Researchers discover new explanation for diabetes and poor growth

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A group of researchers from the University of Copenhagen has taken a significant step towards understanding the reasons for both diabetes and growth hormone deficiency. Their new discoveries centre on the body's ability to regulate certain hormones, and their findings have just been published in the respected scientific journal *PLOS Biology*.

Some people suffering from diabetes or affected by poor growth most likely have problems with the so-called PICK1 protein, a protein that plays a decisive role in the formation of both growth hormone and insulin in the human body.

"We have studied the role played by PICK1 when growth hormone is released by the brain and insulin by the pancreas. Our experiments show that PICK1 deficiency leads to growth hormone and insulin deficiency in both fruit flies and mice. In mice, we can clearly see that the animals become small and fat and less tolerant to sugar when deficient in PICK1. We have reason to believe that the same is true for humans," says Professor Ulrik Gether from the Department of Neuroscience and Pharmacology, who has made the new discoveries together with his research colleagues Ole Kjærulff, Birgitte Holst and Kenneth Madsen.

"Different cells produce different kinds of hormones, and store the hormones for secretion into the bloodstream when required. Up until now, this has been a poorly understood mechanism which, among other things, plays a key role in the development of diabetes and poor growth. However, given what we now know about the PICK1 protein, we are in a

position to say far more about what might have gone wrong when someone is suffering from the two diseases," says Professor Birgitte Holst, explaining that the group wishes to continue looking at whether changes in the PICK1 protein can lead to some people being short, overweight, and diabetic.

Advanced transport system

Hormones are chemicals that regulate the body's functions via the blood in an ingenious transport system. In the so-called Golgi complex – an organelle made up of four to eight flat discs or cisternae arranged in a stack – traffic is bustling with proteins and hormones being modified, sorted and packaged so they can be sent out to destinations both within and outside the cells. These proteins and hormones include insulin and growth hormone. The proteins and hormones are packed into small transport particles called vesicles, and they remain there until the cells receive a signal to send the hormones off. The molecular dynamics that has been mapped through identifying PICK1 has shown itself to be a critical component in relation to diabetes and poor growth.

"The process is comparable to a factory where Lego bricks are packed. If the boxes are not packed properly and cannot be sent out at the right time to the right recipient, it causes problems. In this case with growth hormone and insulin," says Birgitte Holst.

From fruit flies to humans

Ole Kjærulff and his employees started by looking at PICK1 in fruit flies' brains, and then brought in Birgitte Holst, Ulrik Gether and Kenneth Madsen, who all possess expertise within this field of research. Birgitte Holst has looked at how PICK1 deficiency in mice affects their body weight and metabolism, while Ulrik Gether and Kenneth Madsen

have been responsible for aspects to do with cell biology.

"PICK1 is part of the basic cellular process which is vital for fruit flies, mice and probably also humans being able to form and store important hormones such as insulin and growth hormone. We don't yet know exactly what our discoveries mean for the development of diabetes and poor growth in humans, but hopefully our new knowledge will lead to better prevention and treatment in the future," says Ulrik Gether.

Provided by University of Copenhagen