



European  
Crohn's and Colitis  
Organisation

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# ECCO

## News <sup>WINTER</sup>



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\*For Regular Members (incl. Y-ECCO) only; online access only

# ECCO NEWS

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European Crohn's and Colitis Organisation

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# Dear ECCO Friends,

*It is once again time to enjoy ECCO News!*

**And yes, it is that time of the year again:** While the ECCO Office is operating at full speed in preparation for the Congress in Barcelona, I know that many of you will be working very late hours to get your abstracts in before the deadline! These weeks of stress will give way to feelings of satisfaction and quieter weeks prior to Christmas...an ideal time, therefore, to read this ECCO News!

**What will you find in this issue?** Undoubtedly a recommendation for the junior physicians is the interview with the very first ECCO Fellowship awardees, Konstantinos Karmiris and Fabian Schnitzler, who received the Fellowship in 2007. How do they now look back on this period and how has the Fellowship influenced their career? Exploring new horizons and looking outside one's hospital or university is always stimulating, refreshing and often "one of the best times of your life". I am happy to announce that the number of Fellowships will increase in the future.

**You will also find an update on the newest ECCO Guidelines on Extra-intestinal Manifestations,** which will be officially released and presented at the ECCO'15 Barcelona Congress.

**In October, new ECCO Committee Members were elected** and I would like to extend a warm welcome to all newcomers in our family! Of course, it would be unfair not to thank those who will step down in 2015: You will also find their names in this issue and we are grateful to them for the time they have dedicated to ECCO! We hope, of course, that they will stay on board and stimulate many young people to follow in their footsteps!

**Finally, the registration figures for the ECCO'15 Barcelona Congress look very optimistic,** and for those who have not yet registered for the ECCO Congress and want to save money the message is: The late registration deadline ends on February 3, 2015. As always, the true "heart" of the Congress is in the ECCO Interaction: Hearts and Minds, which will take place as usual on Friday evening during the ECCO Congress at the Museu Nacional d'Art de Catalunya. And no, no pizzas on the menu this year but instead, a full three-course buffet dinner!

Enough for now, I think. I hope you are able to spend some time with the family over the Christmas period and I very much look forward to welcoming you in Barcelona in February!

Greetings, and enjoy reading!

**SÉVERINE VERMEIRE**  
ECCO President



Séverine Vermeire © ECCO

Missed an ECCO News issue?  
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# ECCO'15 – Come to Barcelona for IBD!

The 10<sup>th</sup> Congress of ECCO in Barcelona is coming closer and so is the late registration deadline. Benefit from the late registration and register by February 3, 2015 (after this date the onsite registration fees apply)

## Educational programme at ECCO'15:

Educational activities at the 10<sup>th</sup> Congress of ECCO are held from Wednesday, February 18, 2015 to Friday, February 20, 2015. The educational programme covers activities for ECCO's different interest groups, including young gastroenterologists, surgeons, paediatricians, IBD nurses and allied health professionals and scientists. An overview of these activities can be found below. For the detailed final programme please refer to [www.ecco-ibd.eu/ecco15](http://www.ecco-ibd.eu/ecco15). Please note that some of the courses/workshops will run in parallel and that some will have a limited capacity – please register by February 3, 2015.

Wednesday February 18, 2015			Thursday February 19, 2015		Friday February 20, 2015	Saturday February 21, 2015
13 <sup>th</sup> IBD Intensive Advanced Course		8 <sup>th</sup> Y-ECCO Workshop	13 <sup>th</sup> IBD Intensive Advanced Course	Scientific programme Poster exhibition		
Basic ECCO: EduCational COurse for Industry			Cell-based therapy in IBD	Industry exhibition		
	Advanced ECCO: EduCational COurse for Industry		4 <sup>th</sup> S-ECCO IBD Masterclass	Y-ECCO Basic Science Workshop	ECCO Interaction: Hearts & Minds	
6 <sup>th</sup> N-ECCO School			9 <sup>th</sup> N-ECCO Network Meeting			
	2 <sup>nd</sup> N-ECCO Research Networking Forum		4 <sup>th</sup> ClinCom Workshop			
	ECCO-ESGAR MRI Workshop		ECCO-ESGAR Ultrasound Workshop			
	PIBD Update 2015	Global IBD Forum				
ECCO Business meetings						

○ Educational programme      ● Scientific programme

## Look out for our digital oral presentations!

- The **28 best abstracts** (up from 24 in 2014) will receive an **oral presentation** slot in the scientific programme of the 10<sup>th</sup> Congress of ECCO.
- The **next best ~100 abstracts** will be **digital oral presentations**, with a five-minute oral presentation in 10 different rooms on Level 1 on **Thursday, February 19, 2015, 17:15–18:15**. This format was introduced at the last Congress and has proved to be a huge success. Do not miss out on these exciting presentations!
- The remaining accepted abstracts will be displayed as **hard copy posters** throughout the Congress. Please do join our vivid **Guided Poster Session** on **Friday, February 20, 2015 during the lunch break**.

For further information, please refer to [www.ecco-ibd.eu/ecco15](http://www.ecco-ibd.eu/ecco15).

## What's in store for ECCO Members at the ECCO Congress?

ECCO Members attending the 10<sup>th</sup> Congress of ECCO will enjoy a number of highly valuable privileges:



Digital oral presentation at ECCO'14 Copenhagen Congress © ECCO



Congress bags ECCO'15 Barcelona Congress © ECCO

## Special registration privileges:

- Payment of reduced registration fees, with a saving of EUR 300.- to 400.-
- Access to the educational programme (only for Members)

## Onsite privileges:

- General Assembly of ECCO Members  
Thursday, February 19, 2015, 18:30–19:30, Room 111 (CCIB)  
The Annual General Assembly of ECCO Members is ECCO's highest deliberative body and the embodiment of one of the association's most elementary member privileges: The right to vote and help form ECCO's future.
- ECCO Members' Lounge  
ECCO Members have the possibility of enjoying an informal atmosphere with their peers. Meet ECCO Officers and network with colleagues in our lounge located in the entrance hall of the CCIB.

## ECCO Congress bags 2015

This year, our ECCO Congress bags will be produced by Township Patterns®, a company supporting women entrepreneurship in



township communities outside Cape Town, South Africa. Hence, the ECCO Congress bags are more than just a stylish accessory - they are a means of improving the lives of African women who produce them in their own sewing cooperatives.

**Congress bag special:** Every bag will include a copy of JCC – Journal of Crohn's and Colitis Issue 1/2015. Please do not forget to pick up your ECCO Congress Bag!

#### *ECCO Interaction: Hearts and Minds*

"ECCO Interaction: Hearts and Minds" is THE event at ECCO to see and be seen, to network and engage. Anyone who has been to a previous ECCO Congress knows that it is a must and everyone is welcome, but places are limited.

Date: Friday, February 20, 2015

Start time: 20:00

Venue: Museu Nacional d'Art de Catalunya, Palau Nacional, Parc de Montjuïc, 08038 Barcelona, Spain

This event is open to all congress delegates. The price of an entrance ticket purchased in advance is EUR 50.- for ECCO Members and EUR 95.- for non-members. **Please be informed that a three-course buffet dinner is included in the entrance fee.**

Tickets can be purchased during the online congress registration at [www.ecco-ibd.eu/ecco15](http://www.ecco-ibd.eu/ecco15). **Access to the event is strictly limited to those with ECCO Interaction tickets.**



General Assembly at ECCO'14 Copenhagen Congress © ECCO



Members' Lounge at ECCO'13 Vienna Congress © ECCO

# Inflammatory Bowel Diseases

## Barcelona



## 10<sup>th</sup> Congress of ECCO February 18-21, 2015

# ECCO Activities at UEG Week 2014 in Vienna, Austria

October 18–22, 2014

All ECCO Officers met during the UEG Week in Vienna for their ECCO Committee Meetings and ECCO Business Meetings. It was a pleasure meeting you all again. Below I would like to share some insights into the ECCO Activities during this year's UEG Week and wish to remind you that: After the meeting is before the meeting – so I look forward to seeing you all in Barcelona in February at the ECCO '15 Congress.

## ECCO Committee Meetings

The ECCO Officers had a busy schedule on Sunday, when they met for the autumn Committee Meetings. Updates on current projects and many new ideas for future developments have been gathered by each Committee and presented for the Governing Board's approval. As always, the meetings were fruitful and the outcomes will keep everyone busy with follow-up work until the next meeting at the ECCO 2015 Barcelona Congress. Thank you for your productive participation – your initiatives and ideas make ECCO what it is today and what it will become in the future.

## Extra-intestinal Manifestations in IBD – a new consensus

The EIM Consensus Meeting was held on the afternoon of Saturday, October 18. It was a fruitful meeting with more than 20 participants. Once again, one Y-ECCO Member is participating in each working group. This allows our young members to gain an insight into the development of ECCO Guidelines and, ambitious as they are, each Y-ECCO is involved in the development of e-CCO Learning content.

## e-CCO Learning: e-Course on Extra-intestinal Manifestations in IBD

Once again, an e-CCO Learning Meeting took place in line with the Consensus Meeting. Four highly motivated young members of ECCO will participate not only in a working group of the Consensus but also in cooperating to create a comprehensive e-Course on EIM. This e-Course will be structured in a new and exciting way: Each Y-ECCO will create a 'mini-case' on the topic of the respective working group in order to cover as many aspects as possible. Johan Burisch will give an insight into Rheumatology, Tim Raine will examine eye problems, Annemarie de Vries will look at primary sclerosing cholangitis and Pavol Papay will highlight extra-intestinal manifestations connected to skin problems.

Therefore, stay tuned and look up the e-Courses on [www.e-learning.ecco-ibd.eu](http://www.e-learning.ecco-ibd.eu). Launch: 2015

## Talking Heads

For the first time three Talking Heads sessions



EIM Consensus participants © ECCO



Gianluca Sampietro, Fernando Magro, Alessandro Armuzzi © ECCO

on exciting and hot topics in IBD have been recorded:

Marcus Harbord and Peter Irving discuss the communication of risks of disease or treatment with a patient, pointing out the most relevant issues for IBD specialists.

Franck Carbonnel, Joël Doré and Harry Sokol give you an expert's view on faecal transplantation and microbiomes. And an interesting discussion from our P-ECCO Committee Members provides an insight into the use of nutritional therapy in IBD.

Wait for the ECCO eNewsletter announcing the upload of the Talking Heads onto the e-CCO Learning platform [www.e-learning.ecco-ibd.eu](http://www.e-learning.ecco-ibd.eu). Launch: 2014

## IBD Blue Book

For doctors new to gastroenterology, the Education Committee has created something very special: A series of presentations on the most essential topics in IBD, which every medical doctor needs to know according to the Blue Book.

This series will be available for free on the ECCO Website and will give a nice taste of the great educational material ECCO has to offer to its members. Therefore, spread the word and let your colleagues sneak into ECCO Education on the Website [www.ecco-ibd.eu](http://www.ecco-ibd.eu). Launch: 2014

## Podcasts

As last year, the nine ECCO Committee Chairs have been invited to record their information



e-CCO Learning EIM Y-ECCO Task Force (Stephan Vavricka, Tim Raine, Annemarie de Vries, Pavol Papay, Johan Burisch) © ECCO



Jan Gaarenstroom, Nienke Ipenburg © ECCO

on current and future projects in order to use these updates, combined into short podcasts, to inform the General Assembly about ECCO Activities beside the yearly Congress. The talks will be made available to all ECCO Members in the Members' area on the ECCO Website. A video with the highlights will be presented at the General Assembly in Barcelona on February 19, 2015.

## ECCO Dinner at Restaurant Palmenhaus

On Sunday evening all ECCO Officers met in Burggarten of Vienna to enjoy a relaxed evening among the ECCO Family. We welcomed 60 participants including the ECCO Office team. Check out the photos to understand the familial atmosphere within ECCO.

## ECCO Booth at UEG Week 2014

The ECCO Office team was onsite to welcome ECCO Officers and delegates who wanted to find out more about ECCO. Many stopped by to accept a free issue of the Journal of Crohn's and Colitis, as well as the printed version of our society's magazine, "ECCO News". The ECCO Booth was well located and offered an excellent meeting spot for ECCO business and industry meeting participants. Thank you for having stopped by.

**Overall, the numerous activities of ECCO continue to expand in a climate of friendship and networking in accordance with the ECCO Spirit.**

SILVIO DANESE

ECCO News Editor

# Interview with ECCO Fellowship Awardees

Each year since 2006 ECCO has awarded grants and fellowships in order to encourage young physicians in their careers and to promote scientific research in Inflammatory Bowel Disease (IBD) in Europe. The first ever recipients of the ECCO Fellowship were Fabian Schnitzer (FS), Germany and Konstantinos Karmiris (KK), Greece, back in 2007 during the ECCO Congress in Innsbruck, Austria. Since then, many years have passed and ECCO News therefore contacted Fabian and Konstantinos to hear what has happened in the intervening period

**Johan Burisch (JB): Konstantinos, please give readers a short description of the project that was awarded the ECCO Fellowship back in 2007.**

**KK:** The project investigated the long-term benefit of adalimumab in IBD patients who failed to respond to infliximab therapy. The focus was on the influence of adalimumab trough serum concentration and antibodies against adalimumab on clinical outcome. This was an observational study conducted in a tertiary referral centre – the Department of Gastroenterology, University Hospital Gasthuisberg, Leuven, Belgium – in collaboration with the Laboratory of Pharmacology-Toxicology, University Hospital, Tours, France.

**JB: Where did you travel to with the ECCO Fellowship and why did you choose to go there?**

**KK:** I worked on the fellowship project at the Department of Gastroenterology, University Hospital Gasthuisberg, Leuven, Belgium, as mentioned above. Back in 2004, when I was a trainee in Gastroenterology at the University Hospital of Heraklion, Crete, Greece, I had the chance to attend the IBD course for junior gastroenterologists in two successive years. I was inspired and stimulated by the many international colleagues who served as faculty members and decided to focus on IBD. However, it was a young (she still is) lady who made the biggest impression on me: Séverine Vermeire. I decided to contact her, asking for a postgraduate fellowship. She accepted my invitation and before finishing my training in Crete, I visited the IBD centre in Leuven to arrange details. There, I also met for the first time Paul Rutgeerts and Gert Van Assche, another two brilliant scientists and personalities. I was fascinated by the facility, the organisation and the people at the centre. I also had the chance to learn a lot of positive information from a very close friend and colleague who had already been there before me as a fellow: Kostas Katsanos. Séverine proposed that I should apply for the ECCO Fellowship and that was the beginning of a magnificent 1.5-year journey.

**JB: What were the key findings of your project?**

**KK:** We found that 71% and 67% of patients initiating adalimumab therapy showed a response at weeks 4 and 12 respectively. Among them, 61.5% sustained their clinical benefit until the end of follow-up [median (IQR): 20.4 (11.7–30.0) months]. Step up to 40 mg every

week was observed in 65.4%, and 38.5% of patients stopped adalimumab therapy, in most cases due to loss of response. Significantly lower adalimumab trough serum concentrations were measured throughout the follow-up period in patients who discontinued therapy as compared to those who stayed on adalimumab. Antibodies against adalimumab were present in 9.2% of the patients and affected trough serum concentration.

**JB: What has happened since then in terms of your career and collaboration with the hosting department?**

**KK:** Unfortunately, the economic and subsequent social crisis developed in Greece shortly after my return from Belgium. This restricted the available positions for which I could apply



Leuven IBD Group © Leuven IBD Group

due to a state programme to reduce the number of people working in public services such as universities and hospitals and also the financial resources for funding of these services. I managed to find a position as a consultant in the Department of Gastroenterology, Venizeleio General Hospital, Heraklion, the second major hospital in Crete, where I work until today. The hospital is clinically oriented; thus my everyday programme mainly involves endoscopy, outpatient clinic, ward responsibilities and call duties. We have built up a cohort of more than 700 electronically registered IBD patients (one of the biggest in Greece). However, we have no laboratory facility, no fellows, no students and only two trainees. I also have to engage frequently in other non-medical activities (we do not have a secretary in the department so I usually serve as one and in addition I run by myself two or three international observational pharma-initiated clinical trials since we lack a study nurse). Whenever feasible, I aim to initiate or participate in clinical projects, whether national or international, and I maintain a close scientific collaboration with the University Hospital. However, due to the lack of scientific

personnel, I usually have to prepare the protocol, collect data, analyse them and write the abstract or manuscript. Collaboration with the hosting department has not been as fruitful as I would like since I left, but I realise that there are various technical difficulties and that the different priorities and scientific nature of the two departments mean that such collaboration is not easy to accomplish.

**JB: How did the ECCO Fellowship influence your career?**

**KK:** The ECCO Fellowship was a strong initiative for me because it gave me the opportunity to work in an IBD centre with a high impact, to produce high-quality scientific work and to collaborate with very skilled people. It also gave me the chance to become part of a different



Konstantinos Karmiris © Konstantinos Karmiris

culture and to develop strong friendships with colleagues. My mentors influenced my thinking and practice around IBD. I left the centre full of ideas and experience in how to create an IBD centre of excellence, how to set up clinical projects and how to manipulate difficult IBD cases. I hope that I will have a chance in the future to transform these ideas into reality. But above all, the experience taught me the importance of modesty and the negative impact of arrogance, independently of a person's scientific rank. I will try to retain these "lessons" as a guide for my future steps.

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**JOHAN BURISCH**

ECCO News Associate Editor



**Johan Burisch (JB): Fabian, please give the readers a short description of the project that was awarded the ECCO Fellowship back in 2007.**

**FS:** The aim of the awarded ECCO Fellowship "Clinical, apoptotic and immunological genetic polymorphisms as markers to predict short-term outcome to infliximab therapy in Crohn's Disease" was to identify predictors of response to anti-TNF therapy with infliximab in patients with Crohn's Disease (CD). In addition, long-term outcome following anti-TNF therapy in patients with CD was addressed in this project.

A total of 614 patients with CD who had been treated with infliximab between November 1994 and March 2007 were included in the analysis [1]. In a sub-analysis, mucosal healing was addressed before and after the start of anti-TNF therapy with infliximab in 214 patients with CD. Moreover, safety of anti-TNF treatment with infliximab was investigated in these patients [2].

**JB: Where did you travel to with the ECCO Fellowship and why did you choose to go there?**

**FS:** I had the great opportunity to spend my fellowship at the University Hospital Leuven–Gasthuisberg in Leuven, Belgium. I worked in the Centre for Inflammatory Bowel Diseases (IBD) under the supervision of Paul Rutgeerts, Séverine Vermeire and Gert Van Assche. It was the most important experience for my professional career.

The IBD clinic at the University Hospital of Leuven is one of the largest IBD centres in Europe and probably has the most extensive experience using biological therapies in IBD patients. Furthermore, the first patients treated with infliximab in clinical trials were included from the IBD centre in Leuven.

**JB: What were the key findings of your project?**

**FS:** The aim of our clinical trials in Leuven was to identify predictors of a favourable outcome

of anti-TNF therapies in patients with IBD and to describe the long-term outcome of anti-TNF therapies in IBD patients.

For the first time, long-term outcome of infliximab treatment in CD patients and in patients with Ulcerative Colitis (UC) was investigated in clinical trials. Data from the ACCENT I and ACCENT II trials and the ACT I and ACT II trials showed a favourable outcome of anti-TNF treatment with infliximab in UC patients and CD patients over a follow-up period of 1–2 years. No long-term experiences were reported at that time.

During a median follow-up of almost 5 years, we firstly could describe an excellent long-term outcome of infliximab treatment in patients with CD. Sustained clinical benefit was maintained in 63% of CD patients until the end of the follow-up period and disease outcome was favourably modulated in terms of a reduction in the rates of hospitalisation and surgery. A fall in elevated baseline CRP levels and an initial clinical response to infliximab treatment were identified as predictors of a good long-term outcome of infliximab treatment. Comparable results were observed for the long-term outcome of infliximab treatment in patients with UC [3].

In an additional clinical trial, mucosal healing was addressed as a predictor of long-term evolution of infliximab treatment in patients with CD [4]. A total of 214 CD patients underwent endoscopy before and after the start of infliximab treatment and were followed up for a median of almost 69 months. Mucosal healing was described as the most important predictor for long-term outcome of infliximab treatment in patients with CD: Those patients who achieved mucosal healing had significantly lower surgery and hospitalisation rates than CD patients without mucosal healing.

Since then, mucosal healing has been – in addition to clinical response and biological

response – accepted as the most important predictor of long-term outcome in anti-TNF-treated IBD patients.

In addition, the safety of anti-TNF therapies during long-term follow-up was addressed in these clinical trials, with excellent long-term safety profiles for infliximab treatment in patients with IBD. The findings of these clinical trials were of crucial importance for daily clinical practice and for therapeutic decisions in IBD patients treated with anti-TNF therapies.

**JB: What has happened since then in terms of your career and collaboration with the hosting department?**

**FS:** I returned to my home institution, the University Hospital Munich-Grosshadern, where I started a number of new projects focussing on therapy outcomes among anti-TNF-treated patients in a large IBD patient cohort under the supervision of Stephan Brand, which resulted in several publications.

**JB: How did the ECCO Fellowship influence your career?**

For my professional career, the fellowship in Leuven was the most important experience; the clinical experience I obtained in Leuven is of crucial importance for my clinical and academic work in the field of IBD.

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**JOHAN BURISCH**

ECCO News Associate Editor

## ECCO Grant Study Synopses

### Role of rhomboid-like proteins in intestinal damage and repair

#### Aim of research

Intense biosynthesis of secretory proteins makes the endoplasmic reticulum (ER) sensitive to stress caused by misfolded proteins. Accumulation of such misfolded proteins risks stressing the ER, leading to cell death and tissue dysfunction. ER stress is particularly relevant for the professional secretory cells of the intestinal epithelium (e.g. Paneth cells) that protect the epithelium from damage and subsequent inflammation. Understanding the mechanisms that offer protection from ER stress is highly relevant to the development of new strategies for the treatment of Inflammatory Bowel Disease (IBD).

Quality control (QC) machinery in the ER provides a first line of defence against the accumulation of misfolded proteins. Central to this is ER-associated degradation (ERAD), whereby misfolded proteins are recognised, retrotranslocated across the ER membrane and degraded in the cytoplasm by proteasomes. Rhomboid-like proteins are emerging as important regulators of ER QC, particularly at the stage of coordinating dislocation of misfolded proteins into the cytoplasm. The overall goal of the project is to assess the candidacy of rhomboids as novel targets in human IBD.



Colin Adrain © Colin Adrain



**Methodology**

We will examine the role of rhomboids in damage and repair of the intestinal epithelium, in knockout mouse models of experimental colitis. Central is a focus on ER stress in professional intestinal epithelial cells. We will also elucidate, in parallel, the role of rhomboids at a molecular level by identifying novel rhomboid interactors. The role of the novel interactors in the intestinal

epithelium will be tested in rhomboid knockout mouse models.

**Proposed timing**

This ECCO Grant fits within the context of a longer-term programme to investigate the physiological and pathological role of rhomboids. We will study the role of rhomboid-like proteins in experimental colitis during

year 1; the identification of interactors and assessment of their roles in vivo will extend to years 2 and 3.

**COLIN ADRAIN**

ECCO Grant Awardee 2014

**Patient empowerment: Web-based monitoring in children and adolescents with Inflammatory Bowel Disease for better quality of treatment****Aim of research**

Previous research has shown that eHealth and web-based monitoring decrease the time from relapse to remission and improve adherence and health-related quality of life (HRQoL) in adult patients with Inflammatory Bowel Disease (IBD). Therefore it is our hypothesis that eHealth can optimise empowerment and treatment quality in young patients (10–17 years) and support the transition from paediatric to adult gastroenterology care, by involving the patients in their own disease course.

**Methodology**

The adult eHealth web-program Constant Care (ConstantMED©) has been used as a basis to design a web program for young patients. At the web application [www.young.constant-care.com](http://www.young.constant-care.com) the paediatric IBD scores, medication, need for corticosteroids, quality of life, adherence, days of absence from school, need for contact with the hospital, surgery and hospitalisations are registered.

Two studies are designed to evaluate the web program:

Study A: A randomized clinical trial including 10- to 17-year-old IBD patients treated with oral treatment

Study B: A prospective descriptive study including 10- to 17-year-old IBD patients treated with biological therapy (infliximab)

Patients enter their symptoms in the web program and submit a stool sample for faecal calprotectin (FC) analysis at regular intervals. Disease burden is estimated using a combination of FC levels and symptom score and is shown to the patient in a traffic light spectrum, with red indicating severe disease activity, yellow, light to moderate activity, and green, inactive disease. Depending on the colour, different advice is given to the patient. To ensure sufficient follow-up, a medical doctor or IBD nurse monitors the patients by web rounds weekly.



Katrine Carlsen © Susanne Oestergaard

**Proposed timing**

The inclusion period for both studies was September 2013 to February 2014. Forecast end of the study is July 2016.

**KATRINE CARLSEN**

ECCO Grant Awardee 2014

**Gut microbiota, diet and drug usage in Inflammatory Bowel Diseases****Aim of research**

- To characterise inter-/intra-individual variation in gut microbiota composition of IBD patients and healthy control subjects in both Canada and Ireland.
- To find microbial biomarkers associated with inflammation levels and disease phenotypes, or lack thereof.
- To use available metadata (diet, drugs and other life-style data) to investigate whether these biomarkers, or dietary components, could either predict a relapse of symptoms or prolong maintenance of remission.

**Methodology**

Briefly, microbial DNA will be extracted from stool samples using standard protocols followed by amplification of the 16S rDNA V4–V5 region. Following sequencing using Illumina MiSeq, bioinformatic analysis of the sequencing reads will be carried out using the QIIME pipeline along with in-house developed software. Multivariate statistical analysis based

on beta-diversity distances will be used to identify principal coordinate axes that explain most of the biological variance in the context of relevant metadata. The methods include median linear quantile regression and non-parametric Kruskal-Wallis and Mann-Whitney tests of relative taxa abundance, while controlling for multiple testing using the False Discovery Rates methods.

**Proposed timing**

The goal is to collect stool samples from 350 Canadian IBD, 100 Irish IBD and 50 healthy control (HC) subjects at three time points, 3 months apart, amassing 1500 samples in total within the first year of the project. Currently we have collected samples along with the required survey data from 325 Canadian IBD patients at three time points, and from 50 Irish IBD patients and 30 Canadian and 17 Irish HCs at one time point. Thus, the total number of samples collected is 1072, whereof DNA extractions have been carried out on 588 samples. We expect to



Marcus Claesson © T.Tyner, UCC

have collected all 1500 samples ahead of time, i.e. by the end of 2014, and meanwhile have already started sequencing and analysis of the earliest samples.

**MARCUS CLAESSON**

ECCO Grant Awardee 2014

## Impact of Acyl homoserine lactone-driven quorum sensing from Gut microbiota in Inflammatory Bowel Diseases (IMAGIN)

### Aim of research

Studying the impact of Inflammatory Bowel Disease (IBD)-associated dysbiosis on gut inflammation pathways is challenging. The auto-inducer quorum sensing (QS) molecules N-acyl-homoserine lactones (AHLs), a bacterial communication network, have never been studied in the human gut microbiota and are highly suspected to be involved in dysbiosis. Moreover, it has been shown that specific AHLs could interfere with inflammation pathways in extra-digestive models. Encouraging preliminary data from our team clearly indicate that AHL-driven QS occurs in human gut microbiota and that an imbalance in AHL profiles between flares and remission is observed in IBD. We aim to demonstrate through this project that AHLs from the gut ecosystem could participate in gut homeostasis and inflammation in IBD.

### Methodology

We will start by sampling a larger IBD cohort of

IBD patients (n=100 for now), collecting clinical data, peripheral blood mononuclear cells (PBMC) and faecal samples for AHL profiling using HPLC coupled with tandem mass spectrometry (LC-MS/MS) and assessment of microbiota composition by means of real-time quantitative PCR. This step will enable us to refine our initial descriptions of AHL distribution among IBD patients.

In parallel, after identification, molecular characterisation and synthesis of the AHLs of interest, we will perform functional assays in vitro on intestinal and immune cells to detect anti-inflammatory AHLs. We will also study host paraoxonase (PON) activity and its interaction with AHL immunomodulatory effects and identify cellular interactions and mechanisms involved in the anti-inflammatory effect.

### Proposed timing

We propose a 3-year project: One year for the complete sampling, one year (beginning 6 months from the start) for the molecular



Philippe Seksik © Philippe Seksik

characterisation and synthesis of AHLs of interest and one year to study modulation of inflammation and gene expression by AHLs of interest in vitro.

### PHILIPPE SEKSİK

ECCO Grant Awardee 2014

## Validation of the three-year follow-up period of the 2010 and of the one-year follow-up period of the 2011 ECCO-EpiCom inception cohort: Evaluation of changes in medical strategies and surgery rates and their impact on disease activity and disease course

### Aim of research

The ECCO-EpiCom study initiated in 2010 revealed that the incidence rates of Inflammatory Bowel Diseases (IBD) in the participating Western European centres were twice as high as those in Eastern European centres [1]. This difference was confirmed in the second year of the study, when the incidence rates at the individual centre level corresponded to the findings in respect of the 2010 incident cohort [2].

The major aim of this European multicentre study is the data validation of the 3-year follow-up period of the 2010 and the 1-year follow-up period of the 2011 ECCO-EpiCom inception cohort. The primary parameters to be investigated are the evolution of disease activity of Crohn's Disease (CD) and the disease extent of Ulcerative Colitis (UC), the medication profiles, the hospitalisation and surgery rates and their predictors, the malignancy and mortality rates and also the association between disease phenotype, localisation and disease behaviour.

### Methodology

The inclusion period for the 2010 validation cohort was January 1, 2010 to December 31, 2010; similarly, for the 2011 validation cohort it was January 1, 2011 to December 31, 2011. All newly diagnosed IBD patients who lived in the catchment areas of participating centres were included and followed up if they fulfilled the Copenhagen Diagnostic Criteria for CD or UC. In the first year after diagnosis, patients were followed up every 3 months, in the second year every 6 months and in the third year once a year. The participating centres entered the data at diagnosis and the follow-up schemes of the included patients into the web-based EpiCom database [www.ecco-epicom.eu](http://www.ecco-epicom.eu).

### Proposed timing

The data validation of the follow-up schemes of the patients in the 2010 and the 2011 ECCO-EpiCom inception cohort and the statistical analysis will be performed at the Herlev University Hospital of Copenhagen between September 1, 2014 and October 13, 2014.



Zsuzsanna Vegh © Zsuzsanna Vegh

### References

1. Burisch J, Pedersen N, Čuković-Čavka S, Brinar M, Kaimakliotis I, Duricova D et al. East-West gradient in the incidence of inflammatory bowel disease in Europe: the ECCO-EpiCom inception cohort. *Gut*. 2013;63:588–97.
2. Vegh Z, Burisch J, Pedersen N, Kaimakliotis I, Duricova D, Bortlik M et al. Incidence and initial disease course of inflammatory bowel diseases in 2011 in Europe and Australia: Results of the 2011 ECCO-EpiCom inception cohort. *J Crohns Colitis* (2014)

### ZSUZSANNA VEGH

ECCO Grant Awardee 2014

# Publications deriving from ECCO Fellowships and Grants

One of the major goals of ECCO is to encourage research – basic, clinical and translational

To this end, ECCO endows Research Grants and Fellowships on a yearly basis. The Grant and Fellowship awardees are selected in a peer review process involving all SciCom Members as well as external reviewers with expertise in the relevant fields. Outstanding research projects are being submitted each year. It is a genuine pleasure to review the proposals and to witness the increasing scope of the research conducted by ECCO Members. SciCom defined the importance of the proposal to the field of IBD as a major criterion in the selection process. By their nature, projects that are indeed meaningful may impact on the field in various ways, and their results will be accepted for publication in peer-reviewed scientific journals. Some projects may yield results relatively quickly, while in other cases several years may pass between performance of the study and the resultant publication, depending on multiple factors including the complexity of the research, the novelty of the findings and researcher-related issues, to name but a few.

As publication is a clear, easily identifiable deliverable that enables dissemination of knowledge and scientific discussion, we pay specific attention to publications by ECCO Members that report results stemming from an ECCO Grant or Fellowship. Here, we summarise some such publications. The intention of the summary is not to provide an exhaustive report – the number of publications resulting from ECCO Grants and Fellowships since 2008 is almost 30! Rather, we aim to highlight the scope of the research and to demonstrate the ability of ECCO researchers to develop their ideas and hypotheses from the stage of scientifically sound proposals, through well-designed studies to accepted manuscripts. Thus, some selected publications from recipients of Grants and Fellowships that relate to basic, translational and clinical sciences are mentioned. They are arranged according to the respective research area, rather than by chronology. We apologise for not being able to include every publication and every Fellow or Grantee in this summary, and promise to do so in further communications.

**Sofia Maria Buonocore** received the ECCO Grant 2009 for a study entitled „Identification of IL-23 dependent effector pathways in colitis“. This study yielded important insights into intestinal pathology driven by this

intriguing cytokine and the „new cells on the block“, i.e. innate lymphoid cells. In a study published in *Nature* (Buonocore S, et al, *Nature* 2010;464:1371–5), Sofia Maria Buonocore showed that bacteria-driven innate colitis was mediated by IL-23, inducing the production of IL-17 and interferon- $\gamma$  by innate lymphoid cells. The study suggested that these cells may thus be targets for therapeutic intervention.

**Timon Eric Adolph** received the ECCO Fellowship 2012 for his PhD project entitled „Endoplasmic reticulum stress and autophagy converge in the NF- $\kappa$ B signaling pathway“. Timon Eric Adolph and his colleagues relate endoplasmic reticulum stress and autophagy – two major processes that are defective in IBD – with the unfolded protein response in Paneth cells using sophisticated deletion of transcription factor X-box binding protein-1 (Xbp1) in these cells. The authors conclude that Crohn's Disease may thus be a Paneth cell-mediated disease, resulting from the combination of genetic predisposition and environmental effects (Adolph TE, et al, *Nature* 2013;503:272–6; Adolph TE, et al, *Dig Dis* 2012;30:341–6).

**Jan Wehkamp** received the ECCO Grant 2009 for a research proposal entitled „WNT transcription factor Tcf-1 and its role in protective innate immunity in inflammatory bowel diseases“. Jan Wehkamp and his group published findings regarding the importance of aberrant expression of T-lymphocyte specific transcription factors in patients with Crohn's disease, and suggested that the potential implication may be disturbed barrier function (Koslowski MJ et al, *PLoS One* 2009;4:e4496; Beisner J, et al, *Am J Physiol Gastrointest Liver Physiol* 307:G487–98, 2014).

**Holm Uhlig** received the ECCO Grant 2008 for a research proposal entitled „Immunosuppressive drugs and Foxp3+ regulatory T cell activity in inflammatory bowel disease“. His publications include a description of an autoimmune syndrome associated with colitis and with B cell aberrations, as well as increased signaling via the PI3K-AKT pathway (Heindl M, et al, *Gastroenterology* 2012;142:1093–6).

**Silvio Danese** received the ECCO Grant 2008 for his proposal entitled „The role of lymphangiogenesis in IBD pathogenesis“ and Stefania Vetrano received the ECCO Grant 2009 for her proposal entitled „The protein C

pathway in inflammatory bowel disease: A novel mediator of cross-talk between dendritic and epithelial cells“. In their publications these grantees used murine models and human samples to demonstrate the contribution of the lymphatic system to the pathogenesis of IBD as well as intestinal cancer, and to point out new chemokines that may mediate carcinogenesis (Vetrano S, et al, *Gut* 2010;59:197-206) and to connect inflammatory processes and coagulation by focussing on new roles that the protein C system may have in intestinal inflammation (Danese S, et al, *Blood* 2010;115:1121–30).

**Michael Scharl** received the ECCO Grant 2010 for his research proposal entitled „The role of protein tyrosine phosphatase N2 in the regulation of cytokine-induced apoptosis in the intestinal epithelium“. He silenced this protein tyrosine phosphatase in intestinal epithelial cells and showed that this promoted TNF $\alpha$ -induced mitogen-activated protein kinase signaling and the induction of inflammatory mediators. (Scharl M, et al, *Gut* 2011;60:189–97).

**Lael Werner** received the ECCO Fellowship 2011 for his research proposal entitled „Notch in the pathophysiology of Crohn's Disease and Ulcerative Colitis: A possible link to therapeutic TNF $\alpha$  inhibition“. He was able to show that TNF $\alpha$  blockers activated Notch-1 and that Notch-1 inhibition interfered with the effects of TNF $\alpha$  blockers on T cells. Moreover, in his recent publication, differences in Notch-1 expression in inflamed and non-inflamed mucosa were demonstrated, as well as increased Notch-1 expression after treatment with TNF $\alpha$  blockers (Werner L, et al, *Gut* 2012;61:1016–27).

ECCO Fellows and Grantees successfully published results of original and meaningful clinical studies. For instance **Johan Burisch**, who received the ECCO Fellowship 2012 for his study entitled „New Inception cohort in Europe: Is there an East-West gradient in IBD?“, was the lead author for the EpiCom Study assessing epidemiologic trends in the incidence of IBD in Europe, showing a clear East-West gradient, with higher incidences for both UC and CD in Western Europe, and differences in diagnostic procedures and therapeutic and patient management strategies (Burisch J, et al, *Gut* 2014;63:588–97; Burisch J, et al, *J Crohns Colitis* 2014;8:811–8; Burisch J, *Dan Med J* 2014;61:B4778; Burisch J, Munkholm P. *Curr Opin Gastroenterol* 2013;29:357–62; Burisch J, et

al, *Inflamm Bowel Dis* 2014;20:36–46). Another publication by Johan Burisch suggested that environmental factors that are suspected risk factors for IBD, i.e. increased sugar intake and decreased fibre intake, and for UC, i.e. daily fast food consumption and early appendectomy, were more frequent in Eastern Europeans than in Western Europeans. Additionally, Eastern European IBD patients had fewer childhood infections and received more vaccinations (Burisch J, et al, *J Crohns Colitis* 2014;8:607–16).

**Arie Levine** received the ECCO Grant for 2011 for a study entitled „GROWTH Study: Factors predicting relapse and adverse outcomes early in the disease in newly diagnosed pediatric Crohn's disease – a prospective, multi-center prognostication study by The ESPGHAN Porto group“. In his recently published article, Arie Levine reports that treatment with steroids and exclusive enteral nutrition were effective in achieving short-term (12-week) remission, which further predicted one-year remission (Levine A, et al, *Inflamm Bowel Dis* 2014;20:278–85).

**Maria Elkjaer**, who received the ECCO Grant 2009 for her study entitled „Virtual Hospital System in IBD: Patient centered monitoring and web-guided therapy with 5-ASA in ulcerative colitis “Constant-care”: Impact on quality of life

and cost benefit“ also focussed on patients' health management and suggested a web-guided approach for UC patient education and treatment optimisation (Elkjaer M, et al, *Gut* 2010;59:1652–61; Elkjaer M, et al, *Eur J Gastroenterol Hepatol* 2010;22:695–704; Elkjaer M, *Dan Med J* 2012;59:B4478).

**Maria Papp** received the ECCO Grant 2009 for her study entitled „The possible role of von Willebrand factor and its cleaving protease (ADAMTS-13) in the vascular pathogenesis of inflammatory bowel disease“. She focussed on IBD epidemiology and issues related to serological markers associated with IBD (Papp M, et al, *Clin Vaccine Immunol* 2009;16:464–470; Lakatos PL, et al, *Inflamm Bowel Dis* 2009;15:365–374).

Moving from epidemiology and patient health, topics with high relevance to the field of IBD, and thus to ECCO, several ECCO Grantees and Fellows chose to focus on biologic therapies, specifically outcomes of therapy and immunogenicity. To this end, **Kostas Karmiris**, who received the ECCO Fellowship 2007, published a manuscript summarising his findings showing that adalimumab therapy was effective in two-thirds of patients with Crohn's Disease failing infliximab, and that low trough

levels were important for the prediction of adalimumab discontinuation (Karmiris K, et al, *Gastroenterology*. 2009;137:1628–40).

As is evident from this partial review, being an ECCO Grantee and Fellow is a good predictor of performing meaningful research and publishing it in high-ranked journals in the fields of IBD, gastroenterology and related expertise. The scope of research done with the support of ECCO, and the important outcomes and publications, are a vivid and visible deliverable, which is a source of pride and pleasure to us all. We shall continue to report on such outcomes, and urge all authors to update ECCO and SciCom on resulting publications. We look forward to seeing more of these, and have full confidence in the ambition, perseverance and capabilities of our Grantees and Fellows. We wish all past, present and future awardees productive work and continued success that will lead to further contributions to our fight for our IBD patients – and with them – against these complex diseases.

**IRIS DOTAN**  
SciCom Member

## I-CARE (IBD CAncer and seRious infections in Europe), a high-priority Project in IBD

**Evolving treatment algorithms and current guidelines are leading to earlier and wider use of anti-TNF therapy in IBD patients**

**A**nti-TNF and immunosuppressants (IS) in combination are more effective than anti-TNF alone in both Crohn's Disease and Ulcerative Colitis, but this strategy may be associated with an excess risk of malignancies, especially lymphoma, and opportunistic infections. Hence, we must urgently address safety concerns for anti-TNF alone or in combination with IS. Anti-TNF therapy is associated with greater clinical remission rates and steroid tapering in randomised, controlled trials at one year. The potential for disease modification using IS therapy (mainly thiopurines) is questionable, while the impact of anti-TNF on the natural history of IBD (mucosal healing, bowel damage, surgeries and hospitalisations) beyond one year is unknown. Patient-reported outcomes (PROs), including quality of life and disability, will be a major primary end point of future trials. Few data are available on how treatment affects PROs



I-CARE National Coordinators Meeting in Vienna, October 20, 2014 © ECCO



in patients with IBD and the evolution of PROs over time has never been investigated in large prospective cohorts. This is a prerequisite for better assessment of disease burden in IBD and the development of disease-modifying agents for these patients. Anti-TNFs for immune-mediated inflammatory disorders, including IBD, today represent the biggest drug expense in Western countries. Before recommending earlier and wider use of anti-TNF based strategies in order to change patient- and disease-related outcomes, we require more information on the benefit-risk ratio and cost-effectiveness of long-term anti-TNF use. Inherent bias of previous or ongoing registries (no assessment of disease activity/severity etc.) and limitations of clinical trials (short follow-up, underpowered for safety analysis etc.) cannot accurately address these issues. A large statistically powered prospective cross-sectional observational cohort addressing all these issues is eagerly awaited.

The primary objective of I-CARE is to assess prospectively the presence and the extent of safety concerns (risk of cancers, especially lymphoma, and serious infections) for anti-

TNF alone or in combination with thiopurines among IBD patients. We will stratify the risk of cancers and serious infections according to IBD phenotype and disease activity (clinical, radiological and endoscopic).

The four main secondary objectives of the I-CARE project are:

- To investigate prospectively the impact of anti-TNF-based strategies on the natural history of IBD and their potential for disease modification by collecting validated surrogate markers such as mucosal healing and disease complications such as bowel damage (strictures, fistulas, abscess), surgeries and hospitalisations.
- To assess the evolution of PROs on a yearly basis and the impact of anti-TNF agents on PROs in IBD.
- To evaluate the benefit-risk ratio of strategies based on earlier and wider use of anti-TNF therapy for IBD.
- To assess the healthcare costs and cost-efficacy of current therapeutic strategies in IBD.

A total of 800 investigators from 16 countries will

enrol 16,000 IBD patients in I-CARE, a European prospective observational multicentre cohort study.

Each month, every included patient will complete an e-diary containing all predefined clinical elements. The accuracy of all the information entered by the patient will be validated at least once a year by the gastroenterologist.

The study duration of I-CARE is 4 years, with a one-year inclusion period and a three-year follow-up period.

As I-CARE is a European project of the IBD scientific community, the endorsement of ECCO is sought. ECCO will play a crucial role in communication and launching of the project, as did the French scientific societies in launching and promoting the CESAME project.

The first patient should be enrolled in I-CARE in February 2015, probably during the ECCO'15 Congress in Barcelona. We count on you!

#### LAURENT PEYRIN-BIROULET

ClinCom Member & President of ICARE on behalf of the executive committee of I-CARE

## ClinCom's Initiative to review External Study Protocols

**Treatment with anti-TNF $\alpha$  therapies (mainly infliximab and adalimumab) during pregnancy in Inflammatory Bowel Disease patients seems to be safe for the mother and the foetus, at least in the short-term**

However, the widespread use of these medications during gestation is limited due to the scarcity of data on the impact of in utero exposure to anti-TNF drugs on the long-term development of children.

In this respect, we designed a study aiming to assess the influence of anti-TNF treatment on the long-term development of children born to IBD mothers exposed to these medications during pregnancy. Our main objective was to evaluate whether the risk of severe infection (an infection that causes hospitalisation) is higher in children exposed in utero to anti-TNF drugs.

We thought that this was a great opportunity to perform a collaborative study with the European Crohn's and Colitis Organisation (ECCO) Network. The project was

submitted to ClinCom for their consideration. ClinCom Members evaluated the study and made several suggestions that were very helpful, and the final version was considerably improved. We thank them for their help.

Finally, the study was approved by ClinCom, and ECCO is now supporting the project by sending invitations to participate to all ECCO Members.

We strongly recommend proposing studies to ClinCom in order to bolster the collaborative research between ECCO Members.

#### MARÍA CHAPARRO, JAVIER P. GISBERT

Hospital Universitario de La Princesa, Madrid



María Chaparro © María Chaparro

# 36<sup>th</sup> ECCO Educational Workshop in Kuala Lumpur, Malaysia

The 36<sup>th</sup> ECCO Educational Workshop was held in Kuala Lumpur, the capital of Malaysia, on August 24, 2014

The workshop was coordinated locally by Raja Affendi Raja Ali in conjunction with the annual scientific meeting of the Malaysian Society of Gastroenterology and Hepatology (MSGH) and was officiated by the President of MSGH, Sanjiv Mahadeva. The introduction was delivered by Laurence Egan, guest Faculty Member from ECCO and also Professor of Clinical Pharmacology, consultant gastroenterologist and head of the IBD clinic at the University Hospital Galway, Ireland. The other guest Faculty Member from ECCO was Stephan Vavricka, who is head of the Division of Gastroenterology and Hepatology, Triemli Hospital, Zurich, Switzerland.

In total there were 187 participants, including physicians, gastroenterologists, surgeons, pathologists and radiologists. Participants came from Vietnam, Singapore, Thailand, Indonesia, Myanmar, Cambodia, Bangladesh, Brunei, Philippines and also Serbia. Case-based discussions aimed at disseminating the current ECCO Guidelines and fostering their implementation in clinical practice led to extensive debate, especially in the context of geographical variations and differences in expertise. The local Faculty consisted of Ida Hillmi, Muhamad Radzi, Shanthi Palaniappan and Raja



Faculty of the 36<sup>th</sup> ECCO Educational Workshop in Kuala Lumpur (Tan Huck Joo, Sanjiv Mahadeva, Shanthi Palaniappan, Laurence Egan, Stephan Vavricka, Goh Khean Lee, Raja Affendi Raja Ali, Akhtar Qureshi and Ida Hillmi) © Malaysian Society of Gastroenterology and Hepatology

Affendi Raja Ali. The case-based discussions on severe colitis, fistulising Crohn's Disease (CD), refractory colitis, management of infectious complications of IBD, imaging and new diagnostic steps in CD, and complicated ileocaecal CD were discussed and these sessions were very interactive. Laurence Egan also delivered a state of the art lecture on opportunistic infections in IBD, which is very relevant in the local setting.

The informal and formal feedback from both local and international participants, including other South East Asian countries, was excellent overall, with the majority of delegates requesting



KL Goh, Stephan Vavricka, Laurence Egan and Akhtar Qureshi © Malaysian Society of Gastroenterology and Hepatology

that the ECCO Educational Workshop be held again to promote continuing IBD education in the South East Asia region.

**RAJA AFFENDI RAJA ALI**  
Local Workshop Coordinator



# 37<sup>th</sup> ECCO Educational Workshop in Paris, France

Paris hosted the 37<sup>th</sup> ECCO Educational Workshop, the first ECCO Workshop to be held in the country on September 20, 2014

More than 40 gastroenterologists and paediatricians from France, Hungary and Israel actively participated in the meeting, which followed the format of previous ECCO Workshops – case-based discussions aimed at disseminating current ECCO Guidelines and fostering their implementation in clinical practice. Many of the attendees were trainees in Gastroenterology from university hospitals in Paris.

The Faculty consisted of two guest speakers from ECCO, Rami Eliakim from Israel and Peter Lakatos from Hungary, as well as several French Faculty Members – Matthieu Allez, Jean-Pierre Hugot, Laurent Beaugerie and Franck Carbonnel (the last two being former ECCO National Representatives).

The workshop started with a brief introduction by the local organiser Franck Carbonnel and continued with the morning session, which included four case presentations: New-onset ileocaecal CD, paediatric CD,

fistulising disease and management of infectious complications in IBD. Each case was presented in tandem by one fellow gastroenterologist from Paris and one of the Faculty Members.

The workshop continued after the lunch break with another case: Imaging and new diagnostic steps in IBD. The last presentation was the state of the art lecture prepared by Rami Eliakim on IBD in pregnancy, based upon the brand new ECCO Consensus Guidelines.

Judging by informal discussions with participants during and after the workshop, and looking at the evaluation forms completed by them, we have no doubt that the meeting completely fulfilled expectations. The tandem working between the trainees and the Faculty was very much appreciated and encouraged interaction. The success of the workshop was also due to the perfect cooperation and professional assistance of Nicole Eichinger and Phillip Judkins from the ECCO Office and support from our sponsors (Abbvie, Takeda and Hospira).



Faculty of the 37<sup>th</sup> Educational Workshop in Paris, France (Peter Lakatos, Franck Carbonnel, Rami Eliakim, Laurent Beaugerie, Matthieu Allez, Jean-Pierre Hugot) © ECCO

**FRANCK CARBONNEL**  
GuiCom Member





European  
Crohn's and Colitis  
Organisation

# ECCO Educational Workshops – where we have been so far...



-  **1<sup>st</sup> ECCO Workshop**  
Zagreb, **Croatia** - November 10, 2007
-  **2<sup>nd</sup> ECCO Workshop**  
Vienna, **Austria** - December 15, 2007
-  **3<sup>rd</sup> ECCO Workshop**  
Kaunas, **Lithuania** - May 10, 2008
-  **4<sup>th</sup> ECCO Workshop**  
Athens, **Greece** - September 13, 2008
-  **5<sup>th</sup> ECCO Workshop**  
Warsaw, **Poland** - September 26, 2008
-  **6<sup>th</sup> ECCO Workshop**  
Istanbul, **Turkey** - November 8, 2008
-  **7<sup>th</sup> ECCO Workshop**  
Oporto, **Portugal** - November 15, 2008
-  **8<sup>th</sup> ECCO Workshop**  
Haifa, **Israel** - May 5, 2009
-  **9<sup>th</sup> ECCO Workshop**  
Cluj Napoca, **Romania** - June 17, 2009
-  **10<sup>th</sup> ECCO Workshop**  
Oslo, **Norway** - September 4, 2009
-  **11<sup>th</sup> ECCO Workshop**  
Moscow, **Russia** - September 17, 2009
-  **12<sup>th</sup> ECCO Workshop**  
Belgrade, **Serbia** - October 14, 2009
-  **13<sup>th</sup> ECCO Workshop**  
Sao Paulo, **Brazil** - June 19, 2010

-  **14<sup>th</sup> ECCO Workshop**  
Donetsk, **Ukraine** - September 17, 2010
-  **15<sup>th</sup> ECCO Workshop**  
Budapest, **Hungary** - September 18, 2010
-  **16<sup>th</sup> ECCO Workshop**  
Riga, **Latvia** - October 9, 2010
-  **17<sup>th</sup> ECCO Workshop**  
Galway, **Ireland** - October 15, 2010
-  **18<sup>th</sup> ECCO Workshop**  
Sofia, **Bulgaria** - November 11, 2010
-  **19<sup>th</sup> ECCO Workshop**  
Dubai, **UAE** - April 29, 2011
-  **20<sup>th</sup> ECCO Workshop**  
Helsinki, **Finland** - August 26, 2011
-  **21<sup>st</sup> ECCO Workshop**  
Opatija, **Croatia** - September 17, 2011
-  **22<sup>nd</sup> ECCO Workshop**  
Cordoba, **Spain** - November 12, 2011
-  **23<sup>rd</sup> ECCO Workshop**  
Naples, **Italy** - December 1, 2011
-  **24<sup>th</sup> ECCO Workshop**  
Tokyo, **Japan** - June 17, 2012
-  **25<sup>th</sup> ECCO Workshop**  
Athens, **Greece** - July 7, 2012
-  **26<sup>th</sup> ECCO Workshop**  
Durban, **South Africa** - August 10, 2012

-  **27<sup>th</sup> ECCO Workshop**  
Sibiu, **Romania** - September 20, 2012
-  **28<sup>th</sup> ECCO Workshop**  
Bratislava, **Slovakia** - November 16, 2012
-  **29<sup>th</sup> ECCO Workshop**  
Mexico City, **Mexico** - March 7, 2013
-  **30<sup>th</sup> ECCO Workshop**  
Istanbul, **Turkey** - May 2, 2013
-  **31<sup>st</sup> ECCO Workshop**  
Emmetten, **Switzerland** - September 6, 2013
-  **32<sup>nd</sup> ECCO Workshop**  
Gothenburg, **Sweden** - September 20, 2013
-  **33<sup>rd</sup> ECCO Workshop**  
Berlin, **Germany** - November 22, 2013
-  **34<sup>th</sup> ECCO Workshop**  
Prague, **Czech Republic** - March 27, 2014
-  **35<sup>th</sup> ECCO Workshop**  
Sofia, **Bulgaria** - June 13, 2014
-  **36<sup>th</sup> ECCO Workshop**  
Kuala Lumpur, **Malaysia** - August 24, 2014
-  **37<sup>th</sup> ECCO Workshop**  
Paris, **France** - September 20, 2014
-  **38<sup>th</sup> ECCO Workshop**  
Cartagena, **Colombia** - November 22, 2014

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# A new Consensus: Extra-intestinal Manifestations in IBD

**Extra-intestinal Manifestations (EIM) in Inflammatory Bowel Disease (IBD) is the newest ECCO Guideline to be developed**

The process started in spring, with selection of the participants. This caused a problem for us, as far more superb ECCO Members applied than could be accommodated. So after much debate, and some allowance for gender and geographic equity, 25 doctors were chosen and the working groups defined. Four in number, they comprised joints; eyes and skin; liver, biliary and pancreas; and a disparate group containing rarer manifestations. Through the summer these groups reviewed the literature, created a first-draft Consensus Paper and, with much help from ECCO National Representatives and others, thrashed out not just one or two but three iterations of statements. Thus, the stage was set and voting pads ready when we all met recently on a sunny Sunday in Vienna.

As this is a new Consensus, all of the statements were discussed, despite the great majority having already reached the statutory agreement level of >80%. So we were surprised that almost all the statements were changed; and pleased as the changed statements were clearer and, frankly, better. The accompanying ECCO Consensus Paper will be finalised over the next few months, ready for our ECCO'15 Barcelona Congress, where we will delight you by revealing the new EIM Consensus Statements.

Now you might well ask, "What is the strategy for the ECCO Consensus Papers and Statements?". Ten Papers have now been published and another five are to be published in 2015–2016. Over the past few years, several focused Consensus Papers have been written (e.g. Histopathology, Endoscopy, Surgery, Anaemia, Pregnancy) and now comes the one on Extra-intestinal Manifestations. It is planned to update these more specialised Papers approximately every 5 years. The core Consensus Papers (Crohn's Disease and Ulcerative Colitis) will be updated approximately every 3 years and will in future focus more on the modern, state of the art management of active disease and maintenance of remission. Encouragingly, these have become fast-moving fields with the appearance of several different new drugs for treatment of inflammation.

Therefore, subsequent to the Consensus Guidelines on Malignancy in IBD and the ECCO-ESCP Consensus Guidelines on Surgery in CD, there is no plan at present for a new Consensus Paper to appear in the future (as opposed to the updates mentioned above). However, ECCO would never wish you to rest on your laurels.



EIM Consensus participants © ECCO



Tim Raine, Johan Burisch © ECCO



EIM Consensus participants © ECCO

So, annually there will be a Call for 15 ECCO Members to participate in an Expert Review Paper. The first panel has already been convened by Florian Rieder and Axel Dignass, and will meet at ECCO'15 Barcelona Congress to review the management of fibrosis. In 2016, Andreas Sturm and Paolo Gionchetti will co-ordinate a panel to discuss the management of IBD in the elderly, and in 2017 the role of environmental factors in IBD will be discussed. So please look out for requests to help with these endeavours.

We hope you will enjoy reading the latest ECCO Consensus when it is published in Journal of Crohn's and Colitis next year. Beforehand, the statements will be incorporated into the latest version of the e-CCO e-Guide, to be released at ECCO'15 Barcelona Congress. See you in Barcelona.

**FRANCK CARBONNEL, MARCUS HARBORD**

GuiCom Members



Matthieu Allez, Martine de Vos © ECCO



Marcus Harbord, Franck Carbonnel, Tim Raine, Erik Wohlfahrt (CPG IT Support), Stephan Vavricka © ECCO



# ECCO Engagement in the SADEL Project: The first "EU Research Project Fellow"

**In 2012 the European-funded SADEL project (Scaffolds for alternative delivery), part of the Seventh Framework Programme (FP7), started its work on developing a new targeted drug for IBD treatment by making use of the Nanofitin protein scaffold technology**

Nanofitins are artificial proteins that are being developed as alternative tools to antibodies. They show optimal tissue penetration due to their small size and a long half-life in the digestive tract resulting from strong resistance to pH and human intestinal fluids. High affinity for the chosen target results in low effective concentrations, thereby reducing the therapeutic costs. Preliminary data regarding Nanofitins demonstrate a strong potential for optimised pharmacological properties, including reduced immunogenicity.

The therapeutic target chosen by the SADEL consortium is TNF $\alpha$ , a well-known regulator of immune cells and systemic inflammation. The Nanofitin-based drug is supposed to be administered orally, thereby reducing systemic exposure and avoiding the safety issues reported with systemic anti-TNF $\alpha$  antibodies. It is intended to represent the first generation of oral anti-TNF biotherapeutics tackling disease targets in the digestive tract.

The SADEL consortium is a virtual biopharmaceutical company consisting of several small- and medium-scale enterprises, academics, clinicians and pharmaceutical companies with cutting-edge skills such as GMP production, analytics, preclinical and clinical development, licensing and clinical implementation.

ECCO has become part of the consortium in order to advise on designing a clinical phase 1 trial of the new therapeutic product in Ulcerative Colitis and to provide medical and scientific advice, especially in the field of IBD, to all partners in the project. This trial will provide the clinical proof of concept for the effectiveness of Nanofitins and their potential to enlarge the therapeutic armory in IBD treatment.

As a consortium partner with broad IBD-specific knowledge and an excellent network, ECCO will ensure continuous and independent evaluation of both the drug development programme leading towards the clinical trial and the contingency plans in respect of clinical implementation. In order to closely follow the project and to ensure that the intended new therapeutic substance delivers the greatest clinical benefit for IBD patients, ECCO has for the first time designated an ECCO EU Research Project Fellow.

In 2014 I became ECCO EU Research Project Fellow to fulfil this role. Having been engaged in

the field of IBD since 2007, I am currently working as attending physician in the Department of Gastroenterology at the DRK Clinic Westend in Berlin, Germany. Under the overall signing authority of the ECCO President and the direct supervision of Andreas Sturm, as voluntary Senior Expert Officer with the lead in this EU Research Project, I am engaged in ensuring a continuous presence in and provision of clinical advice to the project.

In regular telephone conferences and twice yearly face-to-face meetings, all participants of the consortium meet and discuss new findings and the progress of the project. During these meetings, necessary studies and analyses as well as further investigational steps are settled.

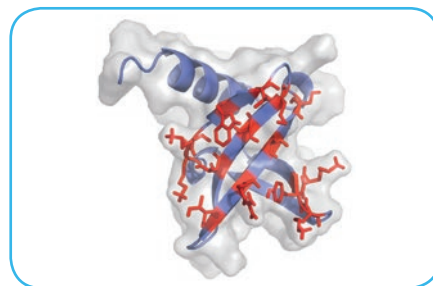
After familiarising myself with the project's 2-year history, I first met the consortium members in February in Copenhagen and was impressed by the high level of assembled expertise: Outstanding experts in different fields and from all over Europe (Austria, Belgium, Denmark, France, Italy, Portugal, Switzerland) were working closely together to achieve the project goal. The scientific and administrative work is meticulous and is distributed into several working packages among the consortium members.

One of the most important tasks for me and the other consortium members in this early phase of the project is to ensure that across the different work packages every researcher acts in compliance with the regulatory requirements of the project and that the gathered data are sufficient for regulatory approval. At the meetings I strongly advocate the clinical point of view, which ECCO believes will be crucial in creating a drug product that optimally meets the IBD patient's needs. Therefore I have helped to clarify the different natures of Crohn's Disease (as a transmural disease) and Ulcerative Colitis (as a mucosal disease), the latter potentially being better reached by oral administration, and have suggested the need to specifically measure mucosal drug concentrations and to study the drug's influence on Extra-intestinal Manifestations.

The more the project develops, the more ECCO will be involved in preparation of the clinical trial design and in disseminating information from researchers to IBD clinicians. Already at the 9<sup>th</sup> Congress of ECCO in Copenhagen, the attentive participant will have been able to



spot the first SADEL poster in the entrance hall, providing information on the project and the progress made to date. If everything advances as desired, you will hear more about this promising project in the future.



Nanofitin © Afflogic Laboratories

**JOHANNES MEIER**  
ECCO EU Research Project Fellow

*SADEL (Scaffolds for Alternative DELivery)  
is a project supported by the  
European Commission through the  
Seventh Framework Programme (FP7)*





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Volume 8  
Issue 12  
December 1, 2014

# JCC

JOURNAL of CROHN'S & COLITIS



Capsule endoscopy in Crohn's Disease  
*See article on page 1598 – 1616*



# JOURNAL OF CROHN'S & COLITIS

International Journal Devoted to Inflammatory Bowel Diseases  
Official Journal of the European Crohn's and Colitis Organisation



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# N-ECCO – Update on current Activities and new Initiatives

## N-ECCO continues to provide educational and networking opportunities for nurses working with patients who have IBD

At the ECCO'15 Congress in Barcelona, the 6<sup>th</sup> N-ECCO School will be attended by 35 nurses who will receive basic education in IBD. A new feature in the programme for 2015 is a talk on adherence. For those interested in attending the School in 2016, please contact the N-ECCO National Representative of your country (please refer to page 34).

The well-established 9<sup>th</sup> N-ECCO Network Meeting will cover a wide variety of subjects presented by expert speakers from several centres in Europe. The programme for the Network Meeting is, as always, based on the suggestions offered by delegates from the previous Network Meeting. The programme for 2015 will include a debate for the first time. Interaction with participants will be encouraged throughout the meeting.

The 2<sup>nd</sup> N-ECCO Research Networking Forum will be of special interest to nurses already undertaking research and to nurses wishing to learn about research or perform research themselves in the future. The programme allows a generous amount of time for discussion and networking with experienced research nurses from the United Kingdom and Scandinavia.



N-ECCO Committee (Lydia White, Palle Bager, Jannette Gaarenstroom, Nienke Ipenburg, Karen Kemp © ECCO)

The complete programmes for the N-ECCO School, N-ECCO Network Meeting and N-ECCO Research Networking Forum are available on the ECCO'15 Congress Website ([www.ecco-ibd.eu/ecco15](http://www.ecco-ibd.eu/ecco15)).

N-ECCO is currently involved in the development of the first N-ECCO e-Learning Cases for nurses. These cases will provide learning opportunities online for all nurses and in particular for nurses whose first language is not English and who wish to study at a slower pace. Many nurses who, due to financial restrictions, are not able to attend ECCO will have

the opportunity via e-COO Learning to gain the knowledge necessary to care for IBD patients anywhere.

One of the aims of N-ECCO, along with providing educational opportunities, is to create opportunities for networking. The N-ECCO Travel Award provides the opportunity for any nurse who is a member of ECCO to visit an established nursing service in another European country. As some nurses may be deterred by language problems, it is also possible for nurses to visit a nursing service in their own country. N-ECCO would like to encourage inexperienced nurses to apply for this exciting opportunity. The next call for applications will be sent out in May 2015.

At the ECCO'15 Barcelona Congress, two Committee Members will be stepping down. We would like to thank Nienke Ipenburg and Lydia White for all the hard work they have done and for their exceptional dedication to N-ECCO.

Hope to see you in Barcelona!

**JAN GAARENSTROOM**  
N-ECCO Chair

# Ileal Pouch Surgery and the United Kingdom Ileal Pouch Registry

## Restorative proctocolectomy (ileal pouch surgery) is a procedure that has transformed the lives of patients with Ulcerative Colitis

Prior to the introduction of this surgical technique in the late 1970s, patients requiring surgery underwent proctocolectomy with permanent ileostomy. The pouch procedure also involves removal of the colon and rectum but preserves the anal sphincter and uses the last 40 cm of small bowel to create a reservoir in place of the rectum. This procedure enables most patients to achieve a normal life with satisfactory bowel function and avoidance of a stoma.

Ileal pouch surgery is a complex operation and significant surgical skill is required to perform it well. It is performed by colorectal surgeons and constitutes a specialist procedure. Pouch surgery is, however, an infrequently performed procedure for many surgeons. In the United Kingdom only 350 ileal pouch operations are performed annually.

In 2010 the Association of Coloproctology of Great Britain & Ireland (ACPGBI) launched a collaboration with Dendrite Clinical Systems to develop the Ileal Pouch Registry. This initiative was led by John Nicholls and myself assisted by a small working group. The aim of the registry was to promote high-quality care for patients undergoing restorative proctocolectomy. The registry permits surgeons to enter patients undergoing pouch surgery within the United Kingdom or abroad. In the United Kingdom there are increasing drives to record outcome of complex procedures on voluntary registers as it is acknowledged that this process is associated with quality improvement. The registry contains details of patients' disease, operation and outcomes – including complications and failures. Importantly, all outcomes associated with surgeons, as well as institutions, are anonymised.

In 2012 the first Ileal Pouch Registry report was published in association with the ACPGBI. The report highlighted the outcomes for 2,383 patients undergoing restorative proctocolectomy. Of these, 2,209 patients had undergone primary pouch surgery and 162 a revision procedure following the failure of primary ileal pouch surgery. The earliest procedure recorded in the registry was carried out in 1977. Accordingly, the registry reflects the outcomes of this surgery since its initial description.

Of the 2,209 patients recorded in the pouch registry as having undergone primary pouch surgery, 80% underwent the procedure for Ulcerative Colitis. Nearly 30% of patients undergoing surgery experienced a complication. Importantly, pelvic sepsis (including anastomotic leakage, abscess or



fistula formation) occurred in 12.7%. Over the long term, pouch failure, defined as loss of anal function due to removal of the pouch or to the formation of an indefinite ileostomy, occurred in 5.2% of patients undergoing a primary procedure. The failure rate was three times higher (15.4%) in those undergoing revisional pouch surgery. Amongst the vast majority of patients pouch function is good. Most patients with pouches open their bowels 5–6 times per day and this function is preserved in the long term, allowing patients to maintain a relatively

normal life.

Although the Ileal Pouch Registry was developed in the United Kingdom, we were encouraged to see a significant contribution from surgeons working in Continental European institutions. It would appear that many European surgeons who dedicate their working lives to the management of Inflammatory Bowel Disease recognise the importance of such an initiative. The Ileal Pouch Registry can be found on the ACPGBI website (and can be accessed directly at [demo.e-dendrite.com/](http://demo.e-dendrite.com/)

[csp/ilealpouch/frontpages/ipdbfront.csp](http://csp/ilealpouch/frontpages/ipdbfront.csp)). We welcome all surgeons wishing to submit their data to register at the above web address.

**OMAR FAIZ**

St Mark's Hospital, Department of Colorectal Surgery

## Changing the Future by Early Intervention

**The Third International Symposium on Pediatric Inflammatory Bowel Disease, endorsed by ECCO and ESPGHAN, was a great success**

Almost 500 participants attended the three-day congress on September 10–13, 2014 in Rotterdam, the Netherlands with Hankje Escher, a former P-ECCO Representative, acting as congress president. The meeting brought together Pediatric Inflammatory Bowel Disease (PIBD) experts and researchers interested in PIBD from 41 countries all over Europe, Asia, America, Australia and New Zealand. The intense programme was full of new research, state of the art knowledge and interactive discussions.

In paediatrics, special consideration in the management of IBD is paid to the restoration of growth and pubertal development. Alarming, final height remains below the fifth centile in 15–30% of Crohn's Disease (CD) patients with paediatric disease onset, though this is less often the case in Ulcerative Colitis (UC). Lessons learned from treating paediatric patients include the need to correct malnutrition and provide nutritional support, to restrict corticoid use to short periods, and to address the importance of control of inflammation while not forgetting the promotion of physical activity to restore bone density. The strategy of treating patients with growth failure is summarised in the recent ECCO-ESPGHAN Guidelines of management of PIBD, which were elegantly presented by Frank Ruemmele, the former P-ECCO Chair. The invited lecture given by the acting P-ECCO Chair, Arie Levine, shed new light on the role of dietary therapy, as did some of the best abstracts selected for oral presentations. Topics addressed exclusive enteral nutrition (EEN), given for 6–8 weeks, as the most obvious and ignored clue to the effect of diet as an environmental factor triggering disease development. Research



Welcome speech by Arie Levine  
© merel van pieterson fotografie



Delegates participating actively in sessions  
© merel van pieterson fotografie

presented by investigators from Glasgow challenged prevailing wisdom concerning the effect of enteral nutrition on the microbiota and protective species, highlighting that we still do not fully comprehend the mechanism of action. Why should we research diet? Modification of

diet offers an intriguing possibility for control of an upstream driver of inflammation without additional drugs. Although EEN may induce attenuation of inflammation and promote weight gain, it does not always work. EEN results in alteration of the intestinal microbiome and changes faecal metabolic activity but this is not maintained when normal diet is resumed. And disappointingly, without additional medication the disease control induced by EEN is not maintained either. So far, the limitations of dietary therapy are incompletely understood, as is the basis for selection of ideal candidates for such therapy. Likewise, evaluation of the role of individual dietary components warrants systematic studies.

Importantly, during this meeting, opinion leaders from Europe, Israel and North America officially started PIBD-NET, a worldwide independent network of PIBD centres, which you will hear of soon!

The closing session challenged everyone to think about and discuss solutions for the future, providing an excellent booster for research. We look forward to the Fourth International Symposium on PIBD in Barcelona in September 2017 and continued enthusiasm in improving the care of our young patients!

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**KAIJA-LEENA KOLHO**  
P-ECCO Member

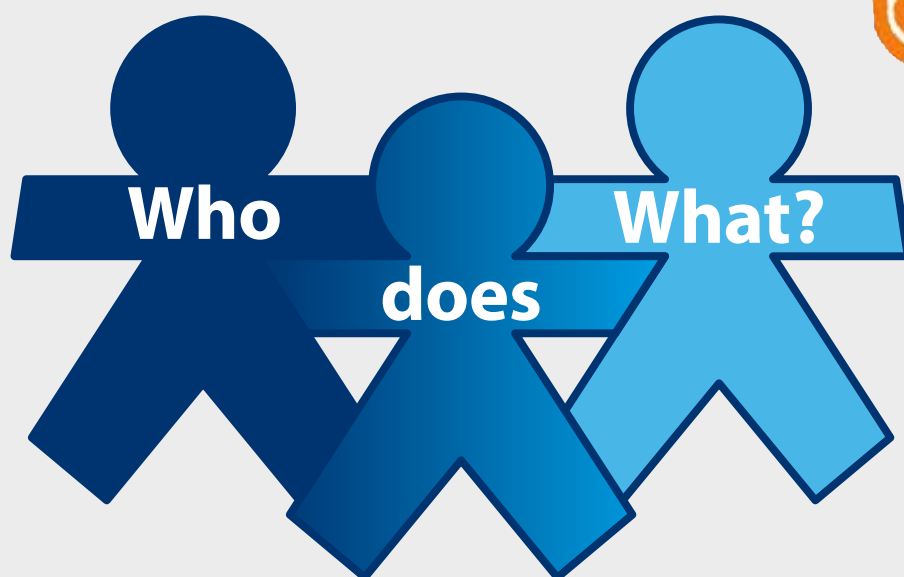


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# Dear Y-ECCO Friends,

Let me give you a short update on what's happening in our group. First of all, I'm happy to announce that Sebastian Zeissig and Tim Raine applied to extend their term on the Committee for one year. I would like to thank them for the outstanding work they have done already and I look forward to working together with them for another year. Yet it has to be said that some other excellent candidates applied for a Y-ECCO Committee position. I can only encourage these people to re-apply next year, as we will have at least three open positions on our Committee for 2016–2019. In the meantime, your help is needed for our growing number of Y-ECCO Activities.

## Y-ECCO Activities at the ECCO'15 Barcelona Congress

As you probably all know by now, each year Y-ECCO organises a workshop aimed at helping Y-ECCO Members to establish their professional careers. Year on year, the feedback from the participants is excellent, and I'm confident that this year's workshop will be a huge success again. The theme for this year is: "Career and job interview workshop – how to sell yourself". It will be a highly interactive workshop where you will learn how to optimise your cover letters, your CV and your performance at job interviews. Our members' meeting and informal networking event will immediately follow the Y-ECCO Workshop: You are warmly invited to join us for a drink – it is a unique opportunity to get to know each other. Y-ECCO will also have a separate corner at the ECCO Interaction: Hearts and Minds on Friday evening. We all hope to see you there!

For the first time, Y-ECCO has organised the Basic Science Workshop, which is scheduled for the Friday afternoon, in parallel with the clinical case-based session. You will find more

information about this workshop in this edition of ECCO News.

## Y-ECCO involvement in ECCO Guidelines

For more than a year now, Y-ECCO Members have been involved in the development of the ECCO Guidelines. Besides being part of the discussion panel, you are asked to develop an e-CCO Learning Case that incorporates all the latest developments covered by the specific Guideline Paper. This is a big opportunity as it is a unique learning process and you will become full co-author of the final manuscript. You can apply at any time and spaces will be allocated on a competitive basis.

## Development of e-CCO Learning

Over the last year, e-CCO Learning has expanded tremendously and the help of Y-ECCO Members is required to ensure its continuing success. You can write an e-CCO Learning Case under the supervision of a senior ECCO Member or you can record a (video) podcast. It's the ideal way to increase your visibility within the IBD Community. Just let us know if you are interested and what your area of expertise is.

## Y-ECCO Literature reviews

The Y-ECCO Literature reviews are now a well-known and highly appreciated part of ECCO News. If you want to write such a review on a recently published landmark IBD paper, please let us know. You will be featured in ECCO News with an accompanying photo and your affiliations.

## Y-ECCO Interview corner

Monica Cesarini has been an excellent Y-ECCO Interview corner Administrator and I would like to thank her for all the hard work she has done. As Monica's term is coming to an end you will

find her last interview in this issue. Starting from Issue 1/2015, her job will be taken over by Nuha Yassin from the UK.

## Clinical Study Protocol submission to Y-ECCO

If you have a good study proposal but you need a large number of patients, you can submit your proposal and protocol to Y-ECCO and we will forward it to ClinCom, who will perform a feasibility analysis and an expert review of your protocol. Once the study has been approved, Y-ECCO will endorse your study by using all possible tools, in order to maximise participation by centres within Europe.

## Y-ECCO co-chairing programme

You can continue to apply for the Y-ECCO co-chairing programme for future ECCO Congresses. This gives you the opportunity to chair a session alongside an experienced ECCO Expert. Selections will be made on a competitive basis.

If you are interested in any Y-ECCO-related activities or if you have ideas for new projects, please let us know by contacting [ecco@ecco-ibd.eu](mailto:ecco@ecco-ibd.eu).

We are looking forward to hearing from you. As always, thank you for all you do for Y-ECCO.



Pieter Hindryckx © ECCO

**PIETER HINDRYCKX**  
Y-ECCO Member

# First Y-ECCO Basic Science Workshop

## Dear Y-ECCO Members,

It is a pleasure to invite you to the first edition of the Y-ECCO Basic Science Workshop, which will take place on Friday, February 20, 2014 as part of the ECCO educational programme of the ECCO Congress. It is targeted at basic scientists and clinicians with an interest in basic science.

We have launched this new workshop to give basic science a more visible platform within ECCO and the ECCO Congress, and to promote scientific exchange and networking among young basic scientists within the IBD Community. The central theme of this year's workshop will be "Host–environmental interactions in intestinal homeostasis and inflammation". There will be one session on "Host–microbial interactions in IBD" and one on "Immunity and genetics in intestinal inflammation". In each session, there will be a general introduction to the topic by an

outstanding scientist in the field (Maria Abreu and Marc Veldhoen), followed by four oral presentations of top-ranked abstracts by Young ECCOs and an interactive discussion on best practices with respect to the research topic.

Selection for oral presentations will be performed on a competitive basis amongst basic science abstracts submitted to the ECCO'15 Barcelona Congress. To be considered for presentation at the Basic Science Workshop, please tick the respective checkbox when submitting your abstract. All abstracts will independently be considered for the main ECCO'15 Congress programme.

Online registration will be available shortly, with a deadline of February 3, 2015. Please register early as spots are limited. The registration fee is EUR 80.- for non-members and EUR 40.- for Y-ECCO Members (and IBD nurse members).



Y-ECCO Committee Members (Tim Raine, Sebastian Zeissig, Pieter Hindryckx, Isabelle Cleynen, Tiago Nunes) © ECCO

We hope to meet you at our inaugural Basic Science Workshop.

**ISABELLE CLEYNEN**  
Y-ECCO Member

## 8<sup>th</sup> Y-ECCO Workshop

Every year, the Y-ECCO Committee organises a specific workshop targeted at our young members (Y-ECCOs) – the Y-ECCO Workshop.

In its eighth edition, the next Y-ECCO Workshop will give guidance and provide practice in the skills of networking, preparing effective cover letters and CVs, and performing well at job interviews. For this edition, the Y-ECCO Committee has come up with a few surprises to make the course more exciting to our members! Instead of traditional lectures, the Y-ECCO Workshop will promote an interactive and fun two-hour session in which participants will practice their skills guided by Judith Martin and Jeffrey Beyer, two renowned specialised trainers experienced in career development, professional communication and intercultural management. Jeffrey Beyer has focussed on teaching and training professional development and communication skills for over 20 years, working on many MBA programmes around the world. Judith Martin is an expert

in global leadership and career development, working together with various multinationals and business schools in Europe and Asia. The interactive activities will include group role-playing, quizzes and games in a laid-back and friendly environment.

Finally, the Y-ECCO experience would not be complete without the Y-ECCO Networking Event, which will take place immediately after the workshop and will offer a perfect opportunity for the younger members of ECCO to get to know each other.

In order to guarantee your presence at the workshop, please register in advance since no onsite registration will be possible and the number of participants is limited (registration deadline: February 3, 2015). We look forward to seeing you all next year in Barcelona!

**TIAGO NUNES**  
Y-ECCO Member



Tiago Nunes and 7<sup>th</sup> Y-ECCO Workshop participants © ECCO



7<sup>th</sup> Y-ECCO Workshop group at ECCO '14 Copenhagen Congress © ECCO

## Y-ECCO Interview corner

*Dear Y-ECCO Members,*

It's a pleasure to introduce the seventh "Y-ECCO Interview corner" interview, with Geert D'Haens.

The rationale of the "Interview corner" is to perform a short interview with a senior ECCO Member, in order to provide advice to young doctors on how to pursue a career in IBD.

We would appreciate your contribution in suggesting questions of interest to the ECCO Office under [ecco@ecco-ibd.eu](mailto:ecco@ecco-ibd.eu). We look forward to hearing from you.

Yours sincerely,

**MONICA CESARINI**  
Y-ECCO Interview corner Admin



Monica Cesarini © ECCO

## Monica interviews Geert d'Haens



Geert D'Haens © ECCO

*You are one of the main characters in the ECCO landscape: What do you think is the main point of this organisation and why should young doctors be part of it?*

As one of the founders of ECCO I have seen an amazing evolution over the years. Beginning with a small group of representatives of National IBD Study Groups, the organisation has now become the largest society devoted to the field of Inflammatory Bowel Disease (IBD). An aspect that has been very positive is the involvement of IBD nurses, surgeons, young investigators, partners from industry and patient associations. They are all "stakeholders"

in the care of patients with IBD. For many initiatives, it is the input and contributions from these different angles that determine their success. Given the large number of ECCO Committees, working parties and scientific initiatives, really everybody who has a desire to contribute can do so. Undoubtedly, many members' careers have benefited from the work they did for ECCO. Starting with small-scale educational initiatives in the early years (advanced courses in Prague and Sardegna, for instance), ECCO took the wonderful initiative to develop Consensus Guidelines under the initial guidance of Eduard Stange from Stuttgart,

Germany. Many important papers that are highly referenced were the first internationally visible product of the organisation that emerged from those meetings. Regular updates will remain a challenge for the future. A further milestone was the start-up of the Journal of Crohn's and Colitis (JCC) (I still remember the voting round I organised for the name of this journal!). Credit and thanks should go to Miquel Gassull from Badalona, Spain for his perseverance in making this initiative a true success. Around the same time we held the first ECCO Congress in Amsterdam at the Academic Medical Center (AMC). Ever since then the ECCO



Congresses have become better and bigger, with attendance now tenfold compared with that first Congress. Another major leap forward was the professionalisation of the ECCO Office in Vienna. Where we started off with only one person and a temporary rented space in Vienna, the machinery behind the ECCO scene has now grown significantly under the leadership of Nicole Eichinger. Daniel Hommes and Simon Travis put a lot of effort into building up that ECCO Office.

A further and logical step is now being taken in the promotion and even coordination of large-scale scientific initiatives such as the ICARE project. So, basically I do not see a reason why young physicians would NOT become part of ECCO: You can learn a lot, you hear the best and most recent research results in the field and you have a great opportunity for network establishment across the continent.

***Would you please tell us some key events that helped you in your brilliant career?***

Being "successful" in your career really depends on many factors. One of the pivotal components, however, is definitely "mentorship". I had the opportunity to work with Steve Hanauer in Chicago for a year in the early nineties, and today I still benefit from that learning experience and even more from the network that came along with a fellowship abroad. So, the number one recommendation I would give to young and ambitious investigators is to move around and try to spend time with the leaders in the field. To become a giant on your own may not be impossible, but examples are, honestly, quite rare. Furthermore, you need

to invest time in research. Thinking of original and creative projects, carrying them out and above all writing them up is a difficult process that we all need to go through at some point. And nobody else will do this job for you. So, to spend nights and weekends on reading and writing is a paramount requirement for the successful investigator and scientist. Never give up! Many things are "thought" to be impossible but are really not for those who are motivated and stubborn.

And finally, when you get to build your own team, be selective in the people you take on board. My personal approach is to try and find collaborators who have the potential to become better than myself. I create the environment, offer help with financial resources and supporting staff and offer assistance in developing original research ideas. Even later in one's career it remains important to work with international experts who can help and push your research forward.

***You are a supporter of many initiatives for young researchers. Could you mention and explain some?***

I have many more research ideas than I can ever carry out myself. So why not stimulate young fellows to spend a few years of research and move the field forward? In the Netherlands it is quite common that motivated young physicians work in a PhD programme for four years before embarking on their training in gastroenterology. At the AMC in Amsterdam it is virtually impossible to enter the training without such a PhD degree. So many young physicians interview to enter the research programmes

for which we have funding. In addition, I host a 'Robarts clinical trial' fellowship, which is a one-year funded research fellowship combined with some clinical practice at the AMC, consistently leading to multiple publications that we develop with the other Robarts offices in London, Ontario and San Diego, California. The upcoming selection round will focus on a candidate who is interested in translational IBD research in close collaboration with the Tytgat GI research institute at the AMC and Gijs van den Brink. With this initiative we wish to set up an evaluation system for 'early drug development' in a limited sample of IBD patients. Furthermore, I try to launch research ideas at National IBD Societies such as the Dutch ICC, the Belgian BIRD and the French GETAID. Over the years, you get to understand which projects belong to the different settings: monocentric, national, international or CRO/pharma driven. All have their specific cost and timely delivery of research results is extremely important to gain and keep momentum. And again: Not to give up is critical in large projects. With the IOIBD ([www.ioibd.org](http://www.ioibd.org)) we also offer travel and scientific grants annually that are worth looking into. My bottom line is simple: Highly skilled and motivated people need support to make their way upward and usually do so with a little help here and there. To see that some of my young "pupils" are on the way to becoming 'giants' is extremely rewarding.

**MONICA CESARINI**  
Y-ECCO Interview corner Admin

## Dear Y-ECCO Members,



Isabelle Cleynen © ECCO

During the past few years, the Y-ECCO Literature reviews have become a fixed and well-received part of ECCO News. The purpose of the literature reviews is to highlight the most recent landmark articles within the field of IBD. The articles can be about clinical phase three trials, epidemiology, endoscopy, basic science etc.

Every Y-ECCO Member can participate in this initiative. The idea is for you to choose a timely and relevant article, and to summarise the key findings and relevance of the paper in one page. Your review will then be published together with a personal picture and a short self-description.

If you are interested in writing a literature review or if you have any questions, you can contact Isabelle ([isabelle.cleynen@med.kuleuven.be](mailto:isabelle.cleynen@med.kuleuven.be)).

**ISABELLE CLEYNEN**  
Y-ECCO Committee Member



Triana Lobatón © Triana Lobatón

In the previous issue of ECCO News we misrepresented the author of "Etrolizumab as induction therapy for ulcerative colitis: a randomised, controlled, phase 2 trial", which should have been Triana Lobatón, Gastroenterology Unit, University Hospital Germans Trias i Pujol, Barcelona, Spain by publishing the wrong photo. We would like to apologise for this mistake and officially introduce you to Triana Lobatón.

## Comparative effectiveness of immunosuppressant and biologics for inducing and maintaining remission in Crohn's Disease: A network meta-analysis

Hazlewood GS, Rezaie A, Borman M, Panaccione R, Ghosh S, Seow CH, Kuenzig E, Tomlinson G, Siegel C, Melmed GY, Kaplan GG. *Gastroenterology* 2014; doi: 10.1053/j.gastro.2014.10.011.

### Introduction

The usage of immunosuppressive drugs in the treatment of Crohn's Disease (CD) has significantly increased in recent decades. Moreover, the introduction of biologics has not only improved the possibilities of treating CD more successfully, but also changed the philosophy of therapeutic approaches in Inflammatory Bowel Diseases (IBD). The most important immunosuppressant drugs are azathioprine (AZA)/6-mercaptopurine (6-MP) and methotrexate (MTX). The most widely used biologic agents belong to the group of anti-tumour necrosis factor (anti-TNF) antibodies (infliximab, adalimumab and certolizumab). Recently, more data have been provided in terms of the efficacy of the anti-integrin antibody vedolizumab in CD [1–3].

Because the number of immunosuppressive drugs and biologics is increasing, it is essential to provide a clear therapeutic algorithm in order to optimise treatment regimens in CD and minimise toxicity [4]. However, the choice of therapeutic strategy is still challenging as head-to-head trials directly comparing different treatments are lacking. Moreover, in the study performed by Stidham et al. it was suggested that adequately powered head-to-head comparative efficacy trials would be very difficult to conduct, and impractical in terms of cost and size, as they would require more than 3,000 patients [5]. Thus, it seems that we have to rely on data from the clinical trials performed so far.

Hazlewood et al. performed a systematic review of MEDLINE, EMBASE, and Cochrane Central databases, through June 2014, in order to identify randomised controlled trials comparing AZA-6-MP, MTX, infliximab, adalimumab, certolizumab, vedolizumab, or combined therapies with placebo or an active agent for induction and maintenance of remission in adult patients with CD.

### Key findings

The authors identified 39 randomised controlled trials. They analysed direct and indirect evidence of the therapeutic efficacy of different treatments

options by comparing the results of multiple studies. Pairwise treatment effects were estimated through a Bayesian random-effects network meta-analysis and reported as odds ratios (OR) with a 95% credible interval (CrI).

It was shown that drugs which were most effective in induction of remission included infliximab + AZA, adalimumab and vedolizumab, when compared to placebo. AZA/6-MP and MTX efficacy did not differ significantly for induction of remission relative to placebo. Pairwise analysis of anti-TNF agents revealed that infliximab + AZA [OR=3.1 (1.4–7.7)] and adalimumab [OR=2.1 (1.0–4.6)] were superior to certolizumab for induction of remission.

In contrast to the data concerning the induction of remission, for maintenance therapy the superiority of all treatments compared with placebo was demonstrated, with the exception of the combination of infliximab and MTX. Infliximab [OR=1.6 (1.0–2.5)], adalimumab [OR=2.9 (1.6–5.1)] and combination therapy with infliximab + AZA [OR=3.0 (1.7–5.5)] were more effective in maintaining remission in comparison with AZA/6-MP alone. When only considering anti-TNF agents, combination treatment with infliximab + AZA and monotherapy with adalimumab were superior to certolizumab. Additionally, it was shown that adalimumab was more effective than vedolizumab as a maintenance therapy in CD.

Interestingly, it was also shown that CD patients treated with AZA/6-MP or MTX were more likely to have an adverse event leading to the withdrawal of the drug, when compared with placebo, most anti-TNF monotherapies, and vedolizumab.

### Conclusions

The cited meta-analysis performed by Hazlewood and colleagues can serve as a guide for practitioners who have to make difficult decisions on the therapeutic approaches in patients with moderate to severe CD. It was shown, in general, that the best treatment option for both the induction and the maintenance of remission is adalimumab or infliximab + AZA. However, the authors indicate that the conclusions drawn from this network meta-analysis have several significant limitations, including the heterogeneity across analysed clinical trials, the reliance mainly on indirect evidence and the fact that only CD patients with moderate to severe disease activity were taken into account as this is the typical definition of study groups in randomised

controlled trials. Thus, it will be essential to perform head-to-head trials directly comparing the efficacy and safety of different immunosuppressive drugs and biologics in patients with CD, although conducting this kind of trial could be very difficult.

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Piotr Eder © Piotr Eder

## PPAR $\alpha$ -UGT axis activation represses intestinal FXR-FGF15 feedback signaling and exacerbates experimental colitis

Zhou X, Cao L, Jiang C, Xie Y, Cheng X, Kruasz KW, Qi P, Sun L, Shah YM, Gonzalez FJ, Wang G, Hao H  
Nature Communication, 2014 September;5:4573

### Introduction

Even though the aetiology of Inflammatory Bowel Disease (IBD) is still largely unknown, it is now widely accepted that the pathogenesis of IBD involves several mechanisms: Genetic and environmental factors, dysregulation of the intestinal barrier function and alteration in the mucosal immune system [1,2]. In particular, traditional therapeutic approaches are designed to target the over-activation and chronicity of mucosal immune responses [3,4]. However, immune suppressor therapies showed variable response rates and notable side effects [3,4], justifying the augmented interest in alternative therapeutic approaches.

In recent years, a huge amount of information has pointed out the importance of a "healthy" intestinal microflora. Indeed, the alteration of gut microbiota, a phenomenon called dysbiosis, has been recognised as a pivotal element in supporting IBD pathogenesis [5,6]. Recently, it has been proved that impaired microbiota enzymatic activity observed in IBD-associated dysbiosis leads to modifications in the luminal bile acid (BA) pool composition [7]. In particular, dysbiosis is responsible for an accumulation of sulphated BAs at the expense of secondary BAs. These changes contribute to the loss of the anti-inflammatory effects of secondary BAs on intestinal epithelial cells, while enhancing chronic inflammation [7].

The mechanisms behind BA dysregulation, however, are still the subject of intensive investigation. In this original research article, Zhou and colleagues clarify how BA homeostasis is altered during experimental colitis, and point out the intestinal peroxisome proliferator-activated receptor  $\alpha$  (PPAR $\alpha$ ) as a novel therapeutic target.

### Key findings

The authors investigated BA amount in several murine compartments, including liver, small intestine, colon, serum, urine, and faeces, and found a compartment-specific dysregulation pattern of BAs after the dextran sulphate sodium (DSS) insult. Importantly, the BA accumulation was evident not only in the faeces, as previously reported [7], but also in the inflamed colon. The levels of BA were significantly lower in the small intestine. The authors also showed that the hepatic expression of the cholesterol 7 $\alpha$ -hydroxylase (CYP7A1) was significantly augmented, supporting the existence of an increased de novo BA synthesis.

The farnesoid X receptor (FXR) is a master regulator maintaining the homeostasis of BAs. Indeed, when BAs are intracellularly accumulated, FXR signals through SHP and FGF15 (FGF19 in human) inhibiting CYP7A1 activity. FXR, as a BA-activated

transcriptional factor, senses the levels of BA and shuts down genes involved in BA synthesis, influx and efflux. However, the authors showed that FXR-FGF15 signaling is compromised during colitis, especially in intestinal epithelial cells: Even if the FXR level was unaffected, the target genes Shp and Fgf15 were significantly reduced.

Since in the small intestine the levels of BA were decreased, the authors investigated whether lower levels of FXR ligands are responsible for the compromised FXR-FGF15 signaling. Both apical and basal transporters of BA remained unchanged, suggesting that the reduced FXR signaling is not due to BA malabsorption. In contrast, the glucuronidation metabolites of BAs were dramatically enhanced in both faeces and urine. UDP-glucuronosyltransferases (UGTs) are enzymes critical for the accumulation of BA metabolites. The authors showed that the several isoforms of UGT are all up-regulated in the small intestine together with an increased enzymatic activity.

Finally, the authors investigated the expression and activity of the peroxisome proliferator-activated receptor  $\alpha$  (PPAR $\alpha$ ), a transcriptional factor involved in regulating the expression of various UGT enzymes. As expected, colitic mice had elevated levels of oleyl ethanolamide (OEA), a natural endogenous lipid that activates PPAR $\alpha$  with high potency. The administration of Wy-14643, a PPAR $\alpha$  agonist, dramatically enhanced DSS susceptibility, augmenting the UGT levels. Ileal expression of FXR target genes Fgf15 and Shp was further decreased, leading to an up-regulation of the hepatic Cyp7a1 and increased BA pool size in faeces and in the inflamed colon tissues. In agreement with these findings, Ppara-null mice were less susceptible to chronic DSS-induced colitis, ileal expression of UGTs was lower than in the WT counterpart and the expression of the hepatic Cyp7a1 was restored. Chronic administration of FGF19 also markedly attenuated DSS-induced colitis, restoring hepatic expression of Shp and Cyp7a1 and ultimately re-establishing the normal levels of BA.

### Conclusion

In conclusion, the accumulation of the lipid endogenous ligand of PPAR $\alpha$  (OEA) over-activate the transcriptional factor, leading to an up-regulation of UGTs. These enzymes promote the accumulation of the glucuronidation metabolites of BAs. This event is critical for the control of BA homeostasis, as it leads to a decreased level of BA in the small intestine and a compromised FXR-FGF15 signaling that ultimately provokes an increased de novo synthesis of BAs from the liver. BA dysregulation augments the severity of DSS-induced colitis that might be dampened by targeting PPAR $\alpha$ .

In the present work the authors identified PPAR $\alpha$  as a novel therapeutic target for the treatment of IBD. Importantly, the authors clarified how BA dysregulation is achieved during the development of experimental IBD. It was not established whether

diet or gut microbiota alteration is implicated in this process. However, this work described a novel and important link between metabolic deficiency and IBD progression.

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### Marco Genua

*Marco Genua is currently working as a post-doctoral researcher in the IBD unit at the Humanitas Research Hospital, Milan, Italy. He has a strong interest in the mucosal inflammatory response driven by innate immune cells during IBD pathogenesis. Currently, Marco Genua is evaluating the relationship between gut microbiota composition and immune cell activities in order to define novel therapeutic target(s).*

Marco Genua  
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## A global consensus on the classification, diagnosis and multidisciplinary treatment of perianal fistulising Crohn's disease

Gecse KB, Bemelman W, Kamm MA, Stoker J, Khanna R, Ng SC, Panés J, van Assche G, Liu Z, Hart A, Levesque BG, D'Haens G, for the World Gastroenterology Organisation, International Organisation for Inflammatory Bowel Diseases IOIBD, European Society of Coloproctology and Roberts Clinical Trials Gut. 2014 Sep;63(9):1381–92. doi: 10.1136/gutjnl-2013-306709. Epub 2014 Jun 20. PubMed PMID: 24951257.

### Introduction

Fistulising perianal Crohn's Disease (CD) represents an aggressive and disabling disease phenotype which can occur in up to 40% of CD patients [1,2] and is a challenging condition to treat. It requires a multidisciplinary approach where a combination of medical and surgical therapies is used. Prior to the era of anti-TNF $\alpha$  therapies, approximately 40% of patients eventually had to undergo proctectomy [3]. The introduction of anti-TNF $\alpha$  therapies has been encouraging as clinical response rates of up to 68% and complete healing rates of 55% have been reported [4]. Real life data, however, suggest that at long-term follow-up for a median of 5 years, less than 50% of patients sustained clinical remission [5]. The surgical treatment of perianal fistulas in patients with CD may sometimes result in significantly high fistula recurrence rates of up to 20% for simple fistulas and between 25% and 50% for complex ones. Combining surgery with anti-TNF therapy achieves better healing rates than using either treatment modality on its own [6].

The dilemma of how to improve the healing outcomes for this challenging condition still persists. The World Congress of Gastroenterology 2013 set up an expert consensus group to assess the best available published evidence and develop an international consensus on the classification and scoring systems, diagnosis, medical treatments and surgical management of fistulising perianal CD. Members of the expert panel voted on each of the statements made and consensus was defined as at least 80% agreement between the members.

### Key findings

The Consensus Statements were divided into four sections:

#### 1. Classification and scoring

A clinically useful scoring system was recommended as it enables the clinician to evaluate disease severity and to determine the optimal management strategy and the response to treatment. It is important to classify fistulas based on whether they are high or low transphincteric fistulas, in addition to the relation of the fistula tract to the anal sphincter muscles and the levator plate (e.g. Park's classification [7]). The presence of a perianal abscess at the time of diagnosis is also important for the classification of fistulas, as is the presence or absence of proctitis as defined by any ulceration and/or stricture in the rectum or inflammation and/or stricture of the anal canal. Combinations of clinical and radiological [magnetic resonance imaging (MRI) or endoanal ultrasonography (EUS)] assessments were advocated for evaluation of Crohn's fistula activity.

#### 2. Diagnosis and follow-up

Six consensus statements were made with regard to the diagnosis and follow-up of fistulas, covering areas from endoscopy to radiological imaging modalities.

Endoscopic assessment of the rectum is essential in the management of Crohn's anal fistula to determine the presence of proctitis, as is examination under general anaesthesia (EUA). Not only does an EUA aid in the diagnosis and classification of anal fistulas, it also has therapeutic benefits, as the drainage of abscesses and placement of setons are key surgical procedures in the treatment of Crohn's anal fistulas. MRI is the gold standard imaging modality for the diagnosis and classification of anal fistulas. Additionally, MRI is used to map out the luminal disease, its severity and any fluid collections. MRI is necessary in identifying trapped sepsis; however, an EUA should not be delayed if sepsis is suspected and an MRI is not immediately available. EUS is also useful in imaging Crohn's anal fistulas and can be used with or without hydrogen peroxide, although it is operator dependent and the views can be quite limited. Other imaging modalities such as computed tomography and fistulography are of limited use in the diagnosis and classification of Crohn's anal fistulas. Perhaps a combination of imaging modalities should be used in conjunction with EUA in order to ensure diagnostic accuracy and optimal management.

#### 3. Short-term medical treatment goals

Abscess drainage and reduction of symptoms are the primary goals, followed by the long-term goals of resolving fistula discharge, improving patients' quality of life, fistula remission, preserving continence and avoiding proctectomy and permanent stoma formation.

The consensus group agreed that corticosteroids and aminosalicylates have no role in the treatment of perianal Crohn's fistulas. Similarly, the evidence regarding the efficacy of methotrexate and cyclosporine is limited. However, the use of antibiotics, especially ciprofloxacin and metronidazole, has been shown to improve symptoms and aid healing as an adjunct to other medical therapies. Thiopurines alone have a moderate effect in treating Crohn's fistulas and tacrolimus is very effective, but caution is required as drug toxicity can have detrimental effects. Combining thiopurines with anti-TNFs leads to higher response and remission rates than use of either drug alone. Infliximab and adalimumab are moderately effective in inducing and maintaining remission. The evidence regarding the utility of certolizumab pegol is, however, insufficient.

#### 4. Surgical management

Surgery for Crohn's anal fistula is mostly in the form of drainage of perianal abscesses and loose/non-cutting seton insertion. It is important to ensure there is no perianal sepsis prior to starting medical treatments. Laying open of the fistula tract is to be used judiciously in superficial and low intersphincteric fistulas. The risk of incontinence may deter the surgeon from performing this procedure in Crohn's anal fistula patients, especially in women with anterior fistulas. Various continence-preserving fistula procedures

have been described but the healing data are not well known. The challenges to definitive surgical procedures are poor wound healing, especially in the presence of active proctitis, when drainage of abscesses and a loose seton may be the only options. Patients with severe and complicated disease which is refractory to medical therapy may benefit from a temporary diverting stoma, although this may not prevent a proctectomy, which is seen as the absolute last resort in treating refractory fistulising perianal Crohn's disease.

### Conclusion

This consensus paper on the management of fistulising perianal CD has highlighted the importance of a multidisciplinary approach to treatment. The expert panel of authors have agreed on key statements that act as a guide to clinicians in the areas of diagnosis of anal fistulas using clinical and radiological techniques, and medical as well as surgical management as guided by radiology. A very useful treatment algorithm will undoubtedly be used globally by surgeons and gastroenterologists who treat patients with this challenging condition.

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# ECCO Country Member Profiles



## Identity card

- Country: **Ukraine**
- Name of group: Ukrainian IBD group
- Number of active members: 43
- Number of meetings per year: 2
- Name of president and secretary: Mykhailo Petrovich Zakharash, Andrey E. Dorofeyev
- National Representatives: Mykhailo Zakharash, Yuriy Vinnyk



## Identity card

- Country: **Croatia**
- Name of group: IBD Group, Croatian Society of Gastroenterology
- Number of active members: 50
- Number of meetings per year: 2-3
- Name of president and secretary of Croatian Society of Gastroenterology: Milan Kujundžić (President), Ivica Grgurević (Secretary)
- Name of president of IBD Group, Croatian Society of Gastroenterology: Boris Vucelic
- National Representatives: Zeljko Krznaric, Brankica Sinčić-Mijandrušić
- Incidence of IBD in the country: Primorsko-goranska County, Croatia, 2000–2004  
UC 4.3/10<sup>5</sup>, CD 7.0/10<sup>5</sup>, Zagreb 2010, UC 3.3/10<sup>5</sup>, CD 3.3/10<sup>5</sup>



## Identity card

- Country: **Greece**
- Name of group: Hellenic Group for the Study of IBD
- Number of active members: 183
- Number of meetings per year: One annual congress
- Name of president and secretary: Spyros Michopoulos (President), Nikos Viazis (Secretary) (until 31/12/2014). From January 1, 2015 until December 31, 2016: Gerassimos Mantzaris (President) and Nikos Viazis (Secretary)
- National Representatives: Epameinondas Tsianos, Ioannis Koutroubakis
- Incidence of IBD in the country: Area of Epirus: Incidence of UC 5.6 per 100,000 inhabitants; Incidence of CD 2.0 per 100,000 inhabitants  
Area of Crete: Incidence of UC 8.9 per 100,000 inhabitants; Incidence of CD 3.0 per 100,000 inhabitants

## Questionnaire – CROATIA



### How did your national group start?

The IBD Group emerged from our national Society of Gastroenterologists.

### How is your group organised in terms of new members joining the group, meetings, election of president etc.?

New members join the group through the national Society of Gastroenterologists. In addition to the gastroenterologists, our membership includes surgeons as well.

Meetings are usually organised three times a year: One during the annual meeting of the Croatian Society of Gastroenterologists and two separate one-day meetings, each on one specific topic.

President and ECCO National Representatives are elected by voting within the Group.

### When did your national group join ECCO?

Our national group joined ECCO at its inception, as Boris Vucelic was one of the ECCO Founders.

### What are your main areas of research interest?

Epidemiology, Basic science, Biologics, Diagnostics, Microbiota

### Does your centre or country have a common IBD database or bio bank?

We started a common country database in 2014.



Brankica Sinčić-Mijandrušić  
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### What are your most prestigious/interesting past and ongoing projects?

Epidemiology, Basic science (Genetics), Microbiota

### Which ECCO Projects/Activities is the group currently involved in?

EpiCom Study

### What are your aims for the future?

We would like to educate our members through training offered by ECCO (Educational Workshops organised by EduCom) and by applying for future grants. Furthermore, we would like to join the new multicentre studies of IBD.

### How do you see ECCO helping you to fulfil these aims?

As previously mentioned, ECCO could help us through its Committees.

### What do you use ECCO for? Network? Congress? How do you use the things/services that ECCO has to offer?



Zeljko Krznaric © Zeljko Krznaric

We use ECCO for networking and participation in the ECCO Congress. Two ECCO Educational Workshops were organised in Croatia (Zagreb, 2007 and Opatija, 2011). We would like to continue the cooperation in all activities offered by ECCO.



Croatian IBD Day 2014 © Croatian IBD group

**ZELJKO KRZNARIC,**  
**BRANKICA SINČIĆ-MIJANDRUŠIĆ**  
ECCO National Representatives, Croatia

## Questionnaire – GREECE



### How did your national group start?

The Hellenic Group for the Study of IBD (EOMIFNE) was founded in 2002. D.G. Karamanolis was responsible for the conception and implementation of the project.

In 1994 the first one-day conference focussing exclusively on Inflammatory Bowel Diseases was organised by the Gastroenterology Department of Hospital Tzaneio Piraeus (Director: D.G. Karamanolis) and the Second Department of Internal Medicine, University of Athens (Director: S. Hadziyiannis). The workshops were repeated in 1995 and 1996.

In 1997, 1998, 1999, 2000 and 2001 the workshops were organised in cooperation with the Department of Gastroenterology at Tzaneio Hospital (Director: D.G. Karamanolis), the Department of Gastroenterology at "Papanikolaou" Hospital, Thessaloniki (Director: G. Kitis) and the University Department of Internal Medicine, Ioannina (Director: E.V. Tsianos). D.G. Karamanolis, G. Kitis and E.V. Tsianos have been designated Honorary Presidents of the Hellenic Group for the Study of IBD.

In 2002 the first official conference of the newly founded Hellenic Group for the Study of IBD took place in Thessaloniki and ever since then the conference has been a very successful annual event of the national group.

### How is your group organised in terms of new members joining the group, meetings, election of president etc.?

New members who want to join the group have to submit an application along with documentation that certifies their interest in IBD. The new members have to be approved by the group's general assembly, which takes place once a year during our congress. The Governing Board

is elected every two years and is responsible for the assignment of the annual congress to a distinguished member of the group. The Governing Board also decides about scholarships and funding of research protocols and studies.

### When did your national group join ECCO?

2003

### What are your main areas of research interest?

- Epidemiology and phenotypic characteristics of IBD in Greece
- Extra-intestinal manifestations in Greek IBD patients
- Biomarkers in IBD
- Anaemia in IBD
- Osteoporosis in IBD
- Clinical and therapeutic trials in IBD
- Pharmacogenetics in IBD

### Does your centre or country have a common IBD database or bio bank?

There is a common IBD database used by the majority of the Greek IBD centres. A bio bank is still lacking in most of the centres.

Since 2012, the Laboratory of Immunology and the Research Laboratory of Gastroenterology at the University of Ioannina have developed an IBD bio bank which currently has samples from 200 patients and 200 healthy matched controls.

### What are your most prestigious/interesting past and ongoing projects?

- Extra-intestinal manifestations in Greek IBD patients
- Development of national guidelines for treatment of UC and CD patients
- Translation of ECCO Guidelines into Greek

### Which ECCO Projects/Activities is the group currently involved in?

Members of the group are participating in various Guideline projects of ECCO.



Ioannis Koutroubakis  
© Ioannis Koutroubakis



Epameinondas Tsianos  
© Epameinondas Tsianos

### What are your aims for the future?

- Development of working research groups on various projects in IBD
- Collaboration of the Greek IBD centres in the development of multicentre epidemiological, clinical and therapeutic studies

### How do you see ECCO helping you to fulfil these aims?

- By supporting research projects with external auditors and expert advice
- By providing grants and financial support to young researchers in IBD
- By helping scientists and doctors from our country to attend meetings for exchange of ideas and to participate in multinational collaboration projects
- By helping our nurses to become more specialised in IBD
- By contacting our patient organisation

### What do you use ECCO for? Network? Congress? How do you use the things/services that ECCO has to offer?

ECCO serves as a platform for gaining expertise, exchanging scientific ideas, working on multicentre research projects and promoting collaboration and friendship among 'IBD-ologists'.

**IOANNIS KOUTROUBAKIS**  
**EPAMEINONDAS TSIANOS**

ECCO National Representatives, Greece

## Questionnaire – UKRAINE



### How did your national group start?

The group started in 2006.

### How is your group organised in terms of new members joining the group, meetings, election of president etc.?

The group has two meetings a year (the first is organised together with the Ukrainian Gastroenterologists Association and the second together with the Ukrainian Coloproctologists Association).

The group is open to new members and membership is free.

Once every four years we hold an election for President and ECCO National Representatives (next due in 2015).

### When did your national group join ECCO?

We joined ECCO in 2008.

### What are your main areas of research interest?

- Mucus barrier and gut flora in IBD
- New biomarkers in IBD
- New treatment

### Does your centre or country have a common IBD database or bio bank?

We are working on this.

### What are your most prestigious/interesting past and ongoing projects?

Mucus barrier and gut flora in IBD

### Which ECCO Projects/Activities is the group currently involved in?

Educational activities

### What are your aims for the future?

- IBD database
- National programme for IBD patients (sponsored by the Government)

### How do you see ECCO helping you to fulfil these aims?

- In the creation of an IBD database
- In the preparation of national standards of diagnosis and treatment for IBD

### What do you use ECCO for? Network? Congress? How do you use the things/services that ECCO has to offer?

Congress, publications

**ANDREY DOROFYEV**  
Former ECCO National Representative, Ukraine



European  
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2015

# Inflammatory Bowel Diseases



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Profession: ☐ Clinical researcher ☐ Dietician ☐ Endoscopist ☐ Fellow/Trainee ☐ Histopathologist ☐ IBD nurse  
☐ Industry ☐ Paediatrician ☐ Pathologist ☐ Pharmacist ☐ Physician ☐ Psychologist  
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