Realizing Our Potential in Biobanking: Disease Advocacy Organizations Enliven Translational Research

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Biobanks are increasingly powerful tools used in translational research, and disease advocacy organizations (DAOs) are making their presence known as research drivers and partners. We examined DAO approaches to biobanking to inform how the enterprise of biobanking can grow and become even more impactful in human health. In this commentary, we outline overarching approaches from successful DAO biobanks. These lessons learned suggest principles that can create a more participant-centric approach and illustrate the key roles DAOs can play as partners in research initiatives. DAO approaches to biobanking for translational research include the following: be outcome driven; forge alliances that are unexpected—build bridges to enhance translation; come ready for success; be nimble, flexible, and adaptable; and remember that people matter. Each of these principles led to particular practices that have increased the translational impact of biobank collections. The research practices discussed can inform partnerships in all sectors going forward.

Background

AS MANY HAVE OBSERVED, science and technology are rapidly changing the questions one can pursue, as well as the tools used to explore essential questions in human health.¹ More than ever, the approach to research is as important as what is being pursued.² There is a growing cadre of people from all sectors of the biomedical research and healthcare systems who are concerned that traditional incentives and competitive research systems are now detrimental to translational research.^{3,4}

If all stakeholders share common goals to accelerate insights from disease biology to enable prevention, symptom management, or even cure, then accelerating research effectively and efficiently requires approaching research practices differently from beginning to end.^{5,6} Effective and efficient approaches to translational research become even more critical with high-stakes projects, such as the President's Precision Medicine Initiative.⁷

A group of nonprofit disease advocacy organizations (DAOs), active in the translational research domain, met to examine how DAOs have pursued biobank research activities

with the aim of improving human health for the populations they serve. DAOs play a significant and growing role in the translational research landscape.^{8,9} Because they often come from outside the traditional biomedical research system, the authors were interested to learn in what ways leadership, practice, and culture may differ from within DAO-managed biobanks.

The insights we frame here can be applied to many aspects of translational research, ultimately leading toward improvements in biomedical research practices. Seeds of innovative practices run throughout all types of organizations¹⁰; our goal is to highlight these principles and associated practices to accelerate change designed to realize the potential of novel partnerships in translational research.

Biobanks form a delicate interface between the science and the people who will benefit, and DAOs are often in a unique position to engage affected individuals, families, and friends, actively promote communications and connections, and guide research directions toward areas of greatest need, and impact within the affected community.¹¹ We invited five DAO-managed biobanks with an international reach to present case studies over the course of 3 days, addressing common practices, key decisions, and examples of tools or

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strategies used to manage the biobank resources. The assembled group then reflected on commonalities between the case studies, resulting in the principles shared here.

DAO Biobank Case Studies

The four case studies we profile here represent international registries and collections of specimens and data accessed by researchers from diverse countries and sectors.*

Genetic Alliance Registry and BioBank

Genetic Alliance Registry and BioBank (GARb)[†] is a cooperative biobank established in 2003 to accelerate drug development, knowing a key rate-limiting step is the availability of well-characterized, well-annotated biospecimens, with associated clinical data. GARb membership is limited to nonprofit organizations, and GARb members own, govern, and provide stewardship for their data and sample collections.

The GARb team works closely with each member organization to help them achieve their research goals; thus, the co-op members benefit from the accrued expertise and experience of the biobank managers. By sharing infrastructure, tools, and best practices, DAOs are able to do more with less. The cooperative model also permits for maximum individual organization control and choice about data sharing, while also facilitating sharing and access due to standardized specimen collection and data management tools.

Chronic Fatigue and Immune Dysfunction Syndrome Association of America

Chronic fatigue syndrome (CFS), a disabling condition that often begins with a sudden flu-like illness, wreaks havoc on nearly every system in the body, yet defies detection using standard medical tests.[‡] For the past 20 years, the CFIDS Association of America (CAA) has funded research aimed at the early detection, objective diagnosis, and effective treatment of CFS. Frustrated with the slow pace, and “one-and-done” research studies, the CAA works more directly with the real stakeholders in CFS research—people whose lives are directly affected by the illness.

As a member of the cooperative Genetic Alliance Registry and Biorepository, the CFIDS has designed the biobank to be an archive of the research results conducted with biobank participants. Stewardship of the samples and data contributed by biobank participants puts CFS patients at the center of research and links projects and findings, even across seemingly different inquiry domains, facilitating greater insight and hypothesis generation.¹² Since starting the biobank in 2010, some of the brightest investigators from the best medical institutions have been enticed into

CFS research using specific granting mechanisms that promote use of the biobank.¹³

Pachyonychia Congenita Project

There are currently no effective treatments for individuals suffering from pachyonychia congenita (PC).[§] Because PC is so rare, most of the information about PC was based on single-case studies, and misinformation proliferated before the foundation created an International Patient Registry with validated data from as many patients as possible in 2004.¹⁴ The PC Project also recognized the need to engage many diverse experts in a team approach to research. Therefore, they organize and sponsor the International PC Consortium (IPCC), which is open to all researchers and physicians who agree to collaborate in helping find effective treatments for PC patients. They sponsor the annual scientific meetings of the PC registry, which feature open cooperative group discussions, where the purposes are to select what actions are most promising and carry out and achieve those goals in the following year(s).

Through the PC Project annual patient support meetings, where affected individuals, family members, scientists, and physicians gather, more accurate knowledge of the disease has been gained, and a stronger understanding developed between these groups.¹⁵ Since clinicians and researchers often only see one person with PC themselves, the patients and families become educators, and an atmosphere of collaboration is created. The registry is used as a catalyst to convene researchers and coordinate a research agenda that will most quickly develop effective, patient-friendly treatments.

PXE International

Pseudoxanthoma elasticum (PXE) is an inherited disorder that causes select elastic tissue in the body to become mineralized.** Early on, in 1995, when the founders of the PXE International’s children were asked for blood samples 2 days in a row, from two different universities, the founders recognized that there was something seriously wrong in science. When they suggested that instead of drawing blood from little children twice, the researchers share, the response was incredulity. They then decided that they would incentivize sharing. They were told that this would be akin to herding cats—which helped them realize that in fact you can herd cats, if you move the food. The “food” was the DNA (the hunt for the gene was on), and thus, the PXE International Registry and BioBank, the first lay-owned and managed entity of its kind in the world, was formed.¹⁶ Requiring the researchers searching for the gene to share data if they used samples from the bank, the foundation was able to create a consortium of almost all the researchers working on the disease in the world.

The data sharing expected goes beyond what the NIH data sharing policies promote. With PXE, researchers shared all findings and processes with the biobank, resulting in accelerated advances toward translational research leading to widespread availability of the diagnostic and several clinical trials.¹⁷ The data sharing approach allows research to be

*The fifth biobank to participate in the case study discussion and analysis was the Multiple Myeloma Research Foundation. However, the representative from the MMRF who attended the meeting had left the organization before we put the article together. We thus do not include the specific case here, although the examples shared informed the development of common principles.

[†]The registry and biospecimen repository information can be found at <http://biobank.org/>. Additional tools for data registries are found at <http://peerplatform.org/>. Accessed in November 2015.

[‡]Since the time of the case study, the organization has changed names. Information can be found on their Web site: <http://solvecfs.org/>. Accessed in November 2015.

[§]The DAO can be found at www.pachyonychia.org/. Accessed in November 2015.

**PXE International can be accessed at www.pxe.org/. Accessed in November 2015.

centrally coordinated, while still allowing embargoing information, so that publishing articles and obtaining grants and other structures in the usual reward systems can occur. Thus, novel collaborations are enabled, and traditional mechanisms for funding and recognition are preserved, resulting in acceleration of the path toward therapies. Dozens of clinical studies have resulted from the biobank and registry.^{8-17,3,**} Figuring out how to meet everyone's needs is part of the key to success and certainly key to continued investments in collaborative research.

DAO Approaches to Biobanking for Translational Research

Lessons learned from the case studies of DAO biobanks suggest principles that can create more participant-centric research approaches and guide biobank management to transform research in ways that impact human health. We outline the overarching principles here.

Be outcome driven

When an organization or a set of researchers are motivated to solve a problem, a collaborative and creative spirit can grow. In general, the current academic or industry-based research incentive structures remain focused on peer-reviewed publications, securing further grant dollars, and protecting patenting rights, which inhibits progress.^{18,19} An outcome focus, in contrast, reminds us why we are investing in significant research infrastructures and projects, with clarity about the ultimate end goals. While all successful organizations lead from their mission, in the case of health research, the goal is improving the health and well-being of people. This mission can be so vast that one can lose sight of how to maintain focus on a specific problem or collection of phenotypes, such that they will, sooner rather than later, beneficially impact affected people. As one case study participant reflected: "We have so many genes, and so few treatments."

Recognizing that not all lines of discovery can be predicted and planned, an outcome focus can involve facilitating connections or dialogues between unfamiliar partners (see section below) to facilitate transforming insights into action. For all biobanks involved in this case study, this means collaborating on the research agenda to assure that unproductive pathways are not repeated. Additionally, the biobanks request all findings (positive and negative) be returned to the biobank so they can be further developed, built upon, or avoided depending on the results.

When health impact is the end goal, not preserving one's ego or intellectual property interests, progress can be made more efficiently. The participation of affected individuals in research meetings can shift the tone and nature of engagement by reminding people why they are working together and what is important. When basic and translational researchers meet and/or work with affected individuals and their families, it connects to the deepest meaning in the work, humanizes the topics, and leads to increasing recognition that each member of the alliance has an essential expertise to contribute.

Forge alliances that are unexpected—build bridges that enhance translation

Gaps in handoffs across researchers are a known challenge for translational science.²⁰ In a time of enormous

culture shift, new alliances are necessary.²¹ Experience shows it takes personal relationships to forge robust alliances. These alliances become productive collaborations when there is a shared sense of purpose toward a common goal and/or an understanding of how incentives can creatively align, while recognizing and valuing diverse needs and interests. Personal connections help all partners recognize what is at stake, and for whom, and facilitate the ability to find common ground.

Seeing diverse perspectives as critical in finding solutions requires moving past a competitive or narrow mind-set and identifying creative ways to frame the problem or pursue the solutions. At best, there is a deep commitment to equality of partners and a reliance on connections and interdependence between the partners. All the biobanks represented here sponsored research meetings, which brought together unusual bedfellows, and often competitors, to share findings and work together on research agendas. A further development has been to create a platform to share and build upon sequencing and identify others working in similar areas.²²

Come ready for success

When discussing case examples of effective and productive practices among the DAOs we assembled, there emerged a clear distinction between practices that worked and those that did not. A major contributing factor required coming to a meeting or opportunity with the sense that there is enough room for everyone to be successful and to have their needs met.

A related attitude that promotes success is an open mind about what might be possible within the opportunity. Sometimes knowing too much, or anticipating an outcome, predisposes the process to a lesser result. Holding a mind-set of possibility helps create those opportunities. Part of being goal focused with each day, each decision, means acting with a certain measured urgency and also endurance (recognizing this is a marathon, not a sprint). DAOs serve affected people and families, and as such, the search for treatments and prevention strategies is a sole focus no matter how hard or long the road.

Be nimble, flexible, and adaptable

The partners at the biobank must be responsive and open to opportunities that may arise from unexpected places or people. This requires truly listening and also not holding too tightly to any given agenda or path, while continuing to make decisions from the core mission and commitments as stated in the first practice on the list. Given the fast-changing pace of practice and the complexity involved with translational health research and practice, staying responsive to emerging needs is key, while providing consistency and sustainability in the face of uncertainty.

The international research meetings the biobank organizations convene are active working meetings, where potential directions are debated. Creative solutions are necessary, particularly when hopeful directions have not panned out. As one participant commented, if a rock blocks the path to the goal, the rock can stay in the path, and we can find another way to accomplish what it is that we truly want to achieve.

Remember that people matter

Managers, researchers, and staff working with the DAO-managed biobanks and research groups value the people

they are serving and keep the needs of the people front and center in their decisions, actions, and priorities. This core commitment and vision run through every action, practice, and person within the organizations. The investment in personal relationships was key with all the case studies, and those relationships pay off. In the PXE International example, participants in the registry complete a 900-item survey of lifestyle and health impacts each year. Having access to this extremely rich data set has meant that researchers and the overall PXE community have a better understanding of the epidemiology and natural history of the disease.

Using DAO Principles in Practice

Enacting the practices described above requires moving beyond slogans to organizational and professional commitments that infuse all aspects of research practice. We have illustrated how these practices are enacted through examples of DAOs engaged in research.

Approaching translational research in new ways requires a culture of communication and collaboration with fellow researchers as well as participant communities—community members can also be researchers. Regulatory and policy changes at the federal level will also help facilitate change within research practices toward more data sharing and more participatory approaches.^{††} Emerging tools and social networks can be leveraged to share as much as possible at levels desired by participants.^{23,24} Generosity of spirit can draw people in and make things happen. Attending to benefits, real benefits, will also help hold biobanks accountable for practices that assure benefits are occurring. If benefits are slow in coming, what can be done differently to accelerate them? Are there new partnerships, better communication, and different research directions that should be pursued? Are there insights coming from other disease sectors that would inform another?

Biobanks currently can be underutilized. Resources may be exhausted on the infrastructure and not on the labor, or there may not be enough for the resource-intensive activity of connecting people, overcoming translational challenges, and taking advantage of opportunities. The renewed approaches to research assure that biobanks are tools that make research more effective and efficient and not simply expensive investments that are underutilized.

Culture change efforts require diverse bedfellows to connect around common interests. Academics, advocacy-based researchers, and industry employees can reconnect with their core commitments and passions to make an impact and help people.²⁵ We all want to make a difference. However, not sharing, cooperating and collaborating, will mean not progressing at rates that will actually help people. As one of our members stated: “Secrecy is a public health problem.” Academic research will benefit from joining in this effort to keep people and health benefit goals at the center of research.²⁶ We need to assure meaningful partnerships with participants and DAOs in ways that transform practices.²⁷ Together we can make advances, and together we can be stronger.

^{††}See, for example, the NIH Genomic Data Sharing Policy from January 2015: <https://gds.nih.gov> and the proposed OHRP regulatory changes guiding protections for research participants: www.hhs.gov/ohrp/humansubjects/anprmcchangeable.html/. Accessed in November 2015.

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