National Institute of Diabetes and Digestive and Kidney Diseases

Pre-Application Webinar

RFA-DK-22-018

Human Islet Research Network (HIRN) Pancreas Knowledgebase Program (PanKbase)

(U24 - Clinical Trial Not Allowed)

Dec 6, 2022

National Institute of Diabetes and Digestive and Kidney Diseases

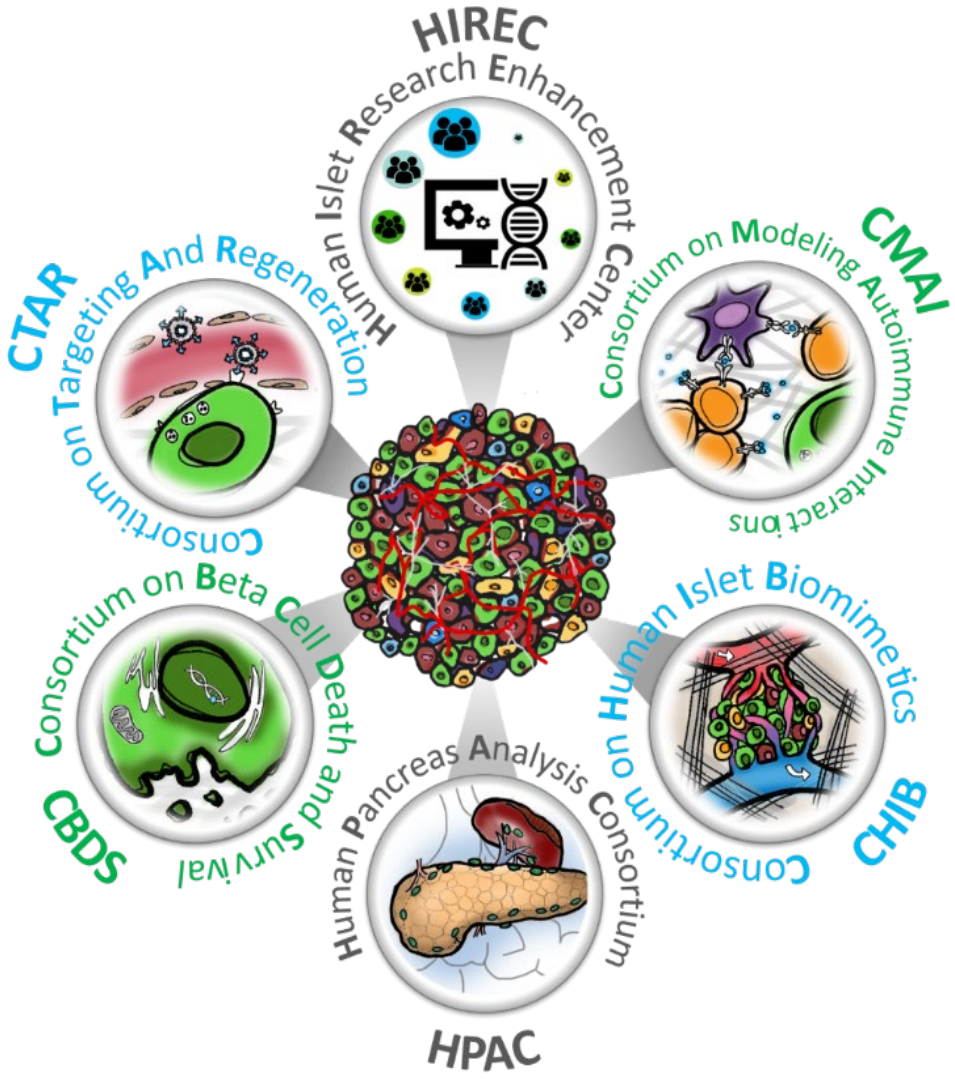
Agenda

1. Presentation ~ 30 min
   - HIRN overview
   - The purpose of PanKbase, a new program of HIRN
   - Design of PanKbase
   - FAQ and answers
2. Open Q&A ~30-45 min
3. Breakout groups (interested people can find collaborators)

** Slides & a FAQ document will be shared through the registration site

** webinar is recorded for NIDDK internal review

Human Islet Research Network (HIRN, https://hirnetwork.org/) overview



Established: 2014

Mission of HIRN:

To better **understand** how beta cells are lost in *human* **Type 1 Diabetes** and to find **innovative strategies** to protect or replace functional beta cell mass in people living with diabetes.

5 research consortia: CBDS, CHIB, CMAI, CTAR, HPAC
1 coordinating center: HIREC

>200 investigators, from ~85 institutes

Human Islet Research Network (HIRN , https://hirnetwork.org/): components

5 research consortia:

- **CBDS: Consortium on Beta Cell Death & Survival,** to discover mechanisms of cellular stress or dysfunction that may contribute to the development of autoimmunity, to identify specific biomarkers of the asymptomatic phase of T1D,….
- **CHIB: Consortium on Human Islet Biomimetics,** combining advances in beta cell biology and stem cell biology with tissue engineering technologies to develop microdevices that support functional human islets.
- **CMAI: Consortium on Modeling Autoimmune Interactions,** developing innovative approaches to model basic aspects of human T1D immunobiology using novel in vivo and in vitro platforms.
- **CTAR: Consortium on Targeting and Regeneration,** to increase or maintain functional beta cell mass in T1D through targeted manipulation of islet plasticity or engineered protection of beta cells from immune-mediated destruction.
- **HPAC, Human Pancreas Analysis Consortium,** investigating the physical and functional organization of the human islet tissue environment, ...

The coordinating center : Human Islet Research Enhancement Center (HIREC)

1 resource generation program, Human Pancreas Analysis Program (HPAP, reside in HPAC)

+ PanKbase

PURPOSE OF THE NEW PROGRAM

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The outstanding challenge in T1D: how is it initiated?

Status

- After decades of extensive research, we still do not fully understand the T1D etiology

Understanding how T1D is initiated is critical for

- Early detection
- Effective biomarkers
- Effective prevention, onset-delay, and intervention approaches

Many un-answered questions

- What are the triggering events?
- How an initial insult leads to perpetuating destruction?
- how the on-site immune cells and islet cells interact?
- The interplay between pro-inflammatory and immune regulatory pathways? The checkpoint?
- The role of metabolic disturbances?
- Effective biomarkers? Biomarkers for subtypes and heterogeneity? Composite biomarkers?
- …

The need of new thinking & approaches

Manuela Battaglia[1] and Mark A. Atkinson[2]

The Streetlight Effect in Type 1 Diabetes

Diabetes 2015;64:1081–1090 | DOI: 10.2337/db14-1208

- The underlying cause of T1D still not known
- No “cure”
- Clinical studies and trials since the early 1980s mostly negative
- Most efforts follow the “safe” research trend of existing dogmas
- Little **pioneer efforts involving unconventional thoughts**
- Need biomarkers that clearly marks the initiation
- Need to develop **combination type of therapy**

The opportunities: emerging, potentially catalyzing

- **<u>Human Big Data</u> at the site and around the time of T1D initiation**
  — becoming available and growing: HIRN and other T1D consortia, investigator generated

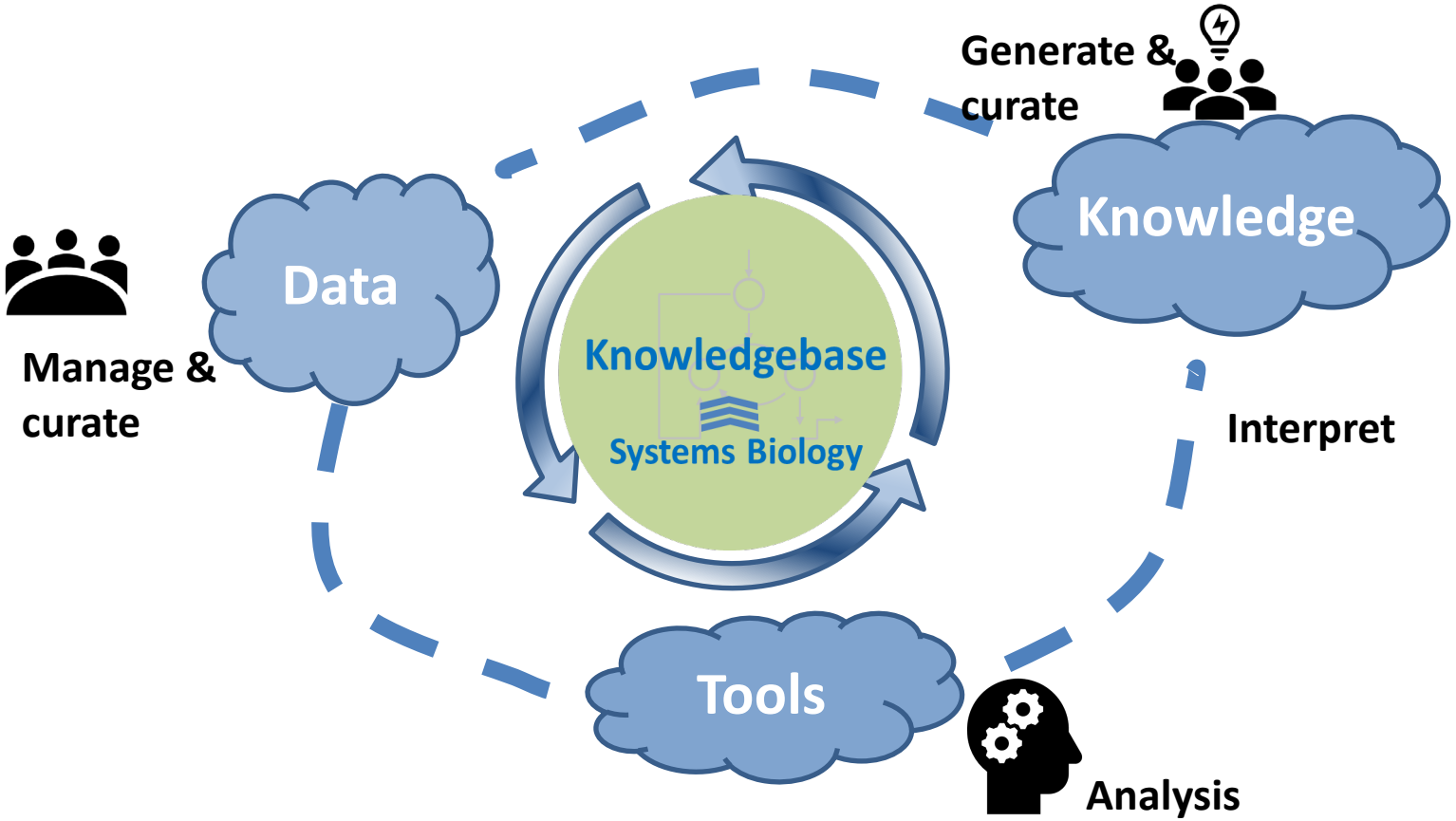
…

- **Extensive relevant <u>knowledge & insights</u> scattered in literature**
  — time to integrate and use them to guide data modeling

- **Abundant advanced data science <u>tools and technologies</u>**
  — can transform the utilization & integration of data and knowledge

- **System Biology**
  — specializes in integration and multi-disciplinary approaches

The gaps in leveraging these opportunities



- Data, tools, and knowledge often locate at different places
- Require different expertise to handle
- The research community could use assistance in linking them, in order to leverage the opportunities

Purpose of the new program

To develop a centralized resource (PanKbase) of the human pancreas for diabetes research that will provide :

- **Access to deeply curated high-quality datasets**
- **Knowledge in computable forms**
- **Advanced data science tools and workflows**
- **An open science platform to**
  - **Connect data, tools and domain knowledge in T1D research**
  - **Enable multidisciplinary collaboration in T1D research**
  - **Accelerate data-driven discovery and innovation, and biomarker and therapeutic target development**

DESIGN OF PANKBASE

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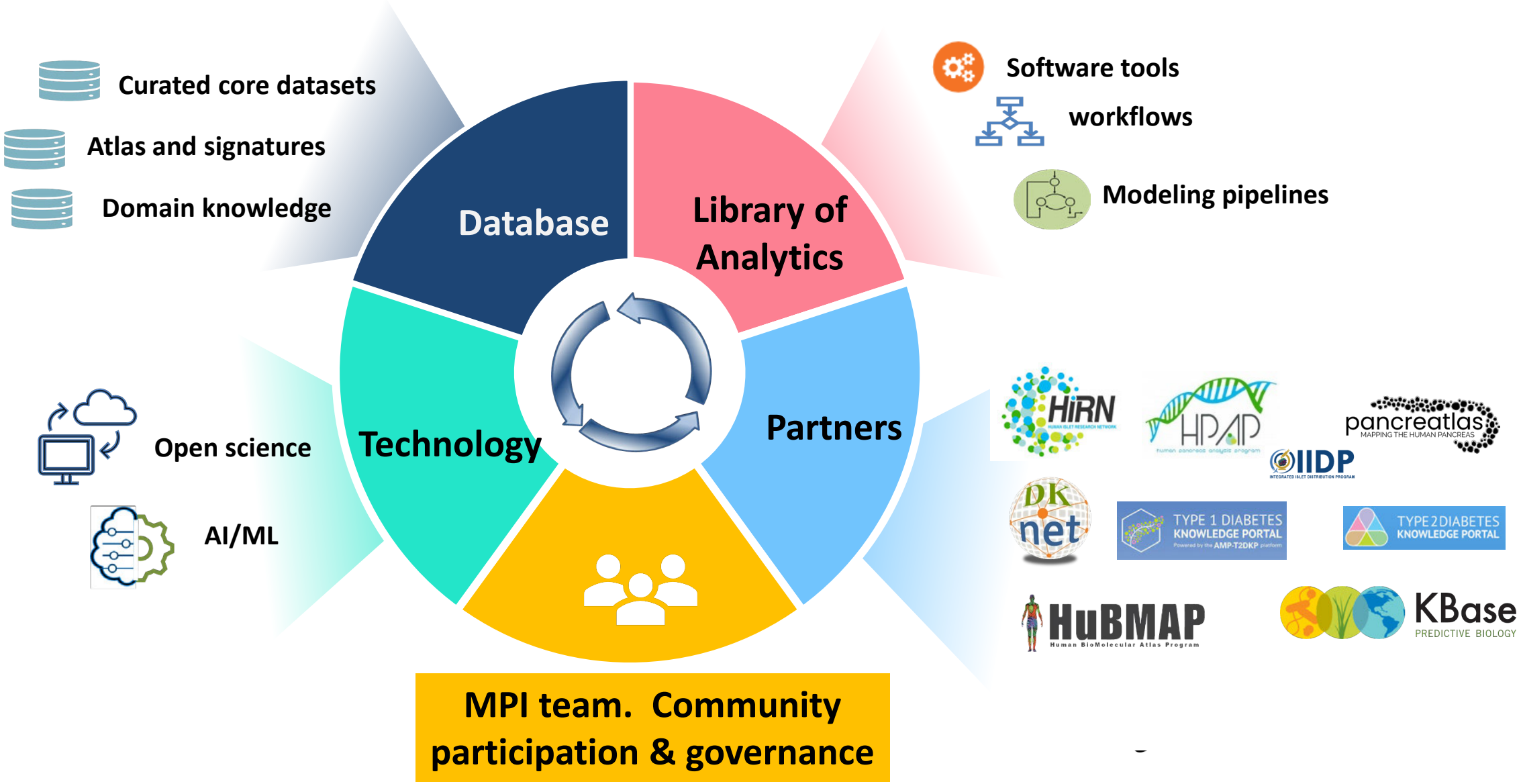
Major components of PanKbase



Designing principles of PanKbase

- **The grand challenge questions in T1D initiation as the driving force and organizing guide**
- **An open science platform for collaboration & innovation**
- **Forward thinking in science**

  Systems thinking beyond individual gene/molecule-centric approaches
- **Forward thinking in technology**

  In cloud, AI/ML ready, technologies supporting open collaboration, FAIR practice and Rigor and Reproducibility
- **Infrastructure building**

  will serve as a model to investigate solutions to community needs in data sharing & utilization, analytical development, collaborations, and innovation and discovery leveraging Big Data

ANSWERS TO SOME QUESTIONS

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MPI team & budget

A minimum of 2 PDs/PIs

The contact PI should be a computational biologist, and the research team should include one islet biologist with extensive experience in human type 1 diabetes pathogenesis as a MPI.

The team should have

- Demonstrated track record of developing community resources such as biomedical data repositories and knowledge portals
- Expertise in modern data science technologies and platforms
- Deep appreciation of the important research questions in diabetes especially in T1D
- Experience in outreach to research communities by effectively communicating and engaging with scientists from diverse backgrounds
- Serious commitment

No requirement regarding seniority of the PDs/PIs

Budget

$3M TC/year for 5 years

Foreign collaborators

Allowed

https://grants.nih.gov/grants/guide/rfa-files/rfa-dk-22-018.html :

Section III. Eligibility Information

- **Foreign Institutions**
- Non-domestic (non-U.S.) Entities (Foreign Institutions) **are not** eligible to apply.
- Non-domestic (non-U.S.) components of U.S. Organizations **are not** eligible to apply.
- Foreign components, as defined in the *NIH Grants Policy Statement*, **are** allowed.

MPIs need to be domestic

Under "**Eligible Individuals (Program Director/Principal Investigator)"**

"The application is required to be submitted as a multiple PD/PI application with a minimum of 2 PDs/PIs, all of whom must have an appointment at a domestic institution. The contact PI should be a computational biologist, and the research team should include one islet biologist with extensive experience in human type 1 diabetes pathogenesis as a MPI. Scientists employed solely by foreign institutions may not serve as one of the PD(s)/PIs of the multiple PD/PI team, although they may be included in the application as collaborators/co-investigators, consultants or other significant contributors.

Cloud computing & Sustainability

Cloud:

Under "Section I. Funding Opportunity Description"

An open science platform

"The platform will be in cloud and friendly for AI/ML application…"

- NIDDK does not have preferences of cloud platforms. Need to follow the NIH's latest Data Sharing and Management policy (https://sharing.nih.gov/data-management-and-sharing-policy).
- Initial hybrid platform is allowed
- NIDDK is exploring/experimenting cloud computing in other consortia and community resources

Sustainability:

- A sustainability plan is required (by the FOA)
- NIDDK is investigating and experimenting with sustainability models

OPEN Q & A

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Thank you

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