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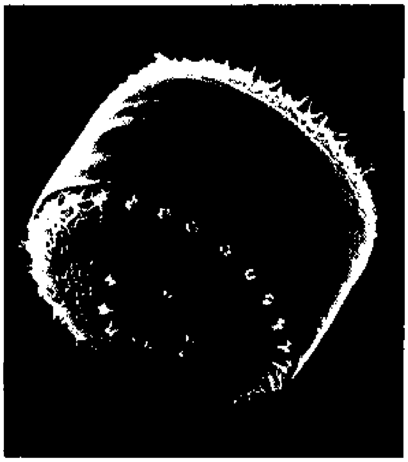
SEA GRANT: A CAPABILITY FOR BIO-TECHNOLOGY RESEARCH



This marine diatom, Thalassiosira weissflagii, *shown here 4,000 times actual size, is commonly used in cryopreservation experiments and has great potential for food chain experiments. It also has been successfully grown as food for the larval stages of organisms in mariculture operations.*

Further information

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Biotechnology, the use of biological systems for the production of goods and services, has expanded rapidly in recent years. The explosive growth of modern biotechnology has been fueled by fundamental breakthroughs in the fields of molecular genetics, cell physiology, biochemistry and biochemical engineering. With new and powerful tools such as genetic engineering, cell culture, plant regeneration, hybridization of organ and tissue cells, embryo storage and transfer and the controlled production of specific antibodies, scientists are beginning to harness the diverse and virtually unlimited capacity of natural systems to produce goods and services of benefit to man.

In agriculture and the chemical and pharmaceutical industries, biotechnology already is producing dramatic results. Improved plant species that can mean increased yields, disease resistance and more efficient harvesting are being developed and tested. The market for genetically-improved plant seeds may reach $8 million in 1985 and $7 billion by the turn of the century. The cancer-fighting drug Interferon, formerly valued at $10 billion per pound, is now produced using biotechnological processes so efficient and inexpensive that researchers can obtain free samples. The cost of cancer treatment with Interferon has correspondingly dropped from $1,000 a day to $30 a day.

Biotechnology using marine organisms and systems is in its infancy compared to its application to terrestrial plants and animals. Biotechnology requires fundamental knowledge about genetics, physiology, biochemistry and bioengineering; however, for marine organisms, this knowledge is largely undiscovered. Similarly, little attention has been given to developing and adapting the tools of biotechnology for the unique requirements of marine systems. Support for biotechnology research and development has focused primarily on terrestrial organisms. For example, in 1983 an estimated $55 million was directed to biotechnology research in agriculture via the state Agricultural Experiment Stations of the Land Grant colleges, and the U.S. Department of Agriculture's Agriculture Research Service. During roughly the same period, Sea Grant support for marine biotechnology research, federal and non-federal funds combined, was less than $8 million.

Much of the current research in marine biotechnology seeks a basic understanding of marine organisms and biological systems associated with persistent marine problems. Areas of research include the biological and biochemical processes of marine biofouling; the metabolic pathways which produce the chemical structure of marine toxins; the isolation, identification and physiology of human pathogens of marine origin; and the understanding of the structure and function of genes in marine plants and animals. Research is underway to identify pharmaceutical and chemical products that may be produced through biotechnology.

Another aspect of marine biotechnology research is the development of techniques for implanting in marine organisms genes which produce certain desirable characteristics. Finally, biotechnology is enhancing ongoing marine research. Applications include the following: Producing and using monoclonal antibodies to detect and diagnose fish diseases caused by marine microbes; developing vaccines for treatment of fish diseases; identifying and producing bacteria which can break down waste products in the marine environment; determining the origins and structure of fish populations; and increasing production of aquacultural systems.

The Challenges Facing Marine Biotechnology

The potential benefits of advances in marine biotechnology are immense. For example, the U.S. seafood industry currently is faced with an annual trade deficit of more than $3 billion and the production of large quantities of waste. Biotechnology can help change these unsatisfactory situations through improvements in fish production, fisheries management and commerical use of wastes. Also, biotechnologically-enhanced aquaculture can create new or alternative job opportunities and sources of food products for the commercial fishing industry.

The marine sector's contribution to the national economy can be dramatically improved as new products, including pharmaceuticals and specialized chemicals, are developed from marine organisms. The U.S. Office of Technology Assessment has estimated that before the year 2000 annual sales of chemicals and drugs produced through biotechnology will reach $15 billion. Marine biotechnology can make a significant contribution to realizing this prediction.

Biotechnology holds promise for solving the problems of disposal of industrial and domestic waste in the marine environment. Genetically engineering marine microbes so they can detoxify wastes or produce useful compounds from them is an avenue of particular promise.

Marine biotechnology offers the United States the opportunity for international leadership. Developed countries throughout the world are making major commitments to the development of biotechnology, but a concerted effort in marine biotechnology has not been mounted. Our nation's competitive advantage in biotechnology can be enhanced by seizing this opportunity.

Current Sea Grant Research Program

Sea Grant is a major source of support for academic research in marine biotechnology. For example, it is the primary national sponsor of research in marine pharmacology and aquaculture. Current Sea Grant research directed to biotechnological development addresses biochemistry, pharmacology, genetic engineering, biochemical engineering, microbiology and botany, in addition to aquaculture. This research program and some of its recent achievements are discussed here.

Researchers at the University of Maryland, Baltimore County, examine an autoradiogram showing the DNA sequence of a plant chromosome.

Biochemistry and Pharmacology

This research examines marine organisms to see if they contain substances that can be used to produce pharmaceuticals. The chemical structures of approximately 40 new compounds from marine organisms have been determined over the past two years.

Working together, researchers at the University of Hawaii and Cornell University have found that halenaquinone, a substance isolated from a sponge, is an antibiotic, and represents a new chemical structural system. At the University of California, three new compounds were isolated and shown to inhibit tissue inflammation at medically significant levels. Two of the compounds also are analgesic and one inhibits sperm motility and cell division. Inhibition of cell division is indicative of ability to stop growth of tumors. Also, scientists at the University of Oklahoma isolated two potential anticancer drugs of high specific activity from sponges. Both drugs are being tested further at the National Cancer Institute.

Scientists at the Massachusetts Institute of Technology (MIT) isolated another substance, not completely characterized, from shark cartilage. It was shown to strongly inhibit the growth of new blood vessels in artifically introduced solid tumors in rabbits, thereby restricting tumor growth. The substance is expected to be applicable in other kinds of antitumor studies. Pharmaceutical firms are expected to secure rights to these discoveries for further investigation and possible commercial development. Several major firms already are contributing funds to several academic projects and providing their services in biological evaluation of new substances.

Researchers at the Universities of Washington and California (Berkeley) and the California Department of Fish and Game are working together to further perfect the ability to predict migratory readiness of salmon by determining the biochemical processes involved with migratory behavior growth. The studies so far indicate that subtle environmental changes may be the key to priming of the thyroid gland that controls physiological changes required for succesful downstream migration and entry to and growth in the ocean.

The U.S. researchers are working collaboratively with researchers in France and Japan. The results of these basic studies, which were the highlight of an international meeting on salmon reproduction held in Seattle in October 1983, are expected to provide the basis for much better management of salmon and greatly increased efficiency in hatcheries.

Genetic Engineering

Genetic engineering is the manipulation of the genetic makeup of organisms. It can be used, among other things, to produce a useful reagent, to control diseases of marine organisms, and to enhance the growth and hardiness of aquacultured species. For example, researchers at the University of Hawaii are developing monoclonal antibodies to ciguatoxin through cell-fusion techniques. Ciguatoxin is the natural substance, transmitted through the food chain to tropical finfish, which causes the disease *ciguatera,* a neural disorder, in humans. It is a significant problem in Hawaii, Puerto Rico, Florida and many other locations where tropical fish species are eaten. If antibodies to ciguatoxin could be produced, they would hasten development of a rapid test of fish with commercial potential, and would allow greater development of fisheries.

Researchers at the University of California, Santa Barbara, have shown that application of insulin and growth hormone accelerates growth in abalone by improving metabolism. On the basis of these findings, they are working to establish recombinant DNA gene banks from molluscan species. These gene banks will be used to identify, select and increase production of genes that produce desirable characteristics, such as disease resistance. This would allow production of strains of abalone with enhanced growth rates, disease resistance, and the ability to synthesize protein and glycogen. The techniques developed would be applicable to other species as well and would significantly advance the science of marine animal husbandry.

Scientists at Johns Hopkins University are learning to manipulate genes and proteins of striped bass which control their resistance to heavy metal pollutants. This research is expected to produce methods useful in genetically improving finfish of all types.

Infectious diseases cause enormous losses of salmonid species in hatcheries and other aquacultural facilities. Researchers with the Oregon, Washington and Maine/New Hampshire Sea Grant College Programs are applying recombinant DNA technology to produce vaccines and diagnostic agents. Their approach is based on determining the fundamental chemical and physiological ways that bacteria and viruses invade and infect the host fish.

Biochemical Engineering

This field of study involves the production of materials or development of processes potentially useful in industry. Researchers at MIT are developing applications for the polymer chitosan, which is derived from the shells of edible crustaceans. In some places, especially Virginia, Alaska and Texas, shells left after processing constitute an enormous waste management problem. Chitosan appears to have good potential for bioproduction or fermentation processes, and research at MIT will provide more information about chitosan's properties.

Research is underway at Cornell University to develop the technology to extract and recover oils and enzymes from fish and other marine organisms. Several fish oils have specific nutritional and potential therapeutic properties, and a number of enzymes from fish are of commercial interest. Traditional methods of extraction and recovery of materials of this type involve application of heat, which denatures protein and destroys enzymic activity. Use of gases, such as carbon dioxide, at certain temperatures and pressures produces fluids that are highly effective solvents. The solvents can be removed through chemically gentle reconversion to the gaseous phase without heating. Use of this technology to isolate biochemicals should present opportunities for expansion of marine commerce by creating new uses of fishery resources.

Microbiology and Botany

Researchers are pursuing specific problems and opportunities, including developing food crops from marine plants, controlling marine fouling and paralytic shellfish poisoning, using chitosan as an agricultural fungicide, and defining the effects of nitrogen metabolism on the chemical composition of macroalgae.

In research aimed at preventing biofouling, for example, investigators at Harvard University have developed a theoretical model of biofouling. The model indicates that the first step in attachment is a reaction between compounds produced by natural bacterial films in seawater and the larvae of biofouling organisms. Their studies so far suggest there may be ways of disrupting this early attachment process.

At the University of South Alabama, Sea Grant scientists have focused their attention on prevention of mineral scaling and biomineral fouling of marine surfaces, costly problems for industry and the military. Sales of antiscalants alone, whose environmental consequences are not fully defined, total several hundreds of millions of dollars annually in the U.S. The research is based on the surprising observation made in 1981 that the organic matrix in oyster shell is a potent inhibitor, rather than an initiator, of growth of crystalline calcium carbonate ($CaCO_3$). The scientists have shown that synthetic substances modeled after the matrix, and matrices of other marine organisms, also inhibit calcium carbonate growth. These observations and studies raise the potential for developing methods to prevent calcium carbonate fouling using fundamental natural processes.

Other current research in this area includes applying modern techniques to improve salttolerant plants for human and animal food and other improvements in agriculture. Highly significant advancements have been made in this field recently at Washington State University. Plant pathologists there have determined that the marine polymer chitosan, derived from crustacean shellfish wastes, is effective in protecting pea seedlings and other crops against pathogenic fungi of the genus *Fusarium*. More importantly, their recent studies have shown that inexpensive treatment of wheat seeds with chitosan will increase yields up to a remarkable 20 percent.

Fields studies of this treatment method are continuing on 320 acres in eastern Washington and six acres in Oklahoma. The researchers will attempt to define the mechanism of chitosan's action. Apparently, chemical subunits of chitosan selectively activate genes which are an essential part of the plant's ability to resist disease. Once the way in which chitosan activates specific plant genes has been determined, it may be possible to expand the use of chitosan and its derivatives to other plant disease problems. Knowledge of the mechanisms by which synthetic compounds affect gene expression also has far-reaching implications in the development of new pharmaceuticals and the treatment of human diseases.

Research Needs and Opportunities

On-going Sea Grant-supported research is addressing novel opportunities and difficult problems whose exploitation or solution will improve the economic posture of the U.S. Its results may include such things as new industrial and agricultural materials; streamlining and simplification of fermentation processes using novel biochemical techniques; increased yields of carrageenan from genetically-improved algae; and use of shark cartilage extract for the treatment of cancers.

An increased level of research effort is essential if progress in marine biotechnology is to continue. Current funding is not sufficient to take advantage of the exciting opportunities which are arising. Examples include the production of marine biomass as raw material for generating energy and chemicals, and the development of novel industrial chemicals and processes from marine bacteria which live in hydrothermal vents in the seafloor and can metabolize hydrogen sulfide, a toxic industrial product.

In marine biotechnology, as in other fields of biotechnology, basic research is particularly needed to determine the structure, function and expression of the genes of plants, animals and microbes. Opportunities for significant commercial application through expanded marine biotechnology are possible in fields including the following:

- Fisheries Enhancement, Management and Protection
- Industrial Materials and Specialty Compounds
- Pharmaceuticals and Enzymes
- Management of Wastes in the Marine Environment
- Environmental Health
- Methods Development and Improvement
- Aquaculture of Plants and Animals

Congress established the National Sea Grant Program in 1966 to accelerate the development, use and conservation of the Nation's marine resources. During its nearly 20 year history Sea Grant has forged an effective partnership with universities, marine industries and governments. The research skills of university scientists from all fields — oceanography, engineering, law, economics, sociology — are combined with a strong commitment to make research findings available to a wide audience through a network of advisory and education specialists. Technical, advisory and public information reports, conferences, workshops and personal contacts by Sea Grant marine agents and university researchers ensure that information needed to use and develop marine resources reaches those who need it.

This experience, coupled with the partnership nature of the program, gives Sea Grant a unique perspective on current and future national needs in marine resource development. This paper is one of a series, each describing an issue of national importance, Sea Grant's contribution to tackling that problem, and priorities for future research.