How diversity of respiratory quinones affects microbial physiology

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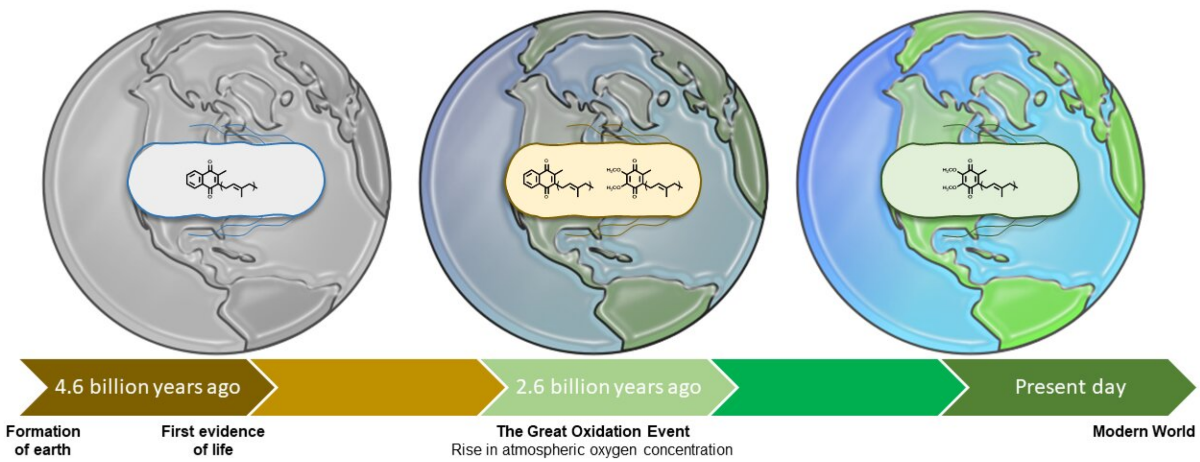

The evolution of respiratory quinones. Credit: Amitesh Anand

A new study provides a fundamental understanding of the diversification of small molecules called respiratory quinones and its adaptive consequences in bacterial species. Bioengineers at the University of California San Diego specifically examined how respiration is affected by different types of quinones present in bacteria growing in aerobic environments.

The team, led by Bernhard Palsson, Galletti Professor of Bioengineering at UC San Diego, and Amitesh Anand, a postdoctoral researcher in the Palsson lab, published their findings Nov. 25 in *Proceedings of the National Academy of Sciences* (*PNAS*).

The process of respiration is dependent on different types of membrane-localized, redox-active small molecules known as respiratory quinones. One type, ubiquinone, is used in modern life forms for aerobic respiration. Historically, its appearance overlaps with the emergence of oxygen on earth. Another type, naphthoquinone, is primarily used in ancient organisms (existing approximately 2.5 billion years ago when the earth had little or no oxygen) for anaerobic respiration.

This quinone diversification overlaps with the oxygenation of the earth's environment and therefore is believed to be an adaptive response to the rise in the oxygen levels. However, a large number of bacterial species still respire aerobically using the ancient respiratory quinone, naphthoquinone.

E. coli and several other bacterial species acquired the ability to produce ubiquinone while retaining the pathways to make naphthoquinone. Interestingly, these bacterial species use ubiquinone for aerobic respiration and naphthoquinone for anaerobic respiration. Bacterial species devoid of ubiquinone, such as Staphylococcus aureus and Mycobacterium tuberculosis, can efficiently respire aerobically using naphthoquinone.

To examine metabolic limitations of aerobic naphthoquinone usage in bacterial species with the ability to produce both types of respiratory quinones, researchers engineered a ubiquinone-deficient strain of *E. coli* to force it to respire aerobically using the ancient respiratory quinone. They then performed an adaptive laboratory evolution of this strain to understand the metabolic challenges that bacterial species face when using the ancient quinone in aerobic environments. The goal was to recreate the conditions during the rapid rise in oxygen in the earth's atmosphere, an event commonly referred to as the Great Oxygenation Event.

The *E. coli* strains that evolved to respire aerobically using naphthoquinone were observed to activate a subset of cellular defense systems that are primarily responsible for mitigating oxidative stress in the periplasmic space. The relatively lower redox potential of naphthoquinone makes it more prone to non-productive electron leakage during the operation of the electron transfer chain in respiration, which can result in the generation of reactive radicals and cause damage to the cell.

By activating a defense mechanism, bacteria experienced a safer operation of the electron transfer chain and showed an improvement in their oxygen consumption. However, activation of this defense mechanism required the bacteria to reallocate finite cellular resources. This restricted the growth capacity of the evolved strains. Researchers hypothesize that this so-called "fear-greed" tradeoff directed the advent of the higher redox potential quinone.

Understanding this fear-greed tradeoff not only advances the basic understanding of microbial bioenergetics evolution, it can facilitate modulation of growth and survival of bacteria, especially a broad range of pathogenic bacteria that respire aerobically using naphthoquinone, researchers said.

More information: Amitesh Anand el al., "Adaptive evolution reveals a tradeoff between growth rate and oxidative stress during naphthoquinone-based aerobic respiration," *PNAS* (2019). www.pnas.org/cgi/doi/10.1073/pnas.1909987116