Salvagene GROUP

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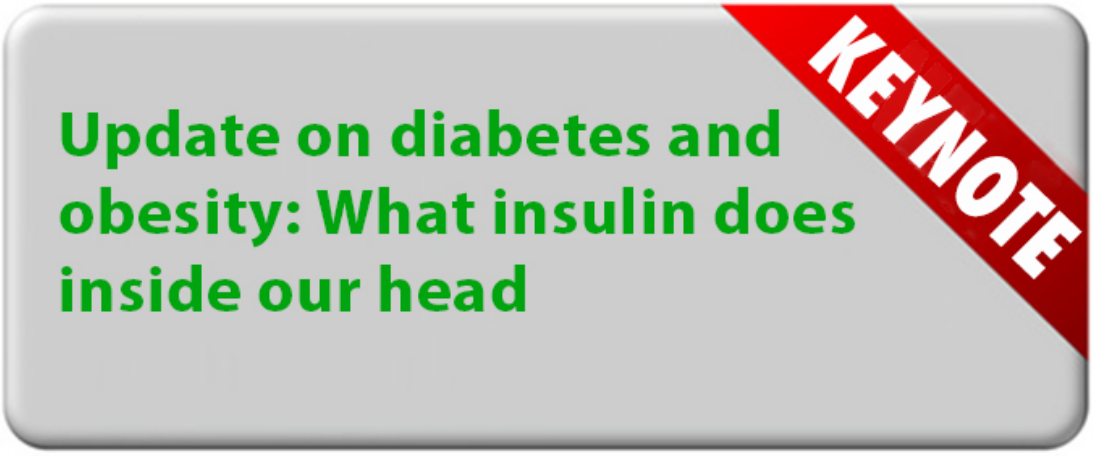

Dear Premium Customers,

Below is an update on previous keynotes and information we have already communicated on diabetes and obesity prevention.

Insulin is a hormone that can control certain brain cells. It has enormous consequences for the body's metabolism. With input from our colleague Jens Claus Brüning at the Max Planck Institute, we explain here the way in which nerve cells react to insulin and the consequences that diabetes has for the brain. The hormone insulin is released by the pancreas as and when a rise in blood sugar level is detected in order to bring it back down again. Three organs play a central role in this process: muscle tissue, fat tissue and the liver. Insulin increases the absorption of sugar in muscles and fat, while in the liver, it inhibits the new formation of sugar. Taken together, this leads to a lower blood sugar level. Receptors for insulin are also found in many other organs, especially in the brain.

The epigenetic state of insulin receptors in the brain in particular has enormous consequences. We have been able to show that

insulin is less effective in lowering blood sugar levels when the insulin receptor is downregulated. This is what causes obesity to develop. It is therefore clear that insulin also has an effect on the central nervous system. It also been possible to identify the nerve networks in the brain by means of which insulin exerts its influence. It is now clear that insulin regulates not only sugar metabolism but also fat deposition and body weight. It is important to note that there are many overweight people in whom insulin no longer works properly in the brain.

Prevention of insulin resistance is one of the key objectives of our Salvagene Premium Program, and from January 2021, we will be implementing a new testing methodology which will involve a significant expansion of our epigenetics module in the area of insulin receptors. It can be shown that there is a greatly increased likelihood of obesity and diabetes if mothers were on a high-fat diet while breastfeeding and thus developed a metabolic disorder. Lactation is one of the most important epigenetic windows during a woman’s life. There is also a second, possibly even more important window, namely the last third of pregnancy. Here, a preventive approach can certainly be taken that also avoids the risk of permanent harm being done to the unborn child.

In this context, we already reported some time ago on a widely circulated epigenetic study from Holland. This shows that the hypothalamus has a network of approximately 3,000 neurons which can suppress food cravings. When these nerve cells are stimulated, they release a messenger substance called pro-opiomelanocortin (C), or PROMC for short. This ensures that you do not feel hungry. We can demonstrate that, although the high-fat diet of mothers leads to this cell network being laid down, it no longer communicates so well to other regions of the brain, and herein lies the increased risk. This is due to epigenetic changes.

In any diabetes prevention strategy, it is important to know that being overweight significantly increases the risk of diabetes. In adult-onset diabetes, insulin is still produced, but it is not as effective as in childhood or youth. The excess calories are generally stored as fat in the adipose tissue. As long as this process continues, there is no major metabolic problem. But at some point, the storage capacity of the adipose tissue becomes exhausted and then, to put it crudely, the fats spill over into the muscles and liver. These organs cannot store the fat in a neutral way. This leads to so-called "lipotoxicity". The insulin can then no longer do its job properly in the liver. We have discovered that a certain type of fat – the so-called "ceramides" – play a decisive role in this process. If the deposition of these ceramides is inhibited, insulin resistance no longer occurs in a high-fat diet.

This is the precise focus of our diabetes prevention program. The substances we are working with include high-dose benfotiamines that inhibit the deposition of ceramides and thus have a different mode of action than other diabetes drugs such as metformin. Benfotiamines do not really have an all-inclusive effect either. This is primarily due to the epigenetic states of the insulin receptors, as well as to the genetic polymorphisms. On this basis, we consider that diabetes overweight prevention has to be adapted to the individual and take place within a completely personalized framework.

Furthermore, there are now so-called "natural SGLT2 inhibitors". They ensure that more sugar is excreted via the kidneys. This not only improves sugar levels, but also reduces the risk of heart disease. The same applies to the so-called "GLP1 analogues". GLP1 is a hormone that is released by the bowel after you have eaten something. It encourages the release of insulin in the pancreatic cells. It has also been shown to have an effect on the brain. This can also lead to significant weight loss. Of course, willpower also plays a big part in this.

We have already discussed the topic of leptin resistance on previous occasions. Adipose tissue forms leptin. This hormone, which was discovered as late as 1994, affects the hypothalamus in such a way that food intake is suppressed as an automatic reflex. At the same time, it also has an effect on the dopamine reward system in the midbrain. Leptin thus regulates the subjective value of food. Fasting leads to a low leptin value, which makes food more attractive. An individual who cannot produce leptin or who is no longer affected by it will essentially have reduced willpower. This molecular insight makes it clear that obesity can be caused by a hormone disorder and that overweight people are not necessarily weak-willed people. The important thing to remember is that, although most overweight people produce leptin, it no longer works properly in their brains. This is similar to insulin resistance. Therefore, both types of resistance – leptin and insulin – play an important role, and it is important to know the epigenetic states of the respective receptors and their changes.

Prevention is therefore much easier to achieve with highly effective measures. **This extension of the epigenetic analyses will be available as of 1st January 2021 for all of our Premium clients.**

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