The Foundations of Research

Private money is playing a bigger role in basic biomedical research these days—and also generating a fair amount of heat about funding strategies

TODAY'S SAVVY SCIENTIST IN SEARCH OF RESEARCH funds knows at least one key to success: diversification. Federal money, the mainstay of university research since World War II, is no longer growing rapidly—and the pie is being divided among an exploding population of eager, well-trained investigators. So whether seeking support for their own labs or for new buildings, departments, and programs, researchers—especially in biomedicine—are leaning ever more heavily on at least one alternative to federal money: private foundations established by wealthy philanthropists.

And with that increased dependence has come increased scrutiny of the strategies these foundations use to decide how to spend their money. The goal of every foundation, according to Thomas Langfitt, president of the Pew Charitable Trusts, is to "find an underfunded area where we can make a difference." In pursuing that quest, foundations have given a boost to many neglected research areas. But there are also downsides to the way foundations go about their business that are part and parcel of the special opportunities they provide. And as investigators become increasingly eager to attract the attention of these private funders, the controversy over the pros and cons of foundation methods can only grow.

Those pros and cons are intimately connected with the main strategies researchers are pursuing today. Those underfunded areas Langfitt refers to are often found on the boundaries of existing disciplines—zones that Jonas Salk (himself a member of the MacArthur foundation board) characterizes as "fertile territory"—where a little watering can sometimes cause a whole new discipline to spring up. For example, foundations exercised their green thumb in the early development of both molecular biology and neurobiology, and more recently in the merging of those fields into molecular neurobiology. In fact, neuroscience remains an enduring interest of foundations—particularly in its most interdisciplinary reaches such as cognitive and computational neuroscience and mental health.

And foundations don't just target specific research areas. Several have taken up the cause of an entire demographic group—young investigators at the beginning of their scientific careers. Often perceived as being at risk in the federal funding system, young investigators are now among the chief recipients of foundation largesse—to the tune of more than $35 million per year (see table on p. 1202).

As this somewhat quirky combination of interdisciplinary research and young investigators suggests, foundations have great latitude in picking their funding targets. Unlike NIH, which tends to follow "well-trodden paths," in the words of Howard Hughes Medical Institute vice president W. Maxwell Cowan, foundations aren't "trammeled by a large bureaucracy, and so can be responsive to new initiatives and developments, and can be focused at critical times in a field or institution." And in such independence lies the great strength—and the great danger—of foundation funding. Independence brings with it the freedom to change goals quickly to meet changing needs at the bench level. At the same time, critics contend that freedom can lead to inefficient—even destructive—funding patterns.

Some critics think, for example, that in the excitement over supporting the best young researchers, too many foundation awards go to the same investigators, while others of equal quality are left wanting. In addition, foundation funding for a "hot" area can disappear as suddenly as it appeared, leaving that once-hot field out in the cold. But while these criticisms are whispered, they are rarely shouted: No scientist wants to alienate an important funding source, especially in these uncertain times.

Despite their few concerns about details, most researchers are behind the idea of supporting the promising young researchers who constitute the future of science. Several foundations started such programs in the 1970s. By now that number has more than doubled and the collective monetary commitment has almost quadrupled. The decisions are typically based on the reputation of the individual researcher rather than the specific project proposed, and the awards range from $15,000 to $100,000 per year in research support for a young professor's first 2 to 5 years, with few strings attached. "We like to call it an insurance policy for risk-taking," says Pew executive director Rebecca Rimel about the Pew Scholars program. "We focus on people who already have a track record

Private Foundations: A Biomedical Sampler

Name & year founded	Source of funds	Annual am't awarded	Type of research supported
Howard Hughes Medical Institute[1]—1953	Hughes Aircraft	$258M (1990)	cell bio., genetics, immunology, neurosci., structural bio.
Lucille P. Markey Charitable Trust—1983	Calumet Farms Racehorses	$58.8M (1991)	broad range of biomedicine
John D. & Catherine T. MacArthur Fdn.—1970	Bankers Life & Casualty; Florida real estate	$30M (1990)	mental health, parasitology
W.M. Keck Foundation—1954	Superior Oil Company	$14M (1990)	broad range
Whitaker—1975	Amp Inc. (elec. connecting devices)	$13.5M (1990)	young investigators, biomedical engineering
Pew Charitable Trusts—1948	Sun Oil Company	$6.75M (1990)	young investigators, cognitive neurosci.
James S. McDonnell Foundation—1950	McDonnell-Douglas Aircraft	$7.5M (1991)	oncology, cognitive neurosci.
Edna McConnell Clark—1950	Avon	$4.1M (1991)	parasitology, inf. diseases of the eye
Charles A. Dana Foundation—1950	Dana Corp. (auto parts)	$4M	training programs in neurosci., aging, environmental health

[1] classified as a medical research organization rather than a foundation by the Internal Revenue Service

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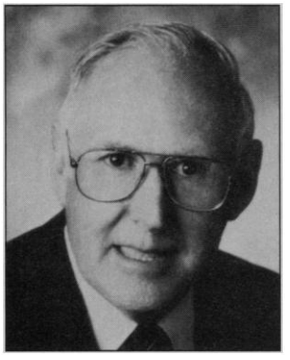
...at a time when they'd like to take some risk in their science, but they can't afford to."

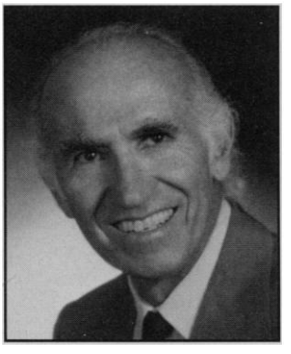
In funding the best young researchers, foundations definitely seem to be getting what they want: a very high benefit-cost ratio. "You have this feeling that you are taking the really good people [who are] destined for success, and giving them a leg up," says oncogene researcher Harold Varmus of the University of California, San Francisco, who sits on the selection committee for the Searle Scholars Program.

The recipients of this generosity seem to be putting the "risk insurance" to good use. "It allowed me to focus on longterm goals, rather than on what I have to do in the short term to get a result, to get another grant," says University of Texas biologist Steven Wasserman of his young-investigator support from both the Markey and Packard foundations. Wasserman also credits Markey—which supports its recipients for up to 8 years beginning when they are still postdocs—with another benefit: allowing him to switch fields (from biochemistry to *Drosophila* development) without having to do a second postdoc. "I might have been able to get a small [NIH] grant, but that only carries you a couple of years before you have to write a renewal," says Wasserman, "and when you're switching fields, a couple of years is too little time to get much accomplished."



Foundations aren't "trammeled by a large bureaucracy, and so can be responsive to new initiatives."

—Maxwell Cowan



"Now and again you may pass the judgment test, sometimes you fail."

—Jonas Salk

Wasserman is hardly unusual in having support from more than one foundation. In fact quite a few of the same names pop up on multiple lists of awardees, and some young scholars as well as selection committee members worry that this clustering of awards leaves many worthy would-be recipients without that extra boost. "It seems to me that the awards are being concentrated on a relatively few people," said one young researcher who doesn't want to be named—partly because he or she doesn't want to sound like an ingrate, having received awards from the Pew, Searle, and Sloan programs, as well as grants from the National Science Foundation and NIH. "I have friends whose work is of equal quality, who are trying to run their labs off a $75,000 NIH grant."

Although most scientists hesitate to blame young researchers for applying for every award they're eligible for, many feel someone should draw the line. "It's my personal feeling that people should get one of these [young investigator awards] and not more," says UCSF's Varmus, adding that "there are people out there who are indisputably excellent, who aren't getting grants."

The problem is that foundations are reluctant to rule out multiple awards, for fear the best scholars will turn their award down in lieu of one that offers more money. "If people can only accept one, you're going to start a bidding war," warns Cedric Chernick, director of the Searle Scholars Program. At least one program—the Pew Scholars program—has a rule on the books against multiple awards, but it has only been loosely enforced in the past. Without such rules, says Varmus, selection committees don't feel they can deny support to a top candidate just because he or she has several other awards. Universities could play a moderating role because they often help select recipients, says Harvard neurobiologist Constance Cepko, who sits on the scholar nominating committee at Harvard Medical School. But such a step would be voluntary—and some universities put their hottest candidate up for every award.

The controversy over how best to support young investigators is minor compared to the differences that arise over other trends in foundation funding. One sore spot, for example, is the never-ending search for novelty. "Foundations don't just put money where it is needed," says one biologist who asked for anonymity. "The concern is always: 'How can we make this something different that hasn't been done before?' They can't just say, 'We want to give money to graduate programs,' they have to give money for students trained in quantum physics who want to work in biology, or some such thing."

Pew's Langfitt counters that foundations must go out on a limb sometimes in seeking new and undeveloped frontiers. And many of those gambles have clearly paid off. The Alfred P. Sloan Foundation, for example, is credited with supporting neurobiology in the early 1970s before it was recognized as a field, and the Rockefeller Foundation for doing the same for molecular biology in earlier years.

In a more recent example of that field-pioneering trend, Maxwell Cowan recalls the Keck Foundation's receptivity in the early '80s, when Cowan, then vice president of the Salk Institute, approached them for support for Salk researcher Ronald Evans to use molecular techniques to study the brain. "Evans had no track record of working on the brain," recalls Cowan—and so he would have been unlikely to get NIH funding for that unique research. Keck came through, and won on two levels. Their investment paid off with important results on patterns of neuropeptide expression in the brain. What is more, it was one of the first steps toward the birth of a field—molecular neurobiology—that within a few years was on its way to recognition as a new and promising research discipline.

Today many foundations continue to hunt for what Stephen Foster, director of program administration for the Charles A. Dana foundation, calls the "leverage points" at disciplinary boundaries. For 4 years the Dana foundation has funded an interdisciplinary program at the University of Washington in which geneticists, toxicologists, and epidemiologists are working together to understand genetic variations in susceptibility to drugs and environmental toxins. The project has already begun to bear fruits such as an understanding of the genetic enzyme deficiency that can increase sensitivity to the insecticide parathion.

The study of neuroscience and mental processes, a popular foundation target for the past 20 years, is full of frontiers to which foundations are flocking. The Pew and McDonnell foundations have a joint program sponsoring eight interdisciplinary centers for cognitive and computational neuroscience, and the MacArthur foundation funds

11 mental health research networks, bringing together clinicians and basic researchers to focus on problems of mental health.

The topics of the MacArthur networks are far-reaching: For example, a network on mental health and the law, headed by psychologist John Monahan of the University of Virginia law school, focuses on resolving such issues as how to determine whether a mentally ill person poses a threat, or when such a person can be judged competent to make decisions. Monahan's network mixes basic scientists, practicing psychologists, lawyers, and policy specialists. "It is inconceivable that a group this large and diverse could have the kind of sustained and intensive interaction that it has had, without the support of the foundation," Monahan says.

But just as there was a potential down side to the foundation strategy of targeting young investigators, there is also a danger in foundations' obsessive search for new horizons. As foundations zero in on this year's exciting new area, they may find themselves moving last year's to the very back burner—sometimes with crushing results. Indeed, at the most general level, some foundation-watchers, such as Pew's Rimel, worry that foundation support for the entire area of biomedicine is heading for a decline, as foundations turn their attention to even hotter topics such as the environment and global poverty. But whether they are making sweeping changes of direction or just a minor course adjustment, foundations are continually changing, and as a result whole fields can be left in the lurch.

In one drama currently being played out, parasitologists are bracing for cataclysm as the MacArthur foundation winds down its funding of their field. Because parasitic diseases are not a national problem in the United States (and parasitology research is not a major mandate of NIH), parasitologists have relied heavily on foundations for funds. The Rockefeller Foundation, once a major supporter, tapered off its parasitology funding in the 1980s, but that gap was filled by a MacArthur program begun in 1985, supporting eight U.S. and three foreign parasitology research networks. "At the time there really wasn't a field of modern parasite biology," says Denis Prager, director of health programs at the MacArthur foundation. "We thought the foundation could make a major contribution [by bringing in] modern biology."

Support for Young Researchers

Name & year program began	Fellows per year	Total award per researcher	Total support per year
Lucille P. Markey Charitable Trust—1985	16	$543,000 to $659,000[2]	about $9.5M
David and Lucille Packard Fdn.—1988[1]	20	$500,000	$10M
Pew Charitable Trusts—1987	20	$200,000	$4M
Searle Scholars Award—1981	18	$180,000	$3.24M
Whitaker Fdn. (bioengineering)—1976	60	$180,000	$11M
McKnight Endowment Fund for Neuroscience—1977	6	$120,000	$720,000
Alfred P. Sloan Fdn. (neuroscience)—1972	16	$30,000	$480,000
NSF Presidential Young Investigator Awards—1984[1]	220 (1991)	$125,000[3]	$35-40M
NIH First Independent Research Support and Transition (FIRST) Awards—1986	425 (1990)	$350,000	$149M

[1] science and engineering, not just biomedicine
[2] includes salary for 2-3 years of postdoc plus 5 years on faculty (higher salary for MDs)
[3] NSF will provide an additional $187,500 if investigator can match that with private funds

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"The money has had a tremendous impact on the field," says parasitologist Lex Van der Ploeg, who heads a MacArthur group at Columbia University. The 11 centers were set up with a focus on bringing in researchers with expertise in molecular biology, and the resulting collaborations have led to such important advances as techniques to transform parasites with foreign DNA. Typical of many of the MacArthur centers, the center headed by Nina Agabian at UCSF gets a full 25% of its funding from MacArthur. And that money is worth twice its face value, says Agabian, because of the freedom with which it can be used. It supports a costly and vital core facility for culturing parasites, floats postdocs until their fellowships begin, and provides a startup fund for high-risk projects. "It has allowed us to be very aggressive about starting new things," Agabian says. The results, in Agabian's and the other centers, have been important insights into the unusual biology of many parasites, which could eventually lead to strategies for their control.

So why is MacArthur pulling out? Has their goal really been accomplished, or is parasitology simply looking a little less attractive than some new interests? "I think we've done what we set out to do," says Prager. "We have attracted new people to the field, they are now publishing in good journals, and I've been told it's a highly competitive system at NIH." But that high competition that Prager boasts of is a double-edged sword, say those in the field. It means that there is a lot of good work being done, and not enough NIH money to support it.

"It's crazy," says Agabian, to withdraw funds when the field is booming with discoveries and new talent is pouring in. Already, she adds, the anticipation of the MacArthur cutback has begun to discourage some good researchers from entering the field. "To abandon a program that has been highly successful doesn't make sense," says Timothy Nilsen, who heads a MacArthur group at Case Western Reserve. "I don't think [MacArthur's] task is finished."

Prager admits that the pull-out will be painful, but he adds that MacArthur is giving projects time to find other funds, by cutting funds gradually over the next 3 years. Some parasitologists, who wouldn't speak for attribution, say they feel abandoned—with no other funds in sight. They have been victimized, they say, by internal politics at MacArthur that have led to the funding turnaround—a charge Prager doesn't deny. "This is a big foundation, with eight big programs that vie for resources," he says, adding that "no foundation can be looked to to provide continued funding in an area. It just can't be."

If the problems associated with quick stops and starts are endemic to foundations, is there a way to make the bumps less jarring? Some scientists suggest that more communication and coordination between foundations may result in smoother transitions. Jonas Salk agrees, recalling that the Rockefeller and MacArthur foundations orchestrated the transition from Rockefeller to MacArthur support of parasitology. But more communication doesn't guarantee that fields won't be phased out, or even that foundations won't reinforce each others' views that it's time to move on. The MacArthur, Rockefeller, and Edna McConnell Clark foundations all get together to discuss parasitology funding, but all three have nevertheless cut their support of the field, despite a Clark foundation report that suggests that other sources of funding are not taking over.

As that example suggests, controversy is bound to keep swirling around many foundation decisions. That, says Salk, is part of the price of freedom: "It's a matter of judgment as to what [foundations] do, when we do it, and when we phase it out," he says. "Now and again you may pass the judgment test, sometimes you fail." ■ MARCIA BARINAGA