

ESPE Sabbatical Leave Program 2004-2005: Report from Prof. Pål R. Njølstad MD PhD, University of Bergen, Norway

First of all, I wish to express my sincere thanks for the ESPE Sabbatical Leave Program for the generous support to my sabbatical stay the academic year 2004-5!! Without this, the research stay would not have been possible.

1. The year was spent as a sabbatical leave in the Lab of Prof C. Ronald Kahn MD at the Joslin Diabetes Center, Harvard Medical School. The aim was to make a mouse model of a novel diabetes gene my laboratory just has isolated, and to use cellular studies to try and understand why our patients get diabetes when they have mutations in this particular gene. The progress of the work was good, and the data are now in the process of being analyzed. This is in line with the plans for the stay. To further continue this project, I have sent one of my MD PhD students, Helge Ræder, for a stay in Kahn's lab from June 2005. Another of my MD PhD students, Mette Vesterhus, will follow Helge Ræder from January 2006.
2. I plan to return to Harvard regularly in order to continue our collaboration and supervise the two students.
3. During my stay I gave one guest lecture at the Rhode Island Hospital, Rhode Island, one at the University of Chicago, Illinois, and one in Malaga, Spain. I attended the American Diabetes Association Annual Meeting in San Diego. I participated in several courses. Moreover, I gave three oral and one poster presentations at Harvard/Joslin Diabetes Center during my stay, and attended several seminars and lectures.
4. Six Pub Med listed papers and two book chapters were published during my year in the US. One paper and one book chapter are in the press and three more papers have just been submitted. Most of this work was partially completed before my stay (see below). Results primarily obtained during the year are currently being analyzed and will be published.
5. Socially, the family and I had a wonderful year in Boston. This city has lot to offer regarding music, museums and other culture. We have left our hearts in Boston and hope not before long to return for shorter stays.

Original papers

1. Sagen JV, Ræder R, Hathout E, Shehadeh N, Gudmundsson K, Bævre H, Abuelo D, Phornphutkul C, Molnes J, Bell GI, Gloyn A, Hattersley AT, Molven A, Søvik O, Njølstad PR. Permanent neonatal diabetes due to mutations in KCNJ11 encoding Kir6.2: Patient characteristics and initial response to sulfonylurea therapy. *Diabetes* 2004; 53:2713-2718.
2. Stene LC, Joner G and the Norwegian Childhood Diabetes Study Group. Atopic disorders and risk of childhood-onset type 1 diabetes in individuals. *Clin Exp Allergy* 2004; 34:201-206.
3. Sagen JV, Pearson E, Johansen A, Spyer G, Søvik O, Pedersen O, Njølstad PR, Hattersley AT, Hansen T. Preserved insulin response to tolbutamide in hepatocyte nuclear factor-1alpha mutation carriers. *Diabetic Medicine* 2005, 22:406-9.

4. Sagen JV, Bauman ME, Salvesen HB, Molven A, Søvik O, Njølstad PR. Diagnostic screening of NEUROD1 (MODY6) in subjects with MODY or gestational diabetes mellitus. *Diabetic Medicine* 2005, 22:1012-5.
5. Shehadeh N, Bakri D, Gershoni-Baruch R, Njølstad PR. Clinical characteristics of mutation carriers in a large family with glucokinase diabetes (MODY2). *Diabetic Medicine* 2005, 22:994-8.
6. Tammaro P, Girard C, Molnes M, Njølstad PR, Ashcroft FM. Kir6.2 mutations Y330C and F333I, that cause neonatal diabetes, decrease K_{ATP} channel ATP-sensitivity. *The EMBO J* 2005, 24:2318-30.
7. Bjørkhaug L, Bratland A, Njølstad PR, Molven A. Functional dissection of the HNF-1alpha transcription factor: A study on nuclear localization and transcriptional activation. *DNA and Cell Biology* 2005, in press.
8. Sagen, JV, Odili S, Bjørkhaug L, Zelent D, Buettger C, Kwagh J, Stanley C, Dahl-Jørgensen K, de Beaufort C, Bell GI, Han Y, Grimsby J, Taub R, Molven A, Søvik O, Njølstad PR, Matschinsky FM. From clinicogenetic studies of maturity-onset diabetes of the young to unravelling complex mechanisms of glucokinase regulation. *Journal of Biological Chemistry* 2005, submitted.
9. H. Ræder H, Bjørkhaug L, Mangseth K, Sagen JV, Johansson S, Hunting A, Følling I, Johansen O, Bjørngaas M, Paus PN, Søvik O, Molven A, Njølstad PR. Hepatocyte nuclear factor-4a mutations in the Norwegian MODY registry: A novel P2 promoter variant co-segregating with late-onset diabetes. *Diabetologia* 2005, submitted.
10. Ræder, H, Johansson S, Holm PI, Haldorsen IS, Mas E, Sbarra V, Neramoen I, Eide SÅ, Grevle L, Bjørkhaug L, Sagen JV, Aksnes L, Søvik O, Lombardo D, Molven A, Njølstad PR. Mutations in gene cause a novel diabetes syndrome. Submitted.

Book chapters

1. Njølstad PR, Søvik O, Matschinsky FM, Bell GI. Permanent Neonatal Diabetes mellitus due to Glucokinase Deficiency. In: Matschinsky FM, Magnusson, M (eds): Glucokinase and Glycemic Disease: From basics to novel therapeutics. Front Diabetes. Basel, Karger, 2004, vol 16, pp 65-74.
2. Gloyn AL, Odili S, Buettger C, Njølstad PR, Shiota C, Magnusson MA, Matschinsky FM. Glucokinase and the regulation of blood sugar: A mathematical model predicts the threshold for glucose stimulated insulin release for GCK gene mutations that cause hyper- and hypoglycemia. In: Matschinsky FM, Magnusson M (eds): Glucokinase and glycemic disease: From basics to novel therapeutics. Front. Diabetes. Basel, Karger 2004, vol 16, pp 92-109.
3. Njølstad PR, Molven A, Søvik O. Diagnosis and management of MODY in a pediatric setting. In: Chiarelli F, Dahl-Jørgensen K, Kiess W. Diabetes in childhood and adolescence. In press, 2005