



A Rare Flower

Families with children facing rare neurodegenerative disease have found a powerful ally in Dr. Maria Escolar

BY EDWARD BYRNES

Dr. Maria Escolar is not a collector, but her office is decorated with a mosaic of colorful artwork. Each piece that graces her walls is a one-of-a-kind original, created mostly in crayon, by a child. This art, which ranges from an exquisitely multicolored beetle to a piece of notebook paper on which is scrawled, “This is Dr. Escolar’s Office,” came from the fertile minds of her young patients—all of whom are, or were, unfortunate victims of some of the rarest diseases known to medicine.

Some of Escolar’s patients, who would have died before their second birthday without treatment, are enjoying their 10th. And many families who have been touched by the care of Escolar and her Program for Neurodevelopmental Function in Rare Disorders (NFRD) go on to offer their assistance to other families who find themselves face-to-face with the reality of having a child with a life-threatening disease. Although it is heart-wrenching to deal with children who are very ill or dying and the family members who love them, Escolar finds her inspiration among them.

“These families are amazing. They have always been

the ones that fuel me to keep on going,” she says.

Escolar, a clinical associate professor in pediatrics at UNC and director of the NFRD at UNC’s Clinical Center for the Study of Development and Learning (CDL), was working as a clinical associate in pediatrics at Duke University Medical Center in 1999 when she came across her first patient with a rare condition called Krabbe’s disease.

Krabbe’s disease belongs to a set of rare lysosomal storage diseases (LSDs) caused by a lack of or defect in enzymes that normally eliminate unwanted substances from the cells of the body. These enzymes are found in the lysosomes of each cell, which break down macromolecules into simpler compounds for elimination or reuse. The defect causes an abnormal accumulation of waste substances, inefficient functioning, and damage to the body’s cells, which ultimately leads to serious

Above: Dr. Maria Escolar (right) reads with patient Caterina Marcus and her mother Claudina during a recent evaluation at UNC’s Clinical Center for the Study of Development and Learning. Photo by Jim Kenny

health problems and in most cases, death. In addition to Krabbe's disease, the LSD family includes more than 40 other conditions, such as Hurler, Hunter's, and Sanfilippo's syndrome, metachromatic leukodystrophy, Tay-Sachs disease, and Sandhoff disease. All are neurodegenerative and fatal.

Escolar came to the US in 1986 from Bogotá, Colombia, after completing her medical degree at Escuela Colombiana de Medicina. She was at Duke, testing children who were receiving umbilical cord blood transplants in an effort to replace the missing enzymes. Her background in neurological development told her that the neurological systems of these children were already too damaged to be helped. They needed help sooner.

"I wanted to see the kids when they were younger and less symptomatic because I thought, with earlier treatment, their outcomes could be better," Escolar said. She began several small projects to evaluate children at younger ages; but to effectively evaluate and help these kids, Escolar knew she needed a multidisciplinary team.

"Duke wasn't interested in supporting that kind of effort; I think partly because they knew UNC already had a big center doing a lot of work in child development. So at that point, I thought I should go to UNC," Escolar said.

Although there weren't any job openings at UNC's CDL, Escolar made a proposal to its leadership: she would find funding for her project herself while getting patient referrals from Duke—all she needed was some clinic space. After some deliberations, they came to an arrangement in which Escolar would serve one day a week as a developmental pediatrician and help with the CDL's clinic in exchange for the clinic space she needed.

With patient referrals from Duke and a foundation grant, she established her Early Childhood Clinic at the CDL in 2000, which evolved into the NFRD program by 2002. The first goal of the clinic was to study rare autosomal recessive diseases to gain an understanding of their natural history.

"Most families who have a child with one of these diseases are very desperate because no one can tell them anything about the disease," Escolar said. "I knew that the only way we can begin to help is to be very systematic about the way we look at these diseases. We have to have a core dataset that will help us understand what the needs of these children are."

Escolar began collecting all the data she could on the rare diseases affecting the children she had been seeing. As word of her clinic spread, Escolar was soon getting referrals from across the country and around the world. She pulled together a multidisciplinary team from across UNC Health Care, including physicians with expertise in genetics, psychiatry, neurology, and other allied health professionals such as audiology and physical therapy.

Escolar's clinical research database grew quickly, so quickly in fact that she soon possessed the largest known database of clinical information on rare neurodegenerative diseases. The database now contains integrated information on 20 diseases and 450 patients from approximately



Escolar and patient Jaxon Cooper, who has Hunter's syndrome. The death of a sibling from the disease at age 14 prompted Jaxon's early testing and diagnosis as a newborn. Jaxon received a cord blood transplantation; and for the six years since then, Escolar and the NFRD has tracked his outcome and provided services that support his development and maximize his function both at school and at home. Escolar says Jaxon's success is an example of one of the basic concepts of her program: early intervention, newborn screening, and the importance of preventing neurological disease before injury occurs.

Photo courtesy of Maria Escolar

1,200 evaluations.

"When families now come to the NFRD, they get a multidisciplinary evaluation of their child so that when they leave, they do so with recommendations for everything from schooling and therapy to palliative medical care," Escolar says. "They get, in one to three

days, what other families may get in six months of going from one appointment to the next, with no one integrating the information along the way.”

When the program began, Escolar and her colleagues put together a combination of tests to be used to gather information on patients’ motor and cognitive skills that could be tracked longitudinally over time. Then, through administering different treatments, they could determine best practices for these patients.

Escolar and her colleagues published retrospective studies about what they had learned. Among many other things, they developed staging systems for the diseases to help clinicians determine the best course of action when they come across a patient with one of these conditions.

“If a clinician sees a child with one of these diseases, they can refer to our staging system and decide if their patient is a good candidate for transplant or if it’s too late and they should work toward improving quality of life. It has helped many clinicians manage these diseases for their patients,” Escolar said.

With this new information, many young patients and their parents are spared unnecessary worry, costly testing, and unnecessary treatments, Escolar says. As more and more health care providers become familiar with Escolar and the NFRD, she and her staff have begun to receive more and more phone calls regarding proper medications and other care related to the treatment and management of pediatric patients with these rare neurodegenerative diseases.

“We now have more experience with these diseases than just about any other place. There have been new discoveries in terms of treatments, such as recombinant enzymes, that can be used instead of or in addition to transplant. There are a lot of different things we can do clinically now that we couldn’t do before. So, there was suddenly a need for clinical trials, and because we have such an extensive database on the natural history of these diseases, many companies became very interested in doing them with us,” Escolar said.

The growth of Escolar’s program has led other clinicians and researchers to seek her out for advice, information, and now, training. Escolar recently created a fellowship program for other physicians to come to UNC and train at the NFRD to ensure that the knowledge and information of the clinic will be spread elsewhere. So far, Escolar has trained two fellows. One, now an attending, continues to see patients at the clinic on a part-time basis, while the other has just begun her third year. Other requests for training fellowships have come from Italy, Canada, South America, British Columbia, and elsewhere.

Additionally, Escolar consults other health care professionals interested in setting up clinical information databases similar to hers. Escolar says that they accommodate these requests so that their model can be replicated in other places; and, as more and more treatment becomes available, it is important for researchers to be able to replicate studies in different populations. “This need for training is growing fast and is now an incredibly important part of what the NFRD does,” she said.

Another area of growth for the NFRD is in imaging research. “Using MRI imaging technology, we’re trying to correlate what happens in the brain with what manifests behaviorally. We might see signs that demyelination is occurring in the brain and the child may be OK. In another case we may see no signs of demyelination in the imaging and yet the child is very sick. So we’re trying to figure out what the MRIs can tell us about function,” Escolar said.

Escolar has begun collaborative imaging studies with the hope of finding ways in which imaging of the brain can inform treatment pre-emptively.

“We are going back and forth between behavioral phenotypes of a disease and the imaging; and, in collaboration with basic researchers with animal models, we can refer to their studies to try to figure out how treatments affect different areas of the brain and see how it affects development and timing of myelination,” Escolar said.

With the addition of the training and imaging components, in addition to seeing patients and maintaining the database, Escolar’s time is at a premium. Though she sees potential for further growth, the current size and structure of the NFRD is pretty close to what she had envisioned from the beginning.

“Where we are now is as big as I wanted [the NFRD] to get. But I can see how it could grow in a virtual way; this infrastructure is unique and I think a lot of other clinicians may want to benefit from it,” said Escolar. “Other researchers may start collaborating with us—using the database to look at other diseases. Things like this could happen that don’t require a lot of additional staff and funding, just the existing infrastructure. One of the fellows we train could begin more of these types of efforts here or in another part of the world. You never know.” [U](#)