

Welcome to the third CRI quarterly newsletter for 2021.

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 Prince Cancer Laboratory, Division of Cell Biology, Department of Human Biology; highlighting the Lab's current research activities, ongoing projects and news. Previous editions of the newsletter are published on the [CRI website](#).

News

- Prof Lynette Denny was a panellist during the recent African Cancer Institute (ACI) Cervical Cancer Elimination webinar. The event was held on 15 September 2021, to mark this year's gynaecological cancer awareness month. Details of the webinar, including recording are available on the institute's [website](#).
- Prof Lynette Denny has been appointed as a Commissioner for the Lancet Commission on Cancer and Health Systems. Recently, she co-authored the "The Lancet Oncology Cancer in Sub-Saharan Africa: A Lancet Oncology Commission". As a member of the WHO Guidelines Development Group for Cervical Cancer Treatment, she also recently co-authored the second edition of the WHO guidelines for screening and treatment of cervical precancer lesions for cervical cancer prevention
- Dr Katherine Antel is the recipient of the NIH Emerging Global Leader Award (FIC K43 TW011986-01) for the 5-year period from 2021-2026. This award is to enable her to become an independent clinical researcher in the field of Diagnostic Pathways of Lymphoma in the South African setting and the unravelling of the pathogenesis of HIV lymphoma. With this grant, she remains on the faculty of Clinical Haematology. During the first 2 years, she will receive training in research methods at the Dana-Farber Cancer Institute in Boston under her new mentor Dr. David Weinstock.
- Dr Nick Jenkins received the Best Oral Presentation [Haematology] Award at the NHLS PathRed 2021

Congress. His work was entitled: Cytogenetically Normal Acute Myeloid Leukaemia at a Single Centre in South Africa. Co-authors included LA Phillips, E Verburgh, M Stone, J Oosthuizen and K Shires.

- The CRI Director Prof Jennifer Moodley has joined the Editorial Board of PLOS Global Public Health, a new Open Access journal addressing global public health challenges and inequities. Prof Moodley will contribute her expertise in oncology and public health cancer research.

Graduation news

- Ms Tareen Dawood was granted her MSc (Biomedical Engineering) degree with distinction. The title of her research was: *Feature detection in ultrasound images for computer aided diagnosis of Hodgkin's Lymphoma*. In this new collaboration between Clinical Haematology and Bioengineering, her primary supervisor was A/Prof Tinashe Mutsvangwa and her co-supervisor was A/Prof Estelle Verburgh. She is now pursuing her PhD studies in imaging at Kings College London.

Upcoming events**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 registration and more information about the conference.



Postgraduate Cancer Research Initiative (PG CRI) 3-minute Thesis Competition 2021

After the successful 3-minute Thesis Competition in 2020, our Postgraduate Cancer Research Initiative (PG CRI) is excited to announce that we will be hosting the competition again this year on 19 October 2021. The competition is a platform for postgraduate students to showcase their cancer-related thesis using 1 non-animated slide and non-scientific language to explain their research topic or proposal to a general audience. There are prizes to be won too! For enquiries, contact Saif Khan (email: khnsai002@myuct.ac.za) or email cri.postgradgroup@uct.ac.za.



3 Minute Thesis Competition
YOUR GRADUATE THESIS
1 SLIDE. 3 MINUTES. WIN PRIZES.
October 19th, 2021
2-4 PM
Cancer Research Initiative
UNIVERSITY OF CAPE TOWN

SAMRC and UCT Gynaecological Cancer Research Centre (GCRC) 2021 Research Indaba

The South African Medical Research Council (SAMRC) and UCT Gynaecological Cancer Research Centre (GCRC) will host the 2021 Research Indaba on 17 November 2021. The event is themed: 'Pathways to the elimination of cervical cancer'. Delegates are expected to register by 31 October 2021. See details [here](#).



SA MRC/UCT Gynaecological Cancer Research Centre
RESEARCH INDABA 2021
Pathways to the Elimination of Cervical Cancer
Wednesday, 17th November 2021
09h30 – 17h00
You are invited to participate in our hybrid meeting where we continue to focus on the WHO Global Strategy to accelerate the elimination of cervical cancer by 2030
Moderated by Prof. Lynette Denny and Chairperson: Dr Nomonde Mbatani
Head of Dept Obstetrics & Gynaecology, UCT/GSH
Speakers
Prof. Anna-Lise Williamson
SAMRCI Chair in Vaccinology, Institute of Infectious Disease and Molecular Medicine, UCT
Prof. Jennifer Meadley
Director, Cancer Research Initiative
Dr Cari van Schoelwyk
DSI-MRC Centre of Excellence in Epidemiological Modelling & Analysis (SACEMA)
Drs Tracey Adams, Linda Rogers, Rakiye Saidu
Dept Obstetrics & Gynaecology, UCT
Dr Nwabisa Giyese
Nelson Mandela Academic Hospital, Witmarsh, WSU
Prof. Sinead Delany-Moretlwe
Director of Research, Wits RH
Prof. Verne Lesnar
Division of Medical Biotechnology, UCT
Dr Nasir Fakih
Dept Radiation Oncology, UCT
Dr Elvis Kidzere
Dept Radiation Oncology, UCT
Neuroscience Institute
J Block New Main Building
Groote Schuur Hospital
Join us for the online meeting: link will be provided after registration
CPD Accreditation: Level 1, & CEUs
For registration and further information, contact:
lavinia.petersen@uct.ac.za; Tel: 021-6505446

Breast Interest Group of South Africa (BIGOSA) 9th Scientific Meeting 2021

BIGOSA is a multidisciplinary group interested in treating patients with breast cancer. The 2021 Scientific Meeting

is scheduled for 16 October 2021. See [website](#) for registration and other details.



Training and Funding opportunities

- **Training:** The African Cancer STARS Training programme (funded by NCI grant D43-CA260640). This program provides mentored training for principal investigators and project managers who are developing cancer research careers in Sub-Saharan Africa.
Deadline: 4 February 2022, see more details on the programme's [website](#).
- **Training:** Free e-learning module on COVID-19 and Cancer Screening offered by International Agency for Research on Cancer (IARC). More details on the module and how to enrol can be found [here](#).
- **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). See [link](#) for more details
- **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). See [link](#) for more details

Special feature – The Prince Cancer Laboratory, Division of Cell Biology, Department of Human Biology, UCT

The primary focus of the research team led by Prof Sharon Prince has been the identification and characterisation of novel drug targets and the design of affordable therapeutic interventions for the treatment of cancers that are highly relevant to South Africa (SA). This includes breast cancer (leading cancer and most common cause of cancer-related deaths in women in SA), cervical cancer (second most common cancer and most common cause of cancer-related deaths in women in SA) and sarcoma (common in African children and young adults). Their research directions has a multi-pronged approach and includes meaningful collaborations with research groups locally and internationally. Notably, these collaborations have led to the development of pre-

clinical drug candidates with a unique focus on cancers afflicting Africa and some of these have been patented. The Prince laboratory currently consists of 1 Hons student, 1 MSc student, 9 PhD students, 3 post-doctoral fellows and 1 scientific officer.



Current Research Team:

Honours student:

1. Talia Gabay (co-supervised with Dr Alexis Mufweba)

Masters student:

1. Carly Burmeister (co-supervised with Dr Georgia Schafer)

PhD students:

1. Ms Victoria Damerell (co-supervised with Prof Michael Pepper, UP)
2. Mr Thato Medupe (co-supervised with Dr S Ngubane, UCT)
3. Mr Mhlahli Mlaza
4. Mr Abid Ali
5. Mr Saif Khan
6. Ms Stephanie Ncube
7. Mr Athi Welsh (co-supervised with A/Prof G Smith, UCT)
8. Ms Claire Bellis
9. Mr Karabo Serala

Postdoctoral fellows:

1. Dr Suparna Chakraborty
2. Dr Arul Jothi Nagarajan
3. Ms Alexis Neumann-Mufweba

Scientific Officer:

1. Dr Supratim Biswas

Current research projects

1. Project title: Investigating the oncogenic roles and regulation of TBX2 and TBX3 in breast, cervical and pancreatic cancer.

Research team members: Prof Sharon Prince, Dr Arul Jothi Nagarajan, Dr Alexis Neumann-Mufweba, Mr Saif Khan, Mr Abid Ali, Ms Stephanie Ncube, Mr Karabo Serala.



Aim: (a) To determine the expression of the human transcription factors TBX2 and TBX3 in cancer; (b) To identify the oncogenic roles of TBX2 and TBX3; (c) To identify more amenable ways of targeting TBX2 and TBX3 by identifying and characterising (i) signalling molecules that upregulate them; (ii) protein partners that cooperate with TBX2 and TBX3 to promote cancer and (iii) TBX2 and TBX3 target genes that mediate their oncogenic roles.

Summary: Compared to conventional anticancer therapies, targeted therapies are expected to be more efficacious with significantly reduced side-effects. In this regard, the Prince laboratory has focused on two highly homologous transcription factors TBX2 and TBX3 which are critical for embryonic development with no known functions in adult tissues. The Prince laboratory and others have shown that TBX2/3 are overexpressed in several carcinomas and sarcomas and that they are required for the progression of virtually all these cancers. This project extends this list to investigating the role of TBX2/3 in cervical and pancreatic cancer. This study aims to identify more versatile ways of inhibiting TBX2/3 by further elucidating members of their signalling axis and potential interacting partners and target genes which may represent novel therapeutic targets in their own

right and results obtained will be used to identify small molecules with anticancer activity.

2. Project title: Identifying compounds/drugs that inhibit the oncogenic transcription factors TBX2 and TBX3 in cancer.

Research team members: Prof Sharon Prince, Drs Supratim Biswas & Suparna Chakraborty, Mr Saif Khan, Mihlali Mlaza & Karabo Serala, and Ms Claire Bellis (UCT), Prof Leticia Costa-Lotufo & Dr Bianca Del Bianco Sahn (University of Sao Paulo, Brazil), Prof Colin Goding (University of Oxford, UK).



Aim: To identify (i) compounds derived from natural marine origin for their ability to inhibit TBX2 oncogenic activity in melanoma, breast cancer, and rhabdomyosarcoma, and (ii) commercially available non-cancer drugs that can inhibit TBX2/3 expression and oncogenic activity in melanoma, breast cancer, cervical cancer, pancreatic cancer and rhabdomyosarcoma.

Summary: The Prince laboratory, in collaboration with the Costa-Lotufo laboratory at the University of Sao Paulo, established a functional chromatography system to identify molecules derived from marine organisms found in Brazil that interact with TBX2 and they recently reported that some of them exhibit anticancer activity by inhibiting TBX2 in melanoma, breast cancer, and rhabdomyosarcoma. In this study, these molecules will be further characterised as lead anticancer agents and based on the success of this screen, the Prince- Costa-Lotufo team will do the same for TBX3.

The pipeline for developing targeted therapies is arduous and costly and to circumvent these challenges, the Prince laboratory in collaboration with the Goding laboratory at the Ludwig Institute of Cancer at the University of Oxford have adopted a second cost-effective high-throughput cell-based drug-repurposing screen to identify commercially available non-cancer drugs that inhibit TBX2/3 expression and oncogenic activity in melanoma,

rhabdomyosarcoma, breast, cervical and pancreatic cancer. Because the latter approach combines targeted and drug repurposing, these drugs are expected to be associated with minimal side effects and to be cost, time and risk effective since the drugs are already approved for clinical use and could potentially impact immediately the lives of cancer patients.

3. Project title: Investigation into the regulation of TBX3 by oncogenic c-Myc and its interaction and co-operation with the human papillomavirus (HPV) oncoproteins E6/E7 to promote cervical cancer progression.

Research team members: Prof Sharon Prince, Dr Alexis Neumann-Mufweba, Mr Saif Khan, Ms Carly Burmeister & Talia Gabay (UCT), Dr Georgia Schafer (ICGEB, Cape Town), Dr Lawrence Banks (ICGEB, Trieste, Italy), Dr Laura Sichero (Instituto do Cancer do Estado de São Paulo, Brazil).



Aim: (a) To determine the association between TBX3 levels, HPV type-specific positivity, and clinicopathological variables, (b) To determine if overexpression of TBX3 in cervical cancer is mediated by the oncogenic c-Myc, (c) To determine the mechanism(s) by which the HPV E6/E7 oncoproteins regulate the pro-proliferative and pro-migratory activity of TBX3, (d) To confirm the requirement of E6/E7 for TBX3 to promote proliferation and migration in non-malignant NIKS keratinocytes (cells of origin of cervical cancer) and (e) To assess the impact of TBX3 targeting commercial drugs on E6/E7 levels and activity in HPV-positive cervical cancer.

Summary: In HPV-associated cervical cancer, the E6 and E7 viral oncoproteins in cooperation with several host factors are crucial for the induction and maintenance of the malignant phenotype. One approach that may facilitate rapid and cost-effective drug development is to identify these host factors and to target them with commercially available non-cancer drugs. In this regard, the Prince laboratory is interested in TBX3 which they have shown is overexpressed in cervical cancer where it specifically promotes proliferation and migration of HPV

positive, but not HPV negative, cervical cancer cells. Their data suggest that the overexpression of TBX3 is a potentially key contributor of cervical cancer progression and that TBX3 co-operates with E6/E7 to carry out these oncogenic functions. The oncogenic c-Myc is also upregulated in cervical cancer and this study test their hypothesis that TBX3 is upregulated by c-Myc and that it co-operates with the HPV E6/E7 oncoproteins to promote cervical cancer cell proliferation and migration.

4. Project title: Investigation of the c-Myc/TBX3/nucleolin axis in the malignant transformation of sarcoma-initiating cells

Research team members: Prof Sharon Prince, Ms Victoria Damerell & Ms Michelle Du Toit (UCT), Prof Michael Pepper & Dr Melvin Ambele (University of Pretoria)



Aim: (a) To investigate c-Myc, TBX3 and nucleolin as combination biomarkers for the detection and diagnosis of sarcomas, and (b) To investigate whether TBX3 and nucleolin on their own or in combination can promote the malignant transformation of mesenchymal stem cells into sarcomas.

Summary: The burden of sarcomas can be reduced if they are detected and treated early which has driven the search for early combination diagnostic markers. This study explores the possibility that TBX3 in combination with c-Myc and nucleolin are important early differential biomarkers of a subset of sarcomas. Furthermore, this study aims to determine whether TBX3 and nucleolin alone or in combination can drive the transformation of MSCs into these sarcoma types. Results emanating from this study will have important implications for the reliable diagnosis and treatment of a subset of highly aggressive sarcomas.

5. Title: To develop novel Platinum Group Metals as anticancer drug leads

Research team members: Prof Sharon Prince & Dr Suparna Chakraborty (Dept of Human Biology, UCT), A/Prof Greg Smith, Dr Siyabonga Ngubane, Mr Athi Welsh & Mr Thato Medupe (Dept of Chemistry, UCT), Prof Selwyn Mapolie & Ms Annick van Niekerk (Dept of Chemistry and Polymer Science, Stellenbosch University)



Aim: To elucidate the anticancer properties and mechanisms of action of transition metal-containing complexes, with the intention of improving target binding (e.g. DNA, biochemically relevant proteins), lipophilicity, solubility, and microsomal stability.

Summary: The Prince group has explored the use of organometallic complexes based on Platinum Group Metals (PGMs) as anticancer agents. South Africa is the dominant PGM producer globally and hence the development of PGM organometallic complexes as potential anticancer drug leads is of value to the pharmaceutical industry and presents a unique opportunity for the beneficiation of locally available resources.

Current research grants and awards

- 2021-2023: MRC self-initiated research grant
- 2021-2023: CRP - ICGEB Research Grant
- 2021-2022: NRF SA / France (PROTEA)
- 2020-2022: NRF Competitive Programme for Rated Researchers grant
- 2019-2021: NRF/ São Paulo Research Foundation (FAPESP) of Brazil Joint Science and Technology Research Collaboration

Current outreach/advocacy

Prof Prince has not only been passionate about research, but she has explored ways of disseminating her knowledge to the public via public talks and getting her laboratory to pioneer and be active in several outreach programs. This includes the CANSA shavathon, an event organised by the team annually in partnership with the Cancer Association of South Africa (CANSA) which began in 2011 and helps to increase the awareness around cancer. In addition, they participate annually in a Learner's Open Day for school learners, in the Science in

Our School (SOS) programme in the Faculty of Health Sciences and they regularly host learners from disadvantaged schools so that they can experience science first-hand and expose them to science as a career.

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

Recent Cancer Publications (Faculty-wide)

1. Bunzli S, O'Brien P, Aston W, et al. Life or limb: an international qualitative study on decision making in sarcoma surgery during the COVID-19 pandemic. *BMJ Open* 2021;11:e047175. DOI: 10.1136/bmjopen-2020-047175
2. Cacciatore S, Wium M, Licari C, Ajayi-Smith A, Masieri L, Anderson C, Salukazana AS, Kaestner L, Carini M, Carbone GM, Catapano CV, Loda M, Libermann TA, Zerbini LF. Inflammatory metabolic profile of South African patients with prostate cancer. *Cancer Metab*. 2021 Aug 3;9(1):29. DOI: 10.1186/s40170-021-00265-6.
3. Davidson A, Mohamed Z. Tackling cancer risk in adolescents and young adults with HIV. *Lancet HIV*. 2021 Oct;8(10):e601-e602. DOI: 10.1016/S2352-3018(21)00246-0.
4. Dzobo K. Integrins Within the Tumor Microenvironment: Biological Functions, Importance for Molecular Targeting, and Cancer Therapeutics Innovation. *OMICS*. 2021 Jul;25(7):417-430. DOI: 10.1089/omi.2021.0069.
5. Ezenwankwo EF, Nnaji CA. Prostate cancer and the added burden of COVID-19 in sub-Saharan Africa: Rethinking regional priorities for responsive and data-driven cancer control programs. *Cancer*. 2021 Aug 23. DOI: 10.1002/cncr.33887
6. Fagan JJ, Noronha V, Graboyes EM. Making the Best of Limited Resources: Improving Outcomes in Head and Neck Cancer. *Am Soc Clin Oncol Educ Book*. 2021 Mar;41:1-11. DOI: 10.1200/EDBK_320923.
7. Fagan JJ. Africa: A Window on Challenges and Opportunities for Head and Neck Cancer. *Laryngoscope Investig Otolaryngol*. 2021 Jun; 6(3): 414–9. DOI: 10.1002/lto.2.554
8. Ferndale L, Moodley M, Chen WC, Wadee R, Wright CA, Parker MI, Willem P, Mathew CG. Processing and Analysis of Tissue Samples from Esophageal Cancer Patients in an African Setting. *Biopreserv Biobank*. 2021 Aug 12. DOI: 10.1089/bio.2021.0030.
9. Moodley J, Harries J, Scott SE, Mwaka AD, Saji S, Walter FM. Exploring primary care level provider interpretation and management of potential breast and cervical cancer signs and symptoms in South Africa. *Ecancer*. 2021; 15:1298. DOI: 10.3332/ecancer.2021.1298
10. Rambiritch V, Verburgh E, Louw VJ. Patient blood management and blood conservation - Complimentary concepts and solutions for blood establishments and clinical services in South Africa and beyond. *Transfus Apher Sci*. 2021 Aug;60(4):103207. DOI: 10.1016/j.transci.2021.103207.
11. Ramorola BL, Goolam-Hoosen T, Alves de Souza Rios L, Mowla S. Modulation of Cellular MicroRNA by HIV-1 in Burkitt Lymphoma Cells— A Pathway to Promoting Oncogenesis. *Genes*. 2021, 12(9), 1302. DOI: 10.3390/genes12091302
12. Ruffieux Y, Dhokotera T, Muchengeti M, Bartels L, Olago V, Bohlius J, Singh E, Egger M, Rohner E. Cancer risk in adolescents and young adults living with HIV in South Africa: a nationwide cohort study. *Lancet HIV*. 2021 Oct;8(10):e614-e622. DOI: 10.1016/S2352-3018(21)00158-2.
13. Serala K, Steenkamp P, Mampuru L, Prince S, Poopedi K, Mbazima V. In vitro antimetastatic activity of *Momordica balsamina* crude acetone extract in HT-29 human colon cancer cells. *Environ Toxicol*. 2021 Nov;36(11):2196-2205. DOI: 10.1002/tox.23333.
14. Toit JD, McDonald A, Brittain D, Cass M, Thomson J, Oosthuizen J, Toit CD, Seftel M, Louw V, Verburgh E. Is Haploidentical Haematopoietic Cell Transplantation Using Post-Transplantation Cyclophosphamide (PTCY) Feasible In Sub-Saharan Africa? *Transplant Cell Ther*. 2021 Aug 31;S2666-6367(21)01167-2. DOI: 10.1016/j.jtct.2021.08.018.
15. Vogel J, De Villiers S, Mugla W, McCaul J, Hosking K, Hilton T. Radiation-Induced pathological fractures of the proximal femur: A case series considering an endoprosthetic solution. *SA Orthop J*, 2021;20(1)
16. Ibraheem A, Pillai C, Okoye I, Smith JJ, Reidy-Lagunes D, Macaulay G, Alatisie O. Cancer Clinical Trials in Africa-An Untapped Opportunity: Recommendations From AORTIC 2019 Conference Special Interest Group in Clinical Trials. *JCO Glob Oncol*. 2021 Aug;7:1358-1363. DOI: 10.1200/GO.21.00096.
17. Kandimalla R, Xu J, Link A, Matsuyama T, Yamamura K, Parker MI, Uetake H, Balaguer F, Borazanci E, Tsai S, Evans D, Meltzer SJ, Baba H, Brand R, Von Hoff D, Li W, Goel A. EpiPanGI Dx: A Cell-free DNA Methylation Fingerprint for the Early Detection of Gastrointestinal Cancers. *Clin Cancer Res*. 2021 Aug 31. DOI: 10.1158/1078-0432.CCR-21-1982.
18. Mbulawa ZZA, Somdyala NI, Mabunda SA, Williamson AL. Effect of Human Papillomavirus (HPV) Education Intervention on HPV Knowledge

and Awareness Among High School Learners in Eastern Cape Province of South Africa. J Cancer Educ. 2021 Sep 28. DOI: 10.1007/s13187-021-02090-3.

19. Shires K, Wyk TV, Wienand K. The expression of multiple cancer/testis antigens can potentially be used to detect circulating disease and clonal evolution in the peripheral blood of multiple myeloma patients. Blood Res. 2021 30;56(3):156-65. DOI: 10.5045/br.2021.2020335
20. Geel JA, Ranasinghe N, Myezo KH, Davidson A, Howard SC, Hessissen L, Bouffet E, Challinor J. Pediatric cancer care in Africa: SIOP Global Mapping process. Pediatr Blood Cancer. 2021 Nov;68(11):e29315. DOI: 10.1002/pbc.29315.

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

Dr Chukwudi Nnaji, email: Chukwudi.Nnaji@uct.ac.za