Characterization Of Antibiotic Resistance Genes In *Enterobacteriaceae* Plasmids From Humans, FoodProducing Animals And The Enviroment

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The family Enterobacteriaceae comprises species of clinically important pathogens which are widely distributed in the environment and in the gastrointestinal tract of animals. Species from this group are frequently reported as etiological agents of life-threatening diseases due to their virulence, including a high level of resistance to multiple antimicrobials. This bacterial family has a propensity to acquire and transfer genetic material, particularly through conjugative plasmids, therefore playing a role in the dissemination of antibiotic resistance genes (ARGs) between bacteria. Therefore, the aim of this study was to investigate the presence of ARGs in Enterobacteriaceae plasmids and to investigate the role played by these mobile genetic elements in disseminating ARGs between humans, animals and the environment. For this, 420 sequences of Enterobacteriaceae plasmids isolated from feces of cattle (n=69), chicken (n=41), swine (n=60), and humans (n=40), as well as soil (n=35) and sewage (n=175), were obtained from the NCBI database, To detect the presence of ARGs, the softwares/databases CARD and RESFINDER were used. The sequence polymorphism and neutrality tests of the most abundant genes were analyzed using DnaSP v.6 and the transfer potential of the plasmids was evaluated using oriTfinder. Lastly, a MOB-based phylogenetic tree was reconstructed using Fastree to make inferences about the plasmids evolution. RESFINDER and CARD predicted 1,046 ARGs among the plasmids analyzed, conferring resistance to 15 classes of antimicrobials. Aminoglycosides (n=322), beta-lactams (n=161) and sulfonamides (n=106) were the classes with the highest numbers of ARGs identified. The highest proportion of ARGs were identified in Enterobacteriaceae plasmids from chicken, while the lowest proportion of ARGs was observed in plasmids from bovine. The genes aph(6)-Id, aph(3'')-Ib, tet(A) and sul2 were the most abundant ARGs identified in this study, being detected in all analyzed ecosystems. The genes aph(3'')-Ib and aph(6)-Id showed a high level of sequence conservation, while tet(A) and sul2 were under positive selective pressure. Most plasmids carried multiple ARGs and were categorized as potentially transferable (62%), of which 88% were predicted as potentially conjugative and 12% as potentially mobilized. Lastly, the MOB-based phylogenetic analysis showed that bacteria from different genera and ecosystems grouped into several clades, showing that plasmids from different sources may share common origins. In conclusion, this study demonstrates a high prevalence of ARGs in plasmids from enterobacteria from different ecosystems, mostly present in potentially transferable plasmids, which highlights the relevance of One Health approaches to tackle antimicrobial resistance in pathogens widespread in nature.

Keywords: *Enterobacteriaceae*, Plasmid, Antibiotic Resistance Genes, One Health

Caracterização De Genes de Resistência A Antibióticos Em Plasmídeos de *Enterobacteriaceae* Isolados de Humanos, Animais de Produção e Ambiente

Plasmídeos conjugativos de enterobactérias contribuem para a disseminação de genes de resistência a antibióticos (GRAs) entre bactérias no ambiente. Neste trabalho o objetivo foi caracterizar GRAs em plasmídeos de Enterobacteriaceae de diferentes ecossistemas e investigar seu potencial de transferência. Os resultados demonstraram a detecção de 1046 GRAs, alguns dos quais estão sob pressão seletiva positiva. Além disso, a maioria dos plasmídeos são potencialmente conjugativos e possuem indícios filogenéticos de compartilhamento de origem. Em conclusão, plasmídeos de Enterobacteriaceae de humanos, animais de produção e ambiente apresentam alta abundância de GRAs e são potencialmente transmissíveis, representando uma ameaça à Saúde Única.