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ARE METALS DRIVING THE EMERGENCE OF SALMONELLA NON-TYPHOID MULTIDRUG RESISTANT CLONES?

Joana Mourão¹; Jorge Machado²; Carla Novais¹; Lúfa Peixe¹; Patrícia Antunes³

¹Chemistry Department, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal

Antibiotic resistant (AB^R) *Salmonella* is a public health threat and might be selected by diverse environmental stressors (e.g. metals) used in animal production setting. We aimed to assess occurrence of known metal^R genes among non-typhoid *Salmonella* belonging to clinical relevant clonal lineages and to characterize the genetic elements linked to their mobilization along with AB^R genes.

Salmonella (n=92) of 16 serotypes, including emergent *S.* 4,[5],12:i:- (n=32) and *S.* Rissen (n=30), and 30 isolates representative of AB^R clones from human/non-human sources from Portugal (2000-2011) were studied. Genes associated with AB^R/integrons (Int), Cu^R(*pcoD*), Ag^R(*silA*), Hg^R(*merA*), As^R(*arsB*) or Te^R(*terF*) were searched by PCR/sequencing. Conjugation assays, genomic location (I-Ceu/S1-PFGE/hybridization) and plasmid (PL) analysis (rep-PCR/sequencing) were done.

Ag^R(72%), Cu^R(57%), Hg^R(47%), Te^R (3%) or As^R(1%) genes were found in different serotypes. All *S.* Rissen (ST469; 60%-*bla*TEM-*aadA*-*sul1*/*sul3*-*tetA*-*dfrA12*) carried *pcoD*+*silA* in chromosome (Ch) as *S.* Typhimurium monophasic variant from European clone (n=17; ST34), which also have co-located AB^R genes (*bla*TEM-*strA*-*strB*-*sul2*-*tetB*) and the majority *merA*. In contrast, *S.* Typhimurium monophasic variant of the Spanish (n=10; ST19) and Portuguese (n=5; ST19) MDR clone carried *merA* and/or *silA* on large non-transferable IncA/C PL (110-170 Kb) or IncR PL (110-140) respectively and MDR *S.* Typhimurium (n=11; 4 clones; ST19/ST313) the *silA* (n=1; DT104 clone) on IncN PL (135Kb) with atypical type I-*sul3* integron, and *merA* (n=3) with *int1*-*oxa30*-*aadA1* (n=2) or *aadA1* (n=1) on transferable IncFII PL (140Kb). In *S.* Enteritidis (ST11) only *merA* (n=2/4) was detected on transferable IncP PL (80Kb) along with *int1*-*dfrA1*-*aadA1*. In isolates of other MDR clones (n=15; 12 serotypes), *merA* (n=13) and/or *silA*+*pcoD* (n=6) were co-located with different Int on large plasmids (>100Kb; IncHI1/IncP/IncI1/NT). The *arsB* (n=1) and/or *terF* (n=3) were located on transferable IncHI2 (240Kb) with *bla*_{CTX-M-9} and in IncP (265kb) and untypable (250kb) PL, with *int1*-*aadA1* or *dfrA1*-*aadA1*/*pcoD*/*silA*/*merA*.

Metal^R genes were often co-located with Int/AB^R genes in diverse PL types carried by clinically relevant serotypes/clones, demonstrating the high genome plasticity of *Salmonella* to acquire different adaptive traits. Continued use of Cu/Ag or Hg environmental pollution might favour the selection of AB^R *Salmonella* by clonal spread and/or PL horizontal transfer.