IBD 2017 – Therapeutic and Biological Barriers

Symposium 209
Berlin (Germany), October 6–7, 2017

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IBD 2017 – Therapeutic and Biological Barriers
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Inflammatory bowel disease: Improved understanding of the disease – targeted treatment

Intensive research activity in recent years has led to a much improved understanding of Crohn’s disease and ulcerative colitis. The resulting increased knowledge of the pathogenesis of these diseases has made it possible to develop new therapeutic approaches that are now becoming established. In addition to new drugs, other innovative new treatment options have also been developed for inflammatory bowel disease (IBD). Even though these treatments are still experimental, it can be assumed that the current period of breakthrough that we are seeing in IBD will lead to further advances in both diagnosis and treatment in the future.

Autologous stem cell transplantation is another innovative approach to IBD treatment. Initial experience with the use of this method in the treatment of IBD indicates that the procedure may trigger a kind of “immunological reset”. However, autologous stem cell transplantation will likely be reserved for serious cases for the foreseeable future.

With the new drug-based therapies, there is a particular focus on local treatment. The rationale behind this focus is based in large part on the positive results achieved with drugs such as mesalazine, and locally active steroids such as budesonide. We are currently seeing significant further development of this concept. Several substances that are locally released (and therefore primarily act locally in the epithelium) are currently in clinical development.

More new systemically active drugs that target the altered signaling that is present in IBD are also likely to be approved. All in all, in light of the many new developments in the field of IBD, it appears fitting to say that we are in the midst of a breakthrough period. The road we are on is leading to a focus on targeted, personalized treatment that is based on the patient’s situation and on the underlying pathogenetic factors of the disease.

Prof. Dr. Britta Siegmund
on behalf of the scientific organizing committee
Crohn’s disease and ulcerative colitis: Overcoming biological and therapeutic barriers

There have been major developments in the treatment of inflammatory bowel disease (IBD). Over the course of the past few years, there has been a steady stream of new biologics that have become available, and other active small molecules are in development. Furthermore, the importance of localized treatment appears to be increasing. The concept of gut-specific efficacy (as it is used in the case of mesalazine and topically active steroids, for example) is currently being developed to a next level. In addition, there is also an increasing focus on overcoming biological and therapeutic barriers in order to establish new treatment options. IBD treatment is therefore increasingly tailored to the patient’s individual situation. This became evident at the 209th International Symposium of the Falk Foundation e.V. in Berlin.

The great efforts that have been made in the field of basic and translational research in inflammatory bowel diseases such as Crohn’s disease and ulcerative colitis are now bearing fruit. B. Siegmund, Berlin (Germany), scientific organizer of the symposium, explained that “Various treatment strategies, and particularly drugs have been developed that allow us to provide an ever more targeted treatment of IBD.” As an example of the marked progress that has been made in the treatment of IBD, B. Siegmund cited the new biologics and new “small molecules” that are profoundly widening the spectrum of treatments available for IBD at the moment. This trend is set to continue in the future thanks to multiple innovative substances that are currently in the pharmaceutical pipeline.

Treatment innovations on various levels

In addition to these new medications, there are also new treatment approaches, such as stem cell transplantation and fecal microbiota transplantation – but these approaches are still experimental. Nevertheless, they have the potential to be prospectively implemented in the therapy of IBD. D. Haller, Freising (Germany), explained that in the case of fecal microbiota transplantation, the aim is to correct the dysregulation of the microbiome, since this has a significant effect on mucosal homeostasis, thus contributing to the pathogenesis of IBD. It is known from cohort studies in IBD patients that changes in the intestinal microbiota certainly can affect disease manifestations. The etiology of this is complex, but it can be assumed that there are various interactions between the genetic predisposition, environmental factors, the intestinal microbiome, and the immune system. Although the links between the factors are well known, it is currently impossible to establish a concrete microbe-based risk profile. For example, the changes in the microbiota and the microbial composition that constitute a clinically-relevant, pathogenesis producing dysbiosis have not been clearly defined. Furthermore, the microbiome itself is affected by environmental factors. Thus, a better understanding of the cross-talk of the intestinal microbiota and the host immune system will be a prerequisite to identify therapeutic strategies.
Local treatments in focus

There is currently a focus on locally-acting treatment procedures for IBD, for example treatment with mesalazine and topically active steroids such as budesonide, which have been in use as standard treatments for some time now. According to B. Siegmund, there are currently several substances in clinical development that are released locally and that primarily deliver their effect via the epithelium. There are various approaches to such treatments. One example is “small-molecule inhibitors”, according to R. Atreya, Erlangen (Germany). According to J. Wehkamp, Tübingen (Germany), attempting to strengthen endogenous mechanisms that work against disease pathogenesis would also be feasible. J. Wehkamp cited the example of defensins, which basically function as endogenous antibiotics, thus affecting the microbiome. Therefore, it would likely be possible to develop functionally active defensins that would modulate the microbiome.

Target-oriented treatment – an option for the future

Prospectively, the novel local as well as systemic treatment strategies will not only offer more options for our patients but will at the same time require to reconsider our treatment algorithms. This is important because according to L. Godny, Petah Tikva (Israel), a customized approach is required due to the heterogeneous nature of IBD. It is therefore crucial that patients are properly stratified, and that the treatment approach is adapted to take into account the current state of scientific knowledge about the disease. According to P.D.R. Higgins, Ann Arbor (USA), treatment must also be optimized for the individual patient’s specific metabolism. In the state-of-art lecture by S. Schreiber, Kiel (Germany), it was made clear that even in the future, it is unlikely that there will be any single treatment that will be optimally suited to all patients with Crohn’s disease and ulcerative colitis. For the moment, there is no sign of a “magic bullet” that can be used to treat all patients. Therefore, in future, the focus will be on the development of customized treatments that are optimized for the patient’s individual phenotype, and the approach that will be taken to achieve this will be combined treatment using new substances and standard therapeutic agents, along with modulation of the microbiome.

Fecal microbiota transplantation – still something of a mystery

The fact that we do not yet know exactly how fecal microbiota transplantation works can be considered one of the most persistent barriers to establishing it as a treatment option for IBD. According to M. Joossens, Leuven (Belgium), the idea is to implant feces from a healthy donor into the gastrointestinal tract of a patient, with the aim of normalizing the dysbiosis. The objective of this treatment is to promote the growth of phyla that have a positive effect, and suppress the growth of those that have a negative effect. However, what actually happens when fecal microbiota transplantation is performed is largely unknown: “We are working with a mechanism that is a mystery to us,” explains the microbiologist.

It therefore comes as no surprise that the success of fecal microbiota transplantation as a treatment is limited to recurrent Clostridium difficile infection, for IBD further clinical studies are required. Among a group of six patients with Crohn’s disease, only one of them exhibited any improvement in their symptoms, and the improvement was temporary. In a group of eight patients with ulcerative colitis, two achieved a remission of more than two years, and one patient achieved temporary improvement of symptoms. On the other hand, in five cases, there was no clinically-relevant change. “These are sobering results,” said M. Joossens.

Target-oriented treatment – an option for the future

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Adapting treatment to the patient’s individual circumstances

The range of treatment options for IBD has expanded significantly in recent years. The challenge now is to manage treatment in such a way that the patient’s symptoms are alleviated in the long term – without side effects as far as possible – and to achieve full remission. Treatment should aim for a remission that lasts so that the patient’s quality of life is improved. Personalized treatment is required in order to achieve this. The parameters of the disease, such as disease activity and the disease site, must be given as much attention as the particular factors relating to the patient. Particular factors relating to the patient may include pregnancy, advanced age, or a history of cancer.

Older patients – frequently a challenge to treat

According to G. Savoye, Rouen (France), treating older IBD patients often represents a particular challenge in the everyday clinical setting. The number of older people with Crohn’s disease and ulcerative colitis is constantly increasing. This is mainly due to demographic change in society – an aging population. Apart from this, there is also “late onset IBD”, in which the disease manifests at a more advanced age.

The practical challenges begin with diagnosis. The symptoms may initially appear to point to other conditions, such as an infection, and may not be recognized as symptoms of IBD at first. For this reason, in the case of older patients in particular, the possibility that the patient may have Crohn’s disease or ulcerative colitis should be taken into account whenever relevant symptoms are present. If IBD is suspected, extra care should be taken due to the fact that older patients are a high-risk group. Treatment for this group must be planned very carefully.

“Multimorbidity is present in almost all cases, so the potential for drug-drug interactions should be taken into account given that the patient may be taking multiple medications,” explains G. Savoye. Special care should be taken when using new substances because in many cases, these substances have not been used in older people sufficiently to ensure their safety for this group. With the modern biologics, there are also some red flags when it comes to side effects. In older patients, some weakening of the immune system can be assumed, and this weakening makes it more difficult to use immunosuppressants. “A very close eye must be kept on the potential of the substances to cause side effects,” G. Savoye emphasizes, specifically highlighting the need for more study data on use in older patients.

However, treatment with established substances such as mesalazine and steroids is usually possible without any problems – although topically active steroids such as budesonide should nevertheless be preferred. Treatment with the standard therapeutic agents is typically sufficient in older people because when IBD occurs in this group, it generally has only a mild or moderate disease course.
IBD treatment after cancer

Similar to treatment at an advanced age, IBD treatment during and after cancer poses a medical challenge according to L. Beaugérie, Paris (France). As a general rule, immunosuppressants should be discontinued if an IBD patient is diagnosed with cancer. The exceptions to this rule are an initial diagnosis of a non-aggressive basal cell carcinoma and controlled cervical dysplasia caused by HPV. Apart from these exceptions, as far as possible, IBD treatment should proceed without any immunosuppressants being prescribed for two to five years after the end of the cancer treatment. This approach should be followed unless it cannot be justified due to the severity of the IBD and there is no therapeutic alternative.

The potential for interactions between the cancer treatment and the natural course of the IBD, and between the cancer treatment and the IBD treatment should also always be taken into account. Furthermore, treatment with docetaxel, sunitinib, sorafenib, or cancer immunotherapies such as CTLA-4 and PD-L1 inhibitors can cause exacerbations of ulcerative colitis. In addition, anti-TNF treatment is absolutely contraindicated in the case of patients with malignant melanoma.

Microbiome equals oncobiome?

Patients with a history of cancer also need to be aware of the increased risk of IBD relapse and of the increased risk of developing other forms of cancer, as L. Beaugérie explains: “This should be taken into account in the case of younger patients in particular.”

C. Jobin, Gainesville (USA), emphasized that carcinogenesis can also be triggered by the microbiome. Furthermore, there is mounting evidence that the microbiome can function as a kind of “oncobiome”. For example, associations have been observed between the strains Escherichia coli and Campylobacter jejuni and an increased risk of colorectal cancer. However, these associations are not yet fully understood. Nevertheless, it is clear that a particular microbiome composition can equate to a risk factor for the development of cancer. Dietary factors can be a decisive factor in this context, but so can chronic inflammatory activity.

Interleukin 1 as the initial trigger of inflammation?

Another thing that remains unclear is exactly how inflammatory processes are initiated. According to B. Simoes Franklin, Bonn (Germany), proinflammatory cytokines of the interleukin-1 family (IL-1) could play a central role here: “Our current knowledge suggests that they may represent the starting point of inflammation.”

It has long been suspected that neutrophils play a central role in this process. Now however, there is growing evidence that this is not true, and that the thrombocytes (platelets) are in fact far more important.
Can we learn something from pouchitis?

The mechanisms of the pathogenesis of IBD are not yet fully understood. I. Dotan, Petah Tikva (Israel), postulates that the occurrence of pouchitis following proctocolectomy and the formation of a pouch as an anal anastomosis could shed some light on the issue. Around 25% of patients undergo proctocolectomy in the course of their disease, and about 60% of those experience pouchitis. This likely occurs through mechanisms that are similar to the mechanisms through which ulcerative colitis and Crohn’s disease manifest.

Fistulating disease – a medical challenge

According to M. Scharl, Zürich (Switzerland), the formation of fistulae in Crohn’s disease is another serious complication. One in two Crohn’s patients develop a fistula in the course of their disease, and about a third experience repeated formation of fistulae. Generally speaking, drug-based treatments are not very effective in dealing with this. Often, the patients have to undergo multiple surgical procedures.

In brief

According to L. de Nes, Amsterdam (The Netherlands), in such situations, it is not unusual for a colostomy bag to be required, and unfortunately, in many patients, the creation of an artificial bowel outlet cannot be reversed. In about one third of cases, an attempt is made to reverse the procedure and restore bowel continuity. However, this is only successful in approximately 17% of patients.

H. Yanai, Petah Tikva (Israel), explains that Crohn’s patients often develop perianal fistulae, which massively impair their quality of life. According to A. Dignass, Frankfurt (Germany), this particularly applies to complex fistulae, which generally cannot be adequately treated through surgery alone. Instead, a multidisciplinary approach is required. Regardless of whether they undergo a surgical procedure, patients usually need to be treated with antibiotics and require anti-TNF treatment; they may also require treatment with newer therapeutic agents such as vedolizumab or ustekinumab. According to A. Dignass, drug-based treatment often initially leads to astounding therapeutic effects. However, the results usually disappoint when an attempt is made to discontinue the medication, meaning that long-term treatment is likely unavoidable.
In the case of severe fistulae that cannot be managed in any other way, D. Garcia-Olmo, Madrid (Spain), postulates that stem cell transplantation can also be considered as a treatment option. Various procedures are currently being tested, with the aim of the treatment always being to achieve an "immunological reset".

**Stem cell transplantation as a last resort?**

A. Radbruch, Berlin (Germany), reports that experience with stem cell transplantation has been gained in other fields, including rheumatology. With stem cell transplantation it is also possible to eliminate the memory cells that cause pathogenesis, to break through autoimmunity, and practically restore tolerance.

M. Allez, Paris (France), points out that a distinction should be made between hematopoietic stem cell transplantation (HSCT) that can be done with autologous stem cells and HSCT that can be done with allogenic stem cells. The results of the ASTIC study show that autologous HSCT can achieve three months of steroid-free clinical remission in 38% of patients with treatment-refractory Crohn’s disease. One in two patients exhibited mucosal healing in the long-term follow-up. “We do not yet expect a cure. However, HSCT appears to be able to modulate the course of the disease in a favorable way,” M. Allez explains.

**Treatment during and after pregnancy**

C.J. van der Woude, Rotterdam (The Netherlands), points out that pregnancy is also a very special treatment situation. If a female patient wants to have children, it is important that she be given comprehensive advice and support. It is also important to try to achieve full remission for at least six months prior to conception because elevated disease activity limits fertility and can also have other unfavorable effects on the course of the pregnancy.

However, in principle, pregnancy is not contraindicated in women with Crohn’s disease or ulcerative colitis, as long as their disease is under control. Most of the drugs that are administered to treat IBD can continue to be administered during pregnancy in order to prevent disease activity flaring up again. In the case of a relapse and elevated disease activity, treatment can generally also be initiated during pregnancy.

In terms of the available drugs, according to C.J. van der Woude, both mesalazine and corticosteroids can be considered low-risk for use during pregnancy. The same applies to thiopurine and anti-TNF drugs. However, we do not yet have sufficient data for a risk assessment of vedolizumab and ustekinumab. There is a clear contraindication for the use of methotrexate and thalidomide.
For and against: Treat to target

There is currently a heated debate about whether the “treat to target” concept, which is already established in rheumatology, should also be applied to IBD. **F. Baert**, Roeselare (Belgium), spoke in favor of adopting such a strategy in order to achieve complete disease management from the very beginning as far as possible. This is because in IBD, clinical activity is only the tip of the iceberg, and certainly does not provide adequate guidance for how to treat.

Rather, the aim of treatment should be to normalize biochemical, endoscopic, and histological activity. In concrete terms, the aim should be complete healing of the clinical symptoms that can be attributed to IBD, including the secondary symptoms such as fatigue or depression. The inflammatory parameters should be normalized and a deep, steroid-free remission as well as mucosal healing should be achieved.

**G. Rogler**, Zürich (Switzerland), spoke against the treat to target concept with the rationale that such a treatment aim always requires invasive treatment, and therefore carries risks for the patient. In his view, aiming for mucosal healing in all patients is also unrealistic: “We are currently only achieving this target in 40% of patients.” The consequence: if we follow the treat to target concept, we are forced to quickly switch medications, leading to frustrated doctors and frustrated patients, because in many patients, this treatment aim simply cannot be achieved. The concept also forces over-treatment, which in turn leads to a substantial cost burden and significant risks of side effects.

Medical challenge: IBD in children

**H. Uhlig**, Oxford (Great Britain), highlighted children with very early disease manifestation as another subgroup of patients that represent a medical challenge. “In concrete terms, we are talking here about children under six years of age,” says H. Uhlig. In these cases, the disease is usually due to a genetic defect. The children affected typically have very severe intestinal inflammation that is also often resistant to treatment.

In order to treat, the genetic defect and its effects must first be identified.

It is therefore necessary to investigate whether the patient may have an impaired barrier function, impaired anti-microbial activity in the bowel, a mutation affecting IL-10 signaling, or impaired regulation of T cell activity (which triggers inflammatory reactions). Information about the cause of the disease can help guide the choice of treatment.
In this context, G. Fiorino, Rozzano (Italy) pointed out that a good response to the modern biologics is far from universal among patients, even though this is often assumed. Only about 40% of IBD patients exhibit a good response to these medications. It is also important to bear in mind that some people exhibit a good treatment response initially, but this effect is lost in the further course. Therefore, regular monitoring is advisable.

Regarding the cost of the medication, P.L. Lakatos, Montreal (Canada), pointed out that biosimilars of biologics for IBD treatment are available.

Involving patients in treatment decisions

When caring for IBD patients, it is also important to directly involve them in treatment decisions. In the opinion of J. Moreau, Toulouse (France), patients are often overwhelmed by the flood of unfiltered information from various sources that is given to them following a diagnosis. Often, they also have to contend with unfamiliar medical jargon. This can lead to feelings of helplessness and of being a victim of circumstances. “Therefore, it is important to ensure that patients are adequately educated. Such patient education should help to meet patients’ needs and should improve their quality of life enormously,” says J. Moreau.

According to M.D. Long, Chapel Hill (USA), it is important to bear in mind that patients’ treatment goals may differ from those of the doctor. Surveys have shown that patients expect effective treatment with long-term efficacy, rapid onset of effect, and low risk of side effects. With regard to the side effects, patients are particularly concerned about the possibility of an increased risk of cancer.

According to P. Munkholm, Herlev (Denmark), patients explicitly want to be involved in treatment. Telemedicine is a useful tool for implementing this approach.
Symposium 210

Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment

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Scientific Organization
F. Magro, Porto (Portugal)
A. Dignass, Frankfurt (Germany)
Poster prizes: Recognizing successful scientists

At the Falk Foundation e. V. symposia, young scientists who present particularly relevant research projects via posters are awarded poster prizes for their achievements on a regular basis. The prize winners of Symposium 209 are:

Poster prize 1: **R. Bruckner**, Zürich (Switzerland), for the poster: "Novel human gut xenograft mouse model for intestinal fistulas."

Poster prize 2: **J.L. Pérez-Hernandez**, Mexico-City (Mexico), for the poster: "Very early-onset inflammatory bowel disease in a patient with an IL10 receptor deficiency due to a novel homozygous IL10RB mutation."

Poster prize 3: **F. Tran**, Kiel (Germany), for the poster: "Atg16L1 orchestrates interleukin-22-signalling in the intestinal epithelium via cGAS/STING."
Causes of IBD: Interplay between many factors
Prize for “outstanding achievements in the field of gastroenterology”

Prof. Dr. Joseph Sung, President of the Chinese University of Hong Kong, received the “International Herbert Falk Award 2017” on the occasion of the 209th Symposium of the Falk Foundation e. V. in Berlin. In his laudatory speech, Prof. Dr. Jürgen Schölmerich, Hofheim (Germany), the coordinator of the prize committee, emphasized that J. Sung was receiving the 40,000 euro prize for his extraordinary achievements in the field of gastroenterology.

J. Sung’s field of research is inflammatory bowel disease (IBD), with a focus on the role of the microbiome in Crohn’s disease and ulcerative colitis. As J. Sung explained in his speech at the award ceremony, the incidence and prevalence of IBD is also steadily increasing in Asia. One reason for this appears to be the increasing adoption of the western lifestyle in Asian countries, as the increase in incidence rates is particularly noticeable in cities, whereas in rural areas, IBD is diagnosed much less frequently.

J. Sung believes that the increase in the incidence of IBD is mainly due to a change in the microbiome, which occurs as a result of changing lifestyles, and he believes that the “rural microbiome” is likely to play a protective role. Conversely, the increasing consumption of fast food and ready meals with a high fat and sugar content, especially in urban areas, appears to be encouraging the development of IBD.

The role of the microbiome as an area of research

J. Sung and his research team are currently investigating the significance of the bacterial colonization of the intestine in early childhood, exactly which factors are responsible for the alteration of the microbiome, how these factors affect the development of IBD, and how the microbiome itself can trigger the development of metabolic syndrome. The scientist is also investigating how certain dietary measures can cause microbial selection, as well as what the significance of potential interactions between the microbiome and viruses, fungi, or even a colonization of the bowel with worms may be.

The “International Herbert Falk Award” is awarded by the Falk Foundation e. V. Freiburg in memory of its founder, Dr. Dr. Herbert Falk. It recognizes candidates with exceptional achievements in the field of diagnostics, treatment and prevention in gastroenterology. The previous prize winners are Professor Dr. Paul Rutgeerts from Leuven, Belgium (2010), and Professor Dr. Claudio Fiocchi from Cleveland, USA (2013).

Herbert Falk (1924–2008) was born in Müllheim in 1924. His family moved to Freiburg, where his father established his own pharmacy, which Herbert Falk later took over. Herbert Falk studied pharmacy and medicine, and ultimately founded Dr. Falk Pharma GmbH in Freiburg, specializing in the development and distribution of drugs for the treatment of diseases of the liver and the digestive tract. The continuing education concept of the Falk Foundation e. V., which was both developed and practiced by Herbert Falk, remains unique to this day. To date, the foundation has held 209 international scientific symposia on topics pertaining to gastroenterology and hepatology, as well as many workshops, seminars and regional training events taking place every year.
Relevant progress is currently being made in terms of our understanding of inflammatory bowel disease (IBD) and in terms of the treatment options. As scientific organizer of the 209th Symposium of the Falk Foundation e. V. in Berlin, Prof. Dr. Britta Siegmund of Charité – Universitätsmedizin Berlin (Germany), explained what new developments this might open up in the future. B. Siegmund believes that we are currently in a “breakthrough period” in inflammatory bowel disease.

Editor: To what extent are we currently experiencing a breakthrough in inflammatory bowel disease?

Prof. Siegmund: There has never been a time with more advances in the field of inflammatory bowel disease than now. We have made great progress in terms of our understanding of the disease, and at the same time, new treatment strategies, and above all, new drugs have been developed. We now have new biologics, as well as new small molecules, which means that we can tailor treatment to the patient’s individual circumstances better than ever. This trend is set to continue, as there are still many more substances in clinical and preclinical development. Apart from this, there are other new treatment approaches, such as stem cell transplantation and fecal microbiota transplantation, which currently are still experimental treatments, but may also have the potential to advance the treatment of inflammatory bowel disease.

Will this also open the door on new therapeutic aims?

The primary aims of treatment in IBD are to relieve the patient’s symptoms, achieve full clinical remission, maintain remission in the long term, and improve the patient’s overall quality of life. The aims are not likely to change any time soon.

To what extent have new treatment strategies already become established in everyday clinical practice?

In recent years, new treatment options such as integrin antagonists, and more recently antibodies against IL-12/IL-23, have made their way into clinical practice. Janus kinase inhibitors are also expected to be approved soon, and more new substances are in the pipeline. The range of treatment options for IBD is therefore continuously expanding, and it can be assumed that new treatment options will continue to make their way into clinical practice in the future.

Does this mean that the established treatment options will become less important?

The established treatment options will continue to play an important role for patients who respond well to them in the future. However, for patients with high disease activity, and patients who do not respond adequately to the standard treatment in general, we now have ever more opportunities to implement targeted treatment using the new drugs. We are also learning from standard treatment. Various approaches aimed at local treatment (as is currently typical in the case of local application of topical steroids and mesalazine) are in development. For example, there are currently several substances in clinical development that are released locally and that primarily deliver their effect via the epithelium. Generally speaking, going forward, new local treatments and new systemic treatment options should make it ever easier to leverage our improving understanding of inflammatory regulation in order to design targeted treatments that are optimized to deal with each patient’s individual disease.

What is the role of the microbiome in this context?

The microbiome shapes the immune system, which in turn can contribute to the development of chronic diseases in the long term. According to current knowledge, faulty development of the microbiome and mucosal immunology appears to contribute significantly to the pathogenesis of IBD. We must therefore improve our understanding of the microbiome in order to better understand IBD. This is a very exciting research area, because a better understanding of the underlying mechanisms may also contribute to the establishment of new treatment options for IBD, such as stem cell transplantation, which may in turn help to make an "immunological reset" possible.
**In light of this, what will the significance of fecal microbiota transplantation be in the future?**

Fecal microbiota transplantation is an interesting approach, but I do not think that it will become a widely used treatment option in the future. Instead, I am convinced that we will develop more elegant ways of influencing the microbiome in a targeted manner.

**The symposium also focused on the situation of older patients with IBD. What makes this issue so relevant?**

Inflammatory bowel disease is generally considered a disease of the young. However, this is only partly true, and demographic changes in society are at the root of the issue. The number of older people in the population is constantly increasing. It follows that the number of older patients with Crohn’s disease or ulcerative colitis requiring treatment in the everyday clinical setting must also increase. Apart from this phenomenon, there is also “late onset IBD”, in which IBD manifests at a more advanced age. Generally speaking, when treating older people, there are specific problems that have to be taken into account, such as the frequent presence of multimorbidity and the large number different medications taken as a result. Older patients are also more susceptible to infections than younger patients – a factor that should be taken into account when treating with immunosuppressants, for example. This example alone makes it clear that in this area too, treatment must be well adapted to the patient’s individual situation.

**What is the role of patient involvement in IBD?**

In the long term, chronic diseases can only be treated by working with the patient. This is why the symposium also focused on strategies for involving patients in their treatment. Good compliance can only be achieved if patients understand the necessity of the treatment and accept the treatment strategies that are adopted. Therefore, we must ask how patients themselves perceive the treatment, how they receive treatment suggestions, and how they can be motivated to cooperate and thereby ultimately exhibit good adherence. In addition, the possibilities opened up by modern telemedicine represent good starting points for involving the patient in treatment planning and monitoring more than ever before. This approach could be of particular interest in regions with relatively few physicians, where it is difficult for patients to present quickly to their treating physician if necessary. However, this is still just the beginning of development in this area, and we need to gain further experience.

**Professor Siegmund, thank you very much for the interview.**
HALF A CENTURY OF PROMOTING MEDICAL EXCHANGE

Conferences that advance medicine and research: 50 years ago, Herbert Falk, MD, PhD, organized a week-long event in Freiburg devoted to the liver – it was his first symposium and the start of an extraordinary success story.

Since then, 207 additional events have been held worldwide, featuring speakers who are pioneers in their fields. To date, more than 130,000 physicians and researchers from around the world have participated in our symposia, and the strong interest in our upcoming events shows that this concept remains appealing. We take great pride in this! Since the very beginning, all of our events – whether large or small – have been based on the principle of providing neutral continuing medical education that benefits research, treatment, and ultimately the patient.

We would like to offer our deepest thanks to everyone who has participated, and we look forward to further advancing scientific dialogue as we continue to advocate for more knowledge sharing and therapeutic progress!

Allow us to welcome you to the Falk Foundation symposia – now and for many years to come!
Speakers, moderators and scientific organizers

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International Symposia and Workshops

Scientific Dialogue in the Interest of Therapeutic Progress

Workshop
Liver-Gut-Microbiome Interactions
Hamburg, Germany
January 25 – 26, 2018

Symposium 210
Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment
Lisbon, Portugal
April 20 – 21, 2018

Symposium 211
XXV International Bile Acid Meeting: Bile Acids in Health and Disease 2018
Dublin, Ireland
July 6 – 7, 2018

Symposium 212
IBD and Liver: East Meets West
Kyoto, Japan
September 7 – 8, 2018

Symposium 213
Tailored Therapies for IBD: A Look into the Future
Milan, Italy
October 5 – 6, 2018

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