

CRI QUARTERLY NEWSLETTER:

Apr – June 2021

Welcome to the second CRI quarterly newsletter for 2021.

We hope that the first half of 2021 was productive and fulfilling for everyone, despite the continuing impact of the COVID-19 pandemic.

Our quarterly newsletters showcase the many cancer-related research activities in the Faculty of Health Sciences to research colleagues, clinicians, funders and the public. In this edition, we have added a special feature of the Division of Haematology (Departments of Medicine and Pathology, UCT), highlighting the Division's current research activities and news or recent accomplishments between April and June 2021. Previous editions of the newsletter are published on the [CRI website](#).

News

- The Prince laboratory hosted Mr Arish Mudra Rakashasa-Loots, from the University of Edinburgh for his PhD rotation (May 2021 to June 2021) which forms part of his degree and Wellcome Trust Fellowship.

Fellowships and awards

- South Dr Walid Mugla (see picture below) has been awarded the first Orthopaedic Sarcoma Fellowship sponsored by ZimmerBiomet to the value of R500k. The 7-month fellowship is being hosted by Dr Thomas Hilton, focusing on the complete management of bone and soft tissue sarcoma patients and joint replacement surgery.



Congratulations to Dr Mugla!

July 2021 graduation news

- Mohsin Khan, PhD: "The molecular role of TBX3 in Malignant Melanoma". Supervisor: Prof. Sharon Prince
- Carly Ann Burmeister, Honours: "Identifying cheap and effective combination therapies for the treatment of cervical cancer". Supervisor: Prof. Sharon Prince
- Linda Mbuthini, MPH: "The cost of providing consultative palliative care services in a tertiary hospital setting" Supervisors: Ms. Lucy Cunnama, Dr. René Krause, Prof. Jennifer Moodley

Congratulations to them!

Upcoming events

SAMRC/UCT GCRC Research Indaba

This will take place on 17 November 2021. Program and registration details will be uploaded onto GCRC website soon (<http://www.samrc-gcrc.uct.ac.za/>)

The 13th AORTIC International Conference on Cancer in Africa

The conference will take place virtually from 5 to 10 November 2021, bringing together multidisciplinary specialists from the global cancer community to reduce the impact of cancer in Africa.

The African Organisation for Research and Training in Cancer (AORTIC) is an Africa-based organisation with members throughout Africa and the international cancer community. Our objectives are to support, integrate, and facilitate evidence-based interventions and innovative programmes towards the prevention and control of cancer in Africa.

See the [AORTIC website](#) for more information about the conference and abstract submission.

Orthopaedic Oncology Session at the upcoming 67th Congress of the South African Orthopaedic Association (SAOA)

The Orthopaedic Oncology session in collaboration with the South African Oncology & Limb Salvage Society (SOLS) under the auspices of the South Africa Orthopaedic Society (SAOA) will be running a morning session as part of the SAOA annual congress. The format of the congress is modified due to the current environment under COVID-19, nevertheless we still have quality local and international speakers presenting, chairing and leading discussions on various Sarcoma topics. See flyer below:

SAVE THE DATE



67TH CONGRESS OF THE
**SOUTH AFRICAN
ORTHOPAEDIC
ASSOCIATION**
30 AUGUST – 2 SEPTEMBER 2021
CTICC, CAPE TOWN, SOUTH AFRICA
CHANGE – BETTER!

**SOUTH AFRICAN ONCOLOGY
& LIMB SALVAGE SOCIETY**
Current / International / Innovation

Tuesday 31st August 2021
07:30- 10:00 & 10:30-12:00
Hall 8.2 – 2nd level @ CTICC2

INTERNATIONAL SPEAKERS:

Mr William Aston	SOLS	London, UK
Prof Henrik Bauer	SOLS	Sweden / Cape Town

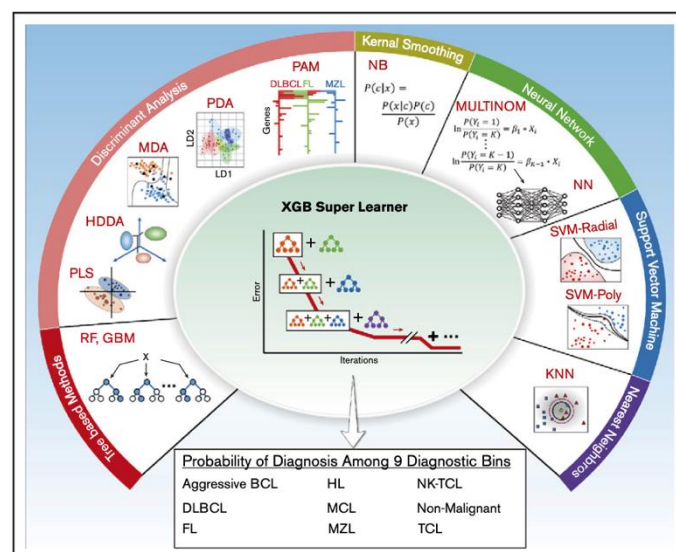
 Visit www.saoa.org.za for more info

Special feature – Division of Haematology, UCT (Departments of Medicine and Pathology)

The division of haematology at UCT encompasses the Groote Schuur diagnostic laboratory and clinical service including stem cell transplantation, as well as the research lab on UCT medical campus, for the diagnosis, study and treatment of all blood disorders and cancers.



Current research projects



Schematic outline of 13 base gene assay learner model – collaboration Weinstock lab at Dana Farber Cancer Institute

1. Title: A novel genetic panel for the diagnosis of lymphoma in a South African cohort – a pilot study.

Research team members: A/Prof Estelle Verburgh, Dr Katherine Antel, A/Prof Jessica Opie, Dr Dharshnee Chetty, Dr Shaheen Mowla, Ms Zahra Latib, Dr Leonardo Rios, Dr Zainab Mohamed, Ms Lillian Andera.

Aim: To determine the diagnostic accuracy of a novel diagnostic platform in a cohort of patients diagnosed with lymphoma at Groote Schuur Hospital from 2005 to 2021.

Summary: A Harvard-based research group has developed a chemical ligation probe-based assay (CLPA) to quantify the expression of 37 genes and assign a

Funding opportunities

- Fund title:** Advanced Development of Informatics Technologies for Cancer Research and Management (U24 Clinical Trial Optional)

Funding amount: \$600,000 per year for up to 5 years

Deadline: 17 November 2021 (17:00 SAST)

Link: <https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-21-015.html>
- Fund title:** Early-Stage Development of Informatics Technologies for Cancer Research and Management (U01 Clinical Trial Optional)

Funding amount: \$300,000 direct costs per year for up to 3 years

Deadline: 17 November 2021 (17:00 SAST)

Link: <https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-21-014.html>
- Fund title:** Exploratory Grants in Cancer Epidemiology (R21 Clinical Trial Optional)

Funding amount: \$275 000 for up to 2 years.

Funder deadline: 8 October 2021 (17:00 SAST)

Link: <https://grants.nih.gov/grants/guide/pa-files/PA-19-277.html>

diagnosis of lymphoma subtype, without pathologist input. This low-cost assay represents a large step forward in lymphoma diagnosis in low-resource settings where costs of ancillary tests are prohibitive and pathology expertise are scarce. However, further research is warranted, particularly in a cohort that includes HIV lymphoma.



Dr Justin du Toit is establishing innovative public-private collaborative research projects in stem cell transplantation.

2. Title: Is Haploidentical Haematopoietic Cell Transplantation Using Post-transplantation Cyclophosphamide(PTCY) Feasible in Sub-Saharan Africa?

Research team members: A/Prof Estelle Verburgh, Dr Justin du Toit, Dr Andrew McDonald, Dr David Brittain, Dr Michael Cass, Dr Jackie Thomson, Miss Jenna Oosthuizen, Dr Cecile du Toit, Dr Matthew Seftel, Prof Vernon Louw.

Aim: To assess the safety and feasibility of haploidentical haematopoietic cell transplantation in South Africa.

Summary: In South Africa, identifying a matched related or matched unrelated donor for haematopoietic cell transplantation is challenging: the ongoing regional HIV epidemic restricts donor eligibility; patients come from highly diverse ethnic populations (limiting the identification of matched unrelated donors); the high financial burden associated with unrelated donor transplantation. Haploidentical stem cell transplant is, therefore, a potentially attractive modality to treat high risk haematological malignancies in this region.

3. Title: Programmed cell death ligand-1 (PD-L1) expression in HIV-associated Diffuse Large B-cell Lymphoma – role and regulation.

Research team members: Zahra Latib, Dr Shaheen Mowla, A/Prof Estelle Verburgh, Dr Dharshnee Chetty.

Aim: To define the role of PD-L1 in Diffuse Large B-cell lymphoma, within the context of HIV infection.

Summary: Expression of PD-L1 has been described as a pro-tumorigenic factor that attenuates the immune response to tumour cells and its upregulation has been implicated in a variety of cancers, including DLBCL. A recent study reported that PD-L1 expression and the number of PD-L1-expressing regulatory B cells are elevated in HIV-patients prior to DLBCL diagnosis, suggesting that PD-L1 is involved in the onset of lymphomagenesis in these patients. Based on the crucial role that PD-L1 expression plays in the immune evasion of tumour cells, this study aims to explore its function and regulation, within the context of HIV infection to further understand the regulation of PD-L1 in HIV-associated DLBCL.



BLOODSA
CONSORTIUM

4. Title: The establishment of a rapid-access lymph node biopsy clinic (BloodSA consortium: pathway to diagnosis)

Research team members: A/Prof Estelle Verburgh, Dr Katherine Antel, Miss Jenna Oosthuizen, Miss Karryn Brown, Prof Vernon Louw, Prof Gary Maartens, Dr Dharshnee Chetty.

Aim: To develop a cost-effective algorithm for the investigation of enlarged lymph nodes in a TB-endemic area

Summary Recognising the significant hurdles to lymphoma diagnosis, we set up a dedicated rapid-access lymph node biopsy clinic with the hypothesis that utilising the latest generation TB molecular test (the Ultra) and the core-biopsy could facilitate diagnosis of lymphadenopathy in a high proportion of patients. From the same cohort we have described how the core-biopsy can be a useful technique during the COVID pandemic. We now publish the outcomes from a larger cohort of 3 years of the lymph node biopsy, with diagnostic evaluation of a core-biopsy for the diagnosis of lymphoma and compare the time-to-diagnosis of lymphoma with a historical cohort. From the data we develop diagnostic algorithm for the evaluation of peripheral lymphadenopathy for patients living in a TB-endemic area.



5. Title: Genome-wide binding of HIV-1 Tat, and analyses of gene networks, in HIV-associated B-cell lymphoma.

Research team members: Dr Shaheen Mowla, Dr Leo Alves de Souza Rios.

Aim: To profile the HIV-1 Tat interactome within the B cell genome using a Chromatin-immunoprecipitation and sequencing (ChIP-Seq) approach and to investigate the role of HIV-1 Tat in the deregulation of the miRNA targetome in B cells using the AGO2-RIP-ChIP assay.

Summary: Recent research has shown that HIV proteins can act as oncogenic agents, directly driving cellular transformation and oncogenesis, and that this is not restricted to CD4+ cells but also bystander cells, including B cells. This proposed research will focus on expanding our understanding of how the HIV-1 protein Tat drives Non-Hodgkin Lymphomas. Cumulative evidence to date shows that HIV-1 Tat is present within B lymphoma cells of HIV infected patients, and that it promotes lymphoma-specific gene expressions and genomic rearrangements in B cells. There is currently no data available on the scope of HIV-1 Tat and B cell genome interactions.



Dr Zainab Mohamed in the multidisciplinary lymphoma clinic with Dr Dharsnee Chetty, PhD student Lillian Andera & others

6. Title: Temporal trends in HIV aggressive lymphoma in Cape Town, South Africa.

Research team members: Ms Lillian Andera, A/Prof Estelle Verburgh, Dr Dharshnee Chetty, Dr Zainab Mohamed, Dr Kudakwashe Simba, Ms Jenna Oosthuizen,

Ms Karryn Brown, Dr Gerdien Kritzing, A/Prof Jessica Opie, Dr Katherine Antel, Dr Sumaiya Cassim.

Aim: To analyse the trends of the aggressive lymphoma subsets diagnosed at Groote Schuur Hospital, Cape Town, South Africa between 2005 and 2020.

Summary: HIV-related lymphomas account for a significant percentage of lymphomas in Sub-Saharan Africa (SSA). There is a lack of adequate well-designed epidemiology studies in both HIV-negative and HIV-positive aggressive lymphomas in SSA, due to underdeveloped referral and diagnostic pathways, and poorly maintained cancer registries. This study will give an accurate indication of the numbers and demographics of patients with different lymphoma disease subsets, their HIV status and the effect of ART coverage in our academic referral centre receiving around half of all public referrals in the Western Province of South Africa.



Ms Melanie Davids, Jenna Oosthuizen and Karryn Brown brilliantly support the division of clinical haematology from the data and research office

Research grants and awards news

- Aaliyah Saferdien and Beatrice Ramorola received the South African Medical Research Council National Health Scholars Programme PhD Award.
- Dr Shaheen Mowla received an FHS Research Stimulus Award for the study entitled 'Epigenetic alterations in Burkitt lymphoma: understanding the role of Activation Induced cytidine Deaminase (AID) as an emerging biomarker'.
- A/Prof Verburgh received an FHS Research Stimulus Award for the study entitled 'A Novel Genetic Panel for the Diagnosis of Lymphoma in a South African Cohort'.
- Dr Dharshnee Chetty, an anatomical pathologist on our interdepartmental lymphoma research team, received an FHS Research Stimulus Award for the study entitled 'Molecular investigation of aggressive Diffuse large B-cell lymphoma, B-cell lymphoma unclassifiable and Burkitt lymphoma subsets diagnosed at Groote Schuur Hospital'.
- Postdoctoral fellow Dr Leonardo Alves de Souza Rios is going on a research visit at University of Groningen, Netherlands, to be trained in an innovative technique

called Ago2 RIP-Chip which will be used to expand molecular studies in lymphoma at UCT.

- Dr Katherine Antel, who recently completed a PhD in lymphoma diagnosis is going to join a leading lymphoma research group at the Dana-Farber Cancer Institute, Boston. She will gain valuable skills in genetic analysis in lymphoma, that she can bring back to further develop lymphoma research here.



Congratulations to Dr Katherine Antel!

Recent or upcoming events

- Establishment of **Weekly Haematology Deep Dive** academic meeting: Under the leadership of UCT Haematology, this virtual weekly meeting has been established for education and development of national collaborations for benign and malignant haematological diseases. Contributors are based at academic centres across South Africa and meetings are attended by professionals working in public and private sector Haematology across Southern Africa. If you are interested in attending, please join at 16-17:30 on Mondays using the following open zoom link. No preregistration is required; sessions are CPD accredited: <https://uct-za.zoom.us/j/99014137741> For queries, please contact Ms Melanie Davids melanie.davids@uct.ac.za
- In collaboration with UCSF, UCT Haematology facilitated a short course on Designing Clinical Research, funded by the NIH Fogarty HIV training grant. Postgraduate students benefitted from the input of both international and local mentors with expertise in haematology and public health.
- Through the division's supplement NIH Fogarty D43 grant, it has been collaborating with Cape Peninsula University of Technology (CPUT) to train post-graduate students at UCT/NHLS in HIV haematology research. This semester, students have been trained

in haematology morphology and have participated in the Fogarty Designing Clinical Research short course.

- A/Prof Estelle Verburch worked with Cancer Alliance to make an awareness & advocacy video on delays in the pathways to lymphoma diagnosis and treatment.
- A/Prof Karen Shires, who is our molecular haematologist, is being joined by a new molecular scientist Marion Stone. Together they will expand our molecular service offering, focusing on minimal residual disease in haematological malignancies.

We look forward to featuring another division/research group in the next quarterly edition.

Recent Cancer Publications (Faculty-wide)

1. Ajayi-Smith A, van der Watt P, Mkwanzazi N, Carden S, Trent JO, Leaner VD. Novel small molecule inhibitor of Kpn β 1 induces cell cycle arrest and apoptosis in cancer cells. *Exp Cell Res*. 2021 Jul 15;404(2):112637. <https://doi.org/10.1016/j.yexcr.2021.112637>
2. Alves de Souza Rios L, Mapekula L, Mdletshe N, Chetty D, Mowla S (2021) HIV-1 Transactivator of transcription (Tat) co-operates with AP-1 factors to enhance c-MYC transcription. *Frontiers in Cell and Developmental Biology*. <https://doi.org/10.3389/fcell.2021.693706>
3. Damerell, V., Pepper, M.S. & Prince, S. Molecular mechanisms underpinning sarcomas and implications for current and future therapy. *Signal Transduction and Targeted Therapy*, 6, 246 (2021). <https://doi.org/10.1038/s41392-021-00647-8>
4. Dzobo K, Sinkala M. Cancer Stem Cell Marker CD44 Plays Multiple Key Roles in Human Cancers: Immune Suppression/Evasion, Drug Resistance, Epithelial-Mesenchymal Transition, and Metastasis. *OMICS*. 2021 May;25(5):313-332. <https://doi.org/10.1089/omi.2021.0025>
5. Fagan JJ, Otiti J, Onakoya PA, Diom E, Konney A, Gebeyehu M, Aswani J, Baidoo K, Koch WM. AfHNS Fellowship: A model to improve access to head and neck cancer care in Africa and Developing Countries. *Head & Neck* 2021;1–6. <https://doi.org/10.1002/hed.26770>
6. Fagan JJ. Semon Lecture: 'Laryngectomy Practice Based on Personal Research', Royal Society of Medicine, 5 November 2020, London, UK. *J Laryngol Otol* 2021;1–5. <https://doi.org/10.1017/s0022215121001511>
7. Kimani, S., Chakraborty, S., Irene, I., de la Mare, J., Edkins, A., du Toit, A., Loos, B., Blanckenberg, A., Van Niekerk, A., Costa-Lotufo, L.V. and ArulJothi, K.N., Mapolie, S. and Prince, S., 2021.

The palladacycle, BTC2, exhibits anti-breast cancer and breast cancer stem cell activity. *Biochemical Pharmacology*, 190, p.114598. <https://doi.org/10.1016/j.bcp.2021.114598>

8. Köhler HF, Mehanna H, Shah JP, Sanabria A, Fagan J, Kuriakose MA, Rene Leemans C, O'Sullivan B, Krishnan S, Kowalski LP. Comparison of different guidelines for oral cancer. *Eur Arch Otorhinolaryngol*. 2020 Oct 15. <https://doi.org/10.1007/s00405-020-06423-8>
9. Matos LL, Forster CHQ, Marta GN, Junior GB, Ridge JA, Hirata D, Miranda-Filho A, Hosny A, Sanabria A, Gregoire V, Patel SG, Fagan JJ et al. The impact of prolonged time to treatment in cancer patients and how to mitigate the risk of dying after the COVID-19 pandemic – a head and neck cancer model. *Cancer Causes Control*. 2021 May;32(5):459-71. <https://doi.org/10.1007/s10552-021-01411-7>
10. Mbulawa ZZA, Somdyala NI, Mabunda SA, Williamson A-L. High human papillomavirus prevalence among females attending high school in the Eastern Cape Province of South Africa. *PLOS One* 2021; 16(6): e0253074. <https://doi.org/10.1371/journal.pone.0253074>
11. Nnaji CA, Kuodi P, Walter FM, Moodley J. Timeliness of diagnosis of breast and cervical cancers and associated factors in low-income and middle-income countries: a scoping review protocol. *BMJ Open*, 2021; May 6, 11:e044093. <https://doi.org/10.1136/bmjopen-2020-044093>
12. Somdyala NIM, Mbuthini L, Müller B, Sithole N, Ncinitwa A, Bradshaw D. Active case-finding method improves completeness and accuracy of data reported to the rural Eastern Cape Cancer Registry in South Africa. *Ecancer*. 2021, 15 1251 <https://doi.org/10.3332/ecancer.2021.1251>
13. van Heerden J, Hendricks M, Poole J, Büchner A, Naidu G, du Plessis J, van Emmenes B, van Zyl A, Uys R, Johani J, Hadley GP, Harrison D, Rowe B, Bassingthwaight M, Moonsamy N, Kruger M; SACCSG Neuroblastoma Workgroup. The implementation of a national paediatric oncology protocol for neuroblastoma in South Africa. *Cancer Causes Control*. 2021 Jul;32(7):725-737. <https://doi.org/10.1007/s10552-021-01424-2>
14. van Schalkwyk C, Moodley J, Welte A, Johnson LF. Modelling the impact of prevention strategies on cervical cancer incidence in South Africa. *Int J Cancer*. 2021 Jun 24. <https://doi.org/10.1002/ijc.33716>
15. Viljoen G, Viljoen N, Fagan JJ, Govender D. Inflammatory leiomyosarcoma of the head and neck: case report. *Int J Surg Case Rep*. 2021 May;82:105907. <https://doi.org/10.1016/j.ijscr.2021.105907>

Please send any cancer-related news, events, publications and conference information for the period July-September 2021 for inclusion in our next quarterly newsletter to:

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