Associate Professor in Data Science Tune H. Pers, this year's recipient of the Danish Diabetes Academy's Young Investigator Award:

In search of the thermostat that controls appetite and fat distribution

Tune Pers hopes ultimately to discover how the brain regulates our metabolism. 'If we can find that out, we can more effectively eliminate the widespread social stigmatization of severely overweight people, and more effectively cure obesity and diabetes', he says.

Might the cause of diabetes be to be found in the brain?
Can we find the thermostat that controls whether we have too big an appetite or store fat too easily? And can we work out how that thermostat reacts to such things as social uncertainty, physical inactivity, stress or perhaps something else again that is responsible for obesity? And, not least, can we learn to adjust the thermostat to stop it causing havoc in the human body?

These are some of the questions that Tune Pers, this year's recipient of the Danish Diabetes Academy's Young Investigator Award, has asked himself – and is working to find answers to.

Tune Pers, 38, is an associate professor in Data Science at the Novo Nordisk Foundation Center for Basic Metabolic Research, also known as the Metabolism Center, at the University of Copenhagen, and he was nominated for the prize by his colleague Professor Torben Hansen.

300,000 people's genetic data compared with their BMIs

Tune Pers has a background unlike anybody else's in the diabetes/obesity research world he moves in, and this is what has brought him the very great successes he has already had. This is because Tune Pers started out studying computer science and economics before taking his master's in bioinformatics, and his ability to handle very large volumes of data truly came into its own a few years ago when he took part in a big research project, the Genetic Investigation of Anthropometric Traits (GIANT) consortium: researchers from more than 20 countries compared genetic data from

300,000 people with their BMIs. At the time, it was the largest study ever to investigate which genetic regions play a part in obesity and how they do it; the result was that the researchers found 147 specific regions in the human genome that affect either how much one weighs as an adult or where fat forms in the body.

The researchers handled the large volumes of data using a new method known as DEPICT (LINK to www.broadinstitute.org/mpg/depict/citation.html), developed by Tune

Pers and his colleagues. In general terms, the method can be used to get closer to knowing what biological processes are involved in complex diseases such as diabetes and severe overweight. The result was published in Nature.

Diabetes and the brain

Today it is the connection between diabetes and the brain that preoccupies him, and he himself says that he hopes ultimately to discover how the brain regulates our metabolism. 'If we can find that out, we can more effectively eliminate the widespread social stigmatization of severely overweight people, and more effectively cure obesity and diabetes, which often go together', he says.

Tune Pers points out that much metabolism research has focused on individual genes, hormones, biological processes and tissues. His approach is to use big data to pinpoint exactly which cell types and bodily processes we need to focus on, and when in life genetics and the environment have most impact on people as regards the development of metabolic disease.

Are we treating symptoms rather than the root of the problem?

The thought that increasingly suggests itself is whether the many challenges facing successful patient treatment might be due to the fact that, after decades of intensive research into diabetes, we are treating the symptoms rather than the root of the problem. The effect of a gastric bypass – the only form of treatment that makes it possible to cure type 2 diabetes with a single intervention – is one thing that has given Tune Pers the idea that we may not yet have got to grips with the root.

'Although the mechanisms underlying the effect of the gastric bypass are still unknown, and although the treatment is typically restricted to extremely overweight patients because of its invasive nature, this 'miracle cure' is still food for thought', he says. Along with his group – and first and foremost postdoctoral researcher Marie Bentsen and PhD student Dylan Rausch – he has investigated whether a single injection of the substance FGF1 into the mouse brain could cure diabetes. It worked, and follow-up analyses of the gene expression data confirmed the cell-type-specific biological processes in the hypothalamus which they subsequently found to be activated by the substance.

The chances of our succeeding in finding out what changes it will take for the brain to cure diabetes permanently are not great. However, that won't stop us venturing out into the unknown – that's where we find the infinite source of energy it takes to find the answers to the big questions. Perhaps, one day, our current and future findings will mean that we can prevent diabetes and severe overweight, or that we can manage with a single one-off, non-invasive intervention', he says.

FACTS
The Danish Diabetes Academy Young Investigators Award is presented each year to a young researcher, below the age of 40, who is engaged in diabetes research in Denmark, and who has shown promising research and made an important contribution to the

understanding and treatment of diabetes.

The Award is presented at the Danish Diabetes Academy Annual Day 12 November 2019.

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