

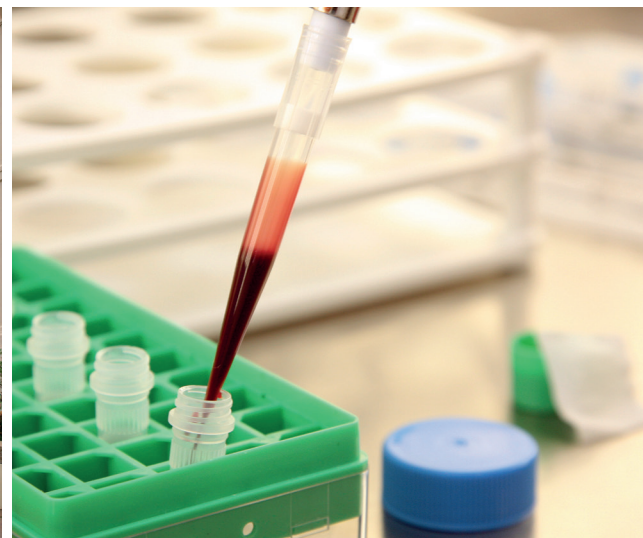


satvi

SOUTH AFRICAN  
TUBERCULOSIS VACCINE INITIATIVE



# ANNUAL REPORT 2014





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# vision

# &

# mission

our  
vision

A World Without TB

our  
mission

Innovative and High Quality  
TB Vaccine Research in  
Africa to Impact the Global  
Epidemic.

# directors foreword



2014 was certainly a year of change for SATVI, with the departure of Professor Willem Hanekom to join the Bill & Melinda Gates Foundation, several longstanding projects reaching successful completion, and two large proof-of-concept efficacy trials starting with a 'bang'. It has also been an extraordinarily busy year, in which the SATVI clinical and laboratory teams have conducted clinical trials of no less than 7 tuberculosis vaccines and a novel jet injector device, in newborn, infant, adolescent, and adult study populations. It was a pleasure to take on the challenge of leading this dynamic research group, given SATVI's solid operational, financial, and academic foundation.

Highlights for the group include approval as an NIH Division of AIDS Clinical Research Site, formal accreditation as a University of Cape Town Research Centre, and renewal of the SATVI Laboratory SANAS accreditation. New operational systems developed by Chief Operating Officer Zameer Brey and Field Site Manager Marwou De Kock have improved efficiency across the board and renovations to the vaccination clinic will streamline procedures for the teams at the Worcester site. SATVI continued an excellent track record of research outputs, with 24 peer-reviewed publications for the year, with high impact publications including the findings of the RIFAQUIN tuberculosis treatment-shortening trial

(Jindani et al), reported in the New England Journal of Medicine. There were many individual achievements, but two deserve special mention — Associate Professor Tom Scriba, Deputy Director Immunology and 2014 recipient of a Silver Medal from the Medical Research Council of South Africa, was awarded a high-profile grant from the MRC Strategic Health Innovation Partnership to study correlates of risk for tuberculosis; and Dr Michele Tameris was awarded her second Wellcome Trust grant, to study community engagement in tuberculosis research through street theatre.

We look forward to working with our international partners and stakeholders on several exciting new projects, with live mycobacterial vaccine trials and innovative, experimental medicine studies on the horizon. Finally, a heartfelt 'thank you' to all our study participants and their families in the Worcester community who support our clinical trials and share the SATVI vision of 'a world without TB'.

Mark Hatherill  
Director



# about SATVI

## WHO WE ARE

**S**ATVI is a tuberculosis research group accommodating several disciplines including paediatrics, infectious diseases, epidemiology, public health, immunology and clinical/biological sciences. SATVI has a large and well-developed clinical field site in the Boland Overberg region, with the core on the premises of the Brewelskloof TB Hospital in Worcester, from where most clinical/epidemiological studies and clinical trials of new TB vaccines are conducted.

The Immunology and Laboratory based work is led by Associate Professor Tom Scriba; and the Clinical Trials work is led by SATVI Director, Associate Professor Mark Hatherill.

## OUR WORK

**T**he South African Tuberculosis Vaccine Initiative (SATVI), which was launched in 2001 at the University of Cape Town (UCT), has developed into a sophisticated world class TB vaccine clinical research facility, with state of the art immunology laboratories located within the Institute of Infectious Disease and Molecular Medicine (IDM) of the University of Cape Town, and at the Worcester field site.

SATVI is regarded as a leader in tuberculosis vaccine clinical research worldwide and is the largest dedicated tuberculosis vaccine research group on the African continent. Our laboratories are accredited, which means adherence to the highest international standards.

SATVI has been extraordinarily productive in terms of clinical trial activities, having conducted 19 Phase I–IV trials of BCG and seven novel TB vaccine candidates, among more than 25,000 research participants, during the last 14 years. The group's publication output, since 2006, totals 130 co-authored papers, with an Average Impact Factor 4.8, of which 105 have a SATVI first or senior author. The active SATVI postgraduate program has also produced 9 PhD graduates and several Masters graduates during the same period.

# governance

## SATVI executive committee and senior research team

*The Executive Committee is comprised of  
the Director, Associate Professor: Mark Hatherill;  
Deputy Director Immunology, Associate Professor: Thomas Scriba;  
Chief Operations Officer: Dr Zameer Brey and  
the Worcester Field Site Manager: Mrs Marwou de Kock.*

## EXECUTIVE COMMITTEE:

### ASSOCIATE PROFESSOR MARK HATHERILL, DIRECTOR



Mark Hatherill is a specialist paediatrician, with accreditation in critical care, and an experienced clinical trialist who is active in the design and implementation of innovative trials of new

TB vaccines through several consortia. He is a Full Member of the Institute of Infectious Disease & Molecular Medicine (IDM) at the University of Cape Town; a member of the SA Department of Health TB Think Tank, Working Group on Diagnostics, Drugs and Vaccines; and a member of the Global TB Vaccine Partnership, Working Group on Experimental Medicine. Dr Hatherill is funded by competitive grants from the Joint Global Health Trials scheme (UK MRC/ Wellcome Trust/DfID) and US National Institutes of Health, and multiple Aeras contracts.

### ASSOCIATE PROFESSOR TOM SCRIBA, DEPUTY DIRECTOR



Tom Scriba (PhD) completed graduate training in T-cell immunology in HIV at Oxford University, in the United Kingdom in 2006. He joined SATVI, within the Institute of Infectious

Disease and Molecular Medicine (IDM) in Cape Town as a post-doctoral fellow where he trained in paediatric and clinical immunology in tuberculosis and vaccinology. In June 2009, he took up a faculty position as a Senior Researcher, and in January 2014 was appointed Associate Professor at the University of Cape Town. He has also been SATVI Deputy Director, Immunology since 2011 and has been centrally involved in correlates of risk of TB studies in infants, following BCG vaccination, and in adolescents, following infection with *M. tuberculosis*.

### DR ZAMEER BREY, CHIEF OPERATING OFFICER



Zameer Brey, is a qualified medical practitioner and holds a MBA and PhD in Lean and Change management from UCT. At SATVI, he has oversight of all operational functions within SATVI including corporate services (HR,

Finance, Risk Management) and is responsible for systems development. Dr Brey has worked in several senior leadership positions where his core role was that of change agent. He has served as a process analyst for the Western Cape Department of Health; as internal consultant to the Deanery of the Faculty of Health Sciences UCT; consulted to the National Departments of Health and Higher Education; and Acting General Manager at the South African Medical

Association. He currently also serves on the Board of the Office of Health Standards Compliance, the South African Medical Association and Groote Schuur Hospital. His accolades include an Allan Gray scholarship in 2008, the Premier's Service in 2009 and being cited in the Mail & Guardian as one of the top 300 youth in South Africa in 2010.

### MARWOU DE KOCK, FIELD SITE MANAGER



Marwou de Kock graduated from the Cape Peninsula University of Technology with a Degree in Biomedical Science; she subsequently completed a Degree in Laboratory Management and is currently busy with her Masters Dissertation

in Clinical Research Administration. She has been working at SATVI since 2002 and has an intricate knowledge of the site, the people and procedures in the laboratory, as well as clinical operations. She started in the SATVI Field Site laboratory and built it up to a world class facility that received SANAS Accreditation in 2010. She is currently responsible for managing the SATVI project office, overseeing and managing service delivery for all operations, as well as coordinating and implementing multiple research projects at the Field Site.



## SENIOR CLINICAL RESEARCH TEAM:

DR MICHELE TAMERIS, PRINCIPAL INVESTIGATOR



Michele Tameris graduated from the University of Cape Town with the MBChB qualification in 1980. Thereafter she worked for many years in the public health sector in Cape Town (Red Cross

Childrens' Hospital and Groote Schuur Hospital) and in Worcester (Eben Donges Hospital and Worcester CDC). In 2003 she joined SATVI as a clinical researcher and since 2005 has been Sub-Investigator on 13 novel TB vaccine trials and Principal Investigator on 3. These trials have been of 7 novel TB vaccines and have included first in man trials, phase 1, 2a and 2b trials including the first phase 2b infant efficacy trial of a new TB vaccine. 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.

DR HENNIE GELDENHUYS, PRINCIPAL INVESTIGATOR



After working in private general practice for 10 years Hennie Geldenhuys joined SATVI full-time in 2007. He is actively involved in the design, conduct, and analysis of

vaccine clinical trials and other research studies in tuberculosis. He has fulfilled the role of Investigator and Principal Investigator on a number of clinical trials, and has published a number of scientific papers. Hennie is based at SATVI's field site in the town of Worcester. His research interests include alternative vaccine administration methods, clinical trials with adolescents, quality management in clinical trials, and the science of translating research protocols into field practice.

DR ANGELIQUE LUABEYA, PRINCIPAL INVESTIGATOR



Angelique Luabeya is a Clinical Researcher and current Principal Investigator on three trials of new TB vaccines (AERAS C035-456, IDRI-TBVPX-203, VPM1002-ZA-2.13TB) involving healthy adult

participants, TB patients and newborns. She has a particular research interest in clinical immunology and health systems in the area of TB prevention in young children, and is also interested in clinical and environmental factors which are associated with the risk of TB infection and disease in our communities.

DR. ADAM PENN-NICHOLSON, POSTDOCTORAL FELLOW



After receiving his PhD in the USA, Adam worked in industry on the development and manufacture of vaccines. He joined SATVI in 2011. Adam's main focus is on the discovery of blood-based biomarkers that prospectively predict TB disease risk, and understanding the biology

involved in progression from latent TB infection to active TB disease. He also provides scientific oversight of several clinical TB vaccine trials currently being conducted at SATVI.

DR ELISA NEMES, SCIENTIFIC OFFICER



Elisa completed her PhD in HIV-specific T cell immunology in Italy and France. She then worked on paediatric immune responses to HIV and TB in Cameroon. She joined SATVI in 2011, where she has been involved in 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 in HIV+ children.



# highlights

2014





SATVI team with Professor Linda-Gail Bekker (UCT Clinical Trials Unit) and delegation from the Division of AIDS (DAIDS), the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institutes of Health (NIH)-during visit to SATVI- August 2014.

## APPROVAL AS NIH NIAID DIVISION OF AIDS CLINICAL RESEARCH SITE (CRS)

The Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), announced in August 2014 that SATVI had met its stringent requirements for participation in international clinical trials. This approval by DAIDS means that the SATVI CRS, part of the UCT Clinical Trials Unit (UCT CTU) headed by Professor Linda-Gail Bekker, will participate in DAIDS-funded clinical research for the development of therapies, interventions and strategies to treat and prevent tuberculosis

## ACCREDITATION AS UCT RESEARCH CENTRE

SATVI was awarded formal accreditation as a Research Centre by the University of Cape Town in June 2014. This accreditation is recognition of SATVI's potential as a growing, highly productive tuberculosis research group; and offers major benefits for the organisation, such as an improved governance environment, five-yearly cycles of strategic review, and the potential to leverage additional funding for students and post-doctoral fellows.



## CLINICAL TRIALS

A DOUBLE-BLIND RANDOMISED, PLACEBO-CONTROLLED, DOSE-FINDING TRIAL OF THE NOVEL TUBERCULOSIS VACCINE AERAS-402, AND ADENOVIRUS-VECTORED FUSION PROTEIN, IN HEALTHY, BCG-VACCINATED INFANTS

(Principal Investigator: Mark Hatherill; Sponsor Aeras)

The SATVI team closed the study database, having successfully completed the follow-up of 166 of the total 487 healthy infants in this multi-centre trial of the safety and immunogenicity of the AERAS-402 candidate vaccine.

PHASE II RANDOMISED CONTROLLED TRIAL TO EVALUATE SAFETY AND IMMUNOGENICITY OF MVA85A AND SELECTIVE DELAYED BACILLE CALMETTE-GUERIN (BCG) VACCINATION IN INFANTS OF HIV INFECTED MOTHERS

(Principal Investigator: Mark Hatherill; Sponsor UCT)

Enrolment of all 248 HIV exposed infants was completed by SATVI and the Stellenbosch University (Principal Investigator: Anneke Hesselning) teams in this trial that will test the safety and immunogenicity of MVA85A vaccination at birth.

A RANDOMISED, PLACEBO CONTROLLED, PARTIALLY BLINDED PHASE II STUDY TO EVALUATE THE SAFETY, IMMUNOGENICITY AND PREVENTION OF INFECTION WITH MYCOBACTERIUM TUBERCULOSIS OF AERAS 404 AND BCG REVACCINATION IN HEALTHY ADOLESCENTS.

(Principal Investigator: Mark Hatherill; Sponsor Aeras)

The enrolment of healthy, QuantiFERON negative adolescents has started in the first trial to test the concept that BCG and the Aeras-404 vaccine might offer protection against primary tuberculosis infection.

EFFICACY OF GSK BIOLOGICALS' CANDIDATE TUBERCULOSIS VACCINE GSK 692342 AGAINST TB DISEASE, IN ADULTS LIVING IN A TB ENDEMIC REGION.

(Principal Investigator: Mark Hatherill; Sponsor GSK)

The enrolment of healthy, QuantiFERON positive adults started in this large, multi-centre trial that will test protection against active tuberculosis disease.





*The SATVI team with Path Representatives, Jennifer Foster and Gene Saxon*

#### COMPARATIVE STUDY OF BACILLE CALMETTE GUERIN (BCG) DELIVERY VIA DISPOSABLE SYRINGE JET INJECTOR AND NEEDLE SYRINGE

(Principal Investigator: Hennie Geldenhuys; Funder Path)  
The BCG Jet Injector trial compared the administration of BCG via the conventional Mantoux method with syringe and needle, to via a novel needle-free jet injector device. The endpoints were safety, injection performance and immunogenicity. The study population consisted of 30 adults and 66 newborns. The trial commenced in 2012, the last study visit was performed in December 2013, with the clinical trial report and manuscript pending publication.

#### A PHASE II, RANDOMISED, OBSERVER-BLINDED, SINGLE CENTRE TRIAL EVALUATING THE IMMUNOGENICITY AND SAFETY OF TWO DOSES OF AN ADJUVENATED TB SUBUNIT VACCINE (AG85B-ESAT-6+IC31) USING 2 DIFFERENT VACCINATION SCHEDULES IN HEALTHY ADOLESCENTS.

(Principal Investigator: Hennie Geldenhuys; Funder Statens Serum Institute (SSI))

In this trial the H1 TB vaccine candidate was tested in 240 adolescents for safety and immunogenicity. The last participant visit was conducted in December 2013. All of the substantial immunology endpoints (Elispot and flow cytometry) were performed by the SATVI laboratory. The clinical trial report and manuscript are in preparation.

#### A PHASE I B, RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED, DOSE ESCALATION STUDY TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF THE IDD 93+GLA-SE VACCINE IN BCG VACCINATED HEALTHY ADULTS

(Principal Investigator: Michele Tameris; Funder Infectious Disease Research Institute (IDRI))

The enrolment of 66 healthy adults (QFT negative and QFT positive) into the 4 cohorts of this Phase 1b safety, immunogenicity and dose finding trial of the adjuvanted vaccine ID93+GLA-SE started in September 2013 and was completed in September 2014. Follow up continues until end June 2015.

#### A PHASE I/II A DOUBLE BLIND, RANDOMISED, PLACEBO-CONTROLLED, DOSE-FINDING STUDY TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF AERAS-456 IN HIV NEGATIVE ADULTS WITH AND WITHOUT LATENT TUBERCULOSIS INFECTION

(Principal Investigator: Angelique Luabeya; Funder Aeras)

This Phase IIa trial of the H56:IC31 vaccine, which incorporates M.tb-specific antigens that target several stages of the complex host-pathogen interaction, is being conducted in HIV-uninfected South African adults with or

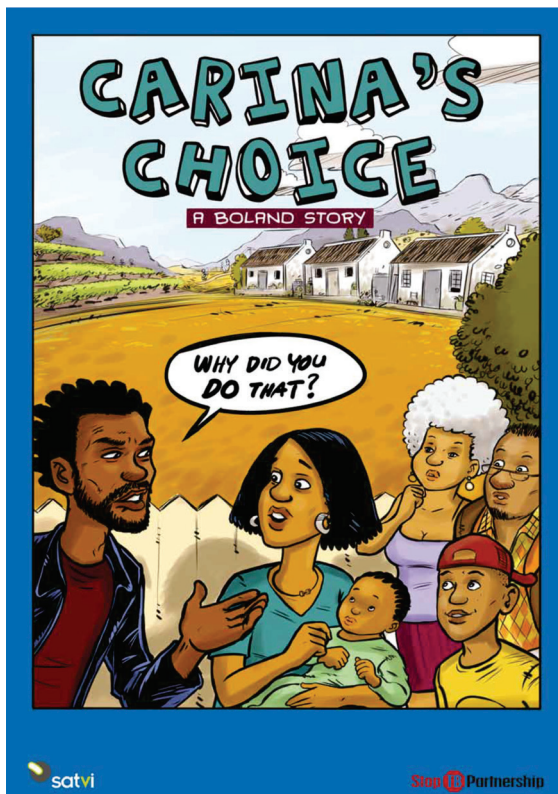
without latent M. tuberculosis infection, in collaboration with Statens Serum Institute (Denmark) and AERAS (USA). The clinical trial has completed enrolment and follow-up of participants will continue until September 2015.

#### UNCONVENTIONAL IMMUNE RESPONSES INDUCED BY BCG-REVACCINATION IN ADULTS WITH M TUBERCULOSIS INFECTION

(Principal Investigator: Mark Hatherill; Funder NIH)

We conducted a clinical trial to investigate the safety and immunogenicity of Bacillus Calmette-Guerin (BCG) revaccination in M. tuberculosis-infected (TST-positive) adults, either following isoniazid preventative therapy or in the absence of preventative therapy. Immune response results show that BCG, as a model for whole mycobacterial vaccines, induces IFN-gamma-expressing NK and NKT cell responses, which appear to persist for many months after vaccination. We are currently characterizing these unconventional "memory" innate responses to BCG vaccination in greater detail. This work is being performed in collaboration with John Johnson and Henry Boom at the Case Western Reserve University in Cleveland, USA.

## AWARENESS-RAISING



## DRAMA SETS THE STAGE

Supported by a Wellcome Trust International Engagement award in 2012, SATVI facilitated a drama production concerning TB vaccine clinical research, "Carina's Choice" with learners from Worcester Secondary School as actors and UCT drama school students as mentors. A very successful roadshow to 8 local high schools reached approximately 8000 adolescents in Q3, 2013. DVDs with English or Xhosa subtitles have been produced for distribution as well as free download access on SATVI website. <http://vimeo.com/103109835>

## BEAT TB – ITS YOUR CHOICE

A second Wellcome Trust International Engagement grant was awarded in October 2014 for a street theatre project to commence in 2015. This will build on work in the first drama project, taking the issue of TB research into the streets, targeting the local adult population.

## IMMUNOLOGY

### TRANSCRIPTOMIC CORRELATES OF RISK OF TB

(Principal Investigator: Tom Scriba; Funders Bill & Melinda Gates Foundation, NIH and MRC-SHIP)

A third of the global population is thought to harbor M. tuberculosis infection, but only 10% of these persons will progress to TB disease. This study aimed to identify and validate blood transcriptomic correlates of risk of TB, in adolescents. We used RNA-sequencing to discover transcriptomic correlates of risk, and developed a real-time PCR test to allow more practical measurement of this biomarker. This new test allows prediction of risk of TB over 1 year with ~90% specificity and ~50% sensitivity, and may be used for targeted preventive treatment of persons at high risk of TB. This work was performed in collaboration with Alan Aderem and Daniel Zak and others at Seattle Biomedical Research Institute in Seattle, USA.



Pharmacy receives "A"-grading from SA Pharmacy Council (SAPC) SATVI'S Pharmacy attained an A-grading from the South African Pharmacy Council which was awarded after a rigorous inspection of all processes, equipment and staff by the SAPC in February 2014.



### APPLICATION OF CYTOMETRY BY TIME-OF-FLIGHT (CYTOF) TECHNOLOGY TO TB IMMUNOLOGY

(Principal Investigator: Tom Scriba; Funder Bill & Melinda Gates Foundation)

Cytometry by time-of-flight (CyTOF) or mass cytometry, allows for the analysis of more than 40 parameters on a single cell level in a single experimental panel by staining cells with heavy-metal-conjugated monoclonal antibodies specific to cell subset, phenotypic and functional markers.

This exciting technology permits unparalleled multi-dimensional analysis of complex cellular subsets.

We are currently optimizing intracellular cytokine staining and HLA tetramer mass cytometry assays and performing head-to-head comparisons with conventional flow cytometry assays. The aim is to integrate mass cytometry into a systems biology platform for identification of correlates of risk of tuberculosis. This work is being performed in collaboration with Holden Maecker and Mark Davis at Stanford University in Palo Alto, USA.

### CHARACTERISATION OF NOVEL MYCOBACTERIA-SPECIFIC NAÏVE-LIKE MEMORY CELLS

(Principal Investigator: Tom Scriba; Funders MRC)

A population of *M. tuberculosis*-specific memory CD4 T cells, which express effector cytokines, but display the unusual memory phenotype CD45RA+CCR7+CD27+, has been described by us and other groups. We aimed to characterize these naïve-like memory CD4 T cells to understand their role in anti-mycobacterial immunity. We detected naïve-like memory cells with HLA class II tetramers in healthy persons with *M. tuberculosis* infection and performed transcriptomic and functional analyses by microfluidic qRT-PCR and flow cytometry. *M. tuberculosis*-specific naïve-like memory CD4 T cells expressed mRNA transcripts of cytotoxic molecules and cytokines, consistent with effector function, and chemokine receptors that suggest migration to inflamed tissues. Investigation of the functional attributes of these naïve-like memory CD4 T cells is on-going.



#### SATVI LABS SANAS ACCREDITED

The SATVI laboratories in Worcester and Cape Town received ISO 15189 Certification from the South African National Accreditation System (SANAS).

## SYSTEMS BIOLOGY OF H1/IC31-INDUCED T-CELL RESPONSES

(Principal Investigator: Tom Scriba; Funders TBVI, Horizon 2020)

The analysis of T cell responses against mycobacterial infection has to date focused on T helper type 1 functions. However, frequencies of functions of mycobacteria-specific Th1 cells do not correlate with risk of TB. The aim of this project was to apply multi-dimensional technologies to identify novel functional and/or phenotypic attributes of antigen-specific T cells induced by vaccination against TB. We combined and optimised Fluidigm BioMark HD microfluidic qRT-PCR technology with HLA class II tetramer staining and flow cytometric cell sorting to analyse transcriptomic and functional attributes of CD4 T cells induced by H1/IC31 vaccination in M. tuberculosis-infected and uninfected adolescents. This work is being performed in collaboration with Peter Andersen and others at Statens Serum Institut in Stockholm, Sweden.

## AWARDS AND PRIZES



*In the 2014 period Tom Scriba, Deputy Director Immunology and Laboratory, was appointed as an Associate Member in the Institute of Infectious Disease and Molecular Medicine (IDM); promoted to Associate Professor; awarded the 2013 Meiring Naudé Medal by the Royal Society of South Africa, recognised for his substantial contribution to medical research in South Africa with a Silver medal in the 2014 Medical Research Council Merit Awards (October 2014) and nominated as finalist in the prestigious NSTF-BHP Billiton Awards for 2013/14.*

# research outputs

I N 2014, the period under review, our publication output was 24 articles in international peer reviewed journals. Twelve of these had first and/or last authors from SATVI. A number appeared in high-impact journals, such as the New England Journal of Medicine (Impact Factor: 53) and Clinical Infectious Diseases (Impact Factor: 9.4). The Average Impact Factor for main author publications was 4.5, and the Average Impact Factor for all publications was 6.6.

## PUBLICATIONS IN PEER REVIEWED JOURNALS

1. Effect of isoniazid therapy for latent TB infection on QuantiFERON-TB gold in-tube responses in adults with positive tuberculin skin test results in a high TB incidence area: a controlled study. Johnson JL, Geldenhuys H, Thiel BA, Toefy A, Suliman S, Pienaar B, Chheng P, Scriba T, Boom WH, Hanekom W, Hatherill M. Chest. 2014;145(3):612-7.
2. Maturation of Innate Responses to Mycobacteria over the First Nine Months of Life. Shey MS, Nemes E, Whatney W, de Kock M, Africa H, Barnard C, van Rooyen M, Stone L, Riou C, Kollmann T, Hawn TR, Scriba TJ, Hanekom WA. J Immunol. 2014;192(10):4833-43.
3. Distinct T-cell responses when BCG vaccination is delayed from birth to 6 weeks of age in Ugandan infants. Lutwama F, Kagina BM, Wajja A, Waiswa F, Mansoor N, Kirimunda S, Hughes EJ, Kiwanuka N, Joloba ML, Musoke P, Scriba TJ, Mayanja-Kizza H, Day CL, Hanekom WA. J Infect Dis. 2014;209(6):88797.
4. The candidate TB vaccine, MVA85A, induces highly durable Th1 responses. Tameris M, Geldenhuys H, Luabeya AK, Smit E, Hughes JE, Vermaak S, Hanekom WA, Hatherill M, Mahomed H, M, Scriba TJ, McShane H, PLoS One. 2014;9(2):e87340.
5. The novel tuberculosis vaccine, AERAS-402, is safe in healthy infants previously vaccinated with BCG, and induces dose-dependent CD4 and CD8T cell responses. Kagina BM, Tameris MD, Geldenhuys H, Hatherill M, Abel B, Hussey GD, Scriba TJ, Mahomed H, Sadoff JC, Hanekom WA; Vaccine. 2014; 14;32(45):5908-17.
6. Safety and reactogenicity of BCG revaccination with isoniazid pretreatment in TST positive adults. Hatherill M, Geldenhuys H, Pienaar B, Suliman S, Chheng P, Debanne SM, Hoft DF, Boom WH, Hanekom WA, Johnson JL. Vaccine. 2014;32(31):3982-8.
7. A controlled trial of sputum induction and routine collection methods for TB diagnosis in a South African community. Geldenhuys HD, Whitelaw A, Tameris MD, Van As D, Luabeya KK, Mahomed H, Hussey G, Hanekom WA, Hatherill M. Eur J Clin Microbiol Infect Dis. 2014, 33(12):2259-66.

8. Time to Symptom Resolution in Young Children Treated for Pulmonary Tuberculosis. Mpofu N, Moyo S, Mulenga H, Luabeya KK, Tameris M, Geldenhuys H, Hussey G, Scriba T, Hanekom W, Mahomed H, Hatherill M. *Pediatr Infect Dis J*. 2014; 33(12):1226-30.
9. Patients with Tuberculosis Disease Have Mycobacterium tuberculosis-Specific CD8 T Cells with a Pro-Apoptotic Phenotype and Impaired Proliferative Capacity, Which Is Not Restored following Treatment. Day CL, Moshi ND, Abrahams DA, van Rooyen M, O'rie T, de Kock M, Hanekom WA. *PLoS One*. 2014;9(4):e94949.
10. Differential leukocyte counting and immunophenotyping in cryopreserved ex-vivo whole blood. Nemes E., Kagina B.M.N., Smit E., Africa H., Steyn M., Hanekom W.A. and Scriba T.J. *Cytometry Part A*, in press.
11. Qualification of a Whole Blood Intracellular Cytokine Staining Assay To Measure Mycobacteria-Specific CD4 and CD8 T cell Immunity by Flow Cytometry. Kagina B.M., Mansoor N., Kpamegan E.P., Penn-Nicholson A., Nemes E., Smit E., Gelderbloem S., Soares A.P., Abel B., Keyser A., Sidibana M., Hughes J.E., Kaplan G., Hussey G.D., Hanekom W.A. and Scriba T.J. *Journal of Immunological Methods*, in press.
12. The Combined Use of M. tuberculosis-specific CD4 and CD8 T-Cell Responses Is a Powerful Diagnostic Tool of Active Tuberculosis. Rozot V, Patrizia A, Vigano S, Mazza-Stalder J, Idrizi E, Day CL, Perreau M, Lazor-Blanchet C, Ohmiti K, Goletti D, Bart PA, Hanekom W, Scriba TJ, Nicod L, Pantaleo G, Harari A. *Clin Infect Dis*. 2014, in press.
13. High-dose rifapentine with moxifloxacin for pulmonary tuberculosis. Jindani A, Harrison TS, Nunn AJ, Phillips PP, Churchyard GJ, Charalambous S, Hatherill M, Geldenhuys H, McIlleron HM, Zvada SP, Mungofa S, Shah NA, Zizhou S, Magweta L, Shepherd J, Nyirenda S, van Dijk JH, Clouting HE, Coleman D, Bateson AL, McHugh TD, Butcher PD, Mitchison DA; RIFAQUIN Trial Team. *N Engl J Med*. 2014;371(17):1599-608.
14. TB Vaccines & Prevention of Infection. Hawn TR, Day TR, Scriba TJ, Hatherill M, Hanekom WA, Evans TG, Churchyard GJ, Kublin JG, Bekker L, Self SG. *Microbiology and Molecular Biology Reviews*. 2014;78(4):650-671.
15. The impact of HIV exposure and maternal Mycobacterium tuberculosis infection on infant immune responses to bacilli Calmette-Guérin vaccination. Jones CE, Hesselring AC, Tena-Coki NG, Scriba TJ, Chegou NN, Kidd M, Wilkinson RJ, Kampmann B. In press, *AIDS*.
16. Safety and Immunogenicity of H1/IC31®, an Adjuvanted TB Subunit Vaccine, in HIV-Infected Adults with CD4+ Lymphocyte Counts Greater than 350 cells/mm<sup>3</sup>: A Phase II, Multi-Centre, Double-Blind, Randomized, Placebo-Controlled Trial. Reither K, Katsoulis L, Beattie T, Gardiner N, Lenz N, Said K, Mfinanga E, Pohl C, Fielding KL, Jeffery H, Kagina BM, Hughes EJ, Scriba TJ, Hanekom WA, Hoff ST, Bang P, Kromann I, Daubenberger C, Andersen P, Churchyard GJ. *PLoS One*. 2014;9(12):e114602.
17. Serum indoleamine 2,3-dioxygenase activity is associated with reduced immunogenicity following vaccination with MVA85A. Tanner R, Kakalacheva K, Miller E, Pathan AA, Chalk R, Sander CR, Scriba T, Tameris M, Hawkrigde T, Mahomed H, Hussey G, Hanekom W, Checkley A, McShane H, Fletcher HA. *BMC Infect Dis*. 2014; 14(1):660.
18. Inflammatory and myeloid-associated gene expression before and one day after infant vaccination with MVA85A correlates with induction of a T cell response. Matsumiya M, Harris SA, Satti I, Stockdale L, Tanner R, O'Shea MK, Tameris M, Mahomed H, Hatherill M, Scriba TJ, Hanekom WA, McShane H, Fletcher HA. *BMC Infect Dis*. 2014;14:314.
19. Analysis of host responses to Mycobacterium tuberculosis antigens in a multi-site study of subjects with different TB and HIV infection states in sub-Saharan Africa. Sutherland JS, Lalor MK, Black GF, Ambrose LR, Loxton AG, Chegou NN, Kassa D, Mihret A, Howe R, Mayanja-Kizza H, Gomez MP, Donkor S, Franken K, Hanekom W, Klein MR, Parida SK, Boom WH, Thiel BA, Crampin AC, Ota M, Walzl G, Ottenhoff TH, Dockrell HM, Kaufmann SH; GCGH Biomarkers for TB consortium. *PLoS One*. 2013;8(9):e74080.



20. Process of assay selection and optimization for the study of case and control samples from a phase IIb efficacy trial of a candidate tuberculosis vaccine, MVA85A. Harris SA, Satti I, Matsumiya M, Stockdale L, Chomka A, Tanner R, O'Shea MK, Manjaly Thomas ZR, Tameris M, Mahomed H, Scriba TJ, Hanekom WA, Fletcher HA, Mc Shane H. *Clin Vaccine Immunol*. 2014;21(7):1005-11.
21. Differential gene expression of activating Fcγ receptor classifies active tuberculosis regardless of human immunodeficiency virus status or ethnicity. Sutherland JS, Loxton AG, Haks MC, Kassa D, Ambrose L, Lee JS, Ran L, van Baarle D, Maertzdorf J, Howe R, Mayanja-Kizza H, Boom WH, Thiel BA, Crampin AC, Hanekom W, Ota MO, Dockrell H, Walzl G, Kaufmann SH, Ottenhoff TH; GCGH Biomarkers for TB consortium. *Clin Microbiol Infect*. 2014;20(4):O230-8.
22. Moxifloxacin population pharmacokinetics and model-based comparison of efficacy between moxifloxacin and ofloxacin in African patients. Zvada SP, Denti P, Sirgel FA, Chigutsa E, Hatherill M, Charalambous S, Mungofa S, Wiesner L, Simonsson US, Jindani A, Harrison T, McIlleron HM. *Antimicrob Agents Chemother*. 2014;58(1):503-10.
23. St John's Wort (*Hypericum perforatum* L.) photomedicine: hypericin-photodynamic therapy induces metastatic melanoma cell death. Kleemann B, Loos B, Scriba TJ, Lang D, Davids LM. *PLoS One*. 2014;9(7):e103762.
24. Qualification of a whole blood intracellular cytokine staining assay to measure mycobacteria-specific CD4 and CD8 T cell immunity by flow cytometry. Kagina BM, Mansoor N, Kpamegan EP, Penn-Nicholson A, Nemes E, Smit E, Gelderbloem S, Soares AP, Abel B, Keyser A, Sidibana M, Hughes JE, Kaplan G, Hussey GD, Hanekom WA, Scriba TJ. *J Immunol Methods*. 2014 pii: S0022-1759(14)00356-1.

# postgraduate students and postdoctoral fellows

*SATVI attracts students from mainly Africa and Europe, who want to study tuberculosis within a clinical research environment. In 2014, SATVI took in one BSc Honours, four MPhil, two MSc and two PhD students, as well as 8 postdoctoral research fellows.*



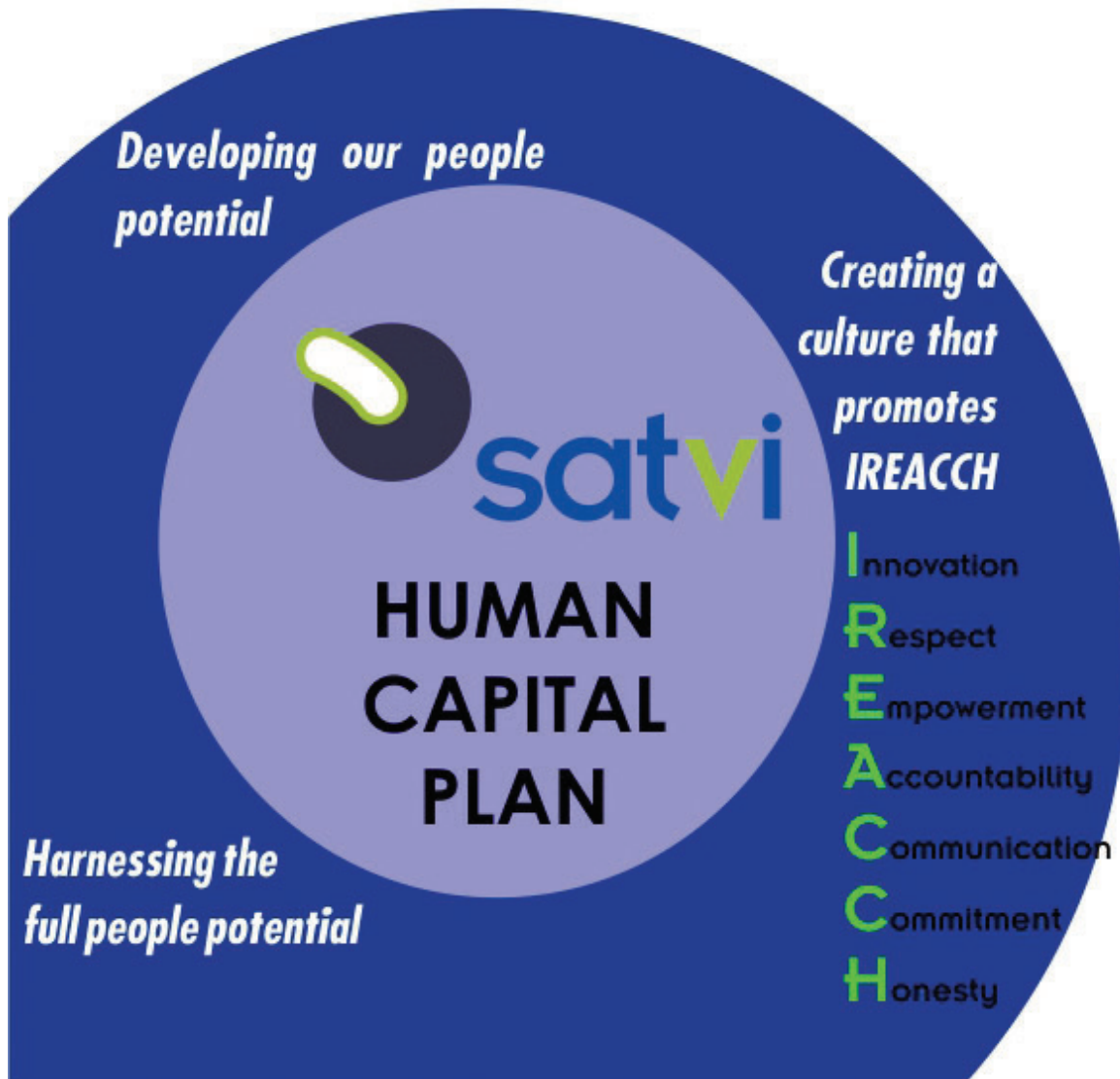
Postdoctoral Research Fellow, Dr Adam Penn-Nicholson presenting a paper titled "M72/AS01E candidate vaccine has an acceptable safety profile and is immunogenic in adolescents in a TB endemic setting" at the UCT Department of Paediatrics and Child Health Annual Research Days held on 29 October 2014 at the Red Cross War Memorial Children's Hospital, Cape Town.



Postdoctoral Research Fellow, Dr Sara Suliman, presenting a paper titled "Validation of Candidate Transcriptomic Correlates of Risk of TB in African Households Contacts of TB cases" at the Institute of Infectious Disease and Molecular Medicine's Ten year Anniversary Symposium on 3 November 2014 in Cape Town.

# SATVI

## staff



THE management team has built further on the 3 year Human Culture and Capital Plan, which commenced in 2012 and which focuses on (1) developing our staff, (2) harnessing the full 'people' potential within the organisation and (3) ensuring the creation of a culture that promotes Innovation, Respect, Empowerment, Accountability, Communication, Commitment and Honesty, which make up the acronym IREACH.

The organisation has continued refining its organisational structure, resulting in a more flat hierarchy, effectively with a smaller top management and a broader middle management. We have implemented the following initiatives to promote teambuilding, innovation and developing it as a research grouping which is rooted in the broader Winelands community:

- Bright Sparks Innovation Program
- Staff Wellness Program
- Women's Day
- Casual Day
- CANSA Tea
- Commemorating Mandela Day
- Secretary and Bosses Day
- Quarterly Staff Meetings and Teambuilding to promote communication, teambuilding, cooperation and cohesion.



SATVI staff who participated in CANSA Tea Day-Stellenbosch-20 September 2014



Staff and Student Induction- Friday 11 July 2014.



Casual Day- Friday 5 September 2014. In support of Casual Day 2014, SATVI staff dressed up to bring out the Bling, put on the ritz, rustle up a little razzle dazzle with outfits inspired by the nightlife of the 1920s, 1930s and 1940s.



Women's Day Challenge "Doeke Friday", 22 August 2014.





Quarterly Staff Meeting, Constantia, 8 August 2014

## QUARTERLY STAFF MEETINGS

The Quarterly Staff Meetings are a platform where the organisation shares its achievements, builds teamwork and prepares for the medium to long term.

## BRIGHT SPARKS INNOVATION PROGRAM

SATVI celebrated the second year of existence of the Bright Sparks Innovation Program which aims to create and nurture innovation amongst staff through the submission of innovative ideas from staff. Some of the submissions received were an online ordering system for medical supplies, the development and implementation of a Staff Wellness Program to promote health and active

lifestyles amongst staff, implementation of Whats App chatgroups to promote internal communication and marketing activations at the local mall.

## WELLNESS

With the support of the SATVI Executive Committee, the Wellness Program was piloted in February 2014, resulting in the establishment of a workplace fitness group which trains three times weekly at the SATVI premises, under the supervision of a fitness instructor. They also participated in several off-site fitness challenges. During November 2014 a Staff Wellness Day was also hosted in Worcester with the support of UCT Wellness and Discovery Health.



Mrs Christel Ferrus having her blood pressure taken at Staff Wellness Day, Worcester – Friday 24 October 2014 .



SATVI Resource Manager, Mrs Linda van der Merwe pedalling the Blenda Venda Bike which makes healthy fruit smoothies.



UCT Dietician consulting with SATVI staff; Mesdames Ameryl van Schalkwyk, Charmaine Abrahams and Dr Michele Tameris



SATVI Health and Safety Committee which organised the Wellness Day- 25 November 2014.

# community involvement



SATVI Organising Social Responsibility Committee – Mandela Day  
– July 2014

Since its establishment in 2001, SATVI has established a good relationship with the community of the Cape Winelands, participating in local organised community structures and supporting organisations in need.

## NELSON MANDELA DAY

For this years' Nelson Mandela Day, we supported the Sean Kelly Centre Multiple Sensory Disabled Children, the Thutuzela Centre for Victims of Family Violence and the Pioneer Hostel for the Blind with equipment and material. Staff also supported the Sean Kelly Centre Multiple Sensory Disabled Children with donations in their individual capacity.

## WORLD TB DAY

For World TB Day (24 March 2014) SATVI hosted a breakfast for staff of the Boland Hospice Home-based Care and a motivational talk, which was given by

Dr Dalene Von Delf from TB Proof, in recognition of the work that they do in the community.

## CANCER TEA DAY

Staff supported the fight against Cancer by hosting two tables at the Annual CANSA Tea which took place in Stellenbosch under the auspices of CANSA South Africa.

## MEMBERSHIP OF MSAT

SATVI is a member of the Worcester Multi-sectoral Action Team (MSAT), whose vision is to work together for the health and wellbeing of the Breederiver community and through which SATVI can support various non-profit organisations on different levels. On World TB Day we hosted a MSAT meeting and introduced community leaders to the SATVI site, and how we conduct clinical research at SATVI. This gave them a better understanding and insight to take back to their various constituencies.



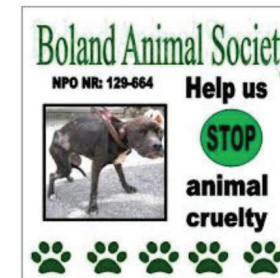


*SATVI team who contributed their off time to make a warm plate of food for the less-privileged in Worcester.*

On Saturday 6 December 2014 the SATVI team participated in the “Pot ve Pens” Campaign, a local initiative to cook warm nutritious meals for the needy in and around Worcester. This is very important for us because through participating in events such as this, we build our relations with other local organisations, show that we care for the less fortunate in the community and build teamwork amongst SATVI staff.



We have supported the following community-based organisations to different degrees:-



Huis Kruger: Huis vir Gestremde Swaksiende

Robertson Kinderhuis

Nuwerus Old Age Home, Worcester

Empilisweni Clinic, Worcester





Chairperson Mrs Belinda Ameterra

# community advisory board

*The Boland Research Community Advisory Board wishes to say thank you to SATVI for fulfilling our dream. Looking back over 2014, we are pleased to say that the consolidation of the CAB with SATVI is an achievement because we worked as a team to achieve one goal.*

Belinda Ameterra

Chairperson

Boland Research Community Advisory Board

THE Boland Research Community Advisory Board (BR-CAB) was re-elected April 2014 and since then has achieved the following:

## WELL FUNCTIONING COMMUNITY ADVISORY BOARD

Since the re-election of the CAB in April 2014, the CAB has elected an Executive Committee from amongst its members at its Annual General Meeting held April 2014, adopted a constitution, held monthly meetings, briefed visiting delegations from the Division of AIDS and the Bill and Melinda Gates Foundation; and has established a Junior CAB which will be built upon in 2015. The CAB is also registered within the ACTG

Network, and has participated in the ACTG Conference held in America during June 2014. The CAB consists of twenty members elected from the Worcester area. The CAB members also underwent training in Good Clinical Practice (GCP).

## RELATIONSHIP BETWEEN SITE AND CAB

The site administration has participated in all the CAB meetings, in addition to providing administrative and logistical support, also updating the CAB members on progress with trial studies. The site has also supported the CAB with a specialist in the form of Reverend David Galetta, who is also the Global CAB Co-Chair and who has assisted the CAB to draft a constitution and prepare a year

plan. During November 2014 the CAB was taken on a tour of the Cape Town SATVI laboratories and participated in a workshop on "The History of Tuberculosis and Correlates of Risk" by Dr Sara Suliman, a Postdoctoral Fellow.



CAB Members during visit to SATVI laboratories at UCT (Cape Town) on 22 November 2014.



CAB members completed Good Clinical Practice (GCP) course, June 2014.





*Dr Hennie Geldenhuys, SATVI Principal Investigator briefing CAB members.*



*CAB members shown around by Dr Sara Suliman, SATVI Postdoctoral Research Fellow.*



# funders



BILL & MELINDA  
GATES *foundation*



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# collaborators





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