of TB/HIV activities and limited integration of TB activities into general health system (http://www.tbcare1.org/countries/africa/SDN/). TB related research in South Sudan is very limited and the epidemiology of TB is not well understood. Prevalence studies using the WHO recommended strategies are necessary, including novel detection technologies (GenXpert). Another important area of research with limited knowledge is the prevalence of drug resistance and molecular epidemiology of M. tuberculosis (Mtbc) strains.
Objectives
Update seminar/conference participants on recent knowledge on TB epidemiology, genomics, diagnostics, TB health information system and on how to conduct operational researches
Facilitate networking and efficient knowledge exchange within ongoing collaborative research projects or for the generation of ideas for new projects
Provide basic bioinformatics knowledge to selected EvoTB research team members from Ethiopia, Sudan and South Sudan
Provide a refresher course on routine diagnostic tests, and to give an insight into more recent tools for microbiological confirmation of tuberculosis

Expected activities
Arrange a research workshop on strengthening research partnership for TB
Arrange a training course in laboratory techniques for detection and immunological responses in TB
Arrange a training course in bioinformatics related to M. tuberculosis
Prepare one new research proposal for GLOBVAC 2015 announcement

Outputs
Established network of TB researchers in Ethiopia, Sudan, South Sudan and other institutions
Defined new concepts for research in TB
Trained 16 persons in modern laboratory techniques for detection of TB
Trained 16 person in bioinformatics

Outcome
Improved collaboration, identification of areas for research, dissemination to Ministry of Health and other partners
Evidence based advice on TB prevention and control to Ministry of Health
Capacity building in TB epidemiology, diagnostics and bioinformatics for medical research scientists and doctors in Ethiopia, Sudan, and South Sudan

References
Yimer et al., APMIS 2013;9:878-85.
Thursday 29th of January 2015

08:30 Registration and coffee

09:00 Seminar opening
Mr. Ayeligne Mulualem ARSHB Head
Prof. Tone Tønjum
Dr. Adane Mihret

09:15 Overview of disease burden, Country update
Convenor: Dr. Solomon A Yimer

Prof. Asma Elsny: Global TB burden and control

To be announced:
Tuberculosis in Sudan

Mr. Gregory Wani: Tuberculosis in South-Sudan

Dr. Andargachew, MOH: Tuberculosis in Ethiopia

10:30 Coffee break

11:00 Tuberculosis update lectures
Convenor: Prof. Brigitte Gicquel

Prof. Tone Tønjum: Genome dynamics driving evolution - relevance for lineage 7
Mycobacterium tuberculosis strains

Prof. Gunnar Bjune: Development of multi-drug-resistant tuberculosis, challenges and solutions
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<tr>
<th>Time</th>
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<tr>
<td>12:30</td>
<td>Lunch</td>
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<tr>
<td>13:30</td>
<td>Tuberculosis update lectures, continue</td>
<td>Convenor: Prof. Asma Elsony</td>
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<td><strong>Prof. Tone Tønjum:</strong></td>
<td>Culture-based mycobacterial diagnostics and drug susceptibility testing</td>
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<td><strong>Prof. Brigitte Gicquel:</strong></td>
<td>Tuberculosis: molecular tools for diagnosis, drug susceptibility testing and isolate characterization</td>
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<td>15:00</td>
<td>Coffee break</td>
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<td>15:30</td>
<td>The cradle of TB, current knowledge on lineage 7</td>
<td>Convenor: Ms. Zebideru Zewde</td>
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<td><strong>Dr. Solomon A. Yimer:</strong></td>
<td>EvoTB project status</td>
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<td>16:15</td>
<td>Discussion on topics of the day and closing remarks</td>
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**Friday 30th of January 2015**

**09:00**  
**Tuberculosis update lectures, continue**  
Convenor: Prof. Gunnar Bjune

**Prof. Brigitte Gicquel:**  
Tuberculosis: New trends in vaccines and drug-designs

**Diagnostic challenges**  
Convenor: Prof. Gunnar Bjune

**Dr. Workabeba Abebe**  
Childhood TB

**10:30**  
Coffee break

**11:00**  
**Diagnostic challenges**  
Convenor: Mr. Gregory Wani

**Dr. Rawleigh Howe:**  
TB and HIV  
To be announced  
TB/DM

**12:00**  
**TB control information system**  
Convenor: Mr. Gregory Wani

**Dr. Laurence Yamuah**  
TB data management and the importance of quality assurance

**12:45**  
Lunch
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<td>13:30</td>
<td><strong>Operational Research</strong>&lt;br&gt;Convenor: Dr. Brita Winje</td>
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<td>14:15</td>
<td><strong>Prof. Gunnar Bjune:</strong> How to conduct operational research</td>
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<td>Workshops to facilitate exchange of ideas within the following topics:</td>
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<td>TB control and prevention&lt;br&gt;Prof. Asma Elsony</td>
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<td>TB operational and basic research needs&lt;br&gt;Prof. Tone Tønjum</td>
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<td>TB data management challenges&lt;br&gt;Prof. Gunnar Bjune</td>
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<td>15:30</td>
<td><strong>Coffee break</strong></td>
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<td>16:00</td>
<td>Feedback from working groups and plenary discussions&lt;br&gt;Dr. Adane Mihretv</td>
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Saturday 31st of January 2015

09:00  Partner research update lectures on tuberculosis
Convenor: Dr. Adane Mihret

Dr. Adane Mihret:
AHRI TB research projects and strategic plan

Dr. Shewki Moga:
EPHI- TB research projects

To be announced
PPM-DOTS Project

To be announced
Heal TB project

10:00  Plenary discussion

10:30  Coffee break

11:00  Partner research update lectures on tuberculosis
Convenor: Dr. Andargachew Kumsa

Dr. Carol Holm-Hansen:
NIPH: Tuberculosis Rapid Test project

Dr. Brita Winje:
NIPH: Cluster studies

Prof. Tone Tønjum:
OUS TB research

To be announced
University of Oslo TB research projects

12:00  Plenary discussion
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<td>12:30</td>
<td>Lunch</td>
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<td>13:30</td>
<td>Plenary final discussions:</td>
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<td>Research needs in Sudan, South Sudan and Ethiopia</td>
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<td>Prof. Tone Tønjum</td>
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<td>14:30</td>
<td>Coffee break</td>
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<td>15:00</td>
<td><strong>Closing remarks</strong></td>
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<td>Prof. Tone on behalf of OUS</td>
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<td>Dr. Brita on behalf of FHI</td>
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<td>Dr. Adane on behalf of AHRI</td>
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