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Invited Commentary

Gut microbiota and pregnancy, a matter of inner life

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More than a century ago, two Nobel Prizes in Physiology and Medicine were awarded to scientists who established the link between microbes and human health. The first one, Robert Koch, linked microbes to infectious diseases, while the second one, Ilya Mechnikov, found that microbes might have beneficial effects on human health. Since then an intricate set of relationships between microbiota and humans has been unravelled. Humans have evolved in – permanent or temporary – intimate association with microbes, contributing to health maintenance or disease.

Look behind your belly button

Over the past 5 years, studies have highlighted some key aspects of the mammalian host–gut microbial relationship. The human gastrointestinal tract contains a diverse collection of micro-organisms totalling about 10^{14} bacterial cells. It is now recognised that gut microbiota play an even more important role in maintaining human health than previously thought[1]. What is becoming clear is that these microbes provide us with essential genetic and metabolic attributes, sparing us from the need to evolve on our own. This includes defence against pathogens at the gut level, immunity, digestion and synthesis of several vitamins. Conversely, accumulating evidence indicates that there are also many factors shaping gut microbiota, such as genetics, drugs and environment[2].

Recently, focus has been placed on therapies that aim to restore a balanced gut microbiota and thereby improving health. However, the mechanisms behind their action on the gut microbiota and their impact on metabolic functions are not fully understood. Today more attention is paid to the role of the balance between gut microbiota and host metabolic functions. The majority of research to date has unveiled a glimpse of the mechanism of action and potential therapeutic role of commensal non-pathogenic microbes (probiotics) on mucosal immunity, inflammatory bowel diseases, allergic diseases and so on[3–6]. As a consequence, most clinical studies in this area have been designed to explore pathological situations rather than physiological or mildly impaired health situations.

Are the gut microbiota involved in glucose homeostasis during pregnancy?

An article in the current issue of the *British Journal of Nutrition* assesses the impact of probiotics and dietary counselling on glucose regulation during and after pregnancy[7]. This is the first study describing the effect of probiotic intake on the health of pregnant women. Previous studies in pregnant subjects were conducted in order to study the impact on the gut microbiota on infant instead of the metabolic homeostasis of the mother.

In this new study, Laitinen *et al.* elegantly demonstrate in a cohort of 256 women that the modulation of gut microbiota composition by probiotics regulates glucose metabolism[7]. The major discovery of the authors is that the blood glucose concentrations were not only lowest in the probiotic group during the first trimester of pregnancy but more importantly over the 12-month postpartum period, while the dietary treatment was interrupted. The maintenance of glucose homeostasis during pregnancy constitutes an important way to reduce the risk of related complications and provides long-term health benefits for the mother and the infant[8,9]. This study is in line with recent evidence showing that gut microbiota are involved in the development of obesity, insulin resistance and related disorders such as type 2 diabetes.

What can we learn from the recent literature? Are the gut microbiota involved in the control of glucose homeostasis?

Authors have highlighted that the differences in energy extraction efficiency from food, leading to a higher fat deposition, may be determined by the gut microbiota[10]. In humans, the relative proportion of the two major representative phyla of bacteria was different between lean and obese individuals, and a similar result was found in a strain of laboratory mice bred to be genetically obese[11,12]. Strikingly, the same authors have also demonstrated that germ-free mice were resistant to a high-fat diet-induced obesity and type 2 diabetes[13], in opposition to the dogma that feeding fat drives the development of obesity and related disorders.

Along this line, our research team argued that the Western diet plays a role in the onset of obesity by reducing or promoting some gut micro-organisms over others in mice models[14,15]. Importantly, the data show that fat feeding strongly changes gut microbiota and especially lowers the well-known probiotic strain *Bifidobacterium* spp. and promotes type 2 diabetes[16,17]. There are several ways to restore the microbial balance, namely by using prebiotics or probiotics. Feeding mice with prebiotic dietary fibres together with the Western diet restored the gut bifidobacteria content, and delayed the onset of obesity, low-grade inflammation, insulin resistance and diabetes[18,19]. Altogether, these findings highlight the role of gut microbiota as an environmental factor involved in the development of

obesity and related disorders. However, what is the role of such intervention in physiological conditions such as pregnancy?

Are the gut microbiota the magic bullet?

This is a revolutionary idea that could change our views about the causes of metabolic disorder and glucose homeostasis control: we depend on the bacteria that inhabit our gut. However, most of the data have been obtained in experimental models, and data obtained in human subjects are scarce. In this new study, the authors have not only challenged the role of the gut microbiota in healthy humans but, more importantly, they have provided the first evidence that the gut microbiota can be involved in the control of glucose homeostasis in healthy pregnant women from early pregnancy for up to 1 year postpartum. Again, in this study, Laitinen *et al.* strongly suggest that the selective modulation of gut microbiota improves serum insulin levels and insulin sensitivity as shown by the homeostasis model assessment (HOMA) and quantitative insulin sensitivity check (QUICKI) indices[7].

Nevertheless, progress in understanding the mechanisms by which the gut microbiota interact with the host will provide a new basis for putative pharmacological or dietary intervention. Moreover, our current knowledge about the complexity of gut microbiota–host interactions remains scare. Therefore, it is difficult to ascertain the exact mechanisms linking dietary habits, gut microbiota and metabolic disorders.

In conclusion, this new study by Laitinen *et al.* adds valuable information about the impact of the host and gut microbiota cross-talk during pregnancy. Taken together with the other experimental studies, this study suggests that, rather than not being useful, changing gut microbiota following probiotic ingestion during pregnancy is probably a new area of intervention to prevent or improve glucose homeostasis in such a context. The mechanism and the relevance in pathological conditions (pregnancy diabetes) remain unknown. Therefore, further clinical trials and multidisciplinary research in this field will provide evidence-based data to take into consideration the gut microbiota to treat or prevent metabolic disorders.

P. D. C. is a researcher from the FRS-FNRS (Fonds de la Recherche Scientifique, Belgium). There is no conflict of interest.

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