



TRIGR Family News

Editor's corner

Dear Study families,

Doctor Marco Songini from Sardinia wrote the editorial this time. The incidence of type 1 diabetes in Sardinia is the second highest in the world which makes the island an ideal region for studying type 1 diabetes.

In the Science Corner we present data on the significance of the gut microbiome in type 1 diabetes and the latest development of a rapid method for analysing diabetes-associated autoantibodies.

Finland's National Study Coordinator Minna Hirvasniemi tells about the importance of the OGTT Study Visit and Juuso tells about his practical experiences of the OGTT.

Matti Koski, Chief Editor

The TRIGR Study in Sardinia

The Sardinia TRIGR study center is one among the 77 centers in Europe, Australia, Canada and the United States participating in the TRIGR study (Trial to Reduce Insulin-Dependent Diabetes in Genetically at Risk).



The Sardinian region is the second largest Italian Island in the Mediterranean Sea. The incidence of type 1 diabetes in Sardinia is the highest in Italy and the second highest in the world after Finland. These countries are so called "Hot spots".

Sardinian genetic and epidemiological background and the geographical isolation make the island an ideal region for investigating environmental, immunological, and genetic factors related to T1D.

In Sardinia, the incidence of T1D in children has been increasing strongly over the last 20 years and continues rising. Consequently several studies have been performed over the years in Sardinia such as the TRIGR study.

The Sardinian TRIGR Center

In the Diabetes Centre of our hospital (St. Michele Hospital) and in collaboration with the Department of Neonatology and Obstetrics we proposed genetic screening of all newborn infants of parents with T1D.



All infants carrying high HLA risk for diabetes were enrolled to the TRIGR study. From 2002 to 2006 altogether 44 children were screened; 17 of them 17 were found eligible (HLA high-risk).

We have now reached the 12th year of the TRIGR study follow-up in Sardinia. Out of the 17 children three have dropped out for logistical problems. Today altogether 10 children and their families continue in TRIGR.

We are happy that all our 10 families have agreed to continue in the follow-up until the youngest participant turns 10 years old. This is very important! I would like to thank all the children and their families taking part in TRIGR for their perseverance!

There is still a long way in front of us if we want to stop type 1 diabetes, but we are confident that researchers and families together will have the answers to the question whether the weaning based on an extensively hydrolyzed milk formula is able to reduce the incidence of type 1 diabetes in children at high genetic risk.



*Doctor Marco Songini
National Investigator of Sardinia*

Welcome to OGTT

In the TRIGR study we perform oral glucose tolerance tests (OGTT) in all participating children at the age of 6 and 10 and also at the final visit. Sometimes there is need to conduct an additional test at some other time point. All our subjects have had at least one OGTT and many of them have already completed their 10 year OGTT's, too. In addition, everyone will have an OGTT at their final visit in 2016 or 2017 depending on the child's birth date.

Why do we perform OGTTs and why it is important to take part in the test?

For the families the OGTT test has many advantages. OGTT generates important information on the child's glucose metabolism and shows whether the glucose tolerance is normal. Currently the OGTT together with diabetes-associated autoantibodies are the only way to provide information on the progression of beta-cell autoimmunity to type 1 diabetes. We have also experienced that a normal OGTT result (reflecting normal glucose tolerance) is a relief for the family.

Only a minority of the TRIGR children have developed signs of autoimmunity. The duration of the prediabetic period may vary from months to decades. In such individuals, type 1 diabetes can be diagnosed and detected in an early phase through an OGTT test (usually in asymptomatic children). An OGTT is essential for detecting asymptomatic diabetes. If the result indicates type 1 diabetes, the test will be repeated to confirm or exclude diabetes in asymptomatic children.

If diabetes have been diagnosed before symptoms in an early phase, the treatment of hyperglycemia is easier. Early insulin treatment facilitates the preservation of residual beta-cell secretion.



*Minna Hirvasniemi,
National Nurse Coordinator in Finland/ Study nurse*

Science Corner

Researchers identified a link between changes in gut bacteria and type 1 diabetes

In the largest longitudinal study to date, researchers at the University of Helsinki, Harvard, MIT and Massachusetts General Hospital have identified a link between changes in gut bacteria and the development of type 1 diabetes (T1D).

Previous studies have identified the possible link between gut bacteria and type 1 diabetes, but this new study is the first to show how specific changes in gut bacteria composition are affecting progression to T1D.

The DIABIMMUNE study followed 33 infants who were at high-risk for T1D from birth until age 3. The researchers found that the children who developed symptomatic T1D experienced a significant drop in the diversity of their gut bacteria soon after the appearance of the first diabetes-associated autoantibodies. It was also find out there was a decrease in specific bacteria known to promote gut health and an increase in harmful bacteria known to promote inflammation. These changes typically occurred

about a year prior to the manifestation of T1D. In addition to teasing out the kinds of gut bacteria changes that may trigger the start of T1D, researchers were also able to identify some patterns of healthy gut bacteria activity that may help protect individuals from developing the disease. In healthy children, gut microbiome varied significantly between individuals, but the functional effects of their gut microbiome remained quite similar during early childhood.

This new knowledge could pave the way for the development of new T1D therapies that are able to slow progression of the disease through manipulation of gut bacteria composition in individuals who are in the early stages of T1D. However, a significant amount of research is still needed to determine whether this recent discovery has therapeutic applications. The next step will be determining what environmental factors may be involved in effecting changes in gut bacteria composition.

The study was published in the February issue of Cell, Host & Microbe 2015;17:260-73.

Rapid assays for detecting diabetes-associated auto-antibodies

Type 1 diabetes (T1D)-associated autoantibodies can be used for diagnosing diabetes and predicting development of the disease. In diabetes research these autoantibodies have been analyzed also from organ donors. Pancreases from autoantibody-negative donors are used for isolating and transplanting islet cells while pancreases from autoantibody-positive donors are used for research purposes, e.g. evaluating mechanisms of beta-cell destruction.

Scandia transplant is a Nordic transplant organization running an organ transplantation program. Nordic transplant units are cooperating with laboratories by reclaiming pancreases and sending them to the laboratory located in University of Uppsala, Sweden.

In the TRIGR Core Laboratory (Children's Hospital, University of Helsinki), diabetes-associated autoantibodies are analyzed by using standard radio binding assays (RBA) since 2002. By this method the results are ready within one day. We have also analyzed serum samples from diabetic children as well as their family members. Our laboratory has also assayed about 1000 samples from organ donors

with RBA assay. Among these donors 5% have been autoantibody-positive.

In the autumn 2013 I started to study in the Master's Degree Program in Clinical Expertise at the Helsinki Metropolia University of Applied Sciences. I was given the opportunity to develop and optimize a rapid assay method for analyzing diabetes-associated autoantibodies in organ donors in my workplace. I developed such an assay for recognizing GAD, IA-2 and ZnT8 autoantibodies. We have now available the rapid method to analyze all three autoantibodies within 2 hours. Usually this analysis would take one day.

The future goal is to get pancreases from autoantibody-positive donors for diabetes research within an appropriate time frame. This rapid method is essential when assessing eligibility of the pancreas for isolating islets for transplantation.



Mevlida Kararic, TRIGR Laboratory, Children's Hospital, University of Helsinki, Finland

Kid's corner

Ava's travel to Lusaka, Zambia

Hi! My name is Ava. I am 10 years old. Some of my favorite things to do are play piano, play basketball, and build robots. I have a pet rabbit named Blu, and my favorite subjects in school are math, and social studies. My dad has type 1 diabetes and that is why I am in the TRIGR study. In September I had the opportunity to travel to Lusaka, Zambia (in the southern part of the African continent) with my family.





This was my 4th trip to Africa! When we are there, my family volunteers with an organization called Alliance for Children Everywhere (ACE). ACE helps orphans and vulnerable children through social welfare, education, and community programs. One of my favorite things to do is to spend time with the smallest babies that have been abandoned or orphaned. They stay in a temporary home called The House of Moses until they can be re-united with their own family, or placed into a new family. While I was there I had the chance to see a baby reconnected with her grandmother, visit many of the schools, and work in the community program. It was a really fun trip! Here are some pictures of me with the babies at the House of Moses, visiting one of the schools, and helping in the community! But, my most favorite thing to do is play with the babies!

Ava and her family, Seattle, WA (USA02)

Leah's letter to her study nurse Karen

I just wanted to say...
 To,
 Karen
 Thank you so much for being so nice and generous to me and my family. Thank you for giving us needles to see if we have diabetes. I really appreciate your hard work at the IWK. Thank you 😊
 xoxo Leah

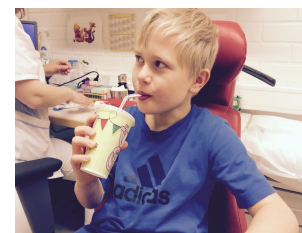


Study Nurse, Coordinator, Karen Scott and Leah (with her siblings). Halifax, Canada (CAN12)

My 10-year TRIGR visit and glucose tolerance test

Hi, my name is Juuso and I just turned 10. I have participated all my life in the TRIGR study. My mom had told me on beforehand what happens during my 10 year TRIGR visit. This time I had to drink a cola flavored sugar drink.

First, my study nurse Minna took my weight and after that we went to the laboratory for taking blood samples. When I sat down to the chair and the laboratory technician started to take blood samples, I was a little bit nervous that it would be painful. Luckily I had had the magic cream in the bends of my arms and the blood draw didn't hurt at all. After the blood sampling I had to drink a cola flavored sugar drink within 5 to 10 minutes. For me it took only one minute 😊.



About 35 minutes after drinking that sugar drink I felt a bit tired as well as hungry since I had not had anything after the evening snack. Another blood sample was taken after 2 hours. After that I was allowed to eat. As breakfast I had a cup of hot chocolate and a croissant.

FINISH!

Juuso, Helsinki, Finland