Galacto-Oligosaccharide has no Effect on Glucose Tolerance, inflammatory Markers or Intestinal Permeability in well-controlled Type 2 Diabetes

Camilla Pedersen[1], Paul Hinton[2], Edith Gallagher[2], Felicity Horton[2], Richard Ellis[3], Umer Z. Ijaz[4], Huihai Wu[1], Etana Jaiyeola[1], Onyinye Diribe[1], Glenn R. Gibson[5], Thibaut Duparc[6], Patrice D. Cani[6], John Wright[1,7], David Russell-Jones[1,7], Roberto La Ragione[1] and M. Denise Robertson[1]

[1]*Faculty of Health and Medical Sciences, University of Surrey, GU2 7XH, UK,* [2]*Medical Physics – Nuclear Medicine, Royal Surrey County Hospital, GU2 7XX, UK,* [3]*Animal and Plant Health Agency, Addlestone, KT 15 3NB, UK,* [4]*School of Engineering, University of Glasgow, G12 8QQ, UK,* [5]*Department of Food and Nutritional Sciences, University of Reading, RG6 6AP, UK,* [6]*Louvain Drug Research Institute, Université catholique de Louvain, Belgium* and [7]*CEDAR Centre, Royal Surrey County Hospital, GU2 7RE, UK*

Aberrant microbiota composition and function have been linked to several intestinal and systemic pathologies, including obesity, the metabolic syndrome and type 2 diabetes[1]. In animal models, prebiotics improve glucose tolerance which may be linked to concurrent favourable changes in the intestinal microbiota, intestinal permeability and endotoxaemia[2].

This is the first study to investigate the link between intestinal permeability, glucose tolerance, and intestinal bacteria in human type 2 diabetes. 30 males with well-controlled type 2 diabetes were randomised to a prebiotic, galacto-oligosaccharide (GOS, 5 g/day), or placebo (maltodextrin) supplementation for 12 weeks. Glucose tolerance, intestinal permeability, endotoxaemia, inflammatory markers and intestinal bacterial composition were assessed at baseline and post-intervention. Intestinal permeability was measured by urinary excretion of ^{51}Cr-EDTA and glucose tolerance by insulin modified IVGTT. Gut microbial community analysis was performed by high-throughput Next-Generation Sequencing of 16S rRNA amplicons and quantitative PCR.

GOS had no significant effects on glucose tolerance, intestinal permeability or inflammatory markers compared with placebo. Non-metric Multi-dimensional Scaling analysis suggested GOS affected intestinal bacterial composition differently to the placebo; however, there were no significant differences in bacterial abundances between treatment groups at any taxonomic level. Nevertheless, changes in the bacterial family *Veillonellaceae* correlated inversely with glucose response (r = −0·90, P = 0·042) and IL-6 (r = −0·90, P = 0·042) in the GOS group. Changes in fasting serum lipopolysaccharide binding protein concentration correlated with fasting blood glucose (r = 0·79, P = 0·0026) in the placebo group.

Lack of effect of GOS in this study may be due to the low dose and the short duration of the supplementation, although concurrent metformin treatment may have masked the effects of GOS. Furthermore, whilst the high heterogeneity of human diabetes compared to animal models may also have played a role, it is also plausible that prebiotics may play a more important role in prevention rather than in the treatment of human type 2 diabetes. However, the small sample size was a limitation of this study.

1. Qin J, Li Y, Cai Z, Li S, Zhu J, Zhang F, *et al.* A metagenome-wide association study of gut microbiota in type 2 diabetes. (2012) *Nature* **490**, 55–60.
2. Cani PD, Neyrinck AM, Fava F, Knauf C, Burcelin RG, Tuohy KM, *et al.* (2007) *Diabetologia* **50**, 2374–83.

Proceedings of the Nutrition Society