IN SILICO DRUG DESIGN AGAINST WOLBACHIAI ENDOSYMBIONT OF BRUGIA MALAYI

JOHN MUTUKU NZAU¹; JOSEPH NG'ANG'A²; JOHNSON KINYUA³

¹Department of Biochemistry, College of Health Science, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000 Nairobi.
²Department of Biochemistry, College of Health Science, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000 Nairobi
³Department of Biochemistry, College of Health Science, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000 Nairobi

Abstract
Lymphatic filariasis, a nematode disease, caused by Brugia malayi and Wuchereria bancrofti. As second causative of morbidity, it continues inflicting socioeconomic burden, pain and suffering amongst endemic areas. This calls for affordable interventions, effective to manage the disease. This study screened Wolbachia endosymbiont of Brugia malayi genome for putative drug targets using GenScan™ and modeled novel drug compounds by use of in silico approach. The target proteins uniqueness was determined using homology search algorithms and BLASTp against human genome. Target sequences were validated by searches against TDR drug targets database. The 3-D structures of the target proteins were modeled and viewed using Cn3D program. Docking was done using Arguslab™ and candidate drug molecules generated. The drug relevant properties of the molecules were predicted using OSIRIS property explorer. The target proteins identified were Glutathione synthetase , MurF protein and MurD ligase .Validation confirmed that they are unique to the parasite, not found in the human genome and are available in the TDR database. Structure prediction revealed target proteins were made of either one or two amino acid chains, their sizes ranged between 305- 445 amino acids, molecular weights (34-48 kDa) and had cysteine, arginine and serine residues in the active sites. Ligand docking work reported 3 molecules glutathione,2-chloro-N-(3-cyano-5,6-dihydro-4H-cyclopenta[b]thiophen-2-yl)-5 (diethylsulfamoyl)benzamide and naphthalene-N-sulfonyl-D-glu derivative as candidate drug molecules. OSIRIS property showed that the molecules had molecular weights (307 - 345 g/mol), Log S values (-4.9 - 0), c Log P values (-4.9-3.5), druglikeness values (-19.1-1.2) and drug score values (0.46 – 0.62). There were no risks of toxicity such as reproductive, irritating and tumorigenic effects reported except for one molecule which had low risk mutagenicity.
References

10. Ayma Aftab, Khalid Masood. (2011). "In silico drug designing via bioinformatics approach." Pakistan times volume 2, no. 1