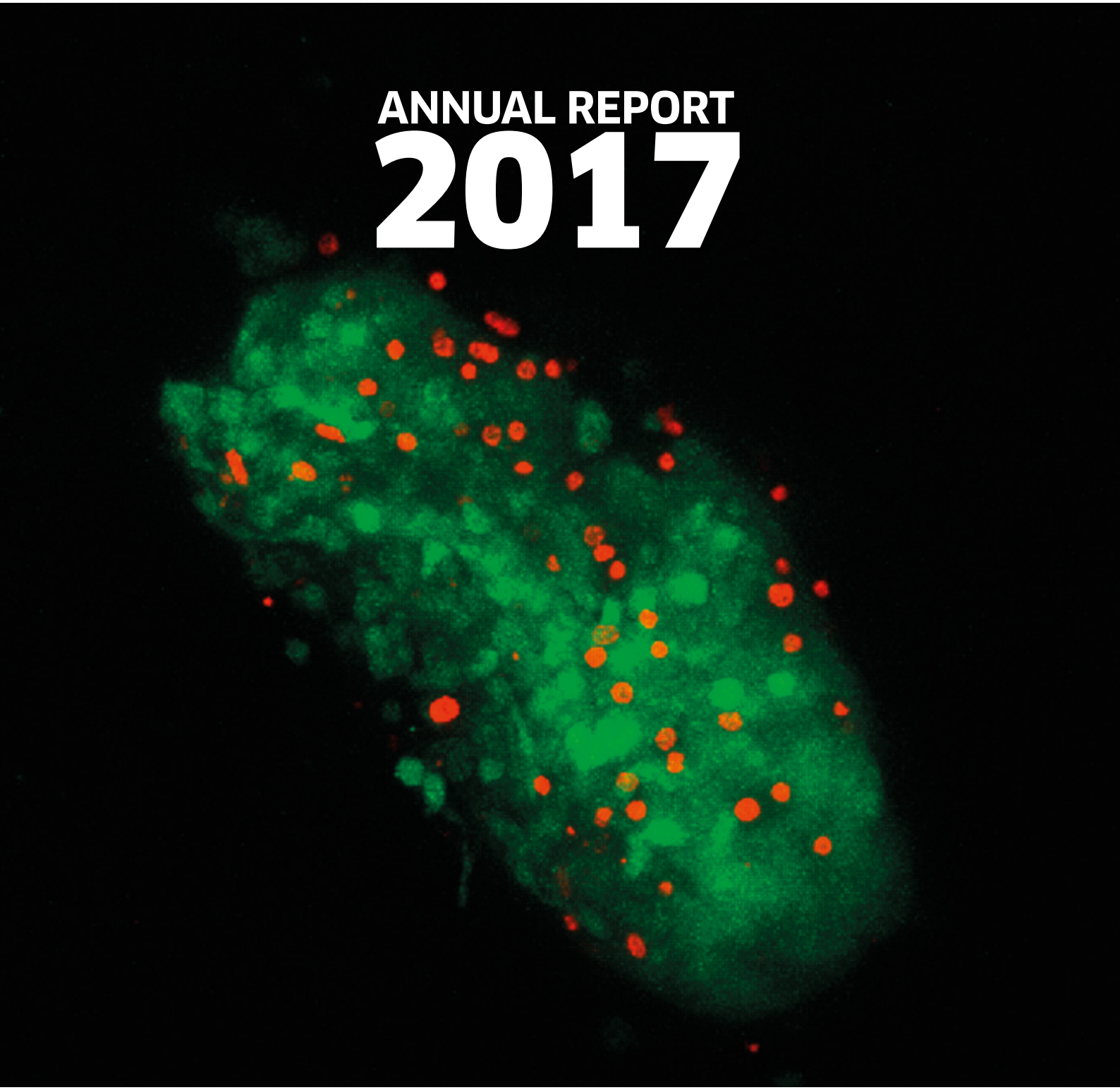
Oslo Diabetes Research Centre

ANNUAL REPORT 2017



Oslo University Hospital

UiO : University of Oslo

ANNUAL REPORT 2017
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Frontpage: Cover picture shows islet amyloid (red) in recent-onset type 1 diabetes. Courtesy from professsor Gunilla Westermark, University of Uppsala, Sweden.

CONTENTS

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KÅRE BIRKELAND
Professor, MD, PhD (Vice Chairman)

TORE JULSRUD BERG
Associate professor, MD PhD

ANNE KAREN JENUM
Professor, MD, PhD

GEIR JONER
Professor, MD, PhD

BENEDICTE LIE
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TROND G. JENSSEN
Professor, MD, PhD

TORE HENRIKSEN
Professor Emeritus, MD, PhD

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FOTO: APELAND/KATRINE LUNKE

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NEW PERSPECTIVES IN DIABETES RESEARCH

There is an urgency for greater action to improve diabetes outcomes and reduce the global burden of diabetes now affecting more than 425 million people, of which one-third are people older than 65 years. The estimates of children and adolescents below age 20 with type 1 diabetes has risen to over a million. If nothing is done, the number of people with diabetes may rise to 629 million in 2045, although positively the incidence has started to drop in some high income countries. At the same time, a further 352 million people with impaired glucose tolerance are at high risk of developing diabetes.

In Norway, 12.000 people get diabetes every year, it is estimated that approximately 245.000 are diagnosed with the disease and probably 50-100.000 more have diabetes, but are not diagnosed yet. Diabetes is a serious disease. In Norway three out of four have at least one complication, one of five get serious eye complications, 500 suffer from amputations and 100 need kidney transplantations every year. The risk of life threatening myocardial infarction and stroke is 2-4 fold increased compared to those without diabetes, and tenfold so in younger age groups.
Several billions of Norwegian kroner are used to treat diabetes every year in Norway, and most of this is spent on diabetic complications. We know from long term clinical studies, including the Oslo Study, that optimal treatment achieving close to normal blood sugar levels can prevent these severe complications. We urge the health authorities to increase spending on diabetes prevention and treatment to save big expenditures in the future - and to save lives and human suffering. It is a paradox that not more research funds are allocated to these issues. Research to prevent these devastating diseases and complications is extremely important both for the individual and society.

Oslo Diabetes Research Center has a strong clinical basis and is the only center in Norway covering the whole life-span of diabetes, from the fetus, through childhood and adolescence to early and late adult life. This life-course approach to diabetes attempts to capture the complex influence of factors operating at different points in life integrating both early-life and adult lifestyle models into a wider framework through an extensive collaboration between our ten established research groups and their collaborators. In the life-course perspective to diabetes we aim to assess how the effect of factors operating at different stages of life, from in utero to late adulthood, might accumulate and interact to determine development of diabetes and its complications later in life. Our ultimate aim is to contribute substantially to prevent diabetes - and in the meantime - its complications.

Our center's 10 research groups are founded in Oslo University Hospital and University of Oslo, mainly in the Faculty of Medicine's three institutes. The center covers nearly all diabetes related research in the Oslo region. In this annual report you may count nearly hundred researchers involved, and you will find description of close to 80 different defined research projects, that include basic science, advanced new laboratory analysis, clinical and epidemiological research. We are turning from pure clinical research into more mechanistic studies, trying to understand the cause and pathogenesis of diabetes and its complications. This applies to both type 1 and type 2 diabetes and other rare forms of diabetes. We also bring this basic science research back to the clinic. We are running 15 randomized, clinical trials, aiming to discover new therapies, and improve known therapies.

This year, we are particularly proud of Cecilie Wium, who received a major grant (NOK 18 Mill) from The Norwegian Research Council for the DIASA project aiming to prevent and improve treatment of type 2 diabetes in immigrants. Cecilie started her research here as a PhD student, continues as post.doc and now Principal Investigator. This highlight the excellence of the Type 2 diabetes research group, steadily improving and expanding.

The nutritional and environmental conditions under which an individual develops from the one cell stage at conception to birth is now known to have major impact on the future health of the newborn child. Inadequate nutrition in this very early (fetal) period of life increases the risk of cardiovascular diseases, diabetes and overweight. Tore Henriksen and his re-

From our annual Oslo Diabetes Research Centre Seminar in Son, April 7-8, 2016. (Photo: Kjersti R. Normann)

search group has recently developed and published a new method to study how maternal nutritional, metabolic and pathogenic factors interact with the placenta. This 4 vessel sampling method is novel in a global perspective, and enables us to study the placenta in vivo by analyzing blood and tissue samples from arterial and venous vessels both on the maternal and fetal side.

The Dahl-Jørgensen group is now involved in a broad international network aiming to establish a vaccine to prevent type 1 diabetes. In the DiViD study a new sensitive assay was able to detect enterovirus RNA in the pancreas in all cases of newly developed disease. The DiViD Intervention Trial is ready to start recruitment to test whether antiviral treatment may save endogenous insulin production in newly diagnosed children with type 1 diabetes. In the EU-project INNODIA (www.innodia.eu) close relatives to patients with type 1 diabetes will be recruited to find persons with prediabetes having high risk of developing the disease, and also trying to establish new preventive treatment for these relatives.

Thus 2017 was again a successful year for the Oslo Diabetes Research Centre. The center is steadily improving it's international reputation. We produced more than one hundred international peer reviewed publications. In this year's annual report you may notice many publications in the highest ranked diabetes related scientific journals.

The centre has no difficulties in attracting young talents for diabetes research. In 2017 we had six Ph.D. dissertation: Kåre Rønn Richardsen, Christin Wiegels Waage, Nicolai Lund-Blix, Jørn Petter Hanto Lindahl, Vibeke Gagnum and Hilde Risstad. We thank and acknowledge them, and are looking forward to include many of them for further research within our center.

In this report you see that the ambitions of each research group are high, and will bring diabetes research in Oslo a big step forward. We work hard to increase funding, and the spirit and enthusiasm is there, never to give in, before getting closer to the targets of prevention and a cure for diabetes.

Knut Dahl-Jørgensen (signature)
CHAIRMAN PROFESSOR DR. MED.

LEADER	WORK PLACE	RESEARCH AREA	E-MAIL
Knut Dahl-Jørgensen (Chairman)	**Pediatric Department, Oslo University Hospital**	**Diabetes in children and adolescents, etiology of type 1 diabetes, complications**	knut.dahl-jorgensen@medisin.uio.no
Kåre I. Birkeland (Vice Chairman)	**Department of transplantation medicine, University of Oslo and Oslo University Hospital**	**Prevention and treatment of type 2 diabetes**	k.i.birkeland@medisin.uio.no
Tore Julsrud Berg	**Department of Endocrinology, Oslo University Hospital**	**Diabetic late complications**	t.j.berg@medisin.uio.no
Geir Joner	**Pediatric Department, Oslo University Hospital**	**Epidemiology and etiology of type 1 diabetes, complications, mortality**	geir.joner@medisin.uio.no
Anne Karen Jenum	**Department of General Practice, University of Oslo**	**Diabetes and primary health issues in primary care**	a.k.jenum@medisin.uio.no
Tore Henriksen / Jens Bollerslev	**Department of Endocrinology and Obstetrics, Oslo University Hospital**	**Diabetes and pregnancy**	tore.henriksen@rikshospitalet.no jens.bollerslev@rikshospitalet.no
Trond Jenssen	**Department of Nephrology, Oslo University Hospital**	**Diabetic nephropathy**	trond.jenssen@rikshospitalet.no
Benedicte Lie	**Department of Medical Genetics, Oslo University Hospital**	**Genetics and epigenetics of type 1 diabetes**	b.a.lie@medisin.uio.no
Jens Petter Berg	**Department of Biochemistry, Oslo University Hospital**	**Metabolomics of hyperglycemia**	j.p.berg@medisin.uio.no
Torild Skrivarhaug	**Pediatric Department, Oslo University Hospital**	**The Norwegian Childhood Diabetes Registry**	torild.skrivarhaug@medisin.uio.no


Serum Sep Clot Activator

Research Group:
CHILDHOOD DIABETES

Group Leader:
Professor Knut Dahl-Jørgensen

KNUT DAHL-JØRGENSEN

Research focus:

The group has four main research areas. The first is the etiology and prevention of type 1 diabetes and autoimmune diseases, especially focusing the role of viruses and the interaction with the immune system in pancreatic and thyroid tissue samples. The last years we have succeeded in detecting a low grade persistent enterovirus infection in the insulin producing pancreatic islets of patients with newly diagnosed type 1 diabetes, and also in the thyroid of patients with newly diagnosed Graves' Disease. This strongly indicates that viruses are important for the development of autoimmune diseases.

The DiViD study has got worldwide attention for its unique collection of pancreatic biopsies in live young adult patients at the onset of type 1 diabetes. We have signed material transfer and research collaboration contracts with 15 international, highly recognized laboratories, and we recently arranged group meetings in Miami in conjunction with the nPOD meeting (www.jdrf.org) to discuss the results and the next steps. This was also the case when we arranged the PEVNET Annual meeting in Oslo in May. Much focus has been on the role of enteroviruses, the insulitis and the role of innate immune system. The last year we have identified several viral "footprints" in the pancreatic islets. We also detected that 43% of the T-cells in the inflamed islets (insulitis) were "resident T-cells", indicating a previous infection. So the evidences for a role of viruses in triggering and driving the process killing the beta-cells are steadily increasing. Also interesting results of increased ER stress and increased proinsulin/insulin ratio in the islets add new aspects to the pathogenesis of type 1 diabetes.

We were granted NOK 9 mill from the Health Region South East in 2016 to start a Scandinavian multicentre, randomized trial (The DiViD Intervention Trial) to study the effect of antiviral treatment aiming to preserve endogenous insulin production at diagnosis, as measured by C-peptide. In addition to standard mixed meal tolerance tests, we will perform filterpaper blood tests for C-peptide monitoring at home. The trial is now approved by the authorities and is ready to start recruiting patients.

The second research area of our group is diabetes late complications. We have long term clinical studies on microvascular complications and the influence of glycemic control and advanced glycation. Recently the risk of early atherosclerosis in childhood onset type 1 diabetes has been the focus in several of our studies, with measurement of vessel wall thickness (IVUS, IMT, MRI) and vessel elasticity, and biochemical markers, as well as clinical data and risk factors. Increased arterial stiffness was reported. Martin Heier has been a postdoc in San Francisco as part of the EU Scientia Fellow Program, studying HDL Cholesterol function, and demonstrated decreased function in children and adolescents with type 1 diabetes. He has now returned to Oslo, planning exciting developments in this (and related) fields. The 10 years follow up of the prospective study "Atherosclerosis in Childhood Diabetes" has started in 2017. This will also include eye examinations and assessment of retinal vessel calibre added by oxymetry. The project aim to develop a new risk score for CVD in childhood onset type 1 diabetes.

In our large, nationwide clinical studies, now as part of the Childhood Diabetes Registry, we focus on important issues as intensified insulin treatment and pumps, diabetic nephropathy, diet, physical activity, quality of life and psychosocial problems and eating disturbances (together with Skrivarhaug's Group).

We became partners in the EU project INNODIA (An innovative approach towards the understanding and arresting type 1 diabetes) www.innodia.eu. This is a broad network of clinical centres and excellent basic research laboratories in Europe. As clinical center we will recruit newly diagnosed patients with

GROUP MEMBERS

AIDA SIMEUNOVIC
MD, PhD student

IDA MARIA MYNAREK
MD, PhD student

THERESE WEIDER
MD, PhD student

HANNA DIS MARGEIRSDOTTIR
MD, PhD, paediatrician, postdoc

MARTIN HEIER
MD, PhD, paediatrician, postdoc

LINE WISTING
PhD, M.Psychol.

DAG HELGE FRØISLAND
MD, PhD, paediatrician, postdoc

SARA HAMMERSTAD
MD, PhD, endocrinologist, postdoc

UNNI METTE KØPP
MD, PhD, paediatrician, postdoc

LARS KROGVOLD
MD, PhD, Assoc. Professor, paediatrician, postdoc

TRINE ROALD
R.N.

HANS JACOB BANGSTAD
MD, PhD

JON HAUG
Dr.Philos, clinical psychologist.

KARI ANNE SVEEN
MD, PhD, consultant (together with Tore Julsrud Berg's group)

type 1 diabetes, and first degree family members, for systematic follow up and make ready for future intervention trials. Such trials aim to prevent diabetes in at risk persons and to preserve endogenous insulin production in newly diagnosed cases. The DiViDInt trial is affiliated to INNODIA.

Projects:
Etiology and prevention of type 1 diabetes and autoimmune diseases:

1. Diabetes Virus Detection Project (DiViD)
2. Diabetes Virus Detection and Intervention trial (DiViDInt)
3. Viruses, genetics and autoimmunity in thyroiditis. A biopsy study.
4. Virus in autoimmune diseases.

Diabetes late complications:

5. Atherosclerosis in Childhood Diabetes – a population-based, prospective study.
6. Long term vascular changes in type 1 diabetes – Clinical aspects and biological markers – 30 years follow-up of the Oslo Study.
7. Advanced glycation of proteins and vascular complications in childhood diabetes.
8. HDL cholesterol function in type 1 diabetes.
9. Diabetic nephropathy: Hypertension and microalbuminuria in Norwegian children with type I diabetes.

Clinical diabetes:

10. Collaboration with the Norwegian Childhood Diabetes Registry (see page 30). A nationwide prospective population-based study for research and quality improvement by means of benchmarking.
11. Children and adolescents with diabetes - present state and future possibilities - A population-based study of factors affecting competences and treatment results in children and adolescents with type 1 diabetes.
12. Eating disturbances in childhood diabetes.
13. Childhood diabetes and celiac disease – a population based study.

Obesity and type 2 diabetes:

14. Pathways contributing to childhood weight development and overweight in Norway. Sub-study of the Mother and Child National Cohort.

Achievements 2017

Detection of a low grade persistent enterovirus infection in the insulin producing islets of Langerhans at diagnosis of type 1 diabetes. In depth description of the insulitis at diagnosis by detection of "resident T-cells" as a prominent feature of the insulitis. Detection of increased proinsulin/insulin ratio and detection of several viral "footprints" in the islets of Langerhans at diagnosis. Detection of amyloid deposits and DNA damage in the islets at diagnosis of type 1 diabetes.

Ambitions 2018-2019

Developing a new risk score for the development of early atherosclerosis in childhood diabetes. Start the DiViDInt, a randomized controlled multicenter trial of antiviral treatment in newly diagnosed type 1 diabetes patients aiming to maintain and restore endogenous insulin production. Finalizing recruitment of INNODIA. Establishing a broader group for the studies of viruses in other autoimmune diseases.

Research Group: TYPE 2 DIABETES AND METABOLISM
Group Leader: Kåre I. Birkeland

Research focus

We focus on epidemiological studies, clinical observational studies and randomized clinical trials in subjects with obesity, prediabetes, gestational diabetes, metabolic syndrome and type 2 diabetes. We design and conduct our own studies, but also participate in international multi-center studies, both researcher initiated and studies sponsored by pharmaceutical companies, (phase II-IV studies). We are also engaged in mechanistic studies and translational research in collaboration with different laboratories.

We aim at contributing to prevention and improved therapy for diseases related to overweight and physical inactivity, primarily type 2 diabetes and its complications. To achieve this, we search for etiological factors in disease development through hypothesis-generating epidemiological and observational studies and seek to test the hypotheses in mechanistic and randomized, controlled clinical trials. We aim to publish our results in internationally well recognized scientific journals and present at national and international meetings. We also engage in popular scientific publishing to increase knowledge about ours and others' research to the public. We collaborate closely and partly overlap with Anne Karen Jenum's group on the STORK-Groruddalen studies, with Elisabeth Qvigstad/Tore Henriksen/Jens Bollerslev's group on the STORK-Rikshospitalet studies and with Cecilie Wium's group at the Lipid Clinic.

Our greatest achievements in 2017:

- The highest number of publications ever from the group (33) and several in high ranked journal (Circulation, Lancet D&E and Diabetes Care).
- Two PhD defenses – Christin Waage and Hilde Risstad.

KÅRE I. BIRKELAND

- A major grant (18 MNOK) from Norwegian research Council to the DIASA project.

Our special focus for the coming years is

- genetics and epigenetics in gestational diabetes.
- diabetes in immigrants.
- mechanistic studies of bone marrow after bariatric surgery, soluble leptin receptors and the glucose lowering effects of probiotics.
- large register-based epidemiological studies in type 2 diabetes.

Projects

1. The FIBERDIA – a randomized controlled trial of the effects of probiotics on glucose metabolism.
2. The DIASA (Diabetes in South Asians) research program.
3. The DAPHNE- , DISCOVER- and DIAFLU studies focusing on large epidemiological register studies of type 2 diabetes in Norway and a substudy of the HUNT-study focusing on anthropometric indices and cardiovascular end-points.

GROUP MEMBERS 2017–2018

KÅRE I. BIRKELAND
Professor, MD, PhD

ANNE KAREN JENUM
Professor, MD, PhD

ANNE-MARIE AAS
Associate Professor, PhD

ANNE-PERNILLE OFSTAD
MD, PhD

CECILIE WIUM
MD, PhD, consultant

CHRISTINE SOMMER
PhD, postdoc

CHRISTIN W. WAAGE
PhD, postdoc

ELINE BIRKELAND
PhD student

ELISABETH QVIGSTAD
MD, PhD, consultant

GUNN-HELEN MOEN
MSc, PhD student

HANNE LØVDAL GULSETH
MD, PhD, senior researcher

HILDE RISSTAD
MD, PhD

INGVILD HØGESTØL
MD, PhD student

KIRSTI BJERKAN
MSc

LINE SLETNER
MD, PhD, researcher

PAZ LOPEZ-DORIGA RUIZ
MD, PhD student

SEDEGHEH GHARAGZLIAN
PhD

SUSANNA E. HANVOLD
MSc, PhD student

ÅSE RUTH EGGEMOEN
MD, PhD student

GRO BOZELIJN
research nurse

GØRIL VINJE
research nurse

ÅSE HALSNE
research nurse

JULIE ONSRUD OPSAHL
Forskerlinjen, Faculty of Medicine

SINDRE LEE-ØDEGAARD
Forskerlinjen, Faculty of Medicine

MANSOORA ALI
master student, NTNU

KJERSTI GJEMS VANBERG
master student, UiO

KRISTINE DUUS MOLVEN
master student, UiO

ODA KRISTINE SMESTU HOLM
master student (UiO)

SANDER RISMYR
master student (UiO)

NADIA KIRYUSHCHENKO
master student (UiO)

MAY-HELEN NYLAND ESPENES
medical student project, UiO

ANNE MARTHE BROBAKK HANSEN
medical student project, UiO

HILDE GJESDALEN
medical student project, UiO

4. Genetic and epigenetic sub-projects under the STORK and STORK-Groruddalen studies.
5. The 4B study: The effect of bariatric surgery on bone marrow fat and glucose metabolism in subjects with type 2 diabetes and morbid obesity.
6. Subprojects under the MyoGlu-study – A controlled, intervention study of high-intensive exercise training in subjects with abnormal glucose tolerance and controls.
7. The HypoAlert-study – An observational study with hypo- and euglycaemic glucose clamp investigations of subjects with type 1 diabetes and hypoglycemia unawareness.
8. 10 year follow up of subjects after bariatric surgery with focus on the prevalence of diabetes and metabolic risk factors.
9. Several multi-center phase II, III and IV clinical trials in collaboration with the pharmaceutical industry.

Ambitions 2018-19

- To publish at least 20 papers each year from the group, also aiming for some in the highest ranked journals.
- To visualize our research to a higher degree to the public.
- To recruit and obtain financial support for at least 1 new PhD or postdoc each year and for one large project every 2-3 year.

Research Group: DIABETIC LATE COMPLICATIONS
Group Leaders: Tore Julsrud Berg

Research focus
Epidemiology and mechanisms of late complications.

Projects
The DIALONG study: A study of long-term survivors with more than 45 years of type 1 diabetes. A large clinical and biochemical study focusing on macrovascular disease, skin and joint complications and quality of life. Three students are now doing their PhD/Dr Phil work in this study and one PhD is using the study as a part in her PhD. Preliminary results are a high prevalence of adhesive capsulitis and shoulder arthrosis.

Kari Anne Sveen holds a postdoc on a study of low grade inflammation against AGEs and inflammatory response in atherosclerosis in diabetes in the DIALONG- and OSLO study in collaboration with professor Jan Nilsson, Malmø.

Tore Julsrud Berg is part of the steering committee of the ROSA 4 study (See report from "Diabetes and related health issues in primary care").

Kristian Folkvord Hanssen has published two more papers on preeclamsia and type 1 diabetes.

TORE J. BERG

Achievements 2017
- Publication of four papers from the DIALONG study.
- Two years postdoctor Scientia Fellow research grant for Kari Anne Sveen.
- Final funding for Dr Phil student in the DIALONG shoulder/hand study.
- Final funding for PhD student in the DIALONG coronary heart disease study.
- Funding for PhD student in the DIALONG quality of live study.
- Funding for PhD student in the ROSA 4 Salten study on quality of care of diabetes.
- One Dr Phil thesis has been submitted.

Ambitions 2018
- Funding for one more PhD student in the DIALONG study.
- Publication of at least five papers from the DIALONG study and one from the ROSA 4 Salten study.

GROUP MEMBERS

TORE JULSRUD BERG
MD, PhD, Associate Professor

KRISTINE B. HOLTE
MD, PhD student

NIELS GUNNAR JUEL
MD, research fellow

ANNE KARIN MOLVÆR
RN, PhD student

KARI ANNE SVEEN
MD, PhD, Scientia postdoc fellow

KRISTINA B. SLÅTSVE
MD, PhD student

KRISTIAN F. HANSSEN
MD, PhD, Senior Professor

Research Group:
CHILDHOOD DIABETES AND DIABETES EPIDEMIOLOGY

Group Leader:
Geir Joner

Research focus
Diabetes epidemiology, causes of type 1 diabetes and prevention, diabetes complications and mortality. Special emphasis on risk factors for type 1 diabetes using epidemiological approaches, including studies of infectious, dietary and other environmental factors, and potential gene-environment interactions. Research to prevent complications and premature death by studying of risk factors is also central in the group's work. The long-time goal is to reduce the incidence of type 1 diabetes in children and reduce the impact of complications of diabetes in children that already have the disease. The most important source for research is the Norwegian Childhood Diabetes Registry with biobank with > 90% of new cases of diabetes below 15 years included, the MOBA-study with biobank and other registers.

Projects
1. The PAGE study (Prediction of Autoimmune diabetes and celiac disease in childhood by Genes and perinatal Environment): Studies of risk factors for type 1 diabetes and for celiac disease in The Norwegian Mother and Child Cohort (MOBA) linked to the Norwegian childhood diabetes registry (PI: Lars Chr. Stene).
2. Biomarkers for intrauterine environment and risk of childhood diabetes. Sera from 30 000 pregnant women linked to diabetes registry to identify women whose children later developed type 1 diabetes selected for biomarker studies, dietary and infectious (Ingvild S. Sørensen).
3. Mortality in a nationwide, population-based cohort of childhood-onset type 1 diabetes in Norway. (PhD-project by Vibeke Gagnum, MD).
4. Cardiovascular and end-stage renal disease in type 1 diabetes with onset before 15 years of age and long duration (project in preparation).

Achievements 2017
The project "Cardiovascular disease and end-stage renal disease in type 1 diabetes with onset before 15 years of age and long duration" has been funded for a phd-student from the Extra foundation. Maryam Saeed, MD, has been appointed as research fellow.
We obtained funding from the South-Eastern Norway Regional Health Authority for postdoc Nicolai Lund-Blix "Early nutrition and risk of islet autoimmunity and type 1 diabetes."
The PAGE-study is in steady progress, several analyses have been completed and results published; several publications are in the pipe-line.
The PhD-students Vibeke Gagnum and Nicolai Lund-Blix have defended their theses.

Ambitions 2018-2019
To be a leading group in epidemiological studies on genetic and environmental risk factors in the etiology of type 1 diabetes in children and adolescents.
To publish more exciting scientific results from the PAGE study.
To get the study "Cardiovascular disease and end-stage renal disease in type 1 diabetes with onset before 15 years of age and long duration" up and running. Long-term follow up of incident cases of T1D 1973-2016 in The Norwegian Childhood Diabetes Registry.

FOTO: ØYSTEIN H. HORGMO, UIO

GROUP MEMBERS

GEIR JONER
Professor, MD, PhD

LARS CHRISTIAN STENE
PhD, senior researcher

TORILD SKRIVARHAUG
MD, PhD, Director
Norwegian Childhood Diabetes Registry

GERMAN TAPIA
PhD, researcher/postdoc

VIBEKE GAGNUM
MD, PhD

INGVILD MENES SØRENSEN
MD, PhD, paediatric endocrinology

NICOLAI LUND-BLIX
cand. scient, PhD, postdoc

MARIA C. MAGNUS
PhD, researcher

KARL MÅRILD
MD, PhD, postdoc

PAZ RUIZ
MD, research fellow

MARYAM SAEED
MD, research fellow

GEIR JONER

Research Group:
DIABETES AND RELATED HEALTH ISSUES IN PRIMARY CARE

Group Leader:
Anne Karen Jenum

ANNE KAREN JENUM

Research focus

We apply a life course approach when studying the causation, care and prevention of type 2 diabetes and cardiovascular complications, and the social and ethnic differences in health. The group members have a diverse professional background, facilitating synergies and convergence in research. We have performed cross-sectional and cohort studies, qualitative studies, an RCT using new technology, systematic reviews and meta-analyses, and are involved in developing culturally sensitive interventions in primary care. The group covers two main areas of research:

1. *The Diabetes Care group* – working with type 2 diabetes, its complication, quality of diabetes care in a multiethnic society and strategies for prevention.
2. *The Mother and Child Health group* – working with the developmental origin of health and disease, not least gestational diabetes and type 2 diabetes, in a Norwegian mother, father and child multiethnic cohort.

Projects:
The Diabetes Care Group

1. *Cardiovascular disease, diabetes and ethnicity, and the quality of diabetes care in a multiethnic general practice population (ROSA 4).* Our multiregional Norwegian research group collected data from primary care from 2014, covering about 11 500 patients in five counties: Oslo, Akershus, Rogaland, Hordaland and Nordland. Later, we have also collected data from hospitals in the same areas. One postdoc (Anh Thi Tran, UiO) and three PhD students are now working with these data; Kjersti Nøkleby (UiO) with issues related to the collaboration between primary care and hospitals for patients in need for shared care, Kristina Slåtsve (UiT/UiO) with data from Nordland in addition to Åsne Bakke (UiB).
2. *The Norwegian study in Renewing Health:* Stimulating self-management in patients with Type 2 diabetes mellitus through tele-care with the Few Touch application and health counseling - a randomized controlled tria, was developed by Faculty of Health Sciences, Oslo and Akershus University College as part of an EU-funded project. Heidi Holmen defended her thesis in 2017 and Astrid Torbjørnsen plans to submit her in 2018.
3. *The need for drug information about diabetes among Pakistani females in Norway.* PhD student Walaa Metwally Ali Abdalaah Abuelmagd plans to submit her thesis in 2018, based on qualitative studies about the need for drug information about diabetes among non-western women, originating from School of Pharmacy, Faculty of Mathematics and Natural Sciences.
4. *Innovative Prevention Strategies for type 2 Diabetes in South Asians Living in Europe* – the EuroDHYAN project, is an EU-funded coordinated effort to target the excessive risk for T2D in South Asian populations in Europe, with partners from Amsterdam, The Netherlands, Edinburgh, Glasgow and Norway (UiO; Jenum; NAKMI). Jenum has led the work with a systematic review and individual data meta-analysis of the findings from relevant behavioural intervention studies, based on all the six eligible trials that were identified. Furthermore, in a submitted paper, we have critically evaluated dietary goals employed in current behavioural interventions. The findings from this EU project will specify HOW to support South Asian people in the uptake and maintenance of a healthy diet and WHAT to focus on.
5. *Follow-up after 16 years of the Romsås in Motion study.* Together with partners at Sogn og Fjordane University College, Faculty of Teacher Education and Sports, we have applied for linkages with sev-

ANNE KAREN JENUM
Professor, MD, PhD, MPH

LINE SLETNER
senior researcher, MD, PhD

TARJA KINNUNEN
ass. prof., PhD, Tampere, Finland

PER LAGERLØV
pediatrician, Professor, PhD

IDUNN BREKKE
Professor, PhD

CHRISTINE SOMMER
PhD, postdoc

KÅRE RØNN-RICHARDSEN
PhD

CHRISTIN WIEGELS WAAGE
PhD

ANH THI TRAN
MD, PhD, postdoc

BJØRN GJELSVIK
MD, PhD

TORE JULSRUD BERG
ass. prof, MD, PhD

ESBEN SELMER BUHL
MD, PhD

NILAM SHAKEEL
PhD student

ÅSE RUTH EGGEMOEN
PhD student

INGUN TOFTEMO
PhD student

MARTHE-LISE NÆSS-ANDRESEN
PhD student

KJERSTI NØKLEBY
PhD student

KRISTINA SLÅTSVE
PhD student

ASTRID TORBJØRNSEN
PhD student

WALAA METWALLY ALI ABDALAAH ABUELMAGD
PhD student

ELIAS NOSRATI
(Cambridge)

ANAM SHAKIL
(Master 2014)

eral Norwegian Health Registers to study the incidence of cardiovascular disease and diabetes, and will develop new projects in 2018.

The Mother and Child Health group

6. *The STORK-Groruddalen cohort study* investigates the role of ethnicity and a range of environmental determinants on the prevalence and development of primarily gestational diabetes (GDM) and intrauterine and childhood growth, http://www.med.uio.no/helsam/forskning/prosjekter/stork-groruddalen/. Data from 823 pregnant women (59% ethnic minorities), were collected from 2008 to 2011. We have developed 11 PhD projects, covering GDM and related maternal health issues, as well as neonatal body composition and fetal and childhood growth. Six PhD students using these data have finished their dissertations, two in 2017 (Kåre Rønn-Richardsen, Christin Wiegels Waage). Åse Ruth Eggemoen and Anne Bærug submitted their theses in 2017. Three have received post-doc grants (Sletner, Sommer and Eggemoen). Sletner later received a four year researcher grant. Further, three PhD projects for general practitioners funded by the Norwegian Medical Association are still ongoing (Nilam Shakeel, Ingun Toftemo and Marthe-Lise Næss-Andresen).
7. *Prediction of gestational diabetes from four Norwegian studies (PreGeDiab4N).* We have in 2017 received approvals from the Regional Ethics Committees to link individual participant data from four Norwegian pregnancy cohorts, first with the aim to develop prediction models to improve screening strategies for gestational diabetes, balancing benefits and harms for women and health care. Second, this new data set gives the possibility to develop new sub-projects with other outcomes, improving the power.

Achievements 2017

Two PhD students finished their dissertation, and two more submitted their theses in 2017. We have published 12 papers, and 15 more are submitted. Sletner has finished her one year visit to our collaborators in Southampton, UK, and have funding for about four more years as a researcher with a project studying placental macroscopic and epigenetic data in STORK G. Jenum has worked much with the EU project EuroDHYAN study. Through 2017 we have included one new member (Kristina Slåtsve), increased the number of subprojects and further strengthened our national and international collaboration.

Ambitions 2018-2019

Beside the planned progress of the ongoing PhD, postdoc and EU-projects, Sletner will perform a pilot study on the stored placenta samples in STORK G, to test their feasibility for epigenetic analyses, and if so plan for further projects. We will also develop new research questions that can be studied in this unique data set. Although the planned follow-up study of mothers and children in STORK G was not funded in 2017, we will refine these plans and work more to get it funded. We will strengthen our national and international collaboration in 2017-2018, facilitating more high quality research related to diabetes and ethnicity. We will further develop some of the ongoing projects by linkages of STORK G with similar national and international studies and for ROSA 4 and MORO, with national registers.

Research Group: DIABETES AND PREGNANCY
Group leaders: Tore Henriksen/Jens Bollerslev

Research focus

The nutritional and environmental conditions under which an individual develops from the one cell stage at conception to birth is now known to have major impact on the future health of the newborn child. Inadequate nutrition in this very early (fetal) period of life increases the risk of cardiovascular diseases, diabetes, overweight and certain cancers.

The research group "The maternal-fetal unit: Metabolic, nutritional, neuroendocrine and vascular interactions" investigates how fetal developmental conditions are formed by studying how maternal nutritional, metabolic and pathogenic factors interact with the placenta. Our research group has recently established a new sampling method that enables us to perform such investigations in a novel way.

The association between the developmental condition of the fetus and future health of the newborn is conceptualized in the term DOHaD (Developmental Origins of Health and Disease or "The Barker hypothesis"). As pointed out in recent international surveys the most effective way of preventing major cardiovascular diseases, diabetes and some forms of cancer is to optimize the developmental environment of the fetus and of early childhood. A variety of factors may influence the condition under which a fetus develops, including maternal obesity and other malnutritional states, infections, preeclampsia with placental dysfunction and exposure to toxic compounds. Worldwide maternal obesity has now become a main risk factor for pregnancy complications and fetal development. In Norway around 20% of young women (mothers to be) are now obese (BMI >30 kg/m2), and obesity has surpassed smoking as a risk factor in pregnancy.

The reason that obesity has adverse effects on pregnancy is primarily not high BMI per ce, but the profound changes in metabolism, endocrinology and inflammation that accompany adiposity. The result is obesity-induced metabolic dysfunction that has large impact on the environment in which the fetus develops. Many of the factors that may cause adverse fetal environments are preventable. However, in order to establish effective preventive measures it is fundamental to understand how a fetus may become exposed to inadequate nutrition and other adverse developmental conditions.

Placenta is situated between the maternal and fetal circulations and virtually any compound being transferred between the maternal and fetal compartments must pass placenta. Thus, placenta plays a central role in determining the fetal nutritional environment.

Projects

1. STORK-Rikshospitalet

The STORK cohort focuses on nutritional, metabolic, neuroendocrine and vascular aspects of the maternal-fetal interaction during development and growth of the fetus.

Two new projects have recently been started based on the STORK cohort.

1. Healthy and unhealthy overweight in pregnancy: A longitudinal study of metabolic status and body mass index (BMI) in relation to pregnancy complications.
   The STORK cohort enables us to analyze subgroups of obese pregnant women with respect to the relation between metabolic profiles and pregnancy outcome. This project is highly relevant in terms of selecting obese women for special pregnancy follow up.
2. Does hypercholesterolemia in pregnancy influence short- and longterm risk for cardiovascular disease in offspring by modulating markers of disease?

The atherosclerotic process is driven by increased cholesterol levels in combination with an enhanced inflammatory response. Hypercholesterolemia is primarily lifestyle induced or it may be caused by a genetic disposition such as familial hypercholesterolemia (FH). Women with FH have been shown to experience very high levels of plasma lipids, in particular LDL cholesterol and they develop a prothrombotic and proinflammatory phenotype during pregnancy compared to non-hypercholesterolemic women. The significance of elevated cholesterol levels and prothrombotic "in utero" environment in relation to markers of risk in offspring has not been thoroughly investigated. The Barker hypothesis suggests that


TORE HENRIKSEN


JENS BOLLERSLEV

the risk of cardiovascular disease in adult life may be determined by an adverse environment before birth. This project aims to generate new knowledge about the effect of hypercholesterolemia during pregnancy and to elucidate if this is associated with increased levels of markers of risk in their offspring.

2. The STORK placenta-study

Transfer of nutrients from mother to fetus

The nutritional and environmental conditions under which an individual develops from conception to birth is now known to have major impact on the future health of the newborn child. In particular, inadequate nutrition in this very early (fetal) period of life may increase the risk of cardiovascular diseases, diabetes, overweight and certain cancers. Other environmental factors, including toxic compounds, may have long term consequences for the developing individual also in absence of structural malformation. Therefore, developmental origins of diseases have become a major conceptual framework and early life intervention is emerging as a primary objective in prevention of diseases. In fetal life placenta, which is situated between the mother and the fetus, is the organ that governs the environmental conditions of the developing fetus. Virtually all substances have to pass this "check-point" before reaching the fetus. The fundamental role of placenta in fetal development is therefore now increasingly acknowledged. Accordingly, our research group has recently developed a new method to study how maternal nutritional, metabolic and pathogenic factors interact with the placenta (The 4 vessel sampling method). The method is novel in a global perspective, and enables us to study the placenta in vivo by analyzing blood and tissue samples from arterial and venous vessels both on the maternal and fetal side. We have currently obtained blood samples from 170 mother-fetus pairs which is almost twice what we considered realistic at the start of the project.

Preeclampsia

Factors originating in placenta are a sine qua non in development of pregnancy induced hypertension (preeclampsia). "The 4 vessel sampling method" offers also a unique opportunity to study that placenta derived factors that induce hypertension during pregnancy. Many of these factors act on the maternal vascular endothelial cells and we have found that in women with preeclampsia, there is increased release of the antiangiogenic factor sFlt from placenta, whereas the proangiogenic factor PlGF shows decreased release.

3. The Norwegian Fit for Delivery (NFFD)

Overweight and obesity have become increasingly prevalent in Norway over the last two decades, also among women of childbearing years. It is now estimated that approximately 20% of all Norwegians are overweight. According to the North Trøndelag population study, the incidence of BMI>30 among women aged 25-30 has increased from 4% during the 1980´s to 12% during the 1990´s.

This is a randomized clinical trial that examines whether a combination of dietary counselling and supervised exercise groups affects pregnancy outcomes, including gestational weight gain (GWG), birth weight, proportion of macrosomic newborns, and use of operative deliveries.

4. SOFUS

SOFUS cohort study studies psychological stress among parents to be who have become to know that their unborn child has a developmental anomaly. The endpoints which are compared to a control group include psychometric and endocrine variables in the mother and circulatory parameters in the fetus.

5. Stork-3

The fetal liver is central in the energy use and metabolism of nutrients during fetal development. This project studies how blood flow in the umbilical vein (coming from placenta) is (re-)distributed between the liver and heart (ducus venosus) at different stages in the fetal development.

Achievements 2017

By employing our unique and large database of 170 mother-fetus pairs we have demonstrated that placenta consumes and turn over a large proportion of

Research Group: DIABETES AND PREGNANCY
Group Leaders: Tore Henriksen and Jens Bollerslev

the glucose and amino acids take up from maternal blood. For example, placenta consumes 20-60 % of the glucose taken up, the remaining is passed to the fetus. This may indicate a large individual variation in placental glucose consumption and may contribute to explain why fetal growth in diabetic pregnancies may be difficult to control by using maternal glucose levels as the only tool.

Further, the non-proteogenic amino acid taurine has a very high concentration in placenta and appears to play an essential role in the homeostatic regulation of placenta (i.e. osmotic balance, anti-oxidative capacity etc).

Our 4-vessel method has been published internationally in form of video presentation with detailed information about the required logistics and methodology, se publication list.

Ambitions 2018-2019

To expand the testing in a human in vivo setting the current, mainly experimentally based, concepts of placental nutrient transport and metabolism.

GROUP MEMBERS

TORE HENRIKSEN
Professor, MD, PhD

GUTTORM HAUGEN
Professor, MD, PhD

JENS BOLLERSLEV
Professor, MD, PhD

SVEIN OLAV KOLSET
Professor

KIRSTEN HOLVEN
Professor, MD, PhD

ELISABETH QVIGSTAD
MD, PhD

TROND MICHELSEN
MD, PhD

KRISTIN GODANG
MSc

THOR UELAND
Post doc

ANNE HELBIG
MD, PhD

CAMILLA M FRIIS
MD, Phd

MARIE CECILIE PAASCHE ROLAND
MD, PhD

ANNE KAASEN
PhD, midwife

LINDA SAGEDA
Phd student

GUN LISBETH OPHEIM
MD, PhD student

ANE MOE HOLME
MD, PhD student

MAIA BLOMHOFF
MD, PhD student

HILDEGUNN HORNE
MD, PhD student

JACOB JUEL CHRISTENSEN
PhD student, Dept. Of Nutrition

ODDRUN KRISTIANSEN
PhD student

FOTO: ØYSTEIN H. HORGMO, UIO

Research Group:
DIABETIC NEPHROPATY
AND TRANSPLANTATION

Group Leader: Trond Jenssen

TROND JENSSEN

Research focus
The Diabetic Nephropathy and Transplantation research group assembles the research activity of three senior researchers and their respective research groups. There is an extensive collaboration between the research groups.

Research focus
Trond Jenssen. Cardiovascular disease and diabetes after organ transplantation. Clinical pancreas and islet transplantation.
Svein O. Kolset. Molecular and morphological changes in the diabetic kidney
Hanne Scholz. Islet cell transplantation: Improvement and optimization of islet isolation, transplantation and clinical outcome

Projects
Trond Jenssen
1. Posttransplant diabetes mellitus (PTDM). Occurrence, pathogenesis, risk factors, follow-up and treatment.
2. Improvement of kidney graft and patient survival in renal transplant patients.
3. Clinical outcome and improvement of beta cell replacement therapy (pancreas and islet transplantation).

Svein O. Kolset
1. Studies on early markers of kidney changes in patients with hyperglycemia (type 1 diabetes) and restored normoglycemia (pancreas transplantation). Studies on syndecan shedding and changes in renal proteome.
2. Syndecans as disease markers in population based studies. Extracellular matrix changes due to experimental diabetic conditions in human glomerular endothelial cells.

Hanne Scholz
1. Improvements of pancreatic islet isolation techniques and evaluation of isolated human islets
2. Investigate the intracellular drug-drug interactions of immunosuppressants in adipose derived stem cells and human islets.
3. Regenerative/repair of the endocrine compartment of the pancreas using adipose-derived stem cells.
4. Development of 3D Bioprinting of biomimetic pancreas to treat diabetes (see picture).

At present (2017/2018) 3 PhD candidates and 1 postdoc fellow are directly involved in the projects. The group published 22 papers in peer reviewed journals in 2017.

Achievements in 2017
Ongoing research grants are upheld.
PTDM and pancreas transplantation group (Trond Jenssen): Inclusion of patients in a researcher initiated, non-sponsered placebo-controlled, randomized clinical trial (SGLT2 inhibition in renal recipients with post transplant diabetes mellitus) was almost completed in 2017. Last patient in (among 50 patients) will be recruited in January 2018, and last patient out will be in August 2018. Renal biopsy sample package for microdissection analysis in kidneys from PTDM patients is completed. Analyses take place in 2018. Several publications have occurred from our renal transplant registry.
Diabetic nephropathy group (Svein O Kolset): The collection of kidney-graft biopsies from transplanted patients with T1DM has been completed. LC-MS/MS analysis has been performed and the proteome from KA and SPK-recipients compared using Scaffold. Further data analysis using the Database for Annotation, Visualization and Integrated Discovery (DAVID), for gene ontology overrepresentation, and the Search Tool for the Retrieval of Interacting Genes/Proteins for protein-protein interaction network analysis is ongoing. Analysis of syndecan-1 and syndecan-4 expression in 1300 participants from the Tromsø study has been completed. The experiments for the project on glomerular endothelial cells in culture have been finalized
Islet transplantation group (Hanne Scholz): The group

GROUP MEMBERS

TROND JENSSEN
Professor

HANNE SCHOLZ
PhD, Leading researcher

SVEIN O KOLSET
Professor

TRINE M REINE
PhD, postdoc

JØRN PETTER LINDAHL
MD

ANDERS HARTMANN
Professor

KARSTEN MIDTVEDT
MD, PhD

SIMEN SCHIVE
MD, PhD student

SHADAB ABADPOUR
MSc, PhD student

MARIT ELIZABETH VON DÜRING
University of Oslo

ESPEN NORDHEIM
MD, PhD student

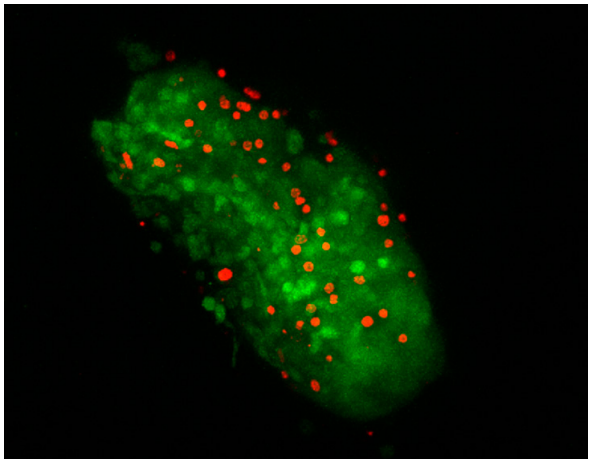
FRANCESCA LANZALACO
(Erasmus student)

THEA ANINE STRØM HALDEN
Postdoc, Dr Scient

has continued to improve the isolation and transplantation method and performed 11 clinical islet transplantations in 2017 (23% increase from 2016). In collaboration with the GI surgery department a new clinical program offering total pancreatectomy with islet autotransplantation (TPIAT) for selected patients with chronic or acute recurrent pancreatitis has been established. PhD candidate Kristine Kloster-Jensen MD delivered her thesis "Functional in vitro studies of immunosuppressive agents in human pancreatic islets" in December 2017. Dr. Scholz became a councilor of the International Islet and Pancreas Transplantation Association (IPITA) (2017-2020). Dr. Scholz is also theme leader (Principle Investigator) aiming to create functional mini-pancreas for "organ on a chip" platform within the newly granted Centre of Excellence led by Prof. Stefan Krauss.

Ambitions for 2018

Trond Jenssen: One candidate is expected to complete his thesis in 2018. Results on microdissection studies from tubular cells from transplanted kidneys will be disclosed. The RCT on SGLT2 inhibition in patients with PTDM will be completed in August 2018, and the results published in the following months. Main results from the ORENTRA trial (an investigator initiated randomized clinical trial on omega-3 substitution in renal transplant recipients and graft function) will be published.



Immunofluorescent image of live (green) and dead (red) cells of a 3D bioprinted human islet. Photo: Shadab Abadpour

Svein O.Kolset: The results from both the transplanted patients, the Tromsø study and the in vitro studies on glomerular endothelial cells will be presented in three different manuscripts to be submitted.
Hanne Scholz: Two PhD candidates are expected to complete their thesis in 2018. The group will focus on refinement of methods for islet isolation and to develop new strategies for cell-based engineering technology to improve the outcome of islet transplantation using adult stem cells. In addition, the group will investigate and develop an organoid model of pancreas (islets).

Research Group:
IMMUNOGENETICS OF AUTOIMMUNE DISEASES

Group Leaders:
Benedicte A. Lie

Research focus
Our main research focus is to identify and functionally characterize genetic factors that predispose to type 1 diabetes and other autoimmune diseases. The genetic risk factors have to a large extent been connected to gene expression and gene regulation of immune cells. To get a deeper understanding of such aspects, we are studying different layers of genomic information; e.g. transcriptome, methylation and microRNA across a wide specter of immune cells both from blood and thymus. These regulatory profiles are investigated against autoimmune genetic risk loci (revealed through genome-wide association studies), and analysed against response to treatment

Projects
1. Characterization of the transcriptome of various immune cells in thymus and profiling of expression of tissue restricted autoantigens.
2. Exploring genetic, epigenetic and environmental risk factors, and their interactions, in rheumatoid arthritis, an autoimmune disease sharing many risk factors with type 1 diabetes.
3. Epigenetic profiling of immune cells from rheumatoid arthritis patients and their correlation with treatment response.
4. Quantification of the expression levels of HLA alleles, the main genetic determinant for autoimmune diseases, on different immune cells from thymus and blood.

Achievements 2017
- Characterized the transcriptome of antigen-presenting cells and T cells from thymus and unraveled the expression profile of risk genes for type 1 diabetes and other autoimmune diseases.
- Discover methylation signatures of CD4 T cells (naïve and memory) that are associated with rheumatoid arthritis and the effect of methotrexate treatment.
- Revealed that patients with coexisting type 1 diabetes and celiac disease are more similar to type 1 diabetes patients in their distribution of HLA class II alleles.
- Explored the HLA association in autoimmune diseases and established a pipeline for quantitatively measure the HLA allelic expression levels.

Ambitions 2018-2019
- Quantitatively measure the expression of different HLA alleles, including type 1 diabetes susceptibility and protective variants, in thymus.
- Test the hypothesis that the immune system is involved in the development of myalgic encephalopathy and chronic low back pain, based on our knowledge from immune genetic studies of established autoimmune diseases like type 1 diabetes.
- miRNA profiling of immune cells from rheumatoid arthritis patients and their correlation with treatment response.

BENEDICTE A. LIE

GROUP MEMBERS

BENEDICTE A. LIE
Professor, PhD

MARTE K. VIKEN
post doc

HANNA HELGELAND
post doc

FATEMEH KAVEH
post doc

INGVILD GABRIELSEN
PhD student

KARI GUDERUD
PhD student

LINE SUNDE
PhD student

FATIMA HEINICKE
PhD student

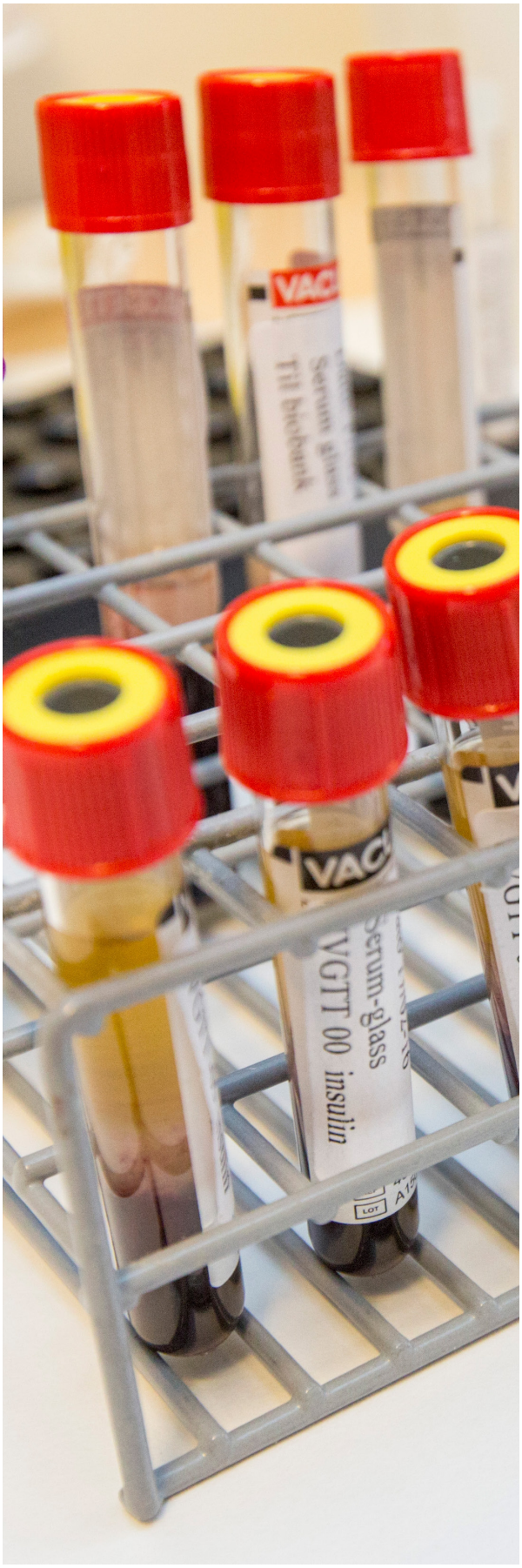
MARIA DEHLI VIGELAND
PhD student

ASGEIR LANDE
PhD student

LILLIAN NERENG
Master student

ANNE RYDLAND
Master student

SIRI FLÅM
Medical Laboratory Scientist



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Research Group:
BIOMARKERS IN ENDOCRINOLOGY AND METABOLISM

Group Leader:
Jens P. Berg


JENS P. BERG

Research focus
Among the research aims of our group is to increase the understanding of mechanisms leading to and metabolic consequences of increased blood glucose by studies of small molecule metabolite profiles (metabolomics). Projects at the Hormone Laboratory study the mechanisms leading to β-cell dysfunction and aim to identify adequate biomarkers to assess changes in β-cell health and function. In addition we focus on the use, quality control, and interpretation of measures of glycemic control such as HbA_{1c} and glycated albumin.

Projects
1. Prediction of early metabolite biomarkers in serum of autoimmune diabetes.
2. Biomarkers of pancreatic β-cell mass.
3. Studies of metabolic profiles in gestational diabetes.
4. Posttranslational modification of proteins and late complications of diabetes.

Achievements 2017
Our group published an article validating a novel capillary electrophoresis based analysis of HbA_{1c} and compared the method with existing HPLC and immunoassay based methods. We deomonstrated that capillary electrophoresis is a precise and convient method for the analysis of HbA_{1c}. The research group has been involved in a multiethnic cohort study of postpartmun HbA_{1c} levels.

The research group was also involved in studies of bile acid profiles up to 5 years after Roux-en-Y gastric bypass and biliopancreatic diversion with duodenal switch to explore the relationship among bile acids and weight loss, lipid profile, and glucose metabolism.

We have also been involved in a case-control study of circulating immunological markers in mid-pregnancy and cord blood plasma from 175 mother/child T1D cases.

Ambitions 2018-2019
Continue studies of proteomic analysis of insulin secreting cells.
Establish and perform studies of clinical samples to evaluate the performance of additional markers of glucose homeostasis such as glycated albumin, fructosamine and 1,5-anhydroglucitol.

GROUP MEMBERS

JENS PETTER BERG
MD, PhD, Professor

PER M. THORSBY
MD, PhD, medical head of Hormone Laboratory

MILAIM PEPAJ
PhD

METTE E. BORNSTEDT
MD

MAY K BREDAHL
PhD

NINA GJERLAUGSEN
MSc

KARI JULIEN
B.Sc.

VIGDIS ENGE
B.Sc.

ANNE NÆRBY
B.Sc.

Research Group:
THE NORWEGIAN CHILDHOOD DIABETES REGISTRY (NCDR)

Group leader: Torild Skrivarhaug

Research focus

The main research focus in this population-based, nationwide childhood-onset diabetes registry:

1) Epidemiology in childhood-onset diabetes, focusing on incidence, prevalence, classification of childhood-onset diabetes in Norway, ethnicity and long-term complications and mortality.
2) Quality in childhood diabetes care – a nation-wide prospective population-based study for research and quality improvement by means of benchmarking.
3) Clinical childhood diabetes, especially focusing on quality of life, diabetes treatment, co-morbidity, eating disorders and the transition from paediatric to adult diabetes care.

Ongoing studies

1. Mortality in childhood-onset type 1 diabetes (T1D). All-cause mortality, SMR, causes of death, relationship between socioeconomic status and mortality in T1D.
2. Co-morbidity in children and adolescents with T1D. Assessing competencies and coping; factors affecting functional and dysfunctional behaviour in children and adolescents with T1D.
3. How do young people with T1DM experience transition from pediatric to adult health care?
4. Classification of childhood-onset diabetes in Norway. To assess the epidemiology of different forms of diabetes and to classify incident cases on the basis of family history, clinical data, C-peptide, autoantibodies and HLA-genotypes.
5. The incidence of severe hypoglycaemia in children with T1D in Norway and in the Nordic countries.
6. The PAGE study (Prediction of Autoimmune diabetes and celiac disease in childhood by Genes and perinatal Environment).
7. Hypoglycemia in children and adolescents with T1D. To determine the prevalence of IAH (Impaired Awareness of Hypoglycemia). Population-based, nationwide study.
8. International HbA1c benchmarking in T1D: Do we need HbA1c variation in addition to average HbA_{1c} values? International joint project.
9. Prevalence of monogenic diabetes in NCDR estimated by targeted deep sequencing. Treament implications?
10. The EURODIAB collaborative group established in 1988, 44 centers representing most European countries and Israel. To study the epidemiology of childhood-onset T1D in Europe.
11. How to implement HrQoL measures in Nordic childhood diabetes registers – Implementing Disabkids as a routine screening tool.
12. Obesity and BMI index standard deviation score in children with type 1 diabetes in the Nordic countries.
13. Cardiovascular disease and end-stage renal disease in type 1 diabetes with onset before 15 years of age and long duration.
14. Developing and validation of a Norwegian PREM tool for children with T1D and their parents.
15. Incidence of diabetes ketoacidosis at the onset of childhood onset T1D in children in the Nordic countries in the period 2010-2014.

TORILD SKRIVARHAUG

16. Long-Term Sulfonylurea Response in KCNJ11 Neonatal Diabetes (SuResponsKIR)
17. EU-IMI 2. NCDR is part of the INNODIA consortium. Started Nov.1, 2015.

At present 2 PhD students and 1 postdoc are directly involved in the projects.

Achievements 2017

Dissertation June 2017; Vibeke Gagnum "Mortality, causes of death and end-stage renal disease in type 1 diabetes".
Conducted two national surveys of Patient Reported Experience Measure:

1) Parents to all children with T1D in NCDR were included.
2) All children with T1D age 12 years +, registered in NCDR and attending diabetes care at Oslo University Hospital, Haukeland University Hospital, Akershus University Hospital and Vestre Viken Hospital were included.

Ambitions 2018-2019

One of the candidates will finish his PhD thesis in 2018.
To publish data on incidence of severe hypoglycemia in children with T1D in Norway.
To publish data on incidence of DKA at the onset of childhood onset T1D in children in the Nordic countries in the period 2010-2014.
To engage a new PhD student in the project "Mortality in childhood-onset type 1 diabetes", to assess the relationship between socioeconomic status and mortality in T1D.

GROUP MEMBERS

TORILD SKRIVARHAUG
Associate Professor, MD, PhD

GEIR JONER, PROFESSOR
MD, PhD

KNUT DAHL-JØRGENSEN
Professor, MD, PhD

LARS CHRISTIAN STENE
Senior researcher, Norwegian Institute for Public Health

VIBEKE GAGNUM
MD, PhD

SIV JANNE KUMMERNES
R.N., diabetes nurse, MSc

ANN KRISTIN DRIVVOLL
MSc

DAG HELGE FRØISLAND
MD, PhD

LINE WISTING
PhD , post doc

MARYAM SAEED
MD, PhD student

PER THORSBY
MD, PhD

KRISTIN HODNEKVAM
MD

NINA GJERLAUGSEN
MSc

FOTO: FREDRIK NAUMANN/FELIX FEATURES


VACU

THESIS 2017

KÅRE RØNN RICHARDSEN. Physical activity during pregnancy through postpartum: A study of predictive and explantory factors in a multi-ethnic population, University of Oslo 2017.

CHRISTIN WIEGELS WAAGE. The postpartum period. A window of opportunity to reduce ethnic differences in women's Health, University of Oslo 2017.

NICOLAI LUND-BLIX. Early nutrition and risk of type 1 diabetes, University of Oslo 2017.

JØRN PETTER HANTO LINDAHL. Pancreas and Kidney Transplantation in Patients with Type 1 Diabetes and End-Stage Renal Disease: Long-Term Outcomes, University of Oslo 2017.

VIBEKE GAGNUM. Mortality, causes of death and end-stage renal disease in type 1 diabetes, University of Oslo 2017.

HILDE RISSTAD. Comparison of variants of gastric bypass and duodenal switch as treatment for severe obisity (BMI 50-60) in randomized controlled trails, University of Oslo 2017.

PUBLICATIONS 2017

International publications:

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INTERNATIONAL INVITED LECTURES / ORAL PRESENTATIONS / POSTER PRESENTATIONS:

Invited lectures:

Dahl-Jørgensen K. Type 1 diabetes goes Viral – is a "guerilla war" going on in the islets? Invited lecture. Second Swedish Diabetes Summit, 21 November 2017, Gothenburg.

Skrivarhaug T. Early pump treatment in children with type 1 diabetes. Experiences from Norway. Children Endocrinology Society Meeting, 7 May 2017; Kosør, Denmark.

Oral presentations:

Abadpour S, et.al. LIGHT/TNFSF14 and glucotoxcicity induce an adverse effect on human islets through elevation of islet dysfunction and apoptosis. 7th EPITA Symposium & 36th AIDPIT Workshop, 28-31 January 2017, Igls, Austria.

Abadpour S, et al. "Transdifferentiation of isolated human exocrine cells to beta-like cells." International Pancreas and Islet Transplantation Association Congress, 21 June 2017, Oxford, UK.

Abadpour S, et al. "Interlukin-22 reverses human islets dysfunction and apoptosis triggered by hyperglycemia and LIGHT." International Pancreas and Islet Transplantation Association Congress, 21 June 2017, Oxford, UK.

Bakke Å, Cooper JG ,Thue G, Skeie S, Carlsen S, Dalen I, Løvaas K, Madsen TV, Oord ER, Berg TJ, Claudi C, Tran AT, Gjelsvik B, Jenum AK, Sandberg S. Type 2 Diabetes in General Practice in Norway 2005-14: Moderate improvements in risk factor control but still major gaps in complication screening. Oral presentation at the 52nd Annual Meeting of the Scandinavian Society for the Study of Diabetes, 19–21 May 2017, Nyborg, Denmark.

Bakke Å, Cooper JG ,Thue G, Skeie S, Carlsen S, Dalen I, Løvaas K, Madsen TV, Oord ER, Berg TJ, Claudi C, Tran AT, Gjelsvik B, Jenum AK, Sandberg S. Type 2 Diabetes in General Practice in Norway 2005-14: Moderate improvements in risk factor control but still major gaps in complication screening. Poster at the 53rd European Association for the Study of Diabetes, 11–15 September 2017, Lisbon, Portugal.

Eggemoen ÅR, Jenum AK, Mdala I, Knutsen KI, Lagerløv P, Sletner L. Vitamin D levels during pregnancy and associations with birth weight and body composition of the newborn: a longitudinal multiethnic population-based study. Nordic congress of General Practice, 14-16 June 2017, Reykjavik, Iceland.

Halden T, et al. "Short term safety of empagliflozin in long term stable renal transplant recipients with post transplantation diabetes mellitus." European Society of Organ Transplantation, 24-27 September, Barcelona, Spain.

Lindahl JP, et al. "Outcomes of pancreas transplantation with duodeno-duodenal enterostomy and endoscopic surveillance.» European Society of Organ Transplantation, 24-27 September, Barcelona, Spain.

Nordheim E, et al. "A single centre experience-Evaluation of biopsy sampling methods of pancreas transplants." American Transplantation Congress, 29 April – 3 May 2017, Chicago, USA.

Nordheim E, et al. "Does duodeno-duodenal anastomosis of pancreas transplants allow for representative endoscopic ultrasound-guided biopsies?" European Society of Organ Transplantation, 24-27 September, Barcelona, Spain.

Nordheim E, et al. "113 concurrent biopsies in pancreas graft recipients: discordant finding between donor duodenum and pancreas grafts.» European Society of Organ Transplantation, 24-27 September, Barcelona, Spain.

Næss-Andresen ML, Berg JP, Jenum AK. Ethnic Differences in Iron Deficiency and Anaemia in early Pregnancy in Oslo. Cross-sectional study from a Population-Based Cohort Oral Presentation/poster. 20th Nordic Congress of General Practice, June 2017, Reykjavik, Iceland.

Reine TM. "Syndecans as markers of diabetic complications - clinical and experimental approaches." Nordic PG meeting 2017, Oxford University, Oxford, UK.

Scholz H, et al. "GPR44 inhibition impoves islets function and survival in transplanted human islets." International Pancreas and Islet Transplantation Association Congress, 21 June 2017, Oxford, UK.

Shakeel N, Sletner L, Falk R, Slinning K, Eberhard-Gran M, Martinsen EW, Jenum AK. Postpartum depression - prevalence and risk factors in a population-based multiethnic cohort study 22nd WONCA

Europe Conference June 28 - July 1, 2017, Prague, Czech Republic.

Shakeel N, Sletner L, Falk R, Slinning K, Eberhard-Gran M, Martinsen EW, Jenum AK. Postpartum depression - prevalence and risk factors in a population-based multiethnic cohort study Nordic congress of General Practice, 14-16 June 2017, Reykjavik, Iceland.

Toftemo I, Jenum AK, Lagerløv P, Falk RS, Sletner L. Prevalence of overweight and thinness in a multi-ethnic cohort of 4 years old children in Norway. Associations with ethnicity, maternal- and early life factors. Nordic congress of General Practice, June 2017, Reykjavik, Iceland.

Poster presentations:

Anderzén J, Hermann JM, Samuelsson U, Charalampopoulos D, Svensson J, Skrivarhaug T, Froehlich-Reiterer T, Maahs DM, Akesson K, Kapellen T, Fritsch M, Birkebæk N, Drivvoll AK, Miller K, Stephenson T, Hofer SE, Fredheim S, Kummernes SJ, Foster N, Amin R, Hilgard D, Rami-Merhar B, Dahl-Jørgensen K, Clements M, Hanas R, Holl RW, Warner JT. International benchmarking in type 1 diabetes: HbA1c increases equally with age, independent of HbA1c at younger age. ISPAD 43rd Annual conference, 18-23. Oct. 2017, Innsbruck, Austria.

Bakke Å, Cooper JG, Thue G, Dalen I, Skeie S, Carlsen S, Oord ER, Løvaas KF, Madsen TV, Tran AT, Jenum AK, Berg TJ, Gjelsvik B, Claudi T, Sandberg S. Type 2 diabetes in general practice in Norway, status and time trends. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Birkebaek NH, Kahlert J, Bjarnason R, Drivvoll AK, Johansen A, Konradsdottir E, Pundziute-Lucka A, Samuelsson U, Skrivarhaug T, Svensson J. The relationship between body mass index standard deviation score, glycemic control and insulin therapy in children with type 1 diabetes in the Nordic countries. ISPAD 43rd Annual conference, 18-23. Oct. 2017, Innsbruck, Austria.

Birkebaek NH, Hanberger L, Charalampopoulos D, Hermann JM, Skrivarhaug T, Akesson K, Warner J, Holl RW, Drivvoll AK, Svensson AM, Stephenson T, Hofer S, Fredheim S, Kummernes SJ, Amin R, Rami-Merhar B, Johansen A, Dahl-Jørgensen K, Hanas R, Svensson J. Centre size may influence HbA1c. An international study. ISPAD 43rd Annual conference, 18-23. Oct. 2017, Innsbruck, Austria.

Cavender MA, Norhammar A, Birkeland KI, Jørgensen ME, Wilding JP, Khunti K, Fu AZ, Bodegård J, Blak B, Wittbrodt ET, Thuresson M, Fenici P, Hammar N, Kosiborod M, on behalf of the CVDREAL Investigators and StudyGroup. Hospitalisation for heart failure and death in new users of SGLT-2 inhibitors in patients with and without cardiovascular disease: the CVD-REAL study. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Eriksson JW, Norhammar A, Bodegard J, Thuresson M, Fenici P, Nathanson D, Kosiborod M, Gulseth HL, Nyström T, Birkeland KI. Dapagliflozin compared to DPP4i treatment is associated with lower risk of kidney disease, heart failure and all-cause death: CVD-REAL Nordic. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Gulseth HL, Bodegard J, Norhammar A, Nathanson D, Thuresson M, Birkeland KI, Eriksson JW, Nyström T. Life years lost and cardiovascular risk in type 2 diabetes patients requiring glucoselowering treatment 2008-2015: nationwide data from Norway and Sweden. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Kinnunen TI, Richardsen KR, Sommer C, Sletner L, Waage CW, Mdala I, Torgersen L, Jenum AK. Ethnic differences in body mass index trajectories from 18 years to 3 months postpartum in a cohort in Norway. 8th Nordic Meeting in Epidemiology and Register-Based Research in Lund, September 13-15, 2017, Lund, Sweden.

Kosiborod M, Cavender MA, Fu AZ, Norhammar A, Birkeland KI, Jørgensen MI, Holl RW, Hammar N, Wittbrodt ET, Bodegård J, Scheerer M, Thuresson M, Fenici P, on behalf of the CVD-REAL Investigators and StudyGroup. Total events of hospitalisation for heart failure in new users of SGLT-2 inhibitors: real world data from 5 countries and more than 298,000 patients: the CVD-REAL study. 53rd European Association for the Study of Diabetes (EASD) annual

meeting, 11-15 September, 2017, Lisbon, Portugal.

Krogvold L, Genoni A, Puggioni A, Campani D, Richardson S, Edwin B, Buanes T, Dahl-Jørgensen K, Toniolo A. Enteroviruses in the pancreas of live adult patients with newly diagnosed type 1 diabetes. Results from the DiViD study. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Mårild K, Thorsen SU, Olsen SF, Holst KK, Tapia G, Granström C, Halldorsson TI, Cohen I, Haugen M, Lundqvist M, Skrivarhaug T, Njølstad PR, Joner G, Magnus P, Størdal K, Ascherio A, Svensson J, Stene LC. Maternal and Neonatal Vitamin D Status and Risk of Type 1 Diabetes in Norway and Denmark. Poster presentation at the Immunology of Diabetes Society (IDS) meeting, January 19-23, 2017, San Francisco, USA.

Mårild K, Vistnes M, Tapia G, Midttun Ø, Ueland PM, Skrivarhaug T, Njølstad PR, Joner G, Størdal K, Stene LC. Possible link between maternal mid-pregnancy macrophage chemoattractants and childhood type 1 diabetes. Poster presentation at the Immunology of Diabetes Society (IDS) meeting, January 19-23, 2017, San Francisco, USA.

Nathanson D, Bodegard J, Norhammar A, Birkeland KI, Nyström T, Thuresson M, Eriksson JW, Gulseth HL. Time-trends in incidence and prevalence of type 2 diabetes patients requiring glucose-lowering treatment from 2007-2015: nationwide data from Norway and Sweden. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Nordheim E, et al. "Endoscopic ultrasound-guided pancreas graft biopsies – the future of graft surveillance?" European Renal Association, 3-6 June, 2017, Madrid, Spain.

Norhammar A, Kosiborod M, Gulseth HL, Eriksson JW, Fenici P, Nathanson D, Bodegard J, Thuresson M, Nyström T, Birkeland KI. Dapagliflozin is associated with lower risk of major adverse cardiovascular events compared to DPP-4i in type 2 diabetes patients. Results from CVD-REAL Nordic. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Persson F, Bodegard J, Nyström T, Nathanson D, Thuresson M, Linnemann Jensen M, Jørgensen M, Birkeland KI, Gulseth HL, Norhammar A, Eriksson JW. Second line treatment after metformin monotherapy of type 2 diabetes in a real life setting 2006 to 2015: nationwide data comparison between Denmark, Norway and Sweden. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Ofstad AP, Sommer C, Birkeland KI, Bjørgaas MR, Gran MJ, Johansen OE, Gulseth HL. Indexes of body fat, but not BMI, are associated with cardiovascular (CV) mortality in subjects with diabetes (DM) during 17 year follow-up in the Norwegian HUNT2 study. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Ruiz PLD, Tapia G, Bakken IJ, Håberg SE, Gulseth HL, Stene LC. Pandemic Influenza diagnosis and subsequent risk of type 1 diabetes (Abstract). Diabetologia 2017;60(Suppl 1):S167-S168. Poster presentation at the 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Samuelsson U, Westerberg L, Aakesson K, Birkebæk N, Bjarnason R, Drivvoll AK, Hanberger L, Skrivarhaug T, Svensson J, Thorsson A. Geographical variation in the incidence of Type 1 diabetes in the Nordic countries. ISPAD 43rd Annual conference, 18-23. Oct. 2017, Innsbruck, Austria.

Schive SW, et.al. Human adipose derived mesenchymal stem cells respond to short term hypoxia by secreting factors beneficial for human islets in vitro and potentiate anti-diabetic effect in vivo. 7th EPITA Symposium & 36th AIDPIT Workshop, 2017, Igls, Austria.

Skrivarhaug T, Drivvoll AK, Kummernes SJ, Svensson J, Fretheim S, Hanberger L, Aakeson K, Konradsdottir E, Bjarnason R, Nordic Childhood Diabetes Registry Study Group, NordicDiabKids. Diabetes ketoacidosis at presentation of childhood-onset type 1 diabetes in the Nordic countries in 2010-2014 – Data from Danish (DanaKid), Iceland, Norwegian (NCDR) and Swedish (Sweadiabkids) nationwide, childhood diabetes registries. ISPAD 43rd Annual conference, 18-23. Oct. 2017, Innsbruck, Austria.

Sletner L, Jenum AK. Accelerated linear growth is observed in ethnic minority infants in Norway, and is preceded by fetal "Catch-down growth". 4th International Conference on Nutrition and Growth. 2.-4. March 2017, Amsterdam, Netherlands.

Sletner L, Hanson MA, Jenum AK. Sex-specific associations between parental factors and fetal growth and body proportions from mid pregnancy until birth; a multi-ethnic cohort study. 10th World Congress on Developmental Origins of Health and Disease. 14.-18. Oct 2017, Rotterdam, Netherlands.

Solbu M, et al. "Syndecan-4 is associated with eGFR and the incidence of myocardial infarction in a general population. The Tromsø Study". American Society of Nephrology, 2017, Philadelphia, USA.

Sommer C, Lee S, Gulseth HL, Jensen J, Drevon CA, Birkeland KI. Plasma soluble leptin receptor predicts insulin sensitivity in humans. 53rd European Association for the Study of Diabetes (EASD) annual meeting, 11-15 September, 2017, Lisbon, Portugal.

Stene LC, Ruiz PLD, Gulseth HL, Tapia G, Bakken IJ, Håberg SE. Pandemic Influenza A H1N1 Vaccination and subsequent Risk of Type 1 Diabetes in Norway. Poster presentation at the Immunology of Diabetes Society (IDS) meeting, Jan 19-23, 2017, San Francisco, USA.

Stene LC, Sørensen IM, Eskild A, Jenum PA, Joner G. Maternal 1,25-dihydroxy-Vitamin D during Pregnancy and Risk of Childhood onset Type 1 Diabetes. Poster presentation at the Immunology of Diabetes Society (IDS) meeting, Jan 19-23, 2017, San Fransisco, USA.

Tapia G, Størdal K, Mårild K, Kahrs CR, Skrivarhaug T, Njølstad PR, Joner G, Stene LC. Antibiotics, paracetamol and infections during prenatal and early life in relation to type 1 diabetes. Late breaking abstract. Poster, at the International Diabetes Federation (IDF) conference, Dec 4-8, 2017, Abu Dhabi, UAE.

Wisting L, Bang L, Natvig H, Skrivarhaug T, Dahl-Jørgensen K, Lask B, Rø Ø. Eating patterns in adolescents with type 1 diabetes: Associations with metabolic control, insulin omission, and eating disorder pathology. EDRS 2017, Leipzig, Germany.

NATIONAL INVITED LECTURES / ORAL PRESENTATIONS / POSTER PRESENTATIONS:

Invited lectures:

Dahl-Jørgensen K. Antiviral treatment at the diagnosis of type 1 diabetes – The DiViDInt Trial. Oslo University Hospital Research Seminars. The insulin producing cell in health and disease. Invited lecture. May 2. 2017, Oslo.

Krogvold L. The pathogenesis of type 1 diabetes: lessons from pancreatic biopsies in the DiViD Study. Oslo University Hospital Research Seminars. The insulin producing cell in health and disease. Invited lecture. May 2. 2017, Oslo.

Skrivarhaug T. Diabetes – many faces. Adolescents and young adults. Diabetes Forum, The Norwegian Diabetes Association, 26. April 2017, Gardermoen.

Skrivarhaug T. Type 1 diabetes in children and adolescents. The Norwegian Childhood Diabetes Registry. The Norwegian Diabetes Association, "Lokallag for barn og unge i Oslo", 10. October 2017, Lillehammer.

Skrivarhaug T. Diabetes – Adolescents and young adults. Diabetes i Nord. Nettverkskonferanse i diabetes, 8. November 2017, Tromsø.

Skrivarhaug T. Diabetes in children and youths. The Norwegian Diabetes Association, Østfold, 11. November 2017, Sarpsborg.

Skrivarhaug T. The Norwegian Childhood Diabetes Registry. The use of data for quality improvement. The Norwegian Diabetes Association, Likefamiliesamling, 10. November 2017, Gardermoen.

Oral presentation:

Reine TM. Increased levels of inflammatory mediators and proinflammatory monocytes in patients with type I diabetes mellitus and nephropathy. Throne Holst Symposium, May 18, 2017, Oslo.

Reine TM. Syndecan-shedding. Molecular Nutrition seminar, Dep of Nutrition, UiO.

Tran AT, Nøkleby K, Jenum AK. Do General Practitioners characteristics matter in the quality of care for type diabetes patients? NAFALM, Norway, 20th September 2017, Asker.

Poster presentations:

Reine TM, et al. Syndecans – New markers of endothelial dysfunction in diabetic nephropathy? Throne Holst Symposium. May 18, 2017, Oslo.

COLLABORATING PARTNERS

Oslo University Hospital/University of Oslo

Harald Arnesen, Professor Emiritus, Centre for Clinical Heart Research
Cathrine Brunborg, Statistician, Centre for Clinical Research
Helene Holm, Midwife/ Diabetes nurse, Dept of Obstetrics and Gynecology
Peter Kierulf, Professor Emiritus, Dep of Clinical Biochemistry
Morten Fagerland, MSc, PhD, Oslo Centre for Biostatistics and Epidemiology
Leiv Sandvik, MSc, Dr. philos., Oslo Centre for Biostatistics and Epidemiology
Ingebjørg Seljeflot, Professor, MD, PhD, Centre for Clinical Heart Research
Kristin Ørstavik, MD, PhD, Dept of Neurophysiology
Bassam Karime, PhD, Dep of Neurophysiology
Kjetil Steine, Ass. Professor, MD, PhD, Division of Medicine and Laboratory Sciences, AHUS
Tone Nerdrum, MD, PhD, Dept. of Cardiology, AHUS
Reidun Mosand, Head of section for diabetes, Dept of Endocrinology
Anders Hartmann, Professor, MD, PhD, Dept of Nephrology
Ludvig Sollid, Professor, MD, PhD, Institute of Immunology
Siri Vangen, Associate Professor, MD, PhD, Dept of Obstetrics and Gynecology
Frode Lars Jahnsen, Professor, MD, PhD, Dept of Pathology
Bjørn Edwin, MD, PhD, Dept of Surgery
Trond Buanes, Professor, Dept of Surgery
Arne Rosseland, Professor, MD, PhD, Dept of Surgery
Jens Ivar Brox, Professor, MD, PhD, Department of Physical Medicine and Rehabilitation
Svein Solheim, MD, PhD, Dept of Cardiology
Nils-Einar Kløw, Professor, MD, PhD, Dept of Radiology
Torbjørn Leivestad, MD, PhD, The Norwegian Nephrology Registry
Anna Varberg Reisæter, MD, PhD, Section of nephrology, Dept of Organ Transplantation Medicine
Mona Svanteson, Researcher, Department of Radiology and Nuclear Medicine
Ylva Haig, MD, PhD, Division of Radiology and Nuclear Medicine
Rune Horneland, MD, PhD student, OUS RH
Bente Halvorsen, Professor, Research Institute for Internal Medicine
Pål Aukrust, Professor, Research Institute for Internal Medicine

Section of Endocrinology, Oslo University Hospital
Department of Medical Genetics, Oslo University Hospital
National Competence Centre for Women's Health, Oslo University Hospital
Hormone Laboratory, Oslo University Hospital
Department of Neuropsychiatry and Psycho-somatic medicine, Oslo University Hospital
RASP (Regional Centre for Eating Disorders), Oslo University Hospital
The Norwegian Childhood Diabetes Study Group

University of Oslo
Hilde Irene Nebb, MD, PhD, Professor, Deputy Dean of Research, Faculty of Medicine, UiO
Frode Rise, PhD, Professor, Dept of Chemistry, University of Oslo
Bernd Thiede, Department of Biosciences, UiO
Håvard Haugen, Professor, Department of Biomaterials, Institute of Clinical Dentistry Faculty of Dentistry, UiO
Department of Biostatistics, University of Oslo

Department of Nutrition, University of Oslo
Lene Frost Andersen, Professor, dr.philos, Head of Dept, Division of Nutritional Epidemiology
Christian A. Drevon, Professor, MD, PhD, Molecular Nutrition
Per Ole Iversen, Professor, MD, PhD, Division of Clinical Nutrition
Margareta Wandel, Professor Emiritus
Line Mariann Grønning-Wang, Associate Professor, MSc, PhD

Institute of Health and Society, University of Oslo
Gerd Holmboe-Ottesen, Professor, dr.philos.
Bernadette Kumar, Associate Professor, PhD and Director of the Norwegian Centre for Minority Health Research (NAKMI)
Bjørgulf Clausen, Professor, MD, PhD
Louise Emilsson, PhD, Postdoctoral Fellow

Akershus University Hospital
Ivar A. Eide, PhD, MD, Renal Unit, Akershus University Hospital
My Svensson, PhD, MPA, Renal Unit, Akershus University Hospital and University of Oslo

Norwegian Institute of public health
Per H. Magnus, Professor, Norwegian Institute of Public Health
Ketil Størdal, MD, PhD, Norwegian Institute of Public Health
Sidsel Graff-Iversen, Researcher, PhD
Wenche Nystad, Director, PhD

Norwegian School of Sports Science
Roald Bahr, Professor, MD, PhD
Sigmund Andersen, Professor, dr. philos.
Finn Skårderud, Professor, MD, PhD

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The Norwegian Knowledge Centre for the Health Services
Lise Lund Håheim, Professor, Institute of Basic Medical Sciences, University of Oslo and The Norwegian Knowledge Centre for the Health Services

Diakonhjemmet Hospital
Karin Magnusson, MSc, PhD, Department of Rheumatology

NTNU
Haakon Stensæth, Associate Professor, MD, PhD, Department of Circulation and Medical Imaging, NTNU
Valdemar Grill, Professor emeritus, Department of Cancer Research, NTNU, Trondheim

Helseundersøkelsen i Nord-Trøndelag (HUNT)
Kristian Midthjell, Professor Emiritus

University of Bergen
Helge Ræder, KG Jebsen Center for Diabetes Research, University of Bergen
Valeriya Lyssenko, Professor, MD, PhD, Department of Clinical Science, University of Bergen

Haukeland University Hospital
Pål Rasmus Njølstad, Professor, MD, PhD, KG Jebsen Center for Diabetes Research, Department of Clinical Science
Oddmund Søvik, Professor Emiritus, Dept of Pediatrics
Trond Markestad, MD, PhD, Dept of Pediatrics
Rolv Terje Lie, Professor, PhD, Dept of Global Public Health and Primary Care
Grethe S. Tell, Professor, MPH, dr. philos., Dept of Global Public Health and Primary Care
Sverre Sandberg, Adjunct Professor, MD, PhD, Dept of Global Public Health and Primary Care
Center for Diabetes Genetics, Haukeland University Hospital
Women's Clinic, Haukeland University Hospital

Bergen University College
Marit Graue, Assoc. Professor, PhD
Marjolein M. Iversen, Assoc. Professor, PhD

Nordlandssykehuset HF
Tor Claudi, MD, Nordlandssykehuset HF

University of Tromsø
Svein Ivar Mellgren, Professor Emiritus, Dep of Neurology
Bjørn Odvar Eriksen, Professor, UIT Arctic University of Tromsø
Toralf Melsom, Associate Professor, UIT Arctic University of Tromsø
Marit Solbu, UIT Arctic University of Tromsø
Svetlana Zykova, Associate Professor, UIT Arctic University of Tromsø

Sørlandet Hospital Kristiansand
Department of Obstetrics and Gynecology

INTERNATIONAL COLLABORATORS

Timothy Lyons, Professor, Queens University, Belfast, Northern Ireland
Alicia Jenkins, Professor, University of Sydney, Australia
John Todd, Professor, University of Cambridge, UK
Flemming Poicot, Professor, Copenhagen, Denmark
Jim McGuire PhD, Steno Diabetes Centre,Copenhagen, Denmark
John Gerich, Professor, Rochester NY, USA
Michael Stumvoll, Professor, Tübingen, Germany
Ashimina Mitrakou, Professor, Athens, Greece
Timon van Haeften, Professor, Holland
Ole Schmitz, Professor, Aarhus, Denmark
Allan Flyvbjerg, Professor, Aarhus, Denmark
Steve Chadban, Professor, Sydney, Australia
Michael N. Oda, Professor, CHORI, Oakland, USA
Vincent Monnier, Professor, Cleveland, USA
Thomas Jansson, Professor, University of Colorado, Denver, USA
Theresa Powel, Professor, University of Colorado, Denver, USA
Yaron Tomer, Professor, Dept. of Endocrinonolgy, Diabetes and Bone Disease, Mt. Sinai Hospital, NY, USA
Chris R. Cardwell, Professor, Centre for Public Health, Queen's University Belfast, Belfast, UK
Janet Svensson, Professor, Department of Pediatrics, Copenhagen University Hospital, Denmark
David R Sell, Assistant Professor, Case Western Reserve University, Pathology
Tuulia Hyötyläinen, Systems Medicine Department, Steno Diabetes Centre, Gentofte, Denmark and VTT Technical Research Centre of Finland, Espoo, Finland
Kathleen Gillespie, BSc, PhD, Diabetes & Metabolism, University of Bristol, UK
Anne-Marie Nybo Andersen, Professor, Section of Social Medicine, University of Copenhagen, Denmark
Steffen Husby, Professor, Dept of Pediatrics, Syddansk Universitet, Denmark
Simon Satchell, MBBS(Lond), PhD(Bristol), MRCP(RCP), CCST Renal Medicine, Academic Renal Unit, University of Bristol, UK
Bo Feldt-Rasmussen, Professor, MD, DMSc, Renal Department Rigshospitalet, University of Copenhagen, Denmark
Esteban Porrini, Researcher, University of Tenerife, Spain
Paul Gatenholm, Professor, Chalmers University of Technology, Gothenburg, Sweden
Maria Sörhede Winzell, PhD, Astra Zeneca R&D, CVMD iMed Bioscience, Mölndal, Sweden
The EURODIAB Group, PI: Professor CC Patterson, Centre for Public Health, Queen's University Belfast, Belfast, UK
The Nordic Childhood Diabetes Registry Study Group
University of Texas, Health Science Center San Antonio, Center for Pregnancy and Newborn Research, Department of Obstetrics and Gynecology, USA
EU-IMI 2, the INNODIA consortium

The DiviD Study Group

Heiki Hyöty, Professor, Dept of Virology, University of Tampere, Finland
Gun Frisk, Professor, University of Uppsala, Sweden
Olle Korsgren, Professor, University of Uppsala, Sweden
Oskar Skog, Assoc. Professor, University of Uppsala, Sweden
Decio Eizirik, Professor, University of Bruxelles, Belgium
Karsten Buchard, Professor, University of Copenhagen, Denmark
Gun Forsander, Assoc. Professor, University of Gothenburgh, Sweden
Henrik B. Mortensen, Professor, University of Copenhagen, Denmark
Johnny Ludvigsson, Professor, Dept. of Pediatrics, University of Linköping, Sweden
Noel Morgan, Professor, University of Exeter, UK
Sara Richardsson, Assoc. Professor, University of Exeter, UK
Bart Roep, Professor, Dept. of Immunlogy, Leiden University, Holland
Mikael Knip, Professor, Dept. of Pediatrics, University of Helsinki, Finland
Gunilla Westermark, Professor, University of Uppsala, Sweden
Yuval Dor, Professor, University of Jerusalem, Israel
Antonio Toliono, Professor, Laboratory of medical Microbiology, University of Varese, Italy
Ben Giepmans, Professor, University of Groningen, Netherlands
Riitta Lahesmaa, Professor, University of Turku, Finland
Matthias von Herrath, Professor, University of California La Jolla, USA
Ian Lipkin, Professor, Columbia University, New York, USA
Ivan C. Gerling, Professor, Memphis, USA
Shiva Reddy, Professor, Auckland University, New Zealand
David Dunger, Professor, University of Cambridge, UK
Malin Thulin-Flodstrøm, Professor, Karolinska Institutet, Stockholm, Sweden
Mark Peakman, Professor, Kings College, London, UK
Mark Atkinson, Professor, University of Florida, USA (nPOD)
Alberto Pugliese, Professor, University of Miami, USA (nPOD)

NOTES

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