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Boston University
School of Medicine

News & Notes

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Researchers identify enzyme that may play role in Alzheimer's disease

In a study presented at the seventh International Symposium on Amyloidosis, School of Medicine researchers have identified an enzyme that may play a role in the formation of senile plaques in the brain of patients with Alzheimer's disease. These plaques are formed when a large protein, the amyloid precursor protein (APP), is broken down into a smaller protein, the amyloid beta protein.

The mechanism responsible for the breakdown of APP is virtually unknown, but, in this *in vitro* study, a protease from a brain with Alzheimer's disease was shown to break down a key bond between two amino acids, methionine and aspartic acid, in the amyloid precursor protein.

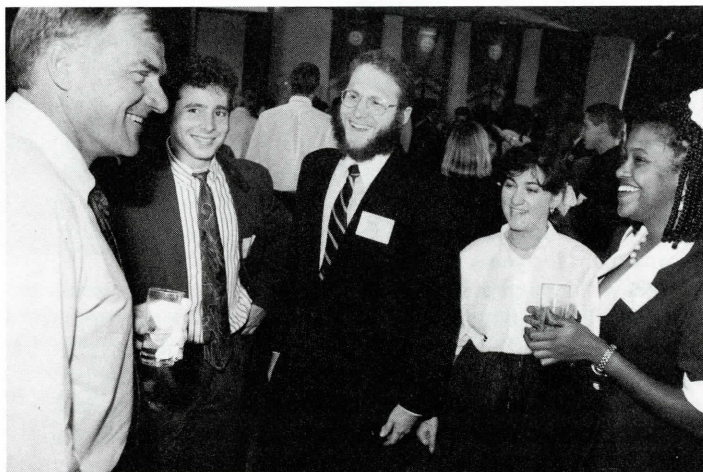
According to Carmela Abraham, PhD, an associate professor of medicine and biochemistry, and Gregory Papastoitsis, PhD, a postdoctoral fellow, these findings suggest that this protease may be initiating the first step in the degradation of APP, but that *in vivo* studies are needed to determine whether it actually plays a role in Alzheimer's disease.

The researchers have found that the protease did not degrade other common proteins, which suggests that it is specific to the amyloid precursor protein. The scientists are developing antibodies against this protease that will allow them to determine how it is distributed in the body. The group is also developing ways to block the production of the protease to prove whether it is, as they suspect, actually involved in Alzheimer's disease.

Lack of activity, television, tied to high body fat in preschoolers

Two School of Medicine investigations, both using data from the Boston University Framingham Children's Study, have identified separate predictors of body fat in early childhood.

In the first study, researchers have found that low levels of activity during the preschool years may predict an increase in body fat in early childhood. In this investigation of 103 preschool-age children, led by Lynn L. Moore, DSc, an assistant professor of medicine, the researchers used electronic body motion sensors attached to the children's waists to measure their activity for two five-day periods each year. The children were studied for a mean time of two-and-a-half years. At annual clinic visits, the researchers used a skinfold test to measure the subcutaneous fat in the children's triceps. Triceps skinfolds are considered the best measure of body fat percentage in young children and these measurements are expected to decrease in the preschool years as children lose their baby fat. In this study, however, Moore found that children with a low level of activity showed an increase in body fat compared to children with higher levels of activity.



Incoming students were welcomed at a reception sponsored by the Alumni Association on Sept. 2. Pictured, Paul M. O'Bryan, PhD, left, an associate professor of physiology, talks with first-year students Ari Schwartz, Amiel Levin, Elaine Melamud and Andra Davis. (photo by David Herwaldt)

In the second study, led by Munro H. Proctor, MD, MPH, an associate clinical professor of medicine, researchers followed the television viewing habits of preschool children for four years. They found that the more hours of television a child watched, the greater the increase in body fat. The amount of television viewed may be an indirect measure of physical activity.

"We are concerned about activity levels in the preschool years not only because they relate to the risk of childhood obesity but because activity levels tend to be fairly stable over time," said Moore, who also contributed to the second study. She added that other studies have shown that if children are not active by late elementary school, they are very unlikely to ever be active as adults. Moore said that future studies will examine whether other factors in elementary school can influence activity levels.

Samet awarded one of 15 national RWJ Faculty Scholars grants

Jeffrey H. Samet, MD, MPH, an assistant professor of medicine, was one of 15 physicians across the country to receive four-year Generalist Physician Faculty Scholars grants from the Robert Wood Johnson Foundation, the nation's largest health care philanthropy.

The grant, part of a wide-ranging effort to counter a nationwide shortage of primary care physicians, is aimed at assisting the career development of generalist medical school faculty members. Grant recipients will conduct research related to gener-

alist medicine and serve as role models to medical students contemplating careers in general internal medicine, pediatrics or family medicine.

The grants are based in part on a recent study that showed that one of the most important factors influencing medical students' choice of medical paths is exposure to top-notch faculty members who are both researchers and clinicians. The perception of generalist medicine as a non-academic specialty may lead them to choose careers in other areas of medicine, some experts believe. It is the purpose of the grant to allow generalists to engage in research while maintaining their clinical expertise.

Samet plans to use the grant to study ways in which care-providers can tailor outreach efforts to certain HIV-infected populations, in order to get them to seek treatment earlier. Through his work in setting up a diagnostic evaluation unit at Boston City Hospital, Samet has found that many people with HIV do not seek treatment for years after acquiring the infection.

Samet will be exploring whether a person's decision to seek treatment is based primarily on the amount of emotional support available at home; whether the person is depressed; the severity of an alcohol or drug addiction, and the extent to which the person is comfortable with the medical system. In addition to seeking ways to target these people, Samet hopes to develop ways to improve patients' adherence to prescribed medical regimens.

Progress shown in development of biocompatible synthetic cornea

Two experiments to determine the biologic response to materials used in synthetic corneas have shed some light on a persistent problem: how to induce the body's own tissue to grow and hold the synthetic material in place.

In one *in vitro* experiment, Vickery Trinkaus-Randall, PhD, an assistant research professor of ophthalmology, was able to induce the growth of corneal epithelial cells on the transparent hydrogel in the center of the synthetic cornea. Epithelial cells normally cover the outside of a natural cornea to protect it, making it smooth and allowing light to pass through it. The researcher also observed that the new cells became confluent, or grew together, and began to make proteins critical to establishing a basement membrane on which the epithelium could be anchored.

In another experiment, Trinkaus-Randall successfully used amines, organic compounds derived from ammonia, to mimic the electrical charges normally found in extracellular matrix proteins to induce cellular growth. The development of a synthetic cornea that could be used to replace a patient's own diseased cornea has long been of concern to scientists. While corneal transplants are common in the United States, many countries, particularly developing nations, do not perform corneal transplants for cultural reasons or because of concerns about infectious diseases.

Researchers propose model for how some tranquilizers may work

Although most drugs work by substituting for, or blocking the activities of, endogenous substances, others, such as Valium and Librium, act as allosteric modulators that change the shape of certain receptors in the brain and thereby affect the way these receptors react to their chemical signals. Modulation is poorly understood, however, and has been of limited use as a basis for pharmacological design. School of Medicine researchers, however, have proposed a model for modulation that may explain how existing modulators work, and could also aid in the design of new pharmacological modulators. The researchers are David Farb, PhD, chairperson of the Department of Pharmacology and Experimental Therapeutics, and Terrell T. Gibbs, PhD, an assistant professor of pharmacology and experimental therapeutics.

According to Gibbs, who recently presented the research at the "Macromolecules, Genes and Computers: Chapter III" meeting in New Hampshire, allosteric modulators work by binding to receptors when they are in the active, rather than the inactive, state. Although these modulators are too weak to turn receptors on by themselves, they can, in effect, help the natural neurotransmitter to pull other receptors into an active state. The receptors then open a sort of macromolecular "gate" and allow the body's own electrical signals to enter.

As Gibbs points out, however, work in this area is still very preliminary: Scientists do not know what it is about a drug binding to a receptor that would cause it to open its gate, and, so far, technologies such as x-ray crystallography, nuclear magnetic resonance and computer modeling have yielded very few answers.



Two exchange students recently arrived at the School of Medicine to participate in the BUSM/Hebrew University-Hadassah Medical School Faculty/Student Exchange Program, which is now in its eighth year. The exchange students, Tali Green and Oren Shibolet, will take part in three rotations at Boston City Hospital and Boston University Medical Center Hospital.

Pictured at a luncheon to honor last year's exchange students are, from left, Asher Yarden, Israeli consul; Dean Emeritus John I. Sandson; Joseph J. Vitale, MD, ScD, a professor of pathology; exchange students Uri Tabori and Hillel Greisner; Louis Kaitz, benefactor of the exchange program; Leonard S. Gottlieb, MD, MPH, chairperson of pathology and laboratory medicine and director of the exchange program; Dean Aram V. Chobanian; Charlotte Kaitz, benefactor of the exchange program; Associate Dean Emeritus Ernest Blaustein, and Edward Alexander, MD, a professor of medicine and a research professor of physiology, and associate director of the exchange program. Both Blaustein and Sandson are members of the exchange program's advisory committee.

Seminars on interdisciplinary perspectives in biotechnology to be held

Boston University Schools of Public Health, Medicine, Engineering, Law and Philosophy have joined together to present "Interdisciplinary Perspectives in Biotechnology," a series of four seminars being held on the Charles River Campus. The first, titled "Genetic Screening under a National Health Care Program," was held on Oct. 15 and featured SPH faculty Wendy K. Mariner, JD, MPH, George J. Annas, JD, MPH, and Michael Grodin, MD, FAAP.

The following is a list of upcoming seminars, each of which will be held from 9 to 11 a.m. at Barrister's Hall in the School of Law, 765 Commonwealth Ave.

On Nov. 19, a seminar titled "Genetic Privacy: Rules for Gene Banks" will be led by Annas and Grodin.

On Feb. 18, David Pollen, MD, a professor of neurology at the University of Massachusetts Medical Center, will present "Hannah's Heirs: The Quest for the Genetic Origins of Alzheimer's Disease."

On March 18, a program on "Biodiversity and the Biotechnology Business" will feature Sheldon Krinsky, PhD, chairperson of the Department of Urban and Environmental Policy at Tufts University, and Rollin Johnson, PhD, from the Center for Science and International Affairs at Harvard University's Kennedy School of Government.

For more information, contact the SPH's Law, Medicine and Ethics Program at x8-4626 (638-4626).

School of Medicine students appointed to AMSA leadership positions

Three School of Medicine students have been appointed to national leadership positions with the American Medical Student Association (AMSA). Giuseppe Ciaravino '95 has been named an associate trustee to the National Board of Trustees; Souman Nandy '96 has been appointed as the co-coordinator of the National Computers in Medicine Task Force, and Mathieu Bermingham '96 has been appointed co-coordinator of the National Medical Education Standing Committee.

Founded in 1950, the AMSA is the largest independent, national organization developed and governed by medical students. AMSA has over 30,000 members, 154 chapters, 16 pre-med chapters and four affiliate foreign chapters. The officers of the School of Medicine AMSA chapter are John Udarbe '96, president, Chrysanthe Gaitatzes '96, recruitment coordinator, and Deborah Martin '96, Task Force/Standing Committee liaison.

Dept. of Pharmacology announces seminar schedule for Nov., Dec.

The following is a list of upcoming seminars sponsored by the Department of Pharmacology and Experimental Therapeutics. Each program will be held from 3:30 to 4:30 p.m. in Room 603 of the Instructional Building and will be preceded by refreshments beginning at 3:15 p.m.



A reception was held on Sept. 20 to honor the 20-year tenure of Daniel Bernstein, MD, associate dean for resources and hospital affiliations. Bernstein recently retired from the School of Medicine.

Bernstein first came to the School of Medicine in 1973 as an associate clinical professor of medicine. In 1977, he was named a clinical professor of medicine and, in 1980, was appointed an associate dean.

Pictured at the reception, Bernstein, left, greets Carl Apstein, MD, a professor of medicine and a research professor of physiology. (photo by Lucy Milne, BUSM Educational Media Support Center)

On Nov. 17, Richard A. Cohen, MD, a professor of medicine, will present "Role of the Endothelium and Potassium Channels in Vascular Reactivity."

On Dec. 1, Keith Miller, PhD, of the Department of Anesthesia at Harvard Medical School and Massachusetts General Hospital, will present "Mechanisms of Action of General Anesthetics on Acetylcholine Receptors."

On Dec. 8, "Dopaminergic Regulation of the Endogenous Opioid System" will be presented by Ellen Unterwald, PhD, from the Laboratory of the Biology of Addictive Diseases at Rockefeller University.

Briefly noted

Harold L. Lazar, MD, an associate professor of cardiothoracic surgery, was recently appointed secretary of the Section of Cardiac Surgery of the American College of Chest Physicians (ACCP)...**Marianne Prout, MD**, an associate professor of medicine and a co-founder of BUMC Hospital's Breast Health Center, recently participated in a Senate field hearing on women's health concerns. The hearing, titled "Improving Women's Health through Early Detection and Prevention Efforts," focused on breast and cervical cancer screening, injury control, violence prevention and sexually transmitted diseases. Held at Simmons College, the hearing was chaired by Sen. Edward M. Kennedy.

Upcoming CME courses

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

On Nov. 6 a seminar titled "Topics for the Practicing Pediatrician: Issues for the 1990s" will be held at the Sonesta Hotel in Cambridge.

The New England Cancer Society's Annual Meeting will take place from Nov. 12 through Nov. 14 at the Colonnade Hotel in Boston.

The Eighth Annual Smithwick Symposium, titled "Challenges in Trauma Care," will be held on Nov. 19 at Boston University Medical Center.

"Current Clinical Pediatrics" is the topic for a seminar that will be held from Dec. 28 through Dec. 30 at the Buena Vista Palace in Walt Disney World, Orlando, Fla.

For further information contact the Department of Continuing Medical Education at x8-4605 (638-4605).

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