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A Specific Mutation in Muc2 Determines Early Dysbiosis in Colitis-Prone Winnie Mice

Dr. Law:
For ReachMD, this is AudioAbstracts, produced in collaboration with the Crohn's & Colitis Foundation. I'm Dr. Ivy Law, an Assistant Project Scientist in the Center for Inflammatory Bowel Diseases at the University of California, Los Angeles, as well as a member of the Crohn's & Colitis Foundation's Rising Educators, Academics, and Clinicians Helping IBD group, or REACH–IBD. Today, I'll be reviewing an article published in the *Inflammatory Bowel Disease* journal titled "A Specific Mutation in *Muc2* Determines Early Dysbiosis in Colitis-Prone *Winnie* Mice."

Inflammatory Bowel Diseases, or IBD for short, describe a group of gastrointestinal disorders that include Crohn's disease and ulcerative colitis. Interactions between environmental factors, host genetics, and gut microbiome play an important role in developing IBD pathophysiology. Focusing on host genetics, the authors of this article studied the perspective changes in fecal microbiota under the influence of *Muc2* mutation, which is a gene encoding for mucin. Mucins are major protein components in the intestinal mucus layer. In fact, the intestinal mucus layer is both a habitat of intestinal microbiome and a barrier that separates the microbiota from the intestinal epithelial cells. To investigate the changes in fecal microbiota, *Winne* mice were the transgenic mouse model used in this study because they carry a missense mutation in *Muc2* and have been shown to have a less compact inner mucus layer that leads to spontaneous development of ulcerative colitis-like symptoms.

In this study, *Winne* mice and their wild-type littermates were separated by genotype and were observed from 4 to 16 weeks. During this period, *Winnie* mice gained less weight and had more watery stools when compared to their wild-type counterparts. Histological evaluation revealed the development of colonic inflammation, indicated by increased epithelial erosion and immune cell infiltration in colons. After confirming the induction of colitis at 16 weeks, DNA was extracted from fecal matter collected at 4, 8, and 16 weeks and was sequenced to reveal differences in fecal microbiota between wild-type and *Winnie* mice.

An analysis of 16S rRNA metagenomics showed that there were differences in relative abundance in bacterial phyla present in fecal samples taken from wild-type and *Winnie* mice. Furthermore, the relative abundance of genus level changed over the period of experiments and also between wild-type and *Winnie* mice. For example, the bacterial genus *Bacteroides* was in higher abundance in *Winnie* mice than in wild-type mice over time; while for genus *Paraprevotella*, its relative abundance was reduced in wild-type mice over time but increased in *Winnie* mice.

It's also important to note that although *Bacteroides* was in higher abundance in *Winnie* mice, previous studies showed the relative abundance of *Bacteroides* was significantly lower in patients with Crohn's Disease or Ulcerative Colitis, especially in the active phase of disease. This observation reflects the potential differences between mouse models and our disease population in pathophysiology and microbiota composition.

Despite the above limitations, the results of this study demonstrate that host genetics is a driving force to modify intestinal microbiome footprint, which is an important element in IBD pathophysiology. Furthermore, this study also provides evidence showing that mutations in *Muc2*, or other alterations in intestinal mucus layers, impact the maintenance of intestinal homeostasis and IBD pathophysiology.

If you're interested in this topic or others on Crohn's disease or ulcerative colitis, the Crohn's & Colitis Foundation's *Inflammatory Bowel Diseases* journal provides the most impactful and cutting-edge clinical topics and research findings. For more information on the Foundation, please visit crohnscolitisfoundation.org.

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