PURDUE INNOVATES | Office of Technology Commercialization

Covalent Inhibitors as Anti-malarial Agents

Nucleic acid delivery system boosting viral surface antigen expression for stronger B-cell response.

Researchers at Purdue have discovered several small molecule drugs that significantly inhibit the growth of the asexual blood stage and the sporozoite hepatocyte stage of the Malaria parasite, Plasmodium falciparum. Recently, resistance to common anti-malaria medications has developed in Asia, South America, and Africa, necessitating the need to develop therapeutics to combat this rise in resistance.

The researchers selected an essential protein to the function of the malaria parasite to target with novel small molecule inhibitors. The selected protein has few known inhibitors and has key differences from the human ortholog. This key difference can be exploited to allow for stronger selection for only the malarial protein, reducing the potential of side effects. The researchers used a known covalent fragment library and were able to identify 6 molecules that showed significant inhibition in vitro at the low to mid micromolar level against three strains of P. falciparum, two of which are multi-drug resistant. Furthermore, these molecules showed high selectivity for the target enzyme in the malaria parasite over the human ortholog.

Technology Validation:

- Inhibitory activity of hit molecules tested in vitro against 3D7, CAM3.II K13 WT, and CAM3.II K13 C580Y malaria strains by exposing each one to a range of concentrations (0.5 â€“ 500 ÂµM) of each molecule and assessing the parasite viability 72 hours later.

- Selectivity of hit molecules for target enzyme over human ortholog assessed by exposing both to varying concentrations of each molecule and measuring the absorbance of the solution over time after initiation with a fluorescent substrate for the enzymes of study.

Advantages:

Technology ID
2023-FLAH-70246

Category
Pharmaceuticals/Drug Discovery & Development

Authors
Daniel P Flaherty
Ryan Imhoff
Caroline Ng

Further information
Joe Kasper
JRKasper@prf.org

Nathan Smith
nesmith@prf.org

View online

- Molecules show significant anti-malarial activity to multi-drug resistant strains

- High selectivity for malarial enzyme over human ortholog

Applications:

- Anti-malaria medications

- Medical diagnostics

Webpage for Additional Information:

Dr. Daniel Flaherty is an Associate Professor in the Department of Medicinal Chemistry and Molecular Pharmacology at Purdue University. Dr. Flaherty received his Ph.D. in pharmaceutical sciences from the University of Nebraska Medical Center. Following this, he became a post-doctoral researcher under the direction of Dr. Jeffrey AubÃ© at the University of Kansas. He has been awarded the Chaney Family Early Faculty Scholar Award in 2023, and the Best Oral Presentation at the 4th International Symposium on Frontiers in Molecular Science in 2022. Dr. Flaherty's lab is particularly interested in developing small molecule drugs for under-explored targets of therapeutic interest.

For further information, visit Dr. Daniel Flaherty's lab website:

https://www.flahertylab.com/

TRL: Medical/Health

Intellectual Property:

Provisional-Patent, 2023-06-02, United States

PCT-Patent, 2024-05-30, WO

Keywords: Inhibitor, Malaria