GUT MICROBIOME

# Gut microbiota drives disease variability in the DSS colitis mouse model

Forster, S. C. et al. *Nat. Microbiol.* **7**, 590-599 (2022)

Inflammatory bowel diseases (IBDs) are disorders of the gastrointestinal tract caused by multiple genetic and environmental factors. Several murine models have been developed to characterize the complexity of IBD pathogenesis and to improve therapeutic options. Among these, the dextran sulphate sodium (DSS)-induced colitis model has been increasingly used for IBD research, despite important experimental variability, which limits the interpretation of the data. In *Nature Microbiology*, Forster et al. report that differences in gut microbiota composition contribute to the variability in disease susceptibility observed in DSS-treated mice.

To identify the factors impacting the DSS model, the investigators administered DSS to 579 genetically identical C57BL/6N mice from 14 distinct parental lineages that were originally derived from a single breeding pair. Analysis of the mice ten days post-DSS treatment revealed considerable differences in intestinal pathology and weight change between mice from different parental lineages, which confirmed disease variability, even among mice sharing a similar genetic background.

To determine whether differences in microbiota composition could explain the phenotypic variation, the investigators colonized germ-free mice with fecal samples from different parental lineages. Following DSS treatment, recipient mice reproduced the disease phenotype observed in the respective donor lineage, indicating that microbiota composition can influence the response to DSS.

Further analysis of the gut microbiome of the mice identified two species, *Duncaniella muricolitica* and *Alistipes okayasuensis* associated with worse disease outcome after DSS treatment. These disease-causing taxa reproduced a severe DSS response when used to monocolonize germ-free mice, confirming the causal link between these species and the severity of DSS colitis. "Our results suggest that the presence of specific gut bacterial taxa before DSS exposure may influence disease severity and outcome, possibly by either priming or protection from disease," explain the investigators in their report.

Finally, the team analyzed mouse microbiome datasets from 31 institutes across 12 countries, which revealed that *D. muricolitica* and *A. okayasuensis* are common, but not ubiquitous, in animal facilities around the world, which may confound experimental results.

"Overall, our work suggests that the application of metagenomics techniques to report microbiota composition, in addition to the genetic and disease phenotypes being described, should represent a standard minimum requirement for the DSS mouse model," conclude the investigators.

Alexandra Le Bras

Published online: 22 April 2022
https://doi.org/10.1038/s41684-022-00975-4