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## Research

The immune genetics of the aetiology and pathogenesis of autoimmune (type 1) diabetes and associated organs-specific autoimmune disorders including celiac disease and narcolepsy are not fully understood. Our research is focused on the role of HLA and non-HLA genes in the etiology and pathogenesis with particular emphasis to uncover the importance of beta cell autoantigens such as GAD65, insulin, IA-2, ZnT8, INS-IGF2 and tetraspanin 7. Humoral and cellular studies are conducted first to detect a trigger that will induce beta cell autoimmunity in children at increased genetic risk. A major effort to identify the trigger of beta cell autoimmunity is carried out in the TEDDY (The Environmental Determinants of Diabetes in the Young) study. A total of 2525 children in Skåne with increased genetic risk for autoimmune (type 1) diabetes were identified at birth (2004-2010) and then followed quarterly until four years of age and thereafter bi-annually until the children turn 15 years of age. TEDDY is supported by the National Institutes of Health (NIH) in the US and is conducted with three clinics in the US, Finland and Germany. In Skåne, we have TEDDY clinics in Malmö, Helsingborg and Kristianstad. Major observations suggest that the association between HLA and autoimmune (type 1) diabetes is secondary to the first appearing autoantibody be it against insulin in children with HLA DR4-DQ8 or GAD65 in children with HLA DR3-DQ2. Studies are also conducted since birth in children born 2000-2004 in the Diabetes Prediction in Skåne (DiPiS) study. Research involves identification of and development of new assays for autoantibodies against novel autoantigens and autoantigen candidates. Studies are conducted in patients with narcolepsy and their controls to identify autoantigens and explain the development of narcolepsy and vaccination with Pandemrix®. Studies on primary prevention is conducted in the GPPAD (Global Platform for the Prevention of Autoimmune Diabetes) consortium and on secondary prevention in TrialNet for which we are the Swedish TrialNet Center. Clinical trials such as the TEDDY Family (TEFA) study is conducted with support from the Juvenile Diabetes Research Foundation (JDRF).

The BB rat is investigated to clarify monogenic type 1 diabetes due to a frameshift mutation in the Gimap5 gene, which is coding for an anti-apoptotic protein. Overall the research aim at the prediction and prevention primarily of autoimmune (type 1) diabetes by combining screening for HLA and non-HLA genes to identify subjects at risk and to measure and develop tests for beta cell autoimmunity and to carry out primary and secondary prevention trials eventually to prevent and thereby cure autoimmune (type 1) diabetes.

## Employment

### Principal investigator

Celiac Disease and Diabetes Unit  
Lund University  
Malmö, Sweden  
2015 Sep 21 → present

### Principal investigator

EXODIAB: Excellence of Diabetes Research in Sweden  
Lund University  
Lund, Sweden  
2010 Jan 1 → present

### Emeritus Professor in Medicine

University of Washington, Seattle  
Seattle, United States  
2009 Jan 1 → present

### Adjunct Professor

Lund University  
Lund, Sweden  
2006 Jan 1 → 2008 Jan 1

**Adjunct Professor**

Lund University  
Lund, Sweden  
1998 Jan 1 → 2005 Jan 1

**Member of the Graduate Faculty**

University of Washington, Seattle  
Seattle, United States  
1997 Jan 1 → 2008 Jan 1

**Robert H. Williams Professor in Medicine**

University of Washington, Seattle  
Seattle, United States  
1995 Jan 1 → 2008 Dec 31

**Adjunct Professor**

Karolinska Institutet  
Stockholm, Sweden  
1995 Jan 1 → 2001 Jan 1

**Adjunct Professor**

University of Washington, Seattle  
Seattle, United States  
1995 Jan 1 → 2007 Jan 1

**Professor of Experimental Endocrinology**

Karolinska Institutet  
Stockholm, Sweden  
1993 Jan 1 → 1994 Dec 31

**Affiliate Professor**

University of Washington, Seattle  
Seattle, United States  
1993 Jan 1 → 1994 Jan 1

**Adjunct Professor**

University of Washington, Seattle  
Seattle, United States  
1991 Jan 1 → 1993 Jan 1

**Visiting Professor**

Université Libre de Bruxelles (ULB)  
Brussels, Belgium  
1990 Jan 1 → 2000 Jan 1

**Professor in Diabetes Research**

Lund University  
Lund, Sweden  
1989 Jan 1 → 1991 Jan 1

**Robert H. Williams Professor in Medicine**

University of Washington, Seattle  
Seattle, United States  
1988 Jan 1 → 1992 Dec 31

### **Adjunct Professor of Medical Cell Biology**

Lund University  
Lund, Sweden  
1984 Jan 1 → 1989 Jan 1

### **Director of Research**

Hagedorn Research Institute  
Gentofte, Denmark  
1979 Jan 1 → 1987 Dec 31

### **Assistant professor**

University of Chicago  
Chicago, United States  
1977 Jan 1 → 1978 Dec 31

### **Associate professor**

Umeå University  
Umeå, Sweden  
1973 Jan 1 → 1979 Dec 31

### **Research Associate**

Umeå University  
Umeå, Sweden  
1970 Jan 1 → 1973 Dec 31

### **Instructor**

Umeå University  
Umeå, Sweden  
1968 Aug 1 → 1970 Dec 31

## **Research output**

### **Islet Autoantibody Levels Differentiate Progression Trajectories in Individuals with Presymptomatic Type 1 Diabetes**

Kwon, B. C., Achenbach, P., Anand, V., Frohnert, B. I., Hagopian, W., Hu, J., Koski, E., Lernmark, Å., Lou, O., Martin, F., Ng, K., Toppari, J., Veijola, R. & T1DI Study Group, 2022 Sep 16, (E-pub ahead of print) In: *Diabetes*.

### **HbA1c as a time predictive biomarker for an additional islet autoantibody and type 1 diabetes in seroconverted TEDDY children**

Salami, F., Tamura, R., You, L., Lernmark, Å., Elding Larsson, H., Lundgren, M., Krischer, J., Ziegler, A-G., Toppari, J., Veijola, R., Rewers, M., Haller, M. J., Hagopian, W., Akolkar, B., Törn, C. & TEDDY Study Group, 2022 Sep 9, (E-pub ahead of print) In: *Pediatric Diabetes*.

### **Temporal changes in gastrointestinal fungi and the risk of autoimmunity during early childhood: the TEDDY study**

Auchtung, T. A., Stewart, C. J., Smith, D. P., Triplett, E. W., Agardh, D., Hagopian, W. A., Ziegler, A. G., Rewers, M. J., She, J-X., Toppari, J., Lernmark, Å., Akolkar, B., Krischer, J. P., Vehik, K., Auchtung, J. M., Ajami, N. J. & Petrosino, J. F., 2022 Jun 7, In: *Nature Communications*. 13, 3151.

### **Telomere length is not a main factor for the development of islet autoimmunity and type 1 diabetes in the TEDDY study**

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**Heterogeneity of beta-cell function in subjects with multiple islet autoantibodies in the TEDDY family prevention study - TEFA**

The TEDDY Family (TEFA) Study Group, 2022 Jan 5, In: Clinical diabetes and endocrinology. 7, 1, 10 p.

**Association of HLA-DQ Heterodimer Residues -18 $\beta$  and  $\beta$ 57 With Progression From Islet Autoimmunity to Diabetes in the Diabetes Prevention Trial-Type 1**

Zhao, L. P., Skyler, J., Papadopoulos, G. K., Pugliese, A., Najera, J. A., Bondinas, G. P., Moustakas, A. K., Wang, R., Pyo, C-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2022, In: Diabetes Care. 45, 7 , p. 1610-1620

**Enteroviruses and Type 1 Diabetes: Multiple Mechanisms and Factors?**

Lloyd, R. E., Tamhankar, M. & Lernmark, Å., 2022, In: Annual Review of Medicine. 73, 1

**Multiplex agglutination-PCR (ADAP) autoantibody assays compared to radiobinding autoantibodies in type 1 diabetes and celiac disease**

de Jesus Cortez, F., Lind, A., Ramelius, A., Bennet, R., Robinson, P. V., Seftel, D., Gebhart, D., Tandel, D., Maziarz, M., Agardh, D., Larsson, H. E., Lundgren, M., Lernmark, Å. & Tsai, C-T., 2022, In: Journal of Immunological Methods. 506, 113265.

**Possible Relationship between the HLA-DRA1 Intron Haplotype of Three Single-Nucleotide Polymorphisms in Intron 1 of the HLA-DRA1 Gene and Autoantibodies in Children at Increased Genetic Risk for Autoimmune Type 1 Diabetes**

Andersson Svård, A., Benatti, E., Lundgren, M., Lernmark, A., Maziarz, M., Elding Larsson, H. & DiPiS Study Group, 2022 , In: ImmunoHorizons. 6, 8, p. 614-629 8.

**Predictors of the Initiation of Islet Autoimmunity and Progression to Multiple Autoantibodies and Clinical Diabetes: The TEDDY Study**

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**Progression of type 1 diabetes from latency to symptomatic disease is predicted by distinct autoimmune trajectories**

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**Rising Hemoglobin A1c in the Nondiabetic Range Predicts Progression of Type 1 Diabetes As Well As Oral Glucose Tolerance Tests**

Vehik, K., Boulware, D., Killian, M., Rewers, M., McIndoe, R., Toppari, J., Lernmark, Å., Akolkar, B., Ziegler, A-G., Rodriguez, H., Schatz, D. A., Krischer, J. P., Hagopian, W. & TEDDY Study Group Colorado Clinical Center, 2022, In: Diabetes Care. 45, 10, p. 2342-2349

**Nine residues in HLA-DQ molecules determine with susceptibility and resistance to type 1 diabetes among young children in Sweden**

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**Beta cell function in participants with single or multiple islet autoantibodies at baseline in the TEDDY Family Prevention Study: TEFA**

Martinez, M. M., Salami, F., Larsson, H. E., Toppari, J., Lernmark, Å., Kero, J., Veijola, R., Koskeniemi, J. J., Tossavainen, P., Lundgren, M., Borg, H., Katsarou, A., Maziarz, M., Törn, C. & The TEDDY Family (TEFA) Study Group, 2021 Apr, In: Endocrinology, Diabetes & Metabolism. 4, 2, e00198.

**Transcriptional networks in at-risk individuals identify signatures of type 1 diabetes progression**

Xhonneux, L-P., Knight, O., Lernmark, Å., Bonifacio, E., Hagopian, W. A., Rewers, M. J., She, J-X., Toppari, J., Parikh, H., Smith, K. G. C., Ziegler, A-G., Akolkar, B., Krischer, J. P. & McKinney, E. F., 2021 Mar 31, In: Science Translational Medicine. 13, 587, eabd5666.

**The Vbeta13 T Cell Receptor Monoclonal Antibody Reduces Hyaluronan and CD68+, CD3+, and CD8+ Cell Infiltrations to Delay Diabetes in Congenic BB DRLyp/Lyp Rats**

Bogdani, M., Faxius, L., Fex, M., Ramelius, A., Wernersson, A., Mordes, J. P., Blankenhorn, E. P. & Lernmark, Å., 2021 Mar 16, In: *Frontiers in Endocrinology*. 12, 629242.

**Children's erythrocyte fatty acids are associated with the risk of islet autoimmunity**

Aronsson, C. A., Parikh, H. M., Lernmark, Å. & TEDDY Study Group, 2021 Feb 11, In: *Scientific Reports*. 11, 1, 3627.

**Plasma Metabolome and Circulating Vitamins Stratified Onset Age of an Initial Islet Autoantibody and Progression to Type 1 Diabetes: the TEDDY Study**

Lernmark, Å. & TEDDY Study Group, 2021 Jan, In: *Diabetes*. 70, 1, p. 282-292 11 p.

**An Age-Related Exponential Decline in the Risk of Multiple Islet Autoantibody Seroconversion During Childhood**

Bonifacio, E., Weiß, A., Winkler, C., Hippich, M., Rewers, M. J., Toppari, J., Lernmark, Å., She, J-X., Hagopian, W. A., Krischer, J. P., Vehik, K., Schatz, D. A., Akolkar, B., Ziegler, A-G. & TEDDY Study Group, 2021, In: *Diabetes Care*. 44, 10, p. 2260-2268

**Associations of breastfeeding with childhood autoimmunity, allergies, and overweight: The Environmental Determinants of Diabetes in the Young (TEDDY) study**

Hummel, S., Weiß, A., Bonifacio, E., Agardh, D., Akolkar, B., Aronsson, C. A., Hagopian, W. A., Koletzko, S., Krischer, J. P., Lernmark, Å., Lynch, K., Norris, J. M., Rewers, M. J., She, J-X., Toppari, J., Uusitalo, U., Vehik, K., Virtanen, S. M., Beyerlein, A., Ziegler, A-G., & 1 others TEDDY Study Group, 2021, In: *The American journal of clinical nutrition*. 114, 1, p. 134-142

**Characteristics of children diagnosed with type 1 diabetes before vs after 6 years of age in the TEDDY cohort study**

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**Complete blood counts with red blood cell determinants associate with reduced beta-cell function in seroconverted Swedish TEDDY children**

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**Etiology of Autoimmune Islet Disease: Timing Is Everything**

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**First-appearing islet autoantibodies for type 1 diabetes in young children: maternal life events during pregnancy and the child's genetic risk**

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**Immunocyte single cell analysis of vaccine-induced narcolepsy**

Lind, A., Salami, F., Landtblom, A-M., Palm, L., Lernmark, Å., Adolfsson, J. & Larsson, H. E., 2021, In: *European Journal of Immunology*. 51, 1, p. 247-249

**Metabolomics Profiling of Patients With A-β+ Ketosis-Prone Diabetes During Diabetic Ketoacidosis**

Jahoor, F., Hsu, J. W., Mehta, P. B., Keene, K. R., Gaba, R., Mulukutla, S. N., Caducoy, E., Peacock, W. F., Patel, S. G., Bennet, R., Lernmark, A. & Balasubramanyam, A., 2021, In: *Diabetes*. 70, 8, p. 1898-1909

**Neutralizing Ljungan virus antibodies in children with newly diagnosed type 1 diabetes**

Lundstig, A., McDonald, S. L., Maziarz, M., Weldon, W. C., Vaziri-Sani, F., Lernmark, Å. & Nilsson, A-L., 2021, In: *The Journal of general virology*. 102, 5, 1602.

**Simplifying prediction of disease progression in pre-symptomatic type 1 diabetes using a single blood sample**

Bediaga, N. G., Li-Wai-Suen, C. S. N., Haller, M. J., Gitelman, S. E., Evans-Molina, C., Gottlieb, P. A., Hippich, M., Ziegler, A-G., Lernmark, A., DiMeglio, L. A., Wherrett, D. K., Colman, P. G., Harrison, L. C. & Wentworth, J. M., 2021, In: *Diabetologia*. 64, 11, p. 2432-2444

**The KAG motif of HLA-DRB1 ( $\beta$ 71,  $\beta$ 74,  $\beta$ 86) predicts seroconversion and development of type 1 diabetes**

Zhao, L. P., Papadopoulos, G. K., Lybrand, T. P., Moustakas, A. K., Bondinas, G. P., Carlsson, A., Larsson, H. E., Ludvigsson, J., Marcus, C., Persson, M., Samuelsson, U., Wang, R., Pyo, C-W., Nelson, W. C., Geraghty, D. E., Rich, S. S., Lernmark, Å. & BDD Study group, 2021, In: EBioMedicine. 69, 14 p., 103431.

**Periodontal conditions, retinopathy, and serum markers in individuals with type 1 diabetes**

Widén, C., Holmer, H., Sättlin, S., Renvert, S., Lernmark, Å. & Persson, G. R., 2020 Nov, In: Journal of Periodontology. 91, 11, p. 1436-1443 8 p.

**Characterization of plasma lipidomics in adolescent subjects with increased risk for type 1 diabetes in the DiPiS cohort**

Andersson Svård, A., Lernmark, Å., Maziarz, M. & DiPiS Study Group, 2020 Oct 8, In: Metabolomics. 16, 10, 109.

**Motifs of Three HLA-DQ Amino Acid Residues ( $\alpha$ 44,  $\beta$ 57,  $\beta$ 135) Capture Full Association With the Risk of Type 1 Diabetes in DQ2 and DQ8 Children**

Zhao, L. P., Papadopoulos, G. K., Kwok, W. W., Moustakas, A. K., Bondinas, G. P., Larsson, H. E., Ludvigsson, J., Marcus, C., Samuelsson, U., Wang, R., Pyo, C-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2020 Jul 1, In: Diabetes. 69, 7, p. 1573-1587 15 p.

**Screening for autoantibody targets in post-vaccination narcolepsy using proteome arrays**

Lind, A., Eriksson, D., Akel, O., Ramelius, A., Palm, L., Lernmark, Å., Kämpe, O., Elding Larsson, H. & Landegren, N., 2020 Apr, In: Scandinavian Journal of Immunology. 91, 4, e12864.

**Longitudinal Metabolome-Wide Signals Prior to the Appearance of a First Islet Autoantibody in Children Participating in the TEDDY Study**

Parikh, H., Lernmark, Å. & TEDDY Study Group, 2020 Mar 1, In: Diabetes. 69, 3, p. 465-476 12 p.

**Hyaluronan deposition in islets may precede and direct the location of islet immune-cell infiltrates**

Bogdani, M., Speake, C., Dufort, M. J., Johnson, P. Y., Larmore, M. J., Day, A. J., Wight, T. N., Lernmark, Å. & Greenbaum, C. J., 2020 Mar, In: Diabetologia. 63, 3, p. 549-560 12 p.

**Absence of Islet Autoantibodies and Modestly Raised Glucose Values at Diabetes Diagnosis Should Lead to Testing for MODY: Lessons From a 5-Year Pediatric Swedish National Cohort Study**

Carlsson, A., Shepherd, M., Ellard, S., Weedon, M., Lernmark, Å., Forsander, G., Colclough, K., Brahimi, Q., Valtonen-Andre, C., Ivarsson, S. A., Elding Larsson, H., Samuelsson, U., Örtqvist, E., Groop, L., Ludvigsson, J., Marcus, C. & Hattersley, A. T., 2020, In: Diabetes Care. 43, 1, p. 82-89

**A combined risk score enhances prediction of type 1 diabetes among susceptible children**

Ferrat, L. A., Vehik, K., Sharp, S. A., Lernmark, Å., Rewers, M. J., She, J-X., Ziegler, A-G., Toppari, J., Akolkar, B., Krischer, J. P., Weedon, M. N., Oram, R. A., Hagopian, W. A. & TEDDY Study Group, 2020, In: Nature Medicine. 26, 8, p. 1247-1255 9 p.

**Decreased HLA-DQ expression on peripheral blood cells in children with varying number of beta cell autoantibodies**

Andersson Svård, A., Maziarz, M., Ramelius, A., Lundgren, M., Lernmark, Å., Elding Larsson, H. & DiPiS Study Group, 2020, In: Journal of Translational Autoimmunity. 3, 100052.

**Hierarchical Order of Distinct Autoantibody Spreading and Progression to Type 1 Diabetes in the TEDDY Study**

Vehik, K., Bonifacio, E., Lernmark, A., Yu, L., Williams, A., Schatz, D., Rewers, M., She, J-X., Toppari, J., Hagopian, W., Akolkar, B., Ziegler, A. G., Krischer, J. P. & TEDDY Study Group, 2020, In: Diabetes Care. 43, 9, p. 2066-2073

**Next Generation HLA Sequence Analysis Uncovers Seven HLA-DQ Amino Acid Residues and Six Motifs Resistant to Childhood Type 1 Diabetes**

Zhao, L. P., Papadopoulos, G. K., Kwok, W. W., Moustakas, A. K., Bondinas, G. P., Carlsson, A., Larsson, H. E., Ludvigsson, J., Marcus, C., Samuelsson, U., Wang, R., Pyo, C-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2020, In: Diabetes. 69, 11, p. 2523-2535

**Plasma ascorbic acid and the risk of islet autoimmunity and type 1 diabetes: the TEDDY study**

Mattila, M., Erlund, I., Lee, H. S., Niinistö, S., Uusitalo, U., Andrén Aronsson, C., Hummel, S., Parikh, H., Rich, S. S., Hagopian, W., Toppari, J., Lernmark, Å., Ziegler, A. G., Rewers, M., Krischer, J. P., Norris, J. M., Virtanen, S. M. & TEDDY Study Group, 2020, In: *Diabetologia*. 63, 2, p. 278-286

**Prospective virome analyses in young children at increased genetic risk for type 1 diabetes**

Vehik, K., Lynch, K. F., Wong, M. C., Tian, X., Ross, M. C., Gibbs, R. A., Ajami, N. J., Petrosino, J. F., Rewers, M., Toppari, J., Ziegler, A. G., She, J.-X., Lernmark, A., Akolkar, B., Hagopian, W. A., Schatz, D. A., Krischer, J. P., Hyöty, H., Lloyd, R. E. & TEDDY Study Group, 2019 Dec, In: *Nature Medicine*. 25, 12, p. 1865-1872 8 p.

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Hampe, C. S., Radtke, J. R., Wester, A., Carlsson, A., Cedervall, E., Jönsson, B., Ivarsson, S. A., Elding Larsson, H., Larsson, K., Lindberg, B., Neiderud, J., Rolandsson, O. & Lernmark, 2019 Nov, In: *Diabetic Medicine*. 36, 11, p. 1375-1383 9 p.

**Autoimmune (type 1) diabetes**

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**Genetic Variation Within the HLA-DRA1 Gene Modulates Susceptibility to Type 1 Diabetes in HLA-DR3 Homozygotes**

Aydemir, Ö., Noble, J. A., Bailey, J. A., Lernmark, Å., Marsh, P., Andersson Svärd, A., Bearoff, F., Blankenhorn, E. P., Mordes, J. P. & Better Diabetes Diagnosis (BDD) Study Group, 2019 Jul, In: *Diabetes*. 68, 7, p. 1523-1527 5 p.

**Predicting Islet Cell Autoimmunity and Type 1 Diabetes: An 8-Year TEDDY Study Progress Report**

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**Maternal dietary supplement use and development of islet autoimmunity in the offspring: TEDDY study**

Silvis, K., Aronsson, C. A., Liu, X., Uusitalo, U., Yang, J., Tamura, R., Lernmark, Å., Rewers, M., Hagopian, W., She, J. X., Simell, O., Toppari, J., Ziegler, A., Akolkar, B., Krischer, J., Virtanen, S. M., Norris, J. M. & TEDDY Study Group, 2019 Feb, In: *Pediatric Diabetes*. 20, 1, p. 86-92 7 p.

**Autoantibodies in Pandemrix®-induced narcolepsy: Nine candidate autoantigens fail the conformational autoantibody test**

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**Eleven Amino Acids of HLA-DRB1 and Fifteen Amino Acids of HLA-DRB3, 4 and 5 Include Potentially "Causal Residues" Responsible for the Risk of Childhood Type 1 Diabetes**

Zhao, L. P., Papadopoulos, G. K., Kwok, B., Xu, B., Kong, M., Moustakas, A. K., Bondinas, G. P., Carlsson, A., Elding-Larsson, H., Ludvigsson, J., Marcus, C., Persson, M., Samuelsson, U., Wang, R., Pyo, C.-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2019, In: *Diabetes*. 68, 8, p. 1692-1704

**Genetic contribution to the divergence in type 1 diabetes risk between children from the general population and children from affected families**

Hippich, M., Beyerlein, A., Hagopian, W. A., Krischer, J. P., Vehik, K., Knoop, J., Winker, C., Toppari, J., Lernmark, Å., Rewers, M. J., Steck, A. K., She, J. X., Akolkar, B., Robertson, C. C., Onengut-Gumuscu, S., Rich, S. S., Bonifacio, E., Ziegler, A. G. & TEDDY Study Group, 2019, In: *Diabetes*. 68, 4, p. 847-857 11 p.

**HLA high-resolution typing by next-generation sequencing in Pandemrix-induced narcolepsy**

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