Diabetes – current and future visions

A leading European diabetes centre in Dresden…

The State of Saxony has made a unique effort to create a place of scientific excellence at the University of Dresden. A central component of this scientific excellence has been created in the field of medicine and biomedical research, especially in the research and treatment of diabetes. Following an international complex review process the 'Technische Universität Dresden' (TU Dresden) has been chosen as one of the 11 German elite universities. Diabetes research is a major focus in the clusters of excellence at the TU Dresden that led to this success.

Currently, more than 300 million people worldwide suffer from diabetes and the number of patients is increasing dramatically. Dresden has a long-standing tradition in the field of diabetes: shortly after the discovery of insulin, it installed the first diabetes clinic in Germany in 1922. Many years later, in 1981, the concept of the metabolic syndrome was also coined in Dresden. Nowadays, it has become one of the largest diabetes centres in Europe.

Professor Stefan R Bornstein, Director and Chair of the Department of Internal Medicine at the University Hospital Carl Gustav Carus Dresden, believes: "Our centre offers several unique features to patients including an islet transplantation programme and the first European Department for the prevention of diabetes. Furthermore, the hospital has one of the largest insulin pump outpatient clinics with more than 400 patients." At large 30,000 patients with diabetes benefit every year from the experienced specialists at our University Hospital Carl Gustav Carus Dresden.

The Dresden diabetes centre has become a part of the new established German health centres and is a key element of the Center for Regenerative Therapies Dresden (CRTD). The diabetes research programme intensively studies ways in which the insulin-producing beta cell can be regenerated and protected so that new therapies to prevent and cure diabetes can be developed. One of these is a unique programme of Type 1 diabetes prevention. Professor Ezio Bonifacio from the CRTD leads an international clinical study in which infants who have a strong genetic predisposition to develop Type 1 diabetes are immunised in an attempt to prevent the disease. Based on a strong interdisciplinary expertise in genetics, cell and developmental biology scientists under Professor Michele Solimena are working to prevent the destruction of insulin producing beta cells and to restore beta cell function and regeneration.

Individual treatment in accordance to the latest research

How is diabetes related to stress and depression?

Comparable to diabetes mellitus, other lifestyle related conditions like stress and stress related diseases are on the rise. This is well documented and reflected by the fact that the levels of cortisol – a major stress hormone – are usually elevated in patients suffering from depression. Cortisol is a major hormone produced by the adrenal gland that is essentially required to adapt the organism's metabolism in response to stressful stimuli. This results in a rapid mobilisation of energy resources to cope with the challenge. However, permanent overproduction of cortisol may also result in negative consequences like loss of muscle mass and impairments of glucose metabolism ranging from increased blood glucose concentrations to diabetes mellitus. A research team under Bornstein and supported by the German Research Foundation (DFG) is currently investigating the shared biology of diabetes and stress.

How is diabetes related to nutrition and the microbiome?

The microbial colonisation of the gut may play a critical role in human health and the number and composition of gut microbes varies between individuals. The human gut microbiome consists of more than 1,000 different germ species and the sum of the gut microbial genomes, the so-called metagenome, exceeds by far the size of the human genome. Novel, cutting-edge sequencing technology (so-called 'next-generation sequencing') has made it possible to characterise the human metagenome and recent studies performed with faecal DNA of individuals from Europe, Asia and the US have suggested an association between specific metagenomic constellations and the risk for obesity and Type 2 diabetes, most likely due to differences in microbial energy metabolism.

Based on this background, the current focus of a novel research project conducted at Dresden diabetes centre is on the metagenome of morbid obese patients with Type 2 diabetes who underwent gastric bypass surgery. Interestingly, shortly after operation a dramatic

improvement of glucose metabolism can be usually observed in these patients, even before weight loss. This study thereby provided the first evidence for an essential role of the gut microbiome in the anti-diabetic effects of gastric bypass surgery.

In the near future further exciting and important insights can be expected from this new field of research. The long-term goal of Bornstein and his team is to develop metagenome-based approaches for the development of novel strategies for the prevention and treatment of diabetes.

Has diabetes a genetic background?
Diabetes is a multifactorial disease and in particular the recent genome-wide association studies (GWAS) have revealed a more or less strong association of several genes with the risk to develop Type 2 diabetes. For example, TCF7L2 has been identified as a gene with the strongest risk associated with its development. However, things are much more complex due to the fact that a variety of other, mostly still unknown factors are essentially involved in the regulation of gene expression. These so-called epigenetic factors may be of environmental or microbial origin and are thought to be the true risk determinants responsible for the interplay of different genes resulting in an individual's risk constellation.

How can we cure diabetes?
A shift in paradigm
For the majority of patients with Type 1 diabetes, treatment with insulin is a very reliable and safe therapy and helps to reduce or prevent diabetes-associated complications. Intensive insulin therapy with several daily injections or with an insulin infusion pump has been shown for many years to be an effective method of maintaining blood glucose concentrations in an acceptable range. However, despite optimal medical therapy, a rare number of patients show a poor control of the disease and experience repeated and unpredictable lapses of blood glucose levels to both ends of the spectrum ranging from severe hypoglycaemia to uncontrolled hyperglycaemia, resulting in severe and potentially life-threatening conditions.

Whole organ pancreas and pancreatic islet transplantation are currently the only options available to replace the insulin-producing ß-cells in patients. Both can provide good control of diabetes and a prevention or stabilisation of diabetic complications. The insulin producing cells are isolated from the pancreas (donor organ), purified and then injected into the blood vessels of the liver of the diabetic patient (recipient) through a small abdominal incision. The pancreatic islet cells engraft in the liver and start to produce insulin. In 2008, the Dresden diabetes centre successfully launched – under Dr Barbara Ludwig – an islet cell transplant programme for the treatment of Type 1 diabetes. This is currently the only active islet transplantation programme in Germany. However, cell and organ transplantation is generally at the price of permanent immunosuppression, thereby making the patient prone to infections and other side effects. Therefore, this therapy is restricted only to a small subset of diabetic patients that need to fulfil a number of specific criteria.

Novel therapeutic options are urgently needed; therefore Dresden scientists currently exploring – together with a biotech company from Israel – a small capsule harbouring insulin producing cells (originally developed in Israel). This bioreactor is designed as an implantable device working as an artificial islet organ in order to supply diabetic patients with insulin. The unique advantage of this novel technique is that it effectively separates the donor cells from the recipient's immune system, thereby making the traditional immunosuppressive therapy completely dispensable.

How can we prevent diabetes?
Type 2 diabetes is the most common metabolic disorder in the world. Currently, with more than 6% of the world's adult population we are experiencing an epidemic growth patients suffering from Type 2 diabetes, in particular affecting more and more young people during their working life. The increasing medical burden of patients with diabetes related complications also results in an enormous economic burden, which could severely impair global economic growth in the near future.

The Dresden diabetes centre introduced the first professorship for research on prevention and care of diabetes in Europe (Professor Dr Peter Schwarz) and offers specialised and customised programmes aimed at an early detection and potential prevention of the disease. The Dresden diabetes competence centre also developed the first European guideline for diabetes prevention and training programmes to educate certified prevention managers. This concept is today used in more than 20 countries EU and also introduced into practical diabetes care.

Our vision

Bornstein: "We follow the vision to promote cutting-edge developments in Dresden that are unique in the world. We look for new and more powerful ways to treat and prevent diabetes in order to better help more people in the future."

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