



White Book on IBD Research

**Roadmap on IBD research grants funded by
IBD patient associations**



United We Stand

Front cover: Radoslaw Ptak/Emily Brochocka from the Polish IBD awareness raising campaign “WC out – coming out from the toilet”.

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1. INTRODUCTION

Research is the main pathway that leads to a better future for people with IBD. Through it we will be able to determine the causes of IBD and hopefully a cure. In a word, research means “HOPE”.

For this reason, people with IBD have great expectations on research and on scientists who dedicate their time, efforts and talent to IBD. Through many talks with national representatives, leaders of research programmes or foundations, and mainly with other patients like me, I’ve noticed a couple of familiar facts. Firstly: many patients associations and foundations around the world are active players in the field of research. Secondly: their role is not always well known, even inside the patients’ community. Thirdly: very often the communication within patients’ organizations about research was not as complete as it could have been.

These are the bases that have inspired my idea of organizing this event. It was a sunny day, in Barcelona, last February when I was talking with a delegate from one of our sister organizations “down-under”, and some question popped up in my mind.

Is it true that IBD - research is only or mainly pharma-led? What is the real amount of money that every year patients from all around the globe take from their pocket and invest in this challenge? Is it possible that two associations are financing the same kind of research at the same time? Is it possible to think about an information model, which can lead each of us, in our everyday fight against IBD, in knowing where the others are investing, in order to evaluate or develop cross frontiers co-operations.?

Amazingly the reaction from all our sister organizations has been not only enthusiastic, but participative. The fact, itself, that we have managed to organize such an event in only nine months, is the symbol of what we can realize in the future together.

In organizing and facilitating this event, I find that EFCCA is offering a way for expressing an incredible potential to every participant, and is expressing its full potential of “federation”.

I believe that this white book, and the results of the overall Symposium, will together represent a milestone. I hope this book can be a handbook, a reference we could all use for getting new ideas in developing research-support strategies.

But above all, I dream this “white book” to become the first step towards a stronger alliance against IBD. I do not have to explain to any of the readers what IBD represent today, and how difficult the challenge is. By getting together in Brussels, we are announcing to IBD that hard times are coming: because patients are today stronger and united, just like our global fight.

Today we are tackling IBD in a more direct way than ever. We are reacting in a creative way and demonstrating our resilience.

Today we are one step nearer to win. Together.

Marco Greco, Ph.D.
Efcca Chairman

2. SETTING THE SCENE

I am really happy to have the opportunity to attend to this symposium, a very special meeting gathering physician, doctors and patients, and where patients from all over the world discuss how to better fund research. The patients that do best are the ones who work with doctors and establish relationships among themselves as well as between patients and doctors in order to gather knowledge and know-how. If we can do that, the IBD community will be the best among patient communities.

In this short introduction I will try to present an update on where we are on IBD research and how the patient community can contribute to it. Environment, genes, microbes and immune system are the four major components related to IBD, but what it is really important is understanding the disease in a very comprehensive fashion. If there are four components, which is the most important? Why do we have IBD today, but didn't 100 years ago? It is not because doctors were not able to diagnose IBD back then, but because IBD was actually not there. Thus, IBD is modern disease. Why? How did it emerge in our society?

My personal view is that we live now in a drastically different environment than a century ago. The other components (genes, microbes and immune system) are still there, but they are probably less relevant. We live in a highly artificial human-modified environment, but as human evolution is very slow, we have not adapted to something that occurred so rapidly. We live in an environment to which we are not prepared for.

What are these environmental factors? Smoking, new diets, medications, geography, social status, stress, etc. All these factors influence our genes and immune system, and the individual response to these environmental challenges determines if we have developed IBD or not. We are no longer conditioned by lot of microbes in the environment; the so-called "hygiene hypothesis". Everything is clean and safe. We get vaccines and antibiotics, and our water is clean; as a consequence, our immune system is not educated to resist the strongest challenges that existed in our previous environment. If we are not able to adapt, we constantly react against. That results in chronic inflammation, in our case IBD.

This is a nice theory, but can we prove that? There is now emerging experimental evidence that the hygiene hypothesis is correct. A study that analyzed two different groups of pigs, one kept in an outdoor environment and the second one indoors with the supply of antibiotics, found that in adulthood, the "dirty pigs" (the ones kept outdoors) had a normal gut flora and immune system, whereas the "clean pigs" had an abnormal gut flora and increased inflammatory and cholesterol pathways. The case of the "clean pigs" mimics what we are exposed as modern humans.

Microbes are critically important; they decide who we are and how healthy we are. They are more powerful than us and indispensable for our health. We acquire them at birth, and they evolve from birth to adulthood modified by genes, foods and the environment. Each one of us has a specific set of microbes. Gut microbes control immunity and inflammation in the intestine, and are crucial for its normal function. After birth, the more frequent and early the use of antibiotics that modifies the flora is, the higher is the risk of developing IBD.

Since the flora is so important, can we change it and make it work to our advantage? We can. Flora needs nutrients just like we do. This question is important in IBD pathogenesis. What we eat today is far from a natural healthy diet, even though we might think we eat healthy. A study, comparing flora between African and European kids showed the dramatic impact of diet on shaping gut microbes: in primitives diets we find old microbes and no IBD, but in current diets modern microbes and IBD.

We can now see the connection between food, microbes and the immune system. Obesity affects a large number of individuals conditioned by lifestyle and diet. There is an essential overlap between the gut flora of obese people and of people with IBD. This means that the change in our behaviours, particularly eating, conditions the probability of diseases such as obesity, IBD, etc., reinforcing the concept that the way we behave conditions these diseases.

Another study conducted in ewes (female sheep) showed that obese mothers have the tendency to deliver newborns with inflamed intestine. This evidence raises one important question: is it the mother that was exposed to a wrong environment, or is it the IBD patient? This is a fundamental question if we want to go back to the causes of IBD.

Moreover, much of what we eat is contaminated by food additives, sweeteners, drugs, cosmetics, etc. These food additives cause changes in bacterial properties.

I would like to add something on the context of cure and treatment of IBD. From 1940's to 2000's we moved from empirical to mechanism-based cure. We try to study the mechanism of inflammation and to intervene to stop different inflammation patterns. Several new medicines have been developed to avoid surgery. Understanding the mechanism of IBD is helping us to improve the therapy and hopefully reach a cure. Still, the risk to fail is there. What we can do to reduce the risk of failure? Difficult questions require multiple joint efforts. We need to work together.

Finding the cure of IBD requires joint efforts of researchers and patient organizations as well as extensive financial resources. Patient organizations should play a leading role to address these challenges.

I would like to conclude with some key messages for the IBD patient organizations:

1. Patient organization cannot just sit and wait for help. They must actively seek it.
2. Do not underestimate the values of individual organizations.
3. All organizations should interact and learn from each other, no matter how small.
4. Each group should promote vigorous and methodical programs and fundraising, but customized to each situation.
5. Keep in mind the big picture, the common goal: what others achieve can help you, and what you achieve can help everybody.
6. Funds should go to the best research, not to "your local researcher".
7. The best hope for a cure should not be just EFCCA, but IFCCA (International Federation of Crohn's and Ulcerative Colitis Associations)

Claudio Fiocchi, M.D.

Professor of Medicine, Cleveland Clinic Lerner College of Medicine

3. COMPILATION OF IBD RESEARCH PROJECTS FUNDED BY IBD PATIENT ASSOCIATIONS

All presentations are available on the EFCCA website.

3.1 ARGENTINA

Association: Fundación Mas Vida de Crohn y Colitis Ulcerosa

Website: www.masvida.org.ar

Description of research: National Fellowship in Epidemiology of IBD in pediatrics in collaboration with the Argentina Society of Pediatrics

Duration / timeframe: 12 months

Funds invested: 30 000 Argentine pesos (4 900 €)

Source of funds for research: Pharmaceutical industry

Aims of study / expected outcomes:

To have a formal record on epidemiology of IBD in Argentina so that actions and strategies can be adopted.

Based on which criteria is this particular research chosen?

Argentina has few epidemiological studies of IBD. It is an initiative of the Foundation in collaboration with the Scientific Society.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Task Team of Hospital Children belonging to Dr. Orlando Alassia Gastroenterology and Nutrition Service. Grants Commission supervised programs and Argentina Society of Pediatrics.

3.2 AUSTRALIA

Association: Crohn's & Colitis Australia

Website: www.acca.net.au

Description of research: The research supports a case for ongoing funding of dedicated IBD nurse positions in public hospitals.

Crohn's & Colitis Australia is seeking a dedicated and ongoing funding stream for IBD nurses affiliated with multidisciplinary IBD services. The reported benefits of an IBD nurse include improved clinical care and safety as well as reduced inpatient health care utilisation, a reduction in hospital admissions and decreased need for surgery.

Duration / timeframe: October 2012 - Dec 2012

Funds invested: \$60,000 Australian dollars (48 000 €)

Source of funds for research: Equal funding was sought from our corporate sponsors. Three organisations undertook to co- sponsor the research.

Aims of study / expected outcomes:

This research is expected to clearly define the problem in Australia, quantify the benefits of employing specialised IBD Nurses in Australian public hospitals and align a strategic response with government priorities. This research will also provide an understanding of current IBD costs on the national economy and a clearer understanding of prevalence of IBD in Australia with a focus on rural/urban split. The new statistics will build on "The Economic Costs of Crohn's Disease and Ulcerative Colitis" commissioned in 2007 by Crohn's & Colitis Australia which for the first time articulated the extent of IBD on the population and on the economy. The report will be used to lobby government and form part of the Crohn's & Colitis Australia 2013 Awareness Month Campaign.

Based on which criteria is this particular research chosen?

This research has been commissioned in response to a number of requests from patients and clinicians who over the years have sought the assistance of Crohn's & Colitis Australia to help lobby state governments to secure funding for IBD Nurse positions in public Hospitals. The research addresses the questions raised by government departments regarding specific geographic need, the economic benefits of funding these positions and consumer perceptions.

Institute, university etc. developing the research; researchers coming from different departments etc.:

The research is being conducted by the management consulting company Pricewaterhouse Coopers (PwC) on behalf of CCA with input from a range of IBD stakeholders including clinicians, nurses and patients. The report also draws on secondary research conducted locally and internationally.

3.3 BELGIUM, CCV

Association: Crohn en Colitis Ulcerosa Vereniging

Website: www.ccv.be

Description of research #1: Butyrate producing bacteria as probiotic treatment in IBD: in vitro characterization of the behaviour of new butyrate producing isolates under gastrointestinal

conditions

Duration / timeframe: 2012-2014

Outcomes: Butyrate producing bacteria as probiotic treatment in IBD: *in vitro* characterization of the behaviour of new butyrate producing isolates under gastrointestinal conditions

A. Geirnaert, N. Boon & T. Van De Wiele

Laboratory of Microbial Ecology and Technology (LabMET), Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, BE-9000 Gent, Belgium

Inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the gastrointestinal tract. The etiology of IBD is still unclear but there is a well-established link between the intestinal microbiota and gut inflammation. Therefore, manipulation of the unbalanced microbial community in IBD is a very attractive therapeutic strategy. Butyrate has well described beneficial effects in IBD, but the delivery into the gut is still problematic. Administration of butyrate producing bacteria that are able to colonize the gut is therefore an elegant solution for the delivery problem. Recently, a novel butyrate producing isolate *Butyricoccus pullicaecorum*, was isolated and showed the production of exceptional high concentrations of butyrate (up to 18 mM) while consuming acetate.

The aim of this project is to characterize the behaviour of *B. pullicaecorum* during gastrointestinal conditions *in vitro*. In a first phase its survival during passage of the upper gastrointestinal tract (stomach, duodenum and jejunum) will be evaluated. Further experiments with the Simulator of the Human Intestinal Microbial Ecosystem (SHIME) will reveal its colonization efficiency at the terminal ileum and different regions of the colon. In a final part some strategies will be developed to stimulate the butyrate production of the supplemented species.

Description of research #2: The role of endothelial dysfunction in IBD

Duration / timeframe: 2011-2013

Funds invested: 3000 € / research project

Source of funds for research: Sponsors (pharmaceutical industry)

Based on which criteria is this particular research chosen?

By the association's medical board

Institute, university etc. developing the research; researchers coming from different departments etc.:

Laboratory of Microbial Ecology and Technology (LabMET) Faculty of Bioscience Engineering Ghent, University of Ghent, Belgium

Department of gastroenterology, Ghent University, Belgium

3.4 BELGIUM, RCUH

Association: Crohn-RCUH

Website: www.mici.be

Description of research: Questionnaire sent to the members of the association to learn about their diseases and lifestyles when they were young.

Duration / timeframe: Around six months

Funds invested: Unknown

Source of funds for research: Own funds

Aims of study / expected outcomes: Trying to detect similar diseases during young age, and to relate it with their current IBD.

Based on which criteria is this particular research chosen?

Based on a doctors' initiative.

Institute, university etc. developing the research; researchers coming from different departments etc.:

It was a small internal research, without links to any university or institute.

3.5 CANADA

Association: Crohn's and Colitis Foundation of Canada

Website: www.ccfc.ca

The Crohn's and Colitis Foundation of Canada (CCFC) was specifically founded in 1974 to "find the cure," and is Canada's largest funder of IBD research and the second largest funder of non-governmental research in the world. CCFC has a well-evolved scientific peer review process for adjudicating Grants-in-Aid applications (currently each GIA being worth \$375 000 [ca. 296 600 €] over three years); well developed research programs and application processes; a robust expert Scientific and Medical Advisory Council; a Board of Directors' Research Committee; and dedicated research administrative staff. While most research funded by CCFC to date has been basic/biomedical research (i.e., pre-human), increasingly CCFC is funding translational, clinical, health services, and population health research as well. CCFC invests in health research to foster advances in prevention, treatments, cures, and health policy. More information on CCFC's research programs can be found at www.ccfc.ca, including Research Annual Reports.

Description of research:

The CCFC has 80 research projects, involving well over 100 scientists. One of the projects is the "Framingham Study" of IBD: the Genetics, Environment, and Microbe (GEM) Project. This initial five-year, \$5.5 million (4.3 million €) investment by CCFC is intended to set in play the identification of the environmental triggers underlying Crohn's disease in genetically at-risk (but currently healthy) individuals aged 6 to 35 years of age.

To date, more than 2000 first degree relatives of people with Crohn's have been enrolled in Canada, U.S.A., and Israel, with close monitoring occurring following the collection of biological samples. Fourteen individuals have newly developed Crohn's disease, thereby demonstrating proof of principle. In order to expand enrolment (including possibly countries in Europe) and sustain current recruitment sites, other funding partners are required.

More information on the GEM Project can be found at www.ccfc.ca and www.gemproject.ca

CCFC took the initial financial risk, but Canada cannot "fund the world" by itself. This is a multiyear (likely decades-long), prospective study with the potential to revolutionize our understanding and management of IBD, just as Framingham (60 years and counting) has done for cardiovascular disease.

CCFC has also endowed a Chair in IBD Research at the University of Calgary plus a Chair in Ulcerative Colitis Research at McMaster University.

Duration / timeframe: 1974 – present, with multi-million dollar annual investment over the past decade

Funds invested: Funds total more than \$76 million to date (60 million €), with recent years' annual investment in the \$5-6 million range (4-5 million €)

Source of funds for research:

As a Canadian registered charity and non-governmental, volunteer-based organization, research funds come from primarily individual donors and supporters via direct mail, major gifts, on-line giving, events (e.g. Gutsy Walk, M&M Meat Shops Charity Barbecue Day, galas, golf tournaments, etc.). Increasingly CCFC is seeking to augment its historic "events-based" community fundraising with leadership fundraising (planned giving, Excellence in Research campaigns, mid-level donor program, etc.). Going forward, CCFC is seeking governmental sources of funding and to expand its corporate bases of support. (Note: with the exception of M&M Meat Shops, most corporate support of CCFC goes towards CCFC's education mandate, rather than research.)

CCFC partners extensively in cost-sharing research arrangements with Canadian federal (e.g., Canadian Institutes of Health Research) and provincial government funding agencies. More recently, CCFC has partnered with a private sector research entity, Vertex Pharma, to enhance outcomes-orientation of CCFC's research investment.

Based on which criteria is this particular research chosen?

CCFC is committed to peer review for major grants: the Grants-in-Aid proposals undergo competitive ranking by MDs and PhDs to ascertain which proposals are scientifically meritorious for CCFC research funding. Recently, CCFC has introduced informed lay reviewers (to provide the patient/parent perspective) to its grant competition process.

CCFC has well developed research program policies and procedures which guide its research funding. Increasingly, CCFC is taking measures to ensure that research (e.g., clinical, epidemiological, and health services) in addition to basic research receives funding. CCFC has also facilitated several quality-of-life surveys in recent years.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Too numerous to list specifically -- refer to CCFC Annual Reports and Research Reports on-line at www.cfc.ca. CCFC funds, or has funded, virtually every Canadian medical school university involved in significant IBD research (which means approx. 15 of 17 medical schools), every Canadian hospital involved in substantive IBD research, and several Canadian veterinary schools. Via the GEM Project, CCFC also funds research occurring in the USA and Israel. Historically, CCFC has had a Visiting Scientist Program, which has placed several European researchers in Canadian IBD research centers.

Outcomes:

For outcomes of research, please refer to CCFC Annual Reports and Research Reports on-line at www.cfc.ca. CCFC-funded researchers are required to submit progress reports and final reports on their research projects, and to speak with CCFC chapter volunteers and donors – the people who made their research funding possible.

Note:

CCFC strongly encourages all IBD organizations to prioritize and fund IBD research. There are too few substantive IBD research funders internationally, particularly given the millions of persons living with IBD worldwide. In addition to helping patients and families cope, collectively we need to offer hope – research is necessary for prevention, treatments, and cures. The Crohn's and Colitis Foundation of Canada is interested in learning more about, and potentially partnering with, European (and other) Voluntary Health Organizations in the realm of IBD research.

3.6 DENMARK

Association: Colitis-Crohn Foreningen

Website: www.ccf.dk

Description of research:

A PhD project examining whether children born by parents with IBD are more likely to get diseases during their life. The following diseases are looked for:

- 1) Autoimmune diseases: IBD, asthma, arthritis in children and diabetes type 1
- 2) Infectious disease: Infections and appendicitis
- 3) Neurological diseases: Epilepsy, spastic paralysis and autistic spectrum disorder (ASD)
- 4) Congenital defects

Duration / timeframe: Children born alive in Denmark between 1977-2009 (ca. 2 000 000 children)

Funds invested: 10 000 € (research funding for about 66 000 € per year)

Source of funds for research: Members donations

Aims of study / expected outcomes:

This knowledge is important towards understanding what influence IBD can have during pregnancy and towards the life of the children. Expect better advice to parents-to-be in the future.

Based on which criteria is this particular research chosen?

This has, to the knowledge of the association, never been looked into.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Epidemiological Department of Aarhus University Hospital.

3.7 FINLAND

Association: CCAFIN

Website: www.crohnjcolitis.fi

Description of research: Supportive information for new IBD patients

Duration / timeframe: 2013-2014

Funds invested: The association doesn't have funds specifically for this purpose. The Finnish association has, however, donated 200 € to the IBD Research Foundation on two occasions.

Source of funds for research: Finnish Foundations

Aims of study / expected outcomes:

Knowledge about what kind of support new IBD patients would like to get from the association and hospitals.

Based on which criteria is this particular research chosen?

This research would support the association's basic services for members.

Institute, university etc. developing the research; researchers coming from different departments etc.:

University hospitals

3.8 FRANCE

Association: AFA

Website: www.afa.asso.fr

Description of research:

As AFA has financed research for 20 years, the spectrum of research is large, including immunology, genetics, and epidemiology. AFA has supported research with 180 grants since

1993 for more than 5 million €. In 2011, 259 000 € was awarded as 12 grants, and additionally, two exceptional grants of 500 000 € about the "physiopathology of ulcerative colitis." In 2012, 9 grants have been awarded for 200 000 €.

Duration / timeframe: 1993/2010

Funds invested: More than 5. 000 000 €

Source of funds for research: Private donations by individuals.

Based on which criteria is this particular research chosen?

To promote, encourage and fund basic research programs, both clinical and therapeutic through grant research projects selected by a scientific committee. Their choice meets two ideas:

- Help to start research groups and achieve the creation of stable structures
- Explore various avenues of research, inflammation, immunology, epidemiology, bacteriology, psychology etc.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Various universities and institutes across France.

3.9 GERMANY

Association: DVVC

Website: www.dccv.de

Description of research #1:

Implementation of a prospective multi-centered clinical study entitled: " Do cutaneous adverse events significantly affect monoclonal antibody based anti-TNF therapies in IBD patients? A national experience throughout all care levels by the German IBD Study Group (GISG)

Duration / timeframe: (presumably) 24 months starting end of 2012

Funds invested: 50 000 €

Source of funds for research: Association/Organisation funds

Aims of study / expected outcomes:

The individual frequency of the various TNF medications and their impact on possible necessary therapeutical changes and further treatment is presently not clear as available data cannot be extrapolated. Depending on the drugs and treatment strategy, 48% to 79% of the patients could continue their current treatment further. This research project aims at clarifying whether the cutaneous changes observed during TNF biological therapies have an impact (primary endpoint) on the further anti-TNF therapy (therapy changes). Within this study, „therapy changes“ are considered as termination of medication, pauses, changes in dosage or changes in the timing of medication of changing the anti-TNF biological therapy. Furthermore,

the study will explore which patient-specific, treatment-specific and quality of life -specific factors influence therapy (secondary endpoint).

Based on which criteria is this particular research chosen?

For all possible grants, the assessment criteria of the applications in the framework of the DCCV research funds are the following:

- 1) Quality of the proposed project / qualification of the applicant
 - Scientific capacity of the application, scientific capacity of the preliminary work, quality of publications
 - Innovation: is the project innovative? Can the project bring a new dimension to the research of inflammatory bowel diseases?
 - Patient orientation: Does the project provide any improvements for patients with inflammatory bowel disease within a foreseeable future?
 - Leveraging effect of a research grant: how big is the expected recognition success (also in relation to costs? Is this a preliminary research project that has the potential to be further funded via major (public) research institutes (fast-start funding)?
- 2) Employment opportunities / scientific context
 - Personal, institutional and contextual requirements
- 3) Purposes and working plan
 - Clear working hypotheses
 - Reasonable focus on the theme
 - Suitability of methodology
 - Feasibility particularly in the framework of fixed or globally conceived timing

Institute, university etc. developing the research; researchers coming from different departments etc.:

Project leader:

Prof. Dr. med. Daniel C. Baumgart

Charité – Universitätsmedizin Berlin, Campus Virchow Klinikum

Medizinische Klinik m.S. Hepatologie, Gastroenterologie, Endokrinologie und Stoffwechselerkrankungen

Augustenburger Platz 1

13353 Berlin

Description of research #2: Detect Dysplasia

The study has explored the most suitable methods for detecting early forms of cancer outbreaks in Colitis ulcerosa patients. For this purpose, the participants underwent two colonoscopies separated by a minimum of 3 weeks and a maximum of 3 months. The colonoscopies were performed using the most recent generation of colonoscopes, once with and once without NBI light.

Duration / timeframe: (presumably) since 2007

Funds invested: 25 000 €

Source of funds for research: Association/Organisation funds

Aims of study / expected outcomes: n/a

Based on which criteria is this particular research chosen?

See above

Institute, university etc. developing the research; researchers coming from different departments etc.:

Project leader:
Prof. Dr. Ludger Leifeld
Medizinische Abteilung
Evangelisches Krankenhaus Köln-Kalk
Buchforststraße 2
51103 Köln

3.10 IRELAND

Association: ISCC

Website: www.iscc.ie

The ISCC is an all-volunteer group with no paid employees. ISCC does not have the manpower to properly assess and select appropriate research projects, nor do they have any experience in this area. Any research projects that the ISCC could potentially support would by necessity have to be small, and the association has decided in the past to instead donate funds to the IBD Research Foundation. To date the ISCC has donated 25 000 € received from ISCC own funds and member fundraising.

3.11 ITALY

Association: AMICI

Website: www.amiciitalia.it

AMICI is currently involved in 5 research projects:

Description of research #1: Prospective study on Clostridium difficile prevalence, antibiotic sensitivity, toxin production profile, genetic polymorphisms in inflammatory bowel disease in north.

Aims to enrol in the study 200 patients (50 Crohn's disease patients in remission and 50 in relapse, 50 ulcerative colitis patients in remission and 50 in relapse) and 50 healthy controls. IBD patients in remission with evidence of CDI will be assessed in the follow-up to look for a disease relapse. Thanks to the deep sequencing new pathogenic factors could be identified: sequencing will be performed to further characterize genetic diversity of C. difficile strains isolated by patients and showing different ribotypes and eventually to identify new potential virulence factors.

Funds invested: 48 000 €

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr. Matteo Martinato (Azienda Ospedaliera - Università di Padova Gastroenterologia)

Description of research #2: The role of lymphatic system in inflammatory bowel disease.

Aim 1. Investigation of structural changes of the lymphatic system in inflammation associated colorectal cancer. This will include: a) quantitative analysis of lymphatic vessel density and morphometry in a relevant experimental model of colitis associated cancer (CAC); b) investigation of the lymphatic endothelial junctions in human IBD, in IBD-related colorectal cancer, and in murine CAC, and c) assessment of the lymphatic endothelium activation state

Aim 2. Define the functional changes of the lymphatic system in IBD and in CAC: This will include: a) isolation and functional characterization of human intestinal lymphatic endothelial cells (HILEC); b) investigation in vitro of intestinal lymphangiogenesis, and c) role of lymphatics in mediating leukocyte in vitro and in vivo trafficking

Aim 3. Investigate the effects of manipulation of the lymphatic system in IBD and in CAC: This will include: a) evaluation of the effect of anti-lymphangiogenic therapy in prevention and treatment of experimental experimental IBD and CAC; b) study of the effect of prolymphangiogenic agents on the progression of IBD and CAC, and c) investigation of lymphatic junctions and leukocyte migration during anti- and pro-lymphangiogenic studies

EXPECTED RESULTS AND ALTERNATIVE APPROACHES: Overall, based on our specific hypothesis and preliminary data, we anticipate that we will find evidence of active lymphangiogenesis in the DSS and AOM model of carcinogenesis. Although descriptive, these data will be necessary to pave the way to use this model to investigate lymphangiogenesis in IBD and CAC. With specific regard to Aim 1, we expect to detect increased lymphangiogenesis also with close association between inflammatory infiltrates and neovascularization. In addition, we expect to detect a high level of expression of ki67+ lymphatic endothelium reflecting endothelial cell activation and lymphangiogenesis. In addition, the whole mounting staining will allow a more detailed spatial visualization of lymphangiogenesis and angiogenesis in the murine colons. Furthermore, we will also further assess the lymphatic structural changes by investigating endothelial junctions. These experiments will help in clarifying a potential involvement of each junctional molecule in mediating leukocyte migration from the gut to the lymph node. Depending on the results, specific KO mouse for VE-cadherin, ZO-1 or JAM-A could be used to further assess a functional involvement of these junctions.

Aim 2 will provide the characterization of HILEC in health and in IBD, helping in screening specific genes involved in lymphangiogenesis. In addition, the use of in vitro and in vivo experiments will help in simulating lymphangiogenesis, and clarifying the functional role of VEGFC and -D in mediating HILEC survival. Finally, by assessing the role of HILEC in mediating leukocyte migration, a functional in vitro and in vivo characterization will be assessed, in relation to the newly formed tumor lymphatic network.

Finally Aim 3, will show in a mechanistic way the therapeutic relevance of manipulating lymphangiogenesis in vivo. By treating colitic mice with anti-lymphatic therapy, we would expect that clinical improvement should be associated with evidence of a decreased vascularization in the mucosa with reduced cancer formation. On the contrary, lymphatic stimulation should be accompanied by disease exacerbation. Once it is demonstrated that lymphangiogenesis is a vital component of IBD and CAC pathogenesis, this could provide the material and conceptual framework for implementing future anti-lymphangiogenic therapies.

Funds invested: 48 000 €

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr. Silvio Danese (Istituto Clinico Humanitas-IRCCS Rozzano MI)

Description of research #3: Therapeutic strategies to alter the natural history of pediatric Crohn's disease: Efficacy and safety.

AIMS OF THE STUDY: To evaluate the effectiveness and safety of IFX as first-line therapy (top-down approach) compared to conventional therapy (step-up approach), based on steroids (CS) and azathioprine (AZA), in pediatric moderate-to-severe CD. The project aims at evaluating if the early neutralization of TNF-may achieve mucosal healing before irreversible tissue damage occurs and thus potentially alter the natural course of the disease (rate and duration of remission, rate of mucosal healing, number of hospitalization and operation, growth parameters, quality of life). The study also would add information about the safety profile of IFX used as first-line therapy in pediatric patients and may add data on the benefit, risks and costs of a reversal of the traditional therapeutic pyramid in pediatric CD, guiding the clinician in deciding in whom, when and how to introduce early aggressive treatment. The primary outcomes are: 1. the proportion of patients with clinical response or clinical remission as determined by the Pediatric Crohn's Disease Activity Index (PCDAI) in the top-down compared to the step-up group; 2. the proportion of patients with intestinal mucosal healing as determined by the Crohn's Disease Endoscopic Index of Severity (CDEIS) at the end of the induction and maintaining phases in the top-down compared to step-up group; 3. the proportion of patients with adverse drug reaction and side effects attributable to therapy during the induction, maintaining and follow-up phases in the two groups. Secondary outcomes are: the mean change in patient length and weight, as assessed by Z-scores in the two groups; the cost-utility and cost-effectiveness of infliximab as first-line therapy.

EXPECTED RESULTS: CD significantly impact patients' daily physical/systemic functioning and contribute to emotional and psychosocial impairments, thereby lowering patients' overall quality of life. A prospective study evaluating the natural course of CD has demonstrated that 30% of patients with chronically or intermittently active disease developed complication requiring hospitalization and surgery in the first years of the diagnosis (4). Remission of CD is associated with a reduced number of hospitalizations and operations, as well as a normalised quality of life. Moreover, in children with CD, maintenance of long period of remission is associated with normal growth and pubertal development. Traditional therapies for CD have no effect in modifying the natural course of the disease. Early use of a therapeutic strategy with the potential to alter the natural course of the disease, healing intestinal mucosa, could potentially reduce all of the complications of the disease, reducing need of hospitalization and surgery, improving overall quality of life, growth and finally reduce direct and indirect costs of the disease. This is of great importance for pediatric patients since young age at onset is thought to be associated with a complicated course of the disease.

We expect the following outputs: 1. Higher rate of remission and mucosal healing in the group of patients treated with IFX as first-line therapy (top-down group) compared to children treated with conventional therapy, based on corticosteroids and immunosuppressors (step-up group) at the end of the induction and maintaining phases (8, 48 weeks of the treatment phase) and at the end of the study (24 months); 2. Lower number of hospitalization and operation in the top-down group compared to the step-up group at the end of the study (24 months); 3. Better growth pattern, due to reduced flare-ups of the disease, in the top-down group compared to the step-up group at the end of maintaining phase (48 weeks of the treatment phase) and at the end of the study (24 months); 4. Good safety profile of IFX used as first-line therapy in pediatric patients with early CD at the end of the maintaining phase (48 weeks of the treatment phase) and at the end of the study (24 months). 4) SIRT1-based therapy as a novel approach for inhibiting gut inflammation –associated colorectal cancer. 5) Genetic predisposition and mechanisms of intestinal fibrosis in Crohn's disease: Basis for therapeutic and diagnostic intervention.

Funds invested: 25 000 €

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr. Marina Aloï (UOC Gastroenterologia, Endoscopia e Epatologia Pediatrica Università di Roma "Sapienza")

Description of research #4: SIRT1-based therapy as a novel approach for inhibiting gut inflammation –associated colorectal cancer

AIM: To determine whether SIRT1 exerts anti-inflammatory functions in the gut.

POSSIBLE RESULTS AND RELEVANCE TO IBD: In recent years there have been considerable advances in our understanding of IBD pathogenesis. Now it is evident that both CD and UC are caused by an exaggerated and inappropriately counter-regulated immune reactivity in the gut wall. Indeed, current therapy for IBD patients is based on suppressing or modulating the immune system. Our observation that in IBD there is a defective production of SIRT1 is novel and links the deregulated SIRT1 expression with intestinal inflammatory diseases in man.

Results from the proposed studies will allow us to ascertain whether enhancing SIRT1 activity is useful to attenuate the ongoing gut inflammation, thereby bringing important rewards in therapy of patients with IBD. The in vivo experiments could help to identify a novel therapeutic strategy for preventing or treating gut inflammation.

Funds invested: 25 000 €

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr. Roberta Caruso (Dipartimento di Medicina Interna Università di Roma "Tor Vergata")

Description of research #5: Genetic predisposition and mechanisms of intestinal fibrosis in Crohn's disease: Basis for therapeutic and diagnostic intervention

Aims: The mainstay of treatment in CD is medical, however, the majority of patients will require at least one surgical treatment during their lifetime. However, surgery is rarely curative as 70% of patients will have endoscopic evidence of stricture recurrence at 1 yr, while at 4 yr 40% will have symptomatic recurrence. Despite advances in CD management in last decades, the incidence of stricture and requirement for intestinal resection have not diminished.

The main limitation of the previous few studies available evaluating the intestinal fibrosis in CD are: a) lack of a valuable animal model; b) difficult access to submucosa and muscular layers where more abundant is the fibrosis; c) retrospective nature of studies; d) poor characterization of myofibroblast population and function; e) scarce information on genetic background of profibrotic phenotype; f) lack of definition of "fibrotic score" with validated correlation with in vivo imaging.

To overcome these limitations an expand working team has been set which combine:

a) excellence in clinical and surgical management of CD patients with high volume of patients in follow-up and undertaking surgical resection;

- b) accurate prospective clinical and morphologic evaluation of patients prior to operation (with entero-MRI and endoscopic biopsies);
- c) extensive morphologic evaluation of surgical samples at stenotic, non-stenotic, and non-inflamed area to quantify the fibrotic burden together with ECM component, matrix metalloproteinase, gelatinase activity, neo-angiogenesis and hypoxia inducible factor evaluation;
- d) extensive functional evaluation of cellular infiltrate with investigation of ligand expression, cytokine production and mRNA expression of transcriptional factors;
- e) extensive evaluation of myofibroblast population provenience and functional characteristics included RNA expression profile of freshly isolated cells); and
- f) DNA and RNA evaluation on a GWA basis of mucosal biopsies obtained at stenotic, non-stenotic, and non-inflamed area.

This approach is thus far unique and will surely contribute to better understanding the fibrotic phenotype both at cellular and clinical level.

Possible Results and relevance: We have assembled an outstanding research team which combine high volume clinical/surgical expertise, long standing experience in immunology and morpho-functional evaluation of chronic inflammation and organ fibrosis, and established competence on genetic predisposition in IBD. We are confident that the originality of the project will shed more light in the mechanism of intestinal fibrosis in CD, by exploring with cutting-edge technologies its morphologic, immunologic, and genetic aspects. The results of the study will hopefully have profound consequences on the CD patients, by better define the in vivo grading, by clarify early pathogenic molecular and cellular changes, and perhaps suggest novel therapeutic approach.

Intestinal fibrosis and stricture formation are often part of the natural history of CD, frequently requiring surgical resection. While an abundance of therapeutic option have become available for the treatment of intestinal inflammation, the treatment options for stricture remain relatively limited to endoscopic pneumatic dilatation and surgical resection, universally accompanied by high recurrence rates. Understanding of intestinal fibrogenesis is slowly increasing also because the transition from the molecular biology arena to clinical trial is hampered by the absence of effective animal models.

This comprehensive, multidisciplinary approach to intestinal fibrosis will surely more clearly elucidate the cellular and molecular mechanisms involved; the identification of a genetic signature of MF expression profile, and possible confirmation at mucosal levels could probably pave the way for a genetic risk prediction of fibrostenosing behaviour. More importantly the validation of correlation between MRI imaging and fibrotic score will clearly enhance the diagnostic/prognostic evaluation of fibrosis. Finally, the clarification of early pathogenic changes of fibrosis, together with the MF interaction with inflammatory, angiogenic, wound healing, and hypoxic mediators, might help for identification of potential anti-fibrogenic compound.

Funds invested: 25 000 €

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr. Stefania Genise (SOD2 GASTROENTEROLOGIA AOU Careggi FIRENZE)

For all research projects by AMICI:

Duration / timeframe: 2 years

Source of funds for research:

Organisation Funds obtained through a percentage of the taxes of citizens

Aims of study / expected outcomes:

Identify the mechanisms of action of the disease and increase the awareness.

Based on which criteria is this particular research chosen?

Projects selected by AMICI's scientific committee.

3.12 ISRAEL

Association: CCFI

Website: www.ccfi.org.il

Description of research: The study will evaluate three proposed different mechanisms that may play a role in nutritionally induced remission.

The study will compare between patients who respond to nutritional therapy and patients who do not respond to it. Patients receiving internal nutrition for six weeks as the sole intervention will be evaluated at 0, 3, 6 and 12 weeks. Patients will be assigned randomly to different weaning diets.

Duration / timeframe: 01.01.2013 – 1.1.2014

Funds invested: Planned budget 60 000\$ (47 000 €)

Source of funds for research: Anticipated grants

Aims of study / expected outcomes:

The goal is to examine the mechanisms involved in response to nutritional intervention in Crohn's disease.

Exclusive internal nutrition can induce remission and mucosal healing, but as opposed to medically induced remission, the mechanism is not understood.

If the nutritional mechanism is understood, environmental factors associated with Crohn's disease could possibly be identified, or ways to achieve the same results without requiring a restrictive diet may be found.

Based on which criteria is this particular research chosen?

This study has potential to improve the quality of life of patients and identify new interventions for achieving remission without suppressing the immune system

Institute, university etc. developing the research; researchers coming from different departments etc.:

Principal investigator: Prof. Arie Levine, Director, Pediatric Gastroenterology Unit, E. Wolfson Medical Center, Holon, Israel Multicenter Israeli study.

3.13 THE NETHERLANDS

Association: Crohn Colitis Ulcerosa Vereniging Nederland (CCUVN)

Website: www.crohn-colitis.nl

Description of research: Work and IBD.

Via questionnaires send to all members aged 18-65. Research done in cooperation with NIVEL (Dutch organisation for research in Health Care). How many patients do work? What problems do they encounter in their work? What are their wishes in order to improve their working conditions? Started in 2011, follow up in 2012.

Duration / timeframe: 2011-2013

Funds invested: 60 000 €

Source of funds for research: CCUF, which is an independent fund related to the association

Aims of study / expected outcomes:

The expected outcomes is that the percentage workers does not differ from the average in the Netherlands (first result). The outcomes will hopefully be evaluated in 2013.

Spin off : Election best employer of the year 2012

Spin off : Development of "tools" to be used by human resource workers.

Based on which criteria is this particular research chosen?

It is an important part of internal research of IBD patients' quality of life. Research about other quality of life aspects is to start end of 2012.

Institute, university etc. developing the research; researchers coming from different departments etc.:

NIVEL

Note: The CCUVN deliberately chose to have an independent fund for financial reasons.

3.14 SWEDEN

Association: The Swedish Stomach and Bowel Patient Organization

Website: www.magotarm.se

Description of research: Oral Health in patients with Crohn's disease

The research consists of two parts. The first one investigated perceived oral health in patients with Crohn's disease in comparison with a control group without CD. This part is finished and verifies that patients with CD perceived their oral health to be worse than those of the other control group.

The second part investigates clinical tests such as more caries, inflammation in gums etc. This study is ongoing but preliminary results are available for some oral diseases.

Duration / timeframe: 2007- ongoing

Funds invested: 31 309 € from the Swedish association

Source of funds for research:

The research has been done by the Department of Dental Medicine, Division of Periodontology, Karolinska Institute, Stockholm, Sweden in cooperation with Gastrocentre at Karolinska hospital, Stockholm. The contribution from the patient association was a part of the total financing.

The Swedish Stomach and Bowel Patient Association is involved in 3 different funds that are supporting research in IBD or wider Stomach and Bowel diseases.

Aims of study / expected outcomes:

An observation of a correlation between worse oral health and Crohn's disease as well perceived as clinically tested is expected.

Based on which criteria is this particular research chosen?

The research was initiated by the Swedish patient organization due to the members experiencing poor oral health. It was estimated that this field should be tested as it was really patient-close.

Institute, university etc. developing the research; researchers coming from different departments etc.: See above

3.15 SWITZERLAND

Association: SMCCV

Website: www.smccv.ch or www.asmcc.ch

SMCCV funds research depending on money left at the end of the year. Decision of who receives money is taken every year individually by the board.

SMCCV has donated 25 000 CHF of funds in 2011 and 2012, respectively, to the IBD Research Foundation (ca. 42 000 €).

3.16 THE UNITED KINGDOM

Association: Crohn's and Colitis UK

Website: www.nacc.org.uk

Description of research #1: UK IBD Genetics Consortium study of anti-TNF pharmacogenomics and IBD genetics in the UK South Asian population.

The last 5 years has seen great progress towards identifying the genetic variants which predispose to Crohn's disease and ulcerative colitis. The progress made is beginning to provide important clues about the causes of these conditions – recognised as the key to the development of better treatments and preventative strategies long-term.

To translate these discoveries into new therapies and improved use of existing therapies for IBD, further genetic investigations are required. This proposal represents the first critical step – to assemble the clinical resources required to undertake these studies.

The key goal is to collect 5000 DNA samples UK-wide from patients with IBD who have not previously participated in our studies. This new collection will focus on:

1. UK South Asians with IBD (a group excluded from genetic studies to date)
2. Selected sub-groups of patients with Crohn's disease who have been treated with the powerful, expensive and potentially toxic anti-TNF antibody therapies infliximab and adalimumab.

This proposal builds on the successes of UKIBDGC and also links the genetic research to the newly created IBD anti-TNF registry. Nation-wide coverage can be achieved through the use of the Clinical Research Network (CRN) and access to the CRN portfolio that Crohn's and Colitis UK support would bring. Through relatively modest financial support from Crohn's and Colitis UK to purchase the DNA extraction saliva kits we can achieve the much larger research objectives of a pharmacogenomics study related to anti-TNF treatment, the additional breadth of including a South Asian population, and increased ability to identify causal genetic variants within many of the ~ 100 areas of the genome already known to influence IBD.

Duration / timeframe: 2012-2013

Funds invested: £30 000 (ca. 37 000 €)

Source of funds for research:

Crohn's and Colitis UK members, local Groups and supporters give or fundraise about £350 000 (435 000 €) every year for research. We also receive occasional legacies specifically for IBD research and sometimes are awarded grants by charitable trusts. All 'in memoriam' donations are directed to research. The Trustees recently transferred £100 000 (124 000 €) from unrestricted funds to maintain levels of research funding at £400,000 (498 000 €) per year.

We have a separate, legally restricted Research Fund which people can choose to give their donations to in preference to or shared with our general unrestricted fund.

Aims of study / expected outcomes:

Studying a large group of UK South Asians with IBD will allow very valuable comparisons with 'European origin' IBD. This will provide critical insights into two key aspects of Crohn's and colitis. Firstly, how the same clinical picture of IBD might arise through different pathways which has the potential to provide insights into causal mechanisms, perhaps including environmental triggers, in both populations. Secondly, where regions of the genome are shown to confer increased risk of IBD in both groups, this could greatly increase our ability to pinpoint the causal genetic variants in both populations, due to their known differences in genetic structure. Such trans-ethnic studies are seen as key next steps in complex disease genetics.

Anti-TNF therapies have revolutionized the management of severe Crohn's disease. However, these powerful medications are not successful in all patients and can result in severe side effects in some. For the anti-TNF antibody study, our goal is to define genetic markers which predict response to or toxicity from these key therapies in Crohn's disease.

Based on which criteria is this particular research chosen?

Crohn's and Colitis UK has three programs of research funding, one of which is medical. Applications are invited each year and typically we receive 25 applications and award 3-5. Applications can be on any aspect of IBD, the charity does not set a priority theme. A panel of 8 doctors/researchers and 4 lay members of Crohn's and Colitis UK assess the applications and recommend which ones should be funded by the Trustees. There is an independent Chairman and external referees reviews are sought. The criteria are the originality and achievability of the research, relevance to the objectives of Crohn's and Colitis UK, (which means basic science is less often funded), quality of the research centre, applicants and consideration of their other IBD research funding, value to Crohn's and Colitis UK members. Strict criteria have to be fulfilled if the research involves the use of animals. Research fellows may be interviewed as part of the process. Our assessment procedure has been awarded a Certificate of Best Practice by the Association of Medical Research Charities, which means that any funded project is counted as part of the national portfolio of research for which hospitals can receive some additional public funding through their local Clinical Research Network (CRN).

This project met the criteria for originality – particularly the South Asian population, achievability (proven methodology), was highly relevant to our objectives (inclusion of ethnic minority population, better IBD treatment, search for the cause), was from an established consortium with a track record of leading research, and was good value for members (builds on other sources of funding but adds an additional dimension to a project that is immediately understandable to our members).

Institute, university etc. developing the research; researchers coming from different departments etc.:

The grant is to the UK IBD Genetics Consortium which involves a broad range of leading IBD units. The grant is held and administered by Dr Miles Parkes at Addenbrookes Hospital, Cambridge.

Description of research #2: Comparison of combination antibiotic and hydroxychloroquine therapy (Ciprofloxacin, Doxycycline and Hydroxychloroquine) with standard therapy (Budesonide) in the treatment of active Crohn's Disease.

Crohn's Disease may be caused by an altered response to intestinal bacteria. There is growing evidence, supported by at least eight independent studies, that a type of E.Coli bacteria may be particularly involved. These bacteria can invade across the gut lining and grow in the tissue

within a type of white blood cell called a macrophage. There is now sufficient evidence to justify trials of therapy targeting the E.Coli living inside the macrophages to see whether this helps to get patients with active Crohn's Disease back into remission.

Antibiotics are often relatively ineffective at killing bacteria 'hiding' inside macrophages. However, in laboratory studies, the researchers have found that a drug called hydroxychloroquine substantially increases the ability of antibiotics to kill the E.Coli isolates that are living inside macrophages. Hydroxychloroquine was initially developed for the treatment of malaria, but is now widely used for its anti-inflammatory activities in rheumatoid arthritis. Recently, it has become standard therapy, in combination with antibiotics, in the treatment of two chronic infections: Whipple's Disease (an intestinal disease) and Q fever (a more generalised illness that commonly affects the heart) – both conditions are known to be caused by bacteria that are replicating within macrophages.

The research is a clinical trial that assesses a combination of antibiotics (ciprofloxacin and doxycycline) and hydroxychloroquine designed to attack E.Coli within macrophages for their efficacy to treat active Crohn's Disease, in comparison (randomised but without placebo-blinding) with standard therapy with the low absorption corticosteroid budesonide.

The trial has already received funding from the National Institute of Health Research through the Liverpool Biomedical Research Centre, allowing us to start the trial in Liverpool. However, the trial would probably take five years to recruit for if it is based at only one centre. The statistician has advised that at least 100 patients are necessary to obtain a clear result.

The funding requested is for additional funding to cover drug and research nurse costs for half the patients (50 with a per capita costing). This allows recruitment at other sites, as well as allowing the trial to be placed on the national CLRN trials portfolio – bringing substantial benefits in terms of recruitment speed and also covering service support costs for recruiting sites.

Duration / timeframe: 2012-2013

Funds invested: £51 000 (63 000 €)

Source of funds for research: See above

Aims of study / expected outcomes:

To discover if this could be a new and relatively safe form of treatment for patients with relapsed Crohn's Disease.

Based on which criteria is this particular research chosen?

Professional initiative, potential new treatment, hospital with a long track record in IBD research, builds on other funding for the research enabling the trial to be multi-centre, quicker and conclusive.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Department of Gastroenterology, University of Liverpool. Grantholder: Professor Jonathan Rhodes

Description of research #3: Managing Fatigue in IBD

40% of people in a Crohn's and Colitis UK survey reported Fatigue as their most troublesome symptom. However, awareness of this in health professionals is low and treatments for it are often lacking.

The Crohn's and Colitis UK 4 year research project (which began in July 2010), will examine the causes of fatigue, pilot a fatigue assessment tool and explore interventions to improve its management in IBD.

The project comprises a number of work packages. Twenty volunteers with IBD were interviewed and the data that emerged from these discussions was used to develop a fatigue assessment tool which is being piloted with 300 people living with IBD who have volunteered to help with this project. Data is being analysed from a questionnaire study of healthcare professionals designed to assess the level of awareness of fatigue. Further stages in the project will be to develop a framework for ensuring that treatable causes of fatigue are actively managed and to trial two additional interventions.

Duration / timeframe: 2012-2014

Funds invested: £481 000 (ca. 598 000 €)

Source of funds for research:

Big Lottery Fund (charitable trust funded by public lottery). The Big Lottery Fund is the largest UK distributor of National Lottery money to good causes. Their mission is to bring real improvements to communities and lives of people most in need. The Big Lottery Fund uses money raised by The National Lottery to fund projects for health, education, environmental and charitable purposes. In 2009/10 they made 14,000 funding commitments totaling £440 million (547 million €) to groups across the UK, ranging from £300 (370 €) to investments of more than £1 million (1 235 000 €).

Aims of study / expected outcomes:

By the end of the project we want to achieve the following outcomes:

- People with IBD will be more confident in requesting assessment and treatment for fatigue.
- Healthcare professionals in 240 IBD clinics will be able to provide greater help to people with IBD to manage their fatigue, through the development, testing and dissemination of a new IBD specific fatigue measurement scale.
- People with IBD will benefit from better assessment and treatment of their fatigue, through the development and evaluation of new interventions.

Based on which criteria is this particular research chosen?

The need for research was identified by Crohn's and Colitis UK from a survey of members which identified symptoms of incontinence, pain and fatigue as ones that were major issues for significant numbers of patients even in remission. 40% of those surveyed identified fatigue as a significant problem in remission. One of the key criteria for the Big lottery Fund was that the research was patient-initiated and led.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Crohn's and Colitis UK identified the need for research on this topic and the potential funding

source. We invited three university hospitals to participate and created a lay-led steering group. We coordinated the drafting and submission of the applications and after receiving funding negotiated the necessary research contracts.

Crohn's and Colitis UK (St Albans)
University College Hospital, London
King's College, London
Addenbrookes Hospital, Cambridge

Description of research #4: Surgery and Me: assessing and ameliorating sexual problems in adolescents with IBD facing surgery

The study aims to identify the psychosexual concerns of adolescents and young adults (aged 16-24 years) with IBD who face surgery with the prospect of stoma formation and to provide support to address these concerns. The research covers:

- an in depth qualitative study to define the breadth of psychosexual concerns in this patient population and identify their needs for support
- the findings of the qualitative analysis will be confirmed through a validated national questionnaire based survey
- will develop and evaluate an educational resource specifically targeted at this patient group based on the needs identified in the first two phases

Duration / timeframe: 2008-2012

Funds invested: £133 000 (165 000 €)

Source of funds for research: See above

Aims of study / expected outcomes:

The study will delineate the range of concerns that adolescents with IBD experience prior to and after surgery. It will then quantify the extent of these concerns in a national sample. Finally, it will generate a targeted educational/support tool and assess its impact.

Based on which criteria is this particular research chosen?

As for previous Genetics submission except that the research programme is our Living with IBD Programme and the assessment panel comprises social science academics, health professionals and lay members. The panel is chaired by a lay member of Crohn's and Colitis UK.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr James Lindsay, Clinical Academic Unit of Gastroenterology, Barts and the London NHS Trust, Whitechapel, London

Description of research #5: A pilot randomised control trial to assess the impact of an interactive IBD electronic record 'IBD Patient View'

The aim is to develop and test an IBD-specific patient record which consists of:

- A secure, personal IBD record, through which the patient can access clinic letters, blood results, medications etc. from anywhere in the world.

- A number of interactive tools to enable the patient to self-assess their symptoms, including disease activity measuring tools where abnormal scores will be highlighted through a trigger email to an IBD Nurse Specialist.
- Access to information used in the hospital self-management programme and to Crohn's and Colitis UK information leaflets.

After development, patients will be randomised over a 6-month period between use of 'IBD Patient View' and standard care.

Duration / timeframe: 2011-2013

Funds invested: £108 000 (134 000 €)

Source of funds for research: See above

Aims of study / expected outcomes:

Improved quality of life, IBD knowledge, disease activity and adherence to medications; reduced health service usage through better supported patient self-management. If the results are positive, the aim is to develop the facility in conjunction with the UK IBD Registry.

Based on which criteria is this particular research chosen?

Health professional initiative based on a long-tradition at Salford Hospital of a commitment to patient self-management; Commitment to future integration to national IBD health service improvement projects; Potential value to patients.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr Christopher Calvert - Salford Royal Hospital Foundation Trust

Description of research #6: An examination of aspects of the occurrence natural history and consequences of inflammatory bowel diseases utilising available electronic records (General Practitioner Research Database and Hospital Episode Statistics)

The research will investigate four aspects of IBD:

- Though it is known that IBD became far more common over the second half of the twentieth century, it is far less certain whether this increase continues, and in what ways any increase may vary by age, gender, region or social class. The first study will ascertain this information in a well-established.
- The NICE appraisal of anti TNF agents demonstrated that the best data NICE could find to describe the natural history of IBD was from a small population in the USA. This study will use the records available to characterise the natural history of IBD among UK patients, in a number of ways, but with particular reference to the proportion of patients remaining under regular follow up, receiving steroids, and undergoing surgery.
- It has been known for many years that IBD patients when in hospital with a flare of their disease are at high risk of VTE. A previous Crohn's and Colitis UK funded study provided evidence that this risk is also high during flares of disease out of hospital. The weakness of this study was that it was not possible from the data available to define when people were in and out of hospital precisely. This study will repeat the research using the linked hospital and GP data now available. This is important because if the risk is high methods of preventing VTE during flares out of hospital should be considered.
- In a disease affecting young adults, reproductive issues are always important to the young patients involved. It remains unclear to what degree fertility overall is affected, and

precisely what the interplay between drugs disease and pregnancy is. We propose to study maternal, and linked maternal child records to determine fertility rates, and the degree to which pregnancy affects disease activity as well as how the drugs used to treat it affect pregnancy outcome.

Duration / timeframe: 2011-2013

Funds invested: £99 000 (123 000 €)

Source of funds for research: See above; through the association's Medical Research Panel.

Aims of study / expected outcomes:

The first study will ascertain whether an increase in IBD continues, and in what ways any increase may vary by age, gender, region or social class. This information will come from a dataset which has now been collected in a reasonably uniform manner for over 20 years.

The second study will analyse the natural history of IBD among UK patients in a number of ways, but with particular reference to the proportion of patients remaining under regular follow up, receiving steroids, and undergoing surgery.

The third study will identify whether there is indeed a high risk of VTE in patients experiencing a flare-up outside of hospital, in which case methods of preventing this can be considered.

The fourth study will determine fertility rates and the degree to which pregnancy affects disease activity as well as how the drugs used to treat it affect pregnancy outcome. As some outcomes (such as congenital malformation) are rare, the research may well be unable to give absolute answers in all these areas, but these data will make an important contribution in this area which is very difficult to study.

Based on which criteria is this particular research chosen?

There is a need for better data on IBD plus the new availability of linked GP and hospital records. Very strong track record in GI epidemiology. Previously delivered on a Crohn's and Colitis UK funded project. Benefit to patients of better understanding of VTE and pregnancy/fertility data.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Dr Timothy Card - Division of Epidemiology and Public Health, Nottingham City Hospital

Description of research #7: Living with IBD: perspectives of gay men and women in the UK

250,000 of the UK population have IBD. We can estimate the figure for those who are gay or lesbian to be about 14,000. The nature of IBD is very likely to be the same in this group, but it is not known if the psycho-social or illness-related concerns are similar or whether there are additional or different issues associated with being gay with IBD.

The study aims to:

- understand the issues and concerns related to IBD amongst the gay or lesbian population and demonstrate whether these are the same or different to the concerns of the non-gay community.
- explore social and psychological aspects of IBD in gay people and how these are managed.

- explore any parallels between disclosing sexual identity and disclosing IBD.
- provide information which will enable Crohn's and Colitis UK to understand the needs of this group.

Duration / timeframe: 2011

Funds invested: £39 000 (49 000 €)

Source of funds for research: See above

Aims of study / expected outcomes:

Helping Crohn's and Colitis UK to be more inclusive towards members with different identities and lifestyles and identify ways of attracting and supporting this group.

Providing evidence to help NHS staff improve their care of people with IBD who are gay. Provide better understanding of the issues surrounding disclosure about illness and what developments in helplines, counseling, information and self-help materials might assist people living with IBD.

Based on which criteria is this particular research chosen?

- Lack of current research.
- Supports Crohn's and Colitis UK objective of inclusion.
- Good track record as an academic institution in similar research and also in research with IBD patients.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Ms Lesley Dibley - Buckinghamshire New University, Uxbridge

3.17 THE UNITED STATES

Association: Crohn's & Colitis Foundation of America

Website: www.ccfa.org

The Crohn's and Colitis Foundation of America (CCFA) is a non-profit, volunteer-driven organization dedicated to finding the cures for Crohn's Disease and ulcerative colitis. It was founded in 1967 by Irwin M. and Suzanne Rosenthal, William D. and Shelby Modell, and Henry D. Janowitz, M.D.

Since its founding over four decades ago, CCFA has remained at the forefront of research in Crohn's disease and ulcerative colitis. Today, CCFA funds cutting-edge studies at major medical institutions, nurtures investigators at the early stages of their careers, and finances underdeveloped areas of research. In addition, CCFA's educational workshops and programs, along with our scientific journal, Inflammatory Bowel Diseases, enable medical professionals to keep pace with this rapidly growing field. The National Institutes of Health has commended CCFA for "uniting the research community and strengthening IBD research."

CCFA's mission is to cure Crohn's disease and ulcerative colitis, and to improve the quality of life of children and adults affected by these diseases. CCFA currently has over 50,000 members, served by the national headquarters, as well as 40 chapters nationwide. Since CCFA is not a government-supported agency, it relies on the support of members and donors to continue the work.

Description of research:

For more than forty years, research supported by CCFA has contributed to the growing body of knowledge and understanding of Crohn's disease and ulcerative colitis, collectively known as inflammatory bowel diseases (IBD).

Today, both CCFA and the National Institutes of Health (NIH) actively support research in the field, and there are approximately 80 new therapies in the pipeline. Below are examples of recent successful research initiatives, studies, clinical trials, and other efforts supported by CCFA that have resulted in new advances in the field.

For a more comprehensive list of research news, visit the News Archive.

CCFA research has contributed significantly to the current hypothesis of the cause of IBD:

- That yet-unidentified environmental agents (such as bacteria) trigger an abnormal immune response in people who carry genes that make them susceptible to Crohn's or colitis.
- That the interplay of genetics, environment, and the immune system accounts for the initiation and perpetuation of the disease.

CCFA research funding has supported:

- Early Research on TNF-alpha, which contributed to the development of infliximab.
- Discovery of the first gene for Crohn's disease, NOD2
- Development of animal models of IBD—vital resources that have greatly accelerated the pace of research
- Understanding and investigation of microbial antigens, bacteria that normally occur in the intestine and that are involved in the body's immune response
- Understanding the function of epithelial barrier cells, which are key to understanding intestinal inflammation
- Understanding and stopping inflammation.
- Early career training for many of the investigators involved in discovery of the IL-23 gene's role in IBD

Clinical Research:

CCFA has sponsored comparative drug trials to find new uses for existing therapies—to enhance the effectiveness of these medications or to minimize harmful side effects:

- Azathioprine in both Crohn's and ulcerative colitis
- Azathioprine and prednisone vs. prednisone alone
- Effectiveness of methotrexate
- Methotrexate vs. 6-MP
- 6-MP vs. 5-ASA.
- Efficacy of infliximab in combination with methotrexate for Crohn's disease - study is ongoing

Key Outcomes in Surgery:

- New surgical technique: improving ileoanal pouch surgery by sparing the anal transition zone. In people who have undergone colectomy, this operation eliminates the need to wear an external pouch in order to eliminate body wastes.
- Understanding the psychological impact of ostomy surgery.

CCFA Contributions to Cancer Research:

- Standard Classification for Dysplasia in IBD—landmark paper that helps physicians evaluate pre-cancerous changes in cells and determine course of action for their patients.
- Studies of markers of cancer risk in chronic ulcerative colitis.

CCFA Contributions to Pediatric Research:

- Prednisone absorption in childhood IBD
- Interventions for bone mineral deficits in children
- Value of serological markers in pediatric IBD
- Alternate-day dosing of prednisone in children
- 6-MP and corticosteroids in newly diagnosed children.

CCFA's Research Investment Portfolio Also Includes:

- Targeting specific "hot areas" for Requests for Applications from researchers
- Identification of the microbial antigens that activate immune responses in the intestine.
- Biomarkers of colon cancer in IBD
- Growth/Bone development - discover how inflammation causes growth failure and bone disease in children with IBD
- Surrogate Markers - RFA Submissions deadline July 1, 2007

Funding government studies CCFA deems essential to IBD:

- CDC/Kaiser Permanente Epidemiology Project, which will help determine how many Americans have IBD and identify differences in treatment patterns
- Building resources that benefit the entire scientific community
- Clinical Research Alliance, a national network of medical centers that participate in clinical trials
- DNA and Cell Line Bank, an important resource for geneticists who are studying IBD.

Duration / timeframe: 1967 - present

Funds invested: 16 million USD annually (12 million €)

Source of funds for research:

Financial support for CCFA Research programs is provided by several different sources including private donors, foundations and for-profit organizations.

Aims of study / expected outcomes:

CCFA's mission is to cure Crohn's disease and ulcerative colitis, and to improve the quality of life of children and adults affected by these diseases.

Based on which criteria is this particular research chosen?

Applications are reviewed in 3 step process:

- 1) Peer Review of Applications

The Research Training Awards Committee is composed of basic and clinical IBD researchers in a variety of fields. The review committee is composed of basic and clinical IBD researchers in a variety of fields. The committee generally has between 15-20 members; leaders in their areas of expertise and 2-3 lay reviewers. In addition, ad-hoc members may be added in order to provide expertise in certain area(s), depending on the composition of topics of the submissions. Each application is assigned a primary and secondary reviewer (and when necessary, a tertiary reviewer). Reviewers are required to prepare a written evaluation of the application, addressing the following Selection Criteria:

- Intellectual background of the applicant
- Applicant's research experience
- Mentor's track record
- Number of important techniques to be learned
- Importance of the research area
- Relevance to IBD
- Applicant's career objectives

All research supported by CCFA must examine aspects of and have a direct application to Crohn's disease and/or ulcerative colitis. It is the applicant's responsibility to explain the relevance of the proposal to IBD. At the Peer Review Committee Meeting, the applications are discussed, and votes are held to either approve or disapprove. If approved, the application is then ranked by each committee member, using a scoring system identical to that previously used by the National Institutes of Health: 1.0 being the highest ranking and 5.0 the lowest.

Note: Lay reviewers actively participate as voting members in the peer-review process. These individuals will look specifically for the relation of the study to IBD as well as the potential for applicants to continue their careers in IBD research. It is the applicant's responsibility to clearly describe these aspects in easily understandable language for the lay reviewers. Failure to do so may result in a lower recommended priority score.

2) Review by Grants Council

Those projects in the fundable range are examined and ranked by the Grants Council in respect to the foundation's goals, as outlined in the document, "Challenges in IBD". (Document may be found on the "Science & Professional" section at www.ccfa.org)

3) Board of Trustees Approval

Following the Grants Council meeting, the Chairperson of the National Scientific Advisory Committee presents the Grant Council's recommendations for funding at the next meeting of Board of Trustees. CCFA's Board of Trustees, with input from the National Treasurer and President regarding budgetary constraints for the fiscal year, then considers the payment of grants.

STATEMENT OF COMMITTEE IMPARTIALITY

To insure that the peer review process undertaken by CCFA's Grants Review Committee is fair and unbiased, the following procedures are in place:

1. An Ad Hoc Review Committee is set up to review any application submitted or sponsored by a Grants Review Committee member during the cycle. This also applies to all committee chairpersons.
2. Committee members are excused from the review room during the discussion of proposals from their own institutions or from collaborating institutions, and do not rank those

applications. Applications and reviews of an applicant's proposal are not available to committee members who have such conflicts of interest.

3. Reviews and applications are treated with utmost confidentiality and are not circulated to anyone outside the review committee membership.

Taken together, these steps attempt to avoid any obvious conflicts of interest among members of the committee.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Benaroya Research Institute; Beth Israel Deaconess Medical Center; Brigham and Women's Hospital, Inc.; Broad Institute, Inc.; Burnham Institute; California Institute of Technology; Cedars-Sinai Medical Center; Children's Hospital Boston; Children's Hospital, Los Angeles; Cincinnati Children's Hospital Medical Center - Research Foundation; Cleveland Clinic Foundation; Clinipace; Columbia University Medical Center; Coriell Institute for Medical Research; Cornell University; Dana Farber Cancer Institute, Inc.; Descartes; Emory University; Federation of Clinical Immunology Societies; Flanders Institute for Biotechnology; Georgia State University; Harvard Medical School; Hebrew University of Jerusalem; Iowa State University of Science and Technology; Joan & Sanford I. Weill Medical College of Cornell University; Johns Hopkins University; Louisiana State University Health Sciences Center-New Orleans; Massachusetts General Hospital (The General Hospital Corp.); Mayo Clinic; Medical College of Wisconsin, Inc.; Medical University of South Carolina; Montana State University; Mount Sinai School of Medicine; National Cancer Institute; New York University School of Medicine; Northwestern University; Research Foundation of CUNY on behalf of Brooklyn College; Research Institute at Nationwide Children's Hospital; Robarts Research Institute; Rosalind Franklin University of Medicine and Science; Saint Louis University; Sanford-Burnham Medical Research Institute; Seattle Institute for Biomedical and Clinical Research; St. Jude Children's Research Hospital; Stanford University; Texas A&M Research Foundation; The Children's Hospital of Philadelphia; The Regents of the University of California, Los Angeles; The Regents of the University of California, San Diego; The Regents of the University of California, San Francisco (Contracts & Grants); The Regents of the University of Michigan; The Rockefeller University; The Scripps Research Institute; The University of Alabama at Birmingham; The University of Chicago; The University of North Carolina at Chapel Hill; The University of Texas Health Science Center at Houston; Trudeau Institute, Inc.; University Clinic of Essen, Medical Faculty of the University-Duisburg-Essen; University of Colorado Health Sciences Center; University of Connecticut Health Center; University of Kentucky Research Foundation; University of Maryland, Baltimore; University of Miami; University of Pittsburgh; University of Texas M.D. Anderson Cancer Center; University of Texas medical branch; University of Washington; UT Southwestern Medical Center; Veterans Medical Research Foundation; Washington University School of Medicine St Louis; Weizmann Institute of Science; Yale School of Medicine

4. IBD RESEARCH FOUNDATION

IBD Research Foundation – the patients’ voice in research

Website: www.ibdresearch.org

The IBD Research Foundation was established in 2008 as an initiative of EFCCA, in order to help EFCCA associations serve their members who would like to contribute to research. Fundraising efforts focus on associations which do not have their own fundraising organization, making available funds for research which otherwise would not have been available. The foundation is open to collaboration with other organizations which support IBD research, in order to support larger IBD research projects together. By supporting IBD related research, the foundation aims to improve IBD treatment and thus contribute to a better quality of life of people with IBD. The ultimate aim of the foundation remains to conquer Crohn’s and Ulcerative colitis by finding a cure.

Although the foundation decides each year how many grants to award and which amount of money will be involved, starting in 2010 the foundation accomplished each year to award three research projects a grant of 5000 € each. Grant applications are not only assessed by renowned peer reviewers, but also by patient reviewers. Since the patient reviewers decide which applications are to be awarded a grant, the foundation guarantees its patients’ perspective in research.

The IBD Research Foundation is currently funding 3 research projects totalling 14 500 €.

Description of research #1: NR4A orphan nuclear receptor signalling: a novel pathway in inflammatory Bowel Disease

Duration / timeframe: 2012-2013

Funds invested: 5000 €

Source of funds for research: Patient associations which are member of EFCCA; private donations by individuals.

Aims of study / expected outcomes:

- To determine the expression of NR4A orphan nuclear receptors in inflammatory bowel disease.
- To determine the subcellular localization of the NR4A receptors (nuclear: cytoplasmic)
- To determine the functional role of NR4A receptors in colonic inflammation and epithelial barrier dysfunction in IBD

Based on which criteria is this particular research chosen?

Criteria of the patients’ representatives committee:

1. Level of innovation
2. Level of interest from a patients’ perspective
3. Budget allocation:
 - Is the allocation of the budget essential for the implementation of the project?
 - Is the allocation of the budget appropriate from a patients’ perspective?

4. Ethical aspects; To what extent do you consider the project ethical?

Criteria of the Scientific review committee:

1. Innovative research?
Scientific importance for the development of
 - Quality of life
 - Knowledge
 - Therapeutic possibilities of IBD
2. Scientific basis (whether the project is based on sufficient scientific evidence)
3. Methods
Do the methods used qualify for achieving the desired results?
Are the results reproducible?
4. Feasibility?
Is the project described in a competent way and what are chances of success?
Consistency of the work?
5. Originality of research
Is the aim of the project and are the main questions to be answered new?
6. Scientific value?
What is the scientific significance of the project? How are questions, methods and originality bringing IBD research further – higher level? What will be gained if the project succeeds?
7. Applicant?
How qualified is the applicant in general for the project? Are there preliminary works in or for the project? Earlier publications? How well is the current state of knowledge taken into account? Is the applicant well supported?
8. Benefits and potential for the patient?

Institute, university etc. developing the research; researchers coming from different departments etc.:

UCD Veterinary Sciences Centre, University College Dublin, Belfield, Dublin 4, Ireland

Supported by: Alan Baird, PhD. Professor and Conway Fellow; UCD Veterinary Sciences Centre, University College Dublin, Ireland

Description of research #2: Development of novel biomarkers for prediction of the outcome of anti-TNF therapy in IBD patients.

Duration / timeframe: January 2012 – September 2012

Funds invested: 4500 €

Source of funds for research: See above

Aims of study / expected outcomes:

To evaluate the efficacy of anti-TNF therapeutics used in IBD in blocking TNF-mediated responses in blood of IBD patients and to identify the predictive factors determining the outcome of anti-TNF therapy which could be detected in blood of IBD patients.

1. What are the efficacies of anti-TNFs measured in blood of IBD patients before the therapy?
2. Do Fc receptors influence the response towards specific anti-TNFs?
3. Can the expression levels of Fc receptors be used as a biomarker suitable for the prediction of anti-TNF response in IBD patients?

4. Do the differences in Fc receptor expression levels found in blood cells of IBD patients correlate with the differences in the intestinal expression levels of the same patients?

Based on which criteria is this particular research chosen? See above

Institute, university etc. developing the research; researchers coming from different departments etc.:

Division of Gastroenterology and Hepatology, Department of Internal Medicine, University Hospital, Zurich, Switzerland

Supported by: Prof. Dr. Dr. G. Rogler Leitender Arzt, UniversitätsSpital Zürich DIM / Gastroenterologie und Hepatologie Zürich, Switzerland

Description of research #3: Modulation of bacterial ligand-induced angiogenesis by probiotics through distinct Toll-like (TLR) and Nod-like (NLR) receptors in IBD.

Duration / timeframe: 01.01.2012 – 31.12.2013

Funds invested: 5000 €

Source of funds for research: See above

Aims of study / expected outcomes:

Probiotics are capable to modulate bacterial ligand-induced mucosal angiogenesis in IBD through TLR- and NLR-mediated recognition.

1. Investigation of in vitro effects of the probiotics E. coli Nissle 1917 or VSL#3 on angiogenesis separately for controls and IBD patients. This will include the investigation of angiogenesis by several functional assays and the evaluation of involved mechanisms and molecules.
2. Evaluation of effects of named probiotics on angiogenesis in vivo. This will include:
 - a. the examination of human colons by conventional white-light illumination and NBI colonoscopy containing the description and classification of vascularisation before and after 12 weeks of probiotic treatment in the same region.
 - b. the evaluation of colon biopsies for angiogenesis before and after administration of E. coli Nissle 1917 or VSL#3 identifying 1.) differences in angiogenesis before and after probiotic treatment and 2.) identification of molecules and receptors relevant to angiogenesis modified by probiotic treatment.

Based on which criteria is this particular research chosen? See above

Institute, university etc. developing the research; researchers coming from different departments etc.:

Charité Universitätsmedizin, Department of Hepatology and Gastroenterology, Augustenburger Platz 1, Berlin, Germany

Supported by: Prof. Andreas Sturm, Professor of Medicine, Charité Universitätsmedizin Berlin

The results of the 2010 grant program are available and as follows:

Description of research #1: The protein C pathway: a novel mediator in intestinal homeostasis in IBD

Duration / timeframe: January 2011 - December 2011

Funds invested: 5 000 €

Source of funds for research: See above

Aims of study / expected outcomes:

The following central hypothesis was proposed to be investigated: The protein C pathway is expressed by DC and epithelial cells, and mediates a novel cell-cell cross-talk that is necessary for intestinal homeostasis.

1. Study the expression and function of the protein C pathway in human IBD
2. Investigate the functional role of the protein C pathway in mediating epithelial homeostasis in a dendritic cell-dependent manner

Based on which criteria is this particular research chosen? See above

Institute, university etc. developing the research; researchers coming from different departments etc.:

Lead researcher: Stefania Vetrano, BSc

Institute:
Laboratory of Immunology and Inflammation
Istituto Clinico Humanitas
20089, Rozzano, Italy

Letter of support by:
Silvio Danese, MD, PhD HEAD, IBD Unit Division of Gastroenterology
Istituto Clinico Humanitas-IRCCS in Gastroenterology, Milan
Francis J. Castellino; Kleiderer-Pezold Professor of Biochemistry
Director, W.M. Keck Center for Transgene Research

Outcomes:

The results have been published by “PNAS - Proceedings of the National Academy of Sciences of the United States of America”:

<http://www.pnas.org/content/108/49/19830.full>

Description of research #2: Exploring the potential of N-palmitoylethanolamine in a mouse model of inflammatory bowel diseases

The study aims at exploring the potential anti-inflammatory properties of PEA in an animal model of colitis, in treating colon inflammation as well as the colitis-related LPS induced systemic inflammation.

Duration / timeframe: January 2011 - December 2011

Funds invested: 4 950 €

Source of funds for research: See above

Aims of study / expected outcomes:

In this grant application we propose to explore the potential antiinflammatory properties of the Nacylethanolamines, and more specifically of N-palmitoylethanolamine, in treating colon inflammation and the related systemic inflammation found during colitis.

Based on which criteria is this particular research chosen? See above

Institute, university etc. developing the research; researchers coming from different departments etc.:

Lead researcher: Prof. Giulio G. Muccioli, PhD

Research institute:
Bioanalysis and Pharmacology of Bioactive Lipids lab
Louvain Drug Research Institute
Université catholique de Louvain, Belgium

Letter of support by:
Prof. M.P. Mingeot – LeClercq; president Louvain Drug Research
Institute; Université catholique de Louvain, Belgium

Outcomes: PEA administration had a beneficial effect on colitis, lowering the macroscopic score as well as pro-inflammatory markers in the colon, liver and brain, although not to a great extent. The administration of a PEA degradation inhibitor, in order to increase the endogenous levels of PEA, was less successful. Moreover the combination of PEA with an inhibitor of its degradation produced the same effects as PEA alone. In conclusion, this study showed a potential beneficial effect for PEA in IBD. Considering that PEA can be metabolized by several enzymes, we propose to explore next the effect of the combination of PEA with another inhibitor of its degradation to try and potentialize its effects.

Description of research #3: Analysis of PPAR- γ haplotype structure and its influence on disease susceptibility, pathogenesis and activity of inflammatory bowel disease.

Duration / timeframe: November 2010 – November 2011

Funds invested: 5 000 €

Source of funds for research: See above

Aims of study / expected outcomes:

The aim is to comprehensively determine PPAR- γ gene variants by sequencing all seven NR1C3 exons which code for the most common PPAR- γ splice variant PPAR- γ 2 and the first 50 bp of the neighbouring intronic regions in 300 IBD patients and compare the sequencing outcome with the sequencing results obtained in 200 non-IBD subjects.

1. Is there a difference in SNP composition and frequency in IBD patients compared to non-IBD control subjects? Is it possible to detect specific PPAR- γ gene variants as putative susceptibility markers for IBD?
2. Do differences in SNP/haplotype composition and frequencies occur between CD patients and UC patients, which would indirectly support the hypothesis of a different pathogenesis?
3. Are there any novel variants of functional relevance within the PPAR- γ gene detectable, which could further explain the mechanisms behind the inflammatory processes observed in IBD patients?

Based on which criteria is this particular research chosen? See above

Institute, university etc. developing the research; researchers coming from different departments etc.:

Lead researcher: Dr. Jessica Mwinyi

Research institute:
Division of Clinical Pharmacology and Toxicology
UniversitätsSpital Zürich
Rämistrasse 100
8091 Zürich

Letter of support by:
Prof. Gerd Kullak-Ublick; UniversitätsSpital Zürich
Klinik für Klinische Pharmakologie und Toxikologie

Outcomes: The results have been published by: “Hindawi Publishing Corporation – PPAR Research”: <http://www.hindawi.com/journals/ppar/2012/349469/>

5. PRIORITIES AND NEEDS OF PATIENT ASSOCIATIONS THAT DO NOT FUND RESEARCH

5.1 BRAZIL

Association: ABCD, the Brazilian Association of Colitis and Crohn's disease

Website: www.abcd.org.br

The Brazilian Association of Colitis and Crohn's disease, has some projects of research.

- 1) Anti IFX antibody detection in Brazilian patients with IBD (does it happen together with loss of response?)
- 2) Nod 2 mutation analysis in Brazilian patients with IBD. Comparison between region north/northeast (more rural and less developed regions) and region south/southeast (more urban and developed regions)
- 3) diagnosis resources in cities with up to 200 000 inhabitants: is it possible to have a safe diagnosis in those places?
- 4) nutritional profile of Crohn's disease patients and evaluation of development in children.

Reasons:

To date, ABCD has no funding.

5.2 BULGARIA

The Bulgarian Crohn's and Ulcerative Colitis Association so far has not and currently does not conduct any research. From the Bulgarian association's point of view, a field of study that deserves attention is *alternative medicine*. Patients' organizations can hardly compete with pharmaceutical companies in funding research of new drugs, but they could concentrate on testing the effectiveness of some alternative medicines or therapies that are already on the market and that claim to reduce the symptoms or even curing Crohn's or Colitis. Members of the Bulgarian association keep posting on the Facebook wall links to (innovative) products - food complements, supplements, therapies, etc. asking if someone has tried them and whether they work. Perhaps inexpensive research would dismiss most of them as 'ineffective' and thus would save desperate patients a lot of money. On the other hand, if the effects of such products are scientifically proven to be effective, they deserve to be made more popular.

Reasons:

Perhaps the reason is that so far no such interest has been demonstrated by the members of the Association. The problem of how to fund research would also inevitably arise.

5.3 CROATIA

Association: HUCUK**Website:** www.hucuk.hr

The Croatian Crohn's and Ulcerative colitis Association HUCUK would create a medical adviser committee that would inform about the ongoing researches across Europe. HUCUK would fund these types of research:

- Genetic research (HUCUK is aware that many genes have already been discovered and that there are many researches done on the subject) because once all the genes are discovered, it will be easier to develop new medications. Genetics is also important for every patient who plans to have a family.
- New medications that are believed to have great potential.
- Influence of the environmental factors in IBD.

A research project HUCUK would like to start on its own would be "Guidelines to define work ability/disability of people with IBD", in other words, disability assessment that is not defined by the Croatian laws.

People with IBD go through long and hard processes of assessment by two types of commissions that are not entirely acquainted with these diseases.

There are 3 groups of IBD recognised by Croatian legislatures which regulate disability and social security rights: patients who were diagnosed before the age of 18, patients who were diagnosed after the age of 18, but couldn't achieve retirement, or aren't able to achieve retirement, and patients who were diagnosed after the age of 18, but due to the disease couldn't work at all, even though they weren't declared unfit to work.

Primary problems in Croatia are achieving rights from the social security and pension system, because there are two types of commissions: a commission to establish physical disability and a commission to establish work ability. The latter is an independent body and doesn't approve the decisions of the commission that establishes physical disability. Each of these commissions is a starting point to achieve rights from the social security and pension systems, and many other rights.

The patients who were diagnosed after the age of 18 and who were never able to work (due to health condition and/or the work market that is usually in favour of healthy persons) are in the worst position because they have no rights in the pension system, not even to receive family pension.

There are no guidelines to define work ability of people with IBD. It is done based on medical documentation by the commission usually consisting of GP's who are not necessarily entirely familiar with the severity of IBD and many complications that come with IBD, especially with Crohn's disease. There are no IBD specialists in the commission. HUCUK considers this to be a huge problem.

In Croatia there is still in force the Physical Disability Law from 1999. It is important to say that a certain number of patients cannot achieve the physical disability rights due to incomplete criteria that are often freely interpreted by the commission (according to the information HUCUK has gotten from the patients).

Reasons:

The main reason is no funds.

5.4 CYPRUS

Association: CYCCA

Website: www.cycca.org

The Cyprian association CYCCA would like to conduct a survey on the number of people suffering from IBD in Cyprus. Besides the number of sufferers, CYCCA wants to investigate the intensity of the symptoms of the patients and other important information such as age of onset, sites of Cyprus that have the most cases, the period needed to be diagnosed, as well as difficulties patients face in their everyday lives.

Reasons:

The biggest problem is the lack of financial resources.

5.5 GREECE

Association: Attica's Society of Crohn's Disease's and Ulcerative Colitis Patients (ASCC)

Website: www.crohnhellas.gr

Reasons:

The main reason is that by law medical research cannot be funded by patients. Even if that was possible, due to the economic crisis neither the private nor the public sector has or is willing to fund research instead of covering the main costs of running their everyday activities. Additionally, ASCC members don't donate money (again due to the economic crisis).

Association: Northern Greece Crohn & Colitis Association

Website: ibd-gr.blogspot.com

The only kind of research at the association is the questionnaires in cooperation with the psychiatric clinic of the Papanikolaou Hospital in Thessaloniki for the diploma of a student, and the questionnaires are done in cooperation with the Gastroenterological institution of Greece (ELIGAST) and in cooperation with Abbott last year. The association also participates this year in the questionnaire of Dr. Triantafylidis and the public Hospital of Nikaia in Athens "Clinical-epidemiological characteristics of patients with CROHN's disease and ulcerative colitis IN GREECE".

Description of research:

Metabolomic analysis refers to the comprehensive study of the many small molecule metabolites present in biological samples, using technologies which enable the analysis of multiple metabolites with high sample throughput.

The use of metabolomic analyses to study inflammatory bowel diseases (IBD) could potentially address key issues of IBD, which are unknown disease etiology and a requirement for improvement of therapy.

Overall, IBD appears to be a complex, multifactorial disease with unknown etiology and a requirement for improvement of therapy. Metabolomic analysis may help address these key issues.

Metabolomic analysis requires analytical technologies that are capable of detecting and quantitating the large number of metabolites in a biological sample.

Metabolomic data consists of measurements of the concentrations of multiple metabolites, which collectively represent the metabolite profile of the sample or organism.

Metabolite profiles produced from metabolomic analysis can be used to discriminate between disease and nondisease states.

Correct diagnosis of CD and UC would assist in disease management, as each disease has different treatment approaches.

Azathioprine and mercaptopurine are thiopurine immunosuppressants frequently used in the treatment of IBD. Although these thiopurines are effective in inducing and maintaining long-term remission for CD and UC, both drugs are not effective in one-third of patients and cause adverse effects in up to one-fifth of patients due to interindividual differences in thiopurine metabolism. Thiopurine metabolism is complex due to the involvement of multiple enzymes. Monitoring the relative levels of toxic and therapeutic thiopurine metabolites in the blood or measuring the activity of thiopurine S-methyltransferase (TPMT), a thiopurine metabolizing enzyme, are carried out to assess therapeutic response and myelotoxicity.

Metabolite profiles for assessment of therapeutic response of IBD patients not only have to consist of drug metabolites, but may also include endogenous metabolites that are affected by the drug treatment. In addition, the use of urinary metabolite profiles to monitor drug would be more convenient than the use of blood samples, as multiple urine samples can be obtained noninvasively.

Metabolite differences reported for IBD patients and controls vary between studies, which may be attributed to differences in sample type, research approach (targeted or nontargeted analysis), and the lack of confirmation of metabolite identity with authentic standards. Further research is required to validate these metabolite differences and improve the accuracy of metabolite markers for IBD clinical applications. Finally, the study of metabolite differences in IBD patients should be extended to other analytical techniques besides NMR to enable the discovery of additional metabolite differences, as no single analytical platform can completely analyze the metabolome.

Duration / timeframe: In the near future, and as long as the funding allows.

Funds invested: Not calculated. It's still a research proposal.

Source of funds for research: Different possibilities – EU Funds? Metabolomic product companies? Cooperation of all of them with universities and institutes (such as the Institute of Nutritional Medicine or the European Institute of Metabolomic Medicine, etc.)?

Aims of study / expected outcomes:

There are only a few studies utilizing metabolomic analysis in IBD research. The results from these studies demonstrate how high-throughput analysis of multiple metabolites to identify metabolic perturbations in IBD may provide new insights into IBD pathogenesis and improve therapy.

Metabolomic analysis can identify specific metabolite profiles of IBD that can potentially be used for disease diagnosis and monitoring.

However, the possible effects of various factors, such as genetic variation, dietary factors, medication, and sample collection have to be taken into account when designing studies to identify accurate metabolite biomarkers.

Based on which criteria is this particular research chosen?

Metabolomic research orientation in relevance with IBD may suggest new therapies not only for the symptoms but also for the cure of IBD and the monitoring of drug side-effects.

Institute, university etc. developing the research; researchers coming from different departments etc.:

Not yet available. Still under investigation.

Reasons:

Low budget of the association (20 €/person/year; not all members pay constantly). The public sector does not fund any research projects, and the private sector is suffering from the economic crisis in the country. So they have a "very low budget story", perhaps only for a few public events in fact, to promote their products.

The main problem of not funding is the economic situation of the country in the one side, and in the other side the amount of money they needed for this kind of research to have reliable and exploitable results. The possible national Fund sources finance only some events like meetings or speeches for the patient associations.

It may be necessary to change some articles in the statute of the association.

5.6 HUNGARY

Association: MCCBE

Website: www.mccbe.hu

The Hungarian association MCCBE is looking to research new medication to better the quality of life.

Reasons:

Lack of financial background.

5.7 NEW ZEALAND

Association: Crohn's & Colitis New Zealand

Website: <http://crohnsandcolitis.org.nz/>

Description of research #1: The GEM Project

CCNZ wanted to be involved in the GEM project (a multidisciplinary human study on the genetics, Environmental & Microbial Interactions that cause IBD), funded by the Canadian Crohn's & Colitis Foundation (CCCF). The aim is to recruit 1st degree relatives from patients with CD and to analyze for genetic predisposition, microbiota, intestinal permeability and environmental factors.

Duration / timeframe: 6 years

Funds invested: n/a

Aims of study / expected outcomes:

Refer to CCCF

Based on which criteria is this particular research chosen?

A networking opportunity (to include Australia) which arose following discussion with CCCF.

Institute, university etc. developing the research; researchers coming from different departments etc.:

We were going to harness the medical resources of the Australia-New Zealand IBD consortium.

Description of research #2: Researching the Oral manifestations of CD as a predictive marker for Intestinal CD

Duration / timeframe: 6 years

Funds invested: not known

Aims of study / expected outcomes:

It is anticipated that oral manifestations of CD will predict intestinal CD onset 10 years earlier.

Based on which criteria is this particular research chosen?

Research by Associate Professor Anita Nolan, Head of Discipline of Oral Medicine University of Otago.

Institute, university etc. developing the research; researchers coming from different departments etc.:

University of Otago New Zealand

Source of funds for research: n/a

Reasons: As for the CCCF study, it is difficult to obtain local funding for overseas managed research. There are no interested parties in funding this [local] research, therefore not able to find the funds.

5.8 NORWAY

Association: LMF

Website: www.lmf norge.no

The Norwegian association, Landsforeningen mot fordøyelsessykdommer (LMF), funds no research directly. Funding research has been done by fundings from hospitals, government, pharmaceutical industry and funds from state-lottery “Extrastiftelsen”. Lottery must be applied to the LMF, and the LMF is applying for funds to the lottery institute.

There has been a 10 years population-based cohort study following IBD patients, and now starting a new 20 years cohort in the same study. It is called IBSEN-study, meaning IBD South East Norway.

5.9 POLAND

Association: J-Elita

Website: www.j-elita.org.pl

The Polish association, J-elita, does not fund any research because they can't afford it and do not wish to take part in something which they can't promise to sponsor from the very beginning to the very end.

Every two years, however, the J-elita organizes a competition for the best BA/MA/PhD thesis about IBD and in this way promotes young scientists who want to learn and write about IBD. Moreover, J-elita is the only patients' association in Poland that grants scientific awards, as in Poland patients' organizations do not follow such practice due to lack of funds. The majority of the research is funded by pharmaceutical companies so no sponsors will give the association money for that.

If the J-elita could fund the research, they would fund ones which aim at finding some innovative cure for IBD.

Reasons:

Lack of funds and problems with reaching the scientists who would be interested in funding the research. The J-elita contacted all the main hospital/university clinics in Poland and sent them an invitation to apply for the grants given by IBD Research Foundation. Unfortunately nobody answered to the invitation. Also in the Association there are no scientists who could decide about which research the J-elita should fund and which should be declined.

5.10 SERBIA

Association: UKUKS

Website: www.ukuks.org

The Serbian association UKUKS is interested in genetics research in terms of congenital factors and predisposition for IBD.

Reasons:

The Serbian association is still evolving and has no supporters/sponsors through which it would sponsor research

5.11 SLOVAKIA

Association: SCC

Website: www.crohnclub.sk

The Slovak Crohn Club does not have research at the moment.

Reasons:

There are no interested parties in funding this research; therefore the association is not able to find funds.

5.12 SLOVENIA

Association: KVCB

Website: www.kvcb.si

The Slovenian association Organization KVČB (Društvo za kronično vnetno črevesno bolezen) does not support research because of lack of funds. The association is interested in the influence of probiotics on the course of disease, genetic manipulation of probiotics, probiotics as vector of active proteins to inflammation place in the digestive system and the epidemiology of IBD. There is a good pool of researchers available, and the association will try to find funds and probably will have some next year.

6. CONCLUSIONS

Following the country-specific presentations, in which Belgium, Brazil, Canada, France, Germany, Israel, Italy, New Zealand, Sweden, the United Kingdom, the USA and in addition the IBD Research Foundation told about their research and fundraising activities and problems related to them, a lively panel discussion under the topic “Paving the way for future scenarios” with the audience took place. The panel discussion was moderated by Prof. Claudio Fiocchi from the Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio, USA, Professor Gerhard Rogler from the University of Zurich, Switzerland, Professor Laurent Beaugerie from the Saint-Antoine University, Paris, France, and Prof. Silvio Danese from the Sacro Cuore University, Rome, Italy, representing the medical and scientific community (for further information, see the end of the conclusions section, and summed up by the EFCCA Chairman Marco Greco). The main points including also concluding remarks from Marco Greco are as follows.

Choosing Meaningful Projects

Although there are many burning questions in IBD research, no matter how much money is raised, it will never be enough for every project. It is therefore important to prioritise and make choices; limited resources require choices, and the choices need to be well done. It is crucial that the scientific community and the patient associations agree on a common research agenda and priorities. A “shopping list” needs to be made, and doctors and patients together should select a few that really can make a difference. Whether it is a cohort study or a study on what kind of bacteria and food modulate IBD is not important; it is the approach that matters.

Although available funds should be directed to meaningful projects, if only large projects are funded, there is a risk that the grants always go to researchers who are already established and able to do the big research. Committed young new researchers should also be attracted into the field to keep it alive and to get new ideas. This can only be done with a strategy that encourages young scientists into research.

Cooperation

Each patient organisation wants to represent the patient, which is correct. The perspective of the patient organisations, however, may be narrower than that of the scientific community that is interested in fighting IBD objectively and as a whole. Small research projects conducted locally or nationally within patient organisations may be useful for patients and physicians in the local community, but not for the scientific community and IBD on a larger scale. Patient organisations can, however, do things that physicians cannot (e.g. they may have the time and resources to phone patients individually after a pre-selected questionnaire). Furthermore, even local projects have the potential to mature over the years and become more meaningful. Smaller and younger patient organizations can learn from the experiences and expertise of more established ones that due to their seniority and structure are able to raise more funds and carry out larger, more meaningful, productive and innovative projects that possess more strength within the scientific community.

No one wants to give up their own perspective, and no one should have to either. Different countries have different needs for patients; the political situation is different from country to country; it might even be that the pathogenesis is different. There are genetic differences between Asian and European populations, and there might be different causes that contribute. It

is therefore still important to have those roots. Nevertheless, the next step is to collaborate, to join forces for common interests; maybe not all interests, but there are some common interests where efforts can be joined.

Today's world is based on network, collaboration and partnership. Without networks and cooperation, success nowadays will no longer be possible. Furthermore, a lot of research funds are spent on ethics committees and bureaucracy. These costs can be reduced by joining forces. The strength in cooperation, however, is not only in raising funds; it's the voice you generate together. Strength lies in numbers.

Role of EFCCA

Creating networks and patient cooperation at the European level is mandatory; however, we cannot achieve something at European level that we cannot first achieve at national level. CCFC (Canada) and CCFA (USA) are very successful because they raise large amounts of funds, have started a long time ago and have many people participating. EFCCA is in a unique position to do the same in Europe at the European Union level as the voice of Europe for lobbying the European Commission in terms of treatment, safety of treatment, and the overall diagnosis of IBD, which is our priority. The voice of EFCCA from all the patients in Europe is extremely important for getting millions from Europe.

A similar symposium could be organized with key scientists or with the key representatives of scientific societies to think about 1) the priorities in the research agenda and 2) meaningful projects. The scientific societies could partner with EFCCA practically in one or two projects. It is relatively easy to design cohort studies where the patients are contacted directly and in which the patients are the subject themselves, contributing directly to the research. In this approach EFCCA has a major role, and once a project is agreed upon, the money will follow more easily.

ECCO (European Crohn's and Colitis Organisation) should also take a more active role in bringing patients and clinicians together and build research strategies for possibly larger scale European projects. Real physical meetings about research priorities are needed instead of e-mails. ECCO should be proactive in organising such a meeting. Representatives of the patient associations pointed out that also the scientific community should speak with a more unified voice; often times, it seems the scientific communities only focus on being the first to publish and on getting money for their own research. As all scientists will need funds for their own research, this is difficult to avoid. A to some extent common research agenda and more networking, however, would be an option.

Closing Remarks from Marco Greco, EFCCA Chairman

Today, we have been given the opportunity to think in a more ambitious way than ever. I strongly believe that today we have a real chance to change the status quo about IBD and IBD research. Hopefully this will be a global journey that we will take together.

When I am asked about my opinion on global or European cooperation, my answer is always the same: IBD doesn't know or care about your nationality when it comes to visit you the first time. Today we are together with a louder voice to say that this is going to stop and to affirm on a global level that we will work together for beating IBD. Whether it is going to take 10, 20 or 30 years, it is going to happen. To make this meeting even more concrete, EFCCA will take the responsibility of having launched this first challenge today by accepting four commitments.

Firstly: EFCCA will be here for you all, whatever your nationality, whatever your country, because when there is an opportunity of cooperating we see a resource and are happy to help you in developing this resource and in optimizing it. I am not only talking to the patients

associations but also to the medical and scientific community. We have never, in the 23 years of history of EFCCA, stepped back from a challenge. We will not do it now either.

Secondly: EFCCA takes the commitment of organising this meeting again – despite the costs and the economic crisis, because this is our *raison d'être*, the sense of our activity – two years from now in 2014 to see if we will be mature enough for catching this challenge and forwarding it.

Thirdly: We announce our commitment to create and support a new platform for making your everyday job in research easier. This White Book will be out of date in a few weeks or months. Thus, we will launch a platform in which you will all be invited to update your data and to keep others in the loop about what you are doing. It is up to you to use this platform and to get the most out of it. Our role is to offer you the necessary instruments.

Fourthly: The intention, as it has appeared here today, of creating an open and continuing discussion forum about these issues. With the idea of tuning the proposals that have come up in the symposium and to transform them into more concrete projects and, more importantly, results.

With these four commitments I hope you see how much we believe in this project, in your work and in the possibility and potential that lies in this cooperation. If you add up all the money in the last years that we have put on the table in the last three years, you will be surprised (see Annexes 3 and 4).

A couple of times today, the word “IFCCA” has come up. EFCCA is a patients’ association and that's what we stand for. If this possibility exists and if you think now is the moment and we can support you in this, then we are ready to make this step forward and go through with this idea. We will try and involve you all. Our structure is such that two non-European countries are already our members; for us there is no problem to cooperate in this way.

If we stay together, we can overcome any bureaucratic barrier. There is no bureaucracy that can resist the impact of a unique voice and an advocated activity. Together we are not only stakeholders but we can be decision makers, and we have the opportunity to do this globally without losing our national identity. I want to close this meeting with the words of a person who has taught me a lot: “There is only one way for doing your job and that is the right way.”

This White Book is the first concrete outcomes of the Symposium. EFCCA and all the involved associations are committed to feed it with real time information.

Introduction of panelists

Claudio Fiocchi is Professor of Medicine, Cleveland Clinic Lerner College of Medicine, and a member of the Lerner Research Institute and Digestive Disease Institute, Cleveland Clinic, Cleveland, Ohio, United States. His research is focused on the pathogenesis of IBD, with the overall goal of uncovering fundamental molecular and cellular abnormalities that underlie the maintenance of a chronic state of inflammation in the intestinal tract. Dr. Fiocchi is the recipient of the Henry Janowitz Lifetime Achievement Award from the Crohn's & Colitis Foundation of America and the Clifford and Jane Anthony Chair in Digestive Disease Research and Education, and is Honorary Foreign Member of the Brazilian Academy of Medicine.

Laurent Beaugerie is Professor of Gastroenterology at Rothschild Hospital, Saint-Antoine University, Paris, France. He studied medicine for six years in Tours University. He then completed his residency at Parisian hospitals, and his fellowship at the Saint-Antoine University, where he has remained ever since. He obtained a PhD in 1996 for his works on the mechanisms and regulation of intestinal transport of passively-absorbed monosaccharides. From 1993 to 1998 he was involved in the work-up of intestinal complications of HIV-infection. His interest then moved to infectious diarrhea and colitis in immunocompetent adults, and to drug-induced colitis. Prof Beaugerie is currently developing a research program on the signals between luminal bacteria and human intestinal epithelium. He is Associate Editor of *Gastroentérologie Clinique et Biologique*, the French indexed journal of Gastroenterology.

Silvio Danese (MD) studied medicine and Surgery at the "Sacro Cuore" University - Policlinico Gemelli in Rome. From 2001 to 2004 he was Research Associate at the "Division of Gastroenterology - Case Western Reserve University, Cleveland, USA" where he dealt with inflammatory bowel diseases under the guidance of Prof. C. Fiocchi. In 2004 he became a specialist in Gastroenterology at the Postgraduate School of the Policlinico Gemelli in Rome. He obtained a PhD studying inflammatory bowel diseases. He coordinated the Centro di Ricerca per le malattie infiammatorie croniche intestinali at Humanitas in Milan (Italy). Since 2007 he is member of the Scientific Committee of ECCO (European Crohn's and Colitis Organization) and he is the current Secretary. Since 2011 is member of the International Organization of inflammatory bowel disease.

Gerhard Rogler is Professor of Gastroenterology and Hepatology at the University of Zurich/Switzerland since 2007. He studied medicine and philosophy at the Universities of Augsburg and Ulm, Germany, finishing his medical studies with the degree of MD in 1993. He habilitated in experimental internal medicine at the faculty of clinical medicine at the University of Regensburg in Germany and became the director of the Gastroenterology and Hepatology division of the Clinic and Policlinic for Internal medicine I at the University of Regensburg in 2002. In January 2011, he became the principal investigator of the Swiss IBD Cohort Study.

ANNEXES

Annex 1. Self-reported amount of funds given to one or more IBD research projects unless stated otherwise by country (for further information, please refer to country-specific data)

Country	€
Argentina	4.900
Australia	48.000
Belgium CCV	6.000
Canada (<i>annual average</i>)	4.500.000
Denmark	66.000
Finland (<i>donated to the IBD Research Foundation</i>)	400
France	1.259.000
Germany	75.000
Ireland	25.000
Israel	47.000
Italy	171.000
The Netherlands	60.000
Sweden	31.309
Switzerland (<i>donated to the IBD Research Foundation</i>)	42.000
United Kingdom	1.169.000
USA (<i>annual</i>)	12.000.000
IBD Research Foundation	29.450

Annex 2. Amounts invested by EFCCA and sister organizations (for further information, please refer to country-specific data)

Association	€
Argentina*	4.900
Australia*	48.000
Canada (annual)	4.500.000
Israel*	47.000
USA (annual)	12.000.000
EFCCA member associations**	2.951.709

* *funds invested in ongoing projects (total invested funds / annually invested funds unavailable)*

** *funds invested in approximately the last 2 years*

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