AUGUST 2002

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Proposed Homeland Security

An Undersecretary for R&D. A “virtual” department. Deal with natural disasters as well as terrorism. Fund research on the psychological and behavioral aspects of terror. Set up an independent think tank. Appoint a public health expert to focus on bioterror. These are all recent suggestions for changes in the President’s proposed Department of Homeland Security, announced in a nationally televised address June 6.

The actual bill, introduced June 18, creates a new department composed of existing government programs now distributed among a dozen federal agencies. The new department would have a budget of $37.5 billion its first year, and about 170,000 employees.

The Homeland Security Act of 2002 would divide the new department into four functional areas: information analysis and infrastructure protection; chemical, biological, radiological, and nuclear countermeasures; border and transportation security; and emergency preparedness and response. An undersecretary would head each area. R&D programs from five current cabinet departments—Health & Human Services, Energy, Commerce, USDA, and Transportation—would be transferred to the new department, and most would be placed in the chemical, biological, radiological and nuclear countermeasures area. The undersecretary for this area would be responsible for setting research priorities and conducting an R&D program to enable the nation to respond to terrorist attacks using weapons of mass destruction.

By far the largest amount of the Department of Homeland Security’s R&D spending would involve civilian biological defense research programs currently operated by the Department of Health & Human Services (HHS). The legislation is vague as to the details, but it appears that the intent is to transfer about $2 billion (but no personnel or laboratories) from the Centers for Disease Control and Prevention and NIH to the new department. The department would then distribute the funds back to NIH and CDC in the form of grants and contracts to carry out bioterrorism-related research. Most of the R&D funds transferred back to NIH would go through the National Institute for Allergy and Infectious Diseases (NIAID).

This strikes many observers from the biomedical research community as a waste of resources, since transferring the funds, only to transfer them back in the form of grants and contracts, will require time and cost money. In addition, Congress is very unlikely to allow such a transfer of funds to occur, especially now that the NIH doubling has just been completed.

Another concern is that the DHS secretary would have the authority to “establish the research and development program, including the setting of priorities” with respect to any responsibilities carried out through the Department of Health and Human Services. The new secretary is supposed to act “in consultation with” the HHS secretary, but the language seems to indicate that DHS has ultimate authority—and is not required to get the Health and Human Services’ secretary’s agreement.

As noted in an analysis of the legislation by the American Association for the Advancement of Science (AAAS), “NIH bioterrorism research grantees and NIH laboratory employees would continue to receive funding from NIH through existing mechanisms, although the ultimate source of funds may change to DHS in a pass-through arrangement. The new coordination and priority-setting powers of DHS, however, would mean that
Department Provoking Controversy

research priorities would be set with strong input from DHS.”

While Congress has pledged to pass this legislation by the end of the year, the details are already beginning to draw fire. This is due to the complexity of the proposal. First, the creation of this department requires the most significant realignment of the executive branch in 60 years. According to the AAAS analysis, the reorganization “could involve the elimination of some agencies, the mergers of others, the transfer of authority over 170,000 federal employees, the physical transfer of an unknown number of civil servants, and the meshing together of nearly two dozen federal units into a new organizational structure.”

Also complicating the picture is the fact that almost 90 congressional subcommittees and committees have some jurisdiction over agencies or programs that would be affected by the reorganization. Some observers believe that this could lead to a reorganization of Congress as well—if not the elimination of some committees or subcommittees—and possibly the creation of a fourteenth appropriations subcommittee to control funding for the new department.

The proposal began to change before it even arrived on Capitol Hill in the form of legislation. For example, a White House publication explaining the new proposal, distributed shortly after the President’s June 6 speech, indicated that the entire Lawrence Livermore National Laboratory would be transferred to the new department. However, the proposed legislation calls for only a few of the laboratory’s programs to be transferred (with no physical transfers of staff or assets likely).

Congressional efforts to keep programs from being transferred to the new department are already underway. Several members of the House Science Committee have made it clear that they will not support transferring the National Institute for Standards and Technology’s (NIST) Computer Security Division to the new department. Rep. Vern Ehlers (R-MI), said this was not a “turf issue,” as he expected the Science Committee would retain jurisdiction over the program regardless of where it was located. Rather, he said that the program was so important to NIST’s mission that the agency would no doubt have to recreate it within two or three years, so there was no point in transferring it.

Science Committee Chairman Sherwood Boehlert (R-NY) said that an undersecretary for research and development is needed in the new department. He stated, “I have come to the conclusion that the bill the Administration has sent us simply does not give R&D a high enough profile to enable the Department of Homeland Security to accomplish its goals. The bill does not even explicitly mention R&D in some critical areas, such as cybersecurity and transportation security, it creates no slot for an official whose primary concern would be R&D, and it does not follow any successful model of R&D coordination.” He declared that when his subcommittee marks up the bill it “will have an undersecretary for R&D with a broad but clear mission and the tools he or she will need to carry it out. I believe the Senate is moving in the same direction.”

Science Committee members also argued that R&D in the psychology of terror should be part of the new department’s mission. Rep. Brian Baird (D-WA) said, “The aim of terrorism is to inflict lasting psychological wounds on its victims. We have seen this in the thousands of people struggling in the aftermath of the attacks of September 11—the family members of the victims, first-responder and rescue personnel, and others. I believe it is critically important to include funding for research on how people cope with such tragedies and provide tools to help repair the psychological impact to our citizens as part of any national homeland defense strategy.”

Boehlert endorsed a recommendation in a recently-released NRC report, “Making the Nation Safer: the Role of Science and Technology in Countering Terrorism,” (see page 16) to establish a Homeland Security Institute, which would function as a kind of “think tank” on long-term security needs. He indicated that the Institute should be located outside the new department, presumably to ensure the objectivity of its advice.

Rep. Nick Smith (R-MI) expressed the view that the new department should focus on natural threats—hurricanes, tornadoes, floods—and not just terrorist threats. He also urged the administration “to guard against being too overzealous, with less emphasis on basic research.”
Former JBC Editor-in-Chief

John Tilston Edsall died June 12 in Boston at the age of 99. An emeritus professor of biochemistry at Harvard University known for his research on the chemistry of proteins and enzymes, Dr. Edsall, an ASBMB member since 1931, served as president of ASBMB in 1958, as president of FASEB in 1959, and was editor-in-chief of the Journal of Biological Chemistry from 1958 through 1967.

“Dr. Edsall became Editor of the Journal of Biological Chemistry in 1958, and was extremely important in drastically changing the overall operation of the Journal to reflect the enormous expansion in biochemistry here and abroad,” recalled Dr. Herbert Tabor, current JBC Editor. “In addition to the reorganization of the structure of the Journal, he also set up strict guidelines for the review process. He always emphasized his uncompromising determination that all decisions and reviews be fair and that they should only be based on the scientific merit of the contributions. The continued success of the Journal is clearly a monument to the framework that he established.”

Dr. Edsall worked in the Department of Physical Chemistry at Harvard Medical School from 1926 to 1954. He was a tutor in biochemical sciences in the Faculty of Arts and Sciences for 40 years, serving as Head Tutor in Biochemical Sciences from 1931 to 1957. In 1954 he moved to Cambridge full-time and became a professor in the Biology Department and later in the Department of Biochemistry and Molecular Biology.

Dr. Edsall’s early research focused on the chemistry and structure of proteins, especially the proteins of muscle and blood. During World War II he was a member of a research program that studied the fractionation of blood plasma proteins for use in medicine and surgery. He also studied light scattering in protein solutions and the interaction of proteins with metallic ions. Later, he conducted research on the structure and function of carbonic anhydrase, an enzyme from red blood cells that promotes the transport of carbon dioxide in the blood.

After Dr. Edsall became professor emeritus in 1973, he gave up laboratory work and devoted himself to writing about the history of modern biological and biochemical science. From 1975 to 1980, he was director of the Survey of Sources for the History of Biochemistry and Molecular Biology.

A memorial service is being planned for sometime this fall.

The following introduction to two JBC Classics is reprinted from the August 16 issue of the Journal for Biological Chemistry. The Classics are available online at http://www.jbc.org/cgi/content/full/277/33/e22

John Edsall: Biochemist, Teacher, JBC Editor-in-Chief, and Responsible Scientist

By Robert L. Hill, Robert D. Simon, and Martha Vaughn

Introduction


John Edsall (1902-2002) was born in Philadelphia to families that had emigrated to America in the 17th century. His mother, Margaret Tilston, was a teacher and his father, David Linn Edsall, was Professor of Medicine at the University of Pennsylvania Medical School. In 1918, David Linn Edsall became Dean of Harvard Medical School, a position he held for seventeen years. The move from Philadelphia to Boston, and Harvard, would mark the beginning of a life-long association of John Edsall with Harvard. At the age of 13, John
was fascinated by a science class at Milton Academy which, along with being raised in a medical family, helped guide him toward medical school and a career in science. At age of 16 he enrolled in Harvard College to study chemistry. He was, by his own admission, an average student but was inspired in his final two years by two teachers/scientists, E. P. Kohler, an organic chemist, and Lawrence J. Henderson, a biochemist and Chairman of the Department of Physical Chemistry at Harvard Medical School (1).

After completing his undergraduate degree in 1923, Edsall started Harvard Medical School where his interest in science and research was further stimulated by Otto Folin’s biochemistry course (Folin is the author of a previous JBC Classic (2)). Most important during his first year was the opportunity to do research with Alfred C. Redfield, Director of the Woods Hole Oceanographic Institute, on the physiology of heart muscle function. This work stimulated a career-long interest in the structure and function of muscle proteins. In 1924, Edsall, along with Jeffries Wyman his college friend and colleague and author of a future JBC Classic, began two years of study at Cambridge University in the Department of Biochemistry chaired by F. Gowland Hopkins (the author of a previous JBC Classic (3)). He took biochemistry courses and did some research but, more importantly, came under the influence of G. S. Adair who, Edsall states, was his “most important contact” at Cambridge (3). Adair was in the process of determining the molecular weight of hemoglobin and describing the oxygen dissociation curves and applying physical chemical principles to the study of proteins. Adair’s work was reported in a previous JBC Classic (4).

Edsall returned to Harvard in 1926 as a third year medical student and started his clinical training much of which he felt was “trivial and stupid” (1) but in spite of this view, decided to finish his medical degree. He had some free time from his clinical studies and began to work with Edwin J. Cohn, the author of a previous JBC Classic (5). Cohn was interested in protein physical chemistry and guided Edsall to examine the globulins of muscle.

Among his early experiments with myosin, actually actomyosin, he was to observe, by refractive index measurements, that myosin solutions made to flow through a capillary exhibited streaming birefringence (10,11). This ordering, induced by capillary flow, was compared to the ordered morphology observed in intact muscle cells by his colleague Alexander von Mural suggesting that the extracted protein(s) represented a basic unit of muscle structure. At the time, there was no good theory that related flow birefringence to the size and shape of the molecules producing it but Edsall determined from hydrodynamic considerations that the dimensions of the myosin molecules must be long and thin in order to explain the ordering induced by capillary flow.

In addition to work on muscle proteins, Edsall and his colleagues in the Department of Physical Chemistry, including Jeffries Wyman, began to systematically study the physical and solution properties of amino acids and small peptides. One of Edsall’s contributions was the description of the amino acid as a dipolar ion or, as he preferred, ionic dipole (3). Using Raman spectroscopy, he showed that both the amino and carboxyl groups of amino acids were charged at isoelectric pH (6).

The two papers reprinted in this installment of JBC Classics are intended to represent a body of work focused on the physical chemistry of proteins. As was common in Edsall’s time, much of his work was published in the chemical literature. The first paper examines primarily the solubility properties of myosin as a function of ionic strength and pH. Further it is reported that the viscosity of myosin was much greater than that of plasma proteins such as albumin. The second paper presents titration data for the protein zein and reports the pK values for the titratable groups, primarily the carboxyl groups and the imidazole of histidine.

Edsall was a devoted teacher but since the Department of Physical Chemistry in the Medical School had few formal teaching responsibilities, he volunteered to be a tutor at Harvard College, a position he held from 1928-1968. He would meet with small groups of undergraduates and advise seniors on their honors research projects. Among the students in Edsall’s groups were R. Gordon Gould, I Herbert Scheinberg, Alton Meister, Alexander Rich, Gary Felsenfeld, Jared Diamond, W. French Anderson, Eliot Elson, Michael Chamberlain, David Eisenberg, Robert Eisenberg, and Joel Huberman. All were to have successful careers in science and medicine (1). He also taught a formal course in the Biology Department of Harvard College on biophysical chemistry.

The beginning of World War II saw the redirection of the work in the Department of Physical Chemistry to the war effort. Led by Cohn, this group spearheaded the national plasma fractionation program. The large scale fractionation procedures they developed provided many protein products essential for the war effort including clotting factors and human albumin as a “plasma extender” for transfusions (5). This applied research also yielded much fundamental knowledge of protein solubility properties and fractionation techniques.
After Cohn’s death in 1953, Edsall moved to Harvard College where he would continue both his research and teaching without the four-mile drive between the Medical School and the College. His research for much of the remainder of his career focused on carbonic anhydrase.

In 1954, Edsall was asked to become a member of the Editorial Board of the *JBC* and in 1958 he was asked to succeed Rudolph J. Anderson as Editor-in-Chief. He accepted and served as Editor-in-Chief until 1967. The Journal editorial offices were established at Harvard and the basic structure of the *JBC* manuscript review process as it exists today was established. The format of the Journal was changed in 1958 to larger pages with 2.4 times the content of the earlier, smaller page format. As a result, the journal became thinner but only for a short time. As Editor, he appointed the first women to the Editorial Board, Mildred Cohn, Sofia Simmons, and Sarah Ratner.

During Edsall’s 10-year term, the size of the Editorial Board doubled from 26 to 54 members (in 2002 the *JBC* Editorial Board has about 500 members). The number of pages published in the *JBC* had also doubled to 5800 since he had become Editor and he felt that there was some sort of limit and it was likely that the *JBC* would fission into sub-specialty journals. It survived that period of growth and remains a general journal of biochemistry and molecular biology. (In 2002 *JBC* will publish over 50,000 pages.) During Edsall’s last year as Editor, page charges of $35 were instituted and were, then as they are now, somewhat controversial though essential to the financial health of the Journal (page charges in 2002 are $65). Edsall was succeeded as Editor-in-Chief by William H. Stein who served only a short term during which he was struck by a crippling paralytic illness. Herbert Tabor served as Acting Editor-in-Chief and in 1971, and with Stein’s resignation, became Editor-in-Chief, a position he retains in 2002 (1, 7).

Edsall was, among his many roles, a vigorous advocate for freedom of scientific inquiry, responsible conduct of research and usage of applied science. In 1954, it was reported at the Annual Meeting of the American Society of Biological Chemists (ASBC) that the United States Public Health Service (PHS) was withholding research support from some investigators because of unevaluated adverse information in their security files. Investigators were not told of this information nor given any opportunity to respond to the alleged charges which, Edsall felt, were irrelevant in any case since none of the research was classified. With a general sense of outrage, Edsall, along with Philip Handler, Wendell Stanley and a few others (1) prepared a resolution to send to the National Academy of Sciences asking for an investiga-
tion of the PHS behavior. At the general business meeting of the ASBMC, the resolution was passed unanimously. The National Academy conducted a thorough investigation with recommendations to President Dwight Eisenhower that grants for unclassified research should be awarded solely on the basis of scientific merit. The Eisenhower administration made this policy effective for all federal granting agencies. During the months it took the National Academy to complete its work, Edsall decided to protest personally. He wrote an article, published in Science (8), condemning what the PHS was doing and declaring his refusal to accept PHS support for his research as long as the practices continued (1). Not until two years later, assured that the practices had stopped, would he apply for and receive PHS research support. Edsall also played an important role in the establishment of the Committee on Scientific Freedom and Responsibility (CSFR) of the American Association for Advancement of Science (AAAS). His article published in Science in 1975 “Scientific Freedom and Responsibility (9) is a seminal and still relevant statement of the issues confronting scientists and citizens.

During the later period of his career, Edsall expanded his half-century of activism as an articulate and effective voice of concern about nuclear, biological and chemical agents for war, environmental degradation and the relationship of technology to society. He died on June 12, 2002, five months before his 100th birthday.

References
2. JBC Classic by Otto Folin
4. JBC Classic by G. S. Adair
5. JBC Classic by Edwin Cohn

JBC Papers Reviewed By Faculty of 1000

Two papers published in the Journal of Biochemistry were highlighted in the March 18 issue of The Scientist. An article on the Faculty of 1000, a new online research service that reviews papers published in the biological sciences, including the following reviews of JBC papers.


“The mode of antiviral action of the interferon-inducible dynamin-like GTPases, the Mx proteins, is still not known. Here it is shown that GTP binding in vitro causes human MxA to self-assemble into helical filaments, a process resembling the GTP-dependent polymerization of dynamin. The authors see these results as supporting the idea that Mx polymerization may play a role in the capture of viral nucleocapsids in vitro. Previous results from this group showing direct interaction been Mx and viral nucleocapsid proteins are consistent with this hypothesis.”

Reviewer: Jonathan Howard of the Institut fur Genetik, Germany

PROTEIN ENGINEERING

“The authors report the basis for design of sequence-specific DNA binding proteins for potential use in gene regulation and nanobiotechnology. A combination of screening and rational design was used to discover zinc-finger peptide sequences relatively specific for each of the possible triplet codons. Assembly of multiple modules gives a process for developing proteins to bind to one’s favorite sequence of DNA, whether as a repressor, a promoter, or to construct a DNA-based device.”

Reviewer: Mark Nelson of E.I. DuPont de Nemours & Co., U.S.
When the National Institutes of Health requested proposals for innovative ideas in immune system suppression from scientists who aren’t immunologists, Dr. Vadivel Ganapathy and his idea qualified.

The Medical College of Georgia researcher has long wondered if the placenta, in addition to supplying a developing baby with the nutrition and oxygen he needs to thrive, was also helping suppress the mother’s immune system so the fetus could survive.

“There is the problem about how pregnant mothers tolerate the placenta and the fetus even though the genetic makeup of the placenta is partly different than that of the mother,” said Dr. Ganapathy, an ASBMB member. The fetus gets half its genetic makeup from each parent, so when this genetically foreign being implants on the uterine wall it should be rejected – like a transplanted organ—by the mother’s immune system.

A major research finding in 1998 from another team of MCG researchers led by Drs. Andrew L. Mellor and David Munn showed that early in pregnancy, at the time of implantation, placental cells express an enzyme, indoleamine 2,3-dioxygenase, or IDO, that locally disables the mother’s immune system. “Our IDO mechanism was one that, if you suddenly interrupt it, the fetus can’t do without,” said Dr. Munn, pediatric hematologist-oncologist and a co-investigator on Dr. Ganapathy’s study. Dr. Munn has no doubt that the body has multiple mechanisms to protect the fetus and so procreation. “I think we can state with confidence that the mother and fetus use multiple mechanisms to make sure that the fetus is not rejected,” he stated.

Evidence about at least one other mechanism began showing up years ago when an article, published in a 1977 issue of the Annals of the New York Academy of Sciences asked, “Progesterone and Maintenance of Pregnancy: Is Progesterone Nature’s Immunosuppressant?”

The question apparently didn’t get answered then, but with the three-year NIH grant Dr. Ganapathy recently secured, it just may.

Progesterone is a female hormone with receptors found throughout the body; physicians and scientists have long known progesterone and estrogen are needed in pregnancy. It’s also known that during pregnancy, the placenta produces a tremendous amount of progesterone, hundreds times more than needed to activate progesterone receptors. Scientists also have known, at least since the 1977 article, that at these high levels, progesterone kills lymphocytes, white blood cells critical to the immune response.

Dr. Ganapathy began to put together an answer to the nearly 30-year-old question when he was looking at the impact of cocaine on the fetus and found a placental protein called sigma receptor interacts with cocaine. In 1996, he cloned the sigma receptor from human placental tissue so he could complete a biochemical profile on exactly how it worked. By then, other scientists had speculated that the ligand or activator of this receptor was progesterone.

“We thought, we can establish that without any doubt by using our cloned receptor,” Dr. Ganapathy said. “So instead of taking tissue and looking at the progesterone binding to it, we can look at the cloned, pure protein receptor and show that progesterone is the ligand. We published that.”
Now he is exploring the rather common-sense hypothesis that since high levels of progesterone are needed to activate the sigma receptor in the placenta and that the high levels occur only during pregnancy, this must be one way the placenta helps control the mother’s immune system so the fetus is not rejected.

“It’s a very positive hypothesis, but it’s still a hypothesis,” Dr. Ganapathy said. “There are progesterone receptors in the placenta and in other tissues but to activate them you only need a tiny amount of progesterone. The placenta is producing a ton of it. Therefore the purpose of the placenta-produced progesterone cannot be to activate progesterone receptors,” he said.

So he is developing a knockout mouse model that is missing the sigma receptor to see if the mice ever get pregnant. He’s betting they won’t.

The work has potential for not only better understanding the mystery of how the fetus survives but also how the immune system works and possibly, why sometimes miscarriages occur.

“Some women who are infertile may have genetic mutations in the sigma receptors so that progesterone is made by the placenta but the receptor is not functional,” Dr. Ganapathy said.

But there may be even more, possibly another ligand or activator for the sigma receptor that would enable use of this process to locally suppress the immune system so organ transplant patients wouldn’t need drugs that more generally suppress, leaving them susceptible to illness and infection. Dr. Ganapathy said a French company is trying to synthesize such ligands.

“It’s a nice theory,” he said; finally he may find if it’s a reality.  

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**Genetically Modified Tomatoes May Help Fight Cancer**

Forget the attack of the killer tomato, this is the attack of the healthy tomato: Scientists from Purdue University and the U.S. Department of Agriculture have developed a tomato that contains as much as three-and-a-half times more of the cancer-fighting antioxidant lycopene.

Dr. Autar Mattoo, an ASBMB member who is research leader at the USDA Vegetable Laboratory in Bethesda, Maryland, said the increase in lycopene occurred naturally in the genetically modified tomatoes. “The pattern for the accumulation was the same as in the control tomatoes,” he noted. “The lycopene levels increased 2 to 3.5 times compared to the non-engineered tomatoes.”

“This is one of the first examples of increasing the nutritional value of food through biotechnology,” said Anvar Handa, Professor of Horticulture at Purdue University.

Lycopene, the pigment that gives tomatoes their characteristic red color, has been the focus of attention since 1995, when a six-year study of nearly 48,000 men by Harvard University found that those who ate at least 10 servings of foods per week containing tomato sauce or tomatoes were 45% less likely to develop prostate cancer.

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**Chairman, Department of Biochemistry**

The Medical College of Wisconsin (MCW) invites established scientists with vigorous research programs and strong leadership skills to apply for the position of Chairman of Biochemistry. The successful candidate will assume leadership of a nationally distinguished department with 12 full-time, funded investigators who are pursuing high-quality research programs as well as contributing to medical and graduate education. Areas of research encompass structural biology, enzymology, biological oxidation, and cellular and molecular biology.

This recruitment is taking place in the context of rapid growth and expansion of the Medical College, and the successful candidate will play a major role in integrating an expanded Biochemistry faculty into MCW initiatives in cancer research, human and molecular genetics, cardiovascular research, and neuroscience.

MCW offers a dynamic intellectual environment in a community with an excellent quality of life. Interested applicants should submit a full curriculum vitae and letter of interest to:

Biochemistry Search Committee, c/o Office of the Dean  
Medical College of Wisconsin, 8701 Watertown Plank Rd.  
Milwaukee, WI 53226

Questions may also be directed to Dr. Paula Traktman, Chairman of the Search Committee, at ptrakt@mcw.edu. For more information, visit the departmental web site at http://www.biochem.mcw.edu/home.html. MCW encourages applications from women and minority candidates.  

EOE/M/F/D/V
Grandad’s Parkinson’s Could Be Fragile X Syndrome

Recent studies at the University of California School of Medicine at Davis, reveal that grandfathers of mentally impaired children could easily be misdiagnosed as suffering from Parkinson’s disease (PD) or other movement disorders, when, in fact, the brain pathology causing their tremor and motor problems may be something entirely different. Their symptoms could be the result of mild changes in the fragile X gene responsible for their grandchild’s retardation. This discovery was made by Paul Hagerman, M.D., Ph.D., Randi Hagerman, M.D., and their collaborators at UC Davis, the University of Colorado, and the University of Manitoba.

Fragile X syndrome, the most common inherited form of mental impairment, affects 1 in 3,000 people worldwide. It is caused by expansions of a three-base (CGG) repeat in the fragile X mental retardation 1 (FMR1) gene. If the expansion exceeds 200 repeats, the gene is generally silenced and, in the absence of its protein product FMRP, mental impairment results. Carriers of the premutation, with an expansion of 55 and 200 repeats, had long been thought to escape clinical involvement. However, the Hagermans’ findings, presented at the European Society of Human Genetics in May and reported in BioMedNet News, challenged that theory with the first report of a new neurological disorder in five premutation carriers over 50.

These patients showed progressive tremor, motor and gait problems, and cognitive decline that were frequently either not diagnosed or misdiagnosed by neurologists who would not have thought of searching for links with fragile X, a syndrome usually spotted in childhood.

The Hagerman team was first alerted to a possible link when their genetics counselor, Louise Gane, asking mothers about their affected child, would often get the reply, “My son’s doing fine but my dad is not doing so well,” recalled Dr. Hagerman. A pattern began to develop with more reports of grandfathers with tremor and/or ataxia problems.

Based on early data from a poll of several hundred affected families, the Hagermans cautiously estimate that as many as one in five males with the premutation could go on to develop the tremor/ataxia syndrome, which can be progressively debilitating.

That estimate is based on a cut-off age of 50, above which, he says, the incidence may well increase. Dr. Hagerman stresses that hard epidemiological data are needed to verify the figures and to understand why some individuals are affected and others are not. Although 1 in 700 men and 1 in 250 women are fragile X premutation carriers in the general population, it is not known how many may be susceptible to this neurodegenerative disorder.

When Dr. Hagerman’s team carried out neurohistological studies on post mortem tissue taken from the brains of five premutation carriers, they found notably different pathology from that of other neurodegenerative disorders such as PD. Specifically, they found changes in the deep cerebellar white matter, which had developed a spongioform appearance. Dr. Claudia Greco, a neuropathologist and collaborator at UC Davis Medical Center, found accumulations of protein-rich clumps or inclusion bodies in the nuclei of both neurons and astrocytes. “They’re most common in the hippocampal formation, with 30-40% of hippocampal neurons showing them,” said Dr. Hagerman. “This type of inclusion is very rare outside this syndrome, but the real puzzle is why these inclusions are forming in the first place, since we don’t know of any abnormal protein product.”

The study of the mechanisms involved in inclusion formation will hopefully lead to molecular treatment of fragile X premutation carriers. (N)

Note: The results of four of the brain studies will be published in the August issue of Brain (Greco, et al. 2002).
University of Michigan Regents Elect Mary Sue Coleman President

Dr. Mary Sue Coleman, has been unanimously elected by the Regents of the University of Michigan as the 13th president of the university. Dr. Coleman, who has served as President of the University of Iowa since 1995 and as a Professor of Biochemistry in Iowa’s College of Medicine and Professor of Biological Sciences in the College of Liberal Arts, will take office August 1. She succeeds B. Joseph White, who has served as interim president since January 1 of this year.

Dr. Coleman’s selection was the culmination of a six-month search, and in announcing her selection, Regent Laurence Deitch highlighted her outstanding academic credentials and accomplishments, calling her “a national leader in higher education,” and “quite simply the best candidate in an extraordinary field and we are fortunate to have her.”

Under Dr. Coleman’s leadership at Iowa, the university increased research funding from $178 million to over $300 million, and increased total annual giving from $82 million to $172 million. She also oversaw major construction projects in liberal arts, medicine, engineering, biology, fine arts, honors center, career center, athletics and recreation, and parking.

In addition to the presidency of Iowa, Dr. Coleman has held posts as provost and vice president for academic affairs (1993-95) at the University of New Mexico, and vice chancellor for graduate studies and research (1992-93) and associate provost and dean of research (1990-92) at the University of North Carolina at Chapel Hill.

She served for 19 years as a member of the biochemistry faculty and as a Cancer Center administrator at the University of Kentucky in Lexington, where her research focused on the immune system and malignancies.

She was elected to the National Academy of Sciences’ Institute of Medicine in 1997, and is a Fellow of the American Association for the Advancement of Science and of the American Academy of Arts and Sciences. She co-chairs the Institute of Medicine’s Committee on the Consequences of Uninsurance.

Molecular and Cellular Proteomics
To Be Included in Medline

The newest ASBMB journal, Molecular and Cellular Proteomics (MCP), has been approved for inclusion in Index Medicus and Medline.

Since this is the first year of publication, all back issues, beginning with the January 2002 issue, will be indexed retrospectively. Such indexing is very important to a journal since Medline searches are one of the primary ways interested investigators are pointed to new journals. Molecular and Cellular Proteomics publishes three types of original articles: research papers, database articles, and technology development articles. Mini-reviews and articles discussing important unresolved issues (perspective articles), as invited contributions, will also be published.

The National Library of Medicine’s advisory committee, the Literature Selection Technical Review Committee, recommended that MCP be added to Index Medicus and Medline. The advisory committee is composed of authorities knowledgeable in the field of biomedicine, such as physicians, researchers, educators, editors, health science librarians, and historians, who review and recommend the journal titles NLM should index. Databases in NLM’s MEDLARS system are available online in the U.S. and throughout the world. Citations from the articles indexed, the indexing terms, and the English abstract printed in the journal will be included in the databases.

ASBMB members are urged to submit papers to MCP and to encourage their libraries to subscribe to MCP, which will only be available for free online access until December 31, 2002. To check out MCP online go to www.mcponline.org.
he Albert B. Alkek Institute of Biosciences and Technology in Houston, Texas, is a new research endeavor sponsored by Texas A&M University. The broad program of the Institute fosters creative research on molecular aspects of medicine and agriculture, provides a forum for the exchange of ideas between the medical and agricultural research communities, and encourages the technology transfer of discoveries from the laboratory to the market place. In the United States, this Institute is unique in its research mission combining medicine and agriculture. IBT scientists also train graduate students and postdoctoral fellows to tackle major scientific questions in a collaborative manner and to applying cutting edge technologies to critical questions in bioscience and medicine.

“The Institute, with its five research centers, continues to develop a unique niche within the Texas Medical Center (TMC),” according to IBT Director Richard H. Finnell, who is also Profes-
A Forum That Brings Medicine and Agriculture Together

By John D. Thompson, Editor

Speaking of the collaboration between diverse disciplines, Wallace McKeehan, Director of the Center for Cancer Biology and Nutrition, said, “I’m here because of this unique setting, in which the Center for Cancer Biology and Nutrition can be a basic research hub in cell and molecular biology and mouse genetics of prostate and liver cancer with spokes running to and from diverse disciplines out on the surrounding wheel. These span frontier horticulture and genetic engineering of plants in the field and food technologies in the strongest agricultural university in the country and all aspects of cancer biology from lab to clinic in the largest medical center in the world.”

Dr. McKeehan also noted, “The IBT is breaking administrative and bureaucratic barriers that are often far more inhibiting to interdisciplinary, collaborative ventures than diversity of themes and distance. For example, where else can a tenured state-salaried professor paid from one state university system (Texas A&M) hold full voting faculty membership and mentor the Ph.D. students in its rival state system (University of Texas)?

“We find ourselves in one of the largest undergraduate teaching university systems and probably one of the most conservative when it comes to the definition of academic tenure and the professor title. Nevertheless, the IBT has managed, with difficulty as you can imagine, to create an atmosphere where a professor is defined as an interdisciplinary, collaborative researcher with specialized advanced students from many backgrounds, levels and objectives, and is encouraged, even aided administratively, to link basic research findings to practical industrial and clinical applications.

This is all without compromise of our pure, basic research foundation.”

Speaking of the medical aspect, Paul D. Gershon, Associate Professor in the Center for Genome Research, said, “My interests are in poly(A) polymerase and a protein combining the sor of Genetics, Toxicology and Biomedical Sciences.

“It has served as a bridge between the multitude of physical and agricultural research strengths and infrastructure located on the Texas A&M University campus in College Station, Texas, some 90 miles to the northwest, and the biomedical research programs of the 41 other TMC institutions in Houston,” he said. “In addition, the IBT has as part of its mission, to develop and commercialize novel research technologies. There have been two start-up companies that have been highly successful during our brief 10-year history.”

“The IBT research strengths have long been focused on cellular signaling in prostate cancer and in extracellular matrix biology,” added Dr. Finnell. “The founding director, Dr. Robert Wells, developed a world-class group of investigators who work on unusual DNA structure and how it relates to human diseases, particularly the trinucleotide repeat disorders. Most recently, we have established a new research center for environmental and genetic medicine. This represents a new direction and emphasis for the IBT in the area of molecular toxicology and environmental health. Research involving environmental toxicants that contribute to the population burden of birth defects and hormone responsive cancers will be the focus of these new investigations.”

“The Institute of Biosciences and Technology is a splendid opportunity for far reaching discoveries at the interface of medicine and agriculture.”

—Dr. Robert Wells
functions of poly(A) polymerase processivity factor with mRNA cap methyltransferase. As a collaboration with the Quirocho group at Baylor College of Medicine, this led to the first crystal structure for an intact poxvirus protein, for an RNA methyltransferase, and co-crystal structure for a protein liganded with a capped mRNA fragment.

**Overview of IBT**

The Albert B. Alkek Institute of Biosciences and Technology is housed in a new 11-story research tower (see photograph) located in the Texas Medical Center in Houston. Eight laboratory floors provide state-of-the-art facilities for the scientists and staff, who will number about 500 when full operation is reached in the future. The Institute came into existence in 1990 and the building was dedicated on August 3, 1992. Dr. Robert D. Wells (Past-President of ASBMB) was the Founding Director (1990-94). The IBT was founded by Texas A&M University and currently is a component of the Texas A&M University System Health Science Center.

**Texas Medical Center**

Called “the largest medical complex in the world” by the New York Times, the Texas Medical Center (TMC) in Houston arose from the generosity of a few visionary businessmen who wanted to give something back to their community. Founded in the 1940s, the Texas Medical Center grew and flourished because of its continuing achievements in healthcare and research.

Covering 670 acres, the TMC now is home to more than 50 member institutions. They are dedicated to providing the best in not-for-profit patient care, research, and education. Indeed, many scientists and academicians whom the world now credits with medical and technological advances have worked at this center. Research plays a central role in the Texas Medical Center, with at least 25 institutions engaged in this function. Approximately $1 billion was the combined total for sponsored research pledged from outside funding. The IBT is centrally located within the Texas Medical Center complex. Major research institutions include Baylor College of Medicine, the University of Texas Health Science Center, and the University of Texas M.D. Anderson Cancer Center.

**IBT Research Organization**

The research programs at the IBT are organized by Centers, each with its own Director. Emerging research areas have stimulated the development of additional centers within the IBT. Original research centers focused on arthritis and bone diseases, cancer biology and nutrition, hereditary diseases, structural biology, genome informatics, and environmental and genetic medicine.

**Technology Transfer**

IBT encourages the commercial development of scientific discoveries. The practical application of technologies will improve both human and animal health while bringing in new sources of research support for the Institute. Virtually all senior IBT faculty have productive working relationships with biotechnology companies, several licensing agreements have been established based on IBT research, and two new companies have been incorporated.

Frederick S. Gimble, Ph.D., Associate Professor in the Center for Genome Research, works with state-of-the-art protein engineering methods to produce novel, extremely specific enzymes that can facilitate the manipulation of complex genomes.

“An historic milestone has been reached with the sequencing of the human genome,” said Dr. Gimble, “and it is clear that this information will have a profound impact on the development of new therapeutics and on methods of combating disease. In the post-genomic era, one goal will be to develop tools that can be used to repair errors within genes that cause inherited disease.”

“My laboratory,” he explained, “is a perfect example of how the pursuit of basic research can result in new discoveries that may eventually lead to clinical applications. For the past several years, our group has studied members

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**In the future, I expect that the conversion of pilot studies initiated at the IBT into research projects performed in collaboration with biotechnology companies will accelerate to generate new products of great benefit to human health.**

— Dr. Frederick Gimble
of a class of enzymes called homing endonucleases that are able to search out a specific sequence within a complex genome, and to cut the DNA at that location. To give one a sense of the specificity of these enzymes, one of the DNA endonucleases that we study cuts at a single site within the 13 million base-pair genome of yeast. This protein is encoded by a ‘selfish’ DNA element that apparently contributes no benefit to its host organism. However, we envision that it will be possible to harness the extreme specificity of these molecules to initiate the DNA repair of defective genes in diseased cells. It has already been demonstrated in model systems using mammalian cells that these proteins can initiate DNA repair. Thus, these reagents fulfill many of the requirements needed to act as “molecular scissors.”

“The Institute of Biosciences and Technology,” stated Dr. Gimble, “is ideally positioned to develop these ideas. It is a facility devoted to research that houses scientists who are applying diverse scientific methods toward the study of a wide variety of biological questions. Our research has benefited immensely not only from our interactions within the IBT but also through our collaborations with scientists at neighboring institutions within the Texas Medical Center.”

A major focus for Dr. Magnus Höök’s laboratory is studies of microbial adherence to ECM components in the mammalian host.

Lab Probes DNA Role in Triplet Repeat Diseases

ASBMB Past President Dr. Robert D. Wells, who founded the IBT, is particularly interested in the role of DNA structure in triplet repeat diseases.

Investigations since 1991 have revealed that approximately 15 human hereditary neurological diseases are caused by the non-Mendelian expansion of simple triplet repeat sequences (CTG/CAG, CCG/CCG, and GAA/TTC). Some of these diseases are myotonic dystrophy, Huntington’s disease, and Friedreich’s ataxia. The clinical observation termed “anticipation” refers to the earlier age of onset and increased severity of the disease through a human pedigree.

This non-Mendelian behavior is correlated with an increase in length of the triplet repeat sequences and is caused by the non-Mendelian expansion process. Dr. Wells’ laboratory is investigating the molecular mechanisms of the genetic instabilities that give rise to the disease etiology in well-defined genetic systems such as Escherichia coli. In addition, studies are underway on the DNA synthetic enzymes (polymerases and topoisomerases) that carry out the expansion process. DNA structural investigations have revealed the presence of a new, unusual conformation (flexible and writhed DNA) which is an intrinsic property of the CTG/CAG and CCG/CCG repeat sequences.

Dr. Wells’ lab is also investigating the biochemical, genetic, and physical bases of the disease etiologies of a number of other devastating and debilitating neurological syndromes.

Graduate Education

An individually tailored curriculum is designed to assure that each graduate student acquires the necessary theoretical background and appropriate knowledge and skills. Graduate students at the IBT enroll in the Graduate School of Biomedical Sciences, Texas A&M University System Health Science Center. Individual IBT faculty also have affiliations with graduate programs of Texas A&M University in College Station in the fields of biochemistry, genetics, nutrition, and some also have adjunct appointments in departments at Baylor College of Medicine, University of Texas Health Science Center, and the University of Texas M.D. Anderson Cancer Center, all of which are located in Houston in the Texas Medical Center.
The United States should take advantage of its scientific and engineering strengths to detect, thwart, and respond to terrorist attacks more effectively, according to a new National Academies report. The report, “Making the Nation Safer: the Role of Science and Technology in Countering Terrorism,” identifies actions, including deployment of available technologies, that can be taken immediately, and points to the urgent need for more research and development in certain critical areas. It proposes that an independent homeland security institute be established to help the government make crucial technical decisions and devise strategies that can be put into practice successfully.

“The scientific and engineering community is aware that it can make a critical contribution to protecting the nation from catastrophic terrorism,” said Lewis M. Branscomb (Kennedy School of Government, Harvard University), co-chair of the Committee on Science and Technology to Counter Terrorism, the NRC committee that wrote the report. “Our report gives the government a blueprint for using current technologies and creating new capabilities to reduce the likelihood of terrorist attacks and the severity of their consequences.” Dr. Branscomb’s co-chair was Dr. Richard Klausner, former director of the National Cancer Institute and currently with the Bill and Melinda Gates Foundation.

The report discusses certain actions that can be taken now to make the nation safer: protect and control nuclear weapons and material, produce sufficient supplies of vaccines and antibodies, secure shipping containers and power grids, and improve ventilation systems and emergency communications. The report offers dozens of specific recommendations on research and development activities that can lead to technologies with the potential for lessening vulnerabilities to terrorism.

For example, advances in biology and medicine can make it possible to produce drugs to fight pathogens for which there are no current treatments. New approaches to making electric-power grids intelligent and adaptive can make them much less vulnerable to attack, allowing power to be preserved for critical services such as communication and transportation. New computer programs for data-mining and information fusion can make it much easier to “connect the dots” among apparently unrelated fragments of intelligence information and to combine sensor readings to allow rapid detection of toxic agents and other threats.

Research also can lead to new emergency equipment, such as better protective gear for rescue workers and sensors to alert them to radiological or chemical contamination and other hazards when they enter a disaster area. Buildings can be made more blast and fire resistant than they are today with improved design standards, and new methods for air filtration and decontamination can lessen casualties from certain types of attacks and greatly speed up recovery.

“These opportunities will go unrealized unless the government is able to establish and execute a coherent strategy for taking advantage of the nation’s scientific and technical capabilities,” added Dr. Klausner. “The federal agencies with science and engineering expertise are not necessarily the same as the agencies responsible for deploying systems to protect the nation, and they all must work together to discover and implement the best counterterrorism technologies.”

The White House Office of Homeland Security is currently responsible for setting a national counterterrorism strategy and coordinating relevant programs. To help determine priorities and create an effective technical strategy, the Office of Homeland Security should establish a new Homeland Security Institute comprised of experts who can analyze vulnerabilities in critical infrastructures and evaluate the effectiveness of systems deployed to reduce them, the committee said. This should include “red teaming” exercises where institute personnel play the role of terrorists to discover weaknesses in U.S. defenses. The institute should be a not-for-profit, contractor-operated organization staffed with people experienced in analyzing complex systems and responding quickly to requests for advice from senior government officials.

The report also recommends that the new Department of Homeland Security, as proposed by President Bush, will need an undersecretary for technology to coordinate science and technology programs within the department and to keep it connected to research-oriented agencies such as the National Science Foundation, National Institutes of Health, Department of Energy, and Department of Defense, as well as the White House’s Office of Science and Technology Policy. The Homeland Security Institute proposed by the committee should support the undersecr-
Technology in War on Terrorism

In a shift that tacitly acknowledges that he lacks the votes, Senator Sam Brownback (R-KS) has scaled back his original proposal to ban all forms of human cloning, and is now talking up the idea of a two-year moratorium.

He also backed out of negotiations with the Senate leadership over how to bring his bill, S.1899, to the Senate floor. Efforts to reach a unanimous consent agreement on the procedure to bring his bill to the floor collapsed in mid-June. Senator Brownback has rejected a proposal to begin debate on his bill collapsed, he tried to amend a bill on terrorism insurance by offering an unrelated amendment dealing with clone patenting. The Senate, after some debate, voted to invoke cloture on the bill. When cloture is invoked, only amendments related directly to the substance of the bill are permitted for consideration. The invocation of cloture was seen as a direct rejection of Senator Brownback's efforts.

Regarding the moratorium, on June 14 ASBMB wrote a letter to Senator Daschle opposing this proposal. The letter can be read in its entirety on the ASBMB website; to find it, click on the link to the public affairs page, then click on “policy statements,” then scroll down to “human cloning.”

The letter notes four objections to a moratorium:

◆ A two-year moratorium puts potentially life-saving breakthroughs further out of reach and may literally mean the difference between life and death for many patients.

◆ A moratorium would delay development of the science behind stem cells. Scientists will be diverted from conducting needed research and, while the moratorium is in effect, new scientists cannot be trained. If the moratorium is ever lifted, rebuilding our research capability would take years. What is worse, the whole field may become stigmatized so that researchers would be reluctant to return to it.

◆ A moratorium, like a permanent ban, will continue to cause private companies to locate “off shore,” and more U.S. scientists will leave and set up research labs overseas.

◆ A moratorium is a ban by any other name. Congress could easily extend it, without debate, much as the “one-year” ban on federal funding for embryo research is extended each year in the Labor-HHS appropriations bill. In short, a moratorium is nothing more than a permanent ban disguised.
Continuing its tradition of strong advocacy for the National Science Foundation, ASBMB urged the Senate to adopt a plan to double the NSF over five years, similar to legislation that has passed the House of Representatives.

In a June 17 letter to the chairs and ranking members of the Senate Committees on Health, Education, Labor and Pensions; and on Commerce, Science and Transportation, then-ASBMB President Robert Wells noted that “We [ASBMB] have long advocated the view that NSF needs and deserves a vastly increased share of federal resources, and explicitly endorsed doubling the agency’s budget over two years ago ...”

“We note that the House of Representatives recently passed H.R.4664, an NSF authorization bill with 15 percent increases authorized in each of the three years of the bill’s duration. ASBMB endorsed this bill when it was introduced in early May, along with about 50 other scientific societies” (editor’s note: see article in ASBMB Today, July 2002). “We believe the bill sets an excellent general direction for NSF during the authorization process, and hope that the Senate bill takes a similar if not even more generous approach ....”

“Specifically, ASBMB supports at least a 15 percent increase in the NSF budget in FY 2003, with similarly-sized increases in each of the next four years. A 15 percent increase this year would mean an increase of about $720 million, to a total of $5.5 billion for FY 2003 ....”

Dr. Wells also said that most of this new money should be spent on NSF’s basic research programs and that there should be a major increase in the average size and duration of NSF grants, as well as funding for more of the most meritorious yet currently unfunded proposals.

After years of lip service but erratic financial support in both the House and Senate—especially when compared to the strong support enjoyed by the National Institutes of Health—NSF is beginning to enjoy a resurgence of interest this year. The House authorization bill, H.R.4664, passed overwhelmingly in June 2002, and prospects for a similar Senate bill seem bright. NSF legislation is being developed that the scientific community “will be really pleased with,” according to a Senate source familiar with the draft bill. Reportedly, the bill commits to a doubling of the NSF budget over five years.

All senators present at a recent hearing on NSF were very supportive of the agency, and the support appears to be both broad and bipartisan. The major issue at this point appears to be time—is there enough of it to pass an NSF bill before the end of the session? Congress will be taking the entire month of August off, and when it returns after Labor Day, there will be only a month left before the beginning of the new fiscal year. In addition, there will be elections this November, and Congress is unlikely to want to linger much into October, particularly with control of the House and Senate being held by such small—and vulnerable—majorities.

ASBMB Welcomes New Ph.D.’s

ASBMB extends its congratulations to these individuals who recently received their Ph.D. degrees. In recognition of their achievement, ASBMB is presenting them with a free one-year membership in the Society. The new Ph.D.’s are listed below with the institution from which they received their degree.

Vijay S. Anandavijayan,
University of Aberdeen

Cheryl L. Baird,
University of Utah

Sapna Mani Chacko,
University of Texas Health Sciences Center

Matthew J. Gage,
Purdue University

Weston R. Gould,
University of Vermont College of Medicine

Michael C. Kersting,
Mississippi State University

Douglas P. Lee,
University of Manitoba

Herbert L. Ley III,
University of Utah

Joseph N. McLaughlin,
Brigham Young University

Maria-Patricia Molina,
City University of New York

Stephen C. Parnell,
University of North Carolina, Chapel Hill

Roopali Roy,
Harvard Medical School

Travis H. Tani,
University of Michigan

DongYan Zhang,
City University of New York
House/Senate Differences Make Rocky Appropriations Process Likely

By Peter Farnham, CAE, Public Affairs Officer

Widely disparate totals for key domestic spending bills indicate that the appropriations process this year is going to be very contentious, with resolutions of the differences in key science-funding bills likely to be delayed until the very end of the year.

Both the House and Senate appropriations committees have completed their so-called 302(b) allocations of domestic discretionary spending for FY 2003. This arcane but very important step helps determine how much money each federal agency will have to spend in the coming fiscal year.

Federal spending is divided into two broad categories—spending that is required by law and thus must be appropriated, and discretionary spending, which Congress decides how to spend. Approximately one-third of the annual federal budget is discretionary spending. The total for discretionary spending each year is set by the congressionally-approved annual budget resolution. This broad discretionary total is then divided up among the 13 subcommittees of the appropriations committee in each house. The term “302B allocation” refers to the section of the Budget Act describing how these allocations are made.

Unfortunately, no budget resolution has been approved this year, so both House and Senate appropriations committees have developed their own discretionary allocations. This has resulted in a Senate total for discretionary spending that is over $11 billion more than the House, including $2.2 billion in “emergency funds” spread over three Senate subcommittees. The different totals, as well as major differences between the internal allocations for certain key funding subcommittees, are sure to generate fireworks over the summer and fall.

For example, the Senate total for the Labor/HHS/Education bill (out of which the National Institutes of Health is funded) is some $4.4 billion more than the House figure. The Senate total for the VA/HUD bill (out of which the National Science Foundation is funded) is some $1 billion higher than the House figure, once $1.5 billion in emergency spending is factored in. A congressional staff member told ASBMB Today that the VA/HUD Subcommittee allocation is so low that the appropriations process “can’t even get started,” and that the allocation was certain to be adjusted.

NIH spending is probably not going to be an item of contention in the final negotiations over the Labor/HHS bill, but any volatile situation involving this bill is a cause for watchful concern in our community.

The VA/HUD bill is more problematical—NSF has never had the support in Congress that NIH has enjoyed (although this may be changing; see story on page 18). In addition, the bills may well get caught up in election year politics. Control of Congress is at stake, with only a six-seat difference between the Republicans and the Democrats in the House, and an even slimmer, one-vote majority for the Democrats in the Senate. Labor/HHS and VA/HUD are the two largest domestic spending bills, accounting for about $225 billion between them. Many politically contentious spending programs beyond science funding are affected by even minor changes in spending in these bills.

Below is a table showing the House and Senate allocations for the 13 appropriations bills, as well as what the President had requested.

### 302b ALLOCATIONS, FY 2003 APPROPRIATIONS BILLS

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<th>House</th>
<th>Senate</th>
<th>President</th>
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<td>Agriculture</td>
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<td>Commerce/Justice/State</td>
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<td>133.99**</td>
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<tr>
<td>VA/HUD/Independent Agencies</td>
<td>91.8</td>
<td>91.4***</td>
<td>92.5</td>
</tr>
<tr>
<td><strong>TOTAL:</strong></td>
<td>748.037</td>
<td>759.867</td>
<td>748.129</td>
</tr>
</tbody>
</table>

*Plus $400 million in emergency funds  **Plus $300 million in emergency funds  ***Plus $1.5 billion in emergency funds
Digital Library Efforts Unveiled

The ASBMB recently unveiled plans to create a peer-reviewed biochemistry and molecular biology digital library. The efforts were discussed in a symposium entitled, “Digital Libraries and Publishing in the Electronic Age” at the Experimental Biology 2002 Meeting in New Orleans. Dr. Marion O’Leary, chairman of the ASBMB Education and Professional Development Committee, moderated the session.

The first speaker of the session was Yolanda George, Deputy Director of Education at AAAS, representing the BioSciEdNet (BEN) collaborative. Ms. George described the history and goals of the collaborative. BEN has 11 member organizations, including ASBMB, and is supported by the National Science Foundation. Its goal is to provide a web portal to a wide variety of resources for biology educators. Its current collections are organized in a Multimedia Auditorium (dynamic and interactive resources), Reading Room (articles, brochures, books), Reference Room (data sets, bibliographies and manuals) and Classroom (pedagogical tools).

The BEN portal provides access to a collection of 680 resources covering 46 biological sciences topics and 25 different resources types ranging from journal articles to simulations from the American Physiological Society, American Society for Microbiology, and Ecological Society of America. By October 2002, 300 additional resources will be available and additional partner sites will connect to the portal including Access Excellence, National Association of Biology Teachers, Science’s Signal Transduction Knowledge Environment, and the Society of Toxicology. With the addition of 2,500 resources over the next two years, the size of the BEN biological sciences collection is expected to grow significantly to fill in the current content gaps.

In addition to the need to collect and review educational materials, BEN has focused on establishing standards for organizing the data and making it available for searching by establishing a series of metatags for different data types. Ms. George also included details on the pioneering efforts of the educators in the American Society for Microbiology, a member of BEN, in developing their digital library (http://www.microbelibrary.org).

Dr. Paul Craig, currently at the San Diego Supercomputer Center on sabbatical from the Rochester Institute of Technology, spoke briefly about the genesis of a digital library within ASBMB as a component of the BEN collaborative. A group of biochemistry and molecular biology educators led by Donald and Judith Voet, co-editors of Biochemistry and Molecular Biology Education (BAMBED) met in March to begin the planning process for the ASBMB Digital Library.

The group also met with Yolanda George (BEN/AAAS), Dr. Terry Woodin (NSF), and Amy Chang (Director, ASM Education Department) to learn more about the BEN collaborative, the NSF

Meeting Focuses on Need for Diversity in Science

A session entitled “Under-representation of Minorities in Science: Can the Pipeline be Fixed?” sponsored by the ASBMB Minority Affairs Committee, was held at this year’s ASBMB Annual Meeting held in conjunction with EB 2002. The session was chaired by Drs. Phil Ortiz and Thomas Landefeld. Following introductory remarks by Dr. Ortiz, the following presentations were made:

- “Attrition of pre-college minority students: stopping the hemorrhage” by Dr. George Negrete from UT-San Antonio;
- “Are faculty fixing the leaks in the pipeline or creating them?” by Dr. Thomas Landefeld from CSU Dominguez Hills;
- “Fixing the leaky pipeline: the role of HBCUs” by Dr. Juliette Bell from Fayetteville State University; and
- “Is there a role for scientific societies in staunching the pipeline?” by Dr. Maria Zavala from CSU Northridge.

The session addressed the problems associated with the efforts to increase the number of minority students both entering and remaining in science. The leaks in the pipeline occur at various sites in the overall process, from pre-college, to admissions, to retention and graduation, through faculty recruitment, appointments and tenure. The session was well attended, the presentations stimulated lively participation from the audience, including references to experiences of individuals as well as suggested ways to address the problems. Plans are underway to make the presentations available, perhaps on the ASBMB website.

This represented the fifth consecutive year when there has been a session at the ASBMB meeting focusing on the important issue of diversity in science.
granting process, and the growing pains other digital libraries have already experienced. The group outlined a tentative organization for this digital library consisting of five divisions: software, visual collections (images, videos, animations, molecular visualizations), curriculum (classroom and laboratory resources, case studies and assessment tools), journal articles (direct links to ASBMB Today and Biochemistry and Molecular Biology Education articles were proposed), and reviews (books, videos, CD-ROM’s, software and websites).

Dr. Craig is heading the initial technical planning for the digital library. Members of the group will comprise the editorial board and will work towards establishing the review process, submission guidelines and evaluation of existing resources. Additional volunteers will be needed as board members once the initial groundwork is laid. The end result of the weekend meeting was a grant request submitted to AAAS to be included in the overall NSF grant request by the BEN collaborative.

The digital library will be managed by the ASBMB, under the supervision of the Education and Professional Development Committee. The purpose of the proposed digital library is to provide an electronically accessible repository of high quality, peer-reviewed instructional materials to be used primarily by educators at the undergraduate, graduate and medical school levels to augment classroom, laboratory and independent learning.

Dr. Craig’s expertise will be valuable to the effort. He enjoys working at the interface between biochemistry and computers. At the Annual Meeting he also described Bioeditor, a software tool designed for annotating macromolecular structures. With Bioeditor a student or teacher can collect text, graphics, web pages, structure and sequence data in a single location. The data can then be incorporated in topics, which can then be opened with Bioeditor or Bioviewer (a read-only version of Bioeditor), or they can be published to a series of web pages.

Bioeditor also uses the Chime plug-in, which enables the user to create animated molecular views. Bioeditor has been written using Visual Basic for the Windows environment; files are saved in an XML format. Two different ideas lead to the development of Bioeditor: a desire to simplify the process of creating animated structure documentaries, so that students and teachers could use the power of the computer without having to learn HTML and/or Javascript, and an effort to reduce the dependence of structure documentaries on available web browsers.
Biotech Funding Plummeted but Despite Downturn 2001 Was Still Second-Best Year on Record

ew financing for U.S. biotechnology companies almost disappeared in 2001, falling 76% below the preceding year, but 2001 was still the second best year on record for biotech financing.

That seeming contradiction was the finding of consulting firm Ernst & Young’s annual report on the industry, which was released in June at the Biotechnology Industry Organization’s annual convention.

According to Ernst & Young, what may have been a collapse for some was a very good year for others. While many startups and small firms have found it hard to get financing, higher-profile companies that had been the favorites of investors when the market was booming tend to be in much better financial shape today.

Ernst & Young partner Chris Nolet said financing in 2001 could best be interpreted as “the after-effects of 2000,” which he called a “breathtaking” year for the industry. However, the bubble burst in the latter part of 2000 as investors fretted about the years of research before many biotech products will enter the market.

At the same time, he said, the financing drought is heightening a longstanding divide between the industry’s most prominent companies and its younger, leaner small fry. Many of the former are sitting pretty. Their stocks may be trading down drastically from a year or two ago, but successful financings in 2000 gave them enough cash to weather a long dry spell. Human Genome Sciences Inc. and Celera Genomics Corp., for example, each have $1 billion or more on hand.

In 1999, only 25% of the companies examined had five or more years of cash. While that figure has risen to 43%, a third of all biotech companies have less than two years of cash on hand, and many of these may have difficulty raising more in the present climate.

Hybrid Magnet Boosts Genomic Sequencing Rates

The University of California’s Berkeley Lab researchers have developed a powerful magnet that obtains DNA samples much faster than commercially available magnetic plates. The magnet, the result of more than a decade of research that led to the development of particle accelerator magnets, can be applied to several emerging biotechnology fields. In addition to gene sequencing, it can be used in the study of what genes do. It can also be used in proteomics, which is the study of how proteins both activate and function in organisms.

Drug Development Network Urged for Europe

European researchers are being rallied to join a collaborative effort to exploit the recently published *Streptomyces coelicolor* genome. Plans for the ambitious program, to knock out every gene in this, the largest bacterial genome ever sequenced, are being hatched by researchers in Britain, who now find themselves in disarray over funding confusion.

Geneticists, microbiologists, and chemists in the UK are poised to begin work on the “Streptomyces Genome Initiative,” a £1.6 million ($2.3 million) project funded by the government’s Biotechnology and Biological Sciences Research Council (BBSRC).

Grant coordinator Mark Buttner, a project leader at the John Innes Centre (JIC) in Norwich, says the goal of the BBSRC project “is to use *S. coeli-

color* as a model for the exploitation of a genome with end-users in mind.”

Nearly 70% of all antibiotics are derived from *S. coelicolor* and its close relatives, the actinomycetes, says Buttner, so the project’s focus is firmly on the production of antibiotics and other secondary metabolites.
Scotland Woos Venture Capitalists With $28 Million Fund

Scotland, long known for enterprise and technical innovation, is pushing to develop activity in such areas as biotechnology, optoelectronics, microelectronics, and nanotechnology. Creation of the Scottish Parliament in 1997 has fostered a stronger impetus for Scottish-based investment initiatives. These efforts are under the jurisdiction of Scottish Enterprise, Scotland's national economic development agency. Scottish Enterprise’s $40 million Proof of Concept Fund has supported more than 40 commercial projects during the last two years.

Clive Reeves, research and development manager for microelectronics at Scottish Enterprise, says that Scottish Enterprise’s efforts have coincided with a growing awareness among venture capitalists and multinational corporations of Scotland’s potential. “It’s actually a coming together of mind-sets,” he said. The most successful projects, he believes, will be those that offer innovation while meeting a market need.

Scottish Enterprise’s about $43 million Proof of Concept Fund supports a project only to the point where it is ready to be commercialized. The reason for this cautious approach is to avoid disrupting established markets. “Scientists,” says Reeves, “tend to drop an idea before the commercial opportunity has been explored, and they move to the next thing that’s going to take them closer to their Nobel Prize.”

Celera Slashes 16 Percent of Work Force in Restructuring

Celera Genomics announced plans to cut 132 jobs, 16% of its work force, as the company best known for sequencing the human genetic code continues to move from selling genetic data to drug development.

Most of the jobs slated for elimination are in the company’s DNA sequencing and online genetic information service, the core business that Celera was founded on four years ago.

“This is really to focus the organization behind our drug discovery business,” said Celera spokesman Rob Bennett.

Philadelphia Pushing to Become Nanotech Center

A coalition led by Drexel University, the University of Pennsylvania, and Ben Franklin Technology Partners-Southeastern Pennsylvania recently received the second installment of its $10.5 million, three-year grant to establish a Nanotechnology Institute in the area. These institutions have also joined with Cheney University of Pennsylvania and Wilkes University in applying to the National Science Foundation for a $17.5 million, five-year grant to establish a center for nanotechnology work on intelligent platforms for tissue engineering and drug delivery.

David E. Luzzi, a materials science professor at Penn who co-directs the institute, says its goal is to coordinate the region’s academic and research strengths to make it a center for nanotechnology; become self-sustaining by helping area institutions pull in research dollars; and boost the number of nanotech jobs in the area.

The nascent company’s existence, and the creation of future companies from the institute, are the result of a new approach by Penn to intellectual property. Historically, the school has relied strongly on licensing, which works well with pharmaceutical products that produce a constant stream of money over a long period of time. To deal with other types of technology, said Luzzi, the university “needs to be flexible enough to do licensing where appropriate and spin out entities” in which it takes an equity stake.

The institute is also interested in training nanotech researchers and employees for the future. That’s why it raised $1.32 million to develop associate degree programs in nanotechnology at community colleges in Pennsylvania, New Jersey, Delaware and Maryland. “The goal is to create a nanobiotechnician,” explained Luzzi.
Calendar of Scientific Meetings

**SEPTEMBER 2002**

5th Siena Meeting “From Genome to Proteome: Functional Proteomics”
September 2–5 • Siena, Italy
Contact: Denis Hochstrasser; Email: pallini@mailsrv.unisi.it
http://www.unisi.it/eventi/proteome

Computational Biophysics:
Integrating Theoretical Physics and Biology
September 7-12 • San Feliu de Guixols, Spain
Contact: Dr. J. Hendekovic, European Science Foundation
Ph. +33 388 76 71 35; Fx. +33 388 36 69 87,
Email: euresco@esf.org

14th Meeting Methods of Protein Structure Analysis
September 8–12 • Valencia, Spain
Contact: Juan J. Calvete; http://www.mpsa2002.ibv.csic.es/
Email: mpsa2002@ibv.csic.es

Fostering Integrity in Clinical Research At Academic Medical Centers
September 9-10 • Baltimore, Maryland
Contact: Tracy Morgan; Ph: 301-443-5330; Fx: 301-594-0039,
Email: tmorgan@osohs.dhhs.gov.

Molecular Targets for Dietary Intervention in Disease
September 19-22 • Iowa State University, Ames, Iowa
Contact: Growth Factor and Signal Transduction Conferences
Ph: 515-294-7978; Fx: 515-294-2244; Email: gfst@iastate.edu;
Website: http://molebio.iastate.edu

7th International Symposium on Dendritic Cells
September 19-24 • Bamberg, Germany
Contact: Prof. Dr. Alexander Steinkasserer
Ph: ++49-9131-853-6725; Fx: ++49-9131-853-5799;
Email: steinkasserer@derma.imed.uni-erlangen.de
Website: http://www.dc2002.de/

American Society for Bone and Mineral Research
24th Annual Meeting
September 20-24 • San Antonio, Texas
Contact: ASBMR Business Office
Ph: 202-367-1161; Fx: 202-367-2161;
Email: ASBMB@dc.sba.com; Website: http://asbmr.org

The Role of Institutional Rules, Guidelines, and Education in Promoting the Responsible Conduct of Research
September 23-24 • Philadelphia, PA
Website: http://www.rowsciences.com/ORIconference/home.html

**OCTOBER 2002**

European Conference on Computational Biology 2002
in conjunction with the German Conference on Bioinformatics 2002
October 6-9 • Saarbruecken, Germany
Contact: http://www.eccb2002.de
Email: eccb.organizers@bioinf.uni-sb.de

Metabolic Engineering IV: Applied System Biology
October 6-11 • Il Ciocco, Castelvecchio Pascoli Tuscany, Italy
Contact: United Engineering Foundation; Ph: 212-591-7836
Fx: 212-591-7441; Email: engfnd@aol.com
Website: http://www.engfnd.org
Registration: http://www.engfnd.org/2ay.html

9th Midwest Platelet and Vascular Biology Conference
October 11-13 • Washington University School of Medicine,
St. Louis, MO
Abstract and registration due August 15, 2002
Website: http://www.biochem.wustl.edu/mwpc9/index.html

Federation of Analytical Chemistry and Spectroscopy Societies
October 13–17 • Providence, Rhode Island
Contact: FACS National Office; http://www.facss.org

The 18th International Conference on Arginine and Pyrimidines
October 13-17 • Giza, Cairo, Egypt
Biennial conference on all aspects of biochemistry and genetics of uptake and metabolism of arginine and pyrimidines.
Contact: Ahmed T. Abdelal, Georgia State University
Email: aabdelal@gsu.edu; Website: http://www.cas.gsu.edu/icap

The Applications of Proteomics
October 16–18 • Lille-Villeneuve d’Ascq, France
Contact: French Society for Electrophoresis and Proteomic Analysis; Tel.: 33-3-20-43-40-97; http://www.sfe-ices.org/
Email: hubert.hondermarck@univ-lille1.fr

18th Asilomar Conference on Mass Spectrometry
October 18–22 • Asilomar, Pacific Grove, CA
Contact: American Society for Mass Spectrometry
http://www.asms.org; Email: office@asms.org; Tel.: 505-989-4517

Fourth HUGO Pacific Meeting and Fifth Asia-Pacific Conference on Human Genetics
October 27–30 • Pattaya, Chonburl, Thailand
Contact: Tel.: 66-2-8892557-8; http://www.mu-st.net/hugothai/
Department Heads Take Note:

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