

## **TRIGR: Approved Ancillary Studies**

PI (whole study group)	Lab	Project Title	Status
Aschemeier Bärbel		Changes in body weight during the first four year of life	The results were presented as a poster at the ISPAD meeting in 2010 Pediatric Diabetes (2010) 11 (Suppl. 14): 35– 113 no manuscript planned
Dosch Michael	Toronto (CAN)	T-cell reactivities in TRIGR probands (Prospective analysis of diabetes associated T-cell abnormalities in the TRIGR North America cohort)	Published: Hadley D, Cheung RK, Becker DJ, Girgis R, Palmer JP, Cuthbertson D, Krischer JP, Dosch HM; TRIGR North America Investigators. Large-scale prospective T cell function assays in shipped, unfrozen blood samples: experiences from the multicenter TRIGR trial. Clin Vaccine Immunol. 2014 Feb;21(2):203-11.
Hyöty Heikki	Tampere (FIN)	Interaction between dietary and viral risk factors in the pathogenesis of T1D	Active - 256 cases= multiple ab+ or T1D - 474 matched controls - CVB3, CVB4 and CVB5 increased 0-6 months before developing T1D ab
llonen Jorma	Turku (FIN)	Genotype and development of diabetes-associated autoimmunity in TRIGR probands	Active HLA DR/DQ genotyping performed on 1628 samples
Knip Mikael/Xavier Ramnik	Helsinki (FIN)	Intestinal microbiota in relation to signs of beta-cell autoimmunity in TRIGR participants	Active Funding for sample collection obtained, Sequencing at Broad Institute waiting for funding
Knip Mikael	Helsinki (FIN)	Frequency of ZnT8 autoantibodies and their contribution to beta-cell autoimmunity in TRIGR participants	Active



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Knip Mikael/Oresic Matej	Helsinki (FIN)	Biomarkers of beta-cell autoimmunity and progression to overt T1D based upon lipidomics/metabolomics and serum proteomics	Waiting for funding
Luopajärvi Kristiina	Helsinki (FIN)	Polarization of the cord blood cell in relation to T1D associated risk genes	Published: Luopajärvi K, Skarsvik S, Ilonen J, Akerblom HK, Vaarala O. <u>Reduced CCR4</u> , <u>interleukin-13 and GATA-3 up-regulation in</u> <u>response to type 2 cytokines of cord blood T</u> <u>lymphocytes in infants at genetic risk of type 1</u> <u>diabetes</u> . Immunology. 2007 Jun;121(2):189- 96.
Luopajärvi Kristiina	Helsinki (FIN)	Insulin specific immunity and T-regulation cells in cord blood cells of TRIGR	Published: Luopajärvi K, Nieminen JK, Ilonen J, Akerblom HK, Knip M, Vaarala O. <u>Expansion of CD4+CD25+FOXP3+ regulatory</u> <u>T cells in infants of mothers with type 1</u> <u>diabetes.</u> Pediatr Diabetes. 2012 Aug;13(5):400-7.
Songini Marco	Cagliari (ITA)	Association of Mycobacterium avium subsp. Paratuberculosis with type 1 diabetes, a possible trigger	Published: M. Niegowska, D. Paccagnini, C.Mannu, C. Targhetta,M. Songini and L. A. Sechi. <u>Recognition of ZnT8, Proinsulin, and</u> <u>HomologousMAP Peptides in Sardinian</u> <u>Children at Risk of T1D Precedes</u> <u>Detection of Classical Islet Antibodies</u> Journal of Diabetes Research. 2016;2016;5842701. doi: 10.1155/2016/5842701
Vaarala Outi	Helsinki (FIN)	Effect of early dietary antigen exposure on T- and B cell immunization to insulin (Effect of early antigen exposure on immunization to insulin and maturation of the mucosal immune response)	Active samples until the age of 3 years have been received and frozen; analyses will be done only after opening of the code



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Virtanen Suvi/Jeff Krischer		Effect of cow's milk intake during childhood on development of islet autoimmunity (Does later cow's milk intake during childhood modify the effects of an early exposure during infancy on the development and progression of beta cell autoimmunity?)	Completed in 2017 (12 TRIGR countries). Data has been sent to the DMU in spring 2018. Next step calculation and analysis
Virtanen Suvi		The role of vitamin D and cow's milk in the development and progression of beta cell autoimmunity	Published: Lehtonen E, Ormisson A, Nucci A, Cuthbertson D, Sorkio S, Hyytinen M, Alahuhta K, Berseth C, Salonen M, Taback S, Franciscus M, González-Frutos T, Korhonen TE, Lawson ML, Becker DJ, Krischer JP, Knip M, Virtanen SM; TRIGR Investigators. <u>Use of</u> <u>vitamin D supplements during infancy in an</u> <u>international feeding trial.</u> Public Health Nutr. 2014 Apr;17(4):810-22.
Virtanen Suvi (Miettinen M, Erlund I, Krischer JP, Niinistö S, Hyöty H, Vaarala O, Honkanen J, Knip M, Cuthbertson D)	Helsinki (FIN)	Fatty acids as putative effect modifiers in the TRIGR study (Effect of early diet and virus infections on immune regulation and the development islet autoimmunity) - Divia	Active Manuscript proposal Association of serum 25- hydroxyvitamin D concentration with the development of islet autoimmunity in children genetically at risk for type 1 diabetes has been accepted by the PPC in February 2018.
Krischer Jeffrey		The Effect of an Extensively Hydrolyzed Infant Formula on the Development of Asthma and Allergic Diseases in Children at Increased Genetic Risk of Type 1 Diabetes	Active 57 centers in 15 TRIGR countries participating
Paolo Pozzilli (Rocky Strollo, Chiara Vinci, Stella Mann, Ernesto Maddaloni, Johnny Ludvigsson, Ahuva Nissim)		Oxidative Insulin as Biomarker for Prediction of T1D	Active Manuscript proposal <i>Oxidative Insulin as</i> <i>Biomarker for Prediction of T1D</i> has been approved by the PPC in March, 2018