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Validation of Methionine Aminopeptidase-1 as a Potential Chemotherapeutic Target for Leishmania major

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Cutaneous leishmaniasis is a vector-borne disease caused by *Leishmania major* affecting millions of people throughout the world. It is an emerging concern in the United States due to military establishments in endemic countries. Treatment for the disease is highly toxic and the lack of vaccines emphasizes on the need for alternative drug treatments. Aminopeptidase inhibitors have shown promising results against malaria and tuberculosis. Methionine aminopeptadse-1 (MetAP1) catalyzes the removal of the N-terminal methionine residue from peptides and proteins. The human MetAP1 has low similarity with the *Leishmania* enzyme making it a potential chemotherapeutic target. The MetAP1 gene was amplified through PCR from *L. major* genomic DNA and cloned into the expression vector pRSET A. The expression and purification of the recombinant enzyme was performed and the biochemical characterization of the enzyme is underway. Transgenic promastigotes of *L. major* (Friedlin clone V1) expressing firefly luciferase were used to determine the antiparasitic activity of putative MetAP1 inhibitors. Eight compounds were tested and three of them showed great anti-leishmanial activity at 0.78μM for 72 hr. with 5-6% survival (IC_{50} = 125 nM). The enzymatic assay using the recombinant enzyme will be developed to determine the inhibitors' specificity.