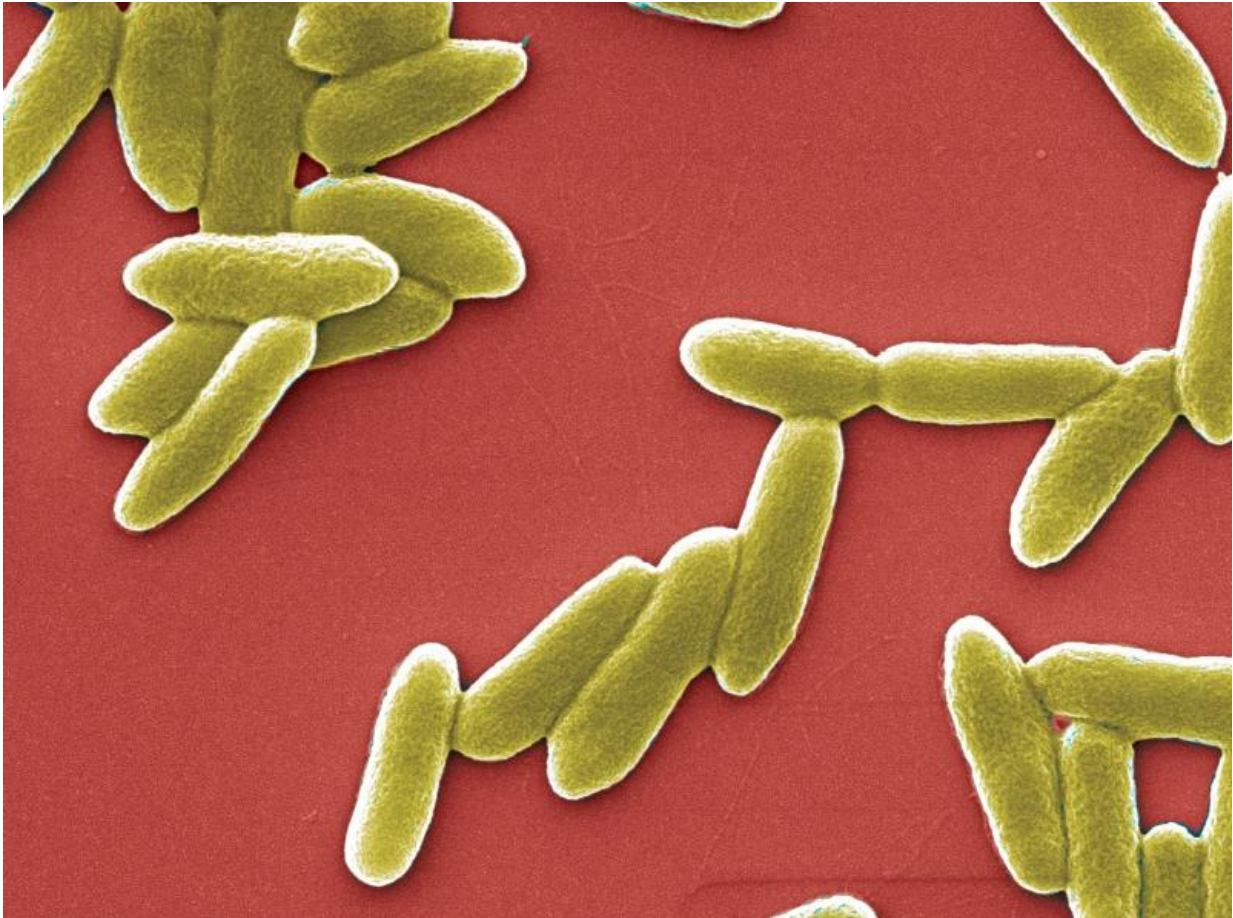


A lead to overcome resistance to antibiotics

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Pseudomonas aeruginosa bacteria. Credit: Karl Perron, UNIGE

Pseudomonas aeruginosa can become a formidable pathogen causing fatal infections, especially in intubated patients, people suffering from cystic fibrosis or severe burns. The presence of certain metals in the

natural or human environment of the bacterium makes it more dangerous and, in particular, resistant to antibiotics of last resort.

A team of researchers from the University of Geneva (UNIGE), Switzerland, has shown that a specific protein of *P. aeruginosa*, called Host factor q (Hfq), is essential for reacting to these metals and acquire these new properties. The results, presented in the special issue Virulence Gene Regulation in Bacteria of the journal Genes, single out the Hfq protein as the Achilles heel of *P. aeruginosa*. Indeed, blocking its action could make this pathogen unable to adapt to a new environment and to resist to certain antibiotics.

Pseudomonas aeruginosa is a ubiquitous [bacterium](#) found in both land and water. This organism is known as opportunistic, as it is able to produce various virulence factors and to adapt to its environment to invade, colonize and survive within human beings, taking advantage of a weakening of its host to become pathogenic. The infections it causes are often difficult, if not impossible to treat because of a resistance to many types of antibiotics.

Abnormal amounts of metals

'We had discovered that high concentrations of metals, such as zinc, could induce a resistance to carbapenems, which are antibiotics of last resort, as well as an increase in the production of [virulence factors](#),' says Karl Perron, researcher at the Department of Botany and Plant Biology of the UNIGE Faculty of Science. This metal may be present in abnormal amounts in the lung secretions of [cystic fibrosis](#) patients and in some urinary catheters, contributing to an increase in the pathogenicity of the bacterium and to treatment failure.

Some antibiotics must penetrate the bacteria to exert their effect. Carbapenems, for example, pass through a specific porin, a sort of

channel normally used to import nutrients. When the bacterium is present in an environment containing an excess of zinc, it becomes resistant to carbapenems. 'We had observed that zinc and other metals induce a suppression of the production of this porin, but we did not know exactly how,' specifies Verena Ducret, biologist in the Geneva group and first author of the article.

Target the bacterium without affecting the host

The team of Karl Perron has solved this enigma by uncovering the central role of a bacterial protein called Host factor q (Hfq). 'This chaperone, a molecular assistant that allows the bacterium to adjust the synthesis of various proteins according to its needs, inhibits the synthesis of certain porins by intervening at several levels of the production chain,' explains Verena Ducret. By studying a bacterium that does not express Hfq, the scientists have thus discovered a real Achilles heel, because the mutant is unable to respond to zinc and other metals. Therefore, it cannot express its virulence or become resistant to carbapenems in the presence of these metals.

Since the different pathways leading to the inhibition of the production of this porin use Hfq, this chaperone becomes a promising therapeutic target. 'We are looking for different inhibitors of Hfq that act on *Pseudomonas aeruginosa* strains. These drugs should counter all of the pathogen's direct and indirect effects without affecting the host cells, because they do not have proteins such as Hfq,' says Karl Perron.

More information: Verena Ducret et al. OprD Repression upon Metal Treatment Requires the RNA Chaperone Hfq in *Pseudomonas aeruginosa*, *Genes* (2016). [DOI: 10.3390/genes7100082](https://doi.org/10.3390/genes7100082)

Provided by University of Geneva

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