CORRESPONDENCE

Some additional considerations on: "Finding the sweet spot: glycosylation mediated regulation of intestinal inflammation"

Mucosal Immunology (2022) 15:525; https://doi.org/10.1038/s41385-022-00512-z

We read with enthusiasm the recent review by Brazil and Parkos 'Finding the sweet spot: glycosylation mediated regulation of intestinal inflammation' in Mucosal Immunology[1]. The authors have elegantly summarised the literature in relation to how chronic inflammation induces changes in intestinal and immune cell glycosylation. We would like to highlight that the interaction between glycome and the microbiome can have systemic effects, as manifested by the changes in the total serum *N*-glycome[2], which occur in recurrent *Clostridiodes difficile* infection (rCDI) patients after successful fecal (or intestinal) microbiota transplantation (FMT/IMT). In our study, we analysed total serum and IgG subclass-specific Fc *N*-glycome profiles in sera archived from two independent trials comparing capsule vs. colonoscopy delivered IMT (discovery cohort)[3] and fresh vs. frozen IMT (replication cohort)[4]. We compared glycan signatures before and again at 4 weeks following IMT. Interestingly, whilst we detected no statistically significant changes in IgG *N*-glycosylation profiles, we identified 11 serum glycans that changed significantly with IMT. Successful IMT associated with decreasing complexity of the serum *N*-glycome, which was mainly driven by a significant reduction in the relative abundance of high-branching, tetragalactosylated, and tri-sialylated glycans and a concomitant increase in low branching, monosialylated, digalactosylated, oligomannosidic, and bisecting *N*-acetylglucosamine glycans. While the mechanisms underpinning IMT remain incompletely understood, the *N*-glycome can serve as a biomarker predicting IMT treatment outcome in rCDI patients[2]. As IMT and other live biotherapeutics are also being explored as potential treatments for other chronic diseases[5,6] including ulcerative colitis, serologic and immune cell glycosylation should be further explored as potential biomarkers to identify patients most likely to respond to this type of treatment, to monitor treatment response and to develop alternative druggable targets to restore intestinal homeostasis.

Tanya M. Monaghan [1,2]✉, Dina Kao[3] and Gordan Lauc[4]
[1]*NIHR Nottingham Biomedical Research Centre, University of Nottingham, Nottingham, UK.* [2]*Nottingham Digestive Diseases Centre, School of Medicine, University of Nottingham, Nottingham, UK.* [3]*Division of Gastroenterology, Department of Medicine, University of Alberta, Edmonton, AB, Canada.* [4]*University of Zagreb, Faculty of Pharmacy and Biochemistry, Zagreb, Croatia and Genos Glycoscience Research Lab, Zagreb, Croatia.*
✉*email: Tanya.Monaghan@nottingham.ac.uk*

REFERENCES

1. Brazil, J. C. et al. Finding the sweet spot: glycosylation mediated regulation of intestinal inflammation. *Mucosal Immunol.* **15**, 211–222 (2022).
2. Monaghan, T. M. et al. Decreased complexity of serum *N*-glycan structures associates with successful fecal microbiota transplantation for recurrent *Clostridioides difficile* infection. *Gastroenterology* **157**, 1676–1678 (2019).
3. Kao, D. et al. Effect of oral capsule vs colonoscopy-delivered faecal microbiota transplantation on recurrent *Clostridium difficile* infection: a randomized clinical trial. *JAMA* **318**, 1985-1993.
4. Lee, C. H. et al. Frozen vs fresh fecal microbiota transplantation and clinical resolution of diarrhea in patients with recurrent clostridium difficile infection: a randomized clinical trial. *JAMA* **315**, 142–149 (2016).
5. Ghani, R. et al. The potential utility of fecal (or intestinal) microbiota transplantation in controlling infectious diseases. *Gut Microbes* **14**, 2038856 (2022).
6. Wortelboer, K. et al. Fecal microbiota transplantation beyond *Clostridioides difficile* infections. *EBioMedicine* **44**, 716–729 (2019).

AUTHOR CONTRIBUTIONS

T.M: conceptualisation, writing original draft, critical revision, final approval. D.K and G.L.: critical revision, final approval.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Tanya M. Monaghan.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 5 March 2022 Accepted: 26 March 2022
Published online: 6 April 2022