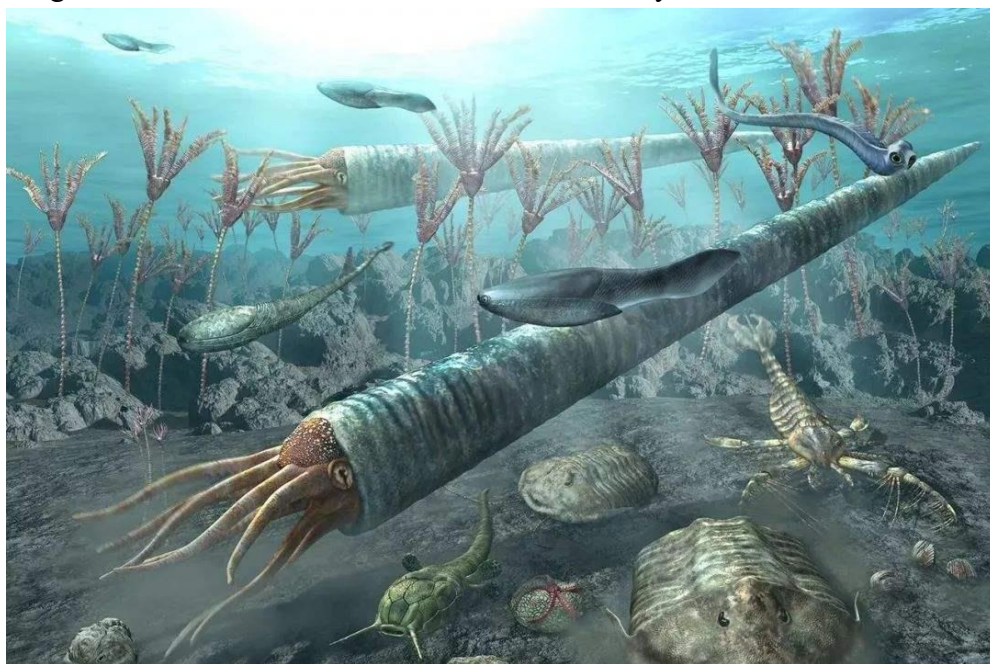


In today's world where disinfectant products emerge one after another, hypochlorous acid (HOCl) disinfectant solution is often misunderstood — some confuse it with “Bleach” (sodium hypochlorite, NaClO) and even question its safety. Unbeknownst to many, this seemingly unfamiliar disinfectant is actually a “natural ally” of the human immune system, a gift from the ocean to life on Earth over hundreds of millions of years, and the most economical and intelligent defensive choice bestowed by evolution.

The Past and Present of Hypochlorous Acid

As early as the distant Phanerozoic Eon, Paleozoic Era, the continuous struggle between life forms and bacteria spurred a silent yet profound revolution — the innate immune defense system based on oxidative bactericidal action quietly emerged. From marine invertebrates to birds soaring in the sky, from tiny arthropods to amphibians and reptiles, and up to humans, this exquisite defense mechanism was continuously optimized throughout the long river of evolution, eventually forming the “Myeloperoxidase (MPO) - Hypochlorous Acid (HOCl)” core innate immune defense system in advanced life forms. This system, like a loyal guard, has always held the front line of the immune battlefield, building an indestructible line of defense for life, achieving indelible merits over hundreds of millions of years of life's evolution.



Origins

Around 3.5 billion years ago, a remarkable organism called cyanobacteria (blue-green algae) became the key force ending the archaean dominance. It performed photosynthesis using chlorophyll, releasing oxygen, gradually transforming the

anaerobic environment upon which early life depended. This initiated a legendary and pivotal evolutionary journey, steering life in a new direction. This seemingly minor change set the stage for the Great Oxidation Event (GOE) around 2.4 billion years ago and the subsequent Cambrian explosion approximately 500 million years ago. Originally adversaries, aerobic and anaerobic bacteria, through prolonged struggle, saw some transition from conflict to cooperation, embarking on a model of “mutualistic symbiosis”: Aerobic bacteria parasitized within archaea that had developed nuclear membranes. The latter provided the former with food like organic acids and CO_2 and a suitable habitat, while the former evolved into the latter’s “mitochondria”, providing energy and power. Simultaneously, they developed oxygen-containing highly reactive substances called Reactive Oxygen Species(ROS), such as H_2O_2 and $\text{O}_2\bullet^-$, forming an ancient and classic chemical weapon system that has been used by life forms ever since, traversing vast stretches of time.



Evolution

During the long course of biological evolution, primitive lower organisms initially relied mainly on ROS, represented by H_2O_2 , as their Version 1.0 chemical weapon to resist pathogens. As species evolved, this arsenal was upgraded to Version 2.0: organisms began synthesizing a new type of “high-explosive” –Hypochlorous Acid (HOCl)—using H_2O_2 and chloride ions (Cl^-) as raw materials. Its bactericidal power is approximately 100 times that of H_2O_2 . Concurrently, the corresponding catalytic enzymes also evolved from scratch, forming the “Myeloperoxidase-like (like-MPO)” enzyme family, such as Dual Oxidase (DUOX) in fruit flies and MPO in mammals, among other key enzymes.

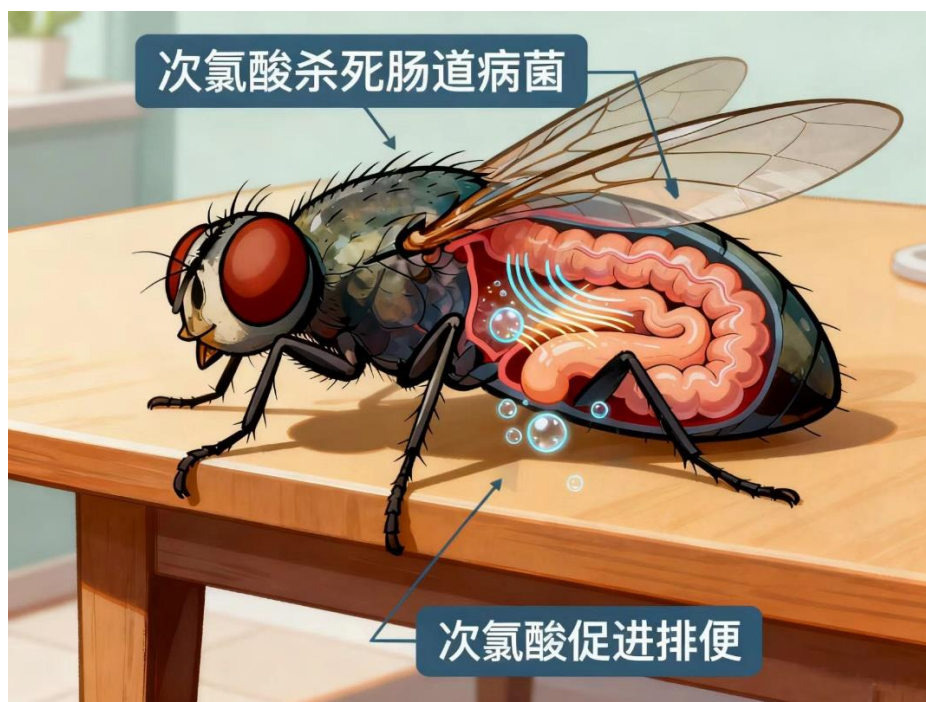
Tracing the Source

Although the exact timing of HOCl ’s emergence cannot be determined from fossils,

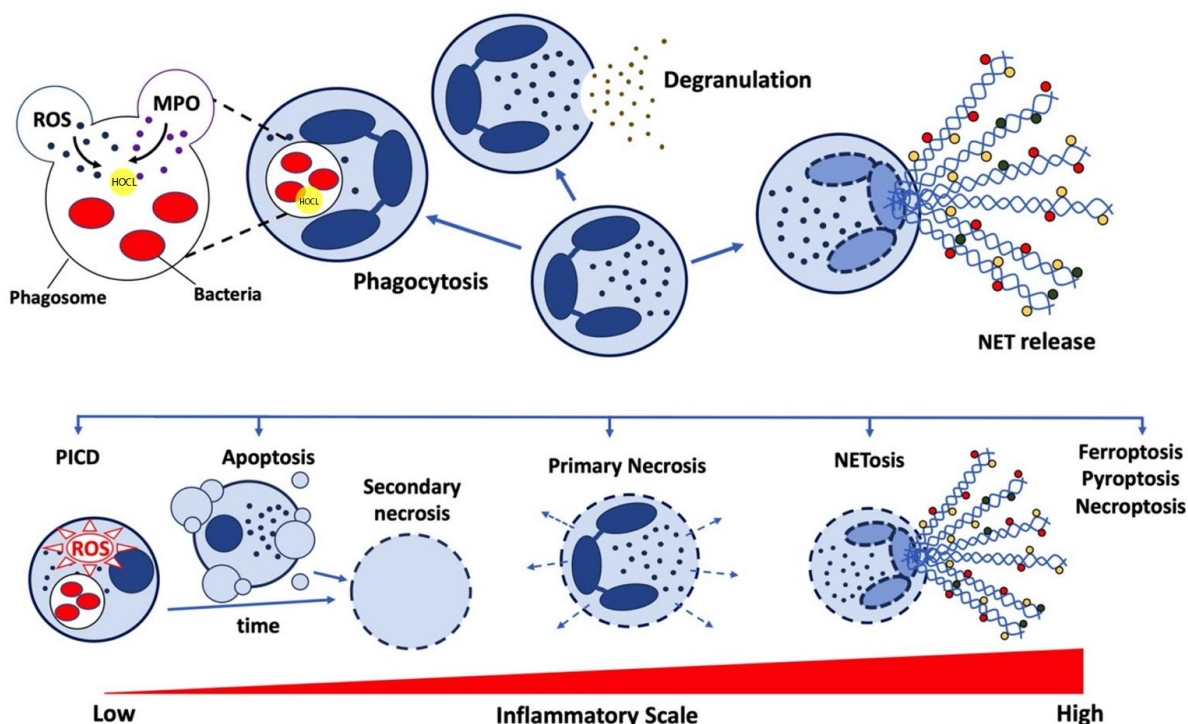
by studying extant primitive organisms, we can still trace the evolutionary trajectory of its immune function. The fact that lower animals possess the ability to use HOCl for immune defense indicates that this mechanism is evidently extremely ancient. In mollusks, the famous Hawaiian bobtail squid (*Euprymna scolopes*) possesses a substance structurally similar to vertebrate MPO, called “squid haloperoxidase (HPO)”, which can convert H_2O_2 in its body into HOCl, thereby helping it resist the myriad bacterial assaults in the ocean. Particularly remarkable is that this squid’s light organ reserves a “VIP channel” for *Vibrio Fischeri* (a bioluminescent bacterium): it can precisely regulate the population and circadian rhythm of *V. fischeri*, causing it to emit blue light only at night, assisting the squid in evading predators. This discovery holds significant evolutionary biological importance. Cephalopod mollusks originated around 500 million years ago in the Paleozoic Era, and they already possessed such a complex HOCl immune system, indicating that the HOCl immune defense function is not a novelty in invertebrates but rather an important immune mechanism likely widespread since ancient times.



How do arthropods like fruit flies, which are exposed to large amounts of food-borne bacteria daily, manage to prevent pathogenic infections? The answer lies in their intricate “Dual-Pathway Regulation of HOCl” mechanism: Firstly, bacteria in the fruit fly’s gut lumen produce uracil, which activates the DUOX pathway and generates HOCl, performing a “chemical clearance” of pathogenic bacteria in the gut lumen. Secondly, HOCl can bind to the chemoreceptor TRPA1(A)10 on intestinal enterochromaffin cells, prompting the release of serotonin, accelerating intestinal peristalsis and excretion, thereby performing a “physical clearance” of the gut lumen. It is this “Kill-and-Flush” combination that significantly reduces the risk of pathogen invasion.



Unlike lower animals that utilize HOCl in a “make-the-most-of-everything” manner, higher organisms tend to enrich the variety of their arsenal and employ a multi-component teamwork mode to achieve efficient pathogen clearance. Taking humans as an example, on the basis of the ROS-centric “Innate Immunity”, the immune system further evolved “Adaptive Immunity” capable of “precise recognition + targeted attack”. Among these, innate immunity is the body’s first line of defense against bacterial invasion, with neutrophils, nicknamed “bomb trucks”, being the core players. They internalize captured bacteria into “phagosomes”, where they generate ROS, primarily HOCl, often ultimately “dying together” with the enemy. Some neutrophils, before succumbing, expel their own DNA strands, forming a trapping net that firmly “ties down” pathogens and exposes them to attack by other immune cells. Unlike the broad-spectrum attack of innate immunity, Adaptive Immunity, centered on T lymphocytes and B lymphocytes, possesses specific recognition and memory functions. This “precision-guided” mode can generate highly efficient targeted antibodies or cytotoxic responses against specific pathogens and enable rapid response upon secondary infection.



The Choice

When we gaze upon the blueprint of life designed by the creator, a profound question arises: Why did life on Earth choose HOCl, with “Chlorine (Cl)” at its core, as a crucial weapon against invading pathogens? To solve this puzzle, we must return to the origin of life — a “photosynthetic revolution” by cyanobacteria. About 2.4 billion years ago, chlorophyll in cyanobacteria captured a single photon from the sun. In that instant, the excited electron broke away from chlorophyll, forcibly seizing electrons from water molecules. The water molecule was split into O_2 , H^+ , and e^- . This process was not only the beginning of photosynthesis but also initiated the first step in converting light energy into electrochemical energy. It is precisely this process of electron gain and loss (redox reactions) that initiated the rhythm of life, driving the respiratory chain and ATP synthesis. Therefore, anions that are abundant and prone to losing electrons are undoubtedly the most economical raw materials for life activities. Cl^- is not only the most abundant anion in the ocean but also the undisputed “champion anion” in the human body, with its concentration far exceeding that of other anions — a resource repository inherited during life’s evolution from the ocean to land. Beyond resource endowment, the property of Cl^- , being prone to lose an electron and become the highly oxidatively active substance HOCl (Cl^+), enables it, within the cyclical electron transfer process of $Cl^- \rightleftharpoons Cl^+$, to create one miracle of life after another.



Revelation

From cyanobacteria challenging the dominance of archaea, to the prolonged struggle between aerobic and anaerobic bacteria, and further to mutualistic symbiosis forming a “community of shared future”, driving life’s evolution from lower to higher forms. Observing the ways of survival in the bacterial world, is human society not much the same?