SANBI
South African National
Bioinformatics Institute

ANNUAL REPORT 2018

FROM HOPE TO ACTION THROUGH KNOWLEDGE

RESPICE PROSPICE
UNIVERSITY *of the*
WESTERN CAPE

Contents

About SANBI

WHO WE ARE

Bioinformatics is a specialist discipline straddling the fields of biology, mathematics and computer science and is integral to modern biological research. The South African National Bioinformatics Institute (SANBI) is situated at the University of the Western Cape in Cape Town (UWC). Our primary focus is the development and implementation of computational methodologies which allow researchers to accelerate their genomics data analyses. SANBI aims to heighten awareness of bioinformatics in South Africa and to assist the country in making optimal use of this technology. As the leading bioinformatics entity in Africa, we continue to foster local and regional collaborations on health-related topics that cover both communicable and non-communicable diseases.

SANBI provides a focus for biological research located in Africa and as such, is dedicated to:

- the development of online specialised resources for genomics and genome informatics;
- capacity development in genomics and bioinformatics in Africa; and
- the development and implementation of genome annotation methods.

OUR VISION

To become a center of excellence, achieving the highest level in research and education in the global, African and South African context.

OUR MISSION

- To conduct cutting edge bioinformatics and computational biology research relevant to South African, African and global populations.
- To develop human resources in bioinformatics and computational biology by educating and mentoring scientists.
- To increase awareness of and access to bioinformatics and computational biology resources.

OUR GOALS

- To generate and publish high quality, relevant bioinformatics research.
- To train and graduate competent and productive researchers.
- To add value to the academic programme of UWC.
- To enhance other research fields through collaborative projects.
- To establish sources of renewable funding to pursue the mission of the institute.

POLICY MANDATES

National Strategic Plan for HIV/AIDS, STIs and TB (2017 - 2022)

The vision and mission of SANBI align with the National Strategic Plan (NSP) 2017 – 2022 that outlines how the country will respond to the prevention and treatment of HIV and AIDS, TB and STIs. Specifically the NSP aims to "...strengthen strategic research activities to create validated evidence for innovation, improved efficiency and enhanced impact...".

The Department of Science and Technology's 10-Year Innovation Plan (2008 - 2018)

One of the five Grand Challenge areas specified in this Plan is the "Farmer to Pharma" value chain to strengthen the bioeconomy. SANBI's genomics programme, which straddles both communicable and non-communicable diseases, aligns clearly with this Grand Challenge.

The SAMRC Act (Act 58 of 1991)

As an extramural unit of the SAMRC, SANBI falls under the legislative mandates of the SAMRC. At Section 3, this Act states that the Legislative Mandate of the SAMRC is: *"...through research, development and technology transfer, to promote the improvement of the health and quality of life of the population of the Republic, and to perform such functions as may be assigned to the SAMRC by or under this Act...".*

Director's Message

One of the key national engagement topics in 2018 has been a national precision medicine roadmap. The South African Medical Research Council (SAMRC) and the Department of Science and Technology held a stakeholder meeting to plot a roadmap for precision medicine in South Africa. In line with this vision and other pan-African and international precision medicine initiatives, SANBI has expanded its research portfolio with the recruitment of Dr Ravnit Grewal, a haematology pathologist, who has established a research group focusing on HIV lymphomas. This exciting new initiative has been realised through funding from the SAMRC. Through Department of Higher Education and Training funding we were successful in recruiting an ex-SANBI student, Dr Ruben Cloete, to establish a research group focusing on molecular modeling.

Our research outputs continue to demonstrate the role of data management and analytics to support precision medicine. We demonstrated the use of next generation sequencing technology to identify disease-associated SNPs. In the infectious diseases space, we demonstrated repeatedly the use of computational tools to identify potential drug molecules against Malaria and Tuberculosis. These analysis pipelines form the cornerstone of our drug discovery toolkit. The role of biological collections cannot be underestimated - we expanded our African footprint with the adoption of our Baobab laboratory information management system in west and east Africa (Ivory Coast and Uganda) as part of our vision to see analytics that underpin the valuable biological collections that span the African continent.

Reflecting on our training programme for 2018, we have maintained our postgraduate outputs and successfully delivered bioinformatics short courses. One of the new training initiatives has been the launch of the Galaxy Africa workshop in April 2018 that attracted researchers and technical staff from seven African countries. There remains a need to ensure that opportunities exist to strengthen our technical support staff who have to maintain and provide a computational environment for researchers to deliver on their data science mandate.

I am sure that 2019 will be as exciting as we build momentum on many of our new initiatives.

Professor Alan Christoffels PhD, M.ASSAf
Director & DST/NRF Research Chair in Bioinformatics and Health Genomics
SAMRC Bioinformatics Unit
South African National Bioinformatics Institute
University of the Western Cape

Year in Review

NEW APPOINTMENTS

In 2018, we welcomed the appointment of haematopathologist, Dr Ravnit Grewal and SANBI alumnus, Dr Ruben Cloete to the SANBI fold.

RESEARCH PROJECTS FUNDING

The midcareer research funding secured the appointment of Dr Ravnit Grewal, who will initiate a programme on pathology and precision medicine at SANBI.

RESEARCH OUTPUTS

A total of 19 journal publications and 1 book chapter were produced in 2018.

RESEARCH HIGHLIGHTS

Drug Resistance Software Solutions

Simon Travers' lab focused on software solutions capable of undertaking DNA-based diagnostics at scale. The TB drug susceptibility testing focused on validation studies while the Sanger sequencing based HIV drug resistance reporting software fully conforms to the World Health Organisation (WHO) drug resistance testing protocols. In August 2018 national laboratories from all over Africa were trained in the HIVDR testing. This solution has been integrated into the Clinton Health Access Initiative's (CHAI) NASCOP system in Kenya, enabling the solution to be used at scale at a national level in Kenya with plans to roll this out globally.

Drug discovery for Tuberculosis

The research by Ruben Cloete and his collaborators at UWC School of Pharmacy demonstrated the value of computational drug design as applied to identifying potential inhibitors for efflux pumps in *M.tuberculosis*. Ongoing studies using a combination of drugs will examine the effect of the drugs on stopping the growth of the bacterium. This could lead to a new drug being included in the treatment regimen to beat drug-resistant TB.

Exome sequencing for clinical research

The rapid update of high throughput sequencing in clinical research globally requires analytical methods to prioritised functionally relevant genetic variants. Work in the Gamieldien lab focuses specifically on analysing large datasets of next generation sequencing reads with a view to identify disease-associated SNPs. Junaid Gamieldien's method published in 2017 has now been applied to a few collaborative projects with the University of Cape Town and Stellenbosch and the resulting publications demonstrate the impact of their computational approach. For example, recently his team used exome sequencing to identify a novel dysferlin mutation in a family with paucisymptomatic heterozygous carriers.

PARTICIPANTS OF THE FIRST GALAXY AFRICA CONFERENCE HELD AT SANBI IN APRIL.

First Galaxy Africa Conference 2018

Data analytics for biology research drives the SANBI/SAMRC Bioinformatics Unit in its mandate to strengthen computational biology capacity in South Africa and across the African continent. To this end, we launched the first Galaxy Africa Conference (**http://galaxyafrica.sanbi.ac.za/**) from 3-5 April 2018 with a focus on bioinformaticians, biologists, and computer scientists from around the African continent. This conference was attended by 44 participants from 7 countries (South Africa, Uganda, Tunisia, Ghana, Sudan and Kenya) (and 12 institutions) and featured 13 speakers over its 3 days.

Natural Products as Anti-malarials

Natural products continue to be an active area of research for our collaborators at the School of Pharmacy. Ex-SANBI student Dr Samuel Egieyeh used available anti-plasmodial bioassay data to build a predictive model that would allow us to predict bioactivity of these natural products before starting an experimental assay. Through this work we can target specific experimental assays more efficiently.

Host-pathogen Protein to Protein Interaction Prediction

The Christoffels' lab in partnership with the Mathematics department at UWC recently published a method of predicting host-pathogen interactions using a machine learning approach. This work stands out from current approaches in that it refines the choice of features that can be used for inter-species protein-protein interaction (PPI) prediction. The achievement lays the ground work for a new project that has started to attempt at improving prediction accuracy using limited experimental data – as is the case for human-*M.tuberculosis* PPI data.

Evolutionary Dynamics of HIV-1

Subtype A is one of the rare HIV-1 group M (HIV-1M) lineages that is both widely distributed throughout the world and persists at high frequencies in the Congo Basin, the site where HIV-1M likely originated. Gordon Harkins in collaboration with researchers from the University of KwaZulu Natal and the University of Cape Town computationally reconstructed, the early spatial-temporal history of the HIV-1M epidemic in order to better understand the evolutionary dynamics of HIV-1M before the onset of the global pandemic. Their published findings suggest that ancestral HIV-1 subtype A viruses may have been genetically predisposed to become major components of the present epidemic.

Because most HIV-1 infections in sub-Saharan Africa are acquired heterosexually through the genital mucosa, understanding the properties of viruses replicating in the female genital tract, and whether these properties differ from those replicating in the blood, is important. Gordon Harkins in collaboration with researchers from the National Institute for Communicable Diseases and the University of Cape Town showed in their published findings that in some women, distinct viral populations exist in the female genital tract and the blood that may impact the efficacy of microbicides and vaccines designed to provide mucosal immunity.

UWC STAFF PARTICIPATED IN THE STUDY OF THE SPEAKING BOOK, "BIOBANKING AND ME".

IN APRIL, SANBI PROVIDED CUSTOMISED BAOBAB LIMS TRAINING TO THE PRECISE NETWORK TEAM.

Community Engagement

The role of community awareness during development of disruptive technologies cannot be reinforced enough. The Christoffels' lab concluded a study on the use of a recently developed health intervention called *"Biobanking and Me"*. The team showed the increase in knowledge gained when using audio and illustrations to communicate the value of storing DNA and carrying out research.

Haematology Malignancies

Ravnit Grewal's publications and research focusses on haematology malignancies, specifically on HIV related lymphomas (HRL). Her research findings which are in keeping with other national and international findings show an increasing trend in HIV related lymphomas over the past decade, in our population in the Western Cape, diseases previously rarely seen in South Africa. It has been well documented that patients living with HIV have a 70-200 times greater risk of developing one of the HRL. Some of her research findings is explored in recent publications in Cancer Management and Research and Leukemia & Lymphoma.

Ilifu Research Cloud for Africa

The Ilifu Project **(http://www.ilifu.ac.za/)** is a big data research project driven by a consortium of 6 South African partner universities and research institutes in the Western and Northern Cape. Astronomy and bioinformatics form key research focii of the project. The SAMRC Bioinformatics Unit staff member Eugene de Beste, played a key role as engineer on the research cloud component of this project, assisting to build the OpenStack cloud (with more than 3,000 CPU cores) and Ceph storage cluster (with more than 2 PB of storage). We also presented this work at the first Ilifu User Workshop, held at UWC in November 2018 and attended by delegates from 4 universities in the consortium.

Increased African footprint of Baobab LIMS for biobanks

Following on from the successful training in 2017, a team from Makerere University, Uganda was hosted by SANBI in February 2018 for a four-day training session on Baobab LIMS. This team has subsequently held two internal training events for professionals at their host institution, highlighting the 'train the trainer' principle.

In March 2018, at the invitation of the West African Health Organisation, the Baobab LIMS team visited the biobank in Abidjan, Ivory Coast to explore possibilities for their use of Baobab LIMS. Similarly in March, SANBI hosted Ismael Kone from the Institute Pasteur in the Ivory Coast, where he was trained on the Baobab LIMS code.

In April 2018, SANBI hosted a 12 -strong team from the Precise Network (**www.precisenetwork.org**), providing customised training for one of their collaborative projects. Since then, this team has been working with the Baobab LIMS team to customise the software to meet the information management needs of their exciting, multi-country research project. Further training events took place at the 4th African Conference on Emerging Infectious Diseases and Biosecurity in Freetown, Sierra Leone and the workshop for Biobanking and Biosecurity in Lagos, Nigeria. A South African trademark application has also been submitted.

Staff

As a research institute, the Director of SANBI reports through the faculty of Natural Sciences to the University of the Western Cape. SANBI comprises a diverse group of research scientists, technical and administrative staff who all contribute to a dynamic productive working environment. Academic staff are tasked with conducting research in their laboratories, securing funding, student graduations and capacity development. The computing infrastructure is maintained and developed by a team of technical staff while administrators ensure the smooth running of daily operations.

SOME OF THE SANBI STAFF DURING A PLANNING SESSION AT THE TYGERVALLEY PROTEA HOTEL.

SANBI STAFF 2018

ACADEMIC		
Name	**Position**	**Funding Source**
Alan Christoffels, Prof	Director & DST/NRF Research Chair in Bioinformatics & Health Genomics, SAMRC Bioinformatics Unit	DST/NRF Research Chairs Programme
Ruben Cloete, Dr	Lecturer	UWC
Junaid Gamieldien, Prof	Associate Professor	UWC
Ravnit Grewal, Dr	Senior Lecturer	SA Medical Research Council
Gordon Harkins, Dr	Senior Lecturer	UWC
Uljana Hesse, Dr	Senior Lecturer in Biotechnology	UWC
Simon Travers, Prof	Associate Professor	UWC

TECHNICAL		
Name	**Position**	**Funding Source**
Hocine Bendou	Software Developer	NIH (H3Africa)
Quinton Coert	Software Developer	EU (B3 Africa)
Eugene De Beste	Systems Administrator	SA Medical Research Council
Phillip Labuschagne	Senior Software Developer	HVTN funding from the Bill and Melinda Gates Foundation
Thoba Lose	Software Developer	SA Medical Research Council
Baruch Lubinsky	Software Developer	DST-HIV funding
Zipho Mashologu	Software Developer	SA Medical Research Council
Campbell Rae	Web Developer	DST/NRF Research Chairs Programme
Peter Van Heusden	Senior Systems Developer	UWC

ADMINISTRATION		
Name	**Position**	**Funding Source**
Margaret Kumalo	Secretary	DST/NRF Research Chairs Programme
Fungiwe Mpithi	Receptionist	SA Medical Research Council
Ferial Mullins	Finance Administrator	UWC
Maryam Salie	Student Administrator	SA Medical Research Council
Junita Williams	Marketing Administrator (part-time)	DST/NRF Research Chairs Programme

Capacity Development

SANBI offers training programmes which are in keeping with its vision of becoming a world-leader in biomedical research and education in the global, African and South African context.

UNDERGRADUATE TRAINING PROGRAMME

Students who are interested in Bioinformatics as a career path are encouraged to take a combination of relevant subjects in Life or Health Sciences, Statistics, Computer Science and Mathematics during their undergraduate degree.

Bioinformatics Module (BTN 315)

Each year the UWC undergraduate Bioinformatics Module is taught to approximately 85 third-year students by the SANBI faculty.

Internship Programme

As part of the DST/NRF Research Chair Programme, SANBI provides a 1-year internship programme to students who graduated with a BSc degree.

POSTGRADUATE TRAINING PROGRAMME

Postgraduate training at SANBI is well-established and alumni are now working all over South Africa and at bioinformatics research sites around the world.

Honours Progamme

Although SANBI does not have an Honours programme, students who attain a pass rate of >60% can include a bioinformatics component to their Honours research project.

Masters Programme

SANBI offers a research MSc in Bioinformatics. Candidates with an Honours (BSc) degree or equivalent in a related scientific subject area may apply. The MSc degree is usually completed within two years.

Doctoral Programme

Candidates should have a Masters degree in Bioinformatics or in a related scientific field subject area such as Computer Science, Mathematics, Biochemistry and Engineering. The PhD degree must be completed within five years although most students aim to complete the degree in three years.

Postdoctoral Programme

Postdoctoral fellows are admitted to the research programme after consultation with a potential SANBI supervisor. Fellowships may last for a maximum of three years.

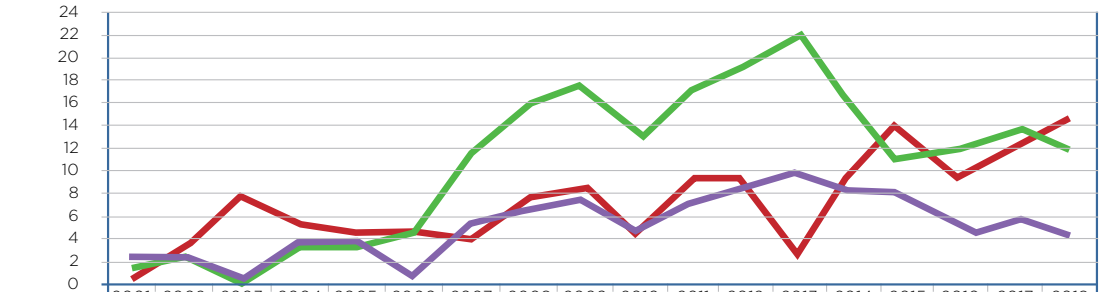
SANBI POSTGRADUATE REGISTRATION

2018 saw the highest number of 15 Masters student registrations of the total of 33 students at SANBI. Additionally, there were 6 Postdoctoral fellows and 12 Doctoral registrations.

While the male to female ratio was split 58% - 42%, it was interesting to note the increase in the number of females registered for PhDs.

The country split was 66% South Africa, 12% Nigeria, 6% India and 3% each from Algeria, Burkina Faso, Congo, Sudan and USA respectively.

SANBI Postgraduate Student Registrations 2001 - 2018:



	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Masters	1	4	8	6	5	5	4	8	9	5	10	10	3	10	14	10	13	15
PhD	2	3	1	3	3	5	12	16	17	13	17	20	22	17	11	12	14	12
Postdoctoral	3	3	1	4	4	1	6	7	7	5	7	9	10	8	8	6	7	6

THESIS COMPLETIONS 2018:

Name	Degree	Supervisor	Thesis Title
Roux-Cil Ferreira	PhD	Simon Travers	Exploring the role of the "glycan-shield" of human immunodeficiency virus in susceptibility to, and escape from, broadly neutralising antibodies.
Philip Labuschagne	PhD	Simon Travers	Development of a data processing toolkit for the analysis of next-generation sequencing data generated using the primer ID approach.
Farzaana Diedericks	Honours	Alan Christoffels	Evaluating In SIlico spoligotyping approaches for *Mycobacterium tuberculosis* strains in South Africa
Ridaa Fredericks	Honours	Alan Christoffels	The use of microsatellite and Cytochrome oxidase 1 (COX 1) gene data in population genetic studies of Hermetia illucens (Black Soldier fly)
Hassan Elamin	MSc in Dentistry	Ravnit Grewal (Co-Supervisor)	Incidence of plasmablastic lymphoma in HIV positive and HIV negative patients in a tertiary hospital in South Africa (2005-2017)
Carla Griesel	Masters in Medicine (Haematology Pathology, Stellenbosch University)	Ravnit Grewal (Co-Supervisor)	The diagnostic utility of Fine needle aspirate (FNA) samples at Tygerberg Hospital

GRADUATIONS 2018:

Name	Degree	Supervisor	Thesis Title
Emil Tanov	PhD	Gordon Harkins	Identification and ranking of pervasive secondary structures in positive sense single-stranded ribonucleic acid viral genomes.
Toluwaleke Ademuyiwa	MSc	Alan Christoffels	Development of opensource laboratory information management system (LIMS) for human biobanking
Gratia Willemse	MSc	Alan Christoffels	The effects of single nucleotide polymorphisms (SNPs) on the acetylation rate and functionality of human N-acetyltranferase-1 (NAT1)
Chantal De Long	BSc Honours Haematology Pathology (Stellenbosch University)	Ravnit Grewal	Evaluation of the Cepheid GeneXpert BCR/ABL Monito and Ultra test kits to identify and monitor the presence of the oncogenic BCR/ABL p210 variant transcript in Chronic Myeloid Leukemia patients

MEMBERS OF THE CHRISTOFFELS LAB CONGRATULATING TOLUWALEKE AT HIS GRADUATION.

Workshops and Courses

Numerous capacity development efforts are organised or hosted by SANBI faculty throughout the year in an effort to further develop human resources in the field of bioinformatics and computational biology.

BIOINFORMATICS TRAINING COURSE

This annual Western Cape course runs for approximately 5 weeks from February at SANBI.

For 2018, there were 24 participants from UWC, University of Cape Town (UCT) and University of Stellenbosch (US) in attendance. The hands-on, practical modules covered the following topics: Introduction to Molecular Biology; Introduction to Linux and Python Programming; Statistics using Python Programming; Scientific Writing; Biodatabases and Next Generation Sequencing; 16S rRNA anaysis and intro to Meta Genomics; Protein Structural Bioinformatics; and Phylogenetics.

WORKSHOPS ORGANISED/PRESENTED BY SANBI

Presenter	Venue	Date	Purpose of Course
Dominique Anderson	SANBI	February	Baobab LIMS training. Training for the Makerere University Biobanking team on the use of Baobab LIMS. Three members from Makerere University in Uganda attended the 4-day course.
Quinton Coert, Hocine Bendou	SANBI	March	Baobab LIMS code modification. Training for Ismael Kone (Institute Pasteur, Ivory Coast) on modification of the LIMS code base.
Dominique Anderson	SANBI	April	Baobab LIMS training. Customised training for the Precise Network Team on the use of Baobab LIMS for their collaborative project. Members who attended included biobank managers, IT managers, and project principal investigators.
Peter van Heusden, Ziphozakhe Mashologu	SANBI	April	Galaxy Africa Conference. Attended by 44 participants from 7 countries. Taught sessions on bacterial variant calling and 16S metagenomic analysis.
Eugene de Beste	Nosy Be, Madagascar	May	JEDI Workshop in Big Data Science. Using CWL and Toil to Wrap an Ad-hoc Astronomy Data Processing Pipeline. Attended by regional postgrad students in Astronomy.
Dominique Anderson	Freetown, Sierra Leone	September	Baobab LIMS practical. 4th African Conference on Emerging Infectious Diseases and Biosecurity. Practical demonstration and training on Baobab LIMS for Bio-repositories held for interested members attending the conference.
Peter van Heusden	Nairobi, Kenya	September	Galaxy workflows at ILRI-BecaHub. “Bioinformatics Community of Practice” course.
Peter van Heusden	Cape Town, South Africa	December	HPC in a Day. Introduction to High Performance Computing workshop at Centre for High Performance Computing (CHPC) National Conference.
Dominique Anderson	Lagos, Nigeria	December	Workshop for Lagos Biobanking and Biosecurity. Training for biobanking staff on the use of Baobab LIMS for sample management.

WORKSHOP ATTENDED BY SANBI

Attended by	Venue	Date	Purpose of Course
Thoba Lose, Ziphozake Mashologu, Tracey Calvert-Joshua, Lynley Abdoll and Mmakamohelo Direko	Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, UCT	14 - 18 May	Genomics of *Mycobacterium tuberculosis* Workshop with theoretical lectures and practical exercises

THE TEAM WHO ATTENDED THE BAOBAB LIMS WORKSHOP FROM BIOBANKING AND BIOSECURITY IN LAGOS, NIGERIA.

THE MAKERERE UNIVERSITY TEAM WHO WERE TRAINED AT SANBI.

Computational Resources

SANBI'S IT TEAM: EUGENE DE BESTE, QUINTON COERT, PETER VAN HEUSDEN, ZIPHO MASHOLOGU AND THOBA LOSE.

SANBI's IT team supports the work of the institute through software development and by crafting our in-house research cloud, data storage and High Performance Computing (HPC) facilities.

SANBI's core server infrastructure comprises two parts: a legacy storage, virtualisation based on Dell EqualLogic SAN, in-house developed research cloud and SGE based HPC cluster, and modernised infrastructure using Ceph storage (based on SuperMicro servers), OpenStack based research cloud and a Slurm based HPC cluster.

On a hardware level both HPC and research cloud are largely based on Dell Blade servers providing a total of 232 CPU cores (spread across the HPC and research cloud infrastructure). Legacy storage provides 30 TB and the Ceph storage 183 TB of storage. Servers are interconnected using 10 Gb Ethernet on fibre.

Internet connectivity is provided by UWC and SANBI is connected to SANReN, the South African Research and Communication network that provides 10Gb/s connections between South African universities and research centers.

COMPUTATIONAL RESOURCES

SANBI HPC Cluster

The cluster hardware configuration was not expanded in 2018 and remains on par with the configuration from 2017. We have 232 CPU cores and 1952 GB of RAM on our Dell cluster.

Server Type	Server Count	RAM	CPU cores
M710HD	6	64 GB - 128 GB	12
M910HD	1	512 GB	16
M620	6	96 GB	12
M610X	2	32 GB	12
M630	3	96 GB - 128 GB	16

All new users in 2018 were hosted on a new cluster running the Slurm job scheduler and backed by our Ceph storage. While some work is still performed on the legacy SGE cluster we are preparing to decommission that cluster in 2019.

Virtual Machine Infrastructure

Experience in building this infrastructure fed into the construction of SANBI's own research cloud. As of the end of 2018, servers providing 64 CPUs and 340 GB of RAM have been provisioned as part of our research cloud. We will complete the provisioning of the new research cloud and decommissioning of legacy virtualisation infrastructure in 2019.

Eugene de Beste spent the past two years developing an openStack research environment as part of his MSc studies. He successfully completed a pilot project (**https://github.com/Banshee1221/Nikeza**) that demonstrated our capabilities in developing and maintaining a research cloud environment that will positively impact adoption of cloud technology in Africa.

DEVELOPMENT ACTIVITIES

Galaxy Africa Conference

The SANBI IT team has developed extensive experience with the Galaxy workflow environment over several years. This motivated our involvement in organising the first Galaxy Africa conference, which was held at SANBI in April 2018. The conference was attended by 44 participants from 7 countries and feature both presentations and workshops on the Galaxy system and its use in bioinformatics. Our work on the COMBAT-TB project was extensively highlighted.

Ilifu Research Cloud

The Ilifu Project (**http://www.ilifu.ac.za/**) is a big data research project driven by a consortium of 6 South African partner universities and research institutes in the Western and Northern Cape. Astronomy and bioinformatics form key research focii of the project. SANBI IT group member, Eugene de Beste, played a key role as engineer on the research cloud component of this project, assisting in building the OpenStack cloud (with more than 3,000 CPU cores) and Ceph storage cluster (with more than 2 PB of storage). We also presented at the first Ilifu User Workshop, held at UWC in November and attended by delegates from 4 universities in the consortium. SANBI servers deployed on the Ilifu infrastructure were also used for a computational chemistry workshop at the CHPC National Conference in December 2018. In 2019 we look forward to building a Galaxy-based bioinformatics science gateway on the Ilifu infrastructure, in collaboration with partners from UCT and US.

MENTORSHIP AND TEACHING

As in previous years, SANBI assisted in the mentorship of students to enter the annual Centre for High Performance Computing national Student Cluster Competition. One team that we mentored qualified to take place in the 2nd round of this competition, held in Cape Town in December.

SANBI TAUGHT JEDI SCIENTIFIC WORKFLOW SYSTEMS IN MADAGASCAR IN APRIL.

SANBI in the Media

During 2018, SANBI contributed 2 articles to the online resource *The Conversation* which is an independent source of news, analysis and expert opinion, written by subject matter academics and researchers. Content is free to read and republish under Creative Commons, allowing access to 22 000 sites worldwide with a global reach of approximately 38 million readers a month.

The Conversation.com
August 9, 2018

How biobanks can help improve the integrity of scientific research

Dominique Anderson, University of the Western Cape;
Alan Christoffels, University of the Western Cape*, and Carmen Swanepoel,* Stellenbosch University

Biobanks are repositories which receive, store, process and disseminate specimens. These include DNA derived from humans and animals; bacterial strains; and environmental samples like plants and soil. Biobanks also provide the vital infrastructure for research to support scientific advancement and innovation. In the developed world, biobanks are well established and generally well funded and supported. There are also biobanks in the developing world like regions in Africa, most notably in South Africa and Nigeria – but the technology is really still in its infancy. Simple issues like internet connectivity, access to reliable water and electricity supply, which are all necessary to run biobanks, are common.

The analytics indicated that this article from August 2018 was read 1239 times and republished 8 times with readers located predominantly in USA, South Africa, France, UK and Australia.

The Conversation.com
May 24, 2018

Science in Africa: homegrown solutions and talent must come first

Alan Christoffels, University of the Western Cape

It's been a recurring refrain: Africa still lags woefully behind the rest of the world in generating new scientific knowledge.

As figures collated by the World Bank in 2014 show, the continent – home to around 16% of the world's population – produces less than 1% of the world's research output.

These are painful admissions to make as the continent prepares to celebrate Africa Day on May 25. But there are several projects and initiatives that offer hope amid all the bad news.

Since publication in May 2018, this article has been read 42 423 times by the majority readers from the USA, UK, South Africa, Canada, Kenya, France and Nigeria. The article was republished 19 times.

Community Engagement

THE BIOBANK SPEAKING BOOK FOR COMMUNITY ENGAGEMENT

"Biobanking and Me" is a battery-operated speaking book which was developed as part of a community engagement and science communication project for the B3Africa Consortium. The team, led by SANBI with inputs from the NSB biobank at Tygerberg Hospital, comprised Anja Bedeker, Dominique Anderson, Thoba Lose, Carmen Swanepoel, Yamkela Mgwatyu, Retha Luus, Renette Blignaut and Alan Christoffels.

The speaking book aims to explain several aspects relating to biobanks, genetic research and research participant rights. The hard-back book recites the printed text to the "reader".

The text is written in simple, plain language that is easy to understand, and each page has a colourful illustration that is representative of the text on the page. Two versions of the book were published, namely an English-and-Afrikaans speaking book (*Biobanking and Me; Ek en biobanking*) and an English-and-isiXhosa Speaking Book (*Biobanking and Me; iBiobanking kunye nam*).

Both the text and soundtrack of each version is bilingual. This offers the reader the option to read and/or listen to the book in one or both languages.

An experimental research design, which incorporates quantitative and qualitative research, was designed to assess the effectiveness and enjoyability of the speaking book. Participants were recruited from different staffing sectors within UWC, including cleaning services, technical services and gardening services. Due to technical aspects of the assessment process, participants were grouped into two main group. The one group was be assessed the first two weeks, and the second group the following two weeks. An additional week was set aside for the focus groups so the interaction ran for 3 days per week, 5 weeks in total.

Each participant received a copy of the book to take home. The collected data analysed thus far has demonstrated an increased participants' knowledge of biobanking and genetics after the introduction of the speaking book.

Furthermore, results indicated that 94% of participants enjoyed reading and/or listening to the book and 77% of participants shared their book with others in their community.

PARTICIPANTS OF THE SPEAKING BOOK STUDY.

Results from this study were presented at the African Society for Laboratory Medicine (**http://aslm2018.org/**) held in Abuja Nigeria on the 10 - 13 December 2018. *Poster - "Understanding Biobanking: The effectiveness of the SANBI Biobank speaking book, "Biobanking and me"*

This study has provided us with a richer understanding of research participants' experience of the speaking book thereby allowing us to determine the effectiveness and enjoyability of the biobank speaking book, and how it can be improved for use in community engagement. Funding would need to be secured in order to produce the book on a large scale and to be able to distribute it in clinics, libraries, hospitals, schools and doctors' waiting rooms.

Because this book can be recreated to cover any topic which may be of interest, it is an excellent tool for other stakeholders to use as a community communication or engagement strategy.

SCHOOL VISIT

ON WORLD TB DAY IN MARCH, STUDENTS IN ALAN CHRISTOFFELS' LAB VISITED SOUTH PENINSULA HIGH SCHOOL IN DIEP RIVER, CAPE TOWN TO SPEAK WITH GRADE 11 – 12 LEARNERS ABOUT TB AND STUDIES IN BIOINFORMATICS AT SANBI.

Research Outputs

SANBI's profile of excellence is reflected in its ability to publish high impact scientific articles in international publications; keynote addresses. invited talks and presentations at conferences. Details of these activities are described in the tables that follow.

JOURNAL PUBLICATIONS

#	Publication (SANBI contributors)	Published Date
1.	*Analyses of HIV-1 integrase sequences prior to South African national HIV-treatment program and available of integrase inhibitors in Cape Town, South Africa.* Dominik Brado, Adetayo Emmanuel Obasa, George Mondinde Ikomey, **Ruben Cloete**, Kamalendra Singh, Susan Engelbrecht, Ujjwal Neogi & Graeme Brendon Jacob. Scientific Reports (2018) 8:4709 DOI:10.1038/s41598-018-22914-5	March
2.	*Unravelling the complicated evolutionary and dissemination history of HIV-1M subtype A lineages.* Marcel Tongo, **Gordon W. Harkins**, Jeffrey R. Dorfman, Erik Billings, Sodsai Tovanabutra, Tulio de Oliveira, and Darren P. Martin. Virus Evolution, 2018, 4(1): vey003 doi: 10.1093/ve/vey003	March
3.	*Identification of proteins in response to terminal drought stress in sorghum (Sorghum bicolor (L.) Moench) using two-dimensional gel-electrophoresis and MALDI-TOF.* **A A Woldesemayat,** DM Modise, BK Ndimba Indian Journal Plant Physiology (2018). https://doi.org/10.1007/s40502-018-0357-9	March
4.	*A 35-gene signature discriminates between rapidly- and slowly-progressing glioblastoma multiforme and predicts survival in known subtypes of the cancer.* **Azeez A. Fatai and Junaid Gamieldien.** BMC Cancer 2018 18:377 https://doi.org/10.1186/s12885-018-4103-5	April
5.	*Renewing Felsenstein's phylogenetic bootstrap in the era of big data.* F. Lemoine, **J.-B. Domelevo Entfellner**, E. Wilkinson, D. Correia, M. Dávila Felipe, T. De Oliveira & O. Gascuel. Nature 556, 452–456 (2018) doi:10.1038/s41586-018-0043-0	April
6.	*Human Leukocyte Antigen-A, B, C, DRB1, and DQB1 Allele and Haplotype Frequencies in a Subset of 237 Donors in the South African Bone Marrow Registry.* Mqondisi Tshabalala, Charlotte Ingram, Terry Schlaphoff, Veronica Borrill, **Alan Christoffels**, and Michael S. Pepper. Journal of Immunology Research Volume 2018, Article ID 2031571, 8 pages	April

#	Publication (SANBI contributors)	Published Date
7.	*Cross-species multiple environmental stress responses: An integrated approach to identify candidate genes for multiple stress tolerance in sorghum (Sorghum bicolor (L.) Moench) and related model species.* **Woldesemayat AA**, Modise DM, **Gamieldien J**, Ndimba BK, Christoffels A. PLoS ONE 13 (3): e0192678. https://doi.org/10.1371/journal.pone.0192678 PMID: 29590108	May
8.	*Minimal residual disease in chronic lymphocytic leukemia: A consensus paper that presents the clinical impact of the presently available laboratory approaches.* Carmen Aanei, Ioana Berindan-Neagoe, Cristina Selicean, Delia Dima, Anca Jurj, Anastasia Melek, **Ravnit Grewal**, Ciprian Tomuleasa Critical Reviews in Clinical Laboratory Sciences, May 2018 DOI: 10.1080/10408363.2018.1463508	May
9.	*Exome sequencing identifies novel dysferlin mutation in a family with paucisymptomatic heterozygous carriers.* **Mahjoubeh Jalali-Sefid-Dashti**, Melissa Nel, Jeannine M. Heckmann and **Junaid Gamieldien** BMC Medical Genetics (2018) 19:95 https://doi.org/10.1186/s12881-018-0613-x	June
10.	*Prediction of human-Bacillus anthracis protein–protein interactions using multi-layer neural network.* **Ibrahim Ahmed**, Peter Witbooi and **Alan Christoffels** Bioinformatics, 2018, 1–6 doi: 10.1093/bioinformatics/bty504	June
11.	*Novel circular DNA viruses associated with Apiaceae and Poaceae from South Africa and New Zealand.* Cécile Richet, Simona Kraberger, Denis Filloux, Pauline Bernardo, **Gordon W. Harkins**, Darren P. Martin, Philippe Roumagnac. Archives of Virology DOI: 10.1007/s00705-018-4031-3	September
12.	*The Westward Journey of Alfalfa Leaf Curl Virus.* Zohreh Davoodi, Nicolá s Bejerman, Cé cile Richet, Denis Filloux, Safaa G. Kumari, Elisavet K. Chatzivassiliou, Serge Galzi, Charlotte Julian, Samira Samarfard, Verónica Trucco, Fabiá n Giolitti, Elvira Fiallo-Olivé, Jesús Navas-Castillo, Nader Asaad, Abdul Rahman Moukahel, Jomana Hijazi, Samia Mghandef, Jahangir Heydarnejad, Hossein Massumi, Arvind Varsani, Ralf G. Dietzgen, **Gordon W. Harkins**, Darren P. Martin and Philippe Roumagnac. Viruses 2018, 10, 542; doi:10.3390/v10100542	October
13.	*Defining the molecular signatures of Achilles tendinopathy and anterior cruciate ligament ruptures: A whole-exome sequencing approach.* Andrea Gibbon, **Colleen J. Saunders**, Malcolm Collins, Junaid Gamieldien, Alison V. September PLoS ONE 13(10): e0205860 https://doi.org/10.1371/journal.pone.0205860	October
14.	*Structural rearrangements maintain the Glycan Shield of an HIV-1 envelope trimer after the loss of a glycan.* **Roux-Cil Ferreira**, Oliver C Grant, Thandeka Moyo, Jeffrey R Dorfman, Robert J Woods, **Simon A Travers, Natasha T Wood**. Scientific Reports volume 8, Article number:15031	October

#	Publication (SANBI contributors)	Published Date
15.	*Use of Flow Cytometry in the Phenotypic Diagnosis of Hodgkin's Lymphoma.* **Grewal R**, Chetty M, Abayomi E-A, Tomuleasa C, and Fromm JR Cytometry Part B June 2018; 9999: 1–12. DOI: 10.1002/cyto.b.21724	October
16.	*Castleman's disease in an HIV endemic area.* Esam-Rajab Mahroug, Candice Sher-Locketz, Minodora-Silvia Desmirean, Emmanuel-Akinola Abayomi, Ciprian Tomuleasa, **Ravnit Grewal** Cancer Management and Research October 2018:10 4553–4563 DOI:10.2147/CMAR.S175648	October
17.	*Mesenchymal stem cells in myeloproliferative disorders – focus on primary myelofibrosis.* Sonia Emilia Selicean, Ciprian Tomuleasa, **Ravnit Grewal**, Graca Almeida-Porada & Ioana Berindan-Neagoe. Leukemia & Lymphoma October 2018 DOI:10.1080/10428194.2018.1516881	October
18.	*Molecular modelling and simulation studies of the Mycobacterium tuberculosis multidrug efflux pump protein Rv1258c.* **Ruben Cloete**, Erika Kapp, Jacques Joubert, **Alan Christoffels**, Sarel F. Malan PLoS ONE 13(11): e0207605 https://doi.org/10.1371/journal.pone.0207605	November
19.	*Developing reproducible bioinformatics analysis workflows for heterogeneous computing environments to support African genomics.* Shakuntala Baichoo, Yassine Souilmi, Sumir Panji, Gerrit Botha, Ayton Meintjes, Scott Hazelhurst, **Hocine Bendou, Eugene de Beste**, Phelelani T. Mpangase, Oussema Souiai, Mustafa Alghali, **Long Yi**, Brian D. O'Connor, Michael Crusoe, Don Armstrong, Shaun Aron, Fourie Joubert, Azza E. Ahmed, Mamana Mbiyavanga, **Peter van Heusden**, Lerato E. Magosi, Jennie Zermeno, Liudmila Sergeevna Mainzer, Faisal M. Fadlelmola, C. Victor Jongeneel and Nicola Mulder. BMC Bioinformatics (2018) 19:457 https://doi.org/10.1186/s12859-018-2446-1	November

CHAPTER IN BOOK

No.	Details	Published Date
1.	*From Spatial Metagenomics to Molecular Characterisation of Plant Viruses: A Geminivirus Case Study.* Sohini Claverie, Pauline Bernardo, Simona Kraberger, Penelope Hartnady, Pierre Lefeuvre, Jean-Michel Lett, Serge Galzi, Denis Filloux, **Gordon W. Harkins**, Arvind Varsani, Darren P. Martin, and Philippe Roumagnac. **Chapter In Book: Advances in Virus Research** ISBN: 978-0-12-814415-2 ISSN: 0065-3527 https://doi.org/10.1016/bs.aivir.2018.02.003	September

PARTICIPANTS OF THE B3AFRICA STAKEHOLDERS MEETING HELD IN NAIVASHA, KENYA IN FEBRUARY.

CONFERENCE PARTICIPATION

Presenter	Conference Details	Date	Title	Oral/Poster
Alan Christoffels	B3Africa Stakeholder Engagement Meeting Niavasha, Kenya	February	Bioinformatics on the back of quality biospecimen collections.	Oral
Peter van Heusden	Galaxy Africa 2018, SANBI	3-5 April	The COMBAT-TB Project: Accessible tools for data intensive *M. tuberculosis* research.	Oral
Eugene de Beste	Galaxy Africa 2018, SANBI	3-5 April	Moving code to data using workflow standards and containers.	Oral
Hocine Bendou	Galaxy Africa 2018, SANBI	3-5 April	From biobanking to bioinformatics.	Oral
Thoba Lose	Galaxy Africa 2018, SANBI	3-5 April	Understanding *M. tuberculosis* variants using Galaxy and the Combat TB Explorer.	Oral
Ziphozakhe Mashologu	Galaxy Africa 2018, SANBI	3-5 April	Using Galaxy for *M. tuberculosis* variant calling.	Oral
Alan Christoffels	SKA Big Data Challgenes in Africa, Madagascar	28-30 May	Bioinformatics in Africa.	Oral
Jamie Southgate	ISMB 2018, Chicago, USA	6-10 July	Establishing the Framework for an African Genome Archive.	Poster

Presenter	Conference Details	Date	Title	Oral/Poster
Peter van Heusden	SA TB Conference, Durban, SA	10 July	COMBAT-TB: Understanding *M.tuberculosis* through better bioinformatics.	Poster
Catherine Rossouw	PATHCONFERENCE, Stellenbosch, SA	August	The impact of archival storage time on the viability of FFPE tissues used for shotgun mass spectrometry analysis.	Poster
Mohd Shahbaaz	Structural Biology 2018, Berlin, Germany	24-26 September	Towards New Therapeutic Derivatives? In silico based design of new kinase inhibitors against *Mycobacterium tuberculosis.*	Poster
Oluwafemi Peter Abiodun	South African Genetics Society (SAGS) and South African Society for Bioinformatics (SASBi), Free State, SA	16-18 October	Exploring the influence of technological, organisational and environmental factors on information security policies and compliance on biomedical data at South African higher education institutions.	Poster
Sarah DeRaedt	South African Genetics Society (SAGS) and South African Society for Bioinformatics (SASBi), Free State, SA	16-18 October	microRNA expression mapping of the developmental life stages of Hermetia illucens (the black soldier fly) to breed for mass protein production.	Awarded Best Poster prize
Susan Alicia Fernol	South African Genetics Society (SAGS) and South African Society for Bioinformatics (SASBi), Free State, SA	16-18 October	An investigation into the genetic basis of autosomal recessive osteogenesis imperfecta type III in a South African family of mixed ancestry.	Poster
Ruben Cloete	South African Genetics Society (SAGS) and South African Society for Bioinformatics (SASBi), Free State, SA	16-18 October	Co-segregating variants in a Parkinsons disease family: characterisation using structural methods.	Oral
Peter van Heusden	Ilifu Users Workshop, UWC, SA	November	Bioinformatics workshops on the Ilifu Research Cloud with Galaxy.	Oral
Ravnit Grewal	4th Global Genomic Medicine Conference , Cape Town, SA	28-30 November	Precision medicine in oncology.	Poster

Presenter	Conference Details	Date	Title	Oral/Poster
Peter van Heusden	CHPC Conference, Cape Town, SA	3 December	High Throughput Computing in bioinformatics: workflows, containers and emerging paradigms.	Oral
Alan Christoffels	African Society for Laboratory Medicine, Abuja, Nigeria (**http://aslm2018.org/**)	10-13 December	Understanding Biobanking: The effectiveness of the SANBI Biobank speaking book, "Biobanking and me".	Poster

ALAN CHRISTOFFELS PRESENTED THE POSTER "UNDERSTANDING BIOBANKING: THE EFFECTIVENESS OF THE SANBI BIOBANK SPEAKING BOOK, 'BIOBANKING AND ME'" AT THE ASLM CONFERENCE IN ABUJA.

INVITED TALKS

Presenter	Conference Name, Venue	Date	Talk Title
Simon Travers	SAMRC/FIND Regional Stakeholders' Summit: AMR + Africa + Diagnostics Isivivana Community Centre, Khayelitsha, Cape Town, SA	30 January	PANEL DISCUSSION: Making it happen: how can diagnostics optimise the use of antibiotics and improve surveillance?
Imogen Wright	NEPAD SANBio BioFISA II Annual Event, Pretoria, SA	27-28 February	PANEL DISCUSSION: Commercialisation of Research Technologies
Simon Travers	PATHRed Innovation Summit, NHLS, Johannesberg, SA	3 August	Cloud technology to improve patient healthcare intervention.
Simon Travers	National Lab Training Centre, Addis Ababa, Ethopia	21-31 August	African HIVDR training workshop in partnership with the US Centers for Diseases Control (CDC)
Simon Travers	Tygerberg Hospital, Cape Town, SA	12 September	Cloud-based HIVDR analysis at scale
Simon Travers	SA Innovation Summit, Cape Town Stadium, SA	14 September	PANEL DISCUSSION: BIOTECH Why isn't more of South Africa's world class life sciences research commercialised?
Alan Christoffels	4th African Conference on Emerging infectious diseases and Biosecurity. Freetown, Sierra Leone	26-28 September	Establishing genomics capacity for disease surveillance.
Alan Christoffels	CHPC Conference, Cape Town, SA	3 December	HPC considerations for public health genomics
Alan Christoffels	Civic Engagement and Stakeholders Meeting on Lagos State Biosecurity Initiative, Lagos, Nigeria	15 December	The role of data and bioinformatics in public health

JOURNAL EDITING AND REVIEWS

PI Name	Journal
Alan Christoffels	Editorial Board Member: Data Journal Reviewer: Bioinformatics, PLoSONE, Journal of Asian Entymology
Junaid Gamieldien	Reviewer: PLoSONE, Biotechniques
Ravnit Grewal	Reviewer: Oncotarget, Haematologica, Oncology Letters
Gordon Harkins	Reviewer: Diversity and Distributions

EXPERT PANEL OR COMMITTEE MEMBERSHIP

PI Name	Committee
Alan Christoffels	Governing Council and Co-Chair: ASBCB
	Advisory Board Member: PHINDAccess: EU-funded project in Tunisia to build capacity in Host-pathogen interaction omic analysis
	Advisory Board Member: Center for Proteomics and Genomics Research
	Advisory Board Member: East African Bioinformatics Network Fogarty Funded Bioinformatics Network in East Africa
	Assessor: NRF Rating Panel
	Member: Global Emerging Pathogens Consortium

THESIS EXAMINED FOR STUDENTS AT OTHER INSTITUTIONS

Examiner	Institution	Degree
Alan Christoffels	University of Cape Town	MSc
	University of Stellenbosch	MSc X3
Ravnit Grewal	University of Witwatersrand	Masters in Medicine x2

EXTERNAL MODERATION

Examiner	Institution	Course
Alan Christoffels	Univerisity of Stellenbosch	3rd year and Honours Bioinformatics Models
Junaid Gamieldien	University of KwaZulu Natal	Genetics Honours

Research Laboratories

RESEARCH LABORATORY OF ALAN CHRISTOFFELS

MEMBERS OF THE CHRISTOFFELS LAB.

HIGHLIGHTS OF THE LAB FOR 2018

The past year has been a productive and exciting year on many fronts. We continue to expand our reputation in biobank informatics with the growth of Baobab LIMS in Africa.

For the past 5 years we have been refining our computer aided drug design as part of the translational work that we do. The past year demonstrates that we have a successful approach to identifying potential drug targets. To this end, we have published papers or submitted papers for publication relating to finding new drugs for tuberculosis.

Two MSc students graduated in 2018 and three students submitted their thesis for examination.

RESEARCH PROJECTS

The projects below underpin our translational work:

Tuberculosis

A comprehensive research programme is underway that includes investigating genetics determinants in both host (Human) and pathogen (*Mycobacterium tuberculosis*) to understand drug resistance, and protein structure determination to inform patient-centric drug design. These findings inform the development of a scientific workflow management system to support reproducible high throughput computational experiments. These workflows form the basis of our COMputational BActerial analytical toolkit for Tuberculosis research (COMBAT-TB)

(**www.combattb.org**) initiative to deploy analytic tools across the African continent.

Search for new anti-malarials

The medicinal benefits of plant extracts generates a plethora of data. In collaboration with the UWC School of Pharmacy, we have published new predictive models using machine learning techniques to identify signatures in common between registered anti-malarial drugs and plant extracts that show anti-plasmodial activity.

Infrastructure for biobanking

The collection and storage of biological material and its associated data are essential to any genetics project with a long term vision. To this end we have contributed to the development of a computational environment to manage and analyse genomic data that is linked to a biobank. Specifically, we have developed an open-source laboratory information management system – Baobab LIMS (**www.baobablims.org**) that is being rolled out across Africa.

HLA Typing

In collaboration with Professor Michael Pepper at the University of Pretoria we are analysing the HLA data for African populations. There remains an important link between HLA diversity and susceptibility to infectious disease. This work will expand with reference to host susceptibility to tuberculosis.

RESEARCH COLLABORATIONS

1. Prediction of human-tuberculosis interaction networks

Collaborating Parties:
Prof Peter Witbooi - Mathematics Department, UWC.

Nature and Purpose:
Use machine-learning techniques to improve the prediction of host-pathogen interactions between human and pathogens.

Output in the last 12 months:
Manuscript in Bioinformatics Journal on human-anthracis protein interactions. This work will now expand to using tuberculosis interaction data.

2. Develop a biobank informatics management system

Collaborating Parties:
B3Africa Consortium funded through Horizon2020 (**www.b3africa.org**).
Precise Network (**www.precisenetwork.org**)

Nature and Purpose:
Development of a laboratory management system that will integrate with other biobanking tools through an open-source platform called Biobank in a Box.

Output in the last 12 months:
We extended our African footprint to the Ivory Coast. Our current funding model is to support research teams who wish to strengthen their laboratories with a tailor-made LIMS.
The LIMS was customised for utility in Kenya, Mozambique and The Gambia.

3. Identification of novel drug targets for drug resistant tuberculosis

Collaborating Parties:
Prof Samantha Sampson and Rob Warren - US
Dr Cedric Wereley - US.

Nature and Purpose:
Current TB drugs are more than 30 years old and have unacceptable efficacy and safety profiles, emphasising the need for new drugs. We have been using computational methods to identify potential drug targets for *M.tuberculosis*. In this regard we have focused on protein kinase inhibitors and also a few essential genes in *M.tuberculosis*.

Output in the last 12 months:
2 compounds were identified as potential inhibitors and experimental assays confirmed their role as inhibitors of mycobacterial growth. A manuscript has been submitted. We also identified compounds that bind more strongly than current first line drugs (isoniazid and Rifampicin). This work has been submitted for publication.

4. Chemo-informatics profiling of plant extracts that show anti-plasmodial activity

Collaborating Parties:
Profs Sarel Malan and James Syce - School of Pharmacy, UWC.

Nature and Purpose:
At least 1000 compounds were identified in plant extracts and show anti-plasmodial activity.

We are using a range of computational tools to compare these compounds with currently registered anti-malarial drugs to identify common signatures and ultimately prioritise the list of compounds identified in plant extracts.

Output in the last 12 months:
Published a paper on predictive models.

5. Computational Bacterial analytical toolkit for Tuberculosis (COMBAT-TB)

Collaborating Parties:
Profs Samantha Sampson and Rob Warren – US.

Nature and Purpose:
Develop a computational platform to store Tuberculosis omic data and to provide a visualisation tool.

Output in the last 12 months:
Submitted the graph database for publication. Added phylogenetic analysis to the toolkit

6. Exploiting protein signatures in Colon Cancer archival biospecimens

Collaborating Parties:
Prof Schneider, Dr Johnathan Rigby – US.

Nature and Purpose:
There are two phases to this project. The first is to assess the stability of the formalin embedded tumor blocks that have been archived for 1-10 years. Our assessment uses proteomic signatures to verify the biological stability of the material. Once this has been completed then we will stratify a cohort of patients to screen for biomarkers

Output for the last 12 months
Mass spectrometry analysis done for the achival tumor samples ranging from 0-5 years. Manuscript in preparation.

7. Dental Genetics Programme

Collaborating Parties:
Prof Manogari Chetty – Dentistry Faculty, UWC.

Nature and Purpose:
We aim to utilise bioinformatics tools to analyse the genetic basis of some of the syndromes observed in the dental clinics.

Output for the last 12 months:
Work on osteogenesis Imperfecta presented at the South African Bioinformatics Society Conference

RESEARCH LABORATORY OF RUBEN CLOETE

HIGHLIGHTS OF THE LAB

In 2018, two students have joined my research lab:
Mr Darren Isaacs - MSc in Bioinformatics funded by the NRF Research Chair.
Miss Rumbie Chitongo - MSc in Bioinformatics funded by the Poliomyelitis Research Foundation.

RESEARCH PROJECTS

My primary research interests focus on understanding drug resistance in *Mycobacterium tuberculosis* and Human Immune deficiency virus (HIV-1) integrase protein and the identification of causal variants in Parkinson's disease development. Tuberculosis and HIV-1 drug resistance is a huge problem in South Africa and calls for the identification of newer drugs to curb the spread of these diseases.

The use of computational methods to speed up the process of drug discovery can reduce the cost and time spent pursuing drugs that later fail in clinical trials. We have developed computational pipelines within my laboratory to interrogate drug targets to screen for drugs that inhibit enzyme targets that can be purchased and tested in vitro for activity against *Mycobacterium tuberculosis*. We also use computational methods to validate mutations and their effects on protein structure and function. This is also very useful to determine if a drug remains within an enzyme active pocket and if the mutation results in reduced binding or no binding. The result of this research may provide improve treatment regimens for South African populations to combat infectious disease and non-communicable diseases like Parkinson's.

RESEARCH COLLABORATIONS

1. Novel drug discovery against Mycobacterium tuberculosis

Collaborating Parties:
Prof Alan Christoffels – SANBI, UWC
Dr Melanie Grobbelaar – US
Prof Samantha Samson – US.

Nature and purpose:
To identify drugs with a new mode of action against Mycobacterium tuberculosis protein targets.

Output in the last 12 months:
Two compounds showed activity against *Mycobacterium tuberculosis* at 50microMolar concentrations.

Future Direction:
Rv2421c and Rv1311 Manuscripts in preparation.

2. Structural impact of resistance associated mutations in the South African HIV-1C integrase protein

Collaborating Parties:
Dr Graeme Jacobs – US.

Nature and purpose:
Firstly, to understand genetic diversity in HIV-1 subtype C integrase gene in South African HIV-1 infected patients. Secondly, to determine if second-line integrase inhibitors will be a viable option for South African patients infected with HIV-1 subtype C.

Output in the last 12 months:
Brado, D., Obasa, A. E., Ikomey, G. M., Cloete, R., Singh, K., Engelbrecht, S., Neogi, U., Jacobs, G. B. (2018). Analyses of HIV-1 integrase sequences prior to South African national HIV-treatment program and available of integrase inhibitors in Cape Town, South Africa. Scientific Reports, 8(1), 4709. PMID: 29549274, PMC5856838.

Future Direction:
Two more manuscripts in preparation.

3. Prioritising mutations identified in South African Parkinson's disease patients using structural methods

Collaborating Parties:
Prof Soraya Bardien – US.

Nature and purpose:
To identify novel genes associated with Parkinson's disease development using Whole Exome sequencing and using structural computational methods to understand the impact of mutations on protein structure and function.

Output in the last 12 months:
None

Future Direction:
Manuscript in preparation.

4. Identification of Mycobacterium tuberculosis efflux pump inhibitors

Collaborating Parties:
Profs Sarel Malan and Jacques Joubert – School of Pharmacy, UWC
Miss Erika Kapp – School of Pharmacy, UWC.

Nature and purpose:
To identify alternative drugs to verapamil and piperine to inhibit *Mycobacterium tuberculosis* efflux pump Rv1258c and restore sensitivity of *Mycobacterium tuberculosis* to Rifampicin.

Output in the last 12 months:
Ten Compounds identified and purchased for synergism assays and one publication.
Cloete R, Kapp E, Joubert J, Christoffels A, Malan S. (2018). Molecular modelling and simulation studies of the *Mycobacterium tuberculosis* multidrug efflux pump protein Rv1258c. PloS One

Future Direction:
Additional manuscripts in preparation.

RESEARCH LABORATORY OF JUNAID GAMIELDIEN

HIGHLIGHTS OF THE LAB FOR 2018:

- Publication of the exome sequencing based findings ending the diagnostic odyssey in a Miyoshi myopathy family having symptomatic individuals in the second generation
- PLoS ONE publication of a whole exome study defining molecular signatures of Achilles tendinopathy and ACL ruptures
- Used whole genome sequencing to identify a likely oligenic mechanism in an individual displaying a complex phenotype of lower and upper motor neuron dysfunction and sensory neuropathy masquerading as limb-girdle muscular dystrophy

RESEARCH PROJECTS

1. Graph knowledgebases for disease genomics

Our oldest project, the BioOntological Graph Relationship (BORG) database, assimilates and integrates multiple disparate sources of genomic and biomedical knowledge and metadata into a unified knowledge graph. We have successfully used it to model and learn the phenotypic features and molecular mechanisms associated with diseases as a means to rapidly prioritise novel candidates identified in genomics studies. The system simulates search paradigms, cognitive processes and biological 'rules' applied by clinical geneticists and biomedical researchers when filtering candidates. The knowledgebase has proven especially useful in our Next Generation Sequencing (NGS) work focused on tendinopathy.

2. Development of an NGS diagnostic framework for atypical diabetes

Among the monogenic forms of diabetes mellitus (DM), Mature Onset Diabetes of the Young (MODY), which has an age of onset of less than 25 years, has been the most intensively investigated in recent years. MODY is a group of clinically heterogeneous, often non-insulin-dependent forms of DM that are defined at the molecular genetic level by deleterious mutations in different genes. As it is estimated that up to 80% of MODY cases go undiagnosed and therefore sub-optimally treated, we have developed a whole exome sequencing (WES) based monogenic diabetes diagnostic workflow and have identified candidate mutations in South African patients, several of which are not in typical MODY genes.

3. Exome and genome sequencing for discovery of candidate causative variants in human diseases

We have several disease NGS projects that benefit from customised versions of our variant discovery pipelines and BORG database:

- Muscular dystrophy
- Motor neuron disease/ALS
- Unknown neuromuscular disorders
- Achilles tendinopathy and cruciate ligament ruptures

4. Transcriptomics profiling to identify circulating biosignatures

- For detection of smoke inhalation injury in burns victims
- For early prediction of likely rapid progressors in cystic fibrosis patients

5. Machine Learning

We apply established machine learning algorithms and latest advances in artificial intelligence approaches to high-value publicly available big biomedical data establish models classification and prediction. Both supervised and unsupervised learning approaches are used to identify features and patterns that can be used to predict clinical endpoints and also potentially novel pathways/networks that contribute to a phenotype of interest. Existing work that has reached a degree of maturity include the use of microarray and RNA sequencing data from repositories such as The Cancer Genome Atlas and the Gene Expression Omnibus to develop models capable of predicting e.g. rate of disease progression and survival in glioblastoma and disease subtype in breast cancer. We are expanding our research to include the use of Computer Vision and Deep Neural Networks to build predictive/explanatory models from both omics and biomedical imaging data.

RESEARCH COLLABORATIONS

1. Exome sequencing of sporadic flail arm ALS

Collaborating Parties:

Dr Mahjoubeh Jalali – Pacific North West Research Institute, Seattle, USA
Prof Jeanine Heckmann – UCT

Nature and Purpose:

To identify causative variants in unrelated but similar cases of flail-arm amyotrophic lateral sclerosis.

Output in the last 12 months:

Participants have been exome sequenced and we are using an ensemble variant discovery approach to identify variants that are likely causative. We are also surveying each exome for the possible presence of structural variation such as copy number variants.

Future Direction:

Genes bearing candidate single nucleotide and short truncating variants are currently being evaluated using a BORG model of motor neuron disease, after which we will verify prior evidence supported candidates using Sanger sequencing. We will search for opportunities to apply the lessons learned and technology developed to data from unsolved ALS cases in public repositories.

2. Exome sequencing in a case of a complex phenotype of lower and upper motor neuron dysfunction and sensory neuropathy masquerading as limb-girdle muscular dystrophy (LGMD)

Collaborating Parties:

Dr Mahjoubeh Jalali – Pacific North West Research Institute, Seattle, USA
Prof Jeanine Heckmann – UCT

Nature and Purpose:

To use whole genome sequencing to identify candidate causative variants in a seemingly atypical case of LGMD.

Output in the last 12 months:

We have applied our filtering approach to a) rule out calpainopathy and b) identify several strong candidate mutations in multiple genes, which suggests that the inheritance mechanism is complex and oligogenic.

Future Direction:

Candidate variants have been confirmed by Sanger sequencing in the proband parents and an unaffected sibling and a manuscript is in preparation.

3. Exome sequencing of atypical diabetes

Collaborating Parties:

Dr Mahjoubeh Jalali – Pacific North West Research Institute, Seattle, USA
Prof Alison September (co-PI) and Prof Naomi Levitt - UCT

Nature and Purpose:

To test an exome-sequencing approach to identifying causative mutations in patients suspected of having mature onset diabetes of the young (MODY).

Output in the last 12 months:

Cases of possible MODY have been exome sequenced and likely pathogenic mutations have been identified and Sanger verified in several patients. Several are in genes that may be linked to glucose homeostasis, but not to MODY.

Future Direction:

Manuscript is in preparation.

4. Identification of genetic biomarkers for risk for musculoskeletal soft-tissue injuries (MSI)

Collaborating Parties:

Dr Colleen Saunders, Prof Alison September and Prof Malcolm Collins - UCT

Nature and Purpose:

To identify candidate Achilles tendinopathy susceptibility genes and variants by comparing whole exome sequences of individuals with severe soft-tissue injuries phenotypes and healthy physically active controls.

Output in the last 12 months:

Manuscript published in PLoS ONE.

Future Direction:

Additional manuscripts in preparation.
Further analysis of the exome data to identify larger structural variants.

5. Identification of signatures of circulating miRNAs predictive of smoke inhalation injury in burn victims

Collaborating Parties:

Dr Kareemah Gamieldien (PI) - Cape Peninsula University of Technology
Dr Wayne Kleintjies - Head of the Tygerberg Hospital Burns Unit

Nature and Purpose:

To identify microRNAs in blood that may be used in the early diagnosis of smoke inhalation related lung injury in burn victims.

Output in the last 12 months:

Sample collection has been completed.

Future Direction:

Small RNAs will be isolated from blood of patients meeting the clinical criteria and will be used for miRNA profiling.

6. Identification of signatures for prediction of treatment-linked survival of cancer patients

Collaborating Parties:

Dr Azeez Fatai – SANBI, UWC

Nature and Purpose:

To build reusable machine learning tools for identifying predictive and prognostic signatures in omics data generated from cancer patients.

Output in the last 12 months:

A manuscript reporting a 35-gene signature discriminating between rapidly- and slowly-progressing glioblastoma multiforme and predicts survival was published in BMC Cancer. Progression-free and overall survival independently of other factors considered.

Future Direction:

We will continue to refine the approach and apply it to available data from other cancers in the public repositories.

RESEARCH LABORATORY OF RAVNIT GREWAL

Research forms a solid academic platform in a tertiary teaching unit and is an integral component of a medical specialist. It is with this belief that I recently joined SANBI in order to pursue my desire to develop and work with a scientific team that will focus on cutting edge health related research in keeping with international trends.

As a Haemato-Pathologist my primary research interest is in HIV related lymphomas. As a consequence of this enquiry, I spearheaded a research group that studied lymphomas as it became evident that we were experiencing a surge in HIV associated complex lymphoma pathology in our laboratory.

As people with HIV on Antiretroviral treatment live longer, research nationally and internationally has demonstrated a rise in certain lymphomas that occur as a consequence of infection with HIV, amongst other pathogenetic mechanisms. Understanding the pathophysiology of these lymphomas in our population specifically is of paramount importance as oncology management practices move towards targeted therapy.

Thus and in keeping abreast with current international research I aim to investigate the role of Precision/Personalised Medicine in Pathology, specifically focusing on the detection of biomarkers for diagnosis, prognostication and management of HIV related lymphomas in South Africa and other African countries.

The way forward in this type of research will be with new collaborations and the use of bioinformatics data to carry out larger scale OMIC research.

RESEARCH COLLABORATIONS

1. Precision medicine and HIV related lymphomas

Collaborating Parties:
Prof Phillip Jermann - Basel University, Institute of Medical Genetics and Pathology
Prof Ciprian Tomuleasa - Iuliu Hatieganu University of Medicine and Pharmacy, Cluj Napoca, Romania
Prof Jonathan Fromm - University of Washington, Seattle, WA, USA

Nature and purpose:
Basel University, Basel, Switzerland: I had the privilege of visiting this institution and meeting with the director of the Molecular Pathology, Dr Philip Jermann, establishing them as our benchmark laboratory for the research that we aim to focus on.

University of Medicine and Pharmacy Cluj Napoca Romania: I have a long-standing collaboration with Prof Ciprian Tomuleasa as we share common interests as haematologists.
We have worked on several projects related to HIV related lymphomas and will therefore continue with this collaboration.

University of Seattle, Washington, USA: Prof Jonathan Fromm is a world authority in flow cytometry of lymphomas. I recently had the honor of publishing a paper on the use of flow cytometry in the diagnosis of Hodgkin lymphoma with Prof Fromm. The incidence of Hodgkin lymphoma has increased in HIV positive patients internationally and in South Africa, hence our shared interest.

Output in the last 12 months:
2 publications and a poster presentation.

Future Direction:
International research in oncology practice is in precision/personalised medicine. In haematology, the 2016 WHO classification update of lymphoid malignancies includes several new entities which are based on molecularly profiling patients. This approach of diagnoses will affect current treatment paradigms and provide a framework for future clinical trials in targeted therapy. Using this mode of therapy however, requires acquiring adequate biopsy specimens, efficient diagnostics and expert pathology review so that the most appropriate combination of drugs are used. Additionally, this ensures accurate conclusions of the drugs being tested and hence the results of the clinical trials. It is therefore incumbent on the treating physicians and pathologists in South Africa to understand these changes. Furthermore it is also our responsibility as Medical specialists to focus our research on prevalent malignancies in this country. The ultimate aim of this research is to offer the most appropriate management options for our population based on our research outcomes.

RESEARCH LABORATORY OF GORDON HARKINS

My research primarily focuses on the evolution and molecular epidemiology of single-stranded DNA and RNA viral pathogens of humans other animals and plants. I seek to computationally determine the evolutionary underpinnings of the emergence and spread of the numerous viral diseases that seriously threaten the health and food security of Africa and the rest of the developing world.

HIGHLIGHTS OF THE LAB:

Six manuscripts were submitted for publication in 2018 four of which were published within the calendar year and the remaining two are under peer review in the journals PLoS Pathogens and the Journal of Virology respectively. A summary of some of the research projects that I have been involved in during a year long sabbatical in 2018 is presented below.

HUMAN-INFECTING VIRAL PATHOGENS

Human immunodeficiency virus

In collaboration with researchers from the University of KwaZulu Natal and UCT we have received funding from the Sub-Sahara Africa Network for TB-HIV Research Excellence (SANTHE) to computationally reconstruct, the early spatio-temporal history of the HIV-1M epidemic in order to i) better understand the evolutionary dynamics of HIV-1M before the onset of the global pandemic and ii) elucidate the factors that mediated the emergence of this important human pathogen. Such an understanding could be crucial both for retracing the earliest evolutionary steps during the emergence of HIV-1M in humans, and accurately reconstructing the ancestral sequences of the major contemporary circulating HIV-1M lineages.

In collaboration with researchers from New York University School of Medicine, Johns Hopkins University and the University of KwaZulu-Natal, South Africa among others; we studied four HIV-1+ Cameroonian individuals, three of them epidemiologically linked in a polygamous heterosexual relationship and one incidence-matched case, over 15 years for heterologous and cross-neutralizing antibody responses, antibody binding, IgA/IgG levels, antibody-dependent cellular cytotoxicity (ADCC), viral epitopes and evolution, and host factors including HLA-I alleles to determine whether correlates of protection are associated with clinical outcome in natural infection.

PLANT-INFECTING VIRAL PATHOGENS

Virulence Evolution

This is a long-term collaborative effort to investigate how the traits of virulence and transmission rates are evolving in viral pathogens important to human health. Using a combination of laboratory experimentation and state-of-the-art computational analyses, we are investigating the spatiotemporal dynamics and evolution of a broad range of viral pathogens focusing primarily on viruses that cause important crop diseases (Maize Streak Disease, Cassava Mosaic Disease and Tomato Yellow Leaf Curl Disease). Collectively, these studies are aimed

at improving our understanding of the different life history strategies of pathogens, including reproduction, migration between and within hosts and virulence. By explicitly connecting our pathogenicity and virulence measurements to the natural history of the pathogen, we are confident this will provide a broader perspective on the evolution of pathogens for which current findings are mainly limited to theoretical or experimental settings.

Viral Emergence

In collaboration with researchers from CIRAD France, the State University of Arizona and UCT, we have adopted a "geo-metagenomics" approach to investigate whether ecological disturbances such as intensive agriculture, cause measureable changes in the spatial and temporal diversity, demographics and evolutionary dynamics of viral communities inhabiting natural ecosystems that are linked to the emergence of socially- relevant crop-infecting geminiviral diseases. Our study population is the fynbos ecosystem situated in the Western Cape region of South Africa – a biodiversity hot-spot which is extremely threatened by increasing human population densities, urbanisation and agriculture. To complement the data on contemporary viral diversity derived from field studies, we are sequencing "ancient" viral genomes present in fynbos plant specimens stored within French and South African herbaria to more accurately estimate when and where, key ancestral plant viruses existed. By producing infectious clones of both these ancient genomes and re-synthesised computationally inferred ancestral genomes, it will be possible to pinpoint when and where over the past few centuries, major changes in virus virulence have occurred. It is hoped that this project will complement the results obtained from our previous work on virulence evolution in Maize streak virus and increase our understanding of the evolutionary and epidemiological processes by which members of this important group of crop pathogens (i) emerged during the colonisation era from their indigenous African hosts, (ii) began causing diseases in crop species introduced by Europeans and (iii) disseminated across the continent from sites of initial emergence to become what are today among the most important biotic threats to African food security.

RESEARCH COLLABORATIONS

1. HIV-1 Recombinants and Epidemiologically Important Subtypes in Africa and Abroad

Collaborating Parties:
Marcel Tongo, Jeffrey R. Dorfman, Tulio de Oliveira - University of KwaZulu Natal.
Darren P. Martin – UCT.

Nature and purpose:
To reconstruct the evolutionary dynamics of HIV-1M before the onset of the global pandemic we analysed all published subtype A near full length sequences together with subtype-A derived genome fragments from 22 different Circulating Recombination Forms (CRFs) using Bayesian spatial diffusion models.

Output in the last 12 months:
An article was published in the journal Virus Evolution in January 2018.

Future Direction:
To investigate the other HIV-1 group M subtypes using a similar analytical approach and perform a comparative analyses with subtype A.

2. Immune Correlates of Disease Progression in Linked HIV-1 Infection

Collaborating Parties:
Ralf Duerr Michael Tuen, Jude S. Bimela, Andrew N. Banin; Sonal Soni; Luzia Mayr; Aubin J. Nanfack; Miroslaw K. Gorny and Phillipe N. Nyambi - New York University School of Medicine, New York, New York, USA.
Jude S. Bimela; Judith N. Torimiro - University of Yaoundé, Yaoundé, Cameroon.
Shilei Ding - Centre de Recherche du CHUM, and Université de Montréal, Montréal, QC, Canada.
Vincenza Itri - Icahn School of Medicine at Mount Sinai, New York, USA.
Allison R. Durham - National Institutes of Health-National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, USA.
Stephen F. Porcella - Rocky Mountain Laboratories, Division of Intramural Research, NIAID, NIH, Hamilton, Montana, USA.
Josephine Meli - Yaoundé General Hospital, Yaoundé, Cameroon.
Marcel Tongo - Institute of Medical Research and Study of Medicinal Plants (IMPM), Yaoundé, Cameroon and Nelson R Mandela School of Medicine, University of KwaZulu-Natal, South Africa.

Xiaohong Wang - Veterans Affairs New York Harbor Healthcare Systems, New York, USA.

Xiang-Peng Kong - Arthur Nádas New York University School of Medicine, New York, USA.

Daniel E. Kaufmann - The Scripps Research Institute, La Jolla, California, USA.

Zabrina L. Brumme - Simon Fraser University, and British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, Vancouver, Canada. Thomas C. Quinn; Andrew D. Redd -Department of Medicine, Johns Hopkins University, Baltimore, USA.

Andrés Finzi - McGill University, Montréal, Canada.

Nature and purpose:
To determine whether correlates of protection are associated with clinical outcome in natural HIV-1 infection in epidemiologically linked individuals.

Output in the last 12 months:
One manuscript has been submitted for publication in PLoS Pathogens that at the time of writing, is under peer review.

Future Direction:
Conduct similar studies involving additional viral subtypes, host, and immune parameters to determine whether the clinical correlation patterns observed in our study are generally applicable and in what extent they mirror correlates of protection in vaccine settings.

3. Virulence Evolution

Collaborating Parties:
Philippe Roumagnac - CIRAD, Montpelier, France.

Darren P. Martin, Adérito Luis Monjane, Dionne Natalie Shepherd - UCT, South Africa.

Philippe. Lemey and Simon Dellicour - Katholieke Universiteit, Leuven, Belgium.

Pierre Lefeuvre and Jean-Michel Lett - CIRAD, Reunion Island.

Arvind Varsani - University of Canterbury, Christchurch, New Zealand.

Nature and purpose:

We have received funding from the National Research Foundation (NRF) to investigate how the traits of virulence and transmission rates are evolving in viral pathogens important to human health. Using a combination of laboratory experimentation and state of-the-art computational analyses, we are investigating the spatiotemporal dynamics and evolution of a broad range of viral pathogens focusing primarily on viruses that cause important crop diseases (MSD, CMD and TYLCD).

Output in the last 12 months:
One manuscript will be submitted for publication in early 2019.

Future Direction:
None

4. Molecular Mechanisms of Viral Emergence

Collaborating Parties:
Pauline Bernardo, Sarah François, Maëlle Deshoux, Denis Filloux, Emmanuel Fernandez, Serge Galzi, Romain Ferdinand, Martine Granier, Michel Peterschmitt and Philippe Roumagnac - CIRAD-INRA-SupAgro, Montpellier, France.

Brejnev Muhire, Darren P. Martin - UCT, South Africa.

Simona Kraberger, Arvind Varsani - University of Canterbury, Christchurch, New Zealand.

Anna-Liisa Laine, Mikko J. Frilander - University of Helsinki, Finland.

Armelle Marais, Thierry Candresse - INRA, UMR Villenave d'Ornon Cedex, France.

Pablo Monge, Fernando Escriu - Unidad de Sanidad Vegetal Zaragoza, Spain.

Nature and purpose:
To investigate whether ecological disturbances such as intensive agriculture, cause measureable changes in the spatial and temporal diversity, demographics and evolutionary dynamics of viral communities inhabiting natural ecosystems that are linked to the emergence of socially-relevant crop-infecting geminiviral diseases such as Tomato yellow leaf curl disease (TYLCD), Maize streak disease (MSD) and Cassava mosaic disease (CMD).

Output in the last 12 months:
A manuscript was published in the ISME journal Nature in 2017 and a further three publications in the scientific journals Viruses, the Archives of virology and Advances in virology were obtained in 2018.

Future Direction:
The rate of discovery of "emergent" viruses has increased over the past two decades. However, it remains difficult to determine whether these viruses are truly emergent, or, if they have simply remained undetected until now. We have shown that one such plant-infecting single-stranded DNA geminivirus species named Euphorbia caput medusae latent virus

displays a high prevalence in samples of the wild spurge Caput medusae collected between Cape Town and Paternoster on the west coast of South Africa is related to other newly discovered species that cause severe infections in French beans in India and alfalfa in France.

5. Viral dynamics

Collaborating Parties:

Alexandre De Bruyn, Mireille Harimalala, Innocent Zinga, Murielle Hoareau, Bernard Reynaud, Jean-Michel Lett and Pierre Lefeuvre - CIRAD, Reunion Island.

Arvind Varsani and Matthew Walters - University of Canterbury, Christchurch, New Zealand.

Darren P. Martin - UCT, South Africa.

Virginie Ravigné - CIRAD, Montpellier, France.

Simona Kraberger - Colorado State University, Fort Collins, USA.

Andrew D.W. Geering, Sharonvan Brunschot and John E. Thomas - University of Queensland, Brisbane, Australia

Kaveh Bananej - Iranian Research Institute of Plant Protection (IRIPP), Iran

Nature and purpose:

To apply recombination analyses and Bayesian phylogeographic inference methods to all available MSV viral sequences and reconstruct a plausible history of ongoing diversification and movements throughout the southern hemisphere with a specific focus on its introduction(s) into Madagascar.

Output in the last 12 months:

None

Future Direction:

In 2017 we secured funding from the National Research Foundation to collect and sequence "ancient" viral genomes present in fynbos plant specimens stored within French and South African herbaria to more accurately estimate when and where, key ancestral plant viruses existed.

6. Endogenous Viral Elements (EVE's)

Collaborating Parties:

Philippe Roumagnac, Denis Filloux and Emmanuel Fernandez - CIRAD, Montpelier, France.

Darren Martin – UCT.

Véronique Jamilloux, Florian Maumus - INRA, URGI, Versailles, France.

Pierre-Yves Teycheney - CIRAD, UMR AGAP, Guadeloupe, France.

Pierre Lefeuvre and Jean-Michel Lett - CIRAD, UMR PVBMT, Réunion Island, France.

Thierry Candresse, Armelle Marais, Sébastien Theil and Chantal Faure - INRA, UMR BFP, Villenave d'Ornon France.

Andrew Geering - the University of Queensland, Australia.

Nature and purpose:

To study endogenous viral elements (EVE's) and their role in virus evolution and their functions in plants to address fundamental biological issues that are critical to the understanding of plant virus evolution and the contribution of plant viruses to both the host genome evolution and biology. This involves approaches in virology, bio-informatics, genomics, proteomics, evolution and synthetic biology, and aims at disentangling key mechanisms of adaptive plasticity of plant and viral genomes such as gene domestication, genetic and epigenetic regulation of plant gene expression and deciphering mechanisms that are central to molecular plant-virus interactions such as recombination, transcriptional or post transcriptional gene silencing.

Output in the last 12 months:

None

Future Direction:

We received funding to support this research from the French National Research Foundation (ANR) in December 2017 and have begun generating data. An initial meeting of all of the major stakeholders was held at CIRAD Réunion Island in September 2017 and a second meeting/ workshop, was scheduled to be held at SANBI in December 2018 to assess the progress made after one year.

RESEARCH LABORATORY OF SIMON TRAVERS

HIGHLIGHTS OF THE LAB

2018 was an excellent year for my research group. We primarily focused on converting a number of years of research into software solutions capable of undertaking DNA-based diagnostics at scale. We now have a complete solution that is capable of enabling next-generation sequencing-based TB drug susceptibility testing. This solution was finalised during early 2018 with the remainder of the year focusing on validation studies.

Further, 2018 saw the completion of our Sanger sequencing based HIV drug resistance reporting software and its incorporation into the Exatype drug resistance testing platform. As well as sample-specific analysis capabilities we have now added quality control and genetic distance measures to the software bringing it to full conformity to the World Health Organisation (WHO) drug resistance testing protocols. In August 2018 we took part in a training workshop with the US Centers for Disease Control (CDC) in Addis Ababa, Ethopia training national laboratories from all over Africa in HIVDR testing. This solution has now been integrated into the Clinton Health Access Initiative's (CHAI) NASCOP system in Kenya with the first samples being processed in the final quarter of the year. This milestone means that from early 2019 our solution will be used at scale at a national level in Kenya with plans to roll this out globally.

2018 was also a productive year for the HIV vaccine projects. Two students, Roux-Cil Ferreira and Phillip Labuschagne, have completed their theses and these are under examination and both of the students are hoping to graduate in early 2019.

RESEARCH PROJECTS

1. The development of computational approaches for highly sensitive analysis of next-generation sequencing (NGS) data.

One of the biggest challenges with NGS is the complexity involved in the analysis of the data. This is particularly difficult for infectious diseases, such as HIV, where it is important to be able to identify pertinent mutations in the infection in the presence of a lot of noise introduced by sample preparation and the sequencing process.

Following on from the launch of Exatype for HIV drug resistance testing in 2016, 2017 focused on the expansion of Exatype to support TB drug susceptibility testing. Exatype for HIV involves mapping sequence data to a single coding region of the HIV genome, while expansion to TB meant that we needed to expand our algorithms to be able to call mutations in both coding and non-coding DNA. This was successfully achieved in 2017 meaning that the Exatype platform is now capable of mapping sequence reads to multiple reference sequences in parallel thereby enabling the accurate, fast analysis of both whole genome and targeted sequencing data.

2017 saw the completion of the underlying database and internal communication protocols to enable the transfer of Exatype outputs into a real-time drug resistance surveillance solution. The next body of work involves the development of analytics and reporting solutions that will mine the underlying database in order to provide end-users with an easy to use surveillance solution.

2. The use of high-throughput sequencing approaches to explore viral and host diversity.

Our work on developing a data analysis pipeline for undertaking sieve analysis to explore the mechanism of viral evasion of vaccine-induced immune pressure focused on the characterisation of recombination in primer ID data. Such data enables the comparison of HIV-1 sequences from vaccine-experienced and vaccine-naïve individuals and allows attribution of vaccine-versus-placebo viral genetic signatures to vaccination. PCR-induced recombination during the sample preparation step, however, can introduce errors into the estimates. We have developed an approach to identify the presence of recombination and minimise the effect that such data would have on analysis.

3. The application of molecular dynamics approaches to characterise the viral epitopes of broadly cross-clade neutralising (BCN) antibodies with a view to identifying novel targets for HIV vaccine design.

The HIV-1 'glycan shield' - the sugars that form a dense layer on the viral surface protein, Envelope - is not only important for its protective qualities but is also a key focus in vaccine research. In recent years, various studies have identified specific glycans that are essential components of broad and potent neutralising antibody epitopes; laboratory experiments have therefore focused on editing the glycan shield in such a way to create, or expose, a glycan-dependent epitope that would increase its sensitivity to neutralisation antibodies. The current understanding is that the removal of a glycan, or a cluster of glycans, creates a gap in the glycan shield, thereby allowing antibodies to bind and neutralise the virus. Our research over the last year has focussed on describing the mechanism by which this happens, and we have presented evidence, beyond the glycan hole/gap view, on how the glycan shield can rearrange to compensate for the loss of a glycan and escape antibody neutralisation. We have carried out a detailed investigation of two different HIV-1 Envelope glycoproteins, using computational molecular dynamics simulations, and show how the loss of a single glycan results in distinct conformational changes of the remaining glycans that form the glycan shield. To our knowledge, this is the first report of how a ripple effect occurs across the surface of the protein when the glycan shield is disrupted, and how this ripple effect is dependent on the original composition of the glycan shield. Our research provides an in-depth description of both the direct and indirect effects of the loss of a specific glycan from two different HIV-1 Envelope glycoproteins, where a series of movement and interaction events has a unique influence on the integrity of an epitope located far from the original mutation. Thus, our work presents novel considerations for laboratory scientists focussing on eliminating or exposing glycan-associated HIV-1 Envelope epitopes.

RESEARCH COLLABORATIONS

1. The role of N-linked glycosylation in the escape of HIV from, and susceptibility to, neutralizing antibodies.

Collaborating Parties:

Dr Oliver Grant, Prof Robert Woods - University of Georgia
Dr Elisa Fadda - Maynooth University, Ireland
Prof Penny Moore - NICD, South Africa
Dr Jeffrey Dorfman, Dr Natasha Wood - UCT

Nature and purpose:

As part of the post-translational processing of a HIV virion carbohydrates are added to the surface of the virion by the hosts glycosylation mechanism. The binding of such N-linked glycans conveys protection to a virion's surface proteins by acting as a shield to avoid detection by the host's immune system. These carbohydrates, however, may comprise a novel target for HIV therapeutics and we are using molecular dynamic simulations to further understand the conservation and dynamics of these carbohydrates and their effect on the accessibility of the underlying protein.

Output in the last 12 months:

Colin Anthony, Talita York, Valerie Bekker, David Matten, Philippe Selhorst, Roux-Cil Ferreria, Nigel J Garrett, Salim S Abdool Karim, Lynn Morris, Natasha T Wood, Penny L Moore, Carolyn Williamson (2017) Cooperation between strain-specific and broadly neutralizing responses limited viral escape and prolonged the exposure of the broadly neutralizing epitope. Journal of Virology 91, 18 (e00828-17)

Thandeka Moyo, Roux-Cil Ferreira, Reyaaz Davids, Zarinah Sonday, Penny L Moore, Simon A Travers, Natasha T Wood, Jeffrey R Dorfman Chinks in the armor of the HIV-1 Envelope glycan shield: Implications for immune escape from anti-glycan broadly neutralizing antibodies (2017) Virology501 (12-24).
Poster presentation at the 24th HIV Dynamics and Evolution meeting – Using molecular dynamics to illustrate the changes in the glycan shields of two HIV-1 envelope trimers after the loss of a glycan.

Future Direction:
This work will continue to focus on studying the effects of glycan addition/removal on the underlying structure of the glycan shield.

2. Development and application of next-generation sequencing for HIV drug resistance genotyping.

Collaborating Parties:
Prof Maria Papathanasopolous - University of the Witwatersrand
Dr Robert Shafer - Stanford University

Nature and purpose:
Next-generation sequencing holds great promise for low-cost, highly scalable HIV drug resistance genotyping but there are a number of hurdles that need to be addressed before these approaches can be used routinely in a clinical setting. We are working on a number of projects with our collaborators to explore the optimal approach to produce and analyse NGS data for HIV drug resistance genotyping.

Output in the last 12 months:
Oral presentations at a number of national and international meetings.
Signature of a contract for use of the Exatype HIV drug resistance testing pipeline through the spinoff company Hyrax Biosciences.

3. Using next-generation sequencing to explore the diversity of the HIV viral quasispecies.

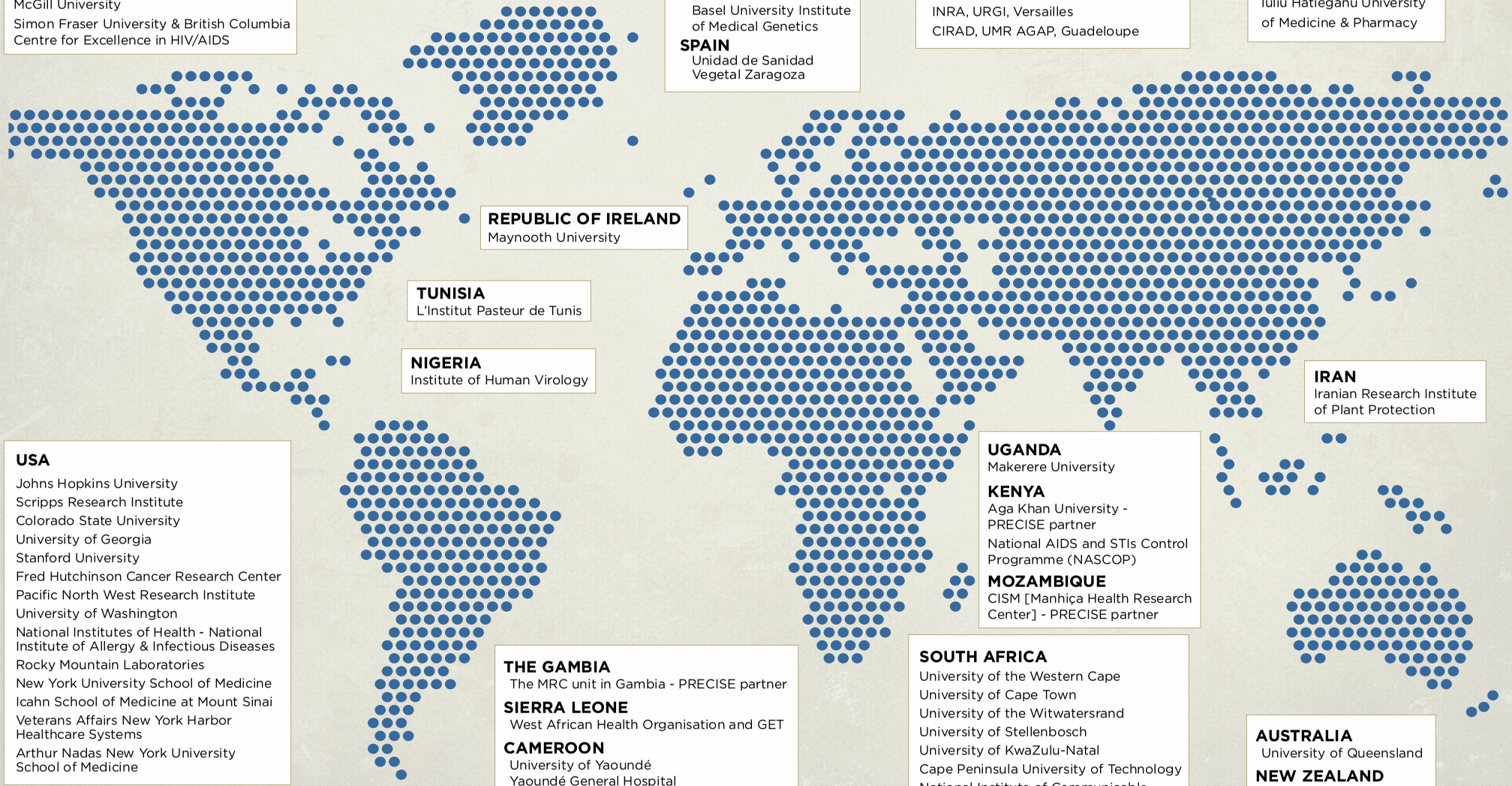
Collaborating Parties:
Prof Lynn Morris - NICD, South Africa
Prof Carolyn Williamson - UCT, South Africa
Dr Paul Edlefsen - Fred Hutchinson Cancer Research Center, Seattle The HIV vaccine trials network (HVTN)

Nature and Purpose:
We are involved in a number of research projects that are harnessing the power of NGS
to enable us to fully understand the diversity of the viral quasispecies in HIV infected individuals. The vast majority of this work is focused on the identification of the potential of individuals to produce broadly cross-neutralising antibodies as well as exploring the viral diversity of breakthrough infections following vaccination with HIV vaccine candidates.

Future Direction:
This pipeline will continue to be developed to support the analysis of data originating from a number of HIV vaccine trails being undertaken in South Africa.

Collaborations

SANBI researchers have established a vast network of partnerships and collaborations with peers all over the world.



CANADA
Centre de Recherche du CHUM
Université de Montréal
McGill University
Simon Fraser University & British Columbia Centre for Excellence in HIV/AIDS

BELGIUM
Katholieke Universiteit

FINLAND
University of Helsinki

SWITZERLAND
Basel University Institute of Medical Genetics

SPAIN
Unidad de Sanidad Vegetal Zaragoza

FRANCE
CIRAD, Montpelier
CIRAD-INRA-SupAgro, Montpellier
INRA, UMR Villenave d'Ornon Cedex
INRA, URGI, Versailles
CIRAD, UMR AGAP, Guadeloupe

ROMANIA
Iuliu Hatieganu University of Medicine & Pharmacy

REPUBLIC OF IRELAND
Maynooth University

TUNISIA
L'Institut Pasteur de Tunis

NIGERIA
Institute of Human Virology

IRAN
Iranian Research Institute of Plant Protection

USA
Johns Hopkins University
Scripps Research Institute
Colorado State University
University of Georgia
Stanford University
Fred Hutchinson Cancer Research Center
Pacific North West Research Institute
University of Washington
National Institutes of Health - National Institute of Allergy & Infectious Diseases
Rocky Mountain Laboratories
New York University School of Medicine
Icahn School of Medicine at Mount Sinai
Veterans Affairs New York Harbor Healthcare Systems
Arthur Nadas New York University School of Medicine

UGANDA
Makerere University

KENYA
Aga Khan University - PRECISE partner
National AIDS and STIs Control Programme (NASCOP)

MOZAMBIQUE
CISM [Manhiça Health Research Center] - PRECISE partner

THE GAMBIA
The MRC unit in Gambia - PRECISE partner

SIERRA LEONE
West African Health Organisation and GET

CAMEROON
University of Yaoundé
Yaoundé General Hospital
Institute of Medical Research and Study

IVORY COAST
Institut Pasteur

SOUTH AFRICA
University of the Western Cape
University of Cape Town
University of the Witwatersrand
University of Stellenbosch
University of KwaZulu-Natal
Cape Peninsula University of Technology
National Institute of Communicable Diseases
HIV Vaccine Trials Network
Tygerberg Hospital

AUSTRALIA
University of Queensland

NEW ZEALAND
University of Canterbury

2018 Financials

SANBI's income and expenditure trends for 2018 are shown in this section.

FIGURE 1.
DISTRIBUTION OF INCOME RECEIVED FROM ALL SOURCES 2018.

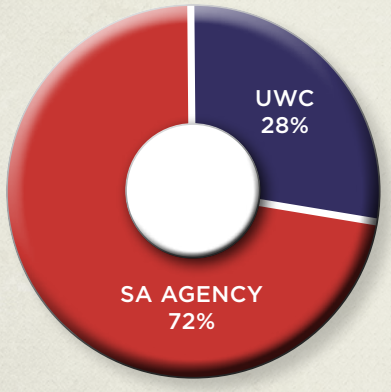


FIGURE 2.
INCOME RECEIVED FROM SA SOURCES.

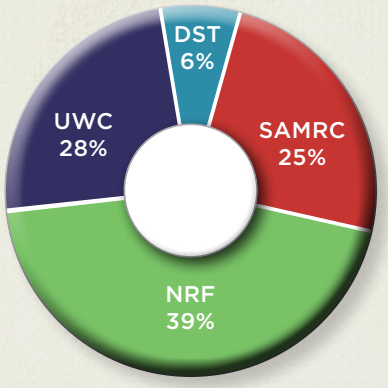


FIGURE 3. INCOME VS EXPENDITURE IN 2010 - 2018.

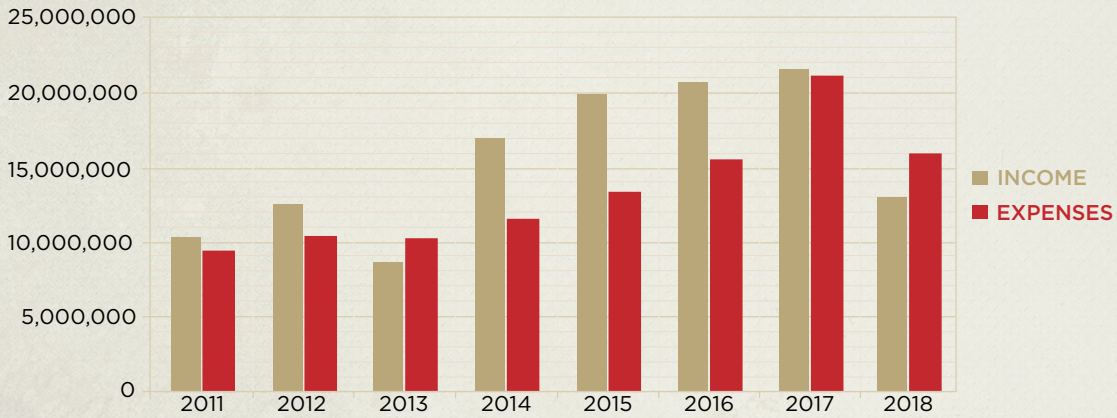
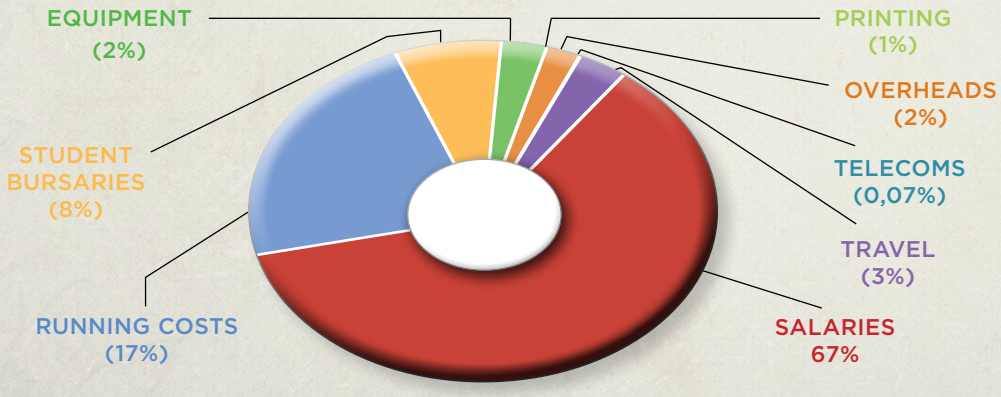


FIGURE 4. EXPENDITURE IN 2018.



Students

POSTDOCTORAL PROGRAMME

IBRAHIM AHMED
Prof Alan Christoffels

DOMINIQUE ANDERSON
Prof Alan Christoffels

JOHANN JOSEF EICHER
Prof Simon Travers

MOHD SHAHBAAZ
Prof Alan Christoffels

RAJAN SHARMA
Prof Alan Christoffels

WESLEY WILLIAMS
Dr Uljana Hesse

**Supervisor in italics*

DOCTORAL PROGRAMME

HOCINE BENDOU

Prof Alan Christoffels

TRACEY CALVERT-JOSHUA

Prof Alan Christoffels

SARAH DERAEDT

Prof Alan Christoffels

SOULEYMANE DIALLO

Prof Alan Christoffels

MMAKAMOHELO DIREKO

Prof Alan Christoffels

ROUX-CIL FERREIRA

Prof Simon Travers

PHILIP LABUSCHAGNE

Prof Simon Travers

BRIDGET LANGA

Dr Junaid Gamieldien

ANATI NKAULE

Prof Alan Christoffels

CATHERINE ROSSOUW

Prof Alan Christoffels

EMILY STANDER

Dr Uljana Hesse

MASTERS PROGRAMME

LYNLEY ABDOLL
Prof Alan Christoffels

PETER ABIODUN
Alan Christoffels

TOLUWALEKE ADEMUYIWA
Prof Alan Christoffels

OLABODE AJAYI
Prof Alan Christoffels

RUMIBIDZAI CHITONGO
Dr Ruben Cloete

EUGENE DE BESTE
Prof Alan Christoffels

FANECHKA ESTERHUYSEN
Dr Junaid Gamieldien

SUSAN ALECIA FERNOL
Prof Alan Christoffels

DARREN ISAACS
Dr Ruben Cloete

YAMKELA MGWATYU
Dr Uljana Hesse

BEN ILUNGA MUTEBA
Dr Uljana Hesse

MUHAMMAD SAEED NATHA
Dr Junaid Gamieldien

JAMIE SOUTHGATE
Prof Alan Christoffels

PETER VAN HEUSDEN
Prof Alan Christoffels

Alumni

STAFF:

Name	Currently
Winston Hide	Chair of Computational Biology, University of Sheffield Adjunct Professor of Bioinformatics and Computational Biology, Harvard School of Public Health, Harvard Stem Cell Institute, Director, HSCI Center for Stem Cell Bioinformatics
Vladimir Bajic	Director & Professor, Computational Bioscience Research Center, King Abdullah University of Science and Technology
Heikki Lehvaslaiho	Senior Research Scientist, Computational Bioscience Research Centre, King Abdullah University of Science and Technology
Tulio de Oliviera	KRISP, Professor
Nicky Mulder	Head Computational Biology Group, Institute of Infectious Disease and Molecular Medicine, UCT
Cathal Seoighe	Stokes Professor of Bioinformatics, School of Mathematics, Statistics and Applied Mathematics, National University of Ireland, Galway
Dale Gibbs	IT Consultant
Samantha Alexander	Administrative Assistant, UCT Faculty of Commerce
Mario Jonas	Data Manager, UCT Computational Biology Group
Nicki Tiffin	Researcher, UCT School of Public Health and Family Medicine
Natasha Schoeman	UWC Student Administration
Long Yi	DevOps Manager, Konga.com

POSTDOCTORAL FELLOWS:

Name	Date Completed	Currently
Soraya Bardien-Kruger	2002	Associate Professor, US
Vladimir Babenko	2002	Senior Staff Scientist, IC&G
Janet Kelso	2004	Max Planck Institute for Evolutionary Anthropology
Raphael Isokpehi	2004	Director of the Center for Bioinformatics & Biology, Jackson State University
Konrad Scheffler	2005	Theodore Gildred Research Facility, University of California, San Diego
Gwen Koning	2006	Global Seed Core Manager – Syngenta Crop Protein AG, Basel, Switzerland
Chris Maher	2007	Assistant Professor, Washington University School of Medicine
James Patterson	2009	
Adam Dawe	2009	
Sunil Sagar	2009	Research Scientist, KAUST
Mandeep Kaur	2009	University of the Witwatersrand School of Molecular and Cell Biology (MCB)
Stuart Meier	2009	Research Scientist, KAUST
Adele Kruger	2010	Wayne State University, Detroit, Michigan

Oliver Hofmann	2010	Affiliated Faculty, Harvard Stemcell Institute, Associate Director at Harvard School of Public Health
Sundarajan Seshadri	2010	Nanyang Technology University, Singapore
Ashley Pretorius	2010	Chief Scientific Officer, Aminotek
Sumir Panji	2012	H3ABioNet Project Manager, UCT
Samson Muyanga	2012	Researcher, Monash South Africa
John Pool	2012	Centre for High Performance Computing
Uljana Hesse	2013	UWC Biotechnology Department
Barbara Picone	2013	Assiciate Editor, Journal of Zoology
Monique Maqungo	2013	Unknown
Edwin Murungi	2013	Department of Biochemistry and Molecular Biology, Egerton University, Njoro, Kenya
Hannah Ajoge	2013	Postdoctoral Fellow, University of Western Ontario, Canada
Natasha Wood	2014	Lecturer, UCT Computational Biology Department
Sarah Mwangi	2016	Postdoctoral Fellow, University of Pretoria, Forestry and Agricultural Biotechnology Institute
Zahra Jalali	2016	Postdoctoral Fellow, University of British Columbia, Centre for Molecular Medicine and Therapeutics
Mahjoubeh Jalali	2016	Postdoctoral Fellow, Pacific Northwest Diabetes Research Institute, Washington

PHD:

Name	Date Completed	Currently
Alan Christoffels	2001	Director, SANBI; DST/NRF Research Chair
Ekow Oppon	2002	Zambia
Junaid Gamieldien	2002	Senior Lecturer, SANBI, UWC
Zhuo Zhang	2007	Research Scientist, University of Singapore
Alan Chong	2009	Research Fellow, Beth Israel Deaconess Medical Centre, Harvard Medical School
Magbubah Essack	2009	Research Scientist, KAUST
Sebastian Schmeier	2009	New Zealand
Ulf Schaefer	2009	Research Scientist, KAUST
Aleksander Radovanovic	2010	Research Scientist, KAUST
Mark Wamalwa	2011	International Livestock Research Institute, Kenya
Musa Gabere	2011	Principal Investigator, King Abdullah International Medical Research Centre
Samuel Kwofie	2011	Biomedical Engineering Lecturer, University of Ghana
Mushal Ali	2013	National Institute of Communicable Diseases, Johannesburg
Kavisha Ramdayal	2014	SAP ERP Analyst, City of Cape Town
Michael Berry	2015	Roche
Azeez Fatai	2015	Senior Lecturer, Lagos State University
Alecia Naidu	2015	SKA, UCT
George Obiero	2015	Postdoc, Germany
Adugna Woldesemayat	2015	Unisa, Pretoria
Darlington Mapiye	2016	IBM, Johannesburg
Rosaline Macharia	2016	Lecturer, University of Nairobi
Colleen Saunders	2016/2017	Research Manager & Msc coordinator, Division of Emergency Medicine, Department of Surgery, UCT

MSC:

Name	Date Completed	Currently
Tzu-Ming Chern	2003	PhD, KAUST
Elana Ernstoff	2003	Unknown
Etienne Swart	2003	Graduate Student, Princeton University
Victoria Nembaware	2003	Training Co-ordinator, H3ABioNet
Zayed Albertyn	2003	Bioinformatics Director, Malaysia
Anelda Van Der Walt	2005	Talrify, Director and Trainer
Faisel Mosoval	2005	Senior Professional Officer, Information Systems and Technology, City of Cape Town
Nothemba Gwija-Kula	2005	Health Consultant, World Bank
Farahnaz Ketwaroo	2005	PhD, UCT
Bukiwe Lupindo	2005	SA Government Administration
Oliver Bezuidt	2007	PhD, University of Pretoria
Eugene Duvenhage	2009	Software Developer, Corporate
Frederick Kamanu	2009	PhD, KAUST
Feziwe Mpondo	2009	South African MRC Research Scientist
Saleem Adam	2011	Unknown
Firdous Khan	2012	PhD UWC Biotechnology Department
Wisdom Akurugu	2013	Bioinformatician, H3ABioNet, Ghana
Fred Nindo	2013	Computational Biology Department, UCT
Ram Shrestha	2013	London, UK
Leendert Cloete	2014	Bioinformatics Scientist, KappaBiosystems, Cape Town
Batsirai Mabvakure	2015	NICD, Johannesburg
Stephanie Pitts	2016	PhD, University of Stellenbosch
Eugene Madzokere	2016	Zimbabwe

HONOURS:

Name	Date Completed
Clifford Omorogie	2001
Grant Carelse	2002
Thurayah Davids	2005
Halimit Ebrahim	2009
Katlego Motlhatlego	2012
Siyanda Tsaba	2012
Stacey Moses	2012
Lynley Abdoll	2015
Warren Jacobus	2015

Funders

Research Institute at the University of the Western Cape since 1997

National Research Foundation funding since 1998

South African Medical Research Council Bioinformatics Unit since 2002

Department of Science and Technology
National Research Foundation Research Chair in Bioinformatics and Public Health Genomics since 2007

B3 Africa funding since 2015

Technology Innovation Agency funding since 2016

Bill and Melinda Gates Foundation funding since 2014

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