

L0009 Massive genome analysis to decipher reservoir and origin of mobile colistin resistance (*mcr*) gene variantsMariem Ben Khedher¹, Seydina M. Diene¹, Sophie Baron¹, Jean-Marc Rolain*¹¹ IHU-mediterranee Infection, Aix-Marseille University, Marseille, France

Background: Nowadays, colistin is used as the last line drug against multidrug resistant bacteria. In 2015, a disturbing new mechanism, a plasmid-mediated colistin resistance gene *mcr-1* has been described and since reported worldwide. Today, seven others *mcr* gene variants (from *mcr-2* to *mcr-8*) have been reported. Here, we conducted a massive bioinformatic analysis of more than 60'000 bacterial genomes to investigate the reservoir and origin of *mcr* variants

Materials/methods: Whole genome data were downloaded from the NCBI RefSeq database and formatted to create a local dataset. Protein sequence of each MCR variant was used as query for the analyses. First, "Rhizome" analysis of MCR-1 was performed by phylogenetic analysis from MCR-1 fragments of 50aa. The eight MCR variants were investigated in downloaded genomes by BlastP analysis using as thresholds e-value 10^{-6} , aa identity $\geq 90\%$, and alignment $\geq 98\%$. Other MCR homologous sequences were also checked with less stringent thresholds. Genetic environment of some MCR variants were analysed into selected genomes.

Results: 60'998 bacterial genomes were downloaded including 25 genera and 701 species (Fig. 1). We have identified 6'172 homologous sequences to MCR-1 in diverse bacterial species. "Rhizome" analysis of this latter reveals a chimeric gene from mainly *Moraxella* species especially from *M. pluranimalium*. BlastP analysis reveals 1'078 positive hits into 11 genera with aa identity $\geq 90\%$ and alignment $\geq 98\%$ (Fig. 1). A highly number of MCR-1 was observed in *E. coli* (n=862). MCR-8 was only detected in *Klebsiella pneumoniae* and *Raoultella ornithinolytica*. Interestingly, MCR-1 and MCR-4 were identified here in *Acinetobacter* species (not yet reported in the literature). Moreover, with BlastP thresholds (50% < aa identity > 90% and alignment > 90%), 1'906 MCR hits in 16 bacterial species were identified. Those being putative MCR variants not yet discovered.

Conclusions: Here, we report a massive bacterial genome analysis and identify plenty *mcr* variant genes in unsuspected bacteria. We describe around 2'000 putative *mcr* genes that could be emerged in gram-negative bacteria. Our approach appears as a powerful tool to exhaustively investigate resistance genes in All available bacterial datasets.

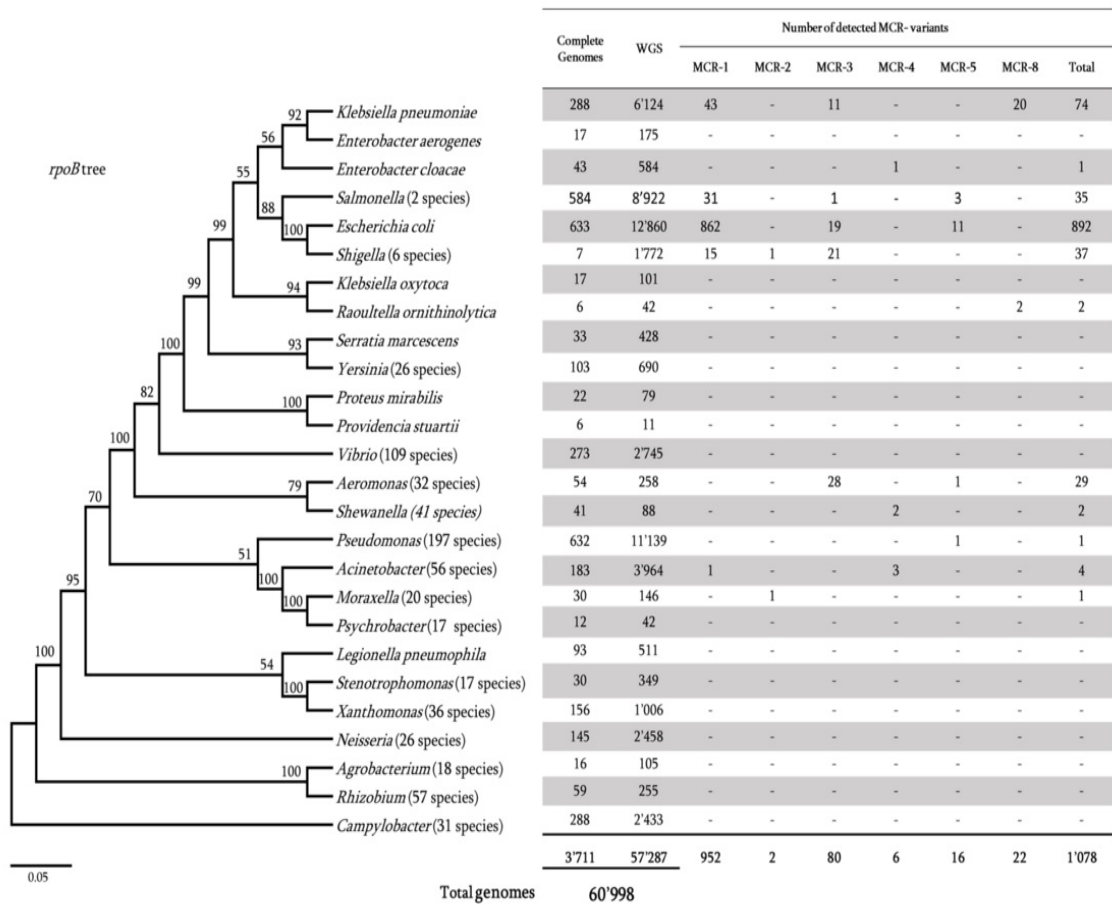


Figure 1: The list of all bacterial species genome analysed here and all detected hits of MCR variants in these genomes.

