Nanotechnology boosts war on superbugs

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This week *Nature Nanotechnology* journal (October 12th) reveals how scientists from the London Centre for Nanotechnology (LCN) at UCL are using a novel nanomechanical approach to investigate the workings of vancomycin, one of the few antibiotics that can be used to combat increasingly resistant infections such as MRSA. The researchers, led by Dr Rachel McKendry and Professor Gabriel Aeppli, developed ultra-sensitive probes capable of providing new insight into how antibiotics work, paving the way for the development of more effective new drugs.

During the study Dr McKendry, Joseph Ndieyira, Moyu Watari and coworkers used cantilever arrays – tiny levers no wider than a human hair – to examine the process which ordinarily takes place in the body when vancomycin binds itself to the surface of the bacteria. They coated the cantilever array with mucopeptides from bacterial cell walls and found that as the antibiotic attaches itself, it generates a surface stress on the bacteria which can be detected by a tiny bending of the levers. The team suggests that this stress contributes to the disruption of the cell walls and the breakdown of the bacteria.

The interdisciplinary team went on to compare how vancomycin interacts with both non-resistant and resistant strains of bacteria. The 'superbugs' are resistant to antibiotics because of a simple mutation which deletes a single hydrogen bond from the structure of their cell walls. This small change makes it approximately 1,000 times harder for the antibiotic to attach itself to the bug, leaving it much less able to disrupt the cells' structure, and therefore therapeutically ineffective.

"There has been an alarming growth in antibiotic-resistant hospital 'superbugs' such as MRSA and vancomycin-resistant Enterococci (VRE)," said Dr McKendry. "This is a major global health problem and is driving the development of new technologies to investigate antibiotics and how they work.

"The cell wall of these bugs is weakened by the antibiotic, ultimately killing the bacteria," she continued. "Our research on cantilever sensors suggests that the cell wall is disrupted by a combination of local antibiotic-mucopeptide binding and the spatial mechanical connectivity of these events. Investigating both these binding and mechanical influences on the cells' structure could lead to the development of more powerful and effective antibiotics in future."

"This work at the LCN demonstrates the effectiveness of silicon-based cantilevers for drug screening applications," added Professor Gabriel Aeppli, Director of the LCN. "According to the Health Protection Agency, during 2007 there were around 7,000 cases of MRSA and more than a thousand cases of VRE in England alone. In recent decades the introduction of new antibiotics has slowed to a trickle but without effective new drugs the number of these fatal infections will increase."

Citation: The article 'Nanomechanical Detection of Antibiotic Mucopeptide Binding in a Model for Superbug Drug Resistance' was published in *Nature Nanotechnology*, October 12 2008

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