

adviser asked him to attend a workshop the foundation had organized and, after spending two days talking with other scientists, Hughes was smitten. He now receives funding from the High Q Foundation in New York — a successor to the Hereditary Disease Foundation — and he finds them a gratifying but demanding partner. High Q expects its researchers to make clear contributions to the search for cures, and leaves little room for academic digressions. "But the benefit of working with High Q is that you get a sense that you're working as part of a community towards a common goal," he says. "There's a kind of excitement to that."

tion called Hunting-

ton's disease. Hughes'

Biomedical researchers have long flirted with private foundations and wooed them into bankrolling their research. Many of these foundations are small entities focused on rare conditions and supported by patient advocates and donations. And in the past, such groups were happy to dole out money, giving academic scientists a relatively free reign to investigate the fundamental

roots of disease. But today the relationships between funders and scientists have become more passionate, needy and complex. Today's disease-focused foundations are becoming frustrated that basic research is not being converted into drugs for sick patients. They prefer to back 'translational' research, which aims to speed progress towards that goal and, to do this, they select research projects carefully and demand that scientists deliver concrete results on time. "The day of simply giving small grants is over. Now, you raise the money, you become educated about the science, and you take a seat at the table and become part of the conversation. It's absolutely new," says Susan Fitzpatrick, vice-president of the James S. McDonnell Foundation, based in St Louis, Missouri.

Researchers, for their part, are keen to help. But they are also attracted by government grants and the greater financial security and intellectual freedom these tend to offer. Through interviews with scientists and the numerous foundations that fund them, Nature gained a broad picture

of the trade-offs involved in these relationships  $\,$ — a picture best illustrated by putting one foundation under the microscope.

## **Fatal attraction**

Jenny Morton first became seriously interested in Huntington's disease in 1991, when she was setting up her first independent laboratory at the University of Cambridge, UK. During her postdoctoral fellowship, she had done a little research on the devastating illness, in which patients' physical and mental faculties inexorably waste away. Then, at a meeting, Morton met a woman whose husband and father-in-law had died of Huntington's and whose two children also inherited the disease. "I thought it was not only an academically interesting subject, but a terrible disease, so I decided to work on it," Morton recalls.

Morton applied for money from the Medical Research Council — the primary public funder of basic biomedical research in the United Kingdom — but was turned down. Like other rare conditions, Huntington's disease simply

doesn't have the same public priority as illnesses that claim many more victims, such as cancer. And because the potential market for treatments is so small, it is unattractive to drug and biotechnology companies.

These factors are frustrating for patients who have these rare conditions, and for the researchers who want to study them. So, in 2002, a group of private donors set up the High Q Foundation. The donors had one goal: to convert the fundamental knowledge about Huntington's disease gained over the past half-century into a cure.

## **Sniffing out success**

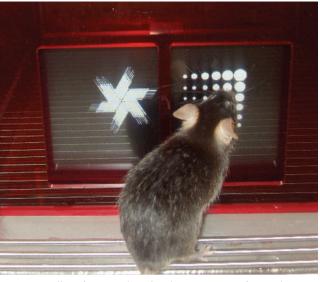
To achieve this goal, High Q and its sister group the CHDI — the successor to the Cure Huntington's Disease Initiative - now function more or less as a biotechnology company. High Q looks for disease targets — biological molecules that behave aberrantly in Huntington's. The CHDI looks for drugs that can correct the behaviour of those targets. For much of this work, the groups fund efforts in the biotechnology industry. But High Q also relies on hand-picked projects by academic researchers such as Morton to aid its quest for targets. "Ninety-five per cent of science works on the principle that the best thing to do is to let good scientists follow their noses," says Allan Tobin, a senior scientific adviser to High Q. "But this is a different attitude. We think we can direct the science."

Morton received her first funding from the Hereditary Disease Foundation in 2002, and now receives around half of her costs from High Q. The money supports studies on mice with characteristic features of Hungtington's disease. Morton also collaborates with doctors, who help her to design her animal experiments so that they are relevant to finding a cure for patients.

Morton sees many benefits to drawing much of her funding from a private foundation, rather than from a public source. For one, the organization is more willing than the government to take risks on new ideas. Five years ago, for instance, she and two other scientists brainstormed an idea for a computerized 'touch-screen' for mice. They hoped it would solve a major problem in the field by allowing them to evaluate the brain functions of animals who were physically incapable of running through a maze but could still touch a screen with their noses.

Some colleagues sneered at Morton's idea because they thought it would be impossible to teach mice with movement disorders to use such a device. Thinking that their derision would be reflected in grant reviews from government agencies, she asked High Q for the money instead, and the foundation gave her a \$350,000 contract for three years to make the touch-screen prototype. Last year, Morton and her colleagues showed that they could teach mice to touch the screen and earn food pellets (A. J. Morton, T. J. Bussey & L. M. Saksida Nature Methods 3, 767; 2006).

Although foundations provide valuable support for new ideas, working with these organizations can also be challenging — and most



The High Q foundation supported development of a touch-screen for disabled

scientists still prefer to work with at least some government grants. For Morton, an important concern is the maintenance of her mice, which costs about £80,000 (US\$160,000) a year. Breeding for experiments has to be planned months or even years in advance, so Morton needs to know that money will be available for those future studies and to keep staff on contracts to do them. This can be done with a typical grant from the Medical Research Council, which runs from three to five years, but High Q's awards are typically only for one year. "Short-term funding when you are trying to keep a long-term project going is very difficult," Morton says.

## Straight and narrow

With their new focus on delivering cures, today's foundations also insist that researchers deliver results or, in the case of high-risk projects, at least show that they tried. Some ask for detailed reports every six months or a year, and make further funding contingent on meeting strict milestones. High Q awards contracts rather than grants to ensure that scientists actually do the work they say they will do, rather than pursuing serendipitous tangents — a luxury that is allowed or even encouraged with government grants. The foundation also insists that researchers share the results of their work as quickly as possible, and discuss unpublished findings openly with colleagues at meetings.

Some researchers find this type of oversight too onerous or controlling. They resent the loss of intellectual freedom and tend to stay away from groups such as High Q. Robi Blumenstein,



"We think we can direct the science." — Allan Tobin

a former businessman who now manages the operations of High Q and the CHDI, acknowledges that their business-like procedures can chafe some academics, but he makes no apolochafe some academics, but he makes no apologies. "We want people to have great ideas, but we need to get them done," he says. "When we switched to this more rigorous model we acknowledged that we weren't going to get everybody to work with us."

Because of the constraints, researchers who do work closely with foundations like these are usually driven by something more than pure intellectual curiosity. Many scientists relish the opportunity to participate in directed, translational research that could benefit patients. Foundations may also allow them to belong to a larger research community of scientists dedicated to the same pressing problem.

In 2003, funding from High Q created the European Huntington's Disease Network, which was the first organization to unite Huntington's disease researchers across Europe and the thousands of patients that they study. "In Europe, there is no network of collaborative research like this in any other neurodegenerative disease," says Sarah Tabrizi, a doctor and researcher at University College London. This network is helping Tabrizi to find biomarkers that may predict the onset of the disease and launch clinical trials to test them. These benefits, she says, far outweigh the inconvenience of complying with short grant cycles and stringent milestones.

But for some, the expectations and sacrifices demanded by foundations are too high. For these researchers, the traditional security of government money offers a more productive union.

Tobin acknowledges that researchers need to make difficult calculations before plunging into a relationship with High Q. "We realize this is an experiment, and it involves a bunch of trade-offs," he says. "The key is that we respect each other." And that, of course, is good advice for any solid partnership — in science, as in other parts of life.

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