Halt-RONIN

Funded by the European Union

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Discovering chronic inflammation biomarkers that define key stages in the Healthy-to-NASH (non-alcoholic steatohepatitis) transition to inform early prevention and treatments strategies.

Grant Agreement No. 101095679

Halt-RONIN Newsletter December 2022-April 2024

Our project aims to **discover chronic inflammation biomarkers that define critical stages in the Healthy-to-NASH (non-alcoholic steatohepatitis) transition to inform early prevention and treatment strategies**.

Our first newsletter provides our latest news and aims to become a forum for analyzing relevant topics in the field of liver diseases and commenting on some of the most relevant articles published during the first year of the project. Halt-RONIN has reached the 18 month of life. This period has been filled with numerous exciting activities, all of which can be explored in our website: https://halt-ronin.com/news/

The meeting in El Escorial "Kick-off meeting Horizon HLTH-2022-STAY-HLTH-02" was a complete success, with lots of new objectives set for the upcoming Halt RONIN project. It was celebrated on May 05-06 2023 in El Escorial, Madrid, Spain. It was organized by the **coordination group, Universidad Complutense de Madrid**. Speakers presented the different research lines of the groups participating in the project, the DUAL animal model, recommendations for the application of Anaxomic´s system biology tools, the advances in the current cohorts of patients under study in Marqués de Valdecilla Universitary Hospital and the ethical regulations. The minutes and the timetable for the meeting can be visited at Kick-off El Escorial

During the Kick-off it was also agreed among the partners the need for a **Biopredic International Workshop** for discussing the existing and novel in vitro models available for the Consortium at Biopredic Int. facilities. It was organized by **Biopredic** and celebrated on July 20-21 2023 at **Rennes University**, France. The minutes and the program can be found at Biopredic International Workshop

On February 8-9th in Edinburgh, we organized our second workshop, **"WP2-WP3 – Modelling health-disease transition in NAFL to NASH in preclinical liver models"**. It was a fantastic experience effectively organized by **Leonard Nelson, PI of The University of Edinburgh and Leader of WP2**. Speakers presented state-of-the-art concepts on the Clinical Perspectives in NAFLD-NASH, HepaRG-based NAFLD-NASH Modelling and 3D multicellular systems, Humanized zebrafish update, Modelling/Transcriptomics/Bioinformatics/Database integration, Steatosite and the Milestones/Deliverables/Discussion of the project. The minutes and the program can be found at Workshop Edinburgh

During this year, we have also organized the **International Seminar Series on Liver Toxicity and Steatotic Liver Disease**. These are taking place every third Wednesday of the month. Until today, we celebrated four seminars:

Date	Speaker	Title
17 January	Prof Jonathan Fallowfield	SteatoSITE: An integrated gene-to-outcome multimodal database for MASLD.
21 February	Dr. Sarp Uzun	Liver injury after SARS-CoV-2 Vaccination and Autoimmune Hepatitis: Molecular and Morphologic Analysis
20 March	Prof. Malu Martínez-Chantar	Translational basic Research: opportunities and challenges
17 April	Prof. Pau Sancho-Bru	Liver Organoids for steatotic liver disease modelling: a new venue of opportunities

You can watch the Seminars again here

Javier Cubero
Coordinator of Halt-RONIN
Complutense University, Madrid

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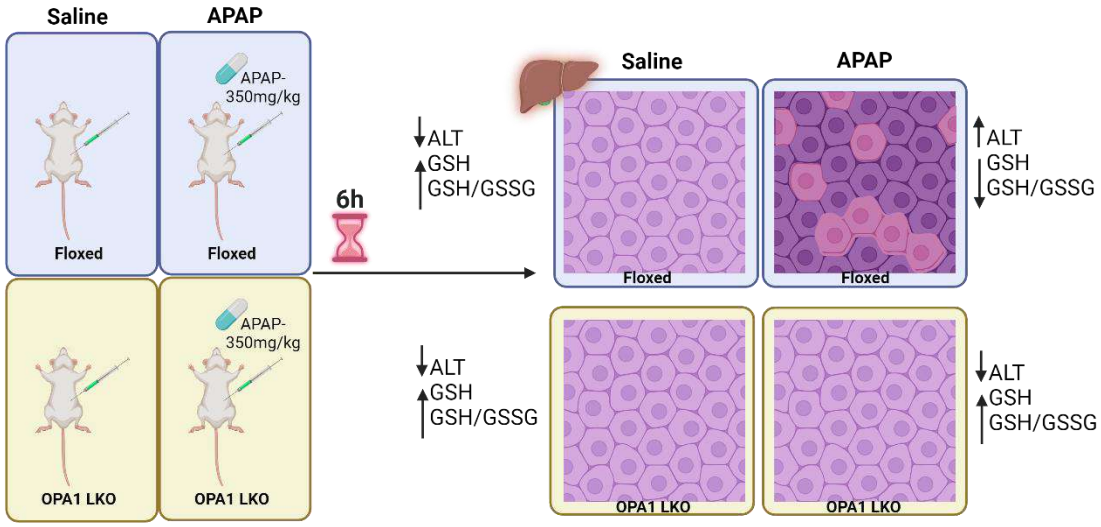
Interesting publications for the consortium:

1. *The mitochondrial fusion protein OPA1 is dispensable in the liver and its absence induces mitohormesis to protect liver from drug-indiced injury.*

MITOHORMESIS, A NOVEL CONCEPT IN DILI

The mitochondrial fusion protein **Optic atrophy 1 (OPA1)** function has been extensively studied for its role in cristae shaping. Alterations of its activity generates mitochondrial failure, however its specific contribution to **liver** function remains unclear. In this study, they have investigated the impact of **OPA1 deficiency** on liver homeostasis and response to **drug-induced injury (DILI)**. Unexpectedly, OPA liver knockout (LKO) mice display healthy without any affection on mitochondrial respiration, even the disruption in cristae morphology. Data suggested that OPA1 is required for proper complex V assembly and LKO protects the liver from drug toxicity. **Acetaminophen (APAP)** overdose is the most common cause of liver failure in humans and is a stablished DILI model. The toxicity of APAP is mainly generated by the conversion of APAP to reactive species by CYP2E1, inducing oxidative stress and mitochondrial damage for hepatic injury. In this study, liver injury was examined 6 hours post APAP administration, 350mg/kg by intraperitoneal injection (IP). Histological analysis by hematoxylin and eosin (H&E) revealed that OPA1 KO mice, almost prevented APAP- induced liver injury. Consistently, serum ALT levels were significantly low in APAP- treated OPA1- LKO mice. The depletion of glutathione (GSH) and activation of JNK by phosphorylation play an important role in APAP injury by amplifying oxidative stress, however OPA1 KO mice maintained significant GSH levels and the ratio GSH/GSSG (oxidised glutathione) in APAP treatment. Surprisingly, the obtained results reveal that **OPA1 is dispensable in the liver**, as its absence does not impair mitochondrial function or overall liver health under normal conditions. Instead, OPA1 **deficiency induces** a compensatory mechanism known as **mitohormesis**, to protect the liver from drug toxicity and steatosis, which can be considered as a mechanism that contributes to liver resilience and **protect against DILI**. These results highlight the complex interplay between mitochondrial dynamics and liver physiology, suggesting that targeting mitohormesis pathways may offer novel therapeutic strategies for liver diseases.



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Access to the original article:

Lee, H., Lee, T.J., Galloway, C.A. *et al.* **The mitochondrial fusion protein OPA1 is dispensable in the liver and its absence induces mitohormesis to protect liver from drug-induced injury**. *Nat Commun* **14**, 6721 (2023). https://doi.org/10.1038/s41467-023-42564-0

Scientific Impact:

According web of science the Impact Factor (IF) of this journal was 16.6 (2022) and it shows a Journal Citation Indicator of 3.24. The Rank (by Journal Citation Indicator) situates this journal in the position 7/134 and the percentile 95.15, poisoning this in the Q1 and D1.

Degree of originality and innovation: The study delves into uncharted territory regarding the role of OPA1 in liver function, shedding light on its dispensability and unveiling its unexpected protective effects. This research pioneers a novel perspective on mitochondrial biology, elucidating the intricate mechanisms underlying liver resilience and highlighting the concept of mitohormesis as a hitherto unrecognized aspect of liver adaptation. **Thematic priority or challenge addressed and contribution to the scientific debate:** The study delves into OPA1's pivotal role in liver function and mitochondrial biology, enhancing our grasp of liver health and metabolic regulation. It uncovers mechanisms behind liver resilience and drug toxicity protection, shedding light on critical liver physiology. Additionally, it challenges conventional beliefs about OPA1's indispensability, introducing mitohormesis as a new adaptation concept. Moreover, it clarifies the complex interplay between mitochondrial dynamics, complex V assembly, and cellular stress responses, pushing forward our understanding of liver pathology and physiology. **Methodological contribution:** 1. Deletion of OPA1 induces a stress response, reshaping liver homeostasis and conferring protection against drug toxicity. 2. OPA1 deletion alters cristae morphology and complex V assembly, triggering a mitohormetic response that enhances liver resiliency.

Interesting publications of the consortium:

1. *Roadmap to DILI research in Europe. A proposal from COST action ProEuroDILINet*

In the current article the aims for a constructive way forward in **Drug-Induced Liver Injury (DILI)** are to highlight the most important priorities in research and clinical science, therefore supporting a more informed, focused, and better funded future for **European DILI research**. This Roadmap aims to identify **key challenges, define a shared vision across all stakeholders** for the opportunities to overcome these challenges and **propose a high-quality research program** to achieve progress on the prediction, prevention, diagnosis and management of this condition and impact on healthcare practice in the field of DILI. This will involve:
1. **Creation of a database** encompassing optimised case report form for prospectively identified DILI cases with well-characterised controls with competing diagnoses, biological samples, and imaging data;
2. **Establishing of preclinical models** to improve the assessment and prediction of hepatotoxicity in humans to guide future drug safety testing;
3. **Emphasis on implementation science** and
4. **Enhanced collaboration** between drug-developers, clinicians and regulatory scientists.
This proposed operational framework will advance DILI research and may bring together basic, applied, translational and clinical research in DILI.

Access to the original article:

Lucena MI, Villanueva-Paz M, Alvarez-Alvarez I, Aithal GP, Björnsson ES, Cakan-Akdogan G, Cubero FJ, Esteves F, Falcon-Perez JM, Fromenty B, Garcia-Ruiz C, Grove JI, Konu O, Kranendonk M, Kullak-Ublick GA, Miranda JP, Remesal-Doblado A, Sancho Bru P, Nelson L, Daly AK, Fernandez-Checa JC. **Roadmap to DILI research in Europe. A proposal from COST action ProEuroDILINet.** *Pharmacol Res*. vol. 200 2024. DOI: 10.1016/j.phrs.2023.107046

Scientific Impact:

According web of science the Impact Factor (IF) of this journal was 9.3 (2022) and it shows a Journal Citation Indicator of 1.91. The Rank (by Journal Citation Indicator) situates this journal in the position 14/278 and the percentile 95.1, poisoning this in the Q1 and D1.

Degree of originality and innovation: Introduction of a comprehensive roadmap for Drug-Induced Liver Injury (DILI) research, emphasizing innovative strategies and collaborative efforts to address key challenges and advance healthcare practices. Proposal for a forward-thinking approach to DILI research, integrating novel methodologies such as database creation, preclinical models, and interdisciplinary collaboration to drive progress in prediction, prevention, diagnosis, and management. **Thematic priority or challenge addressed and contribution to the scientific debate:** This roadmap offers a strategic framework to navigate challenges, fostering informed dialogue and catalyzing advancements in prediction, prevention, and management strategies. By delineating key challenges and proposing a high-quality research program, this article contributes to the scientific discourse on DILI, offering a comprehensive approach to enhance understanding and improve healthcare practices in this field. **Methodological contribution:** This roadmap outlines methodological advancements including database creation, preclinical modelling, and interdisciplinary collaboration, offering a strategic blueprint to advance Drug-Induced Liver Injury (DILI) research. By proposing optimized case report forms, preclinical models, and emphasizing implementation science, this article provides

methodological contributions that promise to enhance the prediction, prevention, and management of DILI, driving progress in both basic and clinical research.

2. *Drug-induced liver injury*

The section II and III of this book, **Role of Sinusoidal Cells in Acute and Chronic Liver Diseases**, unravel the pivotal roles of sinusoidal cells in liver diseases. It encompasses both acute and chronic conditions, elucidating how these cells participate in tissue repair, fibrosis, inflammation, and the progression to liver disease and cancer. We examine their responses to various challenges, emphasizing their multifaceted contributions to hepatic pathology.
Conclusions: LSECs are known actors in the response to injury. Unlike healthy conditions, where LSECs are well fenestrated allowing oxygenation of hepatocytes, and under influence of shear stress, they sustain a vasodilatory phenotype responsible for promoting the quiescent state of HSCs, in intoxications, such as **APAP overdoses**, the loss of their phenotype, combined with activated HSCs, and KCs are responsible for sinusoidal capillarization and perisinusoidal matrix deposition, impairing vascular exchange and heightening the risk of **liver injury**. However, the role of LSECs in iDILI remains elusive. The advancement in in vitro and in vivo models and other researches tools and elucidations of the mechanisms of hepatotoxic drugs such as APAP will help unveil novel functions of LSECs as well as, other hepatotoxic drugs are always in progress.

Access to the original article:

Mesquita M, Andrade RJ, Cubero FJ*. **Drug-induced liver injury (Chapter 9). IN: Sinusoidal Cells in Liver Diseases. Role in their pathophysiology, diagnosis and treatment,** 2024. Editor: Jordi Gracia-Sancho. ISBN: 9780323952620. Elsevier, Amsterdam. Book link

3. *Inhibition of ALK3-mediated signalling pathway protects against acetaminophen-induced liver injury.*

Bone morphogenetic proteins (BMPs) are soluble growth factors that belong to the transforming growth factor (TGF) superfamily. BMP type I receptors ALK2 and ALK3 are abundantly expressed in the human liver and all hepatocyte-derived cell lines, but their effect on acute liver failure (ALF) remains unclear. In this study, we assessed the role of ALK2 and ALK3 in APAP-induced hepatotoxicity. Hepatotoxicity occurs due to an imbalance in hepatic APAP metabolism. APAP overdose caused Glutathione (GSH) depletion, results in the accumulation of the highly reactive specie NAPQI derived from APAP metabolism through the enzyme CYP2E1 which induces oxidative stress and mitochondria damage.
In this study, ALK2/3-inhibited or silenced human hepatoma cell line Huh7 was treated with APAP for 16h. In vivo, an experimental model in mice treated or not with ALK3 inhibitor DMH2 after APAP-induced ALF and sacrificed after 2h and 6h. In vitro, the RTqCR, Western Blot and lactate dehydrogenase (LDH) demonstrated ALK3 inhibition protects against APAP-induced hepatotoxicity and ALK2 over-expression displays an antiapoptotic effect against APAP insult. Consistently, the serum ALT, TUNEL staining, immunohistochemistry and Histological analysis by hematoxylin and eosin (H&E) revealed that DMH2 inhibitor protects against APAP-induced hepatotoxicity in vivo. This study highlights the inhibition of ALK3 protects against APAP-induced hepatotoxicity, providing new mechanistic evidence on the role of BMP signalling in the pathogenesis of liver injury mediated by APAP.

Access to the original article:

Marañón P, Rey E, Isaza SC, et al. **Inhibition of ALK3-mediated signalling pathway protects against acetaminophen-induced liver injury.** Redox Biol. 2024 May;71:103088. doi: 10.1016/j.redox.2024.103088. Epub 2024 Feb 15.

Scientific Impact:

According web of science the Impact Factor (IF) of this journal was 11.4 (2022) and it shows a Journal Citation Indicator of 1.90. The Rank (by Journal Citation Indicator) situates this journal in the position 15/315 and the percentile 95.40, poisoning this in the Q1 and D1.

Degree of originality and innovation: This research introduces a novel approach by investigating the role of bone morphogenetic protein (BMP) receptors ALK2 and ALK3 in acetaminophen-induced liver injury, shedding light on a previously unexplored therapeutic target for acute liver failure. By elucidating the protective effect of ALK3 receptor inhibition against acetaminophen-induced hepatotoxicity, this study pioneers a new avenue for therapeutic intervention in acute liver failure, offering valuable insights into the molecular mechanisms underlying liver injury and potential treatment strategies. **Thematic priority or challenge addresed and contribution to the scientific debate:** This study addresses the urgent need for novel therapeutic targets in the treatment of acetaminophen-induced acute liver failure, highlighting the role of bone morphogenetic protein (BMP) signaling pathways as a potential avenue for intervention. By uncovering the involvement of BMP receptors ALK2 and ALK3 in acetaminophen-induced liver injury, this research significantly advances the understanding of the pathogenesis of acute liver failure and stimulates critical discussions regarding the development of targeted therapeutic approaches. **Methodological contribution:** This study provides a comprehensive assessment of the molecular mechanisms underlying acetaminophen-induced hepatotoxicity, employing both pharmacological inhibitors and lentiviral-mediated modulation of ALK2 and ALK3 expression in human hepatocyte-derived cells. By elucidating the protective effect of ALK3 receptor inhibition against acetaminophen-induced liver injury in both cellular and animal models, this research introduces a novel methodological approach for investigating potential therapeutic targets in acute liver failure.

4. Other publications:

Publications			
Title	**Authors**	**Title of the journal or equivalent**	**DOI**
A Novel Mouse Model of Combined Hepatocellular-Cholangiocarcinoma Induced by Diethylnitrosamine and Loss of Ppp2r5d.	Domènech Omella J, Cortesi EE, Verbinnen I,et al.	Cancers (Basel)	10.3390/cancers15164193
Advancing with cancer immunotherapeutics: CD29+ regulatory T cell antagonism	Cubero FJ, Sarobe P, Tiegs G	Gut	10.1136/gutjnl-2023-331048
Biochimica et Biophysica Acta - Molecular Basis of Disease	Alejandro H Gutierrez, Marina S Mazariegos, Susana Alemany; et al.	Molecular Basis of disease	10.1016/j.bbadis.2023.166660
Breaking the barriers: the role of gut homeostasis in Metabolic-Associated Steatotic Liver Disease (MASLD)	Raquel Benedé, Francisco Javier Cubero, Yulia A. Nevzorova	Gut microbes	10.1080/19490976.2024.2331460

CAP-RNAseq: an integrated pipeline for functional annotation and prioritization of co-expression clusters	Merve Vural-Ozdeniz, Kubra Calisir, Rana Acar, et al.	Briefings in Bioinformatics	10.1093/bib/bbad536
Control Compounds for Preclinical Drug-Induced Liver Injury Assessment: Consensus-driven systematic review by the ProEuroDILI Network	Segovia-Zafra A, Villanueva-Paz M, Serras AS, et al.	Journal of Hepatology	10.1016/j.jhep.2024.04.026
Curcumin encapsulated in milk small extracellular vesicles as a nanotherapeutic alternative in experimental chronic liver disease	Virginia Albaladejo-García, Laura Morán, Ana Santos-Coquillat, et al.	Biomedicine & Pharmacotherapy	10.1016/j.biopha.2024.116381
Dietary and genetic disruption of hepatic methionine metabolism induce acid sphingomyelinase to promote steatohepatitis	Cristina Alarcón-Vila, Naroa Insausti-Urkia, Sandra Torres, et al.	Redox Biology	10.1016/j.redox.2022.102596
Expression of HMGCS2 in intestinal epithelial cells is downregulated in inflammatory bowel disease associated with endoplasmic reticulum stress	Beatriz Martín-Adrados; Stefanie K. Wculek; Sergio Fernández-Bravo; et al.	Frontiers in Inmmunology	10.3389/fimmu.2023.1185517
HILPDA, a new player in NASH-driven HCC, links hypoxia signaling with ceramide synthesis	Jose C Fernandez-Checa, Sandra Torres, Carmen Garcia-Ruiz	Journal of Hepatology	10.1016/j.jhep.2023.05.009
Improving human mesenchymal stem cell-derived hepatic cell energy metabolism by manipulating glucose homeostasis and glucocorticoid signalling	Rodrigues JS, Pereira AF, Camões SP, et al.	Front. Endocrinol	10.3389/fendo.2022.1043543
JNKs protect from cholestatic liver disease progression by modulating Apelin signalling	Mohamed MR, Haybaeck J, Wu H, et al.	JHEP Rep.	10.1016/j.jhepr.2023.100854
Mitochondrial cholesterol: Metabolism and impact on redox biology and disease	Leire Goicoechea, Laura Conde de la Rosa, Sandra Torres, et al.	Redox Biology	10.1016/j.redox.2023.102643
Neuroblastoma RAS viral oncogene homolog (N-RAS) deficiency aggravates liver injury and fibrosis	Zheng K, Hao F, Medrano-Garcia S, et al.	Cell Death and Disease	10.1038/s41419-023-06029-y
Obesity under the moonlight of c-MYC	Yulia A. Nevzorova and Francisco Javier Cubero	Frontiers in cells and developmental biology	10.3389/fcell.2023.1293218
Prior drug allergies are associated with worse outcome in patients with idiosyncratic drug-induced liver injury: A machine learning approach for risk stratification	H. Niu, P. Solis-Muñoz, M. García-Cortés, et al.	Pharmacological Research	10.1016/j.phrs.2023.107030
Roadmap to DILI research in Europe. A proposal from COST action ProEuroDILINet	M.I. Lucena, M. Villanueva-Paz, I. Alvarez-Alvarez, et al.	Pharmacological Research	10.1016/j.phrs.2023.107046
S-Adenosyl-l-methionine restores brain mitochondrial membrane fluidity and GSH content improving Niemann-Pick type C disease	Leire Goicoechea, Sandra Torres, Laura Fàbrega et al.	Redox Biology	10.1016/j.redox.2024.103150
Single Mutations in Cytochrome P450 Oxidoreductase Can Alter the Specificity of Human Cytochrome P450 1A2-Mediated Caffeine Metabolism	Esteves, F.; Almeida, C.M.M.; Silva, S.; et al.	Biomolecules	10.3390/biom13071083
Zonal expression of StARD1 and oxidative stress in alcoholic-related liver disease	Raquel Fucho, Estel Solsona-Vilarrasa, Sandra Torres, et al.	J Lipid Res	10.1016/j.jlr.2023.100413

P11-26 Exosomes derived from primed mesenchymal stem cells improve cell viability on an APAP-induced hepatic injury in vitro model	Serras AS, Camões SP, Rodrigues JS, et al.	Toxicology Letters.	10.1016/j.toxlet.2022.07.476
Abstracts of the 57th Congress of the European Societies of Toxicology (EUROTOX 2023)	Rodrigues JS, Faria-Pereira A, Camões SP, et al.	Toxicology Letters	10.1016/S0378-4274(23)00258-8
Statins improve Liver function and minimize the degree of liver damage by modulating cell death	Hionides, A. et al.	Hepatology	10.1097/HEP.0000000000000580

Communication and Dissemination activities:

Communication Activity Type	Description	Outcome
Meeting	The liver Meeting 2023, Boston, MA (USA) 9-14 Nov. **EXPLORING THE ROLE OF X-BINDING PROTEIN-1 (XBP1) IN THE GUT- LIVER AXIS DURING ALCOHOL-RELATED LIVER DISEASE (ArLD)**. C, Sanz-García, UCM.	Oral communication/ Hepatology page 44 art.42
Poster	The liver Meeting 2023, Boston, MA (USA) 9-14 Nov. **STATINS IMPROVE LIVER FUNCTION AND MINIMIZE THE DEGREE OF LOVER DAMAGE BY MODULATING CELL DEATH**. Hionides, A. et al. UCM	Hepatology Page1133, Art. 2372-C
Meeting	EASL Congress 2023: **"Endoscopy sleeve gastroplasty is an effective treatment in steatohepatitis patients: a prospective, multicenter, randomized trial"**. Dr. Abad, Dr. Calleja, Hospital Universitario Puerta de Hierro	Oral communication
Congress	25th European Congress of Endocrinology ECE2023. Estambul, 2023 Özlem Çelic, IBG	Oral presentation
Meeting	AEEH Congress 2024:**"Validation of the "Rule of 5" from Baveno VII in a multicenter real-life cohort of patients with metabolic-associated dysfunction steatotic liver disease"** Dra. Llop, Dr. Calleja. Hospital Universitario Puerta de Hierro	Oral communication
Congress	9th International Congress of Pathology & 5th Congress of physiological science of Serbia with international participation. Belgrado, 2023 Juan Manuel Falcon, CIC-Biogune	Oral presentation
Poster	ETRS & SPCE-TC. Oct, 2023. **Stem cell-derived hepatocyte-like cells recapitulate cues of insulin resistance progression.** Rodrigues JS et. al., FFUL	Poster
Meeting	2nd PNEV meeting. Lisboa 2023. Invited talk. **Deep molecular characterization of extracellular vesicles as source for low-invasive indicators for pathophisiology.** Juan Manuel Falcon, CIC-Biogune	Oral presentation
Symposium	1st MOVE Symposium Malaga, 2023. **Study of the in vivo biodistribution of hepatocytes-released extracellular vesicles in mouse models for metabolic syndrome progression.** Clara Garcia Vallicrosa, Juan Manuel Falcon. CIC-Biogune. Organization: María Isabel Lucena (Malaga University) and Juan Manuel Falcon (CIC-Biogune)	Poster
Conference	EHD-BBN 2023 congress celebrated in Santander (November, 6-7). **"Loss of CDKN1A protects against masld-induced liver damage and metabolic dysfunction"**. Alejandro H. et al. UCM	Poster
Poster	EUROTOX 2023. **The role of glucose homeostasis and glucocorticoid signalling for the development of relevant hepatic in vitro models for toxicology,drug metabolism and energy metabolism studies.** Raquel B. UCM.	TOP 5 POSTER
Meeting	AEEH Congress 2024: **"Patients with hepatic cirrhosis due to NASH have a higher early cardiovascular risk measured by epicardial fat."** Dra. Hernandez-Conde, Hospital Universitario Puerta de Hierro	Poster

FORUM	Forúm on "**O Teu Futuro, na Saúde**", Colégio Militar, Lisbon, 22 de Nov, 2023. Prof. Joana Miranda, FFUL.	-
Poster	2nd Meeting of the Portuguese Network on Extracellular Vesicles. June 2023. PNEV2023 **Exosomes derived from MSCs primed with APAP injury signals reveal a pro-regenerative signature**. - Serras AS, et al., FFUL	BEST POSTER AWARD
Radio	Radio interview (Radio Alma) and blog mulheres cidadãs: **"Entrevista Joana Miranda, biologa - Mulheres cidadãs**"(radioalma.eu). Prof. Joana Miranda, FFUL	http://radioalma.eu/
Meeting	5th Translational Hepatology Meting of AEEH. "**CDKN1A inhibition protects against chronic inflammation-induced liver damage via modulation of lipid uptake"** Alejandro H et al., UCM.	Poster
Conference	19th European Society for Biomedical Research on Alcoholism **"Exploring the role of X-Binding protein-1(XBP1)in the gut-brain axis during alcohol-related liver disease (ArLD)"** Carlos Sanz. UCM	Oral communication
Workshop	2nd International Workshop on Liver & Gut Fibrosis **"Isolation and characterization of extracellular vesicles (EVs) in faecal matter: Implications for future biomarker discovery"** Raquel Benedé. UCM	Poster
Poster	2nd International Workshop on Liver & Gut Fibrosis. Valencia 26-27/10/2023. **Efficacy of dietary and physical activity intervention in MetALD**. O. Estévez, R. Benedé, H, Leal, et al. UCM	Poster
Workshop	2nd International Workshop on Liver & Gut Fibriosis. **"The heightened importance of the intestinal microbiome in MetALD: role in pathogenesis and impact in therapeutic strategies"** Raquel Benedé. UCM	Poster
Poster	5ªreunión de hepatología traslacional AEEH-Asociación española para el estudio del hígado. **Efficacy of dietary and physical activity intervention in MetALD**. O. Estévez, R. Benedé, H. Leal et. al. UCM	Poster
Workshop	2 International Workshop on Liver and Gut Fibrosis, Spain 22-23Oct2023. E**XPLORING THE ROLE OF X-BINDING PROTEIN-1(XBP1)IN THE GUT-LIVER AXIS DURING ALCOHOL-RELATED LIVER DISEASE (ArLD)**.C.Sanz-Garcia, UCM	Oral Communication
Education and training events:	**Clinical Inmersion in Hepatology:** The Liver Unit at Hospital Universitario Puerta de Hierro (SERMAS) offered a two-day course for specialists interested in expanding their skills in management of advanced liver disease, including NASH. June 2023/ January 2024. Hospital Universitario Puerto de Hierro	-