Bacterial Bleaching of Corals Leads to Hologenome Concept

Efforts to understand how corals developed resistance to pathogens led investigators to develop the much broader concept of the hologenome.

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There is no such thing as a failed experiment, only experiments with unexpected outcomes.
— Richard Buckminster Fuller, American architect and inventor.

Rising temperatures in the Mediterranean Sea each summer lead to bleaching of the stony coral, Oculina patagonica, as it loses its endosymbiotic pigmented algae. In 1996, a former graduate student Ariel Kushmaro here at Tel Aviv University showed that Vibrio shiloi bacteria are responsible for the bleaching disease of O. patagonica.

For the next decade, we continued studying these organisms to better understand the mechanisms of bacterial bleaching of corals, showing that the pathogen adheres to a β-galactoside-containing receptor in the coral mucus, penetrates into epithelial cells, differentiates into a viable-but-not-culturable state, multiplies intracellularly, and produces a peptide toxin that inhibits photosynthesis by algae within the coral. Bleaching of O. patagonica became the best-studied coral disease.

Sometime between 2004 and 2006 that seemingly stable status quo changed, and the corals developed resistance to V. shiloi infection. We no longer could find the pathogen on the corals, and the same strains of V. shiloi that previously infected corals no longer could do so. Our prized model system failed to work anymore. Despite our disappointment over its loss, however, our subsequent efforts to explain what happened led us to something of broader importance: the hologenome concept of evolution.

Initial Focus Was on What Made Corals Resistant to Bleaching

How had the corals become resistant to V. shiloi? Corals possess a restricted adaptive immune system and do not produce antibodies. These facts led us to develop the coral probiotic hypothesis. It posits that the corals acquired beneficial bacteria, or probiotics, from the marine environment that prevent their being infected any longer by V. shiloi. If it is possible to have epidemics of pathogens, we reasoned, why is it not possible to have epidemics of beneficial bacteria? They usually go unnoticed. In support of the coral probiotic hypothesis, we recently showed that treating O. patagonica with antibiotics to kill the beneficial bacteria makes the coral sensitive again to infection and bleaching by V. shiloi.

Sometimes unexpected results in science can lead researchers in new directions. The coral probiotic hypothesis inspired us to consider more generally the role of beneficial microbes in multicellular life forms. For one thing, our finding that symbiotic bacteria protect the host from pathogens proves to be a general phenomenon. The first evidence for the beneficial effects of intestinal microbiota in terrestrial mammals came from studies in the 1950s, showing that animals treated with antibiotics were much more sensitive to infection with pathogens. Since then, we

SUMMARY

➤ When a model system for studying how bacterial pathogens cause the bleaching of sea coral stopped working, efforts to understand what happened led researchers to frame the hologenome concept.
➤ The hologenome concept sees an organism as the sum of its genomic parts, those of both the host and its full microbiome.
➤ The hologenome concept of evolution relies on the continuity of partnerships between holobiont generations, and the microbiota component contributes to the fitness of the holobiont.
➤ The holobiont adds three modes of genetic variation to drive evolution: microbial amplification, acquisition of novel strains from the environment, and horizontal gene transfers.
have learned from many other studies that bacterial symbionts generally provide animal and plant hosts with defensive chemicals that ward off predators, parasites, and pathogenic microorganisms.

During most of the 20th century, microbiological research focused on infectious diseases and the application of model microbial systems to discover a broad array of principles, including in biochemistry, genetics, and infectious diseases. The preponderance of research in microbiology was performed with a limited number of pure microbial cultures under defined laboratory conditions. Insufficient tools were available at that time to study the ecology, natural phylogeny, and evolution of microbes.

The advent of PCR and techniques for sequencing DNA, coupled with bioinformatics for analyzing the data and the cumulative knowledge that had been gained on pure bacterial cultures, opened the door for studying and understanding a fuller depth and breadth of the microbial richness in our world. When these methods were used to examine bacterial communities associated with animals and plants, it soon became apparent that there was a much greater microbial diversity than previously considered and that symbiosis—once thought to be an exceptional phenomenon—is the central hallmark of life on earth.

**The Hologenome Concept of Evolution**

After considering the large body of published data on microbial symbionts from many research groups, we derived the hologenome concept of evolution. To appreciate this concept, a few terms need to be defined. A holobiont is the host plus all its microbial symbionts. The microbiome is the sum of all the microbial genomes. The hologenome is the host genome plus the microbiome. The hologenome concept of evolution posits that the holobiont with its hologenome is a level of selection in evolution.
The concept is supported by a growing body of data that demonstrate:

- All animals and plants harbor abundant and diverse microbial symbionts. In some cases, the numbers of symbiotic microorganisms and their combined genetic information far exceed that of their host.
- The microbiota with its microbiome together with the host genome can be transmitted from one generation to the next with fidelity, and thus it can propagate the unique properties of the holobiont and the species.
- Microbial symbionts and the host interact in a way that affects the anatomy, metabolism, physiology, development, behavior, and overall fitness of the holobiont within its environment. The sum of these interactions characterizes the holobiont as a unique biological entity.
- Genetic variation in the hologenome can be brought about by changes in the host genome and the microbiome. Under environmental change and stress, the microbiome can adjust more rapidly and by more processes than the host organism alone and, thus, can enhance variation and evolution of the holobiont. Evolution of holobionts proceeds via both cooperation and competition.

**Diversity of Microbiota Transmitted between Holobiont Generations**

You may think of yourself as a fully autonomous individual, but like all animals and plants, you are far more complicated—in short, a holobiont, sharing your body with thousands of different species of bacteria, viruses, and protists. In most animals, including *Homo sapiens*, the largest numbers of symbionts are found in the digestive tract. Sometimes, the number of symbiont cells exceeds the number of cells making up the host. Although it often is asserted that the number of cells in the human microbiota is 10 times greater than the number of cells in the human body, the ratio varies and may be closer to 1 than to 10. In some marine sponges, symbiotic bacteria account for 35% of the mass of the organism.

Because of the large number of microbiota in the human gut and the important role they play in health and disease, the collection of microbes within the gastrointestinal (GI) tract is sometimes referred to as our “forgotten organ.” However, the true organs of our body are composed of cells with the same DNA, whereas the GI microbiota comprises thousands of different genomes, such that the total number of bacterial genes there is more than 300 times greater than those present within the human genome.

The hologenome concept of evolution relies on the continuity of partnerships between holobiont generations. Accordingly, both host and symbiont genomes must be transmitted with accuracy from one generation to the next. The accurate transfer of host genome to the next generation is well established.

Until recently, however, the fidelity of transfer of microbiotas was less well established. Nevertheless, we know now that microbial symbionts can be transmitted from parent to offspring in various ways, including via cytoplasmic inheritance, eggs, coprophagy (consumption of feces), direct contact during and after birth, via insect vectors, and from the environment. During vegetative, or asexual, reproduction, the microbiota is automatically transferred to offspring.

In humans, most of the colonization of the newborn gut occurs when the baby transits the birth canal via contact with maternal vaginal and fecal microbes. Furthermore, human breast milk is another source of bacteria to the infant gut. From the point of view of the hologenome concept, it is reassuring to realize that babies acquire microbial diversity from their mother’s milk.

Because some human symbionts are transmitted with great accuracy from mother to offspring for many generations, they have been used as a window into human migration. Many bacterial symbionts co-evolve with their hosts for many generations. For example, ants and great apes have retained many of their symbionts for millions of years.

**Microbiotas are Part of the Holobiont Fitness**

Microbial symbionts contribute to their hosts’ many important functions, including protection against pathogens, provision of nutrients, and energy production—mitochondria and chloroplasts are symbionts that originated from bacteria. In several cases, symbiotic microbes perform processes that the host animal or plants cannot carry out by themselves, including nitrogen fixation in legumes, cellulose degradation in ruminants and termites, photosynthesis by microalgae.
in corals, mollusks, and sponges, and oxidation of inorganic compounds in deep-sea invertebrates. In humans, gut microbiota play an essential role in breaking down dietary fiber, producing vitamins and amino acids, and detoxifying harmful chemicals. In plants, bacteria and fungi interact with the roots and contribute to carbon transfer to soil, nitrate reduction, mineralization of organic materials, and water cycling, all of which promote plant growth.

In mice, chickens, and humans, obesity is correlated with individual hosts carrying a microbiota that differs from the norm. Both microbiota and diet influence obesity, according to Jeffrey Gordon at Washington University School of Medicine in St. Louis, Mo. He and his collaborators infested separate groups of germ-free mice with microbiotas from obese and lean human twins. Mice infected with the bacteria from the feces of the obese twin added significantly greater amounts of body weight than did those mice infected with bacteria from the lean twin. However, because obesity-associated bacteria may be responsible for weight gain during the third trimester of pregnancy, caution should be used in considering them as being only harmful.

In vertebrates, the development of the immune and digestive systems are triggered by and not completed without gut bacteria. To a large degree, we co-develop with our symbionts. Experiments in mice indicate that gut microbiota also affect the brain and behavior. These findings are supported by the fact that there is more than a twofold difference in gene expression in more than 100 genes in the brain between germ-free and conventional mice.

Variation and Evolution of Holobionts

Genetic variation is the raw material for evolution. Without it, evolution cannot occur. For more than 70 years, neo-Darwinists considered chromosomal mutations to be the major source of variation. However, in recognizing the holobiont as a level of selection in evolution, we also can better appreciate three important sources of genetic variation: microbial amplification, acquisition of novel strains from the environment, and horizontal gene transfers.

In this context, microbial amplification refers to changes in the relative numbers of holobiont-associated microorganisms. Such changes are influenced by environmental factors such as diet, changing temperatures, and exposure to toxic materials. An increase in numbers of a particular microbe within the holobiont is equivalent to variation by gene amplification.

Considering the large amount of genetic information encoded in the diverse microbial population of holobionts, microbial amplification is a powerful mechanism for adapting to changing conditions. Microbial amplification at the level of the microbe is pure Darwinian selection, whereas at the level of the holobiont, amplification of a microbe is, in fact, genetic variation within the hologenome.

Acquiring new symbionts from the environment provides another way for introducing variation into holobionts. Animals come in contact with billions of microorganisms in the food they eat, water they drink, air they breathe, and through direct interaction with other animals. Plants contact numerous microorganisms through their roots, the surrounding air, and also by insect vectors. It is reasonable to think that some of these microorganisms become established in the hosts that they encounter. Unlike microbial amplification, acquiring new symbionts can introduce entirely new sets of genes into holobionts.

For example, the ability of some animals to use cellulose and other complex polysaccharides as nutrients was driven by their acquiring bacteria capable of metabolizing those polysaccharides. Both termites and cockroaches gradually internalized microbial consortia from the environment that digest plant litter. Instead of that plant debris decaying in the external environment, it is degraded within the hindgut after being ingested. Similar arguments apply to herbivorous dinosaurs and plant-eating mammals.

Horizontal gene transfer (HGT), also known as lateral gene transfer, refers to the movement of genetic information across mating barriers, namely between more or less distantly related organisms, and thus differs from the standard vertical transmission of genes from parent to offspring. Microbial genes were transferred into animals and plants hundreds of times, according to recent analyses. For example, the gene coding the protein syncytin enables retroviruses to fuse host cells, making it easier from the viruses to spread from one cell to another. Now a version of that protein is required for the placental syncytiotum to develop as an essential barrier to prevent maternal antigens and antibodies entering the fetal
bloodstream. This example of HGT, in which a viral gene transferred and then was integrated into the genome of its mammalian host, probably played a primary role in the major evolutionary leap that led to placental mammals.

New species can arise not only by changes in host genomes but also by changes in their microbiota, according to Robert Brucker and Seth Bordenstein at Vanderbilt University. When they cross-bred recently diverged wasp species, the hybrids died during the larval stage but could be rescued by antibiotics. "In this animal complex, the gut microbiome and host genome represent a co-adapted hologenome that breaks down during hybridization, promoting hybrid lethality and assisting speciation," the researchers concluded.

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Suggested Readings


