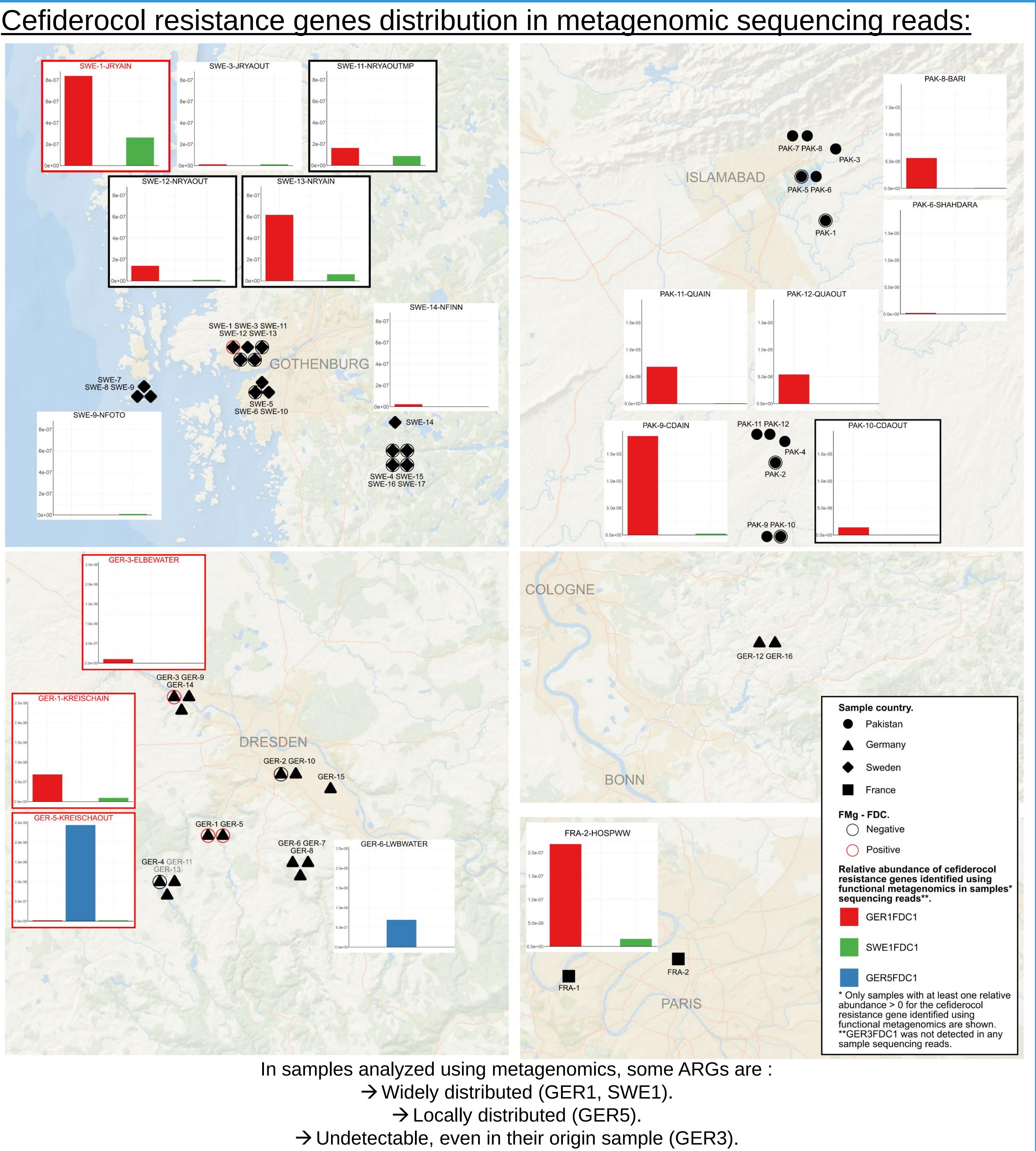
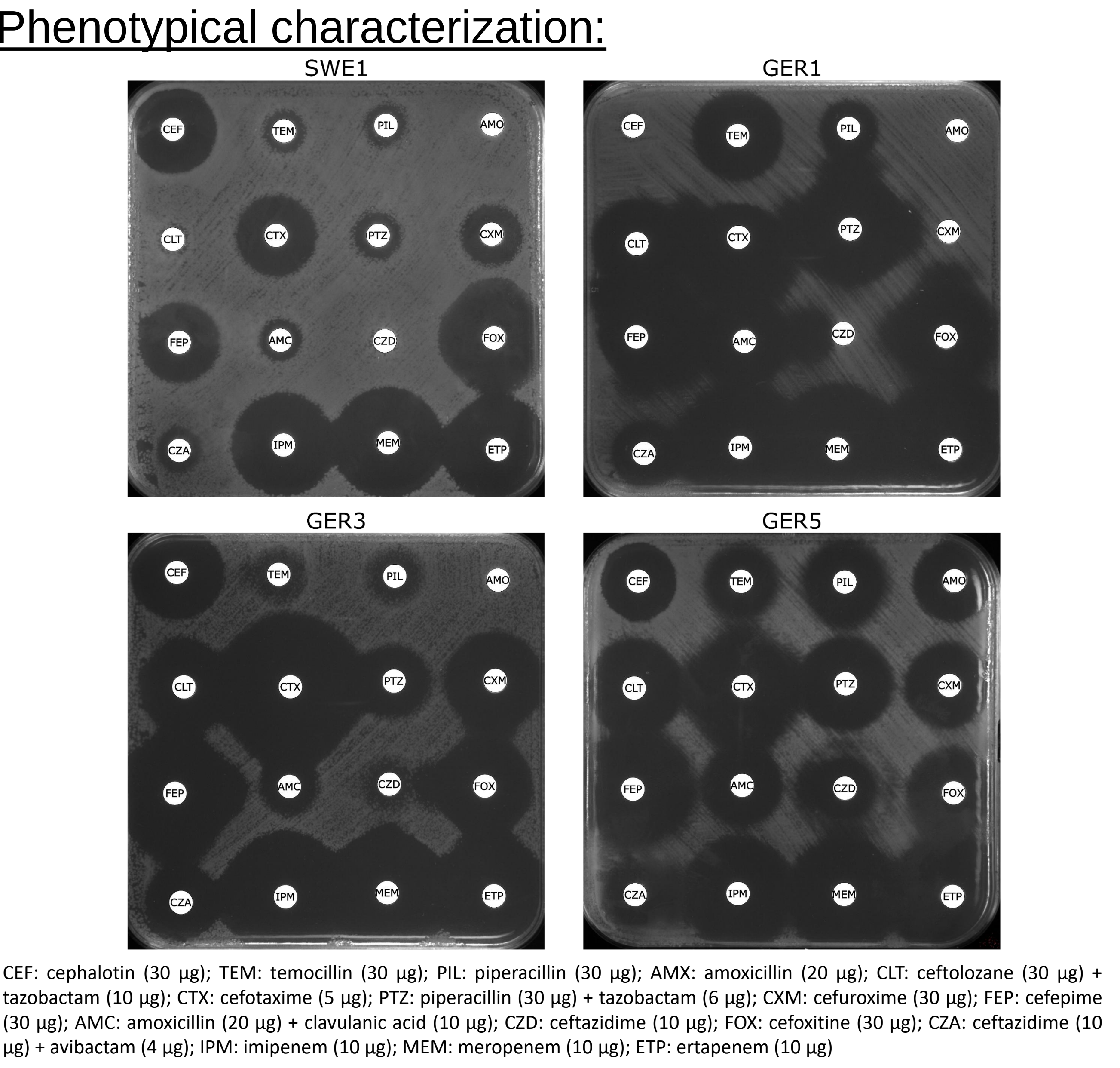
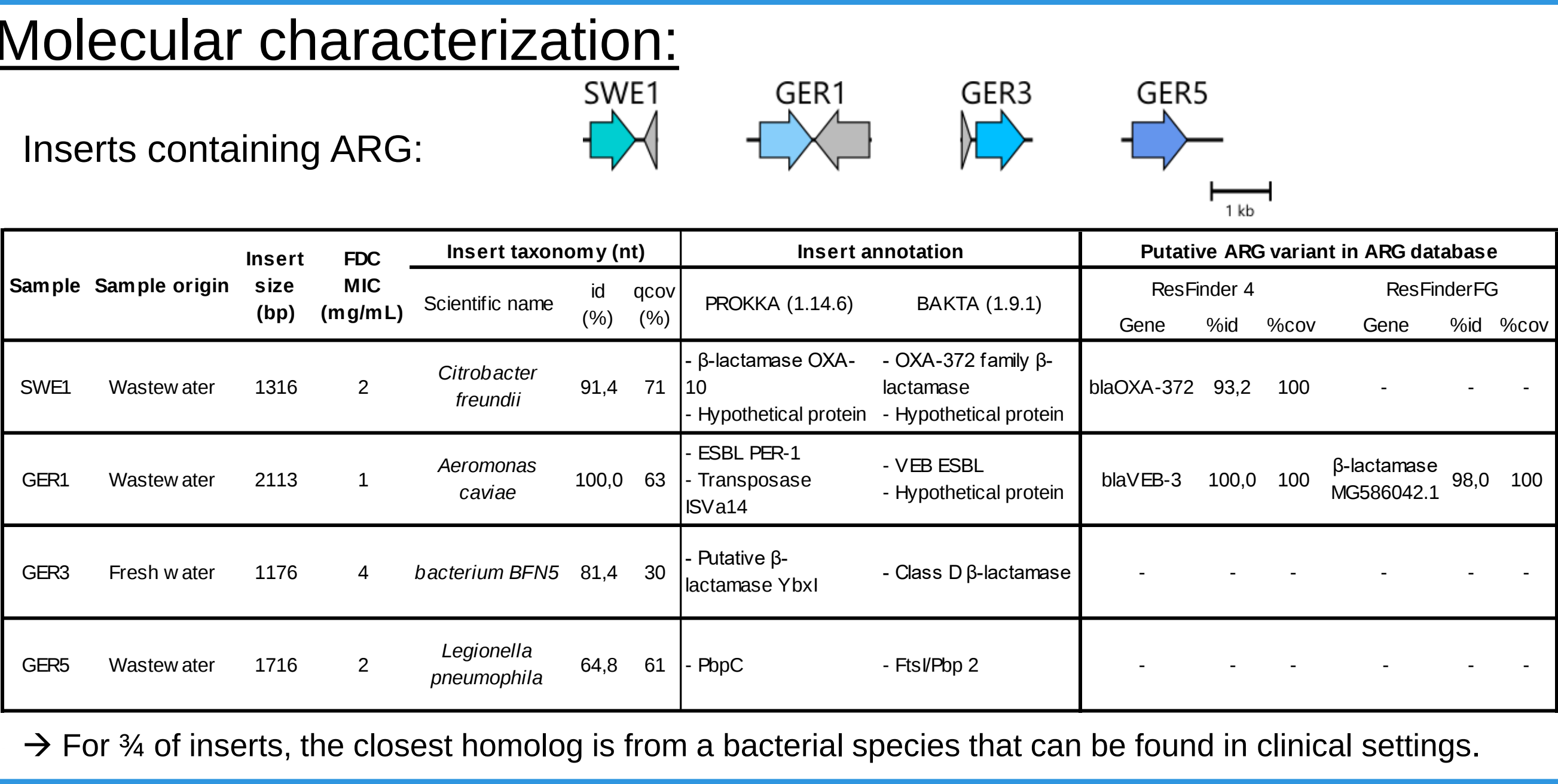
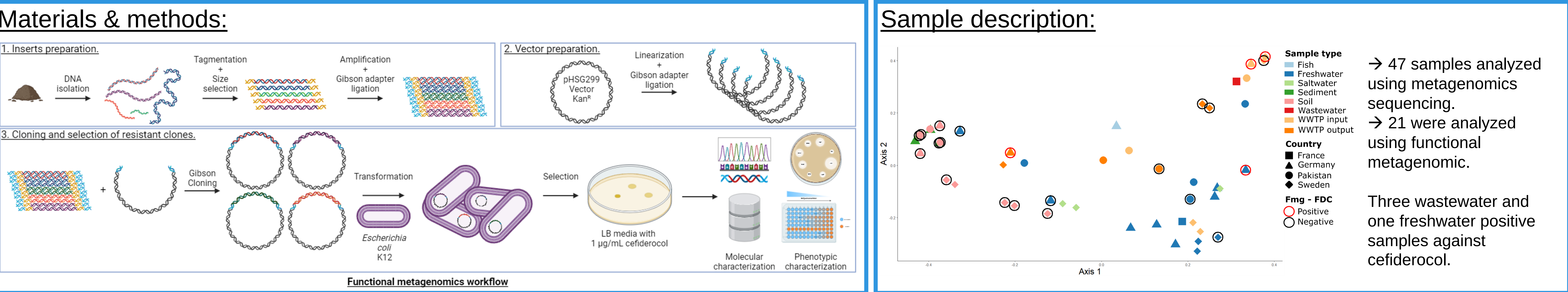


Cefiderocol resistance genes identified by functional metagenomics. P1833

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Background: Emergence of antibiotic-resistant bacteria is a global health crisis in a One Health context. Gram negative bacteria pose a particular threat, employing beta-lactamase enzymes to hydrolyze beta-lactam antibiotics and render them ineffective. While cefiderocol is a new and powerful weapon against these pathogens, knowledge gaps remain regarding resistance mechanisms. This study utilizes functional metagenomics to identify novel genes which expression in *Escherichia coli* confers resistance to cefiderocol.



Conclusion:
Utilizing functional metagenomics, we identified four genes conferring cefiderocol resistance: three beta-lactamases and one PBP encoding gene. This method uniquely enabled the direct characterization of gene function and associated phenotype, a critical advantage over pure computational approaches, particularly for an antibiotic like cefiderocol for which bacterial isolates can have multifactorial resistance mechanisms. The discovery of these genes, some linked to mobile genetic elements and prevalent in wastewater and freshwater, underscores the potential for widespread environmental dissemination of cefiderocol resistance. To fully understand and mitigate this risk, comprehensive functional metagenomic studies are essential.