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Boston University
School of Medicine hosts U.S. Senate field hearing on women's health initiatives

Sen. Edward M. Kennedy chaired a U.S. Senate Labor and Human Resources Committee field hearing on women's health research at the School of Medicine on Jan. 11, acknowledging at the outset that there is a dire need to boost federal funding for women's health research.

Speaking to some 350 to 400 members of the Medical Center community in the Heiber Lounge, National Institutes of Health Director Bernadine Healy, M.D., provided an overview of the NIH's mission to bolster the lagging research in the area of women's health. Her remarks were followed by the testimony of five other prominent female scientists, including two members of the School of Public Health faculty, Hortensia Amaro, Ph.D., an associate professor of social and behavioral sciences, and Lynn Rosenberg, Sc.D., a professor of epidemiology.

“Our knowledge of common disorders is based almost entirely on studies that have used men as the standard to determine research priorities and to evaluate the efficacy of treatments,” said Healy. “As a result, judgments regarding prevention, interventions and treatment therapies for women have sometimes been inappropriate or lacking.”

This is particularly true of minority and low-income women, Rosenberg said. “There is a great need for studies among black women and other minority groups.” Most of the knowledge about the causation and prevention of disease in women has come from studies of white, middle-class women whose lifestyles and health risks may be different from those of minority or poor women. The lack of knowledge about these populations may make treatment and other forms of intervention less effective, she said.

Amaro said that while she applauded the Women's Health Initiative, a 14-year, $625-million clinical study launched by the NIH, it would yield little valuable data on the health problems of minority women, because it grouped women from very different ethnic minorities into one "non-white" category. Even if the data for each minority were reported separately, she said, "the sample size for each group will be too small to provide much-needed information about the health problems of women in Asian, black, Hispanic and Native American communities."

Gene therapy shows promise for treating sickle cell anemia, betal thalassemia

Researchers at School of Medicine and Children's Hospital in Oakland, Calif., have found a way to turn on a fetal gene in patients with two of the most common inherited blood disorders—sickle cell anemia and beta thalassemia—resulting in a promising treatment for these two devastating diseases.

The study, published in the Jan. 14 issue of The New England Journal of Medicine, shows that a compound called arginine butyrate safely and effectively stimulates the production of fetal globin, which, in the developing fetus, substitutes for beta globin, a component of hemoglobin that is defective in patients with these diseases. The trial was a Phase I/II investigation, which was designed to test the safety and, to some extent, the efficacy of the drug. Douglas V. Faller, Ph.D., M.D., director of the Cancer Center, was a key investigator in the study.

While the Food and Drug Administration requires that the drug be tested in larger groups of people before it can be licensed for use, its effect on the six patients studied was so profound that two requested and received "compassionate approval" to continue treatment after the trial ended. One of these patients, who received treatment for the longest duration, had a "complete reversal" of her disease, said Faller. "Looking at her blood, you would not know that she had thalassemia."

In sickle cell anemia, the defective beta globin—which, along with alpha globin, makes up hemoglobin, the oxygen-carrying protein in red blood cells—causes red blood cells to sickle, or form crescent shapes. In beta thalassemia patients, the beta globin gene is either missing or the protein is not produced in sufficient quantities. This results in an overproduction of alpha globin, which is toxic to red blood cells.
Arginine butyrate, which in this study was studied and shown to be safe in people ranging in age from three to 27 years, works by stimulating the production of fetal globin, which in turn suppresses the synthesis of beta globin in patients with sickle cell disease and prevents the sickling of the red blood cells. In beta thalassemia patients, the fetal globin substitutes for the missing beta globin.

Clinical studies in Saudi Arabia in the 1970s found that certain populations of people had the sickle cell mutation, but showed no signs of the disease. An analysis of their blood revealed that, in addition to the defective beta globin, they were also synthesizing fetal globin, a finding that suggested that the continued expression of fetal globin after birth could lessen the effects of sickle cell disease.

These findings led Faller and Oakland pediatric hematologist Susan Perrine, M.D., the principal investigator of this project, to seek populations of infants in which the normal fetal globin switch was inhibited. In 1985, they found that infants of diabetic mothers did not begin the switch in utero. Once the infant was delivered, the switch occurred rapidly, a finding that suggested that an environmental factor present during gestation was somehow preventing the switch. After analyzing several possible factors, Perrine and Faller found that butyrate, a fatty acid in the plasma of the mother, was inhibiting the globin switch. It was this discovery that eventually led to the development of the arginine butyrate infusion.

"This drug acts by activating a dormant fetal gene in the adult, and may be the first example of a new type of therapy for genetic disease, in which drugs are designed to regulate gene expression," noted Faller. He said that a Phase II trial of the arginine butyrate infusion already has begun in California and elsewhere and that a Phase I trial of an oral version of the drug would begin here shortly. The Phase I trial of the oral version already has begun at several other sites in the United States and Canada.

Until now, the only definitive treatment for both diseases has been a bone marrow transplant, a very expensive procedure—it can cost between $250,000 and $1 million—for which fewer than one in four patients is physically eligible. Although it has been used in cancer patients for years, transplantation is still experimental for sickle cell and thalassemia patients. Because it is so risky, transplantation is used only in adults who are suffering acutely from the effects of their disease.

Research shows oncogenic potential for Hox gene 7.1

In one of the first investigations to examine the role of a particular Hox—or homeobox-containing—gene at the cellular level, three School of Medicine researchers have found that forced expression of Hox gene 7.1 in muscle cells delays or prevents entirely their ability to differentiate, or become specialized cells with specific roles, thereby promoting the proliferation of these cells. These findings, published in the Dec. 3 issue of Nature, suggest that Hox 7.1 has oncogenic potential.

Hox genes were first cloned in Drosophila, or fruit flies, in the late 1970s and were linked to changes in pattern formation. Since then, research has established the existence of related genes in vertebrates. However, how Hox genes act at the cellular level remains unclear. While earlier studies have shown that Hox 7.1 is associated with cell proliferation, this is perhaps the first time that the gene has been introduced into cells that normally differentiate. Under the direction of principal investigator David Sassoon, Ph.D., an assistant research professor of biochemistry, this report affirms Hox 7.1's role in regulating cell growth.

This in vitro investigation also confirmed that the transfected cells were capable of anchorage-independent cell growth, one characteristic of tumor cells that distinguishes them from other cell types. Unlike normal cells, tumor cells do not need to anchor themselves to anything to grow, allowing them to migrate freely in the body. Moreover, when the transfecnt cell showing the highest rate of growth in soft agar was injected into nude mice, it produced tumors at all injection sites within two-and-a-half months.

"Hox 7.1 was behaving like an oncogene," said Sassoon. He noted that while several recent studies found that two other Hox genes, Hox 2.4 and Hox 1.1 also were associated with tumor formation, not all Hox genes were oncogenic. The effects of Hox 7.1 on cell differentiation were specific: The study found that a closely related Hox gene, Hox 8.1, failed to have a similar effect. Hox genes are believed to control the way in which body patterns are formed, by producing a protein that binds to DNA, thereby turning other genes on and off in a precise sequence. Scientists believe Hox genes play a significant role in determining the fate of a cell by controlling what type of cell it eventually will become and where it will be positioned in the body, a process that allows an individual to develop from an embryo to adult.
School of Medicine to participate in Generalist Physician Initiative

The School of Medicine was among 18 medical schools recently awarded grants from the Robert Wood Johnson Foundation to participate in the Generalist Physician Initiative, an effort designed by the foundation to counter a national shortage of general physicians by devising ways to encourage medical students to enter generalist careers in medicine.

Working with its affiliated hospitals, community health centers, agencies and community leaders, the School hopes to provide incentives for 50 percent of its graduates to choose careers in family medicine, pediatrics or general internal medicine by the year 2000. It plans to develop a program to help pay the medical education costs of future generalist physicians, who often make less money than medical specialists.

The Robert Wood Johnson Foundation is the nation’s largest philanthropic organization dedicated to improving the health and health care of Americans.

School of Public Health holds third annual ‘right-to-die’ conference

The School of Public Health held its third annual conference on the “right to die” on Dec. 9 in the Keefer Auditorium. The conference addressed such issues as the right to refuse treatment, physician-assisted suicide, religion and health-care proxies, and other issues involving a patient’s right to die.

During the conference, George J. Annas, J.D., M.P.H., co-director of the School’s Law, Medicine and Ethics Program, and Charles H. Baron, LL.B., Ph.D., of Boston College Law School, debated the issue of physician-assisted suicide. Rabbi Joseph Polak of the B’nai B’rith Hillel Foundation and the Rev. Russell E. Smith of the Pope John Center addressed the topic of religion and health-care proxies.

ACS research grants available through the Cancer Center

The Cancer Center at Boston University Medical Center has been awarded an institutional grant from the National Chapter of the American Cancer Society to encourage young investigators (junior faculty) to carry out cancer-related research.

The primary purpose of the grant is to provide “seed” money to allow the initiation of promising new projects or novel ideas that will serve as the basis for future grant applications from other programs. The awards will vary according to the needs of the investigator and should not exceed $12,000. The majority of allocations will be made to persons who have not received prior grant support.

Applications will be awarded on a competitive basis and evaluated according to criteria described in the application forms. Application forms are available from the Cancer Center office, E-124, x4173 (638-4173).

The deadline for applications is April 1, 1993.

Alpert appointed to Governing Council of Institute of Medicine

Joel J. Alpert, M.D., chairman of the Department of Pediatrics, recently was elected to a three-year term on the governing council of the Institute of Medicine, a component of the National Academy of Sciences. As one of 21 members of the governing council, Alpert will be helping to guide the activities of the Institute of Medicine.

Freddo presents Fry Award Lecture

Thomas F. Freddo, O.D., Ph.D., an associate professor of ophthalmology, pathology and anatomy and director of the Eye Pathology Laboratory, presented the 1992 Glenn A. Fry Award Lecture at the American Academy of Ophthalmology meeting held in Orlando in December. The title of Freddo’s presentation was “Aqueous Humor Proteins: A Key for Unlocking Glaucoma?” Freddo was selected to present the lecture by the academy for his achievements in eye/vision research.
Upcoming CME courses

The following is a list of upcoming courses sponsored by the Department of Continuing Medical Education:

Recent Advances in Diagnosis and Management of Infectious Diseases in Children will be held on March 20 at the Marriott Long Wharf Hotel in Boston.

Controversies in Medicine will be held from March 22 through March 26 at the Silvertree Hotel in Smowmass Village, Colo.

Cardiology for the Non-Cardiologist: An Approach for the 1990s will take place at the Royal Sonesta Hotel in Cambridge from April 15 through April 16.

On April 23, The Thyroid: 1993 Update for the Non-Endocrinologist will be held at the Ritz Carlton Hotel in Boston.

Minimal Access Gastrointestinal Surgery will be held from April 15 through April 16 at Boston University Medical Center.

From April 22 through April 24, Athletic Foot Injuries will be held at the Sonesta Beach Hotel in Hamilton, Bermuda.

Current Clinical Pediatrics will be held from April 26 through April 30 at the Hilton Resort in Hilton Head, S.C.

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