

VIROLOGY

MATTERS

DECEMBER 2016

Special
points of in-
terest:

- W Burgers As-
sociate Profes-
sor
- A Khan: MMed
with distinction
- S. Ismail re-
ceived her MSc
with distinction

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Associate Professor

Congratulations to Wendy Burgers who was promoted to Associate Professor.

A/Professor Wendy Burgers is a UCT graduate, with a PhD from Cambridge. Following a post-doc in the Division of Medical Virology, she was awarded a European and Developing Country Clinical Trials P (EDCTP) fellowship (2009), and a Wellcome Trust Intermediate Fellowship (2011). In 2015 she was employed as a senior lecturer in the Division of Medical Virology. Wendy has strong track record in teaching, in particular in training post-graduate students. She was recognised for her publications in high impact journals, ability to raise significant funding from highly competitive sources, and has been an organiser and invited speaker at international conferences. She is a committed member of staff contributing to the University, community and public service.



PhD Graduate

Rubina Bunjun



Thesis Title:

The effect of HIV co-infection on the T cell response to Mycobacterium tuberculosis

Supervisor: Wendy Burgers

Co-Supervisor: Catherine Riou

The HIV and TB co-epidemic is a major public health crisis and an effective TB vaccine is urgently needed. However, robust immune correlates of protection against TB remain undefined, which severely hampers the development and assessment of new vaccines. It is well established that HIV-infected individuals are more susceptible to developing TB. This thesis focuses on mucosal (lung) and systemic immunity to mycobacteria in latent TB infection (LTBI) that may be compromised during HIV infection.

The effect of HIV on immunity at the site of infection, the airways, is not well studied. Bronchoscopy and bronchoalveolar lavage (BAL) was performed and the cellular components, soluble cytokine milieu and viral burden from the airways were characterised. HIV was detected in BAL fluid at similar concentrations as plasma. HIV-infected individuals had signifi-

cantly higher numbers of BAL CD4+ and CD8+ cells compared to HIV-uninfected individuals, which correlated with viral load in BAL. This higher number of BAL T cells in HIV infection was related to both viral load and concentrations of specific chemokines in BAL. The cytokine profile of blood plasma and BAL differed considerably, and HIV infection significantly altered the concentration of several cytokines in BAL and plasma. Taken together, these findings provide evidence for a perturbed lung immune environment during HIV infection.

CD4+ Th1 responses are central to protective immunity to TB. We characterised adaptive immunity to M.tb antigens in BAL and blood, examining CD4 IFN- γ , TNF- α and IL-2 responses. HIV-infected individuals had significantly lower frequencies and absolute numbers of PPD-specific Th1 responses in peripheral blood, despite well preserved CD4 counts. In the lung, a similar decrease in the frequency of PPD-specific CD4 cells was observed in HIV-infected individuals compared to HIV-uninfected individuals. However, in contrast to our findings in blood, there was a normalisation of the absolute number of M.tb-specific CD4+ T cells in BAL of HIV-infected individuals, driven by the infiltration of lympho-

cytes into the airways during HIV infection. Furthermore, our data provide evidence for the compartmentalisation of M.tb-specific CD4+ responses. Thus, despite well-preserved CD4 counts, quantitative rather than qualitative changes in M.tb responses were evident during HIV infection.

Given the evidence of Th1-independent mechanisms contributing to protection against TB, we extended our analysis of systemic mycobacterial immunity to examining Th17 cytokines (IL-17 and IL-22) in response to mycobacterial antigens in LTBI and HIV co-infection. IL-17 and IL-22 are mucosal-acting cytokines, responsible for maintaining epithelial barrier integrity. We found a distinct CD4+ T helper lineage producing IL-22 in the absence of IL-17 and other cytokines that was present at high frequencies in response to M.tb antigens in blood. Moreover, these cells contributed up to 50% to the overall CD4+ T cell response to mycobacteria, equal in magnitude to the Th1 response. Strikingly, we found that mycobacterial Th22 responses were significantly lower in HIV-infected individuals compared to HIV-uninfected individuals. This data suggest a potential role for IL-22 in protection against TB during HIV infection,

MSc Graduate

Sherazaan Ismail



Thesis Title:

Characterisation of HIV-1 Envelope features of breakthrough infections from the CAPRISA 004 Microbicide Trial

Supervisor: Carolyn Williamson

Co-Supervisor: Philippe Selhorst

The CAPRISA 004 trial demonstrated the safety and a 39% efficacy of a 1% tenofovir (TFV) gel for the prevention of HIV-1 acquisition in young African women. It was subsequently shown that women assigned to the TFV arm who became infected had higher viral loads, slower anti-HIV-1 antibody avidity maturation, and higher Gag-specific IFN- γ + CD4+ T cell responses; although replication capacity, as measured by Gag-Pro recombinant viruses, did not differ between arms. We thus aimed to investigate if there were differences in Envelope function, or TFV susceptibility, which may be selected for during transmission in those who became infected despite being assigned to the TFV arm.

Viruses from 39 out of 48 recently HIV-1 infected individuals from the trial (matched on time post-infection and the presence of protective HLAs) were isolated. Isolate *env* genes were sequenced using a single genome amplification approach and were compared to plasma sequences from the same time-point. To evaluate phenotypic characteristics of *env*, inhibition assays were performed using the following inhibitors: tenofovir, maraviroc, T20, PSC-RANTES and anti-CD4 antibody clone SK3. In addition, *envs* for 19 participants were cloned and used to generate pseudoviruses which were evaluated for entry efficiency.

Viral isolates were identical or very similar to viruses in circulation *in vivo*; however had a lower diversity, indicating that they were representative of *in vivo* virus but did not reflect the entire quasispecies in plasma. The TFV arm viruses were not more resistant to TFV than those in the placebo arm. A comparison of variable loop characteristics, distance to a consensus representative of viruses circulating in the region, and sensitivity to inhibitors or entry efficiencies of

the viruses, also found no difference in genotypic nor phenotypic properties between study arms. When assessing the impact of viral phenotype on markers of disease progression, it was found that sensitivity to inhibitors did not contribute to VL or CD4+ count in this cohort. To evaluate envelope in isolation of the rest of the genome, pseudoviruses were generated from 11 participants. We found that PSV entry efficiency did not correlate with VL at isolation, 3 months post-infection and set-point, or with CD4+ counts at set-point. However, pseudovirus inhibitor sensitivities were significantly different to those of isolates for the inhibitors T20, anti-CD4 antibody SK3 and PSC-RANTES.

Overall, the isolate *env* genotypic and phenotypic characteristics investigated in this study did not differ between trial arms. Interestingly, pseudoviruses showed significant differences in their sensitivity to entry inhibitors when compared to their corresponding isolate, highlighting the importance of caution when interpreting data from *in vitro* studies, and motivates for further evaluation of *in vitro* models.

PhD Graduate

Shivan Chetty



Supervisor:
Prof AL Williamson
Co-supervisors:
Dr R Chapman

The development of novel HIV-1 vaccines using modified recombinant BCG

MMed with distinction

Congratulations to **Aabida Khan** who received her MMed with distinction



Postgraduate Students

Lyle Curry



I did my undergrad, Honours and MSc in Molecular Cell Biology working with Prof Nicola Illing at Upper Campus until 2013.

In 2014 I enrolled in the MPhil program for Biomedical Forensic Science at UCT here at Medical Campus where I learnt forensic techniques in toxicology, pathology, genetics and basic anatomy and anthropology. My MPhil dissertation was to evaluate the presumptive test for semen found at crime scenes.

I joined Jo-Ann Passmore's group in 2016 doing a project in collaboration with the Division of Forensic Medicine and Toxicology, with Laura Heathfield as my co-supervisor. The study will look the effects of sexual violence on the immunity in the female genital tract, particularly looking at immune activation and protein biomarkers of inflammation which could lead to increased HIV susceptibility. We will also look at the prevalence of HPV and genital wound in victims of sexual violence.

Sherazaan Ismail



I'm originally from Pretoria but have been living in Cape Town for almost 10 years. I first moved here to pursue my undergrad degree in Molecular and Cell Biology in the Science faculty at UCT. Thereafter, I moved to the Faculty of Health Sciences and completed my BSc Honours and MSc degrees under the supervision of Carolyn Williamson. I am now in my first year of PhD under the joint supervision of Carolyn, and Wendy Burgers. My project forms part of the HIV Cure project and I will be looking at how immune activation influences the latent reservoir of HIV.

Aside from academics I love running, reading, spending time with friends, sunny days on the beach, and rainy days indoors watching movies or reading a good book.

Phindile Ximba



is doing a PhD entitled Recombinant Expression and Characterisation of ZERA-induced HIV-1 envelope Protein Bodies.

Supervisors:
Anna-Lise Williamson; Ros Chapman and Ed Rybicki

Postgraduate Students

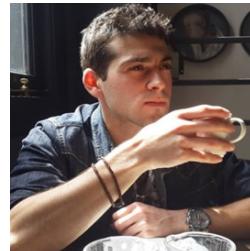
Deelan Doolabh



I was born in Zimbabwe where I grew up and completed both my primary and secondary schooling. I subsequently moved to Cape Town in 2012 for my tertiary education. I attained my BSc in Genetics and Microbiology in 2014. I then moved to the Faculty of Health Sciences and completed my BSc Med Honours in Infectious Diseases and Immunology in 2015. This was in fact my induction into the Division of Medical Virology where I joined the HIV Diversity group. I am currently in my second year of my MSc working on the influence of the genotype of the HIV-1 long terminal repeat on the ability of the virus to establish latency within CD4+ T cells.

Outside of the world of virology I am a pianist and enjoy music in all forms. I am also an avid moviegoer, foodie and enjoy exploring nature.

Emmanuel Margolin



Has registered for a PhD:

Title: Development of an agrobacterium tumefaciens-mediated transient expression platform for the production of soluble HIV-1 subtype C envelope mimetics in plants

Supervisors: Ros Chapman, Ann Meyers, Anna-lise Williamson, Ed Rybicki

Michiel van Diepen



is doing a PhD entitled Generation and characterization of HIV-1 subtype C candidate vaccines that will induce high titre antibody responses to HIV-1 envelope glycoprotein

Supervisor: Anna-Lise Williamson.

Farewell

Andile Nofemela



Andile did his PhD in Virology. He unexpectedly passed away in July.

Nyameka Mhlonyelwa-Mona



After 6 years as the divisional secretary Nyameka resigned to take up a private venture.

We wish her luck and thanks for all she did for the division.



Awards

Harris Onywera

My six-month fellowship under the **CRG–Novartis–Africa Mobility Programme** allowed me to conduct my doctoral research (on genital microbiome, HPV, and HIV) at the Center for Genomic Regulation (CRG) in Barcelona, Spain. I was supervised by Dr. Julia Ponomarenko of the Bioinformatics Core Facility.



During my stint at the institute, I participated in a conference and a number of bioinformatics and statistics workshops. For example, during the conference on “NGS’ 16: Genome Annotation” (2016, April 1-3), at the Barcelona Biomedical Research Park in Barcelona, I did a poster presentation on “Benchmarking 16S rRNA Gene Sequencing and Bioinformatics Tools for Identification of Microbial Abundances”. In 2016, June 29-July 1, I attended a workshop on “NGS Data Analyses: A Practical Introduction”, by ecSeq Bioinformatics, cmt GmbH, Munich, Germany. These improved my metagenomics skills.



While in Barcelona, I learned Spanish, played beach volleyball at the Sotomarrostro Beach, and toured several places notably La Rambla, Montserrat, Plaça de Catalunya, Columbus Monument, Gothic Quarter, the Magic Fountain of Montjuïc, and Camp Nou. Even though I am not a Barcelona FC fan, I enjoyed seeing its football players during their 2015/16 La Liga Champions celebration in La Ramba.



I loved the culture and friendliness of the people, particularly at Dr. Julia’s lab. We would always eat together during lunch – at CRG, the beach, or typical Catalonia restaurants. We had *Biocore*, a WhatsApp group through which we would discuss in advance of what and where we would eat, and/or go for retreats! They introduced me to grilled calçot (onion) eaten with romesco sauce! At the end of my fellowship, they all took me to an Italian restaurant and even bought me gifts! The institute itself has a monthly *Happy Hour* party for people to socialize, and parties to “celebrate” their articles that have been rejected for publications! The fellowship has enabled me to be reasonably conversant with microbiome analyses.

Out of curiosity, I travelled to Brussels in Belgium, where I visited the European Commission, Place de la Bourse, Vrije Universiteit Brussel, Manneken Pis, the Atomium, and the Royal Palace of Brussels.

Finally, when I travelled back to my second home to compete my studies, varsity protests erupted. My experiments (microbiota) also joined the protests – they began failing! Because life on earth is too short to only troubleshoot failed experiments, I opted to go for tandem paragliding and other summertime events. Two days later, all the experiments worked! DIOS es grande (GOD is great)!



Awards

Lindi Masson received the Colin Kaplan Award - she was given this award for her exceptional work on genital inflammation and HIV risk in young women



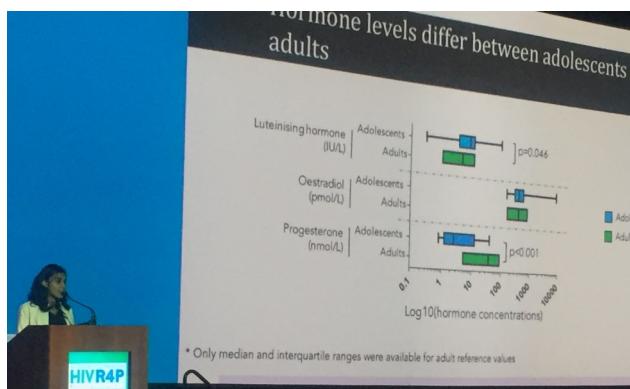
Lindi has performed outstandingly in this area: she has published her work in high impact papers (for example two in Clinical Infectious Diseases, IF 8.8, in the last 2 years); has patented a device to detect inflammation recently awarded R5.7 million to evaluate this device in a clinical trial.

Lindi was also awarded the Faculty of Health Sciences award for best publication

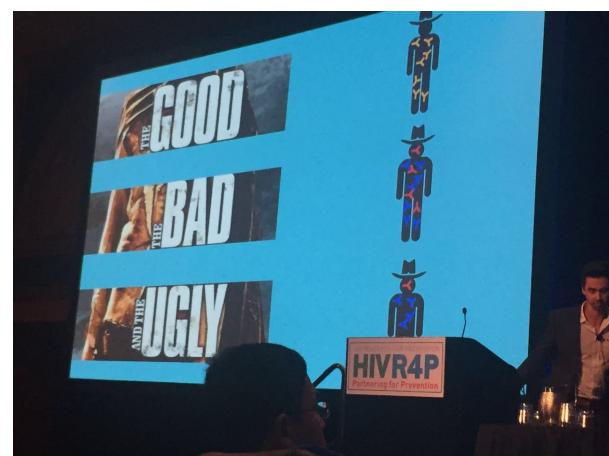
Congratulations to **Smritee Dabee and Daniel Sheward** from the Division of Medical Virology who were awarded HIVR4P New Investigators Awards.

These awards are given to outstanding early-career investigators presenting top-rated work at the HIVR4P meeting, based on high-scoring abstracts.

Smritee works in the IDM research group (GEMS) of Jo-Ann Passmore,



and Daniel is a PhD student in Carolyn Williamson's HIV Diversity Group.



Conferences/Workshops

At the end of June **Anna-Lise Williamson and Niki Douglass** visited MCI Santé Animale, a veterinary vaccine production facility in Morocco. A number of collaborative projects were discussed and Ruzaiq Omar will be going there in December this year.

Tsungai Jongwe's PhD work was presented by Niki Douglas and Anna-Lise Williamson at the International Poxvirus Conference held near Strasbourg at the beginning of July.

Settling down to a feast at the end of the day during Ramadan.



All kitted up to go into the vaccine facility

Conferences/Workshops

Ruzaik Omar

Trip to Morocco in December

"When in Mohammedia one drinks snail soup at the beach, and that's exactly what I did.

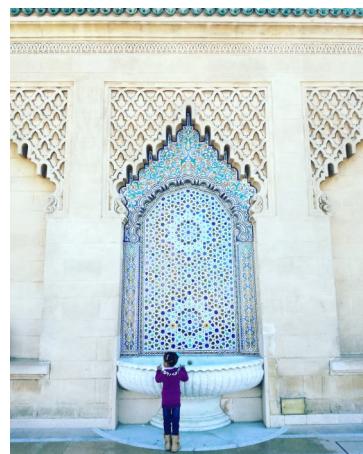
In the long gone year of 2016 we received a visit from members of M.C.I Sante Animale, a GMP veterinary vaccine production company in Mohammedia (Morocco). When an offer was made I seized the opportunity to visit the manufacturing plant.



We have worked on the development of veterinary vaccines within our research lab so it was a fantastic eye opener to see the very end of the vaccine life cycle.



As for Mohammedia, the touristic cities of Rabat, Fes, Casablanca and Marrakech are train rides away and you will never be starved of good food and warm company."



Conferences/Workshops

HIV R4P, Chicago, 2016

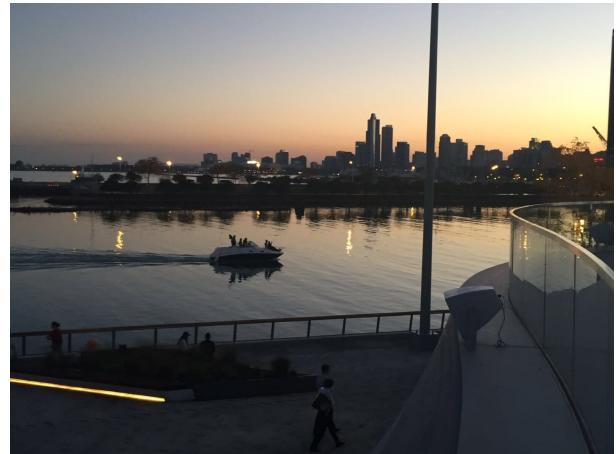
Catherine Riou

I attended the HIVR4P conference in Chicago (17-21 October 2016). The conference was mainly focused on HIV neutralizing antibodies, mucosal immunity and PrEP. The highlights of the conference were for me the plenary session given by Dr D Burton, who gave a brilliant overview on the recent progress in neutralizing antibody-base vaccines and therapy and I also really enjoyed Dr D Farber's talk about the compartmentalization of human immune responses.



Dieter Mielke

It was good to have a large contingent representing UCT at the HIVR4P 2016 conference in Chicago. The conference was packed with informative presentations and discussions, and some interesting talks on stimulating bnAb precursors. Colin, Dan and Sim gave great oral presentations and many of us gave poster presentations. In some of the few free hours, it was fun to explore Chicago a bit: tasting the famous Chicago deep dish pizza, passing many places familiar from movies scenes and gazing into the mesmerizing Cloud Gate ("The Bean").



Conferences/Workshops

Melissa-Rose Abrahams

IAS International AIDS conference and Cure symposium



I was very fortunate to receive a scholarship to attend both the International AIDS Society (IAS) AIDS 2017 conference and the pre-conference 'Towards and

HIV Cure Symposium' in July 2016. Both the symposium and conference were held at the ICC in Durban and were very well supported.

Some very interesting ideas came out of the cure symposium, including that we may need to broaden the 'cocktail' treatment approach to cure strategies since therapy with a single broadly neutralizing antibody (VRC01) was not sufficient to sustain viral control after treatment interruption.

Whether or not active replication and ongoing evolution occurs in the latent viral reservoir remains controversial as one surprising finding was presented on the absence of detectable viral evolution in the reservoir over a period of 16 years!

Application of cancer treatments to induce a state of HIV 'remission' is becoming a hot and fascinating topic, as well as the use of stem cell therapy or gene therapy (such as CRISPR Cas9) to eliminate the reservoir.

The main conference was buzzing with activity. There were thousands of delegates representing those from basic science to social and community tracks and a global village with colourful cubicles and a live band.

Advancing HIV Cure Research Workshop



The first South African 'Advancing HIV Cure Research Workshop' took place in Stellenbosch on the 6-7th October 2016. The workshop was chaired by **Professor Carolyn**

Williamson and **Dr Melissa-Rose Abrahams** and Dr Nigel Garrett from CAPRISA, and was supported by the South African Medical Research Council and the Department of Science and Technology (DST). The workshop assembled key stakeholders and representatives involved in HIV cure research and related fields from institutions across the country and abroad with the goal to discuss the latest findings in the field to identify gaps, and to set priorities for clinical translational cure research in South Africa.

Presentations included advancements in potential interventions to deplete or silence the latent viral reservoir such as the use of broadly neutralizing antibody therapies and gene silencing through targeted stem cell therapy, CRISPR/Cas9 or gene methylation, and the use of targeted radionuclide therapy (conventionally a cancer treatment) for visualizing and targeting anatomical reservoir sites using radioisotopes, and its potential use for assessing efficacy of reservoir clearance in cure trials. The UCT team presented new technologies for characterizing the size and sequence composition of the latent reservoir, including next-generation sequencing and digital droplet PCR, in women from the CAPRISA 002 Acute Infection cohort. This was followed by a presentation on the Females Rising through Education, Support, and Health (FRESH) acute infection cohort, and the proposal of future clinical studies using therapeutic vaccinations. Glaudina Loots (DST), a board member of the IAS Towards an HIV Cure Initiative, stressed the need for collaboration and inter-disciplinary research in particular, between early career HIV and cancer researchers.

Recent Virology Publications

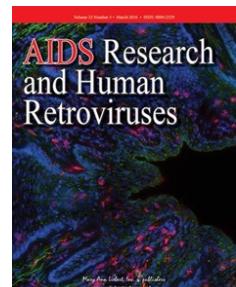


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PLOS ONE



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Clinical
Infectious
Diseases



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Social Responsibility

Debbie Stewart

In South Africa there are over 21,000 children living in 345 registered children's homes. At 18 they usually have to leave when government funding ceases. There is no support system for them and a scarcity of alternative care programmes.



SAYes support young people as they make the difficult transition from children's home to independence at the age of 18. They do this by matching them with a volunteer mentor who offers friendship, guidance and positive role modelling.

SAYes screens, selects, trains and supports volunteer mentors who are individually matched with a young person who is living in or has recently exited from care (aged between 14 and 25). SAYes mentors meet their mentee at least for one hour every week over the course of the year and attend monthly (two-hour) workshops.

I have had an incredibly rewarding year with a young grade 9 mentee.

For more info, see: <http://sa-yes.com/> or if you are interested in becoming a SAYes youth mentor, please visit <http://sa-yes.com/mentors/> or speak to Debbie.

Xhosa Course

Graduation from Xhosa Beginners Course



Congratulations to **Melissa-Rose, Talita York, Danny Sheward and Carina Combrinck** for completing this course

Events



Craig Adams, Sherazaan Ismail, Ruwayhida Thebus and Shireen Ga-lant took part in the K-Way VOP Constantia Valley Grape Run on the 2nd of October

International Pathology Day

International Pathology Day 2016 – not just another obscure day on the calendar. Jane Yates.

What happens in pathology labs and what pathologists do, is generally out of sight. Patients and the public don't directly experience this aspect of their healthcare, even though it is hugely important.

International Pathology Day (this year was the 3rd) is an initiative to highlight how pathology, path labs, lab staff and pathologists contribute to healthcare. The Pathology Learning Centre put together a patient information sheet called "What happens to my blood sample?". This introduces pathology and the different path labs (all 8 of them) and what sort of work they do. The challenge was to write it in an accessible way, without assuming any scientific background on the part of the patient. In the end we got it down to 600 words, as "plain English" as possible; from there it was translated into "plain Afrikaans" and "plain isiXhosa". by Francois Botha (anat path) and Mbali Ndlovu (chem path) respectively. Lynelle Govender (anat path) made the illustrations on her ipad. Jurgen Geitner (PLC) did the design and layout, and the website.

On 16 November we distributed "What happens to my blood sample?" sheets to Groote Schuur patients from a stand on the hospital's main corridor. Our drawcard was a selection of bottled pathology specimens, and NHLS cytology lab staff (Shereen Sirkhotte and Sharon Fenwick) had a microscope and slides to show. Lots of patients and staff stopped to engage with us, the direct interaction was very rewarding and definitely the best opportunity to offer information. Next year



could be the chance for more labs to get involved, it takes a bit of work, so start thinking now about an eye-catching, interactive display or perhaps an online campaign.

For some inspiration visit the brilliant Amsterdam microbiology museum site www.micropia.nl or view these wacky videos by the Royal College of Pathologists Australia <http://worldwithoutpathology.rcpa.edu.au/>



We plan to continue developing www.mybloodsample.uct.ac.za as a repository for patient information.

Photos were taken by Melvin Lawrence (UCT PLC)

Congratulations!



Molly Hanna Masson,
was born 22 September, 3.36 kg.
What a beautiful baby **Lindi Masson!**

Adventure!



Getting a bit as jealous of my boss as well as anxious from staring at a computer screen, I left the country for three months to motorbike through Namibia, Botswana, Zimbabwe, Mozambique, Malawi, and Zambia. Camping in the wild, eating dust, rafting, encountering dangerous wildlife, sandstorms, dealing with friendly or dodgy locals, diving, 4x4, annoying borders & military convoys, mountain hiking... 14 000 km filled with plenty of adventures and memories. Comes highly recommended!



Philippe Selhorst

End of Year Party



Many thanks to
Carolyn and Tim
for hosting the
party.

Photos by **Anna-**
Lise

