Management and integration of diverse data types in Type 1 Diabetes research

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T1D Research Unit

**Mission:**

Pursue a translational research approach to finding new antigen-based immunological and vaccine treatment advances for type 1 diabetes (T1D)

Established in 2012 and headed by Matthias von Herrath, MD

Unit consists of ~20 researchers focused on innovative pre-clinical validation and optimal clinical implementation of known assets rather than on primary discovery
Type 1 diabetes (T1D)

Type 1 diabetes is an autoimmune disorder that develops when the body’s immune system destroys insulin-producing beta cells in the pancreas. As a result, the pancreas stops producing insulin or cannot produce enough insulin on its own.

- Immune response-driven disease
- Polygenetic – over 50 (and counting) genes involved.
- Cause unknown – in addition to genetics, environment may be a major contributor
- Much of what we know mechanistically comes from studies in mice
T1D in Humans

- Approximately 80 children and adults are diagnosed with T1D every day in the U.S.
  - 85% of people living with T1D are adults
  - T1D prevalence in the U.S. among people <20 yrs old rose by 23% between 2001 & 2009
- The rate of T1D incidence worldwide among children >14 yrs old is estimated to increase 3% annually
- About 80% of individuals with T1D have no associated family history
- No gender bias in humans
- No known cure

www.JDRF.org & www.ADA.org
Current Standard of Care

• Type 1 diabetes is a life-long condition that is treatable with **daily** insulin injections, in conjunction with healthy eating and regular exercise.

• Diabetic complications do exist that can increase the risk of problems with your feet, eyes, kidneys, nervous system, or heart.
Complications to finding a successful treatment for type 1 diabetes

- Successful intervention after diagnosis may not be possible
  - Few insulin-producing beta cells remain at diagnosis
  - Cytotoxic T-cells remain present in the pancreas
  - No justification for strong immunosuppression when disease can be ‘managed’ with insulin therapy
Complications to finding a preventive intervention for type 1 diabetes

- Primary at-risk populations are juveniles and young adults
- Lack of definitive susceptibility markers
- Prevention trial challenges:
  - Higher level of trial scrutiny for juveniles
  - Difficult to enrol at-risk patients
  - Safety concerns may be undermining clinical trials
  - Costly and lengthy
Challenge:
An ideal prevention for T1D should have optimal efficacy, patient benefit, and low side-effects.

- Our approach to this challenge:
  - Focus on antigenic therapies already validated in concept
  - Develop robust animal models to validate efficacy and evaluate biomarkers
  - Leverage longitudinal studies to improve biomarker detection in humans
  - Investigate biologics for local suppression of inflammation without systemic side-effects
  - Evaluate combination therapies
Summary of our approach to T1D intervention

Our strategy has four principal cornerstones

- Biomarkers to optimize human dosing
- Close cooperation with key stakeholders at an early stage
- Development of large animal models for tolerance validation
- Careful step-wise clinical strategy (proof of concept trials)
Translating from scientific strategy to systems and infrastructure

Biomarkers:
- Animal and clinical sample management
- Biomarker assay integration
- Analytical, statistical, and visualization systems

Animal Studies:
- Animal care & colony management
- Observational studies
- Sample & assay integration
  Analytics & visualization

Collaboration:
- Data sharing with internal & external partners
- On-demand reporting and visualization

POC Trials:
- Human trial regulatory compliant systems
- Longitudinal and cross-sectional observational studies

All components seamlessly integrated
Infrastructure drivers and considerations

- **Clean slate opportunity** – new scientific outpost 5000 mi from our parent research organization pursuing a novel approach to T1D
- **Ease of use and simplicity** – every researcher needs to interact with the systems in some capacity
- **Add value for researchers** – critical for people to see tangible benefits for their specific work tasks
- **Process and workflow centric** – flexibility to define and customize specific workflows based on unique project and experiment needs
- **Data mobility** – integration of systems, export and sharing of data, etc. The success of data mobility depends on good APIs and/or open data sources.
With a focus on data management

A clearly defined data strategy for each project & site-wide data management goals focused on comprehensive data visibility, simplified data entry and access, and cross-study integration is fundamental to our site.

• Good data management practices begin with clearly defined needs:

  • At the research center level: Data consistency & completeness, analysis methodologies, data integration, & data management; data management systems must meet the needs of the entire site so that experiments & studies can be combined for meaningful longitudinal and meta analysis.

  • At the department level: Needs defined based on types of research conducted (human, animal, in-vitro biology, etc.) focusing on relevant data from materials (compounds, subjects, samples, sample processing, etc.) & from specific assays conducted; all data sources & types must be identified & managed cohesively.

  • At the project level: Identification of project-specific data generated that must be captured; processes & methods to capture & manage data must meet the project’s needs & must be simple to use.

• Buy-in at all levels is critical for success.

  • Key for buy-in: there must be demonstrable value for everyone involved.
LabKey Server – Anchoring our data management infrastructure

- Core to the T1D research unit:
  - Day to day study management. The ability of LabKey to manage & organize experiments & studies while they are being conducted
  - The flexibility of LabKey’s database & data handling capabilities
  - The ability to perform cross-study comparisons

- Simple & flexible data upload for a variety of data types including:
  - Observational data
  - Plate based assays (e.g., Luminex, ELISpot)
  - Flow Cytometry

  *Customizable* reports

- Simple views to quickly understand what is in the system & streamlined methods for preparing data for further analysis
T1D Data Management Infrastructure
Freezer Management – FreezerPro

- Web-based freezer management system
- Flexible and customizable
- Granular permission model
- GLP & HIPPA compliance
- Simple to use barcoding & printing
### Freezer Management Integration

- Samples registered in the FreezerPro database are automatically imported into the appropriate study for use in uploading assay data.
- This simplifies the assay data-association process.
- LabKey-developed feature utilizing the FreezerPro database API.

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• Web-based colony management system
• Similar look and feel to FreezerPro (same company)
• Customizable alerts
• Flexible reporting
• Mobile device support (iPad)
Mouse Colony Database Integration

In a study, mouse colony information from the colony management system, ezColony, is automatically imported as mice are registered to the study.

This integration uses LabKey’s ETL facility to maintain the data feed.

Query snapshots are used to create study datasets from the study query.
Analytics and Visualization Tools Integration

- Ability to quickly and easily export data to our primary analytical tools is paramount.
- LabKey’s flexibility with creating custom data grids, SQL queries, & linking external schemas allows up to easily generate the data shapes required by our analytical tools.
LabKey’s Built-in Analytics and Visualization

![Graphs and data visualizations showing trends in data over time.](image-url)
Managing Complex Animal Studies

- Primarily prevention & intervention animal studies
- Typically >100 animals per study
- Studies run for ~30 weeks
- Thousands of observational data points collected for each study
- Users interacting with data at different levels & in different systems

- LabKey Study Module
- Custom developed worklogs & templates
- Real-time work management system
- More details tomorrow at the LabKey User Workshop
Longitudinal Biomarker Studies

- Proof of concept animal model studies
- Longitudinal human studies of at risk patients
- LabKey Study Module
- Integration with sample management database
- Flow, ELISpot, FluroSpot assay integration
- Custom query, data grids, R-query to simplify external analysis and visualization

Data aggregation and data mash-up analysis

- Need ability to roll-up & combine datasets:
  - Global animal colony diabetes incidence
  - Cross-study control and treatment group analysis
  - Cross-species biomarker correlation
  - Therapeutic comparative analysis & overlay
Our goal is to universally prevent type 1 diabetes

Strategy for a cure

- Biomarkers to optimize human dosing
- Close cooperation with key stakeholders at an early stage
- Development of large animal models for tolerance validation
- Careful step-wise clinical strategy (proof of concept trials)
Acknowledgements

T1D Research Unit Key Contributors

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