

Plan Overview

A Data Management Plan created using DMPTool

Title: Mechanisms and Targeted Control of Pancreatic β -Cell Antioxidant Response

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Project abstract:

Type 1 Diabetes (T1D) is an autoimmune disease caused by progressive destruction of the insulin producing β -cells. The loss of immune tolerance is a result of predisposing genes and environmental factors. However, the exact trigger of autoimmune attack is currently not understood. During the development and progression of T1D, β -cell oxidative stress is a key contributing factor to β -cell dysfunction and destruction. For many years it was thought that β -cells were completely destroyed in individuals with T1D. Recently, this dogma has been challenged by the observation of residual insulin positive β -cells in individuals with long-standing T1D. Similarly, in the nonobese diabetic (NOD) mouse model for T1D, there is a subpopulation of β -cells that are able to withstand prolonged immune attack. These data suggest there is a population of β -cells that are able to adapt and survive during conditions of high stress. To build on these findings, the central goal of this proposal is to define pathways to promote β -cell survival and protection against T1D. I **hypothesize** that *rapid activation of the antioxidant*

response reduces β -cell ROS to repress islet immunogenicity during T1D pathogenesis. I will test this hypothesis through two specific aims. Experiments in **aim 1**, will investigate how β -cell selective loss of NRF2 contributes to the development of autoimmune diabetes. In **aim 2**, I will identify the mechanism controlling β -cell ROS mitigation in early T1D pathogenesis. Completion of these aims will determine the functional role and mechanism of β -cell adaptive redox response *in vivo*. Importantly, this work will identify novel targets to prevent β -cell destruction under diabetogenic conditions, and tools developed and tested as a part of this work can be used in future studies to target therapeutics or imaging probes to the β -cells. These studies will also positively impact my career. Both a comprehensive understanding of islet function in early diabetes pathogenesis and the use of cutting-edge techniques will enable me to develop as a scientist and set me on a trajectory to make real and lasting impacts in the field of diabetes research. This F31 award entails a 2-year training plan designed to achieve 4 main objectives: 1) build a strong understanding of techniques and concepts in diabetes research, 2) train in the generation and use of targeted nanoparticles and pharmacodynamics for diabetes research, 3) train in oral and written presentation of research findings, including grant preparation, and 4) train in the use and handling of mouse models for diabetes research. In addition, the applicant will benefit from the outstanding and collaborative research environment provided by the Center for Diabetes and Metabolic Diseases at the Indiana University School of Medicine. Her training will also benefit from a mentoring and advisory committee consisting of a diverse team of carefully selected and established NIH funded investigators. In summary, the proposed studies and training objectives will provide the applicant with a fertile training environment in which she can become a versatile independent researcher and develop an understanding of β -cell physiology.

Start date: 04-29-2022

End date: 04-30-2024

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Mechanisms and Targeted Control of Pancreatic β -Cell Antioxidant Response

Data sharing plan

How do you plan to provide access to your data?

To increase access to the published research that has been funded, we will deposit peer-reviewed or pre-print manuscripts (with linked supporting data where possible). All the relevant scientific information that derived during this project will be made available to the general scientific community for non-commercial/non-profit uses. Unpublished information and/or resources developed in the course of this project could be made available to interested parties upon request to the Principal Investigator, in writing, or by email. Our lab will reserve the right to request authorship on publications using this reagent. This policy is consistent with the practices of the general scientific community and serves to permit scientific progress by the community, while still preserving our intellectual contribution to the reagents.

All of the animal models expected from this study will have originated at least in part from shared models given to us by other investigators and institutions. Therefore, any distribution of these models will require permission from the original granting institution/investigator.

Other works, including presentations and white papers, will also be made accessible.

When will you make the data available?

The data generated by this project will be made available upon request.

Which archive/repository/central database have you identified as a place to deposit data?

Generated data will be stored on (1) IU's shared cloud system, Microsoft OneDrive, (2) a lab owned, password protected, external hard drive, and (3) Electronic lab notebook, Microsoft OneNote.

Will a data-sharing agreement be required?

A data-sharing agreement will not be required.

What metadata/documentation will be submitted alongside the data?

Metadata will be available upon request.

What file formats will you use for your data, and why?

Data files will be shared in .zip, .tif, .xml format.

What transformations will be necessary to prepare data for preservation/data sharing?

No transformations will be necessary.

Do you need funding for the implementation of this data sharing plan?

No funding is required for the implementation of this data sharing plan.
