MATURE MINOR CONSENT FORM
(Ages ¬15+)

TITLE: Determinants of Partial Remission in Type 1 Diabetes (T1D)

SPONSOR: Alberta Children's Hospital Foundation

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CO-INVESTIAGORS: Dr. Raylene Reimer, Dr. Jon Meddings, Dr. Josephine Ho, Dr. Daniele Pacaud

STUDY COORDINATOR: Heidi Virtanen **403-955-8866**

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

BACKGROUND

We all have a wide variety of bacteria in our gut/bowels. Both animal and human studies found that there is a difference in the composition of bacteria in the gut between those that develop diabetes and those that did not develop diabetes. Specifically, there is evidence linking an abnormal gut bacterial composition with leakiness of the bowel wall, causing inflammation and the development of Type 1 Diabetes (T1D).

At the time of diagnosis, many patients still have *some* functioning beta cells (cells that produce insulin) so that in the first year of T1D, about 50% of patients will experience partial remission. During this period, their insulin requirements are low and they have excellent blood glucose control. We do not know what determines who will experience a partial remission and what determines the duration of partial remission, but it is believed that the gut bacterial composition could be a factor. Since patients who experience partial remission have fewer long-term diabetes-related complications, understanding the relationship between gut bacterial composition, intestinal permeability, and the duration of partial remission is important. To date, there have been no studies evaluating the impact of the gut bacterial composition on partial remission of T1D.

In this small initial study, we will recruit patients with T1D from the diabetes clinic at the Alberta Children's Hospital within one month of diagnosis and follow them for two years, evaluating gut bacterial composition, intestinal permeability and beta cell function.

We aim to enroll a total of 50 patients from the Alberta Children's Hospital diabetes clinic in this study.

WHAT IS THE PURPOSE OF THE STUDY?

This small study will provide a first look at gut bacterial composition and intestinal permeability as factors involved in partial remission of T1D in children newly diagnosed. This information may help us develop therapies to optimize gut bacterial composition at the onset of diagnosis to initiate and/or prolong partial remission, and therefore enhance clinical outcomes and reduce complications.

WHAT WOULD I HAVE TO DO?

There will be a baseline visit and additional visits at 1, 3, 6, 9, 12, 18, and 24 months.

Study visit components are described below, followed by the visit schedule and required components.

Questionnaire (age, gender, date of T1D diagnosis, current medications, other medical conditions, number of episodes of severe hypoglycemia and ketoacidosis, insulin requirements)

Measurements (height, weight)

HbA1c Test and Details about Diagnosis information will be collected from your medical chart. This test measures average blood glucose level for the last 2-3 months prior to the test.

Mixed Meal Tolerance Test you will arrive to clinic fasting. You will get special instructions about diet and insulin dosing before the test. To make the blood sampling easier for the test, an intravenous needle and plastic tube (IV) will be placed in your vein. The IV will be kept in place during the test. Two blood samples, ten minutes apart (one teaspoon of blood for each sample) will be taken through the IV. You will then drink a meal replacement beverage (like "Boost") which has glucose as well as fats and proteins. Blood samples will be drawn through the IV at regular intervals for 2 hours to measure glycemic control and beta cell function (C-peptide, glucose, insulin, proinsulin) in response to a "meal".

Gut Leakiness Test the night before your study visit, after your regular evening meal and 3 hours before bedtime, you will drink a solution containing lactulose and mannitol in 200 mL of water. We will ask you to collect all of your urine for the following 12 hrs and bring it into the clinic within 24 hrs after collection.

Stool Sample will be collected at home. One tablespoon of stool will be placed in a pre-labelled tube, placed in a biohazard bag and stored in the home freezer (-20°C). Stool samples will be brought to the clinic on cold packs within 3 days of collection.

Baseline Visit: Fasting, ~3 hours

- Eligibility Screen and Informed Consent
- Questionnaire
- Measurements
- Mixed Meal Tolerance Test
- Gut Leakiness Test
- Stool Sample

3 Month Visit: ~30 minutes

- Questionnaire
- Measurements
- Gut Leakiness Test
- Stool Sample

6 Month Visit: Fasting, ~3 hours

- Questionnaire
- Measurements
- Mixed Meal Tolerance Test
- Gut Leakiness Test
- Stool Sample

9 Month Visit: ~30 minutes

- Questionnaire
- Measurements
- Gut Leakiness Test
- Stool Sample

12 Month Visit: Fasting, ~3 hours

- Questionnaire
- Measurements
- Mixed Meal Tolerance Test
- Gut Leakiness Test
- Stool Sample

18 Month Visit: ~30 minutes

- Questionnaire
- Measurements

24 Month Visit: ~30 minutes

- Questionnaire
- Measurements

WHAT ARE THE RISKS?

You could have discomfort and/or a bruise when you get your blood drawn. Once in a while, some people may faint. It is rare, but some people may get an infection, a small blood clot, swelling of the vein and surrounding tissue or bleeding where the needle enters the skin. Some people may feel nauseous when they complete the Mixed Meal Tolerance Test. The Mixed Meal Tolerance Test requires drinking a product which contains milk and soy ingredients. People with severe allergies to these could have a reaction. If you have a known allergy to either of these ingredients, please let us know. It is possible we may need to advise you to avoid the Mixed Meal Tolerance Tests.

The intestine leakiness drink contains a small amount of lactulose and mannitol, which are not absorbed into your system, therefore is not likely to cause side effects. Diarrhea and nausea are seen with much higher doses.

ARE THERE ANY BENEFITS FOR ME?

There is no guarantee that you will benefit from this study. During the study we will share with you information about your health and diabetes. The information we get from this study may help us to provide better treatments in the future for patients newly diagnosed with T1D.

DO I HAVE TO PARTICIPATE?

You will continue to have regular standard treatments through the diabetes clinic and your usual diabetes team. Participation in this study is voluntary and you may withdraw from it at any time without jeopardizing your health care. To withdraw, let a member of the research team know that you don't wish to participate anymore. You can contact either the study coordinator (403-955-8866) or investigator (403-955-7819) if you wish to withdraw from the study. Also, let them if you would like your data erased from the study. The researcher can also withdraw you from the study. If new information becomes available that might affect your willingness to participate in the study, you will be informed as soon as possible.

WHAT ELSE DOES MY PARTICIPATION INVOLVE?

There are no other things involved.

WILL WE BE PAID FOR PARTICIPATING, OR DO WE HAVE TO PAY FOR ANYTHING?

The costs of parking for each visit will be reimbursed.

WILL MY RECORDS BE KEPT PRIVATE?

Only the researchers and designated research assistants will have access to the information collected. All paper files will be kept in locked offices at the Alberta Children's Hospital and data will be stored in password protected computers. The University of Calgary Conjoint Health Research Ethics Board will have access to the records.

IF I SUFFER A RESEARCH-RELATED INJURY, WILL I BE COMPENSATED?

In the event that you suffer injury as a result of participating in this research, no compensation will be provided to you by the Department of Pediatrics, the University of Calgary, the Alberta Health Services or the Researchers. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

SIGNATURES

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to your participation as a subject. In no way does this waive your legal rights nor release the investigators, or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your health care. If you have further questions concerning matters related to this research, please contact:

Heidi Virtanen 403-955-8866

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair of the Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Participant's Name	Signature	Date
Investigator/Delegate's Name	Signature	Date

The investigator or a member of the research team will, as appropriate, explain the research and your involvement. They will seek your ongoing cooperation throughout the study.

The University of Calgary Conjoint Health Research Ethics Board has approved this research study.

A signed copy of this consent form has been given to you to keep for your records and reference.