Lysine was the wild-type residue at Vif-22 in subtypes B, D, H, J and K, and sub-subtype F1 (‘K22 variants’). However, the wild-type residue was asparagine in the remaining variants (A1, A2, C, F2, G, CRF01_AE and CRF02_AG; ‘N22 variants’). Interestingly, the change to histidine (codified by codon CAC or CAT) is different according to the original residue. Its emergence requires two changes from K22 (mostly codified by AAA), but only requires a single change from N22 as the wild-type residue (AAC or AAT).

We found a significant 2-fold higher H22 prevalence in N22 variants compared with K22 variants (6.4% versus 2.7%; \( P < 0.01 \)), especially in subtype A1 (17.5%) and recombinants CRF02_AG (11.1%) and CRF01_AE (8.7%). In contrast, subtype C showed a low H22 prevalence (1.6%). Whether this difference is due to the fact that subtype C is the only N22 variant with AAT as the wild-type codon codifying asparagine, unlike the remaining N22 variants (codon AAC), remains to be clarified by additional analysis.

In isolates with both pol and vif sequences from the same specimen available in the LANL-DB (n = 1791), the pol sequence was also downloaded to assess the presence of drug-resistance mutations in protease (PR) and/or reverse transcriptase (RT), which could have been caused by the effect of A3G, i.e. those produced by G-to-A substitutions in a GG-to-GA dinucleotide context: G16E, D30N, M36I, M46I and G73S in PR; and D67N, M184I and G190S/E in RT. The prevalence of these mutations was compared in sequences with (n = 75) or without (n = 1716) the Vif-22H mutation. The prevalence of the PR mutations M36I (81.3% versus 60%; \( P < 0.01 \)) and M46I (8% versus 2.2%; \( P < 0.01 \)) was significantly higher in the Vif-H22 isolates, but the remaining mutations were not significantly different when comparing the two groups: 12% versus 8.3% for G16E, 0% versus 0.8% for D30N and 0% versus 0.2% for G73S in PR; and 0% versus 2.2% for D67N, 2.7% versus 0.2% for M184I and 0% versus 0.9% for G190S/E in RT.

PR-M36I, a minor resistance mutation to protease inhibitors (PIs) according to the International AIDS Society-USA, is also the wild-type residue in most non-B variants but not in subtype B. Nevertheless, an increase in this change has been reported among Vif-H22 subtype B viruses\(^5\) and it is possible that its higher prevalence among Vif-H22 variants is not due just to HIV-1 clade. In fact, polymorphisms in PR-36 play a role in the development of PI resistance and replication capacity depending on viral subtype.\(^6\) On the other hand, whether or not the major PI-resistance mutation M46I can appear more quickly in vivo after virological failure among HIV-1 non-B variants carrying Vif-N22 as wild-type remains to be clarified.

In conclusion, we observed that some of the most prevalent HIV-1 non-B variants (A1, A2, C, F2, G, CRF01_AE and CRF02_AG, which altogether represent over three-quarters of global infections) could follow a shorter route to acquire Vif-22H. This could help the virus to evade therapy through partial hypermutation in resistance-associated positions in the presence of antiretrovirals. Thus, the HIV-1 clade could play a key role in the development of this novel mechanism of resistance to antiretrovirals. However, future studies are needed to understand the predictive value of Vif mutations for treatment failure and establish a causal correlation between Vif function and drug escape during HIV-1 replication.

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### Transparency declarations
None to declare.

### References

### Extended-spectrum β-lactamase blαCTX-M-1 gene carried on an IncI1 plasmid in multidrug-resistant Salmonella enterica serovar Typhimurium DT104 in cattle in France

**Jean-Yves Madec\(^*\), Benoît Doublet\(^2\), Cécile Ponsin\(^1\), Axel Cloeckaert\(^2\) and Marisa Haenni\(^1\)**

\(^*\)Corresponding author. Tel: +33-4-78-72-65-43; Fax: +33-4-78-61-91-45; E-mail: jean-yves.madec@anses.fr

\(^1\)Agence Française de Sécurité Sanitaire des Aliments, Unité Antibiörésistance et Virulencia Bactéries, 31 avenue Tony Garnier, 69364 Lyon, France; \(^2\)INRA, UR1282 Infectiologie Animale et Santé Publique, 37380 Nouzilly, France

**Keywords:** S. enterica, MDR, SG11

Sir, Since the 1980s, multidrug-resistant Salmonella enterica serovar Typhimurium definitive phage type (DT) 104 has been extensively
reported as a cause of infections in humans and cattle due to the dissemination of clonal isolates carrying the Salmonella genomic island 1 (SGI1). SGI1 is mostly responsible for the resistance to a core group of five antimicrobials, including ampicillin/amoxicillin, chloramphenicol/florfenicol, streptomycin/spectinomycin, sulphonamides and tetracyclines (ACSSuT phenotype). In addition, the wide dissemination of plasmidic extended-spectrum β-lactamases (ESBLs) in humans and animals may lead to the emergence of S. enterica carrying both SGI1 and ESBL genes. This was reported for the first time in 2007 in bla\textsuperscript{TEM-52}-carrying Salmonella Agona and Typhimurium from poultry and humans, and in bla\textsuperscript{CTX-M-1}-carrying Salmonella Typhimurium from humans, poultry and domestic animals, with both genes located on IncI1 conjugative plasmids. Yet, this combination has never been described in bovine isolates of S. enterica, despite the epidemic of multidrug-resistant Salmonella Typhimurium DT104 in this animal species and the significant prevalence of ESBLs in Escherichia coli isolates in cattle, especially in France.

Here, we describe a Salmonella Typhimurium strain (isolate 25008) recovered in 2010 from faeces of a diarrhoeic calf and collected through the RESAPATH network, which carries out surveillance of antimicrobial resistance in animal infections in France (www.resapath.anses.fr). This strain displayed the typical penta-resistance conferred by SGI1 and the presence of the island was assessed by PCRs. It was integrated at the specific location described for all other published isolates, as proved by the detection of the chromosomal junctions of the trmE (also called thf left junction) and int2 (right junction) genes of the retron sequence. Furthermore, PCR mapping of SGI1 confirmed the classical organization of the SGI1 backbone and of its complex integron In104, responsible for the ACSSuT phenotype. In addition to the two classical SGI1 integron cassette arrays of 1000 and 1200 bp, an additional 1600 bp product was also detected by integron PCR using primers CS1 and CS2, which carried the dfrA17 and aadA5 cassettes, as shown by sequencing. In addition, strain 25008 was resistant to cefotiofur but susceptible to cefoxitin, with a typical double-disc phenotype. In addition to the two classical SGI1 integron cassette arrays of 1000 and 1200 bp, an additional 1600 bp product was also detected by integron PCR using primers CS1 and CS2, which carried the dfrA17 and aadA5 cassettes, as shown by sequencing. In addition, strain 25008 was resistant to cefotiofur but susceptible to cefoxitin, with a typical double-disc phenotype.

The bla\textsuperscript{CTX-M-1} plasmid transferred in TC-25008 belonged to the IncI1 incompatibility group and to the ST3 group previously detected in avian E. coli isolates, as shown by PCR-based replicon typing and plasmid multicollinear sequence typing, respectively. Since SGI1-carrying Salmonella Typhimurium isolates from humans and healthy poultry were recently reported to harbour ST2/Inc11 bla\textsuperscript{CTX-M-1}-Positive plasmids, we performed EcoRI restriction analysis and showed that plasmids from TC-25008 and the human TCSs (TC-05-9280 and TC-08-843) shared highly similar restriction profiles (Figure 1a). In parallel, PulseNet standard PFGE of XbaI-digested chromosomal DNA carried out on these three SGI1-carrying strains also demonstrated an identical XTMY-1 PFGE profile (Figure 1b), which is the most prevalent one for Salmonella Typhimurium DT104 strains in France.

In this study, we report the first description of multidrug resistance island SGI1 together with ESBL production in Salmonella Typhimurium isolated from cattle, an animal reservoir that mainly supported the epidemic dissemination of the multidrug-resistant DT104 clone but remains nearly free of Salmonella producing ESBLs. Indeed, the current literature strongly indicates that ESBL genes carried by IncI1 plasmids are significantly associated with the avian reservoir of E. coli and Salmonella in Europe. Consequently, in addition to a transfer from poultry to humans, our data now suggest the passage of the same bla\textsuperscript{CTX-M-1}-carrying IncI1 plasmid from poultry to cattle. This hypothesis is further supported by the fact that bla\textsuperscript{CTX-M-1}-carrying IncI1 plasmids (including this one) were detected in >10% of the faecal E. coli from healthy poultry in France, suggesting a strong prevalence of these plasmids in the gut flora of the poultry population. Poultry was also abundantly documented as an important reservoir of S. enterica of various serovars carrying bla\textsuperscript{CTX-M-1} on IncI1 plasmids in Europe and, therefore, might be a starting point for ESBL dissemination to humans and other food animals, such as cattle. These data also further highlight the huge success of ESBL-carrying plasmids in disseminating antimicrobial resistance among different bacterial backgrounds and animal environments. More specifically, considering the important prevalence of SGI1-carrying Salmonella Typhimurium isolates in cattle, the association and...

Figure 1. (a) Restriction analysis (EcoRI) of plasmids extracted from E. coli TCSs. 1, TC-25008; 2, TC-05-9280; 3, TC-08-843; M, molecular weight marker IV (Roche Diagnostics, Meylan, France). (b) XbaI-PFGE profiles of the S. enterica serovar Typhimurium strains. 1, 25008; 2, 05-9280; 3, 08-843; M, lambda ladder (Bio-Rad, Marnes la Coquette, France).
emergence of highly diffusible ESBL gene-carrying IncI1 plasmids in these strains is of concern, and further surveillance of this genotype is warranted, both in humans and animals.

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Transfer of OXA-48-positive carbapenem-resistant Klebsiella pneumoniae from Turkey to France

Marion Levast1, Laurent Poirel2, Amélie Carrér2, Michel Deiber3, Emmanuel Decroisset4, Frank-Olivier Mallaval5, Claire Lecomte6 and Patrice Nordmann2*

1Service de Microbiologie, CH de Chambéry, Chambéry, France; 2Service de Bactériologie-Virologie, INSERM U914 ‘Emerging Resistance to Antibiotics’, Hôpital de Bicêtre, Assistance Publique-Hôpitaux de Paris, Faculté de Médecine, Université Paris-Sud, K.-Bicêtre, France; 3Service de Réanimation Néonatale, CH de Chambéry, Chambéry, France; 4Service de Gynécologie et Obstétrique, CH de Chambéry, Chambéry, France; 5Équipe Opérationnelle d’Hygiène, CH de Chambéry, Chambéry, France; 6CLIN Sud-Est, France

*Corresponding author. Service de Bactériologie-Virologie, Hôpital de Bicêtre, 78 rue du Général Leclerc, 94275 Le Kremlin-Bicêtre, France. Tel: +33-1-45-21-36-32; Fax: +33-1-45-21-63-40; E-mail: nordmann.patrice@bct.aphp.fr

Keywords: outbreak, carbapenemases, importation

Sir,
Carbapenemases possess the most consistent in vitro activity against extended-spectrum β-lactamase (ESBL)-producing Klebsiella pneumoniae. Resistance to carbapenem, while still rare in Enterobacteriaceae, is increasing and represents a significant threat for the management of multidrug-resistant isolates.1 In Enterobacteriaceae, this resistance can be mediated by metallo-β-lactamases (IMP, VIM and NDM), plasmid-mediated clavulanic acid-inhibited β-lactamases (NmcA, IMI, SME, GES and KPC) and the class D β-lactamase OXA-48.2 The OXA-48 enzyme, initially identified from a carbapenem-resistant K. pneumoniae isolate from Istanbul, Turkey, hydrolyses penicillins and imipenem, but spares expanded-spectrum cephalosporins.3 Outbreaks of OXA-48-producing K. pneumoniae and of other enterobacterial isolates have been described in several cities in Turkey.3 Subsequently, single isolates of OXA-48-type-producing K. pneumoniae have been reported from Belgium, the UK, Israel, Morocco, Lebanon and Tunisia.4 We describe here a nosocomial spread of carbapenem-resistant K. pneumoniae strains expressing OXA-48 in a French hospital after a transfer from Turkey.

In late 2010, a pregnant woman was admitted for premature rupture of choriomammatory membranes and fever at the hospital of Chambéry, south-east France. She was treated successively with amoxicillin, metronidazole and netilmicin, then with amoxicillin/ clavulanic acid, and finally with cefixime. She had returned from Kayseri, Turkey, where she had consulted for her pregnancy follow-up at a hospital, but was not hospitalized. There, she