

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

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# Novo Nordisk Research Center T1D Research Unit

- ***Mission:***

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

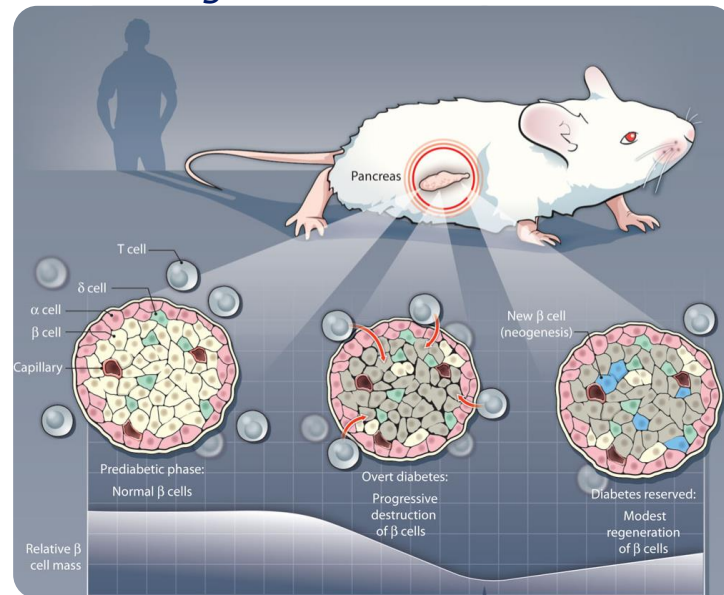
- Established in 2012 and headed by Matthias von Herrath, MD
- Unit consists of ~20 researchers focused on innovative pre-clinical validation and optimal clinical implementation of known assets rather than on primary discovery



# 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



Chong & Bell. 2012. *Sci Transl Med.* 4(133).

# 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



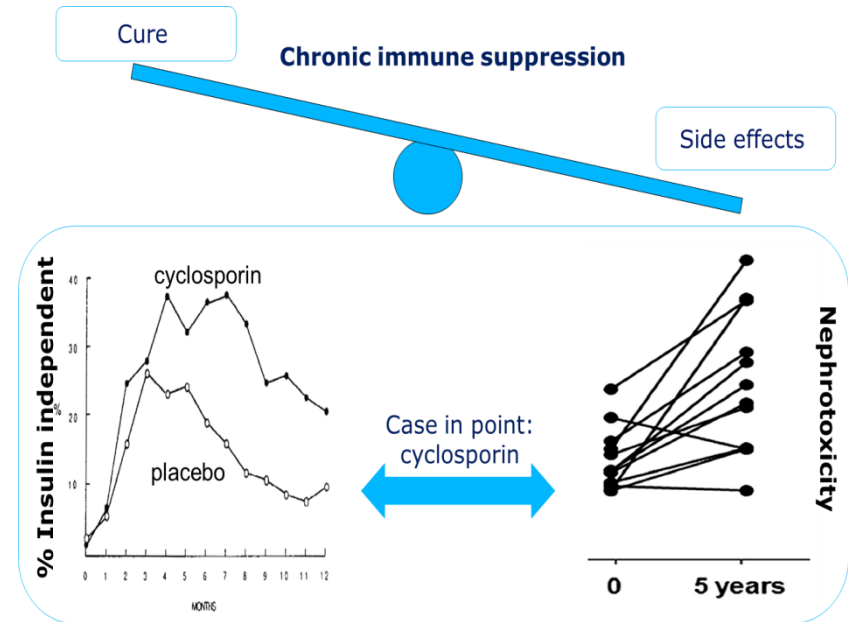
## Current Standard of Care

- 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

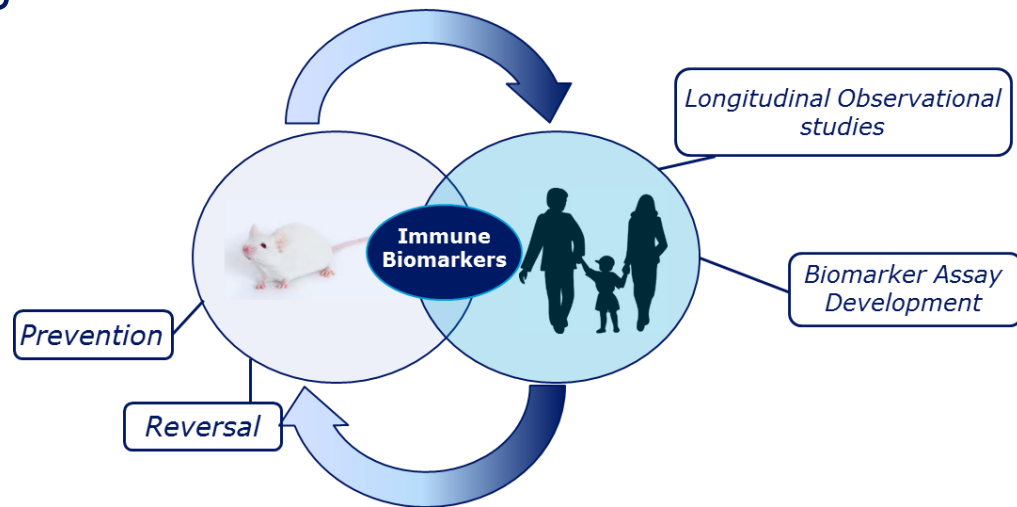


# Challenge:

***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



# 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*

**All  
components  
seamlessly  
integrated**

## 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*

# 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

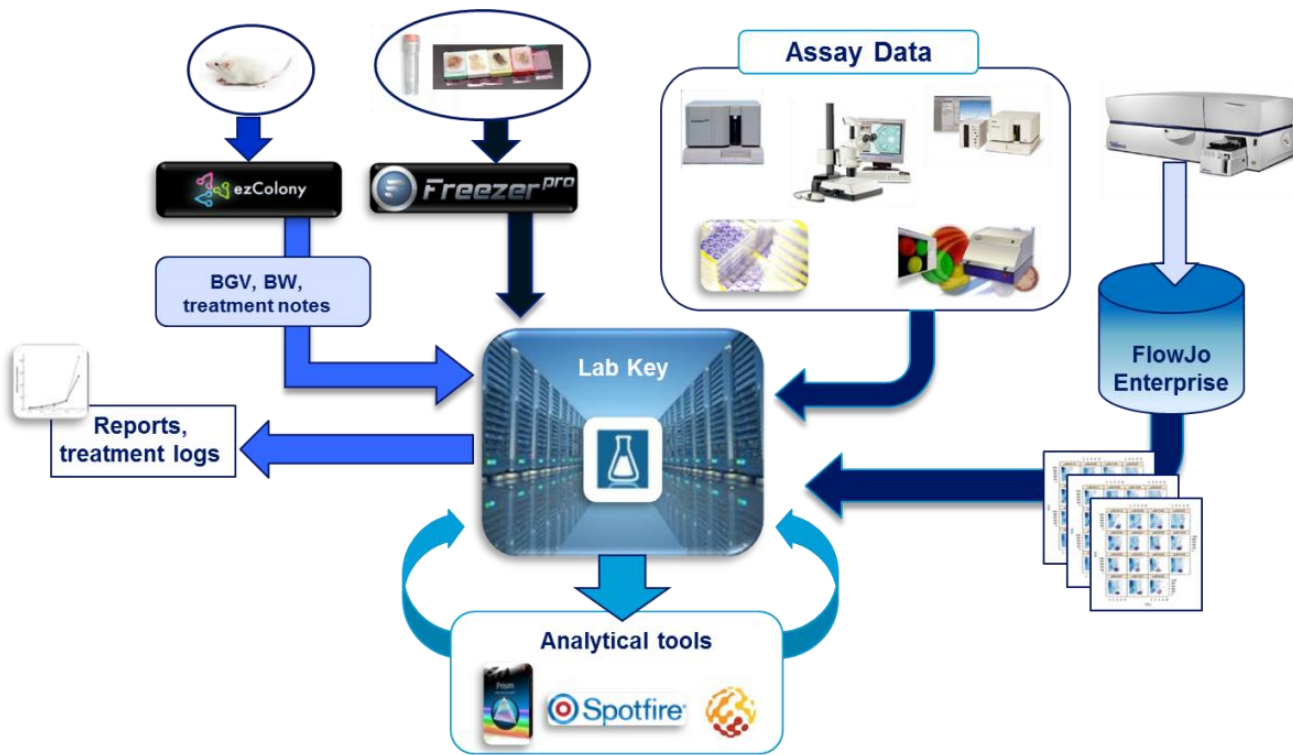
*A **clearly defined** data strategy for each project & site-wide data management goals focused on comprehensive data visibility, simplified data entry and access, and cross-study integration is fundamental to our site.*

- 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

The screenshot displays the FreezerPro web-based freezer management system. The interface is divided into three main sections:

- Left Panel:** A hierarchical tree view showing the freezer structure. It includes 'T1D Freezer Farm (Mezzanine)', 'T1D -20 Freezers', 'T20-1 - Donnie', 'T20-2 - Watson', 'Shelf 1', 'Shelf 2', 'Shelf 3', 'Open Space', 'Rack A' (with boxes 1-20), 'Rack B', 'Shelf 4', and 'Shelf 5'. 'Box 13' is selected.
- Center Panel:** A grid representing the freezer wells. The grid has columns 1-9 and rows A-I. The cell at row H, column 2 is highlighted in blue, indicating the selected sample. A status bar at the bottom of the grid reads '81 vial(s) in 81 wells'.
- Right Panel:** A detailed view of the selected sample, RD79. It includes:
  - ID: 34812**
  - Position:** H / 2
  - Mouse Serum ( )**
  - Barcode:** 1069667
  - RFID Tag:** 355AB1CB00001000011023
  - Total number of RD79 vials in all freezers:** 1
  - Created:** 03/07/2014
  - Updated:** 03/07/2014
  - Notes:** A section with icons for adding notes, printing, and other actions.
  - Metadata:**
    - Date:** 07/15/2013
    - Protocol IACUC:** TBL-02
    - ELN#:** 22362-006
    - Experiment Name (TBL):** Strain NOD
    - Strain:** C44
    - Mouse ID:** RD79
    - Treatment Group:** Isotype Control 25 mg/kg x 6 doses
    - Species:** Mouse
    - Sample Type (T1D):** Serum
    - Notes:** 22 weeks of age, BGV 110
    - Freezing Operator:** AARD

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

# Freezer Management Integration

Mouse ID	Primary Type	Global Unique Id	Derivative Type	Fr Level2	Fr Level1	Fr Position	Fr Container	Freezer	Quality Control Flag	Quality Control Comments	Vial Count	Latest Comments
RD574	Mouse Serum	1071299	Mouse Serum	Rack A	Shelf 3	1	Box 19	T20-2 - Watson	false		1	BGV 600
GR556	Mouse Serum	1071301	Mouse Serum	Rack A	Shelf 3	2	Box 19	T20-2 - Watson	false		1	BGV 600
GR556	Cryomold	1071327	Cryomold	Rack A	Shelf 2	22	Box 13	T80-1 - Homer	false		1	BGV 600
RD574	Cryomold	1071328	Cryomold	Rack A	Shelf 2	19	Box 13	T80-1 - Homer	false		1	BGV 600
GR553	Mouse Serum	1071460	Mouse Serum	Rack A	Shelf 3	3	Box 19	T20-2 - Watson	false		2	BGV 180, 2 weeks post-onset
RD571	Mouse Serum	1071709	Mouse Serum	Rack A	Shelf 3	5	Box 19	T20-2 - Watson	false		2	BGV 192, 2 weeks post-onset
RD569	Mouse Serum	1071742	Mouse Serum	Rack A	Shelf 3	6	Box 19	T20-2 - Watson	false		2	BGV 215, 2 weeks post-onset
BL515	Mouse Serum	1071743	Mouse Serum	Rack A	Shelf 3	7	Box 19	T20-2 - Watson	false		2	BGV 139, 2 weeks post-onset
BK517	Mouse Serum	1071744	Mouse Serum	Rack A	Shelf 3	8	Box 19	T20-2 - Watson	false		2	BGV 416, 2 weeks post-onset
BL510	Mouse Serum	1071745	Mouse Serum	Rack A	Shelf 3	4	Box 19	T20-2 - Watson	false		1	BGV 600
AQ555	Mouse Serum	1071847	Mouse Serum	Rack A	Shelf 3	9	Box 19	T20-2 - Watson	false		1	BGV 600
AQ557	Mouse Serum	1071848	Mouse Serum	Rack A	Shelf 3	10	Box 19	T20-2 - Watson	false		2	BGV 542, 2 weeks post-onset
RD575	Mouse Serum	1071849	Mouse Serum	Rack A	Shelf 3	11	Box 19	T20-2 - Watson	false		1	BGV 600
AQ555	Cryomold	1071850	Cryomold	Rack A	Shelf 2	28	Box 13	T80-1 - Homer	false		1	BGV 600
RD575	Cryomold	1071851	Cryomold	Rack A	Shelf 2	2	Box 13	T80-1 - Homer	false		1	BGV 600
BL510	Cryomold	1071854	Cryomold	Rack A	Shelf 2	25	Box 13	T80-1 - Homer	false		1	BGV 600 (1/2 pancreas 1/2 spleen in OCT)
GR553	Cryomold	1071855	Cryomold	Rack A	Shelf 2	5	Box 13	T80-1 - Homer	false		1	BGV 600 (1/2 pancreas 1/2 spleen)
GR553	Mouse Serum	1071856	Mouse Serum	Rack A	Shelf 3	12	Box 19	T20-2 - Watson	false		2	BGV 600
GR546	Cryomold	1071895	Cryomold	Rack A	Shelf 2	8	Box 13	T80-1 - Homer	false		1	BGV 600, 1/2 pancreas, 1/2 spleen in OCT/Formalin

- 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

# Mouse Colony Management – ezColony

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

ezColony Enterprise™

Rooms, Racks And Cages

Home | Rack K

Search: Live search requires a minimum of 2 characters.

	A	B	C	D	E
7	🟡	🟡	🟡	🟡	🟡
6	🟡	🟡	🟡	🟡	🟡
5	🟡	🟡	🟡	🟡	🟡
4	🟡	🟡	🟡	🟡	🟡
3					
2					
1					2

Cage: KA4 (10000324)  
Cage Type: Holding Cage

Mouse ID	Protocol	Source	DOA	Notes	Genotypes
<input type="checkbox"/> AQ265	JYCI01	JAX	08/21/2013		
<input type="checkbox"/> BL263	JYCI01	JAX	08/21/2013		
<input type="checkbox"/> BK165	JYCI01	JAX	08/21/2013		
<input type="checkbox"/> RD263	JYCI01	JAX	08/21/2013		
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<input type="checkbox"/> AQ266	JYCI01	JAX	08/21/2013		
<input type="checkbox"/> BL264	JYCI01	JAX	08/21/2013		
<input type="checkbox"/> RD264	JYCI01	JAX	08/21/2013		

Animals And Animal Lines

Reports And Audit

Settings And Preferences

Displaying Animals 1 - 8 of 8

Navigation: NNRC Vivarium > ABL-2 Holding Room > Rack K > Cage A / 4

# Mouse Colony Database Integration

Dataset: Mouse Demographics, All Visits >

## Mouse - AQ339

[PREVIOUS MOUSE](#) > [NEXT MOUSE](#) > [SEARCH FOR 'AQ339'](#) > [CUSTOMIZE VIEW](#) >

### 5002: Mouse Demographics

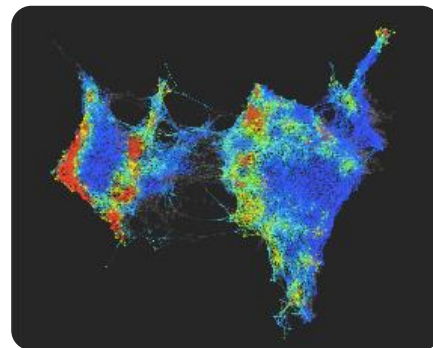
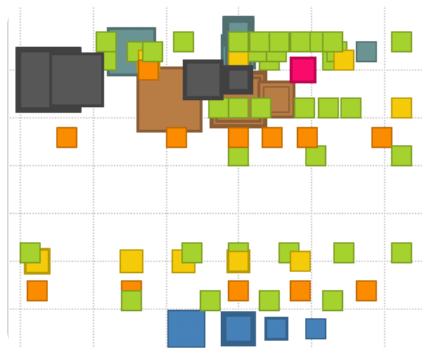
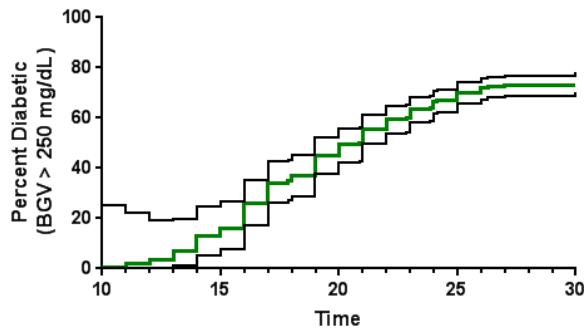
[EDIT DATA](#) >

Animal ID	1439
Protocol	TBL02
Date of Arrival	10-16-2013
Date of Birth	08-20-2013
Age	29 weeks
Sex	f
Mouse Strain	NOD
Mouse Strain Descr	NOD/ShiLTJ - JAX stock#001976
Genotypes	[]
Source	JAX
Block	NNRC Vivarium
Room	Holding Room 1
Rack	Rack E
Cage	EB5
Notes	
Date of Death	
Reason for Death	

- 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

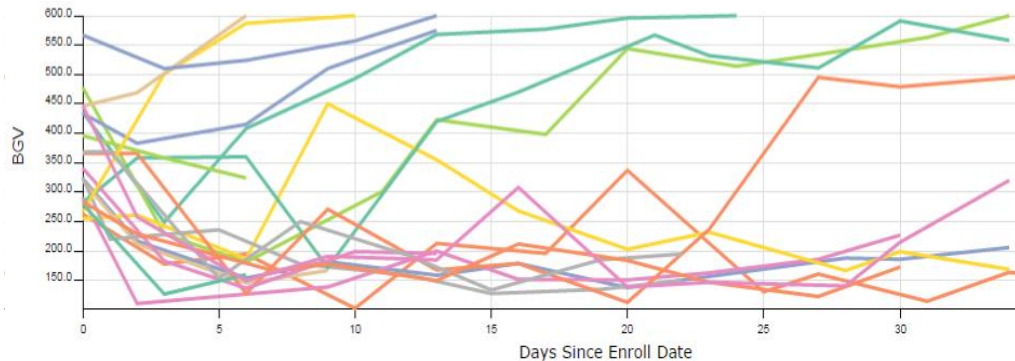
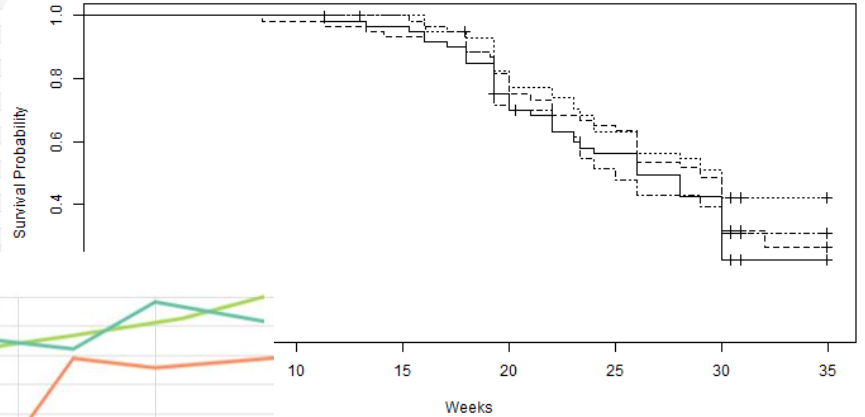
# Analytics and Visualization Tools Integration

- 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

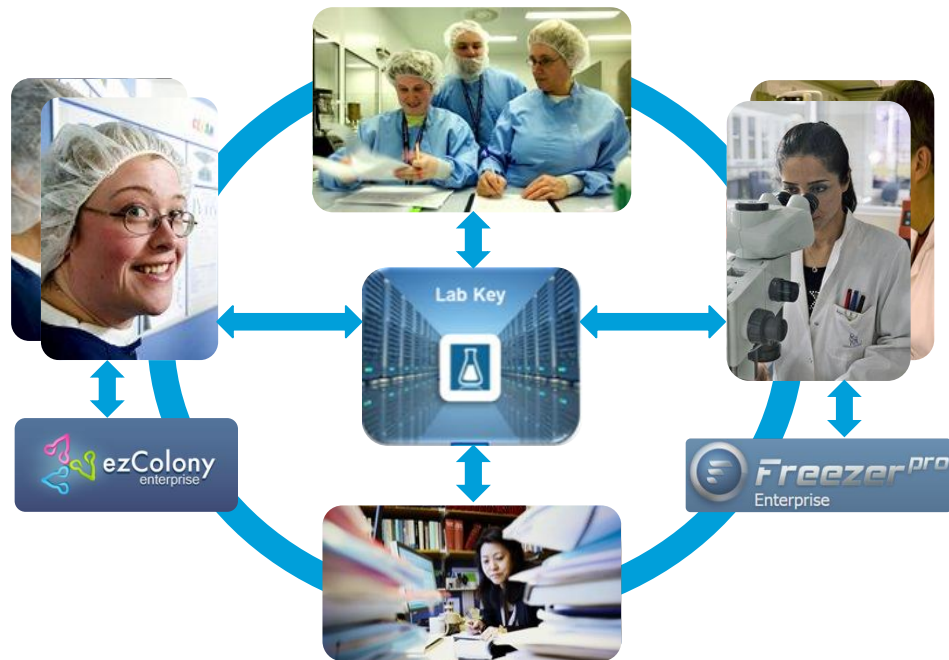
Mouse ID	Treatment Group	Age At Onset	Days Post Onset																																		
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
RD692	Group 1	10.4	277	304		204	127								162			397			359			468				477	566					506			
BL663	Group 1	12.4	420	367		451		571							506																						
BL670	Group 1	13.0	472	472		510		500																													
BL646	Group 1	15.0	292	381		308		421			393					554			507					507			495			525		512				500	
RD670	Group 1	15.4	455	485		429		562			486				500																						
RD664	Group 1	16.0	399	337		497		566			581					596							500														
RD676	Group 1	16.0	363	355		518		432			576					504			592				571				500										
BK640	Group 1	16.4	272	279		520		530			449					573			565				508												500		
RD686	Group 1	17.0	379	434		335		410			459					481			471					500													
RD691	Group 1	17.0	259	277		184		200			163					165			199							299										259	
GR646	Group 1	17.0	352	345		427		492			523					558			500																		
GR656	Group 1	18.0	429	351		308		485			521					500																					
GR663	Group 1	18.4	326	337		298		439			543					560						569				555										500	
AQ679	Group 1	19.0	405	486		253		321			383					188			210							363										378	
GR642	Group 1	20.0	473	412		426		500																													
RD677	Group 1	20.1	303	291	178		222			144					170			175																			
AQ673	Group 1	20.4	294	309		268		368			400					494			469						539												
BL676	Group 1	21.4	296	324		333		316			545					396																					
BK652	Group 1	22.4	368	251		139		414																													
BK656	Group 1	22.4	273	256		298		151																													
GR658	Group 1	23.0	411	420		458																															





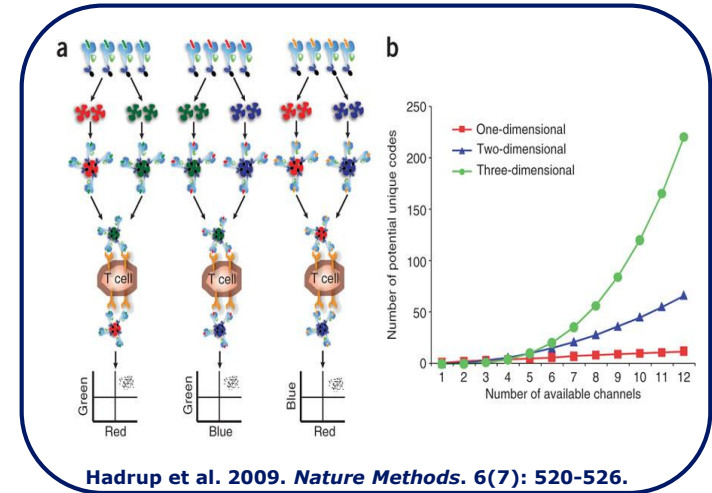
# Managing Complex Animal Studies

- 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



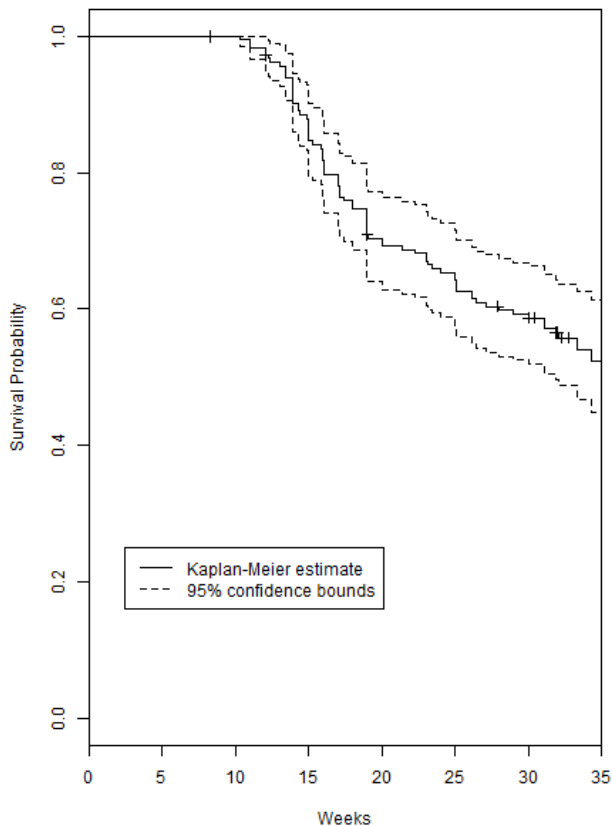
# Longitudinal Biomarker Studies

- 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

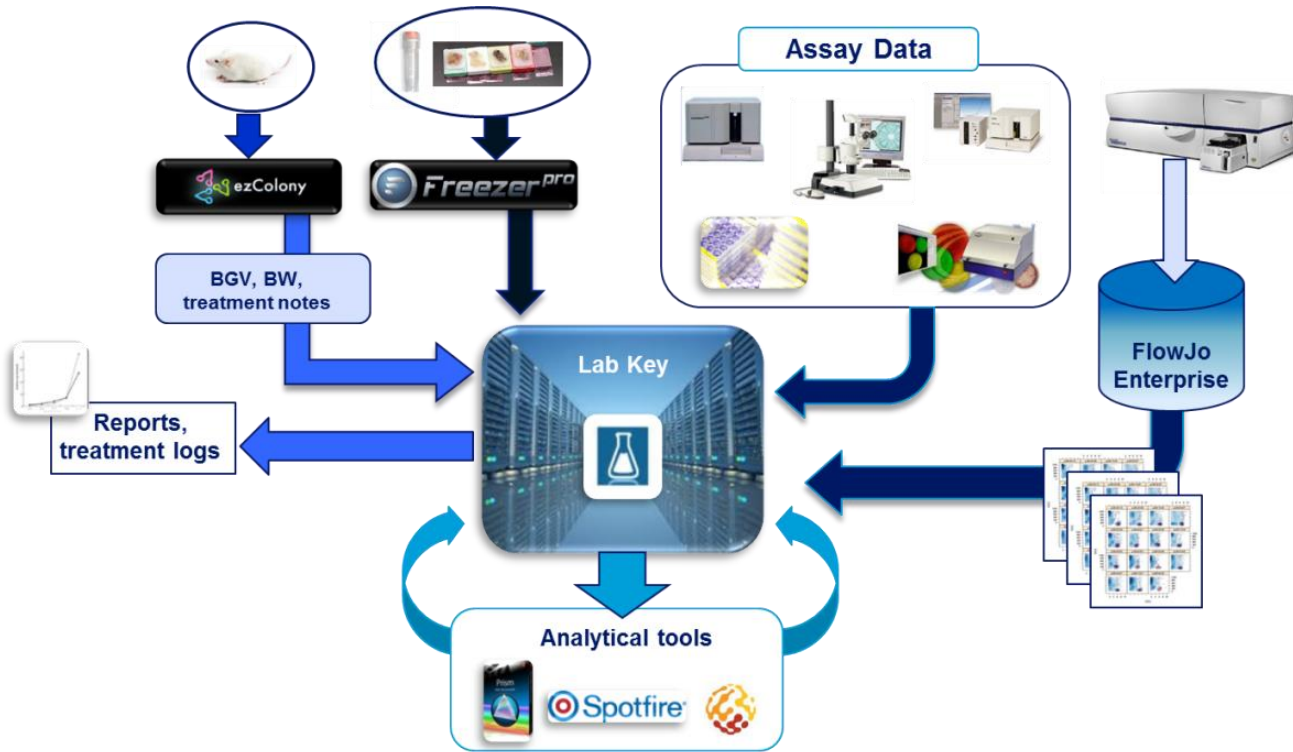


# Data aggregation and data mash-up analysis

Untreated Colony Incidence since Oct 2012



- 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

**Biomarkers to optimize human dosing**

**Close cooperation with key stakeholders at an early stage**

**Strategy for a cure**

**Development of large animal models for tolerance validation**

**Careful step-wise clinical strategy (proof of concept trials)**



# Acknowledgements

## T1D Research Unit Key Contributors

Matthias von Herrath

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Tamar Boursalian

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Jay Chaplin

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