CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

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Project Number

36280

Project Title

Metalloprotease Inhibitors as Lead Candidate Drugs to Treat Lymphatic Filariasis and Other Roundworm Infections

Abstract

Objectives/Goals

Lymphatic filariasis (elephantiasis) is a Neglected Tropical Disease caused by the parasitic nematodes Wuchereria and Brugia. Over 120 million people worldwide are infected and more than 1.4 billion people are at risk of infection. Adult worms live inside lymphatic tissue for several years and chronic infections lead to tissue swelling, pain, and enlarged limbs. Only the adult stage causes the disease and currently, there are no optimal drugs (Ivermectin) that eliminate the adult worms. The focus of this study was to identify a compound or drug that could inhibit the adult worm#s proteolytic enzymes which are important to the worms# survival. Previous results showed that the metalloprotease inhibitor, 1,10-Phenanthroline (1,10P) was highly effective in killing adult Brugia pahangi within 48 hours. In this study, FDA-approved drugs and a preclinical drug that are all metalloprotease inhibitors were assayed with adult B. pahangi in vitro.

Methods/Materials

Worm mortality was quantified using a "Worminator", an instrument that records how many pixels per second are being displaced under a set camera, allowing for an accurate measurement of the protease inhibitor's impact on worm survival. To determine if metalloproteases are also critical to the survival of other parasitic nematodes, the sushi parasite, Anisakis, was assayed with the metalloprotease inhibitors. A spectrofluorometer was used to analyze enzymatic activity

Results

Results showed that Luteolin, 1,10P, and 4,7-D were the most effective drugs in killing the adult stages of Bruiga pahangi with IC50s of 32µm, 15µm, and 7µm, respectively. Luteolin and 1,10P inhibited the motility of the infectious stage of Anisakis in vitro by 85% and 90%, respectively. Biochemical assays showed that Luteolin and 4,7-D inhibited the metalloproteases in Anisakis worm lysates by 100% compared to the control.

Conclusions/Discussion

This study showed that metalloproteases are critical for the survival of Brugia, the parasitic nematode that causes Lymphatic Filariasis as well as, Anisakis, which is also known as the sushi parasite. WHO estimates that over 2 billion people are infected by helminths worldwide and this study suggests that metalloprotease inhibitors may be useful as lead candidates to treat lymphatic filariasis and other roundworm infections.

Summary Statement

This study was able to identify three metalloprotease inhibitors that can be used as an effective treatment to lymphatic filariasis and other roundworm infections

Help Received

My mentor, Dr. Judy Sakanari, supplied with me the compounds, worms, and lab space to conduct my research.

Preliminary