Trial to Reduce IDDM in the Genetically at Risk

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TRIGR Family News

Editor's corner

Dear Study families,

Professor Heikki Hyöty from the University of Tampere in Finland has written the Leading Article about enterovirus analyses currently going on. We may expect interesting results in the near future.

In the Science Corner our local investigator in Helsinki, Dr. Anna Parkkola, has collected and summarized recent interesting scientific publications related to type 1 diabetes.

In the Kid's Corner Brenda Bradley, the National Coordinator of TRIGR Canada, presents the Junior Scientist Award to all of you TRIGR participants.

Please take also a look at the interesting stories we received from Australia and USA.

Matti Koski, Chief Editor

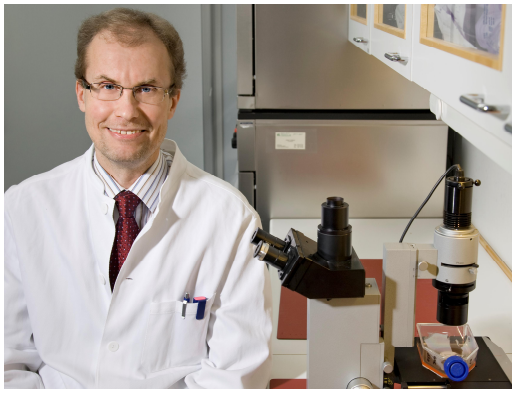
Virus analyses in the TRIGR study

The rapidly increasing incidence of type 1 diabetes (T1D) implies that environmental factors are involved in the pathogenesis of the disease. However, in spite of this quite compelling evidence it has been difficult to identify the exact nature of these factors. Several studies have suggested that exogenous risk conferring and protective factors modulate the risk of T1D, and the research has mainly focused on dietary factors and virus infections which influence the pathogenesis of diabetes in animal models. Recently, increasing interest has focused on their possible interactions since intestinal infections may increase the diabetogenic effect of dietary factors, or vice versa. For example, enteric infections increase the permeability of the gut mucosa and could thus potentiate immunological effects of dietary factors.

Virus infections cause diabetes in animals and one specific virus group, the group of enteroviruses (EVs), has been linked to human T1D in several studies. These viruses occur frequently in young children leading usually to common flu type symptoms. However, they can also cause severe diseases such as paralysis (polio viruses belong to EVs), myocarditis, meningitis, and severe systemic infections. These viruses have also one peculiar feature which increases their relevance in T1D – they can infect insulin producing cells in the pancreas. This kind of pancreatic infection has been described in infants suffering from systemic EV infection. In addition, the virus infects insulin-producing beta cells also in laboratory conditions. Recent studies have detected these viruses also from the pancreas and intestinal mucosa of T1D patients further supporting their role in T1D.

The TRIGR study evaluates whether early exposure to a complex diet in early infancy can modulate the risk of T1D. Since virus infections can interact with these dietary factors we have started an ancillary study to explore the possible effect of EV infections in the TRIGR study. The main aim is to study whether EVs interact with dietary factors and potentiate their diabetogenic effect. These viruses replicate in intestinal mucosa and could create an inflammatory milieu which is favorable for the beta-cell damaging process or increase gut permeability to dietary triggers of T1D. This virus study is carried out by analyzing antibodies against EVs from serum samples collected from TRIGR children during their follow-up. These analyses are currently in progress and we expect to get the first results by the end of this year. However, it will take at least 2 years to complete all the planned analyses and to find out whether such interactions exist. If the result support the effect of EVs this study could open up possibilities to prevent T1D by a vaccine or other

means aimed at eliminating virus-diet interactions in susceptible children.



Heikki Hyöty, Professor of Virology
University of Tampere, Finland

Science Corner

From autoantibodies to clinical type 1 diabetes – a 15-year follow-up

A large study of more than 13 000 children from Colorado, Finland and Germany has characterized the development of type 1 diabetes after the appearance of autoantibodies. The risk to develop type 1 diabetes over the next 15 years after the appearance of the first autoantibody was 13% for children with one autoantibody, 62% for children with two autoantibodies, and 79% for children with three autoantibodies. Among autoantibody-negative children the risk was only 0.4%. Among the risk factors associated with rapid development of type 1 diabetes were early appearance of autoantibodies (before the age of 3 years), and high risk HLA genes (DR3-DQ2/DR4-DQ8). These results confirm that autoantibodies predict type 1 diabetes but unfortunately we still cannot predict the rate of development in an individual child.

Ziegler AG, et al. Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in Children. JAMA 2013;309(23):2473-2479

Patients with longstanding type 1 diabetes still secrete low levels of insulin

It was long believed that at diagnosis of type 1 diabetes most of the insulin secreting beta cells were already destroyed and those still alive were soon eliminated. New findings have now documented that in fact even patients with decades with type 1 diabetes still may have functioning beta cells. In a study by Oram and colleagues, the majority of patients (73%) with type 1 diabetes for over 5 years still secreted low levels of insulin, and the secretion increased in response to a meal. Even after 30 years of type 1 diabetes, 68% of patients still secreted some insulin. These results indicate that some beta cells escape the autoimmune destruction or they are regenerating. These are promising results for the field of immunotherapy research; if we could learn to control the autoimmune attack perhaps we could get the remaining beta cell mass to grow.

Oram RA, Jones AG, Besser RE, Knight BA, Shields BM, Brown RJ, Hattersley AT, McDonald TJ.The majority of patients with long-duration type 1 diabetes are insulin microsecretors and have functioning beta cells. Diabetologia. 2014 Jan;57(1):187-91.

Lipid profile in the prediction of type 1 diabetes

Recently, new areas of research have emerged with the development of novel technology. One such area is the study of metabolites, for example lipids (fat particles) from blood samples. We now have evidence that there are differences in blood lipid profile in children who will later progress to type 1 diabetes, and these differences are present already at birth. These findings indicate that the factors affecting type 1 diabetes development are present very early in life, perhaps even during fetal development. We still need further studies to understand these findings, but perhaps in the future we will have new biomarkers to predict type 1 diabetes development more accurately.

Orešič M, et al. Cord Serum Lipidome in Prediction of Islet Autoimmunity and Type 1 Diabetes. Diabetes *September 2013 vol. 62 no. 9 3268-3274*

Kid's corner

Congratulations TRIGR Participants – Junior Scientist Award

Research is trying to find out something that we don't already know. The TRIGR study is a research study where we are trying to find out why some people get diabetes and others don't. Being part of this study means that you

are like a junior scientist helping in a big research project.

When you plan for your yearly visit with the TRIGR study, do you ever think about all the other children participating in the study? When are they going for their visits, where do they live and how old are they? Often on the very same day children from several different countries around the world are having their visit too.

Since the TRIGR study started in 2002 until the end of February 2014, over 18,000 antibody samples have been collected from all the children in the study. The month of June has had the highest number of tests done, followed by the busy months of May and November. The year 2006 had the most samples in one year! There were over 2,500 samples that year.

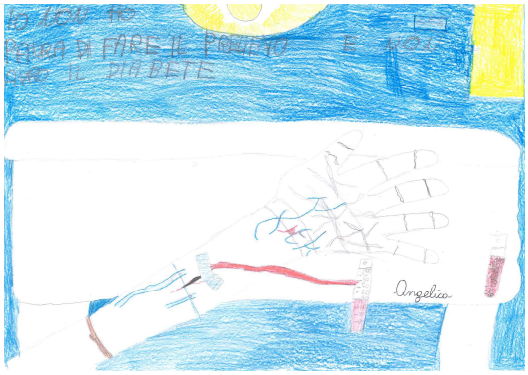
In 2013, the busiest day in the TRIGR study was May 13th. On that particular day 19 children had their blood test. They were from Canada (6 visits), Czech Republic (2 visits), Finland (2 visits), Hungary (2 visits), Italy (1 visit), Netherlands (1 visit), Poland (1 visit) and the United States (4 visits).

At your visits you and your parents give us information called “Data”. The blood test gives us the most important data we need for the study. Each time you have a blood test it plays a very important part in making the study a success.

For all your hard work in the study you have earned the TRIGR Participant Junior Scientist Award!

Brenda Bradley
National Coordinator TRIGR Canada

Angelica from Italy demonstrates the blood drawing



Jordan from Australia

Hi I’m Jordan and I am 7-year-old. I live in North St Marys in Sydney Australia. I live with my mum who is type 1 diabetic. I have a dog called Bobby. I go to St Marys School I am in year 2.

My favourite colour is green, and my favourite vegetable is carrot and fruit is mango. I like playing lots of sport and on the weekends I play football for the colts, and I do swimming lessons.

I enjoy singing and dancing and do dancing for my school. I go to Westmead Hospital each year for my TRIGR visit and see Doctor Neville and Jacki. This year my picture was on the front cover for the TRIGR calendar.

Lucas at Diabetes Congress

Hi, my name is Lucas and I am 8-year-old. I live in Washington State. In 2013, my mother Emily and I attended the ADA congress (American Diabetes Association) Caucus in Washington., DC. Many volunteers and local firefighters all

gave their time to help raise funds for us to attend.

I met with Senator Dave Reichert who presented me with a special medal from Congress. He listened to my concerns about funding for diabetes research. I told him I was in a research study called TRIGR (Trial to Reduce IDDM in the Genetically at Risk). I asked Congress for their help in funding more research.

A girl (Reyanne, also 8 years old) and myself were the youngest to attend. We got up on stage at the ADA that evening to explain to the audience what we accomplished after meeting with some of the Congressmen and Senators. This was an experience I will never forget!

Lucas and Congressman Dave Reichert

Lucas, mother Emily and Senator Maria Cantwell's Aide

Leah´s sailing trip from USA to New Zealand

Hi, my name is Leah. I just turned 8 years old. I have been living on a 38 foot sailboat with my family since 2010. We left Washington State in 2011 to begin our adventure sailing around the world. We have stopped in many ports along the way to New Zealand. We have been to various islands along the west coast of North and South America. In 2012, we set sail to Marquesas, a tiny group of islands in French Polynesia (south of the Equator). We sailed more than 2,700 miles and it took us 26 days. After exploring the beautiful tropical Marquesas Islands, we visited Tuamotu, one of the world's largest coral atolls, then to the Society Islands (Tahiti).

My home aboard the Sailboat "Wondertime"

(L to R) My sister, Holly; my mother, Sara; my father, Michael and me, Leah

In August, we sailed to the tiny island of Niue (1,500 miles NE of New Zealand) then onto to Tonga where we spent the next 3 months. We departed Tonga in November and sailed 12 days to New Zealand which we now call home.

Me and my sister Holly