This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under Marie-Sklodowska Curie grant agreement No 101034285

UNIVERSITY: Center for Applied Medical Research (CIMA University of Navarre, UNAV)

WIT PROGRAMME´S RESEARCH LINE NAME: Hepatology

DOCTORAL PROGRAMME: Doctoral program of applied medicine and biomedicine https://en.unav.edu/web/doctoral-program-of-applied-medicine-and-biomedicine

COMPLETE DESCRIPTION OF THE LINE

Our overarching area of research deals with the identification of novel mechanisms in the development of liver tumors, including metabolic impairment and fatty liver disease, cellular alterations related to chronic liver damage and regeneration, and tissue fibrogenesis. The line of research for the WIT Programme focuses on epigenetic and post-transcriptional processes that modulate gene expression and contribute to liver injury and carcinogenesis. Based on our expertise and previous results, we will build on the role of the splice regulator SLU7 and the histone methyltransferase G9a, their mutual crosstalk and interaction with other epigenetic regulators. We will implement state-of-the art genetic and pharmacological tools, as well as cellular and in vivo experimental models, to unravel fundamental oncogenic mechanisms and potential new therapeutic targets.

RESEARCH GROUP NAME: Hepatic carcinogenesis.

COORDINATOR:

- Avila, Matias A.
- Department: CIMA. Hepatology

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- Telephone number: 34-649186325
- https://cima.cun.es/en/research/research-programs/research-programs-hepatology

MEMBERS OF THE RESEARCH LINE:

Prof. Carmen Berasain, co-supervisor of the WIT Programme awardee.

Dr. Maite G. Fernández-Barrena. Researcher.

Dr. María Arechederra. Researcher.

Dr. Josepmaria Argemí. Clinician-Scientist.

ANOTHER RESEARCH LINES OF THE GROUP:

- Endoplasmic reticulum stress and immunity in liver cancer. In this line we are developing tools to make liver cancer visible to the immune system, even in the two-thirds of patients who do not respond to treatment. To characterize the antitumor response, we have generated tumors that simulate the mutations that appear in human liver cancer. We use high resolution genomic techniques such as RNA sequencing, single cell sequencing, ChIP-seq and ATAC-Seq and we have our own tumor models generated with CRISPR-Cas technology. We are able to test in these clinically relevant systems those targets that give hope of overcoming resistance to tumor death mediated by the immune system.

- Metabolism and new therapies in porphyrias. This line is focused on acute intermittent porphyria (AIP), an orphan genetic disease of hepatic origin. There is currently no specific treatment for this disease, and patients may even require a liver and/or kidney transplant.
AIP patients may experience severe neurological damage and eventually develop liver cancer. The objective of this line is to elucidate the mechanisms of liver injury associated with the disease, and to develop innovative strategies based on gene therapy and cutting-edge biotechnological products.

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- Liquid biopsy in hepatobiliary diseases. Currently, the methods of detection and diagnosis of these diseases have limited sensitivity and specificity, and the majority of patients are diagnosed in an advanced stage without effective therapeutic strategies. Therefore, it is a priority to develop robust and simple methods for the screening and early detection of hepatic (hepatocellular carcinoma, HCC) and biliary (cholangiocarcinoma, CCA) tumors. Liquid biopsy is a non-invasive tool that allows the detection of material from the tumor in body fluids. In this line we aim to develop two liquid biopsy strategies: (1) a strategy for differential diagnosis and early detection of HCCs based on the identification of differential methylation patterns in circulating tumor DNA in serum (Met-ctDNA); (2) a strategy to diagnose the presence of CCAs in patients with biliary strictures, by detecting mutations in the DNA obtained from bile.

- Entities involved in research lines and contact person:

✓ Academic entities:

- University of Pittsburgh. PA, USA. Prof. Ramón Bataller.
- University of Newcastle, UK. Prof. Jelena Mann.
- Friedrich-Alexander University, Erlangen-Nürnberg, Germany. Prof. Claus Hellerbrand.
- Institut Cochin U1016 CNRS 8104 Université Paris Descartes, Paris, France. Prof. Catherine Postic.
- Centre de Recherche des Cordeliers, Inserm UMR1138 Université de Paris, France. Prof. Chantal Desdouets.

✓ Industrial entities:

- CIMA LAB. Diagnostics. Pamplona, Spain. Dr. Gorka Alkorta-Aranburu.

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- Kintsugi Therapeutics. Barcelona, Spain. Dr. Carmen Herrero.
- Moderna Therapeutics. Cambridge, MA, USA. Dr. Joshua Schultz.
- Epizyme Inc. Cambridge, MA, USA. Dr. Veronica Guibaja.

- Group review

Our group is internationally recognised in the field of experimental and translational hepatology. With more than 20 years of experience, we constitute the core of the Hepatology Program of CIMA-University of Navarra. We are part of the Cancer Center of the University of Navarra (CCUN). Profs. Matias Avila and Carmen Berasain are Full Professors of Biochemistry and Director and Sub-Director, respectively, of the Hepatology Program; Dr. Josepmaria Argemí is a Clinician-Scientist; and Drs. Maria Arechederra and Maite G Fernanez-Barrena are Junior Scientists. Currently there are 6 PhD Students in the group, 5 Research Associates (PhD level) and 5 Technicians. Drs. Avila and Berasain have previously supervised more than 15 PhD students and 12 post-docs, including Marie Curie fellows. Our research is mainly focused on the cellular and molecular mechanisms of the liver response to chronic damage and tumor development: regeneration, fibrogenesis, hepatobiliary carcinogenesis and biomarker discovery. Representative publications include PMIDs: 23292666, 28119353, 28082079, 30411380, 25066374, 24865429, 30411380, 31311938, 32327527, 30657957, 33222246, 34331453 34170569, 34285068.

- Link of the group to the "Portal of scientific production"

https://cima.cun.es/en/research/research-programs/research-programs-hepatology

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- Pictures, links… to academic or industrial partners (if any)

  https://www.fau.eu/fau/organisation-and-committees/committees-and-senior-officers/commissions/univisid/21661918/

  https://www.institutcochin.fr/departments/emd/team-postic

  http://www.crc.jussieu.fr/chantal_desdouets.html

  https://research.ncl.ac.uk/fibrosislab/staff/jelenamann/

  https://livercenter.pitt.edu/people/ramon-bataller-md-phd/

  https://www.unav.edu/web/cimalab

  https://www.epizyme.com

  https://www.modernatx.com

  http://kintsugitx.com