

Press release

Inflammatory bowel diseases

The challenging road to personalized medicine

Oxford. The call for personalized medicine, currently heard louder and louder in almost all medical specialties, does not stop at inflammatory bowel diseases. Gastroenterologists hope that this will deliver highly effective and at the same time well-tolerated treatments for each patient. The road to this goal is challenging because it requires intensive basic research in the fields of pathophysiology, genetics and immunology. To state the obvious: Despite all the recent innovations, there is still a considerable “medical need”. “I am predicting that in 20 to 30 years we will have a diagnostic system allowing us to analyze the patients accurately and tell them which medication will be best for them. Before that, however, we still must solve many exciting problems,” says Prof. Markus F. Neurath, Erlangen, Germany, scientific organizer of Symposium 214 of the Falk Foundation e.V.

Although new drugs are constantly being developed, the treatment of inflammatory bowel diseases (IBD) is anything but satisfactory. “Due to complications caused by the disease, 70% of patients with Crohn’s disease still have to undergo surgery in the course of their lives, while the rate for ulcerative colitis is around 30%. In addition, there are many patients suffering from the side effects of the medical treatment protocols currently in use,” said Neurath outlining the current situation. Only in recent years it has been possible to gain deeper insights into the pathophysiology, immunology and genetics on which personalized medicine can build. Yet, it is already feasible to employ the available medications in a more targeted way.

Risks of thiopurines: also a question of genetics

According to Prof. Maria. C. Dubinsky, New York, the favorable effect of thiopurines (e.g. Azafalk®) in combination with TNF-alpha inhibitors on clinical symptoms and mucosal healing is well established. The substance levels of the TNF-alpha inhibitors are higher and the ADA (Anti-Drug-Antibody) titers lower. But the risks of thiopurines, above all myelosuppression and pancreatitis, are also well known. In the future, genetics could potentially facilitate targeted therapy. For example, it appears that certain gene variants of NUDT15 are associated with a significantly higher risk of thiopurine-induced myelosuppression. These patients could be identified by NUDT15 genotyping

prior to treatment. HLA-DQA1-HLA DRB1 polymorphism in particular is associated with a high risk of thiopurine-induced pancreatitis.

Which biologics for which patient?

Biologics are effective, but far less than 50% of those treated achieve complete remission within 52 weeks, Prof. Jean-Frederic Colombel, New York, made clear. Given the increasing number of biologics, he called for more data comparisons from meta-analyses, real-world data and direct head-to-head studies. Ultimately, the goal is to match the right active substance to the right patient. As predictors for non-response to TNF-alpha inhibition he identified higher age, very early onset-IBD (VEO-IBD), biomarkers such as low albumin, but also the gene expression in intestinal tissue, including increased intestinal expression of TNFAIP6, S100A8, IL11, GOS2, and S100A9TREM-1.

Microbiome: Making bacteria colonize

In at least some of the patients with IBD the microbiota plays a significant role in the course of the disease, explained Prof. Ailsa Hart, London. As demonstrated by the positive effects of fecal transplantation in ulcerative colitis it also appears to be a therapeutic target. However, many questions remain unanswered, including which donor will be ideal and which dosage form feasible. At the same time, it must be considered whether it would be enough to transplant "normal" bacteria or whether they would have to be modulated in order to colonize and survive. It is then necessary to find out which patients might benefit from modulating the microbiome and for whom the classical TNF-alpha inhibition would be the right strategy. But above all, it is necessary to find out in which order the available treatment options are employed.

Patient stratification is the future

According to Prof. Geert D` Haens, Amsterdam, only a few evidence-based treatment recommendations take phenotypic biodiversity into account. For him, the future belongs to patient stratification. From his point of view, diagnostic tools to determine the course of the disease will be just as popular in everyday practice as point-of-care diagnostics.

Falk Foundation e.V. honors young scientists **“Recognition and Incentive”**

It is a well-established tradition at the Falk Foundation e.V. symposia that young scientists are awarded poster prizes. This was not different at Symposium 214 in Oxford:

The young researchers at Oxford were eagerly awaiting the award of the poster prizes. “For the young scientists this is a recognition of their work up till now. At the same time, the award is an incentive to pursue this road further and in the long run stay involved in the field of inflammatory bowel diseases,” said Prof. Markus F. Neurath, Erlangen, at the award ceremony. “They see that their work is read and appreciated and that it is worth the effort. Poster prizes such as those awarded by the Falk Foundation e.V. therefore support the scientific commitment in the field of IBD and further advance therapy.”

Awards were presented to the following three researchers:

Dr. Dominik Aschenbrenner, Oxford, for his study: “An IL-1-dependent IL-23 inflammatory monocyte signature correlates with disease severity and treatment response in patients with inflammatory bowel disease”.

Luz del Carmen Martinez-Sanchez, Erlangen, for her study: “Rac1-mediated maintenance of epithelial integrity in the gut”.

Dr. Polychronis Pavlidis, London, for his study: “The interleukin-22 transcriptional programme is activated in human colonic inflammation and associated to anti-TNF-alpha primary non response in Crohn’s disease”.



From left to right: Prof. M.F. Neurath, Dr. D. Aschenbrenner, L. Martinez-Sanchez, Dr. P. Pavlidis, Carola Falk (for Falk Foundation e.V.), Photo: © Kai-Uwe Wudtke, Freiburg, Germany

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