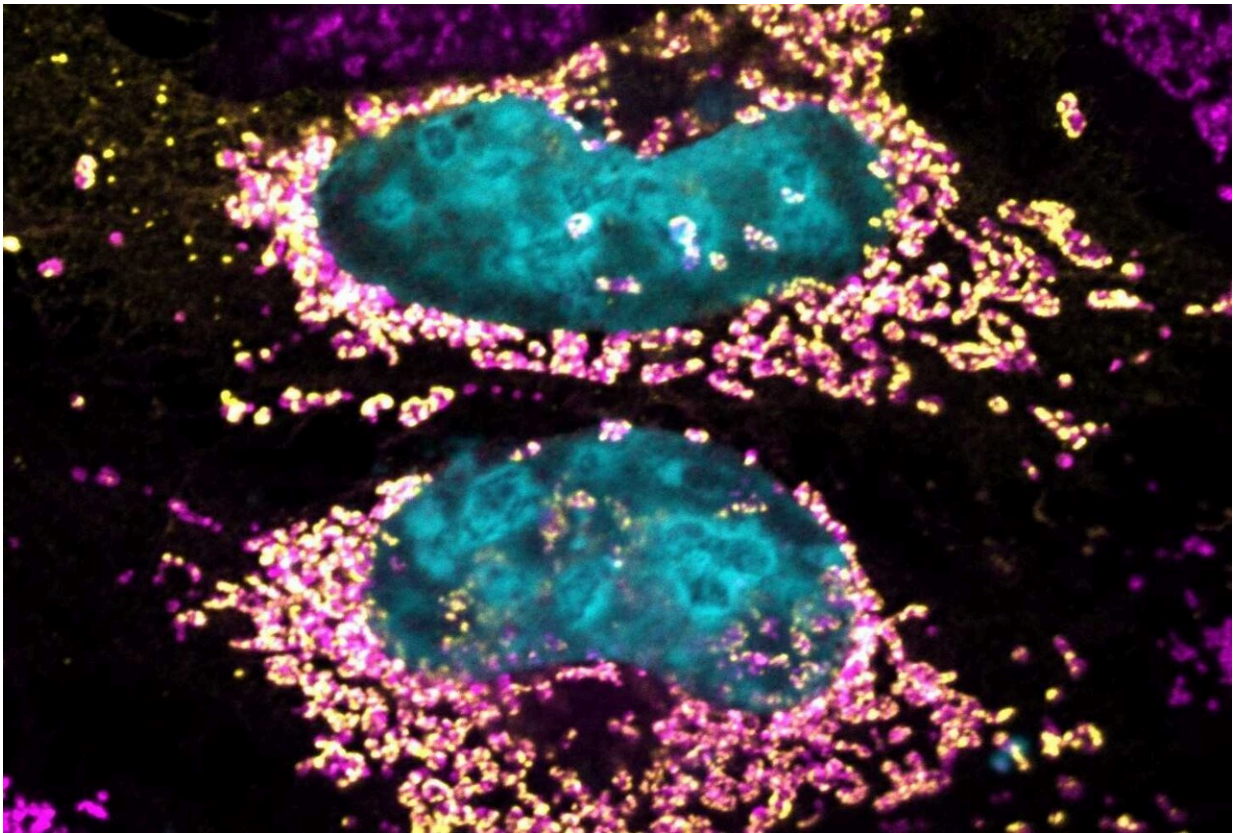


# Study reveals bacterial protein capable of keeping human cells healthy

November 9 2023, by Maria Fernanda Ziegler

---



Human cells showing cell nuclei (cyan), mitochondria (magenta), and the *Coxiella burnetii* protein MceF (yellow). The figure evidences co-location of MceF with cellular mitochondria. Credit: Robson Kriiger Loterio

Researchers at the University of São Paulo (USP) in Brazil, partnering

with colleagues in Australia, have identified a novel bacterial protein that can keep human cells healthy even when the cells have a heavy bacterial burden. The discovery could lead to new treatments for a wide array of diseases relating to mitochondrial dysfunction, such as cancer and autoimmune disorders. Mitochondria are organelles that supply most of the chemical energy needed to power cells' biochemical reactions.

The study is [published](#) in the journal *PNAS*. The researchers analyzed more than 130 proteins released by *Coxiella burnetii* when this bacterium invades host cells, and found at least one to be capable of prolonging cell longevity by acting directly on mitochondria.

After invading host cells, *C. burnetii* releases a hitherto unknown protein, which the authors call mitochondrial coxiella effector F (MceF). MceF interacts with glutathione peroxidase 4 (GPX4), an anti-oxidant enzyme located in the mitochondria, to improve mitochondrial function by promoting an anti-oxidizing effect that averts cell damage and death, which may occur when pathogens replicate inside [mammalian cells](#).

"*C. burnetii* uses various strategies to prevent the death of invaded cells and multiply inside them. One is modulation of GPX4 by MceF, the mechanism we discovered and reported in this article. Reallocation of these proteins in cellular mitochondria enables mammalian cells to live longer even when they're infected with a very large bacterial burden," said Dario Zamboni, one of the corresponding authors of the article and a professor at the Ribeirão Preto Medical School (FMRP-USP).

The study was conducted at the Center for Research on Inflammatory Diseases (CRID), one of FAPESP's Research, Innovation and Dissemination Centers (RIDCs), in collaboration with Hayley Newton, a professor at Monash University in Australia.

"Basically, we discovered a strategy used by *C. burnetii* to keep cells

healthy for longer while replicating intensely. We found that its protein MceF redirects GPX4 to the mitochondria, where it acts as a potent antioxidant, detoxifying the [infected cell](#) and preventing cell components from aging, while allowing replication of the bacterium," said Robson Kriiger Loterio, first author of the article, which derived from his Ph.D. research.

*C. burnetii* is the causative agent of a serious infection called Q fever, a relatively common but infrequently diagnosed zoonosis. According to the authors, agricultural outbreaks are "an increasingly significant economic and public health burden."

The bacterium causes atypical pneumonia in humans and coxiellosis in some animals, such as cattle, sheep and goats. Zamboni explained that it is highly adapted to invade and control macrophages and monocytes—white blood cells that are part of the organism's front-line immune defense—inhibiting the host's responses to the infection.

"The interest of studying this bacterium in depth lies precisely in its ability to subvert cell functions. Unlike other bacteria, which cause disease only when they multiply to reach large numbers, a single *C. burnetii* is enough to make a healthy person sick. So it acts efficiently to modulate the cells it invades. We refer to it jokingly as a brilliant cell biologist because of this ability to modulate everything in host cells," Zamboni said.

Another interesting aspect of *C. burnetii*, he added, is that it replicates in cells for about a week. For comparison, *Salmonella*, which causes severe food poisoning, causes the death of host cells in less than 24 hours.

"Observing *C. burnetii* is a good way to learn about how cells function. In the case of this study, it helped us understand how to treat mitochondrial dysfunction, and provided insights on programmed cell

death in humans," he said.

To analyze the bacterium's capacity to subvert macrophages and act directly on mitochondria, the researchers conducted in vitro assays and experiments involving larvae of the Greater wax moth (*Galleria mellonella*). In this first stage of the study, they investigated more than 80 novel proteins from *C. burnettii* with the potential to interact with host cells and subvert their functioning. "We ended up focusing on MceF because it acts directly on mitochondria, which play a key role in the process of cell death," Zamboni said.

The group will now continue the research on two fronts, one aiming at a deeper understanding of other proteins of interest, and the other involving biochemical studies to find out more about how MceF influences GPX4.

"The nice thing about this research is that by investigating a bacterium we're learning a lot about cell signaling, cell death and novel ways of reversing [mitochondrial dysfunction](#). We don't need to invent a new technique. The process already occurs during the bacterium's interaction with host cells," he said.

**More information:** Robson K. Loterio et al, Coxiella co-opts the Glutathione Peroxidase 4 to protect the host cell from oxidative stress–induced cell death, *Proceedings of the National Academy of Sciences* (2023). [DOI: 10.1073/pnas.2308752120](https://doi.org/10.1073/pnas.2308752120)

Provided by FAPESP

Citation: Study reveals bacterial protein capable of keeping human cells healthy (2023, November 9) retrieved 12 May 2024 from <https://phys.org/news/2023-11-reveals-bacterial->

[protein-capable-human.html](#)

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.