Anders Jahre's Awards for Medical Research 2017

The Jahre Lectures

Thursday 14th September 2017 at 14.00-16.00 hrs
The auditorium, The Radium Hospital research building, Ullernchausseen 70

The lectures are open to everyone.

Programme:

14.00 – 14.45 **Professor Christer Betsholtz**
Integrated Cardio Metabolic Centre, Karolinska Institutet, Stockholm, and Department of Immunology, Genetics and Pathology, Uppsala University, Sweden

The great secrets of the smallest blood vessels

14.45 – 15.10 Break / Refreshments

15.10 – 15.35 **Associate Professor Signe Sørensen Torekov**
Department of Biomedical Sciences, University of Copenhagen, Denmark

Obesity, appetite-regulation and how to maintain a healthy weight loss.
- the biological mechanisms behind healthy sustained weight loss in humans

15.35 – 16.00 **Professor Simon Bekker-Jensen**
Department of Cellular and Molecular Medicine, University of Copenhagen, Denmark

The hardship of life: How cells survive in their hostile environment

Anders Jahre's Awards for Medical Research honor research of outstanding quality in basic and clinical medicine. The prizes are awarded by the University of Oslo and are among the largest within Nordic biomedical research.

ABSTRACTS:

The great secrets of the smallest blood vessels **by Professor Christer Betsholtz**

Blood is transported to and from our bodies' organs by the large blood vessels – arteries and veins, respectively – in which physical quantities such as blood pressure and flow are tightly controlled to ensure effective blood distribution. The microvasculature is instead regulated regarding its permeability for water and solutes, plasma proteins and cells. The nature of the microvascular permeability is organ-specific and under regulation by physiological as well as pathological signals. During development and disease new microvessels may also sprout and remodel through carefully controlled cellular processes, such as migration, growth and division. In my lecture, I will discuss the two principal cell types that build up the microvessels, i.e. endothelial cells and pericytes, and how they communicate with each other and the surrounding cells in angiogenic sprouting and organotypic differentiation. I will illustrate the latter process by the blood-brain barrier, a highly specialized function that ensures that the brain is supplied with sufficient amounts of the right nutrients, while simultaneously protecting it from neurotoxic substances circulating in the blood. I will also show new and unpublished results in which some of the most well hidden secrets of the blood vessels get revealed by single cell RNA sequencing.

Obesity, appetite-regulation and how to maintain a healthy weight loss. - the biological mechanisms behind healthy sustained weight loss in humans **by Associate Professor Signe Sørensen Torekov**

Obesity affects one billion people and impairs all aspects of health. Success rates for maintaining long-term weight loss are very low, thus there is an acute need for more effective treatment strategies. The natural appetite inhibiting hormone glucagon-like-peptide-1 (GLP-1) is secreted from the intestine upon meal intake and reduces blood glucose and food intake. Obese people have low levels of GLP-1, but interestingly a sustained weight loss of 10 kg for one year induces a marked increase in GLP-1. Thus, high levels of GLP-1 seem to be part of successful weight loss maintenance. Treatment with GLP-1 analogues facilitates long term weight loss maintenance accompanied by substantial improvement in metabolic health, compared to similar weight loss obtained by conventional dietary-regimes. Furthermore, obese people can be grouped into high and low immuno-metabolic risk profiles by analyzing the full plasma proteomic profile, which opens up for more personalized treatment strategies. Finally, patients with the genetic heart disease Long QT Syndrome have exaggerated GLP-1 secretion and endocrine pancreatic dysfunction after sugar intake and thereby increased risk of serious hypoglycemia. Therefore, large amounts of sugar intake should be avoided. Conclusively, normalized GLP-1 levels are crucial for both body weight and glucose regulation in humans.

The hardship of life: How cells survive in their hostile environment **by Professor Simon Bekker-Jensen**

In response to harmful environmental conditions and other stresses, cells can mount stress responses that rewire cellular functions to cope with these challenges. Besides serving as acute defense mechanisms, such responses are also required to maintain the fitness of cells over time by constantly responding to low levels of stress originating from e.g. oxidative byproducts of metabolism and gradual age-dependent decay of key cellular constituents.

The MAP kinase p38 is a central transducer of a subset of these responses, activating a plethora of signaling pathways that collectively act to modulate and rewire cellular function to cope with stress. In particular, regulation via p38-, MK2- and 14-3-3 – dependent signaling is emerging as a common effector branch of cellular stress responses. Over the last couple of years, we have contributed to this realization by uncovering and characterizing novel p38-driven stress responses that modulate diverse processes such as protein translation and centrosome functionality. In my talk I will summarize these findings and give an update on our ambitious and ongoing efforts to unravel the poorly defined pathways that govern cell stress-induced activation of MAP kinases. I will also discuss the potential of our discoveries for gaining novel insight into the human aging process and combatting diseases such as cancer.

Popular scientific summary:

The great secrets of the smallest blood vessels **by Professor Christer Betsholtz**

It takes two to tango. Similarly, it takes two cell types to make functional blood vessels: the inner, tube-forming, endothelial cells, and the outer, supporting, pericytes. Pericytes were observed for the first time already 140 years ago, but their importance was hidden until 20 years ago, when they could be deleted and the consequences studied. This was accomplished by gene-knockout in mice for a growth factor, PDGF-B, which is released by endothelial cells to activate a receptor on pericytes, causing them to migrate, grow and attach to the blood vessels wall. I will give examples of how the smallest blood vessels develop organ-specific functions and how endothelial-pericytes signaling takes part in this process. I will also show new data on how the innermost secrets of the vascular cells can be revealed - and even new cell types discovered - using new sensitive techniques.

Obesity, appetite and how to maintain a healthy weight loss. - the biological mechanisms behind healthy sustained weight loss in humans **by Associate Professor Signe Sørensen Torekov**

Obesity affects 1 billion people and impairs all aspects of health; therefore there is an acute need for better treatment strategies. The natural appetite inhibiting hormone GLP-1 is secreted from the gut when you eat and reduces blood sugar and food intake. Obese people have low levels of GLP-1, but interestingly a sustained weight loss of 10 kg for one year induces a marked increase in GLP-1. Treatment with artificial GLP-1 helps to maintain long term weight loss and improves health, also compared to standard diet programs. Furthermore, obese people can be grouped into high and low health risk profiles by analyzing the proteins in the blood, which opens up for more personalized treatment strategies. Finally, the heart disease Long QT Syndrome leads to exaggerated GLP-1 levels and seriously low blood glucose levels upon sugar intake. Normalized GLP-1 levels are crucial for both body weight and sugar regulation in humans.

The hardship of life: How cells survive in their hostile environment **by Professor Simon Bekker-Jensen**

The human organism is made up of billions of cells that live long and largely carefree lifes within the safe confine of our bodies. This popular and simplified notion could not be further from the truth! In fact, all of our cells are constantly exposed to a harmful environment which damages proteins, DNA and other macromolecules. Some of these adverse stimuli can be attributed to external factors (like UV radiation from the sun and perhaps the occasional smoking of a cigarette), but actually most of the damage load is a result of the body's own metabolism and general decay. To stay alive, and to help maintain a healthy organism, all cells are thus equipped with a range of "stress defence mechanisms" which continuously react to the otherwise detrimental effects of their hostile environment. These systems monitor the integrity of our chromosomes and other macromolecular components such as ribosomes and mitochondria. When damaged or unfunctional, these crucial cellular components must be repaired or degraded and replaced to maintain homeostasis. In my lab, we study the molecular architecture of cellular self-defence mechanisms and their implications for human health and disease. Our emphasis is on the links between cell stress responses and human aging, while also investigating whether interference with cellular maintenance may present a new target for cancer treatment.