

Dr George B Stefano

Mitochondria Reconsidered: Unmasking the Ancient Bacterial Legacy in Human Health

doi.org/10.33548/SCIENTIA1317



Although often described simply as the cell's powerhouse, mitochondria began life as bacteria and still carry many bacterial traits. Dr George Stefano, Visiting Professor at Charles University, Prague, explores whether mitochondria should be seen not only as symbiotic partners but also as the most successful chronic infection in history. He highlights how this perspective sheds light on human resilience, viral tolerance, and long-term health. By reframing mitochondria in this way, Dr Stefano and colleagues invite a broader conversation about ageing, disease, and the fine balance between host and microbe that continues to shape human biology today.

Background: From Ancient Bacteria to Cellular Powerhouses

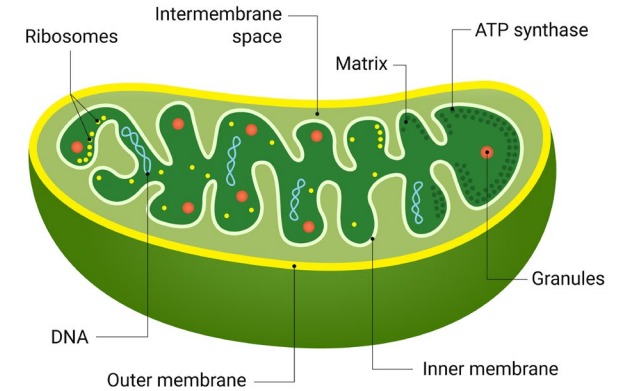
Mitochondria originated more than a billion years ago when an early cell engulfed a bacterium that survived instead of being digested. Over time, this partnership deepened. Most bacterial genes moved into the host cell's nucleus, while the bacteria themselves evolved into mitochondria. Despite this shift, mitochondria still look and behave like bacteria in many ways. Dr Stefano points out that this ancestry means mitochondria may not simply be harmless companions, but instead represent a tolerated long-term infection that became essential for survival.

New Insights into Mitochondria's Role

Modern research has revealed that mitochondria are much more than energy suppliers. They help repair DNA, regulate cell death, and manage the body's immune defences. In bats, for example, mitochondria help balance strong antiviral responses with low inflammation, allowing them to live with viruses that are deadly to other species. Dr Stefano explains that these discoveries show mitochondria as active decision-makers in health, shaping how organisms respond to stress, infection, and ageing.



Mitochondria



Gaps in How We Think About Mitochondria

For decades, mitochondria have been described in textbooks as stable partners in cells. This narrative overlooks their bacterial heritage and underestimates their potential for dysfunction. Dr Stefano argues that by continuing to think of mitochondria only as symbionts, we miss the complexity of their role. Like bacteria, they replicate independently, carry their own DNA, and can even survive outside cells in human blood. These traits make them look less like harmless passengers and more like bacteria that never fully left their infectious roots.

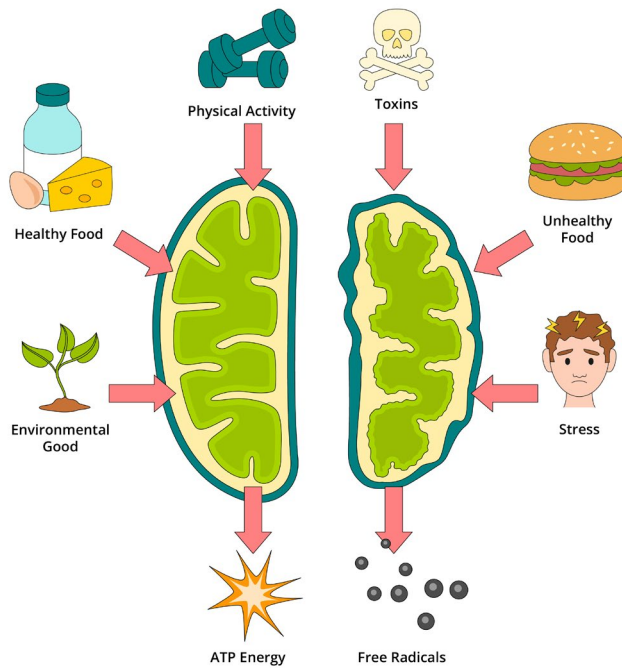
Mitochondrial Quality and Human Disease

When mitochondria work well, they fuel cells and help maintain balance. But when quality control fails, problems arise. Damaged mitochondria can leak signals that trigger inflammation, contribute to neurodegeneration, or drive metabolic diseases like diabetes. Antibiotics, which target bacteria, can also damage mitochondria by mistake, linking treatment side effects to their shared ancestry. Dr Stefano and team highlight that the quality of mitochondrial function is central to human health and that overlooking this connection risks misinterpreting disease.

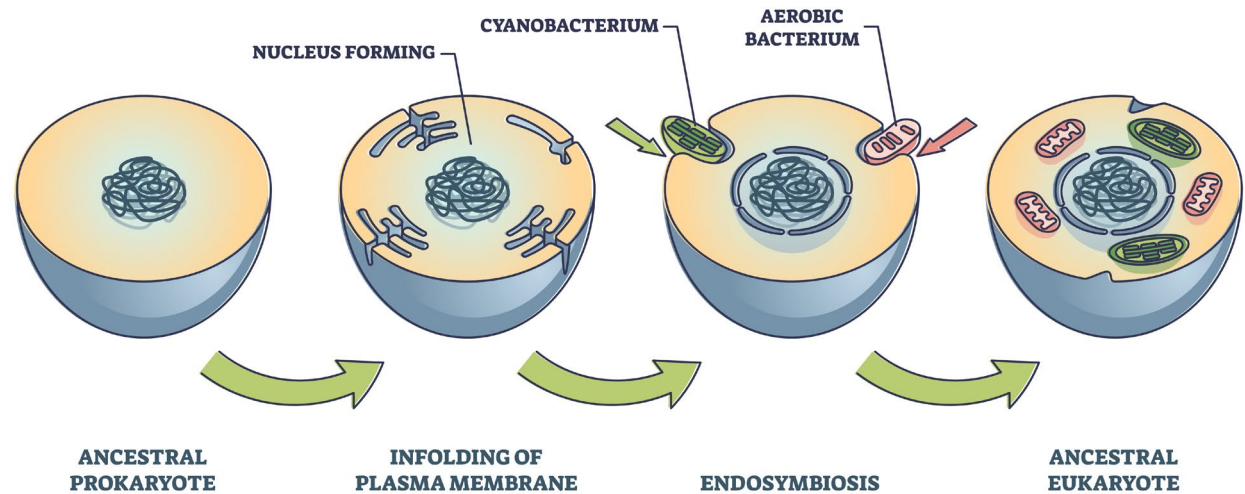
A Total System Perspective on Life and Illness

Dr Stefano and colleagues propose a 'total system' view of mitochondria, where their actions ripple through every aspect of biology. They are involved in immunity, energy, stress responses, and even how we age. Seeing mitochondria as both essential partners and persistent bacterial lodgers allows us to better understand why they influence so many diseases. Just as histology depends on every step of tissue handling, human health depends on the continuous fine-tuning of mitochondrial behaviour.

MITOCHONDRIA & AGING PROCESS



ENDOSYMBIOSIS



What Does the Future Hold: Reframing Mitochondrial Research

Dr Stefano calls for a reevaluation of mitochondria's place in science and medicine. His aim is not to dismiss their life-giving role but to invite dialogue on how their bacterial legacy still shapes us. By recognising mitochondria as both friend and infection, researchers can explore new ways to strengthen resilience, prevent disease, and rethink ageing. This perspective may lead to treatments that protect mitochondria, reduce chronic illness, and help humans live longer, healthier lives.



Article written by Chris Barton, BSc (Hons), MSc



MEET THE RESEARCHER

Dr George Stefano


Charles University, Prague, Czech Republic

Dr George B. Stefano is a neuroscientist and biomedical researcher whose career spans more than five decades. He is Visiting Professor in the Department of Psychiatry at Charles University in Prague and Co-Chair of the Mind-Body Medicine Research Council at Witten-Herdecke University in Germany. Earlier in his career, he served as Distinguished Teaching Professor and Director of the Neuroscience Research Institute at the State University of New York and also held research leadership roles at Harvard Medical School's Mind-Body Medical Institute. He served as Vice Chair of the SUNY Research Foundation Board of Directors, helping steward the systemwide research enterprise. His patents and translational research span Alzheimer's disease, diabetes, cancer, and mitochondrial therapeutics, with several inventions commercialized.

Dr Stefano has published over 500 peer-reviewed papers in journals such as *Science* and *Nature*. His work has uncovered new opioid receptors, advanced understanding of nitric oxide signalling, and highlighted the role of mitochondria in immunity, ageing and chronic disease. Throughout his career, Dr Stefano has secured major funding from the US National Institutes of Health (NIMH, NIDA, Fogarty). His discoveries bridge neuroscience, immunology and integrative medicine. Today, his research focuses on how mitochondrial biology shapes resilience, viral tolerance, and human health throughout life.

CONTACT

gstefano@sunynri.org

 ORCID: 0000-0002-8146-0740



KEY COLLABORATORS

Richard Kream, Neuroscience Research Institute, State University of New York, USA

Pascal Büttiker, First Faculty of Medicine, Charles University, Czech Republic

Martin Anders, First Faculty of Medicine, Charles University, Czech Republic

Tobias Esch, University of Witten/Herdecke, Germany

Maren Michaelsen, University of Witten/Herdecke, Germany

Jiri Raboch, General University Hospital and First Faculty of Medicine, Charles University, Czech Republic

Simon Weissenberger, First Faculty of Medicine, Charles University, Czech Republic



FURTHER READING

Buttiker P, Stefano GB, Weissenberger S, *et al.*, HIV, HSV, SARS-CoV-2 and Ebola share long-term neuropsychiatric sequelae, *Neuropsychiatric Disease and Treatment*, 2022, 18, 2229–2237. DOI: <https://doi.org/10.2147/NDT.S382308>

Das S, Rakshit S, Ahn S, *et al.*, Bat adaptations in inflammation and cell death regulation contribute to viral tolerance, *mBio*, 2025, 16(2), e03204–23. DOI: <https://doi.org/10.1128/mbio.03204-23>

Stefano GB, Kream RM, Weissenberger S, *et al.*, Primordial biochemicals within cocervate-like droplets and the origins of life, *Viruses*, 2025, 17(2), 146. DOI: <https://doi.org/10.3390/v17020146>

Stefano GB, Weissenberger S, Ptáček R, *et al.*, Viruses and mitochondrial dysfunction in neurodegeneration and cognition: an evolutionary perspective, *Cellular and Molecular Neurobiology*, 2024, 44(1), 68–82. DOI: <https://doi.org/10.1007/s10571-024-01503-3>

