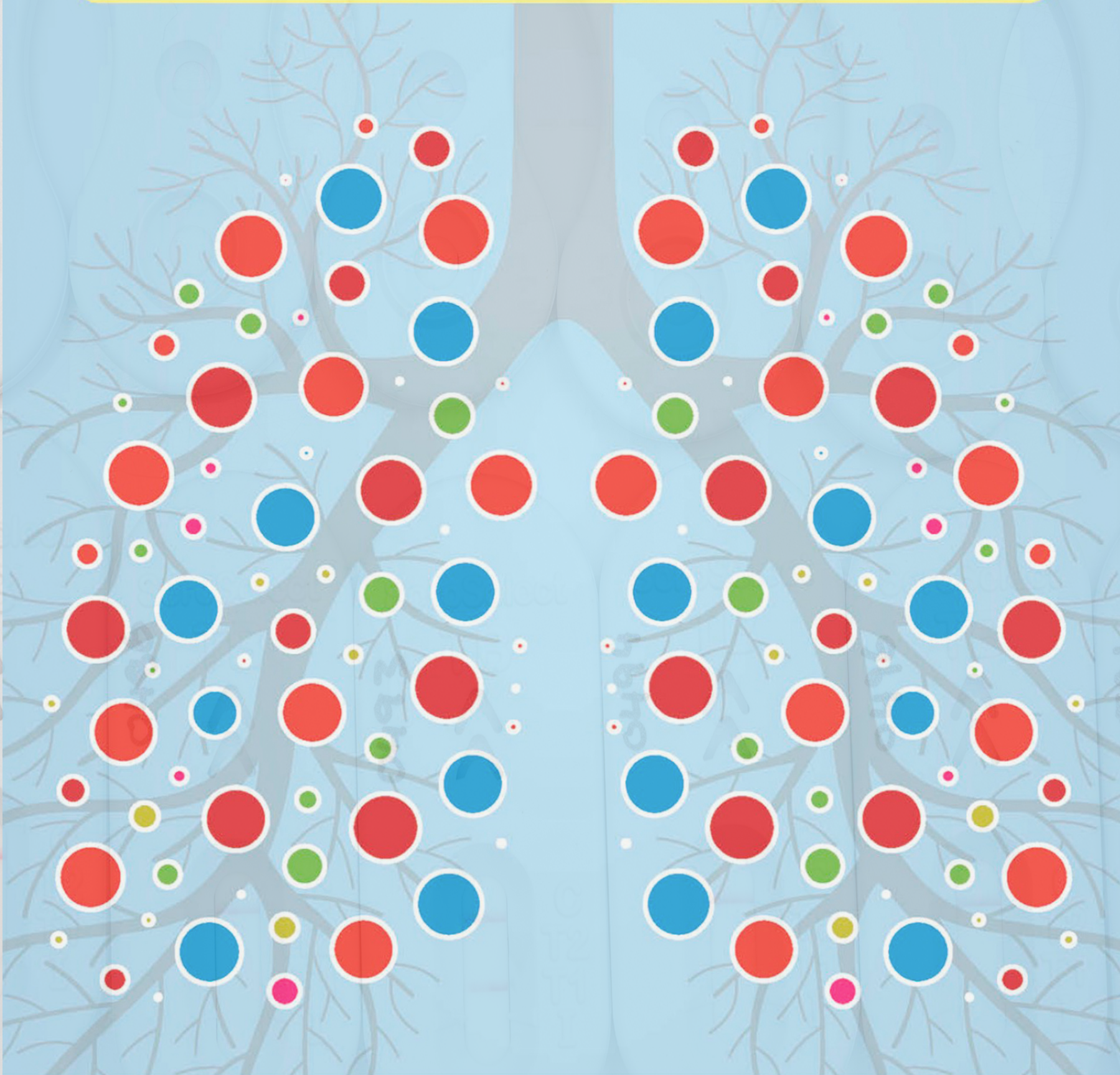




DIAGNOSTIC TESTS AND CLINICAL TRIALS



PREVENTING THE SPREAD OF TB THROUGH NEW DIAGNOSTICS

SeroSelectTB

newsletter

SeroSelectTB project final consortium meeting Moshi, Tanzania

Norwegian Institute of Public Health and KCMC University organized the Final Consortium Meeting at the Weru Weru River Lodge on the foothills of Kilimanjaro in Tanzania.

Professor Kaaya, Vice-Chancellor at KCMC University opened the meeting:

“It is with pride that I welcome you on behalf of the KCMC University. The last time we met I was the Provost, and the institution was a college. This week we host the final consortium meeting as a university, and the SeroSelectTB project has contributed to this evolution.”

“We are doing more than closing a chapter, we are celebrating the partnership and this groundbreaking project. We will also discuss the TB challenges we still need to address. The cornerstone of this meeting is data the analysis and finalizing the multicenter paper.”



Professor Ephata Kaaya, Vice-Chancellor, KCMC University.



SeroSelectTB Consortium. Photo: Jesca Msemu.

Presentations addressed a review of the SeroSelectTB project, achievements and challenges in Tanzania, Ethiopia, and South Africa (details below), the data management program and ongoing data analysis, the SeroSelectTB test kit production, and test performance in detecting HIV coinfectd TB patients. Diagnostic delay, TB diagnostic activities at KNCV, TB research and services in Tanzania, and possibilities for further SeroSelectTB research at the Kibong’oto Infectious Disease Hospital were discussed.



Carol Holm-Hansen, Norwegian Institute of Public Health.



SeroSelectTB in Tanzania: achievements & challenges

Tanzania is among the world’s 30 highest-burden countries for TB and TB/HIV co-infection.

Twenty-one health facilities including dispensaries and health centers were selected from three districts included in the Kilimanjaro region. The healthcare workers were trained on all aspects of the study.



Balthazar Nyombi, KCMC University.

The first participant was enrolled in September 2022, and 4369 participants were enrolled by the end of December 2024. Community engagement was excellent and motivated presumptive TB patients to seek healthcare. A well-characterized biobank was established at KCMC University that can support future studies.

Many challenges were met including a delay securing ethical approvals due to the COVID-19 pandemic, transfer of personnel (clinical officers, laboratory technicians, nurses) to study site facilities, Xpert test results were not always returned from the central laboratory, and the number of patients seeking healthcare was low during the rainy season.

Community Advisory Board presentation

An advisory board (CAB) supported the KCMC University team throughout the study. The board reminded the team that society has been shaped by habits.

The community suggests that SeroSelectTB be introduced to the Ministry of Health as soon as possible. This will reduce the “time wasted” waiting for results from the routine TB tests.

The community trusts researchers and healthcare workers. The participants developed hope for a “lifesaving” diagnostic tool that simplifies testing and thereby motivates persons to seek medical care at nearby dispensaries.

The CAB reported a number of challenges including the need for access to quality and rapid services that can provide fast results and reduce costs, lack of education, poverty, distance to TB testing facilities, and poor public awareness that contribute to the spread of TB.

The CAB recommended that SeroSelectTB researchers should introduce the test to the Ministry of Health to facilitate access to services, to obtain rapid test results, and thereby reduce the spread of TB infections.



Moswery Leocardia

SeroSelectTB in Ethiopia: achievement & challenges

Ethiopia is among the 30 TB and HIV high-burden countries. TB incidence and mortality in Ethiopia is increasing. Our sites were moved from the Bahir Dar in Amhara region to the Sidama region, which is in the high burden TB belt. 85% of the SeroSelectTB participants in Ethiopia are from the Sidama region.

Health extension workers (HEWs) who were responsible for recruiting TB patients, performing the SeroSelectTB test at the health post and referring presumptive TB patients to the health center.

Data and sample collection, additional testing, and uploading data into REDCap were conducted at the health centers. Samples were sent to reference labs with Xpert facilities for confirmatory testing. Community engagement contributed to the smooth implementation of the project by providing a forum for raising awareness, support and solutions.

A total of 2109 total participants were enrolled with 213 TB cases detected (109 in the SeroSelectTB arm and 104 in the Standard-of-care arm). AFB microscopy was performed for 93% of participants, and treatment was initiated following positive AFB microscopy result.

Xpert was performed for only 63% of participants and the results were received after 4-11 days.

Challenges met included delay in TB diagnosis, security issues (Amhara region), infrastructure needs at health sites (lack of power, refrigerators), HEWs' workload (too many activities, campaigns, training), and slow recruitment.



Kidist Bobosha, Armauer Hansen Research Institute.

SeroSelectTB in South Africa: achievements & challenges

South Africa is one of the 30 high-burden countries for TB and HIV with 56,000 deaths due to TB reported in 2023. Social economy is an important factor, and over-crowded housing is at the heart of TB epidemic in South Africa.

REDCap was established, the eCRF designed, and the staff trained prior to recruitment that started in September 2021. Study management, training and retraining was performed throughout the study until recruitment ended in December 2024. In total, 2929 participants were enrolled, 1459 in SeroSelectTB arm and 1470 in Standard-of-Care arm.

Challenges met included disruptions due to inclement weather, transport strikes and protests, loadshedding interruptions, and consent hesitancy among screened participants.

Many lessons were learned. Community engagement, which was performed at the clinics and not in the community, is essential to build trust. Mobile clinics improve access to healthcare and interdisciplinary teamwork is beneficial. Regular QC and feedback meetings are necessary to maintain quality data collection. Future trials should include a fully automated QC process and explore digital participant tracking. Ensuring statistical support and strengthening the community advisory board is essential.



Welile Nwamba, Stellenbosch University.

TB research & services in Tanzania: experience from Kibong’oto Infectious Disease Hospital

Kibong’oto was established in Sanya Juu, West Kilimanjaro as a TB sanatorium in 1926 and in 1956, following the discovery of streptomycin in 1942, became the Kibong’oto Hospital. In 2006 Kibong’oto was given responsibility for managing MDR-TB and HIV care, and was renamed Kibong’oto National TB Hospital. The Kibong’oto Infectious Disease Hospital (KIDH) was established in 2010.

Kibong’oto experienced a six-fold increase in TB during the 1980s at the start of the HIV pandemic.

TB diagnosis at KIDH is especially difficult among patients who have previously had TB.

Post TB lung disease (PTLD) is also a challenge because it is difficult to differentiate active TB from PTLD.

Patients with advanced HIV infection/AIDS cannot produce “good” sputum. TB was detected during autopsy among 45% of HIV-positive patients with an unknown cause of death. Better tests for detecting TB among people with HIV are urgently needed.



Stellah Mpagama, Kibong’oto Infectious Disease Hospital.

Sustainability was a motif throughout the meeting. Importantly, discussions addressing ways in which SeroSelect TB activities - and especially community engagement - could be sustained and lessons learned were led by Abraham Aseffa. Topics included product development (pre-qualification, registration, roll-out), research partnerships and collaboration, responsibility for community engagement (national/regional), the role of and opportunities for post graduate students (use SeroSelect TB data and/or samples for additional investigations), and mechanisms or platforms by which continued research, partnerships, and community engagement can be facilitated.



Carol Holm-Hansen and Abraham Aseffa leading discussion on project sustainability.

The last day was devoted to a working session for all coauthors regarding the multicenter manuscript. Discussions led by Miloje Savic addressed results, data analysis, interpretation, and conclusions. Tables and diagrams prepared for manuscript were presented and reviewed. The meeting concluded with a consortium dinner in the Weru Weru garden with entertainment provided by local Chagga dancers, a Bantu ethnic group from the Kilimanjaro Region, and a taste of the local fermented banana and millet brew, mbege, which has important cultural and nutritional value.



Chagga dancers and mbege tasting at Weru Weru River Lodge, Tanzania. Photo: Carol Holm-Hansen.

A patient's journey

“A patient's journey”, documenting participant enrollment, completing the questionnaire, sample collection, and follow-up during treatment was organized by Gaudensia Olomi from the Health Department at the Kilimanjaro Regional Administrative Secretary's Office in Moshi. Asha Juma Mbwambo was willing to repeat the entire procedure for project documentation purposes.

The visit started at Asha's home, where an interview was conducted. Her daughter was present during the interview while her husband was in the garden. Initially, Asha went to a private health facility where they told her she had “problems” like diabetes or UTI. After having been sick for 2-3 months, she reported to the Kahe Health Center in Moshi District Council (rural), Kilimanjaro region, was diagnosed with TB, and received treatment. The medicines made her feel very sick, but she felt better after a while and continued with the treatment. Asha completed her treatment and reported for all check-ups and 6-month follow-up. At the conclusion of the interview, Asha was asked if she had any advice for others in her village. She said the government should educate the community about TB symptoms; whenever someone feels sick, they should get tested at the health center. Asha stated that the SeroSelect TB test is good, it gives the results quickly, and treatment can be started at once.



Mama Asha at her room where she spent most of her time isolated while following Tb treatment.



The project is very grateful for Asha's willingness to participate and share her experiences.
Asante sana, Asha!

We asked Grant Theron about TB in South Africa



Grant Theron, Stellenbosch University.

GT: TB in South Africa is the single biggest cause of death. And parts of Cape Town have more TB per capita than most other parts of the world. It's almost a situation where TB is killing people in Cape Town every year at the same rate that COVID19 did at its peak. If you think about all the panic and changes that had to be made in response to COVID19, it's very strange and unusual that we don't have that same urgency for TB. In South Africa in general, there are 200,000 to 300,000 TB cases every year. Another thing that people don't understand is that TB mortality in South Africa is also very high, which means that even though we're diagnosing a lot of people, we're probably diagnosing them far too late, when they can no longer benefit from treatment.

MS: Why do you say that you diagnose people way too late?

GT: The fundamental reasons are we've relied on symptoms too much in the past, and we've also relied on people self-reporting to the clinic. And there's a huge amount of stigma associated with TB, probably more so than HIV. That really pushes people back in terms of even wanting to think about TB. And then some people, even when they find out they're TB positive, they are in denial and don't get the support they need to accept the diagnosis and take their treatment.

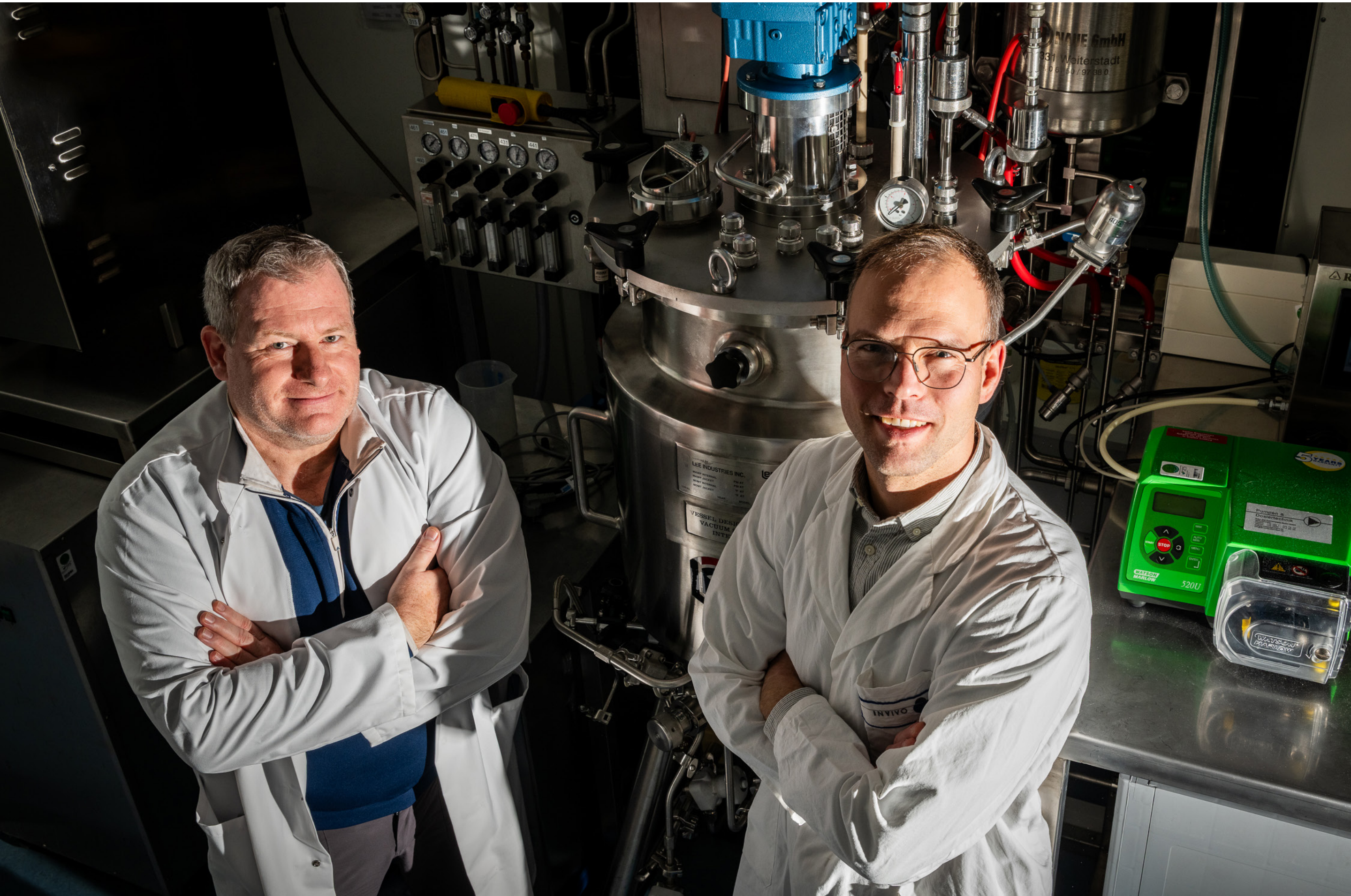
TB has never received the level of effort needed to reduce the stigma. I think a lot of it is tied up with health literacy as well as old beliefs about TB; that if people get TB, it's because of some bad spiritual reason or because of some something bad that their family did.

What some researchers have shown is that with the newer tests, if you do that test in front of the person and they see that specimen go from their own body into the machine and they see the machine say positive on it, they believe it much more. There's much greater buy-in. This is something that the HIV field has done very well.

MS: A rapid test like SeroSelectTB, do you think it would be a useful tool to be employed in the field, going out of the clinics?

GT: Yes, it's just impossible to have everyone with risk factors in the community come to the clinic! A rapid test could reduce the number of people that need to be referred for molecular testing, which is expensive but critical. We can't get away from the need for confirmatory testing. But if you can reduce the number of people incorrectly referred, especially by being able to test a patient in a single encounter because we know they often don't come back, I think it will be a game changer.

At InVivo BioTech Laboratories where protein expression becomes an art



At the site where SeroSelectTB antigens are produced - InVivo BioTech: Christian Schwiebert and Tim Welsink.

More than 100 *Mycobacterium tuberculosis* (Mtb) genes encoding proteins with diagnostic potential were investigated at the Norwegian Institute of Public Health.

Selected proteins were cloned and expressed in a eukaryotic system at InVivo BioTech Services GmbH, Hennigsdorf, Germany.

DNA constructs encoding the selected Mtb antigens for efficient expression as IgG-fusion proteins via transient production in mammalian cell line were designed and optimized. This approach facilitates the purification of correctly folded antigens, an essential process for efficient antibody capture.



*From Start to Finish -
InVivo BioTech Laboratories*



Julius Schlaaf, supervising starter cultures growth.



Tim Welsink with small 1L fermentor.



Juliane Salomon, running protein purification protocol.



Purified antigens ready for shipment to Lateral Flow Labs in Cape Town, South Africa.

Looking ahead

- » The SeroSelectTB project will end on 31 December 2025.
- » Project partners are currently finalizing data analysis and publications.
- » We hope that lessons learned during the SeroSelectTB project will be sustained and activities expanded through local and national initiatives!
- » The SeroSelectTB project website will be updated as activities continue, and publications will be posted as soon as available at <https://www.seroselecttb.org/seroselecttb-publications>.



A view over Kilimanjaro mountain, Tanzania, 2025.

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