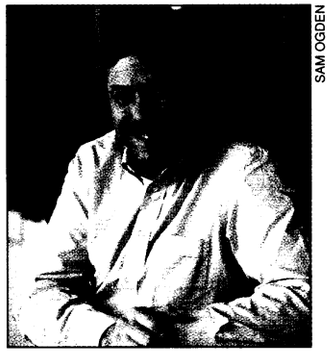
GENOMICS

Whitehead, Three Firms Splice a Deal

CAMBRIDGE, MASSACHUSETTS—"Genomics" is the biotech industry's next unexplored continent: a world where information about people's genes and gene activities will create new ways to diagnose, prevent, and combat disease. Or so researchers and investors hope (*Science*, 7 February, pp. 767–782). Biotech and pharmaceuticals firms are now betting that a good way to stake out commercial territory in this new world is to hire the mapmakers. That's why an unusual new consortium of companies announced last week that it has joined Eric Lander, a gene mapper at the Whitehead Institute for Biomedical Research and the Massachusetts Institute of Technology (MIT), in a 5-year, $40 million effort to develop new "functional genomics" techniques.



SAM OGDEN

Mapping out a deal. Lander lands $40 million for functional genomics.

"Rather than wait and see what happens, we want to pick and choose our path into genomics," says biologist Richard Gregg, a vice president and head of an internal genomics task force at consortium member Bristol-Myers Squibb. "Eric is one of the leaders in thought and technology." A former mathematician and MacArthur Fellow who was elected last month to the National Academy of Sciences, Lander directs the Whitehead/MIT Center for Genome Research, one hub of the massive government-funded effort to locate and characterize the estimated 60,000 to 100,000 genes in the human genome.

Under the deal, announced on 29 April, the New Jersey–based pharmaceuticals giant and two smaller biotech firms—"DNA chip"-maker Affymetrix Inc. of Santa Clara, California, and Millennium Pharmaceuticals of Cambridge, Massachusetts—will give the center equal amounts of cash and equipment for research into faster, more efficient ways to gather and compare genetic data. In return, the companies will receive commercial rights to technologies developed under the program. Most coveted by the firms are automated systems for analyzing, simultaneously and over time, the activities of tens of thousands of genes and proteins in normal and diseased cells. Detailed legal provisions, and the nature of the inventions themselves, will govern which of the firms will get joint or exclusive rights.

The agreement will significantly boost the center's current $14 million annual research budget. That money, most of it from federal grants through the Human Genome Project, has paid for the first rough guides to the 3 billion nucleotides in human DNA: maps studded with thousands of landmarks called "sequence tagged sites" (*Science*, 25 October 1996, p. 540). Lander says he is now eager to see that information put to work in biomedicine. "We've put 7 years so far into building maps and sequences, telling ourselves that this structural genomic information would help change the world. It's time to take that out for a test drive," he says.

Responding to recent concerns that corporate funding could quash the free exchange of scientific data, Lander and the consortium members went out of their way last week to emphasize their "airtight" agreement limiting publication delays to 60 days to allow time for patent filings. Lander, moreover, will divest his stock holdings in both Millennium, which he co-founded in 1993, and Affymetrix, in accordance with the conflict-of-interest guidelines of MIT and the Whitehead Institute.

Industry-university collaborations are common in biotech, and so is "partnering" between pharmaceuticals companies and smaller, idea-driven firms—just last week, for example, Schering-Plough Corp. signed a potential $60 million deal with Myriad Genetics Inc. of Salt Lake City focusing on cancer genetics. But Whitehead Institute director Gerald Fink, a yeast geneticist, says, "It is very unusual to see three companies working together in this way."

Affymetrix President Stephen Fodor predicts, however, that this consortium may well set the tone for future collaborations in biotechnology. "I suspect you will see many of these types of interactions that allow technology to be integrated in new ways by people who ... are not biased by the internal culture of a particular company," says Fodor. "It should be a very powerful way to multiply our resources."

–Wade Roush

NEUTRON RESEARCH

Europeans Plan Their Next Big Source

European neutron-scattering researchers this week announced the next step in their ambitious plan to build the world's most powerful pulsed-neutron source by 2010. On 5 May, a group of five leading research institutions released a feasibility study for the proposed European Spallation Source (ESS), a $1.1 billion neutron facility powered by a 5-megawatt particle accelerator. The 3-year technical study, supported by the European Science Foundation, detailed the technical specifications for the new machine, and the five partner institutions agreed this week to seek funding for a 3-year research and development phase to prove the concept. "In Europe, I think we can do it," says Andrew Taylor of Britain's Rutherford Appleton Laboratory (RAL), secretary of the ESS Council.

The hard part will be to convince European governments to pay for the ESS, but its proponents believe they have a strong selling point in the growing demand for access to neutron beams, from users ranging from individual university researchers to industrial conglomerates. In Europe alone, there are estimated to be roughly 4000 researchers who conduct neutron-scattering experiments in fields including physics, chemistry, materials science, and biology. "What we do is underpin condensed-matter science. ... There is even an applied dimension to it: Understanding how alloys behave under extreme stress at a microscopic level is not a million miles away from designing turbine jet engines," says Taylor.

Europe is currently home to the best of each of the two types of facilities for producing neutrons for research: The Institut Laue-Langevin in Grenoble, France, has the most powerful reactor source, while RAL houses ISIS, the most intense accelerator, or "spallation," source. The ESS would produce neutron pulses that are 30 times brighter than those obtained at ISIS. In 1995, the United States abandoned plans for a more powerful reactor facility, the Advanced Neutron Source (*Science*, 17 February 1995, p. 952), but a new proposal for a National Spallation Neutron Source at Oak Ridge National Laboratory in Tennessee, powered by a 1- to 5-megawatt accelerator, is currently being developed. Japan is also working on two schemes for spallation sources in the 1- to 5-megawatt range.

Like other spallation sources, ESS would use an accelerator to speed protons, bunched together in short pulses, and slam them into a target. The collision generates neutrons by knocking fragments off the target nuclei. ESS's 700-meter linear accelerator would be the most expensive and physically the largest component. Together with the storage rings, it would cost $390 million.

With an energy of 5 megawatts, the proton beam would destroy the solid metal targets used in today's spallation sources. As a result, the target for ESS would have an entirely new design, says ESS Study Group member Tim Broome of RAL. It would consist of liquid mercury, continuously pumped

through a specially designed container at room temperature. "We are completely confident that it will work, but we still have to do some work to establish the real lifetime of the target," says Broome. For example, the team has yet to investigate whether pressure waves created in the mercury by the extremely short, high-power proton pulses would damage the container.

Although ESS still has a long way to go before it produces its first neutrons, researchers are already looking forward to the science that its intense beams would make possible. "We can use it to look at processes in shorter times, we can use it to look at much smaller samples and dilute samples, and we can look at much more subtle effects," says ESS science coordinator John Finney of University College London. For example, researchers would be able to study the folding and denaturation of proteins in solutions and how the interactions between nonpolar groups are modulated by adding particular ions. "This is the kind of thing we cannot even dream of getting a proper answer to now," Finney says.

But before that dream comes true, the participating laboratories—in France, Germany, Switzerland, Denmark, and the United Kingdom—must still secure funding for the next R&D phase from their own governments and the European Union. If they clear that hurdle, the next step would be a 2-year engineering phase, followed by a 6-year construction phase starting in 2002, and a 2-year commissioning phase from 2008. "We have to improve confidence and reduce costs," says Taylor. "We have [technical] solutions, but we have to seek more cost-effective solutions in the long run."

U.S. researchers are looking on with interest. "I think it is an extremely important project for the world, not just for Europe," says Bill Appleton at Oak Ridge National Laboratory. "The total availability of neutron sources is going down, and most sources don't have enough intensity to do the kind of new science that is possible. This source addresses both of these things."

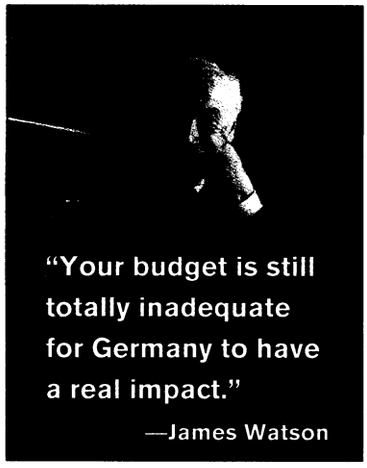
–Alexander Hellemans

Alexander Hellemans is a science writer in Paris.

GENOME RESEARCH

Watson Urges 'Put Hitler Behind Us'

BERLIN—In a keynote speech to a molecular medicine congress here last weekend, one of the world's foremost geneticists—Nobel Prize–winner James D. Watson, co-discoverer of the structure of DNA and a founder of the Human Genome Project—stepped carefully into the ethical minefield of German genetic research and the legacy of Nazi eugenics policies. The time has come, he said, to "put Hitler behind us." He urged Germany to focus on the great benefits that applying genome research can offer humankind, and to put more resources into genetic research. At the same time, Watson warned that geneticists should try to keep decisions about genetic testing and related matters "in the hands of the people" and away from state control. "Genetics as a discipline must strive to be the servant of the people, as opposed to our governments," he told the 1000 delegates. "Never again must geneticists be seen as the servants of political and social masters" who use pseudoscience for despicable ends.



MARGOT BENNETT

In the name of the pseudoscience of eugenics, Adolf Hitler's Nazi regime exterminated millions of Jews, Gypsies, mental patients, and disabled people between 1933 and 1945, and carried out experiments on concentration-camp prisoners. The guilt and horror at that grotesque misuse of science was a major factor in transforming Germany—once a leader in genetics—into one of the most hostile environments for such research and the scientists who do it. In recent years, Germany has begun to emerge from its withdrawal—loosening some strict regulations and slowly rebuilding its genetic research.

Nevertheless, in his speech and at a related news conference, Watson—president of Cold Spring Harbor Laboratory in New York—told German scientists that their nation's genetic research is not moving fast enough. Watson said he was "very happy that Germany has now finally chosen to join" the genome project, but he added: "Your budget is still totally inadequate for Germany to have a real impact. You are putting money in to use the genome, not to get it." Watson also attacked Germany's restrictive laws governing genetic research. "Your regulation of biotechnology has been counterproductive," Watson said, asserting that overregulation had threatened to make Germany "a second-rate nation as far as biotechnology is concerned."

Watson, who is famous for his outspokenness, stepped even further into delicate territory: One reason German genetics has taken so long to recover, he said, is that "Germany never purged itself" completely of the scientists whose work was misused by the Nazis. Watson—who conceded that some Americans, including scientists at Cold Spring Harbor, carried out eugenics research before the Nazi era—said that while some German researchers were punished after World War II, a number of discredited geneticists retained influential university posts. "You never came out and said the bad guys" were bad geneticists, he said, and that failure has hurt later researchers.

Watson's remarks were loudly applauded by many German scientists at the meeting. Detlev Ganten, head of Berlin's Max Delbrück Center for Molecular Medicine, which co-organized the conference, told *Science* he agreed that Germany "never fully purged itself" of the sins of some Nazi-era geneticists and is still "psychologically not well prepared" for such research. He added: "We are grateful that Jim Watson came here with this message. It is very hard for Germans to say it."

But Watson's jabs at Germany's fledgling genome project and the nation's research regulations ruffled some feathers at the Ministry of Education, Science, Research and Technology. Elke Wülfing, the ministry's representative at the conference, told *Science* that the genome project, started 2 years ago (*Science*, 16 June 1995, p. 1556), "is getting an adequate share of the German research budget." Germany now spends about $24 million a year on its genome project, a small fraction of the estimated $3 billion total cost of the entire Human Genome Project. Wülfing said the delay in establishing Germany's project related to "extensive discussions about ethics," and she defended Germany's stance on regulating genetic engineering. "Despite all the known opportunities inherent in biotechnology and genetic engineering, we must not lose sight of the concerns of the general population in the face of the inherent risks," she said.

Watson said he hoped German science will make significant contributions to the genome project: "The gene is still regarded by much of the German population as a bad thing. The time has come to end this." He then added: "Genetics per se can never be evil. It is only when we use or misuse it that morality comes in."

–Robert Koenig

Robert Koenig is a writer in Berlin.