Role of the Advocacy Organization in Rare Disease Research

International Rare Disease Research Consortium
07 November 2014

Sharon F. Terry
President & CEO, Genetic Alliance
Founding CEO, PXE International
President, EspeRare
Principal Investigator, CENA
Elizabeth and Ian diagnosed with pseudoxanthoma elasticum (PXE) 1994

2014

Elizabeth: Teach for America
Ian: Organic Farmer
BioBank

Testing
Clinical Diagnostic Test Development via FDA & CLIA
Regulatory Strategies

Patenting
License & Intellectual Property Management

Gene Discovery

Human Clinical Trials

Drug Screening & Development Approaches

Therapeutics
-- Small Molecules
-- Nonsense mutants

BioBank

Seeing The Light
How The Terry Family's Fight Against Blindness May Change The Course Of Medical Research And IP Law

PXE international

Mutations in a gene encoding an ABC transporter cause pseudoxanthoma elasticum

Mutations in ABCC6 cause pseudo-xanthoma elasticum
Traversing the ‘diagnosed line’, individuals and families journey to seek answers.
Maturing Patient Advocacy

• 1950s-1960s – Medical Models
  ‣ Voluntary Health Agencies

• 1970s – Nascent Patient Movement – Missing Services
  ‣ Self-organized Disease Specific Organizations

• 1980s – Maturing Patient Movement – IS & IT Technology
  ‣ New Alliances and New Strategies Emerge

• 1990s – Powerful Momentum “Patient Power” – Websites & Email
  ‣ Institutionalized Advocacy Coalitions
  ‣ Patient Organized Networked Research Organizations
  ‣ Effecting Broad Change of Public Policy

• 2000s – Successful Models “Research Advocacy” – BioBanks
  ‣ Active Engagement in the Research Enterprise
  ‣ Breaking Conventional Boundaries of the Medical Model
  ‣ Demand for Quality, Services, Choice, & Personalized Delivery
  ‣ Patient Rights Public Policy – Changing the Status-Quo

• 2010s – Networks in the Commons – Translation & Delivery
# Culture Shift in Information Age

<table>
<thead>
<tr>
<th>Industrial Age (old)</th>
<th>Information Age (new)</th>
</tr>
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<tbody>
<tr>
<td><strong>Control</strong> means of production</td>
<td><strong>Open</strong> means of production</td>
</tr>
<tr>
<td>Based on <strong>scarcity</strong></td>
<td>Based on <strong>abundance</strong></td>
</tr>
<tr>
<td><strong>Hierarchical</strong> / Command &amp; Control</td>
<td><strong>Network</strong> / Collaboration</td>
</tr>
<tr>
<td><strong>Linear</strong> / Sequential</td>
<td><strong>Organic</strong></td>
</tr>
<tr>
<td>Win / Lose</td>
<td>Win / Win</td>
</tr>
<tr>
<td>Materials</td>
<td>Information</td>
</tr>
</tbody>
</table>
Needles in Haystacks
But for the advocacy organization, the haystack is made of needles.
Cystic Fibrosis

Cystic fibrosis (CF) is an inherited condition that causes mucus to build up and clog some of the organs in the body, particularly in the lungs and pancreas. When mucus clogs the lungs, it can make breathing very difficult. The thick mucus also causes bacteria to get stuck in the airways, which causes inflammation and infections. These infections can cause chronic coughing, and repeated infections can lead to permanent lung damage (fibrosis) and cysts in the lungs. Mucus accumulation in the pancreas, leading to digestive problems, and is inherited in an autosomal recessive pattern.

Source: Genetic and Rare Diseases Information Center, NHGRI.
Advocacy and Support Organizations

Condition Specific Organizations
Following organizations serve the condition "Cystic Fibrosis" for support, advocacy or research.

**Boomer Esiasion Foundation**
The Boomer Esiasion Foundation is a dynamic partnership of leaders in the medical and business communities joining with a committed core of volunteers to heighten awareness, education and quality of life for those affected by cystic fibrosis, while providing financial support to research aimed at finding a cure.

http://www.esiason.org

**Center for Jewish Genetics**
The Center is dedicated to gathering and disseminating knowledge about Jewish genetic disorders and hereditary cancers. Its mission is to educate and serve health care professionals, clergy and the Jewish community.

http://www.jewishgenetics.org

**Cystic Fibrosis Foundation**
Our mission is to assure the development of the means to cure and control Cystic Fibrosis and to improve the quality of life for those with the disease.

http://www.cff.org
Articles from the PubMed Database

Research articles describe the outcome of a single study. They are the published results of original research. The terms "Cystic Fibrosis" returned 4176 free, full-text research articles on human participants. First 3 results:

Ivacaftor in a G551D homozygote with cystic fibrosis.

Author(s): Michael J Harrison, Desmond M Murphy, Barry J Plant

Genetic interaction of GSH metabolic pathway genes in cystic fibrosis.

Author(s): Fernando Augusto de Lima Marson, Carmen Silvia Bertuzzo, Rodrigo Secolin, Antônio Fernando Ribeiro, José Dirceu Ribeiro
Journal:

Cystic fibrosis (CF) is a monogenic disease caused by CFTR gene mutations, with clinical expression similar to complex disease, influenced by genetic and environmental factors. Among the possible modifier genes, those associated to metabolic pathways of glutathione (GSH) have been ...

The role of serum Pseudomonas aeruginosa antibodies in the diagnosis and follow-up of cystic fibrosis.

Author(s): Last Updated: 26 Sep 2013
Go To URL

Go To URL
Transepithelial nasal potential difference (NPD) measurements in cystic fibrosis (CF).

Author(s): Dorota Sands

The main underlying physiologic abnormality in cystic fibrosis (CF) is dysfunction of the CF transmembrane conductance regulator (CFTR), which results in abnormal transport of sodium and chloride across epithelial surfaces. CFTR function could be tested in vivo using measurements ...


Author(s): Isabelle Sermet-Gaudelus

Cystic fibrosis (CF) is an autosomal recessive lethal disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that encodes for CFTR, an epithelial cell-surface expressed protein responsible for the transport of chloride (Cl(-)). Gating mutations ...

Targeting a genetic defect: cystic fibrosis transmembrane conductance regulator modulators in cystic fibrosis.

Author(s): Nico Derichs
Metabolic Efficiency of Combined Pancreatic Islet and Lung Transplant for the Treatment of End-Stage Cystic Fibrosis

Status: Not yet recruiting
Condition Summary: Cystic Fibrosis; Diabetes Related Cystic Fibrosis

Exocrine Pancreatic Function Testing in Cystic Fibrosis

Status: Recruiting
Condition Summary: Cystic Fibrosis

Circadian Rhythm In Tobramycin Elimination In Cystic Fibrosis

Status: Recruiting
Condition Summary: Cystic Fibrosis

According to ClinicalTrials.gov there are currently 204 additional "open" studies for "Cystic Fibrosis" (open studies are recruiting volunteers) and 604 "Cystic Fibrosis" studies with "all" status. Visit ClinicalTrials.gov now to view them. Or alternatively, consider TrialsFinder for assistance:
The Advocacy ATLAS
Accessible Tools for Leadership and Advocacy Success

www.geneticalliance.org/advocacy-atlas
What are biospecimens and why are they important in drug development?

- **Biospecimens** are biological samples collected from humans such as blood samples, tumor samples, or other tissues. When someone with a disease or condition has a biopsy, surgery, or other procedure, often a small amount of the specimen taken can be stored and used for later research. The specimens are used in biomedical research to learn about how disease affects the human body. To learn more about biospecimens and why they are important for drug development, click on the links below.
  - NCI OBBR: What are Biospecimens and Biorepositories?
  - NCI OBBR: Life Cycle of a Biospecimen
  - NCI OBBR: The Critical Role of Biospecimen in Cancer Research

Testimonials: How we did it

Relevant Publications

Related Tools

- NCI OBBR: Biospecimen Research Database
- NIDDK: Data, Biosample, and Genetics Repository
- NHLBI: Biologic Specimen and Data Repository Information Coordinating Center
- NCI: Specimen Resource Locator
- NCI DTP: Tumor Repository
‘Registry and BioBank in a Box’

• Deliver ‘white label product’
• Deliver technical assistance
• Cooperative – learn from each other
• Low cost and driving lower
• Community based and local trusted entities’
• Global standards and rigor
# Genetic Alliance Registry and BioBank Toolbox

<table>
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<tr>
<th>Where do I begin?</th>
<th>What is a biobank?</th>
<th>Guidelines for considering a registry/biobank</th>
<th>Advocates are leaders in biobanking</th>
</tr>
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<tbody>
<tr>
<td>How do I make this a reality?</td>
<td>Registry/repository start-up guide</td>
<td>Making your organization's biobank a reality</td>
<td>Genetic Alliance registry/repository boot camps</td>
</tr>
<tr>
<td>Is my organization ready?</td>
<td>Organizational readiness checklist</td>
<td>Biobank question &amp; answer session</td>
<td></td>
</tr>
<tr>
<td>How do I select a vendor?</td>
<td>Vendor assessment summary</td>
<td>Vendor assessment worksheet</td>
<td>Landscape analysis manuscript</td>
</tr>
<tr>
<td>Considering Genetic Alliance?</td>
<td>Genetic Alliance BioBank</td>
<td>GARB FAQs</td>
<td>Virtual tour of Genetic Alliance registry solutions</td>
</tr>
<tr>
<td>What else do I need to know?</td>
<td>Biobank governance</td>
<td>Biobank governance checklist</td>
<td>Resource list</td>
</tr>
</tbody>
</table>

*Publications*, *Training/mentoring*, *Videos*, *Webinar*, *Webpage*, *Worksheet*
Platform for Engaging Everyone Responsibly – branded according to the advocacy organizations wishes

The portal fits directly onto any web page and retains the host site’s top and bottom navigation.

The headline, colors, theme, video and other content can be tailored to fit seamlessly into the host site and support each group’s message.

Everything is ready and because it is patient-centric. It supports both new users as well as individuals who may have started on a different organization’s Private Access-enabled site. Everyone benefits!
Users are assisted by highly intuitive, non-coercive trusted, local, “guides”

Multiple guides give an opportunity to use a variety of approaches, and selecting settings that are the most comfortable to each participant. Well known guides can be used across an entire condition, or be specific to an individual disease organization.
To enable ease **and** an extraordinary range of granularity

Each guide suggests his or her ideas as a possible starting point.
To enable ease and an extraordinary range of granularity.

Each guide suggests his or her ideas as a possible starting point.

For multiple categories of uses, and specified usage rights.

Participants use privacy settings to specify who can, and cannot, access or use their de-identified and/or personal contact data, and for what purpose.

Participants may choose to Permit, Decline, or wait for more information before deciding.

<table>
<thead>
<tr>
<th><strong>Advocacy &amp; Support Groups</strong></th>
<th><strong>Researchers</strong></th>
<th><strong>Data Analysis Platforms</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Joubert Syndrome &amp; Related Disorders Foundation (JSRDF)</td>
<td>Researchers recommended by JSRDF</td>
<td>&quot;Show related content&quot; feature</td>
</tr>
<tr>
<td>DiseaseInfoSearch.org listed organizations serving your condition</td>
<td>Researchers recommended by any DiseaseInfoSearch.org listed organization serving your condition</td>
<td>&quot;Compare with others&quot; feature</td>
</tr>
<tr>
<td>All organizations serving your condition</td>
<td>Researchers addressing your condition</td>
<td>Genetic Alliance Translational Research Network</td>
</tr>
<tr>
<td></td>
<td>All researchers</td>
<td>PCORnet: Patient-Centered Outcomes Research Network</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Newly Released Data Analysis Platforms</td>
</tr>
</tbody>
</table>

Participants may choose to Permit, Decline, or wait for more information before deciding.
Longitudinal data and automated reminders

We’re adding ways to easily and intuitively ask about and visualize longitudinal information such as medical and family history, lab values, molecular profiles, and more.

The survey will become one of several sections available for participants to report information.
Longitudinal data and automated reminders

The survey will become one of several sections available for participants to report information. We’re adding ways to easily and intuitively ask about and visualize longitudinal information such as medical and family history, lab values, molecular profiles, and more.

Including the opportunity to set automated update reminders...

...and to chart longitudinal results.

With all this data being moved back into REDCap on a daily basis, and plans to eventually import it into i2b2 and TransSmart for better analytic tools.
“Gamified” Interface for Questions and Answers

Questions appear in a dynamic user interface, and provide immediate feedback on how others responded to the same question...

Participants can review their prior answers, make updates and/or remove the data at any time.
The NaGucer Network Registry will help advance research and improve care!

By sharing our stories in a way that safeguards each individual’s respective privacy concerns, the information we provide can be a vital force in helping to advance research. That’s why the NGF is sponsoring the new Gaucher Network Registry (GNR), the first ever participant powered Gaucher registry. Through learning more about how Gaucher disease affects each individual and -- with express permission -- making it easier for top researchers to contact us about new studies, we can accelerate our quest to find a cure for this debilitating and often fatal disease. Simply click on Start Now! to begin, or Sign In if you are a returning user.

It's quick and simple!

1. Sign Up! (or sign in)
2. Take health survey
3. Let researchers find you
4. Share with others!

Respecting Your Privacy is a Priority

To help us protect your individual privacy in accordance with rules that you establish, we harness the power of Private Access with the specific goal of helping you make your health information available to top researchers - under your own terms.
Let's tell the FDA how important it is to find a cure for Sickle Cell Disease

April 8th is the last day for the Food & Drug Administration (FDA) to hear public comments about sickle cell disease, and our voices need to be heard. This is our opportunity to tell the government about the needs and concerns of millions of Americans affected by sickle cell trait and disease. You can help just by answering a few questions; and if you want, you can also allow researchers to alert you about new studies for which you may qualify...

This is our chance to tell the FDA about the need for more drugs and therapies of people with Sickle Cell Disease

Katrina Rice
44 year old mother of a child with Sickle Cell Disease

We Respect Your Right To Privacy

We understand that many people in our community have concerns about privacy. We are committed to protecting your right to decide how active and open to be. And that's why we're using Private Access to let you establish the rules for who can see your information, when, and for what purpose.
Let's tell the FDA how important it is to find a cure!

By April 8, the FDA needs to hear from us about sickle cell disease, and it's critical your voice is heard. This is our opportunity to tell the government about the needs and concerns of millions of Americans affected by sickle cell trait and disease. You can help just by answering a few questions; and if you want, you can also allow researchers to alert you about new studies for which you may qualify.

“Priorities for research and advocacy should align with real-world perspectives of people who are affected by Sickle Cell Disease.”

Mattie Robinson
Project Manager
William E. Proudford Sickle Cell Fund, Inc.

It's Easy as 1, 2, 3

1. Protect your privacy
2. Tell the FDA your opinion
3. Provide More Health Info
4. Help Sprade The Word!

Respecting Your Right to Privacy

We understand that many people in our community have concerns about privacy. We are committed to protecting your right to decide how active and open to be. And that's why we're using Private Access to let you establish the rules for who can see your information, when, and for what purpose.
Your piece of the puzzle is a critical one!

We do not understand how PXE progresses, or how to slow it down. It is time to change that! Please join our effort to complete the puzzle! Simply click on Start Now! to begin, or Sign In if you are a returning user.

It's quick and simple!

1. Sign Up! (or sign in)
2. Take health survey...
3. Let researchers find you...
4. Share this with others!

Respecting Your Wishes is Our Priority

To help us protect your individual privacy in accordance with rules that you yourself establish, we harness the power of Private Access with the specific goal of helping you make your health information available to top researchers for your condition - under your own terms.
PEER Deployed

• Joubert Syndrome LIFE Registry: https://www.jsrdf.org/JSLIFE
• Gaucher Registry: https://www.gaucherdisease.org/gaucher-network-registry.php
• Pseudoxanthoma Elasticum Registry: https://www.pxe.org
• Registries for All: https://www.reg4all.org
• TrialsFinder: https://www.trialsfinder.org
• Free the Data: https://www.free-the-data.org
• United Mitochondrial Disease Foundation: http://www.umdf.org/site/c.8qKOJ0MvF7LUG/b.9135169/k.D604/Registry.htm
• North Alabama Sickle Cell Foundation: http://sicklecellna.org/peer.php
• Sickle Cell Disease Association of America, Southern Connecticut: http://www.scdaaofsoutherncnt.org/tellthefda.html
PCORnet: the National Patient-Centered Clinical Research Network

The goal of PCORI’s National Patient-Centered Clinical Research Network Program is to improve the nation’s capacity to conduct CER efficiently, by creating a large, highly representative, national patient-centered clinical research network for conducting clinical outcomes research.

The vision is to support a learning US healthcare system, which would allow for large-scale research to be conducted with enhanced accuracy and efficiency.
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The **goal** of PCORI’s National Patient-Centered Clinical Research Network Program is to improve the nation’s capacity to conduct CER efficiently. By creating a large, highly representative national patient-centered clinical research network, we can conduct high quality clinical outcomes research.

The **vision** is to support a learning US healthcare system, which would allow for large-scale research to be conducted with enhanced accuracy and efficiency.

– 1000 researchers, traditional and lay
– 29 funded entities covering all 50 states
– Focus on patient-centered outcomes research
– No “one size fits all”

CENA

– Community Engaged Network for All (CENA)
– 9 disease-specific advocacy organizations, UCSF, UCD
– From hepatitis (affects millions) to Alström syndrome (affects a several hundred)
Patient Powered Research Networks span a range of conditions

<table>
<thead>
<tr>
<th>Organization</th>
<th>PI</th>
<th>Condition</th>
<th>Proposed PPRN Population Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerated Cure Project for Multiple Sclerosis</td>
<td>Robert McBurney</td>
<td>Multiple Sclerosis</td>
<td>20,000</td>
</tr>
<tr>
<td>American Sleep Apnea Association</td>
<td>Susan Redline</td>
<td>Sleep Apnea</td>
<td>50,000</td>
</tr>
<tr>
<td>Cincinnati Children's Hospital Medical Center</td>
<td>Peter Margolis</td>
<td>Pediatric Crohn's Disease and Ulcerative Colitis</td>
<td>15,000</td>
</tr>
<tr>
<td>COPD Foundation</td>
<td>Richard Mularski</td>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>50,000</td>
</tr>
<tr>
<td>Crohn’s and Colitis Foundation of America</td>
<td>R. Balfour Sartor</td>
<td>Inflammatory Bowel Disease (Crohn’s disease and ulcerative colitis)</td>
<td>30,000</td>
</tr>
<tr>
<td>Global Healthy Living Foundation</td>
<td>Seth Ginsberg</td>
<td>Arthritis (rheumatoid arthritis, spondyloarthritis), musculoskeletal disorders (osteoporosis), and inflammatory conditions (psoriasis)</td>
<td>50,000</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
<td>Andrew Nierenberg</td>
<td>Major Depressive Disorder (MDD) and Bipolar Disorder (BP)</td>
<td>50,000</td>
</tr>
<tr>
<td>Univ of California, San Francisco</td>
<td>Mark Pletcher</td>
<td>Cardiovascular health</td>
<td>100,000</td>
</tr>
<tr>
<td>University of South Florida</td>
<td>Rebecca Sutphen</td>
<td>Hereditary Breast and Ovarian Cancer (HBOC)</td>
<td>17,000</td>
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....in both rare and common disorders

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<th>Condition</th>
<th>Proposed PPRN Population Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALD Connect, Inc</td>
<td>Florian Eichler</td>
<td>Adrenoleukodystrophy</td>
<td>3,000</td>
</tr>
<tr>
<td>Arbor Research Collaborative for Health</td>
<td>Bruce Robinson</td>
<td>Primary Nephrotic Syndrome (Focal Segmental Glomerulosclerosis [FSGS], Minimal Change Disease [MCD], and Membranous Nephropathy [MN] Multiple Sclerosis)</td>
<td>1,250</td>
</tr>
<tr>
<td>Duke University</td>
<td>Laura Schanberg</td>
<td>Juvenile Rheumatic Disease</td>
<td>9,000</td>
</tr>
<tr>
<td>Epilepsy Foundation</td>
<td>Janice Beulow</td>
<td>Aicardi Syndrome, Lennox-Gastaut Syndrome, Phelan-McDermid Syndrome, Hypothalamic Hamartoma, Dravet Syndrome, and Tuberous Sclerosis</td>
<td>1,500</td>
</tr>
<tr>
<td>Genetic Alliance, Inc</td>
<td>Sharon Terry</td>
<td>Alström syndrome, Dyskeratosis congenital, Gaucher disease, Hepatitis, Inflammatory breast cancer, Joubert syndrome, Klinefelter syndrome and associated conditions, Metachromatic leukodystrophy, Pseudoxanthoma elasticum (PXE)</td>
<td>50-50,000</td>
</tr>
<tr>
<td>Immune Deficiency Foundation</td>
<td>Kathleen Sullivan</td>
<td>Primary Immunodeficiency Diseases</td>
<td>1,250</td>
</tr>
<tr>
<td>Parent Project Muscular Dystrophy</td>
<td>Holly Peay</td>
<td>Duchenne and Becker muscular dystrophy</td>
<td>4,000</td>
</tr>
<tr>
<td>Phelan-McDermid Syndrome Foundation</td>
<td>Megan O’Boyle</td>
<td>Phelan-McDermid Syndrome</td>
<td>737</td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>Peter Merkel</td>
<td>Vasculitis</td>
<td>500</td>
</tr>
</tbody>
</table>
**EspeRare: Merging patients & commercial interests**

**Mission**

In partnership with advocacy groups, academia and medical reference centers, EspeRare uncovers the potential of existing drugs to address severe therapeutic unmet needs in neurological and immunological rare diseases.

**Strategic Goals**

- **Gives a chance to unexplored therapies in rare diseases:**
  - Identify & drive translational validation of “dormant” opportunities
  - Leverage established patient groups & biomedical networks
  - Invest foundation’s R&D revenues and grants in rare disease programs

- **De-risk early development of rare diseases programs:**
  - Combine not-for profit & public grants with commercial funds/assets
  - Bring Biopharma expertise to academia & patient groups collaborations
  - Translate patient engagement into scientific and regulatory efforts

- **Hand-over programs to commercial partners for late development:**
  - PhII/PhIII ready programs with strong network of patient groups & experts
  - Flexible partnering model, tailored to the asset & disease
EspeRare uncovers therapeutic opportunities and aims to insure treatment access
Include Informed Public in All Stages of Clinical Research

• Participant perspective to study design
  – Protocol Review
  – IRB service
  – Data safety monitoring boards
• Informed decision making
• Reasonable compliance - AIDS Community examples
• Enhanced community education
• Better cohort accrual - Herceptin example
• Improve participant retention
• Advance public trust in research
Advocacy Organizations

- Willing partners
- Ready to work hard
- Have exceptional access
- Are excellent allies
- Add value throughout the system
- Technical assistance for them
For more information:

Sharon Terry
CEO and President, Genetic Alliance, Inc.
(202) 966-5557, Ext. 202
sterry@geneticalliance.org

General Information: http://www.geneticalliance.org/programs/biotrust/cena

Online demo (for JSRDF shown here): http://jsrdf.org/JSLIFE-demo
What do we have to lose?

Everything.