vision and mission

Our Vision
A World Without TB

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

Our Values
Innovation I Respect I Employee Recognition I Accountability I Communication I Commitment I Honesty
Ongoing SATVI projects also reached key targets, including two AIDS Clinical Trials Group therapeutic trials, A5349 and A5343, which are now fully enrolled. A milestone which deserves special mention is that the CORTIS trial has now entered the follow-up phase, with almost 3,000 participants enrolled, having screened more than 20,000 individuals over two years. This is a remarkable achievement given that screening involved real-time processing of many thousands of RT-PCR transcriptomic biomarker assays before randomisation. We now look forward to the release of the CORTIS results late in 2019.

We continue to measure academic success by our scientific outputs and 2018 was not only a record year for publication output, with 37 papers published (11 with a SATVI first or senior author), but also included not one but two landmark TB vaccine papers published in the New England Journal of Medicine. These new data provide much needed impetus to expand and accelerate funding for TB vaccine development. A number of new trials are poised to start in 2019 after many months of preparation, including two dose-ranging studies of the live attenuated M. tuberculosis vaccine MTBVAC, in infant and adult populations; a proof-of-concept Prevention of Recurrence (POR) trial of the adjuvanted protein subunit vaccine H56:IC31; and a trial of preventive therapy for household contacts of MDR-TB patients (PHOENIx).

The success of these new clinical trials will depend as always on the commitment, trust and support for SATVI research in the greater Worcester community, which is affected by an extraordinary burden of TB disease. For the first time, given these exciting new vaccine trial results, it seems we may be closer to relieving the community of that burden and achieving SATVI’s vision of “A World Without TB”.

Professor Mark Hatherill
Director
The South African Tuberculosis Vaccine Initiative (SATVI) is a tuberculosis (TB) research group with a research scope that spans several disciplines including paediatrics, infectious diseases, epidemiology, public health, immunology, systems biology and clinical sciences. Our research focus is understanding the risk for, and protection against, M. tuberculosis infection and TB disease, in order to develop more effective vaccines and preventive strategies.

SATVI was established in 2001 at the University of Cape Town (UCT) and has developed into a sophisticated, world-class TB clinical research centre with state of the art immunology laboratories located within the Institute of Infectious Disease and Molecular Medicine (IDM) of the University of Cape Town. SATVI is regarded as a leader in TB vaccine and prevention research worldwide and is the largest dedicated TB vaccine research group on the African continent. Our laboratories are accredited and adhere to the highest international standards. In addition to our track record in TB vaccine development, our recent work builds on discovery of prognostic biomarkers for TB disease to test screen & treat strategies, based on biomarker-targeted TB preventive therapy.

SATVI has a large and well-developed clinical field site in the Boland Overberg region, with the core facility on the premises of the Brewelskloof TB Hospital in Worcester, from where most clinical/epidemiological studies and clinical trials are conducted. The clinical trials research is led by SATVI Director, Professor Mark Hatherill, and the immunology and laboratory-based research is led by SATVI Deputy Director, Professor Tom Scriba.

Our clinical trial programme has been extraordinarily productive over the past 17 years. SATVI has conducted 28 Phase I–IV trials of BCG and 9 novel TB vaccine candidates among more than 30,000 research participants. Over the last 10 years our cumulative publications include 290 papers, the majority of these with a SATVI first or senior author. Our active postgraduate student programme has also produced 10 PhD graduates and several Master’s graduates during the same period.
governance

EXECUTIVE COMMITTEE

The SATVI Executive Committee is comprised of:

Director, Professor Mark Hatherill
Deputy Director, Professor Tom Scriba
Chief Operations Officer, Dr Masooda Kaskar
Field Site Manager, Mrs Marwou de Kock

From left to right: Professor Tom Scriba, Dr Masooda Kaskar, Mrs Marwou de Kock and Professor Mark Hatherill.
**EXECUTIVE COMMITTEE**

**PROFESSOR MARK HATHERILL**  
**DIRECTOR**

Dr Mark Hatherill (MD, FCPaed) is a specialist paediatrician and clinical trialist who is active in the design and implementation of innovative trials of new TB vaccines and TB preventive therapy strategies, through several consortia. His current academic focus includes development and evaluation of biomarker-targeted interventions and several clinical trials of novel TB vaccine candidates. He is a full member of the Institute of Infectious Disease & Molecular Medicine (IDM) at UCT; member of the WHO SAGE Working Group on BCG Vaccine, the WHO IVR Working Group on TB Vaccines and Co-Chair of the Regional Prospective Observational Research in Tuberculosis (RePORT) South Africa consortium. Dr Hatherill is funded by institutional research grants from the Bill & Melinda Gates Foundation (BMGF), the SA Medical Research Council (SAMRC), US National Institutes of Health, as well as the European & Developing Countries Clinical Trials Partnership and Aeras/IAVI.

**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 is a full member of the IDM, member of the STOP TB Partnership Working Group for New Diagnostics Biomarkers Taskforce and the Collaboration for TB Vaccine Discovery of the BMGF. He is funded by competitive grants from the BMGF, the National Research Foundation (NRF), SAMRC, 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 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 growth and long-term sustainability of the organisation. Dr Kaskar previously occupied several senior leadership positions within 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 the University of Cape Town and an MBA degree from UCT, 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. She is currently responsible for managing the SATVI Field Site, overseeing and managing service delivery for all operations, as well as coordinating and implementing multiple research projects.
senior research team

SENIOR RESEARCHERS

DR MICHÈLE TAMERIS
Investigator

Dr Michèle Tameris graduated from UCT with a MBChB degree in 1980. She worked for many years in the public health sector in Cape Town and in Worcester. In 2003 she joined SATVI as a clinical researcher and since 2005 has been an Investigator on 15 vaccine trials, 6 as Principal Investigator, including 9 trials of novel TB vaccines and the first Phase 2b infant efficacy trial of a new TB vaccine (MVA85A). She has been awarded two Wellcome Trust International Engagement awards (2012 and 2014) for projects using drama to improve community understanding of TB clinical research. She is a member of the Stop TB Working Group on New Vaccines.

DR ANGELIQUE LUABEYA
Investigator

Dr Angelique Kany Kany Luabeya graduated as a medical doctor in 1996 from the University of Kinshasa (MR Congo) and holds a Master’s degree in Epidemiology from the London School of Tropical Medicine (LSHTM). She joined SATVI in 2009 as a clinical investigator from the Africa Centre for Health and Population Studies at University of KwaZulu-Natal and has been involved as Principal Investigator in the implementation and conduct of clinical trials of new TB vaccines (AERAS C035-456, IDRI-TBVPx-203, and VPM1002-ZA-2.13TB) in healthy adults, TB patients and newborns, respectively. She has produced several scientific publications and has a particular research interest in the design and conduct of novel diagnostic studies (TB case-finding by oral swab PCR) and health systems operational research in the area of TB prevention in young children.

DR JUSTIN SHENJE
Investigator

Dr Justin Shenje graduated as a medical doctor in 2004 from the University of Zimbabwe and holds a Master’s degree in Clinical Epidemiology from the University of Pretoria. He joined SATVI in 2015 as a clinical investigator and leads the AIDS Clinical Trials Group (ACTG) trials, serving as Principal Investigator for the A5300, A5343, and A5349 (TBTC Study 31) studies. He has experience with TB prevention, diagnostic and treatment studies, but has a special interest in the application of Geographic Informational Systems (GIS) in mapping local TB incidence rates.
Dr Simon Mendelsohn graduated from the University of Cape Town as a medical doctor in 2011, completing his internship training and community service in Mpumalanga. Thereafter he read for two Master’s degrees at the University of Oxford on a Rhodes Scholarship; in Integrated Immunology (2015) and in International Health and Tropical Medicine (2016), and obtained a Diploma in Tropical Medicine and Hygiene from the Royal College of Physicians (London). Simon joined SATVI on a PhD Fellowship in 2017 and also works as a clinical trial Investigator. He has experience in HIV and TB clinical medicine, most recently with Médecins Sans Frontières implementing an HIV and TB programme in Malawi prisons. Simon’s research interests lie in HIV/TB co-infection from immunological, clinical, and public health perspectives, specifically with developing practical tools for clinical practice.

Dr Hennie Geldenhuys trained in Family Medicine and joined SATVI in 2007. He has fulfilled the role of Principal Investigator on a number of clinical trials. His current focus is coaching and training in private practice, but he remains associated with SATVI as a sessional Sub-Investigator, based at the field site in Worcester, and as clinical quality management consultant for clinical trials.

Dr Elisa Nemes completed her 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. She joined SATVI in 2011, where she has been involved in basic immunology studies, immune-diagnostics, clinical trials of new TB vaccines and studies of host correlates of risk of TB disease in BCG-vaccinated infants; and of BCG/TB immune reconstitution inflammatory syndrome (IRIS) in HIV+ children. She is funded by competitive grants from the Center for AIDS Research (CFAR) and the US National Institutes of Health.
A PHASE IIB, DOUBLE-BLINDED, RANDOMIZED, PLACEBO-CONTROLLED STUDY TO EVALUATE
THE EFFICACY, SAFETY AND IMMUNOGENICITY OF GSK BIOLOGICALS CANDIDATE
TUBERCULOSIS (TB) VACCINE GSK 692342 AGAINST TB DISEASE, IN ADULTS AGED
18-50 YEARS, LIVING IN A TB ENDEMIC REGION

The primary results of this trial of the safety and efficacy of M72/AS01e in adults with latent M.tuberculosis infection against progression to TB disease were recently published in the New England Journal of Medicine and presented at ID Week and the Union World Conference on Lung Health (New England Journal of Medicine. 2018 Oct 25;379(17):1621-1634.). The trial, which concluded in late 2018, was conducted in TB-endemic regions in Kenya, South Africa and Zambia and involved 3,573 HIV-negative adults. Participants who received two doses of either M72/AS01e or placebo 30 days apart and were followed for at least 2 years to detect evidence of pulmonary TB disease, were included in the primary analysis. The primary results demonstrated that M72/AS01e vaccine had an acceptable safety and reactogenicity profile and significantly reduced the incidence of pulmonary TB disease in HIV-negative adults who were already infected with M.tuberculosis at the time of vaccination. Overall vaccine efficacy was 54%, with variation observed across age and gender sub-groups. This result was the first demonstration of protection by a protein-subunit vaccine against TB disease and has potential for major public health impact by reduction of TB transmission. Final results after 3 years of follow-up will be available in 2019.

Clinicaltrials.gov ID: NCT01755598
The results of this proof-of-concept study of vaccine-mediated prevention of M. tuberculosis infection, recently published in the New England Journal of Medicine, demonstrated for the first time that vaccination can reduce the rate of sustained M. tuberculosis infections among healthy adolescents in a high-transmission setting, such as the Western Cape of South Africa (New England Journal Medicine. 2018 July 12;379 (2):138-149. In this trial, revaccination with BCG significantly reduced sustained infections in adolescents with 45.4% efficacy. The H4:IC31 protein subunit vaccine also reduced the rate of sustained infection, although not at statistically significant levels, with 30.5% efficacy. However, the trend observed for H4:IC31 was the first signal of biological efficacy for any subunit TB vaccine in humans. In the trial, M. tuberculosis infections were measured by a blood test (QuantiFERON-TB Gold In-Tube; QFT) converting from negative to positive, and sustained infections were defined by a QFT test that remained positive for at least six months.

These favourable results highlight the importance of investing in new approaches to fight the world’s leading infectious disease killer and for empirical testing of new TB vaccine concepts in clinical trials. The novel prevention-of-infection trial design can be used to inform clinical development of new TB vaccine candidates before entry into large-scale prevention-of-TB disease efficacy trials.

Clinicaltrials.gov. ID: NCT02075203.
THE CORRELATE OF RISK TARGETED INTERVENTION STUDY (CORTIS): A RANDOMISED, PARTIALLY-BLINDED, CLINICAL TRIAL OF ISONIAZID AND RIFAPENTINE (3 HP) THERAPY TO PREVENT PULMONARY TUBERCULOSIS IN HIGH RISK INDIVIDUALS IDENTIFIED BY A TRANSCRIPTOMIC CORRELATE OF RISK

CORTIS builds on a decade-long project to develop a host blood RNA biomarker that predicts whether a person is at risk of developing TB, based on the human immune response (Zak et al, Lancet 2016). In this large clinical trial, we are evaluating whether targeted preventive therapy for people with a positive RNA biomarker test can stop them from developing TB. This international collaboration is led by SATVI in partnership with the Aurum Institute, the Stellenbosch University Immunology Research Group, the Centre for the AIDS Programme of Research in South Africa (CAPRISA), the London School of Hygiene and Tropical Medicine (LSHTM), and the Fred Hutchinson Cancer Research Center (FHCRC).

The trial has recruited almost 3,000 HIV-uninfected adult volunteers from communities with high TB burden at 5 sites in South Africa, who are randomised to either preventive therapy or active surveillance based on their RNA biomarker test result. With CORTIS enrolment complete, our laboratory has processed about 16,000 RNA samples on the Fluidigm RT-PCR platform in the last year, which demonstrates that high-throughput host blood RNA biomarker screening is possible in a TB endemic country. All participants are screened for TB disease at baseline, and through 15 months of follow-up, to evaluate the biomarker for diagnosis of prevalent TB and prognosis of incident TB. Efficacy of preventive therapy (3 months of once-weekly, high dose Isoniazid and Rifapentine) for protection against incident TB will be evaluated in sub-groups of RNA biomarker positive participants in the preventive therapy and active surveillance arms. If successful, CORTIS would provide proof of concept for mass campaigns using a ‘TB screen & treat’ strategy, which has potential for major impact on the global epidemic. Preliminary indications suggest a very high prevalence of TB disease in the CORTIS study population, which is enriched for RNA biomarker-positive persons. Data remain blinded and results are expected late 2019.
THE CORRELATE OF RISK TARGETED INTERVENTION STUDY
HIGH RISK (CORTIS-HR)

National Principal Investigator: Mark Hatherill
SATVI Principal Investigator: Michèle Tameris
Funder: Bill and Melinda Gates Foundation; SAMRC

CORTIS-HR is an observational study of the diagnostic and prognostic performance of the host blood RNA biomarker of TB in HIV-infected persons. This multi-site study enrolled 860 participants and is following them up over a 15-month period to determine if the transcriptomic signature can identify prevalent and incident TB in this population. We anticipate results will be available late 2019.

USING BIOMARKERS TO PREDICT TB TREATMENT DURATION
(PREDICT)

SATVI Principal Investigator: Michèle Tameris
Funding: Bill and Melinda Gates Foundation; EDCTP; ICIDR; RePORT South Africa (Pl Walzl)

This is a prospective, randomized, Phase 2b non-inferiority trial in drug-sensitive pulmonary TB participants. Eligible participants initially receive Isoniazid (H), Rifampin (R), Pyrazinamide (Z), Ethambutol (E) for 8 weeks, then switch to Isoniazid and Rifampicin (HR). Early treatment completion criteria will be evaluated for each participant using all available data at week 16 including GeneXpert results, adherence data and PET/CT scan results. Those who do not meet the early treatment completion criteria at enrolment will be assigned to Arm A and receive standard of care ie 24 weeks of treatment; those who meet early treatment completion criteria, will be randomised at week 16, either to continue therapy to week 24 (Arm B) or to complete therapy early at week 16 (Arm C). All participants will be followed for 18 months from entering the study, with the primary endpoint of treatment success being evaluated at 18 months.
BCG is currently the only licensed TB vaccine, but it provides incomplete protection against pulmonary TB in children and variable protection in adults. It is also relatively contraindicated for HIV-positive persons due to the high risk of adverse events. This multi-site trial of 416 infants evaluated the safety and immunogenicity of the candidate recombinant BCG vaccine VPM1002, in HIV exposed and unexposed neonates, compared with BCG. Enrolment and follow up at all sites is now complete. We anticipate the results of this trial will be made available in the first quarter of 2019.

Clinicaltrials.gov ID: NCT02391415

This study evaluated the biological feasibility of oral swab analysis (OSA) for diagnosis of TB. Oral Swabs were tested from South African adult subjects including sputum GeneXpert® MTB/RIF confirmed TB patients Relative to all laboratory-diagnosed TB, the sensitivity of sputum GeneXpert (1 sample per subject) and OSA (2 samples per subject) were identical at 83.1% and the specificity of OSA was 91.5%. The results confirm and significantly expand our previous finding that M. tuberculosis 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.
TOLERABILITY, AND PHARMACOKINETICS OF BEDAQUILINE AND DELAMANID, ALONE AND IN COMBINATION, AMONG PATIENTS TAKING MULTI-DRUG TREATMENT FOR DRUG-RESISTANT PULMONARY TUBERCULOSIS (ACTG 5343).

Principal Investigator: Justin Shenje
Funders: ACTG, DAIDS

Bedaquiline and Delamanid are novel experimental drugs for the treatment of Multi-drug resistant TB. The safety of the combination of these two drugs with standard MDR treatment has not been investigated, especially for their known effect on the heart. This trial, for which SATVI is one of 3 global sites, tests each drug alone or together in addition to standard MDR- TB treatment, with intensive monitoring for electrocardiogram (ECG) changes and other safety events. Participant enrolment is complete, and study is now in the follow-up phase.

Clinicaltrials.gov. ID: NCT02583048a

A RANDOMIZED, DOUBLE-BLIND, DOSE-ESCALATION CLINICAL TRIAL OF THE SAFETY, REACTOGENICITY AND IMMUNOGENICITY OF MTBVAC COMPARED TO BCG VACCINE SSI IN NEWBORNS LIVING IN A TUBERCULOSIS ENDEMIC REGION WITH A SAFETY ARM IN ADULTS.

Principal Investigator: Michèle Tameris
Funder: Biofabri

The novel vaccine, MTBVAC, is the first recombinant live, whole cell M. tuberculosis vaccine in clinical testing, intended as a BCG replacement vaccine in newborns, or a booster to BCG in older individuals. In this trial we first tested the safety of MTBVAC in 18 BCG vaccinated, TB uninfected adults. After establishing safety in adults, the safety and immunogenicity of 3 doses of MTBVAC was tested in 36 BCG-naïve newborns, compared against BCG. Enrolment and follow up has been completed and results are expected to be published in 2019.

Clinicaltrials.gov. ID: NCT02729571

PHASE I/II, SAFETY AND IMMUNOGENICITY STUDY OF A RECOMBINANT PROTEIN DOUBLE BLIND, RANDOMIZED, TUBERCULOSIS VACCINE (H4:IC31) IN BCG PRIMED INFANTS (P1113, AERAS/IAVI C-015-404).

SATVI Principal Investigator: Michèle Tameris
Funders / Sponsors: Aeras/IAVI, NIAID, NICHD, IMPAACT

This multisite study of 211 participants evaluated the H4:IC31 vaccine, designed as a booster to BCG to provide protection against M. tuberculosis infection and/or TB disease early in life. The trial compared different doses and number of administrations of the vaccine, in infants of different ages. Enrolment and follow up is complete at all sites. We anticipate the results of this trial will be made available in Q1 of 2019.

Clinicaltrials.gov. ID: NCT01861730
We have conducted Phase I/II safety and immunogenicity trials of 9 novel TB vaccine candidates at SATVI. In all these trials, vaccine-induced immune responses were measured using a qualified whole blood intracellular cytokine staining (WB-ICS)/flow cytometry assay. Results from each clinical trial are typically analysed and published separately, which makes the comparison of vaccine-induced immune responses difficult. In this statistical study we leveraged the extensive WB-ICS datasets to perform a direct “head-to-head” comparison of CD4 and CD8 T-cell responses induced by six vaccines that include different antigens delivered in viral vectors, as fusion proteins in adjuvant formulations or in live, whole bacterial vaccines. In collaboration with Francesca Little at the Department of Statistical Sciences, we developed a rigorous and biologically interpretable statistical approach to compare antigen-specific T-cell responses from healthy participants vaccinated with MVA85A, Aeras402, M72:AS01E, H1:IC31, H56:IC31, ID93:GLA-SE, as well as BCG. Our aim was to identify which vaccines induce immune responses that are very similar and the vaccines that induce unique responses, to inform selection of vaccine candidates for down-stream vaccine efficacy testing. M72/AS01E induced the largest CD4 T-cell memory response, but the results suggest a lack of diversity in response profile between different novel vaccine candidates, which has significant implications for future vaccine prioritisation.

The primary aim of this study was to investigate whether room air sampling can identify high risk classrooms where TB transmission is occurring. This research aimed to determine whether an air sampling screening strategy can enable earlier identification of TB patients in classrooms which will enable earlier treatment to reduce spread of TB to other learners. This observational study involved approximately 2,500 learners in two Worcester high schools and three Worcester primary health clinics. Analysis is anticipated to be complete mid-2019.
M. tuberculosis-specific T-cells can recognize bacterial protein fragments using a diverse set of cell surface receptors known as T-cell receptors (TCR). When a M. tuberculosis-specific T-cell recognizes such bacterial protein fragments, it becomes activated and clonally expands to produce thousands of identical copies of itself, so that an army of T-cells that can identify M. tuberculosis can fight the infection. In this project, we are sequencing thousands of individual T-cells to discover the array of TCRs used by the army of M. tuberculosis-specific T-cells from individuals who successfully control their M. tuberculosis infection or those who progress to TB disease. Understanding which T-cell receptors are used by cells in these different people will help us to determine T-cells that are good at controlling the infection and other T-cells that don’t seem to be useful in the fight against M. tuberculosis. We have sorted over forty thousand T-cells that recognize M. tuberculosis and, in collaboration with researchers from Stanford University, have sequenced the TCR from each individual cell. We are currently analyzing the enormous dataset this has generated to determine if the TCR repertoire and/or specific TCRs differ between TB progressors and non-progressors. We anticipate that results from this project will help to identify the bacterial targets that could be included in new TB vaccines that aim to induce T-cell responses.
EVALUATION OF SIX CONCISE HOST-BLOOD TUBERCULOSIS mRNA SIGNATURES IN HIV-INFECTED AND HIV-UNINFECTED SOUTH AFRICAN ADULTS.

Principal Investigators: Mark Hatherill and Thomas Scriba
Project Scientist: Simon Mendelsohn
Funder: Bill and Melinda Gates Foundation, Strategic Health Innovation Partnership (SHIP) of the South African Medical Research Council, Fogarty International Center of the National Institutes of Health (NIH).

A blood-based triage test that allows targeted investigation of individuals with active or sub-clinical TB disease, including asymptomatic individuals at highest risk of progression from M. tuberculosis infection to TB disease, could be used for case finding, help to shorten the time to treatment initiation, or even prevent disease progression before symptoms emerge through targeted short-course preventive therapy.

The aim of this project is to evaluate the performance of six concise PCR-based transcriptomic TB signatures, i.e. blood tests that can predict or diagnose TB, in HIV-infected and HIV-uninfected persons. A prospective head-to-head comparison of these signatures has not previously been done, and it is therefore not known which signature should be advanced for commercial development as a point-of-care test for implementation in field studies. We are measuring the six signatures in samples collected from HIV-uninfected participants of the Correlate of Risk Targeted Intervention Study (CORTIS-01) and HIV-infected participants of the CORTIS-HR, study. By utilising the high-throughput Fluidigm microfluidic multiplex qRT-PCR platform, this project will evaluate which of the six transcriptomic signatures is best at differentiating individuals with prevalent TB from healthy individuals, and which is best at predicting incident TB. Results are expected mid-2019.
This project aimed to deepen our knowledge of the humoral (antibody) response to M. tuberculosis to understand the role of antibody-mediated immunity and the potential of antibodies as biomarkers in TB. In collaboration with Prof. Galit Alter’s team at the Ragon Institute of MHG, MIT and Harvard in Boston, M. tuberculosis-specific antibody responses are being characterized in individuals of the Adolescent Cohort Study and GC6 cohorts. We are comparing antibodies in samples collected at different stages of infection including before acquisition of M. tuberculosis infection, after recent acquisition of infection, in persons who have established (latent) M. tuberculosis infection, in those who revert their IGRA and in those who are progressing to active TB. IgA, IgM and IgG antibodies specific for a variety of antigens including proteins, carbohydrates and lipids are being characterized while isotype/subclasses and the glycosylation profiles of these antibodies are defined. We are also performing functional assays to understand how antibody functions change during the different stages of infection. This study will reveal whether and how antibodies participate in, or may influence the outcome of, M. tuberculosis infection. Moreover, unique changes in M. tuberculosis-specific antibody titers combined with isotype/subclass and glycosylation profiles may be identified as powerful biomarkers that could be translated into inexpensive, easy-to-use serodiagnostic point-of-care tests to accurately identify M. tuberculosis infection, predict control or loss of control of M. tuberculosis infection or be useful for monitoring TB treatment.
planned studies

A PHASE 2A RANDOMISED CONTROLLED DOSE-DEFINING TRIAL OF THE SAFETY AND IMMUNOGENICITY OF MTBVAC IN HEALTHY, BCG NAIVE, HIV UNEXPOSED, SOUTH AFRICAN NEWBORNS.

Principal Investigator: Michèle Tameris
Funders: EDCTP

This planned Phase 2a randomized controlled, dose-defining trial of the safety and immunogenicity of MTBVAC in 99 newborns is planned to start in the first quarter of 2019. Infants will be enrolled sequentially into one of three cohorts to receive a single intradermal dose of MTBVAC 2.5 x 10^4, 2.5 x 10^5 or 2.5 x 10^6 CFU, compared to BCG vaccine (24 BCG; 75 MTBVAC).

The primary objectives of this study are to evaluate the safety, reactogenicity and immunogenicity of MTBVAC at escalating dose levels compared to the BCG vaccine in healthy, BCG naive, HIV unexposed, South African newborns with no known household TB exposure. The secondary objectives of this study are to evaluate QuantiFERON conversion rates in neonates receiving escalating dose levels of MTBVAC.

Clinicaltrials.gov. ID: NCT 03536117

A PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY TO EVALUATE THE SAFETY AND EFFICACY OF H56:IC31 IN REDUCING THE RATE OF TB DISEASE RECURRENCE IN HIV NEGATIVE ADULTS SUCCESSFULLY TREATED FOR DRUG-SUSCEPTIBLE PULMONARY TUBERCULOSIS (STUDY A 055).

SATVI Principal Investigator: Justin Shenje
Funders: EDCTP

The study seeks to evaluate the safety and efficacy of H56:IC31 in the prevention of recurrence of TB in HIV negative individuals who have recently and successfully completed 6 months of TB treatment. The prevention of recurrence study design reduces the required sample size and follow-up period to evaluate vaccine efficacy by targeting individuals with a high incidence of TB, in this case individuals who have recently completed TB treatment. The study is a multi-centre, double blind, randomized clinical trial which aims to recruit a total of 900 participants and follow them up for a period of twelve months.
A MULTICENTRE PHASE III DOUBLE-BLIND, RANDOMIZED, CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF VPM 1002 IN COMPARISON TO BCG.

SATVI Principal Investigator: Angelique Luabeya
Funder: EDCTP
Sponsor: VPM

The VPM1002 (Hyg-) is a recombinant BCG vaccine against M.tuberculosis. This phase III study aims to demonstrate the superiority of VPM1002 (Hyg-) in terms of safety and efficacy in newborn infants vaccinated with VPM1002(Hyg-) compared to those vaccinated with BCG after a follow-up period of 12 months.

PROTECTING HOUSEHOLDS ON EXPOSURE TO NEWLY DIAGNOSES INDEX MULTIDRUG-RESISTANT TUBERCULOSIS PATIENTS (PHOENIX MDR-TB).

SATVI Principal Investigator: Justin Shenje
Funders: DAIDS, ACTG

The PHOENix MDR-TB study is a Phase III, open-label, cluster-randomized, multi-center trial which aims to compare the efficacy and safety of Delaminid versus Isoniazid for preventing active TB disease among high-risk household contacts (HHC) of adults with MDR-TB. The study seeks to recruit 3,452 HHC from multiple sites and follow them for 96 weeks for TB disease. The PHOENix study is expected to start enrolment in early 2019.

MTBVAC PHASE 1B/2A RANDOMIZED, DOUBLE-BLIND, SAFETY, IMMUNOGENICITY, AND DOSE-ESCALATION STUDY IN ADULTS WITH AND WITHOUT LATENT TUBERCULOSIS INFECTION IN SOUTH AFRICA.

Principal Investigator: Angelique Luabeya
Funders: NIH, CDMRP
Sponsor: Aeras/IAVI

This trial will evaluate the safety and reactogenicity of MTBVAC at escalating dose levels compared to BCG vaccine in 144 adults aged 18-50 years with and without latent tuberculosis infection. The participants will be followed for 12 months after vaccination and the estimated study duration (from first participant vaccinated to completion of data collection) is approximately 24 months.
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29. Protein kinase C-delta (PKCδ), a marker of inflammation and tuberculosis disease progression in humans, is important for optimal macrophage killing effector functions and survival in mice.
Mucosal Immunology, 11 (2): 579-580.

30. Functional, antigen-specific stem cell memory (Tscm) CD4+ T Cells are induced by human Mycobacterium tuberculosis infection.
Mpande CAM, Dintwe OB, Musvosvi M, Mabwe S, Bilek N, Hatherill M, Nemes E, Scriba TJ SATVI Clinical Immunology Team.
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Tuberculosis (Edinb), 109: 61-68.

32. Progress and challenges in TB vaccine development.
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33. Comparison of CyTOF assays across sites: Results of a six-center pilot study.

34. Safety and immunogenicity of newborn MVA85A vaccination and selective, delayed Bacille Calmette-Gueerin for infants of Human Immunodeficiency Virus-Infected Mothers: A phase 2 randomized, controlled trial.
Clinical Infectious Disease, 66 (4): 554-563.

35. Helen McShane and colleagues reply to Deborah Cohen.
McShane H, Hill A, Hatherill M, Tameris M, Shea J, Ginsberg A.
British Medical Journal, 26; 360:k236.

36. Comparison of haematology and biochemistry parameters in healthy South African infants with laboratory reference intervals.
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37. Diagnostic performance of an optimized transcriptomic signature of risk of tuberculosis in cryopreserved peripheral blood mononuclear cells.
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awards, honours, accreditations

1. Associate Professor Tom Scriba was promoted to ad hominem Full Professor.
2. Drs. Michèle Tameris and Angelique Luabeya were promoted to Senior Clinical Researchers.
3. Drs. Virginie Rozot and Stanley Kimbung Mbandi were promoted to Research Officers.
4. Dr Virginie Rozot was awarded a Fellowship from the European Developing Countries Clinical Trials (EDCTP).
5. Dr Simon Mendelsohn was awarded a Fogarty PhD Fellowship.
6. Cheleka Mpande won the Best Publication Award from the Institute of Infectious Disease and Molecular Medicine (IDM).
7. Miguel Rodo won an outstanding Poster Award at CYTO 2018.
8. Miguel Rodo was awarded a PhD Bursary from the South African Statistics Association - National Research Foundation (NRF).
9. Dr Pia Steigler was awarded a UCT CIDRI-Africa Postdoctoral Fellowship.
During the year under review we hosted visiting academic, Professor Tom Hawn from the University of Washington (USA), as well as 4 Postdoctoral Fellows, 6 PhD students and 1 Master’s student. We also hosted visiting students Hannah Painter, Lucy Mupfumi, Alexandra Cohn and Charmain Jangano.
WHERE ARE THEY NOW?

Dr Sara Suliman, Postdoctoral Fellow at Brigham and Women's Hospital, Harvard University, USA. Former SATVI Postdoctoral Fellow.

Current Employer:
Brigham has the second largest hospital-based research program worldwide. The division of Rheumatology, Immunology and Allergy houses cutting edge research in several research foci, ranging from autoimmunity to allergy and infectious disease.

Role:
I am currently a senior post-doctoral fellow in the Lipidomic, Immunologic, Metabolomic and Allelic Associations (LIMAA) TBRU consortium. My roles include characterizing innate T cells in tuberculosis and identifying the biological mechanism underlying a genetic locus associated with TB progression risk, which was identified in a Peruvian cohort of household contacts of TB cases. I look forward to opportunities for collaboration with SATVI as I establish more independence as a junior TB investigator.

Dr Adam Penn-Nicholson, Clinical Officer-TB Program at Foundation for Innovative New Diagnostics (FIND), Switzerland. Former SATVI Research Officer.

Current Employer:
FIND is a global non-profit organization that drives innovation in the development and delivery of diagnostics to combat major diseases affecting the world's poorest populations. FIND has been involved in the development and/or delivery of every one of the 10 TB diagnostics recommended by WHO.

Role:
I am responsible for planning, management, monitoring and implementation of diagnostic clinical studies within the FIND TB programme, with a primary focus on evaluation and demonstration studies that enable WHO review and global/national policy making and specimen collection. I build and maintains links with academic institutions, industry partners and national reference laboratories around the world and coordinates site evaluation, training and monitoring visits with clinical and laboratory sites.

Dr One Dintwe, Research Officer/Staff Scientist - HVTN Immunology Laboratory, Vaccine and Infectious Disease Division at the Fred Hutchinson Cancer Research Center. Former SATVI Postdoctoral Fellow.

Current Employer:
CHIL performs assessments of immune responses to candidate HIV and TB vaccines being tested in South Africa and neighboring countries. We also offer training opportunities for Africa scientists with a special focus on clinical laboratory research and advanced lab techniques.

Role:
I oversee a team of technologists working on clinical trials looking at vaccine immunogenicity. I am also involved in developing research aims/projects for our organization and monitoring visits with clinical and laboratory sites.
For Mandela Day SATVI supported several community based soup kitchens, as well as a centre for the physically disabled in and around Worcester.

The “TB Under the Spotlight Science Engagement” programme was conceptualised and presented by scientists from the Division of Molecular Biology and Human Genetics at Stellenbosch University in partnership with SATVI and the Department of Education. Other partners in the initiative include the South African Medical Research Council (SAMRC) and the Department of Science and Technology / National Research Foundation Centre of Excellence for Biomedical Tuberculosis Research. The engagement taught learners about TB signs and symptoms, diagnosis, treatment and how a TB research laboratory works. The programme reached 893 learners in 17 primary and secondary schools in the Cape Winelands District (Worcester, Robertson and Stellenbosch).

Learners could conduct a practical experiment to extract DNA from wheat germ, which is similar to extraction done on the TB germ in laboratories.

Dr Michael Whitfield (SUN), Chloe Shain (UCT-Anthropology), Kelvin Vollenhoven, Professors Rob Warren (SUN) and Tom Scriba (UCT/SATVI).
KICK TB POSTER COMPETITION

SATVI partnered with the District Education Department in hosting the second Kick TB Poster Competition which drew 393 entries from school learners in the district. The poster art, songs, and poetry entries were exhibited at the Hugo Naude Art School in Worcester. This year’s entrants showed that learners knowledge about TB has grown, with some entries explaining latent TB.

Prizes were sponsored by:

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Intermediate Phase: 1st and 2nd prize, Paarl Girls High.

Foundation Phase winners: Dalubuhle Primary School, Franschoek.

Third prize winner, Intermediate Phase, Wellington Primary.

Senior Phase: Writing; 1st prize, St Vincent Primary, Stellenbosch.

Visitors at launch of Art Exhibit, Hugo Naude Art School.

Drs. Angelique Luabeya, Michèle Tameris with Kelvin Vollenhoven during the launch of the Art Exhibit.
funders
collaborators
South African Tuberculosis Vaccine Initiative (SATVI)

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DTP: Kelvin Vollenhoven