

WELCOME TO
T1D EXCHANGE



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WELCOME



Dear Friends and Colleagues,

Welcome to the first T1D Exchange Annual Meeting.

Over the past twelve years I have been inspired by the dedication of the type 1 diabetes (T1D) community, from private and public charities, government, and regulatory agencies, to academic and commercial researchers, business leaders, clinicians, and people living with the disease. I've been impressed with the unwavering commitment to developing new devices and therapies designed to improve overall outcomes, quality of life, and glucose control on the path to cures for T1D.

Throughout this journey, as a funder and stakeholder in the T1D field, I've been frustrated by the efficiency and efficacy of the translation and development process. We have all worked hard to define critical questions and are often discouraged by the cost and the length of time it takes to operationalize projects, programs, and studies. It seems our greatest threats are time and capital – our organization was designed to address these challenges.

T1D Exchange is a living laboratory filled with data, experiences, and people touched by T1D. Our unique model drives efficiency and improves research outcomes by bringing together an integrated Clinic Network, Clinic Registry, Dynamic Biorepository, and the patient/caregiver community, Glu. Maintaining an active database of patients contributing clinical information, real-world insights, and biosamples allows us to present the T1D community opportunities to fulfill important research goals while providing the most comprehensive view of the disease. Our collaborations have proven the efficiency of our model resulting in significant time and cost savings.

We are pleased with our successes over the past three years and are excited to host this first meeting to share our accomplishments, insights, and engage you as T1D stakeholders in the future of the T1D Exchange.

All the very best,

A handwritten signature in black ink that reads "Dana Ball". The signature is fluid and cursive.

Dana Ball
CEO and Co-founder

T1D EXCHANGE: A research and development acceleration platform

T1D EXCHANGE RESEARCH CHARTER

BACKGROUND

T1D Exchange was conceptualized by the type 1 diabetes research and development community as a solution to mitigate barriers and inefficiencies for clinical and translational research. The Exchange was solely funded by The Leona M. and Harry B. Helmsley Charitable Trust from 2009 to 2013. In 2012 a nonprofit organization, T1D First was established to oversee final development and establish a sustainability plan to ensure financial independence through strategic partnerships with industry, government, and charitable organizations.

The overall mission to improve outcomes for people with type 1 diabetes has been a driving force in every decision during the Exchange development process. This mission has been broadly communicated to the type 1 diabetes (T1D) community. Accelerating human-based research and development (R&D) is a key element to achieving this mission. The Exchange has been designed to provide a novel environment that enables faster, high-quality clinical research, development, and healthcare delivery. The Exchange welcomes research ideas and proposals from academic, government, disease organizations, and industry investigators who contribute to achieving the long-term mission.

There are many unmet needs and unanswered questions in type 1 diabetes despite years of research and considerable inefficiencies and inequities in the care of people with T1D. In response to this need, T1D Exchange was conceptualized to provide a patient-centric, real-time health information exchange by supporting care, research, development,

and delivery of information and new treatments to improve outcomes and the lives of people with T1D. To accomplish this goal, the Exchange was envisioned to have three main components: a clinic-based registry to collect data on a large population of people with T1D; a website serving as an online community to provide support for people with T1D as an educational resource and to provide a framework for the conduct of innovative patient-centric research; and a biobank to store biosamples for use by researchers.

To date, most of the studies conducted through the T1D Exchange Clinic Network have been initiated by Exchange investigators. The focus initially was on collecting and analyzing data on the characteristics of Exchange registry participants and designing the annual data collection modules. The first biobank study, residual C-peptide in people with T1D, is currently underway. This study is serving to answer a critical research question while at the same time testing the Exchange biobank infrastructure to ensure seamless execution of future studies and sample procurement. GluU, the direct-to-patient research portal, is under development and the team is conducting surveys and planning future studies.

Now that the core elements of the Exchange R&D platform are operational, the team will be actively accepting requests from the T1D community and looking to establish partnerships that bring complementary resources together to drive toward the Exchange mission.

The Exchange team has established a charter that summarizes the key pillars of its target R&D portfolio, study evaluation criteria and a few examples of potential 2013 research priorities that it believes are critical in making progress toward the Exchange mission. If demand for R&D support exceeds the capacity of the Exchange, the team will use the criteria to prioritize requests. They will also look at ways to expand the scope of external requests, where possible, to align with the research pillars. The Exchange Strategic Alliances team will be proactively seeking partners that may be interested in collaboratively investigating a select group of research priorities.

EXCHANGE MISSION

Improve the lives of all people touched by T1D by facilitating better care and accelerating new therapies through a collaborative data collection and sharing network.

Scope of Research Efforts

T1D Exchange was built to provide a solid foundation and a community resource to encourage new ways of conducting human-based T1D research and development. This broadly includes both observational and interventional studies supporting diagnostic, monitoring, devices, therapeutics, and software solutions. Products being studied can be at any stage of development or already approved but could potentially benefit from additional research.

T1D DISEASE PATHWAYS

Beta Cell Mass & Function

STRESS

CYTOTOXIC DAMAGE

OXIDATIVE DAMAGE

INFLAMMATORY

Metabolic Control

Autoimmunity

Fig. 1

Given the large size of the Exchange population, priorities may be given to certain patient segments where the Exchange could be the only resource available to find enough subjects for a study.

T1D Exchange is a global initiative with its initial registry located in the U.S.

Research Pillars

T1D Exchange has been established in order to facilitate all aspects of T1D research, including the key T1D disease pathways that are currently the focus of most research and development efforts. In addition, the Exchange is including opportunities to drive complications research (Figure 1).

The Exchange research team believes there are four areas likely to improve the quality of life for people with T1D: improved T1D management tools, better insulin, novel biologic interventions, and repurposing of existing non-T1D therapeutics.

In addition to prioritizing research opportunities based on the type of intervention, the Exchange team also wants to ensure that studies are designed to produce safe and “actionable” results that translate into tangible improvements from which people with T1D can benefit as quickly as possible.

The team has established five research pillars that it believes are critically important to linking clinical research and R&D activities to meaningful results. Regardless of the research area, each study should be “optimized” around these pillars (Figure 2).

Improving Patient Outcomes. All Exchange projects should have a focus on improving outcomes for people with T1D. Outcomes should be considered broadly as some interventions may not affect HbA1c but result in other improved outcomes, such as quality of life, that may be important for people with T1D. Another area of opportunity may exist to convert observational studies into interventional studies or use the observational study as a run-in period and then convert to a potential interventional study. This may provide another path to accelerate clinical research.

Sharing Best Practices and Customized Solutions. While all people with T1D are treated with insulin, treatment plans and tools often vary significantly across the T1D community. T1D involves a unique challenge as people are often actively involved in modifying management in real-time. People with T1D, along with their care networks, figure out approaches that work best for them. This has resulted in a wide range of management practices that exist in silos and are not being shared with the broader community. The Exchange provides a vehicle to identify, evaluate, and share these approaches.

Optimizing Healthcare Delivery. The Exchange provides a platform to evaluate new methods of delivering healthcare. Mobile health is considered one of the most important potential changes to how people receive healthcare. This offers a unique opportunity to test and evaluate studies and healthcare solutions through the Exchange and Glu platforms.

Informing Policy Changes. With the rising costs of healthcare, people with T1D face more and more economic challenges when trying to cover the cost of their disease. In addition, when new devices and therapies are approved, access should be available for all eligible. It is important to consider what information should be captured during studies to best position diagnostics, monitoring devices, and therapies for health insurance reimbursement.

Discovery and Translational Research. Some studies may not address any of the first four pillars which are more directly tied to improving care or accelerating new therapies, but are critically important as they generate insight that could open the door for potential future breakthroughs. The Exchange is uniquely positioned to support these studies given access to well-characterized biosamples and trial design capabilities.

SUMMARY

The Exchange is committed to bringing new approaches to T1D research and development that will complement existing efforts and provide a new way for people with T1D to actively engage in finding better, customized day-to-day solutions while exploring disruptive approaches that could change the course of the disease over the long-term.

A critical element of the Exchange’s research charter is providing a highly collaborative environment that ultimately accelerates bringing better solutions for people with T1D as quickly as possible. Now that this environment has been established, the team is looking forward to this next phase in the evolution of the T1D Exchange vision.

EXCHANGE RESEARCH PILLARS

Improve the lives of all people touched by T1D by facilitating better care and accelerating new therapies through a collaborative data collection and sharing network.

IMPROVE

SHARE

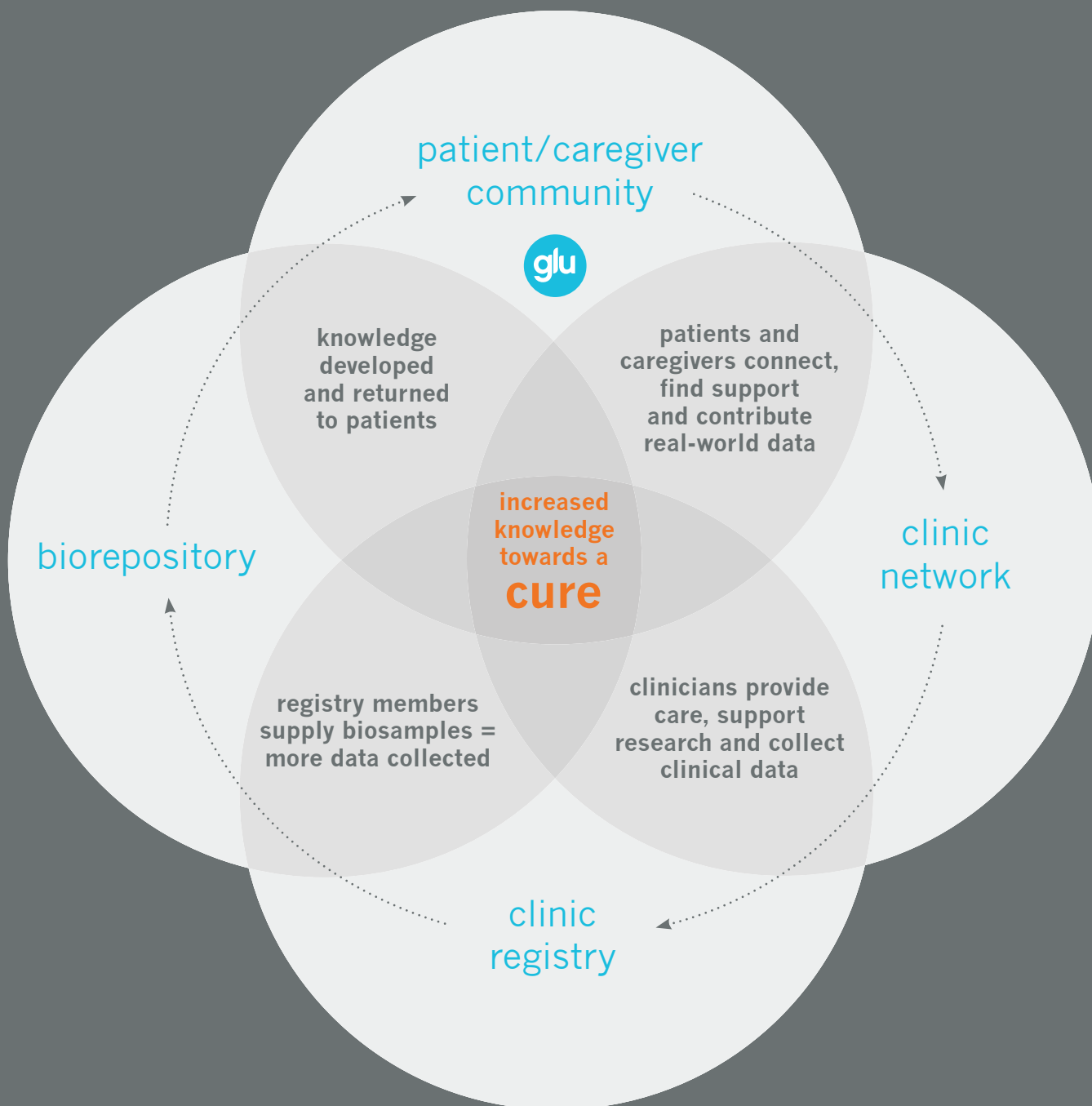
OPTIMIZE

INFORM

DISCOVER

Fig. 2

T1D EXCHANGE MODEL



The Glu online community of patients and caregivers support, empower, and educate one another while participating directly in real-time research and analysis. The platform is designed to accelerate research by amplifying the collective voice of those with type 1 diabetes and their caregivers—via discussions, surveys and studies, and engagement with the wealth of information found within the site. The crowdsourced “citizen science” that emerges from the Glu community offers researchers a fresh perspective to complement traditional methods of inquiry—a minute-to-minute, day-to-day view of how patients actually manage their diabetes.

Data are collected in a variety of ways from the site, ranging from simple polls that do not require IRB approval to complex studies that examine longitudinal data. In this way, the traditional models of research and healthcare delivery are enhanced by direct patient involvement in the discovery process and treatments related to their own health.

To date, Glu is 6,000 members strong—with more people joining daily. Not only have Glu’s citizen scientists shown a high level of interest in participating in studies but they are equally engaged in learning about study outcomes as they are communicated back to the community. The more patients and caregivers feel heard, the more they continue to speak up and become active participants in the search for new treatments and cures.

All aspects of Glu are managed at T1D Exchange’s Boston office by:

- A dedicated team with years of experience in type 1 diabetes, psychology, industry, marketing, communications, and community engagement who actively engage members each and every day.
- A committed team of clinical and market research experts who design, fine-tune, and analyze research approaches and results.

GLU RESEARCH IN ACTION

- The first Glu research abstract was accepted for presentation at the American Diabetes Association’s 73rd Scientific Sessions: Components of Glu, An Online Social Network for Engaging Individuals with type 1 diabetes in Research.
- Glu was used to query patients about injectable glucagon, as part of a study sponsored by an emerging biotech partner interested in improving usability of injectable glucagon through alternative modes of administration. In only ten days data were collected from 126 respondents. Findings were shared with the United States Food and Drug Administration (FDA) to illustrate the shortcomings in current modes of glucagon administration.
- Glu has conducted a number of surveys on topics such as hypoglycemia, healthcare providers, advocacy, food and nutrition, and T1D camps.
- Glu provides directional advice to key diabetes stakeholders as a result of organic discussions that take place within the community. For example, a Glu member initiated a discussion around a new CGM, sharing apprehension about using the device. Other members responded with personal experiences, comparative and contrasting input, and support. As a result, we shared an overview of the discussion with the device maker, including anonymous verbatims.
- Glu will host an observational study, currently in the planning phase, to examine the effect of duration of insulin pump infusion set use on glycemic control and total daily insulin dose in individuals with T1D who are older than 18 years or less than 10 years old.

support **empower** educate

CLINIC NETWORK

The T1D Exchange Clinic Network was formed to support the development of a large registry of adults and children with type 1 diabetes for the purpose of conducting multiple studies proposed by T1D Exchange investigators, and other researchers, patients, and companies.

The network is coordinated by the Jaeb Center for Health Research in Tampa, Florida, under the direction of Roy W. Beck, MD, PhD and consists of 65+ diabetes centers in 32 states, selected to provide a broad representation of geographic locations, practice settings (e.g. university, community, and managed care), and patient characteristics (e.g. age, race/ethnicity, socioeconomic status, and T1D management).

Of the 65+ clinical centers:

- 14 focus primarily on adult T1D patients
- 36 focus primarily on pediatric T1D patients
- 20 serve both adult and pediatric T1D patients
- 54 centers are institution-based
- 15 centers are community-based
- 1 center is managed care-based

LEVERAGING A POWERFUL CLINIC NETWORK

The Clinic Network helps researchers across industries improve the quality and efficiency of clinical trials and epidemiologic studies by centralizing contracting and IRB coordination so that studies move rapidly from concept to protocol development, initiation, and completion.

Because our T1D clinical centers follow more than 100,000 patients overall—and because we have email addresses for approximately 77 percent of the more than 26,000 individuals in the T1D Exchange Clinic Registry—we are able to identify eligible and interested participants for studies more efficiently than ever.

Most recently, clinic network investigators are focusing on two key areas of inquiry based on findings from Clinic Registry data:

- Assess factors associated with severe hypoglycemia in adults with T1D (rationale is based on the surprising finding of a higher-than-expected frequency of severe hypoglycemia in adults with longstanding T1D)
- Assess the value of Metformin in a randomized trial of adolescents with high body mass index (rationale is based in part on registry finding that a substantial number of adolescents with T1D are overweight or obese and have poor diabetes control)

OPPORTUNITIES FOR COLLABORATION

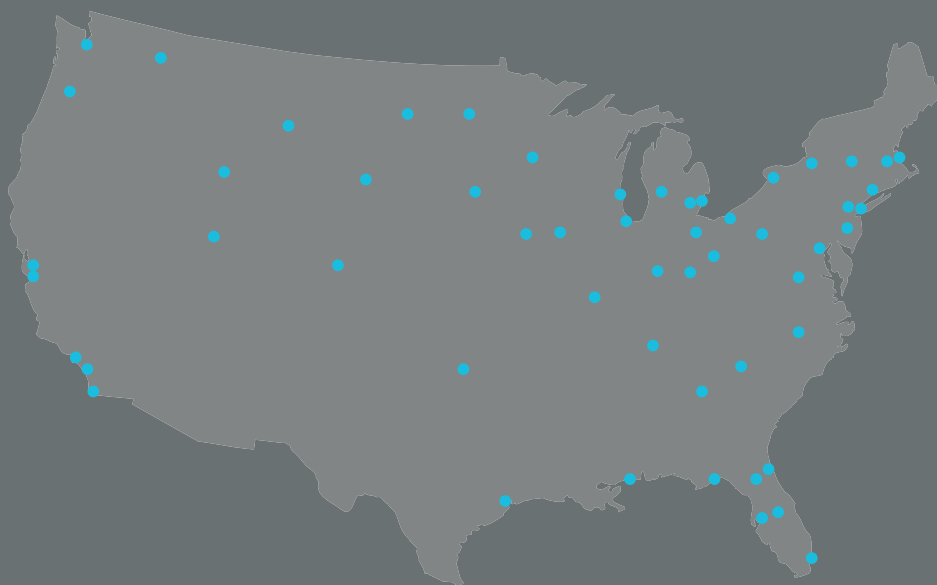
- Access to existing data
- Expansion of Clinic Registry (potential for >100,000 patients)
- Collection of new data to address a specific objective
- Collection of biosamples to address a specific objective
- Conducting investigator-run clinical trials
- Utilization of clinic structure for recruitment for external clinical trials
- Providing expertise on protocol design and statistical analyses

65+

CLINICS IN THE
T1D EXCHANGE
CLINIC REGISTRY

32

STATES WITH
CLINICS, INCLUDING
DAKOTAS, MONTANA,
AND IDAHO



The T1D Exchange Clinic Registry bolsters research and development projects and programs in type 1 diabetes by helping researchers characterize individuals in the United States with T1D, conduct exploratory or hypothesis-generating analyses, and identify participants for future clinical studies. Participants range in age, at the time of enrollment, from less than one year to 93 years, and have lived with the condition anywhere from less than one year to 79 years. More than 1,000 of these patients have had T1D for more than 40 years.

Clinic Registry Data Collection Process:

- A T1D participant questionnaire is completed by the participant or the parent of a participant (if younger than 13 years of age). The questionnaire addresses diabetes history, management, monitoring and complications, general health, lifestyle, family history, socioeconomic factors, and menstrual and pregnancy history.
- Additional information is then extracted from the participant's medical record. The medical record data reflect the diagnosis of T1D, T1D-related events (e.g. severe hypoglycemia and diabetic ketoacidosis), medications, medical conditions including diabetes-related complications, and laboratory results.
- Longitudinal data are collected annually. Participants complete a second questionnaire, similar to the first, to assess changes over time as well as to capture new data for specific research objectives.

Approximately two-thirds of data collected are the same for all participants whereas the remaining one-third can be targeted to address specific research objectives. For example, participants who use a continuous glucose monitor (CGM) may complete a list of questions regarding CGM use or a woman, who reports having been pregnant in the last year, may complete a set of questions about her outcomes and that of her child.

The goal of the Clinic Registry is to update key information from all participant medical records on an annual basis and target subsets with custom questions on an ongoing basis. Both of these tactics are vital to maintaining a current, relevant, view of diabetes management as treatments evolve and maintaining the ability to assess data over time.

The **T1D Exchange Clinic Registry**, representing the United States, is also collaborating with registries from 13 other countries in a study to compare glycemic control among individuals with T1D across countries in the International Collaboration on Glycemic Control that has been organized by the Scotland Diabetes Registry. Collaborations are in progress towards writing joint manuscripts with the DPV registry in Germany and Austria and with the Swedish Diabetes Registry.

KEY FINDINGS FROM THE CLINIC REGISTRY

Already, researchers have made compelling observations from the Clinic Registry data. As of May 2013, the data have been used for 33 abstracts that have been, or will be, presented at national or international meetings. Six manuscripts have been published, one is in process, three have been submitted for publication and are undergoing review, and ten others are in preparation. Below is a sampling of findings:

- 1 Most adults and children with T1D do not achieve goals for glucose control set by the American Diabetes Association.
- 2 Both children and adults who are under excellent glycemic control tend to manage their diabetes differently than those who are under poorer control. These management aspects include decisions on how much insulin to take, when insulin boluses are given, frequency of blood glucose monitoring, and exercise.
- 3 Racial and socio-economic disparities exist in use of insulin pumps and in glucose control. The data show that pump use is much more frequent in Whites than Blacks or Hispanics, a relationship that persists even after adjusting for socio-economic status. In addition, Blacks have higher HbA1c levels than Hispanics or Whites in both pump and injection users.
- 4 The frequency of home glucose monitoring is strongly associated with better diabetes control as measured with HbA1c.
- 5 Continuous glucose monitoring (CGM) is being used by only a small percentage of individuals with T1D, even though substantial benefit has been shown when CGM is used regularly. In addition, data indicate that among individuals who have used CGM, two-thirds stopped using it.
- 6 Severe hypoglycemia resulting in seizure or loss of consciousness occurs more commonly in older adults with longstanding T1D than has been appreciated.
- 7 In both children and adults, the rate of severe hypoglycemia is not higher in individuals with tight glucose control (e.g., HbA1c < 7.0%) than it is in individuals with poorer control (e.g. HbA1c > 8.0%).
- 8 Diabetic ketoacidosis (DKA), which occurs when there is insufficient insulin dosing and a resultant elevation in blood glucose and ketones, does not occur any more frequently in insulin pump users than injection users.
- 9 Adolescents and young adults with T1D have worse glucose control and are at higher risk for DKA than younger or older individuals with T1D.
- 10 Kidney disease (nephropathy) is a common microvascular complication of T1D, of which microalbuminuria (MA) is an early sign. The data show the relationship of MA with glucose control, diabetes duration, and blood pressure.

The T1D Exchange Biobank was established on the conviction that a large repository of biosamples from people with type 1 diabetes would help accelerate basic and translational research across academia and industry. The Biobank is coordinated by the T1D Exchange Biobank Operations Center (BOC) at the Benaroya Research Institute (BRI) in Seattle, Washington, under the direction of BRI Diabetes Research Program Director Carla Greenbaum, MD. The biosamples are stored at the Northwest Lipid Metabolism and Diabetes Research Laboratories at the University of Washington under the direction of Santica M. Marcovina, PhD.

By centralizing thousands of biological samples—together with clinical, demographic, and study-derived information—the Biobank aims to be a world-class resource for innovative research, and a catalyst for exchange of knowledge and collaboration. Specimen types include serum, plasma, white blood cells, DNA, and RNA. It is expected that meaningful data derived from the distribution of biosamples, along with standard clinical and demographic information, will become part of the Biobank, to be shared with other qualified researchers in a virtuous cycle of basic and translational discovery. A Scientific Review Committee of leading experts in diabetes research will review incoming sample requests from qualified researchers and industry partners.

BUILDING A LIVING BIOBANK

At this early stage of development, the focus of the Biobank is to develop its capacity to fulfill requests for samples. To date, most samples have been obtained as part of a standard collection in studies developed by T1D Exchange Clinic Network investigators. But the BOC is also building a “living biobank” in which samples are collected to fulfill a request for specimens not yet in storage.

To build the “living biobank,” T1D Exchange Registry members will be invited to join the T1D Exchange Biobank Study—enabling coordinators to contact participants to schedule a blood draw and collect additional information. As a first step, we have invited more than 1,500 Registry members over age 25 to be part of the T1D Exchange Biobank. DNA samples from these individuals will be distributed to NIH-sponsored researchers from the Children’s Hospital of Philadelphia who are studying the genetic causes of latent autoimmune diabetes of adults (LADA). The first specimens for this study were collected in February 2013. Next, we will invite the approximately 20,000 T1D Exchange Registry participants, who agreed to be contacted for research, to participate. This “living biobank” should prove to be a rich resource for academic and industry investigators alike.

THE BIOBANK VALUE ADD

Biosamples are currently being collected from approximately 1,000 T1D Exchange Clinic Network members as part of the Residual C-Peptide Study, the first large-scale, longitudinal study looking at residual insulin production in type 1 diabetics of varied age at diagnosis and disease duration. Results from the first year of the study are being presented at the American Diabetes Association’s 73rd Scientific Sessions in Chicago and will lead to a manuscript submission later this year.

The well-characterized samples from this large study have proven invaluable to researchers interested in understanding the immune mechanisms in T1D and markers of T1D progression. The BOC is piloting the sample distribution process by fulfilling requests for specific samples collected in the Residual C-Peptide Study by two academic institutions.

In addition to advancing the fundamental goals of the Biobank, the BOC has primary research interests in the association between beta cell function and clinical characteristics of individuals with T1D, as well as in biomarkers and their ability to predict progression of disease in individuals with T1D. Additional interests include the role of beta cell function during pregnancy and in extreme exercisers with T1D.

In 2014, the Biobank will begin accepting sample requests from the entire T1D community and is looking forward to working with industry and academic partners to fulfill these requests. To facilitate this process, interested companies and investigators will be able to search the Biobank database for specific clinical and phenotypic criteria via a web portal and submit a sample request electronically.

PATIENT CHARACTERIZATION



- LABORATORY TEST
- OCULAR HEALTH
- FAMILY HISTORY
- TIME OF DIAGNOSIS
- BLOOD SUGARS
- PAYER/INSURANCE
- DEVICE USE
- MEDICATION USAGE
- PREGNANCY
- INSULIN USE
- MEDICAL PROCEDURES
- PATIENT PHENOTYPE
- CO-MORBIDITY

BECOME A MEMBER

The T1D Exchange Membership Program is currently accepting new members. Your support will help us continue to maintain T1D Exchange and provide our participating organizations with ongoing access to our unique clinical and patient-experience data—as well as the tools and services needed to accelerate device and therapeutic development.

One-year Charter Membership

- Branding: Member organizations will be listed on the T1D Exchange website and their logos will be included in various print and electronic marketing collateral. Members will have the right to review all logo usage to ensure adherence to brand guidelines.
- Annual Meeting: Member organizations will be given two seats to the T1D Exchange Annual Meeting, which convenes stakeholders in the T1D community for a range of objectives.
 - Share research, development, and commercialization successes from the past year
 - Chart clinical studies that will advance T1D research goals for the upcoming year
 - Identify gaps in translational efforts
 - Facilitate opportunities to collaborate
 - Share interesting technology investment opportunities
- State of Diabetes Care Report: This annual T1D Exchange report highlights the latest findings from our studies and surveys.
 - Top 10 findings from the Clinic Registry and Biorepository
 - Key findings from the Clinic Registry, the Glu community, and the Biorepository
 - Overview of research priorities for the next year
- Quarterly T1D Exchange Newsletter: The T1D Exchange Newsletter highlights the latest findings from the Glu community and Clinic Registry members, especially the patient behavior reported via the Exchange's questions, surveys, polls, and studies.

PARTNER WITH US

T1D Exchange has developed a series of specialty services designed to address the needs of its members. Members are encouraged to partner with T1D Exchange on programs created to accelerate study design, patient recruitment, and enable co-creation opportunities that draw on real-world experiences from the patient community.

Exchange 360 Program

An Exchange 360 takes a comprehensive approach coupling real-world data from the Exchange Clinic Registry and the patient/caregiver community, Glu, to understand how people are living with T1D, how they manage their disease on a daily basis, and what their needs are, through behavioral and real-world research. The 360 program allows sponsors to work fluidly from patient insight to product development and access comprehensive data that can support regulatory or commercialization strategies.

Glu Co-Creation™ Program

Glu Co-Creation is a custom program that provides unparalleled insight into patient behavior that enhances partner productivity from discovery to treatment. The program leverages the patient/caregiver community, Glu, to solicit feedback in real-time in an effort to improve products and deliver better outcomes. For example, Glu Co-Creation enables our partners to understand patient response to CGM devices, pumps, and insulin therapies.

Clinical Trial Service

Our Clinical Trial Service offers a rich, centralized resource for study needs that draws from the Clinic Network, the Clinic Registry, and the Biorepository. Additionally, our centralized contracting and coordinated IRB enables expedited protocol design and accelerated recruitment rates.

CONTACT US



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