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# SciSpark

Igniting Ideas, Bridging Minds

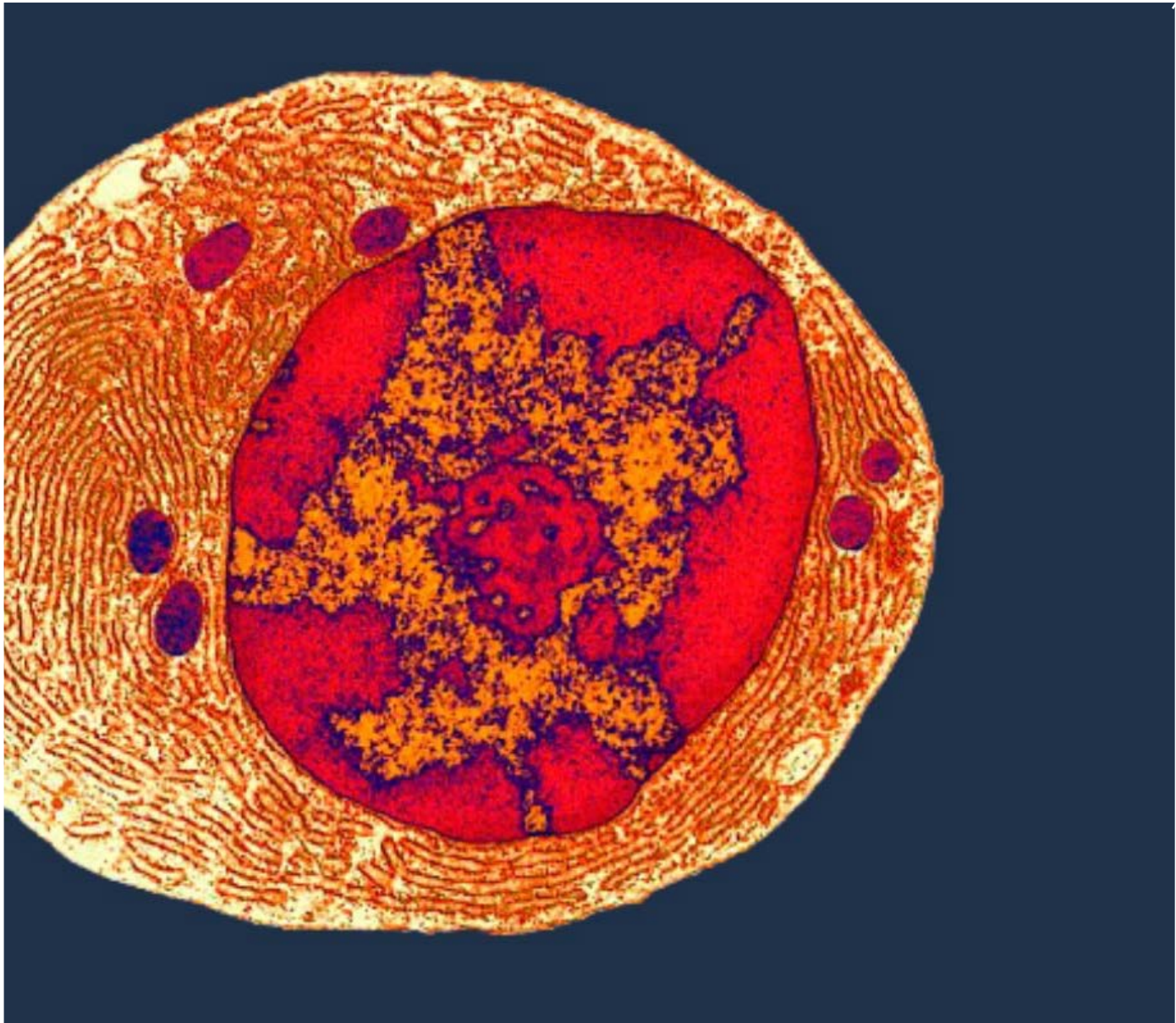
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## What fossils reveal about Evolution, Extinction, and Future

Ammonites, extinct marine mollusks from over 65 million years ago, leave behind intricately spiraled fossil shells that serve as a visual bridge between biology, geology, and time. Their chambered structures, often echoing the golden ratio, reveal nature's deep, mathematical patterns, uniting life, science, and the ancient Earth.





# Evolution of Hemoglobin and Chlorophyll: A Molecular Journey from LUCA

*LUCA'S LEGACY: HOW A SINGLE PATHWAY GAVE RISE TO BLOOD AND GREEN*

By Sajani Prathibha<sup>1,2</sup> & Mahesh Premarathna<sup>1</sup>

At first glance, hemoglobin and chlorophyll might seem like they belong to completely different worlds. Hemoglobin, a red protein containing iron, is found in animal blood and helps transport oxygen throughout the body, playing a key role in metabolism. On the other hand, chlorophyll is a green pigment in plants that captures sunlight and fuels the process of photosynthesis. Although hemoglobin and chlorophyll perform different functions in biology, they share a profound and age-old evolutionary bond in the form of a common ancestry, which is a molecular pathway that emerged right at the beginning of life on Earth.

To understand this connection, we must travel back more than 3.5 billion years to a time before plants, animals, or even complex cells existed. Life's earliest ancestor, known as the Last Universal Common Ancestor (LUCA), is believed to have been a simple organism. However, LUCA likely possessed a sophisticated set of metabolic tools, including the tetrapyrrole biosynthetic pathway. This pathway is fundamental to life today and forms the molecular foundation for the development of heme (a component of hemoglobin) and chlorophyll. The fact that this ancient biochemical machinery is still conserved across bacteria, plants, and animals speaks to its evolutionary significance<sup>1</sup>.

*The evolutionary story of hemoglobin and chlorophyll spans billions of years...How did chlorophyll and hemoglobin evolve together? ...one carrying oxygen, the other capturing light, reflecting nature's adaptive versatility through evolution...However, both are constructed from a common tetrapyrrole ring and a shared biosynthetic pathway*

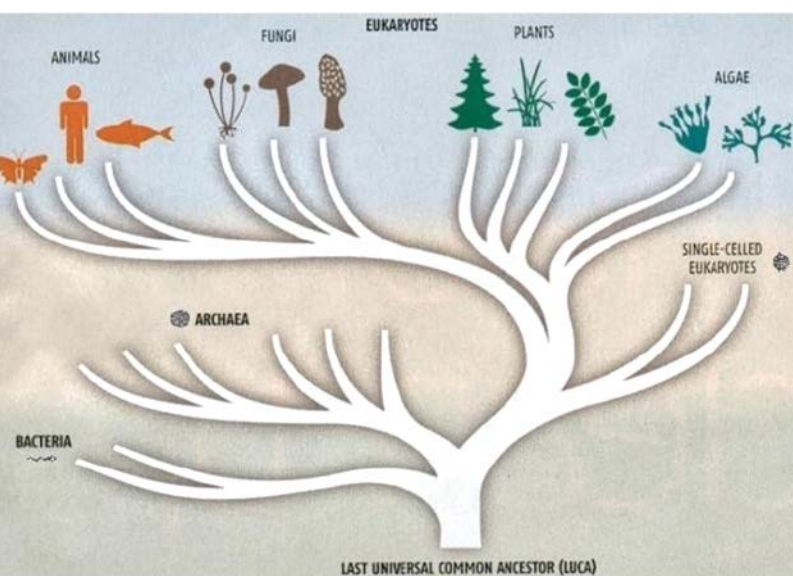
The central player in this shared evolutionary story is tetrapyrrole, a ring-shaped molecular scaffold composed of four interconnected pyrrole units. This scaffold is synthesized through a biosynthetic pathway that begins with 5-aminolevulinic acid (ALA)<sup>2</sup>. Through a series of enzymatic steps, ALA is converted into uroporphyrinogen III, which is then transformed into protoporphyrin IX. At this crucial branching point in evolution, the insertion of different metal ions determined two distinct biochemical destinies: the addition of iron (Fe) by the enzyme ferrochelatase led to the formation of heme, while the insertion of magnesium (Mg) via magnesium-chelatase produced chlorophyll. This single divergence, iron or magnesium, created

molecules that enabled oxygen transport in animals and solar energy capture in plants, respectively<sup>3</sup>.

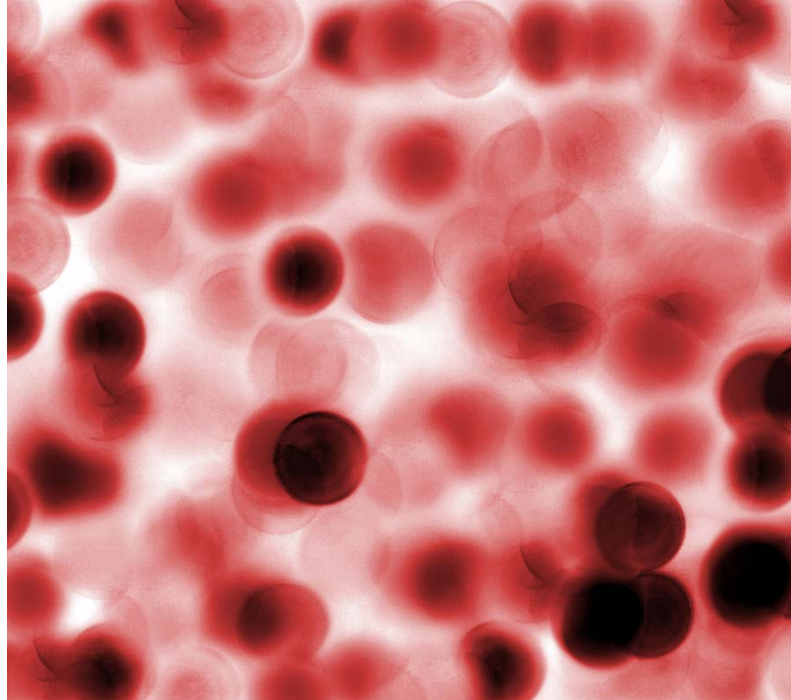
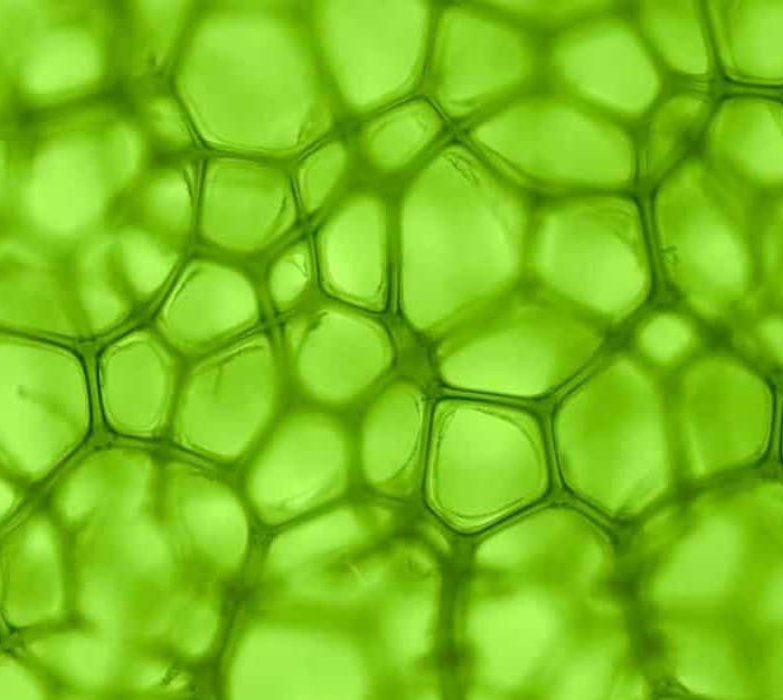
The divergence at protoporphyrin IX marks one of nature's most efficient evolutionary decisions. Heme, the iron-containing product, became central to the function of hemoglobin, which emerged as an essential oxygen carrier in red blood cells. On the other hand, chlorophyll, with its magnesium core, became the main pigment driving photosynthesis, allowing autotrophs to convert light energy into chemical energy. These distinct pathways

underscore how evolution can repurpose a common molecular ancestor to suit vastly different biological functions across species<sup>4</sup>.

The evolutionary story of hemoglobin and chlorophyll spans billions of years. The earliest photosynthetic bacteria, appearing around 3.4 billion years ago, began utilizing primitive chlorophylls. Over time, cyanobacteria developed the ability to perform oxygenic photosynthesis, significantly altering Earth's atmosphere by producing free oxygen. Meanwhile, the incorporation of mitochondria and chloroplasts into eukaryotic cells allowed more complex organisms to harness both respiration and photosynthesis. The emergence of







multicellular animals, around 600 million years ago, brought hemoglobin into widespread use, especially in organisms that required efficient oxygen transport across their growing bodies. These parallel evolutionary paths, both grounded in tetrapyrrole chemistry, reflect nature's ability to adapt and innovate using shared molecular frameworks<sup>5</sup>.

## A New Scientific Vision: Converting Chlorophyll into Hemoglobin

In a daring and visionary step forward, researchers are now proposing something previously unthinkable: to reverse-engineer chlorophyll into hemoglobin not just metaphorically, but literally.

In 2024, a proposal by Israel A. Grillo (McPherson College), this idea is being brought to the laboratory bench. The goal was to synthesize functional hemoproteins like artificial hemoglobin by chemically transforming plant-based chlorophyll into a heme analog and binding it to globin proteins<sup>6</sup>.

This isn't just an academic exercise. If successful, this transformation could redefine the boundaries of synthetic biology, paving the way for synthetic blood substitutes, bioengineered oxygen carriers, and

sustainable heme production<sup>6</sup>.

The conversion process follows a highly sophisticated path, merging organic chemistry, protein engineering, and biotechnology. To make chlorophyll more "heme-like," its phytol tail is removed and aldehyde groups are oxidized. Vinyl groups are introduced through Wittig reactions to match heme's structure. Chlorophyll's chlorin ring is oxidized into a fully conjugated porphyrin ring, mimicking the chemistry of heme using compounds. The magnesium at the center of chlorophyll is replaced with iron ( $\text{Fe}^{2+}$ ) using metalation reactions thus converting it into a synthetic heme.

Globin proteins (alpha and beta chains) are expressed in *E. coli* using recombinant DNA technology. These proteins are then combined with the synthetic heme to create a functional hemoglobin analog. Spectroscopy (UV-Vis, NMR), oxygen-binding assays, and biological models are used to validate whether the new molecule truly behaves like native hemoglobin.

## Implications: Synthetic Blood and Beyond

Should this groundbreaking process succeed, it could usher in an era of plant-based hemoproteins, offering solutions to medical crises such as: Blood shortages in emergency or remote situations, Synthetic oxygen carriers for high-altitude or deep-sea environments, Bio-



compatible heme for tissue engineering or drug delivery<sup>6</sup>. In addition, this approach provides an alternative, green, and sustainable method for the synthesis of intricate molecules that are usually obtained from animal or microbial sources.



*"How did chlorophyll and hemoglobin evolve together?"*

The case of hemoglobin and chlorophyll stands out in regard to molecular homology due to their evolutionary relationship they share, the concept that similar molecules may diverge to perform different and often unrelated functions - one carrying oxygen, the other capturing light, reflecting nature's adaptive versatility through evolution. Both molecules function in different biological contexts. However, both are constructed from a common tetrapyrrole ring and a shared biosynthetic pathway. This common lineage illustrates a fundamental idea in biology: evolution tends to adapt and modify what already exists rather than create something new. Understanding this unifying concept provides insight into the biochemical relationships that unite all beings on Earth, including the oxygen we breathe, the blood in our bodies, and the energy-rich food we consume.

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