

## RESISTANCE TO LAST-RESORT HUMAN ANTIMICROBIAL AGENTS AMONG GRAM-NEGATIVE BACTERIA RECOVERED FROM BARCELONA SEWER RATS (*RATTUS NORVEGICUS*)

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**Abstract** Gram-negative pathogenic bacteria are shared between humans and animals but also the intra- and the inter-species exchange of resistance genes are common among bacteria. Multidrug-resistant bacteria have already been identified from sewage samples but there is little data regarding the potential role of urban rats as reservoirs and source of antimicrobial resistant bacteria relevant to human health. From January-November 2017, 216 rats (*Rattus norvegicus*) were captured with death traps in different sections of the Barcelona sewers. Intra-rectal samples were cultured on selective media to isolate ESBL and/or carbapenemase producing GNB. Species identification was performed by MALDI-ToF/MS and antimicrobial susceptibility by disc diffusion, Etest and microdilution when necessary, following EUCAST guidelines. Detection of genes encoding MCR, ESBLs and carbapenemases was performed by PCR and Sanger sequencing. PFGE was used to study the clonal relatedness. Selected isolates were studied by MLST and also by genome sequencing (MinION platform, Oxford Nanopore). Overall, 229 isolates were recovered from 167/216 (77.3%) rats and were identified, in order of abundance, as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Raoultella ornithinolytica*, *Serratia* spp., *Citrobacter* spp., and *Pseudomonas* spp. Third-generation cephalosporin-resistance was high among *E. coli*, *K. pneumoniae* and *Enterobacter* spp (>50%) associated with carriage of ESBLs. Carbapenem-resistance was identified in 10% of GNB, associated with carriage of KPC, NDM, OXA-48, VIM and IMI carbapenemases. Isolates carrying the same resistant mechanism were not clonally related and overall isolates were clonally diverse. WGS analysis identified NDM and KPC genes in IncX3 and IncFII plasmids, respectively, which were traced to human patients from a local Hospital. There are alarming levels of antimicrobial resistance to clinically relevant antibiotics among BNG colonizing the intestinal tract of Barcelona sewer rats. Although resistant isolates seem to differ between rodents and humans, there is an exchange of resistance genes through the transfer of mobile genetic elements.

**Key words** Bacteria, rats, resistance