Letter of the Chairman

2016 has been the first full year of the European Foundation for the Study of Chronic Liver Failure (EF Clif). The Foundation was constituted on April 8th 2015, from July 2015 became fully operational and in the following November, we were able to start working in our new headquarters. During this year, we have made a lot of progress in finalizing some ongoing studies, while designing and initiating new studies, both clinical (through the EASL Chair) and translational (through the Grifols Chair).

In the clinical research area, we have set up the foundation prospective, for the new key observational multicentre study, following the pathway of the CANONIC, called PREDICT Study. An experienced Principal Investigator has been appointed for two years (starting in January 2017), Prof Jonel Trebicka, to lead this study that is expected to include 1,200 patients with decompensated cirrhosis from more than 50 hospitals from all over Europe.

In the translational research area, under the leadership of Prof’s Richard Moreau and Joan Clària, we initiated several translational research studies, focusing on the antioxidative and antiinflammatory effects of albumin and on the profile of metabolites in serum samples from patients with cirrhosis with and without ACLF by untargeted functional metabolomics and lipidomics.

A major event during 2016 was the organization of the Symposium SYSTEMIC INFLAMMATION AND ORGAN FAILURE IN CIRRHOSIS. THE ACUTE-ON-CHRONIC LIVER FAILURE SYNDROME (ACLF), on April 12th in Barcelona, which was the first international meeting of the EF Clif. Over 200 specialists from all over the world, mostly European hepatologists, participated in just before the start of the 51st Annual congress of the European Association for the Study of the Liver (EASL 2016).

We have already established an ambitious and exciting plan for the 2017 and the following year, with both clinical and translational studies, by optimizing the resources that we will receive from our donors.

Vicente Arroyo, MD
Chairman
The EF Clif is intended to improve the quality of life and to increase the survival of patients with liver cirrhosis.

Supporting high quality research and education on Chronic Liver Failure is our way to pursue it.
Our vocation is helping investigators to achieve their projects and getting the best results. To this end, we finance Research and provide technical support, driven by the idea that research is fundamental to obtain effective treatments for cirrhosis.

We aim to build together an organization that inspires and that is able to contribute to improve the life of cirrhotic patients.
Our organization
European Foundation for the Study of Chronic Liver Failure (EF-Clif)
Board of Trustees

VICENTE ARROYO
M.D.
Emeritus Professor of Medicine, University of Barcelona Medical School, Spain.
Chairman of the EASL Clif Consortium.
Recognition Award, European Association for the Study of the Liver.

Main research interest:
Chronic liver failure, ascites acute bacterial infection in cirrhosis, and acute on chronic liver failure

MAURO BERNARDI
M.D.
Professor of Internal Medicine Bologna University, Italy.
Director, Postgraduate School in Internal Medicine Treasurer, European Association for the Study of the Liver.
Vice-chairman of EASL Clif Consortium.
Distinguished Service Award, Italian Association for the Study of the Liver.

Main research fields:
Cirrhosis and related complications, hepatocellular carcinoma, chronic viral hepatitis, liver transplantation clinical aspects and treatment of alcoholism.

JAVIER JORBA
M.D.
President of Grifols Bioscience Industrial Group.
Member of the Grifols Executive Committee.

IGNACIO CALERO
Lawyer
Lawyer at Osborne Clarke.
Graduated in Law from the Autonomous University of Madrid, Master’s Degree in Corporate Legal Advice from the Instituto de Empresa Business School (Madrid, 2003)
He specializes in Company Law, Competition and Industrial Property.
The scientific activities of the network of hospitals organized in the setting of the EASL Chair are performed under the direction of a Chairman and a Vice-Chairman and of an EASL-CLIF Consortium Steering Committee of 15 additional members.

Paolo Angeli / University of Padova  
Vicente Arroyo / EF Clif, Barcelona  
Mauro Bernardi / Policlinico S Orsola-Malpighi - University of Bologna  
Alexander Gerbes / Munich University Hospital  
Pere Ginès / Hospital Clínic, Barcelona  
Thierry Gustot / Erasme University Hospital, Bruxelles  
Rajiv Jalan / Royal Free Hospital, London  
Richard Moreau / Hôpital Beaujon, Clichy  
Frederik Nevens / Gasthuisberg University Hospital, Leuven  
Marco Pavesi / EF Clif, Barcelona  
Thomas Reiberger / Medical University of Vienna  
Francesco Salerno / Policlinico San Donato - University of Milan  
Faouzi Saliba / Hôpital Paul Brousse, Villejuif  
Fin Stolze Larsen / Rigshospitalet -University of Copenhagen  
Jonel Trebicka / Bonn University Hospital  
Julia Wendon / King’s College Hospital, London  
Reiner Wiest / University Clinic of Visceral Surgery and Medicine-Inselspital, Berne
European Clif Network of Translational Research (Clif- ENTR).
Governing Board

The scientific activities of the European Clif network of Translational Research centres, organized in the setting of the Grifols Chair are performed under the direction of a Director, a Deputy Director and a Secretary.

Director
Vicente Arroyo / Ef Clif, Barcelona

Deputy Director
Richard Moreau / Hôpital Beaujon, Clichy

Secretary
Joan Clària / Hospital Clínic, Barcelona
Our staff

**Management**

*Managing Director*
Josep Mª Torner

**Data Management Centre**

*Head*
Marco Pavesi

*Data Manager*
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*Statisticans*
Àlex Amorós, Elisabeth García

**Assistants**

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Montserrat Carreras

*Scientific Assistant*
Yolanda Godoy
The EF Clif is a Foundation that gives support to the EASL CLIF Consortium and European CLIF Network for Translational Research (ENTR-CLIF) to promote clinical and translational research in cirrhosis.

**Facts and figures**

The EF Clif in numbers

- Only in Europe, about **170,000 citizens** die from cirrhosis every year.
- The cost of cirrhosis represents more than **€15.8 billion** per year in health care and a huge loss in economic productivity.
- This has been our contribution to the fight against this silent disease.
- A network of almost **100 hospitals** in Europe.
- Almost **200 investigators** working on EF Clif sponsored projects.
- More than **1,500,000 €/year** in supporting research.
- **2 chairs** with a continuous commitment to education.
- **19 papers** published in 2016.

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Icons 1, 4, 5, 6 in made by Vectors Market from www.flaticon.com; Icons 2, 7, 8 made by Freepik from www.flaticon.com
The scientific production of the EF CLIF Consortium during 2016 consists of 19 articles.


18. NOVEL APPROACHES AND THERAPEUTICS IN ACUTE ON-CHRONIC LIVER FAILURE Jalan R Liver Transpl. 2016; 22 S14-.

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The increase of the projects in which the EF Clif is getting involved has given the opportunity to include new hospitals during 2016. (*) New centres 2016

<table>
<thead>
<tr>
<th></th>
<th>Country</th>
<th>Hospital Name</th>
<th>Contact Person</th>
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</thead>
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<td>Markus Peck Radosavljevic</td>
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<td>Erasme Hospital. Université Libre de Bruxelles</td>
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<td>Jan Sperl</td>
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<td>Aleksander Krag</td>
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<td>CHU Toulouse</td>
<td>Jean-Marie Peron, Christophe Bureau</td>
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<td>Hôpital Jean Verdier</td>
<td>Roland Amathieu</td>
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<td>Thomas von Hahn, Michael Manns</td>
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<td>Ukraine</td>
<td>Ivano-Frankivsk National Medical University</td>
<td>Virstyk Nataliya</td>
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Activities

12 April 2016

1st Meeting of the EF Clif in Barcelona.

The symposium was the first major scientific event organized by the Foundation, since its establishment in mid-2015, and has served as a public presentation of its activities and projects to the international scientific community in the field of Hepatology. Over two hundred specialists from all over the world, mostly European hepatologists, attended the lectures on the Acute-on-Chronic Liver Failure (ACLF) Syndrome.

27 May 2016

Call for the PREDICT study.

This is the first study which starts under the sponsorship of the EF Clif Foundation and will represent a further advance in the knowledge of ACLF.

19 September 2016

Investigators of the EF Clif hold a workshop in the XXIV Congress of the Latin American Association for the Study of Liver in Santiago de Chile.

The presentations focused on new developments on the characterization, mechanisms and treatments of the ACLF.

12 December 2016

The Cellex Foundation contributes with a donation for the PREDICT Study.

This contribution will allow Dr Jonel Trebicka to join the EF Clif as a Visiting Professor in 2017 and 2018 to lead the future flagship study of the EF Clif.
## New studies calendar

### STUDIES ON ACLF

<table>
<thead>
<tr>
<th>Year</th>
<th>Carbalive</th>
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<th>Promethera</th>
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<tbody>
<tr>
<td>2017</td>
<td>phase 2 -- Carbalive SAFETY -- 48 patients</td>
<td>phase 1B -- Liverhope SAFETY -- 45 patients</td>
<td>phase 2A Study 12 patients</td>
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<tr>
<td>2018</td>
<td>Prevent-ACLF -- 120 patients</td>
<td>phase 2B -- 40 patients</td>
<td>phase 2B -- 40 patients</td>
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<tr>
<td>2019</td>
<td></td>
<td>phase 3 -- 240 patients</td>
<td>phase 3 -- 380 patients</td>
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<td>2020</td>
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### STUDIES ON DECOMPESATED CIRRHOSIS

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<tr>
<th>Year</th>
<th>Aliver</th>
<th>Apache</th>
<th>Predict</th>
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<tr>
<td>2017</td>
<td>Dialive-SAFETY + 2a -- 24 patients</td>
<td>phase 3 -- Apache STUDY -- 380 patients</td>
<td>observational -- 1,200 patients</td>
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<td>2018</td>
<td>Dialive-EFFICACY -- phase 3 -- 126 patients</td>
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<td>2019</td>
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<th>Promethera</th>
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<td>2020</td>
<td>Aliver -- 410 patients</td>
<td>Apache -- Apache STUDY -- 380 patients</td>
<td>phase 3 -- 400 patients</td>
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<td>Aliver -- Apache STUDY -- 380 patients</td>
<td>Apache -- Apache STUDY -- 380 patients</td>
<td>phase 3 -- 400 patients</td>
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This study was aimed to assess the diagnosis criteria, prevalence, clinical features, prognosis and mechanisms of Acute on Chronic Liver Failure in cirrhosis.

Principal Investigator: Richard Moreau (Hôpital Beaujon, Clichy, France).

Data were collected from 1343 hospitalized patients with cirrhosis and acute decompensation from 29 liver units in 8 European countries.

Organ failure and mortality data were used to define ACLF grades, assess mortality, and identify differences between ACLF an acute decompensation.

Diagnostic criteria for ACLF were established based on analysis of patients with organ failure (defined by the CLIF-SOFA score) and high 28-day mortality rate (>15%).

- The results of this prospective observational study were published in 2013 and they have allowed to identify the ACLF as a new clinical entity.
- The description of the natural history of ACLF has led to establish diagnostic criteria and open new perspectives in the study of chronic liver diseases.
- Thirteen ancillary studies have been published, focusing on different aspects of ACLF.
- Eleven additional core and ancillary studies are currently performed, using the database and biological samples from the Canonic Study, which will give a total number of 25 Canonic derived original articles.
Study focused on the effects of albumin administration in the prevention of hepato-renal syndrome and death in patients with cirrhosis, bacterial infections other than spontaneous bacterial peritonitis and high risk of hospital mortality.

Principal Investigator: Javier Fernández (Hospital Clinic, Barcelona, Spain).

This is a phase IV, open-label, multicenter European RCT. Patients with advanced cirrhosis and frequent non-SBP infections were randomized to receive antibiotics or antibiotics plus albumin. The primary goal of the study was to evaluate if albumin administration improves in-hospital survival in this target population. The sample size initially calculated was 512 patients (256 per treatment arm).

From April 2014 to December 2016, 776 patients were screened and 136 patients (17.5%) were included in the study. Hospital Clinic of Barcelona (n=37), University of Padova (n=15), Sapienza University in Rome (n=10), University Hospital in Bonn (n=8), and Erasme Hospital, Brussels and San Giovanni Battista Hospital, Turin (n=8, each) were the centers with the highest inclusion rates. The study has been prematurely interrupted in December 31st 2016 due to the low recruitment rate and the expiration of the study drug. All sites will be closed by the end of April 2017. The final study report will be published no later than 12 months after the finalization of the study.
Ongoing studies

SCotCH
(June 2015-2019)

Study designed to assess the clinical relevance, efficacy and safety in the treatment of hypotensive Cirrhotic Patients with suspicion of sepsis by using low dose cortisone (Supplemental Corticosteroids in Cirrhotic Hypotensive Patients with Suspicion of Sepsis. The SCOTCH – trial).

Principal Investigators: Alexander Willmer (Gasthuisberg University Hospital, Leuven, Belgium) and Javier Fernández (Hospital Clinic, Barcelona, Spain).

This is a phase IV, double-blind, randomized, placebo-controlled, multicenter trial, in cirrhotic patients with septic shock aimed to assess if stress dose steroids treatment improves 28-day mortality in cirrhotic patients with septic shock.

Eight centers are currently active to recruit: Belgium (n=2), Spain (n=4) and Italy and Czech Republic (n=1, each). Regulatory issues are still pending in Germany (n=1), Austria (n=1) and United Kingdom (n=2). Until now, 136 patients have been screened and 31 patients (23%) have been included in the study. We estimate that the inclusion will finish at the end of 2019.
New projects

Predicting Acute-on-Chronic Liver Failure in Cirrhosis (PREDICT)
(January 2017-2018)

The PREDICT Study is designed to prospectively observe patients with cirrhosis and Acute Decompensation (AD) at risk of developing ACLF within three months and to discover new clinical and laboratory predictors of ACLF development, patho-physiological mechanism (using prospective ancillary studies) and potential treatment to prevent ACLF.

Principal Investigator: Jonel Trebicka (Bonn University Hospital, Germany).

The aim of this study is to assess prospectively the critical period prior to the development of ACLF (1), to uncover mechanistic and pathophysiological processes associated with the development and clinical course of ACLF (2) and to identify the precipitating events of ACLF (3).

Specific goals of the study are:

• To identify early clinical predictors, biomarkers, mechanisms and precipitating events during the critical period prior to and involved in the development and clinical course of ACLF (with special emphasis to medical trajectory and drug history) in patients admitted/referred to study centre with acute decompensation of cirrhosis (ascites, GI-hemorrhage, overt encephalopathy, new onset of non-obstructive jaundice and/or bacterial infections) and the chronological relationship of the events with occurrence and dynamics of ACLF development.

• To develop a score predicting ACLF development (CLIF-PREDICT score) and assess 28-day, 90-day, 6-month and 1-year all-cause mortality in cirrhotic patients with acute AD, but without ACLF.

• To serve as a core (hub) study for prospective ancillary studies regarding diagnosis, prognosis and pathogenesis of AD and ACLF.

The population of patients would include ca. 1,200 cirrhotic patients over a twelvemonths period. These patients will be admitted/referred to the study centre because of acute decompensation of cirrhosis (ascites, overt encephalopathy, GI-hemorrhage, new onset of non-obstructive jaundice and/or bacterial infections), without ACLF (as defined according to the CANONIC study) at hospitalization.

After the enrolment visit, the patients will be stratified into two groups:

- Group 1: patients with high risk of ACLF development (CLIF-C AD score ≥ 60).
- Group 2: patients with low risk of ACLF (CLIF-C AD score <60).

The whole cohort will be followed for 3 months, while Group 1 will be followed more closely. Development of ACLF is an end-point and in this case a final visit 7-10 days after ACLF development is planned. Data on liver transplantation, mortality and causes of mortality 3 months, 6 months and 12 months will be collected in the whole cohort.

Prospective collection of biological material and performance of ancillary studies investigating predictors for development and pathogenesis of ACLF.
ALBUMIN AS A DRUG: ANTIOXIDATIVE, ANTI-INFLAMMATORY AND TISSUE PROTECTIVE ACTIONS OF HUMAN ALBUMIN.

Principal Investigator: Joan Clària (Hospital Clínic, Barcelona, Spain).

(June 2016- December 2017)

Albumin plays a modulatory role in systemic inflammation and oxidative stress through its ability to bind and sequester soluble mediators. The main goal of this project is to investigate the mechanisms of action of the anti-inflammatory and anti-oxidative properties of albumin in two ex vivo models. The first model is in leukocytes, which is an appropriate experimental tool for studying the systemic effects of albumin, and the second model is in precision-cut liver slices, which is an appropriate experimental tool for studying the effects of albumin on tissues.

ALBUMIN AS A DRUG: EFFECTS OF ALBUMIN ON GENE EXPRESSION AND SIGNALING IN LEUKOCYTES ISOLATED FROM PATIENTS WITH ACLF.

Principal Investigator: Richard Moreau (Hôpital Beaujon, Clichy, France).

(June 2016-December 2017)

The clinical relevance of albumin is supported by studies showing improved survival in cirrhotic patients receiving albumin infusions. Mechanisms accounting for these beneficial actions point into the direction that albumin modulates a vast network of gene implicated in the control of systemic oxidative stress and inflammation. The main goal of this project is to shed new light on the mechanisms underlying the biological properties of albumin by assessing the effects of albumin on gene expression in leukocytes isolated from patients with decompensated cirrhosis and ACLF.
COMPREHENSIVE UN-TARGETTED METABOLOMIC AND LIPIDOMIC PROFILING OF ORGAN DYSFUNCTION IN PATIENTS WITH DECOMPENSATED CIRRHOSIS AND ACLF.

Principal Investigators: Christophe Junot (CEA, Saclay, France), Richard Moreau (Hôpital Beaujon, Clichy, France) and Joan Clària (Hospital Clinic, Barcelona, Spain). (June 2016-December 2017)

The main goal of this project is to characterize the profile of metabolites in serum samples from patients with cirrhosis by un-targeted functional metabolomics and lipidomics using liquid chromatography-tandem mass spectrometry (LC-MS/MS). The predicted outcomes include the identification of a metabolic signature of ACLF patients, to discriminate patient groups accordingly to etiology (alcohol, virus) or presence of infections and the identification of organ-specific metabolic signatures in these patients.
External projects

New studies
During 2016, the EF Clif has participated in the design and preparation of the following studies.

The APACHE TRIAL (Promoter: Grifols)
The APACHE TRIAL is aimed to study the effects of plasma exchange on short-term survival in patients with ACLF and high risk of mortality.
Principal Investigators: Javier Fernández (Hospital Clinic, Barcelona, Spain) and Fin Stolze Larsen (Rigshospitalet, Copenhagen, Denmark).
(2017-2020)
This is a phase III, multicentre, randomized, open-label trial in 380 patients with ACLF-1b, ACLF grade 2 or ACLF-3a aimed to determine whether plasma exchange with 5% albumin (from 4 to 9 plasma exchange sessions) improves 90-day survival in comparison with standard medical therapy.
The study will be performed in 39 centres, 28 from Europe and 11 from North America. The submission process will start within the second quarter of 2017. The estimated duration of the study is 36 months.

The ALADDIN STUDY (Promoter: Grifols)
The ALADDIN STUDY is a complementary study to the APACHE, aimed to assess the mechanisms of systemic inflammation and ACLF in patients with and without ACLF.
Principal Investigators: Joan Clària (Hospital Clinic, Barcelona, Spain), Richard Moreau (Hôpital Beaujon, Clichy, France) and Ramon Bataller (University of Pittsburgh, USA).
(2017-2020)
The ALADDIN Study is a translational research project coupled to the APACHE Study. It will be performed in blood samples and monocytes and polymorphonuclear leukocytes obtained from patients with ACLF included in the APACHE Study and from an additional group of 150 patients with acute decompensated cirrhosis but without ACLF that will serve as control group. The ALADDIN Study will be performed at the European Centres participating in the APACHE Study.
The ALADDIN Study also includes three ancillary investigations aimed at exploring several specific mechanisms of systemic inflammation, the role of coagulopathy as a potential mechanism of organ failure, and albumin function in decompensated cirrhosis with and without ACLF. This later project will assess the potential role of albumin dysfunction in ACLF, the effect of Plasma Exchange (PE) on albumin function and the potential value of albumin function as a marker of response to PE.
The PRECIOSA STUDY (Promoter: Grifols)

The PRECIOSA STUDY is focused on exploring the albumin dosage for long-term treatment in patients with decompensated cirrhosis.

Principal Investigator: Paolo Caraceni (Policlinico S Orsola-Malpighi, Bologna, Italy).

(2017-2020)

This is a phase IV, European, multicentre, randomized open-label trial in 410 patients with decompensated liver cirrhosis with ascites aimed to determine whether longterm albumin administration (1.5 g/kg body weight every 10 days for 12 months) improves 1-year transplant-free survival in comparison with standard medical therapy.

The study will be performed in about 40 European centres. The submission process will start within the second quarter of 2017. The estimated duration of the study is 36 months

ALIVER (European Union Horizon 2020 Program)

This is a multi-centre, randomised controlled study, to evaluate the safety and performance of The DIALIVE Liver Dialysis Device (LDD) in patients with Acute on Chronic Liver Failure (ACLF) versus standard of care (SOC).

Principal Investigator: Rajiv Jalan (Royal Free Hospital, London, UK).

(2017-2018)

After successful completion of the DIALIVE Safety & Performance study, a second study is planned to assess the efficacy of the DIALIVE to treat ACLF patients. The study hypothesis of the EFFICACY study will be defined based on the outcome of the SAFETY & PERFORMANCE trial.
The aim of the CARBALIVE project is to further develop and validate a novel nanoporous carbon adsorbent (Yaq-001) capable of removing bacterial endotoxin and other metabolic toxins relevant to the progression of bacterial translocation and endotoxemia in patients with cirrhosis and NAFLD.

*Principal Investigator: Rajiv Jalan (Royal Free Hospital, London, UK) (2017-2018)*

The outcome will be a new therapeutic strategy for the treatment of cirrhosis and NAFLD patients ready for further development and clinical application.

**LIVERHOPE (European Union Horizon 2020 Program)**

The objective of LIVERHOPE project is to evaluate a novel therapeutic strategy for patients with cirrhosis based on a combination of rifaximin and simvastatin, targeting the main pathophysiological mechanisms of disease progression, namely the impairment in the gut-liver axis and the persistent hepatic and systemic inflammatory response.

*Principal Investigator: Pere Ginès (Hospital Clínic, Barcelona, Spain) (2017-2018)*

This dual therapeutic approach is supported by preclinical data showing very promising results.

**PROMETHERA**

Promethera Biosciences is a start-up pharmaceutical company that develops innovative therapies for the treatment of liver diseases like HepaStem (Heterologous Human Adult Liver-derived Progenitor Cells).

*Principal Investigator: Frederik Nevens (UZ Gasthuisberg, Leuven, Belgium) (2016-2017)*

The EF Clif has collaborated in the running safety study, in its design and statistical planning, and also in the discussions of a future follow-up efficacy study.
Future projects

In late 2016, The EF Clif has been evaluating new projects to increase the knowledge and understanding of cirrhosis. As a result, some new studies will be designed during 2017.

“Omics” characterization of the ACLF syndrome.

Principal Investigators: Pierre Emmanuel Rautou (Hôpital Beaujon, Clichy, France) and Wim Laleman (Gasthuisberg University Hospital, Leuven, Belgium).

Up to now, the ACLF syndrome has been characterized in patients from the Canonic Study by clinical and standard laboratory data and inflammation and circulatory biomarkers (cytokines, renin and oxidized albumin). In the next two years, the characterization of the syndrome will be completed by genomic, proteomic, lipidomic and metabolomic studies and systemic biological analysis.

Microbiota in ACLF

Principal Investigator: Jonel Trebicka (Bonn University Hospital, Germany).

The PREDICT Study is designed to prospectively observe patients with an Acute Decompensation (AD) at risk of developing ACLF within three months and to discover clinical, laboratory and patho-physiological (using prospective ancillary studies) predictors and mechanisms involved in the development and clinical course of ACLF. Especially gut microbiota has been in the focus of modifying and influencing health and disease in the last years. The overall objective of MICROB-PREDICT is the understanding, prediction and treatment of acute on chronic liver failure. The specific aims are: (A) To define specific gut microbiome and associated host genome, transcriptome and metabolome risk signatures that predict the development of AD and progression to ACLF. (B) From these signatures to develop novel omics-based biomarkers for early diagnosis, prognosis and treatment monitoring. (C) Use the identified risk signatures and biomarkers to evaluate interventions based on microbiome modulation to prevent AD and ACLF development.
Prospective observational study in Acute Alcoholic Hepatitis in Europe

Principal Investigators: Christophe Moreno (Erasme University Hospital, Bruxelles, Belgium) and Ramón Bataller (University of Pittsburgh, USA).

Acute Alcoholic Hepatitis (ASH) is a major cause of ACLF. This association, however, is poorly characterized. Following the end of the PREDICT Study, the EF Clif has decided to explore Acute Alcoholic hepatitis with a project reproducing the methodology used in the Canonic and in the PREDICT STUDY. Samples will be obtained for later translational studies.

The Chinese Canonic Study

Principal Investigator: Hai Li (Ren Ji Hospital, Shanghai, China).

Chinese CLIF Consortium has finished a Chinese Canonic observational Study in 14 University Hospitals from East China. Clinical data and biological samples have been obtained from 1458 patients with cirrhosis. The European CLIF Consortium will participate in the data analysis and exploitation of the results.

The Latin American Canonic Study

Principal Investigator: Flair Carrilho (University of São Paolo, Brasil).

The Latin American CLIF Consortium in collaboration with the EASL-Clif Consortium is planning to develop the Latin American Canonic Study in 1000 patients admitted to a hospital for an acute decompensation in cirrhosis, in University hospitals from Brazil, Argentina, Chile and Mexico. EF Clif supports the project with the design of the e CRF and the economic support for the collection of biological samples and biobanking.