

TITLE: Molecular characterization of nosocomial *Providencia rettgeri* PR2 harboring *bla*_{NDM} gene

AUTHORS: MONTEIRO, A.S.; NUNES-NETO, W.R.; MUNIZ,G.S.; OLIVEIRA, G.C.; SANTOS, V.L.; RABELO, H.P.M.; SOUZA, M.V.D.; MELO, B.O.; BOMFIM, M.R.Q.

INSTITUTION: 1-UNIVERSIDADE CEUMA, CAMPUS RENASCENÇA (RUA JOSUÉ MONTELLO, Nº 1, RENASCENÇA II, CEP 65.075-120, SÃO, LUÍS-MARANHÃO, BRAZIL)

2- UNIVERSIDADE FEDERAL DE MINAS GERAIS (AV. PRES. ANTÔNIO CARLOS, 6627 – CEP: 31270-901, PAMPULHA, BELO HORIZONTE – MINAS GERAIS, BRAZIL)

ABSTRACT:

Providencia rettgeri is a Gram-negative bacillus widely distributed in the environment, and is currently considered an emerging human microbial pathogen associated with nosocomial infections. *P. rettgeri* has a highly dynamic genome, which contributes to its resistance to antimicrobials. The aim of this study was to analyze the antimicrobial susceptibility profile of *P. rettgeri* strains isolated from clinical samples and to conduct a genomic characterization. Eight (08) *P. rettgeri* strains were isolated from blood cultures samples of patients at an intensive care unit. The presence of the *bla*_{NDM} gene was determined by PCR. In addition, the minimum inhibitory concentrations (MICs) of antimicrobials were determined using VITEK automated system and conventional methods. The genome for *P. rettgeri* PR1 strain harboring *bla*_{NDM-1} were sequenced with Illumina MiSeq, and preassembled genomic DNA sequences were annotated using Prokka software. A complementary analysis of the genome was performed using *Rapid Annotation Subsystem Technology (RAST)*. From the eight (08) *P. rettgeri* strains, 07 were harboring the *bla*_{NDM} gene and showed resistance to meropenem and imipenem. The MIC values ranged from 8-128 µg/mL for two drugs. A partial genomic characterization for *P. rettgeri* strain PR2 strain using *RAST* indicated a wide range of genes related to drug efflux pumps and biocidal agents. Were detected in this study 91 genes were related to the subsystem virulence, disease and defense. The genetic systems were characterized, such as the multiple drug extrusion (*MATE*), family-division-nodulation (*RND*), and the major facilitator *superfamily (MFS)*. Partial genomic analysis of the *P. rettgeri* PR2 strain confirmed the presence of the *bla*_{NDM-1} gene and other genes for β-lactamase resistance. In addition, genetic systems for producing and releasing siderophores associated with iron uptake and other genes coding for the heme ring and heme receptors and transporters were identified. About 43 genes were identified and expressed proteins for uptake and metabolism iron. The mobilome analysis of the PR2 strain showed a high concentration of insertion sequences associated with mobile genetic elements, and prophages inserted into the genomes, suggesting the existence of a flexible genome. These *P. rettgeri* strains from clinical samples were highly diverse for antimicrobial resistance which may lead to difficulties for drug therapies against infections caused by this bacterial species.

Keywords: *Providencia rettgeri*, *bla*_{NDM}, antimicrobial resistance