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.

### Funding
This work was supported by grants from Fondo de Investigaciones Sanitarias (FIS 09/00284). G. Y. is supported by Consejería de Educación de la Comunidad de Madrid and Fondo Social Europeo (FSE). A. H. is supported by FIS and Agencia Lain Enralga.

### Transparency declarations
None to declare.

### References

**J Antimicrob Chemother** 2011

DOI:10.1093/jac/dkr014

Advance Access publication 3 February 2011

**Extended-spectrum β-lactamase bla**<sub>CTX-M-1</sub>** gene carried on an Incl1 plasmid in multidrug-resistant**<i>Salmonella enterica</i>** serovar Typhimurium DT104 in cattle in France**

Jean-Yves Madec*, Benoît Doublet, Cécile Ponsin, Axel Cloeaert and Marisa Haenni

1Agence Française de Sécurité Sanitaire des Aliments, Unité Antibiore’sistance et Virulence Bacté´riennes, 31 avenue Tony Garnier, 69364 Lyon, France; 2INRA, UR1282 Infectiologie Animale et Sante´ Publique, 37380 Nouzilly, France

---

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

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

Sir, Since the 1980s, multidrug-resistant <i>Salmonella enterica</i> serovar Typhimurium definitive phage type (DT) 104 has been extensively

---

**References**

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/lorfenicol, 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 blaTEM-52-carrying Salmonella Agona and Typhimurium from poultry and humans, and in blaCTX-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 typical pentaresistance conferred by SGI1 and the presence of the island was assessed by PCRs. It was integrated at the.

Figure 1. (a) Restriction analysis (EcoRI) of plasmids extracted from E. coli Tcs. (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).

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 blaCTX-M-1-carrying IncI1 plasmid from poultry to cattle. This hypothesis is further supported by the fact that blaCTX-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 abundantlymiddleware documented as an important reservoir of S. enterica of various serovars carrying blaCTX-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
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.

Acknowledgements
We wish to thank all the veterinary laboratories participating in the RESAPATH network and, more specifically, the veterinary laboratory from Meurthe-et-Moselle (54) from which strain #25008 was obtained. We thank also Estelle Saras, Christiane Brunet and Véronique Météayer for their skilled assistance, and Dr Alessandra Carattoli for providing the plasmid incompatibility group control strains.

Funding
This work was funded by the Agence Nationale de Sécurité Sanitaire (Anses).

Transparency declarations
None to declare.

References

J Antimicrob Chemother 2011
doi:10.1093/jac/dkq504
Advance Access publication 20 January 2011

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

Marion Levast1, Laurent Poirel2, Amélie Carré2, Michel Deiber3, Emmanuel Decroisette4, 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; 5Equipe 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 expanded-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-48.1 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.2 Outbreaks of OXA-48-producing K. pneumoniae and 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 chorionic 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...