Press Release – UCLouvain Research Obesity - When the intestine loses its ability to communicate to the brain: “Stop, do not eat fat anymore!”

During fat ingestion, if everything works in our body, an enzyme from the intestine transmits to the brain (through the production of molecules) the message “stop, I am not hungry anymore”. This gut-brain axis maintains a balanced food intake. Researchers from the UCLouvain were able to target this enzyme. In overweight or obese subjects this enzyme is dysfunctional, therefore the message “I am not hungry anymore” is no more transmitted. By consequence, the overweight is increasing. These results have been published in the scientific journal *Nature Communications*.

**What are the novelties?**

The team of Patrice Cani (Louvain Drug Research Institute, UCLouvain), is the first one to explain how the gut-brain axis is altered during fat overconsumption:

1) **A high-fat diet alters the gut-brain axis**, through the reduction of the activity of an enzyme (NAPLE-PLD). Therefore the body no longer responds properly to this fat overconsumption, the appetite is not regulated anymore and the subject gains more weight;
2) Mice deleted for this enzyme in the intestine develop a fatty liver, become obese (even more than the wild type mice) and their energy expenditure is reduced;
3) If these mice (without this enzyme) are exposed to a high-fat diet, they are not able anymore to stop eating the fatty diet, and they eat more than the wild type mice exposed to the same high-fat diet.

**How does it work?**

- **Without this enzyme** (or when this enzyme is less efficient due to fat ingestion), we lost the signals informing the brain for stopping eating. In simple, the physiological means by which the intestine activates the appetite-suppressing neurons of the hypothalamus are lost and those same neurons also increase rest energy expenditure. Consequences? We eat more, we expend less energy and by this way we gain weight.
- During their PhD, Amandine Everard, Hubert Plovier and Marialetizia Rastelli, three researchers from the FNRS in the team of Patrice Cani (UCLouvain), they also discovered that in absence of this enzyme the intestine is absorbing more fat and by this way it engorged the liver (which become fatty). This alters the gut microbiota, that will in turn reinforced the vicious circle associated with obesity.
- Finally, the research demonstrates that the administration of the bacteria *Akkermansia* in mice deleted for this enzyme, and thereby harbouring an altered gut-brain axis, is able to reduce the fatty liver and also the food intake. In other words, the bacteria allows to restore the crosstalks, through the message “stop, I am not hungry anymore”.
What are the consequences on obesity?
This research is essential because the discovery of the effects of this enzyme is opening the door for novel potential therapeutic targets (already currently studied in some pharmaceutical societies) to improve the gut-brain axis. Three different approaches are currently tested:

- Administration of specific molecules produced by this enzyme in order to reduce appetite;
- Activation of the enzyme in order to increase the production of molecules and their effects;
- Prevention of the degradation of these molecules in order to maintain their functions.

This research, started in 2010 and financed by the WELBIO-FNRS, the Fonds Baillet-Latour and an ERC, has just been published in Nature Communications. Coordinated by the UCLouvain, this study associates Canadian, Italian, French and Dutch researchers. Contact person (press):

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¹ Akkermansia is gut bacteria with beneficial effects that has been discovered at the UCLouvain by Patrice Cani and his team. This bacteria, alive, is able to reduce the effects associated with obesity and type-2 diabetes in mice.