

MEDIA RELEASE

UP research team discovers new compounds with the potential to eliminate malaria

PRETORIA – The University of Pretoria (UP) has discovered new potent chemical compounds that show potential as candidates for both the treatment and elimination of malaria.

Professor Lyn-Marie Birkholtz, Professor in Biochemistry and South African Research Chair in Sustainable Malaria Control (part of the South African Research Chair Initiative, SARChI), was part of an international team that published this discovery in the journal *Nature Communications* on 11 January. “The breakthrough involves the identification of unique compounds that are able to kill several stages of the malaria-causing parasite and can block the transmission of the parasite between humans and mosquitoes,” she explained.

The deadly human malaria parasite *Plasmodium falciparum* occurs in South Africa. These parasites are transmitted to humans by female *Anopheles* mosquitoes. The only means of killing the parasite itself is to use chemical drugs, but new antimalarial drugs are urgently needed to address the growing concern of antimalarial drug resistance.

Prof Birkholtz describes the parasite as a “shape shifter” since it can take on multiple forms while in humans. Some of the forms cause disease and others allow the parasite to be transmitted back to mosquitoes to continue the life cycle. Prof Birkholtz states: “To eliminate malaria, it is essential that we have the necessary tools to kill all these different forms of the parasite. We can then cure patients of the disease but, importantly, also block the malaria transmission cycle. This is the only way to achieve malaria elimination.”

South Africa is leading regional malaria elimination efforts as part of four frontline countries (Namibia, Botswana and eSwatini) in southern Africa.

In an innovative strategy, the team looked for new chemical compounds that can do exactly this, but that are completely new so that the parasite does not have resistance against them. The team runs a unique research platform on the African continent, in which all of these stages of the malaria parasite can be produced in the lab and be used to test chemical compounds. The team discovered compounds that kill the disease-causing form and compounds that blocked the parasite from infecting mosquitoes in the lab.

Two potent compounds target processes essential to the parasite’s survival: one is a clinical candidate against tuberculosis and blocks cell membrane synthesis and another is an anti-cancer candidate that targets epigenetic mechanisms (mechanisms that control cell fate beyond the genome). “This is the first time that these compounds were shown to have activity against malaria parasites and since they are not toxic to humans, they show the potential to be developed as antimalarials for both the treatment and elimination of the disease,” said Prof Birkholtz.

The discovery was made possible by the team’s use of an open-source chemical compound set called the Pandemic Response Box, developed by the Switzerland-based Medicines for Malaria Venture (MMV) and the Drugs for Neglected Diseases Initiative (DNDi). This compound box contains compounds that can be used for

drug repurposing/repositioning, a process where drugs that have activity against a specific disease (e.g. cancer) can be reused for another disease (e.g. malaria). Dr James Duffy, MMV Project Director, describes the discovery “as an important breakthrough that emphasises the potential to use existing drugs as inspiration for drug discovery projects targeting different diseases. Never before has this been more important than in light of current outbreaks, where the rapid response to discover new chemicals able to kill infectious organisms is essential.”

Prof Birkholtz directs the parasite cluster of the UP Institute for Sustainable Malaria Control (ISMC), a multidisciplinary institute with a focus on integrated innovations towards malaria elimination in South Africa. Professor Tiaan de Jager, Director of the ISMC and Dean of Health Sciences at UP, said: “A discovery of this kind attests to the leading expertise in antimalarial drug discovery at UP, and in South Africa, addressing African-centred societal challenges. This work also shows the commitment of scientists at UP to contribute to the United Nation’s Sustainable Development Goal for Good Health and Wellbeing.”

Prof Birkholtz’s team led the transmission-blocking drug discovery effort as a partner in the South African Malaria Drug Discovery Consortium (SAMDD) that includes two other South African Research Chairs, Professor Kelly Chibale (Chair in Drug Discovery at the Drug Discovery and Development Centre, H3D, at the University of Cape Town) and Professor Lizette Koekemoer (Chair in Medical Entomology at the WITS Institute for Research on Malaria at the University of the Witwatersrand); as well as scientists from the Council for Scientific and Industrial Research and international partners from the USA and Spain. The work has benefitted from sustained funding from the MMV and the Medical Research Council’s Strategic Health Innovation Programme (SHIP) and affirms that investments in health innovations place South Africa at the forefront of discovery.

Captions:

Prof Lyn-Marie Birkholtz

TIP: Chemical compounds are screened for the ability to kill malaria parasites in the lab

Mosquito: A malaria mosquito that has just fed on human blood

Media enquiries

For interviews with Prof Birkholtz, please email Prim Gower at primarashni.gower@up.ac.za or call 083 229 9011.

ABOUT THE UNIVERSITY OF PRETORIA

The University of Pretoria (UP) is one of the largest contact and residential universities in South Africa, with its administration offices located on the Hatfield Campus, Pretoria. This 112-year-old institution is also the largest producer of research in South Africa.

Spread over seven campuses, it has nine faculties and a business school, the Gordon Institute of Business Science (GIBS). It is the only university in the country that has a Faculty of Veterinary Science which is ranked top in Africa, and overall has 120 academic departments, as well as 92 centres and institutes, accommodating more than 55 000 students and offering about 1 100 study programmes.

UP is one of the top five universities in South Africa, according to the 2019-2020 rankings by the Center for World University Rankings. It is also ranked among the top 100 universities worldwide in three fields of study (veterinary science, theology and law), and among the top 1% in eight fields of study (agricultural sciences, clinical medicine, engineering, environment/ecology, immunology, microbiology, plant and animal sciences and social sciences).

In May 2020, the annual UK Financial Times Executive Education Rankings once again ranked GIBS as the top South African and African business school. The University also has an extensive community engagement programme with approximately 33 000 students involved in community upliftment. Furthermore, UP is building considerable capacities and strengths for the Fourth Industrial Revolution by preparing students for the world beyond university and offering work-readiness and entrepreneurship training to its students.

As one of South Africa's research-intensive universities, UP launched the *Future Africa Campus* in March 2019 as a hub for inter- and transdisciplinary research networks within UP and the global research community to maximise 4IR innovation and address the challenges and stresses our continent and world is facing. In addition UP also launched the Javett Art Centre in September 2019 as a driver of transdisciplinary research development between the Humanities and other faculties. In November 2020 UP launched Engineering 4.0. as a hub not only for Smart Cities and Transport, but also to link the vast resources in technology and data sciences to other faculties via Future Africa. These initiatives are stimulating new thinking at the frontier of 'science for transformation'.

For more information, go to www.up.ac.za