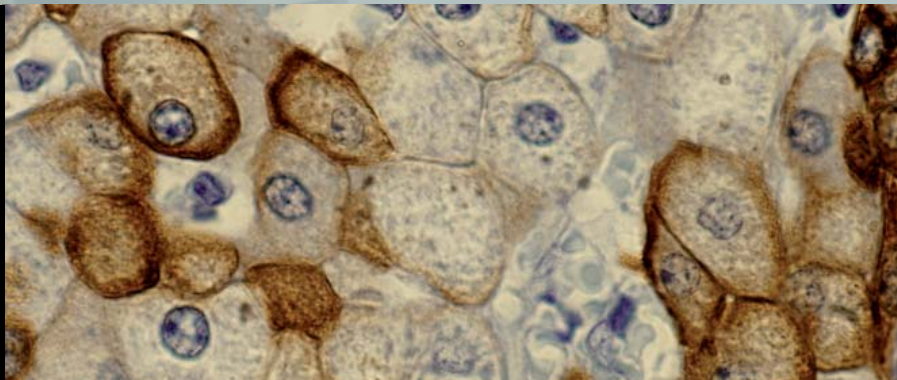


**IDIBAPS**

Institut  
D'Investigacions  
Biomèdiques  
August Pi i Sunyer



# HEPTROMIC

Genomic predictors  
and oncogenic drivers  
in hepatocellular  
carcinoma

HEPTROMIC is a project in the 'Health' Theme of the Specific Programme 'Cooperation' of the European Commission's Seventh Framework Programme



» *Liver cancer is a growing health issue in Western populations. In some countries, death rates increased by up to 50% during the 1990-2005 period.*



» *HEPTROMIC's core team comprises leading European researchers in the basic, translational and clinical fields of liver cancer. Our aim is to lay down a foundation for a sustainable network of expertise based on complex, system level, translational research approaches to liver cancer and closely related disease areas. We expect to open up revolutionary new research horizons in liver cancer over the next decade.*

HEPTROMIC is a 3-year translational research project which aims to solve core problems in the management of hepatocellular carcinoma (HCC), the third most common cause of cancer-related death worldwide. By defining biomarkers for identification of HCC patients with poor-prognosis and novel genetic or epigenetic drivers, HEPTROMIC will achieve the breakthroughs that are critical for developing more personalised therapeutic approaches. Findings obtained from human tissue samples by applying state-of-the-art technology will be confirmed in sophisticated experimental models and translated into novel biomarkers and targets for high-impact clinical use.

## The main ideas supporting HEPTROMIC

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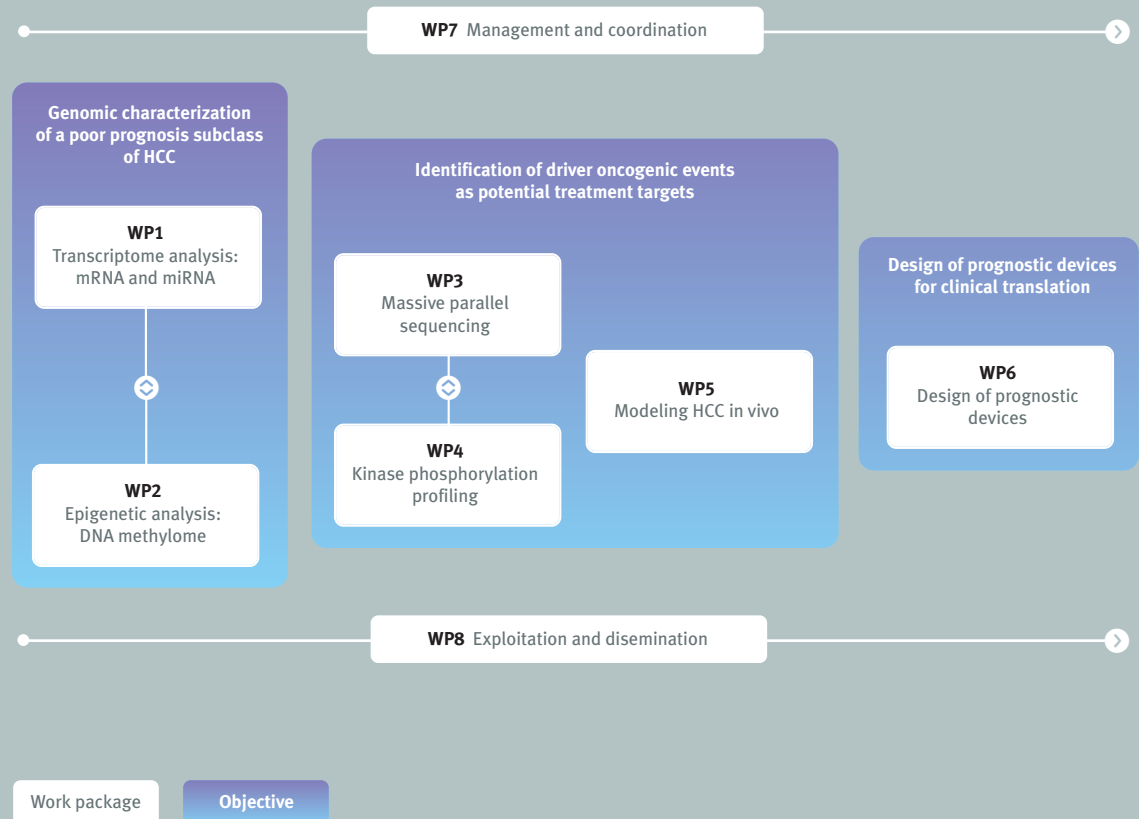
- **The epidemiological impact and lethality of liver cancer.** Hepatocellular carcinoma is a major health problem due to its dismal survival rates. The incidence of the disease is increasing with more than 700,000 new cases per year worldwide, of which 50,000 occur in Europe. The main risk factors are chronic hepatitis (B and C) and alcohol abuse leading to cirrhosis, a true pre-neoplastic condition. One third of cirrhotic patients will develop liver cancer during their lifetime and most of them will die as a result of this complication.
- **The importance of understanding the molecular biology of this cancer.** Robust scientific evidence indicates that HCC is resistant to conventional chemotherapy and, thus, there is a clear need for novel primary systemic therapies for this difficult-to-treat neoplasm. Since molecular therapies could be pivotal in this setting, it is vital that we improve our understanding of the molecular determinants for HCC development and progression.
- **The technological revolution in oncological sciences has the potential to produce a step-change advance in the treatment of HCC.** Novel high-throughput technologies, including the potential to unravel the complete nucleotide sequence of a cancer genome, have changed the way scientists approach human cancer and have only recently made a project like HEPTROMIC possible.
- **Preliminary steps in personalised management of HCC.** Two major advancements could critically improve the outcome of patients with liver cancer: firstly, the identification of crucial molecular subclasses with different prognostic implications, and secondly, the identification of key genetic or epigenetic drivers of specific subclasses which will enable development of more personalised treatment algorithms.

# The HEPTROMIC objectives

- **Genomic characterization of a poor prognosis subclass of hepatocellular carcinoma.** To define the molecular subclass of poor prognosis in patients with early HCC through integrated analysis of mRNA, miRNA and methylome profiles. This will enable clinicians to significantly improve prognostic prediction and to optimise candidate selection for treatments.
- **Identification of driver oncogenic events as potential treatment targets.** To apply state-of-the-art genomic technologies including massive sequencing, kinase profiling and highly sophisticated animal models for pinpointing dominant oncogenic alterations. Ultimately, this will facilitate the development of more effective anti-cancer drugs.
- **Design of prognostic devices for clinical translation.** To achieve effective and efficient clinical translation through the design of prognostic devices to significantly improve prognosis assessment and therapeutic decision-making.

To achieve these objectives, the HEPTROMIC consortium has designed a workplan comprised of 8 work packages.

Diagram depicting objectives and work packages for HEPTROMIC



## Strategic impact

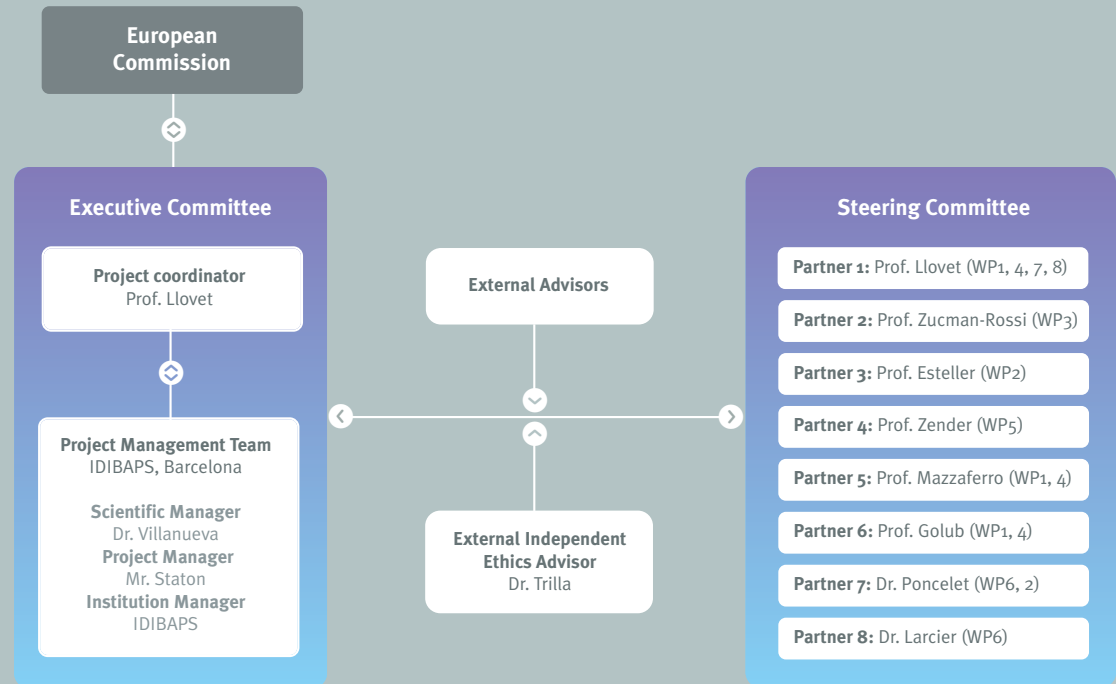
HEPTROMIC is a very bold and ambitious response to the core challenges in a new era of modern oncology. Our aim is to improve health by identifying new genomic predictors and oncogenic drivers of liver cancer and to incorporate these research findings in innovative predictive tools that will contribute to better allocation of resources and refinement of therapeutic strategies. In addition, with two small-medium enterprises in the team, the project will lead to the production of new, knowledge-intensive products, creating sustainable employment and contributing to improving the world competitiveness of the European medical devices sector. We will also help to throw new light on simple processes to link up all the stakeholders in the ‘triple helix’ of researchers and clinicians, business and regulators in the field of liver cancer which we expect will be transferrable to other medical fields.

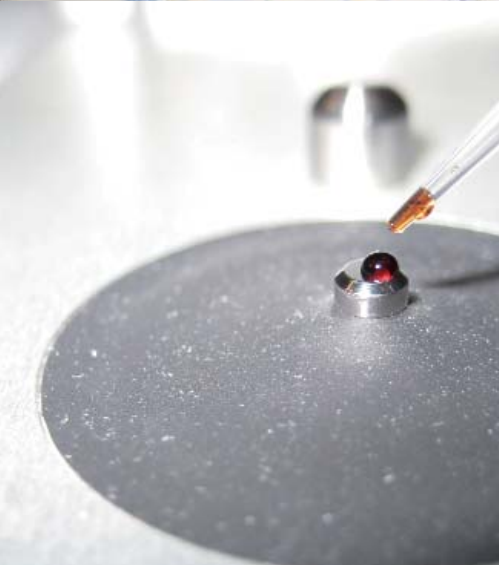
» *HEPTROMIC will optimise decision-making for liver cancer patients by identifying genomic prognostic determinants and oncogenic drivers.*

## The consortium

To achieve its project objectives and help bring about a ‘sea change’ in the treatment of liver cancer, HEPTROMIC has assembled a unique and balanced team with expertise in clinical, translational and basic research. It brings together experts from five European countries and one partner from the USA.

### Flow chart of HEPTROMIC management structure





# Partners

## Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)

Barcelona, Catalonia, Spain

IDIBAPS is a consortium formed by the Catalan Government, the University of Barcelona, the Hospital Clínic of Barcelona and the IIBB-CSIC. It combines high-quality clinical research with high-level translational and basic research to achieve a more effective transfer of scientific advances in the prevention and treatment of the most common health problems.



### Prof. Josep Maria Llovet i Bayer Project coordinator

Josep Maria Llovet, MD is Professor of Research-ICREA in the BCLC Group, Liver Unit, IDIBAPS-Hospital Clinic of Barcelona, Director of the HCC Research Program and Professor of Medicine at the Mount Sinai School of Medicine, New York. Prof. Llovet's research track record includes seminal contributions in the clinical management of hepatocellular carcinoma and the generation of genomic prognostic predictors for this disease.

#### Staff members

Augusto Villanueva, MD.  
Scientific Manager  
Jordi Bruix, MD  
Josep Fuster, MD  
Manel Solé, MD

Victoria Tovar, PhD  
Daniela Sia, PhD  
Clara Alsinet, PhD student  
Helena Cornella, PhD student  
Judit Peix, MSc, Lab manager

## Institut National de la Santé et de la Recherche Médicale (INSERM)

Paris, France

INSERM is a public scientific and technological organization that stresses and nourishes the continuum between the different fields of research in fundamental biology, cognitive and applied medicine and public health to improve the understanding of human diseases, and ensure that patients, the medical community and partners benefit rapidly from the latest research findings.



### Prof. Jessica Zucman-Rossi Partner leader

Jessica Zucman-Rossi, MD, PhD is Professor of Medicine, Oncology, University Paris Descartes, Hôpital Européen Georges Pompidou. She is head of the INSERM unit Functional Genomics of Solid Tumors in Paris. For the last 10 years, Prof Zucman's team has worked to identify new carcinogenetic pathways altered in HCC and benign hepatocellular tumors using a strategy based on the study of large series of human tumors.

#### Staff members

Giuliana Amaddeo, MD  
Sandrine Imbeaud, PhD  
Cécile Billard, PhD  
Gabrielle Couchy, technician  
Karine Poussin, technician  
Ichrafe Ben Maad, technician

## Fundació Privada Institut d'Investigació Biomèdica de Bellvitge (IDIBELL)

Barcelona, Catalonia, Spain

IDIBELL promotes its main research areas (cancer, neurosciences, infectious pathology and transplantation) to establish interrelations among basic and clinical research and healthcare, to stimulate collaborations between IDIBELL researchers and external groups and to produce and disseminate major scientific advances. The Cancer Epigenetics and Biology Program (PEBC ([www.pebc.cat](http://www.pebc.cat))) is IDIBELL's latest research strand, a centre of excellence in the field of cancer epigenetics at Hospital Duran i Reynals.



**Prof. Manel Esteller Badosa**  
Partner leader

Manel Esteller, MD, PhD is a world-renowned leader in the field of epigenetics and epigenomics. Dr. Esteller is the Director of the PEBC, having developed multiple approaches to detect changes in the epigenome of healthy individuals and different diseases, both in humans and animal models.

### Staff members

Anna Portela, PhD  
Fernando Setién, technician, PhD

## Helmholtz Zentrum Für Infektionsforschung (HZI)

Braunschweig, Germany

The HZI has one of the biggest and most modern animal research facilities in Europe. Genome-wide collections (mouse and humans) of microRNA based shRNA libraries were established at the HZI by Prof. Zender's group and will be available to the consortium.



**Prof. Lars Zender**  
Partner leader

Lars Zender, MD, is Professor of Experimental Gastrointestinal Oncology at Hannover Medical School, Germany and head of the Research group Chronic Infection and Cancer, which is located at the HZI in Braunschweig, and at Hannover Medical School. Prof. Zender has very high level expertise in the development of sophisticated animal models in liver cancer.

### Staff members

Tae-Won Kang, PhD  
Anja Kobold, technician  
Anke Samuels, technician

## Fondazione IRCCS Istituto Nazionale dei Tumori (INT)

Milan, Italy

Fondazione IRCCS INT is a public health institute with experimental and clinical units whose activities range from epidemiology (both descriptive and molecular) to rehabilitation and palliative care through innovative prevention, diagnosis and treatment.



**Prof. Vincenzo Mazzaferro**  
Partner leader

Vincenzo Mazzaferro, MD is currently the Director of the Gastrointestinal and Hepato-Pancreatic Surgery and Liver Transplantation Unit of the Istituto Nazionale dei Tumori of Milan and the Vice-Scientific Director for clinical research in the same centre. Prof. Mazzaferro has completed milestone studies for the clinical management of HCC, especially in the setting of liver transplantation.

### Staff members

Carlo Battiston, MD  
Carlo Sposito, MD

## Broad Institute, Harvard

Boston, USA

The Broad Institute is a non-profit research institute whose main focuses include cancer, medical and population genetics, genome biology, psychiatric disease, chemical biology, and computational biology and bioinformatics among others. The Broad Institute's Cancer Program brings together a scientific community focused on understanding the basic molecular mechanisms of cancer and applying this knowledge to transform the practice of cancer medicine.



### Prof. Todd Golub Partner leader

Todd Golub, MD, PhD, is a founding member of the Broad Institute, director of its Cancer Program, Charles A. Dana Investigator in Human Cancer Genetics at the Dana-Farber Cancer Institute, an investigator at Howard Hughes Medical Institute, and professor of pediatrics at Harvard Medical School. Prof. Golub is a worldwide pioneer in array-based gene expression studies and their application for cancer classification and prognosis prediction.

#### Staff member

Yujin Hoshida, MD, PhD  
Jinyan Du, PhD

## Diagenode

Liège, Belgium

Diagenode is an international life sciences company developing and commercialising innovative instruments and reagent systems for life science research and molecular diagnostics.

#### Staff members

Dr. Dominique Poncelet, Partner leader  
Didier Allaer (CEO), founder and specialist in instruments and engineering  
Matarese Filomena, PhD  
Jan Hendrickx, PhD

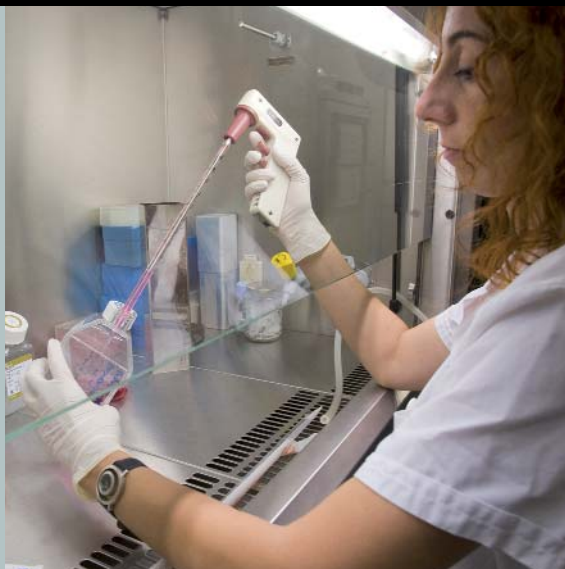
## TcLand Expression SA

Nantes, France

TcLand Expression is a molecular diagnostic company focused on the development and commercialisation of tests aimed at monitoring patients with immunological conditions.

#### Staff members

Dr. Patrick Larcier, Partner leader  
Marina Guillet, PhD, CSO, co-founder and specialist in the analysis of T Cell regulation and transcriptomics  
Alessandra Cervino, VP Biostatistics & Bioinformatics  
Rodolphe Cerval, VP Corporate Business Development



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For further information  
[www.heptromic.eu](http://www.heptromic.eu)

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