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Novel hypothesis on why animals diversified on Earth

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Life and rocks in one picture. Credit: Emma Hammarlund

Can tumors teach us about animal evolution on Earth? Researchers believe so, and now present a novel hypothesis of why animal diversity increased dramatically on Earth about a half-billion years ago. A biological innovation may have been key.

Life on Earth was dominated by microbes for roughly 4 billion years when multicellular life in the form of animals in robust ecosystems rapidly developed. Why animals diversified so late and so dramatically has remained unresolved and is a matter of hot debate.

The diversification of animals occurred over a geologically short period of time known as the Cambrian explosion. Many geologists have assumed that the Cambrian explosion was triggered by an increase of atmospheric oxygen. However, a causal relationship between the Cambrian explosion and increasing atmospheric oxygen lacks convincing evidence.

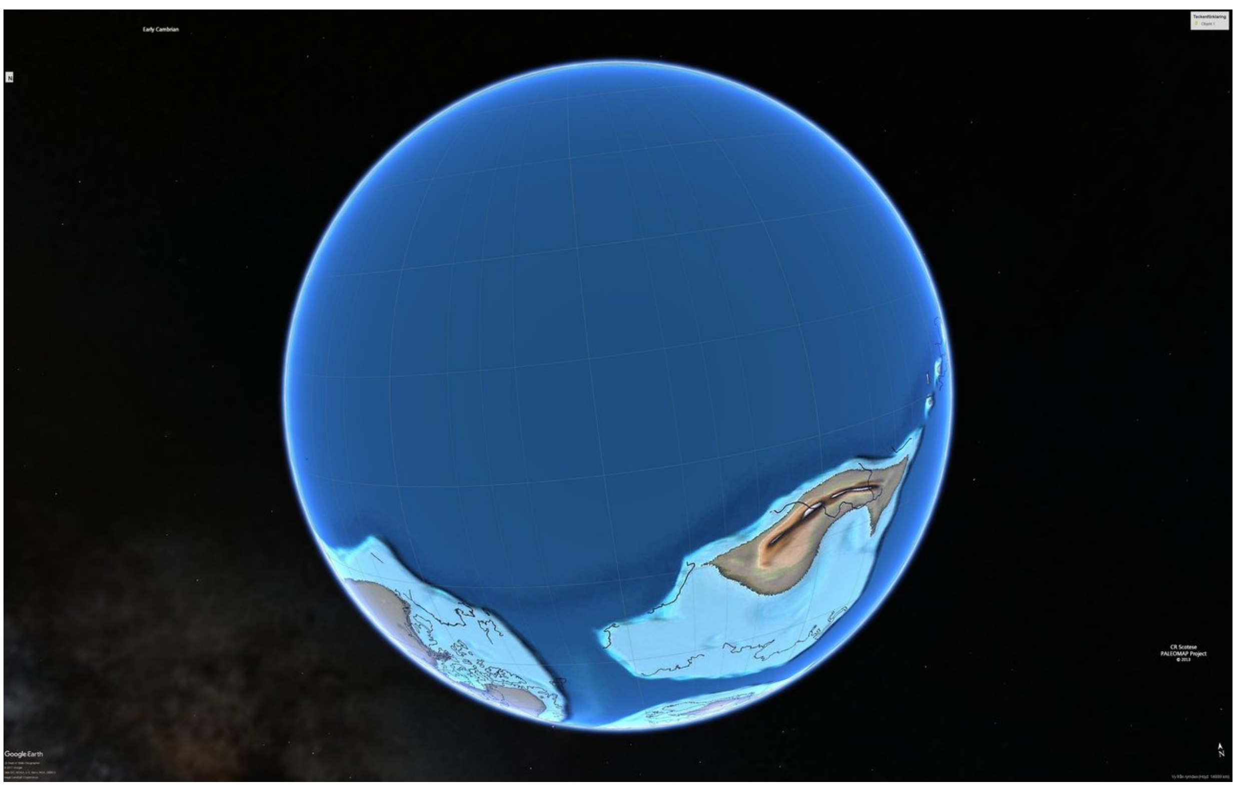
Indeed, research in recent years weakens the support for a correlation between the Cambrian explosion and increasing atmospheric oxygen. For example, dramatic changes in atmospheric oxygen are noted both before and after the Cambrian, but not specifically when animal diversification took off. Simple animals require surprisingly low oxygen levels, which would have been met well before the Cambrian.

"A heated hunt for the geochemical evidence that oxygen increased when animals diversified goes on but, after decades of discussion, it seems worthwhile to consider the development of multicellularity also from other angles," says geobiologist Emma Hammarlund, Ph.D. at Lund University.

In order to understand more about the conditions for multicellular life, Emma Hammarlund contacted tumor biologist, Professor Sven Påhlman at the Department of Laboratory Medicine at Lund University, who has explored the importance of low oxygen concentrations, or so-called hypoxia, in the tumor setting for nearly two decades.

"I wanted to learn what tumor scientists observe on a daily basis, in terms of tissue growth and how it relates to oxygen. Tumours are after all, and unfortunately, successful versions of multicellularity," explains Emma Hammarlund.

The team, which included tumor biologist Dr. Kristoffer von Stedingk at Lund University's Paediatrics division, tackled the historic question of why animals developed so late and dramatically with novel clues from the field of tumour biology. Specifically, they tested whether the same molecular tools exploited by many tumors to maintain stem cell properties could also be relevant to the success of animals in the Cambrian explosion.



Continents and ocean on Earth when animals diversified dramatically in the Cambrian. Credit: Christopher Scotese

Cells with stem cell properties are vital for all multicellular life in order to regenerate tissue. For example, cells in the wall of human small intestine are replaced every two to four days through the division of stem cells.

"Hypoxia is generally seen as a threat, but we forget that oxygen shortage in precise periods and settings also is a prerequisite for multicellular life. Our stem cells are the ones that form new tissue, and they are extremely sensitive to oxygen. The stem cells therefore have various systems for dealing with the effects of both oxygen and oxygen shortage, which is clear in the case of tumors," explains Sven Påhlman.

By studying the ability of tumor cells to imitate the properties of stem cells, Sven Påhlman's team have observed how tumor cells can hijack specific mechanisms that evade the effects of high oxygen on stem cell depletion. As a consequence, the tumor cells are able to maintain stem cell properties, despite being surrounded by the high oxygen concentrations that are present in the body. This same ability, according to the authors, is one of the keys that also made animals so successful.

"The ability to construct stem cell properties despite high oxygen levels, so called 'pseudohypoxia,' is present also in our normal vertebrate tissue. Therefore, we flip the perspective on the oxic setting: While low oxygen is generally unproblematic for animal cells, the oxic settings pose a fundamental challenge for complex multicellularity. Without additional tools, the oxic setting makes tissue-specific stem cells mature too early," says Sven Påhlman.

The new hypothesis holds that the dramatic diversification of animals resulted from a revolution within the animals' own biology, rather than in the surrounding chemistry on Earth's surface. A view that fits with other geobiological observations, such that environments with enough oxygen have been present on Earth since long before the Cambrian explosion.

The hypothesis also has implications for varying capacities to live in oxygenated environments, and perhaps even for how we see cancer as an evolutionary consequence of our ability to live in oxygenated niches. Taking an evolutionary approach is unusual for cancer researchers, even though the development of tumors is generally seen as an evolutionary process.

Similarly, geobiological research rarely apply the cellular perspective. But having combined their expertise, both Emma Hammarlund and Sven Påhlman are surprised that we have not previously wondered about our paradoxical ability to renew tissue in the oxic setting. "Surely, many people who would intuitively disagree. But once you flip the perspective on the oxic niche and start to consider it as challenging for stem cell properties and tissue renewal, then puzzling observations from distant fields starts to fit together. And you can't turn back," says Sven Påhlman.

More information: Emma U. Hammarlund et al. Refined control of cell stemness allowed animal evolution in the oxic realm, *Nature Ecology & Evolution* (2018). DOI: 10.1038/s41559-017-0410-5

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