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# Genetic Alliance Registry and BioBank: a novel disease advocacy-driven research solution

The Genetic Alliance Registry and BioBank was founded in 2003 on the principal that a shared infrastructure would facilitate easy flow of resources and accelerate disease-specific research. Based on the Pseudoxanthoma Elasticum International Registry and BioBank, six disease advocacy organizations came together to identify the best solutions for advocacy organizations to promote and collect biological samples with associated clinical information from their members. This required a flexible system that could accommodate an extensive amount of data and samples, support new avenues of research, yet be adaptable to meet the needs of a variety of organizations, and straightforward to implement and use. After extensive landscape analyses, a cross-disease, infinitely expandable registry and biorepository was established. This article reports on this effort and shares the lessons learned.

**KEYWORDS:** biobank ■ biorepository ■ disease advocacy organization ■ registry ■ translational research

Biobanks are important tools for research, providing well-annotated samples to study diseases, their pathways and mechanisms. Successful biobanks must meet the minimum criteria for sample protocols, data collection, informed consent and stewardship [1,101]. Following standard protocols helps to ensure high-quality sample collection, processing and storage, and using widely accepted or codified standards ensures interoperability. Biologic samples are much more powerful with well-annotated clinical data, which include disease progression, treatment information, demographic information, lifestyle information, family history and other relevant information. Appropriate informed consent is also needed to initiate data and sample collection. Finally, good stewardship is necessary to ensure the judicious use of precious, limited resources.

Disease advocacy organizations (DAO) are involved extensively with registries and biobanks [2]. DAOs are dedicated to specific disease areas and are highly motivated to steward sample collections for the long term. They also have both broad and deep knowledge of their specific field and can promote collaboration and sharing among researchers. DAOs operate within a community of trust with their members, making their members an ideal population from which to recruit participants to establish robust cohorts. We suggest that DAOs should not only be involved, but also often have the passion and capacity to establish and manage these resources. In fact, Genetic Alliance

Registry and BioBank (GARB), Washington, DC, USA, was developed for this purpose – to provide an infrastructure for advocacy organizations to establish and manage their biobanks and registries. Current GARB members are listed in TABLE 1.

## GARB philosophy

The GARB does not exist merely for the sake of having a good, or even excellent, registry and biorepository. It exists to initiate, accelerate, and transform research and services – from basic science to clinical trials to disease management. It is unique in two ways: it is solely focused on improved health, and it is iterative and adaptive to the evolving needs of the community it serves. We recognize that transparency, openness, flexibility and responsiveness are key components of this strategy. Since registries and biorepositories must evolve as technology and science advances, we built a platform that will both test hypotheses and generate hypotheses for future research. Any system that is to provide a robust infrastructure must not only keep pace, but also envision the future beyond its own structure.

## GARB history

### ■ Pseudoxanthoma Elasticum International

The GARB was built on the foundation established by the Pseudoxanthoma Elasticum (PXE) International Registry and BioBank (PIRB), which stored clinical data and biological

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**Table 1. Current Genetic Alliance Registry and BioBank members.**

Member organization	Condition	URL	Founding member	Ref.
CFIDS Association of America	Chronic fatigue syndrome	www.cfids.org		[106]
Children's Tumor Foundation	Neurofibromatosis	www.ctf.org		[107]
Inflammatory Breast Cancer Research Foundation	Inflammatory breast cancer	www.ibcresearch.org	X	[108]
Joubert Syndrome and Related Disorders Foundation	Joubert syndrome	www.joubertfoundation.com	X	[109]
National Psoriasis Foundation	Psoriasis and psoriatic arthritis	www.psoriasis.org	X	[110]
Pseudoxanthoma Elasticum International	Pseudoxanthoma elasticum	www.pxe.org	X	[102]
US Hereditary Angioedema Association	Hereditary angioedema	www.hereditaryangioedema.com		[111]

*CFIDS: Chronic fatigue and immune dysfunction syndrome.*

samples [3]. PXE is an inherited disorder that causes select elastic tissue in the body to become mineralized, resulting in changes in the skin, eyes, cardiovascular system and gastrointestinal system [102]. In 1995, PIRB was the only lay-run BioBank of its kind. The clinical data was stored in a FileMaker Pro database managed in the PXE International office. Blood collection kits consisting of blood vials and a mailer, with a description of the collection protocol and a consent document, were assembled at the PXE International offices. DNA aliquots were stored in rented freezer space at a local academic institution for a small fee. Throughout the late 1990s, PXE International mentored many other disease organizations and helped several to form registries and biorepositories. But this mentoring was labor intensive, and each new registry felt like the reinvention of the wheel. In 1999, PXE International determined that a new, cross-disease model was needed, where organizations could share infrastructure and resources.

#### ■ Establishing GARB

In 2003, PXE International leaders met with several professionals experienced in material transfer and creating registries and biorepositories. These individuals founded a new 501(c)(3) called GARB, built on the foundation of Genetic Alliance, a nonprofit organization focused on transforming health through genetics. The new nonprofit, GARB, established its own governing board consisting of experts in biorepositories and registries, technology transfer, genetics, and ethical, legal and social issues,

with representation from the member organizations. Two of the first accomplishments of GARB were the creation of an Institutional Review Board of experts in the field and development of template documents for each group to customize their study protocol. The six founding disease advocacy organizations each entered into a contract with GARB, and GARB entered into a contract with a commercial biorepository vendor.

The GARB operates in a cooperative model, providing infrastructure, logistics and guidance, while member organizations bring passion, skills and resources to the collective. Member organizations steward, govern, own and manage their data and sample collections; determine what data and samples will be collected; and consent their participants. Collectively, with GARB leadership, members have the ability to determine the attributes of the registry and biobank as a whole and build it to their desired specifications. Customization is essential to address individual data and sample needs for the conditions represented. GARB configures the best possible infrastructure that meets the need of all members, continually updating solutions as science and technology improve.

#### ■ Requirements analysis

Early in its history, it became clear that a robust clinical registry on a central server, with extensive reporting capability and a web interface, and integrated biorepository, were necessary to fully realize the potential of GARB. Major requirements were identified through extensive

discussions with registry and biorepository experts across the world (Box 1). In addition, the following business elements were critical to selecting a new vendor:

- Safeguarding ongoing operations: a service contract for 5 years of service (renewable), with penalties if the vendor cannot provide the service;
- Contracting solely with the vendor, not becoming an asset of the company: if the vendor is sold, GARB has the right to terminate the agreement;
- Safeguarding the resource: if GARB or if the vendor terminate the agreement, the vendor will continue to store samples and data for 18 months, and GARB will continue to pay for that service;
- Safeguarding continued operations: if vendor terminates the contract, is sold or otherwise severs the relationship, GARB assumes the ownership of the servers and the software and training to configure it.

After much searching and interviews with multiple vendors, the board selected a new vendor for the integrated registry and biorepository in 2006.

### ■ Genetic Alliance

Genetic Alliance was the foundation and a key partner of GARB, and in 2008, the two organizations officially merged. Genetic Alliance is the world's leading nonprofit health advocacy organization committed to transforming health through genetics and promoting an environment of openness centered on the health of individuals, families and communities. This was an opportunity for GARB to build on Genetic Alliance's success and unique ability to infuse the healthcare system with individual, family and community perspectives. The Genetic Alliance board assumed governance, and the former GARB board became an advisory board. These additional resources also allowed GARB to hire a full-time director for the first time.

### GARB solution

By joining GARB, DAOs have the flexibility to procure the data and samples required for advancing research in their field. Member organizations own, govern and steward their collections, determining what will be collected, who will it be collected from and who will have access. In this model, there is a

### Box 1. Requirements analysis.

#### Registry

- Database is based on standard vocabularies and messaging
- Database backend is web accessible
- Software is not expensive to license
- Fields are controlled as much as possible to limit variability
- There is a mechanism for quality control
- Registry is browser based
- Participants and providers can enter data that can be reviewed before it is added to the database
- Images and files can be attached/uploaded
- Standard reports are available
- Audit logs are available

#### Biorepository

- Automated as much as possible with barcoded samples, including ordering, shipping and accessioning
- Storage for DNA, RNA, organs, tumors and tissue
- Centralized storage when possible
- Blood collection kits, tissue collection kits and buccal swab kits are provided
- Single or multiple kits can be produced, mailed, tracked and accessioned easily
- All state of the art storage techniques, guidelines and recommendations are followed and are iteratively improved over time
- Audit logs are easily accessible
- Additional genomics services are available as needed

continuum of sampling methods. In the case of PXE International, and several of the other rare conditions, virtually 100% of the individuals registered with the organizations (all cases known to the organization) participate in GARB. In other cases, specific individuals and samples are recruited for specific studies with distinct inclusion and exclusion criteria. Member organizations work closely with their scientific advisory boards, and all protocols are reviewed by the Genetic Alliance Institutional Review Board. GARB provides mentoring and training on biobank operations and the infrastructure described later.

### ■ Infrastructure

The majority of samples are stored locally at a site that GARB contracts for biorepository services and a clinical registry with web-based portals for data entry and management. Gene Logic (MD, USA) has provided these services to GARB, for the registry and general blood, DNA, tissue and organ harvests since 2006. Cell processing and cell line development have been provided by Rutgers University Cell and DNA Repository (RUCDR; NJ, USA) since 2003. Additional services are available upon request from Gene Logic and RUCDR. While the majority of samples are centrally stored at Gene Logic, GARB also has vendor relationships with biobanks in other parts of the USA, such as Rutgers, and in other countries such

as Belgium, South Africa, Italy and Germany, for projects where it was important not to take samples out of these countries. In 2008, Genetic Alliance entered into a strategic partnership with Private Access [103] to provide solutions for clinical trials matching and medical record integration through an individual's privacy directives. Many of the components described have been added over time and additional improvements are planned. Current vendors are listed in TABLE 2.

#### ■ Technical components

The Tissue Repository Information Management System (TRIMS) is Gene Logic's primary vehicle for clinical information management. The TRIMS implementation for GARB is an Application Service Provider model hosted and maintained by Gene Logic with several key components:

- The Tissue Repository Information Management System database is used by member organization administrators, through citrix access, to annotate and maintain clinical and sample data. TRIMS currently supports more than 185,000 records with thousands of standard fields and unlimited customizable fields for the collection of clinical information. TRIMS uses SNOMED CT as the controlled vocabulary for classification of disease and sample morphology, as well as internal standards to control the quality and consistency of entered data;
- Online clinical questionnaire system – this web-based component allows participants or providers to complete customized medical questionnaires and forms. Data entered to the questionnaire database is migrated to the GARB member organizations' TRIMS

databases daily. A clinical questionnaire administration system allows member organizations to assign, manage and approve completed questionnaires;

- Action request system – this web-based portal allows member organizations to request an action that should be performed by Gene Logic biorepository personnel, such as distribution of sample collection kits to participants or samples to researchers. It also provides activity and inventory reporting functionality;
- The Genesis™ Enterprise Software system – this system provides GARB members with extensive search capabilities tailored to the clinical and experimental data stored in the TRIMS warehouse. Genesis provides a collaborative, secure environment that incorporates integrated visualization tools that allow users to examine clinical data and sample attributes simultaneously and perform a wide variety of analyses;
- Data transfer/staging components manage the migration of data between the web portals, the TRIMS database and the Genesis clinical data mining module. Gene Logic provides the chain of custody information and audit tracking for all processes described.

#### ■ Donating data & samples to the biobank

Once a participant has been consented by the member organization, she or he is eligible to donate data or a sample. The participant's name, contact information and the type of kit requested (if a sample will be collected) are entered into the action request system by the member organization. This triggers Gene Logic to accession or register the participant into TRIMS, assemble the kit and send it to the participant. Each kit comes with all necessary components and customized instructions for sample collection. Once the sample donation is complete (in most cases a blood draw by a phlebotomist, nurse or physician, accompanied by a buccal cheek swab), the kit is returned to Gene Logic in a prepaid Fed Ex® mailer. GARB members also collect tissue samples from surgery and organ harvests after autopsy. Customized kits are available, and collection requires collaboration with the institution performing the procedure. Coordination with the local institutional review board, including those in other countries, is usually required. Gene Logic's biorepository receives

**Table 2. Genetic Alliance Registry and BioBank vendors and partners.**

Company	Services	URL	Refs.
Exam One	Contract phlebotomy services	www.examone.com	[112]
Gene Logic	Biorepository, TRIMS registry, Genesis data mining software, Clinical questionnaire interface	www.genelogic.com	[113]
NCBI	dbGaP	www.ncbi.nlm.nih.gov/gap	[114]
Private Access	Dynamic online consenting, clinical trial matching and medical records management	www.privateaccess.info	[103]
Rutgers University	Cell processing and cell line development	www.rucdr.org	[115]

*dbGaP: Database of genotype and phenotype; NCBI: National Center for Biotechnology Information; TRIMS: Tissue repository information management system.*

and accessions all incoming samples. The biorepository then processes and stores the sample according to the protocols agreed upon with GARB. Arrangements can be made to ship multiple kits (e.g., for patient outreach events) or for customized processing. Kit shipment and receipt can be tracked by the member organization within the action request system. For clinical data collection, the member organization sends a request to the participant, parent or provider to complete an online clinical questionnaire, and responses are migrated to TRIMS nightly upon approval by the member organization administrator.

### ■ Making data & samples available to researchers

Member organizations can leverage their collections to promote collaboration and attract new researchers to their field. GARB has developed protocols and material transfer agreements for release of data and samples. Each member organization, with their biobank oversight committee, determines who will have access to their collection. Deidentified data and samples are then released to approved researchers. This system provides researchers with timely access to data and samples that either do not already exist, or exist in fragmented collections split between multiple laboratories unable and possibly unwilling to collaborate. This is all accomplished while maintaining the highest standards of privacy and confidentiality and participant trust.

### ■ Impact on health

Utilizing this infrastructure, GARB members are accelerating translational research. Two groups have identified the gene associated with their condition [4–6], and PXE International has developed and licensed a diagnostic test [7], conducted an epidemiological study, a genotype–phenotype association study, and begun enrolling participants for a clinical trial to test a potential treatment. The National Psoriasis Foundation has just made the largest single collection of psoriasis and psoriatic arthritis samples available to researchers to further elucidate the genetics of this complex disease [104]. Another member is utilizing the infrastructure for adverse event reporting to the US FDA. Our members are collecting robust clinical data that is not currently being collected by other studies and are using the infrastructure for functional studies and biomarker identification. GARB is part of a paradigm shift, where DAO's are

driving participatory research, engaging participants within their community, and convening researchers to accelerate translation.

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### Lessons learned

The past 8 years have taught us the importance of continuing to assess the systems put into place and seek to iteratively improve GARB, through formal and informal landscape analysis, expert interviews and discussions with other biorepository and registry vendors. The most recent landscape analysis was published and includes a tool to assist DAOs in evaluating registry and biorepository vendors [8]. Our philosophy of mindful extensibility, ensuring that the system can be expanded in thoughtful ways, has helped us improve our solutions and make informed decisions about both vendors and features of GARB. Vendor selection is critical, and it is not enough to select a vendor on technology specifications. The vendor must understand the value of advocacy organization-driven research. The for-profit/not-for-profit partnership is often a delicate one to navigate and must be given attention to keep it productive.

In addition, we have learned that collectively, we are only as strong as our individual members. It takes a certain amount of organizational capacity and commitment to establish and maintain a resource such as a registry or biorepository. The leadership of the organization must support this research endeavor, and there must be dedicated personnel, volunteers or paid staff to manage the day-to-day operations. We have created an extensive application process for membership that is designed to assess the potential member's organizational health and support when entering this cooperative model. The biobank director interfaces with the potential and current member organizations and various partners and vendors, and provides training and support as needed to member organizations.

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### Conclusion

Genetic Alliance Registry and BioBank continually strives to provide the best registry and biorepository solutions for members, taking on new capabilities and technologies as they become available. GARB is working to establish a collaboration with the Database of Genotype and Phenotype to allow member organizations to deposit datasets in this public resource. GARB has entered into a formal partnership with Private Access, Inc. (CA, USA) to provide dynamic consenting, clinical trial matching,



and medical record integration to member organizations. Private Access uses technology that extends the current capabilities of internet-based search engines to include the ability for properly authenticated persons such as doctors, family members, researchers and others to search for highly confidential or sensitive personal information based on 'private access' rights that each individual can create to control who can, and cannot, see all or selected parts of his or her personal information [103]. PXE International is the first group to be initiated to the Private Access Suite of Solutions, and additional member organizations are expected to follow in 2011. GARB has begun to offer training to advocacy organizations about all aspects of the nuts and bolts of registries and biorepositories. This includes how-to guides, manuals, boot camps and other resources [105].

### Future perspective

Genetic Alliance Registry and BioBank 'proof-of-concept' model continues to flourish. We have been able to provide sophisticated technical solutions to advocacy organizations at a fraction of market cost, largely owing to cost sharing and the good will of our partnerships. Most importantly, we have developed a system

that allows our member organizations to concentrate on what is important – accelerating discovery for their communities. DAOs are already extensively involved in registries and biobanks, and more DAOs will likely be involved in the future. It will be important to have systems in place, such as GARB, to ensure the success of advocacy-driven research initiatives. Additional inquiries are required to determine the scope of advocacy-initiated biorepositories and registries, and their impact on disease diagnosis, management and treatment. GARB looks forward to extending this system to other conditions and communities, and using the cross-disease analysis capabilities of this system.

### Financial & competing interests disclosure

*Ms Terry is the President of Genetic Alliance BioBank. Dr Horn directs the Genetic Alliance BioBank. Ms Scott and Mr Terry serve on the advisory board of Genetic Alliance BioBank. Mr and Mrs Terry are the founders of PXE International. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.*

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### Executive summary

- Disease advocacy organizations (DAOs) are actively involved in biobanks and registries, collecting a variety of biological sample types and associated clinical data.
- There are numerous advantages for DAO involvement in biobanks and registries, including their connection to the community, extensive disease knowledge, and potential for ongoing stewardship.
- Genetic Alliance Registry and BioBank provides sophisticated infrastructure for advocacy organizations to establish and manage their biobanks and registries.
- Requirements and landscape analyses have been conducted to determine the best solutions for DAO biobanks and registries.
- Expanded DAO involvement in biobanks and registries will help provide additional resources to the scientific community.

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