Molecule designed to tackle drug resistance in hospital acquired infection

New Delhi, Aug 21: Drug resistance is a public health concern that threatens to undermine decades of medical progress. ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.) pathogens cause most nosocomial infections, and are frequently resistant to carbapenem antibiotics, usually leaving tigecycline and colistin as the last treatment options. However, increasing tigecycline resistance and colistin's nephrotoxicity severely restrict use of these antibiotics.

In a Project supported by DBT at IISc Bengaluru, the researchers have designed antimicrobial peptides using a maximum common subgraph approach. Their best peptide (Ω76) displayed high efficacy against carbapenem and tigecycline-resistant Acinetobacter baumannii in mice (Figure 1). Mice treated with repeated sublethal doses of Ω76 displayed no signs of chronic toxicity. Sublethal Ω76 doses co-administered alongside sublethal colistin doses displayed no additive toxicity. These results indicate that Ω76 can potentially supplement or replace colistin, especially where nephrotoxicity is a concern. To the knowledge, no other existing antibiotics occupy this clinical niche. Mechanistically, Ω76 adopts an α-helical structure in membranes, causing rapid membrane disruption, leakage, and bacterial death.

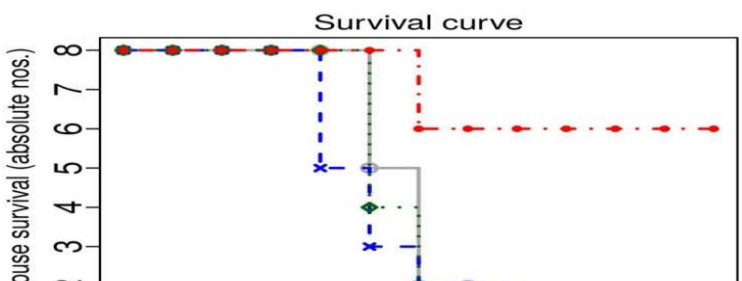

Figure: In vivo efficacy of Ω76 using a BALB/c mouse peritoneal model of infection.

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Link to research paper: https://advances.sciencemag.org/content/5/7/eaax1946.full

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