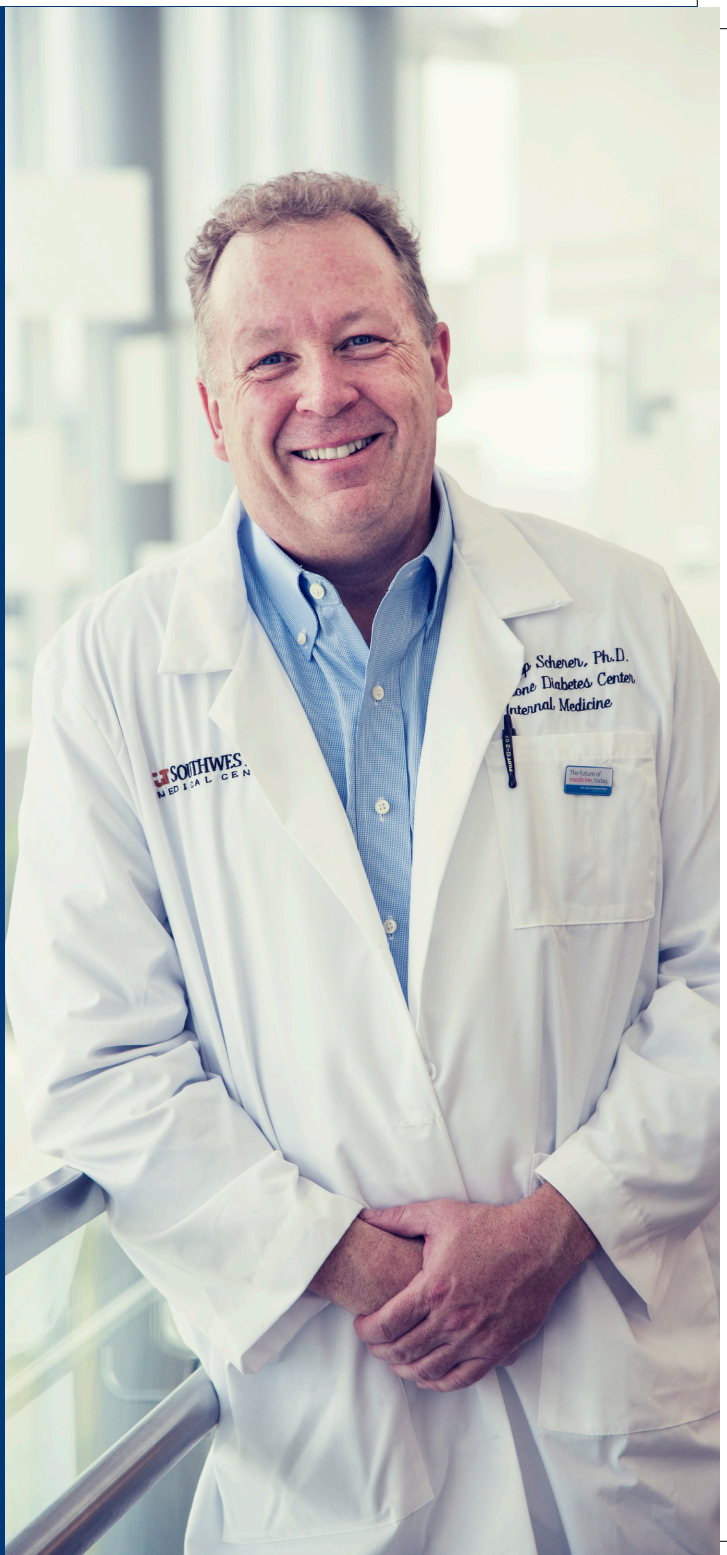
# EASD–
# NOVO NORDISK FOUNDATION
# DIABETES PRIZE FOR EXCELLENCE

# 2017




## PROFESSOR
## PHILIPP SCHERER

# EASD–
# NOVO NORDISK FOUNDATION
# DIABETES PRIZE FOR EXCELLENCE

# The Prize is awarded to an international researcher for outstanding scientific contributions that have increased our knowledge of diabetes.

The EASD–Novo Nordisk Foundation Diabetes Prize for Excellence is being awarded to recognize outstanding research or technology contributions to the understanding of diabetes, its disease mechanisms or its complications.

The Prize is awarded annually to an internationally recognized researcher whose research may focus on prevention, treatment and/or basic research in physiological biochemistry. The research may also be clinically oriented.

In addition, the Prize may be awarded for the "discovery of the decade" within diabetes research.

Established in 2015, the Prize is awarded in collaboration between the European Association for the Study of Diabetes (EASD) and the Novo Nordisk Foundation. It is accompanied by DKK 6 million – of which DKK 1 million is a personal award and the remaining DKK 5 million is for research purposes.

A special prize committee appointed by the EASD decides the winner of the Prize, and the Novo Nordisk Foundation donates the funds accompanying the Prize. Employees of universities, hospitals or other non-profit institutions are considered for the Prize.

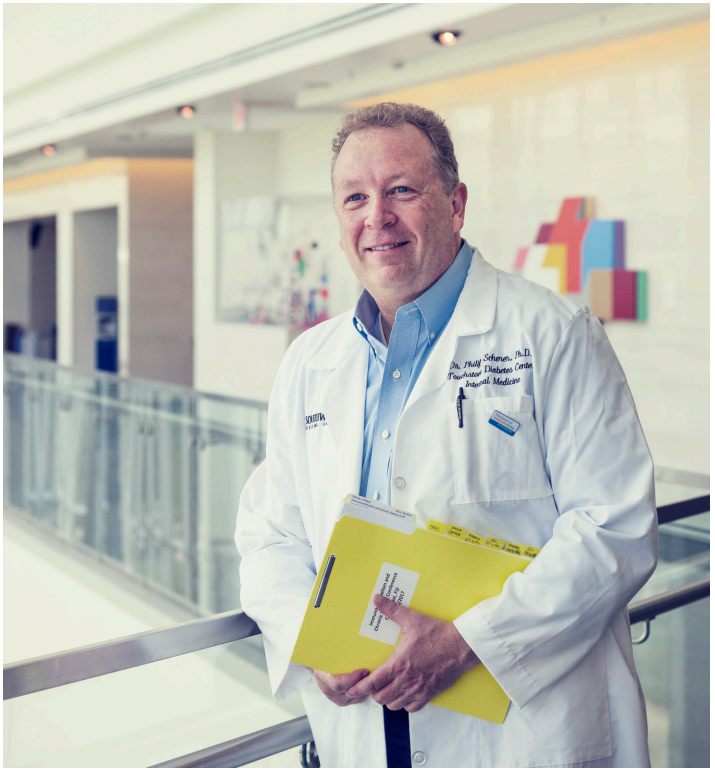
Candidates must be highly renowned and may be of any nationality. The Prize is conferred at the EASD Annual Meeting at which the Prize recipient is invited to give a lecture.

# NOMINATION OF DR. PHILIPP SCHERER

## The 2017 EASD–Novo Nordisk Foundation Diabetes Prize for Excellence is being awarded to Professor Philipp Scherer.

By Juleen Zierath, President, EASD,
and Bernard Thorens, Committee Chairperson

Dr. Scherer is Director of the Touchstone Center for Diabetes Research and Professor of Medicine at the University of Texas Southwestern Medical School in Dallas, United States. Born, raised and educated in Switzerland, he embodies the rich transatlantic scientific exchange in diabetes research.



During his career he has received numerous national and international awards and holds several visiting professorships. He is a sought after expert nationally and internationally, with many contributions to shaping the future of diabetes research in the United States as a member of a number of editorial boards, strategic advisory panels at NIDDK and as Chair of a number of Study Sections at NIH.

Dr. Scherer's work has always ranked amongst the most creative in the field. He discovered adiponectin, which, like the discovery of leptin, ushered in a new era in the study of adipokines and metabolic disease. His comprehensive analysis of adipose tissue physiology and highly innovative approach to science has made him a giant in the world of diabetes research.

Scherer's work has contributed to a completely new approach to the pathophysiology of the metabolic syndrome and type 2 diabetes, two of the most common chronic diseases.

These advances have generated more than 350 publications in journals such as *Nature Medicine*, nearly 40,000 citations (some of his papers have

been cited more than a 1000 times) and an h-index of almost 100. Furthermore, he has authored various reviews, commentaries, book chapters and he holds several patents.

In addition to his personal success, Philipp Scherer is a highly valued mentor. He has been very active with a teaching portfolio spanning the fields of Medical Biochemistry, Medical Physiology, a Cell Regulation Graduate Program, Ethics Sessions for Graduate Students, Human Biology and Disease and Experimental Approaches to Complex Diseases. He leads a large laboratory, fostering not only upcoming scientists, with whom he is also very successful in receiving fellowship awards, but also more seasoned researchers. Those who move on from his laboratory, do so to take up prestigious positions in the academic world.



The Committee of the EASD–Novo Nordisk Foundation Diabetes Prize for Excellence has unanimously decided to award the 2017 EASD–Novo Nordisk Foundation Diabetes Prize for Excellence to Professor Philipp Scherer, a highly distinguished and stimulating speaker who, we are confident, will deliver an outstanding lecture during the 53rd EASD Annual Meeting.

# CURRICULUM VITAE

**Philipp Scherer**
Born, Switzerland
Professor, Gifford O. Touchstone, Jr.
and Randolph G. Touchstone Distinguished Chair in
Diabetes Research, Dallas, Texas, United States

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| 2015 | Banting Medal for Scientific Achievement from the American Diabetes Association |
| 2013 | Naomi Berrie Award for Outstanding Achievement in Diabetes Research from Columbia University |
| 2013 | Britton Chance Memorial Award of the Agency for Science, Technology and Research (A*STAR), Singapore |
| 2012 | O'Donnell Award in Medicine from the Academy of Medicine, Engineering & Science of Texas |
| 2007 | Director of the Touchstone Diabetes Center at the University of Texas Southwestern Medical Center in Dallas |
| 2007 | Professor, Departments of Internal Medicine and Cell Biology, Faculty of UT Southwestern Medical Center |
| 2005 | Outstanding Scientific Achievement Award from the American Diabetes Association |
| 1997 | Professor for Cell Biology and Medicine, Albert Einstein College of Medicine |
| 1995 | Post-doctoral training the Whitehead Institute at MIT in Cambridge, New York |
| 1992 | PhD, the University of Basel, Switzerland |

Professor Scherer has more than 400 publications and more than 40,000 citations.

# The many shades of fat

**Fat is not what it used to be, but in fact it never was. Only a few years ago, fatty tissue was simply considered a storage site for fat. Philipp Scherer has provided some of the most important contributions to dispelling this myth. Today, researchers know that there are healthy and unhealthy types of fat cells but also that fatty tissue constantly influences the rest of the body as if it were an organ.**

If it were a person, it would weigh 400 kilograms. The mouse called the world's fattest weighed five times as much as a normal mouse. Despite this, the mouse was apparently fit and healthy and showed no signs of diabetes.

"The mouse did not produce any leptin, which suppresses appetite. The mouse also secreted three times as much of adiponectin, another important adipocyte-derived hormone that produces healthy fat tissue. This combination meant that the mouse ate without stopping. However, when we examined the mouse, it showed no signs of either diabetes or visceral fat surrounding its organs," explains Philipp Scherer from the University of Texas Southwestern Medical Center in Dallas, United States.

This obese mouse helped to overturn the research world's view of fat and questioned whether fat independently causes obese people to more often develop lifestyle-related diseases or whether other factors decide this.

"I would never recommend counting on becoming obese in a healthy way, but we have definite proof that people who are overweight can actually be pretty healthy, at least at the time we study them. And people who are thin can also have a very unhealthy metabolism, with many of the harmful health effects such as cardiovascular disease and type 2 diabetes that we otherwise associate with being overweight."

Today, leptin and adiponectin play a key role in research on obesity and type 2 diabetes. Researchers have well-founded expectations that learning how to regulate the secretion of these two proteins may contribute to helping the many people worldwide with lifestyle-related diseases to lead better and healthier lives.

## When fat communicates

The fact that two small proteins would play the major role in research on understanding the function and importance of fatty tissue on human health was not in the cards when Philipp Scherer began his research career 30 years ago. He began in the late 1980s in Basle, where France, Germany and Switzerland meet. Here one of the key researchers behind the discovery of mitochondrial DNA, Gottfried Schatz, was based.

"Although this was a different research field, Gottfried Schatz made me understand how incredibly important mitochondrial metabolism is for cells. In addition, proteins need to be targeted to their proper cellular location, and there are critical signals associated with proteins that will traffic them to mitochondria, where complex machinery interprets these targeting signals. Alternatively, they need to be secreted and targeted to the proper cells in distant tissues. These secreted proteins often decisively influence the communication between cells."

This fact was crucial when Philipp Scherer chose to move to the United States to continue his research career after he received his PhD degree in Basle. While he had been studying protein transport in the mitochondria of yeast cells in Switzerland, researchers in the laboratory of Harvey Lodish at MIT in Cambridge had been studying the insulin-mediated transport of glucose across the membranes of fat cells.

"But I soon realized that this research field was very crowded and that I needed to try and find my own niche. I therefore decided to focus on proteins and their effects on how fat cells can communicate with each other and with the rest of the body. So we started to focus on fat cells as secretory cells and examine what they secreted and how this interacted with the rest of the body."

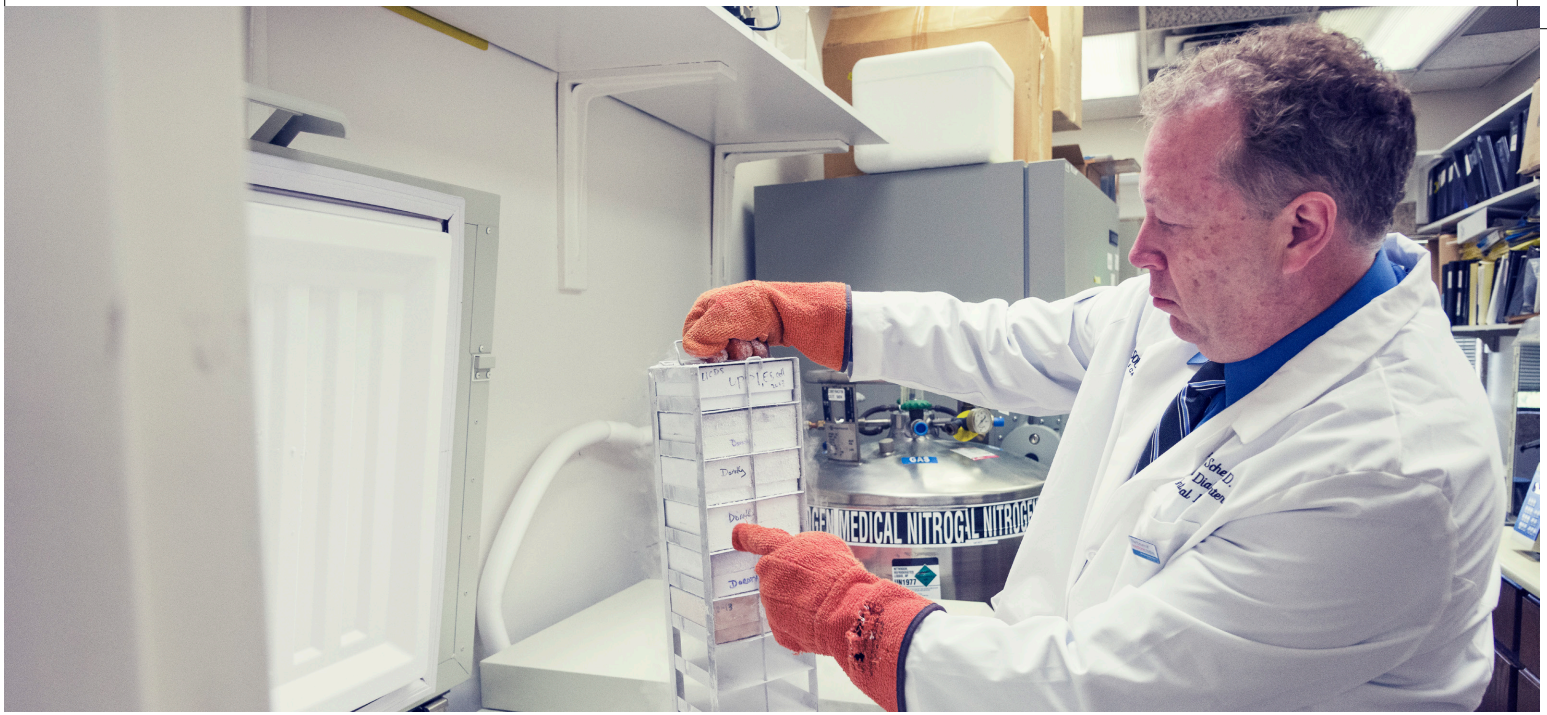
## Hibernating Siberian chipmunks

It soon became apparent that choosing this new angle on the function of fat cells was a quite fortuitous move. Scherer and his colleagues struck gold as early as 1995, and this turned out to be the pivotal moment for Scherer's future research group and for overall research on obesity and diabetes.

"We discovered a previously unknown protein, Acrp 30, solely produced and secreted by fatty tissue. Fat cells secrete abundant quantities of Acrp 30; this increased more than 100-fold during the development of the fat cells themselves and should have interesting regulatory patterns under various metabolic conditions."

Already the following year, Acrp30 was given its current name, adiponectin, by researchers in Japan. However, in 1995, Scherer and his colleagues knew nothing more about adiponectin's function.

"Among other things, its sequence and structure resembled a part of the human immune system, and a protein observed in hibernating Siberian chipmunks. The protein turned out to have effects



on many other tissues in the body. Since then, adiponectin has led us into many new fields. I am still amazed by adiponectin's wide-ranging influence on many metabolic processes."

## Contrary to all expectations

The discovery of adiponectin followed hard on the heels of the discovery of leptin, the other well-known hormone fatty tissue secretes. When leptin is released, it affects the brain, increasing the feeling of satiety and sending the metabolism into overdrive. A lack of leptin may therefore contribute to obesity. The effect of adiponectin, however, totally surprised Scherer and his colleagues.

"Because adiponectin is produced by fat cells and is strongly boosted in the development of the fat cells themselves, we had expected high levels among people who are overweight, but we saw the reverse. Obese people had lower concentrations, whereas people with anorexia, for example, had greatly elevated concentrations of adiponectin."

Now, more than two decades later, the researchers do not fully understand the effects and function of adiponectin, but recent research suggests that fat cells in bone marrow greatly increase their production of adiponectin in times of hunger. In any case, the discovery of leptin and adiponectin launched modern obesity research.

"The discovery of leptin and adiponectin radically changed how researchers perceive fat cells. The last 20 years have taught us that fat cells are not simply a storage location for fat, but rather are extremely active cells that secrete very many physiologically active substances that have powerful effects on other tissue. Today, we know that the communication between fatty tissue, the brain, kidney, pancreas, heart and liver is key to understanding obesity and other lifestyle-related diseases."

## The world's largest mouse

Recent research has shown once again that the amount of fatty tissue is definitely not that important in determining whether a person's metabolism is healthy. Comparing people with healthy versus unhealthy metabolism shows that health is not associated with a person's body mass index but instead with such factors as the concentration of adiponectin.

"We can see, for example, that the prevalence of type 2 diabetes and even insulin resistance as a whole is closely associated with the concentration of adiponectin in the blood. We therefore tried to manipulate mice genetically to produce less leptin but excessive adiponectin to see how this affected their health."

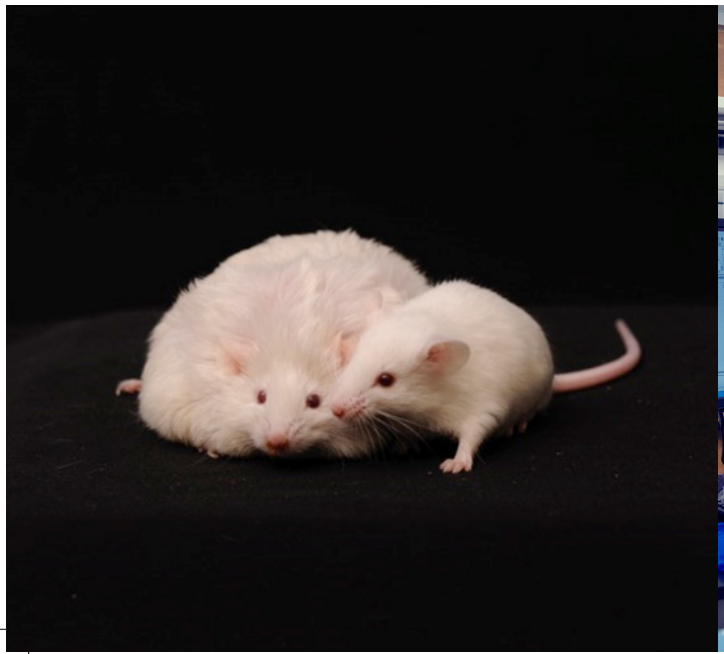
The lack of leptin made the mice constantly hungry. In contrast, adiponectin signalled their brains that they were in a state of starvation. This combination made the mice eat constantly and become fatter and fatter. Despite this, adiponectin apparently also made the mice store the surplus fat and sugar instead of them circulating in the blood.

"This resulted in some grossly overweight mice that actually had improved insulin resistance and no visible signs of type 2 diabetes, and they definitely had no fat or sugar in their blood. In addition, despite their increased fat mass, the mice stored the fat under their skin instead of surrounding their organs."

## Oxygen starvation

The researchers had distinguished obesity as an independent factor from the harmful effects of metabolic diseases. Thus, although obesity is often associated with metabolic diseases, it is apparently not obesity in itself but altered signalling patterns and especially where and how fat is stored that determine whether a person's metabolism becomes healthy or unhealthy and thereby increases the risk of cardiovascular disease and type 2 diabetes.

"Despite being the heaviest mice ever, they could effectively keep all the extra calories and thus the



negative effects away from all other tissue other than fatty tissue, but that was not all. The enormous adipose tissue the mice built up under their skin comprised small fat cells without dangerous inflammation and with an efficient blood supply, which is important for healthy fatty tissue."

The research by Scherer and others has shown that fatty tissue only becomes a health hazard when the oxygen supply declines, since this is especially important for maintaining healthy fatty tissue and metabolism. The fat from surplus food is normally stored as drops in the fat cells, which thus slowly expand. Stress signals are emitted when oxygenation is insufficient, and this ensures that new paths for blood supply are formed so that the fat cells can continue to be oxygenated.

"Storing nutrients for hard times was vital historically. But today, with no shortage of food, the fat stores often grow so much that the blood supply and therefore oxygenation becomes insufficient. This damages the fat cells, which eventually die. This conversion of healthy fatty tissue into unhealthy tissue, sharply increases the risk of lifestyle-related diseases such as type 2 diabetes."



## White, brown and beige

Healthy fatty tissue is therefore not determined by size but more by oxygenation, blood supply and especially hormones signalling from tissue to other organs. Recent research in this field has therefore focused on characterizing fatty tissue. Today, researchers distinguish at least three types of fat: white, brown and, most recently, beige.

White fatty tissue specializes in storing surplus energy as fat, whereas brown fatty tissue can metabolize nutrients and convert their energy into heat. The fatty tissue is brown because of the iron-rich proteins present in the mitochondria – the energy-producing centres in the cells – and more blood vessels.

"We are currently trying to understand what characterizes the different types of tissue and especially how the body could convert one type to another. If, for example, the body could convert the white fat cells to beige or brown ones, this would strongly improve metabolism and the creation of healthy fatty tissue."

Scherer and his colleagues also think that increasing the numbers of brown or beige fat cells or improving their activity may be able to reduce obesity and correct the harmful effects of unhealthy metabolism. Nevertheless, they have no definitive proof that converting fat cells from white to beige or brown is all that is required.

## Body fat as an organ

The research in the past two decades thus shows that the once monochromatic and unequivocal picture of fat has become much more colourful and multifaceted. Philipp Scherer also believes that the time is ripe to perceive fatty tissue completely differently.

“Basically, fatty tissues behave as a distinct organ like any other in the body: an aggregation of cells that performs one or more specialized functions. And the more we study fatty tissue, the more important it appears to be in the human body. For example, recent research has shown that fatty tissue plays a major role in developing cancer and fending off infectious diseases.”

Several parasites target fat cells in such diseases as Chagas disease, caused by *Trypanosoma cruzi*, just as the malaria parasite does in red blood cells. Further, fat cells may apparently also play an important role in breast cancer.

“Fatty tissue plays a major role in several types of cancer in which the tissue is slowly infiltrated by cancer cells. One such example is the lactiferous ducts in breasts, in which cancer cells use the growth factors and other substances secreted by the fat cells.”

## No magic pill yet

Time has thus shown that leptin and adiponectin are just two of the many crucial signalling hormones that fatty tissue secretes to communicate with other tissue and cells. But the focus on these two hormones results from many researchers, including Scherer, considering them to be the key to solving global problems with metabolic diseases such as type 2 diabetes and cardiovascular disease.

“Adiponectin appears to have an incredibly important role. In fatty tissue, it helps to ensure the development of new small fat cells and veins and thereby sufficient oxygenation of the tissue. We have found adiponectin receptors in the liver, heart, kidneys and pancreas, and evidence shows that it directly increases insulin sensitivity in several of these tissues. Adiponectin has also been shown to reduce the risk of blood clots and improve wound healing.”

Philipp Scherer therefore believes that adiponectin is one of the most important biomarkers for determining health, including the risk of type 2 diabetes and cardiovascular disease. Genetic studies have shown that mutations in the gene for secreting adiponectin increase the risk of developing these diseases. Adiponectin and especially the body’s adiponectin receptors are therefore an important target for future treatment.

“Unfortunately, there is no magic pill yet, because adiponectin cannot be used in treatment. It is difficult to produce synthetically and is also unstable as a pill. However, research is already taking place to develop substances similar to adiponectin that can stimulate the adiponectin receptors in the various types of tissue for people who cannot secrete sufficient amounts. This may potentially enable such diseases as type 2 diabetes to be treated and effectively improve insulin sensitivity.”

> My laboratory has the questionable reputation of having made the fattest mouse ever generated in the history of mankind.
>
> - Dr. Philipp Scherer

## Previous recipients of the EASD–Novo Nordisk Foundation Diabetes Prize for Excellence

**2015** Professor Stephen O'Rahilly
**2016** Professor Andrew Hattersley

# THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

The European Association for the Study of Diabetes (EASD) was founded in Montecatini, Italy in 1965.

The mission of the EASD is to promote excellence in diabetes care through research and education. The aims are to encourage and support research, the rapid diffusion of acquired knowledge and to facilitate its application.

EASD embraces scientists, physicians, laboratory workers, nurses and students interested in diabetes and related subjects. Each year, the EASD Annual Meeting brings together over 15,500 medical professionals as well as an online audience of thousands. EASD is the home of diabetes research in Europe.

The Association holds training courses and workshops to attract new talent to diabetes research and to disseminate the latest knowledge. In addition, it has established a large number of study groups focusing on different areas of diabetes research and care and has founded the journal *Diabetologia*.

In 1999, the Association created the European Foundation for the Study of Diabetes (EFSD), which operates on a non-profit basis.

# THE NOVO NORDISK FOUNDATION

The Novo Nordisk Foundation is an independent Danish foundation with corporate interests. Its history goes back more than 90 years.

The objectives of the Foundation are:

1: to provide a stable basis for the commercial and research activities of the companies in the Novo Group; and 2: to support scientific, humanitarian and social purposes.

The vision of the Foundation is to contribute significantly to research and development that improves the health and welfare of people.

Since 2010, the Foundation has donated more than DKK 10 billion (€1.3 billion), primarily for research within biomedicine and biotechnology and diabetes treatment at universities and hospitals in Denmark and the other Nordic countries. The Foundation supports the entire research chain – from education to innovation.

In addition to awarding grants, the Foundation annually awards several honorary prizes to recognize and reward individuals for their unique efforts in research, teaching or other efforts relevant to research.

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