

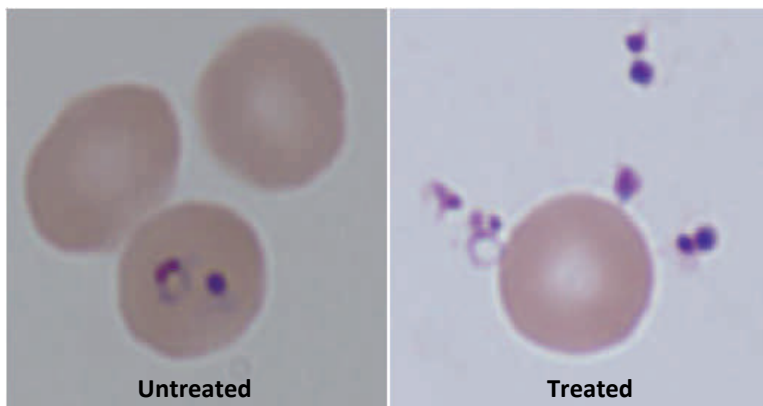


Novel Small-molecule Malaria Therapeutics

Overview of Technology:

Drs. Ian Crandall and Walter Szarek have developed a new class of small molecules that interact directly with the malaria parasite and neutralize its ability to invade red cells—an essential step in its life cycle.

These lead compounds have unique structures and are effective against *P. falciparum* (the most deadly form of human malaria) in culture with IC50s in the picomole and single-digit nM range (as low as 160 pM), compared with values observed for mammalian cells that are 4-5 logs higher—giving a very wide therapeutic window. Initial testing in a mouse model of malaria has shown these compounds to be both efficacious and well tolerated.



Inhibition of Malaria Plasmodium Invasion of Red Blood Cells

These compounds are excellent drug candidates since they have no chiral centers; can be synthesized rapidly and inexpensively; are stable; are soluble, and can easily cross membranes. No cross resistance with current anti-malarials has been observed which is consistent with their novel mechanism of action. Further, they cause parasite death after relatively brief exposure. These compounds have equivalent IC50 values in rodent malarials, which allows drug development using an inexpensive mouse model system. This work originated with tetrazolium based core structures, but has progressed to molecules based on much more stable core structures, generating anti-malarial agents with greater activity.

Malaria produces an estimated 247 million cases per year among 3.3 billion individuals at risk of the disease and results in nearly one million deaths—mostly in children under five years of age. Increasing resistance to current anti-malarials has created a critical need for new, low-cost, effective anti-malarials for the developing world. Additionally, a new, effective and well-tolerated anti-malarial would have a significant competitive advantage in the profitable military and travelers' use markets due to undesirable side-effects of therapeutics currently sold for these markets.

Licensing: This technology is available for licensing/development partnership on an exclusive basis.

Related Publication: Cui, X., Vlahakis, J.Z., Crandall, I.E., and Szarek, W.A. Anti-Plasmodium activity of tetrazolium salts. *Bioorg Med Chem.* **16(4)**,1927-47, (2008)

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