

## Testimony

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Human Services, and Education

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Mr. Chairman and members of the subcommittee,

The patients, patient families, and scientific investigators I represent here today would like to thank you for your constant, tireless, and accomplished leadership on the issues that mean so much to us. We would like to add our voices to all those expressing gratitude, as you serve your final year in Congress, for being the champion you are of the health of our families and nation and the medical research that is improving it. The bipartisan consensus and support you have built for that research has resulted and will continue to result in important breakthroughs that will benefit all of our families. We will find treatments for these diseases being discussed today, and your unflinching commitment at a critical juncture will deserve much of the credit. We are deeply grateful and wish you and your family continued success in all your endeavor.

We thank you, too, for holding these hearings for public witnesses and the hearing for Members of Congress you have scheduled for later this month. These hearings demonstrate once again the importance you place and the time you invest in listening to patient communities and our elected representatives. We especially appreciate your time because you, and we, have so little of it. You are on an accelerated schedule to complete your vital work on our nation's budget. With you, we are racing against the clock as these awful diseases take the lives of our nation's youth.

### **Friedreich's Ataxia**

The disease our group is fighting to conquer is Friedreich's ataxia. Friedreich's ataxia is a rare, genetic, neurological disorder. It afflicts about one in 50,000 people. It is a debilitating, degenerative, and life-shortening disorder. Onset of symptoms is usually between the ages of 5 and 15, sometimes even earlier. These symptoms include muscle weakness and loss of coordination in the arms and legs; impairment of vision, hearing, and speech; aggressive scoliosis (curvature of the spine); diabetes; and a serious heart condition. Most patients need a wheelchair full-time by their late teens or early twenties. Most young people afflicted with this disease die in early adulthood. There are no treatments or cures. Although rare, this disease afflicts males and females across our nation and around the world, including those of various ethnic and racial origins.

### **Growing Hope and Knowledge**

Although we have no treatment or cure, we have growing hope and knowledge of this disease. It was only four years ago that a tremendous breakthrough was announced — the gene

responsible for Friedreich's ataxia was finally located. As you know, such gene identification is a vital step in understanding most diseases and an explosion of research findings followed the discovery. Scientists have since identified the protein that a normal copy of this particular gene forms and the bad copies fail to form. They have further determined that the protein (called Frataxin, after the disorder) is responsible for regulating iron levels in the mitochondria — the energy factories of our cells. Without Frataxin, excessive iron accumulates in the mitochondria, oxidative stress from free radicals damage and kill cells, and the mitochondria produce far less energy than normal. Armed with all this new knowledge, scientists are accelerating their press for breakthrough to treatment. Clinical trials of iron chelators and very promising antioxidants are now underway, attempting to identify compounds to reduce the toxic iron levels and save cells from death to oxidative stress. Scientists are even working hard on a more fundamental, curative approach to repairing the bad gene, breaking down its "sticky DNA" barriers so the gene can be properly transcribed and the protein produced.

### **Congressional Support**

Mr. Chairman, we realize this exciting and hopeful progress would not be possible without the continued, bipartisan support you and your subcommittee have built and sustained for improving the health of the American people. We could not be more grateful for your insightful and effective leadership of the congressional effort to provide for the clinical services, the basic, clinical and translational research, and the infrastructure needed to support it all. We appreciate, for example, the infrastructure support you and your subcommittee are providing through the Health Resources and Services Administration of HHS in the Acadian population of South Louisiana, where Friedreich's ataxia and Usher syndrome (deaf-blindness) occur at frequencies two and a half times those in the general population. Of course, advances made in that special population will be broadly applicable across the country and around the world.

In the vital arena of medical research, we are especially grateful for your leadership in the effort to double the funding for the National Institutes of Health (NIH) over a five-year period. You have heard numerous NIH witnesses over the years testify as to the small percentages of qualified research grant applications actually being funded - good, promising science going undone due to inadequate budgets. You have heard the cheers go up in patient households and labs across the country as you achieved your goal of 15 percent increases in both of the last two years (about \$5 billion more for research). You are hearing again the agitated murmur from the same sources as the administration's budget request is for less than your goal of another 15 percent increase.

We recognize that politics are still being played in determining the level of that requested increase. We recognize, too, that despite the current budget surplus, the Congress must wrestle with difficult funding issues — the national debt, social security, and commitments to other vital obligations such as national security, education, and jobs. However, we know your commitment to medical research and the goal of doubling NIH funding over the five-year period to be unwavering, and we have noted the bipartisan support your commitment enjoys here on the subcommittee and in both chambers. We have faith that you will continue to provide the necessary leadership to permit you and your colleagues to forge the necessary consensus to keep this effort on track. We pledge the continued, unflagging support of our organization and our patient and scientific community to you and this undertaking.

Mr. Chairman, not only do we support your efforts to double the NIH budget, we are among the many who support your approach to doing it in the most effective manner. You are an outspoken champion of avoiding the legislative earmarking of medical research funds for

particular diseases. We have often heard you say that you and your colleagues here are not scientists and should leave scientific judgments to those who are. We agree, too, that none of us should want to pit one disease against another, this week's "disease of the week" against next week's. None of us should seek a system in which our nation's precious medical research resources are decided on the basis of squeaky-wheel, loudest-shout political pressure.

We subscribe to the old mariners' adage, "A rising tide lifts all ships." The increases you are providing in the NIH budget are the rising tide and it is lifting us all. We recognize, too, that we cannot plan or dictate where major, scientific breakthroughs will occur. Most often, scientists don't make scientific advances where they choose to — they make them where they can. The breakthroughs tend to occur wherever the science is readiest, frequently well off the course laid out in advance. The good news here, of course, especially as our general medical understanding grows more and more advanced, is that such breakthroughs are more and more broadly applicable to multiple diseases. For example, as former NIH Director Harold Varmus testified before your colleagues on the Commerce Subcommittee on Health Affairs, "Friedreich's ataxia now joins a growing list of degenerative disorders, such as Parkinson's disease, in which free radicals have been implicated. As with progress in many rare diseases, what we discover about cellular changes and therapeutic approaches in Friedreich's ataxia may lead us to important insights about more common disorders."

### **Congress, NIH, and the Public-Private Partnership**

Mr. Chairman, we would also like to express our appreciation for the role you and your subcommittee have played and continue to play in working with the NIH to optimize its public outreach and its priority setting. Our organization is actively involved with NIH and would like to report that, from our perspective, the NIH leadership has been energetic, enthusiastic, and effective in acting on congressionally mandated recommendations on both fronts.

In fact, the organization I represent, the Friedreich's Ataxia Research Alliance (FARA), was formed in the atmosphere surrounding this effort. We saw that the timing was right and the need clear to form a new non-profit organization devoted to research and education regarding Friedreich's ataxia and the related, early onset, sporadic ataxias. We believed such an organization could make a significant contribution by working with our patient families to support congressional efforts to increase funding for medical research, by working closely with NIH to enhance two-way communications between NIH on the one hand and our patient families and scientific investigators on the other. We were also convinced that we could help raise additional, private funds for research, and encourage more extensive and intensive collaboration among scientific investigators as well as the other grant-making organizations that fund them. We formed a Board of Directors including three leading scientific investigators and lay Members with experience on Capitol Hill, in the Executive Branch, corporate leadership, communications, and fundraising for medical research. We incorporated FARA in September 1998.

### **Public Outreach**

We have been extremely impressed and greatly heartened with the redoubled NIH efforts in public outreach. I was one of many who participated in Dr. Varmus's initial public discussions of his plans to form the Council of Public Representatives to assist NIH in its liaison with the general public and patient advocacy groups, and we have worked closely with the public liaison staffs at NIH that have been enhanced as part of this overall effort. The NIH Institute with overarching responsibility for overseeing research into Friedreich's ataxia, the National Institute of Neurological Disorders and Stroke (NINDS) continues to be absolutely extraordinary in reaching out to our organization and to others. We continue to attend regularly the quarterly

meetings of the NINDS National Advisory Council. The NINDS staff was extremely encouraging and supportive of our early efforts to initiate our new organization, making it clear that they believed we could be helpful in facilitating two-way communications between NINDS and our patient families and scientific community. The NINDS Director also had me and seven other patient group representatives spend a full day with him and his staff discussing the Institute's draft strategic plan and research priorities. At our suggestion, the draft plan and priorities were subsequently sent out for comment to representatives of all patient groups for which NINDS oversees research. The resulting document was distributed widely, along with a subsequent update, as part of an iterative process to develop and refine priorities with public input. I think you'll agree that this process demonstrates a genuine commitment on the part of NINDS to implement the congressionally mandated recommendations regarding public outreach as well as clarity and openness in priority setting.

### **Priority Setting**

We of FARA find the research priorities being established by NINDS as being of exactly the right grain and focus, and I am confident you will too. Without going into any detail, let me just say that these priorities aim not at specific, individual disorders but rather at cross-cutting scientific topics that contain the ingredients for breakthroughs across the full spectrum of disorders in the Institute's purview — topics such as neurogenetics, neurodegeneration, experimental therapeutics, and clinical trials. It is advances in topics such as these that are most likely to permit us to prevent, delay, and treat all the diseases represented here today and restore function lost to them.

### **Collaboration — A Force Multiplier**

As you see, Mr. Chairman, we of FARA are extremely appreciative and respectful of all that you, your subcommittee and NIH do to advance medical science. I do want to suggest, though, as I believe you would, that even after doubling the NIH budget and insuring the high quality of individual research projects, we will not enjoy the type of accelerated progress in finding treatments and therapies we all seek unless we apply energetic leadership and resources to greatly enhance collaboration among all appropriate aspects of medical research. It seems to me that such collaboration is the great force multiplier in our war on disease.

We need greater collaboration among scientists investigating the same diseases, among those investigating different diseases that have aspects in common, among those needing sophisticated, expensive equipment available only to some, and among those in different disciplines that need to be brought to bear on the same problems. Such collaboration is also critical on the NIH campus itself. Free and seamless collaboration across Institute and disciplinary lines, and among the intramural and extramural staffs within the same Institutes, is essential. Extramural staffs must be aware of intramural research projects that could help shed light on — possibly even help orchestrate, guide, or coordinate — extramural projects being funded by the same Institute. Collaboration between NIH Institutes and other HHS organizations is also important.

### *Friedreich's Ataxia — A Case Study in Collaboration*

Mr. Chairman, we are thrilled to report extremely encouraging progress on these collaborative fronts in the work on our disorder. We could not develop treatments without such collaboration. Friedreich's ataxia is a multi-system disorder. It kills cells and severely reduces functions in organs, muscle groups, and skeletal structure literally from head to toe. Our symptoms cut across many fields and NIH Institutes, requiring collaboration among a full range of disciplines

including genetics, molecular biology, neurology, neuroscience, and biochemistry, for example, and among the appropriate Institutes. This collaboration benefits work in other disorders as well. Advances in this research on Friedreich's ataxia provides valuable insights across a spectrum of other, more common disorders and a number of NIH Institutes and disciplines.

A useful illustration of the force-multiplying effect of collaboration, as well as a fruitful public-private partnership in such collaboration, can be found in the international scientific workshop on Friedreich's ataxia held last spring. FARA co-hosted the workshop with our partners at NINDS and received an NIH grant to fund this workshop — the first of its kind. NIH's Office of Rare Diseases provided about half the grant, with the remainder coming from NINDS and several other Institutes with interest and insight into at least some of our symptoms. The event assembled about 80 of the world's leading investigators in projects and disciplines relevant to Friedreich's ataxia so as to foster collaboration among them, integrate the most up-to-date findings, and identify promising new avenues for research. These gifted investigators were eager to get together, take stock, and chart the road ahead so that progress could be accelerated. They get few opportunities to do so. They have not assembled in any number since some of them met in Montreal in 1996 and announced identification of the Friedreich's ataxia gene. So much excitement over new findings has mounted since that meeting and the investigators had not had the opportunity to sit down together to assess where they were and needed to go.

In addition to NINDS, Institutes that provided some funding and / or scientific participants included the Human Genome Research Institute, the Institute of Diabetes and Digestive and Kidney Diseases, the Heart, Lung and Blood Institute, the Institute of Child Health and Human Development, the Institute of Aging, and the Institute of Deafness and Other Communication Disorders. As this list demonstrates, the workshop brought together intramural and extramural investigators from many disciplines, with interests in many symptoms and many diseases to share insights, findings, and plans. Among the rich areas of common ground were such matters as DNA triple-repeat expansions similar to those in brain diseases like Huntington's, various therapeutic approaches such as antioxidation, iron chelation, and gene therapy, which hold hope across a broad spectrum of diseases, as well as clinical studies of diabetes and heart disease.

The impact of the workshop has been profound. The most promising avenues of research were clearly identified. Commitments to increased collaborative efforts on those avenues were made and are being implemented. The NINDS Director, Dr. Gerald Fischbach, and his staff have been phenomenal in their encouragement and support. One exciting illustration of all this energy involves the single most promising near-term development revealed at the workshop — very positive, preliminary results from an antioxidant in an ongoing clinical trial in France. In most Friedreich's ataxia patients in that trial, enlarged heart tissue, the deadliest of our symptoms, has been reduced by about 30 percent. Because the drug is not FDA approved for Friedreich's patients, we need to conduct a clinical trial here in the United States as soon as possible. Towards that end, we have worked steadily with NINDS, investigators around the world, and our patient community. Next week, FARA will fund at NIH a one-day meeting of a steering committee — scientific leaders of intramural and extramural programs here and abroad — to craft the protocols and timelines for that trial. This trial will feature close scientific and financial collaboration among centers and across national borders and organizational lines. Our common goal is a "rolling trial" that opens with this test of antioxidation and does not close until we have an effective treatment for Friedreich's ataxia.

Maximum collaboration as exemplified in this single effort seems to us to be especially important on what appears to be the threshold of a revolution in medical science, based largely on far greater understanding of human genomics and improved, more empowering technologies. Along with increases in funding for medical research, maximum collaboration seems to be a key force multiplier capable of pushing us over that threshold and accelerating progress significantly.

Mr. Chairman, I want to conclude by saying again in what high regard we hold you and the work you and your subcommittee have accomplished and continue to accomplish. You are a true and effective champion of increased funding for medical research and the kind of collaboration essential to its success. We in the Friedreich's ataxia community see the fruits of your labor tangibly before us now. These wonderful scientists WILL find a treatment for this disease, Mr. Chairman, and I don't believe it will take them many more years to do it. Furthermore, that breakthrough in our disorder will be applicable to a broad spectrum of other diseases. And, we will owe much of that sweet success to you and your work with your colleagues here. We are grateful, and pledge our continued, active, energetic support in your efforts to double the NIH budget. Again, we wish you and your family every happiness as you complete this chapter of your public service.