

MITOCHONDRIAL DISEASE FORUM

2016 BIO INTERNATIONAL
CONVENTION

JUNE 6, 2016

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for Biotechnology*



HOPE. ENERGY. LIFE.

The BIO International Convention is an annual event hosted by the Biotechnology Innovation Organization (BIO) attracting over 15,000 biotechnology and pharma leaders, as well as representatives from the patient advocacy community, academia, and the federal government, for one week of intensive networking to discover new opportunities and promising partnerships.

The education program at the BIO International Convention covers timely topics of interest to the biotechnology industry, patient advocacy community, and regulators. In each education session, top thought leaders offer insights on issues essential to the biotechnology industry, including the importance of the patient voice in drug development, review, and approval.

For the very first time, the 2016 BIO International Convention featured a half-day Forum entirely focused on one disease. Working in collaboration with the United Mitochondrial Disease Foundation (UMDF), BIO and UMDF convened thought leaders from the mitochondrial disease patient community, academia, industry, and government for a Mitochondrial Disease Forum (Forum) to examine the challenges and opportunities in mitochondrial disease research. The Forum provided a scientific overview of mitochondrial function and pathology, highlighted the current clinical development pipeline across different biopharmaceutical companies, explored scientific and regulatory needs to advance therapeutic development for mitochondrial disease, and discussed why mitochondrial dysfunction is at the core of human health and a key player in disease formation and progression, and, ultimately, aging.

The Forum was comprised of three individual sessions and attracted over 100 Convention attendees from 19 different countries. This summary provides a brief overview of each Forum session, including the focus of the session and any outcomes derived from the panel discussions, as well as press mentions of the event.

Session One: Understanding Mitochondria and Mitochondrial Disease: A Look at Challenges and Opportunities in Research

Moderator

Michio Hirano, MD, Chief, Neuromuscular Medicine Division and Professor of Neurology, Columbia University Medical Center

Speakers

- Marni Falk, MD, Director, Mitochondrial Disease Clinical Center, Children's Hospital of Philadelphia
- Mark Tarnopolsky, MD, PhD, Professor, Division of Neurology, Department of Pediatrics and Medicine, Head, Neuromuscular and Neurometabolic Disease, McMaster University
- Philip E. Yeske, PhD, Science and Alliance Officer, United Mitochondrial Disease Foundation
- Liz Kennerley, Patient Advocate

An estimated 1 in 4,000 people in the United States live with mitochondrial disease. In recent years, there have been exciting advancements in mitochondrial disease research. We are now gaining a better understanding of mitochondrial disease function/dysfunction and identifying disease-causing mutations. However, a combination of extreme genetic complexity and a constantly-expanding clinical spectrum makes diagnostics and the search for treatments difficult. Translating the exciting discoveries in the lab to effective medical treatments for individuals with mitochondrial disease will require collaboration among all stakeholders.

The Forum kicked-off with a panel that provided attendees with a baseline understanding of the science behind mitochondrial function and pathology and explored the current challenges in mitochondrial research while also highlighting some of the recent advancements in this space.

Dr. Michio Hirano, Chief, Neuromuscular Division and Professor of Neurology, Columbia University Medical Center, kicked off the Forum by walking the attendees through the causes of mitochondrial disease and how it manifests itself, underlying the multi-systemic nature of the disease which contributes to the incredibly difficult task of pin-pointing the exact cause of the condition.

Dr. Marni Falk, Director, Mitochondrial Disease Clinical Center, Children's Hospital of Philadelphia, opened her remarks by discussing the genetic component of mitochondrial disease and its heterogeneity. Dr. Falk explained that mitochondrial disease is difficult to treat, in part, because there are over 300 genes that can carry the disease. Further, the entire body is affected, reducing brain function and, in some cases, even developing into mental disorders.

***“There are now nearly 300 different genes that when they're mutated cause mitochondrial disease which is responsible for half to 60% of the diseases in patients. To treat mitochondrial disease is to treat cancer,”
Dr. Marni Falk, Director,
Mitochondrial Disease
Clinical Center, Children's
Hospital of Philadelphia***

Dr. Mark Tarnopolsky, Professor, Division of Neurology, Department of Pediatrics and Medicine, Head, Neuromuscular and Neurometabolic Disease, McMaster University, discussed his groundbreaking work in the mitochondrial space, as well as the clinical care and therapeutic needs of patients with mitochondrial disease. Through his work, Dr. Tarnopolsky discovered that exercise training can increase mitochondrial production, explaining that lack of exercise can be a major threat to health and increase the effects of aging and chronic disease. Dr. Tarnopolsky coined the term, “exerkines” to describe the communication system between cells in our bodies that work together and “talk” to each other to produce the positive effects of exercise. By

learning how exercise works, perhaps we can get one step closer to understanding mitochondrial disease and its causes.

Dr. Philip Yeske, Science and Alliance Officer, United Mitochondrial Disease Foundation (UMDF), explained the importance of advocating on behalf of patients and the impact it has on advancing the science for mitochondrial disease. Dr. Yeske spoke to the complexity of the disease and the strategy employed by UMDF to be the “dot connector” among stakeholders in the community to help facilitate the exciting research being done to advance development of therapeutics for this disease space.

“Being a patient with a rare disease is the hardest job in the world,” Liz Kennerley, Patient Advocate

Liz Kennerley brought the critically important perspective of a patient living with mitochondrial disease to the discussion. In addition to walking the attendees through a day in her life and the challenges encountered on a day-to-day basis, Liz emphasized how important it is to include patients’ perspectives when developing new therapeutics and treatments. Patients know themselves and the disease they are living with better than anyone and can contribute a tremendous amount of value to the drug development, review, and approval processes.

Translating discoveries in the lab to effective medical interventions for individuals with mitochondrial disease will require collaboration among the patient advocacy community, government, academia, and industry.

Session Two: Drug Development for Mitochondrial Disease: Examining the Current Landscape and Scientific/Regulatory Gaps

Moderator

Marni Falk, MD, Director, Mitochondrial Disease Clinical Center, Children's Hospital of Philadelphia

Speakers

- Matt Kline, MD, MS, FACS, Chief Medical Officer, Edison Pharmaceuticals
- Mark Bamberger, PhD, Chief Scientific Officer, Stealth Pharmaceuticals
- Mark Tarnopolsky, MD, PhD, Professor, Division of Neurology, Department of Pediatrics and Medicine, Head, Neuromuscular and Neurometabolic Disease, McMaster University
- James Valentine, MHS, JD, Associate, Hyman, Phelps & McNamara, PC

In recent years, activity around the development of treatments for mitochondrial disease has seen an uptick. In the United States today, there are four companies actively recruiting patients for clinical trials focused primarily on mitochondrial disease, and several others are in pre-clinical planning. Additionally, infrastructure is being created to facilitate drug development, including clinician and patient-populated registries, a multi-center clinical research network with natural history studies, and, last but certainly not least, increased biobanking efforts.

Despite this progress, however, drug development for this condition remains extremely complex. Challenges include, but are not limited to, the need for better animal models, identification of biomarkers of mitochondrial function, improved clinical trial design, and development of non-invasive endpoints for evaluating effectiveness in trials.

The second panel of the Forum highlighted the current clinical development pipeline across different biopharmaceutical companies and explored the scientific and regulatory needs to advance therapeutic development for mitochondrial disease.

“Each patient would pick one of the other three outcomes which are most bothersome to them and that can be your co-primary endpoint,” James Valentine, MHS, JD, Associate, Hyman, Phelps & McNamara, PC

Dr. Marni Falk convened the second panel of the Forum by explaining the necessity of stakeholders in the mitochondrial disease community to work collaboratively to achieve a better understanding of the condition and, one day, to discover a cure. She asserted that it is imperative for patient perspectives to be taken into consideration early in the drug development process when developing and designing treatments, as well as the importance of personalized medicine to this effort.

Dr. Matt Kline, Chief Medical Officer, Edison Pharmaceuticals, provided an overview of Edison Pharmaceuticals' drug development pipeline in the mitochondrial disease space. Despite a lack of a clear path to a cure, utilization of treatments developed by Edison

Pharmaceuticals by mitochondrial disease patients have led to a reduction in hospitalizations. Dr. Kline walked the audience through a few basic guidelines Edison Pharmaceuticals employs when designing its clinical trials to achieve maximum efficiency and cost-effectiveness, including the importance of appreciating the complicated nature of the disease.

Dr. Mark Bamberger, Chief Scientific Officer, Stealth Pharmaceuticals, discussed his company's use of mitochondrial protective agents to restore mitochondrial bioenergetics, including membrane potential and

respiration under pathological conditions. At this point, the agents appear to target and protect dysfunctional mitochondria without affecting mitochondria and cells. This novel approach could provide therapeutic benefits to mitochondrial disease that would be complimentary to the current standard of care.

Dr. Tarnopolsky provided an explanation of how patients with other various diseases also suffer from mitochondrial dysfunction and the benefit that exercise could have on their conditions and health outcomes.

Mr. James Valentine, MHS, JD, Associate, Hyman, Phelps & McNamara, PC, concluded the conversation by emphasizing the importance of incorporating the patient perspective in the drug development process. Through the utilization of benefit-risk decision-making, the patient voice can be integrated into drug development, review, and approval in a truly meaningful way.

Session Three: Harnessing the Promise of Mitochondrial Research: The Potential to Unlock Answers in Other Diseases and Aging

Moderator

Mark Tarnopolsky, MD, PhD, Professor, Division of Neurology, Department of Pediatrics and Medicine, Head, Neuromuscular and Neurometabolic Disease, McMaster University

Speakers

- Lauren Friedman, PhD, Assistant Director, Scientific Affairs, Alzheimer's Drug Discovery Foundation
- Hani Sabbah, PhD, FACC, FCCP, FHRS, Professor of Medicine, Henry Ford Health System
- Laura Stanley, Executive Director, Foundation for Mitochondrial Medicine
- Baris Bingol, PhD, Scientist, Department of Neuroscience, Genentech

Over the last decade, research has taught us that a better understanding of mitochondrial function will not only be of benefit to patients living with mitochondrial disease, but it will also impact and advance research in a large number of more common conditions that affect millions of people, including Alzheimer's disease, Parkinson's disease, diabetes, ALS, and autism spectrum disorders. Additionally, upon further understanding of the disease, it appears that mitochondrial function is central to the aging process itself.

The final panel of the Forum discussed why mitochondrial dysfunction is at the very core of human health and a key player in disease formation and progression, and, ultimately, aging.

Dr. Tarnopolsky began the final session of the Forum with a discussion of theories as to how and why the human body ages and how this relates to mitochondrial dysfunction. Linking back to discussion earlier in the Forum, Dr. Tarnopolsky touched again on the impact exercise is known to have to ameliorate signs of aging. Dr. Tarnopolsky plans to continue his research regarding exerkines and its therapeutic strategy to slow the progression of age-related and other diseases.

Dr. Lauren Friedman, Assistant Director, Scientific Affairs, Alzheimer's Drug Discovery Foundation (ADDF), spoke to how ADDF accelerates discovery and development of drugs to treat Alzheimer's disease. Building on Dr. Tarnopolsky's opening statement, Dr. Friedman explored the link between mitochondrial dysfunction and the acceleration of the progression of Alzheimer's disease.

Dr. Hani Sabbah, Professor of Medicine, Henry Ford Health System, emphasized the need for cardiovascular health in relation to mitochondrial dysfunction. Every year, over 300,000 people in the United States die from heart failure. By targeting mitochondrial dysfunction, additional energy available to the body can alleviate stress on the heart, potentially decreasing the prevalence of heart disease.

Laura Stanley, Executive Director, Foundation for Mitochondrial Medicine, discussed various collaborative research projects initiated by the Foundation for Mitochondrial Medicine. Ms. Stanley said that developing non-invasive blood tests and improved diagnostics and therapeutic interventions will enhance the current landscape of drug development of for mitochondrial disease.

“What we know is that in Alzheimer’s patients, there is impaired energy utilization...that’s thought to be brought on by mitochondrial dysfunction. Two programs that were funded by Alzheimer’s Drug Development Foundation include drugs looking at therapeutics targeting the mitochondria to treat Alzheimer’s disease,” Dr. Lauren Friedman, Assistant Director, Scientific Affairs, Alzheimer’s Drug Discovery Foundation

Dr. Baris Bingol, Scientist, Department of Neuroscience, Genentech, spoke about his work in the area of Parkinson's disease and its connection to mitochondrial function. Like many of the other affected conditions discussed throughout the Forum, Dr. Bingol explained that improving mitochondrial function can slow the progression of the disease, again illustrating far-reaching implications of a deeper understanding of the condition can have on the development of treatments for a myriad of other diseases.

Press and Social Media Mentions of Mitochondrial Disease Forum at 2016 BIO International Convention

Stem Cellar Blog

[IMAGINE Curing Disease and Saving Lives: BIO 2016 Part 1](#)

By Karen Ring

JUNE 8, 2016

Did you hear that? It's the sound of more than 15,000 people taking a collective breath. That's because we are now at the halfway point of the 2016 BIO International Convention, the world's largest biotechnology gathering with over 900 speakers, 180 company presentations, 19 education tracks, 6 super sessions, and 35,000 partnering meetings. Now that's a lot of stuff!

While many at BIO are focused on partnering – establishing new and exciting relationships with other biotech and pharmaceutical companies to push their products forward – others come to BIO to learn about the latest in research, innovation, and healthcare in the biotechnology space.

With so much going on at once, it's hard to choose where to spend your time. If you follow BIO on twitter using the hashtag #BIO2016, you'll get a condensed version of the who, what, and how of BIO.

For those of you who are more partial to blogs, here's a brief recap of the talks that we've attended so far:

Mitochondrial Disease Education Session

A panel of scientific experts and patient advocates gave an overview of mitochondrial diseases and the latest research efforts to develop therapies for mitochondrial disease patients. Phil Yeske of the United Mitochondrial Disease Foundation described his foundation as the largest funder of mitochondrial research next to the government. Their focus is on patient-centered therapeutic development and they've established a community registry of patients that makes patients the central stewards for research and clinical development.

The most moving part of this session was an impromptu speech by Liz Kennerley, a mitochondrial disease patient and advocate. She bravely spoke about the roller coaster of symptoms affecting all of the organs in her body and aptly described her daily experience by quoting Forest Gump, "Life is like a box of chocolates, you never know what you're gonna get." She ended with the powerful statement that patients are at the core of everything scientists do, and encouraged the panel to engage patients more often because they will tell you everything if you ask them the right questions.

Moving out of Stealth Mode: Biotech journalists offer real-world advice on working with media to tell your story

One of my favorite panels of the conference so far featured three biotech journalists, Christina Farr of Fast Company, Jeff Cranmer of BioCentury, and Alex Lash of Xconomy. It was a dynamic conversation about how biotech companies coming out of stealth mode can best pitch their story to the media. Take home points include:

When pitching to a journalist, make sure that you are honest about what you can and can't say. Have a "BS committee" that can address the validity of your work and your research claims.

When pitching, journalists want to know what the problem is you're trying to solve and how you are trying to solve it better than anyone else.

On press releases: Unless it's a press release from a big name, journalists won't read it. The panel said they would prefer a personalized email detailing a company's background and stage of work. They would also consider reading a press release that included a short personalized email from the company CEO.
Most hated words used to describe research: "Revolutionary" "Game-changing" "Disruptive".

Fireside Chat with University of California President Janet Napolitano

In an intimate Fireside chat, Janet Napolitano described her passion for higher education and making a difference in students' lives. In her new role as the President of the UC system, her main focus is on aligning the policies and initiatives between the UC campuses and promoting research and innovation that can be commercialized around the world.

When asked about how she values basic research compared to applied research, Napolitano responded,

"We want an atmosphere where basic research is supported and one where innovation and entrepreneurship is fostered through incubators and public/private partnerships. We need to make these a tangible reality."

Napolitano also mentioned that the UC system needs support from the private sector and gave PrimeUC – a collaboration with Johnson & Johnson Innovation that is part of her innovation and entrepreneurship initiative – as an example of a step in the right direction. You can read more about PrimeUC in this Event Recap.

From Ebola to Zika, how can we go faster in a global emergency?

I was only able to sit in on part of this expert panel, but here is the gist of their conversation. The global number of human infectious diseases is rapidly increasing every year due to hard-to-control factors like overpopulation, deforestation, and global climate change. As a result, we've had two global health emergencies in the past two years: Ebola and Zika. We were more prepared to deal with the Ebola epidemic because more treatments were already in development. Unfortunately, we weren't as prepared for Zika as it wasn't on the world's radar as a serious disease until 2015.

Martin Friede of the World Health Organization (WHO) said we should take what we learned from the recent Ebola outbreak and apply it to the Zika threat. He said the WHO wants to plan ahead for future outbreaks and remove bottlenecks to health benefits. They want to predict what diseases might surface in the future and have products ready for approval by the time those diseases manifest.

That's all for now, but be sure to read Part 2 of our BIO2016 coverage tomorrow on the Stem Cellar. We will give highlights from an entertaining and fascinating Keynote address with Dr. Bennet Omalu (the doctor who blew the whistle on concussion in the NFL) and Oscar-nominated actor Will Smith (who played Dr. Omalu in the movie "Concussion") on "Knowledge precipitates Evolution". I'll also tell you about an eye-opening Fireside chat with the US Food and Drug Administration Commissioner Robert Califf, and much more!

Mitochondrial Disease News

[Positive Data on Primary Mitochondrial Myopathy Drug Candidate Elamipretide \(Bendavia\) Presented by Stealth BioTherapeutics](#)

By Daniela Semedo, PhD

JUNE 8, 2016

[Stealth BioTherapeutics](#) recently reported positive data from its Phase 2 MMPOWER clinical trial, a double-blind, placebo-controlled study that evaluated the safety, tolerability, and efficacy of [elamipretide \(Bendavia\)](#) in patients with mitochondrial myopathy (MM).

The MMPOWER study investigated Bendavia for the treatment of myopathy (muscle weakness) in patients with genetic [mitochondrial diseases](#). These diseases are a diverse group of rare inherited disorders characterized by systemic [mitochondrial dysfunction](#) that impairs patient health and well-being.

Stealth BioTherapeutics' Bendavia is an investigational drug that targets the inner mitochondrial membrane, and developed for the treatment of several conditions, including cardiorenal diseases and orphan mitochondrial diseases. The drug has the potential to preserve energetics and restore normal energy production in mitochondria while reducing oxidative stress.

The U.S. Food and Drug Administration (FDA) granted Fast Track Designation to Bendavia in January 2016 as a treatment option for primary mitochondrial myopathy in patients with genetic mitochondrial diseases.

Data from the MMPOWER trial will be presented on June 17 at the [Mitochondrial Medicine 2016, the United Mitochondrial Disease Foundation \(UMDF\) symposium](#) June 15-18 in Seattle.

The company recently presented results from the MMPOWER trial at the [BIO International Convention](#) at the Moscone Center in San Francisco, where researchers and biotechnology and pharma leaders discussed the opportunities and challenges inherent to mitochondrial diseases, the current state of drug development, as well as the mitochondrial research potential for other conditions, including aging.

At the convention, Mark Bamberger, the company's chief scientific officer, spoke during the session "[Drug Development for Mitochondrial Disease: Examining the Current Landscape and Scientific/Regulatory Gaps.](#)"

"Mitochondrial medicine has the potential to address numerous rare and common diseases, and as a leader in the space, we are thrilled to participate in these meetings to help bring this conversation to the broader healthcare community and to share updates with those already in the field," said Stealth BioTherapeutics' CEO, Reenie McCarthy, according to a recent [press release](#).

"We especially look forward to presenting positive results from the MMPOWER trial and our ongoing development plans for elamipretide in rare mitochondrial diseases, for which there are currently no FDA-approved treatments."

Stealth BioTherapeutics plans to begin the MMPOWER-2 clinical trial in patients who took part in the MMPOWER study in the second half of 2016.

Yellowhammer News (AL)

Brilliant Alabama researcher named 'future leader' of biotechnology

By Michelle Kilpatrick

JUNE 3, 2016

HUNTSVILLE, Ala. — Alabama is home to one of the world's leading researchers in genomics medicine who is being honored at an international biotechnology convention this summer.

Dr. Howard Jacob of the HudsonAlpha Institute for Biotechnology is being named a "Future Leader" for his work using genetic sequencing and analysis to diagnose and cure childhood diseases. Dr. Jacob will be recognized for his work at the 2016 BIO International Convention in San Francisco later this month.

Dr. Jacob's work with genome sequencing started at the Medical College of Wisconsin, where his team became the first in the world to identify and successfully treat a genetic mutation that was responsible for an undiagnosed illness in a child. Jacob then moved his team to Huntsville in 2015 where he established a medical center at HudsonAlpha to diagnose and treat childhood diseases through genetic sequencing and analysis.

"There are millions of people living with a rare disease and HudsonAlpha uses genome sequencing to find diagnoses and better treatments for those patients," Jacob said. "I'm honored that I have the opportunity to showcase how we are changing lives through genomics."

The "Future Maker" honor is awarded by an international vote and it is presented to researchers whose work has the potential for life-changing implications in the future. Dr. Jacobs is one of three "Future Leader" recipients this year. The other two leaders are Charles A. Mohan, Jr., the founder of the United Mitochondrial Disease Foundation, a leading patient advocacy group for mitochondrial disease, and Dr. Alison Van Eenennaam, an animal genomics and biotechnology cooperative extension specialist at the University of California, Davis who studies the use of animal genomics and biotech in livestock production systems.

BIO President and CEO Jim Greenwood praised the three "Future Makers" for their accomplishments and their ability to be a force for change in the field of biotechnology.

"From biomedical research conducted in outer space to breakthroughs in genome sequencing that are allowing us to cure previously incurable diseases, BIO's featured speakers will showcase a transformative new era of medicine pulled straight from the pages of science fiction," he said.

The BIO International Convention is hosted by the Biotechnology Innovation Organization (BIO), which represents over 1,100 biotechnology companies, academic institutions, and related organizations in more than 30 countries. This year's convention is expected to draw over 15,000 members, who are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products around the world.



Marni Falk, Assistant Prof
 @ChildrensPhila explains how
 genomics is key in exploring
 mitochondrial disease #BIO2016



6/6/16, 4:38 PM



Talk of #exosomes and #CRISPR Cas9
 as therapeutic enablers for
 #mitochondrialdisease by Mark
 Tarnopolsky of @McMasterU.
 #BIO2016

6/6/16, 4:50 PM



UMDF Science
 @UMDFScience



@UMDF partnering with @IAmBiotech
 to present a half-day session
 @BIOConvention on mito disease on
 6/6! goo.gl/prHG4C #MitoBIO2016

6/2/16, 2:53 PM



First up at #BIO2016: Understanding
 #mitochondria & mitochondrial
 diseases, challenges & opportunities in
 research.



6/6/16, 4:08 PM



Discovering Cures
@DiscoverCures



A decade of difference towards treatments and cures - thanks to @UMDF #BIO2016 #MitoBIO2016



6/6/16, 5:10 PM



CIRM
@CIRMnews



Inspiration from #mitochondrialdisease patient @LifeAccrdingLiz. "Patients are at the core of everything." #BIO2016



Liz Kennerley and BIO Intl Convention
6/6/16, 5:06 PM from Moscone Center



UMDF Science
@UMDFScience



The view from the dais during Panel 2 on mito drug development during #MitoBio2016 @BIOConvention - >90 in the room!



6/6/16, 5:49 PM



Discovering Cures
@DiscoverCures



Exciting news for patients with Mitochondrial Disease from Newton, MA-based @StealthBT #BIO2016



Stealth BioTherapeutics Reports Positive Results for Primary Mitoc...
prnewswire.com

6/6/16, 6:19 PM

BIO BUZZ

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BIO International
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Day One | Tuesday, June 7, 2016 | San Francisco



MONDAY recap

Understanding Mitochondria and Mitochondrial Disease



Mitochondrial Disease Researchers Gain Momentum

By Michael Eisenstein

Over the course of an hour, researchers at BIO 2016 on Monday offered their take on the daunting complexities of mitochondrial disease, but patient Liz Kennerley's personal perspective brought things back down to earth. "Imagine that each of your organs... is on its own rollercoaster, so you have ups and downs," she said. "Some-

zing array of other physiological processes. Mitochondria carry their own genome—but are also dependent on proteins produced by the main cellular genome within the nucleus, and mutations in either genome can contribute to mitochondrial disease. Until the advent of genome sequencing technology, homing in on these causative mutations was a Herculean feat. "We really had very low odds of ever solving any one person's disease,"

said panelist Marni Falk, a geneticist at Children's Hospital of Philadelphia. Over the past several years, the extent of this complexity has become clearer, and Falk notes that 300 different genes have been linked to mitochondrial diseases to date.

Per Kennerley's experience, mitochondrial disease can also manifest in many different ways. Moderator Michio Hirano, who leads a neuromuscular disease research center at Columbia

University Medical College, noted that any given mitochondrial disease patient may experience an average of 16 distinct symptoms. These disorders are hereditary, but the severity can vary wildly among family members because of a phenomenon known as 'heteroplasmy'. This refers to differences in the relative amount of healthy and mu-

tated mitochondria in a patient's cells, which can determine the debilitating extent of the disease manifestations.

Panelists described a number of multi-institutional efforts now underway to collect deep, rich datasets that might advance the diagnosis and treatment of mitochondrial disorders. For example, the North American Mitochondrial Disease Consortium (NAM-DC), which comprises 17 research sites in the US and Canada, has built a registry with clinical data from more than 900 mitochondrial disease patients. "That has become a valuable tool for industry – companies have already data-mined our registry to find out what kinds of patients there are out there," says Hirano. Falk and colleagues have also assembled the Mitochondrial Disease Sequence Data Resource (MSeqDR), a free and centralized collection of genetic data encompassing 160 different diseases and 1,363 different disease-related genes.

Such efforts are also being strengthened through the efforts of the United Mitochondrial Disease Foundation (UMDF), a patient advocacy group that represents the largest non-governmental funder of research in this space. Panelist and UMDF Science/Alliance



Panelists on Tuesday afternoon described progress in understanding the complex biological bases of mitochondrial diseases.

times one is worse than the other and then some days it can be the other way around—it's really maddening."

Mitochondrial clinical research has come a long way in a short time. Mitochondria are cellular organelles that generate the ATP molecules that fuel almost every aspect of cellular function, and sit at the hub of a diz-

Officer Philip Yeske described his organization as a “dot connector” between patients, pharma, the research community and other stakeholders. One critical piece of this effort is the UMDF’s Mitochondrial Disease Community Registry, which helps patients to mobilize and contribute data to support clinical research. “If you can’t identify and characterize the patients, you’re not going to have the cohorts necessary to do a clinical trial,” says Yeske.

Patients will also play a crucial role in setting the therapeutic agenda. Given the multi-symptomatic nature of mitochondrial disease, panelist Mark Tarnopolsky of McMaster University and biotech startup Exerkine Corporation pointed out that combination therapies are likely to be a must. Surveys of patients have helped determine priorities in this space – for example, Falk noted that symptoms like exercise intolerance and chronic fatigue are particularly common and broadly debilitating in this community, and treatments for those manifestations top the therapeutic wish-list.

Kennerley concluded the session on a bittersweet note. She recalled some of her friends from the patient community whose lives were cut short by mitochondrial disease, but also added that this strengthened her determination to speak out for more research in this area. “This isn’t just about me, this is about everybody else I know with mito,” she told the audience. “All of you give me hope, and that’s the most important thing in the world when you’re dealing with a disease that you know is fatal.” ▼