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Title

Some additional considerations on: “Finding the sweet spot: glycosylation mediated regulation of intestinal inflammation”.

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*-glycome², which occur in recurrent *Clostridioides 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)⁵ and fresh vs. frozen IMT (replication cohort)⁶. 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 patients². As IMT and other live biotherapeutics are also being explored as potential treatments for other chronic diseases³⁻⁴ 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.

Author contributions

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

Additional information

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Competing interests

The authors declare no competing interests.

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