

How does the gut microbiota respond to iron replacement?

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Interior view of an intestine with Crohn's disease. Credit: Fotolia/ Juan Gärtner

Iron deficiency is often an issue in patients with inflammatory bowel



diseases. An international and interdisciplinary research group under the aegis of the ZIEL Institute for Food & Health (ZIEL) at the TU Munich has now investigated how the intestinal microbiota responds to oral or intravenous iron replacement. Both lead to an improved iron balance but the bacterial community in the gut is substantially altered depending on the route of iron administration.

"Supplying iron either orally or intravenously has a very distinct effect on the intestinal microbiota," says Professor Dirk Haller of the Technical University of Munich (TUM). "The study shows how fragile the stability of the microbial community is, especially in patients with Crohn's disease. Crohn's disease and ulcerative colitis are the two most common forms of chronic inflammatory bowel diseases and are incurable. "These diseases are much more complex than infections driven by commensal bacteria from the normal flora. However, we don't know which bacteria are involved in the disease process," Professor Haller explains. The study, he says, has shown how sensitively the gut microbiota responds to iron replacement.

The result of the human study initiated by ZIEL was published in the February issue of the journal *Gut* of the British Society of Gastroenterology. A team of scientists including Professor Philippe Schmitt-Kopplin of the Helmholtz Zentrum München and Professor Richard Fedorak of the University of Alberta in Canada were involved in the three-month study coordinated by Professor Haller. Previously, the impact of an iron replacement therapy had only been observed in mice, but human data were lacking.

First study on the response of the intestinal microbiota to iron replacement

The 72 subjects of the study were recruited at a Canadian hospital: 31 of



them had Crohn's disease, 32 ulcerative colitis and 19 were anemic due to other causes. Half the subjects took iron sulfate, while the other half received intravenous iron sucrose. The altered bacterial communities and metabolic products were evaluated by high-throughput sequencing and mass spectroscopy of stool samples taken from the patients before and after therapy.

Crohn's disease patients with an unstable intestinal flora particularly benefited from intravenous iron replacement, says Prof. Haller of the Chair of Nutrition and Immunology of TUM. However, the change in the intestinal microbiota showed no influence on disease activity during the study period; this leads to the conclusion that short-term therapy does not lead to exacerbation of the bowel disease but might increase the risk for disease flares due to an instable bacterial ecosystem.

Exemplary cooperation of ZIEL and the Helmholtz Center

For ZIEL Director Haller, this study is an exemplary project designed to translatebasic research into clinical practice. In the past year, ZIEL created a novel infrastructure in microbiome research to allow high-level researchand to intensify international and interdisciplinary cooperation. "In this study we combined microbiome and metabolome expertiseto understand the role of gut bacteria as a true intermediary between environment and the human health," Haller says

More information: Thomas Lee et al. Oral versus intravenous iron replacement therapy distinctly alters the gut microbiota and metabolome in patients with IBD, *Gut* (2016). DOI: 10.1136/gutjnl-2015-309940



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