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Synthesis and biological evaluation of novel antimicrobial cell-penetrating cyclic peptides

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One of the greatest threats to human health in the twenty-first century is the development of antibiotic resistance. Gram-negative pathogens are remarkably successful in evading antibiotic action, due to their ability to maintain the integrity of their cell envelope. Recently, a cyclic octapeptide, named SI24, was identified from a genetic screen as an inhibitor of the σE cell envelope-sensing pathway, which is required for the virulence and viability in several Gram-negative pathogens. SI24 was found to be toxic to *E.coli* bacterial cells when expressed *in vivo*, but was not, however, an effective inhibitor when added exogenously, probably because it cannot cross the cell envelope. On the other hand, positively charged antimicrobial peptides have been considered as potential therapeutic sources of future generations of antibiotics for treating resistant pathogenic microbes because of their broad-spectrum activities. These candidates have been developed as cell-penetrating peptides (CPPs) and have become one of the emerging vehicles for delivery of cargo drugs. We thus hypothesize that conjugation of the cyclic peptide inhibitor SI24 with CPPs could enhance its permeability, and consequently its activity against bacterial cells, providing a paradigm for the development of antibiotics targeting a novel pathway in Gram-negative pathogens.

Biography

Shaima El-Mowafi has completed her PhD from the Pennsylvania State University in 2014. She is currently a Postdoctoral Researcher at the National Research Centre in Egypt.

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