BIOMEDICAL RESEARCH FUNDING

Dexter Takes Over Wellcome Trust's Pot of Gold

LONDON—All researchers struggling for grants must sometimes daydream about what research they would back if they had hundreds of millions of dollars to give away. For Mike Dexter, one of Britain's most distinguished cell biologists, that daydream will become very real next week when he takes the reins of the world's largest private fund for biomedical research, Britain's Wellcome Trust. The Wellcome director plays a key role in determining priorities for the trust's $400 million annual spending on research, most of which goes to researchers in the United Kingdom. "It's exciting to be part of that," Dexter says.

The former head of the Paterson Laboratory at Christie Hospital in Manchester, one of the country's main specialist cancer centers, Dexter takes over from Bridget Ogilvie at a tough time for British science. Public funding for research is being consolidated at fewer departments; money for infrastructure is chronically scarce; the public research budget is stagnant; and a large cadre of researchers are marooned on short-term contracts. All of this has given the trust, with annual spending that almost matches that of the government-funded Medical Research Council (MRC), enormous influence within Britain's biomedical science community (*Science*, 22 November 1996, p. 1292). Dexter's strong record at Paterson is leading to high expectations. "He certainly ensured that research at the Paterson labs was in the international league," says the Paterson's scientific administrator, Graham Cowley.

SUSIE BARKER, HARLEY EVANS

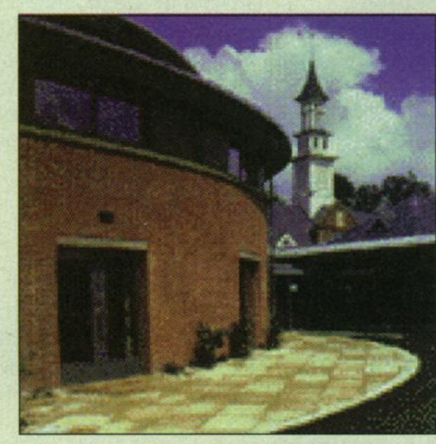
Position of trust. Incoming Wellcome chief Mike Dexter.

The trust, which sold its stake in the Wellcome pharmaceutical company in 1995, has directed most of its support toward researchers in British universities, often offering more generous funding than government sources can and providing equipment and secure, longer term support for key researchers. In recent years, it has also developed a number of initiatives outside universities, including projects abroad and its most expensive venture to date: a flagship genome campus at Hinxton, near Cambridge (see sidebar).

Europe's Cold Spring Harbor

HINXTON, U.K.—Last week, about 300 scientists gathered at this elegant 18th-century country house a few miles south of Cambridge for a symposium to mark the completion of the Wellcome Trust's transformation of the house and surrounding parkland into the hub of the United Kingdom's genome research effort. The new $22 million conference center, in which the symposium was held, aims to provide a venue for cross-fertilization between visiting scientists and the handful of labs on the site: the trust's gene sequencing facility, known as the Sanger Centre; the European Bioinformatics Institute, an outstation of the European Molecular Biology Laboratory; and the U.K. Medical Research Council's Human Genome Mapping Programme Resource Centre.

The campus aims to sequence more than one-sixth of the human genome as well as the genomes of other organisms, ensuring that Britain stays a major player in global sequencing efforts. It also underlines the prominent role that its funder, the Wellcome Trust, has assumed in British science. Set in spacious parkland alongside the River Cam just south of Cambridge, the campus is the trust's most expensive project: It has committed more than $290 million to it over the past 5 years. Wellcome refurbished the hall, built the conference center and Sanger Centre, and provided infrastructure funding for the other, publicly funded labs on site.



WELLCOME TRUST

"Something intangible." Wellcome hopes to create a unique atmosphere at Hinxton.

Steered by program manager Michael Morgan at the Wellcome Trust, the campus project is modeled on the highly successful mix of research and meetings established at Cold Spring Harbor on Long Island, New York, where seclusion and peaceful surroundings play an important role in fostering scientific discussion. "Hinxton is a beautiful setting, and the facilities are fabulous," says plant molecular biologist Michael Bevan of the John Innes Centre in Norwich, who spoke at last week's genetics symposium.

While the refurbished Hinxton Hall provides residential accommodation and a new restaurant, the former stables and kitchen garden at the rear of the house have been turned into a new 300-seat auditorium with adjoining rooms and glass-walled cloisters for poster presentations. "We are trying to create a lovely atmosphere and something intangible too," says Morgan. He says that a diverse menu of meetings is planned to reflect the range of interests and activities across the campus. Jean Weissenbach, head of Genoscope, the French government's genome sequencing center south of Paris, who also spoke at the meeting, was impressed by the campus. "There is nothing equivalent to this in France," he says. "It's a great place, and isolating people from other distractions is extremely fruitful and much better than meeting in a city."

The trust's plans have run into one hitch, however. Wellcome bought 28 hectares of land next to the campus to allow biotech companies to set up shop and benefit from the adjacent research centers. But the local council has objected that the proposal does not fit in with its industrial development plans, and a public inquiry into the trust's planning application was held last week. A report will be submitted to the government for a decision in the fall. Morgan hopes that the plan will be able to go ahead: "It's the U.K. as a whole which will benefit." –N.W.

Dexter says he will push for such efforts to continue, but he believes more could be done to support younger researchers, whose creativity he sees as increasingly squeezed. Although there are no plans yet on the table addressing Dexter's concerns, one of his major worries is the trend for research groups to get larger and for young researchers to be assigned to parts of projects designed by senior researchers. "How often are younger members of a team allowed to develop their own ideas?" he asks. "When I was appointed director of the Paterson, one of the first things I did was to break the departments into smaller groups," he says. "I wanted to give young people space for their own ideas. Seven or eight people is a good size for a group." Dexter approves of the approach taken at the European Molecular Biology Laboratory in Heidelberg, Germany, where young researchers have a guaranteed term of as long as 7 years. That way, they can take risks but also have time to make mistakes, he says.

Dexter is looking forward to exploiting the trust's lack of government bureaucracy to respond quickly to shifting priorities in research. He intends to track rapidly developing fields such as structural biology and research exploiting new gene-sequencing data, increasing the available resources when needed, he says. He also thinks the trust can plug gaps in areas such as clinical research, which he believes has lost out in the molecular biology boom and also suffers because peer reviewers do not understand the ethical constraints on such research.

Dexter's appreciation for clinical research reflects his experience at the Paterson lab, where the staff has close links with hospital-based researchers. His own basic research, on bone marrow cells, helped him devise a technique for culturing them over the long term in the laboratory, which was a boon for clinical cancer researchers. "Good clinical work in the U.K. has almost been destroyed, and we need to think hard about it. We've got to keep looking at the workings of the peer-review system," he says.

Despite his broad ambitions for the trust, Dexter does not see an imperative to expand its overseas projects: "The quality of science in the U.K. is comparable or better than in many other countries. We are still competitive in major areas. To move substantially out of the U.K. would add significantly to our administration costs, but there is nothing to stop us taking money overseas if we decide to," he says.

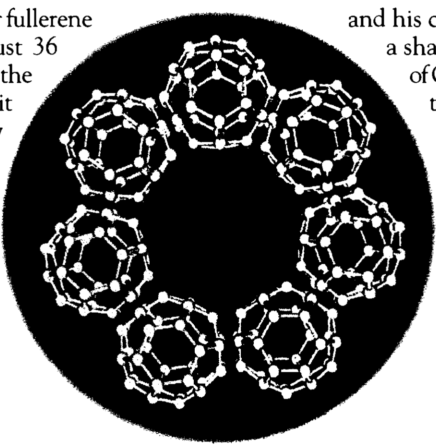
Dexter does plan another kind of outreach, however—to the lay public. He worries that in the public view, science is no longer as appealing or as exciting as it used to be. He thinks negative perceptions of science presented by the media and a weariness on the part of the public barraged with tales of medical breakthroughs may be to blame. "I'm really not sure of the reason," he says. The trust has already made substantial investments in promoting science, such as its $26 million donation to London's Science Museum for its new Wellcome Wing, and Dexter hopes to do more. "In my local pub in Cheshire when I talk to people there is still some real curiosity about research," he says.

–Nigel Williams

CHEMISTRY

New Fullerene Rounds Out the Family

Materials scientists could soon be playing a new ball game. For more than a decade, they have been struggling to turn the 60-carbon soccer balls called buckminsterfullerenes into new materials and compounds. Now, researchers at the University of California, Berkeley, report in this week's issue of *Nature* that they've isolated a smaller fullerene sphere that contains just 36 carbon atoms. Tests on the new fullerene show that it is far more chemically reactive than its larger cousin, which could make it easier to fashion into everything from high-temperature superconductors to high-strength materials.



PISKOTI ET AL.

Buckyball's little brother. C_{36} (yellow) is the first fullerene to have fewer carbons than the original molecule (blue).

Researchers have known for years that the carbon-rich gases from which C_{60} and other, larger, fullerenes condense also contain a 36-carbon form. But the gases normally yield so little C_{36} that researchers had never been able to isolate and examine it. The Berkeley group's success is "really heroic," says James Heath, a chemist at the University of California, Los Angeles, who was part of the team that originally discovered fullerenes in 1985.

The researchers—physicists Charles Piskoti and Alex Zettl, along with chemist Jeff Yarger—started by passing a strong electric arc between a pair of carbon electrodes, in a vacuum chamber containing a whiff of helium. This creates a carbon vapor in which fullerenes of many different sizes take shape, along with piles of carbon soot. When they boosted the helium concentration, Zettl and his colleagues found they got a sharp rise in the production of C_{36}. The helium is thought to cool the vaporized carbon quickly, preserving fullerenes as they form.

After that, "the main hurdle was purifying the C_{36}," says Piskoti, a graduate student in Zettl's lab. The Berkeley team tried two different strategies, both of which worked. In one, they drenched the soot in toluene, a solvent that dissolves and removes C_{60} and C_{70}, then placed the semipurified soot on a tungsten tray and heated it rapidly to about 1500 degrees Celsius. The larger soot particles were unaffected, while the smaller C_{36} molecules evaporated and condensed onto another metal surface above, forming a thin film of pure C_{36}. In their second approach, members of Zettl's team searched until they found other solvents—in this case pyridine and carbon disulfide—that could selectively dissolve C_{36} from the semipurified soot.

After isolating bulk samples of their new fullerene, Zettl and his colleagues took nuclear magnetic resonance spectra to determine the shape of the molecule. Its appearance—like a slightly squashed sphere—bears out theoretical predictions of the most stable closed structure 36 carbons can form. The group also found that these new fullerenes are very reactive and quickly decompose in air, says Piskoti.

This reactivity, due to the strained bonds in the sharply curved structure, could make C_{36} hard to handle, because separate molecules quickly bond together in a jumbled mass. But it could also turn out to be a blessing. Because C_{60} itself is fairly inert, disturbing its structure with additional chemical groups often results in a less stable product. But because C_{36} is unstable to start with, linking other atoms to it could yield stable new substances, which the molecule's unusual structure could endow with useful optical and electronic properties.

Among those properties might be superconductivity. C_{60} can act as a superconductor when it is doped with rubidium, but it loses its superconductivity above 31 kelvin—far below the 135-K record for high-temperature superconductors. But theories suggest that C_{36} should be able to do much better, perhaps even beating today's best ceramic superconductors. Zettl's group is pushing ahead to find out. It's a safe bet that they'll soon have a fair amount of company.

–Robert F. Service