

Microbiota and gut immune system in the pathogenesis of type 1 diabetes

Research group: Arno Hänninen, MD, Ph.D., Docent, Department of Medical Microbiology and Immunology, University of Turku, Kiinamyllynkatu 13; 20520 Turku Tel. +358-2-333 7526 E-mail: arno.hanninen@utu.fi. **Members of the research group** Raine Toivonen, Ph.D. (Academy of Finland postdoctoral research fellow). Rohini Emani, Ph.D.; Sami Pietilä, M.Sc. (registered Ph.D. student), Anna Musku (bioanalyticist).

Project description: Our aim is to define mechanisms linking gut immune system to type 1 diabetes using the nonobese diabetic (NOD) mouse model. Furthermore, we investigate how certain functional properties of gut microbes affect the diversity of microbiota in children. For this, we develop tools for whole-proteome analysis of gut microbiota. With clinical researchers we investigate if certain functional properties affect diabetes risk and other health parameters. We recently found that two common dietary fibers induce abrupt colonization of the gut with a narrow spectrum of microbes, and increase diabetes development in the NOD mouse. We now focus on innate and adaptive immune responses in the distal gut.

Publications:

- Toivonen R, Kong L, Rasool O, Lund RJ, Lahesmaa R, Hänninen A. Activation of Plasmacytoid Dendritic Cells in Colon-Draining Lymph Nodes during *Citrobacter rodentium* Infection Involves Pathogen-Sensing and Inflammatory Pathways Distinct from Conventional Dendritic Cells. **J Immunol.** 196:4750-9, 2016.
- Hänninen A, Toivonen R. On the role of gut bacteria and infant diet in the development of autoimmunity for type 1 diabetes. **Diabetologia** 58:2195-6, 2015.
- Toivonen R, Arstila TP, Hänninen A. Islet-associated T-cell receptor- β CDR sequence repertoire in prediabetic NOD mice reveals antigen-driven T-cell expansion and shared usage of V β J β TCR chains. **Mol Immunol.** 64:127-35, 2015.
- Toivonen RK, Emani R, Munukka E, Rintala A, Laiho A, Pietilä S, Pursiheimo JP, Soidinsalo P, Linhala M, Eerola E, Huovinen P, Hänninen A. Fermentable fibres condition colon microbiota and promote diabetogenesis in NOD mice. **Diabetologia** 57:2183-2192, 2014.
- Emani R, Asghar MN, Toivonen R, Lauren L, Söderström M, Toivola DM, van Tol EA, Hänninen A. Casein hydrolysate diet controls intestinal T cell activation, free radical production and microbial colonisation in NOD mice. **Diabetologia** 56:1781-1791, 2013.
- Alam C, Valkonen S, Palagani V, Jalava J, Eerola E, Hänninen A. Inflammatory tendencies and over production of IL-17 in the colon of young NOD mice are counteracted with diet change. **Diabetes** 59:2237-2246; 2010

Number of Ph.D. degrees supervised 2011-2016: 2

External funding in 2016: Academy of Finland, Diabetes Research Foundation of Finland, Diabetes Wellness Finland, South-West Hospital District of Finland, Emil Aaltonen Foundation, Turku University Foundation.