

The global resistome and frequency of stress-related genes in *Cronobacter* species

FELIPE PINHEIRO VILELA¹, LAURA TONIOLO DIAS¹, JULIANA PFRIMER FALCÃO¹

¹. UNIVERSITY OF SÃO PAULO, SCHOOL OF PHARMACEUTICAL SCIENCES OF RIBEIRÃO PRETO, RIBEIRÃO PRETO / SÃO PAULO, BRAZIL

Cronobacter spp. are emerging environmental bacteria causing opportunistic infections in newborns and children through the consumption of contaminated food items, such as powdered infant formula. In addition to its capacity to survive in low water activity, high temperatures, and acid pH, antimicrobial resistance rates have been increasing among *Cronobacter* species. However, despite the growing concern regarding its infections, few studies have characterized the occurrence of the resistance features in *Cronobacter* in a global scale. Therefore, this study investigated antimicrobial resistance (AMR) and stress-related genes through whole-genome sequencing in 2,132 genomes of *Cronobacter condimentii* (n=2), *Cronobacter dubliniensis* (n=123), *Cronobacter malonaticus* (n=122), *Cronobacter muytjensii* (n=18), *Cronobacter sakazakii* (n=1,739), *Cronobacter turicensis* (n=122), and *Cronobacter universalis* (n=6) from human and non-human sources, isolated between 1970 and 2024 in 27 countries, available at NCBI Pathogen Detection. A total of 99.8% of the genomes harbored at least one AMR gene, and 7.4% presented a multi-drug resistant (MDR) profile. A total of 67 AMR genes related to 11 drug classes were found. Resistance genes to beta-lactams (n=18), aminoglycosides (n=17), quinolones and trimethoprim (n=6, each), respectively, were the most diverse. Fosfomycin resistance gene *fos* (92.3%), beta-lactam resistance genes *bla_{CSA}* (61.1%), *bla_{CSA-2}* (18%), and *ampC* (12.6%), respectively, and colistin resistance gene *mcr-9.1* (5.9%), were the most frequently detected AMR genes among the genomes analyzed. Regarding heavy metal tolerance genes, all genomes harbored *fieF*, a cation diffusion facilitator, while arsenic, copper, mercury, nickel, silver, and tellurium tolerance genes were found in diverse frequencies. Heat (*clpK*, *hdeD-GI*, *hsp20*, *kefB-GI*, *psi-GI*, *shsP*, *trxLHR*, *yfdX1*, *yfdX2*), acid (*asr*), and disinfectant resistance genes (*qac*) were also found. In conclusion, the detection of AMR genes from 11 drug classes and possible MDR strains worldwide evidence the hazard of *Cronobacter* to humans, and the necessity for better surveillance and monitoring by authorities. Moreover, the heavy metal tolerance genes detected alert for the potential co-selection of AMR strains, while acid, heat and disinfectant resistance genes reinforced the capacity of *Cronobacter* to survive and persist in the environment and food.

Agradecimentos: CAPES - Finance Code 001 and FAPESP (processes 2021/07365-0, 2024/18739-7, 2025/01937-3)