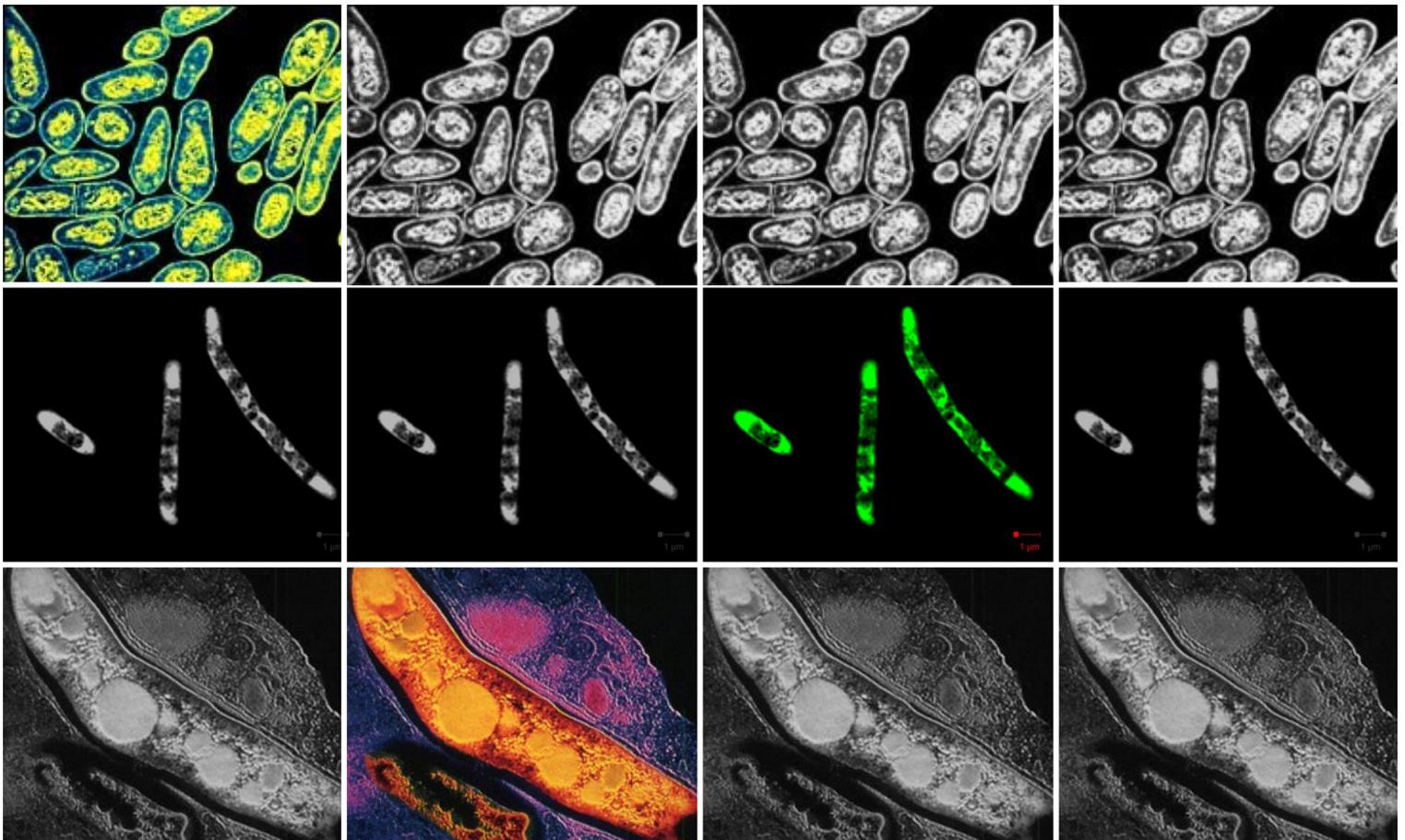
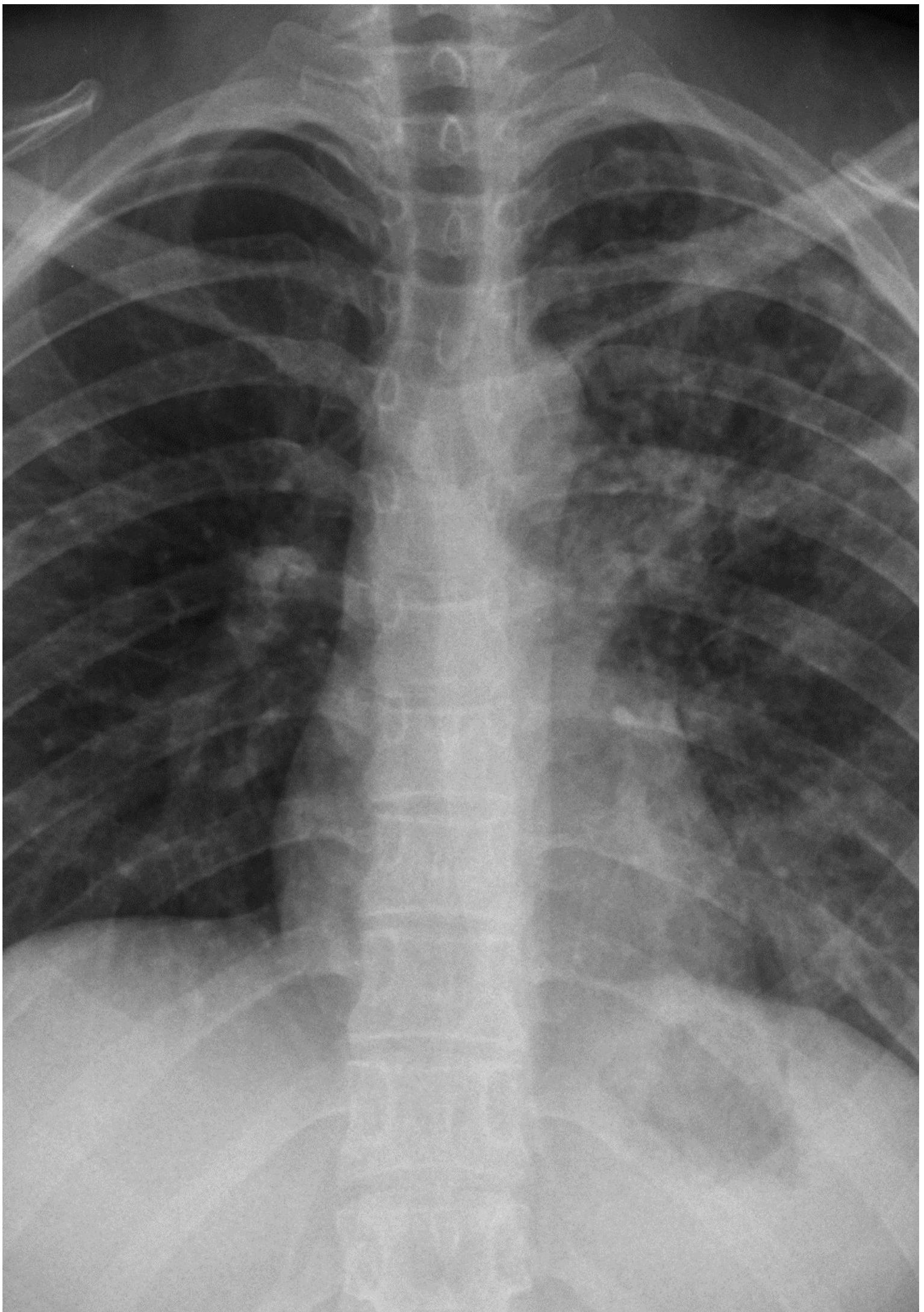
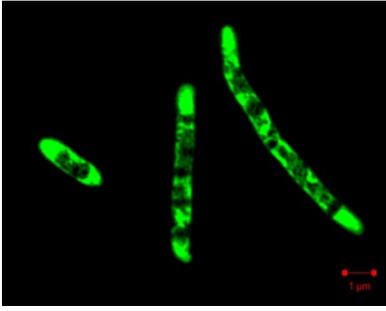


Research seminar: Cradle of TB

January 29th, 2015 – February 13th, 2015
Bahir Dar, Ethiopia







Research seminar: Cradle of TB

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:



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, Deputy 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.

2 Background

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

2 Background

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 114/1000000 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

2 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* (Mtb) strains.

3 Objectives of the seminar

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

Comas et al., Nature Genetics 2013;10:1176-82.

El-Sony et. al., Int J Tuberc Lung Dis. 2002 ;12:1058-66

Firdessa et al. EID 2013;3:460-3.

Tadesse et. al., PLoS One. 2011;12:e28258.

Yimer et al., APMIS 2013;9:878-85.

WHO. Global tuberculosis report 2014. WHO, Geneva, Switzerland.

4 Seminar programme

Thursday 29th of January 2015

08:30	Registration and coffee
09:00	Seminar opening Mr. Ayeligne Muluaem ARSHB Head Prof. Tone Tønjum Dr. Adane Mihret
09:15	Overview of disease burden, Country update Convenor: Dr. Solomon A Yimer
	Prof. Asma Elsony: 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 <i>Mycobacterium tuberculosis</i> strains Prof. Gunnar Bjune: Development of multi-drug-resistant tuberculosis, challenges and solutions

4 Seminar programme

12:30

Lunch

13:30

Tuberculosis update lectures, continue

Convenor: Prof. Asma Elsony

Prof. Tone Tønjum:

Culture-based mycobacterial diagnostics and drug susceptibility testing

Prof. Brigitte Gicquel:

Tuberculosis: molecular tools for diagnosis, drug susceptibility testing and isolate characterization

15:00

Coffee break

15:30

The cradle of TB, current knowledge on lineage 7

Convenor: Ms. Zebideru Zewde

Dr. Solomon A. Yimer:

EvoTB project status

16:15

Discussion on topics of the day and closing remarks

4 Seminar programme

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

4 Seminar programme

13:30

Operational Research

Convenor: Dr. Brita Winje

Prof. Gunnar Bjune:

How to conduct operational research

14:15

Workshops to facilitate exchange of ideas within the following topics:

TB control and prevention

Prof. Asma Elsony

TB operational and basic research needs

Prof. Tone Tønjum

TB data management challenges

Prof. Gunnar Bjune

15:30

Coffee break

16:00

Feedback from working groups and plenary discussions

Dr. Adane Mihretv

4 Seminar programme

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

4 Seminar programme

12:30	Lunch
13:30	Plenary final discussions: Research needs in Sudan, South Sudan and Ethiopia Prof. Tone Tønjum
14:30	Coffee break
15:00	Closing remarks Prof. Tone on Behalf of OUS Dr. Brita on behalf of FHI Dr. Adane on behalf of AHRI Mr. Ayeligne Mulualem, ANRSHB Bureau Head