IL-12, which will probably take place "at two sites," according to a company spokesman.

If the results in HIV research are intriguing, those involving IL-12 and cancer are dramatic. Researchers continue to be surprised at how broad a range of antitumor activity IL-12 shows in preclinical studies. Michael Brunda of Hoffmann-La Roche, whose group reported the first such results last October, summarized the data by saying that IL-12 "appears to have activity against a widespread group of tumors," including renal cell carcinoma, melanoma, colon adenocarcinoma, and 14 other malignancies.

In a mouse model of the B16F16 melanoma tumor, for example, Brunda has shown that researchers can wait 14 days after injecting malignant cells—by which time the subcutaneous tumors have grown larger than a centimeter in diameter—and still inhibit tumor growth with daily injections of IL-12. In a renal cell carcinoma model, direct injections of IL-12 into the tumor led to regression. "Initially we get stasis," says Brunda, "but after prolonged treatment, the tumors go away—and the animals are cured."

Michael Lotze's group at the Pittsburgh Cancer Institute has confirmed many of these results, including a systemic immune response from direct injection of IL-12 into a tumor. In a sarcoma model, where two tumors are generated on either side of a mouse, injection of IL-12 into one tumor causes both to regress. "We were astonished," says Lotze, "to see an effect on subcutaneous tumors. There are very few immunologic therapies capable of causing regression in subcutaneous tumors."

Naturally, with results like these, researchers are eager to see what will happen when IL-12 is used in human trials. Yet hovering over the question of human trials is the issue of toxicity—the issue that caused IL-2 to lose its luster. Several months ago, rumors swept the IL-12 community that primates undergoing toxicology testing at Hoffmann-La Roche had died. In fact, as Roche's Gately explained at the workshop, one of several squirrel monkeys given a maximum daily dose of 50 micrograms per kilogram of body weight experienced lethargy and pulmonary edema and had to be sacrificed; the rest seemed to tolerate that and lower doses well. The main side effect of IL-2—pulmonary edema—has not been seen in any of the mouse toxicology studies, says Gately, who adds that "we think IL-12 is not simply another IL-2."

One side effect of IL-12, however, was underplayed at the meeting: the breakup of the collaboration between Genetics Institute and Hoffmann-LaRoche. The companies cross-licensed their patents in May 1992, when it became clear they were both working on the same molecule—IL-12—under different names: Genetics Institute called it "natural killer stimulatory factor," Hoffmann-LaRoche called it "cytotoxic lymphocyte maturation factor." After the cross-licensing there was initially a remarkable openness about sharing reagents. Last year, however, this happy marriage of scientists ended in a divorce brokered by lawyers. Although the companies are circumspect about the reasons, several researchers familiar with the breakup say Hoffmann favored a conservative approach to clinical trials, while Genetics Institute was in favor of a more aggressive posture.

While most researchers agree the split has not retarded science, there were a few grumbles that the New York meeting was not as open as past conferences and that crucial antibodies are not shared as generously as when feelings were warmer. "I'm not getting those reagents," said one researcher, "which a lot of other people in this room are getting." And, as clinical trials approach, researchers are being told they must choose which company's IL-12 they plan to use. "It's like a child in a divorce," says Lotze. "You have to choose one parent, and you like them both."

Unlike participants in divorces, however, the participants here aren't wasting time on recrimination; they're too busy concentrating on the future—specifically whether the IL-12 story will turn out differently from the tale of IL-2. The answer should come soon. "The real answer to the toxicity question will come in the Phase I trial," says Trinchieri, "and that will be answered this summer."

–Stephen S. Hall

Stephen S. Hall is a writer in Brooklyn, New York.

Additional Readings

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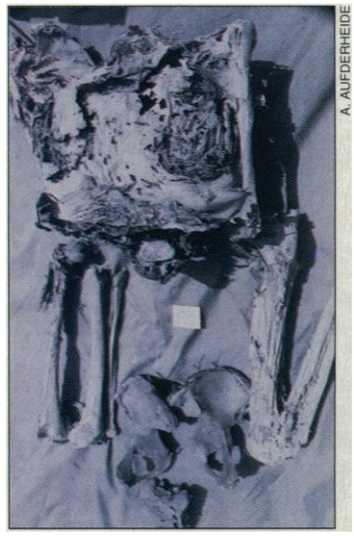
M. Kobayashi *et al.*, "Identification and Purification of Natural Killer Cell Stimulatory Factor (NKSF), a Cytokine with Multiple Biologic Effects on Human Lymphocytes," *Journal of Experimental Medicine* **170**, 827 (1989).

ANTHROPOLOGY

Mummy Settles TB Antiquity Debate

Christopher Columbus, transformed in our politically correct era from courageous hero to imperialist brute, can now be absolved of at least one sin: introducing tuberculosis (TB) to the New World. A group of scientists examining a Peruvian mummy who died 500 years before Columbus set foot on Hispaniola have found DNA specific to the TB bacteria. Their report, marking the first time DNA has been recovered from an ancient sample of a disease-causing organism, was published in the 15 March issue of the *Proceedings of the National Academy of Sciences*. And the research, utilizing the DNA-amplifying polymerase chain reaction (PCR) technique, opens a new avenue of inquiry for scientists trying to reconstruct epidemics of the past.



New World microbes. This 900-year-old mummy had TB DNA.

Previously, paleopathologists had to rely on indirect evidence of disease, such as scars on old bones. "In the past we could only formulate hypotheses about the origin and spread of many diseases," says paleopathologist and physician Bruce Rothschild, director of the Arthritis Center in Youngstown, Ohio. But the advent of PCR, which makes it possible to probe ancient tissues for specific pathogens, changes all that. "Now," says Rothschild, "we can actually go out and test" those hypotheses.

In the case of TB, the direct test solves a longstanding puzzle. Ethnohistorians had suggested Europeans brought TB with them to the New World, because American Indians began suffering devastating TB epidemics in the early 1600s, soon after major European contact began. Paleopathologists, however, had found intriguing—but indefinite—clues indicating that TB was present in the Americas prior to 1492. These clues came from pathological examinations of bone and lung lesions found in some pre-Columbian skeletons and mummies. But those hints weren't conclusive, because many infectious fungi, parasites, and other diseases can leave behind similar marks.

Pathologist Arthur C. Aufderheide of the University of Minnesota's School of Medicine saw a chance for a more definitive answer when he gained access to a 40- to 45-year-old naturally mummified woman who died about 900 years ago. She was one of the Chiribaya people, who inhabited the south coast of Peru, and her fragmented remains had been recovered from a tomb there in 1990.

Aufderheide provided samples of tissue taken from the mummy's right lung and a lymph node to his colleague Wilmar L. Salo, a molecular biologist at Minnesota. Salo removed material from cells in the sample and subjected it to PCR, searching for a segment of DNA unique to the *Mycobacterium tuberculosis* complex (four closely related bacteria, all of which can cause TB in humans). Using the modern TB microbes as a guide, he designed primers to amplify a 97 base pair (bp) sequence of IS 6110, a genetic segment found only in the TB group. Amplification of the 1000-year-old DNA produced a sequence that perfectly matches that of the modern *Mycobacterium*.

The match raises the specter of contamination by modern TB, but Peter M. Small, a molecular epidemiologist at Stanford University and an expert on modern tuberculosis, says Salo's "described attention to detail" in preparing the specimens makes this unlikely.

And the mummy's age makes transmission from European contact 400 years ago equally farfetched, Aufderheide says. His colleagues agree. "This certainly confirms how most of us were interpreting the research," says anthropologist Douglas Uberlacher of the Smithsonian Museum of Natural History. As for the post-contact TB epidemics among American Indians, Aufderheide suspects they were produced by the same forces behind TB's resurgence among homeless populations today—behavioral and environmental changes. "After the arrival of Europeans, the Indians' societies were in upheaval; they were moving away from agricultural or nomadic ways of life to reservations, where there was often crowding, malnutrition, and unsanitary conditions, all of which made people more vulnerable to the disease," he says. Ethnohistorians, too, have been coming to this conclusion, says Dean R. Snow, an ethnohistorian and archeologist at the State University of New York at Albany. "Still, it's nice to have this confirmation," he notes.

With the TB mystery now solved, Aufderheide and others think DNA from mummies and skeletons coupled with the latest PCR techniques and assays is going to have a broad impact on their science, eventually helping them to track ancient epidemics. "That's our whole goal, but we've been frustrated in the past because our techniques were really not good enough," says Aufderheide. For example, scientists couldn't determine whether a person in antiquity had died of a viral infection such as smallpox, measles, or influenza, since these diseases do not alter a skeleton's morphology. Now with PCR and a genetic sequence unique to one of these pathogens, the past lives and deaths of these diseases can be revealed.

–Virginia Morell

NAE Elects New Members

John Gibbons, President Clinton's science adviser, was recently elected to membership of the National Academy of Engineering (NAE). NAE members are elected for their "important contributions to engineering theory and practice." Gibbons, a physicist, was cited "for leadership in a broad spectrum of initiatives toward the development and communication of national policies for technological issues." He was among 79 new members and eight foreign associates whose election was announced last month.

The other new members are:

Richard E. Balzhiser, Electric Power Research Institute; **Craig R. Barrett**, Intel Corp., Chandler, AZ; **Forest Baskett III**, Silicon Graphics Computer Systems, Mountain View, CA; **David B. Bogy**, University of California, Berkeley; **John D. Bredehoeft**, U.S. Geological Survey, Menlo Park, CA; **Wilfried H. Brutsaert**, Cornell University; **John J. Cassidy**, Bechtel Corp., San Francisco, CA; **James A. Caywood III**, DeLeuw, Cather and Co., Washington, D.C.; **Don B. Chaffin**, University of Michigan, Ann Arbor; **Joseph P. Colaco**, CBM Engineers, Inc., Houston; **Donald C. Cox**, Stanford University; **Mangus George Craford**, Hewlett-Packard Co., San Jose, CA; **David N. Cutler**, Microsoft Corp., Redmond, WA; **Stephen H. Davis**, Northwestern University; **Thomas F. Donohue**, GE Aircraft Engines, Cincinnati, OH; **Lewis S. Edelheit**, GE Corporate R&D Center, Schenectady, N.Y.; **Eugene J. Fasullo**, Port Authority of New York and New Jersey; **Bruce A. Finlayson**, University of Washington, Seattle; **Essex E. Finney, Jr.**, Agricultural Research Service; **George M.C. Fisher**, Eastman Kodak Co., Rochester, N.Y.; **Marshall L. Fisher**, University of Pennsylvania; **William L. Fisher**, University of Texas, Austin; **Woodie C. Flowers**, Massachusetts Institute of Technology; **Lambert Ben Freund**, Brown University; **Renato Fuchs**, Chiron Corp., Emeryville, CA; **John L. Gidley**, John L. Gidley and Associates, Inc., Houston; **Elmer G. Gilbert**, University of Michigan, Ann Arbor; **Sidney J. Green**, TerraTek, Inc., Salt Lake City; **Robert W. Gundlach**, Xerox Corp., East Rochester, N.Y.; **George I. Haddad**, University of Michigan, Ann Arbor; **Howard L. Hartman**, consultant, Carmichael, CA; **John M. Hedgepeth**, Digisim Corp., Santa Barbara, CA; **George J. Hess**, Ingersoll Milling Machine Co., Rockford, IL; **F. Kenneth Iverson**, Nucor Corp., Charlotte, NC; **Joseph J. Jacobs**, Jacobs Engineering Group Inc., Pasadena, CA; **Marvin M. Johnson**, Phillips Petroleum Co., Bartlesville, OK; **Anita K. Jones**, U.S. Department of Defense; **Paul G. Kaminski**, Technology Strategies and Alliances, Burke, VA; **John G. Kassakian**, Massachusetts Institute of Technology; **Mark H. Kryder**, Carnegie Mellon University; **Doris Kuhlmann-Wilsdorf**, University of Virginia; **Charles R. Kurkjian**, AT&T Bell Laboratories, Murray Hill, N.J.; **Richard T. Lahey, Jr.**, Rensselaer Polytechnic Institute; **Herbert S. Levinson**, consultant, New Haven, CT; **James D. Livingston**, Massachusetts Institute of Technology; **James E. McGrath**, Virginia Polytechnic Institute and State University; **William McGuire**, Cornell University; **Angelo Miele**, Rice University; **David H. Pai**, Foster Wheeler Development Corp., Livingston, N.J.; **Paul L. Penfield, Jr.**, Massachusetts Institute of Technology; **Richard B. Priory**, Duke Power Co., Charlotte, N.C.; **Robert A. Pucel**, RCP Consultants, Needham, MA; **John R. Rice**, Purdue University; **Reuben Samuels**, Parsons Brinckerhoff, Inc., New York City; **Ronald W. Schafer**, Georgia Institute of Technology; **Gabriel Schmergel**, Genetics Institute Inc., Cambridge, MA; **Lanny D. Schmidt**, University of Minnesota; **Ronald V. Schmidt**, SynOptics Communications, Inc., Santa Clara, CA; **Walter J. Schrenk**, Dow Chemical Co., Midland, MI; **Jerome S. Schultz**, University of Pittsburgh; **Lyle H. Schwartz**, National Institute of Standards and Technology; **Robert J. Serafin**, National Center for Atmospheric Research; **Maurice M. Sevik**, Naval Surface Warfare Center, Bethesda, MD; **Michael F. Sfat**, Bio-Technical Resources, Manitowoc, WI; **Jeffrey J. Siirola**, Eastman Chemical Co., Kingsport, TN; **George F. Sowers**, Law Companies Group, Inc., Kennesaw, GA; **Joel S. Spira**, Lutron Electronics Co., Inc., Coopersburg, PA; **George S. Springer**, Stanford University; **Gunter Stein**, Honeywell Systems and Research Center, Minneapolis; **Olin J. Stephens II**, Sparkman and Stephens, Inc., New York City; **Robert Stratton**, Texas Instruments Inc., Dallas; **George W. Sutton**, Aero Thermo Technology, Inc., Arlington, VA; **James M. Symons**, University of Houston; **Charles P. Thacker**, Digital Equipment Corp., Palo Alto, CA; **Milton H. Ward**, Cyprus Minerals Co., Englewood, CO; **Richard M. White**, University of California, Berkeley; **Savio L.Y. Woo**, University of Pittsburgh; **Aaron D. Wyner**, AT&T Bell Laboratories, Murray Hill, N.J.

The following were elected Foreign Associates:

Gianni Astarita, University of Naples, Italy; **Alec N. Broers**, University of Cambridge, England; **Hans G. Forsberg**, Royal Swedish Academy of Engineering Sciences, Stockholm; **Shinroku Saito**, Nishi-Tokyo University, Kanagawa-ken, Japan; **Jorg Schlaich**, Schlaich Bergermann & Partners, Stuttgart, Germany; **Valerian I. Tatarskii**, University of Colorado; **Shoichiro Toyoda**, Toyota Motor Corp., Aichi, Japan; **Gottfried Ungerboeck**, IBM Zurich Research Laboratory, Rueschlikon, Switzerland.