

Common Cause **A Woman Fights To Unravel Mystery Of Her Rare Disease**

Seeking Treatment, She Hopes
To Benefit From Research
On More-Prevalent Illnesses

Hunting for Clues in Cancer

By **AMY DOCKSER MARCUS**

BOSTON—**Amy Farber** stood before 40 scientists, researchers and physicians in a conference room at Harvard Medical School in May. They were there to hear a lecture about estrogen, and the role it might play in a rare lung disease that strikes mainly women.

But first, Ms. Farber, a 36-year-old anthropologist and an organizer of the conference, spoke. A little over a year ago, she recounted, she was newly married and hoping to start a family when she learned she had lymphangioleiomyomatosis, or LAM, a progressive and fatal lung disease.



Amy Farber

There is no cure and no effective treatment for the disease, which affects perhaps 8,000 people in the U.S. If a treatment isn't found, Ms. Farber worries that the cysts that have invaded her lungs will spread. She knew that eventually she could suffocate to death.

Her voice wavered as she looked at the group, many of whom knew little about LAM and had never known a patient with the disease before. "You are among the scientists most likely to make the breakthrough to save my life and the lives of other women like me," she said.

Finding a cure for rare diseases poses huge challenges. Researchers usually gravitate toward more common diseases, for which better funding is available. That means patients often

end up spearheading efforts to find treatments. They set up foundations to raise money and awareness, hoping to generate new research that might lead to a cure.

Ms. Farber wanted to help with such efforts under way for her disease. But she felt she couldn't afford to wait years to nurture greater researcher interest in LAM or for more scientists to obtain grants to study it. So she also pursued a different route. She approached scientists already studying more-common diseases—particularly cancer and lung diseases—and cajoled them into applying their existing work to solving the problem of LAM.

"I don't have time and don't necessarily even want them to risk whatever it takes to turn themselves into LAM researchers," says Ms. Farber. "I want to leverage what they are already interested in anyway, and use that to find a cure for LAM."

Ms. Farber, who holds a Ph.D. in social anthropology, helped launch medical seminars at Harvard, inviting the small cadre of existing LAM researchers, but also tapping into a network of colleagues to draw oncologists, biologists, pulmonary specialists and others. She brought in people such as Judah Folkman, of Children's Hospital Boston, best known for his work on cancer, and Robert Langer, whose lab at Massachusetts Institute of Technology develops new ways to deliver drugs.

When Ms. Farber wanted to set up a LAM center, she didn't try to lobby for a specialized clinic. Instead, she began talks with the Connors Center for Women's Health and Gender Biology at the Brigham and Women's Hospital, where her 34-year-old husband, Michael Nurok, works as an anesthesiologist. They argued LAM should be studied there, along with other diseases that strike primarily women, such as breast cancer and lupus.

"Amy is trying to save herself," says Paula A. Johnson, who heads the Connors Center. "But what Amy is doing is creating a model for mobilizing forces to look at any disease that might be overlooked because of sheer numbers."

Rare-disease groups often try to generate interest in studying a particular condition by saying it could lead to insights about more-common diseases. "We always present the fact that there are wider implications," says Vicky Whittemore of the Tuberous Sclerosis Alliance, which helps those with a genetic disorder that affects about 50,000 in the U.S. "Otherwise people would say it's an unfortunate situation, but it only affects a small number of people."



Jodi Hilton/Getty Images

Michael Nurok and Amy Farber in their Cambridge, Mass., home, where they launched the LAM Treatment Alliance. But groups devoted to curing rare disorders are also pursuing the strategy of trying to leverage work under way on more common diseases. The ALS Therapy Development Foundation, for example, has set up a lab to screen drugs approved or being developed for other diseases. The group is trying to see if any of those drugs are effective in treating ALS, also known as Lou Gehrig's disease, which affects about 30,000 people in the U.S.

Other researchers are investigating whether certain new treatments for common types of cancer might also work for rare forms. The drug Avastin was approved for colon cancer, but is being tested on other types of cancer, including less common ones, such as ovarian cancer.

The government defines an "orphan" or rare disease as one that affects fewer than 200,000 people. According to the National Organization for Rare Disorders, there are more than 6,000 such conditions, which taken together affect about 25 million Americans. Groups founded by patients continue to increase, because so little is known about most rare conditions. "All these groups start with the hopes of eventually going out of business," says Abbey Meyers, president of NORD. "But most never can."

Many of the scientists and researchers Ms. Farber has consulted support the idea of trying to use what is already being done in other diseases. "Amy's strategy makes sense scientifically," says David Kwiatkowski, an oncologist at Dana-Farber Cancer Institute in Boston, who helped her found the seminar series. "There is this whole field of cancer biology that is developing many techniques designed to study cancer. Why not use those wherever we can to look at this other disorder that doesn't have the same name but has some shared features?"

In December 2004, Ms. Farber was feeling extremely tired and bothered by discomfort in her back and abdomen. At first, no one was sure what was wrong. Blood tests were normal. A chest X-ray turned up nothing suspicious. But a CAT scan showed a mass next to one of her kidneys and small cysts at the base of her lungs. Though the disease is often misdiagnosed, her doctor suspected LAM. Ms. Farber had never heard of it before.

At first, she felt immobilized. Her doctor told her people with LAM have to be careful about flying, because the change in air pressure might raise the risk of lung collapse. Ms. Farber had flown all over the world for work, studying gender roles in Indonesia and spending a year in South Africa researching the well-being of children. Her family lives in California and she regularly visited. But in later months, her fear of flying became so great that twice she took a four-day train ride from Boston to California.

It became hard to sleep or eat. She spent hours watching videos—"Spanglish" with Adam Sandler was a favorite—because it was the only thing that allowed her "to go far away" from her fears. "Worst case thoughts," she wrote one day in a journal entry. "My funeral, M as a single person who lost wife." When her husband had to work nights at the hospital, she had panic attacks, feeling she couldn't breathe.

Ms. Farber's husband learned of a program for LAM research at the National Institutes of Health. In April 2005, she underwent five days of tests at the NIH facility in Bethesda, Md. Her diagnosis was confirmed.

The doctors advised her to think carefully about getting pregnant, out of fear that it might accelerate the disease. The news "forced me to consider that my world, prior life, travels, shared dreams with Michael . . . were perhaps slipping through my fingers," she wrote in an email to a cousin.

She asked doctors at the NIH why they were studying a rare condition like LAM. One reason, she was told, was that it might have implications for cancer, diabetes and obesity. Scientists had discovered LAM is caused by a defect in one of two genes, both involved in regulating cell growth. The process of uncontrollable cell growth that makes LAM deadly is of huge interest to scientists.

For the first time, she began to see her disease in a wider context. "I realized that I needed to look at LAM in a different way," she says.

Her change in thinking came at a time of new developments. Ms. Farber got in touch with the LAM Foundation, a patient-advocacy, research and education group set up in 1995 by Sue Byrnes, whose daughter has LAM. Ms. Byrnes lobbied for the LAM program at the NIH.

In a letter-writing campaign last year, Ms. Farber's family and friends raised \$220,000 for the LAM Foundation.

The foundation's scientific director, Francis X. McCormack, of the University of Cincinnati, is principal investigator for the first LAM treatment trial ever, to be conducted by the NIH's Rare Lung Disease consortium. The two-year trial, expected to start this year, will test a drug called sirolimus in 120 women. The LAM Foundation, a main driver of the trial, is helping fund the more than \$3 million cost.

Several smaller trials are also in the works. Joel Moss, who directs LAM research at the NIH, Dr. Folkman, of Children's Hospital Boston, and others are working to gather data that might lead to testing whether a well-known drug, doxycycline, could prevent LAM from ravaging patients' lungs.

Still, Ms. Farber had no idea how quickly her own disease would progress, and felt research needed to go faster. She was also galvanized to keep looking for additional drugs because of the emerging consensus that, as with cancer and AIDS, single drugs are unlikely to be enough to cure LAM, and "cocktails" of multiple drugs may be more effective.

Ms. Farber started swimming regularly in a pool near her house. In the water, she could "rest her thoughts," she says. "I keep thinking that there is a lot of research that is going on out there that's interesting, but I don't have time, I don't have time."

In April, she and her husband attended the LAM Foundation's annual conference in Cincinnati. She didn't register as a patient, instead signing up as a scientist, spending much of her time attending research presentations. At social events, she spoke with other women—most of them her age—with LAM. Many were wearing what they called their "nose hoses"—supplemental oxygen tubes.

This spring, Ms. Farber, who had been attending Northeastern University School of Law, decided to take a leave to devote herself full-time to finding a treatment for LAM. Every day, she hunted for papers with work that might prove relevant, calling scientists and researchers who in turn suggested other colleagues with whom she should speak. She set up conference calls with scientists around the country, peppering them with questions on how their research might apply to LAM. On a recent day, she got an email, saying a researcher studying a different lung disease at Brigham and Women's Hospital agreed to meet the couple, to see if his work might be useful in treating LAM.

In May, she and her husband launched the **LAM Treatment Alliance**. They hesitated initially about creating a second group for the disease. "With rare diseases like LAM, there are only so many resources to go around," says Dr. McCormack, scientific director of the LAM Foundation. "I do worry about dividing the effort. It hasn't been a problem so far, but I want to make sure we continue to cooperate."

Ms. Farber says she wants to focus solely on ways to speed the search for treatment, without branching into patient-support groups. So far this year, she has raised more than \$500,000. In coming months, her group plans to give out three \$150,000 one-year grants to scientists that the group will recruit, to work on projects it will help shape.

Looking for a Cure			
Advocates for these rare diseases have started foundations to speed up the search for treatments.			
DISEASE	DESCRIPTION	PREVALENCE ¹	ORGANIZATION ²
Amyotrophic Lateral Sclerosis (ALS)	Progressive, fatal neurodegenerative disease	30,000	ALS Therapy Development Foundation
Huntington's disease	Neurological disease leading to dementia and death	30,000	Hereditary Disease Foundation
Niemann-Pick Type C disease	Fatal neurodegenerative disease	500	Ara Parseghian Medical Research Foundation
Rett Syndrome	Neurological disorder almost exclusively diagnosed in females	2,000	Rett Syndrome Research Foundation
Sarcoma	Cancers arising from cells that hold body together	50,000	Sarcoma Foundation of America
Tuberous Sclerosis Complex	Genetic disorder leading to tumors in different organs	50,000	Tuberous Sclerosis Alliance

¹Estimate in the U.S. ²Other groups also support patients with some of these diseases.

The LAM Treatment Alliance's office is currently based in Ms. Farber's home in Cambridge, Mass. In a room she calls "the command center," is a wooden desk built by her father, and two chairs, where she and her husband make calls, send email and plan strategy. "We don't get up from here for hours," she said. A chalkboard listed projects they are working on and questions they want answered. Their wedding picture leaned against it, a reminder of another life. Ray, their dog, rested in the corner.

Ms. Farber was planning a summit to tackle one of the biggest roadblocks in LAM research: getting more cells to study. The cells have proven difficult to grow in the lab. Most cells now come from women at the end stages of LAM, undergoing lung transplants in a bid to extend their lives. Dr. Moss at the NIH says he keeps a backpack in his office, to fly at a moment's notice to the site of a transplant to retrieve lungs for study.

At one of her fund-raisers, Ms. Farber says people repeatedly told her it was hard to believe she had a fatal disease. "You look so healthy," they said. "I kept telling people, 'I wish you could see my lungs.'" But she hasn't been able to bring herself to look at her own scans. "I think about the disease every day, I work on the disease all the time, but I am still too scared to see my lungs," she says.

It was her husband who reviewed all of her scans. When he assesses what they have accomplished so far, he says he is "moderately optimistic" that a drug will be found in time to save his wife. But when he looked at the scans and saw how the cysts continued to grow, it reminded him that their efforts were, "tragic, in the Greek sense of the word," he says. "There is no other choice."

At the May seminar at Harvard, Ms. Farber sat in the front row and took notes as Myles Brown, an oncologist at the Dana-Farber Cancer Institute, spoke. "I am new to the world of LAM," he said. He had spent almost 20 years studying breast cancer, and the role of estrogen in the disease. Given that LAM mostly strikes women, he agreed with LAM researchers who suspected that perhaps, like breast cancer, "it is estrogen-dependent in some way." Dr. Brown wondered if drugs that have helped make such a difference in treating breast cancer could work in LAM.

"I think LAM should be viewed more like cancer," he says. "When it affects people who are so young, it is worthy of aggressive evaluation and therapy."

When a researcher told him about the difficulties of growing LAM cells from patients' lungs, he suggested using a technique that is sometimes applied in cancer research, extracting cells from patients' lymph nodes.

After the meeting, researchers mingled over sandwiches. One offered to show blood samples she had brought. Dr. Nurok remained seated next to Dr. Brown, discussing ideas he had suggested. "What drugs would you want to see tested in LAM, based on your breast-cancer research?" he asked.

Dr. Brown gave him names of some drugs. "I know a doctor in France who has about 30 patients with LAM," Dr. Nurok said, "who might be interested in running a trial using those drugs. Will you help him design a trial if he calls you?" Dr. Brown said he would. By the next morning, Dr. Nurok had already sent an email about the idea to the French researcher.

This is what the couple had wanted, to create an incubator for new ideas and trials. Still, after the seminar, Ms. Farber collected her notes and said, "This is depressing."

The next day, she said she had been moved by all the ideas generated, but "getting from the talk to the action is always so frustrating for me." She headed out for a swim. She wanted to think about what to do next. She needed the reassurance that she was still able to push herself to swim faster and faster. Only then would she let herself come up for air.



The LAM Treatment Alliance is exclusively dedicated to accelerating LAM treatment research. Through diverse partnerships and collaborations, it leverages what is known about relevant common diseases to advance LAM research, and gains insights into treating common diseases through research on LAM. LAM is one of over 6,000 rare diseases affecting over 25 million or 1 in 10 Americans.

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