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Phylogenetic Insights of β-lactam resistance of the CTX-M family

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Bacterial resistance is a major public health concern, particularly against β-lactam antibiotics, one of the most widely used antibacterial drugs. The production of extended-spectrum β-lactamases (ESBLs) is the main defense mechanism found in Gram negative bacteria. Among all the ESBLs, the CTX-M enzymes appear as the most efficient in terms of diffusion in different epidemiological contexts, outnumbering the others. Originated in chromosomal genes of Klyvera spp., the blaCTX-M genes have become associated with mobile genetic elements, such as plasmids, that have mediated inter-replication and dissemination. CTX-M enzymes exhibit a striking plasticity, with a large number of allelic variants belonging to several sub-lineages, which can be associated with functional heterogeneity of clinical relevance. This observational analytical study provides an update of this family, currently with more than 200 variants described, from a phylogenetic, molecular and structural point of view through homology in amino acid sequences. There are currently 6 defined clusters (CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9, CTX-M-25 and CTX-M-151), with the domains CTX-M-1 and CTX-M-9 presenting subgroups, composed mainly of variants identified as hybrids between them (particularly between CTX-M-14 and CTX-M-15).

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