Abstracts

We invited all speakers to send a pitch/abstract/short summary for their presentation. The pitches and abstracts/short summaries are presented in accordance with the conference programme and parallel sessions. [Presentations based on a submitted abstract/summary are marked with an (*).]
### Medical Museion sessions for young investigators, 6 June

<table>
<thead>
<tr>
<th>Hosts: Lykke Sylow, Post doc, Dept. of Nutrition, Exercise and Sports and Kia Ditlevsen, Post doc, Dept. of Food and Resource Economics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Theme 1: Pathways regulating insulin sensitivity and glucose uptake incl. effects of physical activity</strong></td>
</tr>
<tr>
<td><strong>Jonas Roland Knudsen, PhD Student</strong>&lt;br&gt;Dept. of Nutrition, Exercise and Sports, UCPH</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Exercise acutely increases skeletal muscle insulin sensitivity. However, our understanding of the mechanisms behind this health promoting effect is limited. Studies of rodents have implicated the glucose transporter 4 (GLUT4), since prior exercise increases insulin-stimulated insertion of GLUT4 in the surface membrane of the muscle fibers. The aim of this study was to explore the whereabouts of GLUT4 in human muscle in the post exercise period before and during insulin stimulation. We hypothesized that exercise and insulin would cause a redistribution of GLUT4 between different intracellular compartments and the surface membrane. We used correlative light and electron microscopy to identify GLUT4 and compartment protein markers in 70 nm cryo-sections. Exercise accumulated GLUT4 in GLUT4-storage vesicles and the t-tubules. In prior exercised muscle, insulin-stimulation decreased the GLUT4-storage vesicles and increased GLUT4 in early endosomes. In addition, insulin caused accumulation of GLUT4 in the recycling endosomes independent of prior exercise. In conclusion, these data show redistribution of GLUT4 between different compartments in human muscle upon exercise and insulin stimulation.</td>
</tr>
<tr>
<td>¹Molecular Physiology Section, Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, DK</td>
</tr>
<tr>
<td>²School of Biochemistry and Wolfson Bioimaging Facility, University of Bristol, UK</td>
</tr>
</tbody>
</table>

| Naba Hassan, Graduate Student<br>Steno Diabetes Center Copenhagen, the Capital Region Denmark | Combined transcriptomics and metabolomics analyses of adipose tissue in obese subjects reveal pathways associated with insulin resistance*<br>Hassan N., Dahlman I., Kolehmainen M., Legido-Quigley C., Ahonen L., Dragsted L., Ali A. |
|  |
| Type 2 diabetes is a heterogeneous disease and various genetic and environmental components play a role in the etiology of the disease. Understanding the metabolic profiles of tissues involved in the etiology of the disease may provide us with insight into signatures associated with its function. Here we aim to identify metabolic signatures associated with insulin resistance (IR) in human adipose tissue using combined analyses of gene expression, metabolomics and human genome scale metabolic networks (e.g., HMR). Our analyses for the genes associated with HOMA-IR found 62 genes to be significantly dysregulated (Padj < 0.05) in obese participants (N = 56). From the metabolic network based pathway analyses 27 metabolic pathways (Padj <0.05) were found to be dysregulated where 69 metabolites (Padj <0.05) were found to be up-regulated in association with IR. In addition, we found a considerable |
overlap between the lipids represented on HMR and detected on our global Lipidomics UHPLC-QTOF platform. The reporter metabolites and pathways found in our represent putative markers for variation in insulin resistance among obese patients calls for further validation in metabolomics/Lipidomics studies.

Nicolas Oldenburg Jørgensen, Research Assistant
Dept. of Nutrition, Exercise and Sports, UCPH

**Therapeutic potential of direct pharmacological activation of AMPK in the regulation of skeletal muscle insulin sensitivity?**

*Nicolas O. Jørgensen*, Rasmus Kjøbsted, Christian Pehmøller and Jørgen F. P. Wojtaszewski

Metabolic diseases such as type 2 diabetes are associated with skeletal muscle insulin resistance. Interestingly, a single bout of exercise has been found to alleviate this resistance to insulin action. As this effect of exercise is dependent on activation of skeletal muscle AMP-activated protein kinase (AMPK), pharmacological interventions targeting AMPK could potentially improve skeletal muscle insulin sensitivity and consequently metabolic health on a whole body level.

Prior studies have demonstrated that indirect activation of skeletal muscle AMPK by AICAR leads to increased insulin sensitivity for glucose uptake. Therefore, we investigated whether direct allosteric stimulation of skeletal muscle AMPK activity by the novel small molecule PF739 is sufficient to improve insulin-stimulated glucose uptake of isolated skeletal muscle.

We found that direct activation of AMPK in isolated skeletal muscle does not increase muscle insulin sensitivity. However, we believe this might be due to the specific activation pattern of AMPK caused by PF739 rather than a general inability of direct pharmacological AMPK activation to mimic the insulin-sensitizing effect of exercise.

1Section of Molecular Physiology, Department of Nutrition, Exercice, and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark.

2Internal Medicine Research Unit, Pfizer Global Research and Development, Cambridge, Massachusetts, USA.

Steffen H. Raun, Research Assistant
Dept. of Nutrition, Exercise and Sports, UCPH

**Pantothenate Kinase 4 – A novel protein in metabolism**

*Steffen H. Raun, Andreas M. Fritzen, Lisbeth V. Møller, Benjamin L. Parker, Lykke Sylow, Paul Gregorevic, Bente Kiens, David E. James, Erik A. Richter, Maximilian Kleinert*

Pantothenate Kinases (PanKs) are a group of proteins predicted to catalyze the first step of the biosynthesis of Coenzyme A (CoA). PanK4 is one of four isoforms, however the function of PanK4 is not understood.

We found that PanK4 was preferentially expressed in skeletal muscle. During exercise, PanK4 was phosphorylated at Ser-63 in both human (~150%) and mouse (~50%) skeletal muscle. Following exercise training, the expression of PanK4 was also upregulated (~30%) in human skeletal muscle. Overexpression of PanK4 in mouse tibialis anterior muscle was sufficient to increase resting glucose uptake (~80%) in this muscle, while muscle CoA levels were not affected suggesting that PanK4 does not function as a pantothenate kinase. Notably, when a PanK4 mutant that cannot be phosphorylated at Ser-63 was overexpressed, glucose uptake was unaltered.

These data suggest a prominent role of PanK4 regulating skeletal muscle glucose metabolism through a CoA-independent mechanism. This
identifies PanK4 as an interesting therapeutic target in metabolic disorders.

### Theme 2: Personalised approaches, interventions and behavioural concepts

<table>
<thead>
<tr>
<th>Drude Skov Lauridsen, PhD Student</th>
<th>Risk and responsibility: Parental negotiations of having a child “at risk” of obesity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dept. of Food and Resource Economics, UCPH</td>
<td>Studies show that obesity has become increasingly prevalent among young children in both the U.S. and Europe over the last 30 years. This rise has led to a search for the early causes and ways to prevent obesity. While childhood obesity can have multiple causes, parental influence as both causing and being the key to preventing obesity has gained wide usage in media, science and policy. Studies of parental influence are investigating what parents are doing wrong and what is the “right” parental behavior and parenting style to prevent childhood obesity. However, recent studies argue that obesity research has a gender bias as it often focus solely on mothers. The studies contend the framing of mothers is inadvertently reproducing the dominant gendered ideology in which children’s health and wellbeing is a maternal responsibility—thereby neglecting the father or partner, family dynamics and broader sociocultural and economic causes. In effect, mothers are being blamed for the childhood obesity epidemic. As few studies include fathers or the interaction between parents in studies of the prevention of childhood obesity, more knowledge in this area is warranted. This paper investigates how parents negotiate whether their child is “at risk of obesity” and their care practices among families where the mother was targeted based on a high BMI (≥30). The paper analyses 12 in-depth interviews with mothers and fathers who have participated in the SKOT II mother-child cohort study. The parents were asked about their division of food preparation and planning, how they manage their child’s health and weight, and whether they consider their child as “at risk of obesity”. The preliminary results show that parents can differ in their perception of risk and that there are different care strategies to prevent childhood obesity. The paper also discusses parental responsibility in childhood obesity prevention in relation to dominant gender ideologies.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Katharina O Cathaoir, Post doc</th>
<th>Legal issues of personalised medicine in Denmark*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dept. of Law, UCPH</td>
<td>This presentation introduces the potential legal issues of the introduction of personalised medicine in Denmark. The Danish government has placed personalised medicine high on the political agenda. Yet, PM also raises relevant legal concerns. Therefore, this presentation presents the results of a literature review of legal issues pertaining to PM raised in international literature between 2000-2017. The results show that in the context of PM academics have expressed particular concern regarding discrimination and patient autonomy, in particular, informed consent, privacy and confidentiality. These issues are further discussed in the context of Danish law, namely whether Danish law provides adequate protection for the individual, while at the same time providing space for collective goals, such as the good population health and access to effective treatment. From a legal perspective, the establishment of a Danish National Genome Centre and the corresponding amendment to the Danish Health Act is particularly pressing. The Centre has proven controversial and</td>
</tr>
</tbody>
</table>
commentators have argued that the draft legislation breaches individual privacy and violates individuals’ rights. Therefore, the extent to which these concerns are supported by existing practice from Danish and European courts is discussed, as well as relevant principles of international law.

Regitze Anne Saurbrey Pals, Research Assistant
Steno Diabetes Center Copenhagen, the Capital region Denmark

Type 1 diabetes in pre-teenagers: Emerging autonomy in the difficult transition from childhood to adolescence*
Regitze Anne Saurbrey Pals1, Dan Grabowski1

Many children under the age of 12 with type 1 diabetes experience negative psychological symptoms and poor metabolic control. Current interventions have limited effect and rarely engage children actively. Furthermore, the transition from childhood to adolescence and the issue of emerging autonomy in children with diabetes have received little attention. The aim of this study is to explore practices, barriers and strategies related to diabetes care and autonomy in pre-teenagers with type 1 diabetes. The study will inspire the development of a user-driven and practice-oriented intervention to support pre-teenagers with type 1 diabetes.

The study relies on a participatory design and is situated within social constructivism. Following this approach, diabetes care and autonomy include multiple enactments of values and norms related to responsibility, roles and family dynamics. The study is based on participant observation, workshops and interviews with pre-teenagers, their families, peers and healthcare professionals.

Preliminary results include: 1) The children would like their family (especially parents) to talk more positively about diabetes. According to the children, diabetes care does not have to be problem-oriented and based on worries. 2) The children want the healthcare professionals to talk directly to them in ways they can relate to instead of only talking to the parents.

1Diabetes Management Research, Steno Diabetes Center Copenhagen, Niels Steensens Vej 6, 2820 Gentofte

Theme 3: Diet and gut signaling in obesity and insulin action
Anne-Marie Lundsgaard, Post doc
Dept. of Nutrition, Exercise and Sports, UCPH

Mechanisms preserving insulin action during high dietary fat intake in healthy men*
Anne-Marie Lundsgaard, Jørgen F. P. Wojtaszewski, Erik A. Richter and Bente Kiens

Prolonged intervention studies investigating molecular metabolism are necessary for a deeper understanding of the role of dietary fat and carbohydrate in health. To provide mechanistic information about metabolic adaptation to fat-rich diets, healthy men ingested saturated (SFA) or polyunsaturated (PUFA) fat-rich diets for six weeks under weight maintenance. Hyperinsulinemic clamps combined with leg balance technique revealed unchanged peripheral insulin sensitivity, independent of fatty acid type. Both diets increased fat oxidation potential in muscle. Hepatic insulin clearance increased, while glucose production, de novo lipogenesis and plasma triacylglycerol decreased. Intake of fat-rich diets thus induces extensive metabolic adaptations enabling disposition of dietary fat without metabolic complications.
The effect of bacteriophages on obesity*

Caroline M. Junker Mentzel1, Torben Sølbeck Rasmussen1, Lars Hestbjerghansen2, Witold Kot3, Finn Kvist Vognesen3, Axel Kornerup Hansen2, Dennis Sandris Nielsen1*

Several studies have shown that obesity is associated with gut microbiota dysbiosis. In mice, it has also been shown that the obese phenotype is transferable with the gut microbiota. Bacteriophages (phages) are viruses infecting bacteria in a strain specific manner. It is hypothesized that phages can manipulate the gut microbiota and alter the metabolism of the host. Phages were purified from the caecum of C57BL/6N mice, which had been fed a lowfat diet for 14 weeks. 40 male C57BL/6NTac mice were divided in to 5 groups, and fed a high fat diet (60% fat) or a control diet (10% fat) for 12 weeks. One group was fed the low fat control diet (LF) and one group was fed the high fat diet (HF), with no further interventions. One group (HF+P) was orally dosed with a suspension of phages purified from the gut of lean mice. One group was treated with one dose of ampicillin (HF+A) and one group was treated with ampicillin and with phage suspension (HF+A+P). As expected, all groups subjected to high fat diet gained weight faster than the low fat diet group. However, the HF+P group gained significantly less weight and had a significantly better blood glucose profile during an OGTT than the HF group.

1 Section of Microbiology and Fermentation, Dept. of Food Science, Faculty of Science, University of Copenhagen, Denmark
2 Section of Experimental Animal Models, Dept. of Veterinary and Animal Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
3 Section of Environmental microbiology & biotechnology, Dept. of Environmental Science, University of Aarhus, Denmark

*These authors contributed equally to this work

Effects of liraglutide on gallbladder emptying: a randomised, placebo-controlled trial in adults with overweight or obesity*

Christina C. Nexøe-Larsen1, Pernille H. Sørensen1, Helene Hausner2, Mikkel Agersnap2, Mille Baekdal1, Andreas Brønden1, Lea N. Gustafsson3, David P. Sonne1,4, Louise Vedtofte1, Tina Vilsbøll1 and Filip K. Knop1,5,6

Aims: Treatment with liraglutide 3.0 mg has been associated with gallbladder-related adverse events. To assess a potential mechanism, the objective of this single-centre, double-blind, 12-week trial was to compare the effect of a 0.6 mg liraglutide dose and steady-state liraglutide 3.0 mg with placebo on gallbladder emptying in adults with body mass index (BMI) ≥27 kg/m2 and without diabetes.

Methods: Participants were randomised 1:1 to once-daily subcutaneous liraglutide (n=26) or placebo (n=26), starting at 0.6 mg with 0.6 mg weekly increments to 3.0 mg, with nutritional and physical activity counselling. A 600 kcal (23.7 g fat) liquid meal test was performed at baseline, after the first dose and after 12 weeks. The primary endpoint was the 12-week maximum postprandial gallbladder ejection fraction (GBEFmax), measured over 240 min after starting the meal. ClinicalTrials.gov ID NCT02717858.

Results: Baseline characteristics were similar between groups (overall (mean±SD) age 47.6±10.0 years, BMI 32.6±3.4 kg/m2, 50% female). Mean 12-week GBEFmax (-3.7 [-13.1, 5.7]%; treatment difference [95% confidence interval]) and area under the GBEF curve in the first 60 min (-390 [-919, 140] %×min) did not differ for liraglutide 3.0 mg (n=23) versus...
An increase in scientific research associating loneliness with ill health among older people has placed loneliness on the public health agenda. Loneliness is not specifically linked with growing old, but as exposure to risk factors of loneliness generally increases with age, some older people are at risk of long-term loneliness. A broad range of initiatives aspires to combat loneliness among older people through communities and volunteerism and hereby create meaningful social relations. One widespread initiative aiming to do so is the ‘Befriending Scheme’. I will present results from a qualitative research project examining the social relations in a Danish befriending scheme. I apply the concept visiting-friendship to describe the social relation between befriender and
befriendee. Theories on social relations' influence on health form the basis of the visiting-friendship concept. The analysis shows how the visiting-friendship holds possibilities for companionship and attentiveness. Befrienders have the potential to bring back courage in older peoples' life in times containing loss and concerns.

**Morten Arendt Rasmussen, Associate Professor**  
Dept. of Food Science, UCPH and Danish Pediatric Asthma Center, Gentofte Hospital, UCPH

**Analysis of omics data utilizing external knowledge – Examples on microbiome, gene expression and asthma**  
Modern analytical techniques provide an immense amount of data which we wish to turn into knowledge. State-of-the-art multivariate statistical techniques such as partial least squares regression or canonical variates analysis suffers from being too flexible in cases where the signal related to the biological question of interest is small and the number of variables is high. Structured databases mapping omics information to e.g. phylogeny for microbiome or pathways for metabolites, makes can actively be utilized in the multivariate modelling of such data.  
This work presents means for data integration exploiting structured databases to both control overfitting and reveal models enforced to resemble known biology. Specifically, case studies of prediction of asthma at 6 years of age from gut microbiota composition at age one year as well as gut microbiome metabolome interactions in elderly will be presented.

### Session 2: Physical (in)activity in everyday life

**Hosts:** Astrid Pernille Jespersen, Associate Professor, Center for Health Research in the Humanities, the SAXO Institute and Jørn Wulff Helge, Professor, Dept. of Biomedical Sciences

| **Jens Troelsen, Professor**  
Institute of Sports Science and Clinical Biomechanics University of Southern Denmark | **How to promote active ageing based on physical activity measurements and co-design?**  
*Jens Troelsen (presenter), SDU, Sidse Carroll, KADK, Tanja Schmidt, SDU*  
Ageing in place is highly encouraged for both economic reasons as well as for the overall physical, mental and social wellbeing of older adults. Acknowledging that local outdoor communities play a key role, this presentation aims to explore how combined accelerometer, GPS data, observational data and go-along interviews can be utilized to detect movement patterns, and how this broadly-based knowledge can be transferred to a co-design process through the lens of older adults. The presentation is based on preliminary analyses and published scientific papers. |
| **Jonas Salling Quist, Post doc**  
Dept. of Biomedical Sciences, UCPH | **The health effects of active commuting and leisure-time exercise in individuals with overweight and obesity, and the struggles to implement PA in everyday life**  
*Jonas Salling Quist and Astrid Pernille Jespersen*  
Exercise is efficacious for improving cardiometabolic health; however, implementation and maintenance is challenging. Physical activity occurs in several domains of everyday life and active commuting may represent a time-efficient alternative to leisure-time exercise, but whether active commuting conveys health benefits similar to those of leisure-time exercise was unknown. In the GO-ACTIWE randomized controlled trial we investigated effects of 6 months of active commuting and leisure-time exercise of moderate or vigorous intensity 5 days/week on a variety of health outcomes as well as motivators and barriers for engagement in |
regular exercise in physically inactive women and men with overweight and obesity. In a qualitative sub-study, we investigated the participants’ challenges and experiences related to the implementation of exercise and active commuting in everyday life. We observed improvements in several health outcomes including cardiorespiratory fitness, adiposity, and peripheral insulin sensitivity in response to all three types of exercise. In conclusion, active commuting exerts health effects on par with those by leisure-time exercise in individuals with overweight and obesity but issues related to logistics and priorities in everyday life represent important barriers for implementation and maintenance.

Johanne Stubbe T. Kristensen, Associate Professor
Dept. of Systematic Theology, UCPH

Physical activity and the problem of promotion and implementation - A change of perspective

Aske Juul Lassen, Post doc
Center for Health Research in the Humanities, the SAXO Institute, UCPH

Retirement rhythms: Continuing worklife structures in everyday life after retirement*

Aske Juul Lassen, Morten Hjulmand, Kenneth Mertz & Lars Holm This study investigates the daily activity patterns in retirees obtained by qualitative and quantitative data collection methods, and explores how Danish retirees structure their everyday lives in ways resembling work-life. The participants are a subset of older people enrolled in the CALM project (CALM.ku.dk). The qualitative data was collected in experimental workshops, where the participants were asked about their everyday lives. The quantitative data were collected in the same older subjects wearing an Active Pal equipment for 4 days registering sitting/lying, standing, or walking activities continuously during the day. The purpose was to explore agreement between the different assessment methods and the differences and similarities between work-life and retirement rhythms. By understanding such rhythms, this paper seeks to contribute to social theories of retirement and to the understandings of the organisation of everyday life in old age. Such a contribution provides valuable insights into the ways activities and health promotion programmes should be organised and targeted to retirees, as their rhythms of everyday lives should be considered in such endeavours.

Session 3: Intervention research: How to achieve maintained behavioural change?

Hosts: Lotte Holm, Professor, Dept. of Food and Resource Economics and Berit Heitmann, Professor, Dept. of Public Health

Prevention of weight regain - state-of-the-art and research challenges

Health problems associated with obesity are a major healthcare challenge. There are many techniques available to help people lose weight. However, most people re-gain the weight they lose – the real challenge is to maintain weightloss (WLM), but we still don’t know what works best for WLM or why. To better tackle obesity and prevent weight regain, we need to learn more about what behaviour changes to make and how, to best maintain long term weight loss. This is the main research aim of The NoHoW project, which is a European Union H2020-funded project aimed to develop tools to help people maintain
previously lost weight. NoHoW currently carry out a large-scale European randomized controlled trial to test whether different evidence-based and novel behavior change, emotion- and self-regulation techniques delivered via an ICT Toolkit can promote successful WLM.

<table>
<thead>
<tr>
<th>Bodil Just Christensen, Assistant Professor</th>
<th>Instrumentization: an effective strategy for weight loss maintenance?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dept. of Food and Resource Economics, UCPH</td>
<td>A recent study carried out at Hvidovre Hospital suggests that strict rules are the key to weight maintenance. The study investigated the effect of appetite hormones on weight maintenance. 42 participants lost weight on a powder diet and then they were encouraged to maintain the weight loss during the next year. Patients who were good at keeping weight off after losing it didn’t eat to accommodate desire, hunger, or satiety. Instead, they considered eating as a tool with a higher purpose and they devised their own systems for what, how much, and when to eat. These choices were not guided by feelings of hunger and fullness, but by the singular aim of keeping the weight off. They created systematic routines that fit into their daily lives - and stuck to them regardless of feelings of hunger or satiety. What mattered most was that they followed these systematic habits precisely. This approach minimized the number of choices in relation to when, what, and how much they could eat. As a result, the risk of “caving in” went down radically.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thomas Meinert Larsen, Professor</th>
<th>Interventions in achieving/maintaining weight loss loss: how to establish and maintain new habits?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dept. of Nutrition, Exercise and Sports, UCPH</td>
<td>Maintenance of weight loss is by many perceived as almost impossible, and that clear clinical benefits from weight loss are often not achieved. Although there are plenty of evidence that weight loss maintenance is indeed very difficult, there are also many studies that have successfully achieved long-term weight loss and achieved clinical benefits. The presentation will contain an updated review of some long-term studies with successful achievement of weight loss and associated clinical benefits, as well as describe which treatment aspects, such as dietary composition, physical activity, and behavior change techniques seems to be the most promising.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Caroline Sofie Balschmidt, Research Assistant</th>
<th>The cultural archive of colonialism and conceptions of health*</th>
</tr>
</thead>
</table>
| Dept. of Systematic Theology, UCPH             | A structure of inequality in thought and affect based on race was instilled in nineteenth-century European imperial populations and it is from this cultural archive that, among other things, the postmodern sense of self has been formed and fabricated. This formation has had an impact on the postmodern body, by the racialized discourses becoming intertwined with current dominant regimes of truth. This is explicit in the notions of “normal” or “healthy” behavior, which have theoretical and political implications manifested in our understanding of human existence. The disenchantment of the body caused by slavery has created a conflict between the psyche and the body; the spirit and the flesh. In this paper, I discuss how our colonial heritage render postmodern, Western civilizations prone to privilege “healthy” conceptions of the body. I discuss the ways in which an imperial racial economy continues to
underwrite dominant ways of knowing, interpreting, and feeling and how our bodies are affected by them. To understand the notion of otherness that conceptions of health constitutes, the discussion will lean on feminist theology and methodology that can be derived from the discipline.

**Simon Birk Kjær Jensen, MSc Student**  
Dept. of Biomedical Sciences, UCPH

**Diet-induced weight loss improves sleep duration and sleep quality in individuals with obesity**

*Simon B. K. Jensen¹, Charlotte Janus¹, Julie Lundgren¹, Christian R. Juhl¹, Bente Stallknecht¹, Jens Juul Holst¹, Sten Madsbad², Signe S. Torekov¹*

**Background:** Adequate sleep is suggested to be important for metabolic health. Furthermore, epidemiological studies have linked obesity to short sleep and poor sleep quality. Therefore, the aim of this study was to test if a diet-induced weight loss improves sleep in obese individuals.

**Methods:** 55 individuals with obesity (b.w. 109±12 kg, BMI 36±2 kg/m², age 44±11 yr, 31 females) completed a weight loss intervention as part of the S-LiTE study consisting of diet-induced weight loss (8 weeks with a low-calorie diet of 800 kcal/day) followed by one year of weight loss maintenance with exercise and/or the GLP-1 receptor agonist Liraglutide (3 mg/day). Sleep duration (7-day accelerometry, GENEActiv) and sleep quality (total Pittsburgh Sleep Quality Index score) were assessed at baseline and after the diet-intervention.

**Results:** The average weight loss after the 8-weeks diet-intervention was 13.6±5.3 kg (p<0.001). Sleep quality measured by PSQI was 6.5±3.7 at baseline (where >5 denotes poor sleep quality) and decreased to 5.5±3.7 (p<0.05) after weight loss. Sleep duration was increased after weight loss (5.8±1.5 vs. 6.2±1.0 hours; p<0.05).

**Conclusion and follow-up data:** A diet-induced weight loss for 8 weeks increased sleep duration with 24 min/night and improved sleep quality in individuals with obesity. Data from one year of treatment with exercise will be available at the time of the conference.

¹Department of Biomedical Sciences and NNF CBMR, University of Copenhagen,  
²Department of Endocrinology, Hvidovre Hospital, Hvidovre, Denmark.

---

**Parallel sessions 13.45-15.30, 7 June**

**Session 4: Diet, physical activity, health and well-being in children**

**Hosts:** Camilla T. Damsgaard, Associate Professor, Dept. of Nutrition, Exercise and Sports and Bente Stallknecht, Professor, Dept. of Biomedical Sciences

**Camilla T. Damsgaard, Associate Professor**  
Dept. of Nutrition, Exercise and Sports, UCPH

**Foods and nutrients to optimize cardiometabolic health in children**

Elevated blood pressure, dyslipidemia and other cardiometabolic derangements are increasingly seen in children and show tracking into adulthood. A number of studies have shown protective effects of diet in adults but evidence from studies in children is limited, and most dietary recommendations are based on extrapolations from findings in adults. This talk will present promising evidence from our randomized controlled trials on the effect of diet on children’s cardiometabolic health, focusing mainly on n-3 fatty acids, vitamin D and wholegrains, and give directions for future research aimed at preventing cardiovascular disease and type II diabetes from childhood.
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Presentation Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peter Bentsen, Senior Researcher</td>
<td>Health Promotion, Steno Diabetes Center</td>
<td><strong>Education outside the classroom as a holistic ‘add-in’ school-based physical activity promotion intervention for child and youth populations</strong>&lt;br&gt;Children are increasingly sedentary and consequences include declines in mental health, an alarming escalation of obesity and non-communicable diseases such as type 2 diabetes later in life. Schools are frequently used as a setting for physical activity promotion initiatives, but with mixed results. Our research suggests that moving teaching out of the classroom can increase children’s physical activity. Furthermore, education outside the classroom as an initiative to promote physical activity can be joined with the primary aim of the school: education and learning. It offers a novel approach in the fields of education and health promotion practice and policy through its holistic, ‘add-in’ and population-wide health promotion strategy. It is potentially a low-cost and non-invasive solution; however, more research and knowledge on implementation is needed.</td>
</tr>
<tr>
<td>Katrine Strandberg-Larsen, Associate Professor</td>
<td>Dept. of Public Health, UCPH</td>
<td><strong>Disordered eating in early adolescence.</strong>&lt;br&gt;Clinical manifestations of eating disorders are rare among children as they typically debut during adolescence. However, population-based samples of children aged 6-11 years indicate that around one in ten girls and one in twenty boys have disordered eating behaviors. In the Danish National Birth Cohort, children who have been followed from prenatal life were asked about disordered eating behaviors at 11 years. Findings on parental characteristics associated with disordered eating behaviors, and associations between childhood weight trajectories and disordered eating behaviors will be presented. Plans on further use of these data to increase our understanding on the etiology and prognosis of early-onset eating disorder will be presented.</td>
</tr>
</tbody>
</table>
| Theresia Schnurr, Postdoc                   | Novo Nordisk Foundation Center for Basic Metabolic Research, UCPH | **Prenatal exposures possibly modifying the influence of the maternal and child genetics on childhood obesity**<br>*Theresia M. Schnurr¹, Camilla S. Morgen²,³, Ellen A. Nøhr⁴, Torben Hansen¹, Thorkild I.A. Sørensen¹,³*<br>Background: Maternal BMI, smoking, physical activity, coffee consumption and socioeconomic status during pregnancy as well as a genetic predisposition are well-established risk factors for childhood obesity.<br>Objective: The overall objective of this project is to investigate whether prenatal exposures (defined as maternal BMI, smoking, physical activity, coffee consumption and socioeconomic status) interact with the mother’s and child’s genetic predisposition to childhood obesity at 7 years of age.<br>Design: Within the Danish National Birth Cohort (n=100,418), the following mother-child pairs with genome-wide genetic information are available:<br>1. Randomly selected mothers and their children (n=510)<br>2. Obese mothers and their children (n=431)<br>3. Children with the highest BMI at 7 years and their mothers (n=774)
Maternal and fetal genotypes are correlated (r ~ 0.5) and therefore we will explore whether the interactions and associations between maternal and offspring genetic risk profiles and childhood obesity are independent of one another, while taking into account the genetic transmission between mother and child in the available mother-child offspring pairs.

Results: While our preliminary results suggest that there is an interaction between the child genetic risk score and maternal smoking on child overweight, we aim to have additional results generated to be presented at LOM 2018.

1 Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Sciences, University of Copenhagen, Denmark
2 National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark
3 Section of Epidemiology, Department of Public Health, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
4 Research Unit for Gynaecology and Obstetrics, Department of Clinical Research, University of Southern Denmark, Denmark

---

**Health-polarization: Misunderstood perceptions of health as barriers for health behavior change in families with overweight or obese pre-school children**

*Didde Høeg and Dan Grabowski*

To develop tailored family-based interventions to treat and prevent overweight and obesity among children, there is a need for contextual knowledge about potentials and barriers for health behavior change among families. This project is a collaboration between Steno Diabetes Center Copenhagen and Guldborgsund Municipality, which has a high rate of obese citizens. We used a Design-Based Research approach to generate knowledge and to design an intervention tailored to the local context. In total, five participatory workshops with families (45 family members) and five workshops with professionals (31 professionals) were conducted as qualitative data. We found that several parents had perceptions of health being a total absence of everything that taste good and that a healthy lifestyle entails an extreme way of living. This misperception seems to be a huge barrier in these families. The fathers often worry that the family will become fanatically healthy, while the mothers are concerned that the children will be bullied or experience stigmatization because of obesity. These opposing worries regarding health form a vital barrier for the families in terms of becoming healthier. Professionals working with these families should be aware of how to approach these familial barriers in order to best support the families' in becoming healthier.

---

**Session 5: Physiological mechanisms behind the health promoting effects of physical activity**

**Hosts:** Erik Richter, Professor, Dept. of Nutrition, Exercise and Sports and Jesper Lundbye-Jensen, Associate Professor, Dept. of Nutrition, Exercise and Sports

**Zach Gerhart-Hines.**

**Associate Professor**

Novo Nordisk Foundation Center for Basic Metabolic Research, UCPH

**Fiber-type dependent control of skeletal muscle metabolism by the mitochondrial phospholipid cardiolipin**
### Maximilian Kleinert, Post doc
Dept. of Nutrition, Exercise and Sports, UCPH

**The pantothenate kinase 4 is a novel exercise-responsive protein**

Maximilian Kleinert1,2, Steffen H. Raun1, Andreas M. Fritzen1, Rasmus Kjøbsted1, Benjamin L. Parker3, Bente Kiens1, David E. James3, Erik A. Richter1

Pantothenate kinases (PanKs) catalyze the first step in the biosynthesis of coenzyme A. However, PanK4 is a mis-annotated member of the PanK family and its function and regulation are unknown. A single bout of exercise increases the phosphorylation of PanK4 at the Ser-63 residue (p-PanK4) in both human and mouse skeletal muscle. In contrast, stimulation with insulin decreases p-PanK4 in skeletal muscle. Both in situ contractions, via electric stimulation of the sciatic nerve, and in vitro contractions increase skeletal muscle p-PanK4. In vitro, passive stretching of the skeletal muscle or AICAR-induced AMPK activation failed to induce p-PanK4, while increasing cytosolic calcium concentrations augmented p-PanK4.

In summary, we have identified PanK4 as a novel exercise-responsive protein in skeletal muscle. The exercise-induced p-PanK4 is likely mediated by a calcium-dependent kinase.

---

### Thomas Morville, PhD Student
Dept. of Biomedical Sciences, UCPH

**Effects of endurance or resistance exercise on plasma bile acids, FGF19 and FGF21 in humans**

Thomas Morville1, Ronni Eg Sahl1,2, Sam A.J. Trammell2, Matthew P. Gillum2, Jørn Wulff Helge1, Christoffer Clemmensen2

Objective: Exercise has profound pleotropic health benefits, yet the underlying physiological and molecular mechanisms remain incompletely understood. The endocrine fibroblast growth factor FGF21, bile acids (BA) and BA-induced FGF19 have recently emerged as metabolic signaling molecules. Here we investigated whether distinct modes of exercise affect plasma bile acids, FGF19 and FGF21 in healthy humans.

Methods: Ten healthy moderately trained males were enrolled in a randomized, within subjects cross-over study of 1 hour (h) of bicycling at 70% of their VO2peak (endurance exercise (EE)) and 1 h of high-volume resistance exercise (RE). An endocrine time-course of hormones and metabolites was created from venous blood, sampled: pre, post and at time-points 15, 30, 60, 90, 120 and 180 min after exercise.

Results: RE significantly increased circulating glucose (P<0.001), lactate (P<0.001) and insulin (P<0.001) relative to EE, most prominently during the first 30 min post-exercise. EE robustly increased circulating glucagon relative to RE (P<0.001). RE substantially decreased FGF19 (P<0.001),
whereas EE specifically increased FGF21 - peaking 1 h post-exercise (P<0.001). Total plasma BA were significantly decreased 1-3 h following RE (P<0.05). The composition of bile acids changed with both types of exercise. Interestingly, whereas most bile species decreased following exercise, lithocholic acid (LCA) significantly increased (P<0.001) 1-3 h post-exercise following both types of exercise.

Conclusion: Here, we report for the first time that high-intensity RE suppresses the BA-FGF19 axis. EE and RE uniquely modifies the composition of bile acid species in circulation. Notably, both types of exercise increase circulating concentrations of the TGR5 receptor agonist lithocholic acid (LCA). Vigorous EE potently increases circulating FGF21. Future studies are needed to gauge if the herein described exercise-induced alterations in bile acids, FGF19 and FGF21 are underlying some of the health benefits of exercise.

Charlotte Janus, PhD Student (Abstract may be presented by Assoc Professor Signe S. Torekov)
Dept. of Biomedical Sciences, UCPH

Can you exercise your gut? Increased physical activity is associated with increased glucose-induced GLP-1 responses in men
Charlotte Janus1,2, Hanan Amadid3,5, Dorte Vistisen3, Daniel R Witte2,5, Torsten Lauritzen5, Søren Brage6, Anne-Louise Bjerregaard5, Torben Hansen1, Jens Juul Holst1,4, Marit E Jørgensen3,7, Oluf Pedersen1, Anna Jonsson4, Kristine Færch3, Signe Sørensen Torekov1,4.

Physical activity (PA) is a cornerstone in the prevention of metabolic diseases like type 2 diabetes and obesity - conditions in which the secretion of the appetite- and glucose-regulating hormone GLP-1 from intestinal L-cells is reduced. Some studies indicate that acute exercise may increase GLP-1 secretion. However, it is unknown how habitual PA affects GLP-1 secretion. Thus, we examined the association of PA (min/day) at moderate-to-vigorous intensity (MPVA) measured by individually calibrated heart rate and movement sensing for 7 consecutive days with the secretory responses of GLP-1 during an oral glucose test in overweight individuals.

1,326 individuals (mean (SD) age 66.0 (7.1) years, BMI 27.1 (4.5) from the ADDITION-PRO cohort were included. Associations between MVPA and GLP-1 levels in plasma were examined by linear regression analysis (correcting for the effects of age, BMI and insulin sensitivity). MVPA was defined as activity intensity above 3 METs.

In 703 men, fasting levels of GLP-1 were reduced by 19.5% (CI: -33.0; -3.3, P=0.02), and the incremental glucose-stimulated GLP-1 response was increased by 20.0% (2.6;40.3, P=0.02) for every one hour increase in MVPA per day. No associations were found in women.

In conclusion, increases in MVPA per day is associated with decreased fasting and increased glucose-induced GLP-1 responses in overweight men, suggesting increased L-cell sensitivity with physical activity in men.

1Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark.
2Danish Diabetes Academy, Odense University Hospital, Odense, Denmark.
3Department of Clinical Epidemiology, Steno Diabetes Center Copenhagen, Denmark.
4NNF Center for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark.
### Modelling obesity trajectories prior to diabetes - several ways of getting diabetes

Obesity is a well-known risk factor for the development of type 2 diabetes. However, at time of diabetes diagnosis, patients vary greatly with respect to their degree of obesity. This raises the question “Is type 2 diabetes typically characterized by a period of obesity prior to diagnosis?”

Based on an observational cohort of nearly 7,000 men and women, initially free of diabetes, we followed the BMI levels over a median of 14 years in the period 1991-2009. During follow-up 645 developed diabetes. We studied the heterogeneity in BMI patterns of the incident diabetes cases using a data driven method called “latent class trajectory analysis” – a flexible statistical approach for identifying and classifying heterogeneity.

Three distinct patterns of pre-disease BMI were found. A small group of “progressive weight gainers” exhibiting a pattern of consistent weight gain before diagnosis, and another relatively small group of “persistently obese” who were severely obese throughout 15-20 years before diabetes diagnosis. However, the majority of participants belonged to the “stable overweight” group with a trajectory of relatively constant BMI level within the overweight category in the period before diabetes was diagnosed. The results suggest that while obesity is an important risk factor for type 2 diabetes it may not be the main driver of the disease.

### Genetics of obesity and diabetes in Greenland - lessons from indigenous populations

Indigenous people worldwide are in the middle of a social, demographic and cultural transition, which through changes in lifestyle and living conditions results in an epidemiological transition. Inuit are a historically isolated indigenous population, for which both information about the genetic population structure, social transition and the disease pattern is exceptionally good and it is therefore ideal to study the consequences of the social transition on the changing disease pattern in this population. While studies of Greenland Inuit before the 1980s found a low prevalence of type 2 diabetes (T2D) compared to Western populations, two recent population studies among more than 4000 Greenland Inuit found a notably high prevalence of T2D (9%) and pre-diabetes (19%) in the adult population.
We previously identified a loss-of-function variant in TBC1D4 segregating at high frequency in the Greenlandic population displaying a high impact on risk of type 2 diabetes, and recently we discovered a loss-of-function variant in adenylate cyclase 3 (ADCY3) that strongly associates with obesity and type 2 diabetes. The observed effect sizes are several times larger than any previous findings in large-scale genome-wide association studies, confirming the advantage of studying the Greenlandic population due to its extreme demographic history, which allows for the existence of common variations that are rare or absent elsewhere.

Dylan Rausch, PhD
Student
Novo Nordisk Foundation Center for Basic Metabolic Research, UCPH

A single-cell transcriptomics roadmap to investigate diabetes remission induced by the central action of fibroblast growth factor 1 (FGF1)*

Marie A Bentsen¹², Dylan Rausch², Jarrad Scarlett¹³, Kimberly Alonge¹, Pascal N Timshel², Zaman Mirzadeh⁴, Anna Secher⁵, Rasmus Jorgensen⁵, Tune H Pers², Michael W Schwartz¹

Recently, lasting remission of hyperglycemia was achieved in rodent models of type 2 diabetes (T2D) by a single intracerebroventricular (icv) injection of FGF1. While the mechanism underlying this effect is unknown, the lack of association with changes of body fat mass or risk of hypoglycaemia raises the possibility that icv FGF1 normalizes the defended level of glycemia, rather than simply lowering blood glucose levels. Recent work from our lab has identified glucoregulatory neurocircuits in the mediobasal hypothalamus (MBH) as targets for this FGF1 effect. To investigate the mechanism underlying FGF1 action in this brain area, we used large-scale single cell RNA-sequencing to identify and characterize FGF1-responsive cells in mouse MBH. Based on >70,000 single cell MBH transcriptomes from diabetic ob/ob mice harvested 5d after a single icv injection of either FGF1 or vehicle, we identified >20 cell clusters and >900 cell type-specific differentially expressed genes (p<0.01). Among these potential targets of the MBH response to FGF1 in diabetic mice, we found that FGF1 treatment robustly increased the proportion of newly formed oligodendrocytes, a response that can be predicted to yield new mature oligodendrocytes and associated myelination of axons. These preliminary results demonstrate that transcriptional identification and characterisation of icv FGF1-responsive cell clusters may both advance our understanding of brain control of glucose homeostasis and identify novel targets for diabetes prevention and treatment.

This work was supported by funding from the National Institutes of Health (DK101997, DK083042), Novo Nordisk A/S, The Lundbeck Foundation (R190-2014-3904) and Novo Nordisk Foundation (NNF17OC0024328)

¹UW Medicine Diabetes Institute, University of Washington, WA, USA.
²Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, DK.
³Department of Pediatric Gastroenterology and Hepatology, Seattle Children’s Hospital, Seattle, WA, USA.
⁴Barrow Neurological Institute, Phoenix, AZ, USA. ⁵Global Research, Novo Nordisk A/S, Måløv, DK.
Plasma and urinary neutrophil gelatinase-associated lipocalin (NGAL) in obese Göttingen Minipigs with or without streptozotocin induced diabetes mellitus*

Rikke Lindgaard Thomsen, PhD Student
Dept. of Veterinary and Animal Sciences, UCPH

Neutrophil gelatinase-associated lipocalin (NGAL) is considered a promising biomarker of diabetic nephropathy. The aim of this study was to evaluate plasma NGAL (pNGAL), urinary NGAL (uNGAL) and uNGAL/urinary creatinine ratio in obese Göttingen Minipigs (GM) with or without streptozotocin-induced diabetes.

29 castrated male GM were weight stratified into 3 groups according to feeding and diabetes induction: SD (standard chow, n=7), FFC (high fat/fructose/cholesterol diet, n=14) and FFC-DIA (diabetic animals on FFC-diet, n=8). Plasma and urine samples were obtained at mid-study and study end (6 and 12 months after study start). There were no statistically significant differences in pNGAL or uNGAL (both ng/ml) between groups at either mid study or study end. For uNGAL/urinary creatinine ratio (ng/mg) there was a statistically significant higher concentration in FFC (14.28(10.95-23.21)(median(Q1-Q3)); P=0.040) and FFC-DIA (59.39(43.01-142.25); P=0.002) compared to SD (9.00(4.60-12.43) at mid study, in addition FFC-DIA had a higher concentration than FFC (P=0.0003). There was a similar tendency towards a difference between groups (P=0.080) at study end. There were no significant correlations between pNGAL and uNGAL, or between pNGAL and urinary NGAL/urinary creatinine. Ongoing work will elaborate possible associations between NGAL, functional kidney parameters and histopathological kidney changes.

Follistatin overexpression improves insulin action in skeletal muscle*

Xiuqing Han, PhD Student
Dept. of Nutrition Exercise and Sports, UCPH

Increasing studies report Follistatin (FST) overexpression induces muscle growth through inhibiting several ligands of transforming growth factor β superfamily. Apart from the essential role of skeletal muscle in locomotion, skeletal muscle has a critical role in glycemic control as well. However, the effect of FST overexpression on muscle insulin action is unknown. Using muscle-specific recombinant adeno-associated virus-mediated delivery of DNA, the present study investigated the effect of FST overexpression on insulin-stimulated glucose uptake and intracellular signaling in skeletal muscle of mice. As expected, FST overexpression increased muscle mass of TA and EDL. This was accompanied by a ~ 50% increase in insulin-stimulated skeletal muscle glucose uptake and up-regulated Akt/TBC1D4 signaling. Importantly, FST overexpression restored high-fat diet (HFD) induced disturbed insulin action in skeletal muscle. In conclusion, FST overexpression increased insulin-stimulated muscle glucose uptake.
and completely restored HFD-induced muscle insulin resistance. These findings indicate the pivotal role of FST in insulin resistance and have important implications for understanding the potential effect of FST-based therapies.

1Section of Molecular Physiology, Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark
2Faculty of Motor Science, Institute of Neuroscience, Université catholique de Louvain, Louvain-la-Neuve, Belgium
3Muscle Research and Therapeutics Laboratory, Baker IDI Heart and Diabetes Institute, Victoria, Australia.