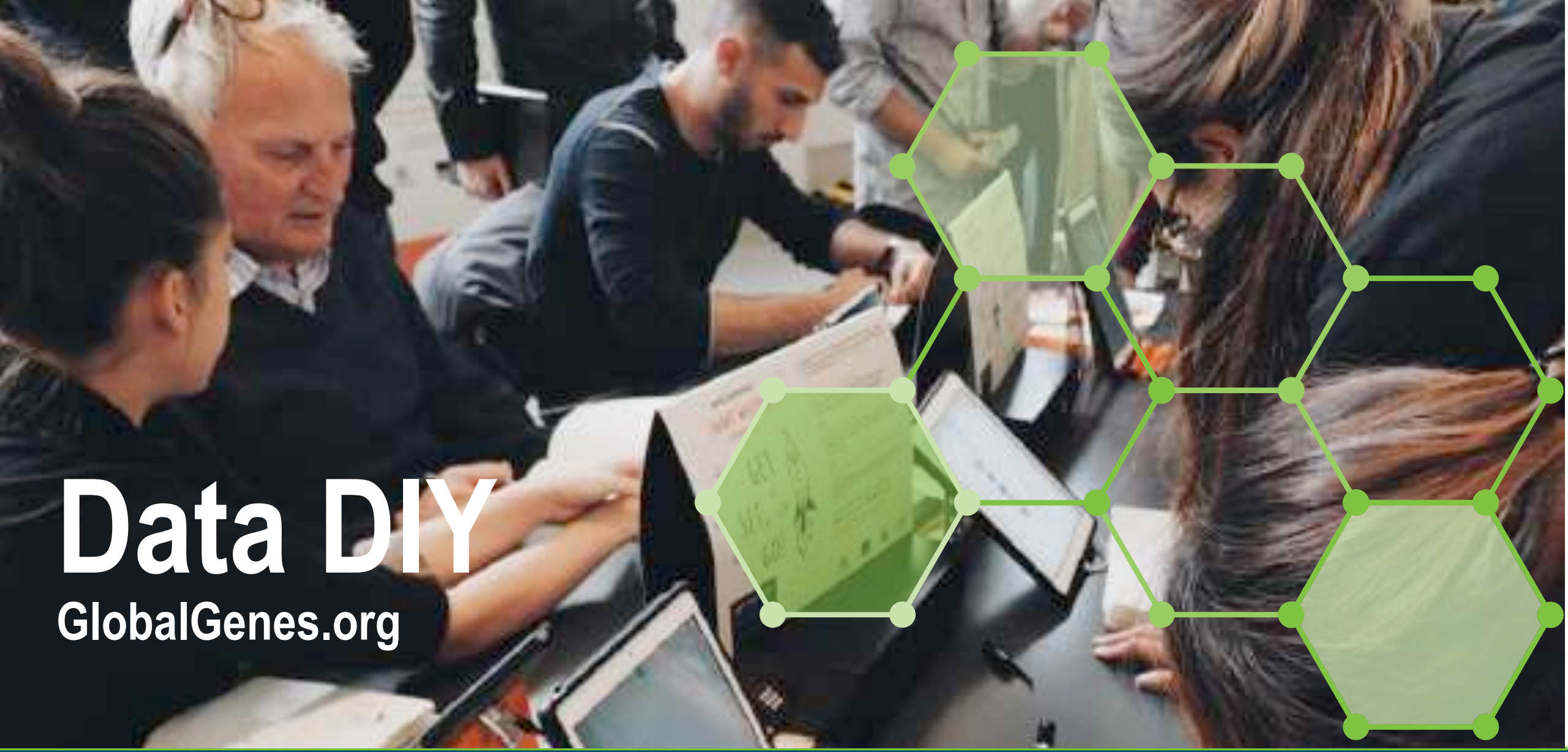

Data DIY

GlobalGenes.org

Global Genes™
Allies in Rare Disease

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Global Genes™
Allies in Rare Disease

Data DIY

Your Involvement in Driving Understanding, Discovery, Diagnosis and Treatments for Rare Disease

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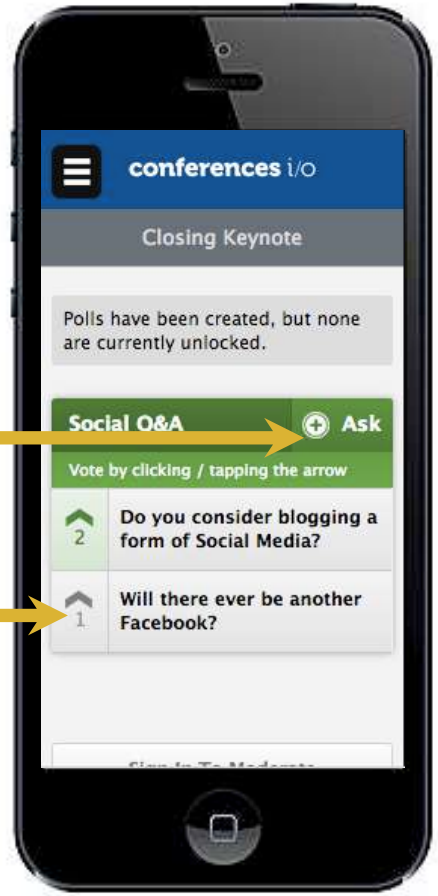
Global Genes Question Wall

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

Ask a Question

Up-Vote a Question



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

Agenda

9:05–9:30	9:30–10:30	10:30	10:45 – 11:45	11:45	12:30–1:45	1:45–2:45	2:45–3:30	3:30–3:45	3:45	4:00–5:00
Welcome & Introduction	**The Whys of Data Collection**	Break	**Data Used for Better Clinical Outcomes and Creating Standards of Care**	Lunch	**Data Collection Without a Roadmap – How Has it Evolved?**	**The How's of Data Collection – What You Need to Know**	**Open Q&A**	**What's Coming Next?**	Break	**Workshop: Making Meaning of Your Community's Data Needs**
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**	**Luke Rosen** Founder **KIF1A.ORG** What is health data and why collecting and sharing it is of increasing importance to rare disease patients and advocacy organizations		**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** Preview of next three series topics and events. Livestream wrap-up.		**Leaders/Mentors** • Scott Demarest • Liz Horn • Megan O'Boyle, • Ethan Perlstein, Steve Roberds • Kari Rosbeck • Luke Rosen Break into groups for mentorship and discussion

Our Speakers

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

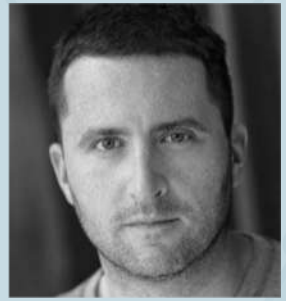
Steven leads the development and execution of scientific strategy through partnerships with individuals affected by tuberous sclerosis complex researchers, healthcare providers, agencies, nonprofits, etc.

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.



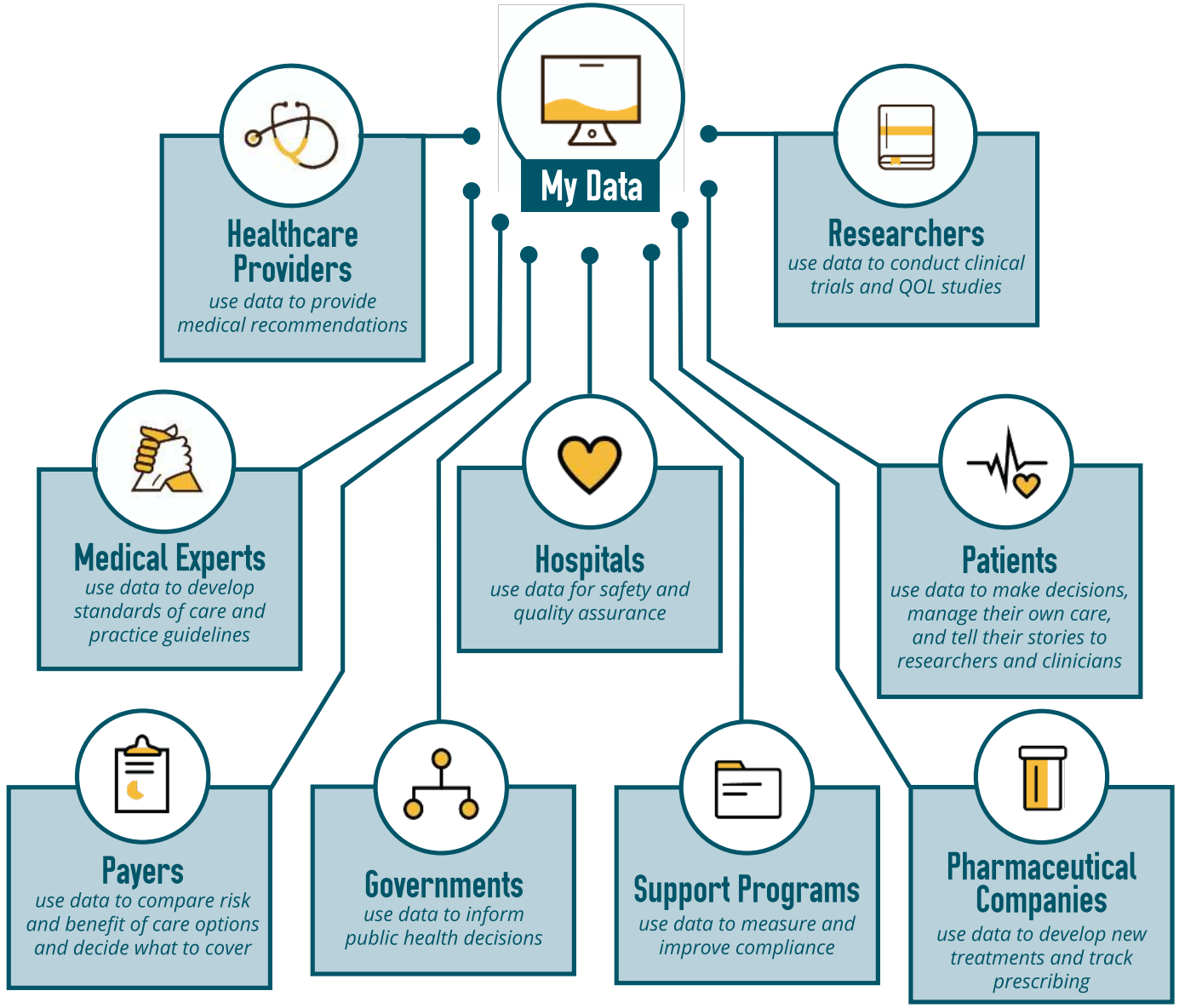
Luke Rosen

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).

The Whys of Data Collection



Graphic icons by Faster Cures and GoInvo. www.heatlhdatabasics.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.

Susannah

My Why







Day 1: The Family

The Pioneers

Expanding the natural history of *KIF1A* associated neurological disorders (KAND)

Lia Boyle[1], Wendy K. Chung[1,2]

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* Assocaited Neurological Disorders.

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***)

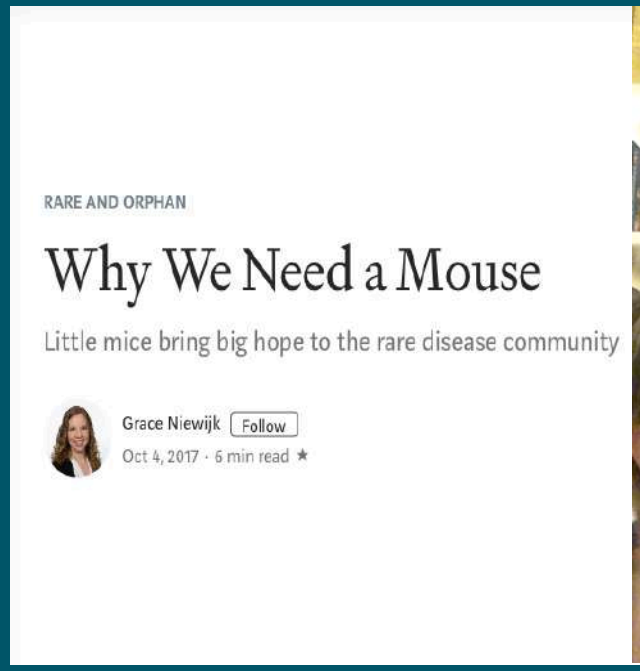
Table 1: Phenotypic manifesations of KAND

	Dominant N=20	Recessive N=2
Neurological Issues	100% (20/20)	100% (2/2)
Hypotonia	80% (16/20)	100% (2/2)
Hypertonia	70% (14/20)	50% (1/2)
Microcephally	40% (8/20)	0% (0/2)
Abnormal MRI	90% (18/20)	50% (1/2)
Developmental delay	100% (20/20)	100% (2/2)
Seizures	45% (9/20)	100% (2/2)
Grand mal	20% (4/20)	50% (1/2)
Petit mal	25% (5/20)	50% (1/2)
Ophthalmological Issues	85% (17/20)	100% (2/2)

22

#WeNeedAMouse

DIY Animal Models


RARE AND ORPHAN

Why We Need a Mouse

Little mice bring big hope to the rare disease community

Grace Niewijk Follow

Oct 4, 2017 · 6 min read ★

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Allies in Rare Disease

#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

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

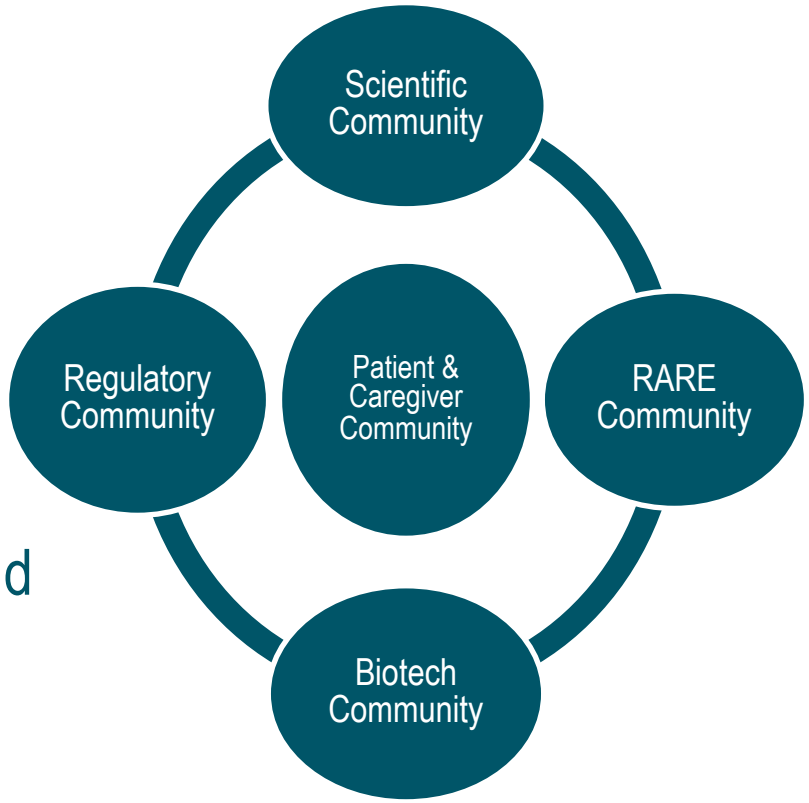
- Detailed patient journey stories freely accessible
- Family advisory board to support formulation decisions
- Detailed understanding of diagnostic pathway
- Rapid response and open dialogue with clinicians
- Rapid response and open dialogue with patient families

Importance of Strong Longitudinal Data in Rare Disease

Accelerating access to treatment & eliminating the placebo arm

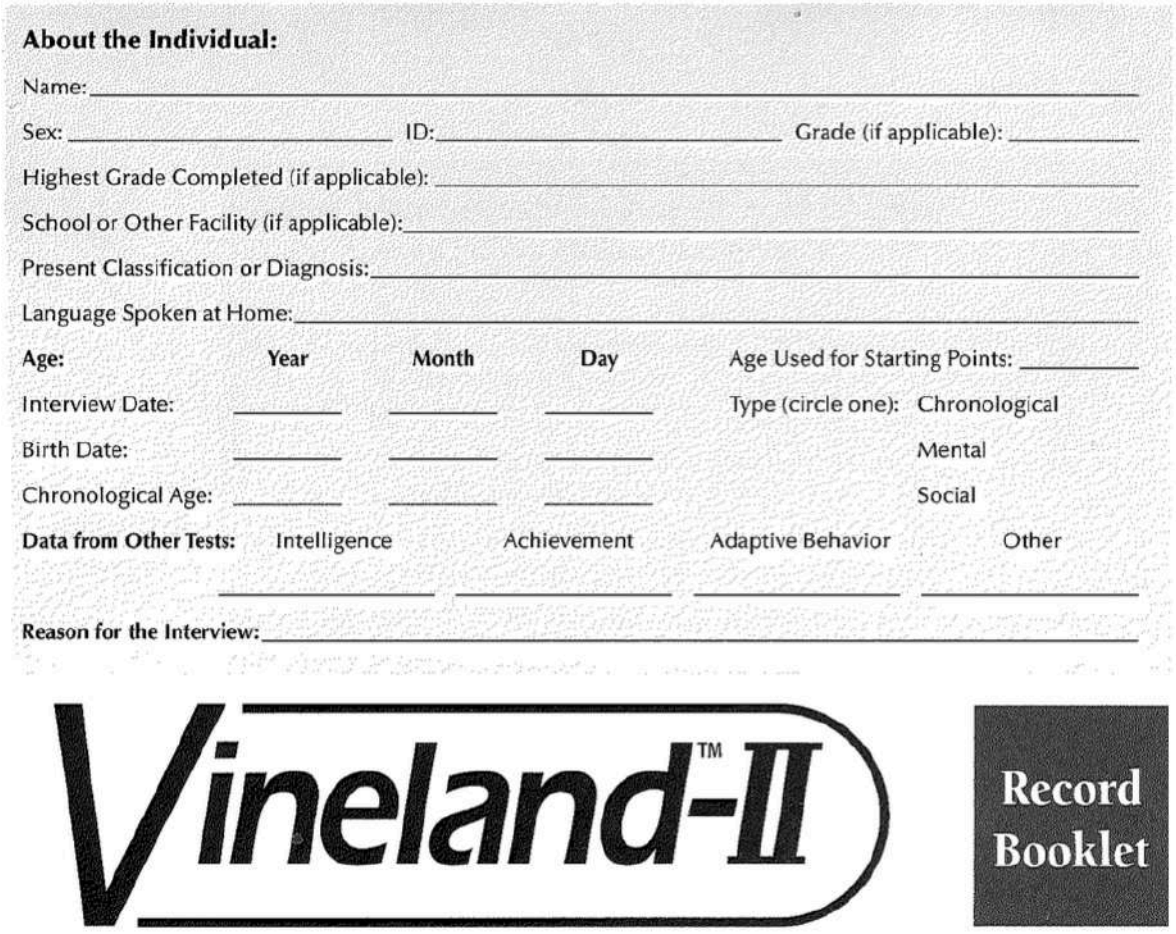
The Community's Why: Precision Natural History

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

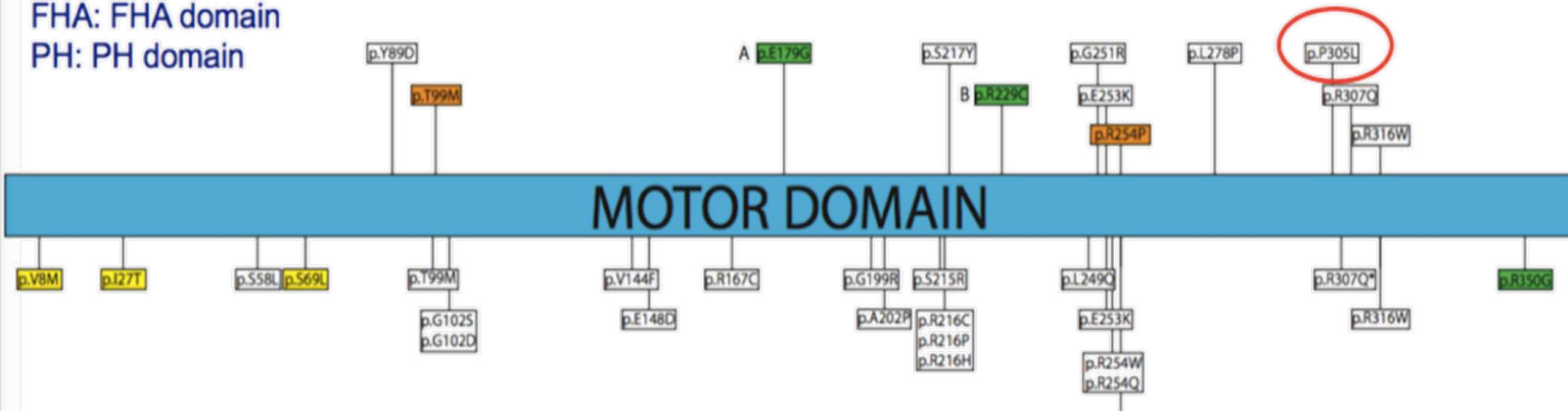


Challenges

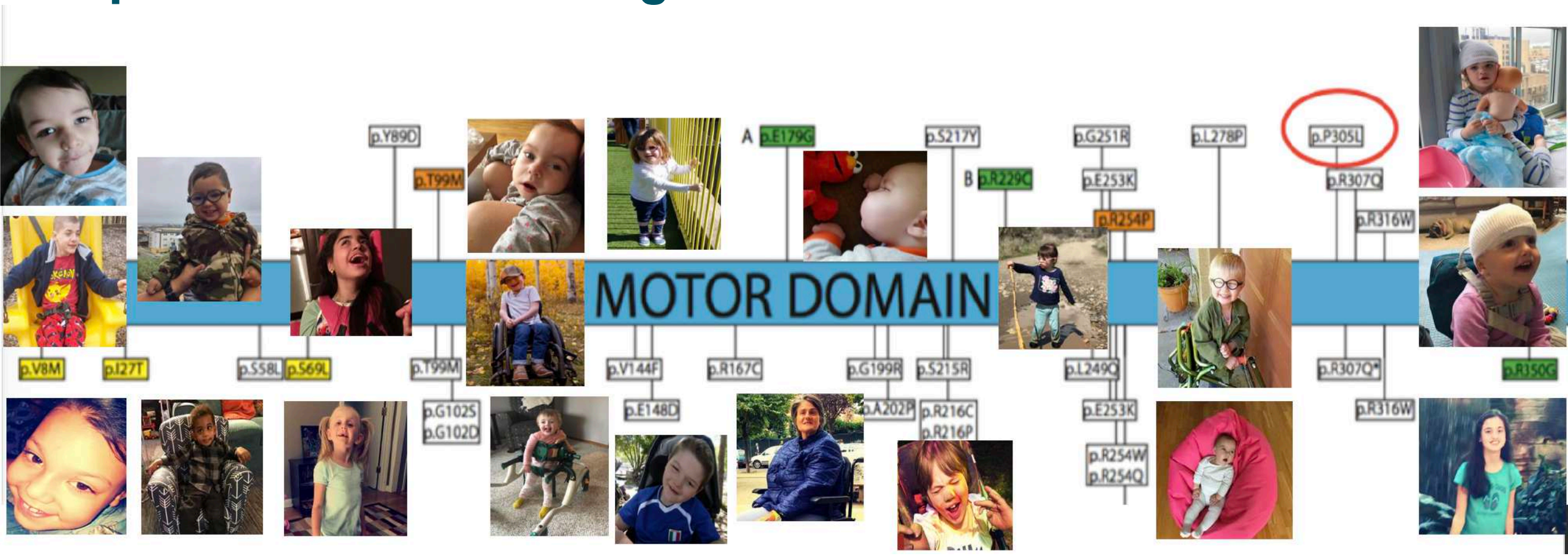
1. Lack of appropriate tools to capture and measure real meaningful change
   - True in rare disease clinical trials
   - Results in missed endpoints and failed trials preventing access to medicines with meaningful therapeutic change
2. Bandwidth: consistent tester in a growing community
3. New biomarkers / re-contacting families
4. **Time is running out: communities don't just grow**



Pre-foundation understanding of KIF1A (2016)



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

Global Genes™
Allies in Rare Disease

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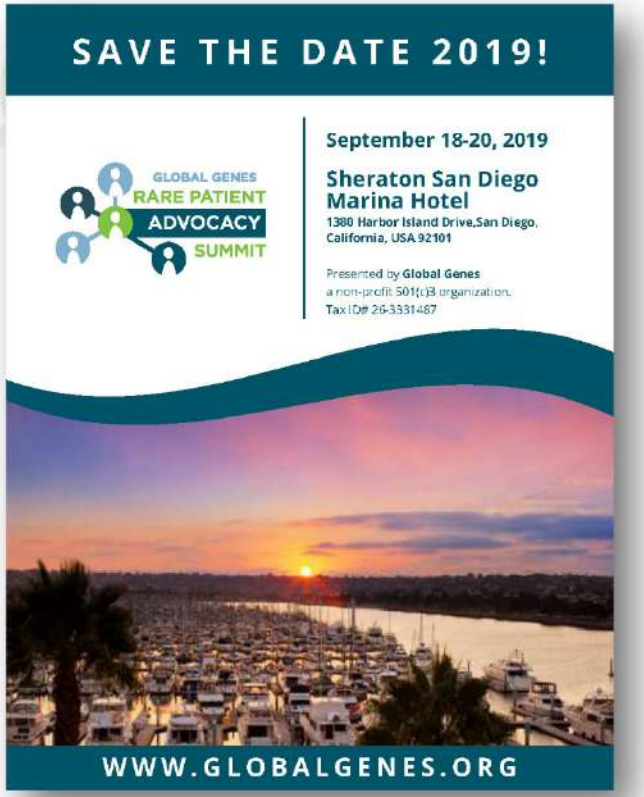
Join us at the Summit for a jam-packed, two-day program filled with TED-style keynotes and five tracks of compelling educational content including: **General Data Protection Regulation: Implications for You and Drug Development.**



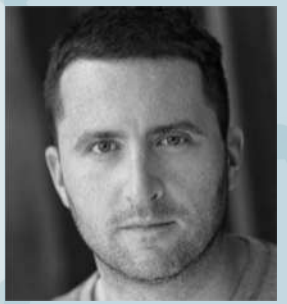
Global Genes, in partnership with the Orphan Disease Center at the University of Pennsylvania School of Medicine, hosts the annual **RARE** Drug Development Symposium designed to connect, educate and inspire rare advocates. The Symposium focuses on the drug development process and the role of rare disease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

Data Used for Better Clinical Outcomes and Creating Standards of Care

MODERATOR

Liz Horn, PhD, MBI
Principal
LHC Biosolutions

Our Speakers



Luke Rosen
Founder
KIF1A.Org

Scott Demarest, MD
Assistant Professor
Dept. of Pediatrics and Neurology CU School of Medicine & Children's Hospital Colorado

Ethan Perlstein, PhD
CEO
Perlara PBC

Steven Roberds, PhD
CSO
Tuberous Sclerosis Alliance

Luke Rosen
Founder
KIF1A.Org

Standard of Care Challenges

- Heterogeneous condition
- Symptomatic treatment strategy
- Treatment resistant

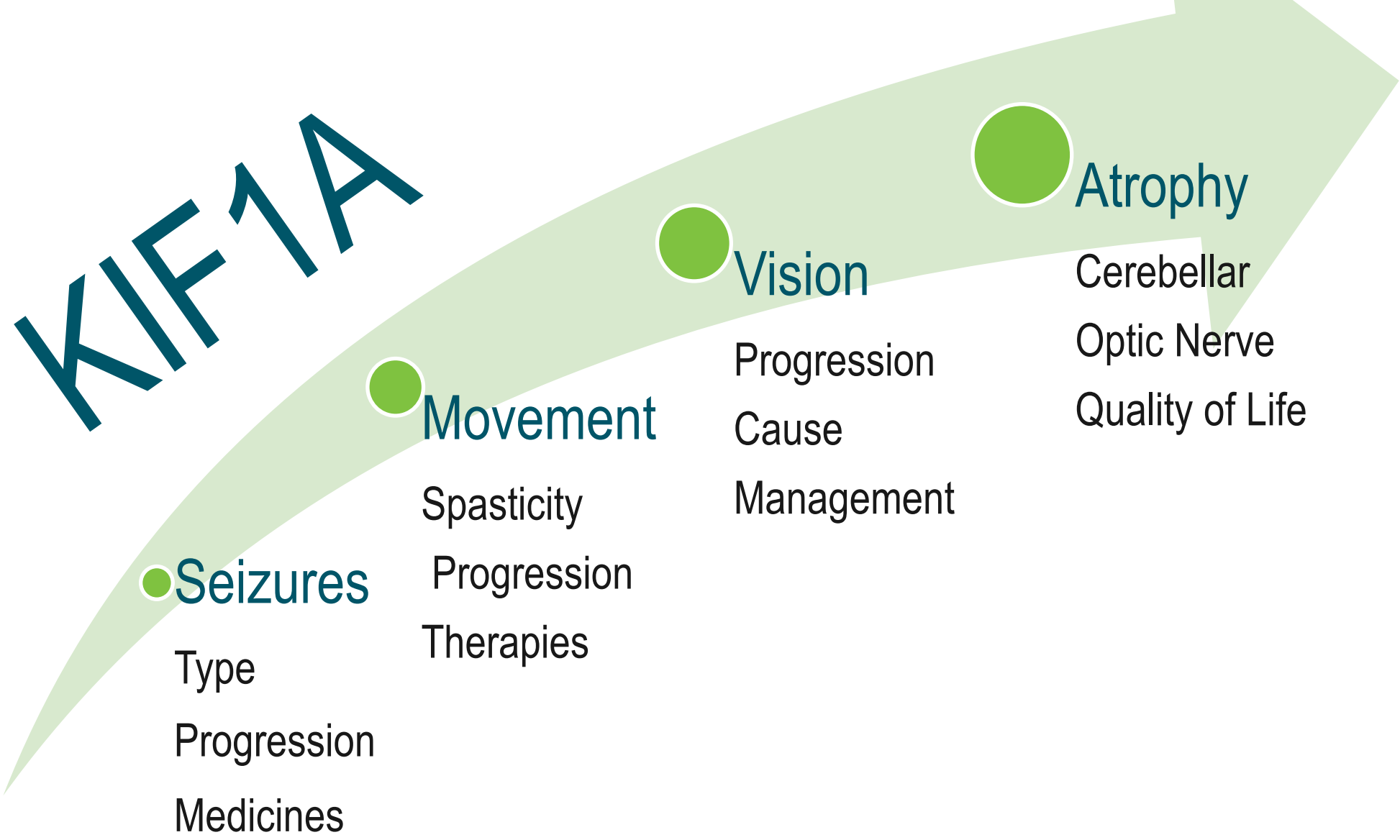
“Care until Cure.” WKC

What is Meaningful Change

Small change, big impact

- Quality of life
- Staying present

Outcome measures & successful trial design


KIF1A
Seizures
Type
Progression
Medicines
Movement
Spasticity
Progression
Therapies
Vision
Progression
Cause
Management
Atrophy
Cerebellar
Optic Nerve
Quality of Life

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-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

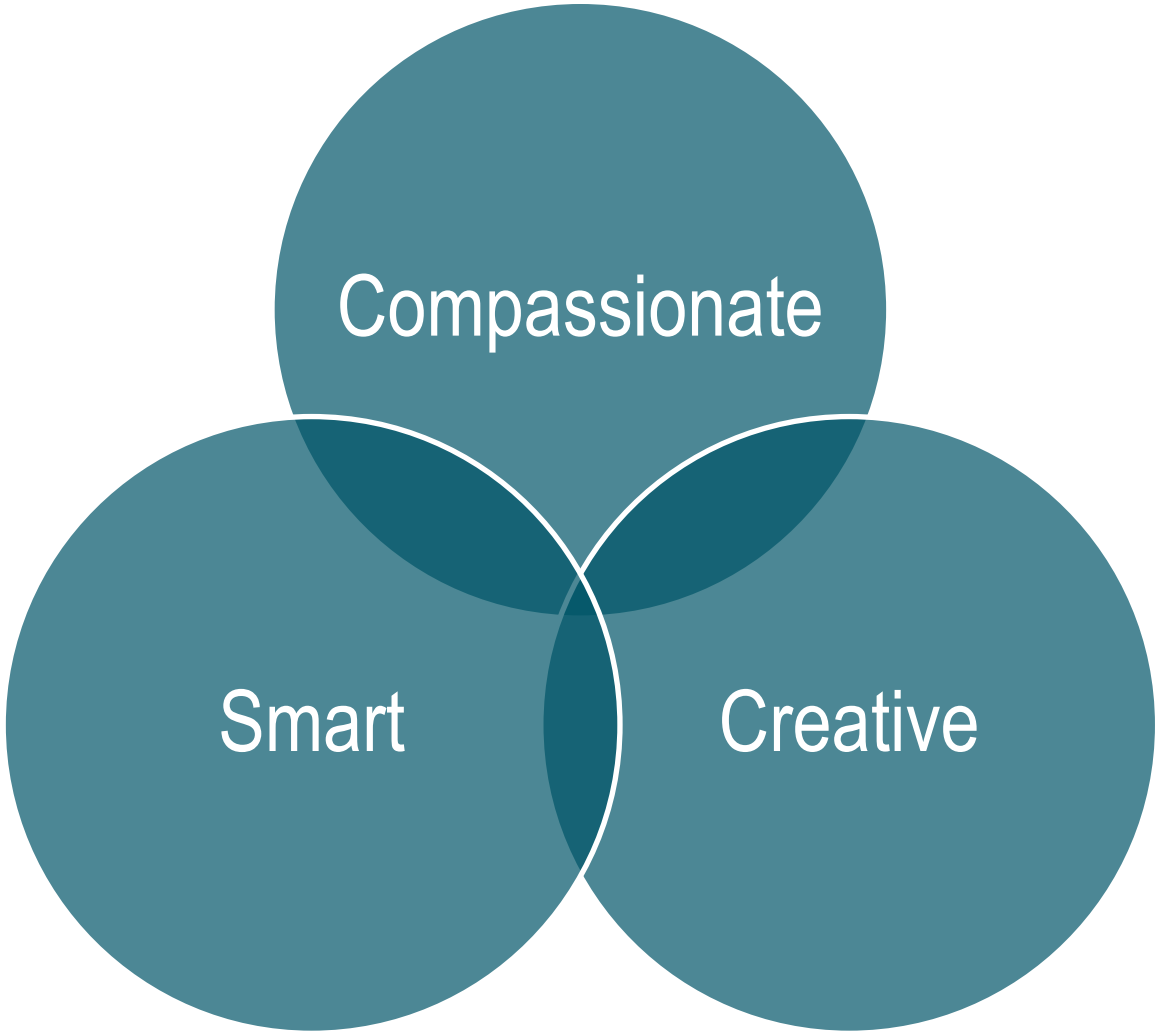
- Doctors are just people – no better, no worse.
- Find the doctors that are interested, curious, invested and support them
- Guidelines are the ideal but Centers of Excellence are a starting point

Doctors are just people and there is a lot of NOISE!

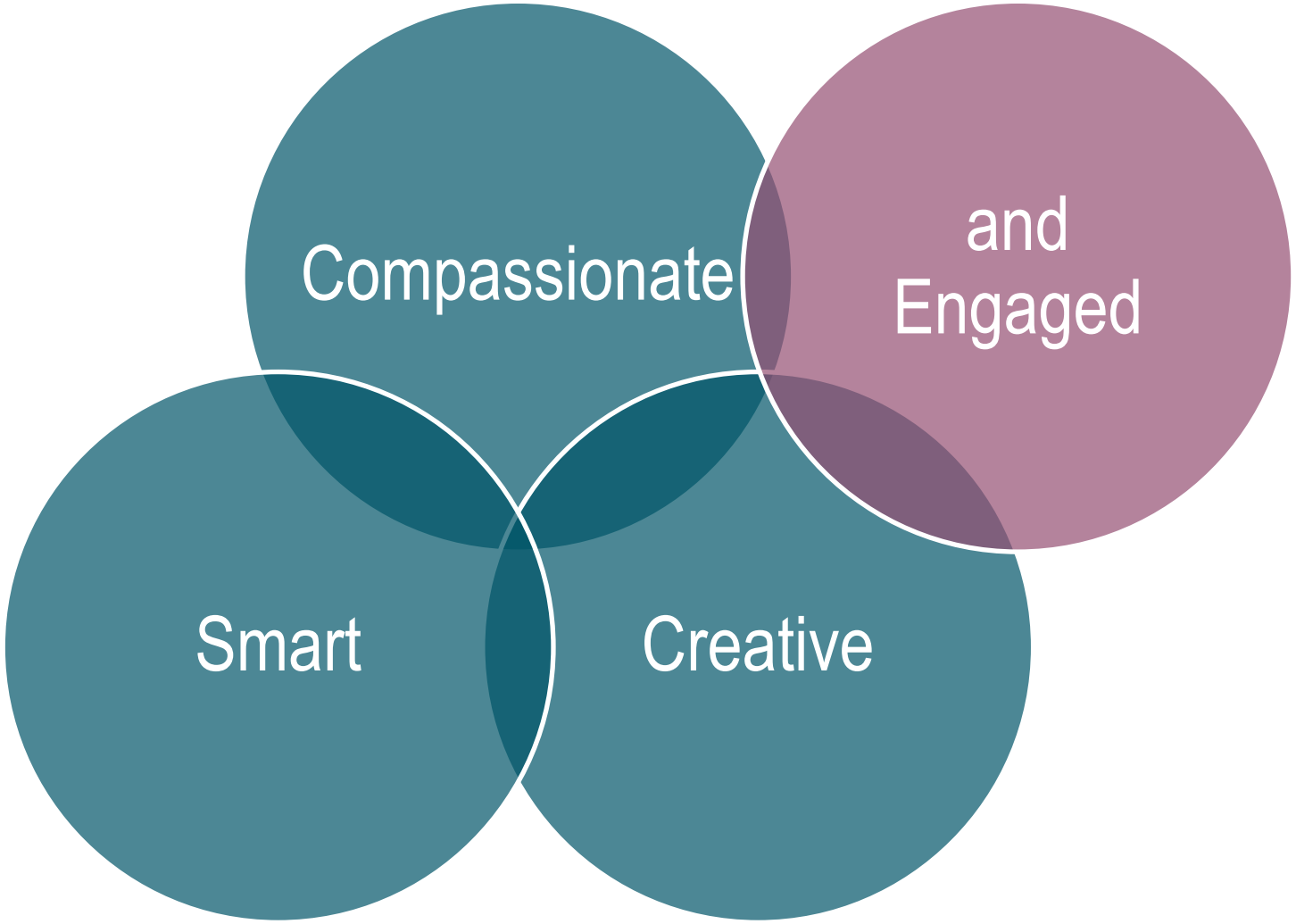
These are not excuses for poor treatment by your doctor, but the truth is that doctors are jugglers:

- 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:



What do you want in your doctor? They have to be:




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

Congenital Disorder of Glycosylation Ia: *PMM2* Gene Sequencing

Results: Two pathogenic variants detected. One copy of a c.415G>A (p.E139K) pathogenic variant and one copy of a c.422G>A (p.R141H) pathogenic variant were detected in the *PMM2* gene of this individual.

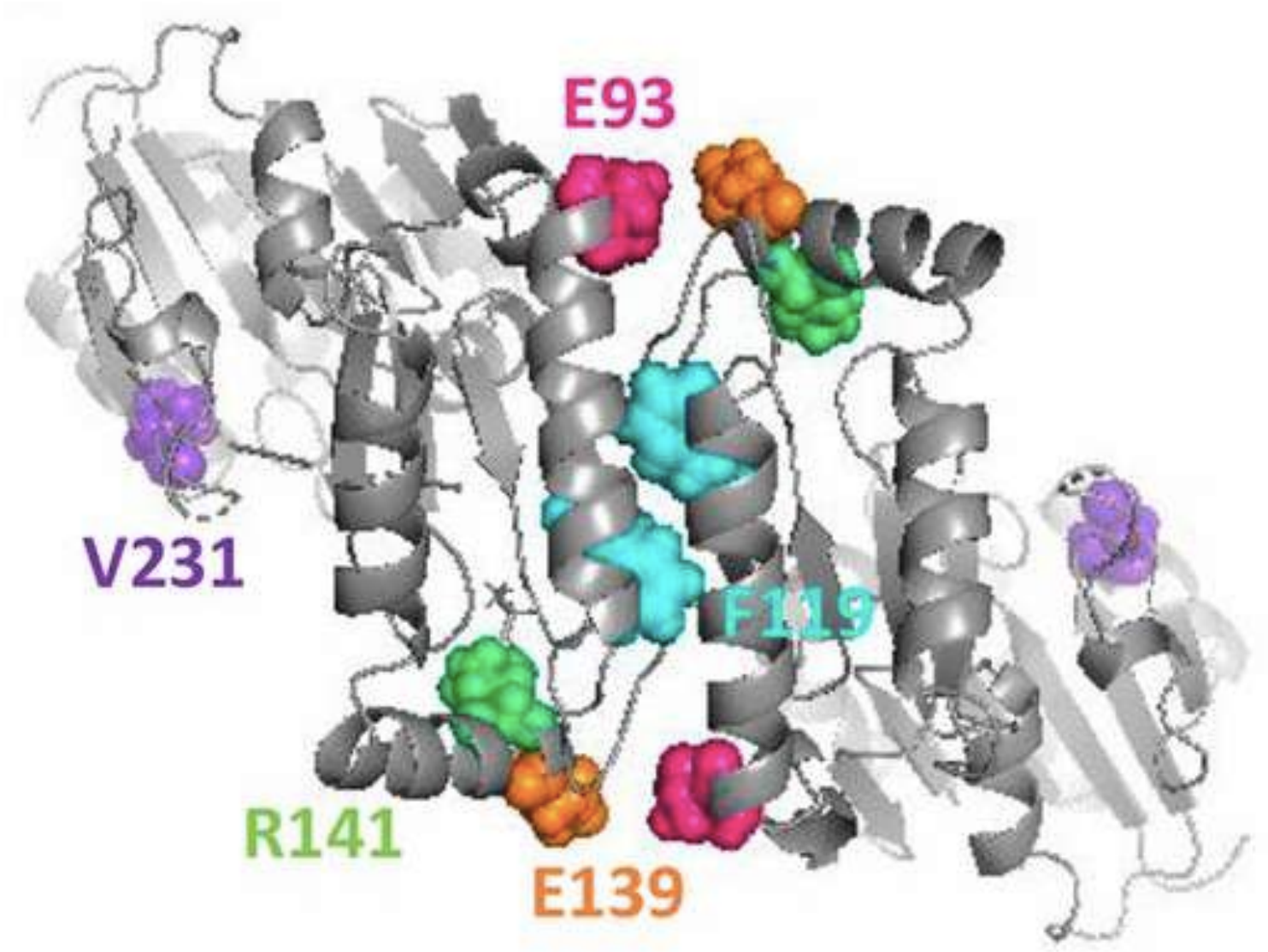
Interpretation

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.

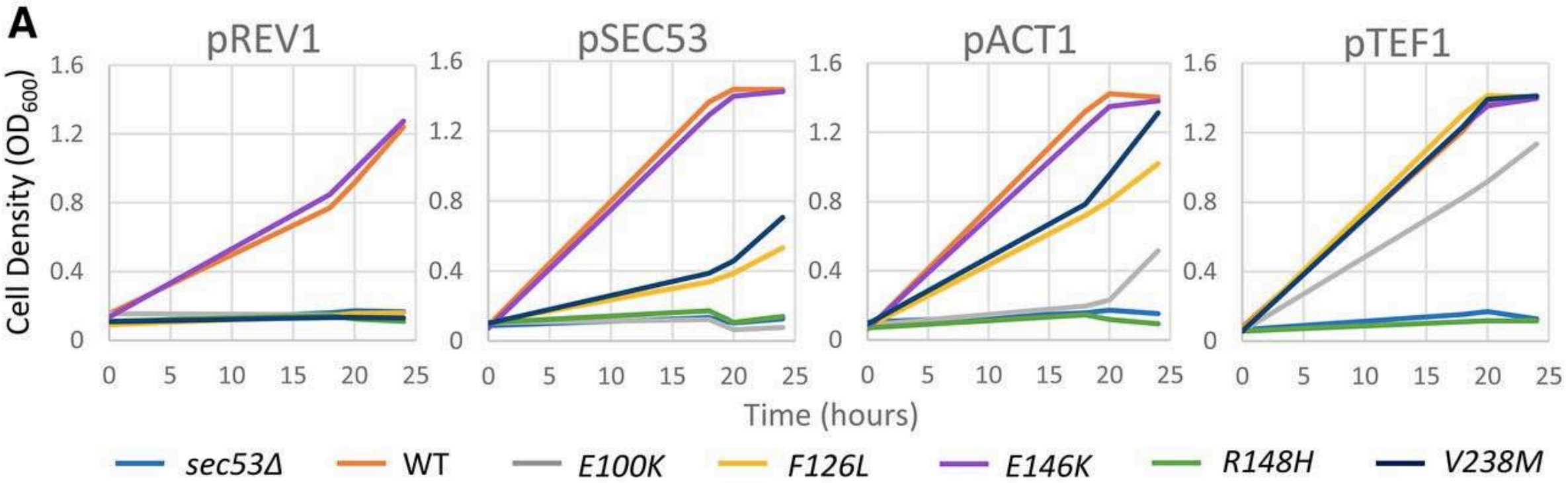
Sequence analysis detected the following:

Gene	Exon/Intron	Nucleotide change	Amino acid change	Zygosity	Type
PMM2	Ex5	c.415G>A	p.E139K	Heterozygous	Pathogenic
PMM2	Ex5	c.422G>A	p.R141H	Heterozygous	Pathogenic

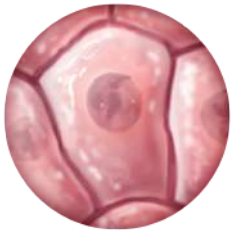
Turning data into discovery

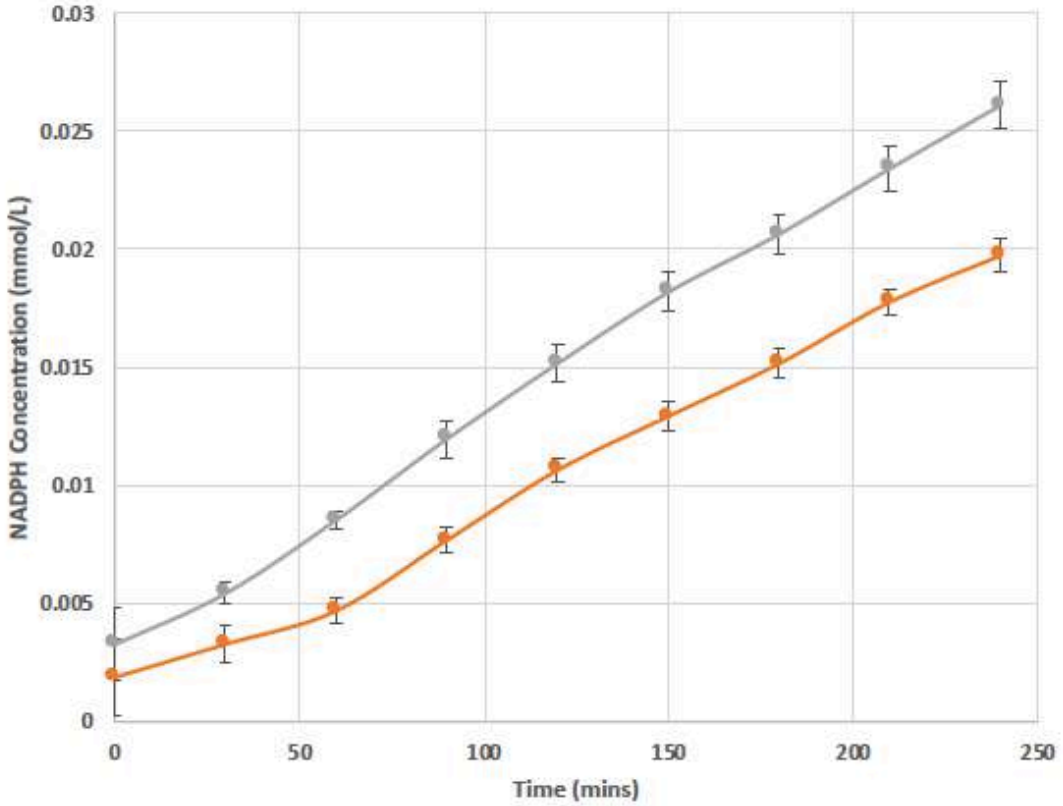


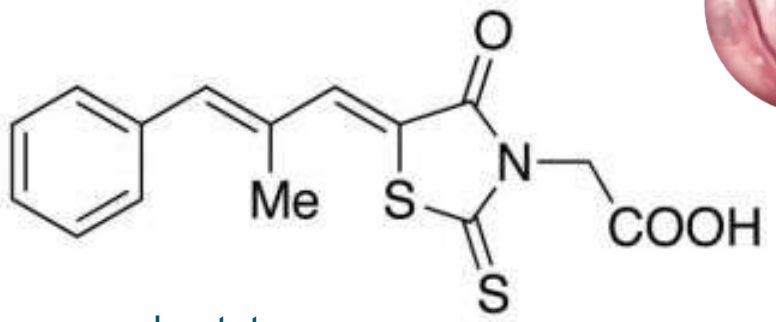
Turning data into discovery



Turning discovery into n-of-1 trial



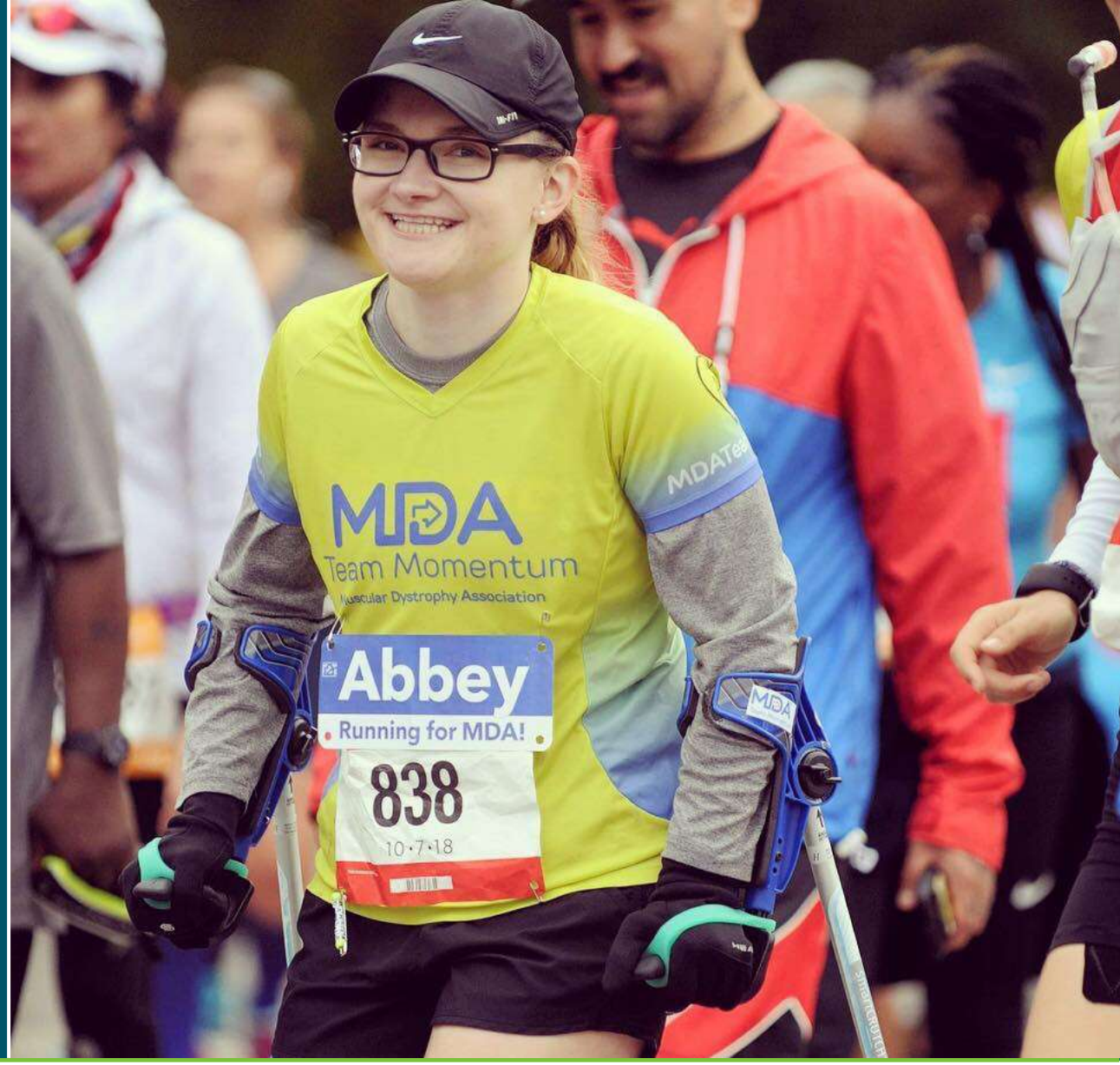




epalrestat

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

TSC NATURAL HISTORY
database

Data Sources for Clinical Data

TSC NATURAL HISTORY database

Participating Institutions

Map Key:

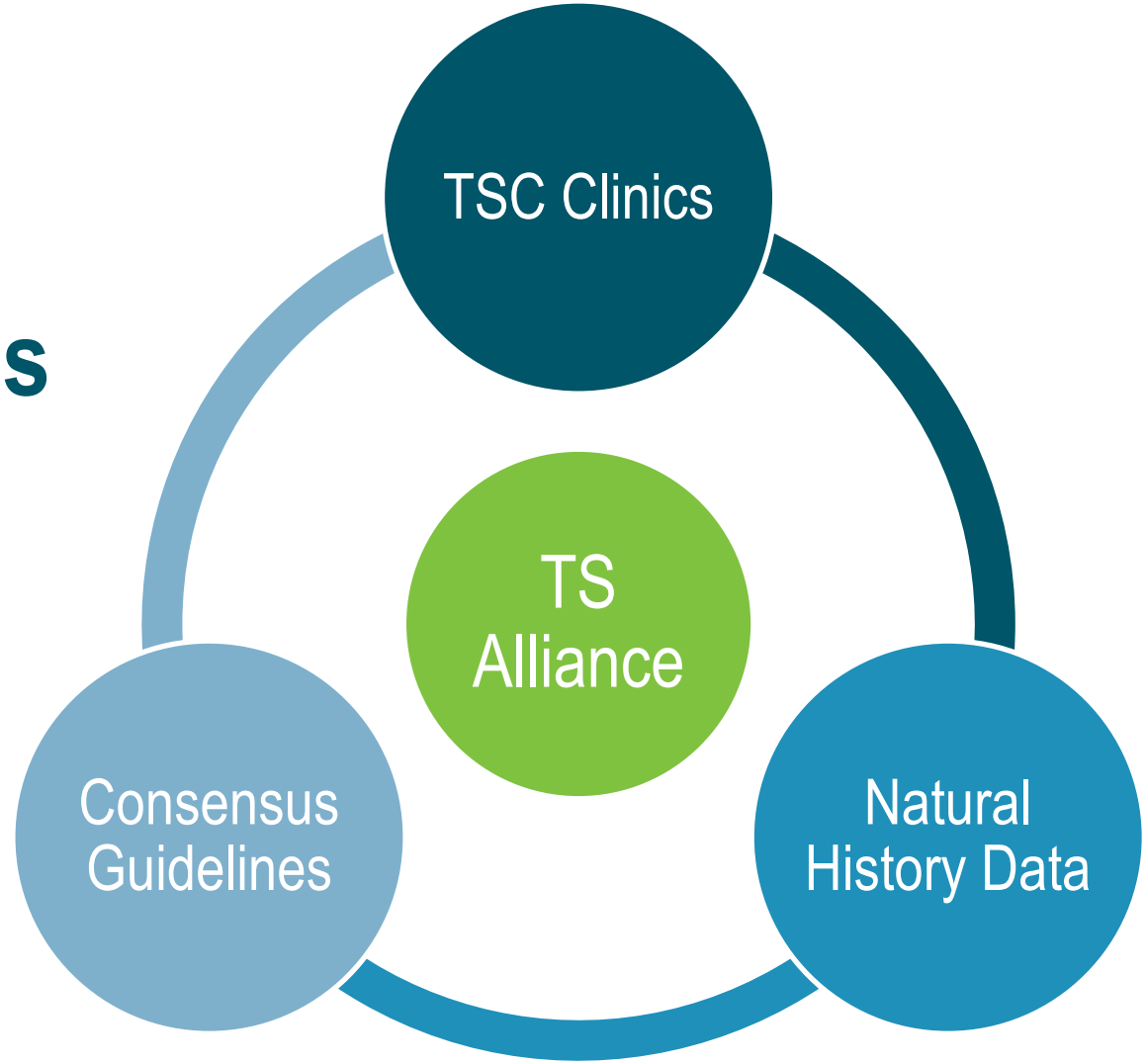
1. Minnesota Epilepsy Group, PA, St. Paul, MN (Michael D. Frost, MD)
2. Texas Scottish Rite Hospital for Children, Dallas, TX (Steven P Sparagana, MD)
3. New York University Langone Medical Center, New York, NY (Josiane LaJoie, MD)
4. Massachusetts General Hospital, Boston, MA (Elizabeth A. Thiele, MD, 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

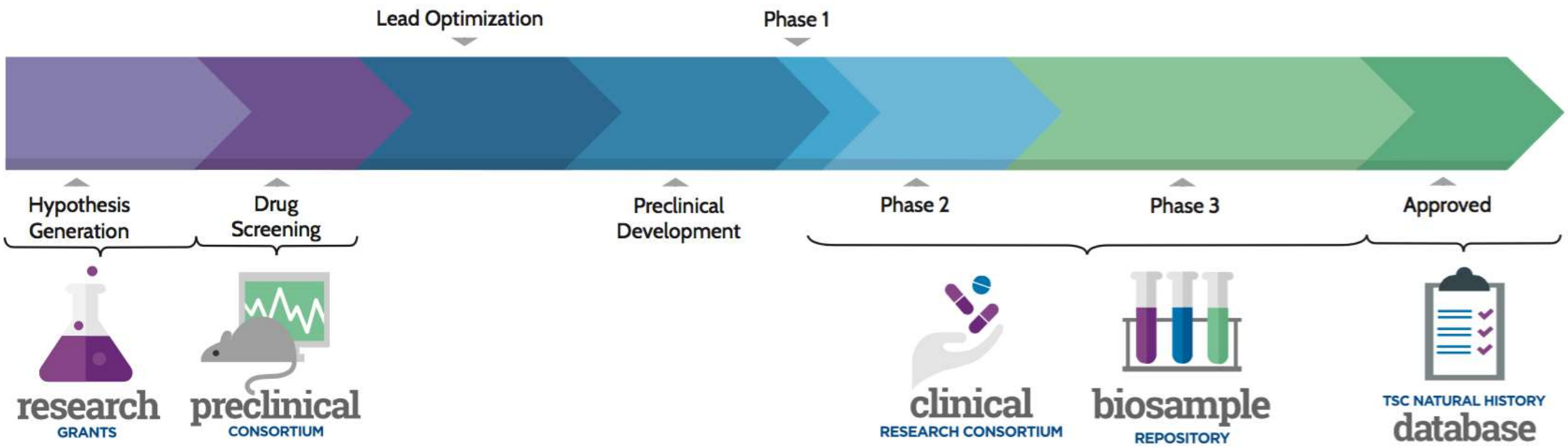
Informing Clinical Consensus Guidelines

- Diagnosis
- Surveillance
- Management



TSC NATURAL HISTORY database

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

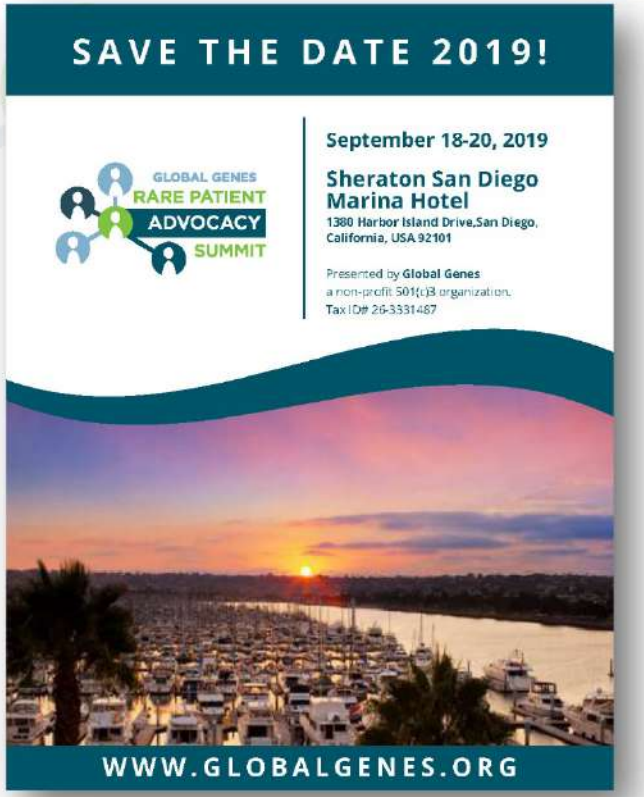
To participate, please visit https://DataDIY.cnf.io with your browser

Lunch
Data DIY

Global Genes™
Allies in Rare Disease

#DataDIY | GlobalGenes.org

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.

Welcome Back

MODERATOR

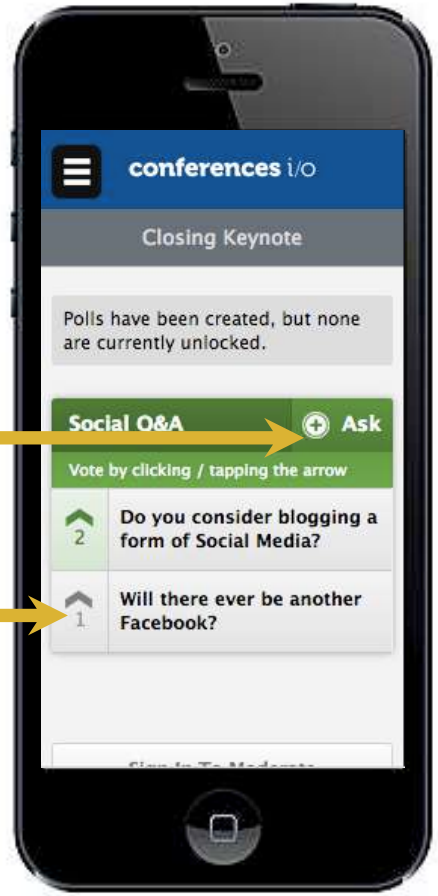
Christian Rubio
VP, Community Development and Engagement
Global Genes

Global Genes Question Wall

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

Ask a Question

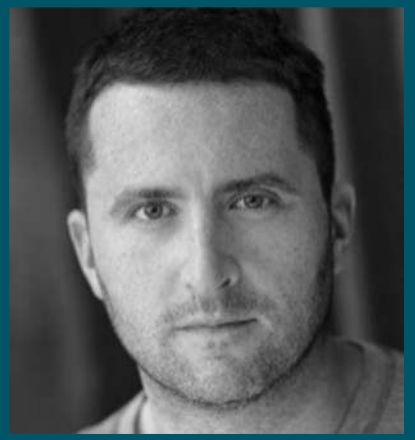
Up-Vote a Question



Note: Responses and submissions are anonymous

Data Collection Without a Roadmap – How Has it Evolved?

MODERATOR



Luke Rosen
Founder
KIF1A.Org

Our Speakers

Liz Horn, PhD, MBI

Principal

LHC Biosolutions

Megan O'Boyle

Principal Investigator International Registry & Data Network

Phelan-McDermid Syndrome Foundation

Kari Rosbeck,

CEO

Tuberous Sclerosis Alliance

Steven Roberds, PhD

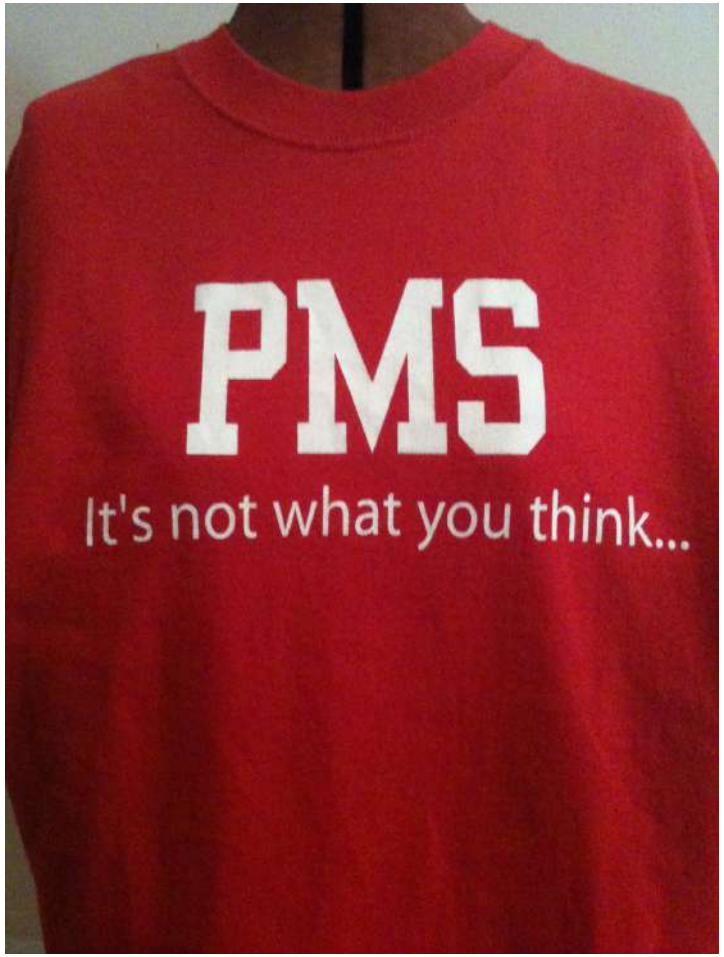
CSO

Tuberous Sclerosis Alliance

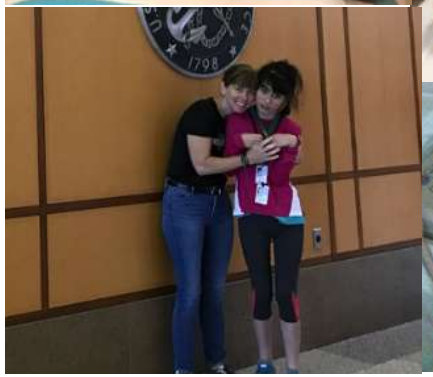
Liz Horn, PhD, MBI
Principal
LHC Biosolutions

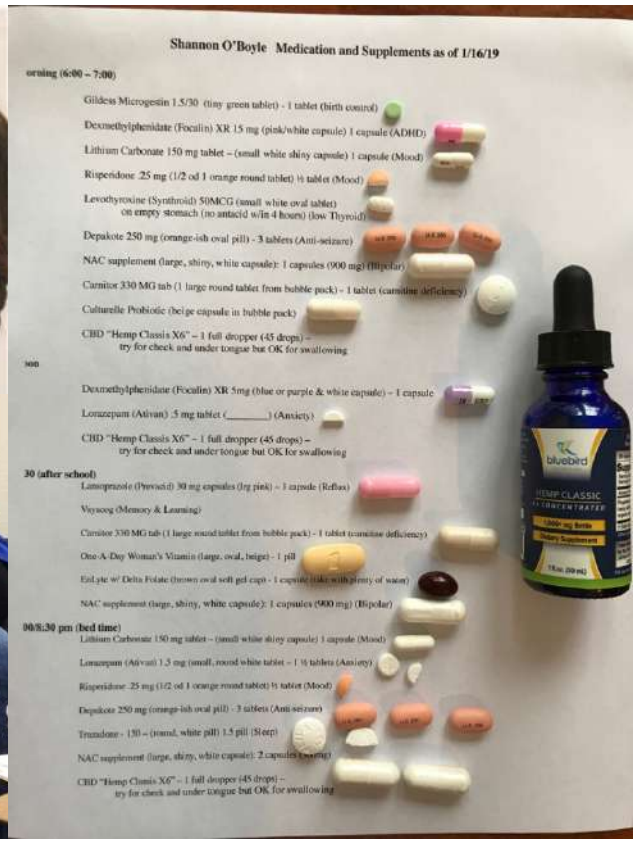
Megan O'Boyle
Principal Investigator International Registry & Data Network
Phelan-McDermid Syndrome Foundation

https://www.pmsf.org/registry/


PMS
It's not what you think...

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
Cusmano-Ozog et al, 2007
Bonaglia, 2006

Who Are We?

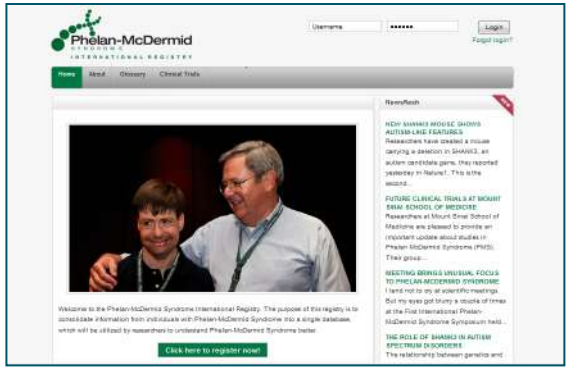
- We are a 16 year-old non-profit foundation with a 3 person office staff
- We do NOT have a Scientific Director
- We DO have a Scientific Advisory Committee
- We have 2,100 known diagnosed members in over 59 countries
- Over 1,300+ members in the International Registry
- 100 families with medical records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

Founder, Sue Lomas

Dr. Katy Phelan

Phelan-McDermid Syndrome International Registry

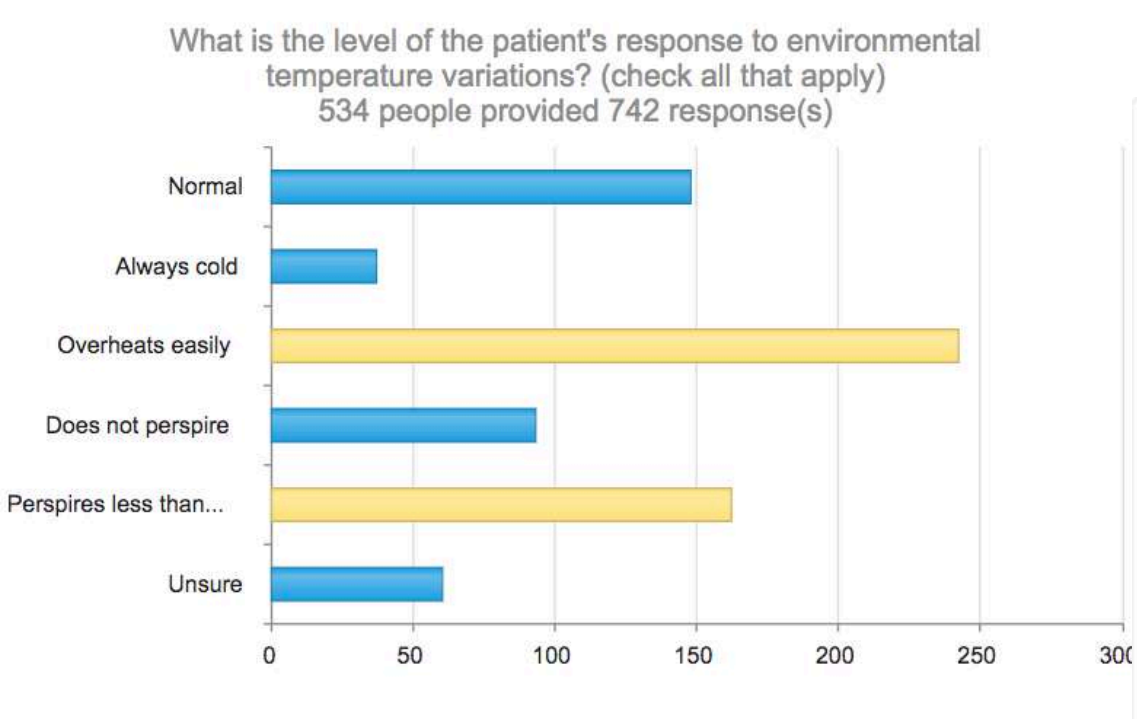
What is the PMSI Registry?

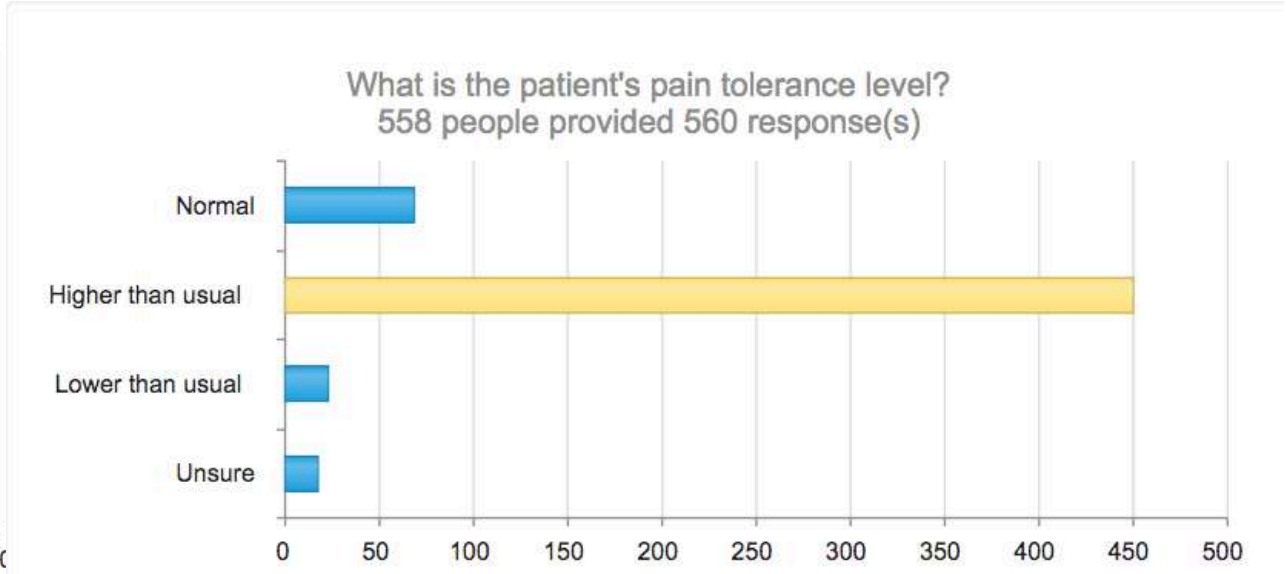


PMS International Registry…

- 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 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

Kari Rosbeck, CEO

Tuberous Sclerosis Alliance

Steven Roberds, PhD, CSO

Tuberous Sclerosis Alliance

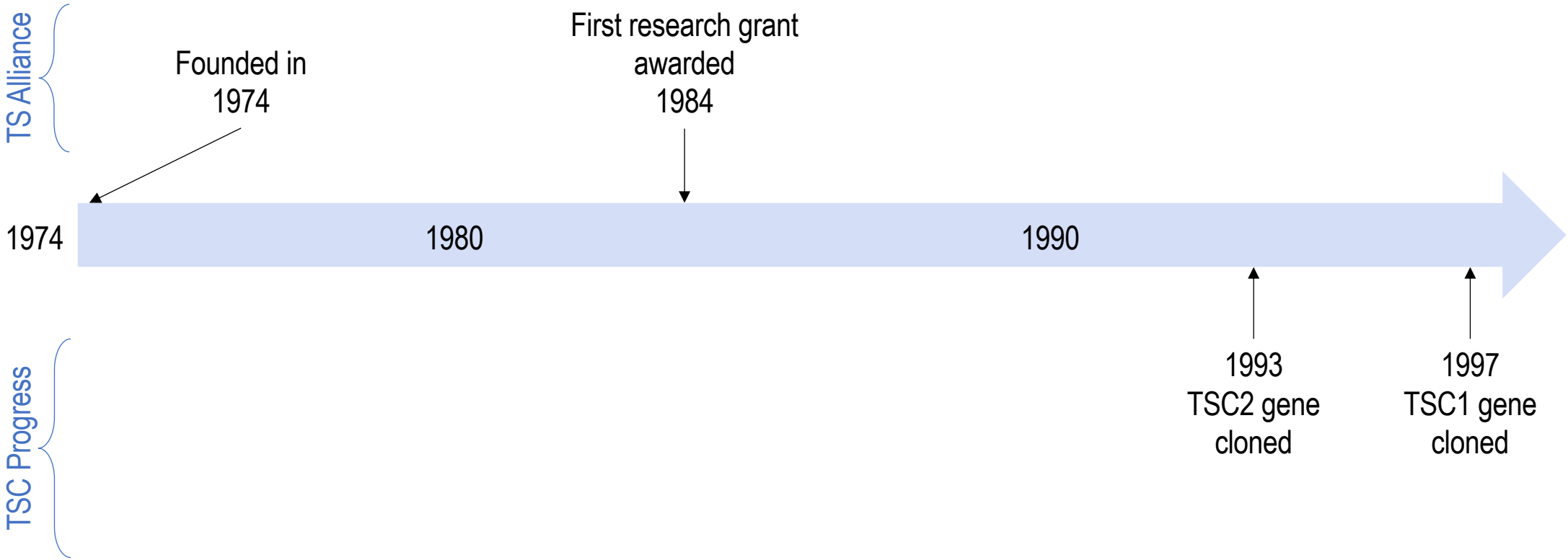
Tuberous Sclerosis Alliance

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

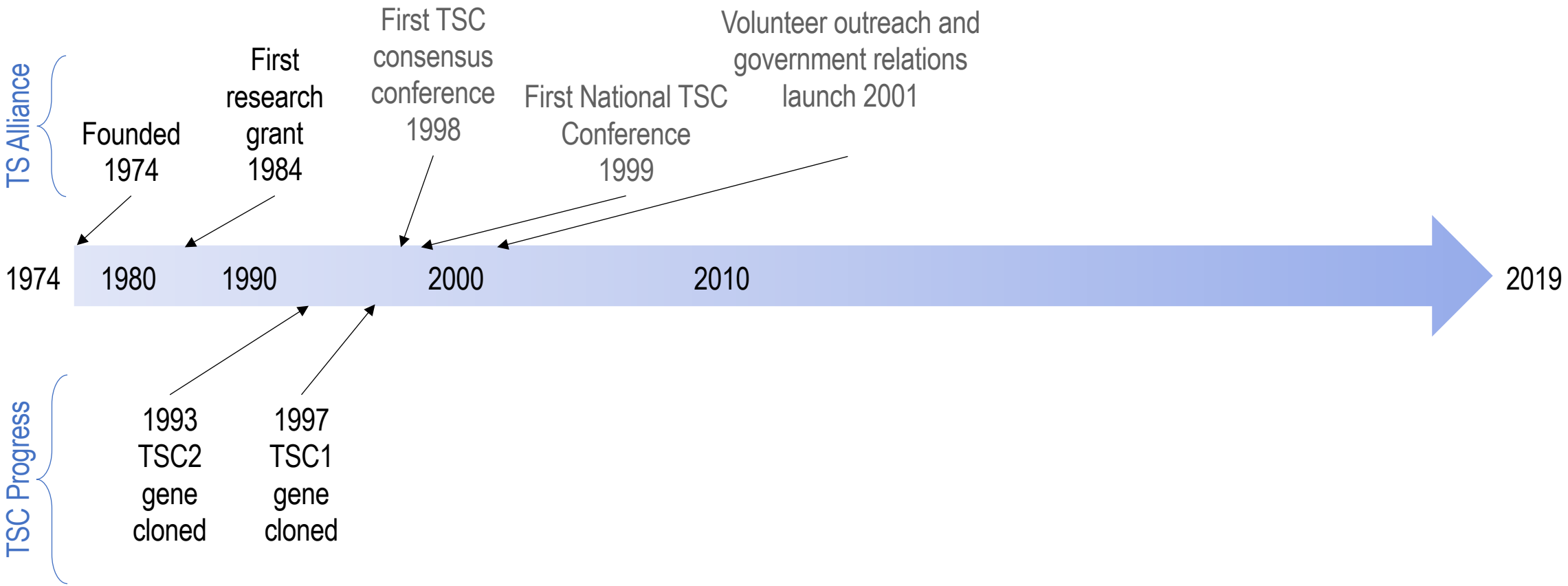
- Developing programs, support services and resource information
- Stimulating and sponsoring research
- Creating and implementing public and professional education programs designed to heighten awareness of the disease

www.tsalliance.org

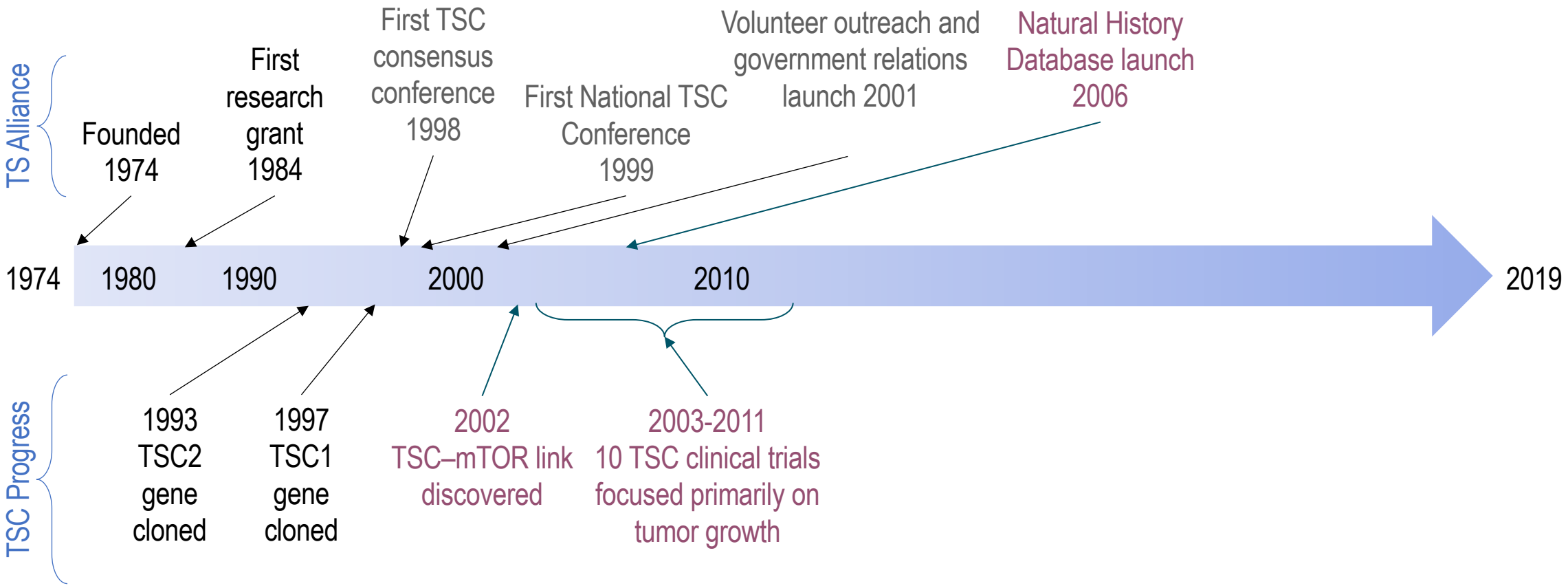
A Key Partner in TSC Advances: The First 23 years



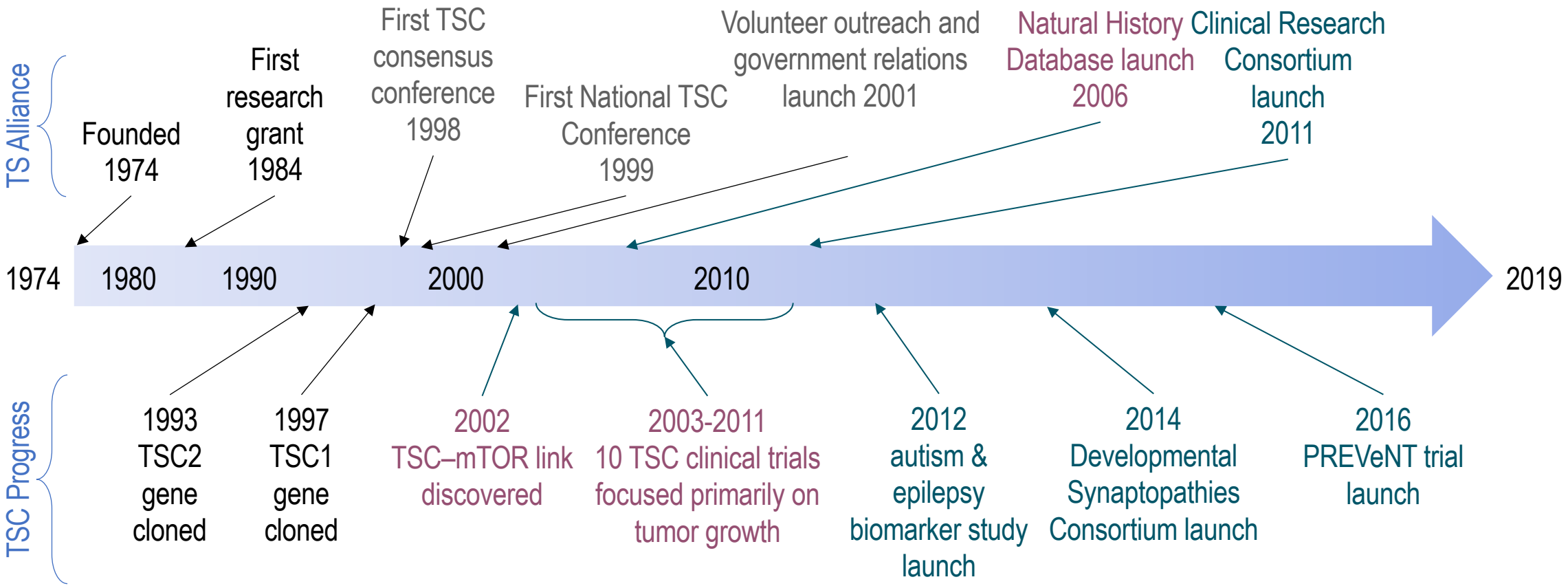
A Key Partner in TSC Advances: The Next 4 Years



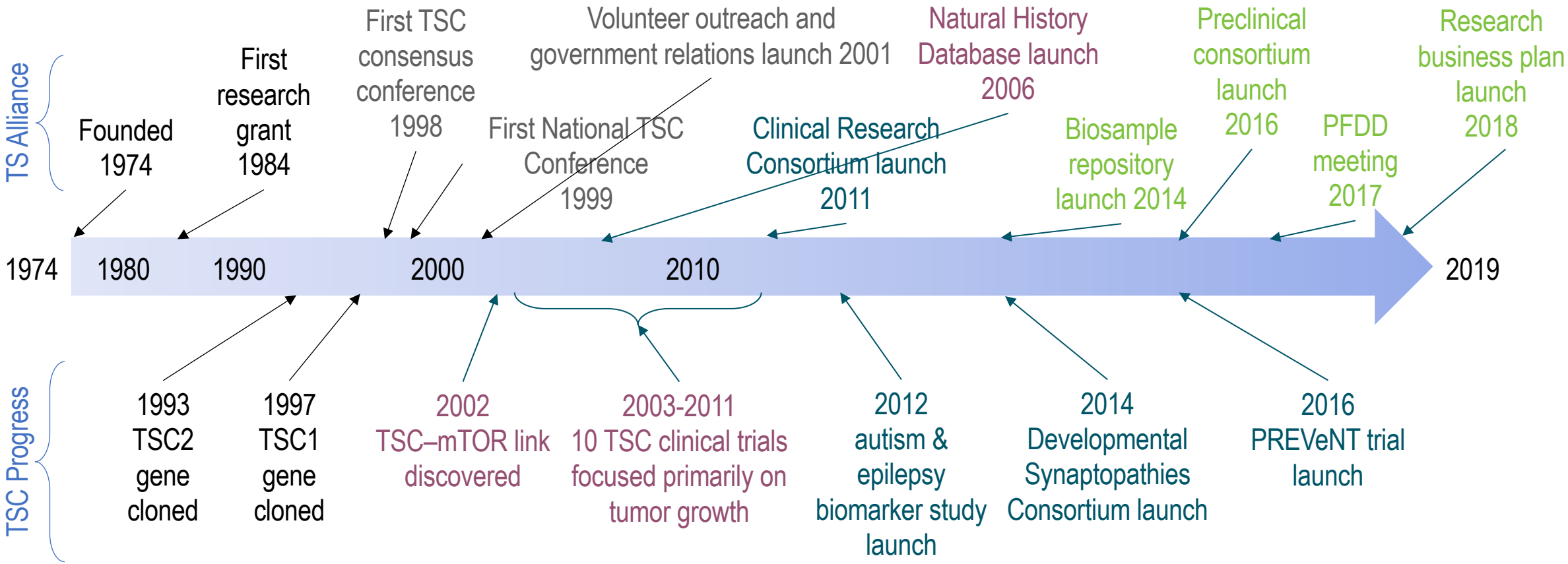
A Key Partner in TSC Advances: The Story Unfolds



A Key Partner in TSC Advances: The Story Unfolds



A Key Partner in TSC Advances: The Story Unfolds



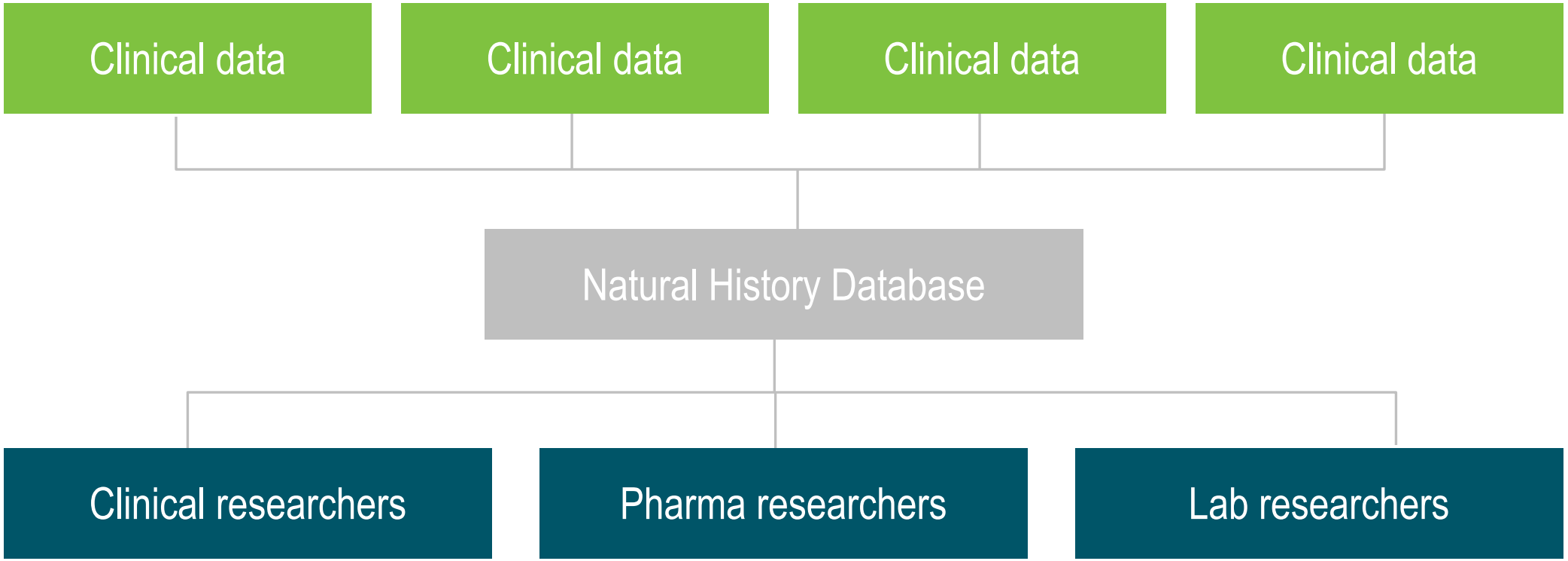
Strategic Decision to Use Clinic-Entered Data

TSC NATURAL HISTORY database

- 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

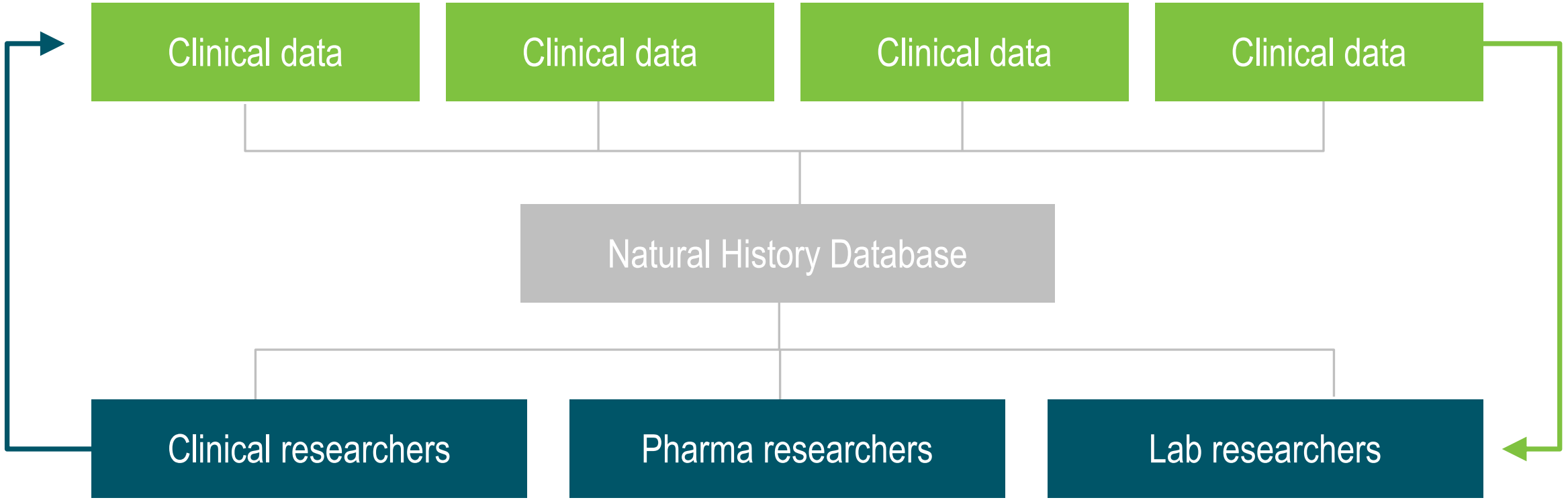
Basic Data Flow

TSC NATURAL HISTORY database



Addition of Questions and Data Refinement

TSC NATURAL HISTORY database

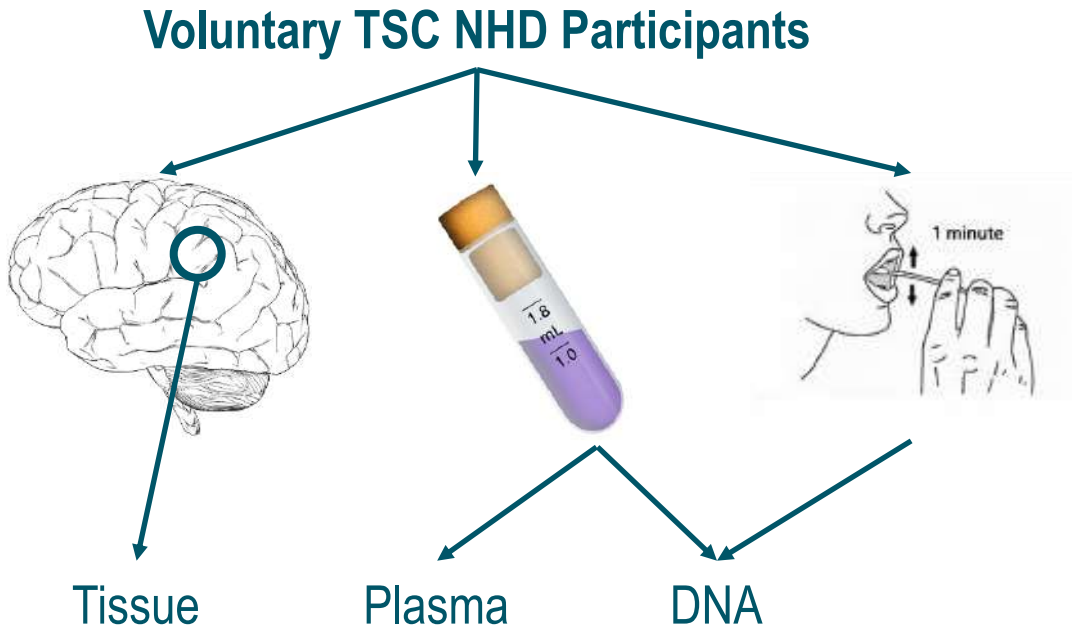


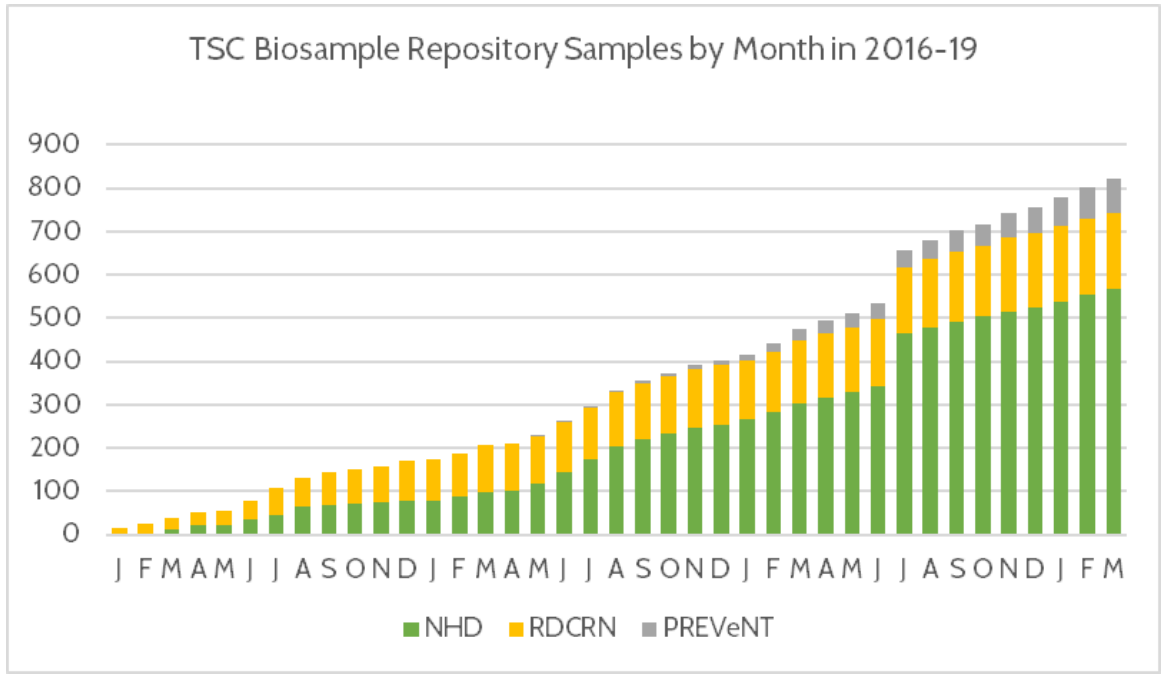
Continuous Improvement and Enhancement

- 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

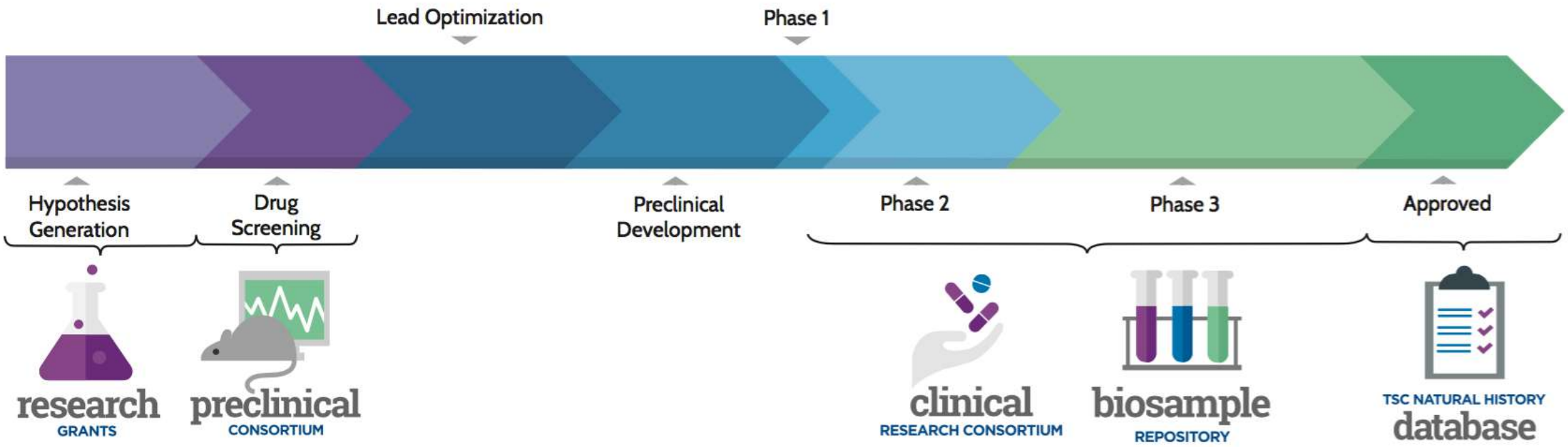
Biosamples Linked to Natural History Data

biosample REPOSITORY





Accelerating Research and Drug Discovery Through Collaborative Projects



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

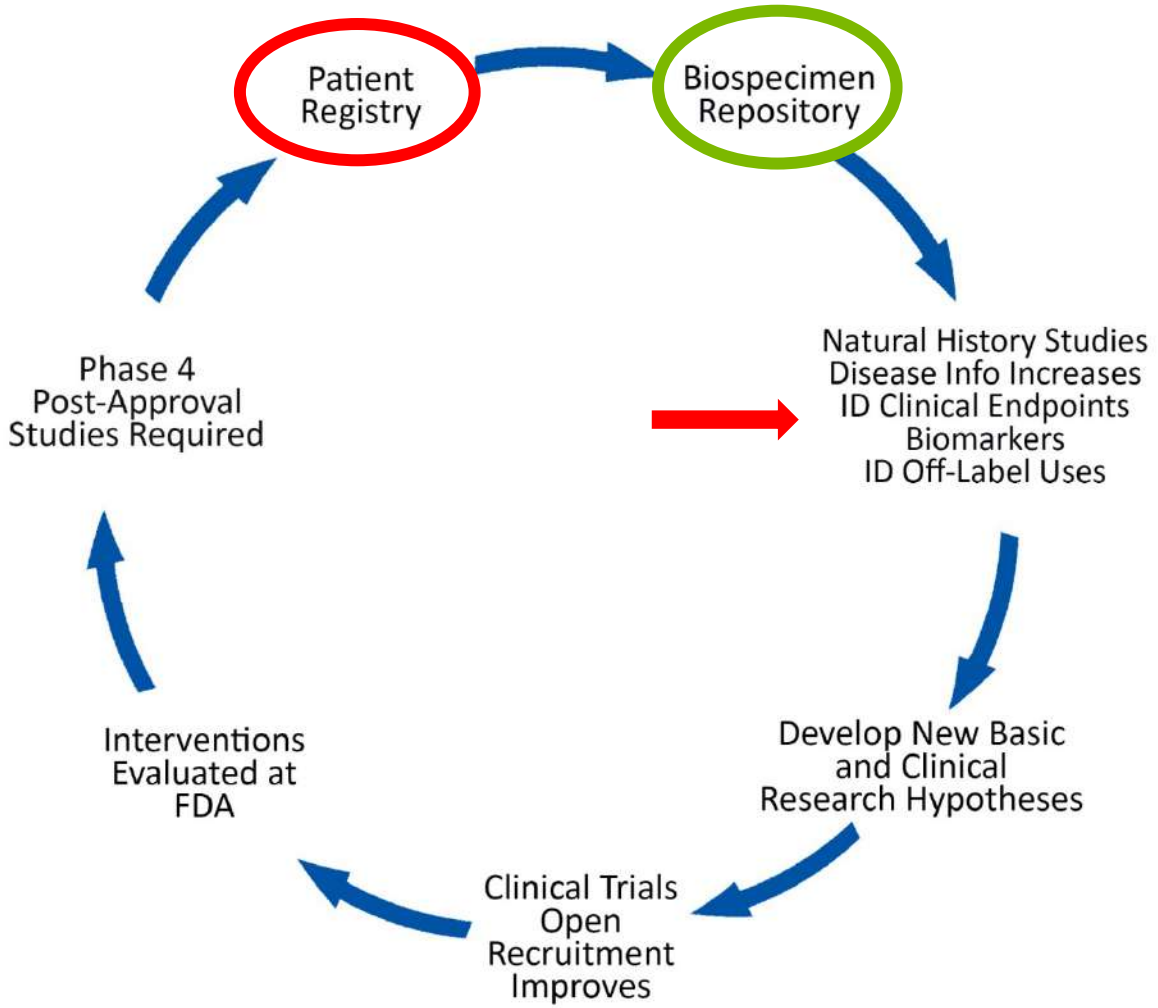
The Hows of Data Collection – What You Need to Know to Structure Your Plan

Liz Horn, PhD, MBI
Principal
LHC Biosolutions

L. Horn, Frogner Park, Norway

Research Engines Drive Progress

Patient registries and biorepositories are research game changers!



L. Johnson, Lymedisease.org

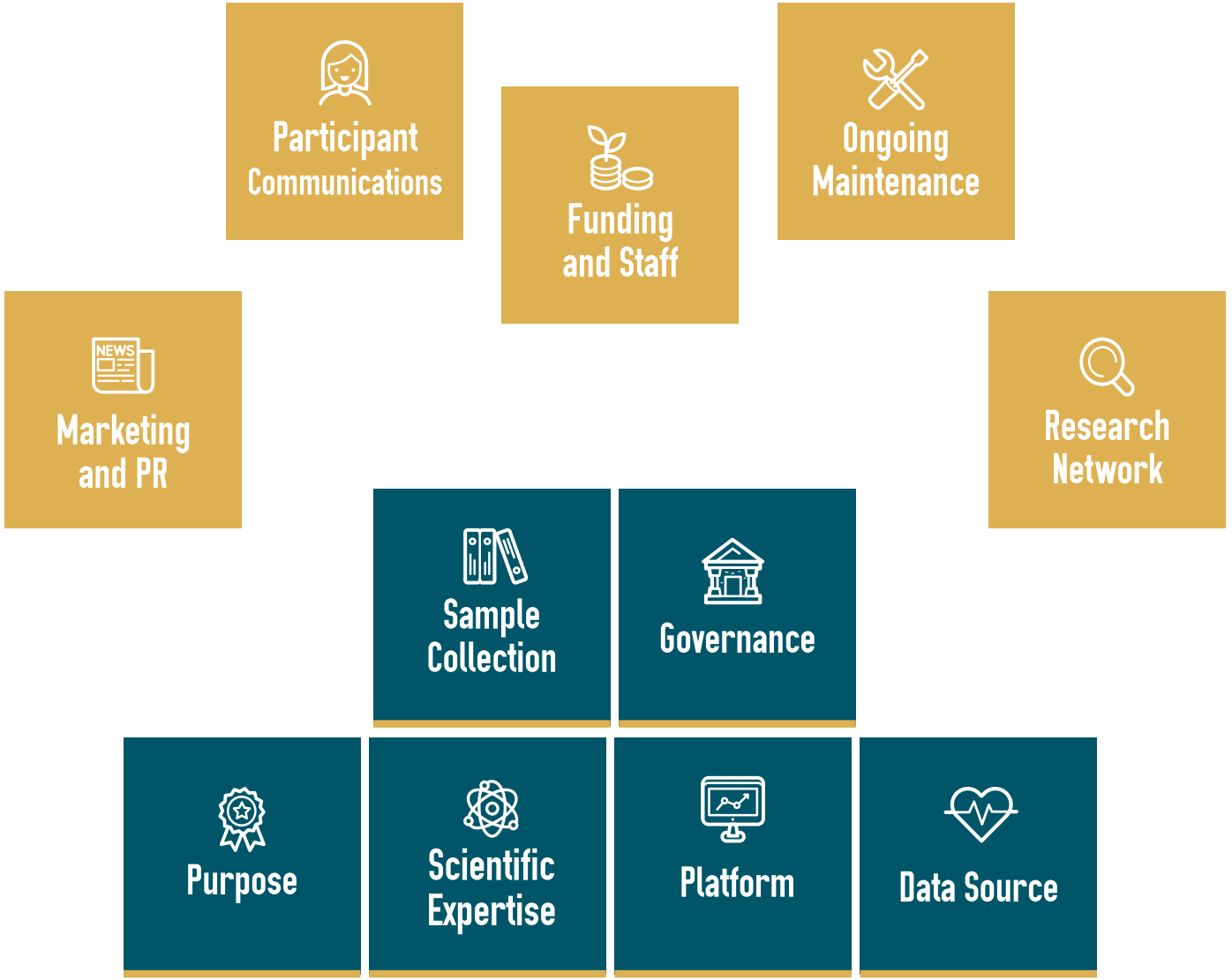
This a time of great opportunity!

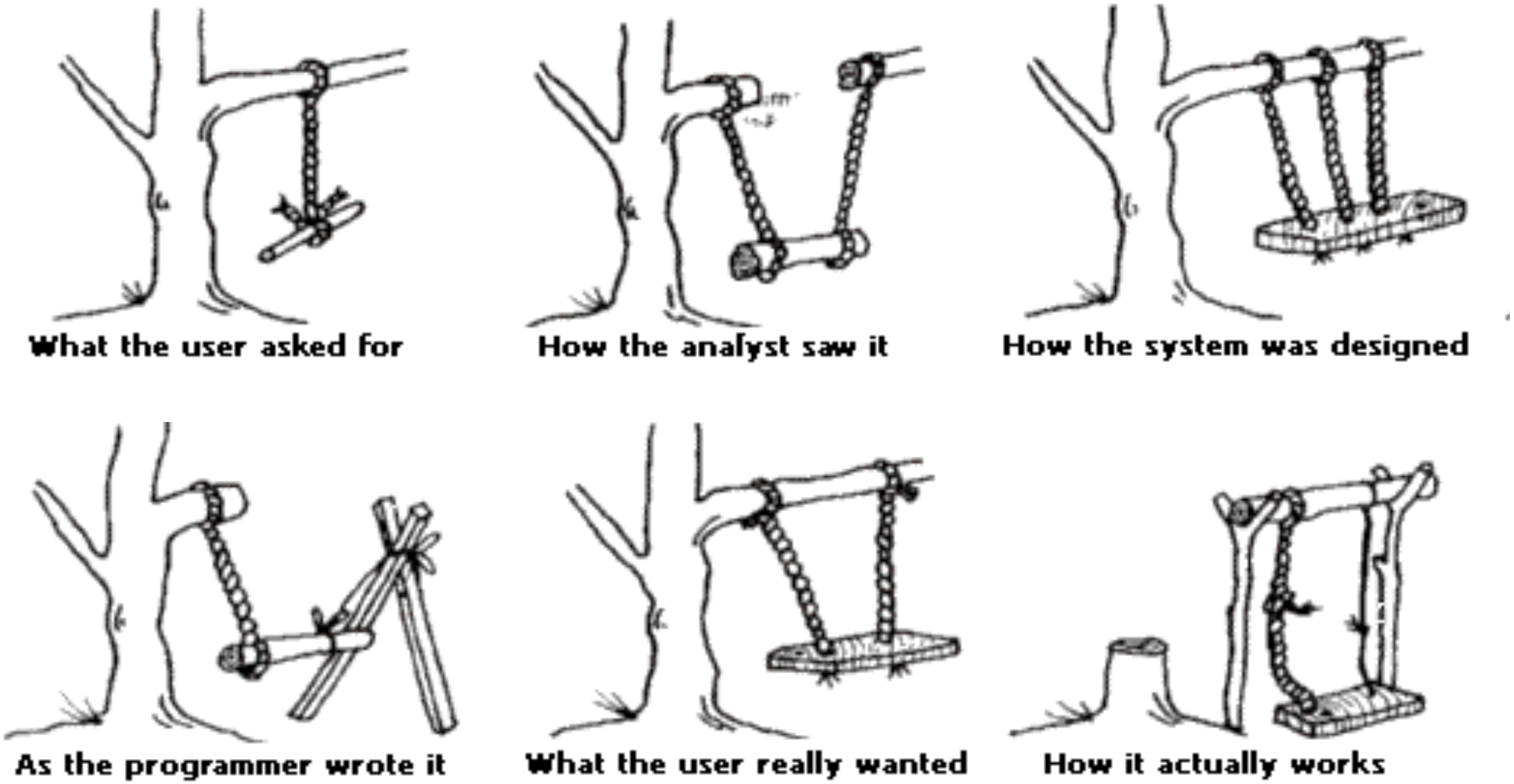
Collaboration is key!

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





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?

Will your data collection project focus on a specific condition?

- ☐ Yes
- ☐ No

If yes, please describe the condition:

_____

_____

Which of the following types of information are you interested in collecting?

Check all that apply.

- ☐ Medical information
- ☐ Demographics (age, sex, etc)
- ☐ Lifestyle information (diet, exercise, etc)
- ☐ Family history
- ☐ Genetic information
- ☐ Diagnosis information
- ☐ Treatment information
- ☐ Quality of life information
- ☐ Other (*describe*) _____

How many participants do you hope to enroll? _____

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

Example from Eye Study

What is your current Marital Status

1. Never married
2. Divorced/separated
3. Widowed
4. Married

Example from WHI

F20 Current marital status

What is your current marital status?

(Mark the one that best describes you)

- Never Married
- Divorced or Separated
- Presently Married
- Widowed
- Marriage-like Relationship

http://rarediseases.info.nih.gov/files/McDonald.pdf

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

Collection

- Sample type
- Donor profile
- Collection timing
- Collection logistics
  - Where
  - When
  - Who
  - How often
- Similar collections?

Processing/Storage

- Location
- Derivatives
- Downstream experiments
- SOPs for extraction
- SOPs for storage

Access

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

Collection Considerations

Blood	Tissue
• DNA, RNA, Protein • PBMCs • Cell lines • Serum, Plasma	• 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

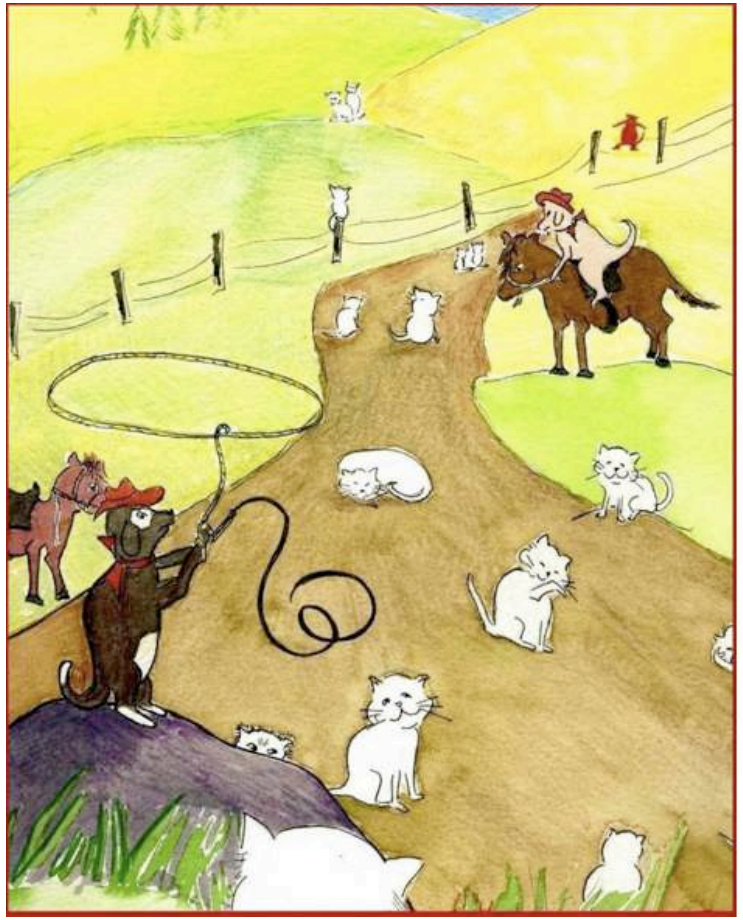
- What tasks do you need assistance with?
- What expertise do you need?
- Who are your current advisors?
  - What is their expertise?
  - What roles do they have in your organization?
  - What other relevant roles do they have?
- What knowledge gaps remain?
  - Medical, scientific, other
- Don’t overlook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

MODERATOR

Christian Rubio
VP, Community Development and Engagement
Global Genes

Data DIY

Your Involvement in Driving Understanding, Discovery, Diagnosis and Treatments for Rare Disease

#DataDIY

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

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

Break
Data DIY

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Allies in Rare Disease

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Workshop

Making Meaning of Your Community's Data Needs

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