DST-NRF CENTRE OF EXCELLENCE

ANNUAL PROGRESS REPORT

Reporting Period

1 January 2015 – 31 December 2015

CONTENTS

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Identification

Name of Director	:	Professor Paul D. van Helden
Names of Node Heads	:	Professor Valerie Mizrahi Professor Bavesh Kana
Name of CoE	:	DST/NRF Centre of Excellence for Biomedical TB Research
Abbreviated CoE Name	:	CBTBR
Host institutions	:	University of Stellenbosch, University of the Witwatersrand University of Cape Town
Date completed	:	08/04/2016

EXECUTIVE SUMMARY

1. Financial Information (Funding of the CoE)

Total NRF funding for 2015 (entire year) – CoE only	:	R 10 758 831
CoE-specific Funding from Host institution in 2015 – WITS	:	R 230 000
– UCT	:	R 150 375
– SU	:	R 817 148
Funding from other sources for the CoE in 2015	:	R 62 920 884
Total funding	:	**R 74 877 238**

Total funding for 2015 for Wits node: **R10 770 183**

- CoE funding from NRF: **R 2 326 031**

- Other funding from NRF: **R 501 169,** made up as follows:
  - Incentive Funding (Kana)[1] R 40 000
  - NRF postdoc supplement[2] R 61 250
  - SA-Swiss Joint Research Grant[3] R 399 919

- Funding from Wits and NHLS: **R 2 535 254,** made up as follows:
  - 10% Wits Institutional Commitment R 230 000
  - Research Incentive Funding R 7 333
  - Salaries R 1 496 621
  - NHLS Research Trust[4] R 499 600
  - TIA – WITS Seed Fund[5] R 301 700

- Funding from other sources: **R 5 407 729,** made up as follows:
  - HHMI IECS grant[6] R 1 272 403
  - DAIDS CTU Supplement R 723 860
  - BMGF Accelerator[7] R 3 186 466
  - MRC Career Development Award[8] R 225 000

Total funding for 2015 for UCT node: **R 15 337 253**

- CoE funding from NRF: R 1 503 754

- Other funding from NRF: R 728 605[9]

- Funding from UCT (*excluding salaries*): R 300 000[10]

- Funding from other sources:[11] R 12 804 894, made up as follows:
  - MRC Unit (MMRU; Mizrahi) R 1 000 000 (1 Apr 2015 – 31 Mar 2016)
  - EU FP7 (MM4TB) (Mizrahi) R 781 053 (1 Feb 2015 – 31 Jan 2016)
  - FNIH (HIT-TB) (Mizrahi) R 3 224 404 (1 Sep 2014 – 31 Aug 2015)
  - MRC SHIP grant (Warner) R 1 374 561 (1 Jan 2015 – 31 Dec 2015)
  - MRC Flagship 1 (Warner/Mizrahi) R 483 243 (1 Jan 2015 – 31 Dec 2015)
  - HHMI SIRS grant (Mizrahi) R 1 130 340 (1 Oct 2014 – 30 Sept 2015)
  - US National Institutes of Health (Warner) R 4 360 350 (1 Jan 2015 – 31 Dec 2015)[12]
  - Wellcome Trust (Warner) R 450 943 (1 Jan 2015 – 31 Dec 2015)[13]

[1] NRF Incentive Funding to BD Kana – Year 5
[2] To C. Ealand
[3] Year 2 SA-Swiss to N. Dhar and B. Kana
[4] Year 1 To B. Gordhan
[5] To B. Kana
[6] Year 4 to B. Kana
[7] Year 2 to B. Kana
[8] Year 1 to C. Ealand
[9] SA/Germany Research Cooperation grant (V. Mizrahi – R 108,900); Competitive Programme for Rated Researchers (D. Warner – R 268,990); UK/SA Royal Society-NRF Seminar (D. Warner; R 63,000); SA/Zambia Research Cooperation grant (D. Warner, R67,715); Community Engagement Award (D. Warner), R 220,000).
[10] Two doctoral fellowships from UCT's Carnegie Corporation *Developing Next Generation Academics* program
[11] Where applicable, external awards include indirect costs (IDC), and ZAR values are calculated based on landed e-rates
[12] UO1 and R21 grants awarded under the NIH-SAMRC South Africa-US program for Collaborative Biomedical Research
[13] Public Engagement award (Eh!Woza project)

Funding for 2015 for SU node: **R 48 769 802**

- CoE funding from NRF : **R 6 930 046**

- Funding from SU: (best estimate): **R 4 815 000,** incl. salaries, student bursaries, excl. space, basic infrastructure, secretary, cleaners.

- Funding from other sources (best estimate): **R 37 024 756**, made up as follows:
  - MRC Centre (estimate of the TB component) R 10 000 000 (incl. salaries)
  - PGWC R 2 495 000 (salaries only)
  - NIH M (X) Dr-TB Late PCR R 1 167 059
  - NIH Altered Immune-endocrine type 2 diabetes R 2 310 889
  - NIH OFX R 31 070
  - NIH Exit Rif R 1 587 786
  - NIH CASS R 306 514
  - NIH Opti Q R 47 091
  - BMGF GC6-74: Cohorts R 1 227 639
  - BMGF Virulence of TB strains R 524 473
  - TANDEM (EU FP7) R 1 324 919
  - FIND R 170 000
  - VPM Clinical trial R 3 328 687
  - Hain Fluorotype R 106 287
  - AERAS Clinical trial project R 2 098 399
  - NRF SARchi R 1 119 038
  - MRC Drug Discovery for Anti-TB Agents R 3 399 123
  - MRC SHIP SATBBI R 3 000 000
  - MRC TB Next R 180 000
  - MRC TB Hart R 549 865
  - MRC SHIP Malt TB Redox R 202 632
  - MRC SHIP - System Imm R 552 020
  - DST TANDEM R 296 266
  - Other NRF funding R 1 000 000

2. Summary of progress against 5 KPAs

(i) Research

The research productivity of the CBTBR remained excellent in 2015 as evidenced by the fact that 84 articles in peer-reviewed journals were published, and 161 conference presentations were made, including 11 plenary/ keynote lectures, and numerous invited talks. Of the research articles published, 70 were in journals with an impact factor (IF) >2.
Progress against targets SLA 5 targets: The outputs under this KPA exceeded the SLA target (≥20 publications of which ≥5 are in journals with an IF ≥2).

(ii) Education and Training

A total of 10 PhD students, 7 MSc students and 9 Honours students from the CBTBR graduated or completed their training in 2015. All these postgraduate students completed degrees within their maximum allowable time agreed upon in the SLA. One postdoc completed training in the UCT node and took up a position at the NICD. A postdoctoral fellow at the Wits node was awarded the prestigious MRC Career Development Award andtransitioned to a fixed term contract post at Wits University in April 2015. A number of new postdoctoral, PhD and MSc students were enrolled in the nodes of the CBTBR, and several students were afforded the opportunity to work in international labs. The student breakdown according gender (59% female) and percentage of postdoctoral fellows (21% of total student complement) exceeded the SLA targets of ≥50% and ≥10%, respectively. The proportion of black students (54%) exceeded the SLA target of ≥50%. The percentage of Honours students was 10% in 2015. *Progress against SLA 4 targets*: The total of 112 postgraduate students associated with the CBTBR in 2015 greatly exceeded the SLA target of ≥35.

(iii) Knowledge Brokerage

The CBTBR continued to contribute to the dissemination of research discoveries through engagement with the scientific community at many meetings and conferences, with stake holders in operational/public health research, policy makers and in some cases, the general public. We continue to strive for country-wide and international publicity in various media platforms, such as radio and press and we continue to be involved in many outreach activities, targeting school teachers and learners, and on science communication in general. We continue to strive for improved communication with metropolitan, provincial and national health authorities, Médecins Sans Frontières (MSF) and NHLS. Our interaction with these stakeholders continues to improve. We now engage more with DoH and NHLS than before and have developed a good relationship with both, such that our phone calls and emails are received and responded to. We continue to advise SANParks, the National Zoological Gardens (NZG) and now also the Namibian Wildlife services, as well as some private entities with regard to TB in wildlife or captive animals. Since July 2015 we housed an NRF-intern science journalist to assist with this overall activity. Perhaps one of our most significant measures of success is that Profs Mizrahi and van Helden served on a WHO panel "Global Framework for TB research" which is aimed at guiding research endeavours for the future to assist in achieving the lofty WHO goal of TB elimination. Participation in this panel led to co-authorship on a paper published in March 2016 in *PLoS Medicine*. The director, co-directors and several team members of the CBTBR also played a major role in discussions, convened by the National TB Think Tank and the SAMRC, that were aimed at developing a national TB research strategy during the course of 2015. This work is ongoing. Prof. Mizrahi continued to contribute to strategic development of the TB Drug Accelerator (TBDA) program of the Bill & Melinda Gates Foundation as a non-member participant at TBDA meetings in Seattle (March) and Beijing (October). Prof Gerhard Walzl continues to be a leading member of the IMPAACT Biomarker Scientific group. He has attended and led meetings aimed at developing a blueprint for such biomarkers.

(iv) Networking

Numerous recent funding opportunities have led to new networking initiatives that have enhanced the local and international footprint of the CBTBR. This activity is extensive, as outlined in Section 4 of the report. Our collaborative links range from institional, regional, local, through Africa to many international consortia and networked partners. The CBTBR regards this activity as central and vital to our activities and encourages it as far as is possible.

(v) Service rendering

Whilst not our major activity, the CBTBR continues with this activity and intends to do so in future. The CBTBR continues to assist with countrywide roll out of the GeneXpert and now provides verification standards to over 20 countries, this innovation has allowed thousands of TB patients to access molecular diagnostics. These verification standards now also fall under the GLI label, for all GLI, CDC and WHO sites. We continue to provide technical/ scientific services to the Eastern and Western Cape Provincial Health Department, Tygerberg Hospital and various TB clinics. We continue with our provision of advice and assistance to individuals, research groups and institutions, locally (including NHLS) and abroad, committee membership and scientific review work at the institutional, regional, national and international levels. We continue to test antimycobacterials for UKZN, NWU, UWC and UCT and international consortia. Members of the CBTBR again played key advisory and participatory roles in the national and regional responses to the extensively drug-resistant (XDR) TB crisis. Assistance to SANParks, NZG, and others, such as the Namibian Wildlife Service regarding TB in wild animals continues to be given. We have extended our service to offering diagnostics and advice to clinicians regarding primary immunodeficiency disorders, which is now incorporated into our TB Genetics research. In addition, we have assisted Tygerberg hospital and veterinary services, as well as SANParks with Toxoplasmosis diagnostics and survey work. Again, this has flowed from our work into "colliding epidemics", where TB is one of the elements involved. .

3. Gender Impact

From the "Science by Women" perspective, it is important to note that 59% of all postgraduate students (including postdoctoral fellows) in the CBTBR in 2015 were female. Two of the three NRF SARChI's granted to SU and closely associated with the CBTBR are female as are two recently appointed NRF Research Career Awardees. Members of the CBTBR are active in SAWISE and Prof Eileen Hoal has been appointed to the Project Team for Women's Career Progression at Stellenbosch University (SU).

PROGRESS REPORT

1. Scientific Research

Overview and Highlights of Progress since the last report:

SU Node

The projects at the SU node are aimed at bridging the gap between basic and clinical research. We undertake many different projects in this field, some of which are listed below: (a) genetics of human TB susceptibility: (b) molecular epidemiology which covers both the drug susceptible and resistant forms of the disease c) evolution of drug resistance (d) mycobactomics (e) diagnostics (f) bacterial genetics (g) immunology (h) surrogate markers for clinical trials (i) drug targets (j) EBA and other drug trials (k) veterinary mycobacteriology and immunology. A few snippets and highlights are shown below.

Epidemiology and Drug Resistance – We have long been of the opinion that standardized regimens are suboptimal for TB treatment in the case of drug resistant TB. Some of our recent work supports this notion. Of 171 patients investigated, 47% would be considered to have started an ineffective regimen with 8% having only one likely effective drug, 9% with two, and 30% with three. We concluded that under current programmatic conditions, nearly half of patients diagnosed with RIF resistant MTB by Xpert also have resistance to at least two additional MDR TB drugs and thus are started on a weakened 5-drug MDR regimen with the indication to adjust therapy not apparent for nearly 8 weeks. Such delays risk worsened outcomes and potentially fuel resistance amplification in the community. For this reason, amongst others, the detection and treatment of XDR-TB requires rapid detailed analysis of the extent of resistance to first, second, and third line antibiotics. We have constructed a multiplexed single-tube LATE-PCR reaction assay that simultaneously generates single-stranded DNA amplicons for the detection of mutations in first line (rifampicin and isoniazid) and second line (fluoroquinolone, aminoglycoside/polypeptide and ethionamide) antibiotics resistance conferring gene targets. A large number of strains that harbor various known combinations of alleles in the 1st line (*inhA*, *katG*, *rpoB*); 2nd and 3rd line (*gyrA*, *gyrB*, *eis*, and *rrs*1401) gene targets have been being analyzed using this assay in order to generate a library of validated fluorescent signatures. This reference library can then be used with appropriate software for comparison of clinical samples and thereby determine detailed nature of drug resistance in that particular MDR-TB or XDR-TB patient. The assay has also been tested on 750 blinded DNA samples isolated from clinical specimens. The assay will also be tested on direct clinical specimens. This technology has been licensed to Hain Lifescience, who in turn has developed a FluoroType MTBDR assay kit which detects resistance to isoniazid and rifampicin. In collaboration with Hain Lifescience we have evaluated the Fluorotype MTBDR assay for the detection of drug resistance in smear positive (n=278), smear negative specimens (n=79), culture negative specimens (n=100) and DNA samples isolated from clinical specimens (n=100).
An assay for the detection of pyrazinamide resistance was constructed at Brandeis University by Michael Whitfield and John Rice. The current design of the assay accurately identified 106/107 pncA mutations.

Recent studies have reported conflicting findings on the genomic stability of *M. tuberculosis* during the evolution of drug resistance. Failure to detect sub-populations by either using stringent filtering approaches or the analysis of single colony forming units may mask the true dynamics of the population causing disease. In this study we aimed to define a reliable cut-off for identification of low frequency sequence variants and to subsequently investigate genetic heterogeneity and the evolution of drug resistance in *M. tuberculosis*. Our data enabled us to define a read frequency cut-off of 30% to accurately detect heterogeneous variants. Using this approach we demonstrated for the first time high genetic diversity between single colonies isolated from clinical samples. Thereafter, we used our read frequency filtering approach to investigate the evolution of isoniazid resistance in *M. tuberculosis* clinical isolates within two patients diagnosed initially with rifampicin mono-resistance. Our findings suggest that the isoniazid selective pressure imposed an evolutionary bottleneck specifically selecting an isoniazid resistant variant thereby dramatically reducing genetic diversity within the mycobacterial population. This was then followed by the subsequent accumulation of new variants in the isoniazid resistant mycobacterial population. The findings of this study demonstrate the presence of numerous sub-populations present within an *M. tuberculosis* clinical isolate, suggesting that the population is dynamic in preparation to respond to a changing environment. These findings have important implications when considering the development of new next generation diagnostic techniques as it is also vital to identify drug resistance causing mutations present in a small sub-population. The resulting datalay a foundation for understanding the population biology of *M. tuberculosis* during disease. In addition, this study highlights the importance of the sequence

read depth obtained using next generation WGS. In order to adequately and reliably detect true drug resistance mutations (or any low frequency variants) it is vital to obtain maximum read depth and quality.

In another project we have successfully developed a method entitled Chromatin Immunoprecipitation – Protein Mass Spectrometry (ChIP-PMS) which allows for the isolation and identification of nucleic acid binding proteins in *M. smegmatis*. This is achieved by affinity purifying protein-nucleic acid complexes on a solid matrix and following tryptic digestion proteins are identified by mass spectrometry. DNA and RNA binding proteins are both nucleic acid binding proteins and have roles in transcriptional regulation, translation as well as DNA replication, repair and recombination. Data obtained from establishing studies in *M. smegmatis* have identified known DNA (DNA polymerase, gyrase, transcription factors) and RNA (RNA polymerase complex, ribosomal complex) binding proteins as well as a number of proteins of unknown function. This method allows for studying the proteins that are involved in transcription and regulation under given experimental conditions i.e. optimal growth vs. hypoxia, but also allows for the identification and classification of novel nucleic acid binding proteins. We aim to apply this method to Severely Attenuated *M. tuberculosis* (SAMtb) under hypoxic conditions using the Wayne model. The identification of proteins that are associated with DNA and RNA in *M. tuberculosis* could potentially identify novel drug targets that are central in limiting the adaption of this pathogen to its host environment thereby having the potential to improve treatment outcomes.

Our deep sequencing protocol has been used to rapidly identify (directly from sputum) mutations associated with fluoroquinoline (FQ) resistance in heterogeneous *M. tuberculosis* populations at a frequency≤1%. This method will allow prompt identification of resistant - and heteroresistant *M. tuberculosis* isolates which will inform our understanding of the mechanism(s) responsible for the evolution of FQ resistance. To date our method is able to identify low-frequency (underlying) resistance strains/clones at a frequency of <1% using deep sequencing. The clinical significance of this method is that it will enable the prompt identification of low-frequency resistance causing mutations thereby guiding the rapid implementation of effective treatment regimens in order to improve treatment success and to interrupt transmission. We found that a certain strain of TB – which has been shown to have the potential to develop drug-resistance to beyond-XDR – harbours a mutation in the *ethA* gene, causing ethionamide resistance, even in otherwise drug-susceptible isolates. This means that patients infected with this strain in an MDR form may be treated with inadequate regimens, as ethionamide resistance testing is not routinely done. In turn this may lead to further resistance acquisition, potentially fuelling the epidemic of beyond-XDR-TB. Furthermore, ethionamide resistance was previously thought to primarily be attributable to *inhA* promoter mutations, which is currently used as a marker for ethionamide resistance on the rapid diagnostic test, Hain MTBDR*plus* v2, which is routinely used. However the presence of this and other *ethA* mutations – sometimes together with an *inhA* promoter mutation – demonstrates that the latter cannot be used alone to determine ethionamide resistance.

Software, developed in our group (USAP), which fully automates the processing of next generation sequencing data for the sensitive detection of genomic variants and detection of disease / resistance causing molecular markers for any organism. The software has been used extensively in our department and has enabled us to analyse over 1500 *Mycobacterium tuberculosis* whole genome sequences as part of various student projects and collaborations. The software is freely available and is described in a manuscript currently being prepared for publication.

Mycobactomics - We have several projects focused on physiology and epidemiology of drug resistant *M. tuberculosis*, as well as aimed at identifying novel anti-mycobacterial compounds to help combat drug resistance. In collaboration with researchers at the University of the Western Cape and the University of Auckland, New Zealand, we are screening novel compound libraries, and characterising the mechanisms of action of active compunds. In partnership with the Institut Pasteur de Tunis, we are investigating genetic variation in a cohort of drug resistant *M. tuberculosis* isolates, with a particular focus on the *ppe_mptr* genes. We also have a collaboration with the Copperbelt University and the Tropical Diseasese Research Institute aimed at elucidating the epidemiology and genetic variation of drug resistant *M. tuberculosis* strains in a high HIV incidence area in Zambia. Appropriate approvals have been obtained, partners identified and sample collection and processing has begun. In other projects, we are investigating the physiological and functional consequences of drug resistance-conferring and compensatory mutations, using a combination of molecular microbiology, proteomics, transcriptomics and bioinformatics. Proteomics approaches are also being exploited to characterise the mycobacterial secretome as well as host responses to mycobacterial infection.

Another area of interest is investigating mycobacterial phenotypic heterogeneity, with a particular focus on mycobacterial persisters. We have developed a flow-cytometry based methodology for enumerating and isolating slow- or non-replicating mycobacteria, and have applied this to demonstrate the emergence of mycobacterial persisters upon macrophage uptake (manuscript under review). We are developing further flow cytometry-based approaches for phenotypic characterisation and rapid counting of mycobacteria.

A major focus are of the group is the PE/PPE proteins of *M. tuberculosis*. Here, we are using a combination of molecular, genomic and computational methods to gain insight into these intriguing protein families which are thought to play crucial roles in host-pathogen interacitons. As mentioned above, we are collaborating with researchers at the Institut Pasteur de Tunis to gain a better understanding of genetic varation and evolution of a subset of the protein families, specifically the PPE_MPTRs, which are unique to pathogenic mycobacteria. We are further collaborating with researchers at the VU Netherlands to investigate the mechanisms and consequences of PE/PPE secretion by *M. tuberculosis*. In other work, we are exploiting computational approaches to explore the relationship between epitope presence and genetic diversity in PPE_MPTR proteins; this work could have important implications for understanding unique aspects of mycobacterial physiology, as well as for vaccine development.

Host Genetics - We investigated the role of gene-gene interactions in genetic susceptibility to TB using a cohort recruited from a high TB incidence community from Cape Town, South Africa. Our discovery data set incorporated genotypes from a large a number of candidate gene studies as well as genome-wide data. After limiting our search space to pairs of putative TB susceptibility genes, as well as pairs of genes that have been curated in online databases as potential interactors, we used statistical modelling to identify pairs of interacting SNPs. We validated the top models identified in our discovery data set using an independent genome-wide TB case-control data set from The Gambia. A number of models were successfully validated, indicating that interplay between the *NRG1- NRG3, GRIK1- GRIK3* and *IL23R - ATG4C* gene pairs may modify susceptibility to TB. Gene pairs involved in the NF-κB pathway were also identified in the discovery data set (*SFTPD - NOD2, ISG15 - TLR8* and *NLRC5 - IL12RB1*), but could not be tested in the Gambian study group due to lack of overlapping data.

Human leukocyte antigen (HLA) genes have been extensively investigated with regards to TB susceptibility in different ethnic populations, often with contradictory results. A few studies of the importance of KIRs have been done in TB. We investigated the role of KIRs and HLA class-I molecules in susceptibility to TB in a South African population. In a sample set comprising 408 TB cases and 351 healthy controls, we show that the *KIR3DS1* gene and KIR genotypes with five or more activating KIRs, and the presence of *3DS1*, protect against developing active TB. Several HLA class-I alleles were identified as susceptibility factors for TB disease. However, none of the KIR-HLA compound genotypes were found to be associated with TB. Our data suggests that the KIR genes may play an important role in TB disease.

Toll-like receptors (TLRs) are involved in the recognition of conserved microbial structures, leading to activation of an inflammatory response and formation of an adaptive immune response. To date, several polymorphisms within the TLR gene family have been associated with susceptibility to tuberculosis, often with varying results across different population groups. Given the importance of pattern-recognition receptors in detecting invading pathogens and the importance of TLRs in the formation of an efficient innate immune response to mycobacteria, we investigated polymorphisms in *TLR1, TLR2, TLR4, TLR8* and *TLR9* in susceptibility to TB i. Our data suggests that polymorphisms within these genes play an important role in susceptibility to TB disease as well as disease caused by specific *M. tuberculosis* strains. Remarkably, *TLR8* polymorphisms located on the X chromosome show sex-specific effects with regards to developing TB disease.

Given the varying and often contradictory results of TLR association studies in different ethnic groups, we also conducted a meta-analysis to investigate the relationship between TLR variants and susceptibility to TB, both across and within specific ethnic groups. An extensive database search was performed for studies investigating the relationship between TLR and TB susceptibility. Data was subsequently extracted from included studies and statistically analysed. Although general associations were identified, most TLR variants showed no significant association with TB, indicating that additional studies investigating a wider range of pattern recognition receptors is required to gain a better understanding of this complex disease.
In 2013, we established a working group of clinicians and molecular biologists to provide clinical and molecular diagnosis to PID patients in South Africa. This working group, called the Primary Immunodeficiency Genetics Network (PIDDGEN), has been actively recruiting PID patients from across South Africa. Over the past two years, PIDDGEN, in collaboration with a number of international partners, has identified several PID-causing mutations and provided molecular diagnosis to a number of patients. To

date, we have sequenced the exomes of 16 patients and where possible, unaffected family members. Through the use of exome sequencing we have identified three putative novel PID-causing mutations in three unrelated patients who suffered multiple or severe episodes of pulmonary TB.

Immunology - We have a specific focus on the discovery of TB biomarkers. The group aims to identify biomarkers of TB disease, infection and markers that will help understand the response to treatment and outcome. Several studies and vaccine trials are ongoing to either discover or validate the markers already discovered through our basic medical research. Prof Walzl is the PI of several of these studies funded through the Bill and Melinda Gates Foundation or the NIH.

Biomarkers for TB treatment response could facilitate clinical trials of new drugs and shortened treatment regimens and might also have application for routine clinical use. We have recruited and followed up cohorts of TB patients from diagnosis to end of treatment and for the subsequent two years to identify treatmentoutcomes like relapse and to discover host biomarkers that predict outcomes. We have used transcriptomic, metabolomics and serum protein assays in collaborative studies to discover biosignatures. We have found that baseline and early treatment markers (including multi-marker models that include clinical and immunological markers) can be used to stratify patients into risk groups for poor outcomes. We have played a central role in a BMGF funded TB treatment response study awarded to the Catalysis Foundation for Health in which we have conducted PET/CT imaging studies at baseline, week 4 of treatment, at end of treatment and one year after end of treatment. Strikingly, only approximately 15% of cured cases have normal fluoro-deoxyglucose isoptope uptake (a marker of inflammation) at end of treatment (EOT), whereas 50% have significant residual inflammation at EOT and 35% have new lesions or intensified lesions. We found that approximately 30% of microbiologically cured patients have MTB mRNA in their sputum at the EOT and all of the 15 cured patients in whom we performed bronchoscopy and bronchoalveolar lavage (BAL) at EOT have MTB mRNA in BAL. If the presence of MTB mRNA at EOT suggests live, albeit not conventionally culturable, bacteria rather than hitherto not described stability of MTB mRNA after chemotherapy-induced bacterial death, this suggest that cured patients did not undergo sterilizing cure and that their immune system is crucial in preventing relapse. Our ongoing work aims to investigate the mechanism for the persistent inflammation and MTB mRNA presence in the lungs at EOT and to apply the most promising markers prospectively to guide treatment-shortening strategies.

Another particular aim is to unravel the link between TB and type 2 diabetes (DM2). Patients with DM2 are three times more likely to acquire TB, however the underlying mechanisms are not understood. As part of a EU FP7 funded project to Prof G Walzl in collaboration with Prof Hazel Dockrell from the London School of Hygiene and Tropical Medicine we have shown that at TB diagnosis the cytokine profile in individuals with TB and DM2 co-morbidity is significantly differenct compared to TB patients without DM2. As expected, pro-inflammatory cytokines are produced at higher concentrations in serum from TB-DM2 patients, interestingly however also anti-inflammatory cytokines are produced at higher concentrations. Dr Ronacher has established new collaborations with Prof Larry Schlesinger (Ohio State University) and Prof Blanca Restrepo (University of Texas) to investigate the role of macrophage function in susceptibility of DM2 patients to TB. Prof Walzl is co-investigator on this study.

Drug Discovery - We have shown for the first time that some artemisins are active against *M.tb*, a project in collaboration with North-West University on the MRC Flagship MalTB Redox project. In this project, Artemisinins effective against malaria disease are evaluated for their efficacy against *M.tuberculosis* as it was observed before that antimalarial drugs also exert some activity against *M.tb* bacilli. We observed so far that certain artemisinin derivatived do show significant effectiveness against strains of *M.tb* and its effect combination with existing antituberculosis drugs are being evaluated. Elesclomol, a registered anti-cancer drug that works on the basis of copper chelation and exerts its effect through free radical killing of cancer cells, is also part of the MalTB Redox project and is presently evaluated against *M.tb* on its own and for synergism with existing antituberculosis drugs.

We have tested novel drugs against Gyrase B of *M.tuberculosis* which has led to a research publication. We have also shown that derivatisation of a natural product, formononetin, can be effectively developed as an antituberculosis drug. These results have also been published. In another project we studied the effect of glutamate homeostasis on the survival of slow growing mycobacteria. We have found that NAD-dependent glutamate dehydrogenase of *M. bovis* BCG is required for resistance against nitrosative stress *in vitro.* We observed that this phenomenon is ameliorated when cells are grown in excess ammonium sulphate, indicating that ammonia production by NAD-dependant glutamate dehydrogenase is required for resistance against nitrosative stress. The results implicate that catabolic glutamate dehydrogenase conveys resistance to nitrosative stress in mycobacteria. The sulfonamides have potential antituberculosis

activity and we have shown that sulfmethoxazole elicits oxidative stress in *M.tb* and could account for its observed synergistic action with Rifampicin against *M.tb*.

Enzymes of the mycothiol and ergothioneine biosynthetic pathways are targets of choice not only because they are unique to mycobacteria but also because it protects mycobacteria against reactive oxygen species. We have knocked out a gene coding for EgtD (an enzyme involved in ergothioneine biosynthesis) from the wild type *M.smegmatis* and the mycothiol deficient mutant (Δ*mshA*) strains. In stress assays we found that the ergothioneine deficient single mutant (Δ*egtD)* and mycothiol deficient single mutant (Δ*mshA)* were slightly sensitive to oxidative stress conditions generated by cumene hydroperoxide relativel to the wild type, while the double mutant (Δ*mshA/egtD)* was significantly affected. This suggests a synergistic anti-oxidative role of ergothioneine and mycothiol in mycobacteria. As opposed to mycothiol, we have shown that ergothioneine is secreted. The *M.tb* mutants have been generated and are currently being investigated.

Animal TB - We have been focusing on discovery and validation of biomarkers with diagnostic potential for detection of TB in several wildlife species. In collaboration with Ezemvelo KwaZulu Natal Wildlife, a study comparing peptide-stimulated plasma cytokine assays for IFN-ɣ and IP-10, demonstrated that IP-10 has improved sensitivity compared to IFN-ɣ in naturally infected African buffaloes. Immunoassays using IP-10 have also shown promise in distinguishing *M. suricattae*-infected meerkats from uninfected animals, which was conducted as part of the Kalahari Meerkat Project in collaboration with the Royal Veterinary College in the UK. Since one of the group's research objectives is to improve sensitivity and specificity of diagnostic tests, studies are underway to investigate the impact of intradermal tuberculin skin test on in vitro cytokine assays in cattle and buffaloes, and serial changes in immune responses over time.

In the past year, the Veterinary group initiated several new research projects, which are fully integrated with the SARCHI for animal TB, Prof Michele Miller. . One of these projects was developing diagnostic tests for warthogs, and using these for epidemiological studies. Commercially available and in-house serological assays were able to detect infected warthogs, demonstrating that this species develops strong humoral responses to bovine TB. This project is being expanded to investigate cell-mediated immune responses in this species. Other progress includes validation of a cytokine gene expression assay for CXCL9 (MIG) in *M. bovis*-infected lions. A study is underway to apply this tool to evaluate prevalence of bovine TB in Kruger National Park lions. Cytokine gene expression assays are also being used to identify biomarkers of immune activation in hyenas and buffalo. These studies will be expanded to include antelope. Characterization of immunological responses in different animal species will be a focus in the coming year as a foundation for understanding variation in presentation and diagnosis of TB.

We have characterised the causative agent of TB in meerkats as a distinct member of the *Mycobacterium tuberculosis* complex (MTBC) and have proposed that it be named *Mycobacterium suricattae*. We used whole genome sequencing to describe the genetic features of *M. suricattae* in an attempt to identify characteristics which may underlie its host specificity. Using this data, we generated a near complete genome assembly, which provides new insight into the genetics of this animal adapted MTBC member. The evolutionary processes included genomic single nucleotide variants (SNV), insertions and deletions as well as IS*6110*-mediated transposition. The insertion points of 21 copies of IS*6110* are described, we confirmed 9 previously reported genomic deletions, and identified a further 6 novel deletions. Our SNV based phylogenetic analysis showed that *M. suricattae* is a novel member of the MTBC, specifically clustering with the recently reported chimpanzee. *M. suricattae* and the chimpanzee bacillus clustered with strains from *M. africanum* lineage 6. The grouping of *M. suricattae*, chimpanzee bacillus and strains from *M. africanum* lineage 6 suggests the presence of a new animal branch, which is distinct from the typical animal branch that includes *M. bovis*, *M. caprae*, *M. orygis*, *M. microti*, *M. pinnipedii*. In the absence of whole genome sequence data for *M. mungi* (which infects banded mongooses) and dassie bacillus (which infects rock hyraxes), we proposed a phylogeny to update the evolutionary history of the MTBC using previously described informative genetic markers.

UCT Node

The research program of the UCT node involves an integrated suite of projects that are aimed at investigating aspects of the physiology and metabolism of *M. tuberculosis* of relevance to TB drug discovery, drug tolerance and drug resistance. As partners in UCT's Flagship 1 project funded by the SAMRC, the UCT node is leading the microbiology component of this interdisciplinary research project on tuberculosis transmission, which has been significantly expanded through new grants from the Bill & Melinda Gates Foundation. Projects are built on areas of fundamental mycobacterial metabolism and

physiology research and on the application of our capabilities in mycobacterial genetics and physiology in the area of drug discovery.

UCT node researchers, Dr. Vinayak Singh and Prof. Valerie Mizrahi, together with MM4TB collaborators in Italy, Switzerland and the UK, identified and validated an exciting new drug target for TB. The target, GuaB2, catalyzes an essential step in the *de novo* purine biosynthesis pathway, as an inosine monophosphate dehydrogenase (IMPDH) enzyme which converts IMP to XMP. The putative target was identified by whole-genome sequence analysis of a spontaneous resistant mutant isolated against a compound that had been shown to have potent activity against *M. tuberculosis in vitro*. After genetically validating a role for GuaB2 in the mechanism of resistance to the compound, GuaB2 was validated as the target by demonstrating profound hypersensitization of *M. tuberculosis* to the compound in a complemented conditional GuaB2 knockdown mutant strain, which showed a Tet-dependent growth phenotype that correlated with both *guaB2* transcript levels, as deduced by droplet digital PCR (ddPCR), and with protein levels, as monitored by western blot analysis. This finding was consistent with extensive biochemical and structural studies performed in our collaborators' laboratories which confirmed the target-inhibitor interaction and elucidated the mechanism of inhibition as well as the mode of inhibitor binding. The conditional mutant was then used to validate GuaB2 as a target *in vitro*, *ex vivo* and *in vivo*. Transcriptional silencing of *guaB2* was shown to result in rapid loss of viability of *M. tuberculosis* in vitro and in THP-1 cells, as assessed by CFU enumeration of silenced cultures on media permissive for growth of the level of *guaB2* transcript as well as the mutant strain. In work done in the lab of our collaborator, Prof. Stewart Cole (EPFL, Lausanne), depletion of GuaB2 was similarly shown to completely abrogate the ability of *M. tuberculosis* to establish an infection in mice, thus confirming a role for GuaB2 in the growth of M. tuberculosis in this animal model. GuaB2 essentiality was subverted in the presence of high concentrations of exogenous guanine supplement (>100μM), presumably through the action of Hpt (hypoxanthine/guanine phosphoribosyltransferase), a key enzyme in the purine salvage pathway. Moreover, the addition of guanine supplement in agar media used to score the viability of GuaB2-depleted cells by CFU enumeration resulted in an increase in culturability up to 7 days post-silencing, confirming that silencing of GuaB2 results in a transient, non-growing but metabolically active state in which *M. tuberculosis* is able to detect, transport and assimilate guanine. However, the profound phenotype of the conditional mutant in mice confirmed that the access of *M. tuberculosis* to guanine is highly restricted in mice. This large consortium project in which UCT node researchers played a leading role is being written up for publication in a top international journal.

Under the auspices of the HIT-TB consortium, funded under the TB Drug Accelerator program of the Bill & Melinda Gates Foundation, UCT node researchers Dr. Joanna Evans and Prof. Valerie Mizrahi have adopted a pathway approach to identify the most vulnerable step/s in the CoA biosynthesis pathway of *M. tuberculosis*. Through transcriptional silencing of seven genes encoding essential enzymes in the CoA biosynthetic pathway of Mtb, *panB*, *panC*, *coaBC* and *coaE* were shown to be essential for growth of Mtb *in vitro*, as evidenced by Tet (inducer)-dependent growth phenotypes displayed by conditional knockdown mutants in these genes. A mass spectrometric method for assessing the impact of gene silencing on the levels of the target protein was developed and applied to the CoaBC mutant to demonstrate almost complete depletion of protein within 5 days of silencing. Interestingly, silencing of *panB*, *panC* and *coaE* was found to have a bacteriostatic effect on *M. tuberculosis* based on CFU enumeration of cultures under conditions of gene silencing, whereas silencing of *coaBC* appeared to be rapidly bactericidal. However, this observation as shown to be attributable to a transient loss of culturability on solid media, as opposed to *M. tuberculosis* cell death, as evidenced by the partial restoration of culturability observed upon supplementation of the agar media with exogenous pantethine, a CoA pathway metabolite that allows CoaBC bypass through the sequential action of the CoaA (PanK), CoaD and CoaE enzymes to produce CoA. By analogy with the guanine rescue phenotype described above for the GuaB2 conditional mutant, this finding confirms that *M. tuberculosis* enters a transient non-growing but metabolically active state of characterized by impaired culturability on solid media upon silencing of CoaBC, in which it can detect, transport and assimilate pantethine, and thus subvert the essentiality of CoaBC. Importantly, however, CoaBC deficiency resulting from prolonged silencing leads to the eventual death of *M. tuberculosis* both *in vitro* and in mice, confirming that *M. tuberculosis* has limited access to pantethine in this animal model. Together, these two studies have highlighted funa number of important issues. Firstly, our findings underscore the severe limitations of the CFU as a surrogate for *M. tuberculosis* viability and reinforce the need for better proxies of cell death. Secondly, our results have profound implications for metabolic targets in terms of the potential for subversion through salvage pathways, and highlight the critical importance of understanding the metabolite access of *M. tuberculosis* in human lesions.

Significant progress was made by postdoctoral fellow, Dr. Raju Mukherjee, on a project aimed at understanding the mechanisms of small-molecule permeation in *M. tuberculosis*. Discovery and differential

proteomics have been applied to analyse the proteome of the well call fraction of *Mycobacterium tuberculosis* with the aim of identifying outer membrane proteins (OMPs) which include porins and major facilitator proteins that are involved in uptake of nutrients and drugs. The cell wall fraction was isolated through differential centrifugation and OMPs were extracted by detergent extraction from both early exponential phase and late stationary phase of growth. Thereafter, differentially expressed proteins were identified and quantified through high resolution mass spectrometry using the MaxQuant-Label free quantification method. In total, 1012 proteins were identified to be present in both samples; of these 769 proteins of unknown function and without an integral membrane protein signature domain were considered for further quantification. 53 and 77 proteins were observed to be down-regulated and up-regulated, respectively, by a factor of more than 2 fold at stationary phase when compared to their levels at the exponential phase. From this pool of significantly differentially expressed proteins, 11 were selected based on their genetic essentiality and propensity to form a β-barrel like structure and were further evaluated for their ability to transport drugs. Three proteins were found to have a role in increasing susceptibility to small hydrophilic drug including isoniazid, ethambutol and moxifloxacin. Ongoing work is aimed at elucidating the mechanisms underlying this phenotype.

Mr. Michael Reiche, MSc student, led an NIH-funded project investigating the kinetics of mutasome protein recruitment and subcellular (co-)localization in mycobacteria. Utilizing a panel of mutant strains expressing fluorescently-tagged recombinant mutasome proteins (ImuA', ImuB, DnaE2), he demonstrated that an N-terminal translational fusion of Venus Fluorescence Protein (VFP) to ImuA' retained full ImuA' function and, following exposure to a sublethal dose of mitomycin C, cells appeared uniformly fluorescent, exhibiting a diffuse yellow signal. In contrast, while an N-terminal translational fusion of enhanced Green Fluorescence Protein (eGFP) to ImuB similarly retained full ImuB function, the recombinant eGFP-ImuB protein appeared to form distinct foci following exposure to a sublethal dose of mitomycin C. Moreover, when the same construct was introduced into another reporter background expressing an mCherry-labelled DnaN protein, there appeared to be almost perfect co-localization of eGFP-ImuB and DnaN-mCherry signals, consistent with the protein-protein interaction inferred from genetic studies. In very recent work, he has generated an mEos-tagged ImuB fusion protein and, moreover, established that this fluorophore enables photoswitching in *M. smegmatis*. These preliminary observations suggest the capacity to tag each of the above proteins with alternative fluorophores that are better suited to single-molecule localization microscopy; these analyses will be conducted at the Advanced Imaging Center of the Howard Hughes Medical Institute in June, 2016, following successful application for access to the iPalm imaging platform.

As part of an SAMRC SHIP-funded project for the development of novel tools for hit triage in TB drug discovery, Drs. Atica Moosa and Krupa Naran have constructed and validated a small panel of three autoluminescent bioreporter strains of *M. tuberculosis* which enable rapid and dynamic detection of compounds whose antimycobacterial mechanism of action involves either disruption of cell wall homeostasis (Pini-LUX) or genotoxic stress (PrecA-LUX, PradA-LUX). The strains contain a luminescence gene cassette from *Photorhabdus luminescens*, and were constructed such that the lux operon (*luxCDABE*) was placed under the transcriptional control of either cell-wall inhibitory (*iniBAC*) or DNA-damage (*recA* and *radA*) inducible promoters. The utility of the resulting reporter strains has subsequently been validated using TB drugs with known mechanisms of action, where a sustained, positive signal can be detected in a dose-dependent and time-dependent manner. Furthermore, the real value of these reporters was demonstrated with compounds such as 5-fluorouracil, whose complex mechanism of action includes inhibition of cell wall biosynthesis and genotoxic stress. As evidence of the value of these reporters, the three LUX strains have been sent to the laboratory of Dr. Clif Barry and Dr. Helena Boshoff at NIAID (USA), where they have been incorporated into routine triage of TB-active compounds derived from partner sites across the Bill & Melinda Gates-funded Tuberculosis Drug Accelerator (TBDA) programme.

Wits Node

The research portfolio of the Wits node can be divided into the following broad thematic areas. The first involves identification and validation of new drug targets for tuberculosis with a major focus on remodelling of the mycobacterial cell wall during growth and pathogenesis. This entails an extensive analysis of enzymes that hydrolyze different bonds in the peptidoglycan polymer using an integrated computational biology, bacterial genetics and microbial physiology approach. In addition to this, mycobacterial energy metabolism has gained recent prominence due to the number of potential new (and existing) TB drugs that target this area of bacterial metabolism and the focus of work ongoing at the wits node lies in further studying the respiratory chain in mycobacteria to uncover new points of vulnerability. DNA repair is also another area of substantive activity where the focus is on identifying the molecular determinants for the

emergence of drug resistant strains. The second prominent area of research involves the identification and characterization of differentially culturable tubercle bacteria (DCTB) in the sputum of patients with active TB disease. In this regard, three prospective observational cohorts have been established to characterize bacterial populations when individuals present with active disease before, during and after treatment. Collaborators include various clinical research units and international experts. A new observational cohort aimed at studying DCTB in drug resistant patients is also being undertaken. The third area of research encompasses the development of novel models for use in counter-screening for tuberculosis drug development. These endeavors are aimed generating various forms of non-replicating, drug tolerant organisms to use for screening against potential novel anti-tubercular agents generated from partners at the H3D-Drug Discovery platform at the University of Cape Town. Finally, the development of novel diagnostic validation reagents is another significant area of activity at the Wits node. In this project, a new generation of reagents, which now serve as industry standards for the validation and quality assurance for GeneXpert, a molecular diagnostic that has been rolled out in South Africa and over 30 other countries, have been developed.

Research highlights over the past year include the discovery of a novel class of druggable peptidoglycan remodelling enzymes, termed amidases, which are now being pursued further. In addition to demonstrating utility for drug development, the Wits node has also described a novel role for these enzymes in coordinating spatial and temporal placement of other cell division proteins. Consistent with this, amidase-defective cells are unable to hydrolyze septal cell walls, resulting in destabilization of the FtsZ ring and in some cases, rotation of the primary axis of the ring to allow for separation of abnormal buds. In addition, a mutant of *M. tuberculosis* that is deleted for the *ami1*-encoded amidase was constructed and subsequent analysis of this strain revealed that it is defective for cell division, forming “ghost” cells that bud from the pole but do not proceed to divide further. Other recent findings from the Wits node on peptidoglycan remodelling have described a role for low molecular weight penicillin binding proteins (LMW PBPs) in mycobacterial cell elongation and division. Wits node researchers have identified a novel essential, LMW PBP, which is required for cell elongation during bacterial growth and remodelling of division scars after daughter cells separate. The cell wall remodelling work at the Wits node also involves an analysis of resuscitation promoting factors (Rpfs). In 2015, the Wits node demonstrated that *rpf* deletion mutants displayed defective biofilm formation, with altered spatial organization of individual cells within the biofilm matrix. This defect is reversed upon provision of culture filtrate from wild type *M. smegmatis*, but not from *rpf* deletion mutants, confirming the requirement for continuous production of Rpfs for biofilm maturation in *M. smegmatis*. Mutants lacking two or three *rpf* genes displayed increased susceptibility to detergent, vancomycin and cephalosporins. Cellular localization studies revealed that both RpfA and RpfB localize predominantly to the septum whilst RpfE localizes to a region between mid-cell and the cell pole, suggestive of specialist function. Single cell time-lapse microscopy identified stochastic *rpf* gene expression, in bursts, within a single colony that is suggestive of cellular scouts, which sense the environment. These effects are currently being studied further.

Bacterial M23 metallopeptidases form part of a highly diverse group of enzymes characterized by their endopeptidase activity in hydrolyzing peptide bonds found within peptidoglycan and elastin. The diversity of the published crystal structures of these peptidases has resulted in lack of clarity regarding their involvement in bacterial cellular processes. The Wits node has undertaken to characterize the functional diversity of these M23 peptidases in mycobacteria and study the relationship between their structure and substrate specificity. In addition, catalytically inert or degenerate Lysostaphin-like metallopeptidases (dLytMs) have drawn much attention as these have been proven to directly regulate the muralytic activity of LytC-type amidases described above. Recent findings from the Wits node outline a role for these proteins in facilitating the final steps of cell division and daughter cell separation. Deletion of multiple m23-metallopeptidases results in failure to complete cell division and abnormal bulging of cells in the septal and polar regions. The placement of future cell division sites is also altered in these mutants. These effects are currently being studied further.

The respiratory chain in *M. tuberculosis* is the target of a recently licensed new TB drug and several existing groups of promising small molecules. The effect of these drugs on cellular metabolism requires further study to elucidate any adaptive consequences of inhibiting the respiratory chain and to highlight possible new vulnerabilities. Work at the Wits node involves an analysis of mutants that lack different components of the mycobacterial respiratory chain. Using existing mutants of *M. smegmatis* and *M. tuberculosis*, defective for the cytochrome *bd* oxidase (CbdO), the Wits node has demonstrated that whilst not essential for growth under carbon-rich conditions, the CbdO is required for optimal ATP production in both *M. smegmatis* and *M. tuberculosis*. They further show that nitrate reductase deficient strains of *M. smegmatis* still retain the ability to assimilate nitrate, possibility through the function of a novel nitrate

reductase that has not been characterized. In addition, loss of CbdO or nitrate reductase results in increased sensitivity to oxidative stress in *M. smegmatis* and *M. tuberculosis*.

The maintenance of genomic integrity during infection is critical for controlling mutation rates and the emergence of drug resistance variants of *M. tuberculosis*. Consequently, DNA repair pathways are predicted to be central in controlling mutation avoidance in mycobacteria. Research at the Wits node is aimed at further understanding the base excision repair (BER) pathway in *M. smegmatis* and *M. tuberculosis*. In 2014, the Wits node published the results of a study that was aimed at understanding the role of Nth, an endonuclease implicated in the BER pathway. In 2015, another study that investigated the combined role of MutY and the Formamidopyramidine (Fpg/MutM) DNA glycosylases was published and demonstrated that deletion of *mutY* resulted in enhanced sensitivity to oxidative stress, an effect which was exacerbated in a Δ*fpg1* Δ*fpg2* double mutant. Furthermore, combinatorial loss of the *mutY*, *fpg1* and *fpg2* genes resulted in a significant increase in mutation rates suggesting interplay between these enzymes in mycobacteria.

To address the issue of appropriate models for TB drug screening, the Wits node undertook to develop 4 distinct counter-screening models to assess new compounds emerging from local drug development initiatives. The approach was geared towards the production of drug tolerant organisms that could be used to identify compounds that selectively inhibit replicating, non-replicating bacteria and the transition from non-replicating persistence to growth. Previous efforts resulted in development of two preliminary screening models that emerged from growing bacteria under carbon starvation conditions or in floating biofilms. In 2015, further refinement of the carbon starvation model was carried out and this is now routinely used to test a select group of compounds from the H3D Drug Discovery and Development Centre at UCT. The Wits node also established a new model for screening that involves nitrate assimilation through the production of ammonia.

The rollout of GeneXpert in South Africa and globally required the establishment of verification and quality assurance systems. The Wits node of the CBTBR has been intimately involved in this process since 2010 through the development of a reliable and robust mechanism for bulk scale manufacture of inactivated tubercle bacteria. In 2015, the Wits node of the CBTBR successfully provided for the entire global demand for verification material. In addition, a new project to develop a second generation of industry standards that are easier to produce, and can be provided at lower cost to developing countries, was undetaken. This initiative has yielded a new set of standards are currently being field tested. If successful, these reagents will revolutionize the global use of molecular diagnostics to detect TB infection.

The Wits node initiated a project in 2012 that was aimed at identification of DCTB in the sputum of patients with active TB disease through supplementation of sputum cultures with culture filtrate from axenic cultures of *M. tuberculosis*. This project has been underway for three years and recruitment has been intensified in the last two years. This work has expanded dramatically to study the prevalence of DCTB in HIV-1-infected and uninfected individuals and to study the dependency of these phenomena on Rpfs. From the 110 individuals assessed in the first study, 19% harboured Rpf-dependent DCTB and no Rpf-independent DCTB. Furthermore, 12% yielded Rpf-independent DCTB with no Rpf-dependent DCTB. In addition, 54 % displayed both Rpf-dependent and Rpf-independent DCTB. Moreover, HIV-1-uninfected individuals and HIV-infected counterparts with CD4 counts >200 yielded higher proportions of DCTB with Rpf-containing culture filtrate. Most probably number assays also allowed for the detection of mycobacteria in 34 patients with no culturable bacteria on solid media. Additionally, the use of Rpf-containing culture filtrate enhanced detection of smear negative individuals. In a separate longitudinal cohort, the Wits node undertook to detect, quantify and characterize DCTB subpopulations in tuberculous sputum during treatment of drug sensitive tuberculosis. The primary aims were to: (I) describe the behaviour of DCTB during treatment with the understanding that these organisms reflect persisters that are tolerant to antibiotic killing (II) assess the presence of DCTB at the end of treatment (III) determine if the quantum or rates of decline in DCTB during treatment is predictive of cure and/or relapse. Thus far, 175 patients have been recruited to the study, with 61 patients successfully completing 6 months of TB treatment. Through this analysis, the Wits node of the CBTBR is now able provide a description of the rates of decline of DCTB during treatment, which are significantly slower than conventionally detectable organisms. The data also suggest the presence of a residual viable population of DCTB at the end of treatment however, this result requires further microbiological confirmation. Collectively, this work from the Wits node has provided novel insight into an important area of TB biology and identified possible alternate endpoints for assessment of new drugs, novel regimens and host-directed therapies.

Joint Research and Training Activities

1. **Wits-SU**.
   The study of iron-sulphur cluster biogenesis in mycobacteria. Prof. Bavesh Kana (Wits node) and Dr. Monique Williams (SU node) are collaborating to study iron-sulphur cluster biogenesis in mycobacteria. This work is funded through the CBTBR and an NRF Research Career Advancement Fellowship awarded to Dr. Williams. Wits-SU

2. **Wits-SU**
   Identification and characterization of DCTB. Prof Bavesh Kana and Prof. Gerhard Walzl intiated a new colloaboration on the study of DCTB in 2015. The main focus in this case is the identification of DCTB after treatment completion in drug sensitive TB patients.

3. **Wits-SU**
   Genotypic characterization of DCTB. Prof. Bavesh Kana and Prof. Robin Warren are collaborating on the genotypic characterization of Rpf-dependent DCTB.

4. **Identification of High-Quality Hits for Tuberculosis (HIT-TB) Consortium.** All three nodes continued to participate in the HITTB consortium, with Prof, Mizrahi as a co-investigator, funded by the BMGF through a subaward from the FNIH, and Profs. van Helden, Kana and Warner funded through SHIP grants from the SAMRC.

2. Education and Training

Breakdown of postgraduate students and postdoctoral fellows in the CBTBR in 2015

Student category	Number/percentage	Target based on SLA4 (for Extension Phase, 2014-2018)
Total number of students	112	≥ 35
% Postdoctoral fellows	21%	≥10%
% PhD students	35%	N/A
% MSc students	35%	N/A
% BSc (Hons) students	10%	N/A
% Women students[a]	59%	≥ 50%
% Black students[a]	54%	≥ 50%

a) Includes postdoctoral fellows

Degrees conferred and postdoctoral fellowships completed

The CBTBR graduated 10 PhD, 7 MSc and 9 Honours students in 2015.

Dissertations and theses

PhD

1. Klopper M. Molecular characterization of the drug-resistant tuberculosis epidemic in the Eastern Cape, South Africa. Promoter: Prof TC Victor; Co-Promoter: Prof RM Warren.
2. Black P. Identification of genes regulating the expression of the Atpbefhagdc Operon in response to rifampicin in multi-drug resistant Mycobacterium tuberculosis strains. Promoter: Prof TC Victor; Co-Promoter: Prof RM Warren.
3. Machado A. Mapping of the distribution of Mycobacterium tuberculosis complex strains involved in bovine tuberculosis in Mozambique. Promoter: Prof PD van Helden; Co-Promoters: Prof RM Warren, Prof G Kallenius
4. Sao Emani C. The role of ergothioneine in mycobacteria. Promoter: Dr B Baker; Co-Promoters: A/Prof IJF Wiid, Dr M Williams.
5. Daya M. Using bioinformatics and biostatistics to elucidate susceptibility to tuberculosis in an admixed population. Promoters: Prof E Hoal; Co-Promoter: Prof. L van der Merwe
6. Theron A. Differential Inhibition of adenylylated and deadenylylated Mycobacteriun tuberculosis glutamine synthetase by ATP scaffold-based inhibitors. Promoter: Prof Ian Wiid; Co-promoter: Prof C Kenyon

7. Koch A. The physiology of drug resistant mycobacteria: implications for pathogenesis. Supervisor: A/Prof Warner Co-supervisor: Prof V Mizrahi.
8. Ditse D. Replication fidelity in mycobacteria. Supervisor: Prof Warner; Co-supervisor: Prof V Mizrahi.
9. Naran K. Mechanisms of antibiotic resistance and tolerance in mycobacteria. Supervisor: A/Prof D Warner; Co-supervisor: Prof V Mizrahi.
10. Kigondu E. Repurposing chlorpromazine and its metabolites for antituberculosis drug discovery. Supervisor: Prof. K Chibale; Co-supervisor: A/Prof D Warner.

MSc

1. Smith, B. Application of Becton Dickinson FACS™ Combinatorial Antibody Profile (FACS™ CAP) technology to the identification of efficiency of tuberculosis therapy. Promoter: Prof G Walzl.
2. Manunu B. Determination of the mechanism of synergy of SQ109 with rifampicin and isoniazid in *Mycobacterium smegmatis.* Promoter: Dr M Williams;. Co-Promoter: Dr SO Friedrich.
3. Visser H. Mechanisms of Resistance to New Generation Anti-TB Drugs. Promoter: Prof TC Victor; Co-Promoter: Dr LV Paul
4. Gallant J. The effect of glutamate homeostasis on the survival of *M. bovis* BCG. Promoter: A/Prof. Ian JF Wiid; Co-Promoter: Dr. AJ Viljoen.
5. Zvinairo K. The influence of small RNAs on the physiology of *mycobacterium tuberculosis.* Promoter: Prof TC Victor; Co-Promoters: Dr LV Paul, Dr E Streicher.
6. Hariparsad S. Biological activity of *Sinularia notanda*. Promoter: Prof D Meyer; Co-Promoter: Prof B Kana
7. Asmal R. Identification and cellular localization of DD-carboxypeptidase-interacting proteins in *Mycobacterium smegmatis* Promoter: Prof Kana

Recruitment of new postgraduate students

A number of new students have joined the team during the course of 2015. Applications from other students are under consideration, pending availability of supervisory capacity, laboratory and office space and/or funding, including bursary support (see above). At the SU node, we enrolled 2 Postdoctoral fellows, 4 PhD students, 9 MSc students and 10 Honours students into the CBTBR in 2015. At the UCT node, 1 Postdoctoral fellow, 1 PhD student and 2 MSc students were recruited. At the Wits node 1 Postdoctoral fellow, 1 PhD student, 4 MSc students and 1 Honours student were recruited in 2015.

Honours and awards to students

- Wynand Goosen received a DAAD – NRF Doctoral bursary.
- Ross McFadyen received a NRF Invitation MSc bursary.
- Charlene Clarke was awarded an NRF Grant Holder Bursary.
- Eduard Roos received an NRF Grand Holder Bursary.
- Roxanne Higgitt was awarded an NRF Invitation Honours Bursary in 2015.
- Taime Olivier was awarded an NRF – MRC Health Scholarship
- Taime Olivier and Ross McFadyen, both from SU node were awarded a Crossley Foundation Award.
- Taime Olivier was selected in the Stellenbosch New voices in science finalist.
- Nastassja Steyn was awarded an NRF Grant Holder Bursary.
- Nastassja Steyn was awarded a Stellenbosch University Merit Bursary.
- Juanelle Du Plessis received an NRF Invitation Doctoral Bursary.
- Marisa Klopper from SU node was awarded a 2015-2016 Stellenbosch University Faculty of Medicine and Health Sciences Subcommittee C Doctoral fellowship.
- Ncite Da Camara, an MSc student from SU node was awarded an NRF Inovation scholarship and a Stellenbosch University travel funding in 2015.
- Micheal Whitfield, a PhD student from Su node, was awarded a NRF – MRC health scholarship.
- Micheal Whitfield received an Ernst and Ethel Eriksen bursary.

- Jomien Mouton was awarded an NRF scarce skills Post-doctoral fellowship.
- Jomien Mouton received a Crossley project funding.
- Jomien Mouton was awarded a Stellenbosch University Faculty of Medicine and Health Sciences travel funding.
- Anzaan Dippenaar was awarded a Claude Leon Foundation Post-doctoral fellowship.
- Anzaan Dipenaar, Margaretha de Vos and Ruben van der Merwe, from SU node received a Swiss South African joint research programme – travel exchange grant.
- Ruben van der Merwe received a SU Scientific travel and Publication incentive fund award.
- Melanie Grobbelaar, a PhD student from SU node received a NRF PhD bursary.
- Melanie Grobbelaar was awarded a Harry Crossley project funding.
- Trisha Parbhoo was awarded a NRF Grant Holder bursary.
- Hanri Visser was awarded a Hanri Crossley scholarship award.
- Jessie Arries and catoline Pule received an MRC NHSP scholarship award.
- Caroline Pule, a PhD student from SU node was awarded a WhiteSci Scientific travel award.
- Caroline Pule, a PhD student from SU node won the prize for best poster presentation at the Euroscicon's TB Summit 2015 in London, UK.
- Caroline Pule won the prize for feedback at Euroscicon's TB SUMMIT 2015 in Lodon, UK.
- Caroline Pule, a PhD student from SU node was awarded an International scientific travel award to attend a conference in UK, RDSD.
- Namaunga Chisompola received a Beit Trust Hardship fund and an Organisation for women in science for the developing world (OWSD) postgraduate fellowship.
- Antoinette Colic received a NRF SARCHi bursary.
- Kenneth Hammond-Aryee, PhD student from SU node was selected in the Finalist written category new voices in science.
- Nikki le Roex, a PhD student from SU node was awarded a KIC Travel Award in 2015.
- Smith B from SU node received a Top Master's Student in the Faculty of Medicine and Health Sciences award
- Juanelle Du Plessis from SU node received a Royal Society (UK)/ Newton Fund International Exchanges Scheme award.
- Happy Tshivhula received the MRC PhD fellow ship for three years
- Happy Tshivhula, Carine Kunsevi (both PhD students) and Dr Léanie Kleynhans (Postdoc) received the Bill and Melinda Travel Award to attend the Keystone meeting on TB and comorbidities in Colorado
- Dr Léanie Kleynhans received the ECI-AAI Travel grant to attend the 4th European Congress of Immunology in Vienna
- Bronwyn Smith was awarded the Stellenbosch University Medal for Top Master's student in the Faculty of Medicine and Health Sciences for 2014.
- Zela Martin, PhD student in the UCT node, was invited to attend the very prestigious 65th Lindau Nobel Laureate Meeting which was held in Lindau, Germany.
- Zela Martin was awarded a Swiss Government Excellence Scholarship to conduct a series of experiments that are critical to her doctoral research. She was also awarded the David and Elaine Potter Fellowship from UCT.
- Antonina Wasuna, from UCT node was selected to participate in the Novartis Next Generation Scientist programme.
- Dr. Nigel Makoah, a postdoctoral researcher from UCT node was awarded an NRF Innovation bursary for 2015-2016. And was also selected for a 1-year Postdoctoral Fellowship sponsored by the Carnegie Corporation of New York

- Charles Omollo, a PhD student who is also supervised by Prof. Kelly Chibale and A/Prof Digby Warner, was awarded an equivalent PhD Fellowship from the Carnegie Corporation.
- PhD student Phia von Coller was awarded an NRF PhD Innovation bursary.
- PhD student Simon Broadley was awarded a 2015 CSIR/UCT Fellowship.
- Master student Michael Reiche, was awarded an NRF Free-standing-Scarce Skills Masters Scholarship as well as an NRF Masters Travel Award in 2015.
- Junior Research Fellow Dr. Joanna Evans was awarded a South African National Research Foundation's Knowledge, Interchange and Collaboration (KIC) Travel Award for attendance at an international conference (Gordon Research Conference on Tuberculosis Drug Discovery and Development, Girona, Spain).
- Dr. Raju Mukherjee was awarded a postdoctoral travel award from UCT to attend the Gordon Research Conference on Tuberculosis Drug Discovery and Development in Girona, Spain.
- Dr. Melissa Chengalroyen was awarded third prize for a poster presentation at the Molecular Biosciences Thrust Symposium held on the 3rd December 2015.
- Zaahida Sheik Ismail, won the prize for best poster presentation in the Communicable and Non-communicable diseases track at the inaugural National Health Laboratory Services Pathology Research and Development Congress (PathReD).
- Dr. Christopher Ealand was awarded the MRC Career Development Award.
- Andrea Papadopoulos was selected by the MRC as a National Health Scholar.

Training courses implemented by staff and students

- Prof. Rob Warren ran a course for postgraduate students at the Honours level from the faculty of Health Sciences. All participants had hands-on experience for the extraction of DNA from *Mycobacterium tuberculosis*, restriction enzyme digests, southern blotting, probe labelling and hybridisation.
- Prof Miller was an instructor at the annual Zimbabwe Wildlife Immobilization and Capture Course. This provides CPD credit for South African veterinarians working with wildlife.

Research Capacity Development workshops run by Prof Corfield:

- Involvement in the PLUME programme aimed at developing research productivity in the Nursing profession.
- SARIMA (SA Research and Innovation Management Association) workshop on "Developing a research profile for early career researchers."
- Oral Communication Skills at SU and UFS for both established and postgraduate researchers.
- Poster presentations and abstract writing at UFS for postgraduate students

Training courses attended by staff and students

Attendees	Training Course	Location/Web address	Start Date	End Date
Klopper M	Health Research Ethics application process: Getting it right.	Stellenbosch University FMHS, Cape Town, SA	29 July	29 Sept
Klopper M	Harry Crossley Grant Writing workshop	Stellenbosch Universtiy FMHS, Cape Town, SA	04 Sept	04 Sept
Botha L	Media Training	SAMRC conference centre, Tygerberg, Cape Town, SA	06 Mar	06 Mar
Borrageiro G	The MIQUE Guidelines: Minimum Information for Publication of Quantitative Real-time PCR Experiments	Tygerberg Campus, Tygerberg, Cape Town, SA	11 Mar	12 Mar

Borrageiro G	Scientific writing for Academic Articles	Tygerberg Campus, Cape Town, SA	18 May	19 May
Borrageiro G	Bioinformatics applied: An introduction to statistics and methods in bioinformatics	Stellenbosch University, Stellenbosch, South Africa	13 July	17 Sep
Borrageiro G	Harry Crossley Grant Writing workshop	Tygerberg Campus, Cape Town, SA	04 Sept	04 Sept
Borrageiro G	Genomics on the move	University of the Witwatersrand, Johannesburg, SA	07 Sept	09 Sept
Hammond-Aryee K	Global Health Diagnostics Course	Mcghill University, Montreal, Canada	06 July	10 July
Brodovcky T, Kunsevi-Kilola C, Tshivhula H, Zass L	Harry Crossely foundation grant writing workshop	Room 4053 B & C, 4th floor, Teaching building, Tygerberg Campus, Cape Town, SA	04 Sept	04 Sept
Stanley K	The Fundamentals of Data Management Training	Washington Duke Inn, Durham, USA	08 Jun	12 June
Stanley K	IATA Dangerous Goods Regulations course	Cpt Airport, Cape Town, SA	19 Nov	20 Nov
Hammond-Aryee K	Global Health Diagnostics	Mcghill University, Montreal, Canada	06 July	10 July
Colic A	Bioinformatics Support Platform Introduction to Bioinformatics Course	SANBI, UWC, Cape Town, SA	16 Feb	02 Apr
Colic A	Gene expression-based Biomarker Discovery	IDM, UCT, Cape Town, SA	24 Aug	26 Aug
Mouton JM	Strengthening Postgraduate Supervision Course	Stias, Wallenberg Centre, Stellenbosch; online, Stellenbosch, SA	15 July	07 Dec
du Plessis J, Klopper M, Grobbelaar M	RNA-Seq Data Analysis with Chipster	Centre for High Performance Computing (CHPC), Cape Town, South Africa	16 Nov	16 Nov
Clarke C, Higgit R	The MIQUE Guidelines: Minimum Information for Publication of Quantitative Real-time PCR Experiments	Tygerberg Campus, Cape Town, SA	11 Mar	12 Mar
Roos EO	Public Speaking Workshop	Willcox Building, Stellenbosch University, Stellenbosch, SA	16 Oct	16 Oct
Schurz H, Bowker NG	GWAS data analysis and results interpretation workshop	African institute for Mathematical science and H3ABioNet, Muizenberg, SA	20 Apr	24 Apr
Schurz H	Genomic Epidemiology in Africa	K-RITH Kwazulu-Natal Research Institute for Tuberculosis and HIV, Durban, SA	21 June	26 June
Schurz H	IDM masterclass on gene expression-based biomarker discovery	MAC room UCT, Cape Town, SA	24 Aug	26 Aug
Da Camara NL, Colic A	Bioinformatics courses	training laboratory of SANBI at the University of the Western Cape, Cape Town, SA	16 Feb	02 Apr
Higgitt RL	Practical course of gene/protein functional networks and interactomes.	UCT Medical campus, Anatomy building, Cape Town, SA	23 Nov	24 Nov
Da Camara NL	Practical Course on Gene/Protein Functional Networks & Interactomes	Health Teaching Labs 1-2, Basement of Anatomy Building, UCT Medical School, Cape Town, SA	23 Nov	24 Dec
Steyn N	Practical Course on Gene/Protein Functional Networks and Interactomes	UCT, Cape Town, SA	23 Nov	24 Dec

Parbhoo T	IUIS-FAIS Southern African Regional Immunology Workshop and 6th Infectious Diseases in Africa Symposium	The River Club, Observatory, Cape Town, SA	20 Oct	23 Oct
Parbhoo T	Scientific writing for theses and dissertations	Stellenbosch University, Cape Town, SA	28 Apr	29 Apr
Bowker NG	Wellcome Trust Exome Sequencing Course	Hinxton, Cambridge, UK	06 Oct	14 Oct
Klopper M	Research in diagnostics for tuberculosis: fundamentals, best practices, and priorities	UCT Lung Institute, Cape town, SA	29 Nov	01 Dec
Schlechter N	Bioinformatics applied: an introduction to statistics and methods in bioinformatics	Natural Sciences Building Room 3011 (NARGA H), Stellenbosch, SA	14 July	17 July
Schlechter N	CRISPR, Duo-link & Next-Gen Sequencing Oligos	UCT, Cape Town, SA	24 Aug	28 Aug
Dippenaar A, de Vos M,van der Merwe R	Sequence Analysis in Molecular Epidemiology of Pathogens	Hotel Falken, Wengen, Switzerland	18 Jan	21 Jan
Dippenaar A, de Vos M, van der Merwe R	Chipster	CSIR, Cape Town, SA	16 Nov	16 Nov
Werely CJ	GCP Beginner's Course	CAB Conference Centre, Brackenfell, Cape Town, SA	08 Apr	09 Dec
Whitfield M	Research in diagnostics for tuberculosis: fundamentals, best practices, and priorities	UCT Lung Institute, Cape Town, SA	29 Nov	01 Dec
Whitfield M	Academic Article Writing	Tygerberg Medical Campus, Tygerberg, Cape Town, SA	18 May	19 May
Williams M	Synnovation Workshop	STIAS, Cape Town, SA	05 Nov	05 Nov
Sampson SL	HERS-SA Academy	Hilton Hotel, Cape Town, SA	06 sept	11 Dec
Chegou NN	6th Advanced Course on Diagnostics (ACDx)	Les Pensieres Conference Centre, Annecy, France	06 Sept	11 Sept
Chegou NN	xMAP Connect 2015	Muziekgebouw aan 't IJ, Amsterdam, The Netherlands	25 Nov	26 Nov
Ngwane A	Computational Biology	Anatomy Building University of Cape Town, Cape Town, SA	23 Nov	24 Nov
Kunsevi-Kilola C	6th African Flow Cytometry Workshop	HVTN Immunology laboratory CHIL, Cape Town, SA	26 Oct	30 Oct
Ealand C, Senzani S, Sheik Ismail Z, Ralefeta D	UCT Microscopy Unit	UCT, Cape Town, SA	01 Jan	31 Dec
Von Coller P	Intermediate Biostatistics class	K-RITH, Durban, SA	01 Aug	31 Aug
Papadopoulos A, Shaku M, Rantsi T, Maphatso M, Moseki M, Senzani S, Sheik Ismail Z	Zeiss Confocal Workshop	Johannesburg, SA	25 Aug	26 Aug
Dakada, H, Swartz K, Tonsing S	GCP	CREDE (Clinical Research Education and Development)	4 Nov	5 Nov
Smith B Gutschmidt A	Best Laboratory Management practices	Cape Town – Chayil Resources	13 Apr	14 Apr
Awoniyi D	Immunology in the Tropics. Makerere/UVRI Infection and Immunity Research Training Programme	MRC/UVRI, Entebbe, Uganda	9 Mar	21 Mar

Awoniyi D	Research in diagnostics for tuberculosis: fundamentals, best practices and priorities	UCT Lung Institute, Cape Town, SA	29 Nov	01 Dec
Du Plessis,N	International Project management Course	The Union's International Management Development Program (IMDP)	2 Dec	2 Dec
Du Plessis,N	GCP Refresher	ERECCA	2 Sep	2 Sep
Beltran C	MPN assay for resuscitation of dormant Mtb	Wits node of the CBTBR	9 Aug	13 Aug

Other capacity development activities

- Prof. Warner served as Convenor, *Laboratory Research Methods* module of the BMedSc(Hons) programme, Faculty of Health Sciences, UCT. Prof. Warner and Dr. Joanna Evans lectured students taking this course.
- Prof. Warner served as Convenor of the *Bacterial Pathogenesis* module of the Infectious Diseases and Immunology Honours Programme in the Faculty of Health Sciences, UCT. Prof. Warner and Dr. Evans lectured in this course.
- Prof. Warner served as Convenor of the *Bacteriology* module of the Intercalated MBChB programme in the Faculty of Health Sciences, UCT. Prof. Warner also lectured in this course.
- Prof. Warner presented the *Tuberculosis* module in the *Defence and Disease* programme in the Department of Molecular and Cell Biology, Faculty of Science, UCT
- Dr. Gordhan taught molecular diagnostics and basic bacteriology in the second year Bioengineering Degree at Wits University.
- Prof. Kana gave delivered lectures on Recombinant DNA and Proteins and Gene Manipulation to the Registrars in 2015 (ANAP7000).
- Prof. Kana delivered a two week lecture series on mycobacteria to the Honours Students in the Molecular Medicine and Haematology Department.
- Both Prof. Kana and Dr. Gordhan taught in the Bachelor of Health Sciences – 3rd Year Molecular Basis of Disease course
- Prof. Warren presented lectures on "Getting Published" as part of the Research Development training programme.
- FamCru & TASK Clinical trials development procedures.
- Dr Jackson served as the course coordinator for the "Molecular Biology" module of the SU Molecular Biology and Human Genetics Honours programme.

Exchange visits

- MSc student from the UCT node, Michael Reiche, received an NRF Travel Award which enabled him to spend three weeks in the USA learning new skills in the fields of microscopy and imaging. He attended the Special Topics Course on Optical Microscopy and Imaging in the Biomedical Sciences (OMIBS) at the Marine Biological Laboratories where he was exposed to theoretical understanding developed during lectures, discussions with faculty, and assignments. This included an in-depth understanding of fundamental aspects of physics as well as the associated cellular biology. Conversations with experts from around the world also proved useful in exposing him to new research ideas and ways of thinking. In addition to the theoretical knowledge, the course also included hands-on use of various imaging techniques on a variety of imaging platforms. The final component of the course comprised of sample preparation methods; image analysis using appropriate software; and the use of controls and correction methods necessary to correctly and accurately measure and quantify samples - 2015
- Michael Reieche travelled to the US NIH in Bethesda, where he presented his research on visualizing the mycobacterial mutasome to members of two collaborating laboratories of the UCT node. Discussions with Dr Roger Woodgate (Laboratory of Genomic Integrity, NICHD) mainly concerned DNA damage in bacteria, repair pathways and methods of investigation, whereas discussion with Drs. Clif

Barry III and Helena Boshoff (Tuberculosis Research Section, Laboratory of Clinical Infectious Diseases, NIAID) focused on holistic approaches to chemotherapeutic targeting of the mutasome. The last stop on Michael's trip was to the HHMI Janelia Research Campus where he met with Drs Teng-Leong Chew and Jesse Aaron at the Advanced Imaging Center to discuss a promising research avenue which formed the basis of a successful application by Digby Warner, Michael's PhD supervisor, to utilise super-resolution imaging equipment at the AIC, under the HHMI Visiting Scientist Program - 2015

- Katrin Jungmann, a doctoral student working under the supervision of Prof. Rolf Müller from the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Germany, spent two months working in the UCT node as part of a South Africa/Germany Research Cooperation Grant to Prof. Mizrahi and Prof. Müller. During this time, she worked on a collaborative research project the supervision of postdoctoral fellow Dr. Atica Moosa.
- Nicole Narrandes undertook a six-month research and training visit to the laboratory of Prof. Kevin Pethe at Nanyang Technological University, Singapore - 2015
- Caitlin Uren visited the lab of Dr Brenna Henn at Stony Brook University in 26 June to 2 July.
- Caitlin Uren visited the lab of Dr Carlos Bustamante at Stanford University from 2-5 July.
- Drs Ronacher and Kleynhans visited the laboratory of Prof Blanca Restrepo (University of Texas) for training in macrophage assays.
- Prof Michele Miller visted Colorado State University on a collaborative project, from the 25-28 January.
- On the 7-19 April, Prof Michele Miller went on a research field work and consultation in Namibia Ministry of Environment and tourism in Waterberg.
- Eduard Roos undertook a research field work to Kruger National Park on the 25 May – 12 June.
- Prof Michele Miller visited Mkuza Game Reserve on 12-18 Sep.
- Professor Michele Miller visited Hluhluwe-iMfolozi Game Reserve on 1 July- 6 August.
- Eduard Roos visited Kruger National park on 30 Nov- 5 Dec.
- Eduard Roos visited Mkuze Game Reserve on 12-18 Sept.
- Taime Olivier went on a research field work to Kruger National Park on 11-15 Sept.
- Wynaand Goosen, Ross McFadyen and Charlene Clarke travelled to Hluhluwe-iMfolozi game reserve on a research field work on 1-30 July.
- Dr Sven Parsons, visited Hluhluwe-iMfolozi game reserve on 1-10 July.
- Charlene Ckarke and Dr. Sven Parsons went on a field visit to the Kalahari meerkat project site on the 1-4 October.
- Juanelle du Plessis visited Imperial College in London.
- Monique Williams visited King's College in London.

Conferences/Symposia Organised (4)

- Prof. Miller served NIH Many Hosts of Mycobacteria symposium invited panel chairperson from the 26th – 27th March 2015.
- Dr Craig Kinnear served on the organizing committee of the Stellenbosch University Faculty of Medicine and Health Sciences Annual Academic Day as the Infectious Diseases representative.
- Dr Craig Kinnear served as the chair of the Stellenbosch University Department of Biomedical Sciences Annual Academic Day.
- Prof. Kana served as chair of the Scientific Organizing Committee for the inaugural National Health Laboratory Service (NHLS) Pathology Research and Development Congress (PathReD) 2015.

3. Knowledge Brokerage

The operational environment

All three nodes are actively involved in the sharing of knowledge amongst researchers within the CBTBR through lab meetings held at least weekly. Journal Club meetings, held weekly at the three sites, also provide an opportunity to share broader-based scientific issues and ideas within the field of biological sciences within and beyond our own institutions. Team members, staff and students also attend numerous local and international conferences, often as invited speakers, where we shared our work with the international community. We have had even more meetings than in the past with health authorities, such as W and E Cape Departments of Health, to share with them our findings and the implication of these. Team members also advised international organisations, such as the TB Alliance and the WHO.

Knowledge translation to stakeholder groups

CBTBR members were involved in numerous public awareness activities countrywide in 2015:

Public awareness, public engagement, and publicity

- Dr. Malherbe was interviewed live for 20 minutes on Radio Sonder Grense (RSG) as well as on Khoisan Community Radio Station on 14 August 2015, regarding TB research, the work of the DST/NRF Centre of Excellence, and Tuberculosis in general. RSG invited him for a follow up discussion 2 weeks later, where he explained what biomedical research is and what one would need to study to go into this occupational direction.Dr. Chegou was interviewed by “The Naked Scientists”, UK, related to new tests for the rapid diagnosis of TB disease at the point-of-care in resource limited settings, on the 19 October 2015, in Geneva.
- Prof. Miller wasfeatured in an article on research group in SU Research Show case 2014.
- Prof. Miller did an article in The Conversations, an online magazine.
- Prof. Miller was interviewed by Business day newspaper.
- Taime Olivier was featured in new voices in Science talk.
- Prof. Miller was interviewed in an article on inaugural speech in SU news online.
- Prof. Miller did an interview with International elephant Foundation newspaper, and was published online.
- Prof. Sampson did an article with an online newspaper called The Conversation on 15 May 2015.
- Prof.Sampson did an article on TB proof blog on 17 July 2015.
- Prof. Sampson participated in a profile piece: FMHS annual publication 2015.
- Caroline Pule did radio interviews about Biomedical research, specifically TB research been done at Stellenbosch University Centre of excellence/DST and NRF.
- Caroline Pule was featured in an article by Science stars magazine under the burner “Motivation about Science careers.”
- On 28 September, Prof. Mizrahi presented a talk at the College of Health Sciences, UKZN, entitled, “Joy, luck, adventures and obstacles: lessons from my journey” at the WILL (Women in Leadership and Leverage) workshop. WILL is an innovative leadership development program with an emphasis on emerging and established women researchers.
- Dr Joanna Evans assisted with conceptualizing and facilitating the Biology Workshops conducted by the Eh!Woza public engagement programme, with the aim of educating learners aged 15 – 17 from Khayelitsha, Cape Town, about the intricacies of biomedical TB research, specifically TB drug discovery.
- Prof. Warner participated in a series of workshops in 2015 that were aimed at equipping Postdoctoral Fellows at UCT with the skills necessary to supervise postgraduate students. These workshops were held in July (13-14) and September (17-18) at Mont Fleur, Stellenbosch.
- Prof. Warner and several members of the UCT node contributed to a series of interactive workshops organized by MMRU alumnus, Dr. Anastasia Koch, and which aimed to expose learners from Ikamva

Youth to current research programmes at UCT around HIV and TB through lectures, tutorials, and practicals.

- Members of the Wits node participated in the University open and exhibition days. They created and manned an exhibit to profile the work done at the CBTBR.
- In March 2015, Prof. Kana served as a judge for the 2014 (to be awarded in 2015) edition of the Discovery Health Journalism Awards. He reviewed health related journalism in different categories, including television, radio, print media and trade publications. He provided feedback to journalists regarding reporting style and made recommendations to improve health reporting in these sectors. Prof. Kana was also invited to attend the awards function on the 27th May 2015, where presentations were made to the journalists with winning entries.
- Prof. Kana participated in the following interview/profile pieces, Television: South African Broadcast Services – SABC1 (30 min profile show for the youth); MNET: Mela (45 min profile show); Radio: South African Broadcast Services, Panel interview on TB (World TB Day)
- Members of the Wits node, together with members from other nodes participated in radio interviews, broadcast in the 9 official languages of South Africa. These interviews profiled the work done in the CBTBR and were also targeted at attracting school children to careers in science.
- Prof. Kana from the Wits node participated in a press conference with Section 27 and TAC where it was announced that Johnny Clegg will be partnering with TAC to raise money for TB awareness. His address to the press highlighted the role that civil society has to play for implementation of the post-2015 WHO strategy. Johnny also handed over a cheque for R 100 000 to TAC to kick-start TB awareness and charged the commercial sector to follow suit.
- Prof. Kana delivered a 30 min public lecture at the National Institute for Communicable diseases this morning. The theme was “The New Post-2015 Global TB Strategy? The End Game” Venue: PRF auditorium, NICD/NHLS, 1 Modderfontein Road, Sandringham, Johannesburg. Chair: Lucille Bloomberg. The title of his presentation: Differential bacterial growth states in active TB disease
- Prof Corfield has continued her involvement in communicating biomedical and biotechnological science through a variety of approaches to a broad audience, ranging from primary and secondary school learners and their teachers, the “man on the street”, medical students and genetic counsellors to members of neighbourhood watches, community policing forums and the SA Police Services. Since 1998, she has encouraged many other scientists and postgraduate students to take part in public engagement and has received support and encouragement for this work from different stakeholders – including outreach funding from the CBTBR and the MRC, the DNA project and the Public Understanding of Biotechnology initiative (PUB) of SAASTA (SA Agency for Science and Technology Advancement, division of the Department of Science and Technology), as well as pro deo work on behalf of her own brand Scibiolosa. The following activities occurred in 2015. She gave DNA Project workshops which focussed on the science of DNA profiling and its application in forensics and crime prevention to relevant mainly adult audiences. She presented her flagship workshop on the science of DNA and its applications in genetics to second year MBChB students as an introduction to the medical genetics module and to genetic counsellors to help them talk to their patients and families in assessable ways. She has used the popular Murder Mystery genre to promote understanding of various sciences, including forensics, space travel and astronomy, to high school learners at Scifest 2015 and at the Zululand Science Centre. She designed and presented a two- day Advanced Biotechnology workshop on behalf of SAASTA/PUB for science centre facilitators from across South Africa. She organised an SAWISE (SA Women in Science and Engineering) Women’s Day event for high school girl learners at the CT Science Centre with the theme “The Science of Health and Beauty”, speakers came from SU and UCT, also included was Valerie’s workshop entitled “HIV comes to the Party”. She has also given talks on “a Careers in Science: one scientist’s journey” to high school learners at the Zululand Science Centre and on “Career Challenges Women Face” at an SAWISE event. Other activities include NRF Ratings workshops given to the Universities of Stellenbosch, the Western Cape and the Free State, and Research Capacity Development workshops at SARIMA, SU and UFS.

4. Networking

Networks and linkages

The three nodes of the CBTBR are involved in wide collaborative networks that involve TB researchers and research institutions in a large number of countries. Maintaining existing collaborative networks and developing new linkages is of critical importance to the CBTBR. For this reason, members continued to devote significant time and effort to networking.

NAME	INSTITUTION	NATURE/ PURPOSE, OUTPUTS AND FUTURE DIRECTION OF COLLABORATION
International (46)		
Dr. Neeraj Dhar	Faculte Des Sciences De La Vie, Global Health Institute Ecole Polytechnique Federale De Lausanne	Collaboration on the study of peptidoglycan remodelling and cell division in mycobacteria and on the use of microfluidics to analyse the impact of drug treatment or target depletion on *M. tuberculosis*.
Prof. Katarina Mikusova	Comenius University, Bratislava	MM4TB collaboration on cell wall biosynthesis
Prof. Česlovas Venclovas	Institute of Biotechnology, Vilnius, Lithuania	Ongoing collaboration on computational biology of *M. tuberculosis* proteins
Dr. Tom Ioerger, Prof. Jim Sacchettini	Biochemistry & Biophysics, Texas A&M University, College Station, TX, USA	Ongoing collaboration on whole-genome sequence analysis of strains of *M. tuberculosis*
Prof. Sir Tom Blundell, Prof. Chris Abell	Cambridge University, UK	Collaborating members of the HIT-TB and MM4TB Consortia
Prof. Stewart Cole and other MM4TB collaborators	EPFL, Lausanne, Switzerland	MM4TB Consortium
Prof. Menico Rizzi	University of Piemonte Orientale, Novara, Italy	Onngoing collaboration on TB drug discovery (MM4TB)
Prof. Hannu Mykyllallio	INSERM, France	Ongoingcollaboration on targeting ThyX for TB drug discovery
Prof. Rolf Müller	HIPS Helmholtz Institute for Infection Research, Saarland, Germany	Ongoing collaboration on the identification of natural products of myxobacterial origin with antimycobacterial activity
Prof. David Russell	Cornell University, USA	Ongoing collaboration on drug permeation
Prof. Dirk Schnappinger, Dr. Sabine Ehrt	Weill Cornell Medical College, Cornell University, USA	Ongoing collaboration on in vivo validation of drug targets
Prof. Kyu Rhee	Weill Cornell Medical College, Cornell University	Ongoing collaboration on metabolomics analysis of conditional mutants of *M. tuberculosis*
Dr. Roger Woodgate	NICHD, NIH	Onoing collaboration on replisone dynamics in mycobacteria. Co-investigator with A/prof. Digby Waner on new five-year UO1 grant from the NIH
Dr. Ian Orme	Colorado State University	Collaboration on characterization of mutant strains of *M. tuberculosis* in the guinea pig model of TB infection.
Dr. Helmi Mardassi	Institut Pasteur de Tunis, Tunisia	Characterisation of LAM evolutionary history (2007-present).

Dr. Wilbert Bitter	Vrije Universiteit, Amsterdam, Netherlands	The trafficking of the *M. tuberculosis* PE and PPE proteins (2006 – present). ESX secretion in Beijing genotype strains
Dr. Philip Supply,	Institut Pasteur Lille	Evaluation of hypervariable VNTR regions for the discrimination of Beijing genotype strains
Dr Bob Horseburgh	Boston University	Deep sequencing for fluoroquinolone resistance
Prof. Sebastian Gagneux	Swiss TPH, Basel, Switzerland	Collaboration on genome sequencing of clinical strains of *M. tuberculosis*
Profs. Larry Wangh and Prof. Barry Kreiswirth	Brandis University, HPRI,	Evaluation of LATE PCR for the detection of resistance to first and second-line anti-TB drugs.
Dr. Clifton E. Barry III, Dr. Helena Boshoff	Tuberculosis Research Section, Laboratory of Host Defenses, National Institute of Allergy & Infectious Diseases, NIH, MD	Ongoing collaboration on the HIT-TB project TB treatment response project with SUNIRG (G Walzl)
Prof Blanca Restrepo	University of Texas	ALERT: Altered endocrine axis during type 2 diabetes and risk for tuberculosis
Dr Mickey Urdea	Catalysis Foundation	Catalysis/Biomarker: Mycobacterium tuberculosis Biomarkers for Diagnosis and Cure
Prof John Belisle	Colorado State University	Biosignatures/ICIDR:
Stefan Kaufmann	Max Planck IIB	TBVac
Hazel Dockrell	LSHTM	TBVac
Prof Tom Ottenhoff	Leiden University	Ongoing collaboration of biomarkers for TB diagnostics
Prof Eric Bottger	University of Zurich	Development and evaluation of novel genetic based diagnostics for drug resistance.
Prof. Timothy Sterling	Vanderbilt University Tuberculosis Center, Nashville, USA	Fluoroquinolone resistance
Prof Megan Murray	Florida University Harvard / Broad institute	Various project including the evolution of XDR-TB strains; other mechanisms of drug resistance (in addition to genomic mutations); mechanisms of resistance to 2nd line drugs; strain fitness; certain strain families may have both increased fitness and increased potential for acquiring drug resistance.
Dr. Karen Jacobson	Harvard University, USA	1) GIS of drug resistant TB in the Western Cape 2) Health systems reserach
Prof. Harald Wiker, Dr Gustavo de Souza	Bergen University and Oslo University, Norway	Ongoing collaboration on *M. tuberculosis* proteomics.
Dr. Hernandez Pando Rogelio	National University of Mexico	Test different drug resistant strains (MDR / XDR) in a mouse model for strain fitness/virulence.
Prof. Ruth McNerey	LSTHM	Whole genome sequencing of drug resistant M. tuberculosis strains
Prof. Anab Pain	KAUST	Whole Genome Sequencing of Mycobacterial Species
Prof. Erwin Schurr	McGill University, Montreal, Canada	Genetic epidemiology. Poster outputs; 4 papers published 2009-2010, one paper in 2013, one in 2014.
Prof. Laurent Abel & Alexandre Alcais	INSERM / Université Paris 5, France	Analysis of genetic epidemiology. Poster outputs; 4 papers published 2009-2010, one paper in 2013, one in 2014.
Dr. Alkes Price	Harvard School of Public Health, Boston, USA	Computational assistance with analysis of admixture mapping. Paper published in 2013

Dr. Brenna Henn	Stony Brook University, New York, USA	Population Ancestry genetic determinations. Paper published in 2013 and 2014
Prof. Stefan Schreiber, Dr. Almut Nebel, Dr. Andre Franke	Christian-Albrechts University, Kiel, Germany	Investigation of candidate genes in TB. Resulted in 4 publications 2007 - 2009. Manuscript in preparation
Dr. Ad Koets	Utrecht University	Host genetics of BTB (WOTRO Integrated program proposal) (2007 - present). Two papers published 2013
Prof. Mary Carrington, Dr. Maureen Martin, Dr. Xiaojiang Gao	Frederick National Laboratory for Cancer Research, Maryland	Investigation of KIRs as TB candidate genes. Paper published 2014
Dr Chris Gignoux	Stanford University, USA	Population Ancestry genetic determinations. Paper published in 2014
Dr John Metcalfe	UCSF	Deep sequenceing to identify heteroresistance
Prof. Annelies van Rie,	UNC	Evaluation of the Xpert MTB/RIF test.
Prof Nalin Rastogi	Pasteur Institute	Spoligotyping TB in Africa
National (37)		
Dr. Musa Mhlanga	Council for Scientific and Industrial Research	Ongoing collaboration to develop methods for super-resolution microscopy in mycobacteria
Prof. Kelly Chibale and other members of H3D	H3D Drug Discovery & Development Centre, UCT	Ongoing collaboration on SATRII, HI-TB and H3-D TB drug discovery projects
Prof. Robert Wilkinson	CIDRI, IDM	Collaboration on sequence analysis of clinical strains of *M. tuberculosis*
Prof. Robin Wood	DTHC, IDM, UCT	Ongoing collaboration on TB transmission
Prof. Adrie Steyn	K-RITH	Ongoing collaboration on SATRII TB drug discovery project
Prof. Tom Scriba	SATVI, IDM, UCT	Ongoing collaboration on TB transmission
Dr. Jeremy Wodward & Prof. Trevor Sewell	UCT	Ongoing collaboration on structural biology and imaging of *M. tuberculosis*
Dr. Lubbe Wiesner	UCT	Ongoing collaboration on pre-clinical pharmacology
Dr. Helen Cox	UCT	Evolution of drug resistance in HIV positive and negative individuals
Prof. Keertan Dheda	UCT	Molecular epidemiology of XDR-TB Whole genome sequencing of XDR-TB
		Collaboration in diagnostic/biomarker project
Prof. Alan Christoffels	SANBI, UWC	Bioinformatic analysis of whole genome sequence data.Wet-lab testing of computationally identified inhibitors
Dr. Nazir Ismail	NHLS	Drug resistant TB in South Africa
Dr. Danie Theron	Eben donges hospital, Worcester	New project on DOTS program on farms.
Prof. Lesley Scott, Prof. Wendy Stevens	University of the Witwatersrand	Ongoing collaboration on the rollout of the GeneXpert diagnostic test and establishment of an external quality assurance system.
Prof. Jonathan Blackburn	IDM, UCT	Collaboration on lipidomic and proteomic analyses of *M. tuberculosis* strains
Prof. Nicola Mulder	CBIO, IDM, UCT	Collaboration on bioinformatic analysis of mycobacterial genomes and transcriptomes
Dr. Violet Chihota	Aurum Health	*M. tuberculosis* strain population structure in Africa.

Prof. Du Toit Loots	North West University, Potchefstroom	Mouse Macrophage metabolome.
Prof. Colleen Wright	NHLS Port Elizabeth	The diagnostic utility of FNAB
Drs. Peter Buss & Markus Hofmeyr	SA National Parks	Development of a gene transcription assay for lions; ongoing project
Dr. Anita Michel, Jacques Godfroid, Koos Coetzer, Nick Kriek	Onderstepoort Veterinary Institute	Non-tuberculous mycobacteria in wildlife (WOTRO Integrated program proposal) (2007 - present).
Dr Chris van der Westhuyzen	CSIR Biosciences,Pretoria	Screen antituberculosis lead compounds
Dr. Richard Haynes	North West University, Potchefstroom	Study novel artemisinins for antimycobacterial activity
Dr Gert Kruger	Chemistry, UKZN, Durban	Screen antituberculosis lead compounds
Mrs Tania Dolby	NHLS , Green point	Collaborator provides routine samples.
Dr. Anneke Hesseling	SU	New collaboration to investigate genotype-immunological phenotype correlations in children. Collaboration of developing a stool TB diagnostic
Prof. Muazzam Jacobs	UCT	New collaboration to assess the impact of steroid hormones on protective immunity to M. tuberculosis in a mouse animal model.
Dr. Elisabetta Walters	Department of Pediatrics and Child Health, Stellenbosch University	Improved detection of *M. Tb* by Xpert MTB/RIF in gastric aspirates and stool samples collected from children with suspected pulmonary TB.
Dr Monika Esser,	NHLS Immunology Unit, Tygerberg Hospital	Identification of gene mutations that cause Primary Immunodeficiency Disorders.
Prof Rafique Moosa	Dept. Medicine, SU	Investigating chromosome 22 genetic polymorphisms as risk factors for HIVAN in South African adults: a pilot case-control study
Prof Ronald van Toorn Dr Regan Solomons	Dept of Medicine, SU	Investigating susceptibility to tuberculous meningitis
Kogie Naido	CAPRISA	Systems immunology project
Gavin Churchyard	Aurum Institute	Systems immunology project
Prof Mark Hatherill Prof Tom Scriba	SA Tuberculosis Vaccine Initiative (SATVI), UCT	CORTIS: The Correlate of Risk Targeted Intervention Study
Prof Mark Cotton	FamCru	CORTIS

5. Service rendering

The following services were provided in 2015:

The provision of scientific/technical service, advice and assistance to local Government, regional services, institutions, research groups and individuals.

Thesis examination

- Prof. Kana served as an external examiner for a PhD dissertation submitted to the University of Kwazulu Natal.
- Dr. Gordhan served as an external examiner an MSc dissertation submitted to the University of Stellenbosch
- Prof. Warner served as external examiner of a PhD submitted to the University of KwaZulu-Natal.
- Numerous external examinations were done by members of the SU node. These include examining PhD or MSc theses for UKZN, SU, WITS, UP etc. Details are not recorded.

Journal editing and reviews

- Prof. Kana reviewed manuscripts for *PLoS One, FEMS Microbiology Letters, mBIO, The FEBS Journal, FEMS Pathogens and Disease, Antimicrobial Agents and Chemotherapy, Infection, Genetics and Evolution, BMC Genomics, BMC Public Health, Scientific Reports, Biochimica et Biophysica Acta: General Subjects and PLoS Pathogens,*
- Prof. Mizrahi served on the Editorial Advisory Boards of *Tuberculosis* and *Cellular Microbiology,* and on the Editorial Boards of *Current Opinion in Microbiology*; *Pathogens & Disease*, and *Emerging Microbes and Infection*. She was also appointed to the Editorial Board of *Cell Chemical Biology* (formerly *Chemistry & Biology*). Prof. Warner served on the Editorial Board of *PLoS One*.
- Members of the UCT node reviewed manuscripts submitted to the *New England Journal of Medicine; Nature Genetics*; *Chemistry & Biology*; *PLoS Pathogens*; *PNAS*; *Antimicrobial Agents and Chemotherapy*; *mBio*; *Lancet Infectious Diseases; Scientific Reports; Genome Biology; Journal of Bacteriology; Current Microbiology; PLoS One*; *Future Medicinal Chemistry; Tuberculosis*; *FEMS Microbiology Letters*; *Environmental Monitoring and Assessment*; and the *International Journal of Infectious Diseases.*
- Most if not all senior members of the SU node review numerous manuscripts for international journals. Records are not kept, but journals include *Nature Reviews, Lancet, Lancet Infectious Diseases, PLoS, J Antimicrobial Chemotherapy, J Mol Med, BMC, Tuberculosis, IJTLD, JID, J Biotech, IJMS, Indian Heart Journal, Cardiovasc. J SA, J Biotech, IJMS, Molecular Biology and Evolution, Journal of Infection in Developing Countries, Journal of Bacteriology, Journal of Medical Microbiology, American Journal of Respiratory Critical Care Medicine, Tuberculosis and Journal of Molecular Biology and Biotechnology.*

Expert Panel or Committee Membership

Expert Panel or Committee	Organisation	Term	Member/ Role
Expert Committee	MSF, GATB, WHO	2008-present	Prof. Walzl
Working Group on New Drugs	Stop TB Partnership	2008-present	Prof. Walzl
Internal Governance and an Institutional scientific advisory committee	SU	2014-present	Prof. Walzl
IMPAACT TB Scientific Committee	NIH IMPAACT	2012-present	Prof. Walzl
Research Committee of Faculty of Health Sciences	SU	2009-present	Profs. Walzl &. Warren
Biomarkers & Clinical Endpoints Workgroup of Critical Path to TB Drug Regimens	NIH	2011-present	Prof Walzl
Consortium for TB Biomarkers (CTB2)	DST	2015-present	Prof Walzl
Ethics Committee for Experimental Animal Research	SU	2008-present	Dr. Wiid
Committee for Postgraduate Education of Faculty of Health Sciences	SU	2008-present	Prof. Gey van Pittius
Centre for Infectious Diseases	SU	2008-present	Prof. Warren
Human Research Ethics Committee of the Faculty of Health Sciences	SU	2009-present	Prof. Gey van Pittius
J-Expert Job evaluation Panel	MRC	2010-present	Dr. Kinnear
Planning Committee of Annual Academic YearDay	Faculty of Medicine & Health Sciences, SU	2012-present	Dr. Kinnear (vice-chair)
Critical Path to Treatment Regimens	NIH/Gates Foundation	2013-present	Profs. van Helden & Warren
ReSeqTB Expert panel	FIND	2015-present	Prof. Warren
Human Research Ethics Committee of the Faculty of Health Sciences	SU	2015-present	Dr. Ronacher
NIH Grants Early Career Reviewer	Center for Scientific Review, NIH	2015-present	Dr. K Ronacher
United States Animal Health Association Scientific Advisory Subcommitte for TB	USA	2015-present	Prof. Miller

Chair of Wildlife TB Study Group of SA	SA	2015-present	Prof. Miller
North American Veterinary Advisor for Elephants, Rhinoceros, and Hippopotamus	Association of Zoos and Aquariums, USA	2015-present	Prof. Miller
Association of South African Women in Science and Engineering (SA WISE) Executive Commitee Member	SA WISE	2015-present	Tashnica Olivier
Invited consultant for Longleat Safari Park, Southampton, UK	UK	2015-present	Prof. Miller
Golden Key International Honour Society, Stellenbosch Chapter - Executive Committee Member	SU	2015-present	Ms. du Plessis
NRF review panel for Postdoctoral fellowships, Bioinformatics and environmental sciences	NRF	2015-present	Dr. Klopper
Biosafety and Environmental Ethics Committee, Stellenbosch University	SU	2015-present	Prof. Sampson
Human Research Ethics Committee Board (HREC1)	SU	2015-present	Dr. Werely.
Ambassador: South African National Tuberculosis Association (SANTA)	SANTA	2015-present	Ms. Pule
Vice-President: South African Association Women Graduates (SAAWG), WC Province Branch	SAAWG, WC Province Branch	2015-present	Ms. Pule
Association of South African Women in Science and Engineering (SA WISE) Executive Commitee Member	SA WISE	2015-present	Ms. Pule
Co-ordinator and Executive Committee Member of Science Stars Mentorship Programme (SSMP)	SA	2015-present	Ms. Pule
ReSeqTB Expert Panel	CPTR	2015-present	Prof. Warren
Diagnostics Panel	CPTR	2015-present	Prof. Warren
Stellenbosch University Sub-Committee C	SU	2015-present	Prof. Warren
Stellenbosch University Clinical Infectious Diseases Managment Committee	SU	2015-present	Prof. Warren
Stellenbosch University Animal Ethics Committee	SU	2015-present	Dr. Parsons
Discovery Expert Group	Gates Foundation	2014-Present	Prof. Mizrahi
Scientific Advisory Board	K-RITH	2014-present	Prof. Mizrahi
Scientific Advisory Committee of SDDC, a structure-guided drug discovery consortium	Structural Genomics Consortium, University of Toronto	2014-present	Prof. Mizrahi
Keystone Symposia Study Group	Keystone Symposia	2014-Present	Prof. Mizrahi
Visiting Scholars and Lecturers Fund Committee	UCT	2014-present	Prof. Mizrahi
Health & Safety Committee of the IDM	UCT	2014-present	Prof. Warner (Chair)
Hazardous Chemical Coordinator of MMRU	UCT	2014-present	Prof. Warner
Lead Academic in charge of the WBS Level 2 BSL III Lab of IDM	UCT	2014-present	Prof. Warner
Education and Equipment Task Teams	UCT	2014-present	Prof. Warner
Board	Sydney Brenner Institute for Molecular Biosciences	2014-present	Prof. Kana
Microscopy and Microanalysis Unit Board	WITS	2014-present	Prof. Kana
Working Group	Global Alliance for TB Drug Development	2014-present	Prof. Kana

University Research Council (URC)	WITS	2014-present	Prof. Kana
FRC Budget task group,	Faculty of Health Sciences, WITS	2014-present	Prof. Kana
Research Entity Forum	Faculty of Health Sciences, WITS	2014-present	Prof. Kana
Research Equipment Review Committee	Faculty of Health Sciences, WITS	2014-present	Prof. Kana
Advisory Board	Faculty of Health Sciences, WITS	2014-present	Prof. Kana
Imaging Committee, Wits University	Faculty of Health Sciences, WITS	2014-present	Prof. Kana
Faculty Research Council (FRC)	Faculty of Health Sciences, WITS	2014-present	Prof. Kana & Dr. Gordhan
Postdoctoral Review Committee	NRF	2014-present	Dr. Gordhan
FISS & TWAS Postdoctoral Fellowships Advisory Panel Meeting.	NRF	2015-present	Dr. Klopper
South African Society of Human Genetics	SA Society of Human Genetics	2015-present	Prof. Hoal
SA Society of Human Genetics	SA	2015-present	Prof. Hoal
National TB think Tank	UCT	2015-present	Prof. Mizrahi
Chaired the Executive Committee of IDM	IDM, UCT	2015-present	Prof. Mizrahi
Chaired the Membership Committee of IDM	IDM,UCT	2015-present	Prof. Mizrahi
Chaired the Faculty of Health Sciences Biosafety Committee.	UCT	2015-present	Prof. Warner
International Union of Tuberculosis and Lung Disease Conference.	UCT	2015-present	Profs. Mizrahi & Warner
Health & Safety Committee of the IDM	UCT	2015-present	Dr. Evans
Operations and Laboratory Management Committee of the IDM	UCT	2015-present	Dr. Mukherjee
Health Sciences Faculty Postgraduate Students Council (HSPSC).	UCT	2015-present	Ms. Koch & Ms. Ditse
SA-Swiss Joint Bilateral Grant Program	Wits	2015-present	Prof Kana
Scientific Advisory Committee	Cape Town HVTN Immunology lab	2015-present	Prof. Kana
Research Entity Review Task Task group	Faculty of Health Sciences, Wits	2015-present	Prof. Kana
URC major and minor Equipment Review Committees	Wits	2015-present	Prof. Kana

Examples of Research Funding Reviews

- Prof. Mizrahi served as a reviewer of research and fellowship applications for the HHMI; the DBT-India/Wellcome Trust Alliance; and the Bill & Melinda Gates Foundation, and as reviewer for promotions at Johns Hopkins University, the Centre for Infectious Disease Research (Seattle); Harvard School of Public Health and the University of Zimbabwe. Prof. Warner served as reviewer for international funding organizations including the Wellcome Trust (UK), the MRC (UK), and DFF-Mobilex (Denmark). He was also a reviewer for major South African funding organizations (NRF, MRC) and the various programmes they administer, including competitive funding for un/rated researchers, and MRC self-initiated research grants, and NRF student funding applications. In addition, he served as an internal reviewer for numerous research proposals considered by the IDM Research Committee, the Human Research Ethics Committee, and the Faculty Biosafety Committee.
- Members of the CBTBR Wits node reviewed for the NHLS Research Trust, Biotechnology and Biological Sciences Research Council (BBSRC, UK), South African Medical Research Council (Newton Fund, SIR and various other programs), National Research Foundation (Rating and Evaluation Program and Competitive Grants).
- Many of the SU node members are either on editorial boards or act as regular reviewers for many journals. A list is not provided, since we have so many of these we do not keep record.

Beneficiation of other researchers by CBTBR

- The SU node also provides infrastructure and intellectual support to groups, even some who are not TB researchers and are therefore defined to be completely outside the CBTBR. For example, the lab housing our CBTBR genetics group also hosts a small group (n=7) of lab researchers, working on the Genetics of Psychiatric Disorders, part of the NRF SARChI research of Prof Soraya Seedat. It also houses a small SU group (Prof Soraya Bardien, n=9) working on the genetics of Parkinsons disease in South Africans. Reserachers from other institutions (Prof eg. K Dheda and his team) also utilise our facilities. Other researchers within SU, such as numerous persons from Paediatrics, Medical Microbiology and Immunology also use our facilities and know how. Our BL3 lab has approximately 70 registered users, of whom about 50 are part of our CBTBR node.
- The UCT node is an integral component of the Institute of Infectious Disease and Molecular Medicine) and a major contributor to the institute's shared research capacity and infrastructure, which is of direct benefit to all member groups involved in TB research. This includes a shared BSL3 laboratory, in which the UCT node has invested considerable resource. This laboratory serves the needs of 45 registered users from across the IDM, 10 of whom belong to the UCT node. The UCT node also provides extensive technical support and assistance in all aspects of mycobacteriology to staff, students and postdocs from the groups of three SARChI chairs, the Clinical Infectious Disease Research Initiative (CIDRI), the SA TB Vaccine Initiative (SATVI), the Desmond Tutu HIV Centre and the Division of Medical Microbiology. The UCT node also provided all of the TB biology expertise and support for the TB drug discovery projects conducted by the H3D Drug Discovery and Development Centre. However, the only outputs reported herein from the UCT node are those funded directly by the NRF grant to the CoE and resulting from the research and training programmes led by the two Team Members in this node, Prof. Valerie Mizrahi and Prof. Digby Warner, and Scientific Staff member, Dr. Joanna Evans.

Other services rendered

- Speciation of Non Tuberculous Mycobacteria (NTM) for Kruger National Park
- Genotyping of clinical isolates (RFLP/mutation detection) for the NHLS, MSF and City Health.
- Prof V Corfield was NRF rating panel moderator in 2015
- Specialist diagnostic service for MDR or XDR TB cases for NHLS, Port Elizabeth.
- Genetic and phenotypic analysis of discordant INH resistant/susceptible isolates from NHLS Port Elizabeth.
- Specialist diagnostic service MDR or XDR TB cases, Brooklyn Chest Hospital, Cape Town.
- Prof. Miller continues to receive and respond to requests for information from South African wildlife veterinarians in private industry, SANParks, EKZN Wildlife, DAFF, National Zoological Gardens, and wildlife researchers. This extends to Namibia, Zimbabwe, and Malawi.
- Hospital medical specialist clinical services, e.g. pulmonology and genetics
- Vakzine Project Management (VPM): phase IIa vaccine trial on tuberculosis
- IDRI- ID93 phase I vaccine trial
- Aeras: C041 biobanking vaccine trial

6. Gender impact of research

Four out of the 13 Core Team Members of the CBTBR are women. In 2015, the CBTBR has also maintained a high percentage of female students (59% of all students and 48% of postdoctoral fellows), which is in line with demographic norms for the Life and Health Sciences at a national level. All three nodes have demonstrated that they are able to provide an environment which is attractive to, and supportive of women researchers at all levels, from Honours students to senior postdoctoral fellows and Team Members, as evidenced by the career progression of Drs. Mohube Maepa (nee Mowa), Katharina Ronacher (promoted to Associate Professor on 6 April 2016) , Monique Williams, Marlo Moller and Lizma Streicher, who have developed into independent investigators and are raising their own grants. Drs Nelita du Plessis, Leanie Kleynhans, Joanna Evans, and others including Dr. Zanele Ditse, Zela Martin and Dr. Anastasia Koch are up-and-coming potential star researchers. At the Wits node, Drs Julian Peters and Melissa Chengalroyen are on a steep upward trajectory in their research careers. In addition, two students from the Wits node Ms. Nicole Narrandes and Ms. Zaahida Sheik Ismail have earned notable recoginition and awards for their research. These developments confirm that the CBTBR serves as a centre in which women researchers are nurtured and developed. Furthermore, as mentioned before, 2/3 SARCHis involved with the Centre are female professors. The SUN node has also recently appointed a new BL3 manager, also a female staff member (Dr N Allie).

HUMAN RESOURCES

1. Core Team Members

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Prof.	Mizrahi	Italy	UCT/NHLS	F	W	50[a]
Dr.	Gordhan	SA	Wits	F	B	100
Prof.	Kana	SA	Wits	M	B	100
A/Prof.	Warner	SA	UCT	M	W	100
Prof.	Hoal van Helden	SA	SU	F	W	100
Dr.	Martinson	SA	Wits	M	W	25[b]
Dr.	Sampson	SA	SU/NRF	F	W	100
Prof.	Van Helden	SA	MRC	M	W	100
Prof.	Walzl	SA	SU	M	W	100
Prof.	Warren	SA	MRC	M	W	100
A/Prof.	Wiid	SA	PAWC	M	W	100
A/Prof.	Theron	SA	SU	M	W	25[c]

a. Director of the IDM
b. Dr. Martinson is also directorof the Perinatal HIV Research Unit (PHRU)
c. Dr. Theron joined the CBTBR in October 2015

2. Scientific Staff

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
A/Prof	Ronacher	Austrian	SU	F	W	100
Dr.	Streicher	SA	SU	F	W	100
Dr	Williams	SA	SU	F	B	100
Dr	Chegou	Cameroonian	SU	M	B	100
Dr.	Loxton	SA	SU	M	B	100
Dr	Kinnear	SA	SU	M	B	100
Dr	Jackson	SA	SU	F	W	100
Dr	Evans	SA	UCT	F	W	100
Prof	Diacon	Swiss	SU	M	W	10[a]
Dr	Sirgel	SA	SU	M	W	100
Dr	Möller	SA	SU	F	W	100
Prof	Tromp	USA	SU	M	W	65[b]
Dr	Du Plessis	SA	SU	F	W	100

a. Director of TASK
b. Appointed as Bioinformatician at SU in May 2015

3. Postdoctoral Fellows

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Dr	Banda	Zimbabwean	SU	Male	Black	100
Dr	Beltran	South African	SU	Female	White	100
Dr	Chengalroyen	South African	Wits	Female	Black	100
Dr	Dippenaar	South African	SU	Female	White	100
Dr	Ealand	South African	WITS	Male	White	100
Dr	Fortuin	South African	SU	Female	Black	15[a]
Dr	Heunis	South African	SU	Male	White	100
Dr	Kleynhans	South African	SU	Female	White	100
Dr	Klopper	South African	SU	Female	White	75[b]
Dr	Leisching	South African	SU	Female	White	100
Dr	Le Roex	South African	SU	Female	White	100
Dr	Majumdar	Indian	UCT	Male	Black	100[c]
Dr	Makoah	South African	UCT	Male	Black	100[d]
Dr	Mashabela	South African	UCT	Male	Black	100[e]

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Dr	Moosa	South African	UCT	Female	Black	100
Dr	Mouton	South African	SU	Female	White	100
Dr	Mukherjee	Indian	UCT	Female	Black	100
Dr	Ngwane	South African	SU	Male	Black	100
Dr	Parsons	South African	SU	Male	White	100
Dr	Peters	South African	WITS	Male	Black	100[f]
Dr	Salie	South African	SU	Male	Black	100
Dr	Singh	Indian	UCT	Male	Black	100
Dr	Styger	South African	SU	Male	White	30[g]
Dr	van der Merwe	South African	SU	Male	White	100

a. Completed in Febuary 2015
b. Commenced in April 2015
c. Commenced in January 2015
d. Completed in December 2015
e. Commenced in January 2015
f. Commenced in January 2015
g. Completed in April 2015

4. Students

Title	First name	Surname	Degree	Institution	Race	Gender	Nationality	Status
Ms	Victoria	Cole	BSc (Hons)	SU	W	F	South Africa	Completed
Ms	Lorinda	du Toit	BSc (Hons)	SU	W	F	South Africa	Completed
Ms	Roxanne L	Higgitt	BSc (Hons)	SU	W	F	South Africa	Completed
Mr	Ziyaadh	Julius	BSc (Hons)	SU	B	M	South Africa	Completed
Ms	Carissa	Kell-Blair	BSc (Hons)	SU	W	F	South Africa	Completed
Mr	Vinzeigh	Leukes	BSc (Hons)	SU	B	M	South Africa	Completed
Mr	Cebisa	Mdladla	BSc (Hons)	SU	B	M	South Africa	Incomplete
Ms	Nandi	Niemand	BSc (Hons)	SU	W	F	South Africa	Completed
Ms	Nombeko	Sikosana	BSc (Hons)	WITS	B	F	South Africa	Completed
Ms	Anel	Sparks	BSc (Hons)	SU	W	F	South Africa	Incomplete
Ms	Talani	van Schalkwyk	BSc (Hons)	SU	W	F	South Africa	Completed
Ms	Jesmine	Arries	MSc	SU	B	F	South Africa	Incomplete
Ms	Rukaya	Asmal	MSc	Wits	B	F	South Africa	Completed
Ms	Nadia	Baartes	MSc	UCT	B	F	South Africa	Incomplete
Ms	Louise	Botha	MSc	SU	W	F	South Africa	Completed
Mr	Nicholas	Bowker	MSc	SU	W	M	South Africa	Incomplete
Ms	Charlene	Clarke	MSc	SU	W	F	South Africa	Incomplete
Ms	Antoinette	Colic	MSc	SU	W	F	South Africa	Incomplete
Ms	Ncite	Da Camara	MSc	SU	W	F	South Africa	Incomplete
Mr	Willem J	du Plessis	MSc	SU	W	M	South Africa	Incomplete
Mr	James L	Gallant	MSc	SU	W	M	South Africa	Completed
Ms	Sidhika	Harisparsad	MSc	UP	B	F	South Africa	Completed
Ms	Ruschca	Jacobs	MSc	SU	B	F	South Africa	Incomplete
Ms	Jessica	Klazen	MSc	SU	B	F	Namibia	Incomplete
Ms	Leigh	Kotzé	MSc	SU	W	F	South Africa	Incomplete
Mr	Bayanika	Manunu	MSc	SU	B	M	DRC	Completed
Ms	Masethabela	Maphatsoe	MSc	WITS	B	F	South Africa	Incomplete
Mr	Rendani	Mbau	MSc	UCT	B	M	South Africa	Incomplete
Mr	Ross	McFadyen	MSc	SU	W	M	South Africa	Incomplete
Mr	Tube	Moagi	MSc	WITS	B	M	South Africa	Incomplete
Mr	Moeketsi R	Moseki	MSc	WITS	B	M	South Africa	Incomplete

Mr	Steven G	Nthambeleni	MSc	WITS	B	M	South Africa	Incomplete
Ms	Trisha	Parbhoo	MSc	SU	B	F	South Africa	Incomplete
Mr	Ditshego	Ralefeta	MSc	WITS	B	M	South Africa	Incomplete
Ms	Tebogo C	Rantsi	MSc	WITS	B	F	South Africa	Incomplete
Mr	Micheal	Reiche	MSc	UCT	W	M	South Africa	Incomplete
Mr	Eduard	Roos	MSc	SU	W	M	South Africa	Incomplete
Ms	Nikola	Schlechter	MSc	SU	W	F	South Africa	Incomplete
Mr	Haiko	Schurz	MSc	SU	W	M	South Africa	Incomplete
Ms	Bevika	Sewgoolam	MSc	UCT	B	F	South Africa	Incomplete
Ms	Zaahida	Sheik Ismail	MSc	WITS	B	F	South Africa	Incomplete
Mr	Kabengele	Siame	MSc	SU	B	M	Zambia	Incomplete
Ms	Bronwyn	Smith	MSc	SU	W	F	South Africa	Completed
Mr	Marvin	Theys	MSc	SU	B	M	South Africa	Incomplete
Ms	Phophi	Tshavhungwe	MSc	SU	B	F	South Africa	Incomplete
Ms	Siyanda	Tshoko	MSc	SU	B	F	South Africa	Incomplete
Ms	Caitlin	Uren	MSc	SU	W	F	South Africa	Incomplete
Ms	Ilana	van Rensburg	MSc	SU	B	F	South Africa	Incomplete
Mr	Kennedy	Zvinairo	MSc	SU	B	M	Zimbabwe	Completed
Ms	Alma	Polson	MSc	SU	W	F	South Africa	Incomplete
Mr	Dolapo	Awoniyi	PhD	SU	B	M	Nigeria	Incomplete
Mr	Germar	Beukes	PhD	WITS	W	M	South Africa	Incomplete
Ms	Phillipa	Black	PhD	SU	W	F	South Africa	Completed
Mr	Simon	Broadley	PhD	UCT	W	M	South Africa	Incomplete
Ms	Nicole	Cardoso	PhD	WITS	B	F	South Africa	Incomplete
Ms	Michelle	Daya	PhD	SU	W	F	South Africa	Completed
Ms	Anzaan	Dippenaar	PhD	SU	W	F	South Africa	Incomplete
Ms	Zanele	Ditse	PhD	UCT	B	F	South Africa	Completed
Ms	Juanelle	du Plessis	PhD	SU	W	F	South Africa	Incomplete
Ms	Melanie	Grobbelaar	PhD	SU	W	F	South Africa	Incomplete
Mr	Kenneth	Hammond-Aryee	PhD	SU	B	M	Ghana	Incomplete
Ms	Elizabeth	Kigondu	PhD	UCT	B	F	Kenya	Completed
Mr	Terry	Kipkorir	PhD	UCT	B	M	Kenya	Incomplete
Ms	Marisa	Klopper	PhD	SU	W	F	South Africa	Completed
Ms	Anastasia	Koch	PhD	UCT	W	F	South Africa	Completed
Mr	Lance	Lucas	PhD	SU	W	M	South Africa	Incomplete
Ms	Adelina	Machado	PhD	SU	B	F	Mozambique	Completed
Ms	Zela	Martin	PhD	UCT	W	F	South Africa	Incomplete
Ms	Marieta	McGrath	PhD	SU	W	F	South Africa	Incomplete
Ms	Amanda	McIvor	PhD	WITS	W	F	South Africa	Incomplete
Ms	Matsie	Mphahlele	PhD	SU	B	F	South Africa	Incomplete
Ms	Krupa	Naran	PhD	UCT	B	F	South Africa	Completed
Ms	Nicole	Narrandes	PhD	Wits	B	F	South Africa	Incomplete
Ms	Tashnica	Olivier	PhD	SU	B	F	South Africa	Incomplete
Mr	Charles	Omollo	PhD	UCT	B	M	Kenya	Incomplete
Ms	Andrea	Papadopoulos	PhD	Wits	W	F	South Africa	Incomplete
Mr	Ray-Dean	Pietersen	PhD	SU	B	M	South Africa	Incomplete
Ms	Caroline	Pule	PhD	SU	B	F	South Africa	Incomplete
Ms	Carine	Sao Emani	PhD	SU	B	F	Cameroon	Completed
Mr	Sibusiso	Senzani	PhD	WITS	B	M	South Africa	Incomplete

Ms	Nastassja	Steyn	PhD	SU	W	F	South Africa	Incomplete
Ms	Anjo	Theron	PhD	SU	W	F	South Africa	Completed
Ms	Phia	Van Coller	PhD	UCT	W	F	South Africa	Incomplete
Mr	Ignatius	Viljoen	PhD	SU	W	M	South Africa	Incomplete
Ms	Hanri	Visser	PhD	SU	W	F	South Africa	Completed
Ms	Antonina	Wasuna	PhD	UCT	B	F	Kenya	Incomplete
Ms	Danicke	Willemse	PhD	SU	W	F	South Africa	Incomplete
Mr	Wynand	Goosen	PhD	SU	W	M	South Africa	Incomplete
Mr	Michael G	Whitfield	PhD	SU	W	M	South Africa	Incomplete

5. Administrative and Other Staff

Title	Surname	Position	Based at	Gender	Race
Dr	Baker	Project Manager	SU	M	B
Ms	Baatjies	MRC Technical officer	SU	F	B
Mrs	Hull-Conrad	Part-time admin clerk	UCT	F	B
Ms	Mohammed	Bookkeeper/ Admin. assistant	Wits	F	B
Ms	Masangana	Laboratory Tech. Assistant	Wits	F	B
Ms	Ralefeta	Research Assistant	Wits	F	B

OUTPUTS

* The Names in bold are CBTBR staff and students

Books / Chapters in Books (Total: 1)

Walzl G, Haks MC, Joosten SA, **Kleynhans L, Ronacher K**, Ottenhoff THM. Clinical immunology and multiplex biomarkers of human tuberculosis. In: Tuberculosis. Editors Kaufmann SHE, Rubin EJ, Zumla A. Cold Spring Harbour Laboratory Press, New York, 2015. P 197-209.

Articles in Peer-Reviewed Journals (Total: 84)

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Plenary/Keynote Lectures (11)
Walzl G. Challenges facing preclinical TB vaccine development. Aeras TB vaccine symposium, 46th Union World Conference on Lung Health, Cape Town, South Africa, 2-6 December 2015.
Walzl G, Ronacher K, Malherbe S, Chegou NN, Stanley K, van der Spuy GD, Kriel M, Kidd M, Warwick J, Barry CE 3rd, Chen R, Dodd L, Johnson JL, Boom WH, Peppard T, Cliff J, Dockrell H, Schoolnik G, Dolganov G, Alland D, Zak D, Winter J. Potential and limitations of current candidate host biomarkers for treatment response. Symposium: Spelunking for Treasure: Searching for Candidate Biomarkers as Prognostic Indicators for Treatment Outcome. 46th Union World Conference on Lung Health, Cape Town, South Africa, 2-6 December 2015.
Mizrahi V. Targeting core metabolic pathways in M. tuberculosis. Plenary lecture, HHMI Science Meeting, Janelia Farm Research Campus, Ashburn, MD, 9-11 June 2015.
Mizrahi V. Targeting core metabolic pathways in M. tuberculosis. Invited lecture, K-RITH, Durban, 26 June 2015.
Mizrahi V. MM4TB Project Update from Cape Town. MM4TB Consortium Meeting #10, Institut Pasteur, Paris, 29 June – 1 July 2015.
Mizrahi V. Targeting core metabolic pathways in M. tuberculosis. Plenary lecture, Gordon Research Conference on Tuberculosis Drug Discovery & Development, Girona, Spain, 12-17 July 2015.
Evans J, Trujillo C, Ehrt S, Boshoff HIM, Schnappinger D, **Mizrahi V**. A pathway approach to identifying vulnerable and bactericidal targets in Coenzyme A biosynthesis in M. tuberculosis. Plenary lecture, Gordon Research Seminar on Tuberculosis Drug Discovery & Development, Girona, Spain, July 11-12 2015.
Mizrahi V. Identifying vulnerable steps in the CoA pathway of M. tuberculosis. Plenary Lecture, Biophysical Society Thematic meeting: Biophysics in the Understanding, Diagnosis and Treatment of Infectious Diseases, Spier Estate, Stellenbosch, South Africa, 16-20 November 2015.
Mizrahi V. Undertaking the full spectrum of research in a TB-endemic country: the example from South Africa. Plenary lecture, 46th Union World Conference on Lung Health, Cape Town, 5 December 2015.
Van Helden PD. Drug resistance and the contribution of zoonotic TB Plenary lecture, 46th Union World Conference on Lung Health, Cape Town, 2-6 December 2015.
Van Helden PD. Bovine TB in wildlife. Plenary Lecture, Workshop on Accelerating bTB Control in Developing Countries, Rabat, Morocco, 2-6 December 2015.

Invited Talks (81)
Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease. 9-11 June 2015. Annual meeting of the Howard Hughes Medical Institute. Janelia Farm Research Campus, Ashburn, Virginia, USA
Kana BD. Detection, quantification and characterization of differentially culturable tubercle bacteria in human TB disease. TB Biomarkers Annual Meeting. 3 – 5 June 2015, the Bill and Melinda Gates Foundation, Seattle, USA.
Kana BD. Differential bacterial growth states in active TB disease. "The New Post-2015 Global TB Strategy? The End Game". 24 March 2015, The National Institute for Communicable Diseases, Sandringham, Johannesburg.
Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease. 26 November 2015, The Institute for Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa.
Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease. 1 October 2015, The Perinatal HIV Research Unit, Soweto, Johannesburg, South Africa
Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease: Separation anxiety and schizophrenia in mycobacterial cells. 16 January 2015, The Kwazulu-Natal Institute for TB and HIV, Durban, South Africa.
Chegou N. Accuracy of a Seven-marker Host Serum Protein Biosignature in the Diagnosis of TB Disease in African Primary Health Care Clinic Attendees Presumed to have TB. 46th Union World Conference on Lung Health, Cape Town, 2 - 6 December 2015.
Chengalroyen M, Beukes G, Gordhan B, Neil Martinson, Otwombe K, Kana B. The detection and quantification of differentially culturable bacilli in patients with active tuberculosis, Oral presentation, 15 – 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa
Chengalroyen M, Beukes B, Gordhan B, Martinson N, Otwombe K, Kana B. The detection and quantification of differentially culturable bacilli in patients with active tuberculosis, Oral Presentation, 24 July 2015, SoMCHAT Young Researchers conference, Chris Hani Baragwanath Hospital, Soweto, South Africa.
Chengalroyen M, Beukes G, Gordhan B, Martinson N, Otwombe K, Kana B. The detection and quantification of differentially culturable bacilli in patients with active tuberculosis, Oral Presentation, October 2015, Postdoctoral Symposium, Wits University, Johannesburg, South Africa.
Gordhan B. The contribution of Nth and Nei DNA glycosylases to mutagenesis in *Mycobacterium smegmatis*. Oral Presentation, 15 – 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa.
McIvor A, Gordhan B, Martinson N, Waja Z, Kana B. Detection of culturable and non-culturable bacteria in patients receiving first-line TB treatment, Oral presentation, 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Peters J, McIvor A, Papadopoulous A, Gordhan B, Kana B. Assessing the utility of Fatty acids in resuscitating DCTB from the sputum of TB infected patients. Oral and Poster. 15 - 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa.
Peters J, McIvor A, Papadopoulous A, Gordhan B, Kana B. Establishing patterns in drug treatment response rates of tuberculosis disease based on non-culturable *Mycobacterium tuberculosis* in sputum. Oral presentation. 24 July 2015, SoMCHAT Young Researchers conference, Chris Hani Baragwanath Hospital, Soweto, South Africa.
McIvor A, Gordhan B, Martinson N, Waja Z, Kana B. Detection of culturable versus non-culturable bacteria in patients receiving first-line TB treatment: An endpoint analysis, Oral presentation, 24 July 2015, SoMCHAT Young Researchers conference, Chris Hani Baragwanath Hospital, Soweto, South Africa.
Ealand C, Kana B. DacB: An essential enzyme for mycobacterial growth, Poster with short talk, 15 - 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa
Ealand C, Kana B. An essential DD-carboxypeptidase determines localisation of peptidoglycan synthesis in mycobacteria, Oral, Health Sciences – Symposium for Postdoctoral and Carnegie Fellows, Johannesburg, South Africa.
Mizrahi V. Global health networks and networking. Invited lecture, Imperial-UCT Graduate Summer School, Global Health Fellows Programme, University of Cape Town, 26 January 2015.
Mizrahi V. The state of TB drug development and the role civil society can play. Treatment Action Campaign & Section 27 Symposium on Tuberculosis, Cape Town, 23 June 2015
Hammond-Aryee K. Genotypic characterization and strain diversity of Toxoplasma gondii from infected human and animal tissues from the Western Cape of South Africa. Talk presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Hammond-Aryee K. Genotypic characterization and strain diversity of Toxoplasma gondii from infected human and animal tissues from the Western Cape of South Africa. Talk presented at the Pathology

research day. FMHS, Stellenbosch University, Cape Town, South Africa, 04 June 2015.
Hoal EG. Genomic Disease Associations in TB in non-Euro-American Populations: The impact of ancestry. Talk presented at the NIAID Workshop on Host Response to TB-HIV Infection: A Genomic Perspective. NIAID, Rockville, USA, 14 January 2015.
Walzl G. Host biomarkers for active TB and for treatment response. South African Thoracic Society Conference, Cape Town, South Africa, 7-10 August 2015.
Walzl G. Deconfounding latent tuberculosis. South African Thoracic Society Conference, Cape Town, South Africa, 7-10 August 2015.
Walzl G. Host biomarkers for active TB and for treatment response. ACTG Annual Meeting, Washington DC, USA, June 2015
Walzl G. Immunodiagnostics of active TB disease. 4th Global Forum on TB Vaccines, Stop TB Partnership Working Group on New Vaccines. Shanghai, China, 21-24 April 2015.
Walzl G, Malherbe S, Ronacher K, Thiart L, Stanley K, van der Spuy GD, Kriel M, Warwick J, Barry CE 3rd, Peppard T, Alland D, Gregory Dolganov, Gary Schoolnik, Winter J. Human TB Treatment Response Studies Using PET/CT Imaging: Inconvenient Observations. Host Response in Tuberculosis- Keystone Symposia. Santa Fe, New Mexico, USA. January 22-27, 2015.
Warren RM. Genesis of drug resistance in Tuberculosis in South Africa. Plenary Talk presented at the PASER, HIVDR in the upcoming fight against antimicrobial resistance. Rainbow Towers Hotel, Harare, Zimbabwe, 08 May 2015.
Warren RM. The eveolving global TB epidemic- Focus on South Africa. Talk presented at the 5th Tuberculosis Control symposium. Education centre, The Woolcock, Glebe, Australia, 03-04 September 2015.
Klopper M. 1.Drug-resistance beyond XDR-TB: a health situation beyond repair? Talk presented at the Ukwanda Sustainable Rural Health Research Days. Worcester Campus, Stellenbosch University, Worcester, South Africa, 18-19 March 2015
Warren RM. Transmission of drug resistant TB- lessons from South Africa. Talk presented at the 5th Conference of the Union Asia Pacific Region. The Hilton Hotel, Sydney, Australia, 31 August - 02 September 2015.
Smith B. Application of Becton Dickinson FACSTM Combinatorial Antibody Profile (FACSTM CAP) technology to the identification of efficiency of tuberculosis therapy. Talk presented at the Stellenbosch University Annual Academic Year day. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Moller M. Population admixture: friend or foe in TB susceptibility. Talk presented at the 6th Biennial Congress of the Southern African Society of Human Genetics. KleinKaap Boutique Hotel, Pretoria, South Africa, 16 August - 19 September 2015.
le Roex N. Disease Control in Wildlife: BTB Test & Cull in African Buffalo. Talk presented at the International Congress of Conservation Biology (ICCB) 2015. Le Corum, Montpellier, France, 02-06 August 2015.
Moller M. Genome-wide association study of ancestry-specific TB risk in the South African Coloured population. Talk presented at the African Symposium on Genome Wide Association Studies for complex disease. African Institute for Mathematical Sciences of SA, Cape Town, South Africa, 23-24 April 2015.
Daya M. Using multi-way admixture mapping to elucidate TB susceptibility in the South African Coloured population. Talk presented at the African Symposium on Genome Wide Association Studies for complex disease. African Institute for Mathematical Sciences of SA, Cape Town, South Africa, 23-24 April 2015.
Klopper M. Next generation sequencing reveals hidden ethionamide resistance as a likely driver towards resistance beyond XDR-TB in a high burden population. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Schlechter N. Identification of novel candidate genes for susceptibility to tuberculosis by identifying disease-causing mutations in individuals with Primary Immunodeficiency Disorders. Talk presented at the 1st Biomedical Sciences Annual Research Day. FMHS, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Tabb DL. Lipid Identification with Greazy and LipidLama. Talk presented at the Special Seminar for Department of Microbiology, Immunology, and Pathology. Colorado State University, Ft. Collins, CO, United States, 10 November 2015.
Whitfield M. Association between Genotypic and Phenotypic Pyrazinamide Resistance in Rifampicin Resistant Mycobacterium tuberculosis Isolates. Talk presented at the 1st Biomedical Sciences Annual Research Day. FMHS, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Whitfield M. Association between Genotypic and Phenotypic Pyrazinamide Resistance in Rifampicin Resistant Mycobacterium tuberculosis Isolates. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 04-06 December 2015.
Kreiswirth B. Virtual sequencing of the entire *pncA* gene target in a single tube using LATE-PCR and Lights-On/Lights-Off probes to predict PZA susceptibility. Talk presented at the 46th Union World

Conference on Lung Health. CTICC, Cape Town, South Africa, 04-06 December 2015.
Kinnear C. Mutation Screening for Primary immunodeficiency disorders in a tuberculosis endemic region: a South African perspective. Talk presented at the 16th Biennial Congress of the South African Society for Human Genetics. KleinKaap Boutique Hotel, Pretoria, South Africa, 16-19 August 2015.
Kinnear C. Primary Immunodeficiency Disease management in tuberculosis endemic regions - are we aware -and how does a registry assist? Talk presented at the 4th African Society for Immunodeficiencies Congress. Hotel el Aurassi, Algiers, Algeria, 29-31 May 2015.
Sampson SL. Devastating Diseases and a Sustainable Society: Learning from the Tubercle Bacillus. Talk presented at the Lustrum conference, Science for Sustainability. Vrije University, Amsterdam, The Netherlands, 26 December 2015.
Sampson SL. Royal Society/Newton Fund International Exchanges Scheme. Talk presented at the Lustrum conference, Science for Sustainability. Vrije University, Amsterdam, The Netherlands, 26 November 2015.
Sampson SL. Single cell elucidation of mycobacterial replication dynamics. Talk presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Sampson SL. Single cell elucidation of mycobacterial replication dynamics. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Chegou NN. Host Serum Biosignatures for the diagnosis of TB disease. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 2-6 December 2015.
Willemse D. Rv1460 is required for growth of Mycobacterium tuberculosis in vitro. Talk presented at the 1st Biomedical Sciences Annual Research Day. FMHS, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Roos EO. Detecting Mycobacterial Infections in African Warthogs (Phacochoerus africanus) Using Serological Methods. Talk presented at the 6th Annual Wildlife Research Symposium. Onderstepoort, Pretoria, South Africa, 19-20 November 2015.
Theron G. Meet the Expert: Opportunities and challenges in TB diagnostic research: Overview and lessons learnt from two large diagnostic RCTs (Xpert and LAM). Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 06 December 2015.
Theron G. Point of care diagnostics for tuberculosis: where are we, and what is next?. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 04 December 2015.
Theron G. Impact of Xpert MTB/RIF on TB case detection and treatment: experience in high-HIV settings. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Peter J, Theron G. Rapid point-of-care urine-based testing for tuberculosis and its impact on mortality: a multi-centre randomised controlled trial. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Lange B, Theron G. Diagnostic accuracy of the Xpert® MTB/RIF cycle threshold level to predict smear positivity in respiratory samples: a systematic review and meta-analysis. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Khaki A, Theron G. The effect of automated nucleic acid amplification assays on mortality in routine care settings: meta-analysis of individual participant data. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Loxton AG. TB immunology Research at Stellenbosch University Immunology Research Group. Annual ACTG Network Meeting, Washington, DC, 22 – 26 June 2015.
Pule C. Deciphering the physiology of drug tolerant and resistant Mycobacterium tuberculosis. Talk presented at the The 9th Annual Medical Research Council Early Career Scientist Conference. SAMRC conference centre, Cape Town, South Africa, 18-20 October 2015.
De Vos M. Rapid Single tube diagnosis of M(X)DR-TB. Talk presented at the Hain LifeSciences TB symposium. Holiday Inn, Harare, Zimbabwe, 25-26 March 2015.
De Vos M. The cutting edge of drug resistance diagnostics. Talk presented at the 6th FIDSSA congress. Champagne Sports Resort, Winterton, South Africa, 05-08 November 2015
De Vos M. Heterogeneity as revealed by whole genome sequencing in Mycobacterium tuberculosis. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
De Vos M. Construction and validation of a three colour single-tube assay for the detection of resistance to first- and second-line anti-TB antibiotics. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Ngwane A. Translational research in tuberculosis drug development. Talk presented at the Postdoctoral Research Symposium. Stellenbosch University, Cape Town, South africa, 29-30 September 2015.
Malherbe S. Evaluating TB treatment responses by [18F]FDG-PET/CT imaging – during and after treatment. 5th TB Biomarker Annual Meeting, Seattle, WA, 4 June 2015.

Miller MA. Elephant medicine and husbandry. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS. Continental Hotel, Canela, Brazil, 06 October 2015.
Miller MA. Tuberculosis in South African wildlife - why is it important? Talk presented at the Stellenbosch University Inaugural Lecture. FMHS, Stellenbosch University, Cape Town, South Africa, 23 June 2015.
Miller MA. Elephant medicine and husbandry. Invited Talk presented at the NIH Many Hosts of Mycobacteria Symposium. TNPRC, Covington, USA, 26 March 2015.
Miller MA. Why is diagnosis of TB so difficult? Talk presented at the BTB Outreach Day. Faculty of Veterinary Science, University of Pretoria, Pretoria, South Africa, 02 March 2015.
Miller MA. Tuberculosis diagnostic challenges in wildife and public health implications. Talk presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 05 December 2015.
Miller MA. Novel approaches to detection of tuberculosis in African wildlife. Talk presented at the US Animal Health Association annual conference. Providence Convention Center, Providence, USA, 26 October 2015.
Miller MA. Serodiagnostics for TB in wildlife species - can these play a role in detecting disease? Talk presented at the South African Veterinary Association Wildlife Group Congress. The Blades, Pretoria, South Africa, 20 March 2015.
Miller MA. Elephant TB - overview of clinical aspects, diagnosis, management and zoonotic risk. Talk presented at the South African Veterinary Association Wildlife Group Congress. The Blades, Pretoria, South Africa, 20 March 2015.
Miller MA. Warthog BTB - are they an underrecognized threat for BTB control?. Talk presented at the South African Veterinary Association Wildlife Group Congress. The Blades, Pretoria, South Africa, 20 March 2015.
Miller MA. Rumenitis and feed management in exotic ruminants. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 03 October 2015.
Miller MA. Restraint, sedation, and immobilization of captive elephants and rhinos. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 03 October 2015.
Miller MA. Hippopotamus medicine and immobilization. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 03 October 2015.
Miller MA. Field research in megavertebrate immobilization. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 05 October 2015.
Miller MA. Translating techniques used with free-ranging megavertebrates to zoo medicine. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 04 October 2015
Miller MA. Tuberculosis in wildlife in South Africa - are we winning the battle?. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 04 October 2015.
Miller MA. Diagnosis, management, and control of tuberculosis in captive elephants and rhinos. Talk presented at the 18th Congress of ABRAVAS and ALVEFAS, Workshop on Megavertebrate Medicine. Continental Hotel, Canela, Brazil, 04 October 2015.
Posters (69)
Senzani S, Bhaskar A, li D, Betzig E, Dhar N, Kana B. Identification and Characterization of Mycobacterial cell wall amidases. Oral and Poster. Swiss South Africa Joint Research Programme, Basel Switzerland.
Chengalroyen M, Beukes G, Gordhan B, Martinson N, Otwombe K, Kana B. The detection and quantification of differentially culturable bacilli in patients with active tuberculosis, School of Clinical Medicine Research Day. September 2015, Wits University, Johannesburg, South Africa
Chengalroyen M, Beukes G, Gordhan B, Martinson N, Otwombe K, Kana B. The detection and quantification of differentially culturable bacilli in patients with active tuberculosis, 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Moseki MR, Kana B. Functional analysis of *cydDC*-encoded type ABC transporter in *Mycobacterium smegmatis*. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Nthambeleni GS, Kana B, Gordhan B. Is there a combined role for the Nth and MutY DNA glycosylases during DNA repair in *Mycobacterium smegmatis*? 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Hassim F, Papadopoulos AO, Kana BD, Gordhan BD. A combinatorial role for DNA glycosylases in mutation avoidance in *Mycobacterium smegmatis*. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Papadopoulos A, Kana B. In silico analysis of M23-domain activators of peptidoglycan degrading amidases

in *Mycobacterium tuberculosis*. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Narrandes N, Kana B. Characterization of the electron transport chain in mycobacteria, 15 - 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa.
McIvor A, Gordhan B, Martinson N, Waja Z,Kana B. Detection of differentially culturable tubercle bacilli by exogenous cyclic-AMP in drug-susceptible patients at baseline, 15 - 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa.
McIvor A, Gordhan B, Martinson N, Waja Z, Kana B. Detection of culturable and non-culturable TB bacteria in patients receiving first-line treatment, 9th Annual SAMRC Early Career Scientist Convention
Shaku M, Kana B. Characterization of LytM domain-containing proteins in *Mycobacterium smegmatis*. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa
Maphatsoe MM, Ealana C, Kana B. Localization of low molecular weight proteins and other potential cell wall remodeling enzymes. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Rantsi TC, Kana B, Gordhan B. Molecular basis of the interplay between the Nth and the Nei DNA glycosylases in the base excision repair pathway in *Mycobacterium smegmatis*. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Sheik Ismail Z, Ealand C, Kana B. Characterization of mycobacterial DD- carboxypeptidases. 15 - 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa. WON FIRST PRIZE
Sheik Ismail Z, Ealand C, Kana B. Characterization of mycobacterial DD- carboxypeptidases. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Ralefeta D, Machowski E, Kana B. Heterologous expression and characterisation of *Mycobacterium tuberculosis* DD-Carboxypeptidases in *Mycobacterium smegmatis*. 15 - 16 April, NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa.
Ralefeta D, Machowski E, Kana B. Mycobacterial DD-Carboxypeptidases: Filling In The Gaps. 3 December 2015, Molecular Biosciences Research Thrust (MBRT) Symposium, Wits University, Johannesburg, South Africa.
Ealand C, Kana B. An essential DD-carboxypeptidase determines localization of peptidoglycan synthesis in mycobacteria, Poster, 9th Annual SAMRC Early Career Scientist Convention.
Naran K. Construction and characterization of bioluminescent *Mycobacterium tuberculosis* reporter strains for mechanism of action studies in new TB drug discovery. Invited talk, K-RITH/IDM Scientific Symposium, Zimbali Lodge, Durban, 22-24 November 2015
Singh V. Identification and validation of GuaB2 as a tuberculosis drug target. Invited talk, K-RITH/IDM Scientific Symposium, Zimbali Lodge, Durban, 22-24 November 2015
Evans J, Trujillo C, Ehrt S, Boshoff HIM, Schnappinger D, Mizrahi V. A pathway approach to identifying vulnerable and bactericidal targets in Coenzyme A biosynthesis in M. tuberculosis. Gordon Research Seminar on Tuberculosis Drug Discovery & Development, Girona, Spain, July 11-12 2015
Singh V, Pato J, Haartkorn R, Warner DF, Rizzi M, Keri G, Mizrahi V. Identification and validation of GuaB2 as a drug target. Gordon Research Conference on Tuberculosis Drug Discovery & Development, Girona, Spain, 12-17 July 2015
Mukherjee R, Ioerger T, Warner DF, Mizrahi V. Permeation in *M. tuberculosis*. Gordon Research Conference on Tuberculosis Drug Discovery & Development, Girona, Spain, 12-17 July 2015
Koch A, Brites D, Evans JC, Seldon R, Oni T, Nicol MP, Warner DF, Mizrahi V, Harris D, Parkhill J, Gagneux S, Martin DP, Wilkinson RJ. High Resolution Snapshot of Genetic Diversity within *Mycobacterium tuberculosis* in a Region of High HIV Co-Infection. Poster, Biophysical Society Thematic meeting: Biophysics in the Understanding, Diagnosis and Treatment of Infectious Diseases, Spier Estate, Stellenbosch, South Africa, 16-20 November 2015
Mukherjee R, Ioerger T, Warner DF, Mizrahi V. Small hydrophilic molecule permeation in *M. tuberculosis*. Poster, Biophysical Society Thematic meeting: Biophysics in the Understanding, Diagnosis and Treatment of Infectious Diseases, Spier Estate, Stellenbosch, South Africa, 16-20 November 2015
Broadley S, Warner DF, Sewell T. Structure determination of proteins involved in induced mutagenesis in Mycobacterium tuberculosis. Poster, Biophysical Society Thematic meeting: Biophysics in the Understanding, Diagnosis and Treatment of Infectious Diseases, Spier Estate, Stellenbosch, South Africa, 16-20 November 2015

Singh V, Kigondu EM, Chibale K, Mizrahi V, Warner DF. Chlorpromazine potentiates the activity of spectinomycin against *Mycobacterium tuberculosis*. Poster, Biophysical Society Thematic meeting: Biophysics in the Understanding, Diagnosis and Treatment of Infectious Diseases, Spier Estate, Stellenbosch, South Africa, 16-20 November 2015.
Bunjun R, Rious C, Soares A, Hanekom W, **Walzl G**, Wilkinson R, Burgers W. Defects in multiple mycobacterial T helper subsets in blood and lungs in early HIV infection. Host Response in Tuberculosis-Keystone Symposia. Santa Fe, New Mexico, USA. 22-27 January 2015.
Corstjens PLAM, Tjon Kon Fat EM, **Chegou NN**, Ottenhoff THM, **Walzl G**, Geluk A. Assessment of lateral flow based assay in six African countries to determine IP-10 levels in stimulated whole blood samples of TB suspects. Host Response in Tuberculosis - Keystone Symposia. Santa Fe, New Mexico, USA. 22-27 January 2015.
Hammond-Aryee K. A high seroprevalence of Toxoplasma gondii antibodies in a population of feral cats in the Western Cape of South Africa. Poster presented at the13th International congress on Toxoplasmosis and Toxoplasma gondii research. Gettysberg College, Pennsylvania, USA, 17-20 June 2015.
Hammond-Aryee K. The prevalence of antibodies to Toxoplasma gondii in sheep in the Western Cape of South Africa. Poster presented at the13th International congress on Toxoplasmosis and Toxoplasma gondii research. Gettysberg College, Pennsylvania, USA, 17-20 June 2015.
Hammond-Aryee K. Genotypic characterization and strain diversity of Toxoplasma gondii from infected human and animal tissues from the Western Cape of South Africa. Poster presented at the59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Dippenaar A. Investigating microevolution in *M. tuberculosis* during transmission. Poster presented at the 36th annual Congress of the European Society of Mycobacteriology. Bellevue Park Hotel Riga, Riga, Latvia, 28 June - 01 July 2015.
Miller M, Parsons S, Buss P, Lyashchenko K, van Helden PD. Detection of immunological responses to BTB in African wildlife. Poster presented at the Keystone Symposium on Immunity to Veterinary Pathogens: Informing Vaccine Development. Keystone resort, Colorado, USA, 20-25 January 2015.
Chegou, N. Diagnostic performance of a seven-marker serum protein biosignature for the diagnosis of active tb disease in African primary health care clinic attendees with suspected pulmonary tuberculosis. The Merck Africa Research Summit, in Geneva, Switzerland, from the 19-20 October 2015.
Da Camara NL. Large pncA deletions in *Mycobacterium tuberculosis* influence rapid detection of pyrazinamide susceptibility. Poster presented at the 5th Conference of The Union Asia Pacific Region. Hilton Hotel, Sydney, Australia, 31 August - 02 September 2015.
Da Camara NL. Targeted deep sequencing to detect heterogeneity in *Mycobacterium tuberculosis* populations. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Kleynhans L, Ruzive S, Van der Spay G, Van Helden, PD, Walzl G, Ronacher, K. Evaluation of the endocrine changes during TB treatment. 4th European Congress of Immunology. Vienna, Austria, 6-9 September 2015.
Sao Emani C, Williams MJ, Wiid IJ, Baker B. Investigation of role of ergothioneine in *Mycobacterium tuberculosis*. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Da Camara NL. Targeted deep sequencing of drug resistance associated genes to investigate heterogeneity in *Mycobacterium tuberculosis* populations. Poster presented at the 1st Biomedical Sciences Annual Research Day. FMHS, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Parbhoo T, Mouton M, Sampson S. Optimization of Flow Cytometric Methods for Mycobacterial Viability Discrimination and Cell Enumeration. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Kriel N, Heunis T, Williams M, Sampson S, Warren RM, van Helden PD. Global/High-throughput analysis of DNA-binding proteins in *Mycobacterium smegmatis*. Poster presented at the 1st Biomedical Sciences Annual Research Day. FMHS, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Kriel N, Heunis T, Williams M, Sampson S, Warren RM, van Helden PD. Global/High-throughput analysis of DNA-binding proteins in *Mycobacterium smegmatis*. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Kriel N, Heunis T, Sampson S, van Helden PD, Warren RM, Williams M. Global/High-throughput analysis of DNA-binding proteins in *Mycobacterium smegmatis*. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Salie M, Daya M, Lucas LA, Warren RM, van der Spuy GD, van Helden PD, Hoal EG, Moller M. An investigation of toll-like receptors in tuberculosis susceptibility reveals sex-specific associations for TLR8

polymorphisms. Poster presented at the American Society of Human Genetics 2015 Annual Meeting. Baltimore Convention Centre, Baltimore, USA, 06-10 October 2015.
Kunsevi-Kilola C, Parbhoo T, Tshivhula H. Identification of distinct bio-signatures in whole blood and live M.tb stimulated PBMCs in TB house hold contacts with and without type 2 diabetes. Poster presented at the 1st IUIS-FAIS Southern African Immunology workshop and 6th Infectious Diseases in Africa Symposium. River Club, Cape Town, South Africa, 20-24 October 2015.
Salie M, Hoal EG. Investigation of TLR in TB susceptibility reveals sex-specific associations for TLR8. Poster presented at the ASHG conference. Baltimore conference centre, Baltimore, USA, 08 October 2015.
Daya M, Hoal EG. Using multi-way admixture mapping to elucidate TB susceptibility in the South african Coloured population. Poster presented at the ASHG conference. Baltimore conference centre, Baltimore, USA, 07 October 2015.
Schlechter N. Identification of novel candidate genes for susceptibility to tuberculosis by identifying disease-causing mutations in individuals with Primary Immunodeficiency Disorders. Poster presented at the Southern African Society for Human Genetics. KleinKaap Boutique Hotel, Pretoria, South Africa, 16-19 August 2015.
Schlechter N. Identification of novel candidate genes for susceptibility to tuberculosis by identifying disease-causing mutations in individuals with Primary Immunodeficiency Disorders. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Leisching G, Pietersen R-D, Mpongoshe V, van Heerden C, van Helden PD, Wiid I, Baker B. The host response to a clinical MDR Mycobacterial strain cultured in a detergent-free environment: A global transcriptomics approach. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Leisching G, Pietersen R-D, Mpongoshe V, van Heerden C, van Helden PD, Wiid I, Baker B. The host response to a clinical MDR Mycobacterial strain cultured in a detergent-free environment: A global transcriptomics approach. Poster presented at the Postdoctoral Research Day. Stellenbosch University, Cape Town, South Africa, 29 October 2015.
Leisching G, Pietersen R-D, Mpongoshe V, van Heerden C, van Helden PD, Wiid I, Baker B. The host response to a clinical MDR Mycobacterial strain cultured in a detergent-free environment: A global transcriptomics approach. Poster presented at the 1st Biomedical Sciences Annual Research Day. FISAN Building, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Dippenaar A. Whole genome sequence analysis of *Mycobacterium suricattae*. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Whitfield M, Streicher EM, Mardarowicsz I, Scott L, Stevens W, Sampson SL, van Helden PD, Warren RM, van Rie A. Association between Genotypic and Phenotypic Pyrazinamide Resistance in Rifampicin Resistant *Mycobacterium tuberculosis* Isolates. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Van Rie A, Whitfield M, Scott L, Warren RM, Voss De Lima Y, Stevens W, Sirgel F. Potential of Rifabutin in the Treatment of Rifampicin Resistant Tuberculosis. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 04-06 December 2015.
Visser H, de Vos M, van der Merwe RG, van Helden PD, Warren RM, Victor TC, Paul LV. Clofazimine: Mechanism of Resistance within *M. tuberculosis*. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 04 December 2015.
Sampson S, Mouton JM, Helaine S, Holden DW. Single cell elucidation of mycobacterial replication dynamics .Poster presented at the New Approaches and Concepts in Microbiology. EMBL, Heidelberg, Germany, 11-14 October 2015.
Chegou NN. Host biomarkers for the diangosis of TB disease. Poster presented at the UNESCO-Merck Africa Research Summit. Maotel Royal Hotel and Eden Palace Au Lac, Geneva, Switzerland, 19-20 October 2015.
Willemse D, Warren RM, Williams MJ. Generation and phenotypic characterisation of Rv1460 mutants of *Mycobacterium tuberculosis*. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Willemse D, Weber B, Warren RM, Williams MJ. Expression and purification of the *Mycobacterium tuberculosis* Rv1460, a possible suf system regulator. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Clarke C. Development of a Diagnostic Assay for *Mycobacterium suricattae* Infection in Meerkats (Suricata suricatta). Poster presented at the 1st Biomedical Sciences Annual Research Day. FMHS, Stellenbosch University, Cape Town, South Africa, 25 November 2015.
Roos EO. Diagnostic Tool Evaluation: Detection of Mycobacterial Infections in Warthogs (Phacochoerus africanus) Using Serological Tests. Poster presented at the 59th Annual Academic Day 2015. FMHS,

Stellenbosch University, Cape Town, South Africa, 13 August 2015.
Theron G. Psychological distress and its relationship with nonadherence to TB treatment: a multicentre study. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 03 December 2015.
Calligaro G, Theron G, Khalfey H, Peter J, Miller M, Michell L, Joubert I, Dheda K. randomised controlled trial of the impact of Xpert® on tracheal aspirates within a burden of disease study in South African intensive care units. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Limberis J, Pietersen E, Jayakumar JJ, Theron G, Dheda K, Smith L, Warren RM, Clark T. Genetic markers of drug resistance and their association with clinical outcomes in patients with MDR-TB or XDR-TB. Poster presented at the 46th Union World Conference on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
De Vos M. Whole genome sequencing reveals genetic heterogeneity and suggests the role of selective bottleneck in defining the population structure of Mycobacterium tuberculosis clinical isolates. Poster presented at the 46th Union World Conferences on Lung Health. CTICC, Cape Town, South Africa, 02-06 December 2015.
Ngwane A, Baker B, Wiid I, van Helden PD. Design, synthesis of in vitro antitubercolosis activity of 2(5H) furanones. Poster presented at the 59th Annual Academic Day 2015. FMHS, Stellenbosch University, Cape Town, South Africa, 05 August 2015.
Kunsevi-Kilola C, Tshivula H. Characterization of human alveolar macrophage and blood monocyte derived macrophage responses to Mycobacterium tuberculosis in TB household contacts with and without type 2 diabetes. Poster presented at the 6th IDA Symposium & African Flow Cytometry Workshop. The River Club, Cape town, South Africa, 20-24 October 2015.

Products / Artifacts / Patents (2)

- **Method for diagnosing tuberculous meningitis**. Inventors: Chegou, NN, Walzl, G, van Furth, AM, Visser, DH, Applicant: Stellenbosch University. South African Provisional patent Application No: 2014/02743, Filing date: 2014/04/15. Worldwide (PCT) application was filed on the 15/04/2015 with application number: PCT/IB2015/052751, Status: Pending
- **Method for diagnosing tuberculosis**. Inventors: Chegou, NN, Walzl, G, Mihret, A, Applicant: Stellenbosch University, Application type: PCT, claiming priority from the South African provisional patent: ZA 2014/01456, Country: PCT / WIPO Application No: PCT/IB2015/051435, Filing date: 2015/02/26, Status: Pending

Honours and Awards to Staff

Prof G Walzl was awarded a Distinguished professorship at Stellenbosch University (2016-2020).
Prof RM Warren was awarded the vice rectors award for outstanding publication numbers.
Prof RM Warren received a Gold Medal for Scientific Excellence from the SA Medical Research Council
Prof. Rob Warren was awarded a rectors award for publication outputs
Prof EG Hoal was elected into a South African Society of Human Genetics
Prof EG Hoal was elected into a SA Society of Human Genetics
Dr CJ. Werely was elected a Member of Human Research Ethics Committee Board (HREC1)
Prof SL Sampson was elected to in the Biosafety and Environmental Ethics Panel
Dr NN Chegou was awarded the Emerging Research Talent by UNESCO and MERK
Professor V Mizrahi was awarded an A1 rating by the NRF. She was also elected as a Fellow of the African Academy of Sciences (AAS)
Prof. V Mizrahi was elected into the College of Fellows of the University of Cape Town. This fellowship is awarded by UCT in recognition of original, distinguished academic work, and was conferred at a graduation ceremony held at UCT on 19 December 2015. Valerie joins a group of 136 active and retired UCT academics who have received this accolade

Prof. D Warner was awarded two grants under the prestigious South Africa-U.S. Program for Collaborative Biomedical Research, a joint initiative of the U.S. National Institutes of Health (NIH) and the South African Medical Research Council (SAMRC). This highly competitive programme saw a total of 31 grants awarded to U.S. and South African scientists in order to support basic and clinical research targeting HIV/AIDS, tuberculosis (TB) and HIV-related co-morbidities and cancers. The first of his grants is for a two-year R21 project, "Drug permeation and activity in *Mycobacterium tuberculosis*-infected macrophages" is being conducted in collaboration with Prof David Russell (Cornell University, USA) and Dr. Lubbe Wiesner (Division of Clinical Pharmacology, UCT). The second award is for a five-year U01 project entitled "Replisome dynamics in *Mycobacterium tuberculosis*: linking persistence to genetic resistance", is being pursued in collaboration with Dr. Roger Woodgate of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, USA
Professor B Kana was selected to represent Wits University at the Higher Education Leadership and Management Program hosted by Higher Education South Africa (HESA - now Universities South Africa). The program involved three workshops that ran from the 25 - 27 February, 22 - 24 April and 24 - 25 June 2015 in Johannesburg
Prof. B Kana from the DST/NRF Centre of Excellence for Biomedical TB Research at Wits University was selected as the Titan for South Africa, the SADC region and the African Continent in the Medical & Veterinary category. CEO Global hosts the annual selection of Titans and Africa's most influential women through a rigorous nomination and judging process that was audited by KPMG in 2015. The Titans - Building Nations program aims to recognize influential men, who embody the spirit of excellence and have made meaningful contributions to their organizations, society and the African continent. These individuals shift the African landscape for the purpose of sustainable growth and display an unwavering commitment to the development of their nations. For more information please visit: Website: www.titans-building-nations.co.za
Professor B Kana was admitted to the Academy of Science of South Africa
Professor B Kana was awarded a B3 rating by the National Research Foundation

Progress of CBTBR Trainees (2005-2015)

Title	Surname, Initial	Training/Deg	Yr completed	Current position
Ms	Cole, V	Hons	2015	Remained in CBTBR for a MSc degree
Ms	du Toit, L	Hons	2015	Unknown
Ms	Higgitt, RL	Hons	2015	Remained in CBTBR for a MSc degree
Mr	Julius, Z	Hons	2015	Unknown
Ms	Kell-Blair, C	Hons	2015	Unknown
Mr	Leukes, V	Hons	2015	Remained in CBTBR as a Research Assistant
Ms	Niemand, N	Hons	2015	Remained in CBTBR for a MSc degree
Ms	Sikosana , N	Hons	2015	Remained in CBTBR for a MSc degree
Ms	van Schalkwyk, T	Hons	2015	Remained in CBTBR for a MSc degree
Mr	Bowker, N	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Clarke, C	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Da Camara, N	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Jacobs, R	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Klazen, J	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Lynch, S-L	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Meyer, L	Hons	2014	Took up a Research assistant position in CBTBR
Ms	Ngakane, L	Hons	2014	Unknown
Mr	Ngqaneka, T	Hons	2014	Unknown
Mr	Nusca, G	Hons	2014	Unknown
Ms	Parbhoo, T	Hons	2014	Remained in CBTBR for a MSc degree
Mr	Schurz, H	Hons	2014	Remained in CBTBR for a MSc degree
Ms	Strauss, C	Hons	2014	Currently pursuing an LLB degree at Stellenbosch University
Mr	Tshehla, E	Hons	2014	Unknown
Ms	van Rensburg, I	Hons	2014	Remained in CBTBR for a MSc degree
Dr	Abrahams, GL	Postdoctoral	2010	Research Officer at UCT 2011-2014; Appointed Lecturer at Rhodes University,2015

Dr	Ahmadou Ahidjo, B	PhD	2011	Postdoctoral fellowship at Johns Hopkins University, 2011-2015; taking up a research position at Aurum Institute in 2015
Ms	Ansarie, M	Hons	2012	Unknown
Ms	Arries, J	Hons	2013	Remained in CBTBR for a MSc degree
Ms	Asmal, R	MSc	2015	Currently working the laboratory of Andries Steyn at K-RITH
Ms	Axcell, A	MSc	2012	Currently completing a PhD in the CBTBR
Dr	Babb, C	PhD	2007	Took up a Scientist post with Wits/NHLS
Dr	Bapela, BN	Postdoctoral	2007	Took up a permanent position at the MRC, retrenched
Ms	Barichievy, S	MSc	2005	Postdoctoral fellow at the CSIR;took up a position in pharma in Sweden in 2014
Dr	Barnard, M	PhD	2013	Took up a Management post with TASK
Dr	Baumann, R	Postdoctoral	2006	Returned to Germany, to private company
Ms	Berrington, C	Hons	2013	Unknown
Ms	Bester, M	MSc	2009	Unknown
Mr	Beukes, G	MSc	2013	Remained in CBTBR for a PhD degree
Dr	Bezuidenhout, J	PhD	2005	Employed as F/T pathologist at Tygerberg Hospital
Dr	Black, JF	Postdoctoral	2010	Took up a position with Livelihoods Foundation
Dr	Black, P	PhD	2015	Took up a Postdoctoral Position in Hong Kong
Ms	Botha, L	MSc	2014	Took up position with TASK
Ms	Botha, J	MSc	2007	Studied pharmacy at UWC
Dr	Botha, MM	PhD	2012	Took up a permanent position at ICON
Ms	Brackin, R	MSc	2005	Completed Electrical Engineering at Wits, and PhD at the CSIR. Currently based at CSIR
Dr	Brown, N	Postdoctoral	2007	Moved to UK
Dr	Bruiners, N	PhD	2012	Took up a Postdoctoral position in the USA
Ms	Carinus, H	Hons	2005	Moved to Dubai
Dr	Chegou, N	PhD	2009	Took up a Senior Scientist position in CBTBR
Dr	Chihota, V	PhD	2011	Deputy Director Research, Aurum Institute
Ms	Coetze, L	Hons	2012	MSc student, UCT
Dr	Conradie E	Postdoctoral	2006	Full-time mother
Dr	Daya, M	Postdoctoral	2015	Took up a postdoctoral position in Denver, USA
Dr	de Vos	PhD	2013	Remained in CBTBR as postdoctoral fellow
Dr	de Wit, E	PhD	2009	Homemaker
Dr	Dippenaar, A	PhD	2014	Remained in CBTBR as postdoctoral fellow
Dr	Ditse, Z	PhD	2015	Unknown
Dr	Djoba, J	PhD	2008	Took up a postdoctoral in Gabon
Ms	Du Plessis, J	MSc	2014	Remained in CBTBR for a PhD degree
Dr	Du Plessis, N	PhD	2012	Remained in CBTBR as postdoctoral fellow
Mr	Du Plessis, WJ	MSc	2014	Remained in CBTBR for a PhD degree
Ms	Du Toit, I	Hons	2006	Planned to do forensics through UNISA
Mr	Dudhia, ZE	Hons	2009	Took a position at Von Seidels Intellectual Property Attorneys
Ms	Ehlers, L	MSc	2014	Took up a position at Winebiotech
Mr	Essone, PN	MSc	2014	Moved to UCT
Dr	Esterhuyse, M	Postdoctoral	2010	Took up a post in Prof Kaufmann's lab (Germany)
Ms	Falmer, A	MSc	2008	Moved to HIV NGO in Paarl
Dr	Fang, Z	PhD	2014	Remained in CBTBR as postdoctoral fellow
Dr	Fenhalls, G	Postdoctoral	2005	Now working in husband's company outside science
Dr	Fortuin, S	PhD	2013	Took up postdoctoral fellow at UCT
Mr	Gallant, J	MSc	2015	Remained in CBTBR for a PhD degree
Mr	Nusca, G	Hons	2014	Unknown

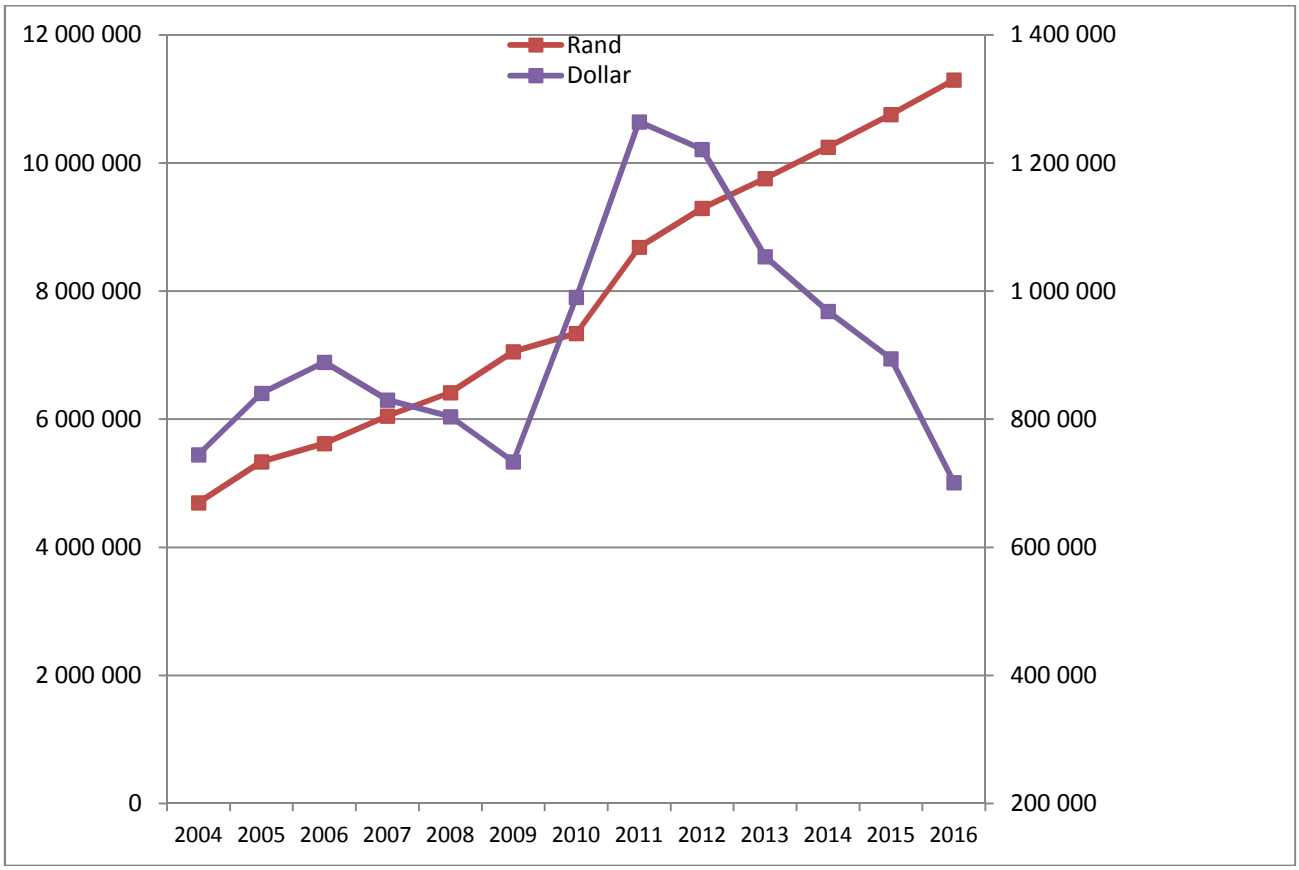
Mr	Goosen, WJ	Hons	2012	Remained in CBTBR for a MSc/PhD degree
Ms.	Goosens, V	MSc	2005	Completed PhD degree in The Netherlands
Dr	Gopinath, K	Postdoctoral	2014	Completed postdoc at UCT in 2014 and moved to Max Planck Institute for Infection Biology, Berlin for second postdoc
Ms	Grobbelaar, M	MSc	2012	Remained in CBTBR for a PhD degree
Dr	Hanekom, M	PhD	2009	Working for TASK clinical trials consortium
Dr	Harper, CJ	Post Doc	2012	Housewife
Ms	Hariparsad, S	MSc	2015	Unknown
Ms	Hassim	MSc	2013	Unknown
Dr	Hayward, D	Postdoctoral	2010	Took up a position at Triclinium
Ms	Heysen, T	Hons	2009	Unknown
Dr	Hoek, K	PhD	2010	Took up a permanent position at the NHLS
Mr	Jennings, G	Hons	2005	Moved to the USA for postgraduate study
Dr	Johnson, R	Postdoctoral	2009	Took up a permanent position at the MRC
Dr	Kigondu	PhD	2015	Returned to Kenya where she took up a position as a Researcher, Centre for Traditional Medicine & Drug Research, Kenya Medical Research Institute, Nairobi, Kenya
Dr	Kleynhans, L	PhD	2012	Remained in CBTBR as postdoctoral fellow
Dr	Klopper	PhD		Remained in CBTBR as postdoctoral fellow
Dr	Koch, A	PhD	2015	Remained in CBTBR as postdoctoral fellow
Ms	Kruger, C	PhD	2009	Took up PhD at Water Health Research Unit, JHB
Mr	Laisse, CJM	MSc	2010	Returned to UEM in Mozambique
Mr	Lambrecht, D	Hons	2005	Left CBTBR to do MSc in Chemistry at SU
Dr	Le Roex	PhD	2014	Remained in CBTBR as postdoctoral fellow
Mr	Limberis	Hons	2013	Registered for anMSc/PhD at UCT
Dr	Loebenberg, L	Post Doc	2012	Took up a permanent position at Afriplex
Dr	Louw, GE	Post Doc	2012	Took up a Postdoc position at NIAID
Dr	Loxton, A	PhD	2009	Took up a Senior Scientist position in CBTBR
Mr	Lucas, L	MSc	2012	Remained in CBTBR for a PhD degree, took a position at Synexa Life Sciences
Ms	Lynch S-L	Hons	2014	Unknown
Mr	Lunn, J	Hons	2013	Took up MSc position at UCT
Dr	Machado, A	PhD	2015	Unknown
Dr	Machowksi, E	Postdoctoral	2006	P/T Senior Scientist in CBTBR
Dr	Macingwana	PhD	2014	Took up Postdoctoral position at Plant Sciences, SU
Ms	Magan, N	Hons	2009	Unknown
Dr	Magwira, C	Postdoctoral	2010	Postdoctoral fellowship in the RMPRU, Wits/NICD; currently seeking employment in Malawi
Mr.	Mahasha, P	MSc	2007	Moved to Univ. of Pretoria, for family reasons
Dr	Makoah, N	Postdoctoral	2015	Took up a position at the NICD in Johannesburg
Mr	Mameja	Hons	2013	Unknown
Mr	Manunu	MSc	2015	Took up a Post with TASK
Ms	Mapela, L	MSc	2012	Unknown
Ms	Martin, Z	Hons	2015	Remained in CBTBR for PhD degree
Dr	Matsoso, LG	PhD	2007	Took a position in a TB-focused NGO in Johannesburg; currently unemployed
Mr	Mazorodze, JH	MSc	2010	Took up a PhD in Bill Jacobs's lab in USA
Mr	Mbouna	Hons	2013	Unknown
Dr	McEvoy, CRE	Postdoctoral	2010	Moved to Australia in March 2010
Ms	Meyer, L	Hons	2014	Unknown
Ms	Mlamla, Z	MSc	2011	Unknown
Dr	Moller, M	PhD	2007	Took up a NRF RCAF position in the CBTBR
Ms	Moolla, N	MSc	2013	Unknown

Dr	Moosa, A	PhD	2012	Remained in CBTBR as postdoctoral fellow
Dr	Mowa, B	PhD	2009	Appointed as Lecturer at Wits after completing postdoc at Wits
Ms	Mpande	Hons	2013	Took up a MSc position in SATVI (UCT)
Ms	Mpongoshe, V	MSc	2014	Unknown
Mr	Mufamadi, S	Internship	2005	Completed MSc at Wits
Ms	Muller, L	Researcher	2006	Project Manager, CBTBR Immunology
Ms	Myburgh, R	Hons	2006	Left the CBTBR to start her family
Dr	Naran, K	PhD	2015	Remained in CBTBR as postdoctoral fellow
Ms	Narrandes	MSc	2013	Remained in CBTBR for a PhD degree
Ms	Ndabambi, S	MSc	2009	Unknown
Dr	Ndwandwe, DE	PhD	2013	Took up researcher post at HPRU (MRC, Durban), currently doing postdoc in Pharmacology at UKZN
Dr	Nel, HJ	PhD	2007	Took a postdoctoral at Trinity College Dublin, Ireland
Dr	Nene, N	PhD	2009	Took up a Postdoctoral at LifeLab in Durban
Dr	Newton-Foot	PhD	2013	Moved to NHLS
Ms	Ngakane, L	Hons	2014	Unknown
Ms	Ngombane, NC	MSc	2011	Returned to MRC
Mr	Ngqaneka, T	Hons	2014	Unknown
Dr	Ngwane, AH	PhD	2012	Remained in CBTBR as postdoctoral fellow
Ms	Ntsapi, MC	Hons	2012	Remained in CBTBR for a MSc degree
Dr	Parsons, S	PhD	2009	Remained in CBTBR as postdoctoral fellow
Ms	Phalane, KG	Hons	2010	Remained in CBTBR for a MSc degree
Ms	Podgorski	Hons	2013	Unknown
Ms	Pule, C	MSc	2014	Remained in CBTBR for a PhD degree
Dr	Ramburan, A	PhD	2009	Took up a permanent position at NHLS, Durban
Mr	Reiche	Hons	2013	Remained in CBTBR for MSc degree
Ms	Richardson, M	PhD	2006	Deceased
Dr	Roberts, T	PhD	2008	Diagnostic Expert, MSF
Ms	Ruzive, S	Hons	2012	Took up a research assistant position in CBTBR
Dr	Salie	PhD	2014	Remained in CBTBR as postdoctoral fellow
Dr	Sao Emani, C	PhD	2012	Remained in CBTBR as postdoctoral fellow
Dr	Savvi, S	PhD	2009	Completed 2 postdocs at UCT; currently working for a biotech company in Cape Town
Ms	Seepe, P	MSc	2011	Unknown
Mr	Senzani	MSc	2013	Remained in CBTBR for a PhD degree
Ms	Serepa	Hons	2013	Unknown
Dr	Sholto-Douglas-Vernon, C	PhD	2005	Employed at St. George's Hospital, London
Dr	Theron, A	PhD	2015	Employed at CSIR
Mr	Siame, KK	Hons	2010	Remained in CBTBR for a MSc degree
Ms	Smith, B	MSc	2015	Remained in CBTBR as Research Assistant
Ms	Steyn, NL	MSc	2012	Remained in CBTBR for a PhD degree
Ms	Strauss, C	Hons	2014	Unknown
Ms	Strauss, O	MSc	2009	Moved to Kayaletsha HIV clinic in Cape Town
Dr	Streicher, EM	PhD	2007	Took up a NRF RCAF position in the CBTBR
Dr	Styger	Postdoctoral	2015	Unknown
Mr	Theys	Hons	2013	Remained in CBTBR for a MSc degree
Ms	Thiart, L	MSc	2014	Unknown
Mr	Tshehla, E	Hons	2014	Unknown
Ms	Tshoko, S	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Uren	Hons	2013	Remained in CBTBR for a MSc degree
Dr	Van der Merwe,R	PhD	2012	Remained in CBTBR as postdoctoral fellow
Dr	Van der Spuy, G	PhD	2009	Remained in CBTBR in MRC Post
Dr.	Veenstra, H	PhD	2007	Retired

Dr	Viljoen, AJ	PhD	2013	Took up a postdoctoral Position in France
Ms	Visser, H	MSc	2015	Remained in CBTBR for a PhD degree
Ms	Wagman, CK	MSc	2012	Took up a position at Police Forensics in Cape Town
Dr.	Warner, DF	Postdoctoral	2007	Moved to UCT in 2011, promoted to Associate professor in the Division of Medical Microbiolog in 2014
Dr	Werely, CJ	PhD	2012	Staff, PAWC (SU)
Ms	Willemse, G-L	Hons	2013	Unknown
Ms	Willemse, D	MSc	2013	Remained in CBTBR for a PhD degree
Dr	Williams, M	Postdoctoral	2014	Took up a NRF RCAF position in the CBTBR
Dr	Wright, CA	PhD	2009	NHLS staff
Mr	Zvinairo, TK	MSc	2015	Remained in CBTBR as Research Assistant

FINANCES

The graph below illustrates the funding to the CBTBR from NRF since inception (in red). Then blue line illustrates the purchasing power of this funding in US dollar terms (similarly, euros). This is provided since the reader should note that this CoE is equipment and consumables intensive, where most of these items are imported. Thus, despite the gratitude we have to NRF for the increases over the years, the increases do not compensate for the drop in purchasing power over the last few years.



The income statement, balance sheet and cash flow statement for period 1 Jan 2015 to 31 Dec 2015 have been reviewed and approved by the external auditors and will be forwarded to the Board.