International MPS awareness day

Q&A with Dr. Emil Kakkis

Q: How did you first get involved with MPS diseases?

A: I was in search of a project for my genetics fellowship at UCLA [University of California, Los Angeles], when Dr. Elizabeth Neufeld was working on cloning the gene for MPS 1. Knowing the importance of this work and how critical it was for the next step towards therapy, it was a perfect match.

Q: How did your education about MPS I begin? Did you have an affected family member?

A: I did not have an affected family member, but got to know a little about the science from Dr. Neufeld's work. My clinical training in the real world of MPS began in June 1991 at a National MPS Society meeting at UCLA. I had never been to a meeting that had scientists, patients and parents all together. For someone not familiar with MPS, there's a certain shock and dismay at looking at how much sickness and trouble these kids have, and yet how well the parents are coping. The kids affected by Sanfilippo would sometimes scream or make odd sounds, or run down the aisle, with a parent chasing right behind. Everyone just kept going on as if nothing happened. Just a routine MPS meeting. This was also my first introduction to activist parents. The parents were often crowding in the back of the sessions designed for scientists, wanting to get involved in the science and learning about what progress was being made. They did not want the softer sugar-coated sessions designed for parents, they wanted to know exactly what was going on, the hard science that would help their kids.

Q: What are some of the unique challenges of developing therapy for rare diseases?

A: When I started MPS work with Dr. Neufeld in the early 90s, the challenge was not being allowed by the whole research system to make something useful happen, to take good science and translate it to a therapy. It was extremely frustrating. There were probably only two or three groups in the world working on MPS 1. There wasn't support or research money at the scale required to do what was really needed to be done. We were developing a manufacturing process to make the enzyme to treat the patients based on an NIH grant that really required at least 100 times more money. The research we were doing had a scientifically sound basis for why it would work, and we knew how we could press forward to make it happen. If we showed that a therapy really works, we thought everything would change. That notion kept me going and it was exactly what happened – we made enough enzyme to successfully treat dogs with MPS 1. That opened the door...

At the same time when we began our work, many families of patients were thinking that research had failed them and had lost faith in what it could deliver. Money raised had been lost in the black hole and nothing good had come of it. None of the research had worked. The challenge then was to get some patients and parents who had been disillusioned by research and whose kids had died, to be interested in supporting it now. Why would it be different this time? But the research was different because we knew better what it was we needed to do, and finally had the means to do it by making the copy of the enzyme using genetic engineering.

Q: Which MPS diseases have you worked on?

A: I started working with Dr. Neufeld on what became Aldurazyme for MPS 1; afterwards I worked with Dr. Hopwood and BioMarin on Naglazyme for MPS 6. The next program I started up was enzyme therapy for Morquio A or MPS IVA at BioMarin, which recently completed a successful trial. Most recently I have been working with Dr. Sly on Sly disease or MPS 7. Ironically, MPS 7 was the first MPS for which the deficient enzyme was identified and the first MPS to be treated in animal models. In some ways it has the best science behind the enzyme therapy, but the least amount of interest to develop it clinically. I think of it as a poster child for the failings of the system, where we know what the science is, we know what to do and how to do it, and yet the patients are not getting the treatment because there just weren't enough patients to attract the money needed for development.

Q: Are you currently working on developing therapy for MPS 7?

A: Yes the team at Ultragenyx is working on it. MPS 7 or Sly disease has been known for 40 years and Dr. Sly has been figuring out every last piece of the MPS 7 biology. It is tragic that we haven't done the one thing that really matters, which is to treat the patients. I wanted to make sure it got done. So we resurrected the program and are working with Dr. Sly on developing enzyme replacement therapy (ERT) for MPS 7. It's a very small patient population but we are being innovative and creative in how we are approaching study development. We have European agreement on a novel study design and a surrogate primary endpoint strategy. Our hope is to start treating patients in clinical studies later in 2013 and if the work is successful, offer it to the public in a couple of years.

Q: Who will be eligible to enroll in the clinical studies? Will everyone receive the enzyme?

A: The first trial is a small open label study in 5 patients, where almost anyone could enroll in the study. The second study has a novel design, with some placebo, although all patients will receive enzyme during the study. The second study might have more requirements to enroll; this is yet to be decided. Both of the trials will be in patients 5 years of age or older, and we expect to study younger patients in subsequent trials. Our goal is to eventually test the enzyme in all patient populations.

Q: How can the patient community support your work?

A: Supporting patients and families participating in the trials is a meaningful and immediately impactful way to contribute. The patient community also needs to continue to support creative research projects that open doors to new treatment strategies. Finally, continue to get the word out to help drive newborn screening. If newborn screening for lysosomal diseases was universal, we would be treating patients from birth and would probably have a much more substantial benefit from treatment based on our research and clinical experience to date. For a disease like MPS, early treatment is an essential part of achieving the best possible result.