

Title:

COMPUTATIONAL MODELS FOR THE DISCOVERY BASED ON THE STRUCTURE OF DRUGS

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Abstract:

CANDIDATES FOR ZIKA VIRUS INHIBITION Currently drug discovery is a widely used tool in the pharmaceutical and medical industry, traditionally this was a trial-and-error method making the processes long and expensive, for this reason the development of virtual screening techniques based on the structure arises as one of the tools to speed up this process. Zika has been considered a serious disease according to the WHO since 2016, due to its effects in neonates who presented microcephaly and Guillan Barre syndrome in other patients. During the investigation, a structure-based virtual screening was used to identify potential inhibitors of the enzyme's protease and methyltransferase of ZIKV, the methodology used arose from a combination of several energy scoring functions using three different molecular coupling programs or Docking software's: Dock6, GOLD and OpenEye. In selecting the best combination of functions, 32 compounds that were reported as active for NS2BNS3 Protease and 50 compounds for NS5 MethylTransferase were used. Using decoy compounds, the method was trained so that together with the ligands they were coupled to the respective enzymes and generated potentially active molecules for these enzymes where 15632 structures with favorable values were obtained. In the search to improve the methodology, a combination of "score" functions were implemented that maximized the enrichment of the compounds. Using the programs described above, it was determined that a combination of the functions 2-4-6 assigned from this molecular coupling software's significantly improved the enrichment values of the molecules. Subsequently, the methodology was evaluated to determine if this combination favors enrichment by calculating the BEDROC and the enrichment factor "EF". During this analysis, it was found that at 1% of the screening recovered three active compounds for NS2B-NS3 and four compounds for NS5. This indicated that the method works, and that the combination of the selected enrichment functions favors the discovery of new drug candidates that inhibit ZIKA.