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Medicines from the Deep Sea: Exploration of the Gulf of Mexico

Cell Mates

Focus
Bacterial endosymbionts and organelles of eukaryotic cells

Grade Level
9–12 (Life Science)

Focus Question
What relationships may exists between endosymbiotic bacteria and common organelles of eukaryotic cells?

Learning Objectives
Students will be able to compare and contrast prokaryotic and eukaryotic cells.

Students will be able to explain the endosymbiont theory for the origin of eukaryotic cell organelles.

Students will be able to explain evidence that suggests an endosymbiotic origin for at least two common eukaryotic cell organelles.

Materials
❒ Marker board, blackboard, or overhead projector with transparencies for group discussions

Audio/Visual Materials
None

Teaching Time
One 45-minute class period, plus time for student research

Seating Arrangement
Groups of 2-3 students

Maximum Number of Students
30

Key Words
Prokaryote
Eukaryote
Endosymbiont
Mitochondria
Plastid
Undulipodium
Microtubule

Background
Despite the many advances of modern medicine, disease is still the leading cause of death in the United States. Cardiovascular disease and cancer together account for more than 1.5 million deaths annually (40% and 25% of all deaths, respectively). In addition, one in six Americans have some form of arthritis, and hospitalized patients are increasingly threatened by infections that are resistant to conventional antibiotics. The cost of these diseases is staggering: $285 billion per year for cardiovascular disease; $107 billion per year for cancer; $65 billion per year for arthritis. Death rates, costs of treatment and lost productivity, and emergence of drug-resistant diseases all point to the need for new and more effective treatments.

Most drugs in use today come from nature. Aspirin, for example, was first isolated from the willow tree. Morphine is extracted from the opium poppy.

Penicillin was discovered from common bread mold. To date, almost all of the drugs derived from natural sources come from terrestrial organisms. But recently, systematic searches for new drugs have shown that marine invertebrates produce more antibiotic, anti-cancer, and anti-inflammatory substances than any group of terrestrial organisms. Particularly promising invertebrate groups include sponges, tunicates, ascidians, bryozoans, octocorals, and some molluscs, annelids, and echinoderms.

The list of drugs derived from marine invertebrates includes:

Ecteinascidin – Extracted from tunicates; being tested in humans for treatment of breast and ovarian cancers and other solid tumors

Topsentin – Extracted from the sponges *Topsentia genitrix*, *Hexadella* sp., and *Spongosorites* sp.; anti-inflammatory agent

Lasonolide – Extracted from the sponge *Forcepia* sp.; anti-tumor agent

Discodermalide – Extracted from deep-sea sponges belonging to the genus *Discodermia*; anti-tumor agent

Bryostatin – Extracted from the bryozoan *Bugula neritina*; potential treatment for leukemia and melanoma

Pseudopterosins – Extracted from the octocoral (sea whip) *Pseudopterogorgia elisabethae*; anti-inflammatory and analgesic agents that reduce swelling and skin irritation and accelerate wound healing

ω-conotoxin MVIIA – Extracted from the cone snail, *Conus magnus*; potent pain-killer

This list reflects an interesting fact about invertebrates that produce pharmacologically-active substances: most species are sessile; they are immobile and live all or most of their lives attached to some sort of surface. Several reasons have been suggested to explain why these particular animals produce potent chemicals. One possibility is that they use these chemicals to repel predators, since they are sessile, and thus basically "sitting ducks." Since many of these species are filter feeders, and consequently are exposed to all sorts of parasites and pathogens in the water, they may use powerful chemicals to repel parasites or as antibiotics against disease-causing organisms. Competition for space may explain why some of these invertebrates produce anti-cancer agents: if two species are competing for the same piece of bottom space, it would be helpful to produce a substance that would attack rapidly dividing cells of the competing organism. Since cancer cells often divide more rapidly than normal cells, the same substance might have anti-cancer properties.

The goal of the 2003 Medicines from the Deep Sea Expedition is to discover new resources with pharmaceutical potential in the Gulf of Mexico. To achieve this goal, the expedition will:

- collect selected benthic invertebrates from deep-water bottom communities in the Gulf of Mexico (sponges, octocorals, molluscs, annelids, echinoderms, tunicates), identify these organisms, and obtain samples of DNA and RNA from the collected organisms;
- isolate and culture microorganisms that live in association with deep-sea marine invertebrates;
- prepare extracts of benthic invertebrates and associated microorganisms, and test these extracts to identify those that may be useful in treatment of cancer, cardiovascular disease, infections, inflammation, and disorders of the central nervous system;
- isolate chemicals from extracts that show pharmacological potential and determine the structure of these chemicals;
- further study the pharmacological properties of active compounds; and
- develop methods for the sustainable use of biomedically-important marine resources.

The last objective is particularly important, since many potentially useful drugs are present in very small quantities in the animals that produce these drugs. This makes it impossible to obtain useful amounts of the drugs simply by harvesting large numbers of animals from the sea. Some alternatives are chemical synthesis of specific compounds, aquaculture to produce large numbers of productive species, or culture of the cells that produce the drugs. Some techniques for producing specific drugs are based on the cells' own machinery for chemical synthesis: enzymes, guided by information contained in the cells' DNA and RNA.

Notice that in addition to selected benthic invertebrates, scientists on the Medicines from the Deep Sea Expedition are equally interested in associated microorganisms as possible sources of useful pharmaceuticals. Many biology students tend to overlook microbial associations in natural communities, but there is mounting evidence that such associations are the basis for most if not all eukaryotic organisms. This activity is intended to highlight these associations, and their possible relationships to common organelles of eukaryotic cells.

Learning Procedure

1. Review the importance of finding new drugs for the treatment of cardiovascular disease, cancer, inflammatory diseases, and infections. Describe the potential of marine communities as sources for these drugs, and introduce the objectives of the 2003 Medicines from the Deep Sea Expedition. Highlight the fact that explorers are focussing on microorganisms as well as the larger benthic invertebrates with which the microorganisms are associated.

2. Briefly review and contrast major characteristics of prokaryotic and eukaryotic organisms:
   - DNA in eukaryotic cells is contained in a membrane-bounded nucleus; DNA of prokaryotic cells is not membrane-bounded and the cells do not have nuclei.
   - Prokaryotes have no tissues or organs; some eukaryotes have extensive tissue and organ development.
   - Prokaryotes exhibit many different forms of metabolism (e.g., anaerobic, facultative aerobic and anaerobic, aerobic); eukaryotes are almost entirely aerobic.
   - Prokaryotes do not have organelles such as mitochondria or chloroplasts; eukaryotes have a variety of organelles, some of which are separated from the cytoplasm by membranes.
   - Most prokaryotes are small cells (1–10 μm), and all are microbes; most eukaryotes are composed of large cells (10–100μm), and many are large multicellular organisms.

3. Briefly review major events in the early history of life on Earth:
   - 4.6 billion years ago – Earth and solar system formed
   - 3.8 billion years ago – First prokaryotes appear
   - 2.2 billion years ago – Photosynthetic prokaryotes produce oxygen
   - 1.4 billion years ago – First eukaryotes appear
   - 700 million years ago – Multicellular plants and animals appear

   Point out that prokaryotes were around for about 2.4 billion years before the first eukaryotes appeared; almost twice as long as the subsequent 1.4 billion years during which the rest of all known living organisms emerged. No intermediate forms between prokaryotes and eukaryotes have been discovered. How did prokaryotes suddenly produce much more complicated eukaryotic organisms? And if the prokaryotes didn't do the producing, what did?

   Tell students that there is increasing evidence that eukaryotic organisms were (and are) the result of symbiotic associations between prokaryotic organisms. At some point in these associations, one (or more) species (called endosymbionts) entered the cells of another species, and performed useful functions. Each species had its own

DNA, and when these organisms reproduced, both were replicated. Eventually, the individual identities of the species disappeared, resulting in a new type of organism. This sort of transformation has actually been seen in the laboratory, and is described in Margulis and Sagan (1986).

Briefly discuss the significance of oxygen-producing prokaryotes. These organisms dramatically changed the environment on Earth. For 1.6 billion years, prokaryotes had been living under essentially anaerobic conditions. Increased oxygen in the atmosphere probably constituted major stress for many organisms, and almost certainly led to significant extinctions. At the same time, these changed conditions created opportunities that may have had a lot to do with the appearance of eukaryotes.

4. Tell students that their assignment is to prepare a written report in which they identify one or more prokaryotes that might resemble precursors of common eukaryotic cell organelles. Reports should include a discussion of any evidence that supports or refutes the theory that these organelles were once separate organisms.

   Assign each student or student group one or more of the following organelles:
   - mitochondria
   - plastids
   - undulipodia and microtubules
   - nucleus

   You may want to provide names of the following prokaryotes as hints:
   - *Bdellovibrio*
   - *Daptobacter*
   - *Thermoplasma*
   - *Cyanobacteria*
   - *Spirochetae*
   - *Eocytes*

5. Have students or student groups present their reports. The following points should emerge in discussing their results:

Mitochondria are responsible for aerobic respiration, and are found in nearly every eukaryotic cell. As a result, all eukaryotes have very similar metabolisms. Prokaryotes include a much more diverse array of metabolic strategies, suggesting that mitochondria may once have been prokaryotes that used aerobic respiration. Mitochondria have their own DNA, mRNA, tRNA, and ribosomes enclosed in mitochondrial membranes. Like bacterial DNA, mitochondrial DNA is not bound in chromosomes. Ribosomes of mitochondria are sensitive to the same antibiotics as those of aerobic bacteria. Endosymbiont theory suggests that predatory aerobic bacteria resembling modern *Bdellovibrio* or *Daptobacter* may have invaded a larger species, perhaps one living in a marginal environment similar to the modern *Thermoplasma* which lives in very hot and acidic waters. The larger bacterium would have provided protection to the smaller invader, which in turn could have helped cope with increasing oxygen in the atmosphere. This theory is boosted by the fact that the DNA of *Thermoplasma* has a protein coating that resembles the histones of eukaryotes.

Plastids contain the chemical machinery necessary for photosynthesis, have their own DNA, mRNA, and ribosomes, and are separated from the rest of the cell by a surrounding membrane. Plastid DNA resembles that of bacteria in the lack of histone, and proteins produced by plastids are very similar to those produced by cyanobacteria, which may have been the endosymbionts that were the precursors of plastids.

Undulipodia are whip-like structures, also known as cilia or flagella, that are composed of nine pairs of microtubules arranged in a cylindrical pattern around another pair in the center. This pattern is found in numerous eukaryote microtubule structures. Microtubules also play a central role in mitosis, and are a major structural component of nerve tissues. Similarities in microtubule organization and chemistry lead evolutionary biologists to believe that these organelles had a common origin. Some endosymbiont theorists have suggested that prokaryotes resembling the highly motile spirochetes may have been the precursors of microtubules.

Several researchers have proposed that the nucleus originated when a swimming eubacterium invaded an archaebacterium similar to *Thermoplasma* that belonged to a group known as eocytes. Eocytes are thermophylic, mostly sulfur-metabolizing organisms that often grow at temperatures above 100°C. This theory suggests that the eubacterium was an obligate anaerobe that oxidized hydrogen sulfide to elemental sulfur. The swimming ability of the eubacterium allowed the symbiotic "consortium" to avoid oxygen and efficiently reach its sources of carbon.

Encourage students to question the endosymbiont theory. Discuss how new technology for DNA analysis and capabilities for studying the ultrastructure of cells contributed to development of this theory. What evidence would provide additional support or contradiction for the theory. How would scientists go about looking for this evidence?

The BRIDGE Connection

www.vims.edu/bridge/ – Click on "Ocean Science" in the navigation menu to the left, then "Chemistry" for resources on drugs from the sea. Click on "Ecology" then deep sea for resources on deep-sea communities. Click on "Human Activities" then "Technology" then "Biotechnology" for resources on biotechnology.

The "Me" Connection

Have students write a short essay describing a symbiotic relationship between two or more species from which they personally benefit.

Connections to Other Subjects

English/Language Arts; Earth Science

Evaluation

Written reports provide an opportunity for evaluation.

Extensions

Log on to http://oceanexplorer.noaa.gov to keep up to date with the latest discoveries of the 2003 Medicines from the Deep Sea Expedition.

Resources

http://oceanica.cofc.edu/activities.htm – Project Oceanica website, with a variety of resources on ocean exploration topics

Margulis, L. and D. Sagan. 1986. Microcosmos. University of California Press. Berkeley.

Margulis, L. and K. V. Schwartz. 1998. Five Kingdoms. W. H. Freeman. New York.

Sagan, D. and L. Margulis. 1988. Garden of Microbial Delights. Harcourt Brace Jovanovich, Publishers. New York.

http://genomics.ucla.edu/eocyte/orignucl.html – Website summarizing evidence for eocytes as the most recent ancestor of eukaryotes

Margulis, L., M. F. Dolan, and R. Guerrero. 2000. The chimeric eukaryote: Origin of the nucleus from the karyomastigont in amitochondriate protists. Proc. National Academy of Sciences 97:6954-6959. Available online at http://www.pnas.org/cgi/reprint/97/13/6954.pdf

National Science Education Standards

Content Standard A: Science as Inquiry

- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard C: Life Science

- The cell
- Molecular basis of heredity
- Biological evolution
- Interdependence of organisms

Content Standard D: Earth and Space Science
- Origin and evolution of the Earth system

Content Standard G: History and Nature of Science
- Nature of scientific knowledge
- Historical perspectives

For More Information

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