The power of giving

The willingness of philanthropies to venture into neglected areas of scientific research is just one of several advantages to private funding

Bill Gates, the founder of Microsoft, does not necessarily enjoy a reputation for being a nice guy. But few could fail to appreciate his humanitarian interests after the Bill & Melinda Gates Foundation kick-started the Global Alliance for Vaccines and Immunization with a US\$750 million grant to increase access to vaccines in developing countries and boost vaccine development. Since its creation in 2000, the foundation, led by Gates' father, William H. Gates Sr, has given more than US\$3 billion to education and global health programmes that are aimed primarily at the developing world. Gates may be the richest private spender on international health, but the money that other private donors and foundations invest also makes a difference, particularly as it demonstrates that private funding is willing to tackle problems that industry and governments cannot, or will not, face.

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At a quick glance, the contribution of private money to research seems rather low: in 2002, non-profit institutions contributed an estimated 4.2% of the total US\$276 billion investment into research and development in the USA; in other countries, statistics show that this per-

centage is much lower (National Science Board, 2004). However, considering the US government contributed only about 12% of the US\$276 billion and more than 70% came from industry, the relative impact of private money on public research becomes more apparent. In addition, private donors have one major advantage over industry or government: they do not have to satisfy shareholders or voters. This freedom, in contrast to restrictions on the use of public money, makes charitable foundations particularly powerful in specific areas. "I think this is an important role for philanthropy," said Susan M. Fitzpatrick, vice president of the James S. McDonnell Foundation (see Table 1 for a list of selected philanthropies and their scientific interests).

Take for instance stem-cell research in the USA. After President George W. Bush decided in 2001 that federal funds could only be used for research on existing stem-cell lines, scientists have increasingly turned to private charities and foundations for money. This May, Houston philanthropists Shahla and Hushang Ansary gave US\$15 million to establish the Ansary Center for Stem Cell Therapeutics at Cornell University's Weill Medical College (New York, NY, USA). The University of Texas Health Science Center (Houston, TX, USA) also recently received a ten-year US\$25 million grant from an anonymous donor, reportedly a grateful patient of James T. Willerson, President of the Center. Private support of politically sensitive research did not start under the Bush administration; when the Reagan administration issued a moratorium in 1988 on federal funding of fetal tissue transplantation research, which

severely restricted research into treatments for Alzheimer's, Huntington's and Parkinson's diseases, the Parkinson's Disease Foundation continued to support research using private funding. At the beginning of the AIDS epidemic in the USA, the Aaron Diamond Foundation was the largest private supporter of AIDS research, spending more than US\$220 million in total.

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Private money can also help projects that suffer from a lack of interest rather than legal or political hurdles. In 2002, the Gordon and Betty Moore Foundation, established by Intel's founder Gordon Moore, decided to support the open-access movement in scientific publishing with a five-year US\$9 million grant to the Public Library of Science (PLOS). The result was *PLOS Biology*, an open-access journal that has probably attracted more attention than Gates' foray into the developing world. The Howard Hughes Medical Institute (HHMI), the US National Institutes of Health, Germany's Max Planck Society, the UK's Wellcome Trust and other research organizations quickly endorsed the PLOS business and publishing model and pledged to cover researchers' publication costs in support. By doing their homework first and investigating the benefits of the project, "we played a bigger role there than just writing a cheque", said Ed Penhoet, Chief Program Officer for Science and Higher Education at the Moore Foundation.

Table 1 | A selection of philanthropies with interests in the biomedical, health or life sciences

Foundation	Web site	Location	Year founded	Funding (US\$, UK£ or €)	Selected areas of interest
Atlantic Philanthropies	www.atlanticphilanthropies.org	Hamilton, Bermuda	1982	Almost \$1 billion to date	Health in developing countries; ageing
Gatsby Charitable Foundation	www.gatsby.org.uk	London, UK	1967	–	Plant science; cognitive neuroscience; mental health
Wellcome Trust	www.wellcome.ac.uk	London, UK	1936	Approx. £400 million per year	Biomedical science; applied clinical research; medicine
Fondation Fyssen	www.fondation-fyssen.org	Strasbourg, France	1979	–	Cognitive mechanisms
Fritz Thyssen	www.fritz-thyssen-stiftung.de	Cologne, Germany	1959	€12 million in 2002	Medicine and natural sciences; molecular pathogenesis and disease research
Volkswagen Foundation	www.volkswagen-stiftung.de	Hannover, Germany	1961	€3 billion to date	Biosciences; communicable diseases in sub-Saharan Africa
Alexander von Humboldt Foundation	www.avh.de	Bonn, Germany	1953	–	Promoting international research cooperation
Fundación Juan March	www.march.es	Madrid, Spain	1955	–	Biological research
Dr Robert C. Atkins Foundation	www.atkins.com	Ronkonkoma, NY, USA	1999	Over \$3 million to date	Nutrition and carbohydrate research
Burroughs Wellcome Fund	www.bwfund.org	Research Triangle Park, NC, USA	1955	Approx. \$25 million per year	Basic medical sciences; emerging infectious diseases; interfaces in science; translational research; science education
Charles A. Dana Foundation	www.dana.org	New York, NY, USA	1950	–	Brain research; immunology
Aaron Diamond Foundation	www.adarc.org	New York, NY, USA	1985–1996	\$220 million total	HIV/AIDS research
Ellison Medical Foundation	www.ellison-med-fn.org	Bethesda, MD, USA	1997	–	Ageing research; infectious disease research
Michael J. Fox Foundation for Parkinson's Research	www.michaeljfox.org	New York, NY, USA	2000	Over \$42 million to date	Parkinson's disease research
Bill & Melinda Gates Foundation	www.gatesfoundation.org	Seattle, WA, USA	1999	Over \$3 billion on health-related grants	Global health; reproductive and child health; infectious diseases, HIV/AIDS, tuberculosis
Howard Hughes Medical Institute	www.hhmi.org	Chevy Chase, MD, USA	1953	–	Biomedical research
W. M. Keck Foundation	www.wmkeck.org	Los Angeles, CA, USA	1954	–	Healthcare; medical research; science; engineering
Lymphoma Research Foundation	www.lymphoma.org	New York, NY, USA	2001	Over \$18 million in total	Lymphoma research
MacArthur Foundation	www.macfound.org	Chicago, IL, USA	1978	Over \$3 billion to date	Population and reproductive health
James S. McDonnell Foundation	www.jsmf.org	St Louis, MO, USA	1950	Over \$264 million to date	Brain, mind and behaviour; complex systems; brain cancer research
Gordon and Betty Moore Foundation	www.moore.org	San Francisco, CA, USA	2000	Over \$650 million to date	Marine microbiology; biodiversity conservation
Open Society Institute	www.soros.org	New York, NY, USA	1993	–	Medicine; public health; science education
Parkinson's Disease Foundation	www.pdf.org	New York, NY, USA	1957	Annual budget of more than \$6 million	Parkinson's disease research
Pew Charitable Trusts	www.pewtrusts.com	Philadelphia, PA, USA	1948	Over \$3 billion to date	Biomedical research and training
Rockefeller Foundation	www.rockfound.org	New York, NY, USA	1913		Global health

While the USA undoubtedly receives the lion's share of philanthropic funding, many foundations increasingly recognize the importance of supporting other, more neglected, regions throughout the world. The HHMI funds scientists in the Baltics, Central and Eastern Europe, Russia and the Ukraine—areas that rarely receive any money for research. The Open Society Institute, founded by Hungarian billionaire George Soros, has foundations in these areas to support public health programmes and initiatives to combat infectious diseases such as AIDS and tuberculosis. The HHMI, the Wellcome Trust, the Rockefeller Foundation, the Volkswagen Foundation, the Gates Foundation and other private charities have begun to support research projects and public health programmes in sub-Saharan Africa.

The freedom inherent in private donations often means that they can be used to support areas of more personal interest. In January 2004, the Lymphoma Research Foundation received an anonymous US\$12.8 million donation to find a cure for mantle-cell lymphoma—an incurable yet relatively rare disease that will kill probably fewer than 2000 Americans this year (American Cancer Society, 2004). The donor was described as a New York-based family affected by mantle-cell lymphoma. Because rare diseases often receive little or no regular funding, private money can make a big difference, but usually only if a philanthropist is personally touched by a disease.

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Such was US actor Michael J. Fox's interest in establishing his own foundation in 2000, after being diagnosed with young-onset Parkinson's Disease almost ten years earlier. The Michael J. Fox Foundation for Parkinson's Research has donated more than US\$42 million in research funding. Larry Ellison, CEO of software giant Oracle (Redwood Shores,

CA, USA), established the Ellison Medical Foundation in 1997 to fund research into ageing and global infectious disease; it is now the largest private source of funding for ageing research, and provides about US\$20 million per year. But sometimes funding choices are not purely altruistic; following the death of her husband, diet guru Robert Atkins, Veronica Atkins now uses the Dr Robert C. Atkins Foundation to support research into the safety and efficacy of low-carbohydrate diets (Blum, 2004). The US\$1.5 million in grants so far has made quite a dent in the field of nutrition research, which enjoys little support from other private funding sources.

Ultimately, "philanthropy allows for a diversity of both decision-making and interest," said Fitzpatrick. In this way, it should complement rather than replace other funding sources. Indeed, "most people have foundation grants and government dollars simultaneously," as any glance at published papers will show. Philanthropy has the power and freedom to take risks, be daring and fund ideas and projects that others do not, or cannot. Wilhelm Krull, secretary-general of the Volkswagen Foundation, described the magic triangle of successful philanthropy as a combination of risk-taking, flexibility and quality assurance.

"It's really more conceptually the idea. Is this a new idea? Is this a new way of looking at a problem, or thinking about a question, or taking an area of research into a slightly new arena that might be difficult for you to do in traditional funding schemes?" Fitzpatrick explained, describing the James S. McDonnell Foundation's philosophy behind funding. On the other hand, "sometimes there's work that's not readily fundable because it seems almost too pedestrian," she said, citing traditional neuroanatomy research as an example. "But yet, it's a fundamental piece of information that, if we don't understand it, we can't go forward." Above all, like any other source of funding, "philanthropy really should be an investment for the acquisition of new knowledge."

According to Penhoet, "the philanthropy business may be the fastest growing business in this country right now." However, outside of specific disease-associated organizations, science is still not a major target for private dollars, which instead go to education, social

services or the arts. And biomedical research still fares better than areas such as geology, environmental research or chemistry. People want their money to go where it will make a difference; because much disease and biomedical research is well-funded through government sources, many foundations, including the Moore Foundation, fund very little biomedical science. "We just couldn't convince ourselves that with US\$200 million, we could really change the face of biomedical science," Penhoet explained. And because the challenges facing the developing world are so immense, many philanthropists feel they are incapable of addressing them. "We don't have the real expertise in Africa so for us to get comfortable making sound investments there, we would have to build up some significant expertise and networks in Africa," Penhoet said.

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Instead, they concentrate more on issues closer to home, such as the Moore Foundation's Wild Salmon Ecosystems Initiative throughout the North Pacific, and one of their latest initiatives—marine microbiology. "We want to advance the field of marine microbiology in a major way," Penhoet explained. The Moore Foundation plans to invest US\$145 million over the next ten years to learn more about the composition, function and ecological role of microbial communities in the ocean, and what role these communities play as the basis of the ocean's food webs and in facilitating the flow of nitrogen, carbon and energy in the ocean. Some of the money will support a sampling expedition across the northwestern Atlantic Ocean—part of the Institute for Biological Energy Alternatives' (Rockville, MD, USA) goal of characterizing microbial community diversity. "The science is tremendously interesting and is not well exploited because it has been poorly funded until now," Penhoet explained. "And new technologies, especially genomics, will have a huge impact on this field."

But philanthropies have the power to impact on more than just science. In a letter to *Nature* soon after President Bush decided to limit support for stem-cell research, Fitzpatrick urged, "Let's use private money to fund the research, let's get the data out there, and let's use the scientific findings to guide policy debates" (Fitzpatrick, 2001). Already, individual states in the USA are debating their stance on stem-cell research; if privately funded research yields positive results, it may influence states to approve further stem-cell research, and even to lift the Bush ban. But the influence of politics should not be underestimated—it took a change in administration before Reagan's moratorium on fetal tissue research was lifted by US President Bill Clinton in 1993. On the other hand, the launch of *PLoS Biology* has already triggered much change and debate in the publishing world (Grivell, 2004).

Indeed, sometimes just a spark of philanthropic interest is enough to convince others of the possibility of change. In 2003, a consortium of scientists led by Richard Klausner of the Gates Foundation pressed for the need for a global HIV vaccine enterprise (Klausner *et al*, 2003) in light of the accelerating global AIDS pandemic, particularly in sub-Saharan Africa and Asia. Even the possibility that Bill Gates may be willing to step in and fund vaccine research has brought together HIV and AIDS experts from government, industry, academia and non-profit organizations worldwide to discuss how to tackle this problem through collaboration and vision.

Nevertheless, large-scale philanthropic funding, as much as it is needed, may also have drawbacks. While it can certainly encourage others to follow suit and put their money to good use, it can discourage potential donors from supporting the same projects. "You know, there's some of each, frankly," Penhoet commented. In areas that were previously underfunded, such as the salmon ecosystem research, "our presence [there] has stimulated a lot of interest," he said. In other areas, however, large grants could give the impression that no more funding is needed. When Gates gave the International AIDS Vaccine Initiative US\$100 million in 2001, other donors—who had been in the final stages of negotiations—pulled back (Strom, 2003).

Ultimately, the sheer size of the Gates Foundation grants might be distracting people from the real strengths and aims of philanthropy. "There's this fascination about 'how much' rather than 'what for'," Fitzpatrick said. Although Gates' millions will undoubtedly have a huge impact on the developing world, bigger is not necessarily better. The Moore Foundation's effect on open-access publishing is proof that even a relatively small amount of money can bring about change. No matter how big or small the grants, the willingness of philanthropies to venture into neglected terrain remains an important support for scientific research.

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Finding my enemy's enemies

The use of friendly microbes to thwart pathogens has a long history. Will the latest wave of discoveries bring us any closer to new biological medicines?

Lin Tao, a researcher at the College of Dentistry at the University of Illinois (Chicago, IL, USA), may have found a way to stop countless infants contracting HIV. This May, at the American Society for Microbiology general meeting in New Orleans (LO, USA), he presented his discovery of a specific strain of *Lactobacillus*, a commensal bacterium in human saliva, which could reduce the likelihood of HIV transmission from mother to breast-fed child. Giving this particular bacterium in the form of lyophilized powder to infants to populate their digestive tract may effectively block HIV from entering its target cells. Around 800,000 infants worldwide contract HIV in this way every year, most of them in Africa. But if Tao's research receives the necessary funding to go into development, a prophylactic against this particularly distressing route of transmission could be in sight. Although the discovery is still some way from application, it reinforces the wisdom that enlisting

your enemy's enemy can be as good as attacking him yourself.

It is simply a case of working out who eats whom

Since the first half of the twentieth century, scientists and medics have realized that the eternal struggles of the microbial world could be exploited for human benefit. Isolating the weapons of these wars provided physicians with a powerful arsenal against disease and infection. No sooner had penicillin been discovered, than pharmaceutical companies brought us even more antibiotics, such as other β -lactams and later polyketides and many other naturally occurring compounds. However, the declining effectiveness of many antibiotics—caused by the misuse of nature's gifts—combined with the convergence of many biological disciplines, is creating a renaissance in the field of biological control of pathogens. The