Disclosures: Giuseppe Cullaro – Ocelot Bio: Consultant, No, No; Novo Nordisk: Stock - publicly traded company (excluding mutual/index funds or pension plans), No, Yes; Eli Lilly: Stock - publicly traded company (excluding mutual/index funds or pension plans), No, Yes; Retro: Consultant, No, No;
Andres Duarte-Rojo – Axcella, Inc: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, Yes; Axcella, Inc: Consultant, No, Yes; Mallinckrodt: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, Yes; Echosens: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No;
Raymond T. Chung – BMS: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Boehringer: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; GSK: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Roche: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, Yes; Janssen: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Salix: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No;
Pratima Sharma: Pratima Sharma, Kavish R. Patidar, Eric Przybyszewski, Robert M Wilechansky, Douglas A. Simonetto, Nneka Ufere, Nabeel Wahid, Sumeet Asrani Disclosure information not available at the time of publication: Tianqi Ouyang, Justin M. Belcher, Kevin R. Regner, Shelsea A. St. Hillien, Jevon Robinson, Andrew Allegretti

12 | SURGICAL BILIARY DIVERSION IS ASSOCIATED WITH AN INCREASED RISK OF LIVER TRANSPLANTATION OR DEATH IN ALAGILLE SYNDROME★

Shannon M. Vandriel[1], Kathleen M. Loomes[2], David A. Piccoli[3], Elizabeth Rand[3], Li-Ting Li[4], Huiyu She[4], Jian-She Wang[4], Rima L. Fawaz[5], Silvia Nastasio[6], Henkjan J. Verkade[7], M. Kyle Jensen[8], Catalina Jaramillo[8], Nathalie Rock[9], Irena Jankowska[10], Piotr Czubkowski[10], Dorota Gliwicz-Miedzińska[10], Henry C. Lin[11], Deirdre A. Kelly[12], Catherine Larson-Nath[13], Florence Lacaille[14], Dominique Debray[15], Saul Karpen[16], Rene Romero[17], Cristina Molera Busoms[18], Étienne M. Sokal[19], Tanguy Demaret[19], Nehal M. El-Koofy[20], Mohamed A. Elmonem[20], Shikha S. Sundaram[21], Alexander Chaidez[21], Palaniswamy Karthikeyan[22], Wikrom Karnsakul[23], Winita Hardikar[24], Sahana Shankar[25], Ruben E. Quiros-Tejeira[26], Seema Alam[27], Pinar Bulut[28], Christina Hajinicolaou[29], Victorien M. Wolters[30], Zerrin Önal[31], Emmanuel M. Gonzales[32], Emmanuel Jacquemin[32], Jérôme Bouligand[33], Lorenzo D'Antiga[34], Emanuele Nicastro[35], Noelle H. Ebel[36], Jeffrey A. Feinstein[37], Björn Fischler[38], Henrik Arnell[38], Susan Siew[39], Michael O. Stormon[39], Kyung Mo Kim[40], Seak Hee Oh[40], Amin J. Roberts[41], Helen M. Evans[41], Maria Camila Sanchez[42], Maria Lorena Cavalieri[42], Way Seah Lee[43], Chatmanee Lertudomphonwanit[44], Ryan T. Fischer[45], Orith Waisbourd-Zinman[46], James E. Squires[47], Cigdem Arikan[48], Jesus Quintero Bernabeu[49,50], Mureo Kasahara[51], Elisa Carvalho[52], Cristina Targa Ferreira[53], Pamela L. Valentino[54], Giuseppe Indolfi[55], John Eshun[56], Pier Luigi Calvo[57], Dev M. Desai[58], Aglaia Zellos[59], Antal Dezsőfi[60], Sabina Wiecek[61], Gabriella Nebbia[62], Raquel Borges Pinto[63], Maria Rogalidou[64], María Legarda Tamara[65], Andreanne N. Zizzo[66], Jennifer Garcia[67], Kathleen B. Schwarz[68], Niviann Blondet[69], Marisa Beretta[70], Thomas Damgaard Sandahl[71], Jernej Brecelj[72], Cristina Gonçalves[73,74], Eberhard Lurz[75], Ermelinda Santos-Silva[76], Nanda Kerkar[77], Quais Mujawar[78], Christos Tzivinikos[79], Uzma Shah[80], Carolina Jimenez-Rivera[81], Jesus M. Banales[82], Richard J. Thompson[83], Bettina E. E. Hansen[84,85], Binita M. Kamath[86] and The Global ALagille Alliance (GALA) Study Group, (1)The Hospital for Sick Children and the University of Toronto, (2)The Children's Hospital of Philadelphia and the University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, (3)The Children's Hospital of Philadelphia and the University of Pennsylvania Perelman School of Medicine, (4)Children's Hospital of Fudan University, the Center for Pediatric Liver Diseases, (5)Yale University School of Medicine, New Haven, CT, (6)Boston Children's Hospital and Harvard Medical School, Boston, MA, (7)University Medical

Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient

Center Groningen, (8)University of Utah, Primary Children's Hospital, (9)Swiss Pediatric Liver Center, University Hospitals Geneva and University of Geneva, (10)The Children's Memorial Health Institute, (11)Oregon Health and Science University, (12)Birmingham Women's & Children's Hospital NHS Trust and University of Birmingham, (13)University of Minnesota, (14)Necker-Enfants Malades Hospital, University of Paris, (15) National Reference Centre for Rare Pediatric Liver Diseases (Biliary Atresia and Genetic Cholestasis), Filfoie, ERN RARE LIVER, Necker-Enfants Malades Hospital, University of Paris, (16)Children's Healthcare of Atlanta, (17)Children's Healthcare of Atlanta & Emory University School of Medicine, Atlanta, GA, (18)Hospital Sant Joan De Déu, (19)Cliniques Universitaires Saint-Luc, (20)Cairo University, (21)Children's Hospital of Colorado and University of Colorado School of Medicine, (22)Leeds Teaching Hospitals NHS Trust, Leeds Children's Hospital, (23)Johns Hopkins University School of Medicine, (24)Royal Children's Hospital, (25) Mazumdar Shaw Medical Center, Narayana Health, (26) Children's Hospital & Medical Center and University of Nebraska Medical Center, (27)Institute of Liver and Biliary Sciences, (28)Phoenix Children's Hospital, (29)Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, (30)University Medical Center Utrecht, (31)Istanbul University Istanbul Medical Faculty, (32) Centre De Référence De l'Atrésie Des Voies Biliaires Et Des Cholestases Génétiques (AVB-CG), Fsmr Filfoie, ERN RARE LIVER, Hôpital Bicêtre, AP-HP, Faculté De Médecine Paris-Saclay, Le Kremlin-Bicêtre, and Inserm U1193, Hépatinov, Université Paris-Saclay, (33)Hôpitaux Universitaires Paris-Saclay, Assistance Publique-Hôpitaux De Paris, Centre Hospitalier Universitaire De Bicêtre, (34)Ospedale Papa Giovanni XXIII, Bergamo, Italy, (35)Ospedale Papa Giovanni XXIII, (36)Stanford University School of Medicine, (37)Stanford University School of Medicine, Lucile Packard Children's Hospital, (38)Astrid Lindgren Children's Hospital, Karolinska University Hospital and Department of Women's and Children's Health, (39)The Children's Hospital at Westmead, (40)University of Ulsan College of Medicine, Asan Medical Center Children's Hospital, (41)Starship Child Health, (42)Hospital Italiano Buenos Aires, (43) University of Malaya, (44)Ramathibodi Hospital Mahidol University, (45)Children's Mercy Kansas City, (46) Schneider Children's Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, (47) UPMC Children's Hospital of Pittsburgh, (48)Koc University School of Medicine, (49)Biodonostia Health Research Institute – Donostia University Hospital –, University of the Basque Country (UPV/EHU), (50) Hospital Universiatri Vall D'hebron, (51)Organ Transplantation Center, National Center for Child Health and Development, (52)Hospital De Base Do Distrito Federal, Hospital Da Criança De Brasília, Centro Universitário De Brasília, (53)Hospital Da Criança Santo Antônio, Universidade Federal De Ciências Da Saúde De Porto Alegre, Complexo Hospitalar Santa Casa, (54) Seattle Children's Hospital, (55)University of Florence and Meyer Children's University Hospital, (56)Le Bonheur Children's Hospital and the University of Tennessee Health Science Center, (57)Regina Margherita Children's Hospital, Azienda Ospedaliera-Universitaria Citta' Della Salute e Della Scienza, (58)Children's Health – Children's Medical Center, (59)Aghia Sophia Children's Hospital, National and Kapodistrian University of Athens, Athens, Greece, (60)Semmelweis University, (61)Medical University of Silesia in Katowice, (62)Fondazione Irccs Ca' Granda Ospedale Maggiore Policlinico, (63)Hospital Da Criança Conceição Do Grupo Hospitalar Conceição, (64)Agia Sofia Children's Hospital, University of Athens, (65)Cruces University Hospital, (66)Children's Hospital, London Health Sciences Centre, Western University, (67) Miami Transplant Institute, University of Miami, (68) University of California San Diego, Rady Children's Hospital San Diego, (69)Seattle Children's Hospital, Seattle, (70)Wits Donald Gordon Medical Centre, University of the Witwatersrand, (71)Aarhus University, (72)University Medical Center Ljubljana, (73)European Reference Network on Hepatological Diseases (ERN RARE-LIVER), (74)Pediatric Gastroenterology/ Hepatology Center Lisbon, (75)Von Hauner Children's Hospital, University Hospital, Lmu Munich, (76)Centro Hospitalar Universitário De Santo António, (77)University of Rochester Medical Center, (78)University of Manitoba, (79)Al Jalila Children's Specialty Hospital, Mohammed Bin Rashid University of Medicine and Health Sciences, (80)Harvard Medical School, Massachusetts General Hospital for Children, Royal Oak, MI, (81)Children's Hospital of Eastern Ontario, (82)Biodonostia Health Research Institute - Donostia University Hospital, Universidad Del País Vasco (UPV/EHU), Centro De Investigación Biomédica En Red De Enfermedades Hepáticas y Digestivas (CIBERehd), (83)Institute of Liver Studies, King's College London, London, United Kingdom, (84)Toronto General Hospital University Health Network, (85)Institute of Health Policy, Management and Evaluation, (86)Division of Gastroenterology, Hepatology and Nutrition, the Hospital for Sick Children, Toronto, ON, Canada

Background: Alagille syndrome (ALGS) is an inherited liver disorder dominated by high γ-glutamyltransferase (GGT) cholestasis. Previous studies have demonstrated limited efficacy of surgical interruption of the enterohepatic circulation in ALGS, with varying degrees of improvement in pruritus and xanthomas. Utilizing the GALA database, we sought to evaluate whether surgical biliary diversion (SBD) alters the natural history of liver disease. **Methods:** Multicenter retrospective analysis of children with clinically and/or genetically confirmed ALGS. Laboratory data were collected preoperatively (−6 to 0 mo) and postoperatively (3 to 12 mo). Paired

Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient

sample t-tests were used to compare continuous variables, and McNemar's tests were used to compare binominal variables pre-and postoperatively. Receiver operating characteristic (ROC) curves were used to determine the optimal laboratory threshold for predicting native liver survival (NLS) following SBD. Cox proportional hazards models were constructed to determine NLS in ALGS-SBD patients. **Results:** Of 1673 ALGS patients, 3.7% (n = 62; 54.8% male) underwent SBD from 26 centers. The median age of SBD was 2.5 years (IQR 1.8 – 4.4). Most ALGS patients underwent a partial external biliary diversion (54.8%, n = 34), followed by a partial internal biliary diversion in 19.4% (n = 12) and ileal exclusion in 12.9% (n = 8). 100% (n = 62) of patients reported pruritus at the time of SBD, and 51.4% (n = 18/35) reported xanthomas. ALGS-SBD patients had a 2.5-fold greater risk of liver transplantation (LT) or death (95% CI 1.6 – 3.9; $p < 0.01$). Following SBD, there were no significant differences in total bilirubin (TB) (8.8 vs. 9.1 mg/dL, $p = 0.51$), ALT (159.5 vs. 189.7 U/L, $p = 0.38$), GGT (495.0 vs. 459.5 U/L, $p = 0.21$) or cholesterol (493.0 vs. 414.6 mg/dL, $p = 0.21$). Availability of serum bile acids (SBA) was limited; however, in 10 patients with SBAs pre-and postoperatively, there was a significant reduction following SBD (257.2 vs. 97.7 µmol, $p = 0.05$). Among these patients, 80% achieved NLS. TB levels < 4.0 mg/dL following SBD were significantly associated with longer NLS ($p = 0.05$; AUC TB, 0.784; sensitivity, 94%; specificity, 52%). There were no significant improvements in pruritus (100% vs. 91.7%, $p = 0.25$) or xanthomas (51.4% vs. 45.1%, $p = 0.67$) after SBD. **Conclusion:** SBD in ALGS was associated with an increased risk of LT or death. SBD may be a marker for severe hepatic phenotype in ALGS. In contrast to PFIC, SBD does not appear to improve NLS in ALGS. However, in a subset of ALGS-SBD patients with SBA, higher rates of NLS were noted in those who experienced a substantial decrease in post-operative SBA levels. These findings also indicate that post-SBD TB levels can be used as a biomarker for NLS. In an era of ileal bile acid transporter (IBAT) inhibitors, SBD may become obsolete in ALGS.

Disclosures: Shannon M. Vandriel – Mirum Pharmaceuticals: Consultant, No, No;
Kathleen M. Loomes – Albireo: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Albireo: Consultant, No, No; Mirum: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Mirum: Consultant, No, No; Travere Therapeutics: Consultant, No, No;
Henkjan J. Verkade – Ausnutria BV, Albireo, Danone Nutricia Research, Intercept, Mirum, Orphalan, and Vivet: Consultant, No, No;
Saul Karpen – Albireo/Ipsen: Consultant, No, No; Mirum: Consultant, No, No; HemoShear: Consultant, No, No; Intercept: Consultant, No, No;
Wikrom Karnsakul – Albireo: Consultant, No, No; Mirum: Consultant, No, No; Travere Therapeutics: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No;
Emmanuel M. Gonzales – Laboratoires C.T.R.S., Mirum, Vivet Therapeutics, and Albireo: Consultant, No, No;
Lorenzo D'Antiga – Albireo, Alexion, Mirum, Selecta, Vivet, Spark, Tome, and Genespire: Consultant, No, No;
Ryan T. Fischer – Albireo and Mirum: Consultant, No, No;
Giuseppe Indolfi – Albireo and Mirum: Consultant, No, No;
Kathleen B. Schwarz – Gilead Sciences, Inc.: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), Yes, No; Sarepta: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; UpToDate: Consultant, No, No; Albireo: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No;
Thomas Damgaard Sandahl – Arbomed: Consultant, No, No; Prime: Consultant, No, No; Alexion: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Univar: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No; Orphalan: Speaking and Teaching, Yes, No; Vivet Therapeutics: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No;
Richard J. Thompson – Generation Bio: Stock – privately held company (individual stocks and stock options), No, No; Generation Bio: Consultant, No, No; Mirum Pharma: Consultant, Yes, No; Albireo Phamra: Consultant, Yes, No; Rectify Pharma: Consultant, No, No; Rectify Pharma: Stock – privately held company (individual stocks and stock options), No, No; Alnylam: Consultant, No, No;

Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient

Binita M. Kamath – Albireo, Mirum, and Audentes: Consultant, No, No; Albireo and Mirum: Grant/Research Support (research funding from ineligible companies should be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds), No, No;
The following people have nothing to disclose: Silvia Nastasio, Deirdre A. Kelly, Étienne M. Sokal, Shikha S. Sundaram, Palaniswamy Karthikeyan, Winita Hardikar, Seema Alam, Emanuele Nicastro, Way Seah Lee, James E. Squires
Disclosure information not available at the time of publication: David A. Piccoli, Elizabeth Rand, Li-Ting Li, Huiyu She, Jian-She Wang, Rima L. Fawaz, M. Kyle Jensen, Catalina Jaramillo, Nathalie Rock, Irena Jankowska, Piotr Czubkowski, Dorota Gliwicz-Miedzińska, Henry C. Lin, Catherine Larson-Nath, Florence Lacaille, Dominique Debray, Rene Romero, Cristina Molera Busoms, Tanguy Demaret, Nehal M. El-Koofy, Mohamed A. Elmonem, Alexander Chaidez, Sahana Shankar, Ruben E. Quiros-Tejeira, Pinar Bulut, Christina Hajinicolaou, Victorien M. Wolters, Zerrin Önal, Emmanuel Jacquemin, Jérôme Bouligand, Noelle H. Ebel, Jeffrey A. Feinstein, Björn Fischler, Henrik Arnell, Susan Siew, Michael O. Stormon, Kyung Mo Kim, Seak Hee Oh, Amin J. Roberts, Helen M. Evans, Maria Camila Sanchez, Maria Lorena Cavalieri, Chatmanee Lertudomphonwanit, Orith Waisbourd-Zinman, Cigdem Arikan, Jesus Quintero Bernabeu, Mureo Kasahara, Elisa Carvalho, Cristina Targa Ferreira, Pamela L. Valentino, John Eshun, Pier Luigi Calvo, Dev M. Desai, Aglaia Zellos, Antal Dezsőfi, Sabina Wiecek, Gabriella Nebbia, Raquel Borges Pinto, Maria Rogalidou, María Legarda Tamara, Andreanne N. Zizzo, Jennifer Garcia, Niviann Blondet, Marisa Beretta, Jernej Brecelj, Cristina Gonçalves, Eberhard Lurz, Ermelinda Santos-Silva, Nanda Kerkar, Quais Mujawar, Christos Tzivinikos, Uzma Shah, Carolina Jimenez-Rivera, Jesus M. Banales, Bettina E. E. Hansen

13 | MiR150 DEFICIENCY IN MACROPHAGES IMPROVES ALCOHOL INDUCED HEPATIC STEATOSIS VIA TRANSFERRING THYROID HORMONE RECEPTOR B ENRICHED EVS TARGETING ADIPOSE TISSUE-LIVER AXIS: THYROID HORMONE RECEPTOR B, A PROMISING THERAPEUTIC TARGET IN ALD

Jing Ma[1], Zhihong Yang[1], Nazmul Huda[1], Yanchao Jiang[1], Hui Gao[1], Il-Man Kim[2] and Suthat Liangpunsakul[3,4], (1)Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, in, (2)Department of Anatomy, Cell Biology and Physiology and Wells Center for Pediatric Research Krannert Institute of Cardiology, Indiana University School of Medicine, Indianapolis, IN, (3)Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, (4)Roudebush Veterans Administration Medical Center, Indianapolis, in

Background: The mechanisms of alcoholic hepatitis (AH) are complex and involve the cross talk between organ systems. MiR150, one of the most abundant microRNAs in immune cells, has been implicated in various liver diseases, but its role in AH pathogenesis remains unclear. We aimed to determine the role of the miR150-mediated immune cells-liver axis in AH pathogenesis. **Methods:** MiR150 levels were measured in serum (S) and liver (L) samples from healthy controls (HC, N = 15 for S, 5 for L), heavy drinkers (HD, N = 17 for S), and AH (N = 65 for S, 5 for L) patients. Correlations between miR150 levels, MELD scores, and serum transaminases were analyzed. Global *miR150* knockout mice (*miR150*$^{-/-}$) and myeloid cell-specific miR150 knockout mice (*miR150*$^{Lyz-/-}$) were generated to assess the function of *miR150* in a chronic plus binge alcohol feeding model. **Results:** Serum and hepatic miR150 level were significantly reduced in AH patients compared to HC. Serum miR150 level negatively correlated with serum AST, but not with MELD score. The level of hepatic miR150 was markedly reduced in mice fed with chronic plus binge alcohol model. Genetic deletion of *miR150* attenuated ethanol-induced liver injury and steatosis, as evidenced by the reduction of ALT, and hepatic triglyceride level. Fatty acid β-oxidation-associated proteins, including PPARα, PGC1α, UCP2, CPT1A, and hormone sensitive lipase, were highly upregulated in both liver and WAT of ethanol-fed *miR150*$^{-/-}$ mice compared to WT mice. To understand how miR150 is involved in alcohol-induced steatosis, we observed a significant increase in the expression of the miR150 target gene, thyroid hormone receptor β (THRB), in the liver, WAT, and circulating extracellular vesicles (EVs). MiR150 deletion contributed to a significant increase in THRB in macrophages and macrophage-derived EVs. Ethanol fed myeloid cell-specific miR150 knockout mice also exhibited elevated THRB levels in the liver, WAT, and circulating EVs. The level of THRB was also increased in the serum EVs of AH patients compared with HC. Deletion of *miR150* in myeloid cells ameliorated ethanol-induced liver steatosis, with upregulated expression of PPARα, UCP2, and CPT1A observed in both the liver and WAT. For the translational aspect of our results, we found that mice treated with THRB agonist, Resmetirom, significantly reduced ethanol-induced hepatic steatosis. The role of miR-150 and ALD pathogenesis is illustrated in the Figure. **Conclusion:** Macrophage-derived miR150 plays a crucial role in controlling the progression of steatosis through the release of THRB-containing EVs. MiR-150 and its target (THRB) may represent potential therapeutic targets for ALD.

Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient