

TITLE: HIGH OCCURRENCE OF HEAVY METALS TOLERANCE GENES IN *KLEBSIELLA* SPP. CLINICAL ISOLATES

AUTHORS: MOREIRA, N.C.¹; ANDRADE, L.N.¹; FERREIRA, J.C.¹; MARTINEZ, R.²; DARINI, A.L.C.¹

INSTITUTIONS: ¹School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo (Avenida do Café, s/n - Campus da USP, CEP 14040-903, Ribeirão Preto - SP, Brazil); ²Ribeirão Preto Medical School – University of São Paulo (Av. Bandeirantes, 3900, Monte Alegre, CEP: 14049-900, Ribeirão Preto - SP, Brazil).

ABSTRACT:

Antibiotic resistance is a major public health problem and a worldwide concern. In this scenario, the use of non-antibiotic antimicrobials, such as heavy metals, has increased aiming control and treatment of bacterial infections and, consequently, heavy metal tolerance genes have been increasingly detected in Gram-negative bacilli. The aim of this study was to investigate and correlate the occurrence of acquired heavy metal tolerance genes and acquired antibiotic resistance genes in *Klebsiella* spp. Clinical isolates from sterile sites from inpatients of a university hospital. This study included 31 *Klebsiella* spp. isolates, corresponding to 24 *Klebsiella pneumoniae*, 3 *Klebsiella variicola*, 3 *Klebsiella oxytoca* and 1 *Klebsiella aerogenes*. In addition, 13 of these isolates were susceptible to third/fourth-generation cephalosporin- and/or carbapenem and 18 isolates resistant to the same antibiotics. PCR was performed to search for acquired heavy metal tolerance genes *silA* (silver), *pcoA* (copper), *merA* (mercury), *arsB* (arsenic) and *terF* (tellurite) as well as acquired beta-lactamases genes (*bla*_{CTX-M}, *bla*_{TEM}, *bla*_{SHV}, *bla*_{BEL}, *bla*_{GES}, *bla*_{VEB}, *bla*_{PER}, *bla*_{BKC}, *bla*_{KPC}, *bla*_{IMP}, *bla*_{VIM}, *bla*_{NDM}, *bla*_{OXA-48}). High frequency of *silA* and *pcoA* genes were detected among the isolates (n=26) regardless of their resistance profile and species. Only two isolates did not harbor both genes. *merA* gene was also found in 10 *silA-pcoA* positive isolates. In addition, 7 isolates also harbored *bla*_{CTX-M group 1} and/or *bla*_{TEM}, *bla*_{SHV}, *bla*_{KPC} genes. Only three isolates did not carry any heavy metal tolerance genes investigated. Antibiotic resistance genes were detected in 17 isolates that harbor *silA* and/or *pcoA* genes. *K. oxytoca* that carried *bla*_{CTX-M group 8} gene and lacked heavy metal tolerance genes was the only exception. Reports of heavy metal-tolerant bacteria from different sources has increased, and the emergence and spread of heavy metal-tolerant bacteria has become a new concern. For this reason, it become important to know the epidemiology of the genetic determinants of heavy metals tolerant genes in different hospital bacteria as well as in bacteria from different settings, such as animal and environmental.

Keywords: heavy metal tolerance, beta-lactamases, *Klebsiella* spp.

Development Agency: São Paulo Research Foundation (FAPESP - Research grant 2018/26232-9 and Ph.D. fellowship, grant 2018/24286-4); Instituto Nacional de Pesquisa em Resistência Antimicrobiana (INCT –MCTI/CNPq/CAPES/FAPs n° 197 16/2014); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil 198 (CAPES) – Finance Code 001; National Council for Scientific and Technological Development (CNPq).