RANDOM SAMPLES

edited by CONSTANCE HOLDEN

Jewish Breast Cancer Gene?

Lending support to observations that Jewish women may be more vulnerable to breast cancer, new research has found that 1 in 100 Ashkenazi Jews carry a particular mutation in *BRCA1*. Defective versions of this gene have been linked to breast and ovarian cancer. The new finding, to be reported in next month's *Nature Genetics*, means large-scale cancer-susceptibility screening is now feasible for the first time.

In the population at large, as few as 1 in 800 people carry one of over 60 different *BRCA1* mutations. But the researchers, led by Lawrence Brody of the National Center for Human Genome Research, report that when they screened the blood of 858 Ashkenazim who were being checked for cystic fibrosis or Tay-Sachs genes, they found that 1% showed a single *BRCA1* mutation.

Assuming that mutation carries a 90% risk of cancer—a rough estimate from studies of all the *BRCA1* mutations—it could account for 16% of breast cancers and 39% of ovarian cancers in Jewish women of Eastern European descent under 50. (In non-Ashkenazim, all the mutations combined cause only 4.1% of breast cancers and 12% of ovarian cancers.) "We can safely say that the frequency of this mutation is higher in the Ashkenazi population than [are] all the *BRCA1* mutations together in the general population," says genetic epidemiologist David Goldgar of the University of Utah, Salt Lake City.

When gene hunters discovered *BRCA1* a year ago (*Science*, 23 September 1994, p. 1796), they found over 60 mutations. That meant widespread screening was unfeasible because every mutation has to be specifically targeted. The new finding means screening for breast cancer susceptibility is possible for 5.5 million Ashkenazi Jewish women around the world, half of whom are in the United States. The researchers, however, are preaching caution.

"We've never screened a population for an adult-onset disease on this scale before," worries Brody. And even if there were enough genetic counselors to help people interpret the information, "we don't know what intervention we should offer. Increased surveillance is one option; prophylactic mastectomy is another. But we don't know whether either is effective."

Lasker Honors T Cell Pioneers

Five scientists whose research helped to solve a basic question in immunology—how T cells recognize foreign proteins—share the 1995 Albert Lasker award for basic medical research, presented on 25 September.

Emil R. Unanue

Together, says Yale immunobiologist Charles Janeway, the winners "defined the state of the field in T cell response." Emil Unanue, chair of the Department of Pathology at Washington University School of Medicine in St. Louis, discovered that scavenger cells called macrophages break down foreign proteins and display fragments on their cell membrane for helper T cells. These cells then trigger an immune response to these fragments, or antigens. Peter Doherty, chair of the Department of Immunology at St. Jude's Children's Research Hospital in Memphis, Tennessee, and Rolf Zinkernagel, director of the Institute of Experimental Immunology at the University of Zurich, Switzerland, established that such T cells recognize the antigen because it is combined with a "self-protein" unique to each mouse strain. Biochemists Jack Strominger and Don Wiley of Harvard University used crystallography to describe the atomic structure of the complex that comprises the self-protein molecule (major histocompatibility complex) and the protein fragments.

Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, says, "It's nice to see them honored as a group for their related achievements." Each winner receives $10,000.

Lady in Amber

This 30-odd-million-year-old damselfly, a relative of the dragonfly, trapped in Dominican amber is one of the stars of an unusual exhibit to open in February 1996 at New York's American Museum of Natural History. Billed as "the most comprehensive exhibition about amber ever mounted," it features about 70 fossil pieces and 60 carved objects. Entomologist David Grimaldi, the exhibit's organizer, calls amber "a completely unique fossil substance." Ironically, he says, resin, which scientists believe trees make as a barrier against insects, has turned out to be "by far the best preserver" of ancient insects. The oldest amber, which takes hundreds of thousands of years to be polymerized from resin, dates from the Lower Cretaceous era 130 million years ago. Grimaldi says amber deposits are still being discovered—including a "very significant deposit" currently being excavated at an undisclosed location in central New Jersey.

AMERICAN MUSEUM OF NATURAL HISTORY

Potential Animal Model For AIDS

AIDS researchers, frustrated in their search for an effective treatment, recently have made headway by heeding an old adage: If you can't beat 'em, join 'em. Combining parts of HIV, the human AIDS virus, with its simian cousin SIV, researchers have developed a virus that could become part of a powerful new monkey model for AIDS drug testing.

HIV-1, the main type of human AIDS virus, is harmless to other animals. The lack of an HIV-1 animal model has hampered attempts to test drugs and vaccines. Over the past 3 years, scientists have been exploring the possibility of hybridizing HIV with SIV. These "SHIVs" should retain enough SIV to make a monkey sick and enough HIV to address specific research questions (*Science*, 24 July 1992, p. 478). But so far, SHIVs have yet to cause disease in monkeys. Now, Klaus Überla of Germany's University of Erlangen-Nürnberg and co-workers have moved the idea closer to reality.

While working in the lab of virologist Joseph Sodroski at Boston's Dana-Farber Cancer Institute, Überla replaced the SIV gene for reverse transcriptase (RT)—an enzyme the virus needs to copy itself—with the RT gene from HIV-1. As the researchers report in the 29 August *Proceedings of the National Academy of Sciences*, this so-called "RT-SHIV" can copy itself. More importantly, the scientists have shown in a small number of monkeys that the RT-SHIV can cause AIDS and thus may be a new tool for testing drugs, such as AZT, that inhibit RT's action.

In addition to evaluating drugs that target RT, Sodroski envisages using the model for other approaches, such as combining monoclonal antibodies directed against HIV with the RT inhibitors. He also hopes SHIVs can be developed that include other HIV genes, such as the one for

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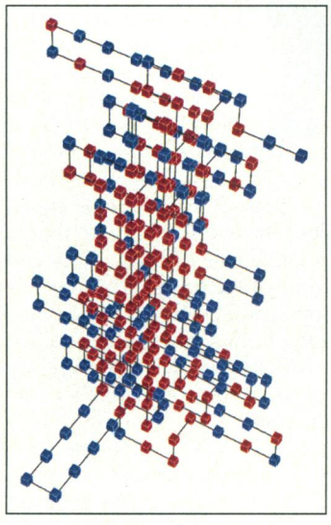
protease, which is the target of promising state-of-the-art drugs. "As your model gets better and more HIV-1–like and the number of agents increase, people will use the models more," Sodroski predicts.

Primate AIDS researchers are impressed by the work. "I think it's wonderful," says Michael Murphey-Corb of the Tulane Regional Primate Research Center. "We really do need this." Murray Gardner of the California Regional Primate Research Center says this is the first documented evidence that SHIVs can produce disease. RT-SHIV may "open the door" to using monkeys to test new AIDS drugs, especially in combination, he says. "Now everything just goes into humans willy-nilly."

Folding Proteins Fast

"The single problem [in biology] with the very largest payoff at this point," says George Rose, a biophysical chemist at Johns Hopkins University, "is a practical way to predict protein structure from amino acid sequence." Now a team from Sandia National Laboratories in New Mexico has an algorithm that may come close to hitting pay dirt.



SANDIA NATIONAL LABS

Fast fold. Computer model for protein triosphosphate isomerase, determined from its amino acid sequence in less than a second. Red and blue boxes are water-hating and -loving amino acids.

Proteins can be composed of sequences of hundreds of amino acids, yet protein function seems to be determined in large part by how those sequences fold up into biologically active conformations. And the number of ways a string of amino acids can be folded is "astronomical," says molecular biologist Jonathan King of the Massachusetts Institute of Technology.

Therefore, several groups are working on algorithms that for the first time will make it possible to predict protein structure—and do it fast—using a computer. Rose, who published the first such algorithm last winter, and Ken Dill, head of the Center for Statistical Physics of Macromolecules at the University of California, San Francisco, have both been working on algorithms that have reduced the time it takes to sort out the structure of small proteins to days or weeks.

But perhaps the most intriguing algorithm comes from mathematicians Sorin Istrail and William Hart at Sandia, who have combined their mathematics with Dill's biological model of protein folding to create an algorithm that may turn out to be several orders of magnitude faster than the competition. The algorithm goes about finding a protein's ultimate shape by finding the minimum energy state of the molecule. It does that by doing what proteins do: first making a big fold in the amino acid chain, which is equivalent to the protein collapsing on itself. It then assumes that hydrophobic amino acids, which dislike water, will migrate toward the center of this fold. There they will join with other hydrophobic amino acids. This stabilizes the protein.

The Sandia algorithm, says Dill, has not yet been validated by testing on proteins with known conformation. But he calls it "a very nice step forward in the computerology of proteins."

Shrinking National Labs

As Congress continues to hammer out a thinner budget for the Department of Energy for fiscal year 1996, most of the nine major DOE labs have reported recent or imminent layoffs. The labs are moving to show they can reform themselves as members of the House Science Committee contemplate measures such as consolidating labs or limiting the kinds of research they do (*Science*, 15 September, p. 1510).

The latest big hit came on 13 September at Los Alamos National Laboratory, when it announced the layoff of 781 employees. About 83% of the jobs cut were support positions; the rest were scientific or technical. The objective, says Los Alamos spokesperson James Danneskiold, is to increase productivity in relation to expenditures by raising the ratio of scientists and technicians to administrative and support staff.

Personnel layoffs and attrition to date:

- Pacific Northwest National Laboratory—About 900 positions, mostly support staff, were eliminated earlier this year.
- Brookhaven National Laboratory—90 employees throughout the lab will be laid off before November.
- Idaho National Laboratory—1250 positions were eliminated a year ago; no further layoffs are planned.
- Sandia National Laboratory—plans to lose about 600 positions from retirement and normal attrition between now and October 1997.
- Argonne National Laboratory—195 positions eliminated last year, 102 through early retirement.
- Lawrence Berkeley National Laboratory—150 support positions were cut in August, and about 13 additional layoffs were announced on 20 September.
- Lawrence Livermore National Laboratory—Staff has been reduced by 15% in the past few years.
- Oak Ridge National Laboratory—22 layoffs this summer from research and support positions.

Materials Science—Live on the Net

Why isn't there more good course software available on the Internet? Materials scientist John Russ and his students at North Carolina State University know one reason: Putting it on-line takes a huge amount of work. It's taken Russ 5 years, with student help, to develop an electronic version of an entire first-year undergraduate materials science course.

The course, "Visualizations in Materials Science (VIMS II)" makes for a giant Web site: **http://vims.ncsu.edu**. Each of the 20 on-line chapters has interactive exercises and illustrative materials, including videos, animated simulations, graphs, diagrams, cartoons, and photos. In the chapter on "nucleation and growth," for example, one can watch a microscope's view of ice dendrites forming in water. The chapter on "ferrous alloys" has a 23-part video tour of the NuCor steel plant in Darlington, South Carolina, complete with sound for those with the right software. "In the science area I'm not aware of anything this complete on the Internet," says Russ. In the past few weeks, he says, "we've had people coming in from literally all over the world using it—[there have been] about 12,000 hits a week on it."

Russ began the project in 1990, developing computer graphics and animations to supplement his teaching. With funding from the National Science Foundation, he turned these graphics into a CD-ROM to accompany the course. Last month, concerned that many people don't have access to CD-ROM players, Russ put the course on the Internet.

"People like John Russ are really ahead of the pack," says engineer Mark DeGuire of Case Western Reserve University. James Wittig, associate professor of materials science at Vanderbilt University, who has used the CD-ROM with his students, notes that most professors simply do not have the time or the resources to do what Russ did. More such courses will require collaboration by "faculty with similar interests from different universities," he says.