

“Endochin-like Quinolones (ELQs) as Broad Spectrum Anti-Parasitic Drugs”

PI: Scott Landfear

Abstract:

This pilot project represents an emergent interdisciplinary collaboration among three established OHSU investigators, Dr. Scott Landfear (MMI), Buddy Ullman (BMB), and Michael Riscoe (VAMC), that will explore the therapeutic potential of the Endochin-like quinolones (ELQs) as broad-spectrum anti-parasitic agents. Several ELQs have already shown remarkable curative properties against two important parasitic infections, malaria and toxoplasmosis, and are currently being readied for clinical trials. The overall objective of this proposal is to examine whether efficacy of these ELQs can be extended to other parasites of medical importance, specifically *Leishmania mexicana*, *Leishmania donovani*, and *Trypanosoma cruzi*, the etiologic agents of cutaneous leishmaniasis, visceral leishmaniasis, and Chagas' disease, respectively. Preliminary data obtained in the Landfear and Ullman laboratories demonstrate that many of the >100 currently available ELQs, synthesized in the Riscoe laboratory, are toxic toward the insect forms of both *L. mexicana* and *L. donovani*, and some ELQs are also remarkably effective against the mammalian form of *L. mexicana*. The three Specific Aims of this proposal will extend the initial observations of ELQ efficacy to the murine model of cutaneous leishmaniasis (Specific Aim 1), improve upon the potency of the current ELQ armamentarium (Specific Aim 2), and extend our drug discovery stratagem to *L. donovani* and *T. cruzi* (Specific Aim 3). The methodology required to accomplish the 3 Specific Aims amalgamates state-of-the-art techniques in molecular parasitology, pharmacology, and medicinal chemistry and will identify 'lead' compounds for treating the 3 diseases. The research in this proposal will be initiated 02/01/2013 and completed by 01/31/2014.