3.7.2 Molecular Hepatology

Publications: 7 | **Q1:** 5

COMPOSITION

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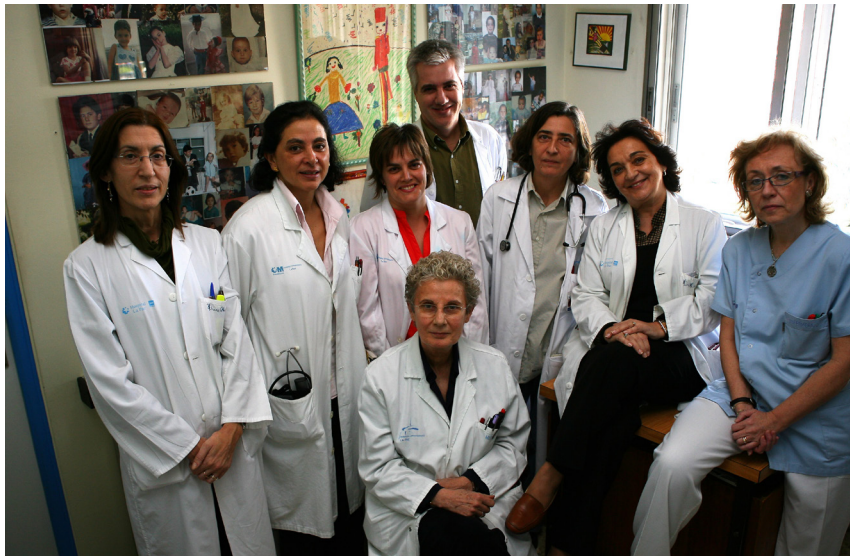
- **David Vicent López.** *Investigador Senior (Contrato Miguel Servet - I2). Hospital Universitario La Paz*

STRATEGIC OBJETIVES

- Our research interest is focused on the study of the molecular mechanisms underlying the most severe paediatric liver disorders, namely cholestasis, which results from the impaired secretion of bile from the liver to the intestine.
- As such, it represents a clinical and biochemical syndrome that is produced by a wide variety of disease processes that affect the liver. Individuals with cholestasis manifest jaundice, severe itching, malabsorption of fats and lipidsoluble vitamins and, in many cases, progressive liver damage. These clinical manifestations are due to the accumulation in blood and tissues of substances normally secreted in the bile, such as bilirubin, bile acids, and cholesterol and to the absence of bile from the intestine.
- When manifested in early infancy, cholestasis is often life threatening and usually requires liver transplantation. Extrahepatic biliary atresia (EHBA), Alagille syndrome and progressive familial intrahepatic cholestasis (PFIC) constitute the main paediatric cholestatic disorders. EHBA is an enigmatic disease of unknown aetiology, characterised by a precocious and accelerated obstruction of the biliary tree. Alagille syndrome is associated with mutations in the Jag1 gene and is characterised by a paucity or absence of intrahepatic bile ducts. PFIC encompasses a heterogeneous group of autosomal recessive diseases that exhibit similar clinical features. These diseases are caused by mutations in proteins located in the canalicular membrane of the hepatocyte and in proteins involved in bile secretion, such as the bile salt export pump (BSEP; ABCB11), the phospholipid transport protein MDR3 (ABCB4) and the aminophospholipid translocase FIC1 (ATP8B1). These cholestatic disorders constitute the most common indication for liver transplantation in childhood.



RESEARCH LINES

- Molecular basis of paediatric liver diseases
- Liver Pathobiology
- Biomarker identification

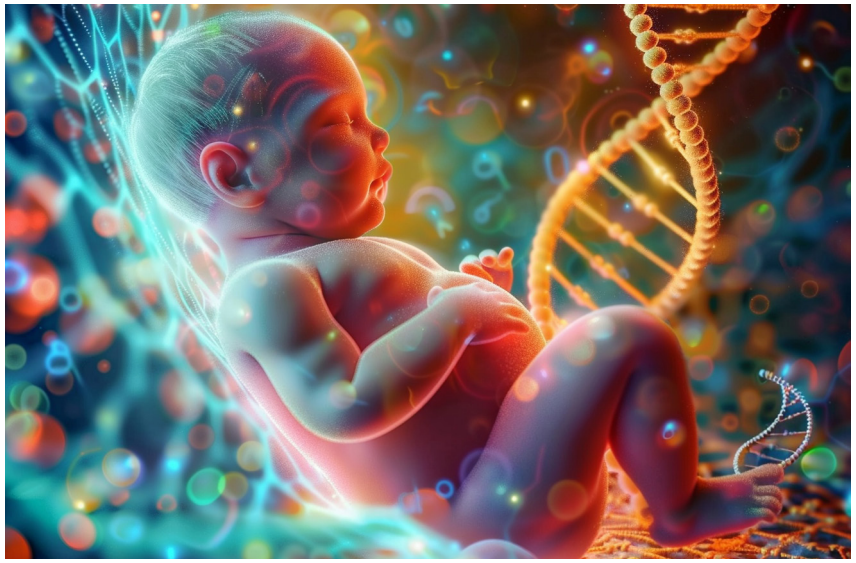
RESEARCH ACTIVITY

Publications

- **Chichelnitskiy E, Goldschmidt I, Ruhl L, Rübsamen N, Jaeger VK, Karch A, Beushausen K, Keil J, Götz JK, D'Antiga L, Debray D, Hierro L, Kelly D, Mclin V, Pawlowska J, Mikolajczyk RT, Bravi M, Klaudel-Dreszler M, Demir Z, Lloyd C, Korff S, Baumann U, Falk CS.** Plasma immune signatures can predict rejection-free survival in the first year after pediatric liver transplantation. J Hepatol. 2024; 81(5): 862-71. Article. IF: 33.0; D1
- **de la Cámara RCM, Torices-Pajares A, Miguel-Berenguel L, Reche-Yebra K, Frauca-Remacha E, Hierro-Llanillo L, Muñoz-Bartolo G, Lledín-Barbacho MD, Gutiérrez-Arroyo A, Martínez-Feito A, López-Granados E, Sánchez-Zapardiel E.** Epstein-Barr virus-specific T-cell response

in pediatric liver transplant recipients: a cross-sectional study by multiparametric flow cytometry. Front Immunol. 2024; 15: 1479472. Article. IF: 5.9; Q1

- **García-Boyano M, Díez MA, Tomé LF, Escosa-García L, Ramos FM, Schuffelmann-Gutiérrez C, Bueno EC, Calvo C, Baquero-Artigao F, Remacha EF.** Ceftazidime-Avibactam Use in a Case Series of Difficult-to-Treat or Recurrent Infections in Pediatric Patients with Complex Chronic Conditions: Effectiveness and Absence of Resistance Development. Antibiotics (Basel). 2024; 13(7): 598. Article. IF: 4.6; Q1
- **Guerrero L, Carmona-Rodríguez L, Santos FM, Ciordia S, Stark L, Hierro L, Pérez-Montero P, Vicent D, Corrales FJ.** Molecular basis of progressive familial intrahepatic cholestasis 3. A proteomics study. Biofactors. 2024; 50(4): 794-809. Article. IF: 5.0; Q1
- **Guerrero L, Vindel-Alfageme J, Hierro L, Stark L, Vicent D, Sorzano COS, Corrales FJ.** Discrimination of Etiologically Different Cholestasis by Modeling Proteomics Datasets. Int J Mol Sci. 2024; 25(7): 3684. Article. IF: 4.9; Q1
- **Li WH, van der Doef HPJ, Wildhaber BE, Marra P, Bravi M, Pinelli D, Minetto J, Dip M, Sierre S, de Santibañes M, Ardiles V, Uno JW, Hardikar W, Bates S, Goh L, Aldrian D, Seisenbacher J, Vogel GF, Neto JS, da Fonseca EA, Costa CM, Ferreira CT, Nader LS, Farina MA, Dajani KZ, Parente A, Bigam DL, Liang TB, Bai XL, Zhang W, Gonsorcíková L, Fronek J, Bohus S, Franchi-Abella S, Gonzales E, Guérin F, Junge N, Baumann U, Richter N, Hartleif S, Sturm E, Rajakannu M, Palaniappan K, Rela M, Pawaria A, Rajakrishnan H, Surendran S, Kumar M, Agarwal S, Gupta S, Asthana S, Bandewar V, Raichurkar K, Spada M, Monti L, Alterio T, Yanagi Y, Uchida H, Komine R, Evans H, Carr-Boyd P, Duncan D, Stefanowicz M, Latka-Grot J, Kolesnik A, Broering DC, Raptis DA, Marquez KAH, Mali V, Aw M, Beretta M, Van der Schyff F, Quintero-Bernabeu J, Mercadal-Hally M, Larrarte K M, Andres AM,**



Hernández-Oliveros F, Frauca E, Casswall T, Jorns C, Delle M, Gupte G, Sharif K, McGuirk S, Superina R, Caicedo JC, Jaramillo C, Bitterfeld L, Kastenberg Z, Shah AA, Domenick B, Acord MR, Mazariegos GV, Soltys K, DiNorcia J, Antala S, Florman SS, Buchholz BM, Herden U, Fischer L, Dierckx RAJO, Hartog H, Bokkers RPH. Incidence, management and outcomes in hepatic artery complications after paediatric liver transplantation: protocol of the retrospective, international, multicentre HEPATIC Registry. BMJ Open. 2024; 14(6): e081933. Article. IF: 2.3; Q2

- **Salinero-Fort M, Mostaza-Prieto JM, Lahoz-Rallo C, Cárdenas-Valladolid J, Iriarte-Campo V, Estirado-Decabo E, García-Iglesias F, Gonzalez-Alegre T, Fernández-Puntero B, Rio VM, Sánchez-Arroyo V, Sabín-Rodríguez C, López-López S, Gómez-Campelo P, Taulero-Escalera B, Rodríguez-Artalejo F, Andrés-Rebollo FJS, De Burgos-Lunar C.** External validation of three diabetes prediction scores in a Spanish cohort: does adding high risk for depression improve the validation of the FINDRISC score (FINDRISC-MOOD)?. BMJ Open. 2024; 14(6): e083121. Article. IF: 2.3; Q2

Research projects

- **Hierro Llanillo L.** Desarrollo de métodos de diagnóstico molecular de enfermedades hepáticas infantiles de carácter hereditario. Fundación ACS. 2005-Ongoing. Managment centre: FIBHULP
- **Hierro Llanillo L.** Diagnóstico molecular de enfermedades hepáticas infantiles de carácter hereditario (PI-426). Fundación ACS. 2012-Ongoing. Managment centre: FIBHULP
- **Hierro Llanillo L.** Estableciendo una base de datos como parte de la red europea de referencia en enfermedades rara hepáticas. R-liver. UE. 2019-Ongoing. Managment centre: FIBHULP
- **Hierro Llanillo L.** Validación de marcadores genéticos y moleculares para el diagnostico de atresia biliar (PI20/01496). ISCIII. 2021-2024. Managment centre: FIBHULP
- **Jara Vega P.** Estudio epidemiológico, observacional sobre el riesgo de desarrollo de síndrome linfoproliferativo en pacientes pediátricos trasplantados hepáticos, en el HULP. Roche Farma S. A. 2008-Ongoing. Managment centre: FIBHULP
- **Romero M, Hierro Llanillo L.** Optimization of spleen VCTE examinations with FibroScan. Echosens. 2022-Ongoing. Managment centre: FIBHULP
- **Ruiz de Valbuena R, Hierro Llanillo L.** A prospective and retrospective cohort study to refine and expand the knowledge on patients with chronic forms of Acid Sphingomyelinase Deficiency (ASMD) (Estudio PIR16183). Sanofi . 2021-. Managment centre:
- **Vicent López D.** Caracterización clínica del nuevo factor de riesgo cardiovascular trimetilamina-D-óxido en pacientes diabéticos obesos. Sección de Endocrinología y Nutrición Severo Ochoa. 2015-Ongoing. Managment centre: FIBHULP
- **Vicent López D.** Contrato Miguel Servet Categoria C (CES06/007). ISCIII. 2008-2025. Managment centre: FIBHULP

Cibers and Retics

- **Hierro Llanillo L.** ERN on Hepatological diseases (RARE-LIVER). EU. (31/12/2024). FIBHULP
- **Jara Vega P.** ERN on Transplantation in children (TransplantChild). EU. (31/12/2024). FIBHULP

Clinical trials

- **Frauca Remacha E.** estudio de fase iii, aleatorizado, doble ciego, controlado con placebo, para evaluar la eficacia y la seguridad de maralixibat en el tratamiento de participantes con prurito colestásico.
  Type/Phase: III
  Sponsored by: Mirum Pharaceutical Inc
  Signature date: 23/10/2024