3.7.2 Molecular Hepatology

Publications:9 | Q1:3

COMPOSITION

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STRATEGIC OBJECTIVE

- 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

- **Delgado-Miguel C, Triana P, Miguel-Ferrero M, Díaz M, Hierro L, Jara P, López-Gutiérrez JC, Oliveros FH.** Mortality predictive factors in congenital hepatic hemangioma: a case-control study. Eur J Pediatr. 2023; 182(4): 1657-63. Article. IF: 3.0; Q1

- **Donà D, Bravo-Gallego LY, Remacha EF, Cananzi M, Gastaldi A, Canizalez JT, Stephenne X, Lacaille F, Lindemans C, Calore E, Galea N, Benetti E, Nachbaur E, Sandes AR, Teixeira A, Ferreira S, Klaudel-Dreszler M, Ackermann O, Boyer O, Espinosa L, Guereta LG, Sciveres M, Fischler B, Schwerk N, Neland M, Nicastro E, Dello Strologo L, Toporski J, Vainumae I, Rascon J, Urbonas V, del Rosal T, López-Granados E, Perilongo G, Baker A, Vega PJ.** Vaccination practices in pediatric transplantation: A survey among member centers of the European reference network TransplantChild. Pediatr Transplant. 2023; 27(7): e14589. Article. IF: 1.2; Q3
- **Felzen A, van Wessel DBE, Gonzales E, Thompson RJ, Jankowska I, Shneider BL, Sokal E, Grammatikopoulos T, Kadaristiana A, Jacquemin E, Spraul A, Lipinski P, Czubkowski P, Rock N, Shagrani M, Broering D, Nicastro E, Kelly D, Nebbia G, Arnell H, Fischler B, Hulscher JBF, Serranti D, Arikan C, Polat E, Debray D, Lacaille F, Goncalves C, Hierro L, Bartolo GM, Mozer-Glassberg Y, Azaz A, Brecelj J, Dezsofi A, Calvo PL, Grabhorn E, Hartleif S, van der Woerd WJ, Kamath BM, Wang JS, Li LT, Durmaz Ö, Kerkar N, Jorgensen MH, Fischer R, Jiménez-Rivera C, Alam S, Cananzi M, Laverdure N, Ferreira CT, Guerrero FO, Wang H, Sency V, Kim KM, Chen HL, de Carvalho E, Fabre A, Bernabeu JQ, Zellos A, Alonso EM, Sokol RJ, Suchy FJ, Loomes KM, McKiernan PJ, Rosenthal P, Turmelle Y, Horslen S, Schwarz K, Bezerra JA, Wang K, Hansen BE, Verkade HJ.** Genotype-phenotype relationships of truncating mutations, p.E297G and p.D482G in bile salt export pump deficiency. JHEP Rep. 2023; 5(2): 100626. Article. IF: 9.5; D1
- **García-Sánchez P, Aguilar-Valero E, Sainz T, Calvo C, Iglesias I, Bueno D, Frauca E, Ramos-Boluda E, Alcolea-Sánchez A, García-Guereta L, Alonso-Melgar A, Esperón F, Mendez-Echevarria A.** Immunocompromised children and young patients living with pets: gaps in knowledge to avoid zoonosis. Transbound Emerg Dis. 2023; 2023: 2151761. Article. IF: 3.5; Q2
- **Gardín A, Ruiz M, Beime J, Cananzi M, Rathert M, Rohmer B, Grabhorn E, Almes M, Logarajah V, Pena-Quintana L, Casswall T, Darmellah-Remil A, Reyes-Dominguez A, Barkaoui E, Hierro L, Baquero-Montoya C, Baumann U, Fischler B, Gonzales E, Davit-Spraul A, Laplanche S, Jacquemin E.** Δ4-3-oxo-5β-reductase deficiency: favorable outcome in 16 patients treated with cholic acid. Orphanet J Rare Dis. 2023; 18(1): 383. Article. IF: 3.4; Q2
- **Goldschmidt I, Chichelnitskiy E, Ruebsamen N, Jaeger VK, Karch A, D'Antiga L, Di Giorgio A, Nicastro E, Kelly DA, McLin V, Korff S, Debray D, Girard M, Hierro L, Klaudel-Dreszler M, Markiewicz-Kijewska M, Falk C, Baumann U.** Diagnosing acute cellular rejection after paediatric liver transplantation-is there room for interleukin profiles?. Children (Basel). 2023; 10(1): 128. Article. IF: 2.0; Q2
- **Lledín MD, Parrón-Pajares M, Morais A, Hernández-Oliveros F, Botella-Carretero JI, Hierro L.** Impact of muscle mass on the prognosis of liver transplantation for infants with biliary atresia. Front Pediatr. 2023; 10: 1093880. Article. IF: 2.1; Q2
- **Pérez-Luz S, Lalchandani J, Matamala N, Barrero MJ, Gil-Martín S, Ramos-Del Saz S, Varona S, Monzón S, Cuesta I, Justo I, Marcacuzco A, Hierro L, Garfia C, Gomez-Mariano G, Janciauskiene S, Martínez-Delgado B.** Quantitative lipid profiling reveals major differences between liver organoids with normal pi*m and deficient pi*z variants of alpha-1-antitrypsin. Int J Mol Sci. 2023; 24(15): 12472. Article. IF: 4.9; Q1
- **Vega MG, Andrade JD, Morais A, Frauca E, Bartolo GM, Lledín MD, Bergua A, Hierro L.** Urea cycle disorders and indications for liver transplantation. Front Pediatr. 2023; 11: 1103757. Article. IF: 2.1; Q2

Research projectsA

- **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. 2021-2023. *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*
- **Jara Vega P.** PaEdiatric Transplantation European Registry (PETER PI-4389). UE. 2019-2023. *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*
- **Jara Vega P.** Support to Generic Services for the ERN TransplantChild (ICT 2372000). UE. 2021-2023. *Managment centre: FIBHULP*

Cibers and Retics

- **Hierro Llanillo L.** ERN on Hepatological diseases. (RARE-LIVER). EU. (31/12/2023). FIBHULP
- **Jara Vega P.** ERN on Transplantation in children. (TransplantChild). EU. (31/12/2023). FIBHULP