

STATE OF THE DONATION

Wealthy philanthropists and private foundations are supporting biomedical research on a grand scale.

Meredith Wadman asks what they get for their money.



B. MELLOR

Scientists arriving at the Stowers Institute for Medical Research in Kansas City, Missouri, might think they've chanced on Xanadu. Limestone floors and fine furniture seduce the eye, and from the expansive gardens comes the soothing sound of fountains. Inside this research palace, funded by a \$2-billion endowment from local mutual-fund magnates Jim and Virginia Stowers, scientists pursue research on fundamental cell biology. Dozens are flush with US\$1 million funding a year, and their work is often destined for stellar publications.

The Stowers are not alone in their generosity; philanthropic foundations have long had an important role in biomedicine, from the birth of the Carnegie Institution in Washington DC in 1902 to the biomedical activism of the Rockefeller Foundation in the 1930s and 1940s. But during the past decade, philanthropists — and the foundations that they establish to distribute their money — have begun funding biomedical science on a particularly striking scale.

Dominating this landscape is the Bill & Melinda Gates Foundation with its plans to nurse the globe to better health, boosted last year by billionaire financier Warren Buffett (see page 254). But there are other donor organizations, many of which fund more basic biological research, ranging from the United States' mighty Howard Hughes Medical Institute (HHMI) to Britain's Wellcome Trust, the world's largest charity exclusively devoted to

biomedicine (see page 251). Their cash is being lapped up by researchers parched by flat funding from the US National Institutes of Health (NIH) and many other sources.

These new givers — the gigaphilanthropists — are perceived to be making an impact on the research landscape that is much greater than the sum of their dollars. "The effect of the private foundations is not reflected in the total funding they supply. They have disproportionate influence," says Hamilton Moses of the Alerion Institute, a Virginia-based think-tank that focuses on innovation in biomedical research. They can, and do, take financial and scientific risks unthinkable with tax-payers' dollars. They fill gaps left by government and industry, dictate exactly what their money is spent on and act quickly compared with the sometimes glacial pace of government agencies. But although those running the organizations are sure that private money buys more and better science than public money, there is little concrete evidence they are right.

The new wealth also comes with strings attached: some funders keep a businesslike control over the direction of the research they pay for and demand a level of accountability that can make researchers uncomfortable (see page 252). Some observers worry about the growing power wielded by the gigaphilanthropists over the research agenda if, as is predicted, charitable giving reaches new heights in the future. They are concerned that too many important decisions with an impact

on biomedicine will be made in the boardrooms of foundations with little scientific expertise — and no public input or accountability. "You may have foundations with assets larger than almost 70% of the world's nations making decisions about public policy and public priorities without any public discussion or political process," says Pablo Eisenberg, a senior fellow and philanthropy-watcher at the Georgetown Public Policy Institute in Washington DC.

Value for money?

By all accounts, the amount of money from non-profit foundations and philanthropists is growing strikingly. In Germany, for example, the Frankfurt-based Hertie Foundation has spent more than €90 million (US\$122 million) on nurturing neuroscience since 2000, compared with a total of €30 million in the previous quarter century.

In Britain, charities fuel more than half of the biomedical research enterprise, led by the Wellcome Trust, which served up £484 million (US\$960 million) in research funding last year compared with £270 million just over a decade ago. In the United States, a wave of philanthropic giving over the past decade has been fuelled by a buoyant stock market and a generation of ageing, affluent baby boomers. Investing in biomedicine allows them to do something that might support the health of their children, and gains them significant tax breaks.

In 2005, a study led by Moses showed that private, non-corporate support for US biomedical

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research leapt 36% to \$2.5 billion between 1994 and 2003 (H. Moses *et al.* *J. Am. Med. Assoc.* **294**, 1333–1342; 2005). Today, “\$5 billion is probably an undercount”, Moses says, when one includes philanthropic funding in all its varieties. This still accounts for no more than 5% of the roughly \$100 billion spent annually in the United States on biomedical research (the biotechnology and pharmaceutical industries account for about 60% of this total and the government, led by the \$29-billion budget of the NIH, for most of the rest). But even so, the massive donations and influence of the US foundations, along with the Wellcome Trust, bear examination.

Linheng Li was one of the first scientists through the door after the Stowers Institute opened in late 2000. Li was intent on ending a 25-year quest by stem-cell scientists to find the ‘niche’ in bone marrow that harbours blood-forming stem cells. In 2003, Li delivered, with a paper in *Nature* describing the cells’ physical and biochemical environment in mice (J. Zhang *et al.* *Nature* **425**, 836–841; 2003), a discovery that had the potential to help researchers grow stem cells outside the body.

Scores of such anecdotes suggest that the munificent backing of a gigaphilanthropist generates more, and more influential, scientific results. But they are just that: anecdotes. There are few if any studies rigorously comparing the productivity of an HHMI investigator, for example, against that of an NIH-funded colleague down the hall.

Such assessments are difficult to make, partly because there are few researchers who rely solely on a single source of funds, philanthropic or public, and so could be sensibly

compared. There is also an ‘apples and pears’ problem, adds Mark Walport, the Wellcome Trust’s director. The trust focuses much of its support on young scientists and building research capacity in the developing world. “It would not be meaningful,” he says, to try to compare the scientific outputs of these programmes with those from senior, independent investigators supported by Britain’s government-funded research councils.

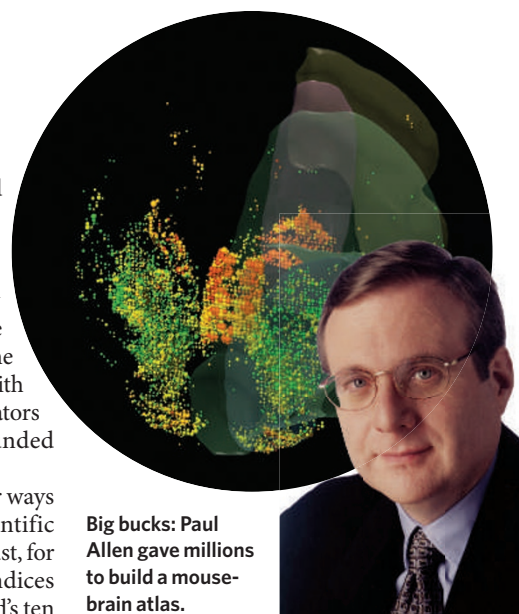
The gigaphilanthropists do find other ways to gauge whether they are getting scientific value for their money. The Wellcome Trust, for instance, has combed global citation indices to establish that it funds five of the world’s ten

most-cited malaria researchers, and four out of the top ten in the cognitive sciences. The Ellison Medical Foundation, based in Bethesda, Maryland, funds ageing research. It is building an electronic archive of every application it receives and it plans — many years hence — to use citations

and other measures to analyse the impact of researchers it backed and those it turned down. Meanwhile, executive director Richard Sprott says he attends as many national and international meetings as he can. “I listen to who’s doing the cutting-edge, exciting stuff. If it’s our people, I think we’re doing okay.”

Tom Cech, the Nobel-prizewinning chemist who has directed the HHMI since 2000, says that the number of plaudits won by its scientists “prove that our investigators are far more successful than average”. Between 1994 and 2007, 89 HHMI investigators were elected to the National Academy of Sciences (NAS) and seven won Nobel prizes. The HHMI has calculated

Big bucks: Paul Allen gave millions to build a mouse-brain atlas.



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that its investigators were more than ten times more likely to be elected to the NAS than US biologists funded by the NIH, and over 16 times more likely to win a Nobel prize in chemistry or medicine. “What we can’t rigorously prove is whether they are more productive because of our support, or simply because we know how to choose winners,” Cech says.

Taking risks

Not every foundation does know how to choose winners, points out Eisenberg. “There are foundation officers who are sharp and knowledgeable, and those who are not,” he says. Without more rigorous comparisons, some observers question whether, dollar for dollar, philanthropic donations guarantee more good science than government or industry does. “I don’t think the data overall would hold up,” says Mary Woolley, president of Research!America, a health-research advocacy group in Alexandria, Virginia. “Plenty of people who have received the Nobel prize were funded by the NIH.”

Philanthropic organizations can certainly put great pressure on their grant recipients to ensure they deliver. At the Stowers Institute, the senior scientists are appraised after five years’ generous funding, when the institute enlists leaders in a researcher’s speciality to evaluate their performance. “The only question we ask is whether the leaders in the field can say definitively, specifically and discretely: ‘This is what this person has done at Stowers that has changed how people think about the field,’” says Stowers’ president Bill Neaves. Since the institute opened its doors, eight of nine senior scientists who have been evaluated have passed that test.

Private foundations have a flexibility and agility with their spending that industry and government agencies do not. They are not answerable to shareholders or venture capitalists; nor do they labour under the political and public scrutiny experienced by the NIH and



The Stower’s Institute provides generous funding but expects star results in return.



Taking a risk: Janelia Farm represents a leap in the dark both for researchers and the HHMI.

other spenders of public money. "When I was at the NIH, we had to ask ourselves a question when contemplating every award: 'Can I live with it on the front page of *The Washington Post*?'", says Sprott, a former director of the National Institute on Aging. That kind of thought process, he says, "tends to make the NIH very conservative".

The NIH, under director Elias Zerhouni, has launched an ambitious effort to battle this conservatism. Since 2004, for instance, Zerhouni has awarded 35 Pioneer awards to individual investigators for high-risk research, delivering around \$2.5 million to each over the course of five years. But for philanthropists, risk-taking is often the rule rather than the exception. "When you are a very small slice of a large pie you not only have the opportunity, but I would say the responsibility, to do something out on the edge," says Cech.

Brain storm

Lately, Cech's organization has been pushing the edge at Janelia Farm, the \$500-million research complex near Washington DC. Since September a cadre of top-tier scientists has been set loose here to try to unravel how information is processed by neuronal circuits — a departure for the HHMI, which until now has supported researchers in their home institutions.

At Janelia Farm, researchers work in small groups without the benefit of tenure or outside funding — but with a freedom from the hassles of grant-writing, teaching and administrative duties that is almost unique in US science. Director Gerry Rubin says that the best science comes from making such an expensive but risky investment, even if nine out of ten projects fail. "We are venture capitalists here," he notes.

The gigaphilanthropists can also move fast. When the US Postal Service was beset by anthrax attacks in the autumn of 2001, researchers quickly realized that they needed to know the background level of anthrax in post offices around the country. "It would have taken the NIH two or three years to solicit and award a grant answering that question," says Sprott. "We could pick up the phone and call the world's top

anthrax expert and ask him to design and carry out the needed study. We had an answer within six months." Ellison's investigator found 15 different strains of anthrax of the kind that infect cattle, sheep and horses; none was the strain being sent through the mail.

Generally, the new philanthropists are not the type to write a cheque and walk away. They are determined to identify and fill key gaps in public funding — and to make sure the work gets done. Take Paul Allen, the Seattle billionaire who co-founded Microsoft with Bill Gates. In 2001, Allen summoned the best and brightest minds he could find in genomics, neuroscience and psychology and asked them what could and should be done to change the field of brain science. In 2003, he and his sister, Jody Allen Patton, signed a cheque for \$100 million to launch the Allen Institute for Brain Science in Seattle*. Last year, researchers there unveiled the Allen Brain Atlas, a three-dimensional map showing where thousands of genes are active in the mouse brain. Some 800 scientists are using the atlas daily, according to the institute.

Like the Allens, foundations "all want mis-



The Wellcome Institute's Mark Walport has hundreds of million of pounds to spend.

sions accomplished", says Donald Brown, president of the Life Sciences Research Foundation, a non-profit organization based in Baltimore, Maryland, that solicits grants from foundations and industry to support postdocs.

Targeted philanthropic spending gets big, expensive projects done fast, but it also draws criticism. Because US charitable foundations are required by law to spend 5% of their assets each year, money can be thrown at projects too quickly for some people's tastes. Gigaphilanthropists can choose to fund research at the whim of their benefactors and the advisers they choose, very different to the extensive consultation with the scientific community that occurs before government money is committed to a big project. In the case of the Allen Brain Atlas, some researchers grumble that the money would have had a far greater impact on neuroscience if it had been spread among a group of top investigators.

More recently, some foundations' alacrity has been taxed as they find themselves scrambling to compensate for the funding freeze at the NIH and keep individual investigators afloat. Some are concerned that this constrains their flexibility — and that they risk being taken for granted. "I worry that we are allowing the government to say: 'We don't have to pay the bill. Private philanthropy will step in,'" says Sprott. "That's not what we want to do."

As Paul Schervish sees it, the current flow of philanthropic money may look a mere trickle by the time today's postdocs retire. In a widely cited 1999 report, Schervish, director of the Center on Wealth and Philanthropy at Boston College, and his colleague John Havens predicted that by 2052 at least \$6 trillion in wealth would be transferred from the estates of older Americans to charity — some \$100 billion more per year than today. That would amount to a significant chunk of cash for biomedicine if, as is the case today, roughly 20% of that money goes to health. "We are going to see substantial foundation growth," says Schervish.

If his prediction pans out, many more researchers will find themselves relying on — and answerable to — the gigaphilanthropists. At the Stowers Institute, the founders have already announced plans to add 56,000 square metres of facilities and 600 people every decade in perpetuity. But in the rich biomedical landscape of the future, it may be just one of many palatial shrines to research.

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For more on philanthropy, see our online special at www.nature.com/news/specials/philanthropy. See also Editorial, page 231.

**Nature* has a commercial collaboration with the Allen Brain Institute in the Neuroscience Gateway.