[1] *Department of Gastroenterology, Erasmus MC, Rotterdam, Netherlands*
[2] *Department of Gastroenterology, Hospital Privado Universitario de Córdoba. Instituto Universitario de Ciencias Biomédicas de Córdoba, Córdoba, Argentina*
[3] *Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis, MN, USA*
[4] *Department of Gastroenterology, Centro de Enfermedades Hepáticas y Digestivas (CEHYD), Bogotá, Colombia*
[5] *Department of Gastroenterology, Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru*
[6] *Department of Gastroenterology, Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil*
[7] *Department of Gastroenterology, Pontificia Universidad Católica de Chile, Santiago, Chile*
[8] *Department of Gastroenterology, Hospital Eugenio Espejo, Quito, Ecuador*
[9] *Department of Medicine, University of Minnesota, Minneapolis, MN, USA*

Introduction and Objectives: Hepatocellular carcinoma (HCC) is the third cause of cancer-related death worldwide. Assessment of genetic components has been used to better stratify those at risk. However, most studies have been performed in Asian or Caucasian populations. Tolloid-like protein 1 (*TLL1*) is one such SNP that has been shown to increase risk in hepatitis C virus (HCV)-associated HCC. We evaluated the risk association of TLL1 in a South American cohort.

Materials and Methods: This is a cross-sectional analysis performed in South Americans with HCC as well as cirrhotic controls through the ESCALON network. We analyzed 120 HCC blood samples and 293 cirrhotic controls from Argentina, Chile, Brazil, Colombia, Ecuador and Peru. The pathogenic variant of *TLL1* (rs1704200) was evaluated using TaqMan-genotyping assay. Multiple logistic regression was used to establish the association between *TLL1* and HCC.

Results: The median age of HCC patients was 68 years (IQR 62-72) and of cirrhotics 64 years IQR 68-70). The most common underlying liver disease in both groups was Non-alcoholic fatty liver disease (NAFLD) at 58% and 59%, respectively. The proportion of individuals who developed HCC with a *TLL1* pathogenic variant (AT/TT) was 18.2% in the South American cohort. The calculated Odds-Ratio (OR) for HCC among South Americans with the TLL1 variant was 0.69 (CI 0.37-1.29), suggesting a non-significant decrease odds for HCC. Interestingly, different results were found when examining HCV-associated HCC (11% of the cases and 6% of controls). The OR for HCV-associated HCC in Latin Americans was 2.07 (CI 0.93-4.58), suggesting a non-significant increased odd of being diagnosed with HCC in South Americans with the variant.

Conclusions: *TLL1* mutations do not seem to associate with HCC development in South American patients with liver disease. However, preliminary results show that the presence of *TLL1* SNP could confer an increased risk for HCC in South Americans with HCV infection.

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P-5 THREE-DIMENSIONAL SINGLE-CELL ATLAS OF LIVER TISSUE ARCHITECTURE

Dilan Martinez[1], Maldonado Valentina[1], Cristian Perez[1], Valeria Candia[1], Hernán Morales-Navarrete[2], Fabián Segovia-Miranda[1]

[1] *Department of Cell Biology, Faculty of Biological Sciences, Universidad de Concepción, Concepción, Chile*
[2] *Department of Systems Biology of Development, University of Konstanz, Konstanz, Germany*

Introduction and Objectives: The liver is an organ that performs a wide variety of functions that are highly dependent on its complex 3D structure. Geometrical models (digital representations of tissues) represent a versatile technique to characterize 3D tissues as well as to get quantitative insights into the link between their structure and function. Until now, these models have only focused on some tissue (sinusoids and bile canaliculi) and cellular components (hepatocytes), leaving out important cellular populations such as stellate cells and Kupffer cells. One of the major bottlenecks for a complete tissue reconstruction is the limitation on the number of markers that can be imaged by fluorescence microscopy (up to 4-5). This study aimed to generate a "3D single-cell atlas of liver tissue architecture", i.e., a full 3D geometrical model which includes all tissue and cellular components simultaneously.

Materials and Methods: We overcome the technical constraints by using deep tissue immunostaining, multiphoton microscopy, deep learning techniques, and 3D image processing. As a proof of concept, we used the 3D atlas to describe the morphological changes that occur in the mouse liver during post-natal early development and adulthood.

Results: We described how liver tissue architecture progressed from post-natal day one to adulthood by a novel set of morphometric cellular and tissue parameters. Our analysis revealed unknown details about the spatial organization of different liver cell types. Unexpected spatiotemporal patterns of non-parenchymal cells and hepatocytes with differing in size, number of nuclei, and DNA content were uncovered. We also provided information regarding the remodeling of the bile canaliculi and sinusoidal networks.

Conclusions: These findings revealed novel characteristics of liver heterogeneity and have important implications for both the structural organization of liver tissue and its functional features. 3D single-cell atlas will provide a powerful tool to understand liver tissue architecture under both physiological and pathological conditions.

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P-6 PATTERNS OF ANTIBIOTIC RESISTANCE IN PATIENTS WITH CIRRHOSIS AND SPONTANEOUS BACTERIAL INFECTIONS: ANALYSES OF THE MULTICENTER STUDY FROM ARGENTINA AND URUGUAY

Sebastián Marciano[1,2], Maria Nelly Gutierrez Acevedo[3], Sabrina Barbero[4], Lorena del Carmen Notari[4], Marina Agozino[5], Jose Luis Fernandez[5], Maria Margarita Anders[6], Nadia Grigera[6], Florencia Antinucci[6], Orlando Federico Orozco Ganem[6], Maria Dolores Murga[7], Daniela Perez[7], Ana Palazzo[7], Liria Martinez Rejtman[8], Ivonne Giselle Duarte[3], Julio Vorobioff[9], Victoria Trevizan[9], Sofía Bulaty[9], Fernando Bessone[9], Marcelo Valverde[10], Martín Elizondo[10], José Daniel Bosia[11], Silvia Mabel Borzi[11], Teodoro E. Stieben[12], Adriano Masola[12], Sebastian Eduardo Ferretti[13], Diego Arufe[14], Ezequiel Demirdjian[14], Maria Pia Raffa[14], Mirta Peralta[15], Hugo Alberto Fainboim[15], Cintia Elizabet Vazquez[16], Pablo Ruiz[16], José Emanuel Martínez[17], Leandro Alfredo Heffner[18], Andrea Odzak[18], Melisa Dirchwolf[19], Astrid Smud[20], Manuel Mendizabal[21], Carla Bellizzi[22], Ana Martinez[22], Jesica Tomatis[19], Andres Bruno[18], Agñel Ramos[13], Josefina Pages[21], Silvina Tevez[5], Diego Giunta[2,23], Adrian Gadano[1,2]

[1] Buenos Aires Italian Hospital, Liver Unit, Buenos Aires, Argentina
[2] Buenos Aires Italian Hospital, Department of Research, Buenos Aires, Argentina
[3] 4 de Junio Hospital, P. R. Sáenz Peña, Argentina
[4] Churruca Visca Hospital, Buenos Aires, Argentina
[5] Güemes Sanatorium, Buenos Aires, Argentina
[6] Germany Hospital, Buenos Aires, Argentina
[7] A.C. Padilla Hospital, San Miguel de Tucumán, Argentina
[8] T J Schestakow Hospital, San Rafael, Argentina
[9] Centenary Provincial Hospital, Rosario Argentina
[10] Bi-Institutional Liver Transplant Unit, Clinics Hospital – Military Hospital, Montevideo, Uruguay
[11] Rossi Hospital, La Plata, Argentina
[12] San Martín Hospital, Paraná, Argentina
[13] Parque Sanatorium, Rosario, Argentina
[14] Sagrado Corazón Sanatorium, Buenos Aires, Argentina
[15] Muñiz Hospital, Buenos Aires, Argentina
[16] Regional Hospital of Rio Gallegos, Rio Gallegos, Argentina
[17] Boratti Sanatorium, Posadas, Argentina
[18] Argerich Hospital, Buenos Aires, Argentina
[19] Rosario Private Hospital, Rosario, Argentina
[20] Buenos Aires Italian Hospital, Infectious Diseases Section, Buenos Aires, Argentina
[21] Austral University Hospital, Pilar, Argentina
[22] Fernández Hospital, Buenos Aires, Argentina
[23] Center for Farmacoepidemiology, Karolinska Insitutet, Stockholm, Sweden

Introduction and Objectives: Selecting an empiric antibiotic treatment in patients with cirrhosis and spontaneous bacterial infections is challenging. It is of paramount importance to have local epidemiological data to maximize pathogen coverage while minimizing the unnecessary use of broad-spectrum antibiotics. This study aimed to describe the patterns of antibiotic resistance of spontaneous bacterial infections according to the site of acquisition.

Materials and Methods: Analysis of the multicenter prospective cohort study of cirrhotic patients with bacterial infections in Argentina and Uruguay (NCT03919032). Only culture-positive spontaneous infections were included in this study: spontaneous bacterial peritonitis (SBP), spontaneous bacterial empyema (SBE), and spontaneous bacteremia (SB). We estimated the proportion of infections that were sensitive to various antibiotics according to where the infection was acquired: community-acquired (CA), healthcare-associated (HCA), or nosocomial (NOS). Approximately 80% coverage is advisable for empiric treatments in stable patients and 90% for critically-ill patients.

Results: The main cohort included 472 patients, of whom 97 presented culture-positive spontaneous infections and were included: with 57 (59%) SBP, 34 (35%) SB, and 4 (6%) SBE. Regarding the site of acquisition, 43% were CA, 36% NOS, and 21% HCA. Gram-positive and negative bacteria were found in 53% and 47% of the infections. The most frequent isolations were Streptococcus spp (26%), E coli (20), K pneumonia (15%), S Aureus (10%), E. faecium (6%) and E. faecalis (4%). Multidrug-resistant organisms (MDROs) were isolated in 35% of the patients. As shown in the table, cefepime and ceftriaxone offer the most rational coverage for CA and HCA infections, and imipenem or meropenem for NOS infections. However, in critically-ill patients, broader-spectrum antibiotics are needed to achieve a coverage closer to 90% (table).

Conclusions: We present, for the first time in our region, evidence-based recommendations for the empirical treatment of spontaneous bacterial infections. Prior colonization and/or infections by MDROs might refine even more the antibiotic selection and should be explored.

Table: Proportion of isolations that were susceptible to selected antibiotics, according to the site of acquisition of the infection (n=97)

	Community Acquired (n=42)	HCA (n=20)	Nosocomial (n=35)
Ceftriaxone	71%	75%	58%
Cefepime	74%	80%	58%
Ceftazidime	40%	35%	33%
Piperacillin-tazobactam	79%	80%	60%
Carbapenems	81%	85%	76%
Imipenem or meropenem	73%	70%	65%
Imipenem or meropenem + Vancomycin	-	-	97%
Ertapenem	73%	70%	65%

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P-7 LIVER INJURY AFTER COVID-19 VACCINATION COMPARED TO POST-INFLUENZA VACCINES: RETROSPECTIVE COHORT STUDY

Marlene Padilla Lopez[1], Natalia Sobenko[1], Valeria Ines Aliperti[2], Vanina Cecilia Stanek[3], Maria Florencia Grande Ratti[4,5], Fernando Ezequiel Jabif[6], Marcelo Gabriel Vallone[6], Alejandra Villamil[1]

[1] Hepatology Section, Buenos Aires Italian Hospital, Buenos Aires, Argentina
[2] Epidemiology Section, Buenos Aires Italian Hospital, Buenos Aires, Argentina
[3] Infectology Section, Buenos Aires Italian Hospital, Buenos Aires, Argentina
[4] Internal Medicine Research Area, Buenos Aires Italian Hospital, Buenos Aires, Argentina
[5] Conicet, Assistant Researcher, Buenos Aires, Argentina
[6] Medical Clinic Service, Buenos Aires Italian Hospital, Buenos Aires, Argentina

Introduction and Objectives: Cases suggestive of immune-mediated acute hepatitis following SARS-CoV-2 vaccination have been reported. The risk of liver injury after Covid-19 vaccination is unknown. This study aimed to estimate the cumulative incidence of liver injury within 90 days after the Covid-19 vaccine, defined as the occurrence of AST and/or ALT increases at least two times the limit of normal or ALP increases at least x 2. To compare with an active comparator group (influenza vaccine).

Materials and Methods: Retrospective cohort study. We analyze a consecutive sample of adult patients vaccinated with Covid-19 vaccines (Sputnik, AstraZeneca/Oxford, Covishield, or Sinopharm) between January 1 and May 30, 2021, and a historical control group vaccinated with influenza between March 1 and July 30, 2019. Qualifying labs were collected as part of routine clinical care or the development of symptoms.

Results: From a total of 29,918 subjects who received the Covid-19 vaccine in 2021 and 24,753 who received the Influenza vaccine in 2019, 130 and 148 patients, respectively, were excluded because of previously altered liver function tests or known hepatic disease. Both groups were comparable in age (73 years old (IQR 65-80), p=0.125) and gender (67% were females). In the Influenza group were more dysmetabolic and immunosuppressed patients.

A total of 269 and 273 patients, respectively, presented altered liver function tests within 90 days post-vaccination. The cumulative incidence of liver injury was 4.6 per 1,000 (95% CI 3.9-5.5) for Covid-19 and 5.1 per 1,000 (95%CI 4.3-6.1) for Influenza (p=0.453). Although, two patients from the COVID group had a more severe injury, with hyperbilirubinemia, development of autoantibodies and requirement of steroids for disease control.