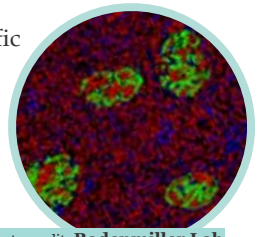
CONSORTIUM ON BETA CELL DEATH AND SURVIVAL (CBDS)

DETECTING AND HALTING BETA CELL DESTRUCTION IN TYPE 1 DIABETES

The autoimmune process that destroys pancreatic beta cells in the early stages of type 1 diabetes begins in a silent mode (that is, before presenting with notable symptoms of the disease). Tests to measure for autoantibodies—specific immune system components in the blood that identify people who are at high risk of developing type 1 diabetes—do not reveal whether a person's beta cells are working properly or whether destruction is occurring at the time of the measurements. This is clearly a key and practical gap in predicting the course of autoimmunity in individuals who are progressing toward diabetes, and who would likely benefit from future therapies to halt the destructive process. Blocking destruction while it is still in its initial stages would be optimal. To bridge this gap, the Consortium on Beta Cell Death and Survival (CBDS) is searching for new biological markers ("biomarkers") of beta cell health, stress, and death that can be easily measured in blood, urine, or saliva, and that can be detected at the earliest onset of autoimmune attack. The Consortium is also developing state-of-the-art tools to study single beta cells or islets in the pancreas at all stages of the autoimmune process. This research should uncover how beta cells initially become stressed and ultimately die in response to the autoimmune reaction, lead to the discovery of improved blood tests for predicting type 1 diabetes, and point to new targets for drug development. Additionally, the CBDS has added three new teams to bring fresh perspectives, expertise, and technologies in pursuit of these important goals.



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University of Zurich

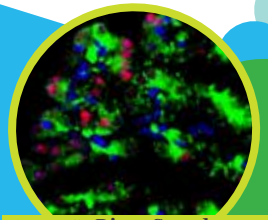

Photo credit: **Diane Saunders, Marcela Brissova, Alvin Powers**
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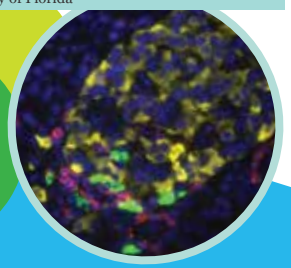

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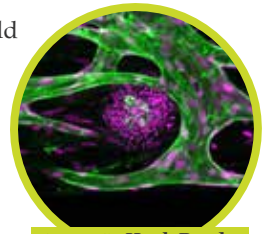
CONSORTIUM ON HUMAN ISLET BIOMIMETICS (CHIB)

MODELING HUMAN PANCREATIC ISLET STRUCTURE, FUNCTION AND ENVIRONMENT

In the human pancreas, insulin-producing beta cells live in islets—small communities of hormone-producing cells, including other cells such as alpha, delta, and PP cells, that all work together to control blood sugar levels. The islet is supported by a network of blood vessels, nerves, and extracellular matrix scaffolding. Recreating this complex islet community in the laboratory would offer several significant benefits. For example, it could improve the ability of beta cells derived from pluripotent cells to work as well as beta cells do in the body. Also, mimicking the islet environment in the lab would help researchers better understand how beta cells are lost to autoimmunity, and it would provide a much-needed platform for testing potential new drugs to protect or restore beta cells in people with or at risk of diabetes. The Consortium on Human Islet Biomimetics (CHIB) combines advances in beta cell biology, pluripotent cell biology, microengineering (building miniature machines or structures—some so small that they might not be visible to the human eye), and related technologies with the goal of developing state-of-the-art microdevices that support three-dimensional islet structure, function, and survival in the lab. CHIB investigators are making excellent progress in creating such devices that will advance the goals of the entire diabetes research community.



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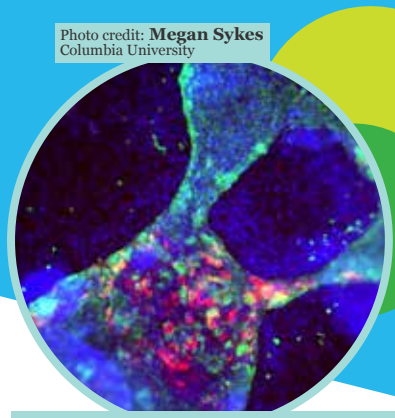
University of California, Irvine

HiRN
HUMAN ISLET RESEARCH NETWORK



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Columbia University

CONSORTIUM ON MODELING AUTOIMMUNE INTERACTIONS (CMAI)

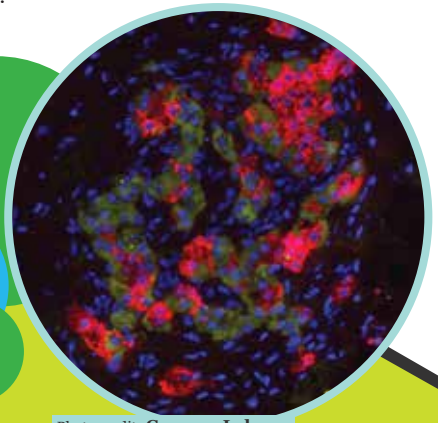
WHY AND HOW DOES THE IMMUNE SYSTEM TARGET BETA CELLS IN TYPE 1 DIABETES?

The autoimmune process that destroys insulin-producing beta cells, leading to type 1 diabetes, begins silently. Clinical symptoms of type 1 diabetes are only obvious after autoimmunity is well underway and the majority of beta cells have been lost. During the progression of autoimmunity, scientists can detect changes in the immune response in the blood of individuals known to have genetic (inherited) risk of type 1 diabetes, but it is much more difficult—if not impossible—to observe what's happening deep within the pancreas where the beta cells reside. For these reasons, it is challenging for researchers to track down the precise molecular and cellular mechanisms of beta cell injury in human type 1 diabetes—and to find ways to intervene in the process. The Consortium on Modeling Autoimmune Interactions (CMAI) is facing this challenge by incorporating human genes, beta cells, and immune cells into mouse and cell models that more accurately mimic human type 1 diabetes than traditional models. CMAI investigators are working together within the Consortium and with investigators across the HIRN Network to refine these models and use them to gain key insights into type 1 diabetes.

CONSORTIUM ON TARGETING AND REGENERATION (CTAR)

REGENERATING INSULIN-PRODUCING BETA CELLS IN PERSONS WITH TYPE 1 DIABETES

Developing strategies to replenish or protect the pancreatic beta cells that are lost or being lost in people with type 1 diabetes (or in those with insulin-dependent type 2 diabetes) is a high priority for diabetes research. Beta cells resulting from such regenerative strategies must be able to survive the autoimmune processes that have destroyed most or all original beta cells and also produce insulin in response to a person's diet and activity—exactly as beta cells work in those without diabetes. The Consortium on Targeting and Regeneration (CTAR) is tackling these problems head-on by learning how to change non-beta cells into insulin-producing cells, designing methods to selectively target molecules to the pancreas that can help replace or regrow beta cells, and developing new drugs to block beta cell death. CTAR investigators are capitalizing on the highly collaborative Network environment to make exciting new advances towards their goal of beta cell regeneration to prevent or reverse diabetes.



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Oregon Health & Science University

HPAP
human pancreas analysis program

HUMAN PANCREAS ANALYSIS PROGRAM (HPAP)

MAPPING THE NATURAL HISTORY OF TYPE 1 DIABETES IN UNPRECEDENTED DETAIL

In the past decade, there have been dramatic advances in our ability to phenotype and molecularly profile human cells and tissues. The Human Pancreas Analysis Program (HPAP) consortium is applying these new technologies to study cells and tissues relevant to the beta cell loss of type 1 diabetes with unprecedented resolution, including at the genomic, epigenomic, protein, and functional levels. The consortium is employing state-of-the-art technologies to determine all aspects of pancreatic islet cell and immune cell biology as they pertain to type 1 diabetes, including in juvenile organ donors. HPAP investigators are profiling both the endocrine and immune systems with multiple modalities. They will make the vast data accumulated available through the open-access resource database (PANC DB), an online database that will be developed through the project. The extensive and high-quality datasets will be made available to HIRN and the diabetes research community-at-large for further discovery.

HIRN
HUMAN ISLET RESEARCH NETWORK

HUMAN ISLET RESEARCH NETWORK

The Human Islet Research Network (HIRN) was established in 2014 to support research that will allow us to better understand how human beta cells are lost in type 1 diabetes, and to accelerate the development of innovative strategies to protect or replace functional beta cell mass in diabetic patients.

HIRN is made up of five consortia:

- Consortium on Beta Cell Death and Survival (CBDS)
- Consortium on Human Islet Biomimetics (CHIB)
- Consortium on Modeling Autoimmune Interactions (CMAI)
- Consortium on Targeting and Regeneration (CTAR)
- Human Pancreas Analysis Program (HPAP)

HIRN investigators continue to develop and apply state-of-the-art tools, reagents, and technologies to advance type 1 diabetes research. HIRN activities are supported by a Coordinating Center and a Bioinformatics Center located at the City of Hope (Duarte, CA).

Connect with us

hirnetwork.org