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Abstracts Book

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C.016 - COMPUTATIONAL BIOLOGY TOOLS IN DESIGN OF AN AGROCHEMICAL AGAINST XYLELLA FASTIDIOSA

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INTRODUCTION The bacterium Xylella fastidiosa causes several diseases in economically important crops. In Brazil, it affects the sweet orange, coffee and plum. In Sao Paulo, 40% of 200 million orange trees have CVC disease caused by action of Xylella fastidiosa, thus causing $100 million expense per year. This Gram-negative bacterium colonizes the xylem vessels in plants and the foregut of some insects that act as vectors of CVC infection. Xylella fastidiosa forms aggregates or bacterial film that usually block the flux of water and nutrients and silently kill the orange trees. OBJECTIVES Since its pathogenicity is related to bacterial motility, the protein PilT from the twitching motility system has been chosen as the host target. Using rational drug design, based on a detailed comprehension of the protein host structure, small molecules were designed in order to block the activity of the protein and provoke the loss of the bacterium pathogenicity. MATERIALS AND METHODS The programs Discovery Studio and Yasara were used in the drug design processes. The homology model for the Xf_PilT protein had been designed. The model has been validated through the analysis of Ramachandran graphs and the use of ProSA web-service. Energy minimization and molecular dynamics were performed in Pipeline Pilot as to optimize the constructed model. Pockets involving the target residues were identified and docking, using virtual high throughput screening (vHTPS), with commercially available compounds (Zinc database) were also performed. DISCUSSION AND RESULTS The selected ligands were improved in order to optimize their affinities using de novo techniques. The best pairs of the protein-ligand were ranked and selected for in vitro tests. CONCLUSIONS Finally, the development of new agrochemicals might be favored by the use of the in silico discovery of the perfect site-targets in the protein and make possible to design the best set of inhibitors as chosen matched guests in any host-guest interaction pair. Keywords: Xylella fastidiosa, PilT, Computational biology tools

C.017 - MOLECULAR MODELING AND DYNAMICS SIMULATIONS OF ANG PROTEIN SIGNAL PEPTIDE IN AMYOTROFIC LATERAL SCLEROSIS

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INTRODUCTION The role of the protein angiogenin (ANG) in angiogenesis is well-established in the literature. Recent studies have found an association between mutations in the signal peptide of ANG and the development of familial amyotrophic lateral sclerosis (fALS). ALS is a progressive, lethal, neurodegenerative disorder, characterized by the degeneration of motor neurons. OBJECTIVES This research aims to investigate, using molecular modeling and dynamics simulation (MD) approach, the conformational changes in the ANG mutant protein structure (M1I, F12S, F12L, G15D, P20S, P21Q, and P21S). MATERIALS AND METHODS Structural theoretical models were created for the wild type protein through ab initio (I-Tasser, QUARK and Rosetta) modeling. The structure of the ANG protein was obtained from I-Tasser modeling. To build the mutant structures, we performed in silico mutagenesis. These structures were energetically optimized by GROMACS package 4.5.5 using an AMBER 99S force field. During energy minimization, both native and mutant structures were solvated in an octahedral box with simple point charge (SPC) water molecules. Initially, the solvent molecules were relaxed, and all of the solute atoms were harmonically restrained to their original positions. Then, the whole molecular system was subjected to energy minimization. DISCUSSION AND RESULTS The theoretical structures were created, and the I-Tasser model was used for the molecular dynamics simulation, which showed conformational alterations in the mutants of the signal peptide ANG protein. CONCLUSIONS Due to the mutations, ANG protein might alter the structure, subcellular location, and functional behavior of protein and play a major role in inducing ALS. Supported by : CAPES-DAAD, CNPq, FAPERJ, UNIRIO. Keywords: ANG, Database, Molecular Dynamics

C.018 - A COMPUTATIONAL MODEL TO DESCRIBE THE ParE-ParD INTERACTIONS AND THE RESIDUES MUTATIONS TO INCREASE THEIR AFFINITY

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INTRODUCTION ParE and ParD are proteins that belong to the toxin-antitoxin system (TA) which is spread all over microorganisms. ParE (12 KDa), the toxin, inhibits the catalytic activity of DNA gyrase, a biological target of antibacterial drugs. ParD (9 KDa) is the antitoxin and neutralizes the ParE action by a stable complex formation. Clarifying the arrangement of this protein complex is crucial the understanding of the mechanism and the identification the main amino acids residues involved in the proteins interactions, to address specific mutations on ParE or ParD proteins and to obtain peptides with more affinity. OBJECTIVES This also can be viewed as an alternative strategy to develop novel antimicrobial drugs with a distinguished mode of action against resistant bacteria, our objective. MATERIALS AND METHODS In our continuous investigation to identify new topoisomerases inhibitors, several fragments of ParE and ParD were synthesized and studied by affinity chromatography and fluorescence assays. DISCUSSION AND RESULTS A ParD peptide analogue, containing the carboxyl-terminal 45 amino acids residues of ParD maintained the same properties of wild type protein and interacting with a ParE derivative (residues Met-1 to Ala-45 of ParE protein). Then, we carried out a computational study with these sequences comprising modeling of these fragments, docking, molecular dynamics with annealing simulation and alanine scanning. The aim of this in silico protocol was to establish a model for describing the molecular interaction between these fragments and to provide a path for choosing specific residues to be mutated which could lead to new ParE derivatives with increased ParD affinity. CONCLUSIONS The results of the computational investigation and the experimental findings were matching and resulted in a minimal ParD sequence, corresponding to an alpha-helix structure, able to interact more strongly with ParE. Keywords: Computational study, ParE-ParD, Residue mutation