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Summary Report

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SYMPOSIUM ON BIOMEDICAL APPLICATIONS OF BASIC RESEARCH

NO0014-88-J-1196

On Monday, August 15, 1988, the symposium entitled Biomedical Applications of Basic Research at the Marine Biological Laboratory was held at the Marine Biological Laboratory, Woods Hole, MA.

The symposium directed at the lay public consisted of 7 scientific presentations, each followed by a discussion period. The purpose of the symposium was to demonstrate how observations by investigators at the Marine Biological Laboratory have led to an understanding of certain human diseases. Presentations were made by scientists from throughout the United States who have been summer investigators at the Marine Biological Laboratory(M.B.L.), and who were able to communicate scientific thought and practice to a large non-scientific audience. The symposium was an important part of the celebration of the 100th anniversary of the M.B.L.

The topics of each presentation and the speakers are listed on the first attachment to this report. Areas of science in which marine biology was shown to have made contributions to an increased understanding of the pathophysiology of human diseases included reproductive physiology, vision, inflammatory diseases, infectious diseases, blood coagulation, and nutrition. Examples of the value of marine biological research for current major biomedical problems in the United States were provided by presentations that dealt with Lyme Disease and AIDS. A test for bacterial endotoxin, developed at the M.B.L., is now used throughout the United States for the detection of this potentially dangerous bacterial product in intravenous solutions and medicines.

Approximately 350 persons attended the symposium. Considerable publicity was achieved for this symposium. Both a press release and an article in the Falmouth Enterprise(the local Cape Cod newspaper) indicated that this symposium was supported by the Office of Naval Research(see attachments). It was the unanimous consensus of those who attended the symposium that it had been highly successful in achieving its goal of demonstrating how basic research is applicable to the study and comprehension of a wide range of human diseases, and that marine biological research is ultimately relevant to the diagnosis and treatment of human illnesses.

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BIOMEDICAL APPLICATIONS OF BASIC RESEARCH AT THE MARINE BIOLOGICAL LABORATORY

*a series of presentations, designed for non-scientists, demonstrating how observations by investigators
at the MBL have been directly relevant to the understanding of human diseases*

Monday August 15, 1988
1:00 p.m. - 5:00 p.m.



Lillie Auditorium
Marine Biological Laboratory

- | | |
|------------------|---|
| 1:00 p.m. | Luigi Mastroianni, M.D.
University of Pennsylvania
<i>In Vitro Fertilization: From Sea Urchin to Human</i> |
| 1:30 p.m. | Robert Barlow, Ph.D.
Syracuse University
<i>Vision in Humans and Horseshoe Crabs</i> |
| 2:00 p.m. | Gerald Weissmann, M.D.
New York University
<i>Marine Sponge Cells Tell Us How Aspirin Works</i> |
| 2:30 p.m. | Andrew Spielman, S.D.
Harvard University
<i>Did Lyme Disease Originate on Naushon Island?</i> |
| 3:00 - 3:30 p.m. | Afternoon Break |
| 3:30 p.m. | Jack Levin, M.D.
University of California, San Francisco
<i>Detection of Bacterial Infections in Humans with
Horseshoe Crab Blood</i> |
| 4:00 p.m. | Hans Kornberg, Ph.D.
University of Cambridge, England
<i>Crossing the Berlin Wall of Bacteria</i> |
| 4:30 p.m. | Virginia Scofield, Ph. D.
University of California, Los Angeles
<i>Marine Invertebrate Immunity: The AIDS Connection</i> |

Wine and cheese reception to follow



MARINE BIOLOGICAL LABORATORY

WOODS HOLE • MASSACHUSETTS • 02543 • (508) 548-3703

PRESS INFORMATION

FOR IMMEDIATE RELEASE:
5 August 1988

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SYMPOSIUM ON BIOMEDICAL APPLICATIONS OF RESEARCH TO HIGHLIGHT MBL COMMUNITY DAY

This year hundreds of thousands of Americans will be infected with bacteria that contain bacterial endotoxin, a substance that can cause shock and death. An estimated 75,000 of these people will die from these infections.

Yet a simple test discovered at the Marine Biological Laboratory in Woods Hole in the late 1960s — a test based on an extract from horseshoe crab blood — can prevent these deaths. Called the Limulus Test (after the scientific name for the horseshoe crab), the diagnostic procedure is being used more and more in hospitals and clinics throughout the country. The test quickly detects bacterial endotoxin in blood and other body fluids, allowing doctors to administer life-saving antibiotics before infection spreads through the body.

Research on the horseshoe crab and other marine animals with important contributions to make to medicine continues at the Marine Biological Laboratory (MBL) today. A review of this research in laypersons' terms is the program of a symposium titled "Biomedical Applications of Basic Research at the Marine Biological Laboratory," to be held in the Little Auditorium of the MBL from 1-5 p.m., Monday August 15, 1988. The symposium, which is free and open to the public, is the centerpiece of MBL Community Day, an afternoon of activities for members of the local community. MBL Community Day is one of many events planned for MBL Centennial Celebratory Week (August 12-19).

The symposium features a series of 20-minute presentations, designed for non-scientists, demonstrating how observations by investigators at the MBL have led to the understanding of certain human diseases. Each presentation will be followed by a 10-minute question-and-answer period. The program will close with a wine and cheese reception.

The talks will be given by scientists from throughout the United States and abroad who are or have been MBL summer investigators, and who are able communicators of science to the lay public. "The program reflects the national and international composition of the scientific community at the MBL during the summer," says symposium organizer Dr. Jack Levin, professor of laboratory medicine and professor of medicine at the University of California School of Medicine, San Francisco, and summer investigator at the MBL for 25 years.

Levin chose to organize a symposium for non-scientists because he wanted to build on the "relatively unique interaction" between the MBL and its local community. "I felt it was important, on the occasion of the 100th anniversary of the Laboratory, to bring to the attention of the public what we do here in terms they could understand, and to provide specific examples of how research at the MBL has directly led to knowledge that

(more)

MBL Symposium/ 2 of 2

contributes to the diagnosis and treatment of human diseases," Levin said.

The symposium opens at 1 p.m. with a presentation by Dr. Luigi Mastroianni of the University of Pennsylvania titled "In Vitro Fertilization: From Sea Urchin to Human." Dr. Mastroianni will discuss studies of reproduction in sea urchins that have led to improvements in reproductive technology for humans, such as test tube fertilization.

At 1:30 p.m. Dr. Robert Barlow of Syracuse University will discuss how studies of vision in horseshoe crabs are helping scientists to understand how the human eye works. His presentation is titled "Vision in Humans and Horseshoe Crabs."

Following Dr. Barlow at 2 p.m., Dr. Gerald Weissmann of New York University will deliver a presentation titled "Marine Sponge Cells Tell Us How Aspirin Works."

At 2:30 p.m. Dr. Andrew Spielman of Harvard University will focus on Lyme Disease, a disease carried by ticks, in a presentation titled "Did Lyme Disease Originate on Naushon Island?"

Following a half-hour break, Dr. Levin will re-open the symposium at 3:30 p.m. with a discussion of the Limulus Test titled "Detection of Bacterial Infection in Humans with Horseshoe Crab Blood."

Levin will be followed at 4 p.m. by Dr. Hans Kornberg of the University of Cambridge in England, whose presentation is titled "Crossing the Berlin Wall of Bacteria." Kornberg will explain how bacteria take up food material — a process that may illuminate how human livers and brains obtain nutrition.

The last presentation, scheduled for 4:30 p.m., will be given by Dr. Virginia Scofield of the University of California at Los Angeles. Focusing on the timely topic of AIDS, Scofield will discuss how immune reactions in marine invertebrates teach us about the human response to the AIDS virus, in a presentation titled "Marine Invertebrate Immunity: The AIDS Connection."

Funding for "Biomedical Applications of Basic Research at the Marine Biological Laboratory" has been provided by the Office of Naval Research.

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The February evening in 1975 after MV Islander hit the MBL's pump-house dock, MBL staff members worked long hours to repair the damage. Confering with diver Daniel H.

Gould are Alan G. Lunn, left, marine contractor Stephen Clark and Stephen A. Mills. (Photo by F.P. Bowles)

Basic Research And Health Is Topic Of Symposium

Hundreds of thousands of Americans become infected each year with bacteria containing an endotoxin that can cause shock and death. But a simple test discovered at Marine Biological Laboratory in the late 1960's, based on an extract from horseshoe crab blood called limulus lysate, can detect the toxin in time to prevent the spread of infection.

As part of its centennial week, MBL is planning a symposium on biomedical applications of research for Monday, Aug. 15, in Lillie Auditorium. The symposium, a review of biomedical research in laymen's terms, is the centerpiece of a planned community day.

A series of 20-minute presentations with question periods to follow will show how observations by investigators at MBL have led to insights into human diseases. The symposium will begin at 1 P.M. in the auditorium on MBL Street, Woods Hole, followed by a wine and cheese reception at 5.

Organizer of the symposium is Dr. Jack Levin, professor of

medicine at the University of California School of Medicine in San Francisco and a summer investigator at MBL for 25 years. He has assembled a group of speakers who have conducted research at MBL over the years on topics with relevance to issues of human health.

The first speaker will be Dr. Luigi Mastroianni Jr. of the University of Pennsylvania. In his talk, titled "In Vitro Fertilization: From Sea Urchin to Human," Dr. Mastroianni will discuss studies of reproduction in sea urchins that have led to such developments as test tube fertilization.

At 1:30 P.M. Robert B. Barlow Jr. of Syracuse University will discuss the ways in which studies of vision in horseshoe crabs are helping scientists understand the way the human eye works. His talk is titled "Vision in Humans and Horseshoe Crabs."

Dr. Gerald Weissman of New York University will speak at 2 P.M. His talk is titled "Marine Sponge Cells Tell Us How Aspirin Works."

At 2:30 P.M. Andrew Spielman of Harvard University will discuss Lyme Disease, carried by ticks and widespread in parts of New England, in a presentation titled "Did Lyme Disease Originate on Naushon Island?"

Following a half-hour break, Dr. Levin will reopen the symposium at 3:30 with a talk titled "Detection of Bacterial Infection in Humans with Horseshoe Crab Blood."

At 4 P.M. Sir Hans Kornberg of the University of Cambridge in England will present a talk titled "Crossing the Berlin Wall of Bacteria." He will explain how bacteria take up food, a process that sheds light on the way human livers and brains obtain nutrition.

The last presentation, at 4:30, will be given by Virginia Lee Scofield of the University of California at Los Angeles. Dr. Scofield will discuss the lessons from immune reactions in marine invertebrates for understanding human response to the AIDS virus. Her talk is

community: The AIDS Connection."

Funding for "Biomedical Applications of Research at Marine Biological Laboratory" has been provided by the Office of Naval Research.



LINKING BASIC BIOLOGICAL RESEARCH TO HUMAN HEALTH PROBLEMS

by Margaret C. Bowles

What do the eyes of the horseshoe crab tell us about the way we see, or the configurations of colonies of sea squirts on underwater surfaces have to say about the response of human immune systems to alien substances? And how do observations of sea urchin gametes contribute to solving the reproductive problems of mankind?

For 100 years many researchers at Marine Biological Laboratory have chosen to study basic biological structures and processes as they occur in the marine organisms that inhabit Woods Hole waters, hoping to shed light on some of the mysteries of human health and disease.

"By looking at simple visual systems, we can obtain insights into complicated ones," longtime summer investigator Robert B. Barlow Jr. said Monday afternoon as he explained the lessons learned over the years from studying the response of horseshoe crab eyes to patterns and levels of light. "That is most of what we do at MBL."

Setting aside the high-context language of the day-to-day practice of basic research for an afternoon, Dr. Barlow and six of his fellow investigators explained to an audience of interested laymen how studies conducted at MBL have contributed to advances in the understanding and treatment of hu-

man health problems.

The occasion was a symposium titled "Biomedical Applications of Basic Research at Marine Biological Laboratory," organized by Dr. Jack Levin of the University of California Medical School in San Francisco as part of the MBL's centennial week activities. More than 300 persons attended the series of presentations in Lillie Auditorium, some coming to hear a single talk, others staying for the whole afternoon.

Questions And Answers

Lively question-and-answer periods followed each 20-minute presentation as audience members contributed observations or brought up issues of concern. Topics ranged from the transportation of nutrients across bacterial cell walls to the changing ecological conditions that contributed to the outbreak of the Lyme disease epidemic in New England over the last decade, from the role of horseshoe blood in detecting bacterial endotoxins to the part marine sponges play in the treatment of rheumatoid arthritis.

Dr. Luigi Mastroianni Jr. of the University of Pennsylvania's department of obstetrics and gynecology opened the symposium with a discussion of in vitro fertilization.

Studies of the eggs and sperm of sea urchins, available in large numbers and easy to observe, have helped clinicians understand and address prob-

lems of human reproduction, he said. Aided by the remarkable advances in recent decades in the techniques of light microscopy, researchers have been able to uncover the finest details of changes that occur in gametes during the process of fertilization.

A time-lapse video sequence filled the large screen behind the speaker with the purposeful movements of sperm and the early stages of a sea urchin embryo undergoing cell division. Armed with basic knowledge of the biochemical environment in which fertilization takes place, physicians are increasingly successful in inducing fertilization outside the human body and implanting fertilized eggs in women who have been unable to conceive naturally, Dr. Mastroianni explained.

Studying Vision

"Have you ever wondered how you see the world around you, far away and close and all in color... or how we see things that aren't there at all?" Dr. Barlow asked as he began the next presentation.

Holding up a large, encrusted specimen with vigorously waving appendages, he explained how the search for a simple visual system had led MBL investigator H. Keffer Hartline to the horseshoe crab. The discovery that adjacent photoreceptors in the horseshoe crab's eyes inhibit each other's response to light and thus enhance their capacity to distinguish borders and edges won Dr.

Hartline the Nobel Prize in 1967, Dr. Barlow noted.

Displaying slides with sequential bands of gray and spinning disk with black and white sections, Dr. Barlow demonstrated that human eyes perceive gradations of color that do not actually exist; perceptions that also serve to enhance boundaries and edges of objects.

Linking studies of the behavior of marine sponge cells with the effects of aspirin and other anti-inflammatory drugs on human beings, Dr. Gera Weissmann traced the history of discoveries that have helped physicians to alleviate the symptoms of inflammatory response, characteristic of painful and disabling diseases such as rheumatoid arthritis.

If one squeezes a sponge, he demonstrated, the primitive community of organisms comes apart into individual cells. But these cells, if left to themselves agglutinate and start to form new little sponge colonies.

Anti-inflammatory agents inhibit the aggregation of sponge cells as they do the clumping of human cells in inflamed joints, offering investigators a simple model for studying the way the work, he said.

Deer, Mice And Ticks

Shifting the focus from cellular to epidemiological research, the fourth speaker in the afternoon introduced the audience to his ideas about the origins and spread of Lyme disease, caused by a tick-borne p-

HEALTH AND DISEASE IS MORE IMPORTANT

parasite.

Andrew Spielman of Harvard University theorized that the decade-old epidemic of Lyme disease spread from Naushon Island near Woods Hole as the deer population of southern New England exploded. During various stages of its development, the deer tick, *Ixodes dammini*, feeds by preference on the blood of deer and mice but will resort to humans in a pinch, he explained.

Lyme disease, characterized by a rash and fever in its early stages and a variety of later complications if left untreated, occurs as an epidemic only where deer ticks flourish, and they are abundant only where deer are abundant, Dr. Spielman said.

The deer tick was found only on Naushon in the 1940's but

spread during the 1960's as the deer population grew, he continued. Tracing the early history of the disease, he showed how changes in land-use patterns affected the numbers and distribution of deer and thus the spread of the disease.

Just as the eyes of the horseshoe crab are of interest to those who study vision, so the creature's blue blood has proved invaluable to pathologists interested in detecting bacterial endotoxins harmful to human health. In the first talk after a short break in the symposium, Dr. Levin described the discovery 25 years ago in the laboratory of Frederik B. Bang at MBL that the horseshoe crab's blood contained a unique anti-bacterial defense mechanism.

Full Of Bacteria

The ocean is full of bacteria, Dr. Levin explained. Cells in the horseshoe crab's blood become active, form clots and trap bacteria they encounter. Studies by Dr. Bang and students of his, including Dr. Levin, led to the development of the *Limulus* amoebocyte lysate test for bacterial endotoxins.

This substance can be used to test food, drugs and medical supplies such as intravenous fluids and machinery such as kidney dialysis or heart-lung machines for the presence of endotoxins produced by bacteria, Dr. Levin said.

Bacteria formed the topic of the next talk, titled "Crossing

the Berlin Wall of Bacteria," by Sir Hans Kornberg of Christ College, Cambridge University.

Dr. Kornberg studies the mechanisms by which food particles pass through the cell membranes of bacteria. He likened the cell membrane to the Berlin Wall and the proteins that stick through it and permit passage of particles in and out to checkpoints. "Here is where your passport is checked, friend or foe," he said.

Understanding how bacteria take up food will help researchers understand how human brains or livers obtain nourishment, Dr. Kornberg pointed out. "If one is interested in transport, as I am, then it is best to look at an organism with vast numbers in which each is similar to the other," he said.

Making a case for the essential unity of life, he concluded, "A lion and a dandelion are very similar at the molecular level. The differences are only important if you meet them in the field."

Immune Reactions

Virginia Lee Scofield of the University of California at Los Angeles brought the symposium to a close with a talk on insights the study of immune reactions of marine invertebrates can offer for the treatment of human immune system diseases like AIDS.

Immune systems protect one's body against infections and tumors by distinguishing between one's own cells and those of others and rejecting

the alien ones, she began. Showing a slide of colonies of tunicates or sea squirts, she pointed out boundaries between clitters where cells of different animals had rejected each other rather than fusing.

Following experiments with tunicate sperm and blood cells, Dr. Scofield and her colleagues tried mixing human sperm with blood cells from a different person to see whether the cells would interact or reject each other. The sperm bound to a penetrated white blood cell, she noted.

The important point, she said, is that the AIDS virus is covered with a protein coat that mimics an important transplant molecule. If her findings are correct, she added, this pathway provides a fast and easy way for the virus to spread.

But also, if she is right, treatments that affect the spread of the disease. Studies she conducted years ago at MBL have led directly to experiments with important public health implications, she concluded.

The talks completed, audience and speakers all crowded Lillie lobby to cover the presentations and consume wine and cheese. Dr. Levin was pleased, both with the response and the efforts of his colleagues to describe their work in non-technical terms.

"I put the fear of God in them beforehand," he said with a chuckle.

The Enterprise

Falmouth, Massachusetts

Monday, Tuesday night,

De August 22, 23, 1988 -
Wed. hall.

Board of Appeals - Wednesday, 7:30 P.M., town hall.