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23 YEARS OF TB RESEARCH

satvi

TOWARDS A WORLD WITHOUT TB

ANNUAL REPORT 2023

vision and mission

Vaccines | Drugs | Diagnostics | Epidemiology | Immunology

Our Mission

Innovative and High-Quality TB Vaccine Research to impact the Global Epidemic

Our Vision

A World Without TB

Our Values

Innovation I Respect I Employee Recognition | Accountability Communication | Commitment | Honesty

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contents

director's foreword

It is a pleasure to present the SATVI 2023 Annual Report, which showcases the breadth and depth of achievements of a truly amazing SATVI Team, whether in the laboratory, in the clinic, or in the community.

It has never been clearer that SATVI is part of a global effort to Stop TB through development and testing of new TB vaccines by multiple stakeholders. For the first time, there is a palpable sense of excitement in our field at the start of a Phase 3 licensure trial of the leading candidate TB vaccine M72/AS01E, for which results may be available within the next five years. Meanwhile, the results of efficacy trials of BCG revaccination for Prevention of Infection (POI) and H56:IC31 for Prevention of Recurrence (POR) indications will challenge our resilience and ability to learn from disappointing findings. Other efficacy trials have already started, including an infant Phase 3 trial of MTBVAC; or are planned, including a Phase 2b trial of MTBVAC in adolescents and adults.

These exciting new TB vaccine trials, in tandem with a number of new trials of the effectiveness of new drug treatment regimens for both drug-sensitive and drug-resistant TB, will form the majority of the SATVI research portfolio for the next five years. However, the third iteration of the RePORT South Africa network will continue the SATVI tradition of conducting large, innovative TB biomarker studies. This edition of the SATVI Annual Report tells the story of one such observational study, the Adolescent Cohort Study, which started almost 20 years ago and has now come full circle, allowing potentially protective *Mycobacterium tuberculosis* antigens to be discovered and incorporated into an early stage mRNA vaccine candidate that has already entered pre-clinical testing.

The future of TB vaccines is bright. The expectation that one or more candidate vaccines currently in efficacy trials will report a signal of protection in the next five years highlights the urgency of understanding how a new TB vaccine would be implemented in the Breede Valley community. We have a short window of opportunity to understand and overcome the drivers of vaccine hesitancy, to optimize the availability and uptake of a new and more effective TB vaccine for the people who need it most.

Professor Mark Hatherill
Director, SATVI

governance & senior clinical research team

EXECUTIVE COMMITTEE

PROFESSOR MARK HATHERILL, DIRECTOR

Dr Mark Hatherill (MD, FCPaed) is a clinical triallist, trained as a specialist paediatrician, who is active in the design and implementation of innovative trials of new tuberculosis (TB) vaccines and preventive strategies, through several consortia. His academic focus includes translational evaluation of new biomarkers and screening tests for TB, and clinical development of novel TB vaccine candidates. He is a full member of the Institute of Infectious Disease and Molecular Medicine (IDM) at the University of Cape Town (UCT), and the South African Principal Investigator of the Regional Prospective Observational Research in Tuberculosis (RePORT) South Africa Consortium.

Dr Hatherill is funded by institutional research grants from the Gates Medical Research Institute, the South African Medical Research Council (SAMRC), the US National Institutes of Health and Civilian Research and Development Foundation (CRDF), and the European and Developing Countries Clinical Trials Partnership (EDCTP).

PROFESSOR TOM SCRIBA,
DEPUTY DIRECTOR IMMUNOLOGY

Dr Tom Scriba (PhD) directs the Clinical Immunology Laboratory at SATVI. He was trained in biological sciences at Stellenbosch University and obtained a DPhil (PhD) in T-cell immunology at Oxford University. He returned to South Africa in 2006 to complete a postdoctoral fellowship in paediatric and clinical immunology in TB and vaccinology at the IDM, UCT.

Dr Scriba's research interests include immunopathogenesis of infectious disease, and in particular *Mycobacterium tuberculosis (M.tb)*, development of immuno-diagnostics, development of novel TB vaccines, discovery of immune correlates of risk of TB disease and correlates of protection against *M.tb* infection and TB disease.

Dr Scriba is a full member of the IDM and of the Collaboration for TB Vaccine Discovery of the Bill and Melinda Gates Foundation (BMGF), and is funded by competitive grants from the BMGF, the National Research Foundation (NRF), SAMRC, the US National Institutes of Health and the European Union.

DR MASOODA KASKAR,
CHIEF OPERATIONS OFFICER

Dr Masooda Kaskar joined SATVI's senior leadership team in 2016 to advance organisational excellence and drive innovation and growth. Her leadership experience spans the corporate, public and philanthropic sectors, with a focus on strategic business development, governance and operations. In her current role she is a key driver of SATVI's transformation efforts and risk management plans to ensure the growth and long-term sustainability of the organisation.

Dr Kaskar previously occupied several senior leadership positions in the pharmaceutical industry. At Novartis she was instrumental in developing and implementing transformational growth plans that resulted in establishing Novartis's leadership position within the industry. She holds an MBChB degree from UCT and an MBA degree from UCT's Graduate School of Business.

MARWOU DE KOCK,
FIELD SITE MANAGER

Marwou de Kock holds a master's degree in clinical research administration from UCT, as well as degrees in biomedical science and laboratory management. She has worked at SATVI since 2002 and has intricate knowledge of the site, the people and procedures in the laboratory, clinical operations, and community engagement. She helped establish the SATVI Field Site Laboratory and developed it into a world-class facility that received SANAS accreditation in 2010.

Ms de Kock is responsible for managing the SATVI Field Site, overseeing and managing service delivery for all operations, and coordinating and implementing multiple research projects.

SENIOR CLINICAL RESEARCH TEAM

ASSOCIATE PROFESSOR ELISA NEMES

Dr Elisa Nemes completed a PhD in HIV-specific T-cell immunology in Italy and France in 2008. She then worked on paediatric immune responses to HIV and TB in Cameroon.

In 2011 Dr Nemes joined SATVI, where she has been involved in basic immunology studies; the development of immuno-diagnostics and clinical trials of new TB vaccines; studies of host correlates of risk of TB disease and correlates of protection from *M.tb* infection and TB disease in infants, adolescents and adults; and studies of BCG/TB immune reconstitution inflammatory syndrome (IRIS) in HIV-positive children. She is funded by competitive grants from the US National Institutes of Health and the Bill & Melinda Gates Foundation.

Dr Nemes was promoted to Associate Professor ad hominem in 2019 and became a full member of the IDM in 2020.

ASSOCIATE PROFESSOR MICHÈLE TAMERIS

Dr Michèle Tameris graduated from UCT with an MBChB degree in 1980. For many years she worked in the public health sector, in Cape Town and in Worcester. In 2003 she joined SATVI as a clinical researcher; she was promoted ad hominem to Senior Clinical Researcher in January 2019, and in January 2022 to Chief Research Officer, with the title of Associate Professor. Since 2005 she has been an investigator on all 32 vaccine trials of 10 candidate TB vaccines that have been conducted at SATVI, including 12 as principal investigator.

Dr Tameris has been awarded two Wellcome Trust International Engagement awards (2012 and 2014) for projects using drama to improve community understanding of TB research and remains actively involved in community engagement and advocacy programmes. She is a member of the Stop TB Partnership Working Group on New Vaccines, leading the Advocacy sub-committee.

ASSOCIATE PROFESSOR DR ANGELIQUE KANY KANY LUABEYA

Dr Angelique Kany Kany Luabeya graduated as a medical doctor in 1996 from the University of Kinshasa (Democratic Republic of Congo) and holds a master's degree in epidemiology from the London School of Hygiene and Tropical Medicine (LSHTM).

She joined SATVI in 2009 as a clinical investigator and has been involved as principal investigator in the implementation and conduct of the clinical trials of several TB vaccines (AERAS C035-456, IDRI-TBVPx-203, VPM1002-ZA-2.13TB, BCG REVAX and MTBVAC) in healthy adults and adolescents, TB patients and newborn infants. More recently she led as SATVI principal investigator on two COVID-19 vaccine trials, the ENSEMBLE study and the SISONKE trial, which vaccinated healthcare workers in South Africa. She also contributed to the implementation of the NOVAVAX COVID-19 vaccine study. She was promoted to chief research officer in 2020.

Dr Luabeya is the principal investigator on several diagnostic studies including TB case-finding by oral swab PCR, molecular confirmation of TB treatment and *M.tb* correlates of risk using molecular epidemiology, conducted in collaboration with the University of Washington and the Columbia University Mailman School of Public Health.

DR JUSTIN SHENJE, CHIEF RESEARCH OFFICER

Dr Justin Shenje graduated as a medical doctor from the University of Zimbabwe in 2004, then completed a master's degree in clinical epidemiology at the University of Pretoria, before joining the SATVI team as a clinical investigator in 2015.

He has been an investigator on two groundbreaking TB drug clinical trials, the A5343 and A5349 studies. The A5343 study showed that Delamanid and Bedaquiline, two new anti-TB drugs, can be safely combined in the treatment of MDR TB; and the A5349 study showed that a four-month Rifapentine-based drug-sensitive TB regimen was non-inferior to the standard six-month drug-sensitive treatment regimen. Dr Shenje is principal investigator on a number of ongoing studies, including the A5400B study, which evaluates the effectiveness of the use of Delamanid in TB prophylaxis of MDR TB household contacts; the A5356 study which seeks to evaluate the safety and efficacy of two linezolid-based MDR TB treatment regimens; the BNT164-02 phase 1 study, which investigates the safety and immunogenicity of two novel mRNA TB vaccines; and the CORTIS KIDS study, a paediatric TB diagnostic study which seeks to evaluate novel diagnostic tests for child household contacts under the age of five years.

DR SIMON MENDELSOHN, CHIEF RESEARCH OFFICER

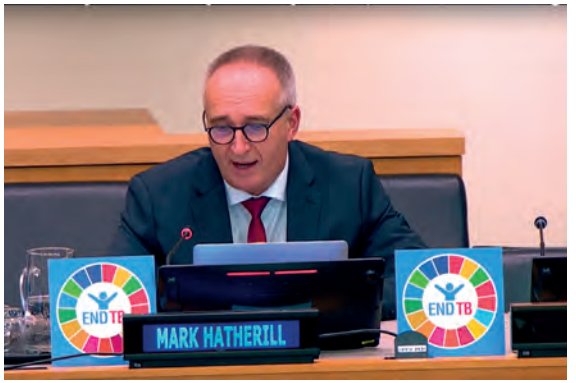
Dr Simon Mendelsohn graduated from the University of Cape Town as a medical doctor in 2011. While on a Rhodes Scholarship he read for two master's degrees at the University of Oxford, in Immunology (2015) and International Health and Tropical Medicine (2016) and obtained a Diploma in Tropical Medicine and Hygiene from the Royal College of Physicians (London). He has experience in HIV and TB clinical medicine; most recently with Médecins Sans Frontières, implementing HIV and TB programmes in Malawi prisons.

Dr Mendelsohn joined SATVI as a clinical investigator in 2017, and in 2022 completed his PhD in Clinical Science and Immunology, which evaluated host-blood gene signatures for the diagnosis and prognosis of pulmonary TB. He is a Senior Researcher and Fellow of the Institute of Infectious Disease and Molecular Medicine, with a research focus on new tests for diagnosing *M.tb* infection and early (pre-symptomatic) TB disease, and biomarkers for guiding TB preventive and curative treatment.

DR NICOLETTE TREDOUX, CLINICAL INVESTIGATOR

Dr Nicolette Tredoux graduated from the University of Stellenbosch in 1998 with an MBChB degree. She worked for many years in the public and private sector in Worcester and Robertson, both as a general practitioner and as a research medical officer. She obtained a postgraduate diploma in occupational medicine at Stellenbosch University in 2015. Dr Tredoux joined SATVI in 2021 as a part-time clinical investigator and has been working there full-time since September 2022.

highlights from 2023



SATVI DIRECTOR CALLS FOR INCREASED INVESTMENT IN TB VACCINE RESEARCH AT UN HIGH LEVEL MEETING ON TUBERCULOSIS, SEPTEMBER 2023.

NEW YORK: On 23 September 2023 our Director, Professor Mark Hatherill, addressed the UN High Level Meeting on TB, calling for a quantum leap in TB vaccine research and for increased development (R&D) funding to deliver the transformative tools needed to end the TB pandemic.

In his presentation, Professor Hatherill reflected on the unprecedented advances made in new diagnostics and treatments to reduce the severity of TB disease and risk of death for TB patients. "Although these advances are necessary," he said, "they are not sufficient to end TB. A vaccine that prevents people from getting TB and infecting others is key to stopping the epidemic."

M72AS01$_E$ TB vaccine

For the first time, the most advanced TB vaccine candidate yet, the M72AS01$_E$, has brought us close to achieving a new, safe and effective TB vaccine. In a *phase 2b trial*, this vaccine has shown 50% protection in adults exposed to TB; it will soon enter a large confirmatory trial, which is expected to deliver results within five years.

If vaccine protection is confirmed, the impact will be transformative for TB control efforts.

Strategy needed

Finance for a comprehensive R&D strategy for all seven late-stage TB vaccines is needed to reach their full potential. There is also a critical shortage of early-stage vaccines in the TB vaccine pipeline, and therefore urgent investment is needed to move the most promising, including mRNA vaccines, through human trials.

"To ensure uptake of vaccines in communities, we need to partner with affected communities in high TB-burden countries to help deliver information about vaccines in ways that resonate with those communities, and to help scientists ask the right questions," said Hatherill. "Which new TB vaccines will be safe and effective in people living with HIV? And in the elderly, infants, and people not yet

> "Over a 25-year period, such an effective vaccine could prevent up to 76 million TB cases and 8.5 million TB deaths, and result in a US$3.8 billion saving in treatment costs."

exposed to TB? We also need to address the fundamental question of how to recognise the protective immune response to vaccination."

This work will require a major leap in annual investment in TB vaccine research, which is currently only 12% of current TB R&D funding and less than a fraction of 1% of the US$100 billion that was committed to COVID-19 vaccine development. The bold response to the COVID-19 pandemic saw 40 efficacy trials, with more than 400 000 volunteers, produce a dozen approved COVID-19 vaccines in only three years.

"By contrast, decades of underfunding for TB vaccines [have] blunted the scope of our ambition. A cautious approach of ad hoc funding of individual vaccine trials did not and will not accelerate TB vaccine development. We need a programme of investment in the entire TB vaccine pipeline – that both tolerates the inherent risk in R&D, and reduces commercial uncertainty – to do the trials that are necessary; and not those trials we think we can afford," Hatherill said.

Collective response

Investment in TB vaccines cannot be left to a handful of funders in low TB-burden countries, he stressed. To ensure an equitable say in the TB vaccine research agenda, and to ensure that the voices of affected communities are heard, stakeholders in high TB-burden countries must contribute their fair share of funding for development. Delivery of a new TB vaccine will require a collective response – from governments, industry, scientists and civil society – to conduct more trials of more vaccines more quickly, and to prepare health systems for their implementation.

In conclusion, Hatherill posited that a new, safe and effective vaccine to break the cycle of TB transmission among adults could be delivered within the next five years. Such a vaccine could save millions of lives, avert the burden of disease for tens of millions of patients and their families, and save billions of dollars in health system costs by 2050.

Supply of the best TB vaccines to the communities that need them will require an immediate quantum jump in investment – not only for accelerated vaccine testing, but also for implementation studies and to ensure sustainable, diversified manufacture.

"The fact that the TB epidemic persists in 2023 is an indictment of our lack of urgency to tackle a pathogen that has affected humans for thousands of years. TB is no less of an emergency than it was 30 years ago.

"We should not need to imagine the bold response to this global health emergency and the rapid mobilisation of funding to make new vaccines against this devastating disease.

"So let us stop imagining and find the political will to deliver these new vaccines to end TB."

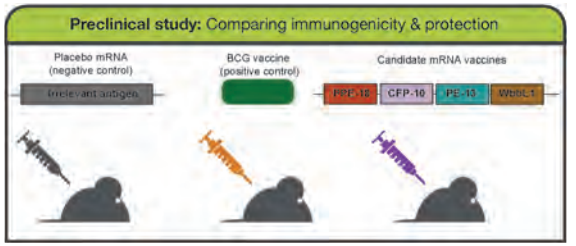
> "Let us imagine that *Mycobacterium tuberculosis* was discovered today, an infectious airborne pathogen that in the coming year would cause 10.6 million people to fall sick with TB, and 1.6 million TB deaths."

TARGETING PROTECTIVE *MYCOBACTERIUM TUBERCULOSIS*-SPECIFIC T-CELL CLONES WITH NOVEL MRNA VACCINES

Principal Investigator: Munyaradzi Musvosvi
Funder: South African Medical Research Council

To date, we have designed and produced research-grade mRNA vaccine candidates that include different polyprotein formulations of the four *M.tb* antigens. Our results show that different formulations result in different patterns of T-cell responses in mice, data which allow us to rationally select the most promising candidates.

We are also performing experiments to determine how well these different mRNA vaccine candidates protect mice against *M.tb* compared to unvaccinated mice. We intend to continue the preclinical assessment of these vaccine candidates, and ultimately wish to select two candidates for evaluation of safety and immunogenicity in phase I trials in humans.



Several novel mRNA TB vaccine candidates are being assessed in preclinical models. This project is supported by the South African mRNA Vaccine Consortium (SAMVAC) and funded by the SA-MRC. SAMVAC was established in response to the lack of local vaccine production capacity during the COVID-19 pandemic.

> In collaboration with researchers at the University of Cape Town, University of the Witwatersrand, and Afrigen Biologics & Vaccines, we are developing a novel TB vaccine that incorporates four antigens discovered in a previous study in which we compared T-cell responses in adolescent TB progressors with those who successfully controlled *M.tb* infection (Musvosvi et al., Nature Immunology 2023).

COMPLETING THE CIRCLE: THE INCREDIBLE SUCCESS STORY OF HOW THE ADOLESCENT COHORT STUDY HAS LED TO THE DEVELOPMENT OF A HOME-GROWN TB VACCINE CANDIDATE

The Adolescent Cohort Study (ACS) was one of three groundbreaking large-scale epidemiological studies conducted by SATVI between 2004 and 2009, among various age and subpopulation groups, to generate data about TB prevalence and incidence in the Breede Valley area, and which eventually would lay the basis for late-phase TB vaccine studies.

The ACS was conducted between 2005 and 2009, under the leadership of Professors Greg Hussey, Hassan Mahomed, Tony Hawkridge, Michèle Tameris and Willem Hanekom, and Ms Fazlin Kafaar, and as many as 120 SATVI staff ventured into schools to reach participants. The study was funded by Aeras and the Bill & Melinda Gates Foundation.

A total of 6 363 adolescents were enrolled (which amounted to 58% of the school-going population of Worcester and surrounding areas), and followed for two years. During the follow-up phase, 67 cases of bacteriologically confirmed TB were detected, suggesting an overall incidence rate of 0.45 per 100 person-years (95% confidence interval 0.29-0.72). Being black or of mixed race, being the child of a mother with education level at primary school or less or unknown, and having a positive baseline QuantiFERON assay or TST emerged as significant predictors of TB disease.

A significant aspect of this research study was the vast number of blood samples collected from participants enabling us to study the immune responses to *M.tb* infection and those associated with TB disease, and to identify immune correlates of risk.

Creating a unique understanding of the immunology of TB

Blood samples collected from the ACS study have provided SATVI researchers, as well as local and international collaborators, with a unique resource to study the immune response to TB. The early and meticulous work of the many nurses, clinical research workers, investigators, data team, and logistics and laboratory staff was pivotal in shaping the study for research on TB in teenagers. The study has resulted in an ever-growing body of research (see list at the end of this section).

For example, the inclusion of both the Tuberculin Skin Tests (TST) and Quantiferon tests in the ACS has allowed us to study immune responses shortly after *M.tb* infection. The insights gained from these studies have been instrumental in developing tests to detect recent infection and to establish the risk of TB in those with a recent infection. Identifying individuals shortly after infection is crucial, because the risk of developing TB is highest during the first two years of infection. This led to the development of methods used as endpoints in the C-040 and BCG REVAX prevention of infection trials.

ACS samples have also been critical to studying differences in immune responses between individuals who successfully control the infection and those who progress to active disease. The insights gained from this research have contributed to the identification of the first immune signatures associated with TB progression. This work directly led to the idea and ultimately the design of the CORTIS-01 trial, which allowed us to test whether a TB risk biomarker can be used to identify those who would benefit most from TB-preventive therapy.

How T-cell responses in non-progressors (controllers) and progressors have informed TB vaccine antigen selection.

More recently, the frozen samples from the ACS have informed the design of a new candidate TB vaccine. One of the challenges TB researchers are faced with when designing a TB vaccine is deciding which parts of the bacterium the immune response should target. *M.tb* is able to produce ~4 000 proteins (Musvosvi, 2023), offering just too many options.

Some vaccine developers have attenuated or weakened the bacterium to the point that it can no longer cause disease, and have used this as the basis for their vaccine – for example, the VPM1002 and MTBVAC vaccines. Others have identified a small number of specific proteins produced by the bacterium and commonly recognised by immune cells that trigger strong immune responses in people who are infected with *M.tb*. Once these specific targets are identified, researchers then examine (in animal studies) whether mice that are vaccinated with new vaccines can control *M.tb* compared to unvaccinated mice. These approaches have been used by virtually all developers in the design of new TB vaccine candidates.

We wanted to use information from people who

successfully controlled their *M.tb* infection, and compare this to immune responses in people who could not control *M.tb* and then progressed to TB disease. Our goal was thus to develop a vaccine by selecting the protein targets that are recognised by immune responses in people who effectively control *M.tb* infection.

To achieve this, we conducted a detailed analysis of T-cells collected from adolescents during the course of the ACS. Specifically, we compared *M.tb*-specific T-cells that target *M.tb* proteins between QuantiFERON-positive adolescents who successfully controlled *M.tb* infection, and QuantiFERON-positive adolescents who developed TB in the ACS. Initially, we identified and isolated individual *M.tb*-specific T cells and then analysed thousands of cells from many participants, utilising a technique called single-cell T-Cell Receptor (TCR) sequencing. Combining this technique with one that allowed us to determine which proteins of the *M.tb* bacterium are recognised by *M.tb*-specific T-cells that are enriched in controllers unlocked the identity of very promising TB vaccine antigens.

The home-grown TITAN-01 mRNA vaccine candidate

Having identified the specific antigen components of the bacterium that the controllers target, we had the necessary information to design a new TB vaccine candidate. With support from the South African Medical Research Council (SA-MRC), we are now undertaking the next steps to develop the vaccine, in partnership with colleagues at the University of the Witwatersrand, the University of Cape Town, and Afrigen Biologics.

The next phase of development includes pre-clinical assessment of several different variants of the vaccine to identify the optimal candidate, while also establishing safety, immunogenicity and protection in the murine model. While it is still early along the vaccine development timeline, we are excited and hopeful about this vaccine contributing to the fight against TB.

ADOLESCENT COHORT STUDY

Selected key references:

Mahomed H, Hawkridge T, Verver S, Geiter L, Hatherill M, Abrahams DA, Ehrlich R, Hanekom WA, Hussey GD; SATVI Adolescent Study Team. Predictive factors for latent tuberculosis infection among adolescents in a high-burden area in South Africa. *International Journal of Tuberculosis and Lung Disease*, 2011; 15(3):331-6.

Mahomed H, Hawkridge T, Verver S, Abrahams D, Geiter L, Hatherill M, Ehrlich R, Hanekom WA, Hussey GD. The tuberculin skin test versus QuantiFERON TB Gold® in predicting tuberculosis disease in an adolescent cohort study in South Africa. *PLoS One*, 2011; 29;6(3):e17984.

Machingaidze S, Verver S, Mulenga H, Abrahams DA, Hatherill M, Hanekom W, Hussey GD, Mahomed H. Predictive value of recent QuantiFERON conversion for tuberculosis disease in adolescents. *American Journal of Respiratory and Critical Care Medicine*, 2012; 186(10):1051-6.

Mahomed H, Ehrlich R, Hawkridge T, Hatherill M, Geiter L, Kafaar F, Abrahams DA, Mulenga H, Tameris M, Geldenhuys H, Hanekom WA, Verver S, Hussey GD. TB incidence in an adolescent cohort in South Africa. PLoS One, 2013; 8(3):e59652.

Andrews JR, Hatherill M, Mahomed H, Hanekom WA, Campo M, Hawn TR, Wood R, Scriba TJ. The dynamics of QuantiFERON-TB gold in-tube conversion and reversion in a cohort of South African adolescents. *American Journal of Respiratory and Critical Care Medicine*, 2015;191(5):584-91.

Zak DE, Penn-Nicholson A, Scriba TJ, Thompson E, Suliman S, Amon LM, Mahomed H, Erasmus M, Whatney W, Hussey GD, Abrahams D, Kafaar F, Hawkridge T, Verver S, Hughes EJ, Ota M, Sutherland J, Howe R, Dockrell HM, Boom WH, Thiel B, Ottenhoff THM, Mayanja-Kizza H, Crampin AC, Downing K, Hatherill M, Valvo J, Shankar S, Parida SK, Kaufmann SHE, Walzl G, Aderem A, Hanekom WA; ACS and GC6-74 cohort study groups. 2016. A blood RNA signature for tuberculosis disease risk: a prospective cohort study. *Lancet*, 2016; 387(10035):2312-2322.

Lindestam Arlehamn CS, McKinney DM, Carpenter C, Paul S, Rozot V, Makgotlho E, Gregg Y, van Rooyen M, Ernst JD, Hatherill M, Hanekom WA, Peters B, Sette A, Scriba TJ. A quantitative analysis of complexity of human pathogen-specific CD4 T-cell responses in healthy M. tuberculosis-infected South Africans. *PLoS Pathogens,* 2016; 12(7):e1005760.

Nemes E, Rozot V, Geldenhuys H, Bilek N, Mabwe S, Abrahams D, Makhethe L, Erasmus M, Keyser A, Toefy A, Cloete Y, Ratangee F, Blauenfeldt T, Ruhwald M, Walzl G, Smith B, Loxton AG, Hanekom WA, Andrews JR, Lempicki MD, Ellis R, Ginsberg AM, Hatherill M, Scriba TJ; C-040-404 Study Team and

the Adolescent Cohort Study Team. Optimisation and interpretation of serial QuantiFERON testing to measure acquisition of *Mycobacterium tuberculosis* infection.
American Journal of Respiratory and Critical Care Medicine, 2017;196(5):638-648.

Scriba TJ, Penn-Nicholson A, Shankar S, Hraha T, Thompson EG, Sterling D, Nemes E, Darboe F, Suliman S, Amon LM, Mahomed H, Erasmus M, Whatney W, Johnson JL, Boom WH, Hatherill M, Valvo J, De Groote MA, Ochsner UA, Aderem A, Hanekom WA, Zak DE; other members of the ACS cohort study team. Sequential inflammatory processes define human progression from *M. tuberculosis* infection to tuberculosis disease.
PLoS Pathogens, 2017;13(11):e1006687.

Scriba TJ, Carpenter C, Carrasco Pro S, Sidney J, Musvosvi M, Rozot V, Seumois G, Rosales SL, Vijayanand P, Goletti D, Makgotlho E, Hanekom W, Hatherill M, Peters B, Sette A, Lindestam Arlehamn CS. Differential recognition of *M.tb*-specific epitopes as a function of tuberculosis disease history.
American Journal of Respiratory and Critical Care Medicine, 2017; 196 (6):772-781.

Penn-Nicholson A, Hraha T, Thompson EG, Sterling D, Kimbung SM, Wall KM, Fisher M, Suliman S, Shankar S, Hanekom WA, Janjic N, Hatherill M, Kaufmann SHE, Sutherland J, Walzl G, De Groote MA, Ochsner U, Zak DE, Scriba TJ, ACS and GC6–74 cohort study groups. Discovery and validation of a prognostic proteomic signature for tuberculosis progression: A prospective cohort study.
PLoS Medicine, 2018; 16(4):e1002781.

Penn-Nicholson A, Mbandi SK, Thompson E, Mendelsohn SC, Suliman S, Chegou NN, Malherbe ST, Darboe F, Erasmus M, Hanekom WA, Bilek N, Fisher M, Kaufmann SHE, Winter J, Murphy M, Wood R, Morrow C, Van Rhijn I, Moody B, Murray M, Andrade BB, Sterling TR, Sutherland J, Naidoo K, Padayatchi N, Walzl G, Hatherill M, Zak D, Scriba TJ; Adolescent Cohort Study team; GC6-74 Consortium; SATVI Clinical and Laboratory Team; ScreenTB Consortium; AE-TBC Consortium; RePORT Brazil Team; Peruvian Household Contacts Cohort Team; CAPRISA IMPRESS team. RISK6, a 6-gene transcriptomic signature of TB disease risk, diagnosis and treatment response.
Scientific Reports, 2020;10(1):8629.

Huang H, Wang C, Rubelt F, Scriba TJ, Davis MM. Analysing the *Mycobacterium tuberculosis* immune response by T-cell receptor clustering with GLIPH2 and genome-wide antigen screening.
Nature Biotechnology, 2020; (10):1194-1202.

Ahmed M, Thirunavukkarasu S, Rosa BA, Thomas KA, Das S, Rangel-Moreno J, Lu L, Mehra S, Mbandi SK, Thackray LB, Diamond MS, Murphy KM, Means T, Martin J, Kaushal D, Scriba TJ, Mitreva M, Khader SA. Immune correlates of tuberculosis disease and risk translate across species.
Science Translational Medicine, 2020;12(528):eaay0233.

Mpande CAM, Dintwe OB, Musvosvi M, Mabwe S, Bilek N, Hatherill M, Nemes E, Scriba TJ; SATVI Clinical Immunology Team. Functional, antigen-specific stem cell memory (TSCM) CD4+ T-cells are induced by human *Mycobacterium tuberculosis* infection.
Frontiers in Immunology, 2021; 9:324.

Mpande CAM, Rozot V, Mosito B, Musvosvi M, Dintwe OB, Bilek N, Hatherill M, Scriba TJ, Nemes E; ACS Study Team. Immune profiling of *Mycobacterium tuberculosis*-specific T cells in recent and remote infection.
EBioMedicine, 2021; 64:103233.

Mpande CAM, Musvosvi M, Rozot V, Mosito B, Reid TD, Schreuder C, Lloyd T, Bilek N, Huang H, Obermoser G, Davis MM, Ruhwald M, Hatherill M, Scriba TJ, Nemes E; ACS Study Team. Antigen-specific T-cell activation distinguishes between recent and remote tuberculosis infection.
American Journal of Respiratory and Critical Care Medicine, 2021; 203(12):1556-1565.

Musvosvi M, Huang H, Wang C, Xia Q, Rozot V, Krishnan A, Acs P, Cheruku A, Obermoser G, Leslie A, Behar SM, Hanekom WA, Bilek N, Fisher M, Kaufmann SHE, Walzl G, Hatherill M, Davis MM, Scriba TJ; Adolescent Cohort Study team; GC6-74 Consortium. T-cell receptor repertoires associated with control and disease progression following *Mycobacterium tuberculosis* infection.
Nature Medicine, 2023; 29(1):258-269.

selection of clinical and immunology studies

TB VACCINE STUDIES

PHASE 3 STUDY MTBVAC 203

MTBVAC in newborns: a randomised, double-blind controlled phase 3 trial to evaluate the efficacy, safety and immunogenicity of MTBVAC administered in healthy HIV unexposed and HIV exposed uninfected newborns in tuberculosis-endemic regions of sub-Saharan Africa

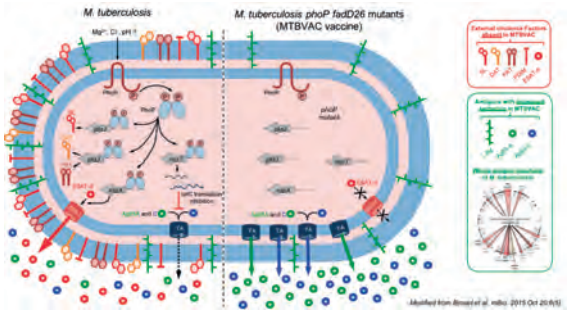
Principal Investigator: Michèle Tameris
Study Coordinator: Danelle van As
Funders: European and Developing Countries Clinical Trials Partnership, Biofabri
Sponsor: Biofabri

ONGOING

MTBVAC 203 is a phase 3 randomised, controlled, double-blind efficacy study of the MTBVAC vaccine (2.5 x 10^5 CFUs) in healthy HIV-unexposed and HIV-exposed, uninfected infants, at four research sites in South Africa, as well as one research site each in Senegal and Madagascar. During the first week of life, newborns are randomised to receive either the MTBVAC or BCG (standard of care) vaccine, and followed up for a minimum of 24 months and a maximum of 72 months.

Enrolment commenced in October 2022. Of the planned 7 120 study participants, vaccine immunogenicity will be measured in the first 460, and reactogenicity in the first 1 000. Efficacy of MTBVAC against TB compared to BCG will be assessed in the 7 000 infants enrolled at South African sites. SATVI will enrol 1 750 infants in this trial.

CLINICALTRIALS.GOV IDENTIFIER: NCT04975178



The phoP and fadD26 rational inactivation in MTBVAC results in virulence attenuation and enhanced immunogenicity relative to the *M. tuberculosis* pathogen. MTBVAC does not secrete ESAT-6, a major virulence factor of *M. tuberculosis*. MTBVAC lacks acyltrehalose-derived lipids, pthiocerol dimycocerosates and sulfolipids involved in virulence and immunomodulation. MTBVAC also secretes higher ammounts of immunogenic proteins, such as the Ag85 complex. (adapted from Broset, E., *et al.*, 2015)

PHASE 2 STUDY MTBVAC 202

A phase 2a randomised, controlled, dose-defining trial of the safety and immunogenicity of MTBVAC in healthy, BCG-naïve, HIV-unexposed South African newborns

Principal Investigator: Michèle Tameris
Study coordinator: Elizabeth Filander
Funders: European and Developing Countries Clinical Trials Partnership (EDCTP)
Sponsor: Biofabri

ONGOING

MTBVAC 202 is a phase 2a randomised, controlled, double-blind, dose-defining study of the MTBVAC vaccine to evaluate the safety, reactogenicity, immunogenicity and potential for IGRA conversion and reversion of MTBVAC in HIV-unexposed, BCG-naïve South African newborns.

In this study, 99 newborns received either BCG (n=24) or MTBVAC (n=75) at one of three dose levels, with sequential enrolment. Enrolment took place between February 2019 and March 2021, with follow-up completed by March 2022. Following unblinded analysis of safety and immunogenicity data, dosage selection was done for the phase 3 efficacy trial, which commenced in October 2022.

Analysis of all data is complete and the manuscript is in press.

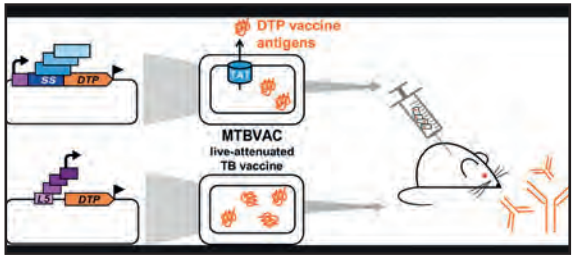
CLINICALTRIALS.GOV IDENTIFIER: NCT03536117

PHASE 1b/2a STUDY MTBVAC A050

MTBVAC Phase 1b/2a randomised, double blind, active-controlled, safety, immunogenicity and dose escalation study in adults in South Africa with and without latent tuberculosis infection (A050)

Principal Investigator: Angelique Kany Kany Luabeya
Study Coordinator: Frances Ratangee
Funders: US National Institutes of Health
Sponsor: International AIDS Vaccine Initiative (IAVI)

ONGOING



This study aimed to evaluate the safety and immunogenicity and establish the optimal dosage in adults of the novel TB vaccine MTBVAC, compared with the BCG vaccine. The study enrolled 144 HIV-negative adults between the ages of 18 and 50 years, with or without evidence of *M.tb* infection assessed by IGRA tests. Participants received a single dose of either the MTBVAC vaccine or the Japan variant of the BCG vaccine. The study completed a 12-month period of follow-up in August 2021. The vaccine was safe and immunogenic in *M.tb*-infected and non-infected participants. The study results are expected to be published during 2024.

CLINICALTRIALS.GOV IDENTIFIER: NCT02933281

PHASE 2 STUDY M72/AS01$_E$ STUDY

A randomised, placebo-controlled, observer-blind, phase 2 study to evaluate the safety and immunogenicity of the investigational M72/AS01$_E$ *Mycobacterium tuberculosis* vaccine in virally suppressed, antiretroviral-treated participants with Human Immunodeficiency Virus (HIV)

Principal Investigator: Michèle Tameris
Study Coordinator: Danelle van As
Sponsor: Bill & Melinda Gates Medical Research Institute, Wellcome Trust

ONGOING

This study was conducted across six sites in South Africa. It assessed the safety and immunogenicity of the M72/AS01$_E$ TB vaccine in virally suppressed, antiretroviral-treated participants with HIV infection, aged between 16 and 35. Enrolment commenced in March 2021 and was complete by June 2021, with follow-up completed in August 2022. Each participant received two doses of the M72/AS01$_E$ vaccine, 28 days apart.

Poorly documented tuberculosis-preventative therapy (TPT) administration and the involvement of clinic staff in the national rollout of the COVID-19 vaccination programme were two of the challenges we encountered in recruitment efforts. The vaccine was well tolerated with no safety signals, was immunogenic, and did not affect HIV viral load or CD4 count. This trial was an important step towards the planned phase 3 efficacy trial of this vaccine to start during quarter two of 2024, because people living with HIV can be safely included. The trial manuscript will be published during 2024.

CLINICALTRIALS.GOV IDENTIFIER: NCT04556981

PHASE 2B STUDY — BCG REVAX

Randomised, placebo-controlled, observer-blind phase IIb study to evaluate the efficacy, safety and immunogenicity of BCG revaccination in healthy adolescents for the prevention of sustained infection with *Mycobacterium tuberculosis*

Principal Investigator: Angelique Kany Kany Luabeya
Study Coordinator: Fazlin Kafaar
Sponsor: Bill and Melinda Gates Medical Research Institute

ONGOING

In a prior Phase 2 trial, BCG revaccination was observed to prevent sustained *M.tb* infection (secondary endpoint, vaccine efficacy [VE] 45%, 95% CI 0.06, 0.68), defined as initial IGRA conversion followed by two additional positive IGRA results three and six months after initial conversion.

We conducted a randomised, double-blind, placebo-controlled phase 2b trial in South Africa to evaluate the safety and efficacy of BCG for the prevention of sustained *M.tb* infection, using the QuantiFERON-TB Gold Plus® assay. IGRA-negative, HIV-negative adolescents 10 to 18 years of age were randomised 1:1 to receive a single dose of BCG or placebo intradermally.

Study follow-up is complete. The primary analysis has been performed, and the results are expected to be published in 2024.

CLINICALTRIALS.GOV IDENTIFIER: NCT04152161

PHASE 1 STUDY — BioNTech

BNT164-02: A phase 1 randomised, placebo-controlled, observer-blind, dose-finding evaluation trial to describe the safety, reactogenicity and immunogenicity of two investigational vaccines against active tuberculosis in BCG-vaccinated, HIV-negative subjects

Principal Investigator: Justin Shenje
Study Coordinator: Christel Petersen
Sponsor: BioNTech

ONGOING

Tuberculosis is the leading cause globally of mortality from a single infectious disease, making developing a vaccine of paramount importance. Currently, the bacillus Calmette-Guérin (BCG) vaccine remains the sole approved vaccine for TB prevention, despite its limited protection. The COVID-19 pandemic resulted in unprecedented efforts to develop vaccines against the virus, resulting in rapid advancements in new vaccine technologies, notably mRNA vaccines.

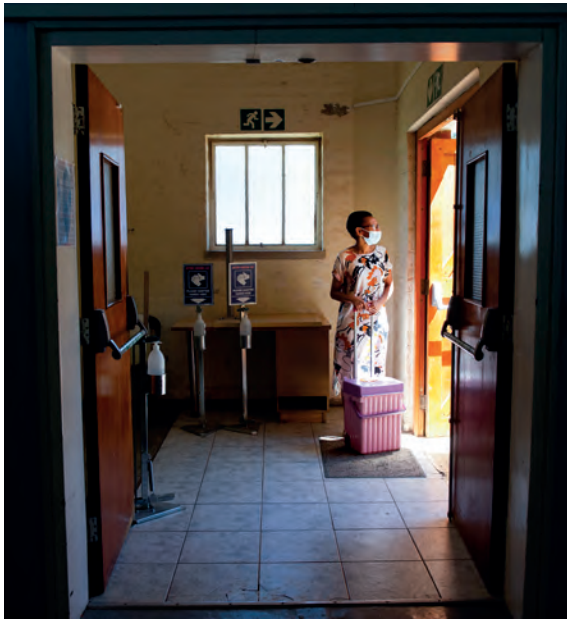
This study aims to evaluate the safety and immunogenicity of various dose levels of two innovative TB mRNA vaccines, BNT164a1 and BNT164b1, both encoding crucial immunogenic antigens of *M.tb*. The study is sponsored by BioNTech.

Participants will receive various doses of one of the two vaccines, or a placebo, and will be followed up over a one-year period. Thus far, data from the vaccine study has not raised any safety concerns. Consequently, the study will escalate vaccine dosage and expand participant inclusion to include a further 540 participants living with HIV.

The study started in July 2023, and the initial phase of the study (which set out to enrol 144 participants) is almost complete.

CLINICALTRIALS.GOV IDENTIFIER: NCT05537038

The BNT delegation visited SATVI on 3 March 2023.



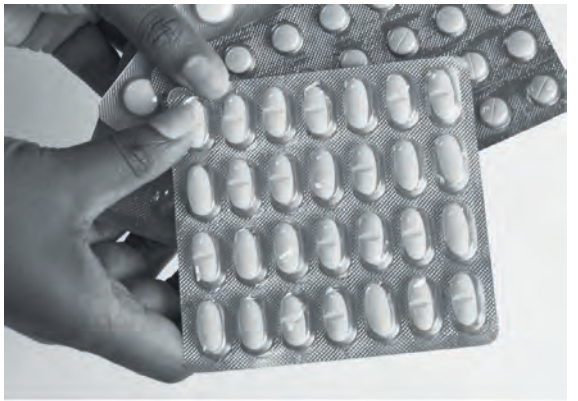
TB TREATMENT STUDIES

PHASE 3 STUDY PHOENIx MDR-TB Study

Protecting households on exposure to newly-diagnosed index multidrug-resistant tuberculosis patients (PHOENIx MDR-TB)

Principal Investigator: Justin Shenje
Study Coordinator: Lynnette Stone
Funder: US National Institutes of Health
Sponsor: Bill and Melinda Gates Medical Research Institute

ONGOING



This study aimed to compare the safety and efficacy of Delamanid with Isoniazid in preventing active TB disease in high-risk household contacts (HHC). It has been established that TB household contacts have a high risk of developing active TB disease; and therefore, the World Health Organisation recommends TB Preventative Therapy (TPT) for high-risk household contacts.

However, to date there has been no consensus on the appropriate TPT regime for drug-resistant TB (DR-TB) household contacts. This phase 3 study will therefore compare the safety and efficacy of Delamanid versus Isoniazid in preventing active TB disease in high-risk household contacts. The study, which started during the fourth quarter of 2019, plans to enrol 352 HHCs, who will receive either Delamanid or Isoniazid over a period of 26 weeks. They will then be followed for the duration of the study, which is 96 weeks.

The study has thus far recruited 57 index cases and 134 high-risk household contacts.

CLINICALTRIALS.GOV IDENTIFIER: NCT03568383

PHASE 3 STUDY A5356

A5356: Safety/tolerability of two Linezolid dosing strategies in combination with a short-course regimen for Rx of drug-resistant TB

Investigator: Justin Shenge
Study Coordinator: Lynnett Stone
Sponsor: National Institute of Allergy and Infectious Diseases
Funder: AIDS Clinical Trials Group (ACTG)

ONGOING

This study aims to assess whether the risk of identified side effects can be mitigated by reducing the dosage frequency of Linezolid from daily to three times weekly, while

increasing the dose from 600 mg to 1 200 mg. The study is sponsored by the ACTG and funded by the US National Institutes of Health.

A variety of new anti-TB drugs including Bedaquiline, Delamanid and Linezolid have recently received approval from both the USA Food and Drug Administration (FDA) and the World Health Organisation (WHO). These advancements present an opportunity to develop safer, shorter, more effective non-injectable anti-TB treatment regimens. However, uncertainty remains regarding the optimal dose of Linezolid. While Linezolid has demonstrated high efficacy, it has been associated with debilitating side effects.

The study plans to enrol 132 patients with multi-drug-resistant TB, who will be randomly assigned to one of the two Linezolid dosage arms. Participants will then receive treatment over 26 weeks, followed by a 46-week follow-up period.

The study, which started in September 2022, has thus far recruited 106 participants, and is anticipated to complete recruitment by July 2024.

CLINICALTRIALS.GOV IDENTIFIER: NCT05007821

PHASE 2 STUDY — PAN TB STUDY

Project to accelerate new treatments for Tuberculosis (PAN-TB)

Principal Investigator: Angelique Kany Kany Luabeya
Study Coordinator: Lisa Beyers
Sponsors: Bill and Melinda Gates Medical Research Institute
Funder: Bill and Melinda Gates Medical Research Institute

ONGOING

PAN-TB PROJECT TO ACCELERATE NEW TREATMENTS FOR TUBERCULOSIS

This phase 2 b/c clinical trial will evaluate whether novel regimens that combine registered products and new chemical entities have the potential to effectively treat drug-sensitive TB (DS-TB) and inform the development of a 'pan-TB' regimen capable of treating all forms of active pulmonary TB.

The two drug regimens, DBQS and PBQS, comprise five antibacterial agents – Bedaquiline, Delamanid, Pretomanid, Quabodepistat [*formerly OPC-167832*] and Sutezolid:

- **DBQS** – Delamanid, Bedaquiline, Quabodepistat and Sutezolid
- **PBQS** – Pretomanid, Bedaquiline, Quabodepistat and Sutezolid

These are designed to explore shorter treatment durations compared to existing drug regimens, without the need for accompanying drug-resistance testing for individuals; with the end goal of identifying a candidate regimen suitable for phase 3 development.

Site Initiation visit, 31 August 2023.

The trial employs an innovative two-stage design to assess the efficacy of the regimens and evaluate their potential to shorten treatment duration.

Stage 1: In the initial stage, the trial will enrol approximately 129 participants. The safety, tolerability, efficacy and pharmacokinetics of the complete DBQS and PBQS regimens, with each drug administered daily for four months (17 weeks), will be evaluated in participants between the ages of 18 and 65 years old who have drug-sensitive pulmonary TB (DSPTB). Approximately 43 participants will receive the six-month (26 weeks) standard-of-care treatment for DS-TB in the countries where trial sites are located.

Stage 2: If successful, the second stage will enrol approximately 400 participants to test the selected regimen at shorter treatment durations, ranging from two to four months, across five arms. An additional 30 to 40 participants will be enrolled in the standard-of-care arm for the second stage of this trial.

CLINICALTRIALS.GOV IDENTIFIER: NCT05686356

DIAGNOSTIC AND BIOMARKER STUDIES

CORTIS KIDS

Study of host blood biomarkers for the diagnosis, prognosis and treatment response of childhood tuberculosis (CORTIS KIDS)

Principal Investigator: Justin Shenje
Study Coordinator: Lisa Beyers
Funder: US National Institutes of Health

ONGOING

> Diagnosing TB in children under five years of age is a challenge, due to the difficulty in sputum collection and the poor sensitivity in this age group.

This observational study will evaluate the diagnostic performance of host biomarkers for diagnosing TB in those with the disease, specifically evaluating and comparing the performance of (1) an RNA transcriptomic signature, (2) a proteomic risk signature, and (3) a T-cell antigen-specific activation assay (TASA) in children under five years of age with a history of TB household contact.

In 2019 the study set out to recruit 435 participants, but despite COVID-19-associated challenges the study was able to recruit 335 participants. Participant follow-up ended in March 2024, and data analysis is ongoing.

BUCCAL SWAB STUDY

Study into tuberculosis case-finding by oral swab polymerase chain reaction (PCR)

Principal Investigator: Angelique Kany Kany Luabeya
Study Coordinator: Christel Petersen
Funders: US National Institutes of Health, Bill & Melinda Gates Foundation

ONGOING

This research will evaluate the feasibility of diagnosing TB from oral swab samples collected from the oral mucosal lining to test for *M.tb* disease, using PCR tests performed on the oral DNA collected from patients with and without TB.

Previous studies (Luabeya et al, 2019) have demonstrated that *M.tb* DNA and/or cells accumulate in the oral cavity of TB patients in amounts that are sufficient to enable non-sputum-based diagnosis of TB.

> Diagnosing pulmonary TB is difficult, due to limited testing, sampling difficulties and test sensitivity issues.

This study evaluates samples collected with tongue swabs for rapid, safe screening for both TB and SARS-CoV-2 (COVID-19). The medical response to the COVID-19 pandemic has highlighted limitations in the testing of symptomatic people. While *M.tb* and SARS-CoV-2 are biologically dissimilar, as respiratory pathogens they share important features, both being airborne diseases with similar clinical presentations including symptoms such as fever, cough, fatigue, difficulty in breathing and chills. In areas where both diseases are prevalent, it is critical to test for both diseases when patients present with common symptoms.

Tongue swabbing can potentially be used to screen simultaneously for COVID-19 and TB in regions of the world where both respiratory diseases are common, because tongue swab samples can be taken from either adults or children, in any setting.

The enrolment of participants in this study is complete. The data analysis is ongoing.

RePORT SA

Study into biomarker approaches for asymptomatic, subclinical and incipient tuberculosis (RePORT SA).

Principal Investigator: Michèle Tameris
Sponsor: University of Cape Town
Study Coordinator: Arina Conradie
Funders: Civilian Research Development Foundation, National Institutes of Health, SA Medical Research Council

ONGOING

This study aimed to discover and validate novel biomarkers to detect symptomatic, subclinical and incipient TB disease in people living with or without HIV.

In this study, samples were collected for multiple biomarkers from household contacts of patients recently diagnosed with TB. Participants were then screened for subclinical TB and followed up for 12 months for incipient TB. The performance of the most promising biomarkers was then compared head-to-head and benchmarked against Target Product Profiles (TPP) for triage, diagnostic and incipient TB tests.

Microbiologically confirmed, prevalent TB was diagnosed in 39 out of 450 (8.7%) participants, of whom 34 of 39 (87.2%) were asymptomatic.

This study was part of a multisite clinical study involving other research sites, which included the UCT-based Lung Institute (UCTLI), the Stellenbosch University-based Immunology Research Group (SUN-IRG), the University of the Witwatersrand-based Perinatal HIV Research Unit (PHRU), the Africa Health Research Institute (AHRI) and the University of Pretoria (UP), as well as international partners and collaborators within the RePORT TB consortium. Funding has been received for Report 3, which is set to commence during quarter three of 2024.

Recruitment at SATVI commenced during quarter one of 2021 and was completed during March 2022, and follow-up was completed during June 2023.

ENDX-TB EXPOSED

Evaluation of new diagnostic tests for active and incident TB in individuals with known TB exposure (ENDX-TB exposed)

Principal Investigator: Justin Shenje
Study Coordinator: Arina Conradie
Funders: US National Institutes of Health, National Institute of Allergy and Infectious Diseases

ONGOING

Current TB diagnostic tools have poor sensitivity, and TB test results are not always available timeously. We need to develop non-sputum-based TB tests that would reduce the risk of transmission and reduce diagnosis time, thereby ensuring earlier initiation of treatment. A few promising blood- and urine-based tests for TB have emerged, such as lateral-flow assays for host proteins, transcriptomic signatures and high-sensitivity urine lipoarabinomannan (LAM) assays.

This diagnostic study evaluated the performance of a range of novel, non-sputum-based TB diagnostic tests, for use at both (1) point-of-care and (2) centralised laboratories, in comparison with conventional TB diagnostic tests.

This multi-centre study recruited adolescent and adult household contacts from sites in South Africa, The Gambia, Uganda and Vietnam who were followed over a 12-month period. During this time participants were monitored for TB signs and symptoms, and underwent standard TB investigation alongside experimental diagnostic tests to identify incident TB cases among the study population. The study completed participant follow-up in September 2023, and is in the manuscript writing phase.

FACE MASK STUDY

Validation of non-invasive, non-sputum screening tests for TB

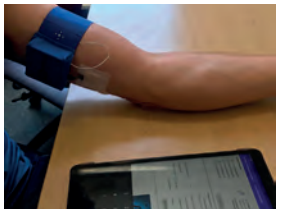
Principal Investigator: Simon Mendelsohn
Study Coordinator: Christel Petersen
Funders: Bill & Melinda Gates Foundation, South African Medical Research Council (SAMRC)

ONGOING

This study aims to validate new, non-sputum tests for diagnosing *M.tb* infection and TB disease. Enrolment of healthy adults and patients newly diagnosed with TB disease started in July 2023, with 75 (25 TB cases; 50 healthy controls) enrolled until the end of December 2023.

Some of the new tests evaluated include face masks fitted with sampling patches, exhaled breath and skin patch chemical signature measurements, oral swabs, chest X-rays with AI computer-aided detection (CAD), and blood collection for specific biomarkers of infection such as *M.tb*-specific T-cell activation assays, *M.tb* cell-free DNA, and *M.tb* complex DNA in CD34+ haematopoietic stem cells.

John Redmond from InspectIR conducting training of SATVI staff.



Skin patch sensor in use.

SELECTION OF IMMUNOLOGY RESEARCH

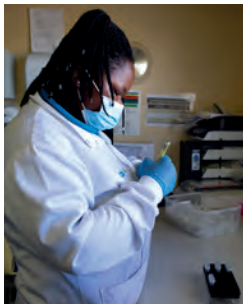
DEVELOPING A SIMPLE AND AUTOMATED METHOD TO MEASURE A T-CELL-BASED TB BIOMARKER

Principal Investigator: Munyaradzi Musvosvi
Funder: Bill & Melinda Gates Foundation

ONGOING

The development of new, non-sputum-based tests to diagnose TB is needed to improve case finding and earlier treatment, ultimately to reduce the burden of TB.

We have been researching a promising blood-based TB biomarker, the TB-TASA test, which has demonstrated high accuracy in identifying persons with TB and the potential to identify healthy persons who are at a high risk of progressing to TB (Mpande et al., 2020).



This candidate biomarker measures HLA-DR expression, which reflects the level of T-cell activation of *M.tb*-specific T-cells. We are addressing several challenges that must be overcome for this test to be adopted for implementation and routine use.

One such challenge is that the test requires trained laboratory technologists who would process the blood samples, and an additional layer of expertise in the analysis of flow cytometry data to interpret the results.

Another challenge is the need for expensive flow cytometry equipment to perform the TB-TASA test.

To address these challenges, we are conducting a proof-of-concept study to automate sample processing and analysis. We are also researching the development and optimisation of sample processing workflows using microfluidic chips, in collaboration with our research partners at the University of Cape Town and Stellenbosch University.

We have developed an automated analysis pipeline, which has been used to analyse flow cytometry data in the MTBVAC study to analyse antigen-specific T-cell responses induced by the MTBVAC vaccine. When compared to manual flow cytometry analysis, it performed at a significantly faster rate, with higher throughput and more reproducibility, while upholding high quality standards.

If this project is successful, the automated processing and analysis platform we are developing will move the TB-TASA closer to clinical translation, and will also improve research workflows used to monitor immune responses in clinical trials.

Worcester laboratory team.

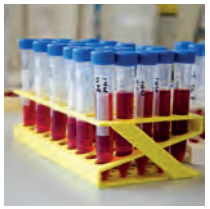
NK CELL DETERMINANTS OF IMMUNITY TO *MYCOBACTERIUM TUBERCULOSIS* IN HUMANS

Principal Investigator: Munyaradzi Musvosvi
Scientist (PhD candidate): Carly Young-Bailie
Supervisor: Dr Virginie Rozot
Co-supervisor: Prof Thomas J. Scriba
Funders: European Developing Countries Clinical Trials Partnership and the National Research Foundation (NRF)

COMPLETE

Natural killer (NK) cells are lymphocytes that can respond to pathogen-infected and neoplastic cells and directly kill target cells or secrete cytokines to modulate and coordinate other immune cells. However, the role of NK cells in TB pathogenesis remains poorly understood.

In this study we characterised NK cells in *M.tb*-exposed adolescents over two years using a CyTOF-based intracellular cytokine staining (ICS) assay to understand peripheral blood NK cell functional changes that occur during progression to TB disease. To understand NK cells in various tissue locations, we also characterised phenotypes and cytotoxic potential in lung, hilar lymph node, bronchoalveolar lavage (BAL), spleen and peripheral blood post-mortem, from TB patients who succumbed to disease and from non-TB controls who died from trauma.



Frequencies of cytokine-expressing peripheral blood NK cells changed over time during TB progression. These cells were lower in samples collected at distal timepoints from TB diagnosis in progressors, but increased significantly to frequencies exceeding controllers at timepoints proximal to TB diagnosis. Importantly, cytokine expression by NK cells during TB disease was dependent on T-cell bystander activation via IL-2; IL-2 neutralisation assay abrogated these responses. Peripheral blood NK cells from TB patients displayed mature, activated phenotypes, expressing higher levels of cytotoxic molecules than NK cells from non-TB controls. In contrast, NK cells in tissues were phenotypically immature, and were enriched in the lungs of TB cases relative to non-TB controls.

These data highlight the dynamic nature of NK cell function during disease progression, and suggest that bystander cytokine activation is an important effector of NK cell responses. The marked differences between peripheral blood and tissue suggest that NK cells in tissues may be playing an immunoregulatory role, perhaps to maintain homeostasis and prevent inflammation-induced tissue pathology.

Cape Town laboratory team

TUBERCULOSIS IN FORENSIC AUTOPSIES

Principal Investigator: Virginie Rozot
Project Scientists: Carly Young-Bailie, Tim Reid, Digby Warner, Atica Moosa, Dharanidharan Ramamurthy, Ben Loos, Alex K Shalek
Funders: Wellcome Leap

COMPLETE

Most human diseases affect specific anatomical locations in the body; but due to the invasive nature of sampling tissues and organs, research into disease is typically done on human blood, or in animal models. This is also true for TB. More effective control of TB is urgently needed, but requires better vaccines, better prognosis and diagnosis tools and improved antimicrobial treatments. These advancements are impaired by the complexity of host-pathogen interactions in human organs, which are chronically understudied.

In collaboration with forensic pathologists we have developed a post-mortem sample-collection platform to address this specific gap.

In persons with possible unnatural cause of death, a medico-legal investigation is undertaken to determine the cause of death. Our study leverages state-ordered autopsies to collect human tissue samples (thoracic draining lymph nodes, non-thoracic draining lymph nodes and blood) at short intervals (<24 hours) after death for immune response investigations. The short post-mortem interval allows us to investigate immune response functions in tissues and determine how these outcomes associate with tissue-specific and other evidence of TB disease pathology, which occurs in a very large proportion of individuals who live in this TB-endemic setting.

Since June 2023, our team has performed 122 autopsies, identified and interviewed 88 next-of-kin, and obtained consent from next-of-kin of 60 deceased family members (68.2% consent success rate) to allow inclusion of material in our research, with 28 refusals. Among the 60 consented cases, 10 had gross pathological evidence of TB at autopsy (16.7%), while 33 of 54 (61.1%) investigated for presence of *M.tb* in lymph nodes tested positive for bacterial DNA.

We have demonstrated the feasibility of this approach, which allows characterisation of immune responses in lymph nodes and identification of those that associate with pathological and microbiological outcomes. A combination of microscopy, flow cytometry, mass cytometry and single-cell RNAseq techniques is currently ongoing to better understand tissue-specific immune control of *M.tb* – or, on the other hand, drivers of immunopathology – and this promises to inform development of new diagnostic tools and vaccine strategies.

Dr Virginie Rozot, Research Officer.

IMMUNOGENICITY OF H56:IC31

Immunogenicity of H56:IC31 vaccination against recurrence of TB in HIV-negative adults successfully treated for drug-susceptible pulmonary TB

Principal Investigator: Tom Scriba
Project Scientists: Anele Gela, Elisa Nemes, members of the H56-POR Consortium
Sponsors: Statens Serum Institut and IAVI
Funder: EDCTP

COMPLETE

Individuals with TB are at high risk of recurrent disease after successfully completing their treatment. A vaccine that can protect against recurrent TB would significantly contribute to control of the TB epidemic. The adjuvanted protein-subunit vaccine H56:IC31, developed by the Statens Serum Institut, has shown acceptable safety and immunogenicity in phase 1/2 clinical trials.

We conducted a randomised, double-blind, placebo-controlled, event-driven phase 2b trial on the H56:IC31 experimental vaccine at five sites in South Africa and one in Tanzania. HIV-negative adults aged 18 to 59 years who were successfully treated for drug-susceptible TB were randomly assigned (1:1) to receive two doses of either H56:IC31 or a placebo, 56 days apart. A total of 831 participants were enrolled.

The first 100 participants randomised at SATVI and one site in Tanzania were included in a vaccine immunogenicity sub-study: 50 participants per site. Immunogenicity data were generated in H56:IC31 and placebo recipients, as per protocol. The primary immunogenicity outcome was antigen-specific T-cell responses that expressed any combination of IFN-γ, TNF, IL-2 and/or IL-17 (ie the total cytokine response), measured at Day 0 or 14 days after the second vaccination (Day 70) in each study arm by whole blood intracellular cytokine staining (WB-ICS) assay. In addition, combinations of IFN-γ, TNF, IL-2 and/or IL-17 expression by antigen-specific T-cells in response to H56:IC31 vaccination were evaluated.

H56:IC31 vaccination induced significant increases in antigen-specific CD4 T-cells expressing any combination of IFN-γ, TNF, IL-2 and/or IL-17 (fold change 3.8, q25 – q75 2.4 – 7.8), which exceeded pre-vaccination responses. Responses in the placebo arm were not modulated by vaccination (fold change 1.0, q25 – q75 0.7 – 1.5). H56-specific CD4 T-cell responses boosted by the H56:IC31 vaccine predominantly comprised cell subsets co-expressing Th1 cytokines. No modulation of CD8 T-cell responses was observed.

Taken together, H56:IC31 was immunogenic in patients who were successfully treated for drug-susceptible TB. Unfortunately, the vaccine showed no efficacy in prevention against recurrent TB. A biorepository of clinical samples (PBMCs, plasma and mRNA) has been collected and cryopreserved, and plans are currently under way to identify immune correlates of risk (COR) to recurrent TB among cases and matched controls, which would allow targeted intervention in those at highest risk for recurrent TB.

research outputs

Note SATVI authors in *bold*

1. ***Musvosvi M***, Huang H, Wang C, Xia Q, ***Rozot V***, Krishnan A, Acs P, Cheruku A, Obermoser G, Leslie A, Behar SM, Hanekom WA, ***Bilek N***, ***Fisher M***, Kaufmann SHE, Walzl G, ***Hatherill M***, Davis MM, ***Scriba TJ***; Adolescent Cohort Study team; GC6-74 Consortium. 2023.
T-cell receptor repertoires associated with control and disease progression following *Mycobacterium tuberculosis* infection.
Nature Medicine, *29(1):258-269.*

2. Swanson RV, Gupta A, Foreman TW, Lu L, Choreno-Parra JA, ***Mbandi SK***, Rosa BA, Akter S, Das S, Ahmed M, Garcia-Hernandez ML, Singh DK, Esaulova E, Artyomov MN, Gommerman J, Mehra S, Zuniga J, Mitreva M, ***Scriba TJ***, Rangel-Moreno J, Kaushal D, Khader SA. 2023.
Antigen-specific B cells direct T follicular-like helper cells into lymphoid follicles to mediate *Mycobacterium tuberculosis* control.
Nature Immunology, s41590-023-01476-3. Epub ahead of print.

3. Rangaka MX, Frick M, Churchyard G, García-Basteiro AL, ***Hatherill M***, Hanekom W, Hill PC, Hamada Y, Quaife M, Vekemans J, White RG, Cobelens F. 2023.
Clinical trials of tuberculosis vaccines in the era of increased access to preventive antibiotic treatment. *Lancet Respiratory Medicine,* 11(4):380-390.

4. Roy Chowdhury R, Valainis JR, Dubey M, von Boehmer L, Sola E, Wilhelmy J, Guo J, Kask O, Ohanyan M, Sun M, Huang H, Huang X, Nguyen PK, ***Scriba TJ***, Davis MM, Bendall SC, Chien YH. 2023.
NK-like CD8+ γδ T cells are expanded in persistent *Mycobacterium tuberculosis* infection.
Science Immunology, 8(81):eade3525.

5. Kurbatova EV, Phillips PPJ, Dorman SE, Sizemore EE, Bryant KE, Purfield AE, Ricaldi J, Brown NE, Johnson JL, Wallis CL, Akol JP, Ocheretina O, Van Hung N, Mayanja-Kizza H, Lourens M, Dawson R, Nhung NV, Pierre S, Musodza Y, ***Shenje J***, Badal-Faesen S, Vilbrun SC, Waja Z, Peddareddy L, Scott NA, Yuan Y, Goldberg SV, Swindells S, Chaisson RE, Nahid P. 2023.
A standardised approach for collection of objective data to support outcome determination for late-phase tuberculosis clinical trials.
American Journal of Respiratory Critical Care Medicine, 207(10):1376-1382.

6. Brough J, Martinez L, ***Hatherill M***, Zar HJ, Lo NC, Andrews JR. 2023.
Public health impact and cost-effectiveness of screening for active tuberculosis disease or infection among children in South Africa.
Clinical Infectious Diseases, 5:ciad449.

7. Krishnan S, Wu X, Kim S, McIntire K, Naini L, Hughes MD, Dawson R, Mave V, Gaikwad S, Sanchez J, Mendoza-Ticona A, Gonzales P, Comins K, ***Shenje J***, Nerette Fontain S, Omozoarhe A, Mohapi L, Lalloo UG, Garcia Ferreira AC, Mugah C, Harrington M, Shah NS, Hesseling AC, Churchyard G, Swindells S, Gupta A; AIDS Clinical Trials Group (ACTG) A5300/ International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) I2003, Protecting Households on Exposure to Newly Diagnosed Index Multidrug-resistant Tuberculosis Patients (PHOENIx) Feasibility Study Team. 2023.
One-year incidence of tuberculosis infection and disease among household contacts of rifampin- and multi-drug-resistant tuberculosis.
Clinical Infectious Diseases, 25:ciad301.

8. Kelley EJ, Henson SN, Rahee F, Boyle AS, Engelbrektson AL, Nelson GA, Mead HL, Anderson NL, Razavi M, Yip R, Ladner JT, ***Scriba TJ***, Altin JA. 2023.
Virome-wide detection of natural infection events and the associated antibody dynamics using longitudinal highly multiplexed serology.
Nature Communications, 14(1):1783.

9. Thirunavukkarasu S, Ahmed M, Rosa BA, Boothby M, Cho SH, Rangel-Moreno J, ***Mbandi SK***, Schreiber V, Gupta A, Zuniga J, Mitreva M, Kaushal D, ***Scriba TJ***, Khader SA. 2023.
Poly(ADP-ribose) polymerase 9 mediates early protection against *Mycobacterium tuberculosis* infection by regulating type I IFN production.
Journal of Clinical Investigation, 133(12):e158630.

10. Hamada Y, Gupta RK, Quartagno M, Izzard A, Acuna-Villaorduna C, Altet N, Diel R, Dominguez J, Floyd S, Gupta A, Huerga H, Jones-López EC, Kinikar A, Lange C, van Leth F, Liu Q, Lu W, Lu P, Rueda IL, Martinez L, ***Mbandi SK***, Muñoz L, Padilla ES, Paradkar M, ***Scriba T***, Sester M, Shanaube K, Sharma SK, Sloot R, Sotgiu G, Thiruvengadam K, Vashishtha R, Abubakar I, Rangaka MX. 2023.
Predictive performance of interferon-gamma release assays and the tuberculin skin test for incident tuberculosis: an individual participant data meta-analysis.
EClinicalMedicine, 56:101815.

11. Gupta-Wright A, den Boon S, MacLean EL, Cirillo D, Cobelens F, Gillespie SH, Kohli M, Ruhwald M, Savic R, Brigden G, Gidado M, Goletti D, Hanna D, Hasan R, Hewison C, Koura KG, Lienhardt C, Lungu P, McHugh TD, McKenna L, Scott C, Scriba T, Sekaggya-Wiltshire C, Kasaeva T, Zignol M, Denkinger CM, Falzon D. 2023.
Target product profiles: tests for tuberculosis treatment monitoring and optmisation.
Bulletin of the World Health Organisation, 101(11):730-737.

12. ***Shenje J***, Raubenheimer P, Wiesner L, Ross I. 2023.
A description of the elevation of pericardial cortisol:cortisone ratio in patients with tuberculous pericarditis. 2023.
Frontiers in Endocrinology, 14:1127550

13. Hillman H, Khan N, Singhania A, Dubelko P, Soldevila F, Tippalagama R, DeSilva AD, Gunasena B, Perera J, ***Scriba TJ***, ***Ontong C***, ***Fisher M***, ***Luabeya A***, Taplitz R, Seumois G, Vijayanand P, Hedrick CC, Peters B, Burel JG. 2023.
Single-cell profiling reveals distinct subsets of CD14+ monocytes drive blood immune signatures of active tuberculosis.
Frontiers in Immunology, 13:1087010.

14. ***Murphy M***, Suliman S, ***Briel L***, ***Veldtsman H***, ***Khomba N***, ***Africa H***, ***Steyn M***, Snyders CI, van Rensburg IC, Walzl G, Chegou NN, ***Hatherill M***, Hanekom WA, ***Scriba TJ***, ***Nemes E***. 2023.
Newborn bacille Calmette-Guérin vaccination induces robust infant interferon-γ-expressing natural killer cell responses to mycobacteria.
International Journal of Infectious Diseases, 25:S1201-9712(23)00069-3.

15. Goletti, D., Al-Abri, S., Migliori, G.B., Coler, R., Ong, C.W.M., Esposito, S.M.R., Tadolini, M., Matteelli, A., Cirillo, D., ***Nemes, E***. and Zumla, A., 2023.
World Tuberculosis Day 2023 theme 'Yes! We Can End TB!'.
International Journal of Infectious Diseases, 130, pp.S1-S3.

16. ***Looney MM***, ***Hatherill M***, ***Musvosvi M***, Flynn J, Kagina BM, Frick M, Kafuko Z, Schmidt A, Southern J, Wilder-Smith A, Tippoo P, Paradkar V, Popadić D, ***Scriba TJ***, Hanekom W, Giersing B. 2023.
Conference report: WHO meeting summary on mRNA-based tuberculosis vaccine development. *Vaccine*, 41(48):7060-7066.

17. Villain E, Chanson A, Mainka M, Kampschulte N, Le Faouder P, Bertrand-Michel J, Brandolini-Bulon M, Charbit B, ***Musvosvi M***, ***Bilek N***, ***Scriba TJ***, Quintana-Murci L, Schebb NH, Duffy D, Gladine C; Milieu Interieur Consortium. 2023.
Integrated analysis of whole blood oxylipin and cytokine responses after bacterial, viral, and T-cell stimulation reveals new immune networks.
iScience, 26(8):107422.

18. Chendi BH, Jooste T, ***Scriba TJ***, Kidd M, ***Mendelsohn S***, Tonby K, Walzl G, Dyrhol-Riise AM, Chegou NN. 2023.
Utility of a three-gene transcriptomic signature in the diagnosis of tuberculosis in a low-endemic hospital setting.
Infectious Diseases (Lond), 55(1):44-54

19. ***Imbratta C***, ***Gela A***, ***Bilek N***, ***Mabwe S***, ***Cloete Y***, Mortensen R, Borges ÁH, Maenetje P, Mlotshwa M, Churchyard G, Sudi L, Sabi I, Meewes P, Wallis CL, ***Hatherill M***, ***Scriba TJ***, ***Nemes E***. 2023.
Qualification of the differential leukocyte count and immunophenotyping in cryopreserved ex vivo whole blood assay.
Cytometry A. 2023 Sep 7.

20. Chihab LY, Kuan R, Phillips EJ, Mallal SA, ***Rozot V***, Davis MM, ***Scriba TJ***, Sette A, Peters B, Lindestam Arlehamn CS; SATVI Study Group. 2023.
Expression of specific HLA class II alleles is associated with an increased risk for active tuberculosis and a distinct gene expression profile.
HLA, 101(2):124-137.

21. Richardson TR, Smith B, Malherbe ST, Shaw JA, Noor F, MacDonald C, van der Spuy GD, Stanley K, Carstens A, Fisher TL, van Rensburg I, Flinn M, Snyders C, Johnson I, Fransman B, Dockrell H, Thwaites G, Thuong NTT, Schacht C, Mayanja-Kizza H, Nsereko M, Tjon Kon Fat EM, Corstjens PLAM, Geluk A, Ruhwald M, ***Penn-Nicholson A***, Chegou NN, Sutherland J, Walzl G; TrENDx consortium. 2023.
Field evaluation of a point-of-care triage test for active tuberculosis (TriageTB).
BMC Infectious Diseases, 23(1):447.

22. Kim S, Hesseling AC, Wu X, Hughes MD, Shah NS, Gaikwad S, Kumarasamy N, Mitchell E, Leon M, Gonzales P, Badal-Faesen S, Lourens M, Nerette S, ***Shenje J***, de Koker P, Nedsuwan S, Mohapi L, Chakalisa UA, Mngqbisa R, Escada RODS, Ouma S, Heckman B, Naini L, Gupta A, Swindells S, Churchyard G; ACTG A5300/ IMPAACT 2003 PHOENIx Feasibility Study Team. 2023.
Factors associated with prevalent *Mycobacterium tuberculosis* infection and disease among adolescents and adults exposed to rifampin-resistant tuberculosis in the household.
PLoS One, 18(3):e0283290.

23. ***Mendelsohn SC***, Verhage S, ***Mulenga H***, ***Scriba TJ***, ***Hatherill M***. 2023.
Systematic review of diagnostic and prognostic host blood transcriptomic signatures of tuberculosis disease in people living with HIV.
Gates Open Research, 5;7:27.

24. Codsi R, Errett NA, ***Luabeya A***K, ***Van As D***, ***Hatherill M***, Shapiro AE, Lochner KA, Vingino AR, Kohn MJ, Cangelosi GA. 2023.
Preferences of healthcare workers using tongue swabs for tuberculosis diagnosis during COVID-19.
PLOS Global Public Health, 3(9):e0001430.

25. Shaw J.A., Meiring M., Allies D., Cruywagen L., Fisher T.L., Kasavan K., Roos K., Botha S.M., MacDonald C., Hiemstra A.M., Simon D., van Rensburg I., Flinn M., Shabangu A., Kuivaniemi H., Tromp G., Malherbe S.T., Walzl G., du Plessis N.; Stellenbosch University Immunology Research Group Bronchoalveolar Lavage Study Consortium (SU IRG BAL Study Consortium, including ***Nemes E***.). 2023.
Optimising the yield from bronchoalveolar lavage on human participants in infectious disease immunology research.
Scientific Reports, 13(1):8859

26. ***Young C***, Suliman S, ***Rozot V***, ***Mendelsohn SC***. 2023.
Meeting report: 6th Global Forum on Tuberculosis Vaccines, 22–25 February 2022, Toulouse, France.
Vaccine, 13

awards, honours & accreditations

SATVI DIRECTOR ADDRESSES UN HIGH-LEVEL MEETING ON TUBERCULOSIS

Professor Mark Hatherill addressed the panel of the UN General Assembly High-Level Meeting on the fight against TB, September 2023.

During September 2023, SATVI Director Professor Mark Hatherill addressed a panel of the UN General Assembly High-Level Meeting on the fight against TB, providing an update on progress with vaccine development and calling for a quantum jump in TB vaccine research and development funding.

Other highlights

- Carly Young-Bailie was elected co-chair of the Stop TB Partnership Working Group on new TB Vaccines.
- Dr Simon Mendelsohn was nominated to the Global TB Bioarchive Steering Committee.
- Dr Justin Shenje was elected Co-Vice-Chair of the ACTG A5414 Protocol Team.
- Dr Viginie Rozot was elected to the UCT Faculty Equipment Committee.
- Yolundi Cloete was appointed to the ACTG Laboratory Technology Committee.

Dr Angelique Kany Kany Luabeya was promoted ad-hominem to Associate Professor.

Drs. Simon Mendelsohn and Justin Shenje were promoted ad-homimen to Senior Research Officers.

postgraduate students & postdoctoral fellows

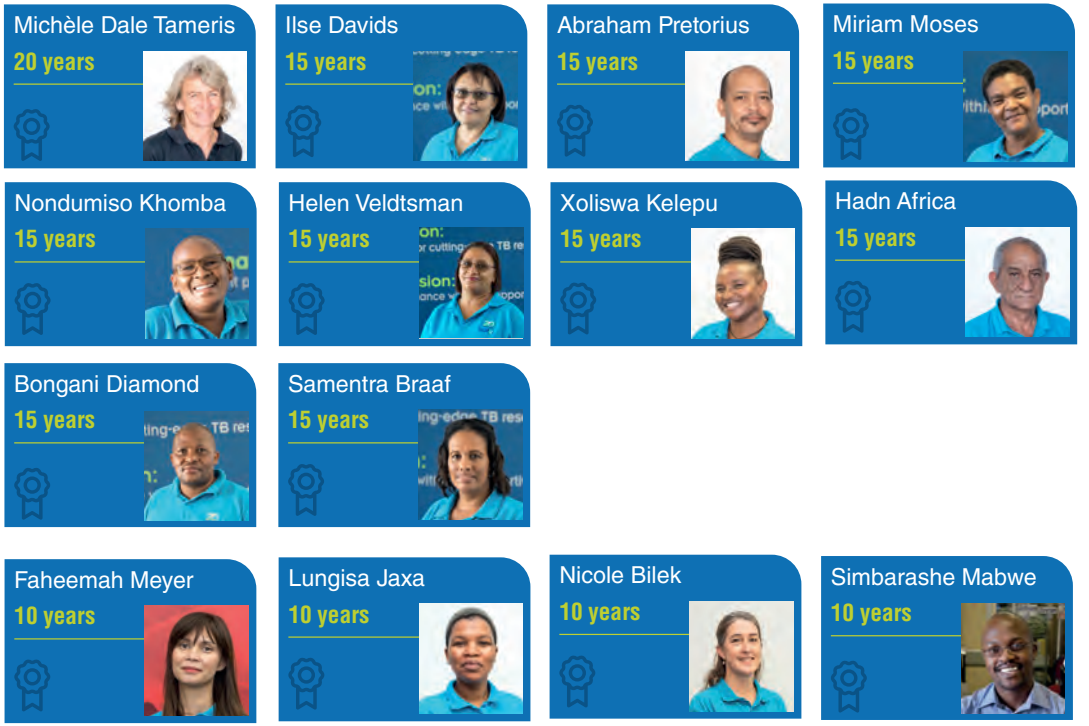
Carly Young-Bailie graduated with a PhD (Supervisors: Virginie Rozot and Tom Scriba).

Dango Mwambene graduated with an MSc (Supervisors: Tom Scriba and Anele Gela).

our staff

LONG SERVICE

The following staff have completed periods of long service:



STAFF WELLNESS DAY

We hosted a Staff Wellness Day at our Worcester field site, providing staff with the opportunity to have a health check-up and access healthy nutrition and financial advice.

UCT Health and Wellness Coordinator, Ms Susan Williams with Mr Habibullah Valley, a member of SATVI Wellness Day Organising Committee.

UCT Food Nutrition presenter with Ms Xoliswa Kelepu.

Access to mental wellness programmes.

JOINT STAFF MEETING

We have initiated a half-yearly joint capacity development session for strategic capacity building across the organisation. During May the Worcester site staff visited IDM in Cape Town where they were welcomed by the Deputy Dean, Professor Collet Dandara, the SATVI laboratory, and the UCT Pathology Learning centre, where they could see TB disease tissue samples, and pulmonary and various forms of disseminated TB.

Professor Collet Dandara, Deputy Dean Postgraduate Education, welcome SATVI staff to the UCT Health Sciences Faculty.

Professor Tom Scriba, Deputy Director.

SATVI staff who attended the programme.

Guided tour of UCT.

Visit to Pathology Learning Centre.

our community & advocacy

WORLD TB DAY

For World TB Day, SATVI has partnered with the Departments of Education and Health in supporting activities at schools and clinics.

Primary Healthcare Clinics

We supported the District Health Department with various TB awareness programmes at clinic level to raise awareness of TB among people visiting the clinic to access health services around World TB Day. The clinics selected were Avian Park, Worcester CDC and Empilisweni Clinic.

World TB Day at Avian Park Clinic.

EDUCATION SECTOR

We supported schools in our district (Cape Winelands) in hosting educational activities which took place on World TB Day. The schools that held World TB Day activities were:

1. Ashton Secondary
2. Avian Park Primary
3. Esselen Park Primary
4. Alfred Stamper Primary
5. SATVI Youth Peer education programme
6. Worcester Secondary High School

World TB Day programme at Esselen Park High School.

Learners produced a drama about TB at Worcester Secondary School.

Dr Nicolette Tredoux presenting a TB talk to learners.

Candle-lighting ceremony for a learner who passed on from TB during 2022 at Worcester Secondary.

Learners from Worcester Secondary who participated in the programme.

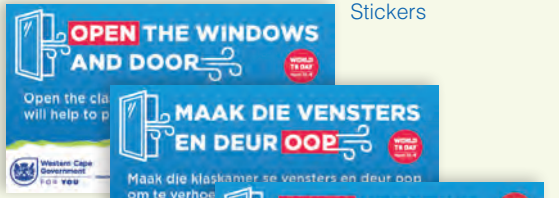
Group discussion of TB education materials, Ashton Secondary High School.

SATVI Communications Manager Kelvin Vollenhoven facilitating a learning session at Ashton Secondary.

Peer educators during World TB Day at Alfred Stamper Primary School, Worcester.

In 2022 we developed a TB Awareness resource kit in partnership with local schools, with a seed grant from the CIDRI-Africa Wellcome Trust. The resource kit consists of banners, stickers, posters and plastic rulers that contain TB messaging, and it was made available to the Department of Education.

Stickers



Wall Banner

Posters

SCIENCE TECHNOLOGY ENGINEERING MATHEMATICS SUPPORT

At the end of 2023 we initiated discussions between SATVI, the ESKOM Expo for Young Scientists and the Cape Winelands district Department of Education to develop plans for the new year to promote Science Technology Engineering Mathematics (STEM) among school learners in the Cape Winelands. These initiatives are aimed at addressing the low post-school uptake of STEM career streams.

GENERAL AWARENESS RAISING AND ADVOCACY

We hosted employees from the Department of Social Services, as well as senior management of the Department of Education, to make them aware of the research work that SATVI does and to raise awareness concerning the occupational risks of working in a high-TB-burden environment.

Other awareness-raising workshops have been conducted, including with the South African Police Service, the Rainbow Chicken plant, and the League of the Friends of the Blind.

Our Communications Manager, Kelvin Vollenhoven, has continued to present monthly TB education talks at Toevlug, an adolescent substance abuse rehabilitation institution.

MANDELA DAY

For Mandela Day we supported several community-based organisations, including a painting project at Steenvliet Primary School, and donating equipment to FEMCET (Touwrsiver), Isiboneli Educare, Comforters Church Educare and Lunathi Creche in Zwelethemba, Worcester.

MANDELA DAY



Painting of Steenvliet Primary School, Touwsrivier.


Donation of equipment and storyreading to FEMCET creche, Touwsrivier.

Donation of equipment to Lunathi Creche, Zwelethemba, Worcester.

COMMUNITY ADVISORY BOARD (CAB)

In the year under review the CAB continued its valuable work in providing feedback and input into research work. During the year, the two CABs associated with SATVI and FAMCRU (Stellenbosch University) were merged into one, to synergise efforts, avoid duplication and stimulate the CAB.

At the end of 2023 the CAB held its last meeting in Cape Town, where they visited the UCT Pathology Museum, to see TB disease manifestations, and the laboratory, where they were able to explore the inner workings. This was followed by an ethics talk, to explain to the CAB how ethics approvals are made.


CAB EDUCATIONAL VISIT TO UCT PATHOLOGY LEARNING CENTRE

Dr Jane Yeats, Director of the UCT Pathology Learning Centre, presented an educational talk on TB in humans, showing CAB members how TB presents in various organs, ranging from the more common TB in the lungs (pulmonary TB) to extra-pulmonary (disseminated) TB.


CAB RESEARCH ETHICS

Ms Ashley Veldsman, a regulatory specialist, presented a talk on research ethics to the CAB in Cape Town.

SOCIAL RESPONSIBILITY- SUPPORT TO COMMUNITY ORGANISATIONS

Khulisa Food Project/SANBI: Biodiversity Conservation Youth Programme, 26 October 2023.

Khulisa/PJ Cona Primary School Environmental Project, December 2023.

CAB VISIT TO SATVI LABORATORY

Dr Nicole Bilek, SATVI Laboratory Manager, gave CAB members a guided tour of SATVI's laboratory facilities.

WORLD AIDS DAY, ZWELETHEMBA

Mrs Linda Sibeko, founder of Ikamva Lethu community organisation speaking at World AIDS Day Programme.

World AIDS Day Programme, Zwelethemba, December 2023.

SOAPBOX SCIENCE ENGAGEMENT

Vanessa Muwango participated in the 2023 Soapbox Science Engagement programme, which took place at the Victoria & Alfred Waterfront, Cape Town.

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