Boom Time for British Biotechnology?

Venture capital is now flowing into small companies and the government is encouraging the commercialization of university research it funds

London. After a relatively slow start in the late 1970's, Britian's biotechnology industry is beginning to pick up speed. Government officials, academics and industrialists all claim that a recent report from the U.S. Office of Technology Assessment (OTA) was excessively pessimistic in its claim that Britain lacks the "dynamism" to produce serious competitors to American companies. They also contest the OTA's conclusion that Britain ranks second behind West Germany among European nations.

"I think that conclusion is completely wrong, particularly if you take the combination of the science and its applications into account" says Gerard Fairtlough, chief executive of Britain's principal biotechnology company, Celltech, which is currently riding a crest of investor enthusiasm.

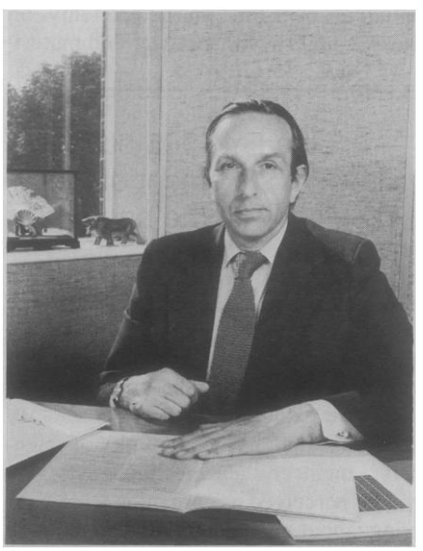
British industry has benefited from various forms of direct government support for biotechnology. Many smaller companies, for example, have made good use of consultancy grants and other special funds offered as part of a $24-million biotechnology package launched by the Department of Trade and Industry in November 1982. Other industrial initiatives in fields such as fermentation technology have been successfully catalyzed by the Biotechnology Directorate of the Science and Engineering Research Council (SERC).

According to Robin Nicholson, chief scientific adviser in Prime Minister Margaret Thatcher's Cabinet Office, broader political changes must also share the credit. "The policy of the government since 1979 has been to free restrictions and to remove barriers to enterprise," says Nicholson. "The relatively healthy state of biotechnology in the U.K. seems partly to reflect the success of those policies."

He picks out, for example, efforts to encourage Britain's venture capital market—now considered the second largest in the world after the United States—through developments such as the Business Expansion Scheme, which allows individuals to write off against tax an investment of up to $60,000 in a small company, provided the money is left in for up to 5 years.

"The Business Expansion Scheme was the first real fiscal change in small company funding for 50 years" says Peter A. Laing of Biotechnology Investments Limited (BIL), a venture capital fund set up by merchant bank N. M. Rothschild in 1981 and chaired by a previous top government science adviser, Lord Rothschild. BIL is said to be the largest biotechnology-oriented venture capital fund in the world. Partly due to this recent flow of venture capital, Britain now has more small biotechnology companies than any of its European competitors.

The government's willingness to let the commercial and industrial communities act as the senior partner in its efforts to boost biotechnology research and development has played a large part in both



Gerard Fairtlough

Celltech chief says OTA misjudged Britain.

the establishment and subsequent operation of Celltech. The company was set up in 1980 primarily at the initiative of the National Enterprise Board, a government body recently amalgamated into the British Technology Group. Although initially providing 44 percent of Celltech's start-up capital, with the four remaining stakes of 14 percent each divided between a group of financial and industrial institutions, the government always intended to hand over its share to private enterprise. It moved in this direction last year when Rothschilds' venture capital company—previously criticized for not investing its funds in any British biotechnology company—bought out a proportion of the government's stock and gained with it a seat on the board of the company.

Like similar companies in the United States, Celltech has actively sought collaboration with larger companies with broader industrial interests or special marketing skills. A joint venture was launched last year with Britain's largest pharmacy chain, Boots, for example, to develop the application of monoclonal antibodies to new diagnostic products. And a technology licensing agreement has been signed with the Japanese company Sankyo to develop tissue plasminogen activator and calcitonin.

Fairtlough says that Celltech, with a current research staff of about 120 scientists and technicians, does not at present share the ambitions of companies such as Genentech to grow into a major corporation. However, with a number of clearly defined product lines, each in a potentially large market, "We could be talking about a turnover of hundreds of millions of dollars in a few years."

Celltech is already earning profits from a reagent for the purification of interferon and has recently created a Culture Products Division which, based on techniques developed with direct government funding, already claims to be the world leader in the in vitro bulk production of monoclonal antibodies.

One reason for Celltech's early success is a unique—and in some quarters highly controversial—agreement with Britain's Medical Research Council (MRC), under which the company was initially given first option on the rights to all results produced in the fields of genetic engineering and monoclonal antibodies in the council's laboratories. These include the prestigious Laboratory of Molecular Biology in Cambridge.

This arrangement was approved by the Conservative government over the opposition of officials in the Treasury, who felt it wrong that one company should be granted exclusive access to what was considered public property. One factor in the decision, it is widely rumored, was the failure in the late 1970's to take out a patent on the technique for producing monoclonal antibodies, which was first developed in the MRC's Cambridge laboratory. Giving Celltech exclusive rights to MRC's work might avoid such lapses in the future.

When Celltech started to register its

first commercial successes, criticism of its deal with the MRC shifted from the political to the industrial community. Both large and small companies complained at being locked out of access to MRC's research. "The academic excellence in places like the MRC should be treated as a national resource and the government should be providing even-handed access to it," says Chris Keightley, managing director of one of the newest and most active small biotechnology companies on the British scene, IO (Bio) Ltd. in Cambridge.

The main product of Keightley's company, set up in 1981 by Acorn Computers and recently recipient of a $1.2-million investment from Rothschild's BIL, is a technique for improving the sensitivity of enzyme-based diagnostic tests. It is based on the research of a scientist whose work was not supported by the MRC, Colin Self of Cambridge University's biochemistry department.

Given the growing pressure to encourage similar initiatives, the MRC has recently renegotiated its licensing arrangements with Celltech. The company will retain first option to developments in fields in which it has already started to develop products. In other fields, however, it will now have to become a competitive bidder, for the MRC is setting up an industrial liaison office to distribute licenses more widely among companies interested in turning its research into commercial products.

The new arrangements have met with general approval in both the industrial and academic worlds. Sydney Brenner, director of the MRC's laboratory in Cambridge, says that at the beginning "there is no doubt that in terms of goodwill, the MRC connection was a major asset to Celltech."

Since then, however, the laboratory has been receiving an increasing number of direct approaches from industry. "In the past, we have had to tell them to go away, since the first options on research in the defined fields had to be offered to Celltech. Now we no longer have to do so."

Brenner and other British scientists point out that there are several differences between the United Kingdom and the United States in the factors affecting the growth of links between the academic biomedical research community and the private sector.

One is a greater reluctance on the part of British academics to get involved in the process of transferring research results from the laboratory, a tradition which is admittedly changing as cuts in government support for the universities as well as general, increase the pressure for university scientists—and universities in general—to look elsewhere for financial support.

A second factor until now has been the tax structure, which has made it more difficult to offer stock options to employees in small companies with initially low turnovers (or profits). The budget proposed in mid-March brings British policy in this area more in line with that in the United States, however.

On the other side of the coin has been a greater willingness to combine public

Pressure for Patent Reform

Cambridge, England. British scientists contend that differences in patent laws between Europe and the United States give U.S. companies a potential advantage in the commercialization of biotechnology. Under European patent laws, a scientific discovery cannot be patented once it has been published in the open literature or even referred to in public debate. In contrast, up to 1 year is allowed after publication for a patent application to be filed in the United States.

"I believe that the greatest inhibitory influence on a closer working relationship between academic and industrial scientists, and the greatest management problem for people like me, comes from this business of prior disclosure," says Sydney Brenner, director of the U.K. Medical Research Council's Laboratory of Molecular Biology in Cambridge, England.

There has long been an awareness of this discrepancy, particularly among patent officers on both sides of the Atlantic, but until now no serious pressure for change. Large corporations, in particular, often welcome being able to scan the scientific literature for new (and unpatented) ideas while employing patent attorneys to keep a close watch on the proposed publications of their own scientists. They tend to argue that they find little wrong with the current system. Robin Nicholson, chief scientific adviser to the British Cabinet, claims that "no one brought the issue to our attention" when his office was preparing a recently published set of recommendations for changes in the British patent law, and expresses some doubt over whether change is really necessary.

Among smaller companies, however, the situation is seen differently. "In this field, the 1-year grace period after publication gives the Americans a considerable competitive advantage" says Gerard Fairtlough, chief executive of Celltech. "I feel that Europe should have the same system."

Although admitting that biotechnology patents can frequently be successfully challenged by sufficiently motivated competitors, such companies also argue that patent rights are seen as crucial assets by potential investors.

Brenner also argues that it would ease the management problem in basic research laboratories such as his—as well as taking some of the pressure off individual scientists—by removing the immediate conflict between the professional demands for fast publication and the commercial demands of patent application. "Patents could be the currency of the interaction between research scientists and industry" says Brenner. "At the moment they are just a burden."

Change will not come easily. Friedrich-Karl Beier, director of the Max-Planck-Institute for Foreign and International Patent Law in Munich, and long a campaigner in favor of a 6-month grace period in Europe to bring it more in line with the United States, points out that this would now require an internationally agreed change in the European Patent Convention. "To do this, it will mean finding sufficient support within the whole European community," says Beier. However, he has already convinced the International Association for the Protection of Intellectual Property to endorse the idea, and suggests that there may be a general move in this direction "within the next 2 or 3 years."

Some British government officials point out that a grace period would help avoid situations—such as that which occurred with monoclonal antibodies in the mid-1970's—where the commercial potential of a discovery is only realized after it has been published, and when it can no longer, under the present system, be patented in the United Kingdom.—**D.D.**

and private ventures, and the lack of any moral imperative frequently felt in the United States to maintain, at least in principle, a sharp dividing line between the two. Furthermore, as with the Celltech/MRC deal, negotiations have often been conducted discreetly out of the public eye.

Either way, there has been little of the public controversy over the restructuring of traditional relationships between the research community and the rest of society that has accompanied similar moves in the United States.

The situation has not been without its critics. Edward Yoxen, lecturer in the University of Manchester's department of liberal studies in science, points out in a recent study *The Gene Business* that many significant policy changes, such as the dispensation on access to MRC research awarded to Celltech, have taken place with little open discussion, even

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though the basic discoveries on which the new technologies are based were financed largely from public funds. "There has been virtually no public debate on this type of issue," says Yoxen.

Few concerns were expressed, for example, over the government's recent decision to drop the "public interest" members from its main regulatory watchdog, the Genetic Manipulation Advisory Group, when this body was recently reformulated as the Advisory Committee on Genetic Manipulation, and its day-to-day responsibilities for registering and monitoring experiments passed to the Health and Safety Executive.

The lack of such debate, however, has certainly not hampered the gradual dismantling of barriers to open cooperation between the academic and the commercial communities, a process openly encouraged by the government. The SERC's Biotechnology Directorate, for example, has recently established what is described as a "protein engineering club," in which major companies such as Glaxo and Unilever will help sponsor research in various academic institutions into ways of producing proteins to order in large quantities.

Similarly, several university institutions are using government money, both from the research councils and the Department of Trade and Industry, to help set up commercial operations. The University of Leicester, for example, has recently obtained backing from five major corporations to establish a center for research into yeast genetics. And the Imperial College of Science and Technology in London has established a company known as Imperial Biotechnology to exploit its research facilities in fermentation techniques.

Keen that the nation should reap a profit from its past and present scientific investments, the government is increasingly engaging in as much industrial planning as it feels it can get away with behind its free-enterprise, non-investment image. Responding to demands from companies such as Imperial Chemical Industries, as well as officials within the SERC, for some form of "national biotechnology program" to cover the spectrum of possible initiatives from tax incentives to information networks, the Department of Trade and Industry has recently set up a special advisory committee made up primarily of senior industrialists to look at areas where an extra push might be useful.

Taken in isolation, none of these moves is itself seen as a guarantee of success. But behind them lie two additional factors that help account for the current bullishness of Britain's biotechnologists. One, as Nicholson of the Cabinet Office puts it, is that "there is more optimism in the business sector than there was 6 or 9 months ago; we certainly started pulling out of the recession faster than either Germany or France."

The other is the gradual emergence of a new spirit of entrepreneurialism among British academics. "In the past, most academics had no idea about how to start up in business; but all that is now changing," says Keightley of IQ(Bio), a Cambridge biochemist who was about to emigrate to the United States when Acorn offered him the opportunity of helping start up the new company.

Similarly, Celltech points out proudly that it has managed to persuade one of the top teams of MRC scientists, headed by immunologist William Hunter of Edinburgh University, to join the company's new venture with Boots. "We have a fabulous opportunity here in Britain," says Keightley. "We are now learning how to capitalize on it."—**DAVID DICKSON**

Meselson Meets a Shower of Yellow Rain from Bees

Matthew Meselson, the Harvard biochemist waging a one-man challenge to the U.S. State Department's version of Yellow Rain warfare, went into the jungles of Thailand last month to test his thesis. He returned at the end of March with a new evidence, declaring the trip a greater success than he had anticipated.

Along with two bee experts who joined him in looking for natural forms of Yellow Rain, Meselson was caught in a 5-minute shower of bee droppings, which he thinks may be the real source of Yellow Rain samples being analyzed by U.S. military labs. Meselson and Thomas Seeley, a biologist at Yale University, last year developed a theory that Yellow Rain spots regarded as chemical weapon deposits were actually the feces of the wild Southeast Asian honey bee, *Apis dorsata* (*Science*, 24 June 1983, p. 1356). The theory was based on the knowledge that honey bees periodically make "cleansing flights" away from the hive, that their droppings contain pollen, and that most of the government's samples of Yellow Rain collected from the environment contain pollen.

Meselson noticed that the government's data on Yellow Rain were gathered in Southeast Asia between February and May. Using funds recently awarded him by the John D. and Catherine T. MacArthur Foundation, he went to Thailand in the middle of this ripe evidentiary season hoping to find proof that Southeast Asian honey bees do produce yellow, pollen-laden rain.

Meselson and Seeley reported at a press conference at Harvard on 28 March that they have proof that *A. dorsata* performs "massive defecation flights which can cover a swath thousands of square meters in area with 100 or more spots of yellowish feces per square meter." They found and studied ten swaths in Thailand and were caught in a bee feces shower that left "about a dozen spots . . . on each member of our three-man team." Meselson says this occurred near a tree in which they had spotted *A. dorsata* nests, but the bees were so far above the ground that he could not see or hear them.