BACKGROUND
Malaria is a mosquito-borne disease caused by the protozoan parasite Plasmodium species, with the most severe form caused by Plasmodium falciparum. The disease is transmitted to people by the female Anopheles vector mosquito. This disease is a leading cause of debilitating illness, with over 200 million cases each year from around the world. The disease is widespread in Africa, and over one million people die of malaria every year on the continent, mostly children under the age of five. Sub-Saharan Africa continues to bear >90% of the disease burden. During the years 2000–2015, remarkable progress was made in controlling the disease, but recently there has been an increase in the burden of malaria cases and progress towards elimination has stalled and at the moment, malaria remains a global health threat. In response to this issue, the WHO has developed a Global Technical Strategy for Malaria (2016–2030) that can be used as a framework to guide countries in their efforts to accelerate progress towards malaria elimination. Malaria elimination not only requires continued control of the Anopheles mosquito vectors and the therapeutic use of antimalarial drugs to cure malaria, but in addition, there is a dire need for agents that block the transmission between human and mosquito, thereby disrupting the parasite lifecycle and preventing new malaria infections.

PROJECT DESCRIPTION
The South African Malaria Transmission-Blocking Consortium (SAMTC) was established to identify and develop compounds that will kill the sexual stages of P. falciparum, which are transmitted to the Anopheles vector. The consortium has developed several in vitro assay platforms targeting different biological endpoints to detect activity of compounds against gametocytes and gametes. A standard membrane feeding assay has also been developed, which will enable the consortium to investigate the complete parasite lifecycle. Clinical isolates from patients with currently-circulating P. falciparum parasite Plasmodium species, with the most severe form caused by Plasmodium falciparum. The disease is transmitted to people by the female Anopheles vector mosquito. This disease is a leading cause of debilitating illness, with over 200 million cases each year from around the world. The disease is widespread in Africa, and over one million people die of malaria every year on the continent, mostly children under the age of five. Sub-Saharan Africa continues to bear >90% of the disease burden. During the years 2000–2015, remarkable progress was made in controlling the disease, but recently there has been an increase in the burden of malaria cases and progress towards elimination has stalled and at the moment, malaria remains a global health threat. In response to this issue, the WHO has developed a Global Technical Strategy for Malaria (2016–2030) that can be used as a framework to guide countries in their efforts to accelerate progress towards malaria elimination. Malaria elimination not only requires continued control of the Anopheles mosquito vectors and the therapeutic use of antimalarial drugs to cure malaria, but in addition, there is a dire need for agents that block the transmission between human and mosquito, thereby disrupting the parasite lifecycle and preventing new malaria infections.

VALUE PROPOSITION
The SAMTC has designed a unique, 3-tiered smart screening cascade to be used as a road map for screening transmission-blocking antimalarial compounds. The combined expertise within the SAMTC has clearly placed it as a main international role player in the field and a reference for interrogating large compound libraries. The SAMTC has built capacity and trained a core group of young scientists in cutting-edge technologies in the malaria field. In addition, this geographically centralised consortium in a malaria-endemic African country with access to malaria patients and African Anopheles vector species, places the group in the unique position of being able to interrogate all stages of the parasite life cycle. It is anticipated that the SAMTC will contribute significantly to the global malaria elimination agenda by spearheading the identification, prioritisation, and development of a new generation of validated compounds with a target candidate profile (TCP) that will block transmission of the parasite to the vector and prevent the spread of the disease (TCP5).

CURRENT STATUS
• More than 25 000 compounds have been screened from approximately 17 distinct chemical backgrounds (libraries) with potential TCP5 activity.
• The SAMTC contributed towards the description of the first South African (and African) antimalarial compound, MMV390048, with transmission-blocking capacity, which is currently undergoing clinical trials in collaboration with Medicines for Malaria Venture (MMV), and was instrumental in the prioritization of a second back-up pre-clinical candidate.
• The SAMTC has also formalised an active partnership with the University of Cape Town's H3D Drug Discovery Platform, to create a single consortium, the South African Malaria Drug Discovery Consortium, which will be funded through various international partnerships and the SAMRC Strategic Health Innovation Partnership (SHIP).

INTELLECTUAL PROPERTY STATUS & PUBLICATIONS
6. Brunschwig et al. (2018) UCT943, a next generation...
A 3-TIERED SMART SCREENING CASCADE FOR MALARIA (CONTINUED)

An in vitro platform for use to screen transmission-blocking antimalaria compounds against gametocytes and gametes


15. Van Voorhis et al. (2016) Open source drug discovery with the Malaria Box compound collection for neglected diseases and beyond. PLOS Pathogens 2016 July 28 https://doi.org/10.1371/journal.ppat.1005763


OPPORTUNITIES

The SAMTC is looking for partnerships for the screening and identification of transmission-blocking antimalarial compounds.

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