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RESEARCH ARTICLE

TAXONOMICAL ANALYSIS OF B-LACTAMASE PROTEINS USING COMPUTATIONAL CHEMISTRY

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ABSTRACT

Currently, it is important to classify the mechanisms by which bacterial resistance occurs, since it represents a serious problem in terms of public health. The goal was to make a phylogenetic analysis of bacterial β-lactamases to prepare a classification based on their molecular sequence, unlike previous classifications. A phylogenetic tree of clinically important bacterial β-lactamases was constructed using their molecular sequences. A cladogram was made to analyze the characteristics of the families and subfamilies. The cladogram analysis shows the existence of three large families of β-lactamases**.** This work represents an advance to classify β-lactamases by their molecular sequence.

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INTRODUCTION

β-lactamic antibiotics are known for inhibiting the activity in transpeptidases and carboxypeptidases due to an acylation in a serine residue in the active site. Specifically, in the PBPs. (Fisher, 2005 and Macheboeuf, 2006). β-lactamases are enzymes, produced by bacteria,that are responsible of the antibiotic resistance that these organisms present during the exposure to antibiotics like penicillin, cephalosporins and carbapenem antibiotics (Murray, 2017 and Jawetz, 2014). Now a days, the reports of antibiotic resistance are raising in more frequent numbers (Wilke, 2005), for which is necessary to do a phylogenetic analysis with the use of the new technologies of molecular biology (Attwood, 2002). This is done to identify the evolution of β-lactamase proteins and their possible impact in the microorganisms of clinical relevance. (Yamada, 2007).

Objective: To construct a phylogenetic tree of diverse β-lactamase enzymes of clinical-relevant bacteria using their molecular sequence. To know the diverse classifications that are shown in the resulting cladogram. To analyze the characteristics of the families and subfamilies of β-lactamase enzymes that will be displayed in the multivariate analysis aided with computational chemistry.

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MATERIALS AND METHODS

A search was conducted in PDB of the selected enzymes (8). The FASTA code of each one was downloaded. In the CLUSTAL OMEGA server, (9) the alignment and multivariate analysis of conglomerates were conducted to build and determine the phylogenetic tree. To finish, a classification was done based on the results of the phylogenetic tree.

RESULTS

The cladogram analysis taken from CLUTAL OMEGA confirms the existence of three large families of beta-lactamases, which were named 1, 2 and 3. The first clade or family has 2 subfamilies, while family 3 has 4 subfamilies (see Figure 1).

DISCUSSION

The analysis of the cladogram shows the existence of three large families of β-lactamases, which we will call 1, 2 and 3. The first clade or family 1, has in turn 2 subfamilies. The first subfamily is made up of active serine hydrolases. The peculiarity of all these β-lactamases is that they have serine in the active site. Thesecond subfamily contains the active β-lactamases hydrolases, highly resistant to inhibitors such as

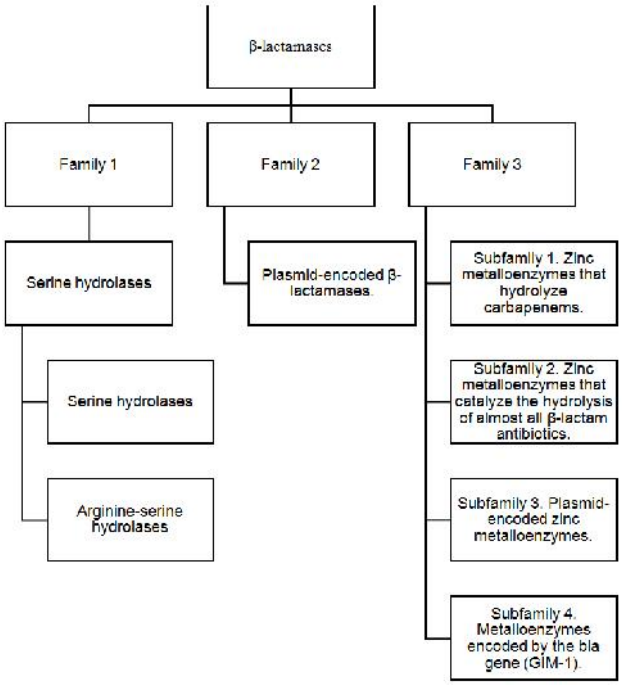

Figure 1. The classification based on the sequential alignment can be classified in 3 families. Family 1 has 2 subfamilies, while family 3 has 4 subfamilies

clavulanate. These have arginine and serine at their active sites.The second family is made up of plasmid-encoded β-lactamases.The third group or family is made up of hydrolytic metalloenzymes, that is, β-lactamases that have metal cofactors in their active site. On the other hand, the Ambler molecular classification, one of the main classifications of β-lactamases, refers to 4 families or classes. Class A that groups serine-penicillinases, class B metalloenzymes, class C a serine-cephalosporinases and class D serine-oxacillinases. In its classification, there is no molecular difference between β-lactamases of chromosomal or plasmid origin, a situation that did occur in our study. With regard to metalloenzymes or class B, Ambler considers 3 subfamilies: B1, B2 and B3. Subfamilies B1 and B3 encompass enzymes with a broad spectrum of action, while B2 are Carbapenemases.

In our case we found 4 subfamilies of metalloenzymes.

- Subfamily 1. Zinc metalloenzymes that hydrolyze carbapenems.
- Subfamily 2. Zinc metalloenzymes that catalyze the hydrolysis of almost all β-lactam antibiotics.
- Subfamily 3. Plasmid-encoded zinc metalloenzymes.
- Subfamily 4. Metalloenzymes encoded by the bla gene (GIM-1).

The proposed classification can be summarized in figure 1.

CONCLUSION

The Ambler classification can be expanded, because it is not based in any phylogenetic analysis. This work can complement and justify the Ambler classification as seen in the results. This investigation represents a first advance to classify the β-lactamases using the protein molecular sequence. Our analysis only includes the FASTA codes of those β-lactamases of clinical-relevant bacteria. In order to create a more exhaustive classification, more enzyme codes are needed.

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REFERENCES

Attwood T, Parry-Smith D, González candelas F. Introducción a la bioinformática. Madrid: Prentice Hall; 2002.

Bank R. RCSB PDB: Homepage [Internet]. Rcsb.org. 2021 [cited 20 January 2021]. Available from: http://www.rcsb.org/pdb/home/home.do

Clustal Omega < Multiple Sequence Alignment < EMBL-EBI [Internet]. Ebi.ac.uk. 2021 [cited 20 January 2021]. Available from: http://www.ebi.ac.uk/Tools/msa/clustalo}

Fisher J, Meroueh S, Mobashery S. Bacterial Resistance to β-Lactam Antibiotics: Compelling Opportunism, Compelling Opportunity†. Chemical Reviews. 2005; 105(2):395-424.

Jawetz E, Melnick J, Adelberg E, Brooks G. Microbiología médica [de] Jawetz, Melnick y Adelberg. México, D.F.: McGraw-Hill Interamericana; 2014.

Macheboeuf P, Contreras-Martel C, Job V, Dideberg O, Dessen A. Penicillin Binding Proteins: key players in bacterial cell cycle and drug resistance processes. FEMS Microbiology Reviews. 2006;30(5):673-691.

Murray P, Rosenthal K, Pfaller M. Microbiologia médica. Barcelona: Elsevier; 2017.

Wilke M, Lovering A, Strynadka N. β-Lactam antibiotic resistance: a current structural perspective. Current Opinion in Microbiology. 2005;8(5):525-533..

Yamada M, Watanabe T, Miyara T, Baba N, Saito J, Takeuchi Y et al. Crystal Structure of Cefditoren Complexed with Streptococcus pneumoniae Penicillin-Binding Protein 2X: Structural Basis for Its High Antimicrobial Activity. Antimicrobial Agents and Chemotherapy. 2007;51(11): 3902-3907.

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