Genetic sequencing
Making progress for diagnosis

Patient communities
Advocates collaborate with industry leaders

MEDIA PLANET

July 2011

RARE DISEASES

3 STEPS TO ADVOCATE FOR RARE DISEASES

ADVOCATING FOR TREATMENTS TO CHANGE MODERN MEDICINE

Discover how the mother of Addi and Cassi Hempel, twins with a genetic disorder, may be developing treatments that could save your life

PHOTO: CHRIS & HUGH HEMPEL

CHALLENGES

STEP 1 BECOME MORE AWARE

Everyone knows someone with a rare disease. Nearly 30 million Americans, or almost one in 10 of us, have diseases considered rare in the U.S. and these tend to be serious and lifelong, affecting not only the patient but the entire family.

Not as rare as you might think

According the National Institutes of Health (NIH), there are nearly 7,000 diseases defined as rare, or affecting fewer than 200,000 Americans by U.S. definition.

Somebody you know has one of these diseases, and the patients and families coping with them need our help. They live with day-to-day challenges that are vastly underserved at this time by our medical and public health systems.

This results in shattered dreams, unnecessary expense, lost productivity, and all too often, premature death.

What are the challenges?

Even though each disease is unique, the problems associated with having a rare disease tend to be consistent. They include:

- Delayed or inaccurate diagnosis
- Difficulty finding a medical expert
- Too little research
- Few, if any, treatment options
- Insurance or other reimbursement problems
- Lack of awareness and understanding of the patient's needs
- A sense of isolation.

Rare diseases are often called "orphans" because they are forgotten and "unclaimed." Many rare diseases are not being studied by any researchers because there is little or no public funding for research.

In fact, much of the research on rare diseases today is being funded by patients, families, and patient organizations raising money through golf tournaments, bake sales, and other means to provide grants for researchers at universities and hospitals.

Seek treatment

Only about 200 rare diseases currently have treatments approved by the U.S. Food and Drug Administration (FDA). That leaves many patients and their families in the position of being treated with products not specifically approved for their disease or not being treated at all.

Furthermore, more than half of the patients are children. The organization I represent—the National Organization for Rare Disorders (NORD)—receives phone calls and emails on a daily basis from parents who are coping simultaneously with the challenges of having a desperately sick child, appealing insurance denials, finding appropriate medical care, and educating their families and friends about their child's disease. It's a lot to deal with, and no one should have to do it alone.

Just by becoming more aware of rare diseases and the needs of the children and adults who have them, you can help. The word "rare" is misleading. These diseases touch lives all around us, and as a society we need to pay more attention.

It could be your son or daughter, or your elderly parent, who is affected. If we all focus a little more on these issues, we could improve millions of lives, reduce unnecessary healthcare spending, and put meaning in the phrase: Alone we are rare. Together we are strong.

PETER L. SALTONSTALL

editorial@mediaplanet.com

"Only about 200 rare diseases currently have treatments approved by the U.S. Food and Drug Administration (FDA). That leaves many patients and their families in the position of being treated with products not specifically approved for their disease or not being treated at all."

Peter L. Saltonstall
President and CEO, National Organization for Rare Disorders (NORD)

WE RECOMMEND

PAGE 4

Wendy White of Siren Interactive, explains how mothers use technology to diagnose their children.

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Publisher: Tristan Vaughan
tristan.vaughan@mediaplanet.com
Business Developer: Mandy Wilczynski
mandy.wilczynski@mediaplanet.com
Designer: Missy Kayko
missy.kayko@mediaplanet.com
Managing Director: Jon Silverman
jon.silverman@mediaplanet.com
Editorial Manager: Luciana Colapinto
luciana.colapinto@mediaplanet.com
Contributors: Nicole Boice, Stephen Groft, Chris Hempel, Michael Joseph, Peter L. Saltonstall, Anne Waters, Wendy White

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INSPIRATION

A mother's medical odyssey with her twins

Question: Why is rare disease research so important?
Answer: Research into ultra rare genetic diseases is helping scientists understand more common diseases such as heart disease and Alzheimer's that affect millions of people.

IDENTICAL TWINS Addi and Cassi Hempel. PHOTO: CHRIS & HUGH HEMPEL

In 2004, Chris and Hugh Hempel were blessed with the birth of identical twin daughters, Addison and Cassidy. When the twins turned three, they contracted a viral infection during an exam, and enlarged spleens were detected. "Nothing to be alarmed about," doctors told them. It was likely mononucleosis. When symptoms did not clear up however, the Hempels took Addi and Cassi to Stanford Hospital where they would embark on what Chris calls "a medical odyssey."

After 18 months of tests with no answers, Chris wondered if her daughters might have a genetic disorder. "I started noticing slight abnormalities with their motor skills, particularly in their balance," said Chris. "I became increasingly alarmed as symptoms worsened and doctors remained baffled."

In October 2007, with the help of doctors at Stanford and Children's Hospital Research Center in Oakland, the Hempels received a diagnosis that Addi and Cassi had been born with Niemann Pick Type C disease (NPC)—an ultra rare and fatal progressive neurological condition caused by inherited genetic mutations on a gene that controls human cholesterol metabolism.

"We were devastated after receiving the diagnosis," says Chris. "Here we are with our twins singing nursery rhymes and the doctors are telling us that in a few short years they will be bedridden and in a complete state of dementia because of cholesterol build up."

Like millions of other people facing rare diseases, the Hempels began their search for treatments only to find limited options. "One option was an experimental drug called Zavesca which provided limited benefit and costs of up to $240,000 dollars per year," said Chris. "First you get hit with a fatal diagnosis, then you find out an experimental treatment costs more than a house."

Soon after the twins' diagnosis, Chris learned that a non-toxic, sugar compound called cyclodextrin could potentially treat Addi and Cassi. Cyclodextrin is used in products ranging from food to cosmetics and even some household products. The compound wasn't deemed to have any active effects until scientists at the University of Texas Southwestern made a surprising discovery; Cyclodextrin seemed to have a profound effect on cellular cholesterol and was actually stopping neurodegeneration in NPC animal studies with mice.

Based on this research, Chris has created a virtual biotech from her kitchen over the past four years; working tirelessly to receive approval from the FDA to treat her twins with cyclodextrin. In April of 2009, the twins started weekly infusions of cyclodextrin into their bloodstreams and recently the FDA allowed injections into their spinal fluid which reaches the brain. Today, Chris is working with doctors at Children's Hospital Oakland, Johnson & Johnson, and Medtronic to receive FDA approval to implant a device into the twins that will be able to deliver cyclodextrin continuously to their brains, similar to a diabetes pump and insulin.

"Cholesterol is one of the biggest killers on the planet, and by understanding this gene that everyone is born with that controls cholesterol, we can gain key insights into why people get heart disease and even dementia," added Chris. "Kids like Addi and Cassi with ultra rare diseases will help solve more common diseases such as heart disease and Alzheimer's that affect millions of people."

MICHAEL JOSEPH
editorial@mediaplanet.com

FACTS

Significant challenges facing treatment development.

- Limited data on the natural history of specific diseases
- Conducting clinical research where the patient numbers are small and those affected are young children with severe, degenerative conditions
- Different regulatory requirements in different countries make access to therapies difficult.

Marc Dunoyer,
President, Asia Pacific/Japan for GSK

There is nothing rare about rare diseases.

- They affect numerous children and their families in the US and approximately 250 million people worldwide. Each year, The Center for Business Intelligence assembles industry and government leaders for two days of case studies, collaboration, communication, and learning. July 12—13, 2011 in Washington, D.C. marked the 6th Annual Rare Disease Leadership Summit. It was there that patient groups, pharmaceutical companies, venture capitalists, pharmacists and political organizations came together to discuss new innovations and collaborative efforts to improve access to care, and share information to save lives.

editorial@mediaplanet.com

NEWS IN BRIEF

Mothers lead the way in researching rare disorders

Few medical conditions are as difficult to diagnose as rare disorders. Many patients wait seven to 10 years before receiving a correct diagnosis, and when the disease is finally given a name, the person behind that diagnosis is often a mom. Why? First, 80 percent of all rare disorders including cystic fibrosis, childhood cancers, and numerous unnamed diseases are diagnosed during early childhood. Second, physicians receive little medical training in rare disorders and can spend an entire career without ever encountering one. Third, and most importantly, is the strength of a mother's instinct to protect her young – she is literally fighting for her children's lives. Empowered by the internet, these mothers research and network with unmatched skill. "The Internet gives patients and caregivers access to medical journals, clinical trial investigators, advocacy organizations and government officials." Additionally, mothers employ the use of social media for sharing news, experiences and resources. "Having support and encouragement right at their fingertips can transform a family's solo ordeal into a shared journey; stripping away feelings of isolation and bolstering their faith and determination." A simple click of a mouse can make a world of difference.

WENDY WHITE
Founder and President, Siren Interactive
editorial@mediaplanet.com

Question: How can new medical technologies improve the diagnosis of patients with rare diseases?
Answer: By employing whole genome sequencing, physicians are now able to provide clearer alternatives and treatment.

STEP 2
UNDERSTAND YOUR GENETIC HISTORY

Genetic sequencing: Empowering diagnosis

A toddler with a mysterious abdomen inflammation endures 100 surgeries. His symptoms continue. Physicians remove his entire colon. Still, no answers. Determined to gather more information to help the boy, they use next generation sequencing to take a genomic assessment of his DNA. There, they find the problem—and the solution—hidden in a DNA mutation.

This Pulitzer-prize winning story was published in the Milwaukee Journal Sentinel about Nic Volker, a recent case of a rare disease diagnosed through genomic sequencing. Over the last half-century, more than 2,000 clinical tests based on genetic information have been developed. Most of these focus on one to a few specific genes to see if a particular variant is present or absent in a given position. This strategy is effective in a majority of cases where there is a clear link between a patient's symptoms and a suspected diagnosis. But sometimes, as in Nic's case, other genes and genetic variants are to blame. Enter whole genome sequencing—a map of the entire human genome—powered by next generation sequencing technology. It emerged two years ago as a service for physicians.

Whole genome sequencing is quickly gaining recognition for its potential in the world of rare diseases, where physicians are challenged with identifying a disorder based on symptoms that don't quite fit with a known disease. When this happens, whole genome sequencing can provide big-picture information about genetic makeup, enabling physicians to make more informed decisions. In some cases, this has really made a difference for patients—so significantly, that insurance companies have reimbursed for the procedure.

Access to this information can end diagnostic odysseys and offer physicians, patients, and their loved ones answers. Still, it's a challenge to evaluate and understand genetic variation. Which genes should be examined, and how can we be sure? How can information be managed to protect privacy? Plus, finding an answer does not mean finding a cure. Nonetheless, patients report that even the worst news can result in better decision-making—such as avoiding additional invasive procedures that would not be successful. As many families suffering with a rare disease know, sometimes any answer is relief in itself.

Despite the current sequencing challenges, there are patients benefiting from whole genome sequencing right now. While not every test yields a conclusive answer, it's a helpful option for physicians, clinical laboratories, and patients like Nic Volker who are working together to solve the mysteries behind these diseases.

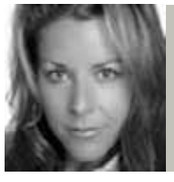
editorial@mediaplanet.com

The Global Genes Project volunteer team is collecting blue jean- and denim-inspired bracelets to give to families living with rare diseases, disorders or conditions. It's part of a campaign called 7,000 Bracelets for Hope. For more information visit globalgenesproject.org

RARE DISEASE AWARENESS DAY

The Global Genes Project

■ **February 29, 2012 is Rare Disease Day,** but at the Global Genes Project, it's rare disease awareness day every day of the year. Since January of 2010, The Global Genes Project has been calling attention to the lack of drug treatments available for millions of people suffering from chronic, life-threatening and fatal rare diseases through its *7,000 Bracelets for Hope* and *Wear That You Care* awareness campaigns. Organizational support for these grass roots campaigns comes from patients, patient advocacy groups, hospitals, research institutes, pharmaceutical companies, consumer brands, and various non-profit foundations.



Nicole Boice
CEO of R.A.R.E. Project and The Children's Rare Disease Network

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DON'T MISS!

Contributing to rare disease solutions through education, advocacy and science

The Center for Rare Disease Therapies at Keck Graduate Institute of Applied Life Sciences (KGI) is a catalyst for positive change that brings together government agencies, pharmaceutical companies, research institutions and advocates to further the development of orphan drugs and to bring relief to patients.

Our accomplishments include partnering with the FDA to educate stakeholders, as well as KGI students, in order to demystify the orphan-drug application process. This endeavor has dramatically increased the number of orphan drug applications approved by the FDA—and boosted the opportunities for new therapies to reach those in need.

To learn more about the Center for Rare Disease Therapies, visit our website at www.kgi.edu/crdt.xml

KECK GRADUATE INSTITUTE
of Applied Life Sciences

DUCHENNE AFFECTS MORE THAN 300,000 WORLDWIDE

Among rare diseases, Duchenne is the world's most common lethal childhood genetic disorder, a rapidly progressive disease that begins with a loss of muscle function and weakness in the lower limbs due to the absence of the muscle protein dystrophin.

Affected muscle fibers eventually die, leading to a steady decline in muscle strength, skeletal deformities, breathing complications and cardiomyopathy. Few individuals with Duchenne live beyond their 20's.

For the over 300,000 males living with Duchenne worldwide, there is hope. Researchers have made significant strides in recent years through gene mutation identification and an understanding of what needs to be done to slow the progression of the disease.

Dr. Eric Hoffman, of Children's National Medical Center in Washington, DC, was part of the team that originally identified the dystrophin gene. His work focuses on a promising therapy called Exon Skipping that will "trick" the gene into producing the necessary protein to rescue muscle cells.

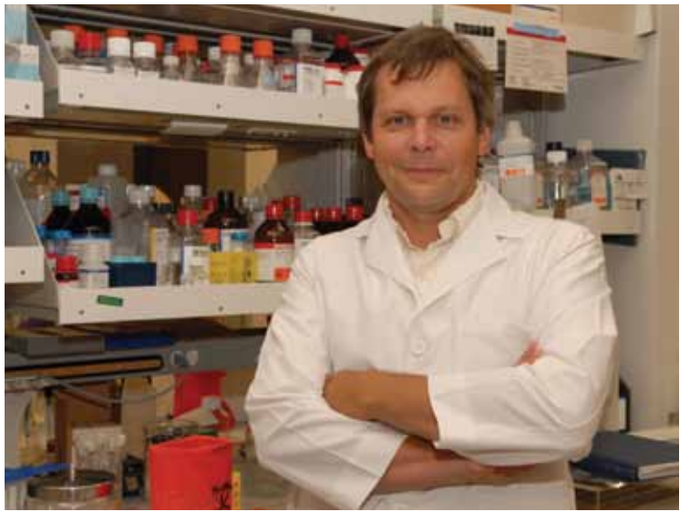
"It is one of the most likely therapies to reach the patient in the short term since clinical trials are already underway," said Hoffman.

Another researcher, Dr. Jeffrey Chamberlin, of the University of Washington-Seattle, has achieved some success delivering genes to mouse muscle using viral vectors – similar to the way the flu invades your body. Animal studies are underway with the hopes of moving quickly to human trials.

In the meantime, two boys die every day from Duchenne and an additional 400 to 600 cases are diagnosed each year. For this generation of Duchenne boys, regulatory hurdles, a lack of research funding and too few human clinical trials are a matter of life and death.

There are many working to find a cure. Among them are two national nonprofits, the Foundation to Eradicate Duchenne (FED) and CureDuchenne.

FED was established in 2002 by Dana and Joel Wood of Alexandria, Va., after their son was diagnosed with the disease. The Woods are both lobbyists in Washington, DC and have been extremely successful in raising federal and private funds for Duchenne research. "Our work at FED is ambitious, with a short-term goal to find a cure," says Joel Wood.



Dr. Eric Hoffman of Children's National Medical Center in Washington, DC. PHOTO: PRIVATE

CureDuchenne, based in Newport Beach, Calif., is a leader in raising funds and awareness. Founders Paul and Debra Miller have a son, 14, with Duchenne. They, too, launched their nonprofit after the diagnosis.

CureDuchenne has raised millions of dollars to fund the most innovative therapies. Its 12-member Scientific Advisory Committee, comprised of the top Duchenne researchers and bio tech executives, provides strategic leadership.

According to CureDuchenne President & CEO Debra Miller, "Six CureDuchenne funded projects have made their way out of the labs and into human clinical trials. We're so close to a cure. When I think of the loss of human life each day, I am even more determined to do whatever it takes to accelerate the research process."

ANNE WATERS
editorial@mediaplanet.com

NEWS

Community collaboration is critical to improving treatment of rare diseases

STEP 3 JOIN A PATIENT GROUP

Very rare diseases carry unique challenges for drug development. Often, little is known about the disease itself, making it difficult to identify targets and design clinical trials, and there are fewer patients to enroll in those trials.

Jamie Manganello Ring
Senior Director, Genzyme Patient Advocacy

Healthcare providers often need education about the disease and about treatment options. Patients and their families may need help coordinating their care from multiple specialists, finding physicians familiar with their condition, proper disease management and treatment options, or navigating their medical insurance. For patients with the rarest conditions, it can be hard to locate other families who know what they're going through and can provide support.

There are a number of ways that people affected by rare diseases can benefit from collaborations with academic researchers, advocacy organizations, and with companies who are developing treatments. At the same time, really listening to patients and advocates is critical for a company to develop treatments that can meet patients' needs.

One way to foster this type of collaboration is for a company to have a dedicated Patient Advocacy function. "A dedicated advocacy function helps ensure that the patient perspective is included in decision making while maintaining open lines of communication between the company and patient groups," explains Jamie Manganello Ring, Senior Director of Patient Advocacy at Genzyme, a Sanofi Company.

Patient organizations and advocacy groups can have an enormous impact on access to treatments. "When we were developing a treatment for Pompe disease, it was very difficult to identify and enroll patients," says Ring. Patient organizations helped find patients and get them enrolled into the trial quickly. Families had also helped design trials that would be feasible for families to participate in and aided in critical communications. "We couldn't have completed the pivotal trial that supported approval without the collaboration of patient organizations all over the world."

In the end, drug companies, patient organizations, families, and advocacy groups all share the same goal: to ensure the best health outcomes and best treatment possible to patients with rare diseases. And companies need to do everything they can to foster open relationships with the community.

KATE LEWIS
editorial@mediaplanet.com

TREATMENT TIPS

How can patients and advocates work together to find treatments?

1. Form a patient advocacy group.
2. Establish a scientific advisory board to stimulate research and gather information for a specific disease state.
3. Develop relationships with strong national patient organizations like NORD and The Genetic Alliance.
4. Work together with the NIH and other pre-existent patient advocacy groups to learn how to build consistent, effective, and efficient advocacy units.
5. Identify goals, academic research institutes, and potential sponsors to support treatment initiatives.
6. Apply for a Research Grant from the NIH.
7. Generate new research studies which decrease gaps in information and identify opportunities for treatment.
8. Stay committed.

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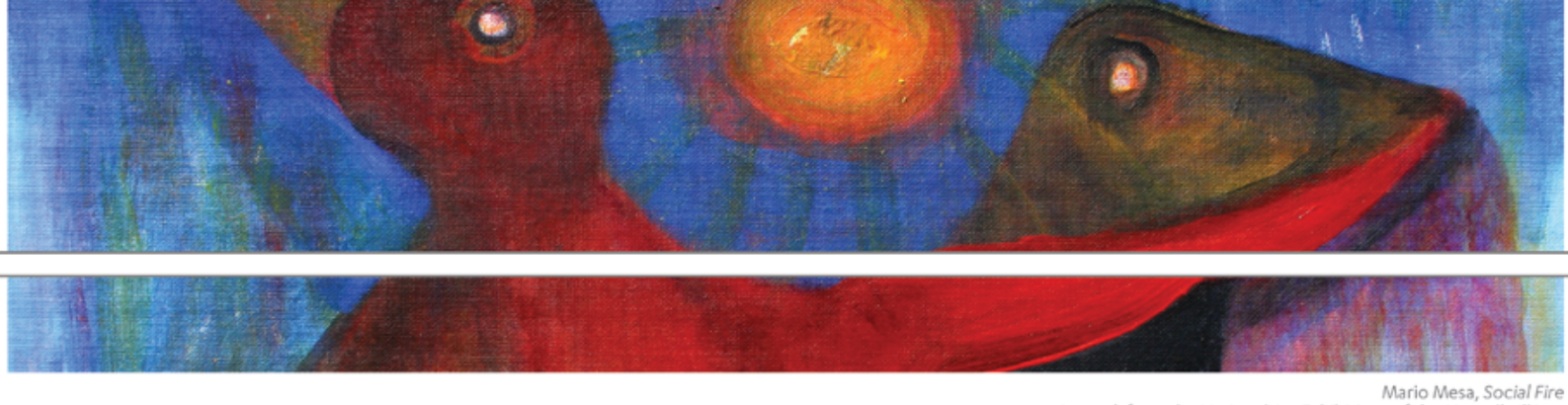

Mario Mesa, *Social Fire*
Artwork from the National Art Exhibitions of the Mentally Ill Inc.
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