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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 Sept 21 → present

Principal investigator

EXODIAB: Excellence of Diabetes Research in Sweden
Lund University
Malmö, 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 Institute

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 Institute

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

β-Cell Function and Glucose Tolerance in Persons With Multiple Islet Autoantibodies Randomized to a Gluten-free Diet

Maziarz, M., Koskenniemi, J. J., Martinez, M. M., Spiliopoulos, L., Salami, F., Toppari, J., Kero, J., Veijola, R., Tossavainen, P., Palmu, S., Aronsson, C. A., Lundgren, M., Borg, H., Katsarou, A., Elding Larsson, H., Knip, M., Lou, O., Dunne, J. L., Törn, C. & Lernmark, Å., 2025 Jun, (E-pub ahead of print) In: Journal of the Endocrine Society. 9, 8, p. 1-13
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Unfolding the Mystery of Autoimmunity: The Environmental Determinants of Diabetes in the Young (TEDDY) Study

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Two DRB3 residues predictively associate with the progression to type 1 diabetes among DR3 carriers

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Considerations for more actionable consensus guidance for monitoring individuals with islet autoantibody-positive pre-stage 3 type 1 diabetes. Reply to Mallone R [letter]

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D. A., Schulman-Rosenbaum, R., Simmons, K. M., Sims, E. K., Skyler, J. S., Speake, C., Steck, A. K., Tonyushkina, K. N., Veijola, R., Wentworth, J. M., Wherrett, D. K., Wood, J. R., Ziegler, A.-G. & DiMeglio, L. A., 2025 Feb 12, (E-pub ahead of print) In: *Diabetologia*.

Early appearance of thyroid autoimmunity in children followed from birth for type 1 diabetes risk

Jonsdottir, B., Clasen, J. L., Vehik, K., Lernmark, Å., Lundgren, M., Bonifacio, E., Schatz, D., Ziegler, A.-G., Hagopian, W., Rewers, M., McIndoe, R., Toppari, J., Krischer, J., Akolkar, B., Steck, A., Veijola, R., Haller, M. J., Elding Larsson, H. & TEDDY Study Group, 2025 Feb, In: *The Journal of clinical endocrinology and metabolism*. 110, 2, p. 498-510 12 p., dgae478.

Amino acids and CART distinguish A-β+ Ketosis-Prone Diabetes from type 1 and type 2 diabetes during hyperglycemic crises

Jahoor, F., Hsu, J. W., Keene, K. R., Peacock, W. F., Huang, X., Guffey, D., Byun, J., Bennet, R., Lernmark, A., Tosur, M. & Balasubramanyam, A., 2025 Jan 16, (E-pub ahead of print) In: *The Journal of clinical endocrinology and metabolism*.

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Joint modeling of multistate and nonparametric multivariate longitudinal data

You, L., Salami, F., Törn, C., Lernmark, Å. & Tamura, R., 2024 Sept 1, In: *Annals of Applied Statistics*. 18, 3, p. 2444-2461

Type 1 diabetes, celiac disease, and autoimmune thyroiditis autoantibodies in population-based type 2 diabetes patients

Lind, A., Cheng-ting, T., Åke, L. & Johan, J., 2024 Sept, In: *Journal of Clinical and Translational Endocrinology*. 37, 100367.

The Influence of Pubertal Development on Autoantibody Appearance and Progression to Type 1 Diabetes in the TEDDY Study

Warncke, K., Tamura, R., Schatz, D. A., Veijola, R., Steck, A. K., Akolkar, B., Hagopian, W., Krischer, J. P., Lernmark, Å., Rewers, M. J., Toppari, J., McIndoe, R., Ziegler, A.-G., Vehik, K., Haller, M. J. & Elding Larsson, H., 2024 May 23, In: *Journal of the Endocrine Society*. 8, 7, bvae103.

Autoimmune Type 1 Diabetes

Akel, O. & Lernmark, Å., 2024 Jan 1, *Textbook of Diabetes*. Holt, R. I. & Flyvbjerg, A. (eds.). Sixth edition ed. Wiley, p. 203-215

Anxiety, depression and quality of life in relation to SARS-CoV-2 antibodies in individuals living with diabetes during the second wave of COVID-19

Lind, A., Yang, C., Hugo, H., Maria, H., Stefan, J., Lernmark, Å., Martin, S., Staffan, T., Cheng-ting, T., Jeanette, W. & Johan, J., 2024 Jan, In: *Diabetes Epidemiology and Management*. 13, 100194.

Assisting the implementation of screening for type 1 diabetes by using artificial intelligence on publicly available data

Teixeira, P. F., Battelino, T., Carlsson, A., Gudbjörnsdóttir, S., Hannelius, U., von Herrath, M., Knip, M., Korsgren, O., Elding Larsson, H., Lindqvist, A., Ludvigsson, J., Lundgren, M., Nowak, C., Pettersson, P., Pociot, F., Sundberg, F., Åkesson, K., Lernmark, Å. & Forsander, G., 2024, In: *Diabetologia*. 67, 6, p. 985-994

Caesarean section and risk of type 1 diabetes

Singh, T., Weiss, A., Vehik, K., Krischer, J., Rewers, M., Toppari, J., Lernmark, Å., Hagopian, W., Akolkar, B., Bonifacio, E., Ziegler, A.-G., Winkler, C. & TEDDY Study Group, 2024, In: *Diabetologia*. 67, 8, p. 1582-1587

Childhood screening for type 1 diabetes comparing automated multiplex Antibody Detection by Agglutination-PCR (ADAP) with singleplex islet autoantibody radiobinding assays

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HLA Class II (DR, DQ, DP) Genes Were Separately Associated With the Progression From Seroconversion to Onset of Type 1 Diabetes Among Participants in Two Diabetes Prevention Trials (DPT-1 and TN07)

Zhao, L. P., Papadopoulos, G. K., Skyler, J. S., Pugliese, A., Parikh, H. M., Kwok, W. W., Lybrand, T. P., Bondinas, G. P., Moustakas, A. K., Wang, R., Pyo, C.-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2024, In: *Diabetes Care*. 47, 5, p. 826-834

Intake of B vitamins and the risk of developing islet autoimmunity and type 1 diabetes in the TEDDY study

Hakola, L., Mramba, L. K., Uusitalo, U., Andrén Aronsson, C., Hummel, S., Niinistö, S., Erlund, I., Yang, J., Rewers, M. J., Akolkar, B., McIndoe, R. A., Rich, S. S., Hagopian, W. A., Ziegler, A., Lernmark, Å., Toppari, J., Krischer, J. P., Norris, J. M., Virtanen, S. M. & TEDDY Study Group, 2024, In: *European Journal of Nutrition*. 63, 4, p. 1329-1338

Oral Insulin Delay of Stage 3 Type 1 Diabetes Revisited in HLA DR4-DQ8 Participants in the TrialNet Oral Insulin Prevention Trial (TN07)

Zhao, L. P., Papadopoulos, G. K., Skyler, J. S., Parikh, H. M., Kwok, W. W., Bondinas, G. P., Moustakas, A. K., Wang, R., Pyo, C.-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2024, In: *Diabetes Care*. 47, 9, p. 1608-1616

Progression to type 1 diabetes in the DPT-1 and TN07 clinical trials is critically associated with specific residues in HLA-DQA1-B1 heterodimers

Zhao, L. P., Papadopoulos, G. K., Skyler, J. S., Pugliese, A., Parikh, H. M., Kwok, W. W., Lybrand, T. P., Bondinas, G. P., Moustakas, A. K., Wang, R., Pyo, C.-W., Nelson, W. C., Geraghty, D. E. & Lernmark, Å., 2024, In: *Diabetologia*. 67, 11, p. 2481-2493

Distinct transcriptomic profiles in children prior to the appearance of type 1 diabetes-linked islet autoantibodies and following enterovirus infection

Lin, J., Moradi, E., Salenius, K., Lehtipuro, S., Häkkinen, T., Laiho, J. E., Oikarinen, S., Randelin, S., Parikh, H. M., Krischer, J. P., Toppari, J., Lernmark, Å., Petrosino, J. F., Ajami, N. J., She, J.-X., Hagopian, W. A., Rewers, M. J., Lloyd, R. E., Rautajoki, K. J. & Hyöty, H. & 2 others, Nykter, M. & TEDDY Study Group, 2023 Nov 22, In: *Nature Communications*. 14, p. 1-13 7630.

Executive Summary: Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus

Sacks, D. B., Arnold, M., Bakris, G. L., Bruns, D. E., Horvath, A. R., Lernmark, Å., Metzger, B. E., Nathan, D. M. & Kirkman, M. S., 2023 Oct, In: *Diabetes Care*. 46, 10, p. 1740-1746 7 p.

Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus

Sacks, D. B., Arnold, M., Bakris, G. L., Bruns, D. E., Horvath, A. R., Lernmark, Å., Metzger, B. E., Nathan, D. M. & Kirkman, M. S., 2023 Oct, In: *Diabetes Care*. 46, 10, p. e151-e199

Polymorphisms in Intron 1 of HLA-DRA Differentially Associate with Type 1 Diabetes and Celiac Disease and Implicate Involvement of Complement System Genes C4A and C4B

Aydemir, Ö., Bailey, J. A., Agardh, D., Lernmark, A., Noble, J., Andersson Svärd, A., Blankenhorn, E. P., Parikh, H., Ziegler, A. G., Toppari, J., Akolkar, B., Hagopian, W. A., Rewers, M. J., Mordes, J. P. & TEDDY Study Group, 2023 Sept 1, (E-pub ahead of print) In: *eLife*. 22 p.

SARS-CoV-2 - No Increased Islet Autoimmunity or Type 1 Diabetes in Teens

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Executive Summary: Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus

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Islet autoantibody screening in at-risk adolescents to predict type 1 diabetes until young adulthood: a prospective cohort study

Ghalwash, M., Anand, V., Lou, O., Martin, F., Rewers, M., Ziegler, A. G., Toppari, J., Hagopian, W. A., Veijola, R., Achenbach, P. (Contributor), Bonifacio, E. (Contributor), Crouch, C. (Contributor), Dunne, J. (Contributor), Elding Larsson, H. (Contributor), Frohnert, B. I. (Contributor), Hu, J. (Contributor), Hyöty, H. (Contributor), Ilonen, J. (Contributor), Jönsson, J. (Contributor) & Killian, M. (Contributor) & 21 others, Knip, M. (Contributor), Koski, E. (Contributor), Li, Y. (Contributor), Li, Z. (Contributor), Liu, B. (Contributor), Lundgren, M. (Contributor), Malhotra, A. (Contributor), Maziarz, M. (Contributor), Meyer, J. (Contributor), Moore, S. (Contributor), Ng, K. (Contributor), Norris, J. (Contributor), Roy, S. (Contributor), Spiliopoulos, L. (Contributor), Steck, A. (Contributor), Stavropoulos, H. (Contributor), Waugh, K. (Contributor), Winkler, C. (Contributor), Yu, L. (Contributor), Lernmark, Å. (Contributor) & Type 1 Diabetes Intelligence Study Group, 2023 Apr, In: *The Lancet Child and Adolescent Health*. 7, 4, p. 261-268 8 p.

Epidemiology and Pathogenesis of Type 1 Diabetes

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Gastrointestinal Infections Modulate the Risk for Insulin Autoantibodies as the First-Appearing Autoantibody in the TEDDY Study

Lönnrot, M., Lynch, K. F., Rewers, M., Lernmark, Å., Vehik, K., Akolkar, B., Hagopian, W., Krischer, J., McIndoe, R. A., Toppari, J., Ziegler, A.-G., Petrosino, J. F., Lloyd, R., Hyöty, H. & TEDDY Study Group, 2023, In: *Diabetes Care*. 46, 11, p. 1908-1915

Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus

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HLA Genotype and Probiotics Modify the Association Between Timing of Solid Food Introduction and Islet Autoimmunity in the TEDDY Study

Uusitalo, U., Mramba, L. K., Aronsson, C., Vehik, K., Yang, J., Hummel, S., Lernmark, Å., Rewers, M., Hagopian, W., McIndoe, R., Toppari, J., Ziegler, A.-G., Akolkar, B., Krischer, J. P., Virtanen, S. M., Norris, J. M. & TEDDY Study Group, 2023, In: *Diabetes Care*. 46, 10, p. 1839-1847

Interaction Between Dietary Iron Intake and Genetically Determined Iron Overload: Risk of Islet Autoimmunity and Progression to Type 1 Diabetes in the TEDDY Study

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Physical Activity and the Development of Islet Autoimmunity and Type 1 Diabetes in 5-15-Year-Old Children Followed in the TEDDY Study

Liu, X., Johnson, S. B., Lynch, K. F., Cordan, K., Pate, R., Butterworth, M. D., Lernmark, Å., Hagopian, W. A., Rewers, M. J., McIndoe, R. A., Toppari, J., Ziegler, A.-G., Akolkar, B., Krischer, J. P., Yang, J. & TEDDY Study Group, 2023, In: *Diabetes Care.* 46, 7, p. 1409-1416

Plasma protein biomarkers predict the development of persistent autoantibodies and type 1 diabetes 6 months prior to the onset of autoimmunity

Nakayasu, E. S., Bramer, L. M., Ansong, C., Schepmoes, A. A., Fillmore, T. L., Gritsenko, M. A., Clauss, T. R., Gao, Y., Piehowski, P. D., Stanfill, B. A., Engel, D. W., Orton, D. J., Moore, R. J., Qian, W.-J., Sechi, S., Frohnert, B. I., Toppari, J., Ziegler, A.-G., Lernmark, Å. & Hagopian, W. & 6 others, Akolkar, B., Smith, R. D., Rewers, M. J., Webb-Robertson, B.-J. M., Metz, T. O. & TEDDY Study Group, 2023, In: *Cell Reports Medicine.* 4, 7, 101093.

Possible heterogeneity of initial pancreatic islet beta-cell autoimmunity heralding type 1 diabetes

Lernmark, Å., Akolkar, B., Hagopian, W., Krischer, J., McIndoe, R., Rewers, M., Toppari, J., Vehik, K. & Ziegler, A.-G., 2023, In: *Journal of Internal Medicine.* 294, 2, p. 145-158

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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

Törn, C., Liu, X., Onengut-Gumuscu, S., Counts, K. M., Moreno, J. L., Remedios, C. L., Chen, W.-M., LeFaive, J., Butterworth, M. D., Akolkar, B., Krischer, J. P., Lernmark, Å., Rewers, M., She, J.-X., Toppari, J., Ziegler, A.-G., Ratan, A., Smith, A. V., Hagopian, W. A. & Rich, S. S. & 2 others, Parikh, H. M. & TEDDY Study Group, 2022 Mar 16, In: *Scientific Reports.* 12, 1, p. 4516

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