Lund University Diabetes Centre (LUDC) was created in 2006 and is funded by a Linneus grant from the Swedish Research Council for a period of ten years. LUDC is today the center for more than 250 persons actively involved in all aspects of diabetes research; the centre is located at CRC in Malmö and BMC in Lund. An LUDC Executive Committee, consisting of coordinator Leif Groop, vice-coordinator Erik Renström and three elected PI:s, takes care of every day questions and supports the LUDC Board.

Diabetes research at LUDC can be subdivided into three parts, discovery, validation and translation. The aim of the discovery is to identify genetic and non-genetic factors responsible for development of diabetes, and in the validation phase to describe how they interact with the environment and cause impairment of insulin secretion and action characteristic of the disease. Ultimately, this knowledge will be translated into the clinic as improved personalized medicine and development of novel therapies.

In the beginning, ten different research areas/groups formed LUDC. Today, the different research areas have merged to 12 interdisciplinary action groups focusing on key problems in the development of diabetes and its treatment. This allows LUDC to maximize the utilization of its broad expertise to address questions of central importance.

The EXODIAB (Excellence of Diabetes Research in Sweden) consortium was created in 2009 as a Strategic Research Area at Lund (70%) and Uppsala Universities funded for at least 5 years by a strategic Research Grant from the Swedish Government. LUDC forms the bulk of the Lund University part of EXODIAB with the addition of the Antidiabetic Food Centre, which has the aim to explore novel food products in the prevention and treatment of diabetes.

A central mission of EXODIAB is to create strong infrastructures which can serve all researchers and shorten the start up time for young researchers - “there is no need for everyone to re-invent the wheels”. A prerequisite for this is access to some of the best and largest biobanks in diabetes research in the world. The creation of several gene atlases for diabetes and the human tissue laboratory (HTL) has been of strategic importance. A big hurdle in diabetes research has always been the difficulty to get access to the key organ in the pathogenesis of the disease, the pancreatic islets. The HTL has to a large extent solved this problem and provides from the Nordic Transplantation Program human pancreatic islets to researchers at LU and UU. The impact of HTL on diabetes research cannot be overestimated.

The central mission of both LUDC and EXODIAB is to prevent and cure diabetes.

“DIABETES CARE AND CURE – LET THE DREAM COME TRUE”
Research area: Genomics

PI Leif Groop, Unit on Diabetes and Endocrinology
Leif.Groop@med.lu.se

Co-PI Marju Orho-Melander, Unit on Diabetes and Cardiovascular Disease – Genetic Epidemiology
Marju.Orho-Melander@med.lu.se

Co-PI Valeriya Lyssenko, Unit on Diabetes and endocrinology
Valeri.Lyssenko@med.lu.se

Vision: To identify the genetic causes of different subgroups of diabetes and explore how these genetic variants interact with environmental factors influencing the pathogenic events leading to diabetes and related disorders like obesity and the metabolic syndrome.

Type 2 diabetes is the fastest growing disease affecting 250 million people worldwide and the number is predicted to double within the next 15 years. T2D is assumed to develop from the interaction between genetic predisposition and an affluent environment.

Diabetes is clearly a much more heterogeneous disease than the simple subdivision into type 1 and type 2 diabetes assumes. Dissection of the genetic heterogeneity of diabetes is a prerequisite for the development of individualized treatment as well as to identify new targets for more efficient therapy. In addition, identification of disease susceptibility genes kicks off possibilities to study gene-environment interactions.

To accomplish this task different strategies are being adopted, including genome wide association studies (GWAS), next-generation sequencing, expression profiling of target tissues (human islets, muscle, fat and liver), as well as studies of epigenetic modifications (DNA and histone methylation, acetylation etc).

A prerequisite for these studies is access to some of the largest and best characterized populations in the field, including the Botnia Study, the Malmö Diet and Cancer Study etc. These studies allow exploration of gene-environment (diet and exercise) interactions as well as prediction of disease development and progression.
Gene variants associated with T2D or glycemic traits.

References:


Research area: Mitochondria group
PI Hindrik Mulder, Unit of Molecular Metabolism
Hindrik.Mulder@med.lu.se
Co-PI Holger Luthman, Unit of Medical Genetics
Holger.Luthman@med.lu.se
Co-PI Charlotte Ling, Unit of Diabetes and Endocrinology
Charlotte.Ling@med.lu.se

Vision:
Our vision is founded on the notion that mitochondrial metabolism in the pancreatic β-cell is responsible for proper insulin secretion. The metabolism of glucose and other fuels translates the rise in extracellular glucose, which is the main determinant of insulin secretion, to intracellular signals that trigger and amplify insulin secretion. Moreover, mitochondrial metabolism in target tissues for insulin, i.e. skeletal muscle, adipose tissue and the liver, may also play an important role in glucose homeostasis. The pathophysiological significance of this notion is underscored by the fact that inherited, albeit rare, abnormalities of mitochondrial DNA lead to a Type 2 Diabetes-like condition. We believe that both common and rare abnormalities of genes that are involved in control of mitochondria play an important role in the development of Type 2 Diabetes. Our assumption is that these genes can be identified by genetic approaches in humans and in animal models of inherited diabetes. The pathogenetic processes can be unraveled by genetic studies and further characterized by functional studies. Learning more about the pathogenesis of Type 2 Diabetes will lead to development of novel treatments for the disease.

References:


Model for a possible role of TFB1M in the development of Type 2 Diabetes (T2D). Mining data from the Diabetes Genetics Initiative Genome-wide Association Study revealed that Transcription factor B1 mitochondrial (TFB1M), a protein which controls translation in mitochondria, is associated with impaired mitochondrial metabolism, reduced insulin secretion and increased future risk of Type 2 Diabetes. The data suggest a model where the risk SNP confers lower TFB1M protein expression. Consequently, mitochondrially encoded proteins will be reduced, oxidative phosphorylation (OXPHOS) restrained, and stimulus-secretion coupling in the β-cell will be abrogated. All this will result in impaired insulin secretion.
Research area: Adipotoxicity – Glucolipotoxicity

PI  Cecilia Holm, Unit of Molecular Endocrinology  
Cecilia.Holm@med.lu.se

Co-PI  Jens Lagerstedt, Unit of Cellular Biomechanics  
Jens.Lagerstedt@med.lu.se

Co-PI  Karin Berger, Unit of Molecular Endocrinology  
Karin.Berger@med.lu.se

Vision: The strong association between obesity and T2DM – “diabesity” - has emphasized the role of adipose tissue and lipids in the development of T2DM. Circulating lipids, in the form of non-esterified fatty acids (NEFA) and triglycerides, are elevated and causally linked to the cardiovascular complications of the disease. Moreover, ectopic lipid deposition (i.e. outside adipose tissue) is believed to be a precipitating event in the development of both islet dysfunction and insulin resistance, the two hallmarks of T2DM. This has been termed ”lipotoxicity” or “glucolipotoxicity”. Besides lipotoxicity, the inflammatory response of hypertrophic adipose tissue expansion contributes to development of insulin resistance through release of cytokines capable of impairing insulin signaling (“adipotoxicity”).

In addition to elevation of circulating lipids T2DM is also associated with altered functionality of plasma high density lipoprotein (HDL). HDL and its major protein component, apoA-I, are central to the reverse cholesterol pathway (removal of excessive and harmful cholesterol), and as such directly important for cardiovascular health. Interestingly, recent studies show that HDL/apoA-I particles can influence insulin secretion of pancreatic beta-cells, and also stimulate glucose uptake in skeletal muscle of T2DM patients. Clearly, these findings add to the complexity of the disease but, importantly, also provide new potential targets in the search to reduce the incidence and complications of T2DM.

The overall objective of our research is to elucidate mechanisms underlying obesity-associated insulin resistance and islet dysfunction and to identify novel targets for the prevention and reversal of these hallmarks of T2DM. More specifically we aim to identify novel factors involved in adipocyte differentiation and determination, describe how lipids are stored and handled in pancreatic beta-cells under normal as well as diabetic conditions, elucidate the role of adiponutrin, a protein implicated in ectopic lipid deposition in liver and unravel the molecular and cellular basis for the HDL/apoA-I triggered enhancement of skeletal muscle glucose metabolism, and explore how such nanostructures can prevent and reverse the state of insulin resistance and thus reduce the incidence of T2DM.
References:

Figure. Schematic representation of mechanisms underlying obesity-associated insulin resistance and islet dysfunction, and the beneficial function of HDL/apoA-I in preventing/reversing their progression (for more details, see text)
**Research area:** GLP-1 Based Therapy

**PI**
Bo Ahren, Unit on Medicine  
[Bo.Ahren@med.lu.se](mailto:Bo.Ahren@med.lu.se)

**Co-PI**
Jenny Vikman, Unit on Medicine  
[Jenny.Vikman@med.lu.se](mailto:Jenny.Vikman@med.lu.se)

**Co-PI**
Nils Wierup, Unit on Neuroendocrine Cell Biology  
[Nils.Wierup@med.lu.se](mailto:Nils.Wierup@med.lu.se)

**Vision:**
Glucagon-like peptide-1 has been developed as a novel therapy of type 2 diabetes, mainly because its dual hormonal action on islet function. Hence, GLP-1 elicits glucose-dependent stimulation of insulin secretion and inhibition of glucagon secretion. A challenge in the development of GLP-1 based therapy is that the active form of GLP-1 is rapidly inactivated through truncation of the peptide by removal of the N-terminal dipeptide end through the enzyme dipeptidyl peptidase-4 (DPP-4). To overcome this problem, two strategies have been developed: the use of GLP-1 receptor agonists, which are largely resistant to the action of DPP-4, and the inhibition of DPP-4, which prevents the inactivation of GLP-1 and thereby enhances and prolongs the action of the endogenous incretin hormone. Our studies aim at elucidating the islet and extra-pancreatic effects of this treatment in animal models of diabetes as well as in subjects with type 2 diabetes, and to identify and examine the positioning of this novel therapy within the management of the disease. Our studies also aim at developing further the GLP-1 based therapy by exploring the activation of the G-protein coupled receptor 119 (GPR119), which is expressed in both insulin- and GLP-1-producing cells, and the activation of which stimulates release of both hormones.

In addition, we search for novel islet and gut messengers e.g. regulatory peptides that modulate islet hormone release. Information about the roles of regulatory peptides in beta-cell function and in type 2 diabetes is still meager and our studies will aid in the search for new strategies for prevention and treatment of type 2 diabetes. A main focus is the regulatory peptide cocaine and amphetamine-regulated transcript (CART). A body of evidence shows that CART has positive effects on glucose homeostasis, i.e. CART increase GLP-1 mediated insulin secretion, inhibits glucagon secretion, CART inhibits glucose-induced cell death, CART is overexpressed in islets of T2D subjects, and CART null mutant mice exhibit severely impaired islet function. These data suggest that CART
is a highly interesting drug candidate, and the so far unknown CART-receptor a potential drug target, for treatment of T2D.

**References:**


Fig.: Result for a study exploring whether DPP-4 inhibition compromises the glucagon response to hypoglycemia, in analogy with its inhibition of glucagon secretion after meal ingestion. Subjects with type 2 diabetes were treated with vildagliptin (a DPP-4 inhibitor) or placebo for four weeks. Thereafter a step-wise hypoglycemic clamp was undertaken (glucose clamped at 7.5, 5.0 and 2.5 mmol/l respectively) after a test meal ingestion, and the glucagon responses to meal versus hypoglycemia were determined. Results show the glucose-dependency of the action on glucagon by DPP-4 inhibition: the response is inhibited at hyperglycemia during meal ingestion but augmented during hypoglycemia. This provides rationale for the conclusion that hypoglycemia is a low risk during
treatment with DPP-4 inhibition. (from Ahrén et al., J Clin Endocrinol Metab 94:1236, 2009).

Eva Degerman                               Lena Stenson                                Olga Göransson

Research area: Cellular signaling in diabetes

PI     Eva Degerman, Unit of Insulin Signal Transduction
       Eva.Degerman@med.lu.se
Co-PI Lena Stenson, Unit of Insulin Signal Transduction
       Lena.Stenson@med.lu.se
Co-PI Olga Göransson, Unit of Protein Phosphorylation
       Olga.Goransson@med.lu.se

Vision: Patients with obesity and type 2 diabetes have a reduced sensitivity to insulin and other hormones in their target tissues, such as skeletal muscle, liver and adipose tissue. This is associated with increased circulating levels of glucose and fatty acids, as well as altered levels of adipocyte-derived hormones and cytokines. The insulin resistance and resulting dysregulated metabolic situation is a cornerstone in the development of diabetes. The exact cellular and molecular mechanisms causing systemic insulin resistance is not known, but its strong link to obesity suggests that primary or secondary defects in adipose tissue is an underlying problem. By dissecting signalling pathways regulating glucose- and lipid metabolism, particularly in adipose tissue, our aim is to identify new molecular targets of relevance for diabetes pathophysiology and drug development. Our research groups focus on the interplay between insulin, cyclic AMP, AMP activated protein kinase (AMPK), a key cellular energy sensor, and AMPK-related kinases. By elucidating such signalling networks we will learn more about the regulation of cellular energy balance and insulin sensitivity. We are also engaged in functional investigation of new risk genes for diabetes, for example TCF7L2 and the GIP receptor, that have emerged from genome wide association studies by other members of the LUDC. At the methodological level we aim at improving techniques related to reversible protein phosphorylation, a key process in signal transduction, as well as imaging of cellular signalling events.
Our vision is to identify new mechanisms and molecular targets of relevance for the treatment of human diabetes and to identify defects in signalling patterns that can predict development of the disease.

References
Interplay between cAMP, insulin and AMPK signalling networks in the regulation of adipocyte functions. The figure illustrates the complex pattern of interactions between interconnected signalling networks in adipocytes. For example, insulin and catecholamines induce the formation of unique multiprotein complexes involving protein and lipid kinases, protein phosphatases, scaffolding proteins and effector molecules at different locations in the cell. These signalling events have important roles for the regulation of lipid and glucose metabolism.
Research area: Islet Patophysiology

PI Erik Renström, Unit of Islet patophysiology
Erik.Renstrom@med.lu.se

Co-PI Albert Salehi, Unit of Islet cell physiology
S_Albert.Salehi@med.lu.se

Co-PI Anders Rosengren, Unit of Islet patophysiology
Anders.Rosengren@med.lu.se

Vision:
The proper function and maintained mass of the pancreatic islets is vital for preventing development of type 2-diabetes. This capacity has in recent years been associated to variations in a large number of genes. The big challenge is to understand exactly how these genetic variations affect cellular functions in the pancreatic islets, in order to identify targets for causative treatment.

Functional gene networks Our aim is to go beyond the single-gene/one-function paradigm and to develop models that take into account the contribution of several genes and their encoded proteins for the altered cellular functions that predispose for type 2-diabetes, and how aberrations in these networks can be corrected by novel treatments. To do this we analyse gene regulatory co-expression networks in pancreatic islets, followed by functional validation experiments, down to detailed molecular level when appropriate.

Protein interactions An important aspect of protein function is their interactions, addressed by discovery techniques (2-hybrid systems) and focused low-throughput methods (e.g. immunoprecipitation, affinity purification), including those that make it possible to characterize interactions in real-time (fluctuation correlation spectroscopy).

Therapeutic targets In addition to the novel targets we expect to identify, G-protein coupled receptors are a class of proteins that already attract massive interest as obvious targets for treatment of type 2-diabetes. Orphan GPCRs will be systematically investigated for their capacity to correct hormone secretion in type 2-diabetes.

References

secretion in vitro and in vivo in mice lacking the chloride transport protein ClC-3 (2009)

*Cell Metabolism* 10(4):309-315

*Topological overlap presentation of clusters of co-expressed genes in donor human islets.*

Analysis was confined to the 5000 most highly expressed genes, which are presented along the x- and y axes. Gene pairs exhibiting the highest connectivity (\(|\text{correlation}|^{10}\)) are denoted in red, whereas pairs without connectivity are in white.
**Research area:** Unit on Vascular Diabetic Complications

**PI** Carl-David Agardh, Unit on Vascular Diabetic Complications
Carl-David.Agardh@med.lu.se

**Co-PI** Jan Nilsson, Experimental Cardiovascular Research Unit
Jan.Nilsson@med.lu.se

**Co-PI** Maria Gomez, Unit on Vascular ET-coupling
Maria.Gomez@med.lu.se

**Vision:** Diabetes is associated with devastating chronic complications including coronary heart disease and stroke (macrovascular complications) as well as microvascular disorders leading to damage of the small vessels of the kidney (nephropathy), eye (retinopathy) and peripheral nerves (neuropathy). These complications impose an immense burden on the quality of life of the patients and account for more than 10% of health care costs in Europe. Novel means to prevent and/or treat these complications are needed. This unit at LUDC focuses primarily on macrovascular complications and retinopathy, both in type 1 and type 2 diabetes. Although hyperglycaemia is one of the most important risk factors for the development of complications, other factors such as oxidative stress, dyslipidemia, inflammation and vasoactive hormones clearly have an impact on the disease. Our goal is to understand the chain of events leading to vascular disease in diabetes, and to develop tools, which can make the development of novel drugs/therapies for prevention and/or treatment more feasible. Important steps are the identification of novel biomarkers for prediction and monitoring of the disease, the development of new treatment approaches and imaging techniques for monitoring the atherosclerotic process and retinopathy and the development of animal models that better reproduce human disease.

**Some examples of specific on-going projects:**

- Recent studies have identified that autoimmune responses against modified self-antigens, such as oxidized LDL, play a key role in atherogenesis. We test the possibility that autoimmune responses against oxidized-LDL, AGE- and aldehyde-modified proteins in the vascular wall may contribute to diabetic complications. If so, we will develop vaccines to modulate these responses.

- We’ve recently shown that hyperglycemia activates the transcription factor NFAT (Nuclear Factor of Activated T-cells) in macro- and microvessels *in vivo*. Activation leads to vasoconstriction, vascular cell proliferation and inflammation. Treatment of mice with a newly developed blocker of NFAT reduces diabetes-driven vascular inflammation in mice. We hypothesize that NFAT acts as a glucose-sensor in the vascular wall, and is a novel target for treatment of macrovascular complications.

- Retinal pericyte loss is one of the early hallmarks of diabetic retinopathy. The underlying mechanisms are not known, but autoimmunity may play a role, as suggested by the presence of circulating anti-pericyte autoantibodies (APAA) in the blood of a substantial proportion of diabetic patients. We propose that APAA might serve as a predictor for impending vascular disease.

- Laser coagulation is the gold standard treatment of diabetic retinopathy. Laser exposure results in hypertrophy and hyperplasia of the retinal pigment epithelium (RPE), but the role of
the RPE is still unclear. We hypothesise that the RPE participates in the beneficial outcome of laser treatment in humans and that identification of released factors can result in new treatment approaches.

Figure legend: a) Confocal image showing VCAM-1 expression (red) and cell nuclei (green) in mouse cerebral microvessels in response to hyperlipidemia, b) Atherosclerotic plaque in the bifurcation of a mouse cerebral artery (white opaque area); c) Serum anti-pericyte autoantibody binding to bovine retinal pericytes (red).

References:


Fluorescence micrograph of immunofluorescent detection of serum antipericyte autoantibody binding site to bovine retinal pericytes in vitro.
Research area: Pancreas development and human embryonic stem cell differentiation

PI Henrik Semb, Stem Cell Center
Henrik.Semb@med.lu.se

Co-PI Isabella Artner, Stem Cell Center
Isabella.Artner@med.lu.se

Vision: Type I diabetes results from specific autoimmune mediated destruction of beta cells. Considerable efforts are now focused on trying to develop functional insulin-producing cells from adult and embryonic stem cells as a consequence of encouraging results obtained in reversing type I diabetes upon human islet transplantation. Thus, a hope is that human embryonic stem cells (hESC) can be used in this endeavor due to their remarkable differentiation potential. In fact, recent studies report that insulin+ cells can be produced from embryonic stem cells. However, these cells differed significantly from mature pancreatic beta cells in lacking proper glucose responsiveness. Ultimate success in developing therapeutically useful cells will depend on a fundamental understanding of the regulatory factors that are required for controlling the specialized genetic programs associated with the formation of functional beta cells. To work towards successful islet transplantation we are studying the mechanisms governing beta cell differentiation in the embryonic pancreas (specifically the role of transcription factors). Knowledge obtained for these experiments is directly applied in our experiments to differentiate hESCs into transplantable insulin producing cells. Ultimately our results will be applied to develop novel protocols to generate unlimited amounts of beta cells (from hESCs). The goal of our program is to accelerate the production of a cell-based therapy for diabetic patients.

References:


Figure legend:
Expression of MafA, Pdx1, and Ngn3 induces insulin production in the chick gut endoderm. This over-expression experiment illustrates the significance of these transcription factors to insulin production and beta cell differentiation.
Research area: Autoimmune diabetes pathogenesis, prediction and immune interventions

PI Åke Lernmark, Unit on Diabetes and Celiak
Ake.Lernmark@med.lu.se

Co-PI Corrado Cilio, Unit on Diabetes and Celiak
Corrado.Cilio@med.lu.se

Co-PI Annelie Carlsson, Unit on Paediatrics, Lund
Annelie.Carlsson@med.lu.se

Vision: The research focus of the group is to uncover the etiology and pathogenesis of autoimmune diabetes (T1D). The long-term goal is to predict and to develop novel approaches that could prevent or revert the disease process. The current research on the dissection of T1D genes in humans and in several animal models is directed to the identification of genetic factors within and outside the Major Histocompatibility Complex (MHC) that are critical to disease risk. The focus is also to identify markers that predict either islet autoimmunity, T1D, or both as well as to monitor immunotherapeutic strategies to prevent and cure T1D. With the help of a large longitudinal international NIH-funded study, the TEDDY study, we will be able in the near future to dissect the role of environmental factors impinging on the risk for T1D. Extensive analysis of lymphocytes and their antigen-specific cellular responses is undergoing to identify immunological inflammatory changes (immunological footprint) that could mark the reactivation and progression of organ-specific autoimmunity and that could also contribute to the pathogenesis of T2D diabetes. The detailed analysis of circulating lymphocytes and their antigen-specific cellular responses will be also instrumental to monitor immunotherapy clinical trials. The study of components of the innate immunity, which represent the interface between infections and adaptive immune responses, will complement the extensive studies aimed at defining the environmental factors leading to diabetes. Finally, we will study the interplay between immune cells and the pancreatic islet by studying the immunological responses in pancreatic lymph nodes and in T cell infiltrating the islets in organ donors with T1D, T2D or only autoantibody positive through a well established collaboration with Olle Korsgren in Uppsala (Nordic Islet Transplantation Network). The strong translational focus of our research platform is reflected by the development of autoantibody and T cell assays to predict and improve diabetes classification as well as ongoing immunomodulatory clinical trials (GAD65 vaccination) to halt beta cell autoimmunity.

In summary, our research contributes to 1. Genomics in diabetes (HLA and non-HLA genes in type 1 diabetes and dissection of diabetes genes in the NOD mouse and the BB rat); 2. Inflammation (islet inflammation, systemic immunological responses in autoimmune diabetes); 4. Islet dysfunction (NOD mouse, BB rat and human islet studies of stress related factors) and 7. Novel therapies (alum-formulated GAD65 immunomodulation Phase II and III clinical trials, immunomodulation using modified lactobacilli).
References

Research area: Cellular regulation of islet hormone secretion

PI: Lena Eliasson, Unit on Islet cell exocytosis
Lena.Eliasson@med.lu.se

Co-PI Patrik Rorsman, Oxfod Centre for Diabetes, endocrinology & metabolism
Patrik.Rorsman@med.lu.se

Co-PI Jonathan Esguerra, Unit on Islet cell exocytosis
Jonathan.Esguerra@med.lu.se

Vision: The main focus of our research is to investigate the cellular mechanism by which insulin and glucagon is secreted with a specific interest in how microRNAs (miRNAs) are involved in this regulation. MicroRNAs are a class of recently discovered non-coding regulatory RNA molecules that affect gene expression by binding to 3’-untranslated regions of messenger RNAs (mRNAs), preventing the translation of the mRNAs. Our vision is that we will: 1) Reach a better knowledge regarding the cellular regulation of the stimulus-secretion coupling in the pancreatic hormone secreting cells and how disturbances in these processes are involved in diabetes development. 2) Achieve a better understanding of miRNAs and their role in insulin-and glucagon-secretion and in diabetes development. 3) Identify miRNAs that will work as biomarkers for diabetes and its complications.

References:


The figure describes the cellular regulation of insulin secretion. Insulin is released upon high glucose. The stimulus-secretion coupling (black arrows) describes the involvement of the mitochondria generating high ATP-levels and the closure of the $K_{ATP}$ channels. The sulfonylurea receptor (SUR) is part of the KATP-channels and the binding site of sulfonylurea used in treatment of diabetes. The binding of sulfonylurea to the channel results in closure of the channel. The closure of the $K_{ATP}$ channels leads to depolarization of the cell membrane and opening of voltage-dependent $Ca^{2+}$-channels (VDCC). The increase in intracellular calcium ($Ca$) initiates exocytosis of the insulin containing secretory granules. Insulin secretion can be amplified by incretins such as GLP-1 and GIP (dotted arrows). GLP-1 agonists are currently used in treatment of type 2 diabetes, why it is important to further examine the role of incretins in both insulin- and glucagon secretion. Currently we are investigating how miRNAs can influence the stimulus-secretion coupling in the insulin secreting beta cells on several levels. Mature miRNAs are generated from pre-miRNAs (grey arrows) and inhibit the translation of several target proteins that might influence the insulin secretion process at different levels.

Research area: Tailoring of foods for metabolic benefits/Antidiabetic Foods

**PI**  Inger Björck, AFC  
Inger.Bjorck@appliednutrition.lth.se

**Co-PI**  Maria Johansson, AFC  
Maria.Johansson@appliednutrition.lth.se

**Vision Antidiabetic Food Centre (AFC)**

The vision of AFC is to constitute an environment that stimulates establishment of innovative and preventive food concepts thus providing community benefits and sustainable growth by preventing obesity, type 2 diabetes and other manifestations of the insulin resistance syndrome (www.ffsc.lu.se/afc). Collaboration within EXODIAB makes possible exploitation of synergistic competences regarding research techniques. Additionally, EXODIAB collaboration provide substantial added value by allowing for studies of the therapeutic potential of prototype foods.

Research activities within AFC focuses on studies of various food factors and/or properties of importance for metabolic risk factors. One recent finding concern the link between colonic fermentation of indigestible carbohydrates, and systemic benefits probably mediated through stimulation of GLP-1.


Facilitated flow of Innovations within LUDC/EXODIAB

One of the major priorities within LUDC/EXODIAB is to accelerate the rate of innovations developed from inventions and discoveries in the area, to secure that the benefits reach the public and to reach the scientific goal of developing novel therapies for prevention and treatment of diabetes and its complications. Interaction between academia and the industry is a key component of this consortium.

In order to realize this goal, an Innovation Officer (IO) with an extensive experience from the Life Science industry has been hired: her task is to manage relationships with the industry and accelerate the rate of innovation coming from LUDC/EXODIAB.

The vision is to develop LUDC/EXODIAB to become a major partner to the industry in supporting the development of novel treatment approaches, thus strengthening the consortium, resulting in attracting new and ambitious PhD students and funding collaboration projects. The IO will also help the EXODIAB members with commercialization along the conventional, intellectual property based path.

How will we innovate?

3 ways have been identified for securing that research results lead to better patient treatment:

- shorter term collaborations, testing of “leads” within existing models
- longer -term, strategic collaborations , investigating biological systems
- Identifying areas for IP activities leading to start-ups

A centralized approach to customer contacts is preferred, the one point of contact being the IO. A Commercial Advisory Board (CAB) will be created to bring market needs and industry competence into the selection process. Project teams will be created for each collaboration.

The IO focuses on four programmes to secure increased innovation:

- Seminars to increase focus on innovation
- Running the CAB to identify potential and prioritize projects
- Building relationships with the industry and increasing market knowledge
- Linking to existing Innovation Systems at LU

LUDC/EXODIAB has the vision to collect the value of its commercial activities in a commercial entity (holding?) called DiaBridge that will market its services and projects to industrial partners.
Long-term vision for flow of innovations within LUDC/EXODIAB. At the interface between Academia and the business sector is a Commercial Advisory Board that oversees development of innovation projects funded by agencies such as VINNOVA, SSF, or in collaboration with industrial partners. When such projects have developed their commercial potential sufficiently for being launched on the commercial market they will be transferred to DiaBridge.