DST-NRF CENTRE OF EXCELLENCE

ANNUAL PROGRESS REPORT

Reporting Period

1 January 2014 – 31 December 2014

CONTENTS **Page**

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	:	24/04/2014

EXECUTIVE SUMMARY

1. Financial Information (Funding of the CoE)

Total NRF funding for 2014 (entire year) – CoE only	:	R 10 247 458
CoE-specific Funding from Host institution in 2014 – WITS	:	R 230 000
– UCT	:	R 143 215
– SU	:	R 817 148
Funding from other sources for the CoE in 2014	:	R 55 866 456
Total funding	:	**R 67 304 277**

Total funding for 2014 for Wits node: R 11 910 684

- CoE funding from NRF: **R 2 215 267**
- Other funding from NRF: **R 501 000,** made up as follows:
  - Incentive Funding (Kana)[1] R 40 000
  - Incentive Funding (Gordhan)[2] R 40 000
  - NRF postdoc supplement[3] R 45 000
  - SA-Swiss Joint Research Grant[4] R 376 000
- Funding from Wits and NHLS: **R 1 694 254 ,** made up as follows:
  - 10% Wits Institutional Commitment R 230 000
  - Research Incentive Funding R 37 692
  - Salaries R 1 426 562
- Funding from other sources: **R 7 500 163,** made up as follows:
  - HHMI IECS grant[5] R 1 234 560
  - SHIP – MRC[6] R 237 936
  - DAIDS CTU Supplement R 1 883 511
  - BMGF Accelerator[7] R 4 144 156

Total funding for 2014 for UCT node: R 11 563 549

- CoE funding from NRF: **R 1 432 147**
- Other funding from NRF: **R 330 023**[8]
- Funding from UCT and NHLS: **R 1 738 638**[9]
- Funding from other sources:[10] **R 8 062 741,** made up as follows:
  - MRC Unit (MMRU; Mizrahi) R 1 198 387 (1 Apr 2014 – 31 Mar 2015)
  - EU FP7 (MM4TB) (Year 4) (Mizrahi) R 796 001 (1 Feb 2014 – 31 Dec 2014)[11]
  - FNIH (HIT-TB) (Mizrahi) R 3 522 629 (1 Mar 2014 – 28 Feb 2015)[12]
  - MRC SHIP grant (Year 1) (Warner) R 1 006 513 (1 Jan 2014 – 31 Dec 2014)
  - MRC Flagship 1 (Year 1) (Warner/Mizrahi) R 439 211 (1 Jan 2014 – 31 Dec 2014)

[1] NRF Incentive Funding to BD Kana – Year 4
[2] NRF Incentive Funding to BG Gordhan – Year 5
[3] To CS Ealand
[4] Year 1 SA-Swiss to N. Dhar and B. Kana
[5] Year 3
[6] Year 2 To B. Kana and BG. Gordhan
[7] Year 1
[8] SA/Germany Research Cooperation grant (V. Mizrahi – R 77,000); Competitive Programme for Rated Researchers (D. Warner – R 190,023); UK/SA Royal Society-NRF Seminar (D. Warner; R 63,000)
[9] Salaries
[10] Where applicable, grant awards from external funders include indirect costs (IDC)
[11] Year 3 of five-year grant (total €331,667 - including IDC), calculated at exchange rate of R12/€
[12] Year 4 of 5-year grant from FNIH (sub-contractor on grant from BMGF), calculated at exchange rate of R11/$
[6] Calculated at exchange rate of R11/$

- HHMI SIRS grant (Year 3) (Mizrahi) R 1,100,000 (1 Jan 2014 – 31 Dec 2014)[6]

Funding for 2014 for SU node: R 43 830 044

- CoE funding from NRF : **R 6 600 044**
- Other Funding from SU: (best estimate): **R 4 500 000,** incl. some salaries, student bursaries, excl. space, basic infrastructure, secretary, cleaners.

- Funding from other sources (best estimate): **R 32 730 000**, made up as follows:
  - MRC Centre (estimate of the TB component) R 8 300 000 (incl. salaries)
  - PGWC R 2 330 000 (salaries only)
  - MRC SHIP Funding (x2) R 1 800 000
  - EDCTP R 1 600 000
  - BMGF R 3 500 000
  - Harry Crossley Foundation R 100 000
  - IMPAACT R 300 000
  - EU FP7 (European Union) R 1 900 000
  - SARChI R 5 500 000
  - ACTG R 600 000
  - HPTN/DAIDS R 1 900 000
  - NIH R 3 900 000
  - 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 2014 as evidenced by the fact that 64 articles in peer-reviewed journals were published, and 118 conference presentations were made, including 6 plenary/ keynote lectures, and numerous invited talks. Of the research articles published, 55 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 6 PhD students, 7 MSc students and 15 Honours students from the CBTBR graduated or completed their training in 2014. All these postgraduate students completed degrees within their maximum allowable time agreed upon in the SLA. Two postdocs completed training in the UCT node. Both moved on to contract academic positions, one in Germany and the other in the UCT node. A postdoctoral fellow at the Wits node was awarded the prestigious MRC Career Development Award and will be transitioning to a fixed term contract post at Wits University. 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 (57% female) and percentage of postdoctoral fellows (24% of total student complement) exceeded the SLA targets of ≥50% and ≥10%, respectively. The percentage of black students (50%) met the SLA target of ≥50%. The percentage of Honours students was 17% in 2014.
Progress against SLA 4 targets: The total of 89 postgraduate students associated with the CBTBR in 2014 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. During 2015 we hope to house a full time science journalist intern (NRF sponsored) to assist with this overall activity. Perhaps one of our most significant measures of success is that Profs Mizrahi and van Helden were asked to serve 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.

(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 and some idea of our networks can be gained from the details provided in section 4 of the report. These range from 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. Moreover, The CBTBR provides quality control reagents for this instrument, now globally. The material from the CBTBR will 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, the gold mines, 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, 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. SU continues to provide a genotyping service to the NHLS in Green Point to identify laboratory contamination and to identify the reasons for discordance between the Xpert and culture. SU is also assisting the NHLS to determine the reason for discordance between phenotypic isoniazid resistance and the absence of its detection on the MTBDRplus line probe assay.

3. Gender Impact

From the "Science by Women" perspective, it is important to note that 57% of all postgraduate students (including postdoctoral fellows) in the CBTBR in 2014 were female. Two of the three NRF SARChI's recently 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.

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 (in collaboration with Prof L Wangh and Dr J Rice at Brandeis University, USA) 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. These gene targets are analyzed at end-point in the same tube by hybridization to sets of Lights-On/Lights-Off probes labeled in a three colors. The reaction also contains an amplifiable and a non-amplifiable internal control to guarantee reliability and a proprietary reagent is included to ensure primer specificity throughout amplification. A large number of strains that harbor various combinations of alleles in the 1st line (*inhA, katG, rpoB*); 2nd and 3rd line (*gyrA, gyrB*, *eis, and rrs1401*) gene targets are being analyzed using this assay in order to generate a library of fluorescent signatures that can distinguish all drug resistant mutations from H37Rv, a drug sensitive reference strain, as well as from each other. Each strain containing a variant sequence displays its own fluorescent signature in the appropriate color within the temperature range assigned for binding of the relevant probes. 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. Subsequently the assay will be tested on 1000 blinded DNA samples isolated from clinical specimens, as well as 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. We are now evaluating this kit in collaboration with Hain Lifescience for the detection of drug resistance in smear positive and smear negative specimens.

Pyrazinamide (PZA) forms part of the front line anti-tuberculosis (TB) treatment regime along with rifampicin (RIF); isoniazid (INH); and ethambutol (EMB). PZA forms an integral cornerstone of this treatment regime due to its unique ability to target persister cells. However, routine drug susceptibility testing for PZA is not done due to technical challenges; including false positivity related to the acidity of the media, inoculum size and the critical concentration used. It is understood that single nucleotide polymorphisms (SNPs) in the *pncA* gene are the primary mechanism of resistance to PZA. To further our current outstanding of the genetic basis of PZA resistance we used a targeted DNA sequencing approach to identify SNPs in the *pncA* gene. In order to relate genotype to phenotype, resistance was also determined using the BACTEC 960 PZA DST. To date a cohort of INH mono-resistant; RIF mono resistant; and multi-drug resistant TB (MDR-TB) isolates from South Africa have been characterised. An excellent correlation between genotype and phenotype was observed, however this study did identify (SNPs) which conferred resistance at a lower concentration of PZA. This information will inform the interpretation of rapid molecular assays to ensure that PZA susceptibility is accurately defined. This is vital for the tailoring of MDR-TB treatment regimens, drug resistance surveillance and for clinical trials aimed at developing treatment shortening regimen which include PZA.
We have identified a number of large deletions of the pncA gene. These deletions makes it impossible to PCR amplify the region and thus predict drug resistance. This is of particular importance, since the deletion will mean that the M. tuberculosis strain will be resistant, but amplification failure will interpreted as a negative isolate. Currently these deletions identified are being validated and a manuscript are in preparation to raise awareness of this potential cause of drug resistance and reason for false negative results in molecular drug resistant diagnostics.

Another project aims to establish a method for the isolation and identification of DNA binding proteins in *M. tuberculosis*. To achieve this, DNA binding proteins are cross-linked to DNA and captured onto a solid matrix. Following, on-matrix tryptic digestion the DNA binding proteins are identified using mass spectrometry. We propose calling this method Chromatin Immuno-precipitation - Protein Mass Spectrometry (ChIP-PMS). Preliminary data obtained using *M. smegmatis* confirmed that our method selectively enriched for proteins known to be bound to DNA including the RNA polymerase complex as well as other expected proteins such as ribosomal proteins, other RNA associated proteins and proteins required for energy metabolism (i.e. providing energy for replication and transcription). We are in the process of validating the reproducibility of the ChIP-PMS method. This method will be used to study changes that occur in the regulome when *M. tuberculosis* is cultured under different environment conditions for example, antibiotic exposure and hypoxia. We believe that the identification of proteins that are associated with DNA in *M. tuberculosis* will enable the identification of novel drug targets that have the potential to improve treatment outcomes.

We have collected all drug resistance *Mycobacterium tuberculosis* strains in the Western Cape since 2001 and this has become an immensely rich source for various different ongoing studies. A database with routine lab data and genotyping data of the strains and Strain bank currently has more than 27000 isolates. This database and strain bank was instrumental in a molecular epidemiological study to compare different time windows of the XDR TB epidemic. We are retrospectively studying the XDR TB epidemic in the Western Cape Province from 2006, when the first outbreak of XDR-TB was reported in KwaZulu-Natal. We are assessing how the strain population has changed and the impact of treatment regimens on the epidemic over time. We have extensively mined the database to be able to accurately determine transmission/acquisition of resistance of XDR-TB. This study will lay the foundation for future Molecular Epidemiology studies of XDR-TB.

In terms of Heteroresistance in *Mycobacterium tuberculosis* we have identified *Mycobacterium tuberculosis* isolates with heteroresistance to various drugs including Rifampicin. Furthermore, we have also identified isolates that are resistant to Rifampicin, but no mutation has been identified by Sanger sequencing. In collaboration with UCSF we were able to identify underlying resistance/susceptible strains by Deep Sequencing, since the current molecular diagnostics and Sanger sequencing will not detect the underlying strains less than 10% of the population.

The admixed South African Coloured population has a high incidence of TB. Computational and statistical techniques were applied to a large case-control genotypic data set to generate hypotheses regarding genetic factors that underpin TB progression. A panel of ancestry informative markers was developed for the complex admixture in the population and the importance of adjustment for ancestry in association studies demonstrated. The role of gene-gene interactions was investigated, and validated in a cohort from The Gambia. Genome-wide admixture mapping was used to identify regions of the genome that harbour novel TB susceptibility genes.

Identifying novel susceptibility genes against the backdrop of a complex disorder is challenging and we have therefore started investigating individuals who have Primary Immunodeficiency Disorders (PIDDs) in which one of the primary features is increased TB susceptibility. We hypothesise that identifying the mutations in these individuals, will provide us with novel candidate genes to test for association with TB susceptibility in the general public. To date, we have sequenced the exomes of 10 PIDD-affected individuals and their available family members to identify these disease-causing genes. In addition, we have been able to provide a genetic diagnosis for a number of PIDD patients.

We investigated how the human leukocyte antigen (HLA) class-I molecules, which have T cell antigen presentation capabilities and influence NK cell activity, impact *Mycobacterium tuberculosis* strain susceptibility in a South African population. We showed that the Beijing strain occurred more frequently in individuals with multiple tuberculosis (TB) disease episodes, and the HLA-B27 allele lowered the odds of having more than one disease episode. Associations were also identified for specific HLA types and disease caused by the Beijing, LAM, LCC, and Quebec strains. In addition, HLA types were associated with disease caused by strains from the Euro-American or East Asian lineages, and the frequencies of these alleles in their sympatric human populations identified potential co-evolutionary events between host and pathogen.

We investigated disease-specific biomarkers of childhood TBM in a cohort of children aged 3 months-13 years with symptoms and signs suggestive of meningitis. Cerebrospinal fluid (CSF) and serum from 56 patients with

and 55 patients without TBM were assessed for 28 soluble mediators. Unsupervised hierarchical clustering analysis revealed a disease-specific pattern of biomarkers for TBM relative to other types of meningitis. A biomarker-based diagnostic prediction model for childhood TBM based on CSF concentrations of interleukin 13, vascular endothelial growth factor, and cathelicidin LL-37 is presented with a sensitivity of 0.52 and a specificity of 0.95. These data highlight the potential of biosignatures in the host's CSF for diagnostic applications and for improving our understanding of the pathogenesis of TBM to discover strategies to prevent immunopathological sequelae.

The host immune and endocrine systems are tightly linked and it has been shown recently that endocrine alterations occur during infection with *Mycobacterium tuberculosis* (Mtb) as well as during active tuberculosis (TB) disease. Our study evaluates hormonal changes in patients newly diagnosed with TB before, during and at the end of successful treatment and establishes the relative contribution of endogenous hormones to immune modulation and mycobacterial killing.Blood plasma was collected at diagnosis, week 4 and month 6 from 27 successfully cured patients and 10 patients who failed standard TB treatment. Luminex bead array assay or ELISA were used to quantify Leptin, Ghrelin, Amylin, Cortisol, T3, T4, Estradiol, Progesterone, Adiponectin, Growth Hormone, Dehydroepiandrosterone (DHEA) and Testosterone. The differences in hormone levels particularly cortisol between the two outcome groups and significant changes of hormone levels during treatment which correlated to serum immune markers. We then assessed the ability of these hormones *in vitro* to directly alter cytokine production and mycobacterial growth inhibition in peripheral blood monocytes with and without T-cells of healthy individuals latently infected with Mtb. We could show that immune activation during active TB is associated with an endocrine dysregulation and that several hormones can directly alter monocyte and/or T cell function and thus mycobacterial growth inhibition. A manuscript of this work is currently prepared for submission to an international journal.

In collaboration with UCT, UWC; Univ Texas, and Univ Zurich we have investigated optimising drug exposure in tuberculosis treatment regimens to minimise selection of drug resistance. Reassessing of breakpoints for drug susceptibility testing of anti-tuberculosis drugs indicated that the current critical concentrations used for drug susceptibility testing may lack the ability to detect strains within a predominant wild-type population that have acquired mutational resistance. Research has also been conducted to evaluate a TB resistance line probe assay for rapid detection of genetic alterations associated with drug resistant *M. tuberculosis* strains. These investigations have improved our knowledge and capacity to better understand the complexity of TB treatment which is important to make informed decisions regarding dosing recommendations. These findings provide important information that could be used to influence TB treatment strategies which is essential to prolong the life span of existing and new anti-TB drugs and to minimise the emergence and spread of drug-resistant strains.

We have shown for the first time that some artemisins are active against *M.tb*, a project in collaboration with North-West University and the MRC. We have tested novel drugs against Gyrase B of *M.tuberculosis* which has led to a research publication in an international scientific journal. 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. These findings also include whole genome sequence analysis of *M. bovis* BCG lacking glutamate dehydrogenase which identified a putative single nucleotide polymorphism unique in the protein kinase H gene. PknH is involved in the signal cascade to combat nitrosative stress and induce dormancy in mycobacteria. The results implicate that catabolic glutamate dehydrogenase conveys resistance to nitrosative stress in mycobacteria. We investigated the role of the genes involved in ERG biosynthesis in relation to the level of ERG, and mutants bearing deletion in each gene involved in ERG biosynthesis were generated in CDC1551. The sensitivity to current anti-tuberculosis drug of these strains was not altered.

A major focus of the Veterinary Immunology group has been the discovery and validation of novel diagnostic biomarkers of bovine TB in African buffaloes. Following a screen of candidate plasma cytokines, the proteins IP-10 and MCP-1 were identified as novel markers of particular interest and are currently under further investigation. In pilot studies, IP-10 was shown to increase the sensitivity of conventional interferon-gamma

release assays in buffaloes and to have at least a similar sensitivity to such assays in cattle. The cattle work was done in partnership with a new collaborator at University College Dublin, Ireland. Other work concluded in the past year was a pilot study evaluating new commercially available cattle assays for BTB in buffaloes. This study has been expanded into a larger and more comprehensive program which will be initiated this year.
In the last year the Veterinary group has also expanded its focus on TB in lions. The development of a diagnostic assay for TB in this species was completed and this test validated in a cohort of *M. bovis*-infected and -uninfected animals. This test will now be used to screen a set of banked plasma samples obtained from over 100 lions from the Kruger National Park. Other progress by the Veterinary group includes investigation of humoral responses to TB in a variety of wildlife species including buffaloes, lions, white rhinoceroses, and meerkats. Preliminary results show that serological assays may be useful adjunct tests for detecting infection and disease. Research is being expanded to include serological assays for screening additional species such as warthogs and kudus. Examining cell-mediated and humoral host responses to TB in wildlife will provide increased understanding of pathogenesis and new tools for epidemiological studies. In collaboration with researchers from the Royal Veterinary College in the UK, the Veterinary group is investigating new methods of detecting TB in Kalahari meerkat populations. Assays for cytokine production, gene expression, and humoral responses have been developed and demonstrate differences between TB-infected and uninfected animals.

In terms of funding awards, Rob Warren was awarded two MRC flagship subcontracts to work together with MEDUNSA and UCT on an RCT to investigate the usefulness of a new MDR-TB treatment regimen as well as to study the immunology of TB at the site of the disease. Gerhard Walzl served as principal investigator on two multi-site Bill and Melinda Gates Foundation funded projects and two EDCTP projects, as well as co-investigator on another BMGF grant and an FP7 grant, on NIH and Wellcome Trust grants. He was awarded a DST/SHIP bioinformatics grant to develop TB biomarker bioinformatic capacity in SA. and was awarded a SARChI chair in TB biomarkers. Two other SARChI chairs were awarded to Stellenbosch University by the NRF, one to Prof Samantha Sampson, who took up her post in late 2013. The other to Prof Michele Miller, who took up her post in January 2014. During the course of the past year Prof Miller has secured funding from the American Association of Zoo Veterinarians as well as the Wildlife Disease Association.

UCT Node

In a major study published in December 2014 in *Chemistry & Biology*, UCT node researchers, led by Dr. Vinayak Singh and Prof. Valerie Mizrahi, together with MM4TB collaborators led by Prof. Katarína Mikušová from Comenius University in Bratislava, demonstrated that 5-fluouracil (5-FU) has a particularly complex mechanism of antimycobacterial, targeting four different pathways in cellular metabolism. Phenotypic approaches which harness the power of post-genomic technologies are playing a pivotal role in identifying small molecules that display whole-cell activity against *M. tuberculosis* and can be used as chemical probes to discover new drug targets and reveal metabolic vulnerabilities in this formidable human pathogen. In this study, we used a combination of chemical genetics, trace metabolite labelling, macromolecular incorporation assays and protein biochemistry to investigate the mechanisms of resistance and action of 5-FU, a compound that has been in use for more than five decades as an anticancer drug and whose antibacterial activity has been well documented. In this paper, we show that metabolism of 5-FU to FUMP constitutes the first and only route of activation of this pro-drug, consistent with deficiencies in the pyrimidine salvage pathway of Mtb. Resistance of Mtb to 5-FU is mediated either by mutations in *upp* that abrogate FUMP production, or by mutations in *pyrR* that impair the repressor function of the pyrimidine regulator and result in overproduction of UMP through *de novo* biosynthesis, which rescues the cell from the toxic effects of downstream metabolites of 5-FU. These include uracil mimetics that were shown to act on cell envelope biogenesis, RNA synthesis, DNA synthesis and thymidylate synthesis. While modest hypersensitisation conferred by conditional depletion of the flavin-dependent thymidylate synthase, ThyX, implicated ThyX inhibition in the mechanism of action of 5-FU, the inhibition of mycolyl arabinogalactan peptidoglycan is likely to constitute the principal mechanism of bactericidal action of this drug.

A rigorous genotypic and phenotypic characterization of a suite of conditional mutants in essential steps in the coenzyme A biosynthetic pathway was completed as key step towards the identification and validation of novel anti-tubercular drug targets within this pathway. Emphasis over the past year was focused on assessing the impact of transcriptional silencing of the *panB*, *panE*, *panK*, *coaBC*, *coaD* and *coaE* genes on the viability of *M. tuberculosis*. Interestingly, *coaBC* silencing was found to be uniquely bactericidal in *M. tuberculosis* in vitro. In

collaboration with Prof. Dirk Schnappinger and Sabine Ehrt at Cornell University, *coaBC* silencing was also shown to result in rapid loss of viability of *M. tuberculosis* during both acute and chronic infection in mice. Current emphasis is focused on using mass spectrometry to investigate the relationship between transcriptional silencing, protein depletion and viability of *M. tuberculosis*. The large panel of conditional mutants generated in the UCT node has provided an important resource for ranking target in terms of vulnerability and kinetics of cell death upon target depletion *in vitro*, *ex vivo* and *in vivo*. This work has attracted significant interested within the TBDA and has led to the establishment of two new collaborations to rapidly advance drug discovery efforts focused on CoaBC.

Outstanding progress has been made on establishing a TB drug screening facility at UCT under the auspices of the UCT node and the MRC/NHLS/UCT Molecular Mycobacteriology Research Unit, in collaboration with the H3-D Centre for Drug Discovery and Development. This facility provides a critically important platform for the supporting the large suite of drug discovery projects underway in the UCT node and is also used by the SHIP unit of the MRC as a national facility for small-molecule screening for anti-tubercular agents provided by laboratories from across the country. Over the past year, the TB screening facility has achieved several key milestones including the validation and use of a Hamilton *STARlet* automated liquid handler for primary screening of all compounds and extracts; the establishment of a fully computerized, quantitative platform for determination of anti-mycobacterial inhibitory activity and storage of MIC analyses on the CDD database; the development by PhD student Ms. Krupa Naran and postdoctoral fellow, Dr. Atica Moosa, of bio-reporters for rapid early detection of genotoxic and cell wall-damaging agents; and the construction and genotypic confirmation by Dr. Moosa of *M. tuberculosis* mutants for early assessment of inhibition of promiscuous targets. All of these assays have now been incorporated into the standard screening and biology triage algorithm in the UCT facility and, moreover, have been made available within the TBDA as part of a set of assays for hit triage developed within the HIT-TB consortium in collaboration with Drs. Clifton E. Barry II and Helena Boshoff (NIAID). As a result of these developments, the TB drug screening platform at UCT – of which these assays are essential components – is entering a phase of rapid growth in terms of the number of compounds/extracts that we will be screening. The facility currently screens ~500 compounds/extracts per week, including re-screens and counter-screens. We have received ~120 priority TB "actives" sourced from across all TBDA participant sites, and will continue to receive selected compounds for analysis in the reporter assays. We have established a sizeable international (University of Lisbon) and local (Rhodes University, North West University, University of Limpopo) network of chemistry research groups who supply compounds for assay against *M. tuberculosis*. We have begun to expand into natural product extracts and compounds, with partnerships internationally (Helmholtz Institute for Pharmaceutical Research Saarland, Germany) and locally (Rhodes University, University of the Western Cape). All of these are in addition to the compounds we continue to receive from established local (H3-D, UCT Chemistry) and international (HIT-TB) sources for both primary and SAR screens, as well as downstream analysis of identified actives. We have made significant progress in the rapid set-up and automated analysis of 2D and 3D combination screens, and these are scheduled for introduction as standard assays within the next 6-12 month period. In summary, the UCT facility has now assumed a position as the centre of choice for anti-TB screening and preliminary biology assessment in South Africa and, simultaneously, has established small but highly significant role within the TBDA.

Significant progress was made on a study that aimed to elucidate the structure-function relationships determining the differential fidelities of the *dnaE1*- and *dnaE2*-encoded mycobacterial PolIIIα subunits under conditions of genotoxic stress. To this end, PhD student Zanele Ditse explored the role in DnaE1 intrinsic fidelity of highly conserved PHP domain residues by site-directed replacement of targeted amino acids, resulting in a panel of *Mycobacterium smegmatis* mutants carrying selected *dnaE1* alleles. A complementary approach investigated the contribution of the mycobacterial proofreading DnaQ subunit homolog to the maintenance of DnaE1-dependent replicative fidelity by generating a targeted *dnaQ* knockout mutant. The third component of this study focused on the inferred role of a highly-conserved N-terminal extension and C-terminal pentapeptide motif in the function of the alternative, error-prone DNA PolIIIα subunit, DnaE2. Replacement of wild-type *dnaE1* with mutant *dnaE1*^{E133A} and *dnaE1*^{D228N} alleles resulted in reproducible increases in the spontaneous mutation rate of 3-fold and 10-fold, respectively. This result confirmed the predicted role of highly conserved PHP-domain residues in DnaE1 intrinsic fidelity and, significantly, provided the first evidence of mutator alleles in mycobacteria. A reproducible, but not significant, loss in fidelity (~1.4-fold increase in mutation rate) was observed for a *dnaQ* knock-out mutant compared with the wild-type strain; moreover, DnaQ was shown to be dispensable for DNA damage-induced mutagenesis and damage tolerance. In contrast, a second *dnaQ* homolog, *dnaQ-uvrC*, which comprises an N-terminal 3'-5' exonuclease domain and a C-terminal

UvrC-like endonuclease domain, was shown to be required for DNA damage survival, suggesting a role in SOS-mediated DNA repair. Finally, targeted deletion of conserved N- and C-terminal regions in DnaE2 had no effect on DNA damage tolerance or induced mutagenesis, indicating that these domains are not crucial for the function of the error-prone polymerase under conditions of genotoxic stress. In summary, these results reinforced the notion that the mycobacterial replisome differs in key respects from the well-characterised *E. coli* model, and so urge further work to elucidate the composition and regulation of the protein complex which governs DNA replication and repair in a major human pathogen.

In other publication highlights from the UCT node, Profs. Digby Warner and Valerie Mizrahi published an editorial in the *New England Journal of Medicine* that accompanied the publication of three papers reporting the outcomes of phase 3 clinical trials of fluoroquinolone-containing regimens for the treatment of tuberculosis. They also published a review article in *Trends in Microbiology* which explored the topic of diversity and disease pathogenesis in *M. tuberculosis* and together with doctoral student Ms. Anastasia Koch, they also published a review article in *Genome Biology* on the prospects for translating genomics research into new tools for tuberculosis control. Published online on 7 November 2014, this article has been designated as "Highly Accessed" having been accessed 4629 times since publication. Prof. Warner published a chapter entitled, "*Mycobacterium tuberculosis* metabolism" in the book, "Tuberculosis", a subject collection from the Cold Spring Harbor Perspectives in Medicine, edited by Stefan H.E. Kaufmann, Eric J. Rubin and Alimuddin Zumla.

Wits Node

The research portfolio of the Wits node is focused on identification and validation of new drug targets for TB. The major emphasis is on remodelling of the mycobacterial cell wall during growth and pathogenesis. For this, the Wits node has undertaken an extensive analysis of enzymes that hydrolyze different bonds in the peptidoglycan using an integrated computational biology, bacterial genetics and biochemical approach. 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 Wits node is currently involved in further studying these aspects in mycobacteria. Another prominent area of research involves the identification and characterization of differentially culturable tubercle bacteria 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.

Outstanding progress was made on various projects aimed at further understanding cell wall remodelling. *N*-Acetylmuramoyl-L-alanine amidases (amidases) are a group of peptidoglycan degrading enzymes that have been implicated in the final stages of daughter cell separation during cell division. In addition, these enzymes are involved in remodeling of the cell wall during stress conditions in other organisms. Their role in mycobacteria has remaining largely unexplored. The Wits node has studied two amidase homologues in *M. smegmatis* and identified a single, essential amidase (MSMEG_6935 – Ami2), which could serve as a novel drug target in *M. tuberculosis*. Single-cell time-lapse microscopy demonstrated that depletion of Ami2 results in immediate cessation of cell elongation, followed by cell death. Deletion of another amidase (MSMEG_6281 – Ami1) leads to the formation of cellular filaments. Cellular localization studies revealed that Ami1 localizes in punctate foci along the lateral axis of the mycobacterial cell, in a manner that has not been reported for any amidase in bacteria. Conversely, Ami2 localizes to the cell pole and in most cases, localization is only observed on one pole, a pattern which is retained for localization of Ami2 in the Δ*ami1* mutant. Moreover, formation of new FtsZ contractile rings continues in Δ*ami1* mutant cells, which are blocked for replication. In some cases up to three rings form in one cell. Collectively, these data describe non-redundant and essential roles for mycobacterial amidases in cell division and growth. In a second related project, the role of DD-Carboxypeptidases (DD-CPases), which are proposed to play an important role regulating biosynthesis of cross-linked peptidoglycan in bacterial cells, was explored. Work at the Wits node entailed characterization of these enzymes as potential drug targets. A comparative genomics analysis of these and other peptidoglycan degrading enzymes in 19 mycobacterial species was conducted and demonstrated a notable level of redundancy for each class of enzyme. These data were published in 2014. *M. tuberculosis* and *M. smegmatis* encode 3 and five distinct DD-CPase homologues and it was demonstrated that depletion of *dacB* in the latter, using two distinct approaches, resulted in reduced PG synthesis at one growth pole with a decrease in cell size, presumably due to loss of bipolar growth. Consistent with this, abnormal bends/distortions developed on

cell poles as a result of *dacB* depletion. Increased expression of *dacB* led to a higher frequency of longer of cells, suggestive of a role in maintaining cellular shape. In addition, deletion of more than one DD-CPase homologue leads to defects in cell morphology, whilst overexpression results in a 3-8 fold increase in growth rate. These and other related effects are being explored currently. The third component of peptidolgylcan remodelling research at the Wits node involves analysis of resuscitation promoting factors (Rpfs), which are a group of peptidoglycan degrading enzymes that have been implicated in stimulating the growth of dormant bacteria. They are of particular interest as they have been postulated to modulate growth of *M. tuberculosis*, thereby promoting reactivation of infection in individuals that harbor latent tuberculosis infection. In this regard, studies at the Wits node demonstrated that deletion of *rpfB* in *M. smegmatis* leads to an overall reduction in cell length and collective deletion of *rpfA* and *rpfB* results in colony morphology defects and in the inability to form mature, ruffled biofilms. In addition, continuous production of Rpfs is required to maintain the structure of mycobacterial biofilms, suggesting that paracrine signalling is essential in these processes.

In a project that involved all three nodes of the CBTBR, enzymes involved in molybdopterin-cofactor (MoCo) biosynthesis in *M. tuberculosis* were studied. Previous work from the CBTBR demonstrated that MoaX, a novel fused molybdopterin synthase is cleaved into two constituent components. In current work, a collaboration between the Wits and UCT nodes, the cleavage of MoaX was confirmed along with the demonstration that this processing is essential for catalysis and that incorrect post-translational processing results in the formation of a defective enzyme. MoCo can be converted to *bis*-molybdopterin guanine dinucleotide (*bis*-MGD) through the activity of a guanylyltransferase, MobA. A collaborative study, between all three nodes of the CBTBR and international investigators, demonstrated that *bis*-MGD production is required for assimilatory and respiratory nitrate reductase activity in *M. tuberculosis* and that loss of this form of MoCo results in no survival defects in human monocytes or mouse lungs but leads to reduced persistence in the lungs of guinea pigs. These findings on MoCo biosynthesis were compiled into two manuscripts, both of which were accepted for publication in 2014.

The Wits node is also involved in TB drug development efforts with a specific focus on developing 4 distinct counter-screening models to assess new compounds emerging from local drug development initiatives. The overall approach is geared towards the production of drug tolerant organisms that could be used to identify compounds that selectively inhibit replicating and non-replicating bacteria. Previous efforts resulted in development of two preliminary screening models that resulted from growing bacteria under carbon starvation conditions or in floating biofilms. In 2014, the carbon starvation model was refined by optimizing plate format and other technical issues to control for evaporation, pipette error, operator bias. These efforts led to the development of a streamlined protocol, which was used to test a select group of compounds from the H3D Drug Discovery and Development Centre at UCT. Further refinements to the biofilm model were also made in addition to the development of new screening model based on hypoxic growth.

The maintenance of genomic integrity during infection is critical for controlling mutation rates and the emergence of drug resistance variants in *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. The functionality of the mycobacterial Nth homologue was confirmed followed by the demonstration that deletion of *nth* resulted in increased UV-induced mutagenesis and combinatorial deletion with the Endonuclease VIII homologues resulted in reduced survival under oxidative stress conditions and an increase in spontaneous mutagenesis to rifampicin. These data confirm a role for Nth in BER and mutagenesis in mycobacteria. In a second study, the combined role of MutY and the Formamidopyramidine (Fpg/MutM) DNA glycosylases was investigated where it was 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.

The rollout of GeneXpert in South Africa and globally required the establishment of verification and quality assurance systems. The Wits node 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 2013, the CBTBR provided for greater than 80% of the global demand for verification material. In 2014, the Wits node continued to produce and supply reagents for quality assurance of new GeneXpert units placed

throughout South Africa and supported the establishment of routine TB testing in prisons and several mining sites. In addition, the verification material produced by the Wits node for the CBTBR has received full WHO endorsement and has been rolled-out in 22 countries for use in instrument verification. These efforts are now being commercialized through the development of a company that will be spun out of Wits Enterprise.

The Wits node initiated a project in 2012 that was aimed at identification of differentially culturable tubercle bacteria (DCTB) in the sputum of patients with active TB disease through supplementation of sputum cultures with culture filtrate, from *M. tuberculosis*. This project has been underway for two years and recruitment has been intensified in the last 18 months. The findings of this study revealed that both HIV infected and uninfected patients with active pulmonary TB disease at baseline retained a detectable proportion of DCTB, which were enumerated using the most probable number (MPN) assay. Comparisons between these two groupings for HIV status, CD4 count, and various laboratory diagnoses revealed no significant differences. In two distinct follow up studies the bacillary sputum burden – measured by four readouts – in HIV-infected and uninfected adults was determined during the course of TB treatment. The results thus far revealed comparable declines in colony forming units and time to positivity on MGIT between smear positive and smear negative individuals. Furthermore, it was confirmed that the GeneXpert cycle threshold is a poor proxy for treatment response in smear negative individuals.

Joint Research and Training Activities

1. **UCT-Wits-SU.** The project on the biosynthesis and function of molybdopterin in mycobacteria is a strong collaboration between the three nodes. This resulted in a publication in *Infection & Immunity* involving researchers from all three nodes as well as international collaborators from UMDNJ and the University of Colorado. This paper was selected by the editors of this journal as being of significant interest and was thus featured on IAI Spotlight. All these nodes have been involved and worked together in the search for new candidate TB antibiotics.

2. **SU-UCT.** Prof. van Helden and Prof. Mizrahi are co-PIs on the ACTG/IMPPACT International TB Specialty Laboratory (PI: Prof A Diacon, SU)

3. **Wits-SU**. Prof Rob Warren and Dr Lizma Streicher sent in vitro mutatnts resistant to either fluoroquinolones or aminoglycosides were sent to Prof Kana for development of a standardized panel for the evaluation of the performance of the MTBDRsl line probe assay as well as other assays under development. In addition, an isolate with an rpoB 533 mutation was sent to Prof Kana to enhance his culture panel for quality control of the Xpert MTB/RIF

2. Education and Training

Breakdown of postgraduate students and postdoctoral fellows in the CBTBR in 2014

Student category	Number/percentage	Target based on SLA4 (for Extension Phase, 2014-2018)
Total number of students	89	≥ 35
% Postdoctoral fellows	24%	≥10%
% PhD students	33%	N/A
% MSc students	26%	N/A
% BSc (Hons) students	17%	N/A
% Women students[a]	57%	≥ 50%
% Black students[a]	50%	≥ 50%

a) Includes postdoctoral fellows

Degrees conferred and postdoctoral fellowships completed

The CBTBR graduated 6 PhD, 7 MSc and 15 Honours students in 2014.

Dissertations and theses

PhD

1. Dippenaar A. A phylogenomic and -proteomic investigation into the evolution and biological characteristics of the members of the Group 2 Latin-American Mediterranean (LAM) genotype of Mycobacterium tuberculosis. Promoter: Prof NC Gey van Pittiius. Co-Promoter: Prof RM Warren
2. Fang Z. Structural and functional studies of Mycosin-3, and essential sybtilisin-like serine protease in mycobacterium tuberculosis. Promoter: Prof NC Gey van Pittiius. Co-Promoter: Prof RM Warren
3. Essone Ndong P. Development of immune-based TB tests suitable for resource limited settings. Promoter: Prof G Walzl
4. Salie M. The role of the major histocompatibility complex and the leukocyte receptor complex genes in susceptibility to tuberculosis in a SA Population. Promoter: Prof E Hoal. Co-Promoter: Dr M Moller
5. Macingwana L. Investigation of the activity of sulfonamide anti-bacterial drugs in *Mycobacterium tuberculosis* and the role of oxidative stress on the efficacy of these drugs. Promoter: Prof. IJF Wiid. Co-Promoter: Dr B Baker
6. Le Roex N. Host genetic factors in susceptibility to mycobacterial disease in the African buffalo, *Syncerus caffer*. Promoter: Prof E Hoal. Co-Promoters: Prof Paul van Helden, Assoc Prof Ad Koets

MSc

1. Rabie U. Contribution of the Placenta to the diagnosis of congenital tuberculosis. Promoter: Prof CA Wright. Co-Promoters: Prof RM Warren, Dr KGP Hoek, Dr A Bekker
2. Pule C. Defining the role of efflux pump inhibitors on anti-TB drugs in rifampicin resistant clinical *Mycobacterium tuberculosis* isolates. Promoter:Prof TC Victor Co-Promoters: Dr G Louw, Prof RM Warren
3. Du Plessis J. Deciphering the impact of rpoB mutations on the gene expression profile of *Mycobacterium tuberculosis*. Promoter: Prof TC Victor Co-Promoter: Prof RM Warren
4. Botha L. Characterizing the proteomes of selected members of the Mycobacterium tuberculosis complex. Promoter: Prof RM Warren; Co-Promoter: Prof Nico Gey van Pittius
5. Mpongoshe V. Gene expression changes in macrophages infected with pathogenic *M. tuberculosis* and non-pathogenic *M. smegmatis* and *M. bovis* BCG. Promoter: Dr B Baker. Co-Promoter: Prof. IJF Wiid.
6. Ehlers L. Investigation of the molecular mechanisms of immune modulation by the contraceptive Medroxyprogesterone acetate (MPA) on immune responses to mycobacteria. Promoter: Dr K Ronacher
7. Thiart L. Evaluation of micro RNA expression profiles during BCG infection in the presence and absence of endogenous and synthetic steroids and possible implications on the host immune response to the pathogen. Promoter: Prof G Walzl, Co-Promoter: Dr N Chegou

Recruitment of new postgraduate students

A number of new students have joined the team already or will do so during the course of 2014. 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 7 Postdoctoral fellows, 3 PhD students, 4 MSc students and 14 Honours students into the CBTBR in 2014. At the UCT node 2 MSc students and 1 Honours student were recruited. At the Wits node 1 PhD student and 2 MSc students were recruited in 2014.

Honours and awards to students

- Mr. Sibusiso Senzani, PhD student from the Wits node was selected from ca 500 presenters at the 4th South African TB Conference to receive the first prize for the Discovery Health Clinical Excellence Award.
- Mr. Sibusiso Senzani won the prize for best poster presentation by a student at the biennial Wits Health Sciences Research Day
- Mr. Ditshego Ralefeta, MSc student at the Wits node won third prize for his poster presentation at the Wits Molecular Biosciences Research Thrust Symposium
- Mr. Sibusiso Senzani won the first prize for best oral presentation at the Wits Molecular Biosciences Research Thrust Symposium

- Ms. Zaahida Sheik Ismail, MSc student from the Wits node won first prize for the best poster presentation from the Faculty of Health Sciences at the Wits Cross-Faculty symposium.
- Mr. Sibusiso Senzani won first prize for the best oral presentation from the Faculty of Health Sciences at the Wits Cross-Faculty symposium. Mr. Senzani then went on to compete across all Faculties and won the prize for best research across all faculties at Wits University.
- Dr. Krishnamoorthy Gopinath won the University of Cape Town (UCT) Faculty of Health Sciences Prize for Best Publication (Basic Laboratory Sciences) in 2013 by a Young Investigator for his paper entitled "A vitamin B_{12} transporter in *Mycobacterium tuberculosis*" published in *Open Biology* in 2013.
- MSc student Zela Martin was nominated to attend the 65th International Nobel Laureate Meeting, Lindau, Germany and has progressed through to the final round [Notification that her nomination was successful was received in March 2015]. She was also awarded a prestigious 2015 David and Elaine Potter Fellowship for her doctoral studies at UCT
- MSc student Michael Reiche was awarded a NRF Scarce Skills Masters bursary
- Malherbe F.Awarded the prize for best oral presentation at the Congress. September 2014 – South African society of Nuclear Medicine Congress, Durban
- Michael Whitfield was awarded a NRF Travel Award, and a Faculty Travel Award in 2014
- Nastassja Steyn was awarded a NRF Grant Holders Bursary, and a Merit Bursary Stellenbosch University in 2014
- Anzaan Dippenaar was awarded a Claude Leon Foundation Postdoctoral Fellowship in 2014
- Marisa Klopper was awarded a SACEMA Doctoral scholarship in 2014
- Tashnica Olivier was awarded a NRF Grant Holder Bursary (SARChI Animal TB) in 2014
- Charlene Clarke was awarded a NRF Grant holder Bursary (SARChI Animal TB) in 2014
- Ruben van der Merwe was awarded a Faculty travel award in 2014
- Margaretha de Vos was awarded a Faculty travel award in 2014
- Jomien Mouton was awarded a Mary Veenstra prize for best student poster presentation at the Microscopy Society of South Africa's Annual Conference in 2014
- Jomien Mouton was awarded a NRF Grant Holder-linked Bursary (SARChI Mycobactomics) in 2014
- Lara Meyer was awarded a NRF Grant holder Bursary (SARChI) in 2014
- Lizma Streicher was awarded a Bill and Melinda Gates foundation keystone travel scholarship to Keystone symposium, Keystone, Colorado in 2014
- Melanie Grobbelaar was awarded a Bill and Melinda Gates foundation keystone travel scholarship to Keystone symposium, Keystone, Colorado in 2014
- Lizma Streicher was awarded a NRF Research Career Advancement Award in 2014
- Monique Williams was awarded a NRF Research Career Advancement Award in 2014
- Juanelle du Plessis was awarded a NRF Innovation Doctoral Scholarship, Stellenbosch University Postgraduate Merit Bursary, and a WhiteSci Travel Award in 2014
- Caroline Pule was awarded a Singapore International Pre-graduate Internship Attachement Award (SIPGA),a WW ROOME Private Bursary, a Stella and Paul Lowenstein Charitable and Educational Trust, a National Scientific Travel Award from SU Research Development and Support Division (RDSD), a Distinguished Young SA Women Scientist Doctoral Fellowship, a Prestigious Rectors Award for exceptional excellence: succeeding against all odds, and a Prestigious National Health Scholarship Programme Award (NHSP) from SAMRC and DoH in 2014
- Suereta Fortuin was awarded a DRD travel award, and a Faculty travel award in 2014
- Philippa Black was awarded a NRF DST Innovation Doctoral Scholarship, a Merit Bursary from SU and an NRF Travel Award in 2014
- Zhuo Fang was awarded a NRF Grant-Holder Bursary in 2014
- Jesmine Arries was awarded a National Health Scholarship Programme (NHSP) Award - SAMRC in 2014
- Tiaan Heunis was awarded a DST NRF Innovation Postdoctoral Fellowship, a Faculty Travel Award and a Wellcome Trust Travel Bursary in 2014
- Danicke Willemse was awarded a NRF Innovation Doctoral Scholarship, a Ernst and Ethel Eriksen Bursary, and a Harry Crossley Research Grant in 2014

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.

Other Workshops

- Prof Warren was part of the organising committee for the XDR-TB Workshop, Cape Town, October 2014
- Prof Warren is part of the organising committee for the TB conference to be held in Durban June 2014.
- Presentation skills/conference communication skills workshop for postgraduates and scientists
  Prof Corfield developed this workshop and has fine-tuned it over the years of presentations. During 2014 she facilitated the workshop for several different audiences:
  Dept of Biomedical Sciences, FMHS, Stellenbosch University. BSc Hons students - February
  Foetal Alcohol Spectrum Disorder Research Unit, Stellenbosch University - February
  Research Development Stellenbosch University. Students and lecturing staff - May and November
  Postgraduate Research Office University of the Free State. Postgraduate students - July
  Research Africa Independent grants platform - February in Stellenbosch and August in Johannesburg

Training courses attended by staff and students

Attendees	Training Course	Location/Web address	Start Date	End Date
Kana B, Gordhan B, Peters J, McIvor A, Beukes G, Papadopoulos A, Chengalroyen M	Good Clinical Practice Course	University of Witwatersrand, Johannesburg, South Africa	7 Oct	8 Oct
van Coller P	Biostatistics Training Course	K-RITH, Durban, South Africa	26 May	30 May
Evans J, Singh V, Swart C, Fortuin S, Fang Z, Heunis T	IDM Masterclass on Mass Spectrometry	UCT, Cape Town, South Africa	14 Oct	16 Oct
Arries J, Heunis T, Fortuin S	5th ACGT Proteomics Workshop	Stellenbosch University, Cape Town, South Africa	15 Sep	17 Sep
Fortuin S	6th Max Planck Summer school	Bathesda, Maryland, USA	21 Jul	25 Jul
Hammond-Aryee K	African Doctoral Academy (introduction to SPSS)	Stellenbosch University, Cape Town, South Africa	23 June	27 Jun
Williams M	Article writing retreat (SU MERC programme)	Stellenbosch University, Cape Town, South Africa	29 Oct	30 Oct
Heunis T	Joint EMBL-EBI/Wellcome Trust Course: Proteomics Bioinformatics	Cambridge, United Kingdom	10 Nov	14 Nov
Arries J, Pule C	Mass Spectrometry Based Proteomics Practical Course	CAF, Stellenbosch University, Cape Town, South Africa	07 Aug	11 Aug
Arries J, Theys M	Mass Spectrometry of Small Molecules: LC-MS	Central analytical Facility, Stellenbosch University, Cape Town, South Africa	07 Jul	07 Jul
Olivier T	Short Course in Clinical Research Skills	Cape Town, South Africa	01 Jul	01 Jul
Williams M	SU Mentoring symposium	Cape Town, South Africa	19 Nov	19 Nov

Mouton J	Technical Forum on Microscopy, Microscopy Society of South Africa Annual Conference	Stellenbosch, South Africa	02 Dec	02 Dec
Warren RM	DOH Think tank	Sheraton Hotel	12 Mar	12 Mar
Borrageiro G, Boolay S, Olivier T, Hammond-Aryee K	Roche MIQE Gene Expression WORKSHOP	Stellenbosch University, Cape Town, South Africa	10 Jun	11 Jun
Glanzmann B	South African Human Genome Project Workshop 1 (Training in NGS analysis)	South African National Bioinformatics Institute UWC, Cape Town, South Africa	28 July	31 July
Glanzmann B, Ntsapi C	South African Human Genome Project Workshop 2 (Understanding and characterising Southern African genomes)	Sydney Brenner Institute for Molecular Bioscience (SBIMB), University of the Witwatersrand, Johannesburg, South Africa	28 July	31 July
Neethling A, Visser H, du Plessis J, Pule C, Arries J, Heunis T, Steyn M	EMBO Practical Course on Computational Analysis of Protein-Protein Interactions	Faculty of Health Sciences Barnard Fuller Building Anzio Road 7925, Cape Town, South Africa	29 Sep	03 Oct
Bardien S, Boolay S	NIH grant writing workshop	Stellenbosch University, Internal Medicine Division, Tygerberg, South Africa	15 Oct	16 Oct
Salie M, van der Merwe C	Confocal Microscopy Course	Central Analytical Facility, Stellenbosch, South Africa	16 Oct	17 Oct
van der Spuy GD	Bqyesian Statistics	Stellenbosch, South Africa	20 Oct	24 Oct
Lucas LA Kleynhans-Cornelissen L	Systems Biology of Disease Summer Course	Institute of Systems Biology, Seattle, USA	28 July	01 Aug
van der Spuy GD	Biostatistics with R	Div. Molecular Biology & Human Genetics, Cape Town, South Africa	08 Apr	30 Apr
van der Spuy GD	Project Management	Stellenbosch University, Cape Town, South Africa	23 July	23 July
Schlechter N, Daya M, van der Spuy G, McGregor N, Uren C, Banda E	Next Generation Sequencing Workshop	Seminar Room, Fisan Building, Stellenbosch University, Cape Town, South Africa	01 Oct	12 Dec
Schlecheter N, Steyn N	International Software Carpentry Workshop	UCT, Cape Town, South Africa	27 Nov	28 Nov
Schlechter N	Next Generation Whole Exome sequencing and bioinformatics data analysis	Institute for Clinical Molecular Biology at Christian Albrechts University of Kiel, Germany	15 Apr	19 Jun
Schlechter N	Next Generation Sequencing	Central Analytical Facility, Stellenbosch University, Cape Town, South Africa	9Jul	10Jul
Loxton AG, Muller L, Ronacher K,du Plessis N,Kleynhans L Ehlers L,Chegou N	GCLP	Presented by CLS, UCT, Cape Town, South Africa	13 May	15 May

Other capacity development activities

- Prof. Warner served as Coordinator of the "Cloning Techniques" module of the BSc (Med) (Hons) programme, Faculty of Health Sciences, UCT. Dr. Joanna Evans lectured, and PhD students Phia van Coller, Anastasia Koch, Zanele Ditse and Krupa Naran tutored 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. Dr. 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. Dr. Warner also lectured in this course.
- Prof. Warner lectured 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 2014 (ANAP7000).
- Prof. Kana delivered a two week lecture series on mycobacteria to the Honours Students in the Molecular Medicine and Haematology Department.
- Prof Warren and Dr Kinnear presented lectures on "Getting Published" as part of the Research Development training programme.
- Dr Kinnear served as the course coordinator for the "Molecular Biology" module of the SU Molecular Biology and Human Genetics Honours programme.

Exchange visits

- Doctoral student, Anastasia Koch was awarded a Fogarty AIDS and TB Training & Research Programme (AITRP) fellowship. This prestigious award funded a 3-month training visit to Prof Tom Ioerger's laboratory at Texas A&M University where she was trained in the application of bioinformatics tools for analyzing mycobacterial genomes.
- Dr. Joanna Evans undertook a three-month training visit to the laboratory of Drs. Barry and Boshoff at the NIAID as part of the HIT-TB project funded by a grant to Prof. Mizrahi. During this time, she developed methods for identifying and quantifying intermediates in the coenzyme A biosynthetic pathway, and applied these in analyzing the impact of conditionally regulating the expression of essential steps in the pathway.
- Mr. Sibusiso Senzani conducted a 1 month working visit at the Howard Hughes Medical Institute Janelia Research Campus, USA.
- Dr. Christopher Ealand conducted a 1 month working visit in the laboratory of Dr. Carolyn Bertozzi at the University of California Berkley, USA.
- Prof. Bavesh Kana, Dr. Bhavna Gordhan, Ms. Julian Peters, Mrs. Amanda McIvor, Mr. Germar Beukes, Ms. Andrea Papadopoulos and Dr. Chengalroyen attended a two day training course on Good Clinical Practice.
- Ms Nikola Schlecter visited the laboratory of Andre Franke at Institute for Clinical Molecular Biology, Christian-Albrechts-University in Kiel, Germany 15th April to 19th June where she was trained in whole exome sequencing (WES) data analysis.

Conferences/Symposia Organised (3)

- Prof. Kana served on the organizing committee of the Wits Faculty of Health Sciences Research 2014.
- Prof. Kana served as the overall Conference Chair for the 4th SA TB conference, ICC, Durban, 10-13 June 2014.
- 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.
- Prof. Mizrahi chaired the Ten-Year Anniversary Symposium of the IDM, UCT, Cape Town, 2-4 November 2014

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 numerous meetings 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 2014:

Public awareness, public engagement, and publicity

- Members of the Wits node participated in the Wits Cross-Faculty Open Day, November 2014. They created and manned an exhibit to profile the work done at the CBTBR.
- In March 14-15, Prof Kana served as a judge in the 2013 (to be awarded in 2014) 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 where presentations were made to the journalists with winning entries.
- Prof. Kana participated in the following interviews, *Television:* South African Broadcast Services – TB in South Africa (Morning live show); DSTV Channel 404 – TB (Health Talk show); *Radio*: South African Broadcast Services, Africa Channel – Panel interview on TB, Lotus FM – TB in South Africa (Desi Drive show), East Coast Radio – TB (Evening Talk show), Classic FM – TB in the mines (Classic Business & Politonomy show).
- Professor Kana Chaired a press conference with Minister Aaron Motsoaledi on Department of Health National Plan for TB control.
- Professor Kana Chaired a Press Briefing Session with representatives from the Treatment Action Campaign, Section 27 and Medecins Sans Frontieres advocacy groups on breaking down the barriers to treatment of MDR TB.
- Siamon Broadley (PhD student, UCT node) wrote a commissioned piece entitled, “Structural Biology – Why The Fuss?” for the Public Understanding of Biology - Young Science Communicators Writing Initiative, January 2014.
- Prof. Warner gave an invited talk on “What it means to be an academic in the 21st century” At the launch of the 2014 Carnegie Fellowship programme, UCT, 26 May 2014.
- Prof. Warner delivered an invited talk on “The changing nature of the role of the institution and challenges for supervisors with regards to research students” at a series of UCT Postdoctoral Supervision Training Retreats, Mont Fleur, Stellenbosch, 22nd-23rd January; 29th -30th May; 9th-10th June, 2014; and 23rd-24th October, 2014.
- World TB Day 2014. On World TB day, the Wits node of the CBTBR conducted an awareness campaign to raise the profile of TB disease in the public consciousness. CBTBR staff and students displayed chest X-rays on their upper bodies in an awareness campaign targeted at higher education learners.
- Prof Gerhard Walzl was interviewed live for 20 minutes on Radio 2000 on 10 March 2014, regarding the TB Awareness Month of March. He answered various questions concerning tuberculosis and the risk factors associated with the disease.
- Prof Sampson wrote 2 opinion pieces for popular press, including The Sowetan newspaper and spice4life (online lifestyle magazine), for World TB day, to highlight the urgency of the TB epidemic, to raise public awareness of the drug resistant TB epidemic and to highlight NRF-funded research efforts towards tackling this problem and impact on society.

Outreach activities

- PhD students Anastasia Koch and Zanele Ditse from the UCT node, together with PhD student Olivia Carulei from the Division of Medical Virology at UCT, and two South African artists (Ed Young and Herman de Klerk) established collaboration with Ikamva Youth (http://ikamvayouth.org), an NGO that aims to empower youth through education. During this project two resources were produced alongside learners in Khayelitsha. The first is an infographic that describes the natural history of TB, with a focus on the biology of the disease and the importance of seeking treatment for TB. The second resource is a 20-minute video consisting of a series of interviews with learners. The video highlights youth attitudes towards TB and documents personal experiences (http://cargocollective. com/ehwoza/).The success of this project, funded by the UCT node, resulted in an application led by Anastasia Koch for a Wellcome Trust International Engagement Award, which was granted in February 2014. The project aims to produce two types of content: websites that describe methodology, results and relevance of high-impact TB studies coming out of the home of the UCT node – the Institute of Infectious Disease and Molecular Medicine – and videos that explore attitudes to research in the community and how biomedicine can be used to address specific questions related to TB control in that environment. The youth group will steer production so that media is relevant to their demographic – learners will describe what kind of digital and visual language resonates with them and will best communicate biomedical concepts within their communities. This project will provide learners the opportunity to stimulate discussion around the social and biomedical issues that surround TB disease and research more broadly. An additional benefit is that, through interaction with artists, learners will gain insights into digital media production. In its most basic form, the project aims at decreasing current taboos and stigmas surrounding TB.
- UCT node PhD student, Anastasia Koch, contributed to the *PLOS Speaking of Medicine* blog with a description of the EH!WOZA community engagement project that she developed. This innovative project, which is funded by a Wellcome Trust International Engagement Award, was kick-started in 2013 with seed funding from the CBTBR. This contribution can be found at:
  http://blogs.plos.org/speakingofmedicine/2014/06/12/ehwoza-leaving-lab-addressing-tb-stigmas-taboos/
- Prof. Digby Warner was awarded a three-year Community Engagement Funding Instrument grant from the NRF for a project entitled, “Eh!Woza! Lab coats in the community: the dynamics of engaging communities and biomedical scientists.” Anastasia Koch is a co-investigator on this grant which builds upon the success of the Eh!Woza project that she was instrumental in developing together with colleagues from the Institute of Infectious Disease and Molecular Medicine at UCT and two Cape Town-based artists. This latest award follows on the heels of a Wellcome Trust International Engagement Award to Anastasia and Eh!Woza colleagues. Seed funding for this project was provided by the UCT node of the CBTBR in 2013.
- CBTBR SU node staff and student donated bags to Faseka high School in Guguleto. The learners appreciated it a lot. These were grade 11 pupils from one of their science classes. Khethelo explained where the bags came from and that it is meant to encourage them to study hard for their exams, get good grades and to pursue some kind of tertiary education, especially in the science, technology and engineering fields. The outreach was organised by SU node students Stefanie Malan and Khethelo Xulu.
- Prof Corfield has continued her involvement in outreach activities that engage the general public in a greater awareness of biomedical science and biotechnology, and in novel ways to communicate these complex sciences, through activities with many different audiences, ranging from primary and secondary school learners and their teachers, 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 of SAASTA (DST), as well as her pro deo work and contract work under the name of Scibiolosa (her own initiative setup since retirement– in which she calls herself “a scientist@large”).
  Work with the DNA Project to promote understanding of forensic DNA profiling:
  The workshops given were sponsored by the DNA project (an NGO promoting awareness of crime scene preservation of DNA evidence). This has become more important with the recent passing of the DNA Forensic Act which allows the establishment of a DNA forensic database in South Africa. A total of 12 workshops were given, including 9 Community workshops, attended by members of Community Policing Fora, Neighbourhood Watches and the SAPS which were held across the greater Cape Town area, including Khayelitsha and Mitchells Plain (Manenberg and Samora Machel were cancelled due to violence).

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 (54)		
Dr. William MacKenzie	Centers for Disease Control and Prevention, USA	Collaboration on the detection and characterization of Rpf-dependent bacterial populations in sputum. Project funded by the Division of Aids at the NIH.
Prof. Michael Barer, Dr. Galina Mukamolova	University of Leicester, UK	Collaboration on the detection and characterization of Rpf-dependent bacterial populations in sputum and in the lungs of infected mice. Project funded by the Division of Aids at the NIH..
Prof. Gilla Kaplan	Public Health Research Institute, International Center for Public Health, Newark, NJ	Prof. Kaplan serves as the international member on the Board of the CBTBR. She and Dr. Kana serve on the CU-SA Fogarty AITRP Advisory Board. Dr Kana collaborates with Dr. Kaplan, Prof Mizrahi and Dr Williams on a project aimed at further understanding molybdopterin biosynthesis in mycobacteria, which resulted in a publication in 2014.
Dr. Carolyn Bertozzi	University of California Berkeley	Collaboration on the use of novel bioorthogonal chemistry derivative to probe peptidoglycan remodelling in mycobacteria
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.
Dr. Eric Betzig	Howard Hughes Medical Institute	Collaboration on the development of novel imaging methods for mycobacteria
Dr. Ian Orme	Colorado State University	Collaboration on characterization of mutant strains of *M. tuberculosis* in the guinea pig model of TB infection.
Dr. Kevin Pethe	Institute Pasteur - Korea	Collaboration on characterization of compounds that target the mycobacterial respiratory chain.
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. 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	New collaboration on targeting ThyX for TB drug discovery
Prof. Rolf Müller	HIPS Helmholtz Institute for Infection Research, Saarland, Germany	New collaboration on the identification of natural products with antimycobacterial activity
Prof. David Russell	Cornell University, USA	Existing collaboration on vitamin B_{12} transport and metabolism, and new collaboration on drug permeation
Prof. Sebastian Gagneux	Swiss TPH, Basel, Switzerland	Collaboration on genome sequencing of clinical strains of *M. tuberculosis*
Prof. Dirk Schnappinger, Dr. Sabine Ehrt	Weill Cornell Medical College, Cornell University, USA	Collaboration on in vivo validation of drug targets
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.
Prof. Kyu Rhee	Weill Cornell Medical College, Cornell University	New collaboration on metabolomics analysis of conditional mutants of *M. tuberculosis*
Dr. Roger Woodgate	NICHD, NIH	New collaboration on replisone dynamics in mycobacteria
Prof. Sarah Fortune	Harvard School of Public Health	New collaboration on replication fidelity in mycobacteria
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 Eric Bottger	University of Zurich	Development and evaluation of novel genetic based diagnostics for drug resistance.
Prof Edward Nardell	AIR facility, Witbank	Transmissibility of drug resistant TB

Prof. Timothy Sterling	Vanderbilt University Tuberculosis Center, Nashville, USA	Fluoroquinolone resistance
Prof Megan Murray	Florida University Harvard / Broad institute	Development of a novel TB diagnostic for drug resistance.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. All of these projects involve whole-genome sequencing, proteomics, microarray. Prof. Murray is directly involved in project planning, paper writing, funding proposals (NIH, Wellcome trust).
Dr. Karen Jacobson	Harvard University, USA	1) GIS of drug resistant TB in the Western Cape 2) MDR treatment outcome in Brewelskloof Hospital Treatment outcome of M(X)DR-TB
Prof. Harald Wiker, Dr Gustavo de Souza	Bergen University and Oslo University, Norway	Ongoing collaboration on the *M. tuberculosis* phosphorylome New collaboration on the detection of drug resistance by single run multi-locus sequencing. New collaboration on the *M. tuberculosis* secretome.
Dr. Anita Schurch	RIVM, Netherlands	Ongoing collaboration on *M. tuberculosis* genome evolution.
Dr. Hernandez Pando Rogelio	National University of Mexico	Test different drug resistant strains (MDR / XDR) in a mouse model for strain fitness/virulence. The isolates are the same as described above and will compliment the data obtained by molecular investigations. To determine whether reinfection induces reactivation.
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
Prof. Harriet Mayanja	Makerere University, Uganda	Collaborators on BMGF-funded project.

Dr. Carol Holm-Hansen	Norwegian Institute for Public Health	Collaboration on BMGF Grand Challenge Exploration grant, 2010-2011
Dr. Christoph Lange, Dr. Barbara Kalsdorf	Clinical Infectious Diseases Centre for Clinical Studies, Medical Clinic,Research Centre Borstel, Germany	Collaboration on TB diagnostic study 2011
Dr. Jeff Boyle	Qiiagen, US	Collaboration on diagnostic TB study
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
Prof Sivaramesh Wigneshweraraj	Imperial College London	Structure-function relationships in Mycobacterium tuberculosis RNA polymerase
Prof Anne Bowcock	Imperial College London	Exome sequencing of patients with Mendelian susceptibility to Mycobacterial Disease
Dr Lucy Collins	London Research Institute	Investigating difference in autophagy induction by different *M.tuberculosis* strains using correlative light and electron microscopy.
National (36)		
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.
Dr. Musa Mhlanga	Council for Scientific and Industrial Research	Ongoing collaboration to develop methods for super-resolution microscopy in mycobacteria
Prof. Jonathan Blackburn	IDM, UCT	Collaboration on lipidomic and proteomic analyses of *M. tuberculosis* strains
Prof. Kelly Chibale	H3-D Drug Discovery Centre, UCT	Ongoing collaboration on SATRII, HI-TB and H3-D TB drug discovery projects
Prof. Nicola Mulder	CBIO, IDM, UCT	Collaboration on bioinformatic analysis of mycobacterial genomes
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	New 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	New collaboration on structural biology and imaging of *M. tuberculosis*
Dr. Violet Chihota	Aurum Health	*M. tuberculosis* strain population structure in Africa.
Dr. Gavin Churchyard	The Aurum Institute	Collaboration on the detection and characterization of Rpf-dependent bacterial populations in sputum. Project funded by the NIH. The Wits node also collaborating with Dr. Churchyard on several other ventures under the auspices of the Wits-Aurum Coalition.
Dr. Helen Cox	UCT	Collaboration on drug resistance in Khayelitsha, Western Cape. Impact of mixed infection on treatment outcome.

		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
Dr. Grant Theron	UCT	Measuring infectiousness through cough aerosol sampling.
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.
Dr. Else Marais	Wits/NHLS	Ongoing collaboration on the molecular epidemiology of drug resistant TB in Gauteng.
Dr. 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).
Prof. Kelly Chibale	Dept Chemistry & H3-D Centre for Drug Discovery & Development, UCT	Screen antituberculosis lead compounds
Dr Chris van der Westhuyzen	CSIR Biosciences,Pretoria	Screen antituberculosis lead compounds
Dr. Richard Haynes Kenyon	North West University, Potchefstroom	Study novel artemisinins for antimycobacterial activity
Dr Gert Kruger	Chemistry, UKZN, Durban	Screen antituberculosis lead compounds
Prof. Ivan Green	Dept Chemistry, UWC	Screen new compounds and derivatives for antituberculosis activity
Mrs Tania Dolby	NHLS , Green point	Collaborator provides routine samples.
Dr. Anneke Hesseling	SU	New collaboration to investigate genotype-immunological phenotype correlations in children.
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. Anita Michel	Faculty of Veterinary Science, University Pretoria	Assessment of novel biomarkers for the diagnosis of TB in cattle; this work is ongoing
Dr Monika Esser,	NHLS Immunology Unit, Tygerberg Hospital	Identification of gene mutations that cause Primary Immunodeficiency Disorders.
Prof S. Schaaf and E. Zöllner	Dept. of Paediatrics and Child Health, FHMS, SU	Investigting the genetic aetiology of TB and Insulin Dependant Diabetes Millitus.
Dr. Ben Loos	Dept. Physiological Sciences, SU	Investigating differences in autophagy induction by different *M tuberculosis* strains using super-resolution confocal microscopy.

5. Service rendering

The following services were provided in 2014:

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 Pretoria.
- Dr. Gordhan served as an external examiner an MSc dissertation submitted to the University of Stellenbosch
- Prof. Warner served as external examiner on MSc dissertations 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 WITS, Pretoria, UCT, UWC and other universities and Universities of Technology. Details are not kept.

Journal editing and reviews

- Prof. Kana reviewed manuscripts for *PLoS One*, *Journal of Bacteriology, South African Journal of Science, Journal of Infectious Diseases, BMC Genomics, PLOS One, Antonie van Leuwenhoek, Antimicrobial Agents and Chemotherapy*, *BMC Public Health, BMC Biochemistry*, *Journal of Bacteriology*, *Molecular Microbiology*.
- Prof. Mizrahi served on the Editorial Advisory Boards of the *Biochemical Journal; Tuberculosis*; *Cellular Microbiology,* and the Editorial Boards of *Current Opinion in Microbiology*; *Pathogens & Disease*, and *Emerging Microbes and Infection*. Prof. Warner served on the Editorial Board of *PLoS ONE*.
- Members of the UCT node reviewed manuscripts submitted to *Nature Genetics, Science, Science Translational Medicine, eLife, Nucleic Acids Research, Cell Reports, Scientific Reports, PLoS Pathogens, Frontiers in Molecular Biosciences, Molecular Microbiology, Antimicrobial Agents and Chemotherapy, mBio, Proceedings of the National Academy of Sciences USA, Microbiology, Future Microbiology, Emerging Microbes and Infections, Tuberculosis, Journal of Antimicrobial Chemotherapy, International Journal of Tuberculosis & Lung Disease; International Journal of Infectious Disease.*
- 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. G. Walzl
Working Group on New Drugs	Stop TB Partnership	2008-present	Prof. G. Walzl
Internal Governance and an Institutional scientific advisory committee	SU	2014-present	Prof. G. Walzl
IMPAACT TB Scientific Committee	NIH IMPAACT	2012-present	Prof. G. Walzl
Research Committee of Faculty of Health Sciences	SU	2009-present	Profs. G. Walzl & RM. Warren

Ethics Committee for Experimental Animal Research	SU	2008-present	Dr. I. Wiid
Committee for Postgraduate Education of Faculty of Health Sciences	SU	2008-present	Prof. NC. Gey van Pittius
Centre for Infectious Diseases	SU	2008-present	Prof. RM. Warren
Human Research Ethics Committee of the Faculty of Health Sciences	SU	2009-present	Prof. NC. Gey van Pittius
J-Expert Job evaluation Panel	MRC	2010-present	Dr CJ. Kinnear
Planning Committee of Annual Academic YearDay	Faculty of Medicine & Health Sciences, SU	2012-present	Dr CJ. Kinnear (vice-chair)
Critical Path to Treatment Regimens	NIH/Gates Foundation	2013	Profs. PD van Helden & RM Warren
Discovery Expert Group	Gates Foundation	2014	Prof. V. Mizrahi
Board of Directors	K-RITH	2014	Prof. V. Mizrahi
Scientific Advisory Board	K-RITH	2014	Prof. V. Mizrahi
Scientific Advisory Committee of SDDC, a structure-guided drug discovery consortium	Gates Foundation, Structural Genomics Consortium, University of Toronto	2014	Prof. V. Mizrahi
Scientific Advisory Committee	TB Alliance	2014	Prof. V. Mizrahi
Steering Committee	WHO Consultation for Research on TB Elimination, Stockholm,	2014	Prof. V. Mizrahi
Keystone Symposia Study Group	Keystone Symposia	2014	Prof. V. Mizrahi
Reviewe panel for the International Pre-Doctoral Fellowships program	HHMI	2014	Prof. V. Mizrahi
Council of Scientific Advisors	International Centre for Genetic Engineering and Biotechnology, Italy	2014	Prof. V. Mizrahi
Visiting Scholars and Lecturers Fund Committee	UCT	2014	Prof. V. Mizrahi
Executive and Membership Committees	IDM, UCT	2014	Prof. V. Mizrahi
Health & Safety Committee of the IDM	UCT	2014	Prof. Warner (Chair)
Institutional Biosafety Committee	UCT	2014	Prof. Warner
GMO Committee	UCT	2014	Prof. D. Warner
Hazardous Chemical Coordinator of MMRU	UCT	2014	Prof. D. Warner
Lead Academic in charge of the WBS Level 2 BSL III Lab of IDM	UCT	2014	Prof. D. Warner
Education and Equipment Task Teams	UCT	2014	Prof. D. Warner
Health & Safety Committee	IDM, UCT	2014	Dr. J. Evans
Operations & Lab Management Committee	IDM, UCT	2014	Dr. A. Moosa
Health Sciences Faculty Postgraduate Students Council	UCT	2014	Ms. Koch, Ms. Ditse
Advisory Committee	CU-SA Fogarty AITRP	2014	Prof. B. Kana
Board	Sydney Brenner Institute for	2014	Prof. B. Kana

	Molecular Biosciences		
Board of the Microscopy and Microanalysis Unit	WITS	2014	Prof. B. Kana
Working Group	Global Alliance for TB Drug Development	2014	Prof. B. Kana
University Research Council (URC)	WITS	2014	Prof. Kana
Graduate Sciences Committee	Faculty of Health Sciences, WITS	2014	Prof. Kana
FRC Budget task group,	Faculty of Health Sciences, WITS	2014	Prof. Kana
Executive Committee of the School of Pathology	Faculty of Health Sciences, WITS	2014	Prof. Kana
Research Entity Forum	Faculty of Health Sciences, WITS	2014	Prof. Kana
Research Equipment Review Committee	Faculty of Health Sciences, WITS	2014	Prof. Kana
Advisory Board	Faculty of Health Sciences, WITS	2014	Prof. Kana
Imaging Committee, Wits University	Faculty of Health Sciences, WITS	2014	Prof. Kana
Faculty Research Council (FRC)	Faculty of Health Sciences, WITS	2014	Prof. Kana & Dr Gordhan
Postdoctoral Review Committee	NRF	2014	Dr. Gordhan
Research Entity Review Task Group	Faculty of Health Sciences, WITS	2014	Dr. Gordhan

Examples of Research Funding Reviews

- Prof. Mizrahi served as a reviewer for the HHMI and as reviewer for promotions at Johns Hopkins University. Prof. Warner served as reviewer for international funding organizations including the Wellcome Trust (UK), the MRC (UK), and the India Alliance (a partnership between The Wellcome Trust, UK and the Government of India). He was also a reviewer for the NRF and MRC and the various programmes they administer, including international collaborative programmes (Japan-SA; Germany-SA), competitive funding for un/rated researchers, and MRC self-initiated research grants, Thuthuka, and NRF student funding applications. In addition, he served as an internal reviewer for numerous research proposals considered by the IDM Research Committee and Institutional Biosafety Committee.
- Members of the Wits node reviewed for the British Medical Research Council (UK), NHLS Research Trust, Biotechnology and Biological Sciences Research Council (BBSRC, UK), SA Medical Research Council (various programs), National Research Foundation, and Faculty Research Committee Grants (Wits).
- 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, mostly students) 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, and from time to time hosts a research student working on diseases of the prostate from our division of Urology. All of the PIs involved have or have had NRF support. We are also fully integrated with three SU Based TB SARCHI's and their researchers and students. A UCT based SARChI (Prof 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 50 registered users from across the IDM, only 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) and the SA TB Vaccine Initiative (SATVI). 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 the member of the Scientific Staff, Dr. Joanna Evans.

Other services rendered

- Speciation of Non Tuberculous Mycobacteria (NTM) for Kruger National Park
- Genotyping of clinical isolates (RFLP or mutation detection) for the NHLS, MSF and City Health.
- Prof V Corfield was NRF rating panel moderator in 2014
- Specialist diagnostic service for MDR or XDR TB cases for NHLS, Port Elizabeth.
- Specialist diagnostic service for suspect extra-pulmonary TB cases, Brooklyn 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
- Cellestis: Evaluation of new peptide to diagnose TB

6. Gender impact of research

Four out of the 13 Core Team Members of the CBTBR are women. In 2014, the CBTBR has also maintained a high percentage of female students (57% of all students and 52% 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, 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 Zanele Ditse, Zela Martin and 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.

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.	Gey van Pittius	SA	SU	M	W	5[b]
Prof.	Hoal van Helden	SA	SU	F	W	100
Dr	Martinson	SA	Wits	M	W	25[c]
Dr.	Sampson	SA	SU/NRF	F	W	100
Prof.	Van Helden	SA	MRC	M	W	100
Prof.	Victor	SA	PAWC	M	W	50[d]
Prof.	Walzl	SA	SU	M	W	100
Prof.	Warren	SA	MRC	M	W	100
A/Prof.	Wiid	SA	PAWC	M	W	100

a. Director of the IDM
b. Appointed as deputy dean for Research in September 2012
c. Dr. Martinson is also directorof the Perinatal HIV Research Unit (PHRU)
d. Retired in July 2014

2. Scientific Staff

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Dr.	Ronacher	SA	SU	F	W	100
Dr.	Streicher	SA	SU	F	W	100
Dr	Abrahams[a]	SA	UCT	M	B	10
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[b]	SA	SU	F	W	100
Dr	Evans	SA	UCT	F	W	100[c]
Prof	Diacon	Swiss	SU	M	W	10
Dr	Sirgel	SA	SU	M	W	100

a. Dr. Abrahams' contract ended February 2014. Appointed as a Lecturer in the Dept of Biochemustry & Microbiology at Rhodes University, March 2015
b. Seconded full-time toSU from MRC
c. Promoted from postdoctoral to Junior Research Fellow at UCT in September 2014.

3. Postdoctoral Fellows

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Dr	Banda	Zimbabwean	SU	Male	Black	100
Dr	Chengalroyen	South African	Wits	Female	Black	100
Dr	Dippenaar	South African	SU	Female	White	100
Dr	Du Plessis	South African	SU	Female	White	100
Dr	Ealand	South African	Wits	Male	White	100
Dr	Fortuin	South African	SU	Female	Black	100
Dr	Gopinath	Indian	UCT	Male	Black	50[b]
Dr	Heunis	South African	SU	Male	White	75[a]
Dr	Kleynhans	South African	SU	Female	White	100

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Dr	Leisching	South African	SU	Female	White	100
Dr	Le Roex	South African	SU	Female	White	100
Dr	Möller	South African	SU	Female	White	100
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	Salie	South African	SU	Male	Black	100
Dr	Singh	Indian	UCT	Male	Black	100
Dr	Styger	South African	SU	Male	White	100
Dr	van der Merve	South African	SU	Male	White	100

a. Commenced in April 2014
b. Completed in June 2014

4. Students

Title	First name	Surname	Degree	Institution	Race	Gender	Nationality	Status
Mr	Nicholas	Bowker	Hons	SU	White	Male	South Africa	Completed
Ms	Charlene	Clarke	Hons	SU	White	Female	South Africa	Completed
Ms	Ncite	Da Camara	Hons	SU	White	Female	South Africa	Completed
Ms	Ruschca	Jacobs	Hons	SU	Black	Female	South Africa	Completed
Ms	Jessica	Klazen	Hons	SU	Black	Female	Namibia	Completed
Ms	Sasha-Lee	Lynch	Hons	SU	Black	Female	South Africa	Completed
Ms	Lara Maria	Meyer	Hons	SU	White	Female	South Africa	Completed
Ms	Lerato	Ngakane	Hons	SU	Black	Female	South Africa	Completed
Mr	Thobile	Ngqaneka	Hons	SU	Black	Male	South Africa	Completed
Mr	Giovanni	Nusca	Hons	UCT	White	Male	Italy	Completed
Ms	Trisha	Parbhoo	Hons	SU	Black	Female	South Africa	Completed
Mr	Haiko	Schurz	Hons	SU	White	Male	South Africa	Completed
Ms	Christine	Strauss	Hons	SU	White	Female	South Africa	Completed
Mr	Enock	Tshehla	Hons	SU	Black	Male	South Africa	Completed
Ms	Ilana	van Rensburg	Hons	SU	Black	Female	South Africa	Completed
Ms	Jesmine	Arries	MSc	SU	Black	Female	South Africa	Incomplete
Ms	Rukaya	Asmal	MSc	WITS	Black	Female	South Africa	Incomplete
Ms	Louise	Botha	MSc	SU	White	Female	South Africa	Completed
Mr	Willem	du Plessis	MSc	SU	White	Male	South Africa	Incomplete
Mr	James L	Gallant	MSc	SU	White	Male	South Africa	Incomplete
Mr	Wynand	Goosen	MSc	SU	White	Male	South Africa	Incomplete
Ms	Sidhika	Hariparsad	MSc	UP	Black	Female	South Africa	Incomplete
Ms	Zela	Martin	MSc	UCT	White	Female	South Africa	Incomplete
Mr	Ross	McFadyen	MSc	SU	White	Male	South Africa	Incomplete
Mr	Katiso	Mgadi	MSc	SU	Black	Male	South Africa	Incomplete
Ms	Vuyiseka	Mpongoshe	MSc	SU	Black	Female	South Africa	Completed
Mr	Steven	Nthambeleni	MSc	WITS	Black	Male	South Africa	Incomplete
Mr	Ditshego	Ralefeta	MSc	WITS	Black	Male	South Africa	Incomplete
Mr	Michael	Reiche	MSc	UCT	White	Male	South Africa	Incomplete
Ms	Nikola	Schlechter	MSc	SU	White	Female	South Africa	Incomplete
Ms	Zaahida	Sheik Ismail	MSc	WITS	Black	Female	South Africa	Incomplete
Ms	Bronwyn	Smith	MSc	SU	White	Female	South Africa	Incomplete
Mr	Marvin	Theys	MSc	SU	Black	Male	South Africa	Incomplete
Ms	Phophi	Tshavhungwe	MSc	SU	Black	Female	South Africa	Incomplete

Ms	Siyanda	Tshoko	MSc	SU	Black	Female	South Africa	Incomplete
Ms	Hanri	Visser	MSc	SU	White	Female	South Africa	Incomplete
Mr	Michael	Whitfield	MSc	SU	White	Male	South Africa	Incomplete
Mr	Kennedy	Zvinairo	MSc	SU	Black	Male	Zimbabwe	Incomplete
Mr	Dolapo	Awoniyi	PhD	SU	Black	Male	Nigeria	Incomplete
Mr	Germar	Beukes	PhD	WITS	White	Male	South Africa	Incomplete
Ms	Philippa	Black	PhD	SU	White	Female	South Africa	Incomplete
Mr	Simon	Broadley	PhD	UCT	White	Male	South Africa	Incomplete
Ms	Michelle	Daya	PhD	SU	White	Female	South Africa	Incomplete
Ms	Zanele	Ditse	PhD	UCT	Black	Female	South Africa	Incomplete
Ms	Juanelle	du Plessis	PhD	SU	White	Female	South Africa	Incomplete
Ms	Lizaan	Ehlers	PhD	SU	White	Female	South Africa	Incomplete
Mr	Paulin	Essone	PhD	SU	Black	Male	Gabon	Completed
Mr	Zhuo	Fang	PhD	SU	Black	Male	China	Completed
Ms	Melanie	Grobbelaar	PhD	SU	White	Female	South Africa	Incomplete
Mr	Kenneth	Hammond-Aryee	PhD	SU	Black	Male	Ghana	Incomplete
Ms	Marisa	Klopper	PhD	SU	White	Female	South Africa	Incomplete
Ms	Anastasia	Koch	PhD	UCT	White	Female	South Africa	Incomplete
Mr	Lance	Lucas	PhD	SU	White	Male	South Africa	Incomplete
Mr	Lubabalo	Macingwana	PhD	SU	Black	Male	South Africa	Completed
Ms	Marieta	McGrath	PhD	SU	White	Female	South Africa	Incomplete
Ms	Amanda	McIvor	PhD	WITS	White	Female	South Africa	Incomplete
Ms	Krupa	Naran	PhD	UCT	Black	Female	South Africa	Incomplete
Ms	Nicole	Narrandes	PhD	WITS	Black	Female	South Africa	Incomplete
Ms	Tashnica	Olivier	PhD	SU	Black	Female	South Africa	Incomplete
Mr	Charles	Omollo	PhD	UCT	Black	Male	Kenya	Incomplete
Ms	Caroline	Pule	PhD	SU	Black	Female	South Africa	Incomplete
Ms	Carine	Sao Emani	PhD	SU	Black	Female	Cameroon	Incomplete
Mr	Sibusiso	Senzani	PhD	WITS	Black	Male	South Africa	Incomplete
Ms	Nastassja	Steyn	PhD	SU	White	Female	South Africa	Incomplete
Ms	Sophia	van Coller	PhD	UCT	White	Female	South Africa	Incomplete
Mr	Ignatius	Viljoen	PhD	SU	White	Male	South Africa	Incomplete
Ms	Antonina	Wasuna	PhD	UCT	Black	Female	Kenya	Incomplete
Ms	Danicke	Willemse	PhD	SU	White	Female	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	Peachy	Bookkeeper/ Admin. assistant	Wits	F	B
Ms	Masanga	Laboratory Tech. Assistant	Wits	F	B
Ms	Ndlovu	Research Assistant	Wits	F	B
Ms	Papadopoulos	Research Assistant	Wits	F	W

OUTPUTS

* The Names in bold are CBTBR staff and students

Books / Chapters in Books (Total: 3)

Du Plessis N, Walzl G. Helminth-M. TB co-infection. Adv Exp Med Biol. 2014; 828:49-74. doi: 10.1007/978-1-4939-1489-0_3. Review. PubMed PMID: 25253027.
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Williams MJ, Mizrahi V, Kana BD. (2014) Molybdenum cofactor: a key component of *Mycobacterium tuberculosis* pathogenesis? *Crit Rev Microbiol*. 40(1): 18-29. (IF=6.09)
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Arora K, Ochoa-Montano B, Tsang PS, Blundell TL, Dawes SS, **Mizrahi V**, Bayliss T, Mackenzie, CL, Cleghorn LAT, Ray PC, Wyatt PG, Uh E, Lee J, Barry CE III, Boshoff HI. (2014) Respiratory flexibility in response to inhibition of cytochrome *c* oxidase in *M. tuberculosis. Antimicrob. Agents Chemother*. 58(11):6962-6965. (IF=4.45)
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screening and target identification-driven drug repositioning in antituberculosis drug discovery. *Bioorg Med Chem.* 22(16):4453-4461. (IF=2.33)
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Roug A, Geoghegan C, Wellington E, Miller W, Travis E, Porter D, Cooper D, Clifford D, Mazet J, **Parsons SDC**. (2014) Utility of a fecal real-time PCR protocol for detection of *Mycobacterium bovis* infection in African buffalo *Syncerus caffer*. *Journal of Wildlife Diseases* 50(1): 140-142. (IF=1.31)

Salie M, Van Der Merwe L, **Möller M**, **Daya M, Van Der Spuy GD, Van Helden PD**, Martin MP, Goa X, **Warren RM**, Carrington M, **Hoal EG**. (2014) Associations between Human HLA Class-I Variants and the *Mycobacterium tuberculosis* Subtypes Causing Infection. *Journal of Infectious Diseases* 209(2): 216-223. (IF=5.48)

Streicher EM, Maharaj K, York T, Van Heerden CJ, Barnard M, **Diacon AH**, Mendel CM, Bosman ME, Hepple J, Pym A, **Warren RM, Van Helden PD**. (2014) Rapid sequencing of the Mycobacterium tuberculosis pncA gene for the detection of pyrazinamide susceptibility. *Journal of Clinical Microbiology* 52(11): 4056-4057. (IF=4.23)

Sutherland J, **Loxton AG**, Haks MC , Kassa D, Ambrose L, Lee JS, Ran L, Van Baarle D, Maertzdorf J, Howe R, Mayanja-Kizza H, Boom WH, Thiel BA, Crampin AC, Hanekom W, Ota MO, Dockrell HM, **Walzl G**, Kaufmann SHE, Ottenhoff THM. (2014) Differential gene expression of activating *Fcγ* receptor classifies active tuberculosis regardless of human immunodeficiency virus status or ethnicity. *Clinical Microbiology and Infection* 20(4): 230-238. (IF=5.20)

Todorov SD, Gombossy De Melo Franco B, **Wiid IJF**. (2014) *In vitro* study of beneficial properties and safety of lactic acid bacteria isolated from Portuguese fermented meat products. *Beneficial Microbes* 24: 1-16. (IF=1.50)

Van Crevel R, Dockrell HM, Eckold CE, Cliff JM, Moore D, Griffiths UK, Laurence YV, van Crevel R, Netea MG, Aarnoutse R, Lachmandas E, Kaufmann SH, Beigier-Bompadre M, Leitner S, Löwe D, Golinski R, Ottenhoff TH, Haks MC, Joosten SA, Vrieling F, **Walzl G, Ronacher K, Malherbe S**, **van der Spuy G**, Critchley JA, Kerry SR, Pearson F, Hill PC, McAllister SM, Ioana M, Panduru NM, Riza AL, Cimpoeru A, Nicoli R, Wijmenga C, Kumar V, Ugarte-Gil C, Lopez S, Coronel J, Alisjahbana B, Ruslami R, Soetedjo NN,

Santoso P, Koesoemadinata RC, Schacht C, Büch J. (2014) TANDEM: understanding diabetes and tuberculosis. *Lancet* 2(4): 270-272. (IF=39.21)
Van Der Merwe RG, Van Helden PD, Warren RM, Sampson SL, Gey Van Pittius NC. (2014) Phage-based detection of bacterial pathogens. *Analyst* 139(11): 2617-2626. (IF=3.91)
Wallis RS, Dawson R, **Friedrich SO, Venter A**, Paige D, Zhu T, Silvia A, Gobey J, Ellery C, Zhang Y, Eisenach K, Miller P, **Diacon AH**. (2014) Mycobactericidal Activity of Sutezolid (PNU-100480) in Sputum (EBA) and Blood (WBA) of Patients with Pulmonary Tuberculosis. *PLoS ONE* 9(4): 1. (IF=3.53)
Zvada SP, Denti P, **Sirgel FA**, Chigutsa E, Hatherill M, Charalambous S, Mungofa S, Whitney K, Simonsson ASH, Jindani A, Harrison T, Mcilleron H. (2014) Moxifloxacin population pharmacokinetics and model-based comparison of efficacy between Moxifloxacin and Ofloxacin in African patients. *Antimicrobial Agents and Chemotherapy* 58(1): 503-510. (IF=4.45)

Conferences/Meetings Attended & Invited Talks/Seminars Presented (Total: 118)

Plenary/Keynote Lectures
Kana BD. Academic Career Management. Plenary lecture presented at the SA PhD Project – KwaZulu Natal Regional Conference. Coastlands Convention Centre, Umhlanga Rocks. 18 – 19 November 2014.
Mizrahi V. Targeting pyrimidine metabolism in *M. tuberculosis*. Plenary lecture, Microbiology after the genomics revolution: Genomes 2014, EMBO Conference, Institut Pasteur, Paris, 24-27 June 2014.
Mizrahi V. Targeting core metabolic pathways in Mycobacterium tuberculosis. Plenary presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Falls, Zambia, 27-29 August 2014.
Mizrahi V. Targeting pyrimidine metabolism for TB drug discovery. Keynote lecture presented at the South African Immunology Society (SAIS) Conference, Cape Town, 03 February 2014.
Mizrahi V. The practice of research and publication in South Africa, Keynote lecture, UCT Libraries Research Week, Cape Town, 12 May 2014.
Streicher EM. The molecular war against drug resistant tuberculosis. Plenary speaker at the SACORE scientific meeting, Lilongwe, Malawi, 24-31 August 2014.
Invited Talks
Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease: Separating anxiety and schizophrenia in mycobacterial cells. Invited lecture presented at the Weill Cornel Medical College, New York, USA, 9 September 2014
Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease: Separating anxiety and schizophrenia in mycobacterial cells. Invited lecture presented at the Rutgers Medical School, New Jersey, USA. 10 September 2014
Ealand CS, Kana BD. *dacB*: an essential enzyme for mycobacterial growth. Oral presentation at the Wits Faculty of Health Sciences Research Day and Expo. Johannesburg, South Africa,17 September 2014.
Ealand CS, Kana BD. *dacB*: an essential enzyme for mycobacterial growth. Oral presentation at the 4th SA TB conference. International Convention Centre, Durban, South Africa, 10 – 13 June 2014.
Chengalroyen MD, Beukes G, Gordhan B, Martinson N, Otwombe K, **Kana BD.** The detection and quantification of differentially culturable bacilli in patients with active tuberculosis. Oral presentation at the 4th SA TB conference. International Convention Centre, Durban, South Africa, 10 – 13 June 2014.
Machowski E, Ealand CS, Senzani S, Kana BD. How Flexible Can Mycobacterial Cell Walls Be? A Bioinformatic Approach. Oral Presentation at the 4th South African TB Conference. Durban, South Africa, 10-13 June 2014.
Senzani S, Kana BD. Identification and Characterisation of Mycobacterial cell wall amidases. Oral presentation at the 4th SA TB conference. International Convention Centre, Durban, South Africa, 10 – 13 June 2014.
Senzani S, Kana BD. Identification and Characterisation of Mycobacterial cell wall amidases. Oral presentation at the 6th Cross Faculty Graduate Symposium 2014, University of the Witwatersrand, Johannesburg, 28 - 29 October 2014.
Senzani S, Kana BD. Identification and Characterisation of Mycobacterial cell wall amidases. Oral presentation at the Molecular Biosciences Research Thrust 2014 Symposium, 4th December 2014.
Beukes G, Chengalroyen M, Martinson N, Gordhan B, Kana BD. The effect of temperature on culture

filtrates in stimulating bacterial culturability in tuberculous sputum. Oral presentation at the 4th SA TB conference. International Convention Centre, Durban, South Africa, 10 – 13 June 2014.
Narrandes NC, Kana BD. Characterisation of the mycobacterial electron transport chain: Implications for drug efficacy. Oral presentation at the 4th SA TB conference. International Convention Centre, Durban, South Africa, 10 – 13 June 2014.
Narrandes NC, Kana BD. Characterisation of the mycobacterial electron transport chain: Implications for drug efficacy. Oral presentation at the Biannual Faculty of Health Science Research Day and Postgraduate Symposium, 17 September 2014.
Sheik Ismail Z and Kana BD. Characterisation of mycobacterial DD-Carboxypeptidases. Poster and oral presentation at the 6th Cross Faculty Graduate Symposium 2014, University of the Witwatersrand, Johannesburg, 28 - 29 October 2014.
Mizrahi V. Tuberculosis drug development: lessons learned and future prospects. 36th Bernard Pimstone Memorial Lecture, Department of Medicine Research Day, University of Cape Town, 9 October 2014.
Mizrahi V. The IDM Today. Plenary lecture, Ten-Year Anniversary Symposium, Institute of Infectious Disease & Molecular Medicine, University of Cape Town, 2 November 2014.
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.
Warner DF. Mechanisms of replication fidelity in *Mycobacterium tuberculosis*. South African Society for Biochemistry and Molecular Biology (SASBMB), Goudini Spa, 6-9 July, 2014.
Warner DF. A vitamin B_{12} shot for *Mycobacterium tuberculosis*. Invited lecture, K-RITH Seminar Series, KwaZulu-Natal Reseach Institute for TB and HIV (K-RITH), Durban, 25 April, 2014.
Warner DF. A vitamin B_{12} shot for *Mycobacterium tuberculosis*. Invited lecture, Department of Biomedical Sciences, Stellenbosch University. 2 June, 2014.
Ditse Z, Mizrahi V, Warner DF. Replication fidelity in the microevolution of *Mycobacterium tuberculosis*. 9th International Conference on the Pathogenesis of Mycobacterial Infections, Grand Hotel Saltsjöbaden, Stockholm, Sweden. 25-29 June 2014.
Ditse Z, Mizrahi V, Warner DF. Replication fidelity in the microevolution of *Mycobacterium tuberculosis*. IDM Ten-Year Symposium, University of Cape Town, 2-4 November 2014.
Ditse Z, Mizrahi V, Warner DF. Replication fidelity in the microevolution of *Mycobacterium tuberculosis*. UCT-KRITH Retreat, Devon Valley Hotel, Stellenbosch 6-7 October 2014.
Broadley SG, Warner DF, Sewell BT. Structure determination of ImuC from *Mycobacterium tuberculosis*. Poster presented at the South African Society of Biochemistry and Molecular Biology conference. Cape Town, 6-9 July 2014.
Chegou NN, Sutherland, JS, Mayanja-Kizza H, Howe R, Van der Vyver M, Kassa D, Crampin AC, **Walzl G**, AE-TBC Consortium. Utility of Mycobacterium tuberculosis-specific host cytokine signatures in whole blood culture supernatants in the diagnosis of Tuberculosis disease. Talk presented at the 7th EDCTP Forum, Theme: The partnership journey: New horizon for better health. 30 June – 2 July 2014.
Chegou NN, **Loxton AG, Walzl G**. Utility of M. tuberculosis specific host cytokine signatures in whole blood culture supernatants as diagnostic markers tuberculosis disease. Talk presented at the Seventh EDCTP Forum. The Partnership Journey: New Horizon for Better Health. Maritim proArte Hotel Berlin, Berlin, Germany, 28 June - 02 July 2014.
Loxton AG. TB Biomarkers: Diagnoses, treatment response and cure. Oral presentation at TB vaccine meeting, Les Diablerets, Switzerland 28-31 January 2014
Warren RM. Next Generation Sequencing: Applications in Tuberculosis. Invited talk presented at the NHLS Cape Town, South Africa, February 2014.
Warren RM. Emergence and spread of extensively and totally drug-resistant Mycobacterium tuberculosis. Invited talk presented at the ICAAC, Washington, USA, 7 September 2014.
Warren RM. Comparative Genomics of Drug-Resistant TB. Invited talk presented at the 4th TB Conference, Durban, South Africa, 10-13 June 2014.
Warren RM. Phenotypic and extended DST. Invited talk presented at the XDR-TB Workshop, UCT, Cape Town, South Africa, 10-12 October 2014.
Warren RM. Genesis of MDR and XDR-TB: Can we prevent this from happening in the future? Invited talk presented at the XDR-TB Workshop, UCT, Cape Town, South Africa, 10-12 October 2014.
Warren RM. Drug resistant tuberculosis: Creating the monster. Talk presented at the K-RITH Seminar series. K-RITH, University of KwaZulu-Natal, Durban, South Africa, 30 May 2014.

Sampson SL. In vivo imaging of Mycobacterium tuberculosis infection. Talk presented at the UK-SA Seminar on Imaging in Host-Pathogen Interactions. Cape Town, South Africa. November 2014.
Whitfield M, Streicher EM, York T, Mardarowicz I, Scott L, Stevens W, **van Helden PD, Sampson S, Warren RM**, Van Rie A. Association between Genotypic and Phenotypic Pyrazinamide Resistance in Rifampicin Resistant Mycobacterium Tuberculosis Isolates. Talk presented at the 4th SA TB Conference 2014. Durban ICC, Durban, South Africa, 10-13 June 2014.
Whitfield MG, Streicher EM, York T, Mardarowicz I, Scott L, Stevens W, **van Helden PD**, Van Rie A, **Warren RM**. Association between Genotypic and Phenotypic Pyrazinamide Resistance in Rifampicin Resistant Mycobacterium tuberculosis Isolates. Talk presented at the 9th International Conference on the Pathogenesis of Mycobacterial Infections. Grand Hotel Saltsjöbaden, Stockholm, Sweden, 26-29 June 2014.
Van Helden PD. Crossroads in TB research: where are we heading?. Talk presented at the 9th International Conference on the Pathogenesis of Mycobacterial Infections. Grand Hotel Saltsjobaden, Stockholm, Sweden, 26-29 June 2014.
Van Helden PD. Chalenging Dogmas using Molecular Biology to understand TB. Talk presented at the SASBMB Biennial Conference. Goudini Spa, Worcester, South Africa, 6-9 July 2014.
Whitfield MG, Streicher EM, York T, **Mardarowicz I**, Scott L, Stevens W, **van Helden PD**, van Rie A, **Warren RM**. Association between Genotypic and Phenotypic Pyrazinamide Resistance in Rifampicin Resistant Mycobacterium tuberculosis Isolates. Talk presented at the 58th Annual Academic Day. Tygerberg, Cape Town, South Africa, 13 August 2014.
Malherbe ST. Measuring TB treatment response through PET/CT. Talk presented at South African Society of Nuclear Medicine 16th Biannual Congress. Maharani Hotel, Durban, South Africa, 21 September 2014.
Malherbe ST. TB treatment response. Talk presented at the The Spinal Surgery Masters Symposium. Protea Vinyard Hotel, Cape Town, South Africa, 01 November 2014.
Malherbe ST. Measuring Tb treatment response through PET/CT imaging. Talk presented at the H3-D TB drug development Symposium. Zambezi Sun, Livingstone, Zambia, 27-29 August 2014.
Malherbe ST. Measuring TB treatment responses through 18-FDG-PET/CT.Talk presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Lucas L. Circulating MicroRNAs: Potential markers of early treatment response in pulmonary Tuberculosis. Talk presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Du Plessis J. The role of Bcells during Mtb infection. Talk presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Mgadi K. Role of monocytes in TB-Diabetes disease. Talk presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Streicher EM. Rapid prediction of Pyrazinamide resistance by pncA gene sequencing. Talk Presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Streicher EM. Shifting the Blame: Transmission vs Acquisition of XDR-TB. Talk Presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Pule C. The effect of efflux pump inhibitors on First and Second-Line anti-tuberculosis drugs differs in rifampicin mono-resistant clinical Isolates of *Mycobacterium tuberculosis*. Talk Presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Van der Merwe R. WGS pipeline applications to interrogate genetic diversity among clinical strains of *Mycobacterium tuberculosis*. Talk presented at the 4th South African TB Conference, Durban, South Africa, 10-13 June 2014.
Hammond-Aryee K. Toxoplasma gondii seroprevalence in humans and animals in Africa. Talk presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
De Vos M. Construction of a Three Color Single-Tube Assay for Resistance to First, Second, and Third Line Antibiotics used to Diagnose and Treat XDR-TB. Talk presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Van der Merwe R. A Whole Genome Sequencing approach to investigate the evolution of drug resistance in the Western Cape of South Africa. Talk presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Aywoniyi D. Evaluation of cytokine responses against novel Mtb antigens as diagnostic markers for TB disease. Talk presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South

Africa, 13 August 2014.
Paul L. Validation of novel isoniazid resistance causing mutations in the KatG catalase-peroxidase of Mycobacterium tuberculosis. Talk presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Miller M. Mycobacterial infection and tuberculosis in free-ranging African lions (Panthera leo): potential impact of environmental mycobacteria on diagnostic testing. Talk presented at the American Association of Zoo Veterinarians Conference, Orlando, USA, 19-24 October 2014.
Miller M. Effect of azaperone on blood pressure and other cardiorespiratory parameters in etorphine-immobilized free-ranging African elephants (Loxodonta africana) – role in managing anesthetic complications. Talk presented at the American Association of Zoo Veterinarians Conference, Orlando, USA, 19-24 October 2014.
Pule C. The effect of efflux pump inhibitors On First and Second-Line Anti-Tuberculosis Drugs Differs in Rifampicin Mono-Resistant Clinical Isolates of Mycobacterium Tuberculosis. Talk Presented at the European Society of Mycobacteriology 35th Annual Congress,Vienna, Austria, 29 June - 02 July 2014.
Miller M. Detection of immunological responses to Mycobacterium bovis in naturally infected African lions (Panthera leo) in Kruger National Park, South Africa. Talk presented at the V Annual Research Symposium in Wildlife Health, hosted by National Zoological Gardens, Pretoria, South Africa, 20-21 November 2014.
Streicher EM. Shifting the Blame: Transmission vs Acquisition of XDR-TB. Talk presented at the XDR-TB workshop UCT, Cape Town, South Africa, 10-12 October 2014.
Posters
Kana BD. Amidase_3 domain-containing N-acetylmuramyl-L-alanine amidases play essential, non-redundant roles in growth and cell division in Mycobacterium smegmatis. Poster presentation at the Annual HHMI Scholars Meeting, 3-5 September 2014.
Kana BD. Amidase_3 domain-containing N-acetylmuramyl-L-alanine amidases play essential, non-redundant roles in growth and cell division in *Mycobacterium smegmatis*. Poster presentation at the Gordon Research Conference on Bacterial Cell Surfaces, 22 - 27 June 2014.
Chengalroyen MD, Beukes G, Gordhan B, Martinson N, Otwombe K**, Kana BD.** The detection and quantification of differentially culturable bacilli in patients with active tuberculosis. Poster presentation at the Molecular Bioscienes Research Trust. University of Witwatersrand, South Africa, 4 December 2014.
Chengalroyen MD, Beukes G, Gordhan B, Martinson N, Otwombe K, **Kana BD.** The detection and quantification of differentially culturable bacilli in patients with active tuberculosis. Poster presentation at the Faculty of Health Sciences Biennial Research Day and Postgraduate Symposium. University of Witwatersrand, South Africa, 17 September 2014.
Senzani S and Kana BD. Identification and Characterisation of Mycobacterial cell wall amidases. Poster presentation at the Wits Health Science Research day and post graduate Expo 2014, Faculty of Health Science, University of the Witwatersrand, Johannesburg, 17 September 2014.
Beukes G, Chengalroyen M, Martinson N, Gordhan B, Kana BD. The effect of temperature on culture filtrates in stimulating bacterial culturability in tuberculous sputum. Poster presentation at the 6th Biennial Research Day and Postgraduate Expo 2014, Faculty of Health Science, University of the Witwatersrand, Johannesburg, 17 September 2014.
Beukes G, Chengalroyen M, Martinson N, Gordhan B, Kana BD. The effect of temperature on culture filtrates in stimulating bacterial culturability in tuberculous sputum. Poster presentation at the 6th Cross Faculty Graduate Symposium 2014, University of the Witwatersrand, Johannesburg, 28 - 29 October 2014.
Beukes G, Chengalroyen M, Martinson N, Gordhan B, Kana BD. The effect of temperature on culture filtrates in stimulating bacterial culturability in tuberculous sputum. Poster presentation at Molecular Biosciences Research Thrust 2014, University of the Witwatersrand, Johannesburg, 4 December 2014.
Sheik Ismail Z, Kana BD. DD-Carboxypeptidases affect crosslinking in mycobacteria. Poster presentation at the 4th Annual SA TB Conference, 2014, ICC, Durban, 10 – 13 June 2014.
Sheik Ismail Z, Kana BD. Characterisation of mycobacterial DD-Carboxypeptidases. Poster presentation at the 6th biennial Research day and Postgraduate Expo 2014, Faculty of Health Science, University of the Witwatersrand, Johannesburg, 17 September 2014.
Sheik Ismail Z, Kana BD. Characterisation of mycobacterial DD-Carboxypeptidases. Poster presented at the Molecular Biosciences Research Thrust 2014, University of the Witwatersrand, Johannesburg, South

Africa, 4 December 2014.
Ralefeta D, Machowski E. and Kana BD. Heterologous expression and characterisation of *Mycobacterium tuberculosis* DD-Carboxypeptidases in *Mycobacterium smegmatis***.** Poster presentation at the 6th Cross-Faculty Graduate Symposium 2014. University of the Witwatersrand, Johannesburg, South Africa, 28 - 29 October 2014.
Ralefeta D, Machowski E. and Kana BD. Heterologous expression and characterisation of *Mycobacterium tuberculosis* DD-Carboxypeptidases in *Mycobacterium smegmatis*. Poster presentation at the Molecular Biosiences Research Trust Research Day 2014. University of the Witwatersrand, Johannesburg, South Africa, 04 December 2014.
Kigondu E, Singh V, Warner DF, Chibale K. In vitro synergistic interactions and possible mechanism of action of chlorpromazine and its metabolites in combination with anti-TB drugs against *Mycobacterium tuberculosis*. Poster presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Fals, Zambia, 27-29 August 2014.
Moosa A, Mizrahi V, Warner DF. Smart screening for TB drug discovery. Poster presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Falls, Zambia, 27-29 August 2014.
Naran K, Mizrahi V, Warner DF. An SOS-deficient mutant of *Mycobacterium tuberculosis* for use in phenotypic anti-TB drug screens Poster presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Falls, Zambia, 27-29 August 2014.
Omollo C, Kigondu E, Warner DF, Chibale K. In vitro synergistic interactions of fusidic acid with known anti-tuberculosis drugs. Poster presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Falls, Zambia, 27-29 August 2014.
Wasuna A, Moosa A, Warner DF, Chibale K. Mutation in fusA1 causes in vitro resistance of *Mycobacterium tuberculosis* to fusidic acid. Poster presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Falls, Zambia, 27-29 August 2014.
Evans JC, Abrahams GL, Mizrahi V. Identification of vulnerable steps in the Coenzyme A biosynthetic pathway of *Mycobacterium tuberculosis*. Poster presented at the Keystone Symposium on Novel Therapeutic Approaches to Tuberculosis. Keystone, Colorado USA, 30 March - 4 April 2014.
Broadley SG, Warner DF, Sewell BT. Structure determination of ImuC from *Mycobacterium tuberculosis*. Poster presented at the Higher European Research Course for Users of Large Experimental Systems. Grenoble, France, 23 February - 26 March 2014.
Broadley SG, Warner DF, Sewell BT. Structure determination of ImuC from *Mycobacterium tuberculosis*. Poster presented at the International Conference on the Crystallization of Biological Macromolecules. Hamburg, Germany, 17-20 September 2014.
Hammond-Aryee K. Toxoplasma gondii IgG Antibody Avidity testing at National Health Laboratory Services, Tygerberg Academic Hospital Cape Town. Poster presented at the African Society of Laboratory Medicine Conference, Cape Town, South Africa, 30 November - 04 December 2014.
Willemse D. Expression of the *Mycobacterium tuberculosis* SufR homologue. Poster presentation at the SASBMS conference, Cape Town, South Africa, 6-9 July 2014.
Black P. Novel mechanisms contrubuting to evolution of drug resistance in *Mycobacterium tuberculosis*. Poster presented at the 35th Annual Congress of the European Society of Mycobacteriology, Vienna, Austria, 29 June - 02 July 2014.
De Vos M. Construction of a Three Color Single-Tube Assay for Resistance to First, Second, and Third Line Antibiotics used to Diagnose and Treat XDR-TB. Poster presented at the 45th Union World Conference on Lung Health, Barcelona, Spain, 28 October - 01 November 2014.
De Vos M. Detecting resistance to nine anti Tuberculosis drugs in a single reaction tube. Poster presented at the 45th Union World Conference on Lung Health. Barcelona, Spain, 28 October - 01 November 2014.
Steyn N. Investigating the localisation of the ESX-3 secretion system in *Mycobacterium smegmatis*. Poster presented at the 52nd Annual Microscopy Society of Southern Africa (MSSA 2014) hosted by Stellenbosch University, Cape Town, South Africa, 2-5 December 2014.
Mouton J. Single cell elucidation of mycobacterial replication dynamics. Poster presented at the 52nd Annual Microscopy Society of Southern Africa (MSSA 2014) hosted by Stellenbosch University, Cape Town, South Africa, 2-5 December 2014.

Hammond-Aryee K. Current Toxoplasma gondii seroprevalence studies in humans and animals in the western cape and policy implications. Poster presented at the 58th Annual Academic Day, Stellenbosch Univerrsity, Cape Town, South Africa, 13 August 2014.
Klopper M. Deciphering the Evolution of Totally Drug-Resistant tuberculosis: A catalogue of genome variation at single-base pair resolution. Poster presented at the 58th Annual Academic Day, Stellenbosch Univerrsity, Cape Town, South Africa, 13 August 2014.
Black P. Novel mechanisms contrubuting to evolution of drug resistance in *Mycobacterium tuberculosis*. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Fang Z. Functional study of Mycosin-3, an essential subtilisin-like serine protease in *Mycobacterium tuberculosis* - A proteomic approach. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Bowker N. Detection of novel TB susceptibility variants using next generation sequencing of the Major Histocompatibility and Leukocyte Receptor Complexes. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Goosen WJ. The Use Of Mycobacterium Bovis-Specific Antigens For The Diagnosis Of Tuberculosis In African Buffaloes (Syncerus Caffer).. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Kayigire X. Quantification of viable Mycobacterium tuberculosis using propidium mononazide combined with Xpert MTB/RIF. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
McFayden R. Investigating the Humoral Immune Response to *M. bovis* Infection in African Buffaloes (Syncerus caffer). Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Sao Emani C. Ergothioneine is secreted by slow growing mycobacteria. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Schlechter N. Identification of novel candidate genes for susceptibility to tuberculosis by identifying disease-causing mutations in individuals with PIDs. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Theys M. Characterising two essential penicillin-binding proteins of *Mycobacterium tuberculosis*. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Visser H. Deciphering the Resistance Mechanisms of *Mycobacterium tuberculosis* to Clofazimine. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Uren C. Fine-scale population structure between the Nama and Khomani San of Southern Africa. Poster presented at the 58th Annual Academic Day, Stellenbosch University, Cape Town, South Africa, 13 August 2014.
Fortuin S. Whole genome sequencing and Proteomic analysis of a heteroresistant *Mycobacterium tuberculosis* clinical isolate suggest in vitro evolution lead to an altered metabolic state of the *rpoB* resistant strain. Poster presented at the SACORE scientific meeting, Lilongwe, Malawi, 24-31 August 2014.
Miller M. Use of rapid serological assays for detection of *M. bovis* in free-ranging African lions (Panthera leo). Poster presented at the VI International M. bovis Conference, Cardiff, Wales, 16-19 June 2014.
Fortuin S. Whole genome sequencing and proteomic analysis of a heteroresistant *Mycobacterium tuberculosis* clinical isolate suggest in vitro evolution lead to an altered metabolic state of the *rpoB* resistant strain. Poster presented at the Wellcome Trust Emerging Scientific Researchers Conference, Uganda, 19-24 May 2014.
Uren C. Fine-scale population structure between the Nama and Khomani San of southern Africa. Poster presented at the Society of Molecular Biology and Evolution Annual Conference. Hilton Hotel, San Juan, Puerto Rico, 8-12 June 2014.
Uren C. Investigating fine-scale population structure between the Nama and Khomani San of southern Africa. Poster presented at the SASBi-SAGS Joint Congress. Kwalata Game Ranch, Tswane, South Africa, 23-26 September 2014.

Kleynhans L, Ronacher K, Walzl G, Loxton AG, Malherbe ST. Evaluation of the endocrine changes during TB treatment. Poster presented at the H 3-D Drug Discovery & Development: Innovative approaches to TB drug discovery: Laboratory to Bedside. Zambezi Sun, Livingston, Zambia, 27-29 August 2014.
Williams MJ. Biosynthesis of *bis*-molybdopterin guanine dinucleotide is dispensable for virulence of *Mycobacterium tuberculosis* in mice. Poster presented at the South African Society for Biochemistry and Molecular Biology Conference. Guidini Spa, Cape Town, South Africa, 6-9 July 2014.
Lucas LA, Walzl G, du Plessis J, Mgadi K. Circulating MicroRNAs: Potential Markers of Early Treatment Response in Pulmonary Tuberculosis. Poster presented at the 4th SA TB Conference. Durban ICC, Durban, South Africa, 10-13 June 2014.
Salie M, van der Merwe L, Möller M, Daya M, van der Spuy G, van Helden PD, Warren R, Hoal EG. Associations Between Human Leukocyte Antigen Class I Variants and the *Mycobacterium tuberculosis* Subtypes Causing Disease. Poster presented at the IUATLD. Barcelona Conference Centre, Barcelona, Spain, 30 October 2014.
Whitfield MG, Streicher EM, York T, **Mardarowicz I**, Scott L, Stevens W, **Van Helden PD,** Van Rie A, **Warren RM**. Association between genotypic and phenotypic pyrazinamide resistance in *Mycobacterium tuberculosis*. Poster presented at the 16th International Congress on Infectious Diseases. CTICC, Cape Town, South Africa, 02-05 April 2014.
Kigondu E, Singh V, Warner DF, Chibale K. In vitro synergistic interactions and possible mechanism of action of chlorpromazine and its metabolites in combination with anti-TB drugs against *Mycobacterium tuberculosis*. Poster presented at the H3-D Symposium on Innovative Approaches to TB Drug Discovery: from Bench to Bedside. Victoria Fals, Zambia, 27-29 August 2014.
De Vos M, Rice J, Rice L, Kreiswirth B, Kurepina N, **Streicher EM, van Helden PD, Warren RM**, Wangh L. Evaluation and Validation of a Highly Multiplexed LATE-PCR Single-tube Assay for M(X)DR-TB. Poster presented at the 16th International Congress of Infectious Dieseases. CTICC, Cape Town, South Africa, 02-05 April 2014.

Honours and Awards to Staff

Prof RM Warren was awarded the vice rectors award for outstanding publication numbers.
Prof G Walzl was awarded the vice rectors award for outstanding publication numbers.
Prof. B Kana was selected for the award of a Higher Education Leadership and Management (HELM) Fellowship for 2015. The HELM fellowship aims to provide enabling learning opportunities for middle and senior managers in both the academic and non-academic fields. This opportunity enables them to gain the knowledge and skills required for playing a constructive managerial role in advancing overall institutional performance within the framework set by legislation, national higher education policies and governance arrangements, a variety of system and institutional planning measures including those related to teaching and learning and research, and the funding of higher education institutions. Prof. Kana was one of 4 academics selected from Wits for this program.
Prof. B Kana was awarded the First Time Inventor's Prize from Wits Enterprise for the development of a globally marketable product. This award is given to staff or students at Wits University for pioneering approaches to developing patentable ideas and products.
Prof. B Kana was part of the team that was awarded the Gauteng Accelerator Programme (GAP) innovation completion. The GAP is an initiative of The Innovation Hub, a subsidiary of the Gauteng Growth and Development Agency and is implemented by The Innovation Hub in partnership with a number of industry and public sector stakeholders that include the Mobile Applications Laboratory of Southern Africa (mLab), Technology Innovation Agency (TIA) and the Climate Innovation Centre (CIC), Swedish, Smart Living Challenge, Merck Sharpe & Dohme (MSD) and in collaboration with Pfizer Inc., New York and Emory University (Atlanta, Georgia in USA). The Wits team won First prize for compiling a business plan for SmartSpot, a company that will be spun out of Wits University to market verification and quality assurance reagents for TB molecular diagnostics.
Prof. Warner was promoted *ad hominem* to Associate Professor in the Division of Medical Microbiology, Department of Clinical Laboratory Sciences at UCT.
Prof. Mizrahi received an Excellence Award from the University of Cape Town.

Progress of CBTBR Trainees (2005-2014)

Title	Surname, Initial	Training/Deg	Yr completed	Current position
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	Unknown
Ms	Strauss, C	Hons	2014	Unknown
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 as a 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	Axcell, A	MSc	2012	Working at the NHLS
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	2014	Took up a Postdoctoral Position in Hong Kong
Ms	Botha, L	MSc	2014	Took up PA position in CBTBR
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	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	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 MSc studentship at the MRC
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	Remained in CBTBR as postdoctoral fellow
Mr	Gallant, J	Hons	2013	Remained in CBTBR for a MSc degree
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	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	Kleynhans, L	PhD	2012	Remained in CBTBR as postdoctoral fellow
Ms	Koch, A	MSc	2011	Completed PhD degree in CBTBR at UCT in 2014. Currently doing postdoc at UCT
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	Unknown
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
Mr	Lunn, J	Hons	2013	Took up MSc position at UCT
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

Mr	Mameja	Hons	2013	Unknown
Ms	Mapela, L	MSc	2012	Unknown
Ms	Martin	Hons	2013	Remained in CBTBR for MSc degre
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	Mlamla, Z	MSc	2011	Remained in CBTBR for a PhD degree
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
Ms	Naran, K	MSc	2010	Completed PhD at UCT in CBTBR; currently doing postdoc in the UCT node
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	Ngombane, NC	MSc	2011	Returned to MRC
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
Ms	Sao Emani, C	Hons	2010	Remained in CBTBR for a PhD degree
Dr	Savvi, S	PhD	2009	Completed 2 postdocs at UCT; currently working for a biotech company in Cape Town
Ms	Seepe, P	MSc	2011	Remained in CBTBR for a PhD degree
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
Mr	Siame, KK	Hons	2010	Remained in CBTBR for a MSc degree
Ms	Steyn, NL	MSc	2012	Remained in CBTBR for a PhD degree

Ms	Strauss, O	MSc	2009	Moved to Kayaletsha HIV clinic in Cape Town
Dr	Streicher, EM	PhD	2007	ook up a NRF RCAF position in the CBTBR
Mr	Theys	Hons	2013	Remained in CBTBR for a MSc degree
Ms	Thiart, L	MSc	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	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Wagman, CK	MSc	2012	Took up a position at Police Forensics in Cape Town
Dr.	Warner, DF	Postdoctoral	2007	Moved from NHLS to UCT as CBTBR Team Member
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	Hons	2012	Remained in CBTBR for a MSc degree

FINANCES

The income statement, balance sheet and cash flow statement for period 1 Jan 2014 to 31 Dec 2014 have been reviewed and approved by the external auditors and will be forwarded to the Board.