GEORGE MASON UNIVERSITY

MEPicides: INFECTIOUS DISEASE PRODRUGS

GMU-22-019

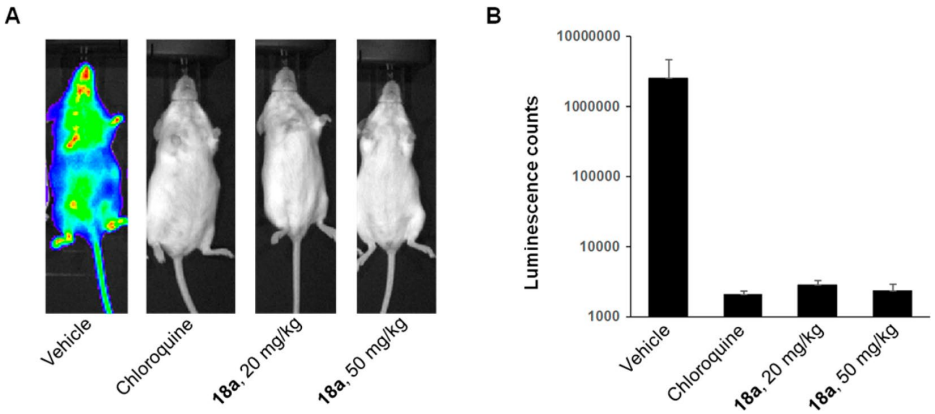
TARGETING MALARIA AT ITS CORE: A BREAKTHROUGH IN SAFE, POTENT TREATMENT

In collaboration with George Washington University, Mason's groundbreaking research has led to the development of MEPicide compounds. MEPicides are a novel class of antimalarials. The Mason MEPicides target the DXR enzyme in the metabolic pathway (MEP) of the malaria parasite, *Plasmodium falciparum*. The lead compound (18a) delivers potent, selective action with minimal toxicity, offering a new solution against drug-resistant malaria.

Key Features

- **Targeted Action:** Inhibits the essential DXR enzyme in the parasite's MEP pathway, leading to effective antimicrobial activity
- **High Potency:** The 18a lead compound shows an IC50 of just 13nM against parasite growth, comparable to first-line treatments like artemisinin
- **Novel Mechanism:** The unique mode of action combats drug-resistant malaria strains
- **Low Toxicity:** Exhibits no significant inhibition of human HepG2 cells, suggesting excellent safety and selectivity
- ***In Vivo* Efficacy:** Proven in mouse models, reducing parasitemia significantly without adverse effects

MEPicides represent a favorable avenue for next-generation antimalarial therapies.



Compound 18a is effective in an in vivo mouse model of efficacy. Mice were infected with P. berghei parasites expressing luciferase. From day 2 to day 7, mice were dosed daily with vehicle, 20 mg/kg chloroquine, 20 mg/kg 18a, or 50 mg/kg 18a. Mice were imaged using an IVIS imager at 7 days postinfection (A) and parasitemia was quantified (B). All doses were administered intraperitoneal (IP) injection.

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