Europe Seeks Strategy for Biology

A consensus is growing that greater coordination is needed in biological research, in particular on genome sequencing. But differences remain on how this can best be achieved.

Bonn

If the United States gets a human genome sequencing project off the ground and Japan launches its Human Frontiers Science Program, what should Europe do to get into the act?

The question has been exercising the minds of a growing number of European scientists, science policy-makers, and politicians, who are concerned that the U.S. and Japanese projects could produce important scientific, industrial, and commercial spin-offs. Europeans are looking at ways to structure their own efforts in modern biology in ways that would permit them to be effective partners—and not merely junior partners—in both projects, while promoting an independent European capability in the field.

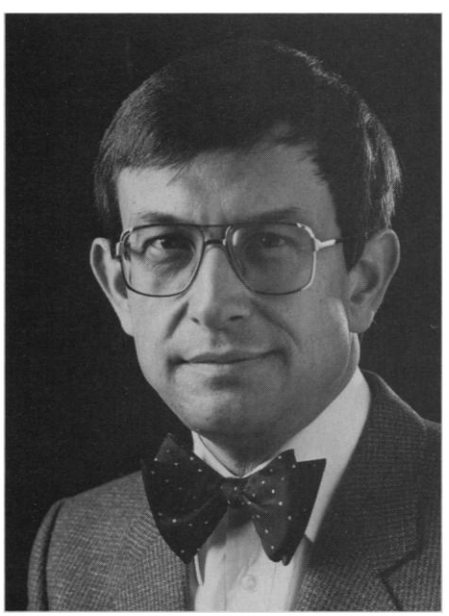
Starting last Monday, a series of key meetings are being held under the auspices of the Brussels-based Commission of the European Economic Community (EEC) to explore the possibility of building both a scientific and political consensus in support of closer European cooperation in biology.

Several suggestions have been circulating around European capitals. They range from the creation of a new center for research in human genetics, through a biotechnology version of the French-inspired EUREKA program, to a suggestion put forward informally by West Germany's science minister Heinz Riesenhuber that Europe should launch its own version of Japan's human frontiers program.

Riesenhuber, who is the current chairman of the council of EEC research ministers, has played a key role in stimulating the debate. He is keen that agreement should be reached both on the best ways to support biological research, and—a particularly thorny topic in West Germany—on the legal, ethical, and environmental regulations it is required to meet. He hopes to be able to present firm proposals to his fellow research ministers at their next meeting on 29 June (the day before the end of his 6-month period as chairman).

One prominent argument in favor of closer European collaboration is that, overall, Europe's combined scientific output in fundamental research related to biotechnology, measured for example by the number of papers published in leading journals, is significantly larger than that of the United States, yet its biotechnology industry is smaller. A failure to exploit biological research more vigorously could have serious implications for industrial competitiveness, some European politicians and industrialists are warning.

Detailed knowledge of the human genome, for example, could open up vast new global markets in diagnostics and therapeutic agents, and this knowledge could become a highly profitable commodity from which countries without an adequate research base may be excluded, they suggest.



Heinz Riesenhuber. *German research minister has played a key role in stimulating the debate.*

René Sautier, the recently retired president of the French chemical and pharmaceutical company Sanofi, points out in a report on the biotechnology industry, commissioned by Prime Minister Jacques Chirac and presented to him last month, that the first to successfully develop techniques for the diagnosis of polygenic disorders would have an advance of several years on their competitors. "It is certainly one of the areas which, because of its nascent character, justifies an initiative supported by public research funds, accompanied by industrial financing, at the French, if not European, level," says Sautier.

Even French President François Mitterrand has been expressing interest. In his reelection manifesto, he pointed out that the project to sequence the entire human genome "would cost less than a voyage to the moon," and went on to complain that "none of our European nations consecrates a serious part of its budget to it."

Many scientists accept that closer collaboration on, for example, research in genome sequencing is needed to avoid duplicated efforts and to increase the strength of Europe's research infrastructure in human genetics. "There is a strong case for European scientists getting together in this field" says Sir Walter Bodmer, director of the Imperial Cancer Research Fund (ICRF) in London and a leading molecular geneticist.

Yet the growing agreement that some form of joint action is appropriate has been tempered by warnings that the nature of the science is such that excessive centralization could be counterproductive. It is a dilemma that remains both hotly debated and unresolved. There is also considerable support for the view that any cooperative action should grow from the abilities and needs of individual research groups and companies, rather than according to priorities laid down from outside. Cooperation "has to be based on the strengths of those who are already doing things," stresses Bodmer.

There are two separate lines along which research cooperation could develop. They represent different—and in some respects conflicting—approaches to creating a framework for boosting European efforts in advanced biological research in general and genome sequencing research in particular.

One would involve organizing a European program primarily around the European Commission, building on research projects that are currently being funded under different, relatively unrelated, programs. The other would be a more technology-oriented strategy based on the approach that has been used for the development of EUREKA, a program of joint development projects each financed by private and public funds. EU-

REKA, which was launched at the initiative of France in 1985, is now supported by 19 European governments and has a total planned budget in excess of $5 billion.

The European Commission is already funding a number of research projects involving genome sequencing—for example, a project on the genetics of drosophila being carried out by research teams in the United Kingdom, West Germany, and Greece. In addition, two new projects are under consideration. The first is a proposal to launch a European-wide effort to sequence the yeast genome, a project that could involve up to 40 laboratories in the 12 member states of the EEC. "If it works, it could be extended to larger projects, such as human genome sequencing," says EEC adviser and project coordinator André Goffeau of the University of Louvain in Belgium.

In addition, it is being proposed by the commission that $18 million which EEC research ministers have already decided should be spent on research in predictive medicine over the next 5 years be allocated specifically to studying the human genome.

Some commission officials feel that it should be possible to bring these efforts together and to develop them into a single European genome program, allowing direct linkage, for example, to the work on biological data processing and storage currently being financed at the European Molecular Biology Laboratory (EMBL) in Heidelberg.

"What we might do is something comparable to the research network called BRAIN that we have already established in adaptive intelligence and neurocomputing, essentially establishing links between researchers already working in fields relevant to an overall theme" says Charles White, secretary of the commission's Committee for the European Development of Science and Technology (CODEST).

As for the EUREKA program, a proposal for a project that would include joint development work on genome sequencing technologies has already been put together by two research supplies and equipment companies—Amersham International in the United Kingdom and Bertin et Compagnie in France—together with two leading European research institutes—the ICRF in London and the Centre d'Etude du Polymorphisme Humain (CEPH) in Paris.

Initial plans are relatively modest, covering primarily the joint development of research equipment and supplies. If successful, however, the project's promoters, which include Bodmer of the ICRF and CEPH director Jean Dausset, the 1980 Nobel Prize winner for medicine, hope that it will become the kernel of a much larger development program, forging a strong alliance

Focus on the Genome

Paris

Slowly but steadily, research on the human genome is climbing into the top ranks of the scientific agenda in European nations.

Government agencies, tightly strapped for research funds, have been cautious about committing themselves to providing extra money. Over the past year, however, a growing number of initiatives have been launched aimed at raising the profile of genome research in general and human genome sequencing in particular—in some cases with new financing being earmarked from outside the conventional biomedical research budget.

■ The French government has agreed to make an extra 8 million francs ($1.4 million) available for human genome research, identified as a new national priority by Prime Minister Jacques Chirac. The money is being allocated by a committee chaired by Nobel Prize winner Jean Dausset, founder and director of the Centre d'Etude du Polymorphisme Humain (CEPH), whose carefully documented collection of DNA samples could become the focal point of an international sequencing effort.

Half the money will be used to support research into sequencing areas of the genome considered to have particular medical importance; the other half for developments in data processing. Committee member Jean Frézal, professor of genetics at Necker Hospital for Sick Children in Paris, says the committee is likely to support "a handful of rather big projects to study, say, the fragments of a chromosome of interest to a particular research group."

■ Britain has set up a special committee of the Medical Research Council, jointly chaired by MRC secretary Dai Rees and Walter Bodmer, director of the Imperial Cancer Research Fund (ICRF). The committee is intended to coordinate research associated with human genome sequencing, described by Rees as "a matter of the highest priority."

Funds have already been allocated to research on techniques of human genome sequencing to be carried out by Sidney Brenner at the University of Cambridge. In addition, according to Rees, the human genome has been agreed on as one of the principal focal points of a new national postgraduate center for medical education and research (to be formed out of two existing institutions), and meetings have been held with 40 top British scientists to discuss a strategy for genome research that will be put forward to the government jointly by the MRC and privately funded research groups such as the ICRF.

■ In Germany, although no formal program has yet been launched, discussions within the federally funded Deutsche Forschungsgemeinshaft (DFG) have led to a decision to hold a meeting in July bringing together scientists working on cloning, on data handling, and on the development of sequencing apparatus.

"The least we are hoping for is an annual conference to coordinate efforts in these three fields," says Ernst Winnacker, vice president of the DFG and director of the Gene Center in Munich. Beyond that, he adds, discussions are taking place about putting in an application for a major grant to the West German research ministry, the BMFT.

For the past 3 years, the DFG has allocated about $500,000 a year to research on the human genome research. Officials in Bonn say that a significant increase in funding for this research is now highly likely.

■ Perhaps most ambitiously, the Italian government has announced that it will allocate about $10 million over the next few years to a national effort to sequence a particular 50-million-base chromosomal fragment known to be responsible for mental retardation. The task will be carried out by research groups throughout the country, and the whole effort is being coordinated by Renato Dulbecco of the Salk Institute.

In all these countries, there is a growing feeling that scientific and industrial interest in both the United States and Japan means there should be more European cooperation. "Many of us feel that, in order to both collaborate scientifically and compete technologically with the United States and Japan, countries like Germany cannot work in isolation, but that there must be coordination at the European level," says Winnacker of the DFG. ■ **D.D.**

across Europe between research laboratories, research equipment producers, and eventually pharmaceutical and chemical manufacturers. Italian, Swiss, and German companies are said to have already expressed interest, besides those in France and the United Kingdom.

Given the two slightly different approaches, each with its supporters, the need now, as some see it, is to generate a political consensus behind a common strategy for stimulating closer cooperation. Such a common strategy, it is argued, might also be used to dampen the public disquiet that has surfaced in several European countries (in particular West Germany) over the ethical implications of modern biological research—particularly genetics research affecting humans.

On 11 April, the research ministers of the 12 member states of the EEC gave their informal backing during a lunchtime discussion in Luxembourg to Riesenhuber's proposals to explore ways of generating such a consensus. In particular, they agreed that German and European Commission officials should jointly oversee plans for four separate meetings over the next 2 months, each aimed at addressing separate issues.

The first was the meeting held in Brussels on 2 May. Planned as a detailed discussion of both the proposed contents of the Japanese human frontiers program and of the possibilities for greater research cooperation in Europe, it was attended by 50 to 60 top European scientists as well as representatives from the commission's various scientific and industrial advisory boards. "The idea is to have a broad discussion among scientists about what should be done, just as we did before we set up EMBL in the early 1970s," CODEST member François Gros, former director of the Institut Pasteur in Paris told *Science* before the meeting. "After one or two meetings of this type, the EEC Commission will be in a better position to decide on the appropriate form of European activity."

If all goes according to plan, the 2 May meeting will, at the discretion of the German government and the Commission, be followed by an informal meeting of research ministers to discuss what type of European program might be endorsed on 29 June. And two parallel meetings will discuss the ethical and legal dimensions of biological research, particularly that concerning recombinant DNA techniques and genome sequencing.

As for Japan's Human Frontiers Science Program, the European ministers have already agreed on a common approach, which they will present if, as currently anticipated, the program is discussed at the Toronto summit in June. They have agreed that the type of research envisaged under the Japanese program is appropriate for international collaboration, and that Europe should play a significant role in it; for the time being, however, their contribution to the program will be more in kind than in new research money.

There are some differences of opinion, however. Riesenhuber, for example, has expressed both support for and caution about the Japanese initiative. Referring recently to the danger that it could become a new brain drain of European expertise in molecular biology and neurosciences to Japan, he has emphasized the need to ensure a "real partnership" with Japanese scientists, suggesting that Europe should aim to make the same overall level of financial contribution as the Japanese. British officials, in contrast, say they are waiting to see how the program develops before deciding to commit any funds to it.

Agreement on the appropriate form of a purely European initiative to stimulate advanced biological research is still proving elusive. But, according to German officials at least, the positive interest expressed informally by the research ministers indicates that substantial developments may take place over the next few months. "There is a lot going on," says a top BMFT official in Bonn, "and it looks as things are really beginning to move." ■ **DAVID DICKSON**

Field Test Data Inadequate, OTA Says

More research must be conducted to support risk assessment evaluations of outdoor tests of genetically engineered organisms, says the Office of Technology Assessment (OTA). "To dispel speculation, increasing the general knowledge base about organisms intended for environmental applications is paramount," says OTA. Not only will this bolster public confidence, the agency says in its latest report on biotechnology,* but additional data also should lead to some relaxation of federal regulations.

The findings are part of an overview prepared at the request of Congress on the use of engineered organisms in agriculture and for tackling environmental pollution. OTA's report examines historical introductions of new and modified organisms and plants as well as recent field trials.

The study should serve as a useful reference for members of Congress and the general public trying to make sense of the conflicting statements of social activists and industry. The report concludes that:

- With adequate review, the small-scale field tests that occur in the next several years are not likely to pose an environmental problem that cannot be controlled.
- Small field experiments are likely to be the only way potential risks from some proposed commercial uses of genetically engineered organisms can be evaluated.
- There are reasons to be cautious because significant areas of uncertainty exist, especially in the realms of microbial ecology and population dynamics.

In addition, OTA recommends that the National Science Foundation, the Department of Agriculture, and other federal research agencies consider targeted research initiatives covering interactions between competing organisms, gene regulation, and related issues affecting microorganisms. Along with this effort there also is a need for greater interdisciplinary research among microbiologists, geneticists, plant pathologists, agronomists, ecologists, and evolutionary biologists, says OTA.

"Specific data and basic, broad-based information. . .to develop capabilities for generic risk assessment and management strategies are lacking," observes OTA, which suggests that federal regulation of the biotechnology industry could benefit from better data. "With many commercial applications of biotechnology reaching the field test stage," the agency comments, "regulators need clear risk assessment and risk management guidelines."

As more data are gathered regarding various classes of organisms, regulation of some field tests can be relaxed, if not abandoned. "It should be possible now, or become possible in the near future to sort planned introductions into broad categories for which low, medium, or high levels of review are appropriate," says OTA.

The current regulatory mechanism set up by the Biotechnology Science Coordinating Committee (BSCC) in June 1986 is inadequate, OTA says. The BSCC, which is part of the Office of Science and Technology Policy, "lacks the power to impose its decisions" upon regulatory agencies such as the Environmental Protection Agency or the Department of Agriculture, the agency notes. As a result, OTA adds, there are inconsistencies in the regulatory approaches used by executive branch agencies. ■

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**Field Testing Engineered Organisms: Genetic and Ecological Issues* is the third of a series titled "New Developments in Biotechnology." Copies of the report (OTA-BA-350) are available from the U.S. Government Printing Office.