BIO_09 - Structural modeling of two anti-*Acinetobacter baumannii* monoclonal antibodies and the target surface protein

Laianne Dias Inácio[1]; Juliana Georg da Silva[1]; Anna Érika Vieira de Araújo[1]; Cristiane Pinheiro Pestana[1]; Milena Mouta Verdan França Carvalho[1]; Alexandro Guterres[1]; Mayla Abrahim Costa[1]; Ana Paula Dinis Ano Bom[1]; José Procópio Moreno Senna[1].
[1]Fiocruz/Bio-Manguinhos

Introduction: *Acinetobacter baumannii* is a multidrug-resistant bacterium associated with nosocomial infections, being considered a global threat to public health and a critical priority for the development of new therapeutic options. In this scenario, monoclonal antibodies (mAbs) emerge as specific and promising approach. Bioinformatics has tools capable of modeling biological macromolecules, as well as, evaluating the possible regions in which antibody-ligand recognition occurs. Identifying possible antigenic regions in a target, as well as, the paratope in an antibody, are important for studies of mAb affinity maturation, development of synthetic peptides, among other approaches.

Objectives: To perform the structural modeling of two mAbs and the target protein of *A. baumannii*, predicting the possible epitopes.

Methodology: Sequence of variable regions of two mAbs, obtained by hybridoma technology, were previously obtained by Sanger sequencing and analyzed by IgBlast tool. Then, mAbs had their structure modeled by ABodyBuilder program. Initially, the signal peptide of the target recombinant protein was identified by SignIP 5.0 program and removed for the structural modeling step by AlphaFold 2 program. All models of mAbs and target protein generated were validated by Ramachandran Plot using the MolProbity program, and the most promising ones were selected for the prediction of epitopes by Seesar 13.0.5 program.

Results: Structure of mAb 1 validated by MolProbity showed good reliability with 90.1% of amino acid residues in favorable regions, 98.6% of residues in allowed regions and only 3 residues as outliers. The mAb 2 also showed good reliability with 88.6% of the residues in favorable regions, 97.5% of the residues in allowed regions and only 5 residues as outliers. In the target protein, 36 residues that constitute the signal peptide were identified and removed. Then, its structure was generated by AlphaFold 2 obtained a pLDDT of 89.8 and its validation indicated that 97.4% of the residues were in favorable regions, 99.5% of the residues in allowed regions and only 4 residues as outliers, featuring high reliability. In addition, in this structure were predicted 12 possible binding regions, which will be subsequently tested through molecular docking.

Conclusion: Modeled structures of both mAbs and the target protein showed good reliability. In addition, it was possible to map the possible epitopes of the target protein for later molecular docking stage. These results are important tools in order to identify the regions of greater affinity with the mAbs generated.

Keywords: Structural modeling; Prediction of epitopes; Antimicrobial resistance