Mitochondrial Disease Roadmap to a Cure
Mitochondrial Disease Community Registry Update

Southeast Regional Mitochondrial Medicine Symposium

April 2017

UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

HOPE. ENERGY. LIFE.

Guiding Principles of a Roadmap Project

- **Global in scope**
  - Opportunity to identify partners around the world, each with unique capabilities
- **Community-Driven**
  - UMDF would like to steward and manage the project, but broad stakeholder involvement/buy-in is mission critical
- **Leverage knowledge/experience of UMDF SMAB to jump-start the process**
  - Allowed framework to be quickly created
- **An iterative process**
  - Versions will be renewed on a regular basis, reflective of changes in landscape

UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

HOPE. ENERGY. LIFE.

Why does our community need a Roadmap?

"If you don't know where you are going, any road will get you there."

Lewis Carroll (George Harrison, *Any Road)*

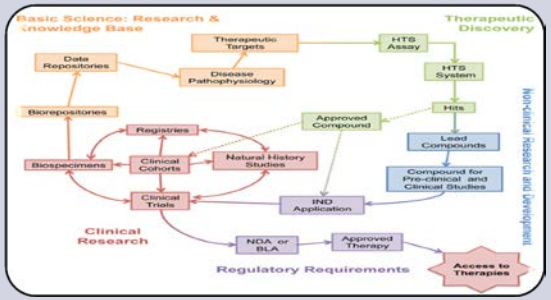
- UMDF's Mission: "…is to find treatments and cures for Mitochondrial Disease…"
- Desire of the UMDF Board of Trustees
- Timing: Significant progress towards therapeutics, understanding mitochondrial biology, increased interest of pharma, increased government awareness.
- UMDF could be the steward for aligning resources in the most efficient and effective manner

The Roadmap is simply a mechanism for identifying, aligning and mobilizing all the various activities and resources necessary to accelerate the discovery of treatments and potential cures.

UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

HOPE. ENERGY. LIFE.

Mitochondrial Disease Roadmap
A 3-Pillar Approach



Diagnosis

- Increase Awareness
- Improving Diagnoses
- Developing Tools to Measure Mitochondrial Health/Disease

Therapeutic Development

- Facilitating Drug Development
- Identifying & Funding Gaps, from Basic Science to Clinical Trials

Patient Care

- Personalized Medicine
- Patient/Clinician Education
- Developing Coordinated Care Models
- Establishing Centers of Excellence

Summary Findings – Diagnosis Pillar

Current Landscape

- Challenging due to extreme complexity of disease
- **Broad need to better identify and characterize patients**

Key Existing Assets

- Patient Registries: NAMDC/RDCRN/MDCR/MSeqDR/Global DBs
- Patient Biobanks: NAMDC/Mayo (limited)

Key Needs

- Improved diagnostic methods
- Consensus indices to measure mitochondrial health
- **Increased patient access to genetic testing**

Near-Term UMDF Focus

- **MDCR Growth: create infrastructure to support research data**
- Improved Patient Biobanking: utilize MDCR to steward biosamples in collaboration with Mayo

Diagnosis

- Increase Awareness
- Improving Diagnoses
- Developing Tools to Measure Mitochondrial Health/Disease

Summary Findings – Therapeutic Development Pillar

Current Landscape

- Rapidly advancing activity in both academia and industry
- Committed pool of clinician researchers in place, but shallow and stretched thin, making clinical trial expansion challenging

Key Existing Assets

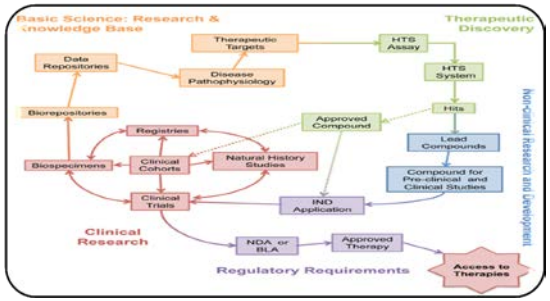
- Patient registries and biobanks
- **UMDF Grants: advance basic, translational and clinical projects**
- Availability of translational tools (limited)

Key Needs

- **Broad stakeholder consensus on priority research topics**
- Development of additional translational tools and validated outcome measures
- Increased collection of natural history data

Near-Term UMDF Focus

- Evolve to increased focus on directed funding of priority topics
- **Financially support industry-sponsored pilot clinical investigations**



Therapeutic Development

- Facilitating Drug Development
- Identifying & Funding Gaps, from Basic Science to Clinical Trials

Summary Findings – Patient Care Pillar

Current Landscape

- Small group of highly expert clinicians
- **Complexity of disease demands involvement of many specialties- a difficult reimbursement scenario**

Key Existing Assets

- Handful of Centers of Excellence (CoE) established
- UMDF Grand Rounds

Key Needs

- **Validation, standardization, support and oversight of CoE models + additional locations**
- Expanded educational tools for patients and clinicians
- Increased advocacy around insurance reimbursement in coordinated care models

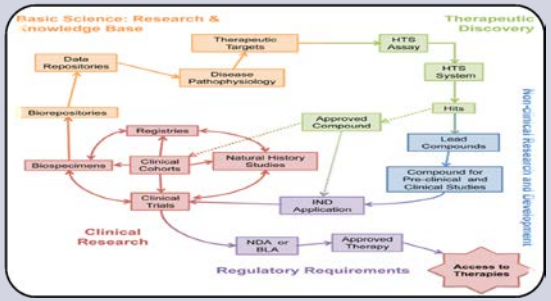
UMDF Focus

- **Development of oversight process for Centers of Excellence**
- Collection of patient care experience to support advocacy efforts

Patient Care

- Personalized Medicine
- Patient/Clinician Education
- Developing Coordinated Care Models
- Establishing Centers of Excellence

Key Assets Aligned to Roadmap



Diagnosis	Therapeutic Development	Patient Care
• Increase Awareness		• Personalized Medicine

Mitochondrial Disease Community Registry
- Multi-stakeholder governance
- Increased data collection
- International deployment

MSeqDR – Genomic Data
- Patient eConsent via MDCR

Education
- Online materials
- Symp/Grand Rounds

Scientific Investment Portfolio
- Academic research grants
- Support of MDCR/MSeqDR/NAMDC
- Funding pilot clinical trials

Patient Care Project
- MMS Project
- Coordinated care

Mitochondrial Disease Community Registry

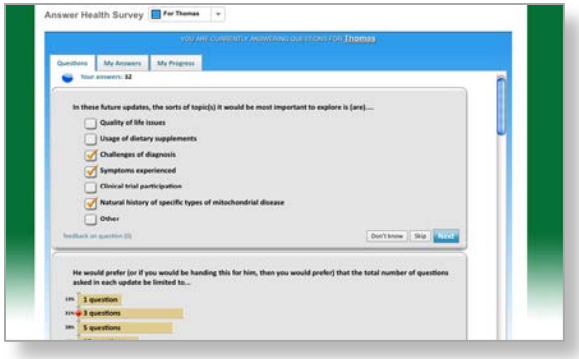
- Goals for a Patient-Populated Registry
  - Keywords: Sustainable, Compatible, Valuable
  - UMDF as steward, not owner
    - Registrants should have full control of who may see their data, analyze their data and who may contact them
  - Patient-populated in order to cast a wider net
    - Complementary, NOT competitive to NAMDC
  - Collect contact and health information
    - Collection of health information over time (longitudinal)
    - Ability to accept study/trial proposals from researchers, query the database and supply de-identified data

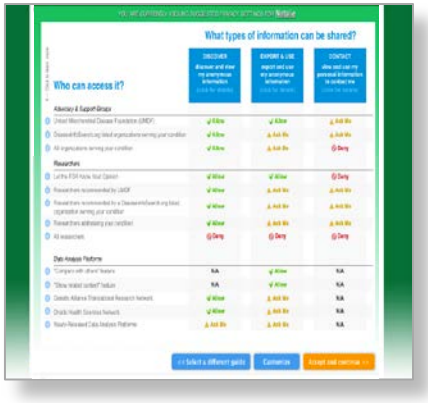
UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

HOPE. ENERGY. LIFE.

Mitochondrial Disease Community Registry

www.umdf.org/registry





Who?

Patients, caregivers & family members

Confirmed diagnosis ***NOT*** required

Why?

Need patient data collected over time in order to improve diagnoses and develop treatments

Key

Registrants have full control of privacy settings

- Allow, deny or "ask me"
- Who can see anonymous data
- Who can analyze anonymous data
- Who can contact you about research studies and clinical trials

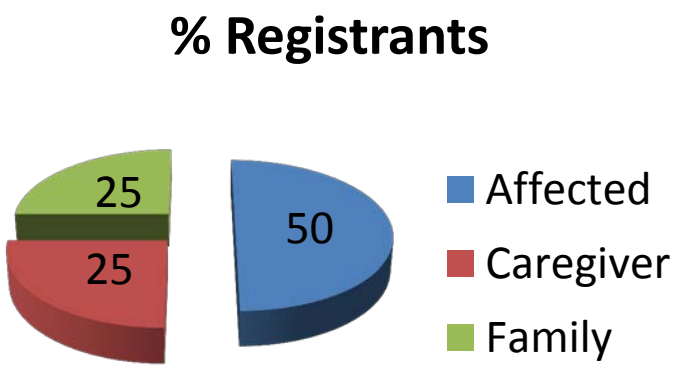
UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

HOPE. ENERGY. LIFE.

PLEASE REGISTER & SHARE!

MDCR Current Status

- Launched August 2014
- March 2017: ~2,050 registrants
- Baseline survey
  - ~100 Q's/~150K Responses
  - Baseline demographics
  - Diagnostic State
  - Opinions on patient-centered drug development
- International: 46 countries represented!
  - ~90% from the US



UNITED MITOCHONDRIAL DISEASE FOUNDATION℠
HOPE. ENERGY. LIFE.

MDCR Data Mining Project

Analysis of Data Collected
2014-2016

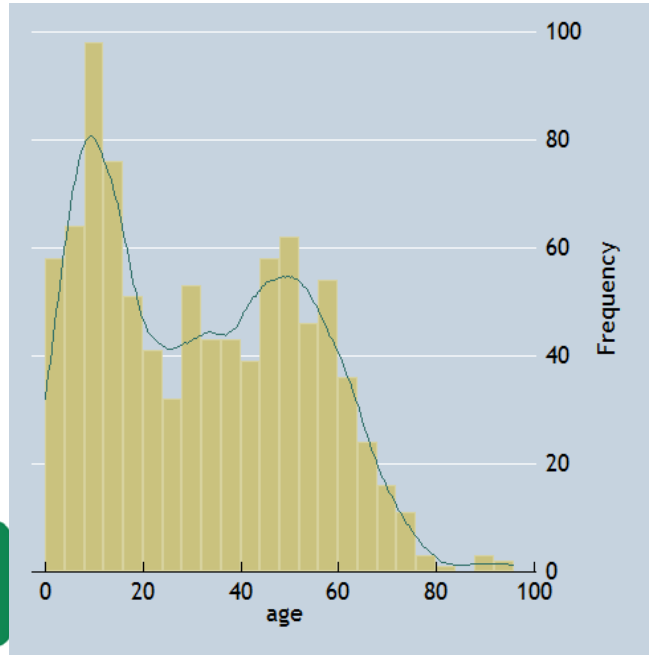
UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

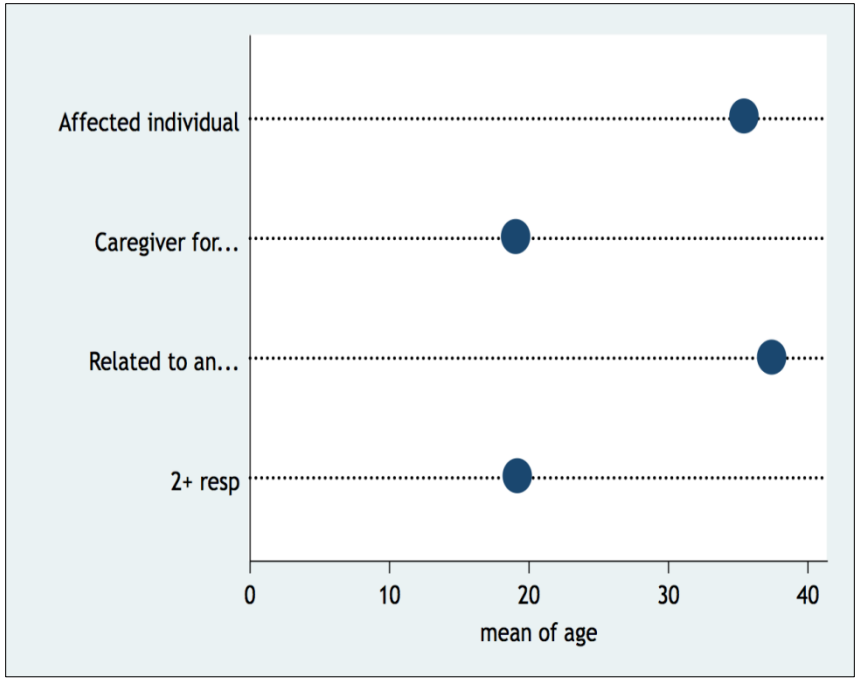
HOPE. ENERGY. LIFE.

Demographics

- Gender
  - Greater female participation
- Age
  - Majority between 20-40
  - Caregivers responding for younger probands
  - 99.7% living

My gender (self-identified) is...	No.	Column %	Cumulative %
Female	523	62.3	62.3
Male	308	36.7	99
Other (specify on next question)	3	0.4	99.4
skipped	5	0.6	100
Total	**839**	**100**	





Mito Disease Diversity

- Broad syndrome representation
- Disorder vs. Age/Race relationships too thin for substantive conclusions

I was diagnosed with (or may have) one of the following	No.	Col %	Cum %
Alpers syndrome	1	0.9	0.9
Encephalopathy	11	9.6	10.5
KSS (Kearns-Sayre Syndrome)	20	17.5	28.1
Leukoencephalopathy	1	0.9	28.9
LHON (Leber Hereditary Optic Neuropathy)	1	0.9	29.8
MELAS	12	10.5	40.4
Myoclonus Epilepsy Ragged-red Fibers	3	2.6	43
Mitochondrial DNA Depletion Syndrome	11	9.6	52.6
MNGIE	8	7	59.6
Multiple Respiratory Chain Enzyme Deficiencies	25	21.9	81.6
NARP	6	5.3	86.8
Pearson syndrome	2	1.8	88.6
SANDO	1	0.9	89.5
Sensory Ataxia Neuropathy	12	10.5	100
Total	**114**	**100**	

mitochondrial dis dx	racecat				
	asian	white	other rac	2 + races	Total
Complex I Deficiency	1	1	0	0	2
Complex III Deficienc	0	0	0	1	1
Complex IV Deficiency	0	0	0	2	2
CPEO	0	0	1	0	1
Encephalomyopathy	0	0	0	1	1
Encephalopathy	0	0	0	1	1
MELAS	0	0	0	2	2
MNGIE	0	1	0	0	1
Multiple Respiratory	0	0	0	1	1
NARP	0	0	0	1	1
Total	1	2	1	9	13

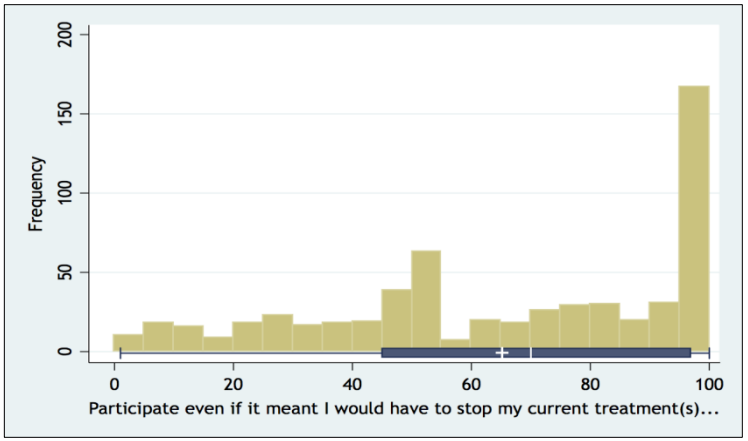
	My gender (self-identified) is...					
	Female		Male		Total	
I was diagnosed with (or may have) the following	No.	Col %	No.	Col %	No.	Col %
Alpers syndrome	0	0	1	2.6	1	1
Encephalopathy	4	6.8	5	13.2	9	9.3
KSS (Kearns-Sayre Syndrome)	11	18.6	7	18.4	18	18.6
Leukoencephalopathy	0	0	1	2.6	1	1
LHON (Leber Hereditary Optic Neuropathy)	1	1.7	0	0	1	1
MELAS	7	11.9	2	5.3	9	9.3
Myoclonus Epilepsy Ragged-red Fibers	1	1.7	0	0	1	1
Mitochondrial DNA Depletion Syndrome	5	8.5	5	13.2	10	10.3
MNGIE	5	8.5	2	5.3	7	7.2
Multiple Respiratory Chain Enzyme Deficiencies	14	23.7	9	23.7	23	23.7
NARP	5	8.5	0	0	5	5.2
Pearson syndrome	0	0	2	5.3	2	2.1
SANDO	0	0	1	2.6	1	1
Sensory Ataxia Neuropathy	6	10.2	3	7.9	9	9.3
Total	59	100	38	100	97	100

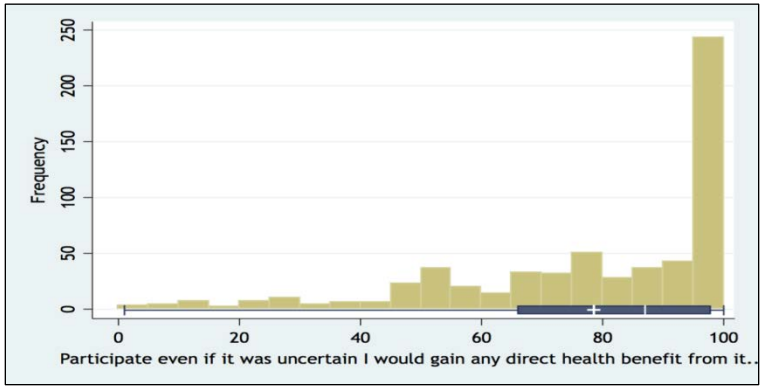
UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

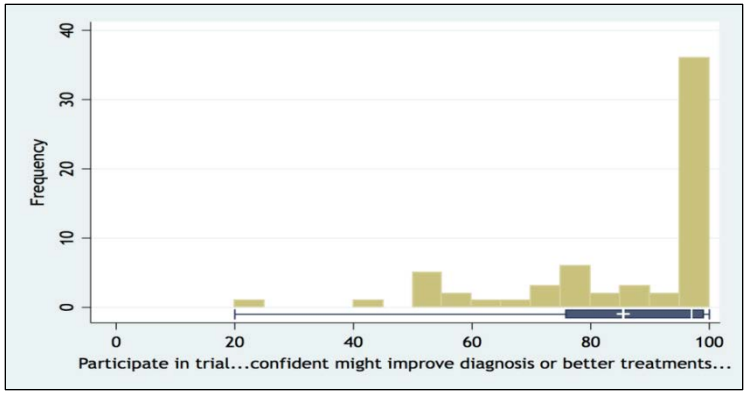
HOPE. ENERGY. LIFE.

Willingness to Participate in Research

- Generally high willingness/interest in community to HELP with clinical studies







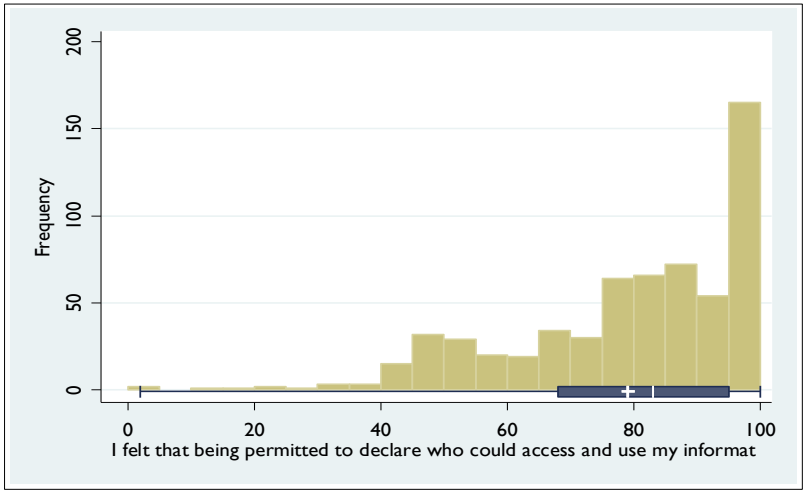
Response to "I am not interested in participating in research because..."				
Item	Yes	%	No	%
"Do not want to be a guinea pig"	3	0.20%	5	0.33%
"The project was not recommended by a doctor"	1	0.07%	7	0.46%
"Results may not be kept private or confidential"	0	0.00%	8	0.53%
"The project will take a lot of time"	0	0.00%	8	0.53%
"Not paid for taking part"	0	0.00%	8	0.53%
"The project involves medical tests, like drawing blood or having x-rays"	1	0.07%	7	0.46%
"The research might reveal something bad"	0	0.00%	8	0.53%
"No obvious benefit to self or family"	1	0.07%	7	0.46%
"Worried about privacy"	0	0.00%	8	0.53%
"Don't know"	3	0.20%	5	0.33%
"Would rather not say"	1	0.07%	7	0.46%
"Would rather not say"	1	0.07%	7	0.46%
Total	1509			

UNITED MITOCHONDRIAL DISEASE FOUNDATION℠

HOPE. ENERGY. LIFE.

Miscellaneous

- High marks for PEER platform experience
- High interest in sharing of genetic testing results



	I have access to the results of genetic testing…						
f I could control who aw my information, I vould be willing to sk my health roviders to update ny profile and/or link ll or some of my ealth records to it…	Although I/he/she recall(s) that genetic testing was performed, I/he/she do/does not have a copy of the report and would not be inclined to request a copy for this purpose.	Genetic testing was never done.	Genetic testing was performed and I/he/she have/has a copy of a report from the doctor or testing lab that lists the genetic variations that are a possible cause of the medical condition.	Other (please specify)	While I/he/she do/does not have a copy of the report, I/he/she recall(s) that genetic testing was performed. I/he/she would be willing to request a copy of the report if this would be useful to gathering information concerning the mitochondrial disorder.	skipped	Total
efinitely not	0	0	1	0	0	0	1
efinitely would want	1	11	12	3	5	0	32
omewhat likely	0	5	5	0	1	0	11
omewhat unlikely	0	0	2	0	0	0	2
Incertain	0	1	10	2	3	1	17
ery likely	0	6	9	2	5	0	22
ery unlikely	2	1	0	0	0	0	3
kipped	0	0	0	0	1	0	1
otal	3	24	39	7	15	1	89

MITOCHONDRIAL DISEASE FOUNDATION℠
HOPE. ENERGY. LIFE.

Near-Term Growth Initiatives

- Increased MDCR Activity
  - Advisory Board in place and recommended:
    - Philip Yeske, UMDF; Amy Goldstein, CHOP; Michio Hirano, Columbia; Jodie Vento, UPMC; Jodi Wolff, Santhera Pharma
    - Regular communication with registrants- plan developed & data mining project complete
    - More frequent, simple surveys- One launched, one in dev, many conceptualized
    - Broaden type of data collected- expand to include genomic & biosamples
- Increased Partnering/Internationalization
  - MDCR is now ready to be broadly deployed
    - IMP and AMDF also very interested in utilizing PEER
  - Establishes a central global repository of patient-derived data on a single platform
    - Flexible platform ideal for driving large global priorities while also allowing or local customization