



# FOR **Ourselves** AND **Others**



Patient  
advocacy groups  
push their  
agenda:  
**FIND A CURE.**

BY  
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PHOTOGRAPH  
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Richard Siravo,  
with a photograph of  
his son, Matty



**M**atthew Siravo died on May 11, 2003. The cause: cardiac arrest and massive brain damage induced by a grand mal epileptic seizure lasting ninety minutes two days earlier. Matty's death certificate was signed on Mother's Day. He was five.

Within a month, Matty's parents, Richard and Debra Siravo, had parlayed their grief into the first of what would become a trio of annual fundraising events—a golf tournament, a 5K road race, and a winter ball—all intended to increase epilepsy awareness, support families coping with the diagnosis, educate physicians and school personnel, and fund basic research. To date, the family's Matthew Siravo Memorial Foundation, based in Wakefield, Rhode Island, has raised more than \$600,000, established a visiting professorship in pediatric neurology at Hasbro Children's Hospital, and awarded \$50,000 to support a pilot study of the biochemical pathways affected by anti-seizure medications.

In late November 2007, the foundation hosted a symposium for Brown physician-scientists as part of an effort to cultivate local scholarship on epilepsy and expedite the search for a cure. "When Matty was first diagnosed, we felt as though here in Rhode Island there were very limited resources for parents and families struggling with epilepsy," says Richard Siravo, who now serves as the foundation's full-time executive director and staffs the state's only resource center for families dealing with diagnosis and treatment. "We surround ourselves with folks who have children with epilepsy, so we have a lot of pressure on us and a great burden on our shoulders to commit our funds to research."

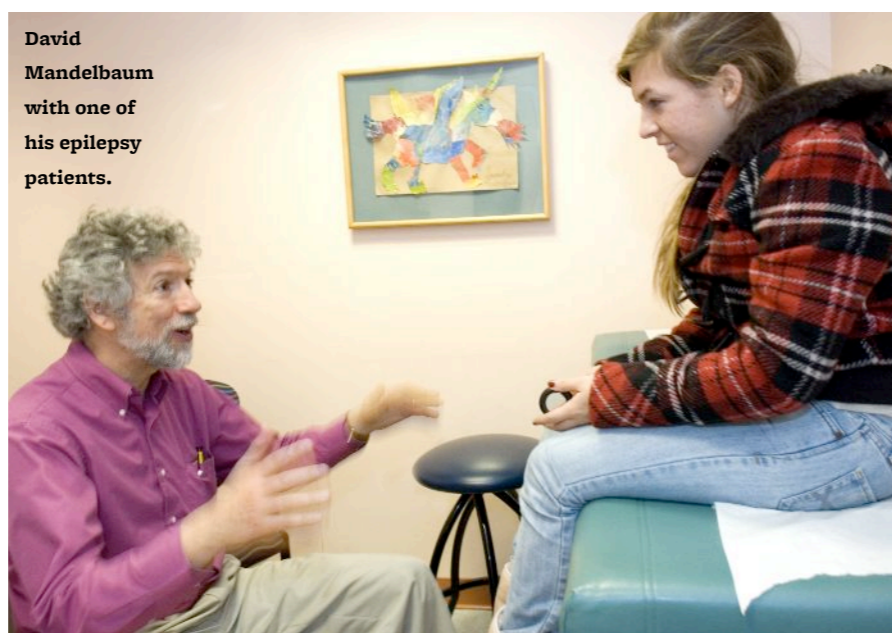
The Siravos aren't alone. Nationwide, as the Internet makes it possible for families

faced with rare and tragic diagnoses to find one another and share the stories of the poorly understood diseases that afflict their loved ones, patient advocacy groups are forming at a record pace. Back in the days of manual typewriters and party telephone lines, most groups struggled to share information on symptoms, treatments, and coping. Now they're drumming up interest among researchers and facilitating the search for cures, in the process delving into the genetic roots of disease and funding investigations of biomedical fundamentals. "There's no doubt that without these independent funding agencies and advocacy groups, there are niche research programs

that would never see the light of day or never even be initiated," says Dr. Tom Tracy, vice chair of the Department of Surgery at Alpert Medical School and pediatric surgeon-in-chief of the division of pediatric surgery at Hasbro Children's Hospital, who serves on the Matthew Siravo Memorial Foundation's Professional Advisory Board. "They're essential to this kind of work."

#### A LITTLE HELP FROM OUR FRIENDS

**The grants from such groups** aren't huge, often just \$100,000, spread over two years—but it's enough to get a scientist interested, launch a pilot study, and collect preliminary data to support a more ambitious grant application to a federal agency, says Professor of Medicine Sharon Rounds, the chief of pulmonary/critical care and of the Medical Service at the Providence VA Medical Center and former president of the American Thoracic Society. "It's a small portion of total biomedical funding," says Rounds, who serves as co-chair of the Scientific Advisory Committee that reviews all grant applications considered by the ATS,



David Mandelbaum with one of his epilepsy patients.

ROBIN D. BLOSSOM

which collaborates with patient interest organizations to fund a wide range of inquiry. "But for a young person starting out, it's seed money to get them off the ground and running. For the patient interest organization it's a way to attract investigators into research that's relevant to their disease."

Perhaps even more important than attracting new researchers is the continuity patient interest organizations provide in the face of shifting federal priorities. "There's always a political, cultural impact on where public dollars go. That's inevitable," says Director of Child Neurology at Rhode Island and Hasbro Children's hospitals David Mandelbaum, who received funding from the National Alliance for Autism Research. "Now autism is very prominent, but there was a time it wasn't and the only way to get money was through NAAR and some of these other organizations. These are the kinds of agencies that not only generate investigations in areas that might not be getting the focus, they can also provide bridge money for the lean years."

As with autism, funding for AIDS research has ebbed and flowed, with patient

many people do you know who have muscular dystrophy? But Jerry Lewis has been doing his telethon for years and raising money for MD." The trick, he and Rounds agree, is balancing the need for investigation of orphan diseases that afflict small numbers of patients with the imperative to achieve the greatest good



Walter Atwood

with the limited research dollars in the federal budget.

"Do the little ones get a disproportionate share of the pie?" asks Rounds. "Sure they do. But because of the work that's done in understanding the mechanisms of the disease, they provide scientific insight that's relevant to other diseases."

Molecular biologist Walter Atwood investigates the JC virus, a human poly-

cell model to understand how the virus attacks oligodendrocytes, the neural cells affected both by PML and MS.

"The stem-cell research is expensive," says Atwood, "and the money provided by the pilot project grant will allow us to bring this technology into the laboratory." If all goes well, says Atwood, whose primary support comes from two longstanding National

### "CAN THESE FAMILIES dictate what constitutes good science? ARE THE STUDIES BEING DONE IN AN OBJECTIVE, SCIENTIFIC WAY?"

advocacy groups such as ACT-UP and the Gay Men's Health Crisis working to keep the disease in the public spotlight for two decades. Ditto for myriad breast cancer groups and the families of kids with juvenile diabetes.

Often, says ethicist and Clinical Assistant Professor of Emergency Medicine Jay Baruch, patient advocacy groups address inequities in public funding. "From a justice perspective, there are maladies that will be left out of the fray," says Baruch, who serves as director of Brown's medical ethics curriculum. "How

omavirus that can precipitate the fatal demyelinating disease Progressive Multifocal Leukoencephalopathy in AIDS patients. Recently, the disease PML occurred in two multiple sclerosis patients and in one Crohn's disease patient being treated with immunosuppressive drugs and a new medication known as Tysabri. This prompted Atwood to apply for a small pilot project grant from the National Multiple Sclerosis Society. The application was funded, making Atwood the first Brown researcher to receive funding from the Society. The appli-

Institutes of Health awards, the relationship could yield further funding. "Potentially, if this pilot project goes forward and we make good progress, we would be in a position to apply for a larger chunk of money."

#### MAKING IT REAL

**When it comes to** patient advocacy groups, money is only part of the equation, says Rounds, who spent five years in the nineties working on cystic fibrosis after the CF Foundation awarded her a small, two-year grant to extend her research in that

direction. As a professional organization representing 18,000 members, the ATS has institutionalized its collaboration with patient interest organizations, creating a Patient Advisory Roundtable to inform research priorities and co-funding grants with such groups as the AlphaOne Foun-

PRF's education and public awareness committee. "I dove in and immersed myself in the field of progeria, and pushing the field forward has been incredibly important," says Gordon, who helped isolate the progeria gene in October 2002, co-authored an April 2003 *Nature* article detailing the mutation

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dition, the LAM Foundation, and the Longevity Foundation. At every session of the ATS's annual meeting, patients make five-minute presentations on living with the condition under consideration by the assembled researchers. Says Rounds, "I have seen physicians and scientists in tears at the end of these presentations. You would think that doctors would understand the importance of the work from the patient's perspective, but to be honest with you, we need to be reminded from time to time of what's really important."

For Leslie Gordon, PhD ScM'91 MD'98, it's impossible to forget what's really important. As a thirty-one-year-old pediatrics intern at Rhode Island Hospital in 1998, Gordon heard what few specialists ever say: "Your son has progeria." Within a month, Gordon had quit her internship, and before the year was out she had devoured everything that had been published on the fatal condition—which causes what looks like rapidly accelerated aging and affects only about forty children around the world—and found a research position at Tufts University School of Medicine to study it.

In 1999, Gordon and husband Scott Berns, MD, MPH, founded the Progeria Research Foundation at their kitchen table. Gordon serves as medical director; Berns serves as chairman of the board and heads

behind the disease, and in early 2006 co-authored two reports in the *Proceedings of the National Academy of Sciences* describing a mutant form of protein that damages blood vessel cells (see *Brown Medicine*, Spring 2006). The finding may shed light on the progression of progeria and atherosclerosis, a leading cause of heart attacks and strokes. "Living with a child who has progeria certainly makes [the work] more directed and more time-sensitive."

In the eight years since its inception, PRF has distributed \$1.5 million in research grants, established a cell and tissue bank, organized and run five scientific workshops on progeria, all of which were co-funded by the NIH, and conducted lobbying that resulted in language in the Children's Health Act of 2000 supporting progeria research. In May 2007, PRF began funding a clinical drug trial at Boston Children's Hospital, a two-and-a-half year, \$2 million effort, for which Gordon serves as a co-investigator.

"Everything we fund is funded with an eye toward...finding a cure for progeria," says Gordon, who highlights the possibilities for gaining a better understanding of the healthy aging process through PRF-funded investigations. "Certainly there's a lot of basic science that's essential to building toward a clinical trial or finding the gene for your syndrome, but the mission itself is medically based."

**QUALITY ASSURANCE**

**Scientists**, on the other hand, tend to focus their attention on the mechanisms of molecules, organs, and pathologies. "There's a dynamic tension between the scientific world and the patient world," says Rounds. "The scientists will say there's not going to

be a cure until we understand the mechanisms of disease. And the patients and families say, 'We need a cure. My child is going to die.'" Furthermore, says Baruch, there's a question of whether advocate-funded research affects the outcome—akin to a study on the health effects of cigarettes funded by Philip Morris or a nutritional analysis of soda funded by Coca-Cola. "Can these families dictate what constitutes good science?" he asks. "Are the studies being done well, in an objective, scientific way? That's one thing. The second is that if the people funding it are doing it to get a certain answer, and they're not getting it, are they squelching that answer?"

To optimize the quality and credibility of the science they fund, organizations assemble a professional advisory board to evaluate grant proposals and guide the allocation process.

"The principle of peer review, having your application submitted to rigorous analysis, that's the bottom line," says Mandelbaum, who is professor of clinical neurosciences (neurology) and serves on the Siravo Foundation's Professional Advisory Board. "If it's not subjected to peer review, the quality of the science could be poor. With the National Alliance for Autism Research, I had to write a proposal, submit it to their advisory board, submit a budget. The process

is quite indistinguishable from the formal process of any other granting agency."

Rigorous peer review has been critical for PRF, says Gordon, because the quality of the data her group funds propels the research to the next level. "We seek to partner with the NIH, complement the NIH, work with the NIH," she says. "We wanted to give laboratories a chance to get start-up data to garner larger grants from the NIH. Where a lab might have been doing nothing on progeria, now they can go to the NIH and say 'Here's what we've got, will you fund us?'"

Mandelbaum sees an added benefit in peer review—allowing scientists to do their best, most objective work, while patient interest organizations deploy the passion and dedication that makes them incredibly effective advocates. "You need that dispassionate jury to allocate the funds, but to get the money obviously you want the passion of the advocate," he says. "It's a good combination if they're kept separate."

But even with dispassionate peer review, advocate-funded research isn't without its challenges. Grants from the NIH include close to 50 percent funding for overhead—expenses associated with actually running a lab. Unlike many interest group-funded grants which preclude coverage for overhead, Atwood's MS Society award includes a 10 percent overhead account, which he credits with having facilitated Brown's willingness to accept the funds. "Most societies are like that," says Atwood. "They want their money to be used for research. They don't want the money to be used for the light bulbs and electricity we use in the building to actually do the work."

Many smaller foundations also explicitly preclude salary support for clinicians whose research endeavors compete with responsibilities to generate revenue through patient visits. "Time is the most important commodity," says Mandelbaum, whose NAAR grant allowed him to hire a statistician and a

research assistant, and dedicate some of his own attention to a languishing dataset accumulated through an NIH-funded project. "You're often asking people to spend their nights and weekends to do the work that is made possible by the non-salary support money."

**MAKING IT PERSONAL**

**Meanwhile**, Baruch credits patient interest organizations with an ability physician-scientists simply don't have—putting a name and face to the diseases legislators crafting federal budgets might otherwise fail to recognize.

"If there's an identifiable face to a person who needs a certain treatment, people are more apt to do everything, or go to more extreme measures and make more of a financial commitment," says Baruch, citing Michael J. Fox's work on behalf of Parkinson's awareness and funding. Rounds, who takes vacation time from her appointment at the VA Hospital to lobby for funding for the NIH and VA on behalf of the ATS, says nothing compares with the power of a patient to bolster a scientist's message about the need for research funding.

"When a doc goes and lobbies for funding from the NIH, there's a lot of self-interest involved and the legislators and their assistants say, 'Sure, they're lobbying for themselves,'" says Rounds. "When you go with a patient who's wearing oxygen, who has to catch his breath before finishing a sentence, it has a visceral impact and the message from the professional comes through much more effectively."

While the Siravo Foundation hasn't yet launched a lobbying effort, the Progeria Research Foundation has seen a significant rise in awareness of its cause during the past eight years. From 1950 through 2002, only 104 peer-reviewed articles tackled the topic of progeria. From 2003 to 2005, there were fifty-two.

"One of the most amazing things I've experienced is the number of volunteers, researchers, and physicians who just want to help these children," says Gordon. "That's been a privilege for me and given me a lot of hope over the years."

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**Scott Berns and Leslie Gordon enjoy life with their son, Sam.**