A molecular mechanism of anti-microbial resistance

Description: A project team reports a mechanism of possible microbial resistance to antimicrobial peptides.

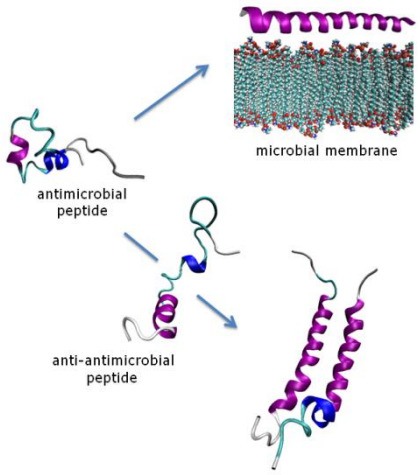

Image caption: Two scenarios of antimicrobial peptide action: (top) an antimicrobial peptide binds to microbial membranes and forms membrane-disrupting helical structures or (bottom) when challenged by an anti-antimicrobial peptide it forms a biologically inert helical complex.

Article: Antimicrobial peptides are natural antibiotics found in all multicellular organisms. These molecules are viewed as potential drug candidates in the post-antibiotic era because widespread microbial resistance against them has yet to emerge.

The use of these peptides in medicine may trigger the development of antimicrobial resistance in a fashion similar to that currently occurring with more conventional antibiotics such as methicillin and vancomycin. However, the mechanism of action of antimicrobial peptides, which target and rapidly destroy bacterial membranes, lends credibility to the view that this is unlikely to happen. To acquire resistance against such formidable agents, microorganisms would need to re-build their genetic apparatus, which is an extremely high price to pay.

In a recent study, a research team comprising scientists from NPL, University of Bristol, University of Edinburgh, University of Oxford and IBM explored the effect of peptide sequences designed to be antagonistic towards antimicrobial peptides. The research showed that these 'anti-antimicrobial' sequences interact with the antimicrobial peptides to form inert molecular complexes, known as helical oligomers.

The team then studied the structural and biological properties of these inert assemblies in biologically relevant environments, using a combination of spectroscopy, microscopy, bioassays and molecular dynamics simulations. The findings, reported in the *Journal of Biological Chemistry* (http://www.jbc.org/content/early/2013/06/04/jbc.M113.459560.abstract) suggest that antagonistic sequences secreted by bacterial cells or expressed on their surfaces may cause efficient anti-antimicrobial responses. Although this remains to be shown in nature, this research offers a molecular rationale for these responses with potential implications for antimicrobial resistance.