GUT MICROBIOTA
RESEARCH & PRACTICE
edited by ESNM

SHORT CHAIN FATTY ACIDS

A selection of content from the Gut Microbiota for Health 2016

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EDITORIAL

In searching for the molecular mechanisms connecting dietary fibre to positive gastrointestinal and metabolic effects and lower body weight (Slavin, 2013), research in the past several decades has centred around a group of molecules called short-chain fatty acids (SCFAs), which are produced by bacteria when they ferment non-digestible carbohydrates. As a young cell biologist recruited to the French National Institute for Agriculture and Food Research (INRA) in the early nineties to study how dietary fibre impacts human health, I rapidly focused my research on these SCFAs, especially on butyrate. The study of these molecules has revealed local, intermediary, and peripheral effects on host tissues, showing how they may influence different aspects of host health through complex mechanisms.

Effects in gastrointestinal tract

The main role of SCFAs is as an energy source for host colonocytes through β-oxidation. SCFAs regulate cell proliferation through the release of growth factors or gastrointestinal peptides (e.g. gastrin), or through modulation of mucosal blood flow (Blottiere *et al.,* 2003). SCFAs are also known to influence genes that regulate cell proliferation and cell cycle (Siavoshian *et al.*, 2000). For example, the transcription factor AP-1 (activator protein-1) is implicated in cellular proliferation, transformation and death—and in 2012 our group demonstrated that SCFAs (in particular, butyrate) regulate the AP-1 signaling pathway (Nepelska *et al.,* 2012).

Butyrate indeed stands out as an important SCFA for regulating gene expression in the intestine. Our group previously found that MUC gene expression and mucin secretion were regulated by butyrate: its effects on different MUC genes could influence the characteristics of mucus gel and, thus, its protective ability. Further, we discovered that this upregulation of colonic mucins was enhanced when butyrate was the major energy source of the colonocytes (Gaudier *et al.,* 2004).

SCFAs have further effects in the intestine: they also appear to influence gastrointestinal motility (Cherbut *et al.,* 1997) in a complex manner that has been noted in humans and investigated in many animal models.

Effects on energy metabolism

SCFAs provide around 10% of daily energy for a human host but their role in metabolism is not fully understood. These molecules appear to have beneficial effects on host energy metabolism, including a role in reducing plasma concentrations of free fatty acids (Ge *et al.,* 2008) and cholesterol (Fushimi *et al.,* 2006), and/or decreasing plasma glucose levels (Sakakibara *et al.,* 2006). Work from our laboratory in collaboration with the Karolinska Institute in Stockholm had to do

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with ANGPTL4 (angiopoietin-like 4), a metabolism-altering protein produced by human intestinal epithelial cells. In an experiment with germ-free mice, we found that butyrate induced intestinal ANGPTL4 gene expression; this occurred with direct oral administration of butyrate, or with colonization with the SCFA-producing bacteria *Clostridium tyrobutyricum* (Korecka *et al.,* 2013). The molecular mechanisms of how SCFAs regulate metabolism, however, are not fully understood, and despite the observation that SCFAs may ultimately protect against obesity, they also provide calories that could contribute to obesity (Morrison & Preston, 2016).

Effects on immune system

In the late nineties, we and others reported that SCFAs, especially butyrate, display anti-inflammatory effects with potential applications to inflammatory bowel disease (Segain *et al.*, 2000). More recently, their role in the generation of differentiation of regulatory T cells has been revealed (Furusawa *et al.*, 2015). Through their known activation of G protein-coupled receptors and their influences on the activity of particular enzymes (namely lysine/histone deacetylase) and transcription factors, SCFAs influence the development, survival, and function of intestinal epithelial cells and leukocytes (Corrêa-Oliveira *et al.,* 2016). Very recent work showed that dietary fibre and SCFAs induced expression of the RALDH1 enzyme (a vitamin A converting enzyme) in intestinal epithelial cells, and that the RALDH1 expression levels in small intestinal epithelial cells correlated with a number of immune cell changes: altered dendritic cell activity, increased regulatory T cells, and higher luminal IgA production (Goverse *et al.,* 2017).

Effects on cancer

Several links exist between SCFAs and cancer—in particular, colorectal cancer (CRC). SCFAs may play a role in protection against CRC, perhaps by altering the intestinal environment or by modulating the local immune system in a way that reduces cancer risk (Keku *et al.,* 2015). In the years ahead, more research is needed on dietary fibre and SCFAs as they relate to CRC risk.

Conclusions

SCFAs are emerging as important molecules for host health. SCFA production is influenced by food intake and diet-induced changes in the gut microbiota (Ríos-Covián *et al.,* 2016), leading some to hypothesize that SCFAs constitute a key link between diet, microbiome, and health. There is still much to learn about the extent of SCFAs' effects on the human body, and probably even the brain. By combining mechanistic research with well-designed clinical studies we will advance knowledge of human SCFA production, uptake, and excretion, and the pathways by which these affect overall health.

Dr. Hervé M. Blottière

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Dietary fibre/short-chain fatty acids and vitamin A may protect mice against peanut allergy via gut microbiota

ALLERGIES, FOOD & INTOLERANCES, GUT MICROBIOTA, RESEARCH & PRACTICE
Published on September 21, 2016 by Andreu Prados

Andreu Prados holds a Bachelor of Science Degree in Pharmacy & Human Nutrition and Dietetics. Science writer specialised in gut microbiota and probiotics, working also as lecturer and consultant in nutrition and healthcare.

The incidence of food allergies has increased dramatically in Western countries over the past 20 years and the gut microbiota seems to be a promising target for preventing and treating them. However, mechanisms by which gut microbiota is involved in the loss of oral tolerance remain unclear.

A recent study, led by Dr. Charles Mackay from the Monash Biomedicine Discovery Institute and Department of Biochemistry and Molecular Biology at Monash University in Clayton (Australia), has found that the development of food allergies in mice could be linked to dietary elements including fibre and vitamin A.

The researchers examined the beneficial roles of dietary fibre in peanut allergy using mice. Mice were fed on diets either depleted or enriched in fibre for at least 2 weeks. High-fibre feeding enhanced the activity of mucosal CD103+ dendritic cells (DCs), which are the main regulators of immune tolerance through promoting the differentiation of naïve T cells into regulatory T (Treg) cells in the mesenteric lymph nodes (MLN). The fibre achieved this effect by upregulating retinoic acid-synthesizing (RALDH) enzyme activity and enhancing antigen-specific Treg cell responses.

To study the effects of dietary fibre on oral tolerance in vivo, zero-fibre- and high-fibre-diet-fed mice were subjected to a model of oral tolerance involving multiple challenges with peanut extract. Antigen-challenged high-fibre-diet-fed mice contained a greater proportion of CD103+ DC and Treg cells in the MLN 3 days after tolerance induction. Besides this, total cell numbers in the MLN of high-fibre-fed mice were also significantly lower, which indicates a reduced inflammatory response.

Zero-fibre- and high-fibre-diet-fed mice had an induced food allergy in an experimental model of peanut allergy. Protection from food allergy under the high-fibre diet was associated with reduced clinical symptoms of anaphylaxis on day 28-which correlated with lower levels of serum immunoglobulin E (IgE)-and an increased proportion of both CD103+ DCs and Treg cells

Zero-fibre- and high-fibre-diet-fed mice had an induced food allergy in an experimental model of peanut allergy.

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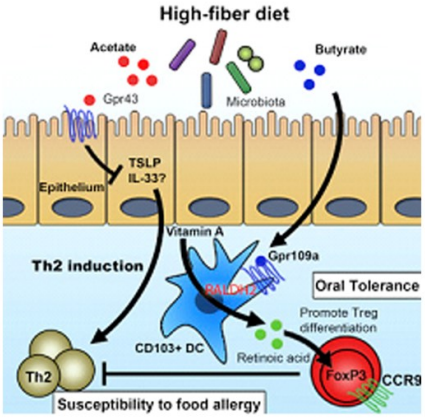
in the MLN (correlated with lower total cell numbers in the MLN). Other improved features observed in high-fibre-diet-fed mice were decreased production of T helper (Th)-2 cytokines IL-4, IL-5, and IL-13 from lymphocytes from the MLN and preserved gut epithelial permeability. High-fibre-mediated protection against food allergy relied on vitamin A metabolism and took place via promoting immunoglobulin A (IgA) and T follicular helper and mucosal germinal centre responses. Altogether, these results suggest that high-fibre feeding may enhance oral tolerance and protect mice against peanut allergy.

In order to study the role of gut microbiota composition in the protective role of high-fibre feeding in food allergy, germ-free mice inoculated with zero-fibre or high-fibre microbiota had a food allergy induced. Mice reconstituted with high-fibre microbiota had significantly better clinical anaphylaxis scores and a greater proportion of Treg cells compared to mice reconstituted with zero-fibre microbiota. Furthermore, the researchers investigated whether short-chain fatty acids (SCFAs), the end products of fermentation of dietary fibres by the anaerobic intestinal microbiota, could mediate the beneficial effects of dietary fibre in the experimental model of food allergy. Mice were fed with acetate, butyrate, or propionate for 3 weeks prior to initial sensitization and throughout the experiment. Mice fed with acetate and butyrate showed a reduction in anaphylaxis clinical scores and total serum IgE levels, which correlated with the induction of CD103+ DCs and Treg cell responses and a lower total cell numbers in the MLN. However, SCFAs did not protect mice against food allergy in the absence of a gut microbiota. Besides SCFAs, another pathway by which gut microbiota can protect against food allergy involves commensal bacteria-induced MyD88 signalling. The authors also found that the beneficial effect of dietary fibre in mouse peanut allergy involved activity of SCFA receptors GPR43 and GPR109a, by influencing CD103+ DC responses and gut epithelial integrity.



CREDIT: TAN *ET AL.*/CELL REP 2016

To sum up, dietary fibre/SCFAs together with vitamin A and a healthy gut microbiota play key roles in protecting mice against peanut allergy. According to the researchers: "These findings support the notion that diets deficient in fibre, typical of many Western countries, could underlie the rise of food allergies in recent decades".

Dietary fibre/SCFAs together with vitamin A and a healthy gut microbiota play key roles in protecting mice against peanut allergy.

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Fitness may predict a diverse gut microbiota in healthy people

GUT MICROBIOTA, MOOD & WELLBEING, RESEARCH & PRACTICE
Published on September 14, 2016 by Andreu Prados

Andreu Prados holds a Bachelor of Science Degree in Pharmacy & Human Nutrition and Dietetics. Science writer specialised in gut microbiota and probiotics, working also as lecturer and consultant in nutrition and healthcare.

It has been previously found that exercise may play an important role in the overall health of the host by contributing to the diversity of gut microbiota. However, extreme dietary differences, especially high protein intakes, amongst the elite athletes studied may confound interpretations about the specific role of exercise in determining gut bacterial richness. How physical fitness contributes to intestinal microbial diversity is currently not known.

A recent study, led by Dr. Deanna L. Gibson from the Department of Biology at the University of British Columbia (Canada), has found that cardiorespiratory fitness is correlated with increased microbial diversity and increased production of faecal butyrate in healthy humans.

The researchers used high-throughput sequencing to analyse faecal microbiota of 39 healthy participants with similar age, body mass index, and diet, but with varying cardiorespiratory fitness (CRF) levels, as assessed by the peak oxygen uptake (VO2peak). Faecal short-chain fatty acids (SCFAs) were also analysed using gas chromatography.

Diet was not a confounding factor across fitness groups, as there was a lack of distinct dietary patterns amongst all fitness groups (low fitness, n=14; average fitness, n=12 and high fitness, n=13). It was shown that VO2peak, an indicator of physical fitness, accounted for more than 20% of the variation in taxonomic richness, after accounting for all other factors such as diet. Although VO2peak was not associated with specific bacterial taxa, it was correlated with distinct microbiome functions including chemotaxis, motility, and fatty acid biosynthesis.

VO2peak was strongly correlated with faecal butyric acid, which was represented primarily across high and average fitness participants.

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Fitness may predict a diverse gut microbiota in healthy people

Increased butyrate levels were explained by increased abundances of key butyrate-producing taxa (*Clostridiales, Roseburia, Lachnospiraceae,* and *Erysipelotrichaceae*) among physically fit participants.

In conclusion, CRF, independent of diet, is correlated with increased microbial diversity and production of faecal butyrate. These findings support the use of exercise as an adjuvant therapy in combating those conditions associated with reduced microbial diversity such as diabetes, colorectal cancer, and inflammatory bowel disease.

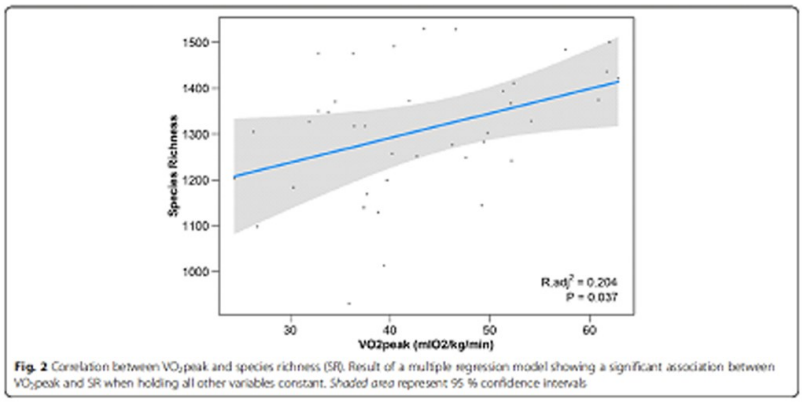

Fig. 2 Correlation between VO_2peak and species richness (SR). Result of a multiple regression model showing a significant association between VO_2peak and SR when holding all other variables constant. *Shaded area* represent 95 % confidence intervals

CREDIT: ESTAKI *ET AL.*/MICROBIOME 2016

These findings support the use of exercise as an adjuvant therapy in combating those conditions associated with reduced microbial diversity.

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An update on the link between short-chain fatty acids, diet, and human health

DIET, RESEARCH & PRACTICE, SCFA
Published on March 18, 2016 by Andreu Prados

Andreu Prados holds a Bachelor of Science Degree in Pharmacy & Human Nutrition and Dietetics. Science writer specialised in gut microbiota and probiotics, working also as lecturer and consultant in nutrition and healthcare.

A recent review, led by Dr Nuria Salazar from the Institute of Dairy Products of Asturias (Spain), belonging to the Spanish National Research Council, summarizes the up-to-date scientific evidence regarding the role of short-chain fatty acids (SCFAs) in host health and the impact of diet on their production.

SCFAs are the end products of fermentation of non-digestible carbohydrates (CHO) and proteins in the large intestine by the anaerobic intestinal microbiota. Acetate, propionate and butyrate represent 90-95% of the SCFAs present in the colon, whereas branched-chain SCFAs produced from dietary protein that is unabsorbed in the small intestine only represent 5% of total SCFAs production. Lactate is also produced by some members of the microbiota and is recycled into different SCFAs in order to avoid metabolic acidosis in the host.

SCFAs are produced by colonic microbiota through several metabolic pathways. Acetate is the most abundant one in the colon. It is noticeable that low levels of butyrate- and propionate-producing bacteria have been linked to inflammatory disorders, such as ulcerative colitis and asthma.

There is a high inter-individual gut microbiota variation, even among healthy individuals, both in organismal composition and in metabolic function. Diet impacts the gut microbiota composition and activity and, as a result, SCFA production may be affected. For instance, it has been found that high dietary fibre intake from fruit, vegetables, and legumes is linked to a rise in health-promoting SCFAs. Indeed, SCFA levels may be considered as a biomarker of a healthy status. Both epidemiological and intervention studies carried out with different populations have shown

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An update on the link between short-chain fatty acids, diet, and human health

that dietary components have an impact on microbial composition and can modulate the synthesis of SCFAs. The profile of SCFAs synthesized and their presence in faecal content may one day help us to distinguish populations with diseases such as obesity and irritable bowel syndrome. Knowing the SCFA profile in a person might shed light on how bacteria contribute to gut microbiota dysbiosis, which perhaps could be modulated by appropriate probiotics.

SCFAs have several effects on human health. They play an important role in the maintenance of the gut barrier function by reducing luminal pH and inhibiting some pathogenic microorganisms. Besides this, during intestinal absorption, SCFAs (mainly butyrate) are used as a source of energy by colonocytes and bacterial communities. SCFAs have also been reported to protect against the development of colorectal cancer and to control intestinal inflammation. Butyrate and propionate serve a number of epigenetic functions such as balancing histone acetylation and deacetylation activity, which can explain in part their biological effects. In addition, a new field of research shows that SCFAs may have a critical role in appetite regulation and energy homeostasis.

In conclusion, although it can be hypothesized that high levels of SCFAs are beneficial for host health, their role in the interplay between diet, gut, microbiota, and host energy metabolism is likely more complex. Further studies are needed in order to elucidate the role of SCFAs in mammalian energy metabolism and develop personalized strategies to mitigate disease risk through modulating SCFA production.

Knowing the SCFA profile in a person might shed light on how bacteria contribute to gut microbiota dysbiosis, which perhaps could be modulated by appropriate probiotics.

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Ríos-Covián D, Ruas-Madiedo P, Margolles A, Gueimonde M, de los Reyes-Gavilán CG, Salazar N. **Intestinal short-chain fatty acids and their link with diet and human health.** Front Microbiol. 2016. doi:10.3389/fmicb.2016.00185.

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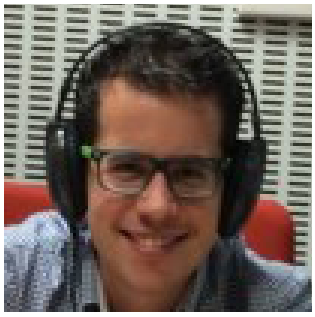
The role of gut microbiota composition and microbial metabolites in fat partitioning and carbohydrate metabolism in youth

GUT MICROBIOTA, GUT MICROBIOTA COMPOSITION, OBESITY, RESEARCH & PRACTICE, SCFA

Published on November 14, 2016 by Andreu Prados



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A previous study by Reijnders *et al.* has added to the body of research calling into question some direct and simple associations found between the gut microbiota and metabolic disorders.

Now a recent study, led by Dr. Nicola Santoro from the Department of Paediatrics at Yale University in New Haven, Connecticut (USA), has found that the gut microbiota of obese youth may drive a higher accumulation of energy than that of lean adolescents through an elevated production of short-chain fatty acids (SCFAs) and a higher capability to oxidize carbohydrates.

The researchers analysed the gut microbiota of 84 children and teenagers (7-20 years old; the participants included 27 youth who were obese, 35 who were severely obese, 7 who were overweight and 15 who were normal weight); in these individuals, body fat distribution was measured by fast-magnetic resonance imaging, de novo lipogenesis (DNL) was quantitated using deuterated water, and the capability of gut microbiota to ferment carbohydrates (CHO) was assessed by 13C-fructose treatment in vitro in faecal material. The participants also provided blood samples and kept a three-day food diary. Researchers measured plasma SCFAs but not faecal SCFAs.

The composition of the gut microbiota was associated with the degree of obesity and the distribution across body fat depots. Specifically, researchers found a significant association between the *Firmicutes* to *Bacteroidetes* ratio, and the abundance of *Bacteroidetes* and *Actinobacteria*, with body mass index (BMI), visceral and subcutaneous fat. These data show that children and teenagers who are obese have different gut microorganisms than their lean counterparts.

In addition, plasma levels of acetate, propionate, and butyrate were associated with weight gain (expressed as changes of BMI/year) over a 2-year period independent of age, gender, and ethnicity (84 subjects were analysed at baseline and 72 subjects were analysed at follow-up). Strikingly, plasma SCFA concentrations were also linked to hepatic DNL in obese adolescents. Besides this, the rate of CHO fermentation from the gut microbiota was higher in obese than in lean subjects.

In conclusion, this study has shown for the first time that for similar amounts of dietary energy,

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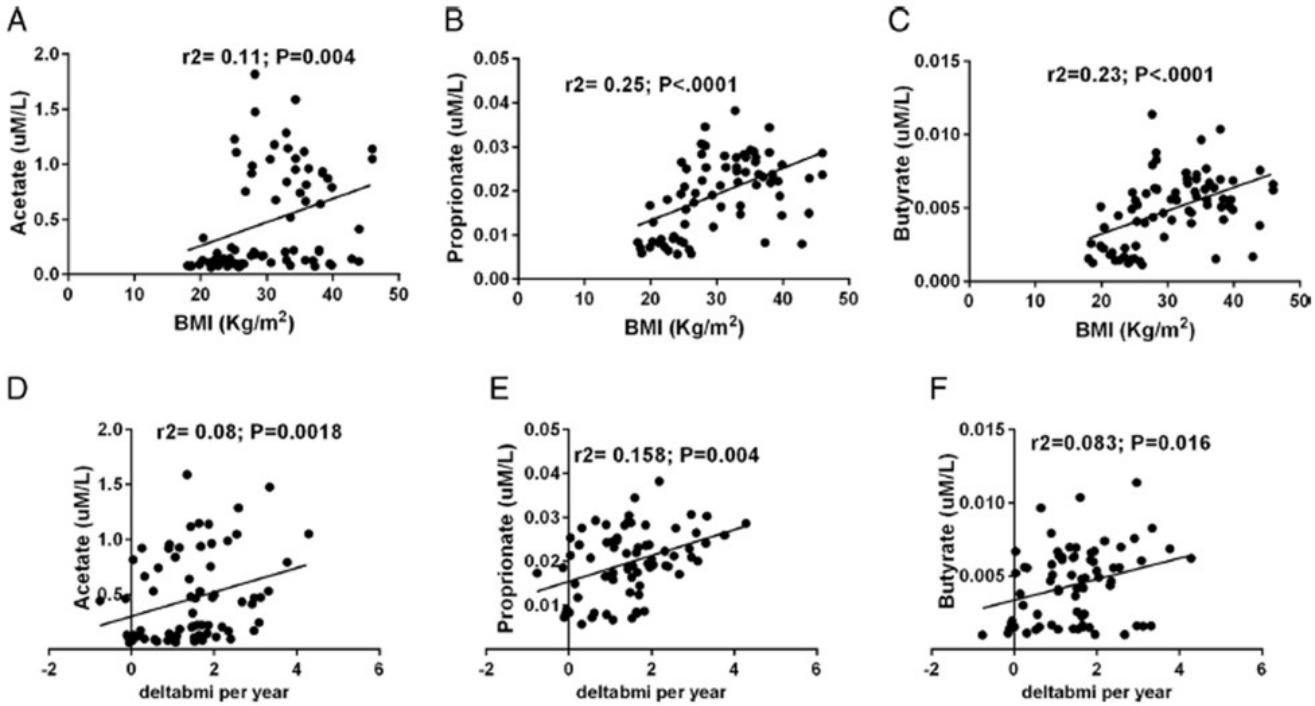
The role of gut microbiota composition and microbial metabolites in fat partitioning and carbohydrate metabolism in youth

in children and adolescents the composition of the gut microbiota is associated with increased fat deposits. The gut microbiota of obese youth may drive a higher accumulation of energy than that of lean counterparts through an elevated production of SCFAs as measured in the plasma, which in turn could enhance hepatic DNL causing lipid accumulation in all the fat depots.

This trial has highlighted the need for more follow-up studies to more deeply investigate the relationship between changes in gut microbiota composition and activity and both microbial metabolites and host metabolism. Although this study showed levels of plasma SCFAs were linked to obesity, other work tends to show SCFAs are beneficial for health.



CREDIT: GOFFREDO *ET AL.*/J CLIN ENDOCRINOL METAB 2016

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The role of short-chain fatty acids in driving obesity: Should we blame acetate?

FIBERS, GUT MICROBIOTA COMPOSITION, METABOLIC CONDITIONS, OBESITY, PREBIOTICS, RESEARCH & PRACTICE, SCFA
Published on August 5, 2016 by Patrice D. Cani

Professor Patrice D. Cani is researcher from the Belgian Fund for Scientific Research (FRS-FNRS), group leader in the Metabolism and Nutrition research group at the Louvain Drug Research Institute (LDRI) from the Université catholique de Louvain (UCL), Brussels, Belgium, and WELBIO (Walloon Excellence in Lifesciences and BIOtechnology) investigator.

In a recent paper by Perry *et al.*, researchers describe an investigation into the putative mechanisms by which gut microbiota alterations may lead to obesity, insulin resistance, and metabolic syndrome. Authors describe increased production of acetate by altered gut microbiota in rats. They link this to activation of the parasympathetic nervous system, increased glucose-stimulated insulin secretion, higher ghrelin secretion, hyperphagia, and obesity. Thus, they point to increased acetate production as a driver of metabolic syndrome.

Those in the field have known for decades that microbes produces acetate (see here, for example) and that this acetate may contribute to changes in liver lipid metabolism as well as glucose metabolism and food intake. Thus, it is well known that chronically increasing acetate abundance can drive lipogenesis. A link between acetate and diabetes has been also shown in the past, although it is still debated.

The association between microbes and neuronal routes, in addition, has been well described: for example, here.

The key contribution of this paper by Perry *et al.* is the discovery that in vivo turnover of acetate is specifically influenced by the gut. In addition, they used a collection of interesting and sophisticated tools to demonstrate that acetate can directly increase glucose-stimulated insulin release, affecting both the gut-brain axis and peripheral sites.

Attributing all of the observed effects to changes in acetate, however, is likely premature. Among the short-chain fatty acids (SCFAs), acetate is probably the most debated in terms of its beneficial or detrimental metabolic effects.

In the paper by Perry, *et al.*, authors did not discuss another key body of work showing that prebiotic fermentation by the gut microbiota can increase the abundance of SCFAs, including (in some studies) the overall pool of SCFAs. For example, it has been shown that acetate is increased with prebiotic fructooligosaccharides (FOS) (see here), and that this is associated with reduced body weight and fat mass, decreased diabetes, and a lower food intake. Another related paper by Gary Frost and colleagues showed that prebiotics such as inulin (C13 labeled) increased acetate that reached the brains of rats and reduced ghrelin production, leading to a reduction in food

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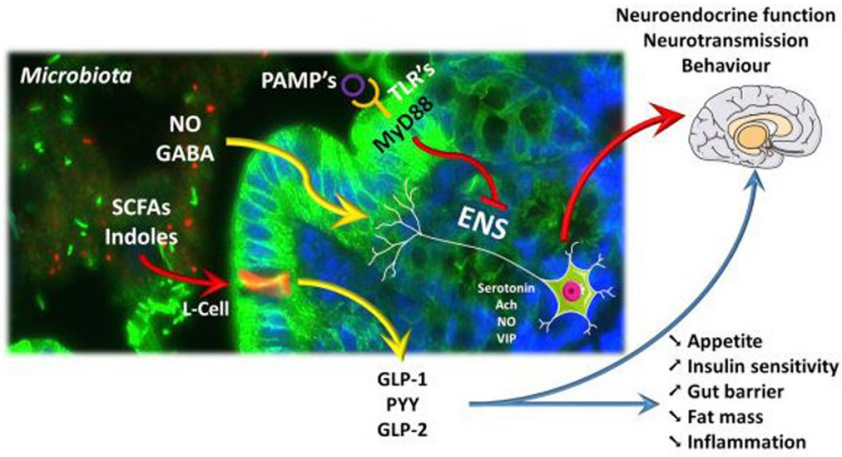
The role of short-chain fatty acids in driving obesity: Should we blame acetate?



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intake, body weight, and fat mass through mechanisms involving neuronal activity. The effects of acetate in this context, therefore, seem to be contrary to those in the current study Perry and colleagues.

Another complexity not explored in the Perry, *et al.* work is that the microbiota rapidly transform acetate into other SCFAs. The 10 days of intragastric infusion of SCFA probably changed both the microbiota and the overall SCFA profile in the gut. Ratios of SCFAs are also important to consider: if the ratio of acetate to propionate is changed, for example, the real abundance of acetate can be increased. So here it remains unclear whether the observed effects are attributable to the acetate itself or to products of the cross-feeding.

A key question about these mechanisms is what drives the secretion of specific hormones. The authors used a protocol of acetate administration for 10 days, and the intragastric route means it would be rapidly absorbed—but this may also change hormonal routes. Thus, the question of whether changes in secretion of specific hormones is due to luminal mechanisms (in the intestine/stomach) or blood-driven mechanisms is not yet resolved.

In the Perry, *et al.* study, acetate probably did strongly contribute to the changes observed in the rodents, but unfortunately the authors did not put their findings into the general picture of the important literature showing that fermentation of specific dietary fibres may have an impact on SCFAs (including acetate) and on metabolism. As an ultimate example, the recent paper by De Vadder *et al.* elegantly shows that, in response to dietary fibres, another product of microbiota fermentation (succinate) can be a precursor of glucose production in the gut but can improve glucose homeostasis by a mechanism depending on intestinal neoglucogenesis.

Thus, addressing the central idea of the Perry, *et al.* paper when it comes to humans, acetate may or may not be the driver of obesity; most likely, it is dependent on the microbiota and the dietary fibres used (e.g. resistant starches, prebiotics). Overall, it seems the story of how the gut microbiota drive obesity is not yet complete.

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http://www.gutmicrobiotaforhealth.com/en/role-short-chain-fatty-acids-driving-obesity-blame-acetate/

SELECTED CONTENT

Conserving and restoring the human gut microbiome by increasing consumption of dietary fibre

DIET, FIBERS, RESEARCH & PRACTICE
Published on MAY 9, 2016 by Andreu Prados

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Modern lifestyle and Western diet have led to a substantial depletion of gut microbial diversity, which is linked to many non-communicable diseases (NCDs). In a recent commentary published in Trends in Endocrinology & Metabolism by researchers from the University of Alberta (Canada), it has been argued that we need to reconsider nutritional recommendations to focus on fibre in an attempt to restore proper composition and function of the 'disappearing' gut microbiome.

Recent research in this area suggests that dietary fibre recommendations should be refigured in future. Although dietary fibre intake recommendations for adults range from 18-38 g/d (see table below), this seems not to be enough to prevent NCDs. Beneficial effects of dietary fibre have been broadly studied, but only in recent years have researchers investigated to what extent they are mediated by changes in both composition and function of the gut microbiota. Microbiota-accessible carbohydrates (MACs) found in plant-derived fibre are the primary substrates for certain gut bacteria in humans. In fact, rural human communities from South America and Africa have a low prevalence of NCDs and this fact has been related to a higher gut microbiota diversity, driven by a market economy based on vegetables, fruits, wild game meat and fish for sustenance without including flour-like products and processed food. This suggests that following a plant-based diet is a nice step forward in order to keep a more diverse gut microbiota, as it prioritizes at the first level the consumption of vegetables, fruits and legumes, which are known to be rich sources of dietary fibre; the current Western diet is high in fat and simple carbohydrates and low in fibre. A second step may be fibre supplementation of widely consumed foods (fortified foods) or even taking fibre supplements if healthy eating habits are achieved.

Although revised recommendations should move in the direction of increased dietary fibre, there is still no consensus about the ideal daily amount. A recent study, led by Dr. Kishore Vipperla from the Division of General Internal Medicine at the University of Pittsburgh (USA), showed that moving African Americans to a traditional South African diet with a daily dose of 55 g of dietary fibre- mainly in the form of resistant starch-and reduced fat and protein improved mucosal biomarkers of colon cancer risk within just 2 weeks. Together, these results suggest that current guidelines

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Country/Region		Recommended fiber intake (g/day)	Median intake (g/day)	Body issuing the requirement
US and Canada	Males	38	16.5-19.4	North America – Jointly use the IOM report from the National Academy of Sciences
	Females	25	12-15	
France	Males	30	21	*Agence française de sécurité sanitaire des aliments* (French food safety agency)
	Females	25	17	
Germany	Males	30	24	German Nutrition Society
	Females	30	21	
Japan	Males	30	17	Japanese Ministry of Health
	Females	25	17	
UK	Males	18*	15.2	UK Department of Health
	Females	18*	12.6	
FAO/ WHO		>25		WHO/FAO
		>20		

*Lower requirements due to use of the NSP method.

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for the consumption of fibre rich foods are too low and increasing the fibre recommendation to more than 50 g/d in African Americans, and perhaps in all populations consuming a Western diet, is likely to have an immediate effect on colon cancer risk. This level of fermentable fibre intake in human subjects correlates well with estimates of dietary fibre intake for ancient diets and traditional high-fibre diets in the Mediterranean, Africa and China.

Even now, dietary fibre intake in most countries around the world is far below recommended levels. The gap between dietary fibre recommendations and intakes is so extreme in Western countries, as most Westerners only consume half of the amount of dietary fibre recommended by guidelines; this has been referred as the "fibre gap". A study in mice showed that loss of gut bacteria diversity related to low-fibre diet may be inherited and irreversible over generations. Thus, enriching the food supply with dietary fibre might have an essential role in preventing lost of certain beneficial bacterial species. Beyond boosting the consumption of dietary MACs, the researchers suggest reintroducing missing taxa that were lost through modernization, which can be achieved either by administering probiotics (food) or live biotherapeutics (drugs).

In conclusion, it's time to change nutritional recommendations to focus on fibre, as it is the primary substrate for nourishing gut microbial communities. Concomitantly, people should be encouraged to consume quantities of fibre that more closely match the recommendations. Enriching the food supply with dietary fibre seems a plausible approach.

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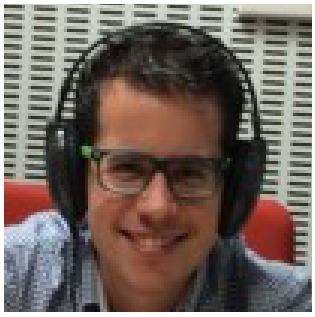
SELECTED CONTENT

Mice study shows low-fibre diet may decimate gut bacteria diversity over generations

DIET, FIBERS, RESEARCH & PRACTICE
Published on March 9, 2016 by Andreu Prados



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According to a recent study by Stanford University School of Medicine researchers, gut microbe deterioration from low-fibre diets may be inherited and irreversible over generations.

Microbiota-accessible carbohydrates (MACs) found in plant-derived fibre have a beneficial impact on gut microbiota. In the study, mice colonised with human gut microbes were fed a diet rich in dietary fibre (high-MAC) for 6 weeks and divided into two groups. One group was fed a low-MAC diet for 7 weeks, after which they returned to the high-MAC diet for a further 6 weeks. The control group was fed a high-MAC diet throughout the experiment. In both groups, diets were identical in terms of protein, fat and calorie content. After the first 7-week period, 60% of the bacterial species in the low-fibre group showed a dramatic decline in abundance compared with only 11% of the control group. When these mice were returned to a high-MAC diet, 33% showed a lower rate of abundance. The control group did not change significantly. Although gut bacteria in the mice that had consumed a low-fibre diet partly recovered, one-third of the original species did not see their gut microbiota fully restored despite their return to a high-fibre diet.

To study the influence of the different diets on subsequent generations, the researchers bred mice from the two groups and weaned their pups over four generations. By generation four of fibre deprivation, there was an irreversible disappearance of more than two-thirds of the bacterial species identified in the first-generation's gut microbiota. This result was driven by the low-MAC diet and switching low-MAC-diet mice to the high-MAC diet did not influence the outcome. Although high dietary fibre was insufficient in restoring microbiota composition or diversity to control levels, faecal transplantation together with a high-MAC diet did

Adopting a high-fibre diet may be beneficial for the gut microbial ecosystem of both the person consuming the diet and their future generations.

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result in microbiota diversity and composition restoration in the fourth-generation low-fibre mice.

These results support a model in which consuming a modern diet low in fibre could contribute to bacteria loss in the intestine over generations and may be responsible for the less diverse microbiota observed in the industrialised world compared with the diet among hunter-gatherers and rural agrarian populations.

In conclusion, according to the model used, adopting a high-fibre diet may be beneficial for the gut microbial ecosystem of both the person consuming the diet and their future generations. In short, these results suggest that gut microbiota diversity is a key regulator of host health.

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