Researchers make significant step forward in combating antibiotic resistance

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The research led by Durham University, which involved colleagues at the University of Birmingham, is a significant development in combating antibiotic resistance; it will pave the way for the creation of the inhibitors to counteract the process, allowing a renaissance in the use of antibiotics.

Antibiotic resistance is a global problem. The World Health Organisation (WHO) estimates that for tuberculosis alone multi-drug resistance accounts for more than 150,000 deaths each year. WHO warns of "a doomsday scenario of a world without antibiotics," in which antibiotic resistance will turn common infections into incurable killers and make routine surgeries a high-risk gamble.

Certain types of bacteria are a scourge of the hospital environment because they are extremely resistant to antibiotics and consequently difficult, if not impossible, to treat. This group of bacteria is classified as 'gram-negative' because their cells have a double membrane or outer layer, compared with gram-positive bacteria, which just have one outer layer.

Not only are these cells difficult to penetrate in the first instance, due to their double membrane, but they have effective 'pumps' which quickly reject anything that interferes with the activity of protein-building within the cell and the development of the protective cell wall.

This research, which was funded by the Wellcome Trust, gives for the

first time a clear insight into how these protein components of the pump work together to transport an antibiotic from the cell.

Examples of gram-negative bacteria include those which cause food poisoning, meningitis, gonorrhoea and respiratory problems. Since the antibiotic is an interfering agent, many of these pathogenic bacteria use the membrane pumps to transport the medication out of the cell.

The pumps are made up of three different proteins within the cell that work together to bring about the movement. Research lead, Professor Adrian Walmsley from Durham University's School of Biological and Biomedical Sciences explained:

"Patients with bacterial infections are often treated with antibiotics, but since many strains are resistant to one or more of these drugs, clinicians often try to bring such infections under control by prescribing a combination of different types of antibiotics in the hope that they will override the resistance mechanisms. This sometimes works, but other times it does not. Pumps exacerbate this situation by reducing the effective concentration of the drug inside the cell. "

"By investigating how these pumps function, we have been able to identify the molecular events that are involved in binding and transporting an antibiotic from the cell. This advance in our understanding will ultimately aid the development of 'pump blockers'. This is important because these pumps often confer resistance to multiple, structurally unrelated, drugs; which means that they could also be resistant to new drugs which have never been used before"

Dr Vassiliy Bavro from the the Institute of Microbiology and Infection at the University of Birmingham said: "This study greatly expands our understanding of the mechanistic aspects of the pump function, and in particular challenges our previous concepts of energy requirements for

pump assembly and cycling. By elucidating the intricate details of how these essential nanomachines come together, it also provides a new working model of their functional cycle in general, paving the way to development of novel approaches to disrupting their function."

Dr Ted Bianco, Acting Director of the Wellcome Trust, said: "A world without antibiotics is a world where simple surgery becomes a life-threatening procedure, where a scratch from a rose might prove fatal, and where diseases like tuberculosis return with a ferocity not seen in Britain since the Victorian era. This is why fundamental research to understand the mechanisms of antibiotic resistance is so important. Only when we know what we're up against can researchers begin to design new antibacterial agents to help us win the war against bacterial infections."

Provided by Durham University