

#### Reagan Haney

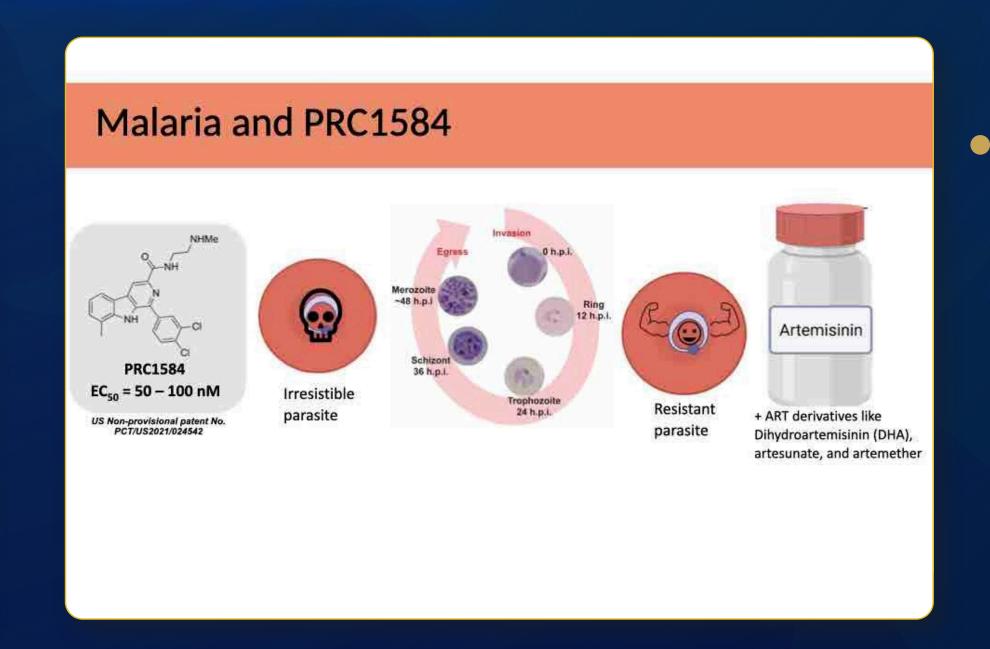
Ph.D. Candidate, Biochemistry and Molecular Biology Second Year ARCS Scholar Herz Global Impact Award



### Deciphering the mechanism of action of β-carboline derivatives – A novel class of antimalarials

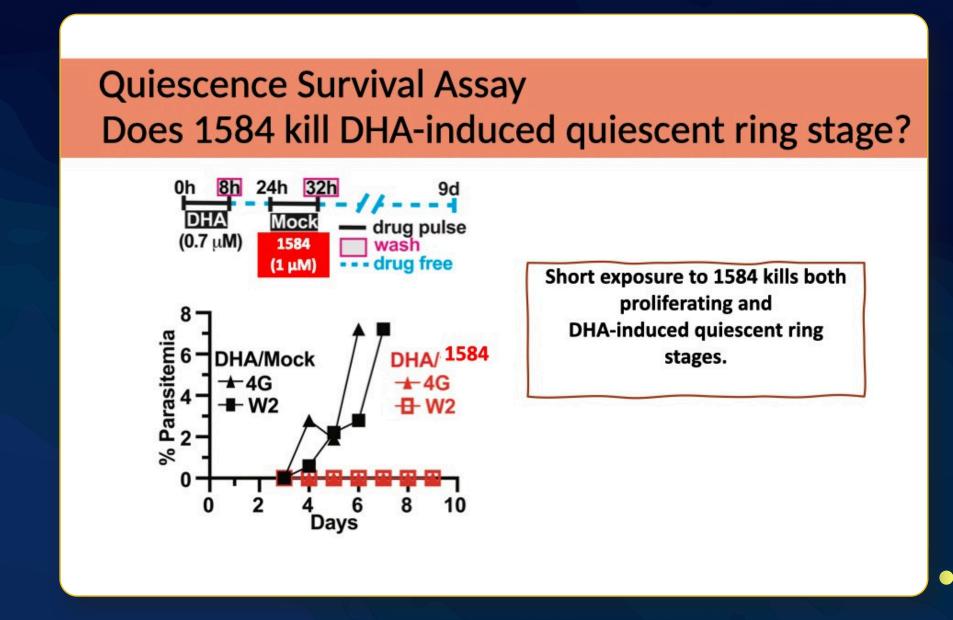
Malaria is a devastating disease that caused approximately 619,000 deaths in 2021 worldwide. Cases of malaria have increased from previous years in part by the quick development of resistance to current antimalarials. Due to the rising resistance to current antimalarial drugs such as chloroquine and artemisinin, there is an urgent need to discover and develop new drugs that engage new targets in the malaria parasite. This research focuses on a novel antimalarial called PRC1584.

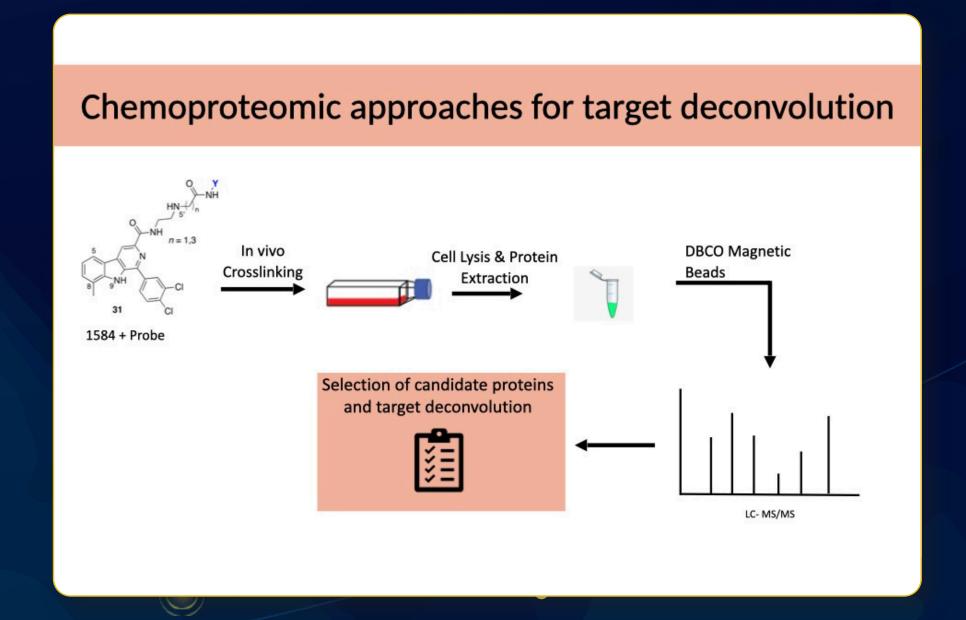
## Malaria is a life-threatening disease caused by Plasmodium parasites that are transmitted to humans when infected female Anopheles mosquitoes take a blood meal. Sponsoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Spinosoles develop Spinosoles develop Life Cycle of the Malaria Parasite Intervalvation to mosquito Spinosoles develop Spinosoles de



#### Early Lead Criteria for Antimalarials Global Health Innovative Technology (GHIT) Fund and Medicines for Malaria Venture (MMV) devised the following PRC1584 disease-specific criteria for early leads for malaria. Image » Treatment P. berghei <100 nM for sensitive and multidrug-resistant EC<sub>50</sub> strains of plasmodium spp. Selectivity >100 in mammalian cells Day 5 (2T) Day 7 (4T) Index When administered orally in blood stages of infection: In vivo Clearance at a dose that eradicates efficacy 90% of the target (<50 mg/kg) (four doses over 4 days) Unable to generate resistance Irresistible

# • Quiescence - is the altered ring stage development in artemisininresistant *P. falciparum* in which ring stages persist for extended periods of development in the absence of drug. 8-hour DHA exposure





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