Structural and functional insight of Mobilized Colistin Resistance-1 variants

Tasnimul Arabi Anik¹, Dipta Chandra Pal¹, and Atiq Abrar Rahman¹

¹University of Dhaka

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Abstract

Mobilized Colistin Resistance-1 (MCR-1) is a transferase enzyme that confers resistance to polypeptide antimicrobial called colistin (polymyxin E) by modifying lipid A of the Gram-negative bacterial cell membrane. The rapid dissemination of MCR-1 and its variants has become a public health concern. So far, thirty-six variants of MCR-1 have been reported across the world. These variants have been detected in 109 different bacterial species. They differ from each other either by single (29 variants) or multiple (7 variants) substitutions. These substitutions mostly occur in the transmembrane domain of MCR-1. While the MCR-1 is 91% conserved overall, the catalytic domain is more stable with 93.6% of the residues unchanged. In this review, we have summarized the crystal structure of MCR-1 and provided a comparative analysis of all mutants. Besides, we have highlighted the differing amino acid substitutions in the two domains of MRC-1 and in the α-helix, β-sheets, and loops of cMRC. Moreover, we have focused on residues that may have a role in catalysis and can be exploited as potential drug targets. The impact of these changes and the function of active site residues need to be thoroughly understood to design drugs that are effective against all the variants of MCR-1.

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