



March 14-15th, 2015, Barcelona

Fact sheet #4

Crohn's disease: Gut microbial collaborations trigger inflammatory diseases

Only to a small extent have the underlying causes of Crohn's disease and ulcerative colitis been revealed so far. This is a major obstacle for a fundamental improvement of diagnostic and therapeutic approaches. Recent findings presented by Prof. Dirk Haller (Technische Universität München, Munich, Germany) at the Gut Microbiota for Health World Summit that took place in Barcelona, March 14-15, 2015, give reason to hope that this situation might be overcome in the near future. One key to the solution is the gut microbiota composition.

In Europe about 500 out of 100.000 persons suffer from ulcerative colitis (UC) and 320 from Crohn's disease (CD). In North America UC affects 250 and CD 320 per 100,000.

Over the past decades inflammatory bowel diseases (IBD) have become a major burden in many countries of the world. IBD are caused by a complex interplay of genetics, gut microbes and environmental factors. Meanwhile 163 genetic regions have been identified that are involved in the onset of IBD and increase the risk to develop these diseases. However, genetic factors alone do not

induce IBD, another important player being the gut microbiota as Prof. Dirk Haller (Technische Universität München, Munich, Germany) pointed out. Patients with ulcerative colitis and Crohn's disease are characterized by changes in the gut microbial ecosystem, although it is unclear whether this is cause or consequence of the disease. In order to look into the mechanisms underlying the genesis of Crohn's disease Prof. Haller used germ-free mice in which part of their immune defense was genetically modified, thus increasing their susceptibility to inflammatory diseases. However, in spite of their genetic predisposition the mice did not develop IBD as long as they remained germ-free. The situation changed after several strains of intestinal microbes had been introduced into their guts.



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Bacterial collaboration induces disease

One of the crucial questions is whether single microbial species or strains can be identified as “malefactors” that trigger the disease, or if we are dealing here with a collaborative action that involves different kinds of bacteria, depending on the specific composition of the gut microbiota. His findings suggest that the latter is true: “We found that the transfer of dysbiotic microbial ecosystem – that is, a compositionally imbalanced microbiota – induced Crohn’s while the transfer of unrelated microbial consortia or single bacterial strains, although commonly associated with CD, did not have this effect. All our results point towards a community effect of the complex microbiota and gain of aggressive, or loss of protective mechanisms, rather than the selection of aggressive phylotypes as single agents causing Crohn’s disease,” said Prof. Haller

“Understanding the true nature of a dysbiotic and disease-conditioning microbiota seems of essential importance to judge the risk of relapse in IBD patients after therapeutic intervention.”

Prof. Dirk Haller

To accurately identify detrimental microbial profiles is highly important for future clinical applications: “Understanding the true nature of a dysbiotic and disease-conditioning microbiota seems of essential importance to judge the risk of relapse in IBD patients after therapeutic intervention.” The same applies to fecal microbiota transplantation (FMT). This therapy has proven quite successful for treating Antibiotics-associated diarrhea (AAD), but not – so far – for treating IBD.

“In AAD-patients the microbiota diversity is so heavily reduced that the transfer of mostly any microbiota with normal diversity is likely to improve the patient’s intestinal health. But with IBD things seem to be more intricate. To successfully apply FMT in Crohn’s patients it will be crucial to find appropriate donors whose microbiota meets exactly the required compositional type. Investigations to fill the remaining gaps of knowledge are under way and will hopefully improve the situation of IBD patients in the near future”, explained Prof. Haller.

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