DST-NRF CENTRE OF EXCELLENCE

ANNUAL PROGRESS REPORT

Reporting Period

1 January 2012 – 31 December 2012

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Identification

Name of Director	:	Professor Paul D. van Helden
Names of Node Heads	:	Professor Valerie Mizrahi Dr 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	:	18/02/2013

EXECUTIVE SUMMARY

1. Financial Information (Funding of the CoE)

Total NRF funding for 2012 (entire year) – CoE only	:	R 9 294 747
CoE-specific Funding from Host institution in 2012 – WITS	:	R 220 000
– UCT	:	R 127 911
– SU	:	R 778 236
Funding from other sources for the CoE in 2012	:	R 36 753 576
Total funding	:	**R 47 174 470**

Funding for 2012 for Wits node: (Total: R 7,552,825)

- CoE funding from NRF: **R 2,009,313**

- Funding from WITS and the NHLS: **R 1,760,702**, made up as follows:
  - WITS R 1,180,181[1]
  - NHLS R 580,521[2]

- Funding from other sources:[3] **R 3,782,810**, made up as follows:
  - HHMI IECS Award R 2.077,958[4]
  - NIH Subcontract R 194,796[5] (1 Oct 2012 – 31 Dec 2012)
  - MRC Career Development Award R 250,000 (2 Jan 2012 – 31 Dec 2012)
  - TIA (SATRII) R 850,000 (1 Apr 2012 – 31 Mar 2013)
  - CAPRISA R 130,000 (2 Jan 2012 – 31 Dec 2012)
  - NRF Incentive Funding R 80,000 (1 Apr 2012 – 31 Dec 2012)
  - MRC Research Day Awards R 15,000
  - CDC GeneXpert EQA funding R 185,056

Total funding for 2012 for UCT node: (Total: R 9,319,370

- CoE funding from NRF: **R 1,299,000**

- Funding from UCT and NHLS: **R 1,751,562**, made up as follows:
  - UCT R 651,562[6]
  - NHLS R 1,100,000[7]

- Funding from other sources:[8] **R 6,268,808**, made up as follows:
  - MRC Unit (MMRU) R 1,029,129 (1 Apr 2012 – 31 Mar 2013)
  - MRC (Salary) R 378,000 (1 Jan 2012 – 31 Dec 2012)
  - EU FP7 (MM4TB) (Yr 2) R 925,885 (1 Feb 2012 – 31 Dec 2012)[9]
  - FNIH (HIT-TB) R 2,662,294 (1 Mar 2012 – 28 Feb 2013)[10]
  - TIA (SATRII) R 1,000,500 (23 Mar 2011 – 30 Sep 2012)
  - HHMI SIRS grant (Yr 1) R 273,000 (1 Oct 2012 – 31 Dec 2012)[6]

[1] Made up of Friedel Sellschop Research Award to B. Kana for three years – 2012, the final year, 10% CoE Institutional commitment, co-funding for MRC Career Development Award to B. Kana, salary allocation and major equipment co-funding
[2] Salary allocation
[3] Where applicable, grant awards from external funders include indirect costs
[4] Year 1 of 5-year grant from the HHMI – 10% of funds are retained by WITS as indirect costs
[5] Once-off supplement to the PHRU CTU from the NIH, funds shown are those spent in 2012, 8% of funding is retained by the WITS Health Consortium as indirect costs
[6] Salaries and running costs
[7] Salaries
[8] Where applicable, grant awards from external funders include indirect costs (IDC)
[9] Year 2 of four-year grant (total €331,667 - including IDC), calculated at exchange rate of R11.1/€
[10] Year 2 of 3.5-year grant from FNIH (sub-contractor on grant from BMGF), calculated at exchange rate of R8.2/$
[6] New five-year $500,000 grant, began on 1 October 2012. Amount shown is the proportional grant for the 2012 calendar year.

Funding for 2012 for SU node: (Total: R30 302 275)

- CoE funding from NRF : **R5 986 434**

- Other Funding from SU: (best estimate): **R3 200 000,** incl. some salaries, student bursaries, excl. space, basic infrastructure, secretary, cleaners.

- Funding from other sources (best estima**te):** **R21 115 841**, made up as follows:
  - MRC Centre (estimate of the TB component) R 6 100 241 (incl. salaries)
  - PGWC R 2 100 000 (salaries only)
  - NWO R 350 000
  - EDCTP R 2 700 000
  - BMGF R 4 100 000
  - Welcome Trust R 1 200 000
  - Harry Crossley Foundation R 157 600
  - IMPAACT R 300 000
  - RCB (Germany) R 200 000
  - VPM (Germany) R 1 500 000
  - DF (Germany) R 350 000
  - K-RITH R 33 000
  - NIH R 100 000
  - Cellestis R 550 000
  - Other NRF funding R 1 375 000

2. Summary of progress against 5 KPAs

(i) Research

The research productivity of the CBTBR remained excellent in 2012 as evidenced by the fact that 2 book chapters, 47 articles in peer-reviewed journals, 3 non-peer-reviewed articles were published, and 101 conference presentations were made, including 9 plenary/ keynote lectures, and numerous invited talks. Of the research articles published, 40 were in journals with an impact factor (IF) >2.

Progress against targets SLA 4 targets: The outputs under this KPA greatly exceeded the SLA target (≥10 publications of which ≥5 are in journals with an IF ≥2).

(ii) Education and Training

A total of 2 postdoctoral fellows, 8 PhD students, 7 MSc students and 9 Honours students from the CBTBR graduated or completed their training in 2012. All these postgraduate students completed degrees within their maximum allowable time agreed upon in the SLA. A number of new postdoctoral, PhD and MSc students were enrolled in the nodes of the CBTBR. A number of students were afforded the opportunity to work in international labs (details provided below).

Progress against SLA 4 targets: The total of 84 postgraduate students associated with the CBTBR in 2012 is more than triple the SLA target of ≥25. The student breakdown according gender (69% female) and percentage of postdoctoral fellows (18% of total student complement) equalled or exceeded the SLA targets of ≥50% and ≥10%, respectively. The percentage of black students (53%) exceeded the SLA target of ≥50%. The percentage of Honours students was 11% in 2012. No honours students were rejected unless they did not meet the entrance requirements set by the university.

(iii) Knowledge Brokerage

Members of the CBTBR continue to disseminate scientific information at the operational, scientific community and stakeholder levels as far as possible. Apart from enjoying country-wide and sometimes international publicity in various media platforms, the CBTBR continued to be involved in many outreach activities, targeting school teachers and learners, and on science communication in general. We continue to strive for improved comunication with metropolitan, provincial and national health authorities, MSF and NHLS. Our interaction with these stakeholders continues to improve, even if still failry low key. We continue to advise SANParks, the NZG and Johannesburg Zoo, as well as some private entities with regard to TB in wildlife or captive animals.

CBTBR members continue to be engaged with the media to develop more accurate and meaningful science communication channels between various media stakeholders and the basic researchers through participation in the adjudication panel for the Discovery Health Journalism Awards. CBTBR members also participated/ran workshops at local conferences which were aimed at assisting postgraduate students at developing academic careers in science.

For the first time, the CBTBR has prepared an MRC "Policy Brief" concerning recommendations for TB treatment in the case of drug resistant disease. This policy brief was prepared in consultation with the MRC and was released in January 2012.

(iv) Networking

The CBTBR played a key role in facilitating the SU-UCT collaboration that led to the award of the ACGT/IMPAACT/HVTN International Tuberculosis Speciality Laboratory (ITBSL) in 2012 to a consortium led by Prof. Andreas Diacon from SU. The consortium also includes Profs. van Helden and Walzl from SU, and Profs. Hanekom, Nicol and Mizrahi from UCT,

The UCT node has made good progress on strengthening collaboration within UCT, particularly with the H3-D Centre for Drug Discovery and Development (led by Prof. Kelly Chibale) and the Demsond Tutu HIV Centre. This node is also in discussion with groups at Harvard University, University of Pittsburgh and K-RITH on various collaborative projects. The Wits node continues playing the leading role in an international collaboration between Wits University, the USA National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the University of Leicester, the Perinatal HIV Research Unit (PHRU) and the Aurum Institute which involves the detection and characterization of non-replicating bacterial populations in the sputum of patients with active TB disease. The Wits node has also initiated a new collaboration with PATH, a US-based organization, which will assist the node on the commercialization of reagents used in the validation of novel diagnostics. In this context, the Wits node will be forming new collaborative links with groups in India and China. The SU node continues to be a major partner in numerous international links, now even including Saudi Arabia fr wnhole genome sequencing and including various BMGF grants (e.g. Prof. Walzl via Prof. Kaufmann in Berlin on GC6). Furthermore, Prof Walzl has other BGMF grants: 1) Biomarker Discovery with a consortium including Drs. Clif Barry (NIH), David Alland and others, 2) Hazel Dockrell (LSHTM) on surrogate markers. The CBTBR partners extensively in Africa, for example through an EDCTP grant supporting an African/European consortium with 7 African and 5 European sites.

The CBTBR regards this activity as central and vital to our activities and encourages it as far as is possible.

(v) Service rendering

Activities in this area include the provision of technical/ scientific services to the Eastern and Western Cape Provincial Health Department, the gold mines, Tygerberg Hospital and various TB clinics, the 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 candidate drug compounds for UKZN, UWC and UCT. 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, Johannesburg Zoo and others regarding TB in wild animals continues to be given, and to the AACL for companion animals. The SU node continues to assist the MRC (Delft) and SAAVI with TB infection problems in their animals. The Wits node continues to play an important role in the national rollout of the GeneXpert diagnostic platform which promises to revolutionize TB diagnostics in South Africa. In this regard, the Wits node has been involved in the establishment of the external quality assurance system for this platform, The Wits node has further assisted the Contract Laboratory Services division of the NHLS to establish DNA extraction methodologies for strain typing for samples in the REMOX clinical trial and continues to provide support where necessary. The SU node developed a new sample collection vial for fine needle aspirates for TB diagnosis. This vial system is being rolled out by NHLS.

3. Gender Impact

From the "Science by Women" perspective, it is important to note that 69% (unchanged since 2011) of post graduate students in the CBTBR in 2012 were female. The very high representation by women at the lower levels of this research enterprise is consistent with the broader demographic picture for the Health Sciences in SA.

PROGRESS REPORT

1. Scientific Research

Research progress is summarised briefly in the Appendix; only the joint research and training activities are outlined here.

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 UCT and Wits nodes. A key researcher in this project is Dr. Monique Williams, whose appointment is in the MRC/NHLS/UCT Molecular Mycobacteriology Research Unit (UCT node of the CBTBR) but is seconded full-time to the SU node. This collaboration has yielded a review article, which is in press in a high-impact journal This secondment has enabled Dr. Williams to participate in several core SU projects studying drug resistance and efflux. The second collaboration between the three nodes nodes is on the TIA-funded SATRII project. Researchers at the three nodes together form the Biology component of the SATRII project.

2. **Wits-SU**. Dr Melissa Chengalroyen from the Wits node spent two weeks at the SU node to obtain training on DNA fingerprinting methodologies to distinguishing *M. tuberculosis* strains. Dr Chengalroyen has now established the relevant methods at the Wits node and continues to work with Dr Streicher at the SU node on interpretation of the data.

2. Education and Training

Breakdown of postgraduate students and postdoctoral fellows in the CBTBR in 2012

Student category	Number/percentage	Target based on SLA4 (for Performing Phase, 2009-2012)
Total number of students	84	≥ 25
% Postdoctoral fellows	18%	≥10%
% PhD students	34%	N/A
% MSc students	37%	N/A
% BSc (Hons) students	11%	N/A
% Women students	69%	≥ 50%
% Black students	53%	≥ 50%

Degrees conferred and postdoctoral fellowships completed

The CBTBR graduated 2 postdoctoral fellows, 8 PhD, 7 MSc, and 9 Honours students in 2012.

Dissertations and theses

PhD

1. Moosa A. Molecular mechanisms of transport and metabolism of vitamin B_{12} in mycobacteria. Supervisorer: D Warner. Co-supervisor: V Mizrahi
2. Kleynhans L. The impact of the steroid hormones medroxyprogesterone acetate, cortisol and progesterone on protective immunity to tuberculosis. Promoter: G Walzl
3. Du Plessis N. The impact of Nippostrongylus Brasiliensis infection on host immune responses and susceptibility to Mycobacterium tuberculosis in a murine co-infection model. Promoter: G Walzl
4. Ngwane A. Elucidation of the mechanism of action of a furanone based compound (F1082). Promoter: I Wiid, Co-Promoter: PD van Helden
5. Bruiners N. Investigating the Human M. tuberculosis interactome to identify the host targets of ESAT-6 and other mycobacterial antigens. Promoter: NC Gey van Pittius, Co-Promoter: RM Warren

6. Van der Merwe R. Development of a novel fluorescent-marker phage technology system for the early diagnosis of tuberculosis disease. Promoter: RM Warren
7. Werely CJ. Pharmacogenetics of Arylamine N-acetyltransferase genes in South African populations. Promoter: PD van Helden
8. Botha MM. Regulators of dormancy/viability of *Mycobacterium tuberculosis* inside the human macrophages. Promoter: I Wiid

MSc

1 Axcell A. Genotypic and phenotypic heterogeneity of *Mycobacterium tuberculosis* recovered from patients with drug-resistant pulmonary tuberculosis. Promoter: B. Kana

2 Mapela L. Characterization of Resuscitation Promoting Factors in *Mycobacterium smegmatis.* Promoter: B. Kana

3 Black P. Identification of genes regulating the expression of the *atpBEFHAGDC* operon in response to rifampicin in multi-drug resistant Mycobacterium tuberculosis strains. Promoter: TC Victor

4 Grobbelaar M. Adaptation of the *Mycobacterium tuberculosis* transcriptome in response to rifampicin. Promoter: TC Victor

5 Lucas L. Toll-like receptor genes and their pathway: role in susceptibility to pulmonary tuberculosis in a South African population. Promoter: E Hoal

6 Wagman C. Genetic studies on susceptibility to pulmonary tuberculosis mediated by MARCO, SP-D and CD14: molecules affecting uptake of *Mycobacterium tuberculosis* into macrophages. Promoter: E Hoal

7 Steyn N. Investigating the localisation of the ESX-3 secretion system in *Mycobacterium smegmatis*. Promoter: NC Gey van Pittius, Co-Promotor: RM Warren

Research interns (MRC sponsored)

1. Ms P Seepe (Research Intern) Registered for 2nd year of PhD degree in 2012

Recruitment of new postgraduate students

A number of new students have joined the team already or will do so during the course of 2013. 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 4 Postdoctoral fellows, 6 PhD, 5 MSc and 8 Honours students into the CBTBR in 2012. At the UCT node 1 Postdoctoral fellow, 1 PhD students and one Honours student were recruited. At the Wits node 1 Postdoctoral fellow and 1 MSc student were recruited in 2012.

Honours and awards to students

- Dr Christopher Ealand, Ms Farzanah Hassim, Ms Nabiela Moola, and Mr Sibusiso Senzani were all invited to give oral presentations at the MRC Early Career Scientists Conference 2012, 24th – 25th October 2012. Ms Moola and Mr Senzani both won first and second prize respectively for best oral presentation by an MSc student.
- Mr Sibusiso Senzani was invited to give an oral presentation at the DST/NRF Centre of Excellence Director's Forum. Sanlam Centre, Pretoria, South Africa. 13th November 2012
- Mr Sibusiso Senzani received a scare skills MSc bursary from the NRF. Ms Rukaya Asmal, Ms Farzanah Hassim and Ms Nabiela Moola received MSc bursaries from the NRF. Mr Germar Beukes, Ms Rukaya Asmal, Ms Farzanah Hassim and Ms Nabiela Moola received the postgraduate merit award from Wits University
- Dr Christopher Ealand was awarded a CAPRISA postdoctoral scholarship for partial salary funding.
- MSc students, Ms Lusanda Mapela and Ms Amanda Axcell both graduated with distinction.
- Dr. Monique Williams was awarded a Columbia University-Southern African Fogarty AITRP Traineeship and a PHRI-AURUM-Global Infectious Diseases Research Fogarty Traineeship which enabled her to undertake 6 months of postdoctoral training in TB basic sciences in the laboratory of Dr. Gilla Kaplan at the PHRI at UMDNJ (New Jersey).

- Dr. Vinayak Singh was awarded a Keystone Symposia Global Health Travel Award to attend the Keystone Symposium on Tuberculosis: Understanding the Enemy, to be held at Keystone Resort, British Columbia, Canada, in March 2013.
- Ms. Anastasia Koch received the Benfara Scholarship from UCT and a DAAD-NRF Joint Scholarship; Ms. Krupa Naran was awarded a scholarship from the Ernst and Ethel Eriksen Trust, a UCT Equity Scholarship and a DAAD-NRF Joint Scholarship; Ms. Zanele Ditse was awarded the Marion Beatrice Waddel Scholarship, an Equity Scholarship from UCT and a DAAD/NRF Joint Scholarship.
- CBTBR students from all three nodes received various scholarships and travel grants in 2012
- Mrs M. Klopper, received the L'Oréal-UNESCO Regional Bursary for Women in Science Fellowship Sub-Saharan Africa, 2012
- Mrs M. Klopper, was awarded a SACEMA PhD bursary, 2012
- Mr. M Salie and Miss M. Grobbelaar were awarded MRC PhD Bursaries, 2012
- Dr E Streicher, Dr G. Louw, Mrs M de Vos, Miss M. Grobbelaar, Ms. P Black were awarded the Bill and Melinda Gates Global Health Travel grant (Keystone Symposium: E1, Drug Resistance and Persistence in Tuberculosis, Kampala, Uganda, May 2012)
- Mrs M. de Vos, awarded a NRF scarce skills Doctoral Fellowship: Stellenbosch University Postgraduate Merit bursary, 2012
- Mr M. Salie, DAAD-NRF Joint In-Country Doctoral Scholarship, 2012
- Mr M. Salie, Miss J. du Plessis and Ms A Dippenaar were awarded Harry Crossley Funding, 2012
- Mr M. Salie, EMBL Travel Grant and Registration Fee Waiver, 2012
- Miss J. du Plessis, received a SU Postgraduate Merit Bursary, 2012
- Miss J. du Plessis, was awarded the UMDNJ Global Infectious Diseases Scholarship, 2012
- Mr A. Viljoen and Mrs C. de Villiers were awarded DAAD-NRF Scholarships for PhD, 2012
- Mr M. Salie, Ms A. Dippenaar were awarded International Office Overseas Conference Grants, 2012
- Ms. M. Daya, received a full fee scholarship (17th Summer Institute in Statistical Genetics (SISG) for 3 modules: Bayesian Statistics for Genetics, MCMS for Genetics, Mixed Models in Quantitative Genetics), 2012
- Mr. M. Salie, received the SU-FMHS Scientific Travel-Scientific Visit grant (Stanford University)
- Miss S. Fortuin, received the MRC PhD Internship, 2012
- Miss S. Fortuin, received the Pasteur Institute travel award (Proteomics and drug design Course, Tunisia), 2012
- Miss S. Fortuin, was awarded Welcome trust travel award (6th Annual Directors meeting, Ghana), 2012
- Ms. N. Le Roex, Finalist in the Popular Science Article category at the New Voices in Science colloquium, Stellenbosch University, December 2012.
- Dr A Loxton, received the SU Scientific Travel Award (AIDS 2012 meeting, Washington, USA), 2012
- Dr A Loxton, obtained the ERS International travel award Vienna, Austria, September 2012

Hosting of international exchange students

Mr. Felanji Simukonda (Karonga Prevention Study (KPS), in Malawi), Mrs. Anna-Ritah Namuganga (Uganda - Case Western Reserve Collaboration Immunology Laboratories at the Joint Clinical Research Centre, Makerere University) visited the SUN-IRG unit for training on laboratory procedures and conduction of specialized experiments on a collaborative biomarker research project, the African European Tuberculosis Consortium (AE-TBC) study in 2012.

Molecular Epidemiology Course

Prof. Rob Warren ran PCR training courses in 2012 and trainees included Gershvin Arries, Xavier Kayigire, Bayanika Manunu from CCTR and 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 *Mycobacteria tuberculosis*, restriction enzyme digests, southern blotting, probe labelling and hybridisation. The course equipped all participants with the necessary skill to enable them to perform PCR.

Other Training courses

Ms. Amour Venter also conducted initiation training for the laboratory personnel involved with clinical drug trials on the following protocols:

- TB Alliance protocol number NC-002-(M-Pa-Z); 06 March 2012
- Protocol TBTC Study 29X; 06 March 2012
- TB Alliance protocol number NC-003-(C-J-Pa-Z); 11 September 2012
- AstraZeneca protocol DMID 11-0006; 08 November 2012

Other Workshops

- Prof G van der Spuy presented on CRF design and data capture a workshop in Windhoek, July 2012.
- Prof G Walzl presented a workshop on Laboratory accreditation in Windhoek, July 2012.
- Prof G van der Spuy Presented 'Data Management - Principles & Practice' module at the Faculty of Medicine and & Health Sciences Workshop 'Project Management for the Research Team' on 28 August 2012 held at Tygerberg Campus.

Training courses attended by staff and students

Training Course	Attendee/s
Advanced TB Research course, 06-09 March 2012, at the UCT Lung Institute	Dr N. Chegou, Mr P. Essone Ndong
Proteomics & drugs design Course, Institute Pasteur, Tunis, 20-24 March 2012	Ms. S. Fortuin
'GCP for the Research Team' Course, Tygerberg Campus, Stellenbosch University, 26-27 January 2012	Drs A. Loxton, M. Kriel, N. Chegou, L. Kleynhans, N. du Plessis, Mrs L. Muller, Ms K.Stanley
SAMU/MSF DR-TB Workshop. Title: Drug resistant TB and genetic mutations	Dr. EM Streicher
Secretary course on 24 April 2012 held in Rondebosch	Ms L Vos
Performance Management Workshop on 17 April 2012 at Devon Valley, hosted by Stellenbosch University	Mrs L Muller, Dr D. Kriel
Basic isiXhosa course, Masazane 1, 14 Feb-19 April 2012, Tygerberg Campus	Mrs S. Mcanda, Prof. I. Wiid
Grant Writing Course, STIAS, Stellenbosch, 18 April 2012	Dr N. Du Plessis
Mass Spectrometry and Proteomics Course during 18th-25th April 2012, at University of Southern Denmark, Odense, Denmark	Mr. KK Siame
HR: Building effective Relationships 11-12 of June hosted by human resources of Stellenbosch University at Lancerac Manor	Dr. K. Ronacher-Mansvelt
GCP course, Tygerberg Campus, Stellenbosch University, 14-15 June.	Dr. K. Ronacher-Mansvelt
Helping students to avoid plagiarism and use Harvard referencing correctly on 30 May 2012 at SU Language Centre	Ms G Durrheim
Hain Lifescience SA (Pty) Ltd Mini Symposium, Vineyard Hotel and Spa, Newlands, Cape town. 24 May 2012	Dr E Streicher
The Keystone Symposia on Drug Resistance and Persistence in Tuberculosis on 13-18 May 2012 held at Kampala, Uganda.	Ms PA Black
Keystone Symposia on Drug Resistance and Persistence in Tuberculosis, Kampala, Uganda, 13-18 May 2012	Drs E. Streicher, G. Louw, A. Ngwane, Ms M. Grobbelaar, Mrs M. de Vos
Population Genetics workshop hosted by UCT, 4-8 June 2012	Drs. M. Moller, M. Daya & N. Roetz
Partek workshop Workshop (Next Generation Sequencing and Microarray Data Analysis), SANBI, UWC, 23-27 July 2012	Ms P. Black, Ms M. Grobbelaar, Mr. M Salie

Workshop in Windhoek, Various topics related to consortium studies, July 2012	Profs G. van der Spuy, G. Walzl, Dr M. Kriel, Ms. K. Stanley
New Voices in Science: Writing Workshop, Stellenbosch Univ, 4 September 2012	Mr. M Salie
New Voices in Science: Science Communication Workshop, Stellenbosch Campus, 11 June 2012	Ms. N. le Roex
17th Summer Institute in Statistical Genetics (SISG), Seattle, USA, 9th-20th July	Ms. M. Daya
Mass spectrometry based Proteomics workshop, Tygerberg Campus, Stellenbosch University,11 July 2012	Mr RD Pietersen, Ms. A. Dippenaar, L. Vos
Two-week course entitled, "Introduction to statistics and its applications in Biology (level II)" from 9-20 July 2012 at SACEMA, Stellenbosch	Dr. N. Chegou
SASBMB/FASBMB Congress 2012 in the Drakensberg, from 29 Jan - 1 Feb 2012.	Mr P Essone Ndong
Advanced TB Diagnostic research course at UCT Lung Institute, 6-9 March 2012	Mr P Essone Ndong
Workshop hosted by the Dept Molecular and Cell Biology, University of Cape Town & the Centre for Proteomic and Genomic Research, 19-21 September 2012	Ms L. Vos, Ms M. McGrath
Seminar on the UniProt and Tuberculist databases, UCT, 1-2 November 2012	Ms M. McGrath
Web seminar on the PATRIC website presented by the PATRIC website organisation, 27-30 Nov 2012.	Ms L. Vos, M. McGrath
Workshop in scientific writing skills for theses, 22-23 August 2012	Ms M. McGrath,
Workshop in scientific writing skills for academic articles,28-29 August 2012	Ms M. McGrath,
ARESA (Advanced Research Ethics Training in Southern Africa) seminar, Newlands, Cape Town, 30-31 August 2012	Dr. M. Moller, Mr. M. Salie, Prof E. Hoal
DAIDS Good Clinical Laboratory Practise Training Course, Johannesburg, 28–30 August 2012	K Stanley
EMBO Proteomics bioinformatics course: Computational Biology: from genomes to cells and systems, Girona, Spain, 14-20 October 2012	Ms A Dippenaar
Novartis Next Generation Scientist in Basel, Switzerland from 01 June-31 August 2012	Dr A Ngwane
Microbiome Master Class, IIDMM, UCT, October 2012	Ms A Koch
Novartis Next Generation of Scientist 2011 and 2012 reunion, KZN University, Durban, 28-30 November 2012	Dr A Ngwane
Workshop in scientific writing skills for academic articles. 28-29 August 2012. Stellenbosch University	Dr M de Vos

Staff members studying for higher degrees (all registered at SU)

- Cedric Werely (PGWC) completed his doctoral degree, working on Arylamine N-acetyltransferase genes in Tuberculosis to study the influence of host genetics on disease susceptibility.

Other capacity development activities

- Prof. Warren presented two lectures in the MBChB module on Infections and Clinical Immunology in 2012. Title: Molecular Epidemiology of Drug Resistant TB in South Africa.
- Dr. Warner (organiser), Prof. Mizrahi and Dr. Evans lectured in the Bacterial Pathogenesis module of the Infectious Diseases and Immunology Honours course, UCT, 2012
- Dr. Warner lectured on the Medical Microbiology component of intercalated MBChB programme, UCT Faculty of Health Sciences
- Dr. Kana lectured in the Molecular Medicine and Hematology Honours program in the School of Pathology.
- Dr Gordhan and Dr Kana ran a gene cloning course for Honours students in the School of Pathology
- Dr Kana lectured in the Human Genetics Honours program at Wits University.
- Dr Kana lectured in the Postdoctoral Forum in the Faculty of Health Sciences.

Exchange visits

- Prof. Peter Schwartz and Dr. Massimiliano Gnecchi of the University of Pavia, Italy, for purposes of establishing a new cell culture technique for collaborative study on LQT syndrome, 29-February 2012
- Dr. Clif Barry (NIH), Dr. Jelle Thole (Tuberculosis Vaccine Initiative) visited the SU node for an evaluation visit from the SA Accreditation System (SANAS) and was recommended for Accreditation by the assessors, 01 March 2012
- Dr. Nazir Ismail (NICD), Discussions on collaboration, 2012
- Dr. Chikwe Ihekweazu (NICD), Discussions on collaboration,2012
- Dr. Johan van Heerden (NHLS), Discussions on collaboration,2012
- Dr. Karen Jacobson (Harvard), Discussions on collaboration, 2012
- Dr. Bernd Eisle and Dr. Ankita Minhas (Vakzine Project Management (VPM) Germany), for the ongoing phase IIa TB vaccine trial, 17 April 2012
- Prof. Kevin Fennelly (University of Florida), setting up the Andersen impactor to measure transmissibility of TB cases, 23-25 April 2012
- Prof. D.R. Sherman (Seattle Biomedical Research Institute), student exchange, 22-February 2012
- Dr. Annette Roug (PhD candidate in wildlife epidemiology at University of California, Davis, USA), to evaluate an RT-PCR assay for screening African buffalo faeces for M. bovis, August 2012
- Drs. Akin Jenkins & Calvin Gomo (Veterinary Faculty, University of Pretoria), Performed diagnostic screening for bovine tuberculosis in dairy cattle in Western Cape herds, September 2012
- Dr. Jelle Thole and the TB Vaccine Initiative (TBVI) visited the CBTBR SU node on 25 October 2012
- EDCTP – High Level delegation visited the CBTBR SU node on 05 November 2012
- The UCT node hosted many visitors in 2012, including Drs. Eric Rubin (Harvard), Dr. David Sherman (Seattle Biomed), Dr. David Russell (Cornell), Dr. Clif Barry and Dr. Helena Boshoff (NIAID), Prof. Stewart Cole (EPFL)
- Dr C de Chastellier (INSERM, France), Dr Y Lemmer (CSIR) and Prof J Verschoor (Univ. Of Pretoria) – visited for discussions on EM and Nanoparticle technology, December 2012
- Dr. Bavesh Kana visited K-RITH for collaborative discussions, May 2012
- Dr. Bavesh Kana visited Prof. Michael Barer at the University of Leicester for collaborative discussions, 2012
- Dr. Bavesh Kana visited Dr. Neeraj Dhar, EPFL, Switzerland for collaborative discussions, September 2012
- Dr. Williams was awarded a CU-SA Fogarty Fellowship to train in Dr. Kaplan's laboratory in 2012. Also in 2012, Dr Williams spent three weeks at the Wits node to conduct lipid analyses on mycobacterial strains.
- Mr. Andile Ngwane visited Novartis Institutes for Biomedical Research in Basel, Switzerland, for the Novartis Next Generation of Scientist Programme, 01 June- 31 August 2012
- Ms. Natalie Bruiners visited the Public Health Research Institute, New Jersey, for research training, June-Dec 2012
- Ms. Philippa Black visited Prof. Christopher Sassetti's lab in Worcester, USA to receive training in molecular techniques such as transposon mutagenesis and DNA library preparation. 1-31 October 2012.
- Ms. Margaretha de Vos visited Prof. Larry Wangh's lab at Brandeis University, Waltham, MA, USA to receive training in LATE-PCR and Lights-on/lights-off probes techniques. 15 October - 1 November 2012
- Ms. Juanelle du Plessis visited Prof. David Sherman's lab in Seattle, USA to receive microarray and data analysis training. 01 July - 31 October 2012
- Mr. Muneeb Salie visited Prof Carlos Bustamante/Dr Brenna Henn Lab, Stanford University, USA, for training in software for statistical analysis of population admixture and next-gen sequencing, 12 October – 2 November 2012

International Conferences Organised (2)

- Bovine Tuberculosis Conference, Skukuza, Pretoria, South Africa September 2012
  Prof. Paul van Helden was part of the organising committee for this conference.
- 3rd SA TB Conference, Durban, South Africa, 12-15 June 2012
  Dr Bavesh Kana was part of the organising committee for this conference and chaired the Basic Sciences Track.

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. We also attend numerous local and international conferences, often as invited speakers, where we share our work with the international community. We have had numerous meetings and contacts with health authorities, such as W and E Cape Departments of Health, to share with them our findings and the implication of these. These are just some of the bodies we have met with. Team members also advise international organisations, such as GATB and WHO.

Knowledge translation to stakeholder groups

CBTBR members were involved in numerous public awareness activities countrywide in 2012:

Public awareness, public engagement, and publicity

- Prof. Mizrahi delivered her Inaugural Lecture entitled, *"*Knowing the Enemy: Survival and Subversion Strategies of *Mycobacterium tuberculosis"* at UCT on 22 August. This public lecture attracted a wide audience from across Cape Town.
- On 20 November, the Health Sciences Postdoctoral Association (HSPDA) of UCT held its inaugural Postdoctoral Research Day as part of the Faculty Centenary Celebrations. UCT node postdoctoral fellow, Dr. Joanna Evans, chaired this event, and Drs. Vinayak Singh and Krishnamoorthy Gopinath served on the Organising Committee. Postdoctoral fellows from across the University were invited to participate, with the aim of increasing awareness of the research being carried out by postdocs in other Faculties and encouraging further academic interaction between UCT postdocs. As a result, the audience of approximately 170 people, comprising postgraduate students and staff members as well as postdocs, was treated to a selection of presentations that covered topics ranging from Astronomy and Chemistry to Zoology and Immunology. Three distinguished plenary speakers, Emeritus Prof. Wieland Gevers (IIDMM, UCT), Prof. Anusuya Chinsamy-Turan (Zoology, UCT) and Prof Robert Millar (IIDMM, UCT) delivered excellent lectures centered around the theme of how to succeed as a postdoc in academia. The Faculty of Health Sciences, together with IIDMM, sponsored a very generous sum of R12000 prize money for the top three presentations in both the oral and poster categories, which were decided upon by a selection of academics from within the Faculty. This event was a great success that was thoroughly enjoyed by all who attended.
- Members of the UCT node also participated in a number of outreach activities:
  a. Prof. Mizrahi interviewed by SABC radio and SABC television at the 3rd SA TB Conference in Durban. Television interview was broadcast on the main news bulletins on SABC1, SABC2, SABC3 and e-TV on June 12 and June 13, 2012.
  b. Ms. Anastasia Koch is a member of the Health Sciences Postgraduate Students Council (HSPSC), and serve as the co-head of the Social Responsiveness Portfolio. The aim of the portfolio is to provide a space and structure for HSF postgraduate students to contribute to community outreach initiatives, and to develop a culture of social responsiveness within the HSF. Events that have been arranged by this portfolio include: a postgraduate students quiz night that was held on 4 October 2012 to raise money for Friends of the Children's Hospital Organization, and workshops with postgraduate students to plan a series of health-related events to be held in partnership with Ikamva Youth in Khayelitsha in February 2013.
  c. Two Grade 11 students from the LEAP school (http://leapschool.org.za/) were hosted by PhD students, Anastasia Koch and Zanele Ditse, in August 2012. The students, who are interested in pursuing a career in scientific research, spent two days in the MMRU to find out what a career in biomedical research might entail.
  d. Dr. Evans participated in the Pinelands High School Careers Evening (21 June 2012) and advised learners on careers in Microbiology/Molecular Biology.
- Dr. Warner adjudicated essays submitted to the Royal Society of South Africa Schools Essay Competition in June 2012.

- On the 19th September 2012, the Faculty of Health Sciences at Wits University hosted their biennial Health Sciences Research Day. This event was chaired by Dr Bavesh Kana from the Wits node and the other members of the node were extensively involved in organization of the day, coordinating exhibitions and review of the abstract book. The day was a phenomenal success and served as a wonderful platform to garner greater enthusiasm for research within and across many different disciplines. The event was attended by over 1000 delegates, with 90 oral and 187 poster presentations, covering topics within five themes: Clinical Research and Therapeutics for Health; Diseases of Lifestyle; Education, policy and systems; Infectious Diseases and Molecular and Comparative Biosciences. Research Day 2012, which fell under the auspices of the Wits90 celebrations, was held in the spirit of celebrating the Faculty's achievements in research, which was reflected in the record number of abstract submissions and overall increased attendance by researchers, exhibitors, government officials, senior visitors from other Faculties and senior University staff. The Deputy Minister of Health, Dr Gwen Ramokgopa gave the opening address which was followed by plenary lectures by Dr Jonathan Lewis (Director of ZIOPHARM Oncology) and Professor Shabir Madhi (Executive Director of the National Institute for Communicable Diseases (NICD) and Director of the Respiratory Meningeal Pathogens Research Unit). Three round table discussions were convened in the afternoon, where top, highly qualified experts gathered to tackle different issues (A world without AIDS; Eliminating TB and Colliding Epidemics – Africa in Transition). Dr Kana, along with other members of the organizing committee raised R 463 000 in sponsorship to fund the event, R 187 500 of which was disbursed as awards for excellent research presentations. The Health Science Research day 2012 promoted a renewed passion for scientific research and related activities and would not have been possible without the extensive involvement and time commitment from the Wits node of the CBTBR.
- During the Wits Health Sciences Research Day 2012, the members of the Wits node of the CBTBR created an exhibit to profile the work done on TB at Wits University. There was significant contact with undergraduate and postgraduate students from various disciplines, many of whom wanted to know more about TB.
- Dr Bavesh Kana participated in an open round table discussion at the Wits Health Sciences Research day on strategies for eradication of TB in South Africa, 19th September 2012. This discussion was attended by a broad spectrum of people from within and outside the University.
- Dr. Christopher Ealand and Ms Nicole Narrandes participated in the Wits Cross-Faculty Open Day. They created and manned an exhibit to profile the work done at the CBTBR to high school students.
- In July 2012, Dr Bavesh Kana was invited to participate in the Talking Heads program. This program involved the gathering of 50 of the most interesting thought leaders/experts in South Africa. Each of these leaders meets with 4 groups of 6-8 people from the general public to discuss their area of expertise. Dr Kana was engaged in this program as an expert and used the opportunity to profile the TB problem and the work done at the CBTBR to members of the general public/other professionals.
- In March 2012, Dr Kana served as a judge in the 2011 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. Dr Kana was also invited to attend the awards function where presentations were made to the journalists with winning entries.
- Dr Bavesh Kana also had the opportunity to provide mentorship and advice to postgraduate students, nurses and community health care workers on building academic careers in science at two local conferences. The first workshop was conducted at the South African Society for Biochemistry and Molecular Biology 2012 Meeting, 29 January – 1 February 2012, Champagne Sport Resort, Drakensberg, South Africa. This was a unique opportunity to provide career guidance to MSc, PhD students and postdocs with varying research backgrounds. The second workshop was held at the Research Capacity Building Session of the 3rd SA TB Conference, 12-15 June 2012, International Convention Centre, Durban, South Africa. In this case a broader local audience of postgraduate students, nurses and clinicians attended to seek his advice on pursing academic research.
- Dr Bavesh Kana was invited to give a talk at the Midrand Graduate Institute on developing research careers in the South African setting. He addressed an audience comprising undergraduate and postgraduate students. Senior members of the academic staff also attended.
- Prof. Warren presented two lectures in the MBChB module on Infections and Clinical Immunology in 2012. Title: Molecular Epidemiology of Drug Resistant TB in South Africa.

- Numerous radio, TV and newspaper interviews locally and abroad. Owing to extreme administrative burden, opportunistic interviews, no accurate records were kept.

Outreach activities

Prof Corfield has continued her involvement in outreach activities that engage the general public in a greater awareness and appreciation of biomedical science; since 1998, she has received support and encouragement for this work from different stake holders and has actively encouraged the participation of others in these events. These activities have been undertaken with "outreach" funding from the CBTBR or with the Community Liaison Office/Research Translation Office of the MRC, with Ms Benita Mayosi.

A highlight of 2012 has been that Prof Corfield was judged the most worthy recipient of the 2011/2012 NSTF-BHP Billiton Award in the category "To an Individual or a Team for an outstanding contribution to SETI through Science Communication for Public Awareness over the last 5 years – sponsored by the South African Agency for Science and Technology Advancement (SAASTA)". The award was made to Prof Corfield for producing a package of innovative SETI-based public engagement activities which she shares with other scientists and science communicators through training workshops and printed/electronic/DVD resources. This award requires that the winner presents a series of lectures to high school learners (particularly), Prof Corfield presented the first of these in August 2012 to learner visiting iThemba Labs, Western Cape. The title of her presentation was "A different scientist's journey; enjoying the ride" which traced her interest and education in science from primary school to doctorate and her 47 year career in varied natural science disciplines, including the last 26 years of research in CBTBR investigating the molecular genetics of heart disease.

Prof Corfield continued to promote the use of the Murder Mystery genre to engage the general public in the science underpinning DNA forensics and in the ethical issues that this technology raises. She has written three more "who-dun-it" scenarios which have been used in public engagement activities, at Scifest Africa 2012 and the CT Science Centre, also train science graduates in public engagement skills.

During 2012, Prof Corfield was involved in other activities that furthered public awareness of various aspects of science. One of these is the continued rollout of the DNA Project, an organisation which seeks to raise awareness of the importance of DNA forensic evidence through many activities. During 2012, Prof Corfield has presented, *DN: CSI*, which she has helped develop with other trainers working with the DNA Project, to the South African Police (SAPS), security companies, school learners of all ages and the general public. Again in 2012, in response to the need to raise awareness of the range of health-related careers available to school learners, Prof Corfield presented a talk entitled "Careers in Health Care" to Stellenbosch University's bridging programme.

The activities in which Prof Corfield and members of CCBTBR were involved in 2012 are detailed below:

February 13 DNA:CSI workshop Pinelands High School

February 16 DNA:CSI workshop Diep River SAPS

March 10 and 11 Scifest Africa Sci-friend science communication training workshop run in conjunction with international science communicators

March 14-20 Scifest Africa daily DNA Detective (7); DNA:CSI (7); Murder Mysteries (2) workshops

May 21 "Careers in Health Sciences" presentation to bridging course learners at Stellenbosch University

June 25 DNA:CSI workshop Group 4 Security Services (2)

August 15 NSTF BHP Billiton presentation to high school learners visiting iThemba labs

October 31 Murder Mystery staff training and presentation at CT Science Centre as part of their Public Understanding of Biotechnology programme

December 5 Member of discussion panel at Teachers' Forum to discuss Body Worlds exhibition

4. Networking

New networks and linkages

- The Wits node is playing the leading role in an international collaboration between Wits University, the USA National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the University of Leicester, the Perinatal HIV Research Unit (PHRU) and the Aurum Institute. This new collaborative project is led by Dr. Bavesh Kana from the Wits node and involves the detection and characterization of non-replicating bacterial populations in the sputum of patients with active TB disease. The funding for the project was awarded in 2012 and Dr Kana was invited to the University of Leicester for collaborative discussions and to give a presentation of the research being conducted at the Wits node of the CBTBR.
- Dr. Bhavna Gordhan from the Wits node is involved in a collaborative research project that falls under the auspices of the South African Tuberculosis Research and Innovation Initiative (SATRII), an initiative which encompasses all three nodes of the CBTBR. Dr. Gordhan has to date screened over 500 small compounded for anti-tubercular activity and has contributed to telephone conferences and face to face meetings on this collaborative project.
- Dr. Bavesh Kana continues to collaborate with Dr. Lesley Scott and Professor Wendy Stevens from the Department of Molecular Medicine and Hematology at Wits University. Their partnership has allowed for the development of a robust external quality assurance system for rollout of the new GeneXpert TB diagnostic system in South Africa. The Wits node is playing a critical role in this venture which will help to bolster the national TB control program further testifying to the impact of the CBTBR on TB control in South Africa and internationally. There has been significant recent interest in this work by the WHO, PATH, FIND and other key stakeholders involved in TB control.
- Further collaborative links at the Department of Molecular Medicine and Hematology at Wits University, through the Wits of the CBTBR includes collaboration with Dr. Melinda Suchard on characterization of the immune response in humans when challenged with mutant mycobacterial strains, defective in cell wall remodeling. Dr Suchard and Dr Kana are currently co-supervising a MMed student working on this project.
- The Mycobacterial Referral Laboratory at the National Health Laboratory Service (Johannesburg, Central branch) currently collaborates with the Wits node on a project aimed at the characterization of discordant rifampicin resistant mutants in the Gauteng region. The strains selected for this study would comprise those samples that give inconsistent phenotypic resistance data when compared to the rifampicin resistance genotype provided by the line probe assay. The project represents an important partnership between the CBTBR and the national diagnostic platform for TB in South Africa.
- Dr Melissa Chengalroyen from the Wits node spent two weeks at the SU node to obtain training on DNA fingerprinting methodologies to distinguish *M. tuberculosis* strains. Dr Chengalroyen has now established the relevant methods at the Wits node and continues to work with Dr Streicher at the SU node on interpretation of the data.
- Dr. Monique Williams from the SU node and Prof Valerie Mizrahi (UCT node) is collaborating with Dr. Bavesh Kana and Ms. Nicole Narrandes at the Wits node on a project aimed further understanding the biosynthetic pathway for molybdopterin cofactor (MoCo) biosynthesis. This is a collaborative project that also involves Dr. Gilla Kaplan from the Public Health Research Institute in the USA. Dr. Williams was awarded a CU-SA Fogarty Fellowship to train in Dr. Kaplan's laboratory in 2012. Also in 2012, Dr Williams spent three weeks at the Wits node to conduct lipid analyses on mycobacterial strains.

Existing 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
Dr. William Mac Kenzie	Centers for Disease Control and Prevention, USA	Collaboration on the detection and characterization of Rpf-dependent bacterial populations in sputum. Project funded by the NIH.

Prof. Michael Barer and Dr. Galina Mukamolova	University of Leicester, UK	Collaboration on the detection and characterization of Rpf-dependent bacterial populations in sputum. Project funded by the NIH
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.
Prof. Gilla Kaplan and Dr. Dorothy Fallows	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 and Dr. Fallows on an NIH funded project to study hetero-resistance in TB patients with active disease. Ongoing collaboration on mouse phenotyping of mutant strains
Prof. Lesley Scott	University of the Witwatersrand	Ongoing collaboration on the rollout of the GeneXpert diagnostic test and establishment of an external quality assurance system.
Dr. Melinda Suchard	University of the Witwatersrand	Ongoing collaboration of immunological characterization of mutants defective for cell wall turnover/remodeling
Dr. Chris Edlin	iThemba Pharmaceuticals	Ongoing collaboration on SATRII initiative for TB drug discovery
Prof. Mary Gulumian	National Institute of Occupational Health	New collaboration on the study of DNA repair in mycobacteria
Prof. Jim Phillips	National Institute of Occupational Health	New collaboration on the further understanding cell wall metabolism in mycobacteria
Prof. John D. McKinney	École Polytechnique Fédérale de Lausanne (EPFL), Switzerland	Collaboration on the mechanisms of propionate catabolism, funded by a grant from Swiss/ SA Joint Research Programme.
Dr. Clifton E. Barry III and Dr. Helena Boshoff	Tuberculosis Research Section, Laboratory of Host Defenses, National Institute of Allergy & Infectious Diseases, NIH, MD	Ongoing collaboration on the IMTB project, and new collaboration on the HIT-TB and SATRII projects
Prof. Česlovas Venclovas	Institute of Biotechnology, Vilnius, Lithuania	Ongoing collaboration on the structure and function of a novel mutagenic complex in mycobacteria.
Dr. Tom Ioerger & Prof. Jim Sacchettini	Biochemistry & Biophysics, Texas A&M University, College Station, TX	Collaborating on whole-genome sequence analysis of strains of *M. tuberculosis*.
Prof. Sir Tom Blundell and Prof. Chris Abell	Cambridge University, UK	Collaborating members of the HIT-TB and MM4TB Consortia
Prof. Chris Sassetti	University of Massachusetts, USA	Collaboration on carbon metabolism in *M. tuberculosis.*
Prof. Stewart Cole	EPFL, Lausanne,	MM4TB Consortium

& Dr. Ruben Haartkoorn	Switzerland	
Prof. Jonathan Blackburn	IIDMM, UCT	Collaboration on lipidomic and proteimic analyses of *M. tuberculosis* strains
Prof. Kelly Chibale	H3-D Drug Discovery Centre, UCT	Oollaboration on SATRII and H3-D TB drug discovery projects
A/Prof. Nicola Mulder	CBIO, IIDMM, UCT	Oollaboration on bioinformatic analysis of mycobacterial genomes
Prof. Robert Wilkinson	CIDRI, IIDMM	Co-applicant on several new grant applications
Prof. Robert Doyle	Syracuse University	New collaboration on vitamin B12 biosynthesis
Prof. David Russell	Cornell University	New collaboration on vitamin B12 transport and metabolism
Dr. S. Sampson	Imperial College, UK	The evolution and function of the PE and PPE gene families (2001-present) & the ESAT-6 secretion system interactome (2007- present).
Dr. H. Mardassi, Mr. A. Karboul and Mr. A. Namouchi	Institut Pasteur, Tunisia	Characterization of *M. tuberculosis* lineages through the PE/PPE gene family (2002 - present)
Dr. W. Bitter and Mr A. Abdallah	Vrije Universiteit, Amsterdam, Netherlands	The trafficking of the *M. tuberculosis* PE and PPE proteins (2006 – present).
Dr. John Ho	Cornell University, New York, USA	Characterization of *M. tuberculosis* lineages through the PE/PPE gene family (2007 –2009).
Prof. J. Ho, Dr. A. Gibson and Prof. R. Huard	Cornell University, New York, USA	The dissemination of the major RDRio sub-lineage of the LAM *M. tuberculosis* spoligotype family in Luso-American countries, Portugal and Africa
Dr. H. Mardassi	Institut Pasteur de Tunis, Tunisia	Characterisation of LAM evolutionary history (2007-present).
Prof. A. Steyn	K-RITH	The ESAT-6 secretion system interactome (2007-present).
Prof. Dr. VPMG Rutten, Dr. I. van Rhijn, Dr. A.P. Koets	Utrecht University	Non-tuberculous mycobacteria in wildlife (WOTRO Integrated program proposal) (2007 - present).
Dr R. Anthony	KIT The Netherlands	MLPA assay for the detection of ofloxacin resistance.
		Identification of ofloxacin and amikacin heteroresistance.
Prof D. van Soolingen	RIVM The Netherlands	Evolution of the Beijing genotype Lineage
		Evaluation of the MIRU-VNTR typing method
Dr K Kremer	RIVM The Netherlands	Whole genome sequencing of Beijing genotype strains
Dr V Dartois	Novatis Singapore	MassArray detection of mutations conferring drug resistance
Prof E Bottger	University of Zurich	Development and evaluation of novel genetic based diagnostics for drug resistance.
		Evolution of ofloxacin resistance

Prof E Nardell	AIR facility, Witbank	Transmissibility of drug resistant TB
Prof. Erwin Schurr	McGill University, Montreal, Canada	Genetic epidemiology. Poster outputs; 4 papers published 2009-2010.
Prof. Laurent Abel & Alexandre Alcais	INSERM / Université Paris 5, France	Analysis of genetic epidemiology. Poster outputs; 4 papers published 2009-2010.
Dr Alkes Price	Harvard School of Public Health, Boston, USA	New collaboration. Analysis of admixture mapping. Manuscript in preparation
Dr Brenna Henn	Stanford University, San Francisco, USA	Population Ancestry genetic determinations. Manuscript in preparation
Dr. Ingileif Jonsdottir	deCODE, Iceland	Genetic susceptibility to TB.
Dr. Lluis Quintana-Murci	Institut Pasteur, Paris, France	Genetic susceptibility to TB and population structure. Paper published 2010.
Prof. Stefan Schreiber and Dr. Almut Nebel	Christian Albrechts University, Kiel, Germany	Investigation of candidate genes in TB. Resulted in 2 co-authored publications in 2007, and 2 co-authored publications in 2009.
Prof .Megan Murray	Harvard / Broad institute	Various project including the evolution of XDR-TB strains; other mechanisms of drug resistance (in addition to genomic mutations); mechanisms of resistance to 2nd line drugs; strain fitness; certain strain families may have both increased fitness and increased potential for acquiring drug resistance. All of these projects involve whole-genome sequencing, proteomics, microarray. Prof. Murray is directly involved in project planning, paper writing, funding proposals (NIH and Wellcome trust).
Dr K Jacobson	Harvard University	1) GIS of drug resistant TB in the Western Cape 2) MDR treatment outcome in Brewelskloof Hospital Treatment outcome of M(X)DR-TB in Khayelitsha
Dr. Judith Nagy	Imperial College London	Proteomics of large clusters (more transmitted) vs. small clusters (less transmitted) in the same strain family after other criteria to select isolates have been taken into consideration. The aim is to identify proteins differentially expressed in the same strain family which may give them an advantage to transmit better than others.
Prof. Harald Wiker and Dr G 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, The Netherlands	Ongoing collaboration on *M. tb* 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.
Dr. Helen Cox	MSF	Collaboration on drug resistance in Khayelitsha, Western Cape. Impact of mixed infection on treatment outcome.
Prof. Tom Alber	Berkeley	Collaboration on the *M. tuberculosis* lipidome.
Prof. Brigitte Gicquel	Pasteur Institute	Collaboration on mutation in *M. tuberculosis* DNA repair genes.

Prof K Dheda	UCT	Molecular epidemiology of XDR-TB
Prof R McNerey	LSTHM	Whole genome sequencing of drug resistant M. tuberculosis strains
Dr. Kim Mallard	LSTHM	Whole genome sequencing of *M. tuberculosis* strains
Prof Anab Pain	KAUST	Whole Genome Sequencing of Mycobacterial Species
Prof. Kathy Eisenach	Arkansas, USA	Mechanisms of strain fitness in an in vitro THP-1 cell line model. Project is in planning phase.
Prof. Stefan Kaufmann	Max Planck Institute for Infection Biology, Berlin, Germany	Collaborators on BMGF-funded project.
Prof. Henry Boom	Cleveland, Ohio, US	Collaborators on BMGF-funded project.
Prof. Hazel Dockrell	London School for Hygiene and Tropical Medicine, UK	Collaborators on BMGF-funded project, Co-applicants on grant application to BMGF.
Dr. Mark Doherty	Statens Serum Institute, Kopenhagen, Denmark	Collaborator on BMGF-funded project, collaborators on NIH-sponsored study
Dr. Martin Ota	MRC, The Gambia	Collaborators on BMGF-funded project.
Prof. Harriet Mayanja	Makerere University, Uganda	Collaborators on BMGF-funded project.
Prof. Willem Hanekom and Dr. Hassan Mahomed	SATVI, UCT	Collaboration on TB vaccine studies
Dr. Carol Holm-Hansen	Norwegian Institute for Public Health	Collaboration on BMGF Grand Challenge Exploration grant, 2010-2011
Dr. Christoph Lange and 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	R&D, Cellestis, Australia	Collaboration on diagnostic TB study 2010-2011
Dr. Volkmar Schoellhorn	Auto-Immune Diagnostics (AID)	Collaboration on TB diagnostic study 2010-2011
Prof N. Beyers, Dr A. Hesseling, Dr S. Tonkin, Prof B. Marais	SU	Non-tuberculous Mycobacteria (NTM) - Prevalence and Clinical relevance in HIV-infected and HIV-uninfected children (2006 - present).
Prof. N. Beyers	DTTC, SU	Ongoing collaboration of the molecular epidemiology of *M. tuberculosis* in the W. Cape.
Dr. A. Michel, J. Godfroid, K. Coetzer, N. Kriek	Onderstepoort Veterinary Institute	Non-tuberculous mycobacteria in wildlife (WOTRO Integrated program proposal) (2007 - present).
Dr Mary Jackson	Colorado State University	Screen anti-TB compounds against RIF-resistant *M. tuberculosis* strains.
Dr Dorian Bevec	MondoBiotech, Switzerland	Screen peptides for anti-TB activity.
Prof. Kelly Chibale	Dept Chemistry, UCT	Screen antituberculosis lead compounds
Dr Corli Witthuhn	Food Science, SU	Fermentation Processes to kill *M. Tuberculosis*
Dr Thavi Govender	Dept. Chemistry, UKZN	Test antituberculosis activity of existing antituberculosis drug derivatives. K. Onajole 2009

Prof Green	Dept Chemistry, UWC	Screen new compounds and derivatives for antituberculosis activity
Dr. S. Todorov	Univ. Sao Paulo, Brazil	Antituberculosis activity of Bacteriocins Todorov, 2008
Dr C. Kenyon	CSIR, Pretoria	Dormancy regulators of M.tb in human macrophages.
Dr. Haynes	Hong Kong University of Technology	Testing new compounds for antituberculosis activity
Prof Peter Folb	Pharmacology, UCT	Testing derivatives of Diphenyl Oxazole for antituberculosis activity
Ms. Marlein Bosman	NHLS , Green point	Collaborator on all our projects – provides routine samples.
Lily Telisinghe, Dr Salome Charalambous	Arum Health	TB in the correctional services
Dr Nazir Ismail	NHLS	Drug resistant TB in South Africa
Dr. Sias May	TB Control program in Suidkaap/ Lawaaikamp	TB Control strategy.
Dr. Danie Theron	Eben donges hosp, 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.
Prof C. Reinecke, Dr du Toit Loots	North West University	*M.tuberculosis* metabolome.
Prof C Wright	NHLS Port Elizabeth	The diagnostic utility of FNAB
Dr. Alistair Calver	Gold Mine, Northern Cape	Ongoing, outbreak of drug resistance in a setting with a good control program.
Prof. Willem Hanekom	IIDMM, UCT	Sharing of technology (multicolour FACS, Luminex machine), sharing of samples, manuscript accepted for publication.
Prof. Frank Brombacher	IIDMM, UCT	Sharing of expertise (murine helminth models).
Dr A. Hesseling	SU	New collaboration to investigate genotype-immunological phenotype correlations in children.
Prof. Keertan Dheda	Lung Institute, UCT	Collaboration in diagnostic/biomarker project.
Dr. Anna Mandalakas	Case Western Reserve University, USA	Collaboration of diagnostic studies in paediatric TB.
Dr. Marc Jacobsen	Bernhard Nocht Insitute, Hamburg, Germany	Collaboration on helminth/TB co-infection studies.
Dr. Muazzam Jacobs	University of Cape Town	New collaboration to assess the impact of steroid hormones on protective immunity to M. tuberculosis in a mouse animal model.
Prof Annelies van Rie	UNC	Treatment of HIV infected Children with Rifabutin
		Evaluation of the Xpert MTB/RIF test.
Profs L Wangh, B Kreiswirt, F Drobneiwski	Brandis University, HPRI, QMUL	Evaluation of LATE PCR for the detection of resistance to first and second-line anti-TB drugs.
Dr. Ian Orme	Colorado State University, Colorado, USA	Virulence of TB strains in a guinea pig model: impact on Vaccine development

5. Service rendering

As per our Business Plan for the current phase of the CBTBR, the following services were provided in 2012:

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

Thesis examination

- Dr. Kana examined a PhD thesis for Stellenbosch University and an MSc Dissertation for WITS University.
- Dr. Warner examined a PhD thesis for the University of Oslo, Norway, and will travel to Norway in 2013 for the examination *viva*. Dr. Williams examined a PhD thesis submitted to Stellenbosch University and Dr. Evans examined Honours projects submitted to UCT.
- 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

- Dr Kana reviewed manuscripts for *Antimicrobial Agents and Chemotherapy*, *PLoS One*, *PLoS Pathogens*, *Tuberculosis*, *Antonie van Leeuwenhoek Journal of Microbiology*, *The Journal of Infectious Diseases*, *Vaccine*, *Molecular and Cellular Biochemistry*.
- Prof. Mizrahi served on the Editorial Advisory Boards of the *Biochemical Journal, Tuberculosis*, *Cellular Microbiology,* and the Editorial Board of *Emerging Microbes and Infection*. In 2012, she also reviewed manuscripts submitted to *Nature Genetics, E-Life, PLoS Pathogens,* and *Cell Host & Microbe.*
- Dr. Warner reviewed manuscripts submitted to *PNAS*, *PLoS Pathogens, Molecular Microbiology, Tuberculosis, Journal of Infectious Diseases, Journal of Clinical Microbiology, PLoS One* and *Journal of Infectious Diseases*. Dr. Abrahams reviewed a manuscript for *PLoS One*.
- 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

- Dr. Kana served on the Advisory Committee of the CU-SA Fogarty AITRP.
- Dr. Kana served on the Steering Committee for the Wits-Aurum Coalition and chairs the Projects Committee for this venture
- Dr. Kana served on the University Research Council (URC) at Wits University
- Dr. Kana and Dr. Gordhan served on the Faculty Research Council (FRC), Faculty of Health Sciences Wits University
- Dr. Kana and Dr. Gordhan served on the Postgraduate Committee, Faculty of Health Sciences Wits University
- Dr. Gordhan served on the Research Entity Review Task Group, Faculty of Health Sciences Wits University
- Dr. Kana chaired the Wits Health Sciences Research Day Committee (2012)
- Dr. Kana was elected to serve on the FRC Budget task group, Faculty of Health Sciences Wits University
- Dr. Kana served on the Faculty Advisory Board, Faculty of Health Sciences Wits University
- Dr. Kana served on the Executive Committee of the School of Pathology, Faculty of Health Sciences Wits University
- Dr. Kana served on the Research Entity Forum, Faculty of Health Sciences Wits University
- Dr. Kana served on the Faculty of Health Sciences Research Equipment Review Committee, Wits University
- Dr. Kana served on the URC major and minor Equipment Review Committees, Wits University
- Dr. Kana served on the Research Coordinators Committee, Faculty of Health Sciences, Wits University
- Dr. Kana served on the Faculty of Health Sciences Imaging Committee, Wits University

- Dr. Kana served on the Faculty Graduate Studies Committee Working Group on Research Output Guidelines, Faculty of Health Sciences, Wits University
- Dr. Kana served on the Molecular Biosciences Thrust Committee, Faculty of Health Sciences, Wits University
- Dr Gordhan served on the BTC Scholarship Selection Committee
- Dr Gordhan served on the NRF Postdoctoral review Committee
- Prof. Mizrahi served as a member of the Board of Directors, KwaZulu Natal Research Institute for TB and HIV (K-RITH), University of KwaZulu Natal, South Africa
- Prof. Mizrahi served on the Council of Scientific Advisors of the International Centre for Genetic Engineering and Biotechnology (Trieste, Italy)
- Prof. Mizrahi served as a member of the Scientific Advisory Board of K-RITH, University of KwaZulu Natal
- Prof. Mizrahi served on the Search Committee of K-RITH, University of KwaZulu Natal
- Prof. Mizrahi served as a member of the Scientific Advisory Committee of the Global Alliance for TB Drug Development (TB Alliance, New York)
- Prof. Mizrahi served as a member of the SACEMA Trust and also as a member of the SACEMA Management Board, Stellenbosch University
- Prof. Mizrahi was appointed to, and served on the Visiting Scholars Fund Committee, UCT
- Prof. Mizrahi served on the Research Funding Task-Team of the University Research Committee, UCT
- Prof. Mizrahi served on the Internationalisation Task Team of the University Research Committee, UCT
- Prof. Mizrahi served on the Area Stakeholders Committee, Carnegie Corporation Developing the Next Generation Academics Programme, UCT
- Prof. Mizrahi chaired the Executive Committee of the IIDMM, UCT
- Prof Mizrahi chaired the Membership Committee of the IIDMM, UCT
- Prof. Mizrahi was appointed to the Senior Council on Research, Faculty of Health Sciences, UCT
- Dr. Warner served as a member of the Steering Committee, iThemba Pharmaceuticals, Johannesburg
- Dr. Warner served as a member of the Institutional Biosafety Committee, UCT
- Dr. Warner served as a member of the GMO Committee, UCT
- Dr. Warner served as the MMRU Hazardous Chemical Coordinator, IIDMM, UCT
- Dr. Warner served as the Lead Academic in charge of the WBS Level 2 Biological Safety Level III laboratory, IIDMM, UCT
- Dr. Warner served on the Integrated Education Committee of the IIDMM, UCT
- Dr. Warner served on the Abstract Review Committee of the 3rd SA TB Conference (TB/HIV Integration Conference), Durban, 12-15 June 2012
- Dr. Evans served on the Health & Safety Committee of the IIDMM, UCT
- Ms. Moosa served on Operations and Laboratory Management Committee of the IIDMM
- Dr. Evans chaired the UCT Health Sciences Postdoctoral Association (HSPDA) and Drs. Gopinath and Singh served on the leadership committee of the HSPDA.
- Ms. Koch served on the UCT Health Sciences Faculty Postgraduate Students Council (HSPSC) and headed the Social Responsiveness portfolio.
- Profs van Helden and Walzl served on MSF, GATB, WHO and Stop TB Partnership.
- Profs Walzl and Wiid served on the Ethics Committee for Experimental Animal Research of Stellenbosch University.
- Prof Warren served on the Centre for Infectious Diseases of Stellenbosch University.
- Profs Walzl and Warren served on the Research Committee of Stellenbosch University, Health Sciences.
- Prof Gey van Pittius served on the Committee for Postgraduate Education and Health Research Ethics Committee of Stellenbosch University Faculty of Health Sciences.

Examples of Research Funding Reviews

- Dr. Kana served as a reviewer for MRC Career Award Applications, NRF Rating and Evaluation program, NRF postdoctoral program and the NRF SA-France research program. Dr Kana also served as an external reviewer for the Portuguese Foundation for Science and Technology – 2012 Investigator Program. Dr Gordhan was part of a panel at the NRF post-doctoral and PDP workshop where she gave input on the NRF review process for fellowships and discussed some of the common mistakes and omissions on the applications. Dr Gordhan also assisted with the selection of the Postgraduate Degrees Awards for the best MSc and PhD thesis submitted to the Faculty of Health Sciences, Wits University for 2012. Both Dr. Gordhan and Dr. Kana served on assessor committees at Wits University for MSc and PhD proposals. Dr. Gordhan reviewed an application for the NHLS Research Trust grant program.
- Prof. Mizrahi served as a reviewer for the Wellcome Trust, the Bill & Melinda Gates Foundation and Seattle Biomed. She also served as a reviewer for promotion at the University of the Witwatersrand. Dr. Warner reviewed grant applications submitted to the Wellcome Trust, the NRF, and the MRC. He also served as an internal reviewer for numerous research proposals considered by the IIDMM Research Committee.
- Many of the SU node members are either on editorial boards or act as regular reviewers for many journals. Again, a list is not provided, since we have so many of these we do not keep record.

Other services rendered

- Dr Gordhan and Dr Kana reviewed abstracts submitted for the MRC Early Career Scientists Conference 2012, 24th – 25th October 2012.
- Dr Gordhan was invited to participate in the DST Scientific meeting: India-South African bilateral meeting, 21st -22nd February 2012.
- Speciation of Non Tuberculous Mycobacteria (NTM) for Kruger National Park
- Genotyping of clinical isolates (RFLP or mutation detection) for the NHLS and MSF.
- Prof V Corfield was NRF rating panel moderator in 2012
- Specialist diagnostic service for MDR or XDR TB cases
- Specialist diagnostic service for suspect extra-pulmonary TB cases
- Hospital medical specialist clinical services, e.g. pulmonology and genetics
- Weekly tutorials/practicals to Clinical Genetics registrars in molecular genetics by CBTBR staff during 2012 (Prof Corfield and Mrs de Villiers).
- Seegene (Korea): We are currently in a collaborative venture with Seegene, Inc. to design and improve *M. tuberculosis* diagnostics. Seegene is a molecular diagnostic company based in Korea well known for its pioneering R & D activities and novel technologies. Seegene has enhanced the sensitivity and specificity of PCR (polymerase chain reaction) that enables them to provide multiplex PCR products by which multiple target genes of pathogens can be simultaneously detected, saving time and cost.
- AID (Germany): Evaluation of a genetic drug susceptibility test.
- Hain Life Sciences (Germany): Evaluation of the MDRTBsl genetic drug susceptibility test.
- Vakzine Project Management (VPM): phase IIa vaccine trial on tuberculosis
- Cellestis: Evaluation of new peptide to diagnose TB

6. Gender impact of research

"Science for Women" (gender-sensitivity of the research agenda)

The work being undertaken in the CBTBR is aimed at contributing towards global efforts in researching and developing new laboratory-based tools for reducing the societal burden of TB. TB is the greatest single infectious cause of death in young women, and causes more deaths among women than all causes of maternal mortality combined. The particularly high rates of HIV co-infection in women are expected to fuel an increased prevalence of TB in women over time. In addition to the disease burden, TB also imposes a massive, but largely hidden burden of social impact on women.

"Science by Women" (the participation by women in the research programme)
Five out of the 13 Core Team Members of the CBTBR are women. In 2012, the CBTBR has also maintained a high percentage of female students (69% of all students and 57% 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 Core Team Members. These indicators 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
Dr.	Kana	SA	Wits	M	B	100
Dr.	Warner	SA	UCT	M	W	100
Prof.	Gey van Pittius	SA	US	M	W	10[b]
Prof.	Hoal van Helden	SA	US	F	W	100
Dr.	Ronacher-Mansvelt	SA	SU	F	W	100
Dr.	Streicher	SA	SU	F	W	100
Prof.	Van Helden	SA	MRC	M	W	100
Prof.	Victor	SA	PAWC	M	W	100
Prof.	Walzl	SA	US	M	W	100
Prof.	Warren	SA	MRC	M	W	100
Dr.	Wiid	SA	PAWC	M	W	100

a. Director of the IIDMM
b. Appointed as deputy dean for Research in September 2012

2. Postdoctoral Fellows

Title	Surname	Citizenship	Institution	Gender	Race	% Time spent in CBTBR
Dr.	Chegou	Cameroonian	SU	Male	Black	100
Dr.	Chengalroyen	South African	Wits	Female	Black	100
Dr.	Du Plessis	South African	SU	Female	White	75[a]
Dr.	Ealand	South African	Wits	Male	White	100
Dr.	Evans	South African	UCT	Female	White	100
Dr.	Gopinath	Indian	UCT	Male	Black	100
Dr.	Kirsten	South African	SU	Female	White	50[b]
Dr.	Kleynhans	South African	SU	Female	White	75[c]
Dr	Louw	South African	SU	Female	Black	75[d]
Dr.	Loxton	South African	SU	Male	Black	100
Dr.	Möller	South African	SU	Female	White	100
Dr.	Moosa	South African	UCT	Female	Black	65[e]
Dr.	Parsons	South African	SU	Male	White	100
Dr	Roetz	South African	SU	Female	White	100
Dr	Singh	Indian	UCT	Male	Black	100

a. Commenced in April 2012
b. Left the SU node in July 2012
c. Commenced in April 2012
d. Left the SU in September 2012
e. Commenced May 2012

3. Students

Title	First Name	Surname	Degree	Institution	Race	Gender	Nationality	Status
Ms	Munadia	Ansarie	Hons	UCT	Black	Female	South African	Complete
Ms	Lisa Jane	Coetze	Hons	SU	White	Female	South African	Complete
Mr	Willem Jacques	Du Plessis	Hons	SU	White	Male	South African	Complete
Mr	Wynand Johan	Goosen	Hons	SU	White	Male	South African	Complete
Ms	Claudia	Ntsapi	Hons	SU	Black	Female	South African	Complete
Ms	Sheena	Ruzive	Hons	SU	Black	Female	Zimbabwean	Complete
Ms	Siyanda	Tshoko	Hons	SU	Black	Female	South African	Complete
Ms	Hanri	Visser	Hons	SU	White	Female	South African	Complete
Mr	Tawanda	Zvinairo	Hons	SU	Black	Male	Zimbabwean	Complete
Ms	Rukaya	Asmal	MSc	Wits	Black	Female	South African	Incomplete
Ms	Amanda	Axcell	MSc	Wits	White	Female	South African	Complete
Mr	Germar	Beukes	MSc	Wits	White	Male	South African	Incomplete
Ms	Philippa	Black	MSc	SU	White	Female	South African	Complete
Ms	Michelle	Daya	MSc	SU	White	Female	South African	Incomplete
Ms	Juanelle	Du Plessis	MSc	SU	White	Female	South African	Incomplete
Ms	Lizaan	Ehlers	MSc	SU	White	Female	South African	Incomplete
Ms	Melanie	Grobbelaar	MSc	SU	White	Female	South African	Complete
Ms	Andrea	Gutschmidt	MSc	SU	White	Female	German	Incomplete
Dr	Kenneth	Hammond-Aryee	MSc	SU	Black	Male	Ghanian	Incomplete
Ms	Farzanah	Hassim	MSc	Wits	Black	Female	South African	Incomplete
Mr	Lance Andrew	Lucas	MSc	SU	White	Male	South African	Complete
Ms	Lusanda	Mapela	MSc	Wits	Black	Female	South African	Complete
Ms	Angela Maria	Menezes	MSc	SU	White	Female	South African	Incomplete
Ms	Nabiela	Moolla	MSc	Wits	Black	Female	South African	Incomplete
Ms	Vuyiseka	Mpongoshe	MSc	SU	Black	Female	South African	Incomplete
Ms	Nicole	Narrandes	MSc	Wits (co-sup UCT)	Black	Female	South African	Incomplete
Mr	Paulin Essone	Ndong	MSc	SU	Black	Male	Gabonese	Incomplete
Ms	Khutso Germina	Phalane	MSc	SU	Black	Female	South African	Incomplete
Ms	Caroline	Pule	MSc	SU	Black	Female	South African	Incomplete
Ms	Carine	Sao Emani	MSc	SU	Black	Female	Cameroonian	Incomplete
Mr	Sibusiso	Senzani	MSc	Wits	Black	Male	South African	Incomplete
Ms	Sirkka	Shikongo	MMed	Wits	Black	Female	South African	Incomplete
Mr	Kabengele Keith	Siame	MSc	SU	Black	Male	Zambian	Incomplete
Ms	Nastassja Lise	Steyn	MSc	SU	White	Female	South African	Complete
Ms	Marisa	Tait	MSc	SU	White	Female	South African	Incomplete
Ms	Leani	Thiart	MSc	SU	White	Female	South African	Incomplete
Mr	Albertus	Viljoen	MSc	SU	White	Male	South African	Incomplete
Ms	Louise	Vos	MSc	SU	White	Female	South African	Incomplete
Ms	Chandré Kim	Wagman	MSc	SU	Black	Female	South African	Complete
Ms	Danicke	Willemse	MSc	SU	White	Female	South African	Incomplete
Mr	Marinus	Barnard	PhD	SU	White	Male	South African	Incomplete
Ms	Maria	Botha	PhD	SU	White	Female	South African	Complete
Dr	Adane Mihret	Bekele	PhD	SU	Black	Male	Ethiopian	Incomplete
Ms	Natalie	Bruiners	PhD	SU	Black	Female	South African	Complete

Ms	Marieta	Burger	PhD	SU	White	Female	South African	Incomplete
Ms	Margaretha	De Vos	PhD	SU	White	Female	South African	Incomplete
Mrs	Anzaan	Dippenaar	PhD	SU	White	Female	South African	Incomplete
Ms	Zanele	Ditse	PhD	UCT	Black	Female	South African	Incomplete
Ms	Nelita	Du Plessis	PhD	SU	White	Female	South African	Complete
Mr	Zhuo	Fang	PhD	SU	Black	Male	Chinese	Incomplete
Ms	Suereta	Fortuin	PhD	SU	Black	Female	South African	Incomplete
Mr	Xavier	Kaygire	PhD	SU	Black	Male	Rwandan	Incomplete
Ms	Elizabeth	Kigondu	PhD	UCT	Black	Female	Kenyan	Incomplete
Ms	Leanie	Kleynhans	PhD	SU	White	Female	South African	Complete
Ms	Anastasia	Koch	PhD	UCT	White	Female	South African	Incomplete
Mrs	Lungile	Kwitshana	PhD	U Kwazulu Natal	Black	Female	South African	Incomplete
Ms	Nikki	Le Roux	PhD	SU	White	Female	South African	Incomplete
Mr	Lubabalo	Macingwana	PhD	SU	Black	Male	South African	Incomplete
Ms	Atica	Moosa	PhD	UCT	Black	Female	South African	Complete
Ms	Zandile	Mlamla	PhD	SU	Black	Female	South African	Incomplete
Ms	Matsie	Mphahlele	PhD	SU	Black	Female	South African	Incomplete
Ms	Krupa	Naran	PhD	UCT	Black	Female	South African	Incomplete
Ms	Duduzile	Ndwandwe	PhD	Wits (sup UCT)	Black	Female	South African	Incomplete
Ms	Mae	Newton-Foot	PhD	SU	White	Female	South African	Incomplete
Mr	Andile	Ngwane	PhD	SU	Black	Male	South African	Complete
Mr	Muneeb	Salie	PhD	SU	Black	Male	South African	Incomplete
Ms	Prudy Mashika	Seepe	PhD	SU	Black	Female	South African	Incomplete
Ms	Michelle	Smit	PhD	SU	White	Female	South African	Incomplete
Ms	Anjo	Steyn	PhD	SU/CSIR	White	Female	South African	Incomplete
Mr	Ruben	van der Merwe	PhD	SU	White	Male	South African	Complete
Mr	Ignatius	Viljoen	PhD	SU/UP	White	Male	South African	Incomplete
Mr	Cedric John	Werely	PhD	SU	Black	Male	South African	Complete

4. Administrative and Other Staff

Title	Surname	Position	Based at	Gender	Race
Dr	Abrahams[a]	Research Officer	UCT	M	B
Dr	Baker	Project Manager	SU	M	B
Mrs	Hull-Conrad	Part-time admin clerk	UCT	F	B
Ms	Peachy	Bookkeeper/ Admin. Assistant	WITS	F	B
Ms	Magobo	Research Assistant	Wits	F	B
Ms	Motsi	Research Assistant	Wits	F	B
Ms	Serapa	Research Assistant	Wits	F	B
Ms	Nkomo	Laboratory Assistant Technical	Wits	F	B
Dr	Williams[b]	Senior Scientist	UCT	F	B

a. Seconded full-time to NIAID,NIH
b. Seconded full-time to SU node

OUTPUTS

* The Names in bold are CBTBR staff

Books / Chapters in Books (Total: 2)

De Wit E, Moller M, Hoal EG. (2012) Genetic Perspectives of Tuberculosis in Southern Africa. In: Genomics and Health in the Developing World, D Kumar (Ed) Oxford University Press, New York
Warner DF, Mizrahi V. (2012) Tuberculosis Drug Discovery: Target Identification and Validation. *In*: Drug Discovery in Africa (Chibale, K.C., Davies-Coleman, M. & Masimerembwa, C., eds.), Springer, ch. 3, pp. 53-84

Articles in Peer-Reviewed Journals (Total: 47)

Griffin JE, Pandey AK, Gilmore SA, **Mizrahi V**, McKinney JD, Bertozzi CR, Sassetti CM. (2012) Cholesterol catabolism by Mycobacterium tuberculosis requires transcriptional and metabolic adaptation. Chem Biol. 19(2): 218-227. (IF=5.976)
Warner DF, **Mizrahi V**. (2012) A pseudokinase debut at the mycobacterial cell wall. Sci Signal. 5(208):pe3. (IF=7.500)
Warner DF, **Mizrahi V**. (2012) Approaches to target identification and validation for tuberculosis drug discovery: a UCT perspective. S Afr Med J. 102(6): 457-460. (IF=1.610)
Abrahams GL, Kumar A, **Savvi S**, Hung AW, Wen S, Abell C, Barry CE III, Sherman DR, Boshoff HIM, **Mizrahi V.** (2012) Pathway-selective sensitization of Mycobacterium tuberculosis for target-based whole-cell screening, Chem Biol. 19:844-854. (IF=5.976)
Barnard M, **Gey van Pittius NC**, **van Helden PD**, Bosman M, Coetzee G, **Warren RM**. (2012) Diagnostic performance of Genotype® MTBDRplus Version 2 line probe assay is equivalent to the Xpert®MTB/RIF assay. J Clin. Microbiol. 50(11):3712-3716. (IF=4.258)
Chegou NN, Black GF, **Loxton AG**, **Stanley K**, **Essone PN**, Klein MR, Parida SK, Kaufmann SH, Doherty TM, Friggen AH, Franken KL, Ottenhoff TH, **Wazlz G**. (2012) Potential of novel *Mycobacterium tuberculosis* infection phase-dependent antigens in the diagnosis of TB disease in a high burden setting. BMC Infect Dis. 12(1):10. (IF=3.011)
Chegou NN, **Essone PN**, **Loxton AG**, **Stanley K**, Black GF**, van der Spuy GD**, **van Helden PD**, Franken KL, Parida SK, Klein MR, Kaufmann SHE, Ottenhoff TH, **Walzl G**. (2012) Potential of Host Markers Produced by Infection Phase-dependent Antigen-stimulated Cells for the Diagnosis of Tuberculosis in a Highly Endemic Area. PLoS ONE. 7(6):e38501. (IF=4.610)
Chihota V, **Müller B**, Mlambo C, Pillay M, **Tait M**, **Streicher EM**, Marais E, **Van der Spuy G, Hanekom M**, Coetzee G, **Trollip A**, Hayes C, Bosman M, **Gey van Pittius NC**, **Victor TC, Van Helden PD, Warren RM**. (2012) The population structure of multi-and extensively drug-resistant tuberculosis in South Africa. J Clin Microbiol. 50(3): 995-1002. (IF=4.258)
Cohen T, **van Helden PD**, Wilson D, Colijn C, McLaughlin MM, Abubakar I, **Warren RM**. (2012) Mixed strain *Mycobacterium tuberculosis* infections: implications for tuberculosis treatment and control. Clin Microbiol Rev. 25(4):708-719. (IF=19.832)
De Beer JL, Kremer K, Ködmön C, Supply P, van Soolingen D,Global network for the molecular surveillance of tuberculosis 2009 (Consortium of authors include **Warren RM** (2012) First worldwide proficiency study on variable numbers of tandem repeats typing of Mycobacterium tuberculosis complex strains. J Clin Microbiol. 50(3): 662-669. (IF=4.258)
Diacon AH, Maritz S, Venter A, Van Helden PD, Dawson R, Donald P. (2012) Time to liquid culture positivity as a substitute for colony counting on agar plates in early bactericidal activity studies of antituberculosis agents. Clin. Microbiol Infect 18(7): 711-717. (IF=4.034)
Diacon AH, Dawson R, du Bois J, Narunsky K, **Venter A**, Donald PR, van Niekerk C, Erondu N, Ginsberg AM, Becker P, Spigelman MK. (2012) Phase II Dose-Ranging Trial of the Early Bactericidal Activity of PA-

824. Antimicrob Agents Chemother. 56(6):3027-3031. (IF=4.680)

Diacon AH, Donald PR, Pym A, Grobusch M, Patientia RF, Mahanyele R, Bantubani N, Narasimooloo R, De Marez T, van Heeswijk R, Lounis N, Meyvisch P, Andries K, McNeeley DF. (2012) Randomized pilot trial of eight weeks of bedaquiline (TMC207) treatment for multidrug-resistant tuberculosis: long-term outcome, tolerability, and effect on emergence of drug resistance. Antimicrob Agents Chemother. 56(6): 3271-3276. (IF=4.680)

Donald PR, **Maritz JS, Diacon AH.** (2012) Pyrazinamide pharmacokinetics and efficacy in adults and children. Tuberculosis (Edinb) 92(1): 1-8. (IF=3.149)

Drewe JA, O'Riain MJ, Beamish E, Currie H, **Parsons S**. (2012) Survey of infections transmissible between baboons and humans, Cape Town, South Africa. Emerg Infect Dis 18(2): 298-301. (IF=6.996)

Gey van Pittius NC, **van Helden PD**, **Warren RM**. (2012) Characterization of Mycobacterium orygis. Letter in Emerg Infect Dis. 18(10):1708-1709. (IF=6.689)

Hatherill M, Verver S, Mahomed H; **Taskforce on Clinical Research Issues, Stop TB Partnership Working Group on TB Vaccines (Walzl, G)**. (2012) Consensus statement on diagnostic end points or infant tuberculosis vaccine trials. Clin Infect Dis. 54(4): 493-501. (IF=7.898)

Hesseling AC, Kim S, Madhi S, Nachman S, Schaaf HS, Violari A, **Victor TC**, McSherry G, Mithell C, Cotton MF. (2012) High prevalence of drug resistance amongst HIV-exposed and –infected children in a tuberculosis prevention trial. Int J Tuberc Lung Dis 16(2): 192-195. (IF=2.426)

Katale BZ, Mbugi EV, Kendal S, Fyumagwa RD, Kibiki GS, Godfrey-Faussett P, Keyyu JD, **van Helden PD**, Matee MI. (2012) Bovine tuberculosis at the human-livestock-wildlife interface: Is it a public health problem in Tanzania? A review. Onderstepoort Journal of Veterinary Research. 79(2):1-8. (IF=0.890)

Kiser JJ, Zhu R, D'argenio DZ, Cotton MF, Bobat R, McSherry GD, Madhi SA, Carey VJ, Seifart HI, **Werely CJ**, Fletcher CV. (2012) Isoniazid Pharmacokinetics, Pharmacodynamics, and dosing in South African infants. Ther Drug Monit. 34(4):446-451. (IF=2.605)

Loxton AG, Black GF, Stanley K, Walzl G. (2012) Heparin-Binding Hemagglutinin Induces IFN-γ+ IL-2+ IL-17+ Multifunctional CD4+ T Cells during Latent but Not Active Tuberculosis Disease. Clin Vaccine Immunol. 19(5): 746-751. (IF=2.567)

Macingwana L, Baker B, Ngwane A, Harper C, Cotton M, Hesseling A, **Diacon A, van Helden PD, Wiid I**. (2012) Sulfamethoxazole enhances the antimycobacterial activity of Rifampicin. J Antimicrob Chemother. 67:2908-2911. (IF=4.480)

Mandalakas AM, Kirchner HL, Lombard C, **Walzl G**, Grewal HMS, Gie RP, Hesseling AC. (2012) Well-quantified tuberculosis exposure is a reliable surrogate measure of tuberculosis infection. Int J Tuberc Lung Dis. 16(8):1033–1039. (IF=2.426)

Mbugi EV, Katale BZ, Kendall S, Good L, Kibiki GS, Keyyu JD, Godfrey-Faussett P, **van Helden PD**, Matee MI. (2012) 'Tuberculosis cross-species transmission in Tanzania: Towards a One-Health concept. Onderstepoort Journal of Veterinary Research. 79(2):1-6. (IF=0.890)

Mbugi EV, Kayunze KA, Katale BZ, Kendall S, Good L, Kibik GS, Keyyu JD, Godfrey-Fausett P, **van Helden PD**, Matee MI. (2012) 'One Health' infectious diseases surveillance in Tanzania: Are we all on board the same flight? Onderstepoort Journal of Veterinary Research. 79(2):1-7. (IF=0.890)

McEvoy CRE, Cloete R, Muller B, Schurch AC, **van Helden PD**, Gagneux S, **Warren RM**, **Gey van Pittius NC**. (2012) Comparative analysis of *Mycobacterium tuberculosis* PE and PPE genes reveals high sequence variation and apparent absence of selective constraints. Plos One 7(4): e30593. (IF=4.610)

Miller M, Joubert J, Mathebelu N, De Klerk- Lorist L, Lyashchenko KP, Bengis R, **van Helden PD**, Hofmeyer M. Olea–Popelka F, Greenwald R, Esfandiara J, Buss P. (2012) Detection of antibodies to tuberculosis antigens in free –ranging lions (Panthera Leo) infected with Mycobacterium bovis in Kruger National Park, South Africa. JZWM 43(2): 317-323. (IF=0.710)

Muller A, **Möller M**, Adams LA, **Warren RM, Hoal EG**, **van Helden PD**. (2012) Comparative analysis of putative TB-susceptibility gene, MC3R (Melanocortin-3-receptor), and pseudogene sequence in cattle (Bos taurus), African buffalo (Syncerus caffer), hyena (Crocuta crocuta), rhino (Ceratotherium simum) and other African bovids and ruminants. Cytogenet Gen Res. 136(2): 117-122. (IF=2.074)

Mukinda FK, Theron D, **Van der Spuy GD**, Jacobson KR, Roscher M, **Streicher EM**, Musekiwa A, Coetzee GJ, **Victor TC**, Marais BJ, Nachega JB, **Warren RM**, Schaaf HS. (2012) Rise in Rifampicin-monoresistant Tuberculosis in Western Cape, South Africa. Int J Tuberc Lung Dis 16(2): 196-202. (IF=2.426)
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Seddon JA, Hesseling AC, Marais BJ, **Jordaan AM, Victor TC**, Schaaf HS. (2012) The evolving epidemic of drug-resistant tuberculosis among children in Cape Town, South Africa. Int J Tuberc Lung Dis. 16(7):928–933. (IF=2.426)
Seddon JA, **Jordaan AM, Victor TC**, Schaaf HS. (2012) Discordant Drug Susceptibility for Mycobacterium tuberculosis within Families. Pediatr Infect Dis J. 31(7): 783-785. (IF=3.271)
Seddon JA, Visser DH, Bartens M, **Jordaan AM**, **Victor TC**, van Furth AM, Schoeman JF, Schaaf HS. (2012) Impact of drug resistance on clinical outcome in children with tuberculous meningitis. Pedriatr Infect Dis J 31(7): 711-716. (IF=3.271)
Seddon JA, **Warren RM**, Enarson DA, Beyers N, Schaaf HS. (2012) Drug-resistant tuberculosis in children is caused by transmission and amplification of resistance within families. Emerg Infect Dis 18(8):1342-1345 (IF=6.996)
Sirgel FA, Tait M, Warren RM, Streicher EM, Böttger EC**, van Helden PD, Gey Van Pittius NC,** Coetzee G, Hoosain EY, Chabula-Nxiweni M, Hayes C, **Victor TC,** Trollip A. (2012) Mutations in the rrs A1401G Gene and Phenotypic Resistance to Amikacin and Capreomycin in Mycobacterium tuberculosis. Microb Drug Resist. 18(2): 193-197. (IF=1.847)
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Streicher EM, Bergval I, Dheda K, Bottger E, **Gey van Pittius NC**, Bosman M, Coetzee G, Anthony R, **van Helden PD**, **Victor TC**, **Warren RM**. (2012) Mycobacterium tuberculosis population structure determines the outcome of genetic based second-line drug testing. Antimicrob. Agents Chemother. 56(5): 2420-2427. (IF=4.680)
Streicher EM, **Müller B**, **Chihota V**, Mlambo C, **Tait M**, Pillay M, **Trollip A**, Hoek KGP, **Sirgel FA, Gey van Pittius NC**, **Van Helden PD**, **Victor TC**, **Warren RM**. (2012) Emergence and treatment of multidrug resistant (MDR) and extensively drug-resistant (XDR) tuberculosis in South Africa. Infection, Genetics and Evolution. 12(4):686–694. (IF=3.055)
Van Rie A, Mellet K, John M-A, Scott L, Page-Shipp L, Dansey H, **Victor TC, Warren RM.** (2012) False positive Rifampicin resistance on Xpert®MTB/RIF: case report and clinical implications. Int J Tuberc Lung Dis 16(2): 206-208. (IF=2.426)
Van Schalkwyk C, Cule M, Welte A, **van Helden PD, van der Spuy G,** Uys P. (2012) Towards eliminating bias in Cluster Analysis of TB Genotyped data. PloS One. 7(3):e34109 (IF=4.610)
Van Soelen N, Mandalakas AM, Kirchner HL, **Walzl G**, Grewal HM, Jacobsen M, Hesseling AC. (2012) Effect of Ascaris Lumbricoides specific IgE on tuberculin skin test responses in children in a high-burden setting: a cross-sectional community-based study. BMC Infect Dis. 12(1):211 (IF=3.236)

Visser ME, **Stead MC**, **Walzl G**, **Warren RM**, Schomaker M, Grewal HM, Swart EC, Maartens G. (2012) Baseline predictors of sputum culture conversion in pulmonary tuberculosis: importance of cavities, smoking, time to detection an w-beijing genotype. PloS One 7(1): e29588. (IF=4.610)
Weiner B, Gomez J, **Victor TC**, **Warren RM**, Sloutsky A, Plikatis BB, Posey JE, **van Helden PD**, **Gey van Pittius NC**, Koehrsen M, Sisk P, Stolte C, White J, Gagneux S, Birren B, Hung D, Murray M, Galagen J. (2012) Independent large scale duplications in multiple *M. tuberculosis* lineages overlapping the same genomic region. PloS One 7(2): e26038. (IF=4.610)
Zhu R, Kiser JJ, Seifart HI, **Werely CJ**, Mitchell CD, D'Argenio DZ, Fletcher CV. (2012) The Pharmacogenetics of NAT2 enzyme maturation in perinatally HIV exposed infants receiving isoniazid. J Clin Pharmacol. 52(4): 511-519. (IF=3.387)

Non Peer-Reviewed Articles (Total: 3)

Van Helden PD. (2012) Simplicity. EMBO reports 13:172. (IF=7.488)
Van Helden PD. (2012) The cost of research in developing countries. EMBO reports 13(5): 395. (IF=7.488)
Van Helden PD. (2012) Not too much and not too little. EMBO Reports. 13:942.

Published Abstracts (Total: 0)

Technical Reports (Total: 0)

Products / Artefacts / Patents (Total: 0)

Conferences/Meetings Attended & Invited Talks/Seminars Presented (Total: 92)

Plenary/Keynote/ Distinguished Lectures
Mizrahi V. Development and Application of New Tools for TB Drug Discovery: A View from South Africa. Keynote lecture presented at the 4th Annual CEND Symposium: Fighting the Diseases of Poverty, Centre for Emerging and Neglected Diseases, UC Berkeley, 13 January 2012
Mizrahi V. New Tools for TB Drug Discovery. Plenary lecture delivered at the Symposium on Scientific Advances in TB Pathogenesis and Treatment, 10th Conference on Retroviruses and Opportunistic Infections (CROI 2012), Seattle, WA, 5-9 March 2012
Mizrahi V. Drug Resistance in TB: Scope of the problem and underlying mechanisms. Lecture presented at the pre-Symposium Workshop. Keystone Symposium on Drug Resistance and Persistence in Tuberculosis, Speke Resort, Kampala, Uganda, 13-18 May 2012
Mizrahi V. Mechanisms driving mutations to drug resistance. Plenary lecture presented at the Keystone Symposium on Drug Resistance and Persistence in Tuberculosis, Speke Resort, Kampala, Uganda, 13-18 May 2012
Mizrahi V. New Tools for TB Drug Discovery. Plenary lecture presented at the 3rd SA TB Conference 2012, Durban, 12-15 June 2012
Mizrahi V. Knowing the Enemy: Survival and Subversion Strategies of Mycobacterium tuberculosis. Inaugural Lecture, University of Cape Town, 22 August 2012.
Mizrahi V. New Tools for Tuberculosis Drug Discovery: A South African Perspective. Wolfson Colloquium, University of Cape Town, 4 September 2012.
Mizrahi V. Pathway-selective sensitization of *Mycobacterium tuberculosis* for use in target-based whole-cell screening. Invited lecture presented at the H3-D Symposium on New Paradigms in Drug Discovery: Challenges and Opportunities in Africa, 16 October 2012.
Kana B. Peptidoglycan remodelling during mycobacterial growth and persistence. Opening talk in the "Innovations from Africa Theme". Kwazulu-Natal Research Institute for TB and HIV (K-RITH) Opening Scientific Symposium. Hilton Hotel, Durban, South Africa. 10th October 2012.

Invited Talks
Mizrahi V. New Tools for TB Drug Discovery. Invited lecture presented at the Department of Medicine Seminar Series, University of Cape Town, 15 March 2012
Evans J, **Mizrahi V**. Identifying vulnerable targets in the CoA biosynthetic pathway of *M. tuberculosis*. Lecture presented at the Kick-Off meeting, High-Quality Hits for Tuberculosis (HIT-TB) Consortium, Cambridge, UK, 27 March 2012
Mizrahi V. Mechanisms driving mutations to drug resistance. Lecture presented at the IIDMM/ICGEB Seminar Series, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, 9 May 2012
Singh V, Warner DF, **Mizrahi V**. Pyrimidine metabolism in *M. tuberculosis* – an update from UCT. Invited talk presented at the Fourth Consortium Meeting, More Medicines for Tuberculosis (MM4TB), Tällberg, Sweden, 5-6 July 2012
Gopinath K, McKinney JD, Mizrahi V, **Warner DF**. BacA is essential for vitamin B_{12} transport in *M. tuberculosis*. Invited talk presented at Tuberculosis 2012, Paris, 11-15 September, 2012
Gopinath K, McKinney JD, Mizrahi V, Warner DF. Identification of genes requires for transport and assimilation of vitamin B12 in *M. tuberculosis*. Invited talk presented at the Vitamin B12 Symposium, Nancy, France, 20-22 September 2012.
Mizrahi V. Pathway-selective sensitization of *Mycobacterium tuberculosis* for use in target-based whole-cell screening. Invited talk presented at the H3-D Symposium on New Paradigms in Drug Discovery, Cape Town, 16 October 2012.
Kana B. Remodelling the mycobacterial cell wall for new TB drugs. Invited talk at École polytechnique fédérale de Lausanne EPFL. Lausanne, Switzerland, 7th September 2012.
Kana B. Remodelling the mycobacterial cell wall for new TB drugs. Invited talk at the University of Leicester. Leicester, United Kingdom. 10th July 2012.
Kana B. Peptidoglycan remodelling during TB infection. Invited talk at the Kwazulu-Natal Research Institute for TB and HIV (K-RITH), Durban, South African, 31st May 2012.
Kana B. Career Guidance for young scientists and NRF ratings. Oral presentation at the Research Indaba. Midrand graduate institute. Johannesburg. 22nd October 2012.
Kana B. How to Build an Academic Career in Science. Oral presentation at the Research Capacity Building Session of the 3rd SA TB Conference. International Convention Centre, Durban, South Africa. 12-15 June 2012.
Kana B. Building an Academic Career in Science. Invited talk given at the Career Guidance for Young Scientists Workshop at the SASBMB/FASBMB Congress 2012 - The South African Society of Biochemistry and Molecular Biology. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, 29 January – 1 February 2012.
Hassim F, Gordhan B. Construction and phenotypic characterization of *M. smegmatis* mutants deficient in the MutY DNA glycosylase. Oral presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Hassim F, Gordhan B. Construction and phenotypic characterization of *M. smegmatis* mutants deficient in the MutY DNA glycosylase. Oral presentation at the MRC Early Career Scientists Conference 2012, 24th – 25th October 2012.
Narrandes N, Mizrahi V, Kana B. Functional characterization of molybdopterin synthase encoding genes in mycobacteria. Oral presentation at the SASBMB/FASBMB Congress 2012 - The South African Society of Biochemistry and Molecular Biology. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, 29 January – 1 February 2012.
Narrandes N, Mizrahi V, Kana B. Functional characterization of molybdopterin synthase encoding genes in mycobacteria. Oral presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Sensani S. My Journey at the CBTBR. Oral presentation at the DST/NRF Centre of Excellence Director's Forum. Sanlam Centre, Pretoria, South Africa. 13th November 2012
Senzani S, Kana B. Analysis of peptidoglycan degrading amidases. Oral presentation at the MRC Early Career Scientists Conference 2012, 24th – 25th October 2012.
Moolla N, Gordhan B. Construction and Phenotypic Characterization of Mycobacterium smegmatis Mutants

Deficient in the Nth DNA Glycosylase. Oral presentation at the MRC Early Career Scientists Conference 2012, 24th – 25th October 2012.
Ealand C, Kana B. The role of mycobacterial DD-carboxypeptidases in peptidoglycan remodeling and turnover. Oral presentation at the SASBMB/FASBMB Congress 2012 - The South African Society of Biochemistry and Molecular Biology. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, 29 January **–** 1 February 2012.
Ealand C, Kana B. The role of mycobacterial DD-carboxypeptidases in peptidoglycan remodeling and turnover. Oral presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Ealand C, Kana B. The role of mycobacterial DD-carboxypeptidases in peptidoglycan remodeling and turnover. Oral and poster presentation at the MRC Early Career Scientists Conference 2012, 24th – 25th October 2012.
Hoal EG. Genomics of Infectious Diseases in Africa. Invited talk presented at the Golden Helix Symposia: Genomic Medicine: Translating Genes into Health. 18-21 April 2012. Turin, Italy.
Warren RM. Characterizing Drug-Resistant TB epidemics in South Africa. Invited talk presented at Stellenbosch University. 19th April 2012.
Le Roux N. Host genetic susceptibility to M. bovis in buffalo. Talk presented at the Annual Bovine TB Workshop, Kruger National Park, May 2012.
Grobbelaar M. Adaptation of the Mycobacterium tuberculosis transcriptome in response to Rifampicin. Talk presented at the Keystone Symposia, Uganda during 13-18 May 2012:.
Parsons SDC. Adaptation of the QuantiFERON TB-Gold assay for the diagnosis of TB in wildlife. Talk presented at the International Wildlife TB Conference, Skukuza, Kruger national Park, South Africa, May 2012.
Parsons SDC. Development of a Gene Expression Assay for the diagnosis of TB. Talk presented at a meeting of the BTB Study Group, Skukuza, KNP, September 2012.
Warren RM. Deciphering the Epidemiology of drug-resistant tuberculosis through comparative genomics. Invited speaker at the 6th Annual New England TB Symposium, Focus on Drug-resistance, Broad Institute, Cambridge, 28 June 2012.
Le Roux N. Novel SNP identification and association with bovine TB in African buffalo. Invited talk presented at the International Society of Animal Genetics (ISAG) 2012 conference, Cairns, Australia, 15-20 July 2012:
Klopper M. Molecular characterization of the drug-resistant tuberculosis epidemic in the Eastern Cape, South Africa. Talk presented at SACEMA Research day, Stellenbosch, April 2012.
Streicher EM. Mycobacterium tuberculosis population structure determines the outcome of genetic based second-line drug resistance testing. Talk presented at the Keystone Symposium, Drug Resistance and Persistence in Tuberculosis, Kampala Uganda, May 2012.
Fortuin S. The evolution of the Mycobacterium tuberculosis proteome. Invited speaker at the Welcome Trust All Directors Meeting, Accra, Ghana 2012.
Fortuin S. Identification of virulence proteins of Mycobacterium tuberculosis. Invited speaker at the Southern Africa Consortium for Research Excellence Annual Meeting, Gaborone, Botswana, September 2012.
Fortuin S. The phosphoproteomes of a hypo- and hyper-virulent clinical M. tuberculosis Beijing strains. Talk presented at the Stellenbosch University 56th Annual Academic Year day 2012, 15-16 August 2012.
Van Helden PD. Molecular Epidemiology of Mycobacterium TB. Invited talk presented at the SA Clinicians Society Conference 2012, Cape Town, South Africa, 25-28 November 2012.
Van Helden PD. Antibiotics and omics of TB. Invited talk presented at the Structural Biology in the Bio Economy Conference, Cape Town, South Africa, 2-4 December 2012.
Walzl G. TB biomarkers in peripheral blood. Invited talk presented at the 43rd Union World Conference on Lung Health, Kuala Lumpur Malaysia , 13-17 November 2012.
Walzl G. Clinical impact of recent advances for the prevention, diagnosis and treatment of tuberculosis. Invited talk presented at the European Respiratory Society Annual Congress, 1-5 September 2012, Vienna, Austria.
Walzl G. Lessons from the search for biomarkers for active TB and TB treatment response. Invited talk presented at the Joint EVI/TBVI Symposium. Les Diablerets, Switzerland, 31 January 2012.

Walzl G. Utility of multiplex cytokine arrays in TB biomarker discovery. Invited talk presented at the Tuberculosis Research Unit Annual meeting, Cleveland, USA, 26-27 November 2012.
Le Roux N. Novel SNP identification and association with bovine TB in African buffalo. Talk presented at the International Wildlife Tuberculosis Conference, Kruger National Park, South Africa, 9-12 September 2012.
Werely CJW. TB treatment considerations for neonates and infants. Talk presented at the 43rd Union World Conference on Lung Health, Kuala Lumpur, Malaysia, 13-17 November 2012.
Posters
Koch, A., Mizrahi, V., Warner, D.F. Physiology of drug-resistant mycobacteria: implications for pathogenesis. Poster presented at the Keystone Symposium on Drug Resistance and Persistence in Tuberculosis, Speke Resort, Kampala, Uganda, 13-18 May 2012.
Mapela L, Beukes G, Senzani S, **Kana B.** Peptidoglycan remodelling in mycobacterial growth and pathogenesis. Poster presentation at the Tuberculosis 2012: Biology, pathogenesis, intervention strategies. Institut Pasteur, Paris, France, 11th-15th September 2012.
Kana B. Resuscitation promoting factors in bacterial growth and cell wall remodelling - Extreme Makeover for the Cell wall. Poster presentation at the Annual HHMI Scholars Meeting. HHMI Headquarters, Chevy Chase, Maryland, USA. 14-17 February 2012.
Asmal R, Kana B. Identification and cellular localization of DD-Carboxypeptidase-interacting proteins in Mycobacterium smegmatis. Poster presentation at the 4th Cross Faculty Graduate Symposium: Showcasing Postgraduate Research at Wits 2012. Wits University – Professional Development Hub, Johannesburg, South Africa. 19th and 22nd October.
Asmal R, Kana B. Identification and cellular localization of DD-Carboxypeptidase-interacting proteins in Mycobacterium smegmatis. Poster presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Hassim F, Gordhan B. Construction and phenotypic characterization of *M. smegmatis* mutants deficient in the MutY DNA glycosylase. Poster presentation at the SASBMB/FASBMB Congress 2012 - The South African Society of Biochemistry and Molecular Biology. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, 29 January – 1 February 2012.
Narrandes N, Mizrahi V, Kana B. Functional characterization of molybdopterin synthase encoding genes in mycobacteria. Poster presentation at the Tuberculosis 2012: Biology, pathogenesis, intervention strategies. Institut Pasteur, Paris, France, 11th-15th September 2012.
Narrandes N, Mizrahi V, Kana B. Functional characterization of molybdopterin synthase encoding genes in mycobacteria. Poster presentation at the 4th Cross Faculty Graduate Symposium: Showcasing Postgraduate Research at Wits 2012. Wits University – Professional Development Hub, Johannesburg, South Africa. 19th and 22nd October.
Senzani S, Kana B. Analysis of peptidoglycan degrading amidases. Poster presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Senzani S, Kana B. The role of resuscitation promoting factors in peptidoglycan hydrolysis and reactivation from dormancy in Mycobacterium smegmatis. Poster presentation at the SASBMB/FASBMB Congress 2012. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, 29 January – 1 February 2012.
Beukes G, Mapela L, Kana B. The role of resuscitation promoting factors in peptidoglycan hydrolysis and reactivation from dormancy in Mycobacterium smegmatis. Poster presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Moolla N, Gordhan B. Construction and Phenotypic Characterization of Mycobacterium smegmatis Mutants Deficient in the Nth DNA Glycosylase. Poster presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Moolla N, Gordhan B. Construction and Phenotypic Characterization of Mycobacterium smegmatis Mutants Deficient in the Nth DNA Glycosylase. Poster presentation at the SASBMB/FASBMB Congress 2012 - The South African Society of Biochemistry and Molecular Biology. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, 29 January – 1 February 2012.
Goosens V, Mizrahi V, **Gordhan B.** The role of DNA glycosylases in mutagenesis and adaptation to stress in mycobacteria. Poster presentation at the Keystone Symposia |Drug resistance and persistence in

tuberculosis. Kampala, Uganda. 13th – 18th May 2012.
Chengalroyen M, Kana B. The role of resuscitation promoting factors in the reactivation of Mycobacterium tuberculosis in sputum. Poster presentation at the Wits Health Sciences Research Day & Postgraduate Expo 2012. Wits Medical School, Johannesburg, South Africa, 19th September 2012.
Chengalroyen M, Kana B. A tool to improve the diagnosis of Mycobacterium tuberculosis. Poster presentation at the Spring Science Showcase. Delta Environmental Centre, Johannesburg, South Africa, 9th September 2012.
Chengalroyen M, Kana B. The role of resuscitation promoting factors in the reactivation of Mycobacterium tuberculosis in sputum. Poster presentation at the SASBMB/FASBMB Congress 2012 - The South African Society of Biochemistry and Molecular Biology. Champagne Sports Resort, Drakensberg, KwaZulu-Natal, **29** January – 1 February 2012.
Moller M. A CD14 promoter polymorphism is implicated in tuberculosis susceptibility in a South African population. Poster presented at the 62nd Annual Meeting of the American Society of Human Genetics, San Francisco, USA, 6 – 10 November 2012.
Daya M. A panel of ancestry informative markers for the South African Coloured population. Poster presented at the 62nd Annual Meeting of the American Society of Human Genetics, San Francisco, USA, 6-10 November 2012.
Salie M. HLA class-I supertypes are associated with specific M. tuberculosis strain infections. Poster presented at the 62nd Annual Meeting of the American Society of Human Genetics, San Francisco, USA, 6-10 November 2012.
De Vos M. Increasing levels of rifampicin resistance in Mycobacterium tuberculosis results in minor changes in the genomes of in vitro rifampicin resistant mutants. Poster presented at Keystone Symposium: E1, Drug Resistance and Persistence in Tuberculosis, Kampala, Uganda, May 2012.
Black PA. Regulatory response to Rifampicin in multi-drug resistant Mycobacterium tuberculosis strains. Poster presented at the Keystone Symposia on Drug Resistance and Persistence in Tuberculosis, May 2012.
Salie M. Poster presented at the EMBO|EMBL Symposium: New Perspectives on Immunity to Infection, Heidelberg, Germany, 19-22 May 2012.
Louw GE. Mycobacterium tuberculosis sputum cultures show polyphenotypic rifampicin resistance. Poster presented at Keystone Symposium, Drug Resistance and Persistence in Tuberculosis, Kampala Uganda, May 2012.
Le Roux. Novel SNP identification and association with bovine TB in African buffalo. Poster presented at the International Society of Animal Genetics (ISAG) 2012 conference, Cairns, Australia, 15-20 July 2012.
Willemse D. Regulation of efflux in rifampicin resistant mutants of Mycobacterium tuberculosis. Poster presented at the EMBO Tuberculosis 2012: Biology, pathogenesis, intervention strategies Conference, Institut Pasteur, Paris, France, 11-15 September 2012.
McGrath M. Nucleoside analogs and their possible role in the emergence of TB drug resistance. Poster presented at the EMBO Tuberculosis: Biology, Pathogenesis, Intervention strategies Conference, Paris, France, 11-15 September 2012.
Viljoen A. Genetic study of the nitrogen assimilatory pathways of Mycobacterium bovis BCG. Poster presented at the EMBO Tuberculosis: Biology, Pathogenesis, Intervention strategies Conference, Paris, France, 11-15 September 2012.
Sao Emani C. The role of ergothioneine in the physiology of Mycobacterium smegmatis. Poster presented at the EMBO Tuberculosis: Biology, Pathogenesis, Intervention strategies Conference, Paris, France, 11-15 September 2012.
Fortuin S. A phosphoproteomic approach to characterise mechanisms of virulence in clinical M. tuberculosis Beijing strains. Poster presented at the Keystone Symposia (Proteomics, Interactomes), Stockholm, Sweden 2012.
Fortuin S. The phosphoproteomes of a hypo- and hyper-virulent clinical M. tuberculosis Beijing strains. Poster presented at the MRC Early Career Scientist Conference, 25 October 2012.
Fang Z. Mycosin-3 of Mycobacterium tuberculosis, functional and structural studies. Poster presented at the Structural Biology in the Bio Economy Conference, Cape Town, South Africa, 2-4 December 2012.
Parsons SDC. Development of a diagnostic gene expression assay for tuberculosis in African buffaloes

(Syncerus caffer). Poster presented at the 8th Conference of the Federation of African Immunological Societies, Durban, December 2012.
Parsons SDC. A novel "dassie bacillus" variant isolated from meerkats. Poster presented at the International Wildlife TB Conference, Skukuza, KNP, September 2012.
Dippenaar A. Evolution of the members of the group 2 Latin American-Mediterranean (LAM) genotype of M. Tuberculosis. Poster presented at EMBO course: Computational Biology: from genomes to cells and systems, 14-20 October 2012.
Ngwane A. Identification of a novel anti- M. tuberculosis compound (F1082) for TB drug development. Poster presented at Keystone Symposium, Drug Resistance and Persistence in Tuberculosis, Kampala Uganda, May 2012.
Ngwane A. Evaluation of Vav1Contribution in B cell Activation and Immunosuppression. Poster presented at Novartis Next Generation of Scientist Meeting, 23 August 2012.
Loxton A. The frequency of CD103 as a marker of regulatory CD4+ T-cells and suppressor CD8+ T-cells is not affected by ARVs, but has a negative correlation with absolute CD4 cell numbers. Poster presented at the XIX International AIDS Conference, Washington DC, USA, 22-27 July 2012.
Loxton A. Regulatory T-cells and high levels of FOXP3 mRNA lead to decreased immune responses during HIV-TB co-infection .Poster presented at European Respiratory Society (ERS) 2012 Conference, Vienna, Austria, 1-5 September 2012.

Other Relevant Outputs (including honours and awards to staff)

SARCHi Research Chairs: The NRF has provisionally allocated 3 new SARCHi's to the CBTBR in 2012, evidence of the strength of the CBTBR and the NRF's confidence in the entity
Dr Bavesh Kana was selected as an Early Career Scientist of the Howard Hughes Medical Institute after a fiercely competitive process which involved almost 800 applicants worldwide. Dr. Kana is one of only 26 scientists from around the world to receive this prestigious award and represents one of only two awards made in Africa. The award comes with a $ 715 000 research grant, over the period of five years, Further details for this award can be found at http://www.hhmi.org/research/iecs/
Dr. Bavesh Kana was appointed as one of the top 200 Young South Africans by the Mail and Guardian newspaper. The Mail and Gaurdian 200 Young South African list comprises those individuals who are expected to make a significant impact in South Africa and play a key leadership role in the country. More details on this can be found at http://ysa2012.mg.co.za/
Dr Bhavna Gordhan was honored for her research achievements and leveraging significant research funding at the 2012 Annual Faculty of Health Sciences Research Awards.
Dr Bhavna Gordhan was awarded the Keystone Symposia Global Health Travel Award to attend the Keystone Symposium on Drug resistance and persistence in tuberculosis. Kampala, Uganda. 13th – 18th May 2012.
Dr Bavesh Kana was selected as an Early Career Scientist of the Howard Hughes Medical Institute after a fiercely competitive process which involved almost 800 applicants worldwide. Dr. Kana is one of only 26 scientists from around the world to receive this prestigious award and represents one of only two awards made in Africa. The award comes with a $ 715 000 research grant, over the period of five years, Further details for this award can be found at http://www.hhmi.org/research/iecs/
Prof. Mizrahi was selected as a Senior International Research Scholar of the HHMI and awarded five-year a $500,000 research grant. This highly prestigious SIRS award was given to 13 basic science researchers from countries outside the USA. This is Prof. Mizrahi's third award from the HHMI. Details of this award can be found at http://www.hhmi.org/news/SIRS20120926.html.
Dr. Williams was awarded a Columbia University-Southern African Fogarty AITRP Traineeship and a PHRI-AURUM-Global Infectious Diseases Research Fogarty Traineeship, July-Dec 2012

Progress of Students Who Have Qualified or Trained in the CBTBR (2005-2012)

Title	Surname, Initial	Training/Degree	Yr completed	Current position
Dr	Abrahams, GL	Postdoctoral	2010	Appointed as Research Officer at UCT nodein 2011Seconded for 3 years to Dr. Clifton Barry's lab at the NIAID
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
Mr	Barnard, M	MSc	2005	Unemployed
Dr	Baumann R	Postdoctoral	2006	Returned to Germany, to private company
Ms	Barichievy, S	MSc	2005	Sydney Brenner postdoctoral fellow in the lab of Dr. Musa Mhlanga at the CSIR
Ms	Bester, M	MSc	2009	Remained in CBTBR for a PhD degree
Dr	Bezuidenhout, J	PhD	2005	Employed as F/T pathologist at Tygerberg Hospital
Dr	Bintou, AA	PhD	2011	Took up a postdoctoral position with Prof. Bishai, John Hopkins University, USA
Dr	Black, JF	Postdoctoral	2010	Took up a position with Livelihoods Foundation
Ms	Botha, J	MSc	2007	Studying pharmacy at UWC
Ms	Brackin, R	MSc	2005	Took up a PhD position at CSIR
Dr	Brown, N	Postdoctoral	2007	Moved to UK
Ms	Carinus, H	Hons	2005	Moved to Dubai
Dr	Chegou, N	PhD	2009	Remained in CBTBR as postdoctoral fellow
Dr	Chihota, V	PhD	2011	Deputy Director Research, Aurum Institute
Dr	Conradie E	Postdoctoral	2006	Full-time mother
Dr	de Wit, E	PhD	2009	Housewife
Dr	Djoba, J	PhD	2008	Took up a postdoctoral position in France
Mr	Dudhia, ZE	Hons	2009	Took a MSc studentship at the MRC
Ms	Du Toit, I	Hons	2006	Planning to do forensics through UNISA
Ms	Ehlers, L	Hons	2010	Remained in CBTBR for a MSc degree
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	Fenhalls, G	Postdoctoral	2005	Now working in husband's company
Ms.	Goosens, V	MSc	2005	Took up PhD studentship in the Netherlands
Dr	Hanekom, M	PhD	2009	Remained in Lecturer's post
Dr	Hayward, D	Postdoctoral	2010	Took up a permanent position at Triclinium
Ms	Heysen, T	Hons	2009	Unknown
Ms	Hoek, K	PhD	2010	Took up a permanent position at the NHLS
Dr	Johnson, R	Postdoctoral	2009	Took up a permanent position at the MRC
Mr	Jennings, G	Hons	2005	Moved to the USA for postgraduate study
Ms	Koch, A	MSc	2011	Remained in CBTBR for a PhD degree
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	Loxton, A	PhD	2009	Remained in CBTBR as a postdoctoral fellow
Dr	Machowksi, E	Postdoctoral	2006	P/T Senior Scientist in CBTBR
Ms	Magan, N	Hons	2009	Unknown
Dr	Magwira, C	Postdoctoral	2010	Took up a second postdoctoral fellowship in the RMPRU, Wits/NICD
Mr.	Mahasha, P	MSc	2007	Moved to Univ. of Pretoria, for family reasons
Dr	Matsoso, LG	PhD	2007	Took a position in a TB-focusd NGO in Johannesburg
Mr	Mazorodze, JH	MSc	2010	Took up a PhD in Bill Jacobs's lab in USA
Dr	McEvoy, CRE	Postdoctoral	2010	Returned to Australia in March 2010
Ms	Mlamla, Z	MSc	2011	Remained in CBTBR for a PhD degree
Dr	Moller, M	PhD	2007	Remained in CBTBR as a postdoctoral fellow
Dr	Mowa, B	PhD	2009	Appointed as Lecturer at Wits after completing postdoc
Mr	Mufamadi, S	Internship	2005	Completed MSc at Wits
Ms	Muller, L	Researcher	2006	Full-time mother
Ms	Myburgh, R	Hons	2006	Left the CBTBR to start her family
Ms	Naran, K	MSc	2010	Remained in the CBTBR for a PhD degree
Ms	Ndabambi, S	MSc	2009	Unknown

Mr	Ndong, PE	Hons	2010	Remained in CBTBR for a MSc degree
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
Ms	Newton-Foot, M	MSc	2009	Remained in CBTBR for a PhD degree
Ms	Ngombane, NC	MSc	2011	Returned to MRC
Dr	Parsons, S	PhD	2009	Remained in CBTBR as postdoctoral fellow
Ms	Phalane, KG	Hons	2010	Remained in CBTBR for a MSc degree
Dr	Ramburan, A	PhD	2009	Took up a permanent position at NHLS, Durban
Ms	Richardson, M	PhD	2006	Deceased
Dr	Roberts, T	PhD	2008	Took up a permanent position at CPGR, UCT
Ms	Sao Emani, C	Hons	2010	Remained in CBTBR for a MSc degree
Dr	Savvi, S	PhD	2009	Doing second postdoc at UCT
Ms	Seepe, P	MSc	2011	Remained in CBTBR for a PhD degree
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	Strauss, O	MSc	2009	Moved to Kayaletsha HIV clinic in Cape Town
Dr	Streicher, EM	PhD	2007	Remained in CBTBR as postdoctoral fellow
Ms	Thiart, L	Hons	2010	Remained in CBTBR for a MSc degree
Dr	Van der Spuy, G	PhD	2009	Remained in CBTBR in MRC Post
Dr.	Veenstra, H	PhD	2007	Housewife
Mr	Viljoen, B	Hons	2009	Remained in CBTBR for a MSc degree
Dr.	Warner, DF	Postdoctoral	2007	Moved from NHLS to UCT as CBTBR Team Member
Dr	Williams, M	Postdoctoral	2009	Given an MRC-funded post in the MMRU, , seconded to SU node, 2001-2012
Dr	Wright, CA	PhD	2009	Remained in University Post
Ms	Ansarie, M	Hons	2012	Unknown
Ms	Coetze, L	Hons	2012	Unknown
Mr	Du Plessis, WJ	Hons	2012	Remained in CBTBR for a MSc degree
Mr	Goosen, WJ	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Ntsapi, MC	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Ruzive, S	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Tshoko, S	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Visser, H	Hons	2012	Remained in CBTBR for a MSc degree
Mr	Zvinairo, TK	Hons	2012	Remained in CBTBR for a MSc degree
Ms	Axcell, A	MSc	2012	Working at the NHLS
Ms	Black, P	MSc	2012	Remained in CBTBR for a PhD degree
Ms	Grobbelaar, M	MSc	2012	Remained in CBTBR for a PhD degree
Mr	Lucas, L	MSc	2012	Remained in CBTBR for a PhD degree
Ms	Mapela, L	MSc	2012	Unknown
Ms	Steyn, NL	MSc	2012	Remained in CBTBR for a PhD degree
Ms	Wagman, CK	MSc	2012	Remained in CBTBR for a PhD degree
Ms	Botha, MM	PhD	2012	Took up a permanent position at ICON
Ms	Bruiners, N	PhD	2012	Remained in CBTBR as postdoctoral fellow
Ms	Du Plessis, N	PhD	2012	Remained in CBTBR as postdoctoral fellow
Ms	Kleynhans, L	PhD	2012	Remained in CBTBR as postdoctoral fellow
Ms	Moosa, A	PhD	2012	Remained in CBTBR as postdoctoral fellow
M	Ngwane, AH	PhD	2012	Remained in CBTBR as postdoctoral fellow
M	Van der Merwe,R	PhD	2012	Remained in CBTBR as postdoctoral fellow
M	Werely, CJ	PhD	2012	Staff, PAWC (SU)
Dr	Harper, CJ	Post Doc	2012	Housewife
Dr	Loebenberg, L	Post Doc	2012	Took up a permanent position at Afriplex
Dr	Louw, GE	Post Doc	2012	Took up a permanent position at K-RITH

FINANCES

The income statement, balance sheet and cash flow statement for period 1 Jan 2012 to 31 Dec 2012 are currently under review by the external auditors and will be forwarded to the Board as soon as it becomes available.

APPENDIX: Scientific Research Report

THEME I: FUNDAMENTAL RESEARCH ON ASPECTS OF THE PHYSIOLOGY AND METABOLISM OF MYCOBACTERIA OF RELEVANCE TO TUBERCULOSIS DRUG RESISTANCE AND DRUG DISCOVERY

The research program of the UCT node involves an integrated suite of projects that are aimed at investigating aspects of the physiology and metabolism of *M. tuberculosis* of particular relevance to TB drug discovery and drug resistance. Projects 1-4 are built on areas of fundamental mycobacterial metabolism and physiology research for which the MMRU is internationally recognized – the metabolism of DNA, nucleotides and cofactors. Research on DNA metabolism is focused on further investigating the structure and function of the novel mutasome discovered by UCT node researchers and on exploring the mechanistic basis of replication fidelity in mycobacteria. A new study on nucleotide metabolism initiated in mid-2011 aims to identify and exploit vulnerabilities in pyrimidine biosynthesis for drug discovery. Cofactor metabolism is a major thematic area of research in the UCT node, focusing on vitamin B_{12} (cobalamin), molybdenum cofactor (MoCo), vitamin B5 (pantothenate) and coenzyme A. Our work on vitamin B_{12} is focused on elucidating the mechanisms of *de novo* biosynthesis of vitamin B_{12}, its transport into mycobacteria and the role of the B_{12}-dependent methylmalonyl pathway in priopionate catabolism in *M. tuberculosis*. This work, which has led to the identification of proteins involved in the transport and assimilation of B_{12} in *M. tuberculosis* (publication in press). Ongoing studies on the mechanism of molybdenum cofactor (MoCo) biosynthesis – a collaborative project involving all three nodes of the CBTBR, have focused on the late-stage step in the pathway. With the support of two Fogarty training fellowships, Dr. Monique Williams spent 6 months in the lab of Dr. Gilla Kaplan (PHRI, UMDNJ) where she has characterized a MoCo-deficient mutant strain in murine and macrophage infection models. Finally, we have significantly expanded our efforts on TB drug discovery through participation in the HIT-TB (TB Drug Accelerator, BMGF), MM4TB (EU FP7) and SATRII (TIA) consortia, and through strong collaboration with Prof. Kelly Chibale's group (H3-D Drug Discovery Centre) on SATRII and other studies. Dr. Warner has led the Biology component of SATRII, and Prof. Mizrahi has played an instrumental role in aligning SATRII with the HIT-TB program. Importantly, our drug discovery projects that focus on specific enzymes/pathways in DNA and cofactor biosynthesis as potential drug targets fall are highly integrated with our fundamental research in these areas of mycobacterial metabolism.

Current projects and sub-projects

1. **Mechanisms of DNA repair, replication and mutagenesis in mycobacteria**
   a. Mechanisms of mutagenesis in Mycobacterium tuberculosis: structural and functional characterisation of the DNA polymerase accessory factors encoded by Rv3394c and Rv3395c
   b. Replication fidelity in mycobacteria
2. **Physiology of drug-resistant mycobacteria: implications for pathogenesis**
3. **The biosynthesis, transport and function of vitamin B_{12} in mycobacteria and the role of B_{12}-dependent enzymes in mycobacterial growth and persistence**
   a. Mechanisms of propionate catabolism in M. tuberculosis: Identification of genes required for vitamin B_{12} transport in M. tuberculosis
   b. Molecular mechanisms of transport and metabolism of vitamin B_{12} in mycobacteria: role of alternate B_{12} co-factors

   Highlights: A novel vitamin B_{12} transporter identified last year was confirmed, and furthermore, key components of the B_{12} assimilation and corrinoid salvage systems in *M. tuberculosis* were identified. Specifically, an ABC transporter, Rv1819c, implicated previously in *M. tuberculosis* pathogenesis, was shown through a rigorous suite of genetic and physiological experiments, to be essential for corrinoid transport in *M. tuberculosis*. Furthermore, Rv1314c, the putative PduO-type adenosyltransferase, was identified through a forward genetic screen, and found to be essential for the assimilation of exogenous vitamin B_{12} (provided in the form of cyanocobalamin) by *M. tuberculosis*. This work has been accepted for publication in *Open Biology*, a new open-access journal of the Royal Society of the UK (http://rsob.royalsocietypublishing.org/site/misc/about.xhtml)

4. **Tuberculosis drug discovery: SAR studies o*n novel antitub*erculars and elucidation of mechanisms subverting drug efficacy in mycobacteria**
   a. *Structure-activity relationship studies on novel anti-tubercular compounds*
   b. *Elucidation of mechanisms subverting drug efficacy on mycobacteria*

5. **Identification of vulnerable targets in the coenzyme A pathway**
   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. This project is built upon the methodologies developed in the MMRU under the auspices of the TB Drug Accelerator program funded by the Bill & Melinda Gates Foundation, as described in a major paper published in *Chemistry & Biology* in July 2012.

6. **Targeting pyrimidine metabolism for TB drug discovery**
   Novel insight into the mechanism of anti-tubercular action of 5-fluorouracil were obtained by the isolation, and subsequent genotypic and physiological analysis of mutants of *M. tuberculosis* that are resistant to this tool compound. These studies have revealed a potentially exploitable vulnerability in pyrimidine metabolism in *M. tuberculosis* which has significant implications for the discovery of novel anti-mycobacterial agents.

7. **Characterization of DNA repair pathways in mycobacteria**

   Background: *M. tuberculosis* possesses multiple pathways for DNA repair and the maintenance of genomic integrity under stress conditions encountered during infection. The possible role that these pathways play in the emergence of drug resistance have formed the basis of a large project at the Wits node, specifically aimed at further understanding the base excision repair pathways and roles of the Formamidopyrimidine DNA glycosylases (Fpg/MutM/Fapy). Furthermore, the MutY, Endonuclease VIII (Nei) and Endonuclease III (Nth) DNA repair enzymes have also been the subject of study at the Wits node

   Research Highlights: For the first time, researchers at the Wits node have confirmed the functionality of the mycobacterial Nth homologue through heterologous complementation studies. Moreover, we have now demonstrated that MutY plays a critical role in the control of genomic stability and modulation of mutation rates to rifampicin. Work presented from this project at the 2012 MRC Early Career Scientists Conference was awarded first prize in the MSc category.

THEME II: BASIC SCIENCE RESEARCH ON KEY PATHWAYS IMPORTANT FOR MYCOBACERIAL GROWTH AND THEIR ROLE IN THE CLINICAL MANIFESTATION OF TB DISEASE

The Wits node of the CBTBR takes a multipronged approach at addressing key questions relevant to the development of new interventions and modalities to address the TB problem in South Africa and globally. The research enterprise is divided into several main thematic areas where significant focus is placed on basic science research aimed at further understanding the physiology of *M. tuberculosis* during different disease states. A major focus of the Wits node is the characterization of cell wall remodeling enzymes and the role that these play in the complex manifestation of clinical TB disease which ranges from latent TB infection to chronic, active granulomatous disease. In this regard three groups of peptidoglycan (PG) degrading enzymes are being studied. Other projects include a study of the mycobacterial respiratory chain and characterization of the molybdopterin biosynthetic pathway, the latter being conducted as a three-way collaboration between all three nodes of the CBTBR. Further niche areas include a description of the bacterial metabolism and physiology during TB infection through the identification and characterization of dormant bacteria populations in the sputum of South African patients with active TB disease. The Wits node has also placed significant effort into the development of essential tools/reagents to be used for the search for new TB drugs and to aid the rollout of novel diagnostic tests for TB in South Africa, through the national TB control program. Further detail and some key highlights from all projects are given below.

1. **Identification and characterization of dormant bacterial populations in the sputum of patients with active TB disease**

   Background: This project is aimed at identification of resuscitation promoting factor-dependent (RPFd) organisms in the sputum of patients with active TB disease. These bacteria are non-culturable and hence

are not identified using routine culture. Moreover, they are phenotypically resistant to chemotherapeutic intervention and their presence in sputum may have significant consequences for disease treatment and transmission. The Wits node aims to identify these dormant bacteria through supplementation of sputum cultures with culture filtrate, from *M. tuberculosis*, containing resuscitation promoting factors (Rpfs) with the concomitant use of an Rpf deficient mutant as a negative control.

Research Highlights: During 2012, significant effort was placed on securing high quality sputum material for use in this study. All the relevant protocols and ethic clearance certificates were obtained. A sample flow from the clinical trial site at Chris Hani Baragwanath Hospital, in Soweto, to the Wits node of the CBTBR was established. Substantial effort was also placed in optimization of the methodology to reliably detect and quantify dormant organisms. Thereafter, 40 sputum samples were processed, approximately 30% of these were TB positive and RPFd bacteria were identified in numerous samples although, the proportion was variable between patients.

2. Characterization of resuscitation promoting factors in mycobacteria

Background: Rpfs have been previously implicated in growth stimulation of dormant bacteria and consequently have attracted significant interest due to the possible roles that they play in reactivation TB disease in those individuals harboring latent TB infection. The Wits node has been active for many years in further dissecting the role of these enzymes under various different laboratory conditions.

Research Highlights: During 2012, an in vitro model of mycobacterial dormancy was established at the Wits node through modification of published method. The model was then used to test a panel of mycobacterial mutants defective for various *rpf* genes and these experiments identified a critical role for Rpfs in the establishment of the dormant state in mycobacteria. Microfluidic growth experiments, conducted with a collaborator in Switzerland implied an important role for Rpfs in bacterial cell division and growth.

3. Characterization of *N*-Acetylmuramoyl-L-alanine amidases in mycobacteria

Background: *N*-Acetylmuramoyl-L-alanine amidases (amidases) are a group of PG degrading enzymes that are critical for bacterial cell division and as such represent a potential new source of TB drug targets. This project is aimed at characterizing the functions of these enzymes in bacterial growth.

Research Highlights: Characterization of the multiple amidase homologues in *Mycobacterium smegmatis*, a close relative of *M. tuberculosis*, through gene knockout/knockdown has identified a single, essential amidase (MSMEG_6935) which is could serve as a novel drug target and is currently being characterized further. Work presented from this project at the 2012 MRC Early Career Scientists Conference was awarded second prize in the MSc category.

4. Characterization of DD-Carboxypeptidases in mycobacteria

Background: DD-Carboxypeptidases (DD-CPases) play an important role in the expansion and cross-linking of the PG layer in bacterial cells and through their activity, they can modulate cell growth. Work at the Wits node entails characterization of these enzymes as potential drug targets and further study of their impact on dormancy and reactivation of bacterial growth in latent TB infection.

Research Highlights: There are five distinct DD-CPase encoding genes in *M. tuberculosis* and *M. smegmatis*. Work at the Wits node involving knockout/knockdown of these homologues has now identified a single essential gene, *dacB*, which is currently being studied.

5. Molybdopterin cofactor biosynthesis in mycobacteria

Backgrounds: Several enzymes involved in molybdopterin biosynthesis in *M. tuberculosis* have been shown to be essential for in vitro growth, under carbon limiting, nitrate replete conditions. This project aims to further characterize these biosynthetic enzymes and to further unravel the functional basis, in any, for the genetic redundancy that exits in this pathway.

Research Highlights: Previous work identified a novel, fused molybdopterin synthase in *M. tuberculosis*, encoded by MoaX. However, the functional consequences of this genetic fusion of the two components that make up this enzyme were unknown. A key research highlight for this project is our demonstration that MoaX gets cleaved into its two constituent components and that this cleavage occurs at a glycine which forms the substrate for a subsequent adenylation reaction.

6. Tuberculosis drug discovery: SAR studies on novel antituberculars

Background: This project falls under the auspices of the South African Tuberculosis Research and Innovative Initiative (SATRII) and involves all three nodes of the CBTBR. The research comprises in vitro screening of potential new antitubercular compounds and subsequent determination of mode of drug action. Chemistry support for the synthesis of small compounds is provided by chemistry groups at UCT and iThemba Pharmaceuticals

Research Highlights: Thus far, just over 500 compounds have been screened at the Wits node for in vitro bactericidal activity. Of these, 3 compounds with promising in vitro activity have been advanced to mode action studies.

7. Establishment of an external quality assurance assay for GeneXpert

Background: The GeneXpert is a novel nucleic acid amplification diagnostic platform that will allow for the detection of TB infection within a time frame of 2 hours and promises to make a significant impact on TB detection and control. The national rollout and uptake of this technology is dependent on the presence of a robust external quality assurance (EQA) program that allows for initial verification and subsequent continuous assessment of instruments in the field.

Research highlights: The Wits node of the CBTBR has played a pivotal role in the establishment of the EQA program through the provision of high-quality, killed mycobacteria for standardization of instruments in the field. A method was developed for the production of bulk scale, chemically killed pathogenic mycobacteria which are enumerated and then shipped to testing sites as dried cultures spots (DCS). Due to the effort of researchers at the Wits node, thousands DCS cards were created in 2012 and shipped to almost all sites with GeneXpert machines, rolled out through the National Health Laboratory Services. The uptake of this new diagnostic tool, at this scale, would not have been possible without the assistance provided by the Wits node of the CBTBR.

THEME III: BRIDGING THE GAP BETWEEN BASIC AND CLINICAL RESEARCH

The projects under this theme are often 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, including Mycobacteria/Helminth co-infections (h) surrogate markers for clinical trials (i) drug targets (j) EBA and other drug trials. The CBTBR operates two category 3 biosafety level labs for this work. This work also takes place within the MRC Centre for Molecular and Cellular Biology.
The African Region has approximately one quarter of the world's cases, and the highest rates of cases and deaths relative to population. Southern Africa is the epicentre of the dual human immunodeficiency (HIV) and TB epidemic with high rates of drug-resistance in some communities. In South Africa, the TB epidemic has reached alarming proportions with an estimated incidence of 500,000 cases diagnosed each year. Of these, approximately 330,000 cases are estimated to be co-infected with HIV leading to an over mortality of >100,000 cases per year. Drug resistance continues to emerge as a serious factor threatening the success of the National TB Control Programme. In 2011, the number of laboratory-confirmed MDR-TB cases increased to 10,085, of which only 5,643 cases were started on treatment. Retaining patients on treatment is challenging especially if treatment may be of the order of 24 months (MDR-TB treatment) leading to high default rates which implies that treatment success is only of the order of 40%. This drops to a dismal 20% in the cases with XDR-TB. More recently, Totally drug resistant (TDR)-TB has been reported in the Eastern Cape where genotypic and phenotypic drug susceptibility testing has demonstrated resistance to at least 10 available anti-TB drugs making this form of the disease almost untreatable. This is supported by the fact that only 8.5% of cases showed culture conversion after 0.5 years of treatment, while mortality was 58% in the first year of treatment.

DRUG RESISTANT TUBERCULOSIS

1. The evolution of second-line drug resistance in *Mycobacterium tuberculosis*

This study aims to describe the proteomic changes associated with the emergence of resistance to amikacin and ofloxacin in *Mycobacterium tuberculosis* with the view to determine how these may alter bacterial physiology.

2. **Factors influencing MDR treatment default in a rural setting**
   This study aims to identify factors which influence treatment adherence in patients discharged from a MDR-TB hospital using a multivariate analysis.

3. **Emergence and spread of XDR-TB and TDR-TB in South Africa**
   This study describes the molecular epidemiology of M(X)DR-TB in the Eastern Cape province of South Africa and has shown clonal spread of a highly resistant strain which contains markers to suggest resistance to all available anti-TB drugs.

4. **Molecular epidemiology of XDR-TB in Western Cape, South Africa**
   This study describes the molecular epidemiology of M(X)DR-TB in the Western Cape province of South Africa during the period 2007 to 2011. Analysis of this data suggests that the current treatment regimen and management of MDR patients are inadequate to prevent amplification of resistance.

5. **Evolution of MDR in isoniazid mono-resistant cases**
   This study aims to investigate the outcome of isoniazid mono-resistant TB in a setting where the diagnostic algorithm is based only on the detection of rifampicin resistance.

6. **The emergence of fluoroquinolone resistance during treatment of MDR-TB.**
   This retrospective folder review aims to identify risk factors associated with the emergence of ofloxacin resistance.

7. **Treatment response in patients diagnosed with XDR-TB in the Eastern Cape, South Africa**
   This study aims to describe treatment outcomes in patients infected with highly resistant atypical Beijing genotype strains.

8. **Effect of rifampicin on the MICs of first and second line anti-TB drugs in rifampicin resistant *Mycobacterium tuberculosis* isolates**
   This study aims to determine whether inappropriate treatment of rifampicin resistant TB stimulates tolerance towards other anti-TB drugs.

9. **Selective use of rifabutin in the treatment of MDR and XDR Tuberculosis**
   This study aims to demonstrate that rifabutin may be used as an effective drug for the treatment of M(X)DR-TB with the characteristic *rpoB*516 mutation. Thereby improving treatment outcome.

10. **Resistance profiling in therapeutically destitute patients with XDR-TB**
    This study aims to describe the level of resistance to all anti-TB drugs used in South Africa in order to identify alternative therapeutic options.

11. **Targeted sequencing of drug resistant *Mycobacterium tuberculosis* isolates**
    This study aims to capture all drug resistant isolates from the Western Cape with the view to describe their epidemiology.

12. **The influence of rifampicin heteroresistance on the performance of molecular based drug resistance diagnostics**
    This study aims to determine the sensitivity of molecular based diagnostics for the detection of underlying rifampicin resistance.

13. **Geospatial mapping of drug susceptible and drug resistant tuberculosis as a tool to guide TB control**
    This study aims to develop statistical models to describe the spatial distribution of TB cases over time with the view to inform TB control.

14. **Development of an electronic record system in a rural Tuberculosis hospital in South Africa**
The study has developed an electronic database for the capture of clinical information on MDR-TB cases and will be expanded to include drug susceptible TB for adults and paediatrics.

***MYCOBACTERIUM TUBERCULOSIS* DIAGNOSTICS**

1. **Sensititre for the rapid determination of *Mycobacterium tuberculosis* Minimum Inhibitory Concentrations**
This study has tested the performance of the sensititre plate in relation to MGIT based MIC determination and targeted DNA sequencing.

2. **Optimising the impact of Xpert MTB/RIF on treatment outcomes of drug resistant Tuberculosis**
This study aims to determine whether the implementation of the Xpert MTB/RIF test will prevent the amplification of resistance.

3. **Evaluation and validation of a highly informative LATE-PCR single tube assay for M(X)DR-TB**
This study aims to develop a simple genetic based test for the detection of *M. tuberculosis* and resistance to five anti-TB drugs.

4. **Evaluation of Line-probe assays for the detection of first and second line drug resistance in *Mycobacterium tuberculosis***
This study has demonstrated that the MTBDRplus assay is as sensitive as the Xpert assay for the detection of *M. tuberculosis* and rifampicin resistance. This test will complement the Xpert assay and will provide additional information on isoniazid resistance. The diagnostic performance of the MTBDRsl assay allowed for the accurate detection of fluoroquinolone and aminoglycoside resistance. In addition this assay reduced the time to diagnosis by more than 40 days thereby improving treatment outcome and preventing amplification of resistance.

5. **Rapid genetic detection of pyrazinamide susceptibility: an essential eligibility criterion for entry into clinical trials**
This study aims to develop a rapid molecular screening process for the identification of mutations in the pncA gene conferring resistance to pyrazinamide.

6. **Rapid diagnosis of tuberculosis lymphadenitis using Xpert MTB/RIF assay**
This study aims to develop guidelines for the diagnosis of TB lymphadenitis using the Xpert MTB/RIF assay.

7. **Molecular detection of transrenal DNA as a diagnostic for *Mycobacterium tuberculosis* disease**
This study aims to develop a novel PCR method for the detection of small fragments of DNA as molecular diagnostic for TB.

8. **Identification of laboratory based diagnostic delay in a high through put routine diagnostic laboratory**
This study aims to retrospectively review diagnostic records to identify processes which influence the time to issuing of a diagnosis.

9. **Identification of novel pathways leading to isoniazid resistance**
This study aims to use whole genome sequencing analysis of *M. tuberculosis* strains lacking classical isoniazid resistance conferring mutations with the view to identify novel mechanisms of isoniazid resistance. This information will be used to improve the sensitivity of current molecular based tests.

10. **Mycobacteriophages as novel diagnostics for *Mycobacterium tuberculosis***
This study aims to engineer mycobacteriophages as tools for rapid diagnostics.

MYCOBACTERIAL PHYSIOLOGY

1. **Investigating the localisation of the ESX-3 secretion system in *M. smegmatis***

This study aims to determine the localisation of the ecc fusion proteins in wild type *M. smegmatis* and in the *M. smegmatis* ESX-3 knock-out strain. This information will provide novel insight into the position of secretion systems in the cell wall of *M. tuberculosis*.

2. **Nucleoid gene regulation in *Mycobacterium tuberculosis***
   This study aims to develop the methodology to identify all DNA binding proteins with the view to understanding their regulatory role in gene expression.

3. **Structural and Functional Analysis of Mycosin-3, an essential subtilisin-like serine protease in *Mycobacterium tuberculosis***
   This study aims to determine structure and function of Mycosin-3 and to determine its role in bac*terial pathogenesis.*

4. ***Ident*ification of sensory mechanisms involved in drug tolerance**
   This study aims to use transposon mutagenesis to identify genes involved in the induction of drug resistance after exposure to rifampicin.

5. **Regulation of efflux in rifampicin resistant mutants of *Mycobacterium tuberculosis***
   This study aims to describe the promoter function regulating Rv1258c.

6. **The effect of SQ109 on efflux in *Mycobacterium smegmatis***
   This study aims to identify genes involved in SQ109 resistance

7. **The function of mycobacterial esx secretion systems and their substrates**
   This study aims to determine the functional role of esx3 in the acquisition of iron.

8. **Energy metabolism and its role in drug resistance**
   This study aims to demonstrate how ATP production provides energy for efflux systems.

9. **Factors influencing mutation rate in *Mycobacterium tuberculosis***
   This study aims to determine whether antiretroviral drugs influence the mutation rate in *M. tuberculosis* and thereby the emergence of drug resistance.

10. **PPE esterase activity**
    This study aims to close and characterize the esterase activity of three different PPE genes.

11. **Characterization of host pathogen interactions using Yeast2hybrid systems**
    This study aims to identify host-proteins which interact with esx6 with the view to determine how the secretion of esx may reprogram the human macrophage.

12. **Does reinfection induce reactivation?**
    This study aims to use the murine infection model to determine whether reinfection can induce reactivation of a latent infection.

13. **Compensatory mutations involved in restoring fitness in drug resistant isolates**
    This study aimed to identify whether compensatory *rpoC* mutations were associated with the transmission of rifampicin resistant *M. tuberculosis*.

MYCOBACTOMICS

1. **Development of bioinformatic algorithms for the analysis of whole genome sequencing data**
   This study aimed to combine a suite of algorithms to optimally predict single nucleotide polymorphisms, insertions and deletions.

2. **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***

This study aimed to describe the evolutionary history of the LAM genotype both at the level of phylogenetics, as well as phyloproteomics.

3. **Deciphering the Meerkat bacillus genome**
   This study aims to described the genomic structure of the uniquely identified meerkat bacillus with the view to identify the genetic basis of host pathogen compatibility

4. **Reconstructing the evolutionary history of *Mycobacterium bovis* in South Africa**
   This study aims to compare the genome sequences of *M. bovis* isolates cultured from different sites in South Africa in order to determine the phylogeny and spread of *M. bovis* strains in South Africa

5. **The genetics of treatment failure**
   This study aims to use whole genome sequencing in conjunction with comprehensive clinical data to identify the mechanisms leading to treatment failure.

6. **Genetic mechanisms underlying phenotypic heterogeneity in drug resistant clinical isolates**
   This study aims to use whole genome sequencing to identify the genetic basis of phenotypic heterogeneity in clinical isolates of rifampicin resistant tuberculosis.

7. **Genetic heterogeneity at the site of disease in XDR-TB cases**
   This study aims to culture and sequence *M. tuberculosis* clones from different sites within the granuloma from lung resections.

8. **Transcriptomic response to rifampicin in rifampicin resistant *Mycobacterium tuberculosis* isolates**
   This study aims to establish the analysis pipelines for transcriptomic data with the view to determine how rifampicin impacts on gene expression.

9. **Effect of *rpoB* mutations on gene expression in *Mycobacterium tuberculosis***
   This study aims to determine whether different mutations in *rpoB* influence gene expression, thereby explaining the prevalence of these mutations in drug resistant TB.

10. **Transcriptomic adaptation in response to the evolution of TDR-TB**
    This study aims to determine how the accumulation of different resistance conferring mutations influences gene expression in closely related clinical isolates.

11. **Genomic and phyloproteome analysis of Principle Genetic Group 1 *Mycobacterium tuberculosis* strains**
    This study aims to use the combination of whole genome sequence data and proteomic data to describe the evolution of Principle Genetic Group 1 strains.

12. **The role of IS*6110* in shaping mycobacterial physiology**
    This study aims to identify the position of IS*6110* insertions in the genomes of different *M. tuberculosis* isolates and to identify domains deleted through homologous recombination between adjacent elements.

13. **Whole genome sequencing as a tool to identify PAS resistance**
    This comparative study aims to identify novel genetic mechanisms of PAS resistance.

14. **Proteomic analysis of some of the *Mycobacterium tuberculosis* complex members**
    This study aims to characterize the proteomes of *M. bovis*, *M. orygis*, *M. caprae, M. pinnipedii* and the meerkat bacillus. This study aims to identify proteins involved in host pathogen compatibility.

15. **Comparative label-free quantitative mass spectrometry analysis**
    This study aims to determine:
    a. Proteome and Phosphoproteome of closely related hypo and hyper-virulent *M. tuberculosis* clinical isolates
    b. Proteome of Rifampicin-mono-resistant *M. tuberculosis* isolate and its wild type progenitor

c. Proteome of clinical multi-drug resistant isolate in the before and after exposure to rifampicin during mid-log growth
d. Identification of *M. tuberculosis* surface antigens in strains representative of the major lineages of the global phylogeny.

16. **Annotation and functional analysis of hypothetical proteins in *Mycobacterium tuberculosis***
This study aims to determine the function of hypothetical proteins with the view to address this knowledge gap.

MOLECULAR IMMUNOLOGY: IMMUNE RESPONSES IN TB, HIV and WORM INFECTIONS

1. **Co-infection with *Nippostrongylus brasiliensis* and BCG or *M. tuberculosis***
It was found that *N. brasiliensis* infection, followed 5 days later by BCG infection leads to decreased BCG growth in the lungs of co-infected mice compared to mice with BCG infection alone. This effect is not seen with Nippostrongylus MTB co-infection. Work completed- 1 manuscript published (du Plessis et al, 2012) Acute helminth infection enhances early macrophage mediated control of mycobacterial infection.

2. **Biomarkers of protective immunity and surrogate markers of TB disease in Africa - Gates Grand Challenge project 6-74.**
The aim of this project is to find biomarkers for protective immune responses against TB by longitudinal follow-up of household contacts of TB patients and by comparing responses in progressors to active disease with those in non-progressors. The study was completed in Dec 2012.

Database design
Prof Gian van der Spuy has designed and created a unified database for the consortium using a Microsoft Access interface and stores the data in a MySQL back-end. The database was locked in December 2012.

Specific sub-studies in the GC6-74 project:
Diagnostic pilot study: a direct comparison between different tests for latent TB infection was conducted as such comparisons have been lacking in high TB prevalence areas. This work has been completed.

Contribution to host gene expression profiling: We have recruited more than 120 participants with well defined TB infection and disease status. Data from the study were published in Clin Microbiol Infect. (see publication 19).

Screening new TB antigens: 86 antigens (85 obtained from Leiden University and one from MPIIB) were screened in 61 participants for their ability to induce IFN-γ production in the whole blood assay. This work has been completed and published- Potential of novel Mycobacterium tuberculosis infection phase-dependent antigens in the diagnosis of TB disease in a high burden setting. Chegou NN, Black GF, Loxton AG, Stanley K, Essone PN, Klein MR, Parida SK, Kaufmann SH, Doherty TM, Friggen AH, Franken KL, Ottenhoff TH, Walzl G. BMC Infect Dis. 2012 Jan 20;12:10. doi: 10.1186/1471-2334-12-10

3. **Identification of biomarkers that is able to predict tuberculosis treatment response**
Host or bacterial surrogate markers for successful TB treatment outcome in pulmonary TB patients are urgently needed to aid clinical trials of new TB drugs. The analysis of this work is on-going and a manuscript is in prep (Ronacher et al)
A second study in Collaboration with the Catalysis Foundation for Health assesses the utility of FACS^{TM} CAP technology (assessment of >200 cell surface markers on PBMCs) in TB treatment response biomarker discovery. This study is ongoing.

4. **Diagnosis of latent TB infection in adults and children**
We are performing the laboratory component of several studies that focus on diagnostic aspects of latent TB infection with the use of the new interferon gamma release assays (IGRA's), namely the Quantiferon TB (QFT) and T Spot TB assays. All the IGRA studies have been completed and 2 manuscripts published - Detecting Tuberculosis Infection in HIV-Infected Children: A Study of Diagnostic Accuracy, Confounding

and Interaction and Well-quantified tuberculosis exposure is a reliable surrogate measure of tuberculosis infection.

Cellestis Formulation study 2- study to improve the diagnostic ability of the available Quantiferon test- study completed and results are being analysed by Cellestis (Qiagen).

Evaluation of the dual-colour ELISPOT assay for discrimination between latent and active TB disease: In collaboration with Borstel Research Centre and a private company Autoimmun Diagnostika GmbH we are evaluating the potential of cells producing Interferon-gamma and Interleukin-2 simultaneously to distinguish between the latent and active form of TB disease. This study is completed and a manuscript for submission has been prepared (Ndong et al)

Systems Biology Approach to the Mechanisms of TB Latency and Reactivation. This study combines access to unique clinical specimens (peripheral blood cells, plasma, broncho-alveolar lavage specimens) from epidemiologically well characterized persons with MTB infection in US, Uganda and South Africa with experts in the use of proteomics, genetic epidemiology and cytokine biology for a multidisciplinary systems biology approach to LTBI and its progression to active TB.

5. **The evaluation of *Mycobacterium tuberculosis* specific host cytokine signatures in whole blood culture supernatants as diagnostic biomarkers for active TB infection**
   An EDTP-funded grant was awarded to the SUN-IRG to establish a consortium of 7 African institutions in 6 African countries plus 5 institutions in 4 European countries to find host markers for active TB lead by Gerhard Walzl. This study is ongoing and has produced scientific papers already. (e.g. Chegou et al, 2012).

6. **TB Vaccine studies and vaccine-site preparation studies**
   We have conducted a Phase IIb TB vaccine immunogenicity study (48 newborns) with the German vaccine developer Vakzine Projekt Management (VPM) and Prof Mark Cotton of KIDCru. This study was successfully completed and data analyses are currently underway.
   We have an ongoing EDCTP funded study with Dr Alexander Pym as PI to build capacity development in the field of clinical trials in Africa ~ Trial of excellence for Southern Africa (TESA)

7. **Immune Endocrine Interactions during TB**
   We have previously shown in humans and in a mouse model that contraceptive hormones affect anti-mycobacterial immune responses and TB disease severity (Kleynhans et al 2011 PlosOne, Manuscript submitted to Infection and Immunity 2012). Due to the close link between the immune and the endocrine system we have now initiated a study to assess whether endogenous hormones can serve as markers of TB treatment response or TB disease severity. We are also trying to elucidate the underlying molecular mechanisms of the immune endocrine interactions during TB.

HOST GENETICS (BIOINFORMATICS AND GENOME WIDE AND CANDIDATE GENE STUDIES)

1. **A biostatistical investigation of gene-gene interactions associated with the host genetics of Mycobacterium tuberculosis**
   The role of epistasis in susceptibility to tuberculosis infection is studied in 950 samples genotyped using the Affymetrix 500 000 SNP chip, using data mining and machine learning methods, including multifactor-dimensionality reduction (MDR), random forests and neural networks.

2. **A panel of ancestry informative markers for the complex five-way admixed South African Coloured population**
   The minimum number of AIMS to distinguish the 5 ancestral populations of the SAC will be developed to assist genetic association studies and other investigations on this population.

3. **Ancestral components of a South African multi admixed Population determined by a novel Proxy Ancestry Selection Method**

A new algorithm, PROXYANC, is being applied to the SAC data on nearly 1000 individuals to accurately determine the ancestral components of the population. The LD in the population appears to result from admixture rather than population bottlenecks.

4. **Genetic studies on susceptibility to pulmonary tuberculosis mediated by MARCO, SP-D and CD14: molecules affecting uptake of *M.tuberculosis* into macrophages**
   Eleven SNPs in these three genes are being investigated and the results analysed for association to disease, linkage disequilibrium, haplotypes and gene-gene interactions. The role of a promoter SNP in CD14 is assessed in gene-expression analysis was conducted with qPCR and a reporter gene assay

5. **Associations between human HLA class-I variants and the *Mycobacterium tuberculosis* subtypes causing infection**
   Host-pathogen co-evolution – the idea that the human host and the pathogen have genetically adapted to each other due to long term interactions – is emerging as an important factor in influencing disease outcome. Evidence for this can be seen from studies which have shown the adaptation of M. tuberculosis strains to specific human populations, even in cosmopolitan settings. In our study we aim to identify the human genetic factors that could play a role in this co-evolution process.

6. **The role of Killer Cell Immunoglobulin-like Receptors and the Human Leukocyte Antigen class-I Receptors in Susceptibility to TB**
   The KIRs and HLA class-I molecules have been shown to play a vital role in the immune response to infectious diseases. We investigate the role of the 16 KIR genes and their HLA class-I ligands as susceptibility factors for susceptibility to TB.

7. **HLA class-I allelic diversity in South African populations**
   HLA data for various populations demonstrates significant differences in allele frequencies between different geographical populations, with some alleles completely absent from certain populations. Given the importance of the HLA genes in various biological processes, in the case of vaccine efficacy, identifying the allelic repertoire could allow us to design vaccines better suited to specific populations**.**

8. **Polymorphisms in Toll-like receptor genes alter susceptibility to TB**
   The Toll-like receptors are involved in the recognition of conserved microbial structures, which results in the activation of an inflammatory response and formation of an adaptive immune response. The various Toll-like receptor genes are involved in the recognition of different pathogens (TLR1/2 – triacylated lipopeptides, TLR2 – PAMPs, TLR4 – LPS, TLR8 – ssRNA and TLR9 – unmethylated CpG rich bacterial DNA), thus making these genes suitable candidates for disease susceptibility studies.

9. **Genome-wide association study of ancestry-specific TB risk in the South African Coloured population**
   Admixture mapping is suitable for less complex admixed populations than the SAC, and we are combining a GWAS approach with the determination of ancestry-specific risk. Confounding due to socioeconomic status has been excluded.

VETERINARY TUBERCULOSIS

1. **Novel SNP Discovery in African Buffalo, Syncerus caffer, Using High-Throughput Sequencing**
   We have identified approximately 6.5 million novel SNPs in the African buffalo genome. Bta4 (*Bos taurus*) gene annotation was added to the nearly two million SNPs identified within whole gene regions. Selected SNPs were subject to validation and fluorescent genotyping in approximately 900 African buffalo samples

2. **Gene polymorphisms in African buffalo associated with susceptibility to bovine tuberculosis infection**
   SNPs identified as above in genes or pathways of interest were tested for association with skintest positive status in 900 buffalo and three polymorphisms in previously unreported genes were found to be implicated.

3. **Prevalence & incidence changes in bovine TB in African buffalo in Hluhluwe iMfolozi Park**

An epidemiological dataset collected over a seven year period is being collated and analysed to identify changes due to the test and cull BTB programme.

PHARMACOKINETICS

1. **Isoniazid Pharmacokinetics in low-birth weight South African infants in the era of HIV**.

2. **Pharmacokinetics of twice daily vs once daily dosing with granular slow-release para-aminosalicylic acid in adults on second-line anti-tuberculosis and antiretroviral treatment**

3. **Pharmacokinetics and Toxicity of second line anti-tuberculosis drugs in HIV infected and uninfected children**

4. **Investigating the effects of nucleotide variation on the structure and function of human NAT1**

TARGETS AND NEW DRUG DEVELOPMENT

1. **Nitrogen metabolic pathway in the *Mycobacteria***
   The study focuses on nitrogen metabolism in mycobacteria in order to better understand how nitrogen metabolism may be regulated in disease-causing mycobacteria.

2. **Elucidation of mode of action of a furanone based antituberculosis compound**
   F1082 is a furanone based compound with specificity towards M.tuberculosis and works synergistically with rifampicin against M.tuberculosis. Mechanisms of action are investigated.

3. **Investigation of the synergistic effect of Sulfamethoxazole and Trimethoprim in combination with first-line TB drugs**
   Sulfamethoxazole and Trimethoprim (BACTRIM), as individual drugs as well as in combination with each other and first-line TB drugs against Mycobacterium tuberculosis showed synergism with Rifampicin. Proteomics and animal model studies ongoing.

4. **Eliminating *M.bovis* from raw milk with Kefir fermentation**
   Effective assay methods for M.bovis in raw milk are developed along with methods to effectively eliminate M.bovis through various fermentation methods.

5. **Differential inhibition of adenylylated and deadenylylated *Mycobacterium tuberculosis* glutamine synthetase by ATP scaffold-based inhibitors**
   Glutamine Synthetase comes in an adenylylated (extracellular) and deadenylylated (intracellular) form in M.tuberculosis. Drugs are designed to target the adenylylated form which is fatal for *M.tb*.

6. **Synergism between para-amino salycilate (PAS) and pyrazinamide (PZA) against M.tb**.
   PAS and PZA are both only effective in an acidic environment. Synergism between these drugs against *M.tb* show border levels of synergism.

7. **Bactrim resistance in HIV/TB patients**
   To evaluate BACTRIM in combination with rifampicin, *M.tb* strains from HIV/TB and TB patients are evaluated for Sulfamethoxazole resistance/sensitivity in a project with Desmond Tutu Centre

8. **Drugs designed against mycothiol and ergothioneine pathway enzymes**
   Mycothiol (MSH) and Ergothioneine (EGT) is a major low molecular weight cellular thiol responsible for protection of bacteria against oxidative stress. The design of drugs and inhibitors against enzymes of the MSH and EGT pathways are based on the fact that they are synthesised by mycobacteria but not eukaryotes, and may be important for its survival. We will evaluate the role and association of MSH and EGT in the survival of mycobacteria in macrophages.

ANTIMYCOBACTERIAL CLINICAL TRIALS

1. EBA studies

We have noted a constant increase in demand for sites able to perform clinical trials at a quality adequate for registration of novel anti tuberculosis drugs and regimens. Requirements of Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) must be met. All documentation needs to be complete and ready for inspection by national and international regulatory authorities. A recent survey conducted by the CDC suggested that more frequent inspections are on the cards. Only few centres globally can currently fulfil those requirements. 2011 has seen more drug trials conducted than ever before in our centre. At the level of EBA studies (2 weeks study duration, Phase IIA), we have tested the nitroimidazole derivative PA-824 in various dosages. For the first time we were evaluating combinations in EBA studies (TMC207, PZA, PA-824, and Moxifloxacin) and have completed the clinical evaluation of SQ-109 as well as PNU-100480. We participated in a phase IIB study (8-week duration) of Rifapentine versus Rifampicin added to HZE in the first 2 months of treatment in adults with pulmonary TB (Study 29). A large Phase III trial (full treatment duration REMoxTB) was initiated at the centre in 2007 to investigate if tuberculosis treatment duration can be shortened from 6 to 4 months by incorporating Moxifloxacin into the regimen. More than 10,000 samples have been processed for this ongoing study so far. MDR and XDR tuberculosis trials have seen the completion of recruitment of two trials with TMC207 for which follow-up is ongoing.

DATA MANAGEMENT

1. Due the extensive data requirements of the SU node of the CBTBR, we have chosen to manage our own information technology systems. We currently have in excess of 110 computers in the centre, including 5 Linux-based servers which supply the infrastructure requirements of staff and students involved in our many projects. All these systems are developed and maintained in-house by Prof G van der Spuy. Amongst the various services provided by the server platforms are three key components.