Potential Inhibitors of Ldlip3 Lipase Targeting Pathogens Lipid Metabolism to Combat Leishmaniasis

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Visceral Leishmaniasis caused by leishmanial species mainly by *Leishmania donovani*, most common in India and is spread through sandflies. Shakarian *et. al.* characterized LdLip3 an exported/secretory novel lipase and proved

that its mRNA is constitutively expressed by both the promastigote and amastigote. Leishmania are typically opportunistic facultative lipid scavengers and earlier studies have shown amastigotes have elevated fatty acid metabolism compared to promastigotes. Extensive use of pathogen's lipid metabolism especially in utilizing the host lipids for energy metabolism and in virulence highlights the importance of exported lipid catabolizing enzymes. Current study aims finding LdLip3 as drug target which would aid in combating Leishmaniasis. Since the structure of *Leishmania donovani* LdLip3 enzyme is not yet known, we modelled the 3D structure followed by the identification of leishmanial specific potential inhibitors utilizing Structure Based Drug Design approach using NCI diversity set and ZINC database. The identified potential inhibitors with higher predicted free energy of binding towards LdLip3 than human lipase which might selectively kill the parasite will be used to exploit the potential of natural products to be anti-leishmanial drugs. ZINC02141591 was the best hit with difference in free energy of binding of -2.38 which might be a potential non-covalent inhibitor. LdLip3 represents a suitable and promising drug target and is also a step towards understanding and targeting pathogen's lipid metabolism, thereby addressing novel therapeutic molecules to combat leishmaniasis.