Data DIY
GlobalGenes.org
Data DIY
Your Involvement in Driving Understanding, Discovery, Diagnosis and Treatments for Rare Disease
Global Genes Question Wall

To participate, please visit https://datadiy.cnf.io/ with your browser

Note: Responses and submissions are anonymous
Welcome and Introduction

Christian Rubio
VP, Community Development and Engagement
Global Genes

Nicole Boice
Founder
Global Genes

Heidi Bjornson-Pennell
Patient Engagement Strategist, Science Policy
Chan Zuckerberg Initiative
<table>
<thead>
<tr>
<th>Time</th>
<th>Session / Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:05–9:30</td>
<td>Welcome &amp; Introduction</td>
</tr>
<tr>
<td>9:30–10:30</td>
<td>The Whys of Data Collection</td>
</tr>
<tr>
<td>10:30–10:45</td>
<td>Break</td>
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<tr>
<td>10:45–11:45</td>
<td>Data Used for Better Clinical Outcomes and Creating Standards of Care</td>
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<td>11:45–12:30</td>
<td>Lunch</td>
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<tr>
<td>12:30–1:45</td>
<td>Data Collection Without a Roadmap – How Has it Evolved?</td>
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<tr>
<td>1:45–2:45</td>
<td>The How’s of Data Collection – What You Need to Know</td>
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<td>2:45–3:30</td>
<td>Open Q&amp;A</td>
</tr>
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<td>3:30–3:45</td>
<td>What's Coming Next?</td>
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<tr>
<td>3:45–4:00</td>
<td>Break</td>
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<tr>
<td>4:00–5:00</td>
<td>Workshop: Making Meaning of Your Community's Data Needs</td>
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**Panel**
- How patients and clinicians are using health data, including novel forms, to accelerate clinical impact, inform better outcomes and gain insights into improving standards of care.

**Panel**
- Hear from organization leaders about their data collection journey, key insights and lessons learned along the way.

**Liz Horn**
- Principal, LHC Biosolutions
- Understanding the steps for structuring your data strategy and high level data sharing partnership models.

**All Presenters**
- Christian Rubio, Global Genes
- Liz Horn, LHC Biosolutions
- Break into groups for mentorship and discussion.

**Leaders/Mentors**
- Scott Demarest
- Liz Horn
- Megan O’Boyle
- Ethan Perlstein
- Steve Roberts
- Kari Rosbeck

**Break**
- Christian Rubio, Global Genes
- Preview of next three series topics and events.
- Livestream wrap-up.

**Break**
- Christian Rubio, Global Genes
<table>
<thead>
<tr>
<th><strong>Our Speakers</strong></th>
</tr>
</thead>
</table>
| **Scott Demarest, MD**  
Assistant Professor  
Dept. of Pediatrics and Neurology  
CU School of Medicine & Children’s Hospital Colorado |
| Scott’s clinical practice and research focus on the evaluation and treatment of early life genetic epilepsies. |
| **Liz Horn, PhD, MBI**  
Principal  
LHC Biosolutions |
| Liz is principal at LHC Biosolutions where she builds research initiatives with nonprofit organizations, focusing on registries and biobanks. |
| **Megan O’Boyle**  
Principal Investigator  
International Registry & Data Network Phelan-McDermid Syndrome Foundation |
| Megan is the principal investigator (PI) for the Phelan-McDermid Syndrome (PMS) international registry and the PMS data network. |
| **Ethan Perlstein, PhD**  
CEO  
Perlara PBC |
| Ethan founded Perlara PBC, the first biotech public benefit corporation partnering with families, organizations and researchers to cure diseases previously thought too rare to matter. |
| **Steven Roberds, PhD**  
CSO  
Tuberous Sclerosis Alliance |
| Steven leads the development and execution of scientific strategy through partnerships with individuals affected by tuberous sclerosis complex researchers, healthcare providers, agencies, nonprofits, etc. |
| **Kari Rosbeck**  
CEO  
Tuberous Sclerosis Alliance |
| Kari joined the Tuberous Sclerosis Alliance in 2001 and became president and CEO in 2007. She’s been involved in nonprofit fundraising and volunteer management for more than 30 years. |
| **Luke Rosen**  
Founder  
KIF1A.Org |
| Luke Rosen is the co-founder of KIF1A.ORG, a research and advocacy organization working to develop treatment for KIF1A Associated Neurological Disorder (KAND). |

Global Genes  
Allies in Rare Disease

#DataDIY | GlobalGenes.org
The Whys of Data Collection

Graphic icons by Faster Cures and Golivo. www.healthdatabasics.org
The Whys of Data Collection
Why health data is vital to rare disease patients and advocacy organizations

Luke Rosen
 Founder
 KIF1A.org
DISCLAIMER

The material presented in this presentation is for informational purposes only. The views expressed in presentations are those of the speaker(s) and not, necessarily, of Ovid Therapeutics.
My Why
Day 1: The Family
The Pioneers
Expanding the natural history of *KIF1A* associated neurological disorders (KAND)

Lia Boyle¹, Wendy K. Chung¹,²

¹) Columbia University College of Physicians and Surgeons, New York, NY, ²) Department of Pediatrics, Columbia University Medical Center, New York, NY

**Introduction**

- *KIF1A* encodes for a kinesin responsible for anterograde axonal transport of synaptic-vesicle precursors and neurotransmitters.
- Pathogenic variants in *KIF1A* have been associated with distinct disorders including the peripheral nervous system disorder hereditary sensory neuropathy IIC (HSN2C), the central nervous system upper motor neuron disorder hereditary spastic paraplegia-30 (SPG30), as well as a complex syndrome with a constellation of symptoms including axonal hypotonia, peripheral spasticity, intellectual disability, and variable cerebellar and cerebral atrophy (MRD9).
- Although pathogenic variants in *KIF1A* were initially assigned to each of these distinct diagnostic categories based on phenotype and mode of inheritance, as we expand our understanding of the natural history of these disorders, these discrete disorders are really a spectrum of clinical severity across *KIF1A* Associated Neurological Disorders.

**Table 1: Phenotypic manifestations of KAND**

<table>
<thead>
<tr>
<th></th>
<th>Dominant N=20</th>
<th>Recessive N=2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurological Issues</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotonia</td>
<td>80% (16/20)</td>
<td>100% (2/2)</td>
</tr>
<tr>
<td>Hypertonia</td>
<td>70% (14/20)</td>
<td>50% (1/2)</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>40% (8/20)</td>
<td>0% (0/2)</td>
</tr>
<tr>
<td>Abnormal MRI</td>
<td>90% (18/20)</td>
<td>50% (1/2)</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>100% (20/20)</td>
<td>100% (2/2)</td>
</tr>
<tr>
<td><strong>Seizures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grand mal</td>
<td>45% (9/20)</td>
<td>100% (2/2)</td>
</tr>
<tr>
<td>Petit mal</td>
<td>25% (5/20)</td>
<td>50% (1/2)</td>
</tr>
<tr>
<td><strong>Ophthalmological Issues</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>85% (17/20)</td>
<td>100% (2/2)</td>
</tr>
</tbody>
</table>

**Methods**

- Cohort includes 22 individuals, 1 of whom (an individual with the p.E253K variant) died prior to study enrollment.
- 14 males, 8 females, 5 months - 21 years old (mean=8.1 years, median=5.6 years)
- 20/22 individuals are heterozygous with one pathogenic variant. 17/20 variants are confirmed de novo, though parental testing is not available for 3/20.
- 2/22 individuals are compound heterozygotes with one variant inside the motor domain and one outside.
- Data collected includes caregiver reported medical history (Table 1), copies of clinical genetic test reports (Figure 1), and Vineland Adaptive Behavior Scales-II (VABS-II) (Figure 2)
#WeNeedAMouse

DIY Animal Models

RARE AND ORPHAN

Why We Need a Mouse
Little mice bring big hope to the rare disease community

Groco Kneisz [Follow]
Oct 4, 2017 - 6 min read

Global Genes

#WeNeedAMouse Youtube

#DataDIY | GlobalGenes.org
THE WHY:
First Message to Families

1. Welcome, you are not alone
2. You’re doing everything right
3. We’re in this together and you’re supported
4. I’ll never ask you to do something that I wouldn’t do myself
5. You must enroll in our natural history study or our children will die
Foundation Readiness

The reason industry says “no” to investment in rare disease programs & how to make them say “yes”
Industry Challenges: Rethink Rare

• Rare, genetic disease excluded because sponsor might not be willing to…
  – Start from scratch with community engagement/data collection
  – Validate existing data
  – Add indication to a late phase, crowded pipeline

• Gross misconception of rare, genetic disease prevalence
  – Exponential growth of communities with no approved treatment options
    • KIF1A – Individuals identified with diagnosis in 2016: ~25
    • KIF1A – Individuals identified with diagnosis today: 200+
  – By the time a program is in phase 2 the population will be “marketable”
Tee it up for Industry: Impossible to Say “No”

• Bring prepared and efficient tools to the table
  – Cross off community-driven line items for every function (registry, meaningful change etc.)
  – Bring validated data ready to employ (natural history study, individual’s genetic confirmation etc.)
  – Advocate for company (integrate company into community, take part in regulatory engagements etc.)

• Care only about what matters most: KIF1A.ORG has no interest in…
  – Intellectual property
  – Patents
  – Profit of any kind

We are a group of patients, caregivers, advocates, family members and scientists focused on one thing: giving our children a meaningful and happy quality of life before time runs out
Accept the Burden: Line Items by Function

Primary Functions of Biotech Research & Development

1. Pre-Clinical
2. Clinical Development / Operations
3. Regulatory
4. Market Access
Dear Biotech:

These tools support your process and make KIF1A.ORG the ideal partner to efficiently and urgently develop therapeutics for our rare disease.

The following tools are freely available to the entire scientific community, including pharma and biotech.

Sincerely, Our Community
## Pre-Clinical Preparation

- Detailed natural history and genotype/phenotype studies
- Detailed and re-contactable patient registration
- List of pathogenic mutations
- Animal models and iPSC lines of mutations with diverse phenotypes
- Rapid response and open dialogue with clinical research team
- Rapid response and open dialogue with families and foundation
Clinical Trial Readiness

- Detailed re-contactable patient registry to support rapid enrollment
- Global map of patient locations to support trial site feasibility and selection
- Center of excellence with trial experience and capabilities ready to activate
- Families willing to support trial design and protocol development
- Meaningful clinical endpoints and outcome measures
Advocacy for Regulatory Approval

- Educated families to advocate with company for approval
- Detailed description of impactful and meaningful outcome measures
- Structured PFDD model prepared with clear message
- Impactful videos of families illustrating unmet needs and meaningful change
- Physicians ready to advocate for approval
- Data on frequency and global need for treatment
Advocacy for Market Access

- Detailed patient journey stories freely accessible
- Family advisory board to support formulation decisions
- Detailed understanding of diagnostic pathway
- Rapid response and open dialogue with clinicians
- Rapid response and open dialogue with patient families
Importance of Strong Longitudinal Data in Rare Disease

Accelerating access to treatment & eliminating the placebo arm
The Community’s Why: Precision Natural History

1. Understand progression of degenerative disease
2. Clinical picture of new disorder with 80 different disease-causing mutations, varying in severity and phenotype
3. Eliminate placebo arm of future open-label clinical trial: small population + small trial = every individual potentially benefits and stays on drug without waiting for commercialization
4. Close the circle between research, medical, regulatory, industry and patient communities
5. Understand what matters most to families and develop meaningful clinical outcome measures
Challenges

1. Lack of appropriate tools to capture and measure real meaningful change
   - True in rare disease clinical trials
   - Results in missed endpoints and failed trials preventing access to medicines with meaningful therapeutic change

2. Bandwidth: consistent tester in a growing community

3. New biomarkers / re-contacting families

4. Time is running out: communities don’t just grow
Pre-foundation understanding of KIF1A (2016)

NC: Neck coil
CC: Coiled coil
FHA: FHA domain
PH: PH domain
Impactful understanding of KIF1A
KEY TAKEAWAYS

1. Partnerships with researchers can be powerful – if they are open to sharing data

2. Natural history studies enhance disease understanding and may replace placebos in trials

3. Families can provide important data on how different mutations affect different individuals
Questions?

Global Genes Question Wall
To participate, please visit https://DataDIY.cnf.io with your browser

Thank you Luke@KIF1A.org
Break
Data DIY
Join us at the Summit for a jam-packed, two-day program filled with TED-style keynotes and five tracks of compelling educational content including:

- General Data Protection Regulation: Implications for You and Drug Development.

Global Genes, in partnership with the Orphan Disease Center at the University of Pennsylvania School of Medicine, hosts the annual RARE Drug Development Symposium designed to connect, educate and inspire rare advocates. The Symposium focuses on the drug development process and the role of rare disease advocates.
Data Used for Better Clinical Outcomes and Creating Standards of Care

Liz Horn, PhD, MBI
Principal
LHC Biosolutions
Luke Rosen
Founder
KIF1A.Org
Standard of Care Challenges

- Heterogeneous condition
- Symptomatic treatment strategy
- Treatment resistant

“Care until Cure.” WKC

What is Meaningful Change

Small change, big impact

- Quality of life
- Staying present

Outcome measures & successful trial design
KEY TAKEAWAYS

1. Standard of Care in many genetic disorders is symptomatic management of multiple implications from the genetic change

2. To design successful clinical trials, we need to understand what truly matters to families and what a meaningful therapeutic change really is
Scott Demarest, MD
Assistant Professor
Dept. of Pediatrics & Neurology
CU School of Medicine & Children’s Hospital Colorado
Who am I?

• Child neurologist and epileptologist
• My sub sub-specialty is in genetic causes of early-life epilepsies
• My care and research are oriented toward improving the lives of patients and families with these rare diseases

Disclosures

• I have consulted for Upsher-Smith and Biomarin on an unrelated subject matter
• I have funding from the International Foundation for CDKL5 Research
Punch-line

• Doctors are just people – no better, no worse.
• Find the doctors that are interested, curious, invested and support them
• Guidelines are the ideal but Centers of Excellence are a starting point
Doctors are just people and there is a lot of NOISE!

These are not excuses for poor treatment by your doctor, but the truth is that doctors are jugglers:

• See more patients
• See them faster
• Bill more
• Don’t forget that test
• You need to see that patient in the hospital
• What about that test you ordered

• Write that letter of medical necessity
• See more patients
• Finish your notes
• See more patients
• Finish your notes
• “I really need to set up that database…”
What do you want in your doctor? They have to be:

- Compassionate
- Smart
- Creative
What do you want in your doctor? They have to be:

- Compassionate
- Creative
- Smart
- Engaged
You want this guy!
Support them when they are engaged!

Things that take time, money and/or effort:

- Specialty clinics
- Multi-disciplinary clinics
- Creating programs initiatives
- Creating care protocols
- Standardizing care protocols
- Creating care guidelines
- Implementing care guidelines
- Getting an IRBs
- Creating databases (especially with the right data)
- Input of data
- Data analysis
- Publishing
- Creation of research networks
- Doctors are unlikely to ask for money!
How to you get there?

• Start with one engaged provider and expand the network by supporting them
• Create hubs of care with groups of providers that have more experience and a willingness and INTEREST in see your rare disease
• Centers of Excellence
• Eventually you collect large amounts of data and write guidelines…
KEY TAKEAWAYS

1. Doctors are just people – no better, no worse
2. Find the doctors that are interested, curious, invested and support them
3. Guidelines are the ideal but Centers of Excellence are a starting point
Ethan Perlstein, PhD
CEO
Perlara PBC
Say hi to Maggie and her parents
The single most important piece of data

<table>
<thead>
<tr>
<th>Congenital Disorder of Glycosylation Ia: PMM2 Gene Sequencing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Results:</strong> Two pathogenic variants detected. One copy of a c.415G&gt;A (p.E139K) pathogenic variant and one copy of a c.422G&gt;A (p.R141H) pathogenic variant were detected in the PMM2 gene of this individual.</td>
</tr>
</tbody>
</table>

**Interpretation**

A sample from this individual was referred to our laboratory for molecular testing for congenital disorder of glycosylation type Ia (CDG Ia). CDG Ia is the most common form of CDG reported and is caused by deficiency of the enzyme phosphomannomutase, which converts mannose-6-phosphate to mannose-1-phosphate. The clinical presentation of CDG Ia is highly variable with infantile, childhood, and adult presentations. Pathogenic variants in the PMM2 gene cause CDG Ia. Two pathogenic variants within the PMM2 gene, one inherited from each parent, are required to cause the disease.

Sequence analysis detected the following:

<table>
<thead>
<tr>
<th>Gene</th>
<th>Exon/Intron</th>
<th>Nucleotide change</th>
<th>Amino acid change</th>
<th>Zygosity</th>
<th>Type</th>
</tr>
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<tbody>
<tr>
<td>PMM2</td>
<td>Ex5</td>
<td>c.415G&gt;A</td>
<td>p.E139K</td>
<td>Heterozygous</td>
<td>Pathogenic</td>
</tr>
<tr>
<td>PMM2</td>
<td>Ex5</td>
<td>c.422G&gt;A</td>
<td>p.R141H</td>
<td>Heterozygous</td>
<td>Pathogenic</td>
</tr>
</tbody>
</table>
Turning data into discovery
Turning data into discovery

A

**Cell Density (OD$_{600}$)**

<table>
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<tr>
<th>Time (hours)</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>pREV1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pSEC53</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pACT1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pTEF1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Graphs**

- **pREV1**
- **pSEC53**
- **pACT1**
- **pTEF1**

**Lines**

- **sec53Δ**
- **WT**
- **E100K**
- **F126L**
- **E146K**
- **R148H**
- **V238M**

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Turning discovery into n-of-1 trial

epalrestat
KEY TAKEAWAYS

1. You can’t embark on a cure odyssey without taking a first step: mutation–models–medicine
2. N-of-1 cure odysseys are now a reality because highly motivated families get up to speed within WEEKS of a diagnosis
3. More Organic Intelligence, less AI
Steven Roberds, PhD
CSO
Tuberous Sclerosis Alliance
About Tuberous Sclerosis Complex

Tuberous sclerosis complex (TSC) is a genetic disorder that causes tumors to form in vital organs, primarily the brain, eyes, heart, kidneys, liver, lungs and skin.

- TSC affects approximately 1 in 6,000 live births.
- An estimated 50,000 Americans have TSC and more than 1 million worldwide.
- No two people are affected the same way, not even identical twins.
- Neurological manifestations are often the most devastating – affecting almost all with TSC in some manner, from mild to severe.
- TSC is a leading genetic cause of autism and epilepsy.
Vision for the TSC Natural History Database

• Better understand progression of TSC to improve health care
• Follow all manifestations of TSC over a person’s lifetime
• Identify cohorts for future clinical studies and trials
• Serve as a resource to researchers to hasten discovery of new therapies
Data Sources for Clinical Data

Participating Institutions

Map Key:
1. Minnesota Epilepsy Group, PA, St. Paul, MN (Michael D. Frost, MD)
2. Texas Scottish Rite Hospital for Children, Dallas, TX (Steven P Sparagana, MD)
3. New York University Langone Medical Center, New York, NY (Josiane Lajoie, MD)
4. Massachusetts General Hospital, Boston, MA (Elizabeth A. Thiele, MD, PhD)
5. Children’s National Medical Center, Washington, DC (William McClintock, MD)
6. University of Chicago, Chicago, IL (Patricia Ogden, APN, FNP, NP-C)
7. UCSF Benioff Children’s Hospital, Oakland, CA (Rachel Kuperman, MD)
8. University of California Los Angeles (UCLA), Los Angeles, CA (Joyce Y. Wu, MD)
9. University of Texas Health Science Center, Houston, TX (Hope Northrup, MD)
10. University of Alabama, Birmingham, AL (Bruce Korf, MD, PhD)
11. Cleveland Clinic, Cleveland, OH (Ajay Gupta, MD)
12. Children’s Hospital Colorado, Aurora, CO (Susan Koh, MD)
13. Nicklaus Children’s Hospital, Miami, FL (Ian O’Neil Miller, MD)
14. Loma Linda University Medical Center, Loma Linda, CA (Stephen Ashwal, MD)
15. University of Pennsylvania, Philadelphia, PA (Katherine Nathanson, MD)
16. Boston Children’s Hospital, Boston, MA (Mustafa Sahin, MD, PhD)
17. Cincinnati Children’s Hospital Medical Center, Cincinnati, OH (Darcy A. Krueger, MD, PhD)
18. Washington University, St. Louis, MO (Michael Wong, MD, PhD)
Natural History Data Use Examples

• Epilepsy treatment patterns, e.g., drugs, surgery, second surgery
• Correlation of early-onset seizures with drug-resistant epilepsy
• Genotype-phenotype relationships
• Changes in patterns of renal tumor monitoring and treatment with availability of mTOR inhibitor therapy
• Informing clinical consensus guidelines regarding brain tumor monitoring
Informing Clinical Consensus Guidelines

• Diagnosis
• Surveillance
• Management
Accelerating Research and Drug Discovery Through Collaborative Projects
KEY TAKEAWAYS

1. Ensure diversity of data sources – not only ethnic diversity, but different centers of excellence

2. Data are not static – continuous learning and adaptation will be required
Questions?

Global Genes Question Wall

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Lunch
Data DIY
SAVE THE DATE 2019!
September 18-20, 2019
Sheraton San Diego Marina Hotel
1888 Harribank Blvd. San Diego, California, USA 92101
Presented by Global Genes
and the University of Pennsylvania Orphan Disease Center
Call 201-353-6837

REGISTER TODAY!
June 7, 2019
Philadelphia, PA
Presented by Global Genes and the University of Pennsylvania Orphan Disease Center

Don’t Stop Innovating: Patients’ Role in Breakthrough Ideas

Global Genes, in partnership with the Orphan Disease Center at the University of Pennsylvania School of Medicine, hosts the annual RARE Drug Development Symposium designed to connect, educate and inspire rare advocates. The Symposium focuses on the drug development process and the role of rare disease advocates.

Join us at the Summit for a jam-packed, two-day program filled with TED-style keynotes and five tracks of compelling educational content including:

General Data Protection Regulation: Implications for You and Drug Development.

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WWW.GLOBALGENES.ORG

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Welcome Back

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VP, Community Development and Engagement
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Global Genes Question Wall

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Data Collection Without a Roadmap – How Has it Evolved?

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Founder
KIF1A.Org
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<td></td>
<td>Principal</td>
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</tr>
</tbody>
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Liz Horn, PhD, MBI
Principal
LHC Biosolutions

Megan O’Boyle
Principal Investigator International Registry & Data Network
Phelan-McDermid Syndrome Foundation

https://www.pmsf.org/registry/
Shannon Colleen O’Boyle (18 years old, DX @ 8 months, Del 22q13.31-13.33 (6.27Mb))
What does Phelan-McDermid Syndrome (22q13 deletion/mutation) look like?
Characteristics of PMS

Core features

- Developmental (intellectual) disability (100%)
- Absent or delayed speech (100%)
- Autism spectrum disorder (84%)
- ADHD
- Hypotonia
- Regression

Other features

- Seizures (40+ %)
- Gastrointestinal dysfunction
- Sleep issues
- Psychiatric regression
- Decreased perception of pain
- Habitual chewing or mouthing
- Temperature regulation issues
- Cardiac complications
- Renal conditions
- Lymphedema
- Minor dysmorphic features (long eyelashes, dysplastic ears, fleshy hands)

Dhar et al, 2010
Phelan 2007
Phelan, 2008
Phelan et al, 2001
Cusimano-Dogg et al, 2007
Bonaglia, 2006
Who Are We?

• We are a 16 year-old non-profit foundation with a 3 person office staff
• We do NOT have a Scientific Director
• We DO have a Scientific Advisory Committee
• We have 2,100 known diagnosed members in over 59 countries
• Over 1,300+ members in the International Registry
• 100 families with medical records integrated with registry data

Founder, Sue Lomas

Dr. Katy Phelan
Newsflash

Sign in to Reconsent
Welcome to the Phelan-McDermid Syndrome International Registry. Please sign in to review and complete the new Informed Consent. There are new data sharing options, including the option to participate in the Phelan-McDermid Syndrome Data Network (PMS_DN). Once you have answered the 8 questions in the informed consent, check "Yes, I agree to participate in the Registry." If you have any questions, please contact the Registry Coordinator at PMSR@PMSF.org.

Welcome to the Phelan-McDermid Syndrome International Registry. The purpose of this registry is to consolidate information from individuals with Phelan-McDermid Syndrome into a single database, which will be utilized by researchers to understand Phelan-McDermid Syndrome better.
What is the PMSI Registry?

PMS International Registry...

• Collects contact info (for foundation use only)
• Collects Genetic Reports (curated/de-identified by a trained genetic counselor)
• Asks 100 clinical (medical) questions (organized by organ)
• Asks 100 developmental questions
• Asks 100 questions re: adolescent & adult patients
• Asks 100 additional questions submitted by a researcher (data will be “protected” for one year then it will become part of the data available to the entire research community)
Returning Data to Families

- What is the level of the patient's response to environmental temperature variations? (check all that apply)
  - 534 people provided 742 response(s)
  - Normal
  - Always cold
  - Overheats easily
  - Does not perspire
  - Perspires less than...
  - Unsure

- What is the patient's pain tolerance level?
  - 558 people provided 560 response(s)
  - Normal
  - Higher than usual
  - Lower than usual
  - Unsure
What advantages do patient groups have by creating their own registry?

- Contact information
- Trust of their members
- Consent to be re-contacted
- Ability to inform and recruit patients
- Means of communications:
  - Social Media
  - Newsletters
Why a patient group sponsored registry?

• Decrease patient survey fatigue
• Data can be shared with more researchers faster for less $
• Increase in researcher access to data
• Researcher can post Q&A on the PMSIR registry faster and for less
Who gets what?

• Patient Support Group gets…
  – Info about the condition

• Researchers get …
  – Data about the patients

• Pharmaceutical companies get …
  – Data to improve selection of appropriate candidates for clinical trials
Value to researchers…

• Get data from more patients
• Get data faster
• Get data for less $$ (saved funds can be spent on more studies)
• Be able to re-contact patients through support group
• See data that may not have been of interest but becomes valuable
How did we accomplish what others said we couldn’t? We:

• Found the right vendor
• Compiled potential Q&A
• Consulted with researchers about the Q&A
• Created necessary documents: Informed Consent, IRB protocol, marketing materials, etc. (with the help of outside advisers)
• Beta tested
• Marketed
• Returned data to patients/families whenever possible
• Will re-access the registry after 2 years and change as needed
Why did we put our limited time & resources into building a patient registry?

- Better characterize syndrome
- Educate and empower families
- Improve diagnosis and clinical care
- Provide data for pre-clinical and clinical research
- Identify cohorts
- Facilitate recruitment & reduce enrollment lag
- Connect families to research opportunities
- Collecting patient contact information (for communications and recruitment)
What we’ve learned…

Patients/families have limited time:

• Short, specific surveys are best

• Ability to go back to finish is preferred

• Too many questions can be overwhelming

• Parents can’t remember answers and that makes them feel like “bad” parents

• If the first experience took too long then they are less likely to update annually – diminishing the longitudinal data
KEY TAKEAWAYS

1. Participating in the registry empowers parents/families

2. Families are using PMSIR to inform their physicians about the syndrome and specific conditions
Tuberous Sclerosis Alliance

The TS Alliance, founded in 1974, is committed to finding a cure for tuberous sclerosis complex while improving the lives of those affected by:

• Developing programs, support services and resource information
• Stimulating and sponsoring research
• Creating and implementing public and professional education programs designed to heighten awareness of the disease

www.tsalliance.org
A Key Partner in TSC Advances: The First 23 years

- Founded in 1974
- First research grant awarded in 1984
- TSC2 gene cloned in 1993
- TSC1 gene cloned in 1997
A Key Partner in TSC Advances: The Next 4 Years

TS Alliance
- Founded 1974
- First research grant 1984


TSC Progress
- 1993 TSC2 gene cloned
- 1997 TSC1 gene cloned

First TSC consensus conference 1998
First National TSC Conference 1999
Volunteer outreach and government relations launch 2001

1994

TS Alliance

TS Progress

#DataDIY | GlobalGenes.org
A Key Partner in TSC Advances: The Story Unfolds

1974
- Founded
- First research grant

1984
- First TSC consensus conference

1984
- TSC2 gene cloned

1988
- TSC1 gene cloned

1993
- First TSC Conference

1998
- Volunteer outreach and government relations launch 2001

2001
- Natural History Database launch

2002
- TSC–mTOR link discovered

2003-2011
- 10 TSC clinical trials focused primarily on tumor growth

2019
A Key Partner in TSC Advances: The Story Unfolds

TS Alliance
- Founded 1974
- First research grant 1984

TS Progress
- 1993 TSC2 gene cloned
- 1997 TSC1 gene cloned
- 2002 TSC–mTOR link discovered
- 2003-2011 10 TSC clinical trials focused primarily on tumor growth
- 2012 Autism & Epilepsy biomarker study launch
- 2014 Developmental Synaptopathies Consortium launch
- 2016 PREVeNT trial launch

- First TSC consensus conference 1998
- First National TSC Conference 1999
- Volunteer outreach and government relations launch 2001
- Natural History Database launch 2006
- Clinical Research Consortium launch 2011

Timeline:
- 1974: Founded
- 1980: First research grant
- 1990: First TSC consensus conference
- 2000: First National TSC Conference
- 2010: Volunteer outreach and government relations launch
- 2011: Natural History Database launch
- 2012: Autism & Epilepsy biomarker study launch
- 2014: Developmental Synaptopathies Consortium launch
- 2016: PREVeNT trial launch
- 2019: Clinical Research Consortium launch
A Key Partner in TSC Advances: The Story Unfolds

1974 Founded

1980 First research grant 1984

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2003-2011 10 TSC clinical trials focused primarily on tumor growth

2011 Clinical Research Consortium launch

2012 Natural History Database launch 2006

2014 Clinical Research Consortium launch 2011

2016 Biosample repository launch 2014

2017 Developmental Synaptopathies Consortium launch 2016

2018 PREVeNT trial launch 2012

2019 Volunteer outreach and government relations launch 2001

Global Genes

#DataDIY | GlobalGenes.org
Strategic Decision to Use Clinic-Entered Data

- Existing network of TSC Clinics
- Estimated 50,000 Americans with TSC provides large sample size
- Shifts burden of medical record translation from parents and caregivers to clinic staff (but needs significant financial support)
- All data collection requires IRB-approved informed consent
Basic Data Flow

Clinical data → Clinical data → Clinical data → Clinical data → Natural History Database → Clinical researchers → Pharma researchers → Lab researchers
Addition of Questions and Data Refinement

Clinical data

Clinical researchers
Pharma researchers
Lab researchers

Natural History Database
Continuous Improvement and Enhancement

• Growth of custom-built database

• Pharma partnership enabled second-generation database
  – Win-win collection of data on manifestations of high priority to patients and pharma: TAND, epilepsy, SEGA, renal
  – Platform established for clinical study data and reports
  – Database ownership remained with TS Alliance
  – Non-exclusive data access by pharma partner

• Addition of sub-projects suggested by researchers
Biosamples Linked to Natural History Data

Voluntary TSC NHD Participants

- Tissue
- Plasma
- DNA

TSC Biosample Repository Samples by Month in 2016-19

- NHD
- RDCRN
- PREVeNT
Accelerating Research and Drug Discovery Through Collaborative Projects

Hypothesis Generation

Drug Screening

Preclinical Development

Lead Optimization

Phase 1

Phase 2

Phase 3

Approved

research

preclinical

GRANTS

CONSORTIUM

clinical

biosample

RESEARCH CONSORTIUM

REPOSITORY

TSC NATURAL HISTORY DATABASE

Global Genes

#DataDIY | GlobalGenes.org
KEY TAKEAWAYS

1. Putting patient advocacy groups at the center contributes to long-term sustainability of data programs, as opposed to one-off projects.

2. Begin where you are, learn by talking to other groups in your situation and grow as resources allow.

3. Demand collaboration and obtain continual input of multiple stakeholders.
Questions?

Global Genes Question Wall

To participate, please visit https://DataDIY.cnf.io with your browser
The Hows of Data Collection – What You Need to Know to Structure Your Plan

Liz Horn, PhD, MBI
Principal
LHC Biosolutions
Research Engines Drive Progress

Patient registries and biorepositories are research game changers!

L. Johnson, Lymedisease.org
This a time of great opportunity!

Collaboration is key!
The Patient Community is Vital

• Understand the unmet needs of the community
• Develop trust within the community
• Leverage scarce resources
• Facilitate collaboration between stakeholders
• Committed to the cause
• Stewards of the collection
• Bring multiple stakeholders together
Building Blocks

- Participant Communications
- Funding and Staff
- Ongoing Maintenance
- Marketing and PR
- Research Network

- Sample Collection
- Governance
- Purpose
- Scientific Expertise
- Platform
- Data Source
What the user asked for

How the analyst saw it

How the system was designed

As the programmer wrote it

What the user really wanted

How it actually works

http://codejunkie.net/graphics/gigo.jpg
Considerations

• Data only or data with biological samples?

• What information/samples should be collected?

• Who will manage collection?
  – How will the information/samples be collected?
  – How/where will the information/samples be stored?

• Who can access the collection?

• Who will advise you?

• Resource and financial considerations
What will you collect?

<table>
<thead>
<tr>
<th>Will your data collection project focus on a specific condition?</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If yes, please describe the condition:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Which of the following types of information are you interested in collecting?</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Medical information</td>
</tr>
<tr>
<td>☐ Demographics (age, sex, etc)</td>
</tr>
<tr>
<td>☐ Lifestyle information (diet, exercise, etc)</td>
</tr>
<tr>
<td>☐ Family history</td>
</tr>
<tr>
<td>☐ Genetic information</td>
</tr>
<tr>
<td>☐ Diagnosis information</td>
</tr>
<tr>
<td>☐ Treatment information</td>
</tr>
<tr>
<td>☐ Quality of life information</td>
</tr>
<tr>
<td>☐ Other (describe)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How many participants do you hope to enroll?</th>
</tr>
</thead>
<tbody>
<tr>
<td>--------------------------------------------</td>
</tr>
</tbody>
</table>
# Data considerations

## Types of information
- Medical information
- Participant demographics
- Lifestyle information
- Family history
- Genetic information
- Diagnosis/treatment information
- Quality of life metrics
- Who enters info?

## Standards/Sources
- Facilitates pooling of data
- No uniform standard exists
  - HL7, LOINC, SNOMED-CT, RX-Norm
- Standardized instruments
- Questions others used
  - NHANES, PROMIS, PhenX, db-GAP, PRISM

## Access
- Who can access
- Who determines access
- SOPs for access
- SOPs for distribution
- Governance
- Stewardship
- Returning results (aggregate, IRRs, IFs)
- Collaboration

---

**Data commons/repository**
Questionnaire considerations

• What information will you collect?
• What format will the questionnaire be?
• Who will design the questionnaire?
• Who will enter the information?
• How often will information be updated?
• What questionnaires/ instruments currently exist?
Sources for questions

• Use standardized data collection instruments when available

• Use questions that others have used on a large scale
  – NHANES (National Health and Nutrition Examination Survey)
  – PROMIS (Patient-Reported Outcomes Measurement Information System)
  – PhenX (consensus measures for phenotypes and exposures)
  – dbGaP (database of Genotype and Phenotype)
  – PRISM (Patient Registry Item Specifications and Metadata for Rare Diseases)
Different answer choices

<table>
<thead>
<tr>
<th>Example from Eye Study</th>
<th>Example from WHI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is your current Marital Status?</strong></td>
<td><strong>F20 Current marital status</strong></td>
</tr>
<tr>
<td>1. Never married</td>
<td>(Mark the one that best describes you)</td>
</tr>
<tr>
<td>2. Divorced/separated</td>
<td>- Never Married</td>
</tr>
<tr>
<td>3. Widowed</td>
<td>- Divorced or Separated</td>
</tr>
<tr>
<td>4. Married</td>
<td>- Presently Married</td>
</tr>
<tr>
<td></td>
<td>- Widowed</td>
</tr>
<tr>
<td></td>
<td>- Marriage-like Relationship</td>
</tr>
</tbody>
</table>
Measures are more meaningful than descriptors

- Hyperlipidemia – yes/ no
- Kept the descriptor but lost the measurement
- In the 1970’s, high cholesterol >300
- Then it changed to normal cholesterol <250
- Changed again to <200
Patient entered vs. provider entered data

• Hot topic with strong opinions
• Influenced by resources
  – Providers need compensated to enter data
• Research shows patients can accurately enter certain information
• Complex information can be obtained from provider/medical record
• Questionnaire must be designed for who will be entering it
Who will be eligible?

Who will be eligible to participate in your data collection project?

☐ Anyone who would like to submit their data, whether or not they have a diagnosis
☐ Only those who have been diagnosed with this condition by a healthcare provider
☐ Other (describe) _______________________

______________________________
Are you interested in biological samples?

Are you interested in collecting biologic samples?
- Yes
- No
- Maybe in the future

If yes, what physical samples would you like to collect?
- Blood and/or serum
- Buccal swabs
- Urine
- Tissue
- Other (describe)

How many samples do you hope to collect?
Biobank Planning Considerations

• What biological samples will you collect?

• What sample associated data will you collect?
  – How will the data/samples be collected?
  – How/where will the data/samples be stored?

• Who will manage collection?

• Who can access the collection?

• Who will advise you?

• Resource and financial considerations

• Biobank business plan
## BioBank considerations

<table>
<thead>
<tr>
<th><strong>Collection</strong></th>
<th><strong>Processing/Storage</strong></th>
<th><strong>Access</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sample type</td>
<td>• Location</td>
<td>• Who can access</td>
</tr>
<tr>
<td>• Donor profile</td>
<td>• Derivatives</td>
<td>• Who determines access</td>
</tr>
<tr>
<td>• Collection timing</td>
<td>• Downstream experiments</td>
<td>• SOPs for access</td>
</tr>
<tr>
<td>• Collection logistics</td>
<td>• SOPs for extraction</td>
<td>• SOPs for distribution</td>
</tr>
<tr>
<td></td>
<td>• Where</td>
<td>• Cost Recovery</td>
</tr>
<tr>
<td></td>
<td>• When</td>
<td>• Governance</td>
</tr>
<tr>
<td></td>
<td>• Who</td>
<td>• Stewardship</td>
</tr>
<tr>
<td></td>
<td>• How often</td>
<td>• Returning results (aggregate, IRRs, IFs)</td>
</tr>
<tr>
<td></td>
<td>• Similar collections?</td>
<td>• Collaboration</td>
</tr>
</tbody>
</table>

- **Processing/Storage:**
  - Location
  - Derivatives
  - Downstream experiments
  - SOPs for extraction
  - SOPs for storage
Collection Considerations

**Blood**
- DNA, RNA, Protein
- PBMCs
- Cell lines
- Serum, Plasma

**Tissue**
- DNA, RNA, Protein
- Cell lines
- FFPE, Frozen sections
- Whole tissue

- Collection at point of care
- Collection at outreach events/ individual kits to donors
- Collection at autopsy
Who will help you?

Who will help you create a plan for your data collection project?

☐ Scientific advisory board
☐ Medical advisory board
☐ Researchers who will likely use our data and samples
☐ Medical experts
☐ Other advocacy organizations with registries/repositories
☐ Other (describe) ____________________

______________________________
Medical and scientific advisors

• Knowledge experts
• Champions of your organization
• Key stakeholders
• Competitors
• Politically complex (collaborators, allies, frenemies, enemies)
• Volunteers
Roles for advisors

• Study design
• Questionnaire development
• Registry/ biobank oversight
• Recruitment partner
• Data use committee
• Promote registry to other investigators
• Users of data
Common advisory structures

• Medical board
• Scientific advisory board
• Registry/biobank oversight committee
• Other task forces/committees/working groups
• Ad-hoc advisors
Mapping the landscape of your advisors

- What tasks do you need assistance with?
- What expertise do you need?
- Who are your current advisors?
  - What is their expertise?
  - What roles do they have in your organization?
  - What other relevant roles do they have?
- What knowledge gaps remain?
  - Medical, scientific, other
- Don’t overlook organizational politics
Cultivating new advisors

• Network at scientific meetings
  – Go to relevant posters and talks
  – Introduce yourself and follow-up after the meeting

• Ask current advisors to recommend other advisors

• Consider timing in their career

• Consider working with them on a pilot project
Tips for working with advisors

- Be clear on expectations
- Understand roles, responsibilities and decision making
- Discuss time commitment and deliverables
- Communicate regularly
- Acknowledge your advisors
  - Within your community
  - To their peers

dancingcatstudio.com/whimsicalcatart.htm
Lessons learned

• Don’t duplicate efforts – registries and biobanks are expensive and administratively burdensome
• Develop partnerships to share data and resources
• Ensure registry/ biobank is sustainable over time
• Use common data fields/ controlled vocabulary to allow comparison with multiple data sets
• Follow best practices
• Retention is key - it is much harder to recruit new participants than to keep those that are participating
• Prior proper planning prevents poor performance
• Stewardship is important
• Good partners are essential
• People matter
The Importance of Planning

• Solicit input before you build
• Find out what researchers need, and how they need it
• Define goals based upon needs
• Ensure consent language doesn’t unnecessarily restrict future use
• Develop a business plan
Discussion

L. Horn, Stonehenge, England
Open Q & A

Global Genes Question Wall

To participate, please visit https://DataDIY.cnf.io with your browser
What’s Coming Next?

Christian Rubio
VP, Community Development and Engagement
Global Genes
Data DIY
Your Involvement in Driving Understanding, Discovery, Diagnosis and Treatments for Rare Disease

Workshop#2 (2nd of 4 Part Series)
Data Trusts, Governance and Collection Platforms
Know Your Rights, Responsibilities and Opportunities
WASHINGTON, DC
Wednesday July 17, 2019 - Friday July 19, 2019

#DataDIY

Workshop#3 (3rd of 4 Part Series)
DEVELOPING COLLABORATIVE RESEARCH NETWORKS
October 24-25 | Philadelphia, PA

Workshop#4 (4th of 4 Part Series)
DATA SHARING FOR SCIENCE COLLABORATIONS
January 2020 | Houston, TX

GLOBALGENES.ORG/EVENT/DATA-DIY

#DataDIY | GlobalGenes.org
Break
Data DIY
Workshop
Making Meaning of Your Community’s Data Needs