

genetically isolated population also has well-established genealogical records that date back to the first Scandinavians who settled on the island in the ninth century.

Even if Celera's original business model of selling access to sequence data has turned out to be unviable, it has nevertheless benefited research as a whole. The Human Genome Project started without any private sector impetus, but the public effort was largely accelerated in response to Celera, owing to fears that a private company could end up controlling the intellectual property rights to the human genome. This race to the finish resulted in the Project being completed earlier than expected, and gave scientists worldwide an enormously valuable research tool. In addition, the public data have been continuously improved and updated, to almost match the quality of Celera's proprietary data.

Will a public-private competition, similar to that which drove the Human Genome Project, happen again? It is already occurring, many say, but with less fanfare and in the opposite direction. In the 1990s, the efforts of the publicly funded project prompted Celera to join the fray. Today, public initiatives are staking a claim on industry's turf. Chapman believes that the work of Celera and Perlegen Sciences (Mountain View, CA, USA) in the area of genetic haplotypes—adjacent SNPs that are typically inherited together—prompted the establishment of the International HapMap Project in 2002. This seeks to catalogue haplotypes for use in identifying genes that are important in disease, and in individual responses to pharmaceutical drugs and the environment. Perhaps in response to commercial efforts, the National Cancer Institute developed the Cancer Genome Anatomy Project to compile gene expression profiles on normal, precancerous and cancerous cells.

Celera's legacy also extends beyond genetics. In 2004, the National Institutes of Health (Bethesda, MD, USA) established the PubChem chemical database. The project is, at least in part, intended to

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counter industry's increasing monopoly on chemical compounds. "It's like a public version of the big compound libraries that big pharmaceutical companies have in-house," said Ehlers. The project provides information on the biological activity of small molecules, along with their chemical structures, and allows researchers free access to carry out computerized screening, structure modelling and drug design.

So, how will history view Celera and its challenge to the public sequencing project? It is too early to judge it as a success

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or failure, as the story is not yet finished. "They did the right thing by their shareholders," Chapman said, before pausing. "Strike that: they did the right thing by a subset of their shareholders. Should they have gotten out earlier? I don't know. But they pushed science forward."

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The squeaky wheel gets the grease

Research funding is not necessarily allocated to those who need it most

A recent television advertisement in the USA featured a woman in her 30s remarking that, since she was a teenager, she had feared getting breast cancer. After all, one in seven women is now diagnosed with the disease, up from one in nine when she was younger. After years of regular breast self-examinations and mammograms, she was diagnosed with cancer—lung cancer, despite being a non-smoker. The voice-over at the end of the advertisement commented that nearly twice as many women now die from lung cancer each year than from breast cancer.

How the issue—and fear—of breast cancer came to occupy such a prominent place in the consciousness of women worldwide, while lung cancer stealthily became the new killer, illustrates the power of public relations campaigns and patient activism. Together, these forces have brought numerous diseases, including breast cancer, prostate cancer and HIV/AIDS, to the attention of millions. They have raised record amounts of private funding for research and are putting considerable public pressure on the government to adjust its biomedical research agenda. As philanthropic funding is limited, various patient groups fiercely vie for

the public's attention and contributions—and ultimately government funding. The public is increasingly confronted with 'duelling' statistics—which disease is worse, has higher mortality and is harder to treat—that compete for their attention and dollars. There is no parallel campaign, however, to raise money to develop new drugs for tuberculosis, even though one-third of the human race is infected, and 1.75 million died of the disease in 2003.

The Prostate Cancer Foundation (PCF; Santa Monica, CA, USA) is one such activist group, which has mounted an aggressive awareness campaign to draw attention to their cause. Junk-bond millionaire and prostate cancer patient Michael Milken founded PCF in 1993 to fund applied research, and the foundation now boasts an advisory board with former US presidents and numerous captains of industry. Its website and public relations material issue dire warnings that "without improvements in diagnosis and treatment, by 2015 the number of new [prostate cancer] cases will increase 50% from about 230,000 today to over 300,000...A non-smoking man is more likely to get prostate cancer than lung, bronchus, colon, rectal, bladder, lymphoma, melanoma, oral and



kidney cancers combined.” What PCF does not say is that prostate cancer has the highest five-year survival rate of all cancers, according to the National Cancer Institute (NCI; Bethesda, MD, USA), and that mortality rates have drastically declined as screening has increased.

Faced with various patient advocacy groups and their respective public relations campaigns, the difficult question for health officials is which disease should receive the most research funding, and why? The diseases that affect the most people, or the ones that kill the most? Is it the years of life lost or the amount of dollars spent on healthcare? The number of new cases per year or the growth rate of the disease? What effect, if any, do other funding sources have on federal funding?

The most prevalent cancers in the USA may serve as an example of how funds are currently distributed (Table 1). The NCI did not comment on its criteria for allocating research funds, but “the ACS allocates research funds on the basis of ‘scientific excellence’ rather than prevalence or mortality,” according to John Stevens, Vice President for Extramural Grants at the American Cancer Society (ACS; Atlanta, GA, USA). By contrast, lupus, a life-threatening autoimmune disease that largely affects minorities, has a much lower profile. Although 1.5 million US citizens suffer from lupus, the National Institutes of Health (NIH; Bethesda, MD, USA) allocated only US\$88 million for

research in 2005, down from US\$96 million in 2003. Lupus will receive another US\$25 million from non-profit organizations, according to Duane Peters, Vice President for Advocacy and Communications at the Lupus Foundation of America (Washington, DC, USA). There are about one million patients diagnosed with HIV/AIDS in the USA, and research received a total of US\$2,981 billion from the NIH this year.

Another disease playing catch-up is sickle cell anaemia, a painful condition that can halve lifespan and that affects 72,000 Americans, mostly African Americans. Research into this disease only really got underway in the 1970s in response to the civil rights movement in America, which brought the concerns of African Americans to the attention of the public and the government. The race component of sickle cell anaemia helped fuel more recent research into health disparities in the USA, and spawned attempts to redress racial and economic imbalances.

Not surprisingly, every patient advocacy group makes a case that their disease requires more research funding—PCF maintains that patient numbers are steeply rising each year to ‘epidemic’ proportions, in spite of the fact that most men with prostate cancer will not die from the disease. Lung-cancer groups point to extremely low one- and two-year survival rates, which they believe explains why the need for research money for their disease is more pressing than for breast or prostate cancer.

To understand how patient advocacy shapes US research funding, it is instructive to look at the early history of philanthropy and activism. In the 1930s, the USA began “waging a war of propaganda against [cancer]...using both hope and fear...The emphasis on mobilizing the public against the cancer nemesis was most pronounced in the US, with its rich historical legacy of citizens forming interest groups in order to promote social reform,” wrote Barron Lerner, a physician and historian from Columbia University (New York, NY, USA; Lerner, 2001). He described the creation of the NCI in 1937, and at almost the same time, the founding of the forerunner of the ACS, which declared that it would “fight cancer with publicity”, and the formation of a philanthropic ‘Women’s Field Army’ to raise money for cancer research and break the silence surrounding the disease. Breast and prostate cancer patient advocates still present statistics of escalating incidence—fear—and note that screening and more research for treatments and cures can reduce mortality—hope.

Lerner noted that when discussing disease, war metaphors abounded in publicity throughout the Second World War and the

As philanthropic funding is limited, various patient groups fiercely vie for the public’s attention and contributions—and ultimately government funding

Table 1 | Prevalence of selected diseases in the USA and research spending by the US National Institutes of Health

Disease	People affected in 2002 ¹ (millions)	Estimated new cases in 2005 ²	NIH funding million US\$ ³ 2004	2005 (estimated)
Breast cancer	2.29	212,930	708	716
Prostate cancer	1.83	232,090	378	381
Lung cancer	0.350	172,500	297	300
Colorectal cancer	1.05	145,290	297	298
Brain cancer	0.102	18,500	187	190
Ovarian cancer	0.170	22,220	112	113
HIV/AIDS	1.0 (from 2003 ⁴)	2,850	2,981	
Parkinson's Disease	1.5 ⁵		224	232
Lupus	1.5 ⁶		87	88
Sickle cell anaemia	0.080 ²		90	91

Sources: ¹US National Cancer Institute (Bethesda, MD, USA): www.cancer.gov; ²American Cancer Society (Atlanta, GA, USA): www.cancer.org; ³US National Institutes of Health (Bethesda, MD, USA): www.nih.gov; ⁴Centers for Disease Control & Prevention (Atlanta, GA, USA): www.cdc.gov; ⁵American Parkinson Disease Association (Staten Island, NY, USA): www.apdaparkinson.org; ⁶Lupus Foundation of America (Washington, DC, USA): www.lupus.org.

Cold War. The use of celebrity spokespeople also began in the 1940s. But while US President Richard Nixon declared a “war on cancer” in 1971, the turning point in the public’s awareness of the disease came in 1974, when two politicians’ wives, Betty Ford and Happy Rockefeller, went public with their struggles with breast cancer. In 1982, the first breast cancer philanthropy and advocacy group, the Susan G. Komen Foundation (Dallas, TX, USA), was founded. Four years later, Komen’s founder and two patients formed the National Alliance of Breast Cancer Organizations (New York, NY, USA), an umbrella organization of 375 members.

By this time, the AIDS epidemic was underway. In the early 1980s, its sufferers received neither media attention nor research funding—US President Ronald Reagan could not even bring himself to utter the word ‘AIDS’ in public. This changed when a critical mass of patients, friends and families, and celebrity spokespeople made their presence known on Capitol Hill and in the White House. By 1989, they had succeeded: the government was spending US\$74.5 million on breast cancer annually, and over US\$2 billion on HIV/AIDS, although breast cancer killed more than 40,000 women in 1989 as compared with 22,000 AIDS patients in the same year (AP, 1989; Lerner, 2001).

“As my father used to say, ‘the squeaky wheel gets the grease’,” said Kevin Frost, Vice President for Global Initiatives at the American Foundation for AIDS Research (AmfAR; New York, NY, USA). “In the first

ten years of the AIDS epidemic, activism played an enormous role in funding research for the disease.” One of many patient advocacy groups, AmfAR has raised and invested more than US\$233 million for its programmes and awarded grants to more than 2,000 research teams worldwide since it was founded in 1985.

Cancer and AIDS activists have raised the use of celebrity spokespeople to a new height, and others have learned to do the same

Similarly, when breast cancer activists founded the National Breast Cancer Coalition (NBCC; Washington, DC, USA) in 1991, their goals were to improve access to screening and treatment, increase research funding and improve the role of women in healthcare policy. Using some of the same grass-roots techniques used by AIDS activists, NBCC and other advocacy groups pushed for an increase in federal funding for breast cancer research to US\$550 million a year by 1996, and have been instrumental in getting legislation passed for health coverage of mammograms and outlawing outpatient mastectomies. Activists also copied the looped red AIDS ribbon—in pink—to symbolize their cause. Breast cancer became “the darling of corporate America”, endorsed and funded by Revlon’s Ronald Perelman, cosmetics queen Evelyn Lauder and designer

Ralph Lauren (Belkin, 1996). ‘Race for a Cure’ mini-marathons still frequently take place throughout the country, along with other very visible fundraising events, which continue to raise large amounts of money for breast cancer research.

Cancer and AIDS activists have raised the use of celebrity spokespeople to a new height, and others have learned to do the same. “We clearly see the benefit for the American psyche that associating a celebrity with a disease is of big value, and we have used it effectively,” said Frost. Were it not for high-profile spokespeople, such as US General Norman Schwarzkopf and Harry Belafonte for prostate cancer, Sharon Stone for HIV/AIDS, Michael J. Fox for Parkinson’s disease, and now Nancy Reagan for stem-cell research, most Americans might tune out these causes.

Since the early 1990s, the combination of patient-celebrities and high-profile philanthropists has created new powerhouses of advocacy and fundraising for diseases such as spinal cord injury, brain cancer and Parkinson’s disease. The money raised by such venture philanthropic organizations (VPOs) has been significant and has greatly benefited treatment-orientated research (Edelson, 2005). Some examples of VPOs are Accelerate Brain Cancer Cure (Burlingame, CA, USA), founded by the Case family on behalf of AOL founder Steve Case’s brother, who later died of brain cancer; the Bill and Melinda Gates Foundation (Seattle, WA, USA), which distributes US\$600 million a year for infectious diseases and children’s health; Milken’s PCF, which has raised more than US\$230 million since 1993; the Christopher Reeve Paralysis Foundation (Springfield, NJ, USA); and the Michael J. Fox Foundation for Parkinson’s Research (New York, NY, USA), which has raised US\$52 million in less than five years, including US\$10 million specifically for stem-cell research.

In parallel, NIH’s research budgets for diseases that are represented by well-organized patient advocacy groups have changed accordingly. The NIH research budget for Parkinson’s disease has largely increased over the past ten years to an estimated US\$232 million in 2005; Fox’s foundation has added to this clout. The Case Foundation has also energized drug development in a research area that was largely ignored until recently. Although only about

17,000 patients are diagnosed each year with primary brain cancer, it is one of the most lethal cancers, killing almost all patients within two years.

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The NIH budget for prostate cancer rose from US\$25 million in 1992 to US\$381 million in 2005, and PCF has been instrumental in jump-starting research and drug development, including research on biomarkers. "When we started, there was no funding and no baseline of research," said CEO Leonard Michelson. However, PCF still sees itself as the underdog, which it has made part of its public relations image. "It is difficult to do clinical research because the disease is so heterogeneous and so slow-growing, it is difficult to recruit patients for lengthy clinical trials, and because it metastasizes diffusely, it is difficult to image its spread," said Craig Dionne, Executive Vice President of Research and Therapeutics.

There are also no good surrogate markers yet, he added: "Prostate cancer research still lags behind that of breast cancer."

Unlike cancer or AIDS, lupus has no celebrity spokespeople and a less organized and active patient population, which has most likely affected their ability to lobby the US government for more research funding, according to Peters. Insufficient research and a lack of new drugs is tied to funding and is self-perpetuating, he said. A recent Phase III trial for Riquent® (La Jolla Pharmaceuticals, San Diego, CA, USA), the first drug in decades that reduces lupus-related renal complications, had problems with statistical significance, partly because the disease has no unambiguous biomarkers, so the trial lacked clear endpoints. By contrast, the problem of reliable biomarkers is one that PCF has been able to address with increased research funding, noted Michelson.

A lupus patient may argue that his or her disease receives only a fraction of the research money—public and private—that is spent on cancer or HIV/AIDS. Nevertheless, were it not for patient activism and lobbying, many diseases, including breast and prostate cancer and HIV/AIDS, would receive much less attention and research funds, although some of this is diverted from other diseases. For the

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most part, the increasing influence of patient advocacy groups is a positive development. It is also an unavoidable part of a democratic society in which people with similar interests join together to maximize their influence on the public and the government. Although the advocacy groups who make the most noise reap the most rewards, hopefully the increased attention towards improved healthcare and research funding will eventually benefit society as a whole, and the benefits will trickle down to patients with less high-profile diseases.

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