Discovery in the fight against antibiotic-resistant bacteria

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For four years, researchers at Universite catholique de Louvain have been trying to find out how bacteria can withstand antibiotics, so as to be able to attack them more effectively. These researchers now understand how one defense mechanism works and the results of their research have been published in the prestigious scientific journal *Cell*.

There are two main families of bacteria : those that are surrounded by a single membrane (or one outer wall) and those that are surrounded by two membranes (or two outer walls). The team of Jean-François Collet, professor at the de Duve Institute at UCL, looked at this second type of bacteria.

For a bacterium to survive, it has to keep its two outer walls intact. If one of these walls is damaged, the bacterium dies. So it was vital for the UCL researchers to analyse the protection mechanisms of these bacterial "walls' (to find their weak spot), so as to be able to fight these defence systems more effectively by developing new antibiotics.

The researchers examined a protein that is found between these two protective walls, known as RcsF. When all is well, this protein is continually sent to the second outer wall. However, if the bacterium is attacked (by an antibiotic, for instance) the machinery that sends RcsF to the outer wall no longer works: instead of being on the second outer wall, RcsF is stuck between the two fortifications (membranes), from where it sends out an alarm signal. This signal prompts the bacterium to trigger defence systems (by sending other back-up proteins) so as to resist the

attacking antibiotic.

In this process, the UCL researchers succeeded in discovering how the protein RcsF manages to sound the alarm. In practical terms, when it is stressed, stuck between the two walls, RcsF contacts another protein, IgaA. The interaction between these two proteins raises the alarm.

What was the point of discovering this alarm mechanism?

In terms of basic research, the researchers wanted to understand how the alarm system worked. They made a twofold, unexpected discovery: the fact that the protein RcsF positions itself on the second outer wall (on the surface of the bacterium) and the fact that it interacts with a second protein, IgaA. This discovery gives rise to other interesting questions, since it suggests that other proteins may take the same path;

In terms of applied research, given that this alarm helps defend bacteria against antibiotics, the UCL researchers aimed to gain a better understanding of how these proteins work so as to be able to develop new antibiotics, which would bypass this alarm system and hence, ultimately, fight more effectively against bacterial infections (such as urinary infections linked to the bacterium Escherichia-coli, for example). To be specific, the researchers believe that it will be possible to use the proteins in this system as a target to break through the bacteria's defence system and create new antibiotics.

The resistance of certain bacteria to antibiotics is currently a major health problem. More and more bacteria are becoming resistant to the antibiotics available at the moment, because they are acquiring new defence mechanisms. The UCL discovery could therefore provide a response to this growing problem.