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

Moser, Matthew

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