

# The Metalloprotease Inhibitor, 1, 10 Phenanthroline, as a Lead for Finding Drugs to Kill *Brugia pahangi* Worms

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The objective of my project was to inhibit the proteolytic enzymes of adult and microfilariae *Brugia pahangi* using protease inhibitors to see if these inhibitors could kill these parasites. I tested various classes of protease inhibitors (serine, cysteine and metalloprotease) on the adult and microfilarial stage of *Brugia pahangi* as well as on the adult and larval states of *Caenorhabditis elegans*. The worms were incubated in 24-well plates. The inhibitors were added in high and low dosages. The survival of the adult *Brugia* worms was quantified using a "Worminator," while the survival rates of the small worms (microfilariae and *C. elegans*) were recorded visually using a microscope. I used a scale from 0 to 5, with 0 = dead and 5 = very active. The metalloprotease inhibitor, 1,10 Phenanthroline (1,10 P) caused the greatest mortality on the adult *Brugia* at high (120uM) and low (24uM) concentrations within the first 24-hours of the assay. The microfilariae were not only killed by 1,10 P but also with high concentrations of a cysteine protease inhibitor, K11777. The low concentration did not have any effect on the microfilariae. *C. elegans* adults and larvae were killed by high concentrations of 1,10 P. Overall the metalloprotease inhibitor 1,10 P had the greatest effect on both the parasitic worm, *Brugia* and the free-living nematode, *C. elegans*. To see if I could find other metalloprotease inhibitors that were structurally similar to 1,10 P, I used the ZINC database to find other drugs. There was only one drug that had a similar chemical structure to 1,10 P and I would be interested in investigating this drug, as well as other metalloprotease inhibitors, on the worms to determine if they could be a potential anti-parasitic drug.

## Awards Won:

Fourth Award of \$500