TITLE: Spatial location of the main resistance-causing mutations in *Escherichia coli* RNA Polymerase β subunit: a bioinformatics approach

AUTHORS: SOLANO, C.M.; LEITE, J.S.; SILVA, F.H.C.F.L.; FACHIN, L.P.

INSTITUTION: CENTRO UNIVERSITÁRIO CESMAC, MACEIÓ, AL (R. da Harmônia - Farol, Maceió - AL, 57081-350)

ABSTRACT:
The biomedical community knows about bacterial resistance to antibiotics almost since the early antibiotic era. However, the main concerns has only emerged within the past twenty years, when resistant strains have emerged with dangerous regularity. In view of this, caution is required regarding its medical prescription and due to the consequent public health problems. Such resistance may occur through different mechanisms, including missense mutations, in which a specific position of the bacterial gene undergoes a mutation; or by the incorporation of a resistance gene from another microorganism, through a plasmid. Resistance caused by missense mutations, which are the main interest to this work, involves the acquisition of permanent changes in the bacterial genetic code, within the antibiotic compound's target proteins. Such aspect leads to the transmission of these characteristics to the next bacterial generations, making the bacteria and their offspring permanently resistant. In this context, as part of the initial steps of a research line on the characterization of the effects of the missense mutations that cause antibiotic resistance on the conformation and dynamics of their target proteins, the present work aims to show which regions of a bacterial protein's missense mutations occur most frequently. In this context, in this study, one of the proteins most affected by such mutations, the β subunit of *Escherichia coli* RNA Polymerase, was chosen. Bioinformatics tools, including the Swiss PDB Viewer program, were used to mutate the wild-type protein, and visualize the three-dimensional location of the mutated amino acid residue. As a result, it was observed that the Asp516Val, His526Tyr and Ser531Leu mutations, which are located nearby in the linear sequence of the protein, are also spatially located, in the region of the Rifamycin binding site, specifically in a cavity inside the protein. Based on these results, it is expected that the obtained data will contribute to future studies aiming to identify the influence of the mutation on the antibiotic compound's binding to such protein and, based on such studies, to propose chemical modifications in these bioactive agents for the development of new antimicrobial agents.

Keywords: mutations, bioinformatics, antibiotics, resistance-causing, bacterial.