

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Hepatobiliary Cancers: Pathobiology and Translational Advances (EK29)

Scientific Organizers: Alphonse E. Sirica, Gregory J. Gores and Lopa Mishra

Supported by the Directors' Fund

Fatty Liver Disease and Multi-System Complications (EK28)

Scientific Organizers: Jay D. Horton, Morris J. Birnbaum and Hannele Yki-Järvinen

March 22-24, 2021 • Virtual at your computer

Sponsored by Merck & Co., Inc. and Novo Nordisk A/S

MONDAY, MARCH 22

Welcoming Remarks and Keynote Session (Joint) (8am Denver/Mountain Time Start)

***Jay D. Horton**, University of Texas Southwestern Medical Center, USA

***Alphonse E. Sirica**, Virginia Commonwealth University, USA

Helen H. Hobbs, University of Texas Southwestern Medical Center, USA

[NOT AVAILABLE ON DEMAND] *PNPLA3's Role in NAFLD*

Hashem B. El-Serag, Baylor College of Medicine, USA
Changing Epidemiological Trends in Non-Alcoholic Fatty Liver Disease versus Viral-Associated Hepatobiliary Cancers

Non-Alcoholic Fatty Liver Disease, Liver Inflammation and Fibrogenesis in the Pathogenesis of Hepatobiliary Cancers (Joint) (9:10am Denver/Mountain Time Start)

***Jay D. Horton**, University of Texas Southwestern Medical Center, USA

***Alphonse E. Sirica**, Virginia Commonwealth University, USA

Lopa Mishra, George Washington University, USA
A TGF- β -ALDH2 Axis in Obesity, Metabolic Syndrome, and HCC

Maria Rescigno, Humanitas University, Italy
The Gut-Liver Axis in Liver Cancer Risk Conditions

Daniel A. Heller, Memorial Sloan Kettering Cancer Center, USA
Lipid Dysregulation in Inflammation, NASH, and Cancer

Juan R. Sanabria, Marshall University/Case Western Reserve University, USA
Short Talk: The α 1-Na/K-ATPase/Src-p/PI3K Pathway Modulates the Survivin-SMAC Apoptotic "Switch" in NASH Related Hepatocellular Carcinoma: A Translational Study

Career Roundtable (Joint) (12:30pm Denver/Mountain Time Start)

Kendra K. Bence, Pfizer Inc., USA

Augusto Villanueva Rodriguez, Icahn School of Medicine at Mount Sinai, USA

Xin Wei Wang, NCI, National Institutes of Health, USA

Poster Session 1 (Joint) (2pm Denver/Mountain Time Start)

Tumor Microenvironment and Hepatobiliary Cancers (3pm Denver/Mountain Time Start) (EK29)

***Lopa Mishra**, George Washington University, USA

Silvia Affo, Columbia University, USA
Role of Cancer Associated Fibroblasts in Cholangiocarcinoma

Amaia Lujambio, Icahn School of Medicine at Mount Sinai, USA
Mechanisms of Immune Escape in Hepatocellular Carcinoma

Alphonse E. Sirica, Virginia Commonwealth University, USA
The Desmoplastic Reaction and Intrahepatic Cholangiocarcinoma Progression: CAFs, Select Molecular Drivers, and Prognostic Implications

***Gregory J. Gores**, Mayo Clinic, USA
Targeting the Tumor Microenvironment for Cholangiocarcinoma Therapy

Yuhua Xue, University of Pittsburgh, USA
Short Talk: p-Ezrin (Thr567) Synergizes with Akt Signaling to Accelerate Yap Mediated Cholangiocarcinogenesis but Correlates with a Favorable Prognosis in Human Intrahepatic Cholangiocarcinoma (ICC) Patients

Wen-Xing Ding, University of Kansas Medical Center, USA
Short Talk: SQSTM1/p62 Inhibits whereas Nrf2 Promotes Tumorigenesis by Inducing Cell Population Remodeling and Metabolic Reprogramming in Mouse Livers with mTORC1 Activation and Defective Autophagy

Haichuan Wang, University of California, San Francisco, USA
Short Talk: Requirement of Hippo Signaling Cascade during AXIN1 Mutation Driven Hepatocarcinogenesis

Juan Pablo Unfried, University of Navarra, Spain
Short Talk: Long Non-Coding RNA NIHCOLE Promotes the DNA Damage Repair of Hepatocellular Carcinoma Cells

Genetics of NAFLD (3pm Denver/Mountain Time Start) (EK28)

***Jay D. Horton**, University of Texas Southwestern Medical Center, USA

***Henry N. Ginsberg**, Columbia University Vagelos College of Physicians and Surgeons, USA

Elizabeth K. Speliotes, University of Michigan, USA
Use of GWAS to Identify SNPs Associated with NAFLD

Noura S. Abul-Husn, Icahn School of Medicine at Mount Sinai, USA
Genomics and Liver Disease in Diverse Populations: From Biobanks to Patients

Karthickeyan Chella Krishnan, University of Cincinnati, USA
Short Talk: Mouse and Human Population Studies Revealed Sex-Specific Roles of Liver Pyruvate Kinase in Promoting NAFLD/NASH

Mohammad Kabbani, Rockefeller University, USA
Short Talk: Human Hepatocyte PNPLA3 148M Exacerbates Rapid Non-Alcoholic Fatty Liver Disease Development in Chimeric Mice

Ester Dohnalkova, Mayo Clinic, USA
Short Talk: Hepatocyte-Specific Deletion of ROCK1 Prevents Liver Inflammation and Fibrosis in Murine Nonalcoholic Steatohepatitis

Neil A. Youngson, Institute of Hepatology, UK
Short Talk: Acetyl-CoA Metabolism Drives Epigenome Change in Steatosis Leading to Widespread Abnormal Transcription and DNA Damage

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NAFLD and CVD (5:10pm Denver/Mountain Time Start) (EK28)

***Henry N. Ginsberg**, Columbia University Vagelos College of Physicians and Surgeons, USA
The AAA Atpase Torsin A, a New, Potent Player in VLDL Secretion, NAFL, and NASH

***Jay D. Horton**, University of Texas Southwestern Medical Center, USA
Molecular Mediators of NAFLD and Hyperlipidemia

TUESDAY, MARCH 23

Hepatobiliary Cancer Biomarkers and Molecular Subtypes (8am Denver/Mountain Time Start) (EK29)

***Gregory J. Gores**, Mayo Clinic, USA

***Alphonse E. Sirica**, Virginia Commonwealth University, USA

Yujin Hoshida, UT Southwestern Medical Center, USA
Liver Cancer Risk-Predictive Molecular Biomarkers Specific to Clinico-Epidemiological Contexts

Augusto Villanueva Rodriguez, Icahn School of Medicine at Mount Sinai, USA
Liquid Biopsy in Hepatobiliary Cancers

Jessica Zucman-Rossi, University Paris Descartes-HEGP, France
Mechanisms of Liver Carcinogenesis Define Specific Molecular and Phenotypic HCC Subgroups

Jesper Bøje Andersen, University of Copenhagen, Denmark
Defining Distinct Subtypes of Intrahepatic Cholangiocarcinoma by Molecular Profiling: Diagnostic, Prognostic, and Therapeutic Applications

Robert F. Schwabe, Columbia University, USA
Discovery of Subgroup-Specific HCC Master Regulators by Systems Biology Approaches

Kerstin Seidel, Genentech, USA
Short Talk: Notch Inhibition Regresses Progenitor-Like HCCs by Inducing Hepatocyte Differentiation through Controlling C/EBP α Expression and HNF4 α Activity

Sungjin Ko, University of Pittsburgh, USA
Short Talk: NOTCH-YAP1/TEAD-DNMT1 Axis Drives Hepatocyte Reprogramming into Intrahepatic Cholangiocarcinoma

Role of Lipids in NAFLD (8am Denver/Mountain Time Start) (EK28)

Mitchell A. Lazar, Perelman School of Medicine, University of Pennsylvania, USA
Circadian Contributions to NAFLD

***Catherine Postic**, INSERM Institut Cochin, France
Altered Insulin Signaling and Glucose Toxicity in NAFLD

***Hannele Yki-Järvinen**, University of Helsinki, Finland
Effects of Genetic Risk Factors for NAFLD on Hepatic Lipid Metabolism

Eran Elinav, Weizmann Institute of Science, Israel
Host Microbiome Interactions in Health and Disease

HongMin Ni, University of Kansas Medical Center, USA
Short Talk: Lack of VMP1 Impairs Hepatic Lipoprotein Secretion and Promotes Nonalcoholic Steatohepatitis in Mice

Joanne Hsieh, Columbia University, USA
Short Talk: Sexually Dimorphic Mechanisms of Action of TTC39B in Hepatic Lipogenic Gene Expression

Xiao-Wei Chen, Peking University, China
Short Talk: An ER Lipid Scramblase (ELS) Safeguards Lipoprotein Biogenesis and Lipid Homeostasis

Zhaoyue Zhang, Princeton University, USA
Short Talk: Serine Catabolism Generates NADPH to Support Hepatic Lipogenesis

Meet the Editors (Joint) (12:30pm Denver/Mountain Time Start)

Elena Bellafante, Med - Cell Press, UK

Francesco Giovinazzo, Frontiers Journals, Italy

Xin (Cindy) Sun, Journal of Experimental Medicine at Rockefeller University Press, USA

Poster Session 2 (Joint) (2pm Denver/Mountain Time Start)

Genomics, Molecular Heterogeneity, and Precision Medicine in Hepatobiliary Cancers (3pm Denver/Mountain Time Start) (EK29)

***Lopa Mishra**, George Washington University, USA

***Alphonse E. Sirica**, Virginia Commonwealth University, USA

Irene Oi Lin Ng, University of Hong Kong, Hong Kong
Molecular Biomarkers in Hepatocellular Carcinoma

Xin Wei Wang, NCI, National Institutes of Health, USA
Causes and Functional Intricacies of Intertumor and Intratumor Heterogeneity in Primary Hepatobiliary Cancers

Renumathy Dhanasekaran, Stanford University, USA
Implications of Genetic Heterogeneity in Hepatocellular Carcinoma (HCC)

Teh Bin Tean, Duke-NUS Medical School, Singapore
Genomic and Epigenomic Studies of Cholangiocarcinoma and their Clinical Implications

Josep Llovet, Icahn School of Medicine at Mount Sinai, USA
Immune Therapies for HCC: is NASH-HCC Responding Different

Bangyan Stiles, University of Southern California, USA
Short Talk: Heterogeneous Liver Cancer Development Promoted by PTEN Regulated beta-Catenin and SOX9 Signal

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Chungui Xu, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospi, China

Short Talk: Gender Distinct in Genomic Features of HBV-Related Hepatocellular Carcinoma

Pathways to NASH (3pm Denver/Mountain Time Start) (EK28)

***Morris J. Birnbaum**, Pfizer Inc., USA

Mark A. McNiven, Mayo Clinic, USA

Lipid Droplet Formation and Lipophagy in Fatty Liver Disease

***Tobias Walther**, Harvard/HHMI, USA

Lipid Droplet Biology in NAFLD

Annelise Poss, University of Utah, USA

Short Talk: Ceramides as Mediators of Endoplasmic Reticulum Stress in NASH

Cholsoon Jang, University of California, Irvine, USA

Short Talk: The Small Intestine Shields the Liver from Fructose-Induced Steatosis

Kahealani Uehara, University of Pennsylvania, USA

Short Talk: Activation of Hepatic mTORC1 Protects Against NASH via Dual Regulation of VLDL- TAG Secretion and De Novo Lipogenesis

Sabine Daemen, Washington University in St. Louis, USA

Short Talk: The Hepatic Crown-like Structure in NASH: A Nexus between Monocyte-Derived Macrophages, Hepatic Stellate Cells, and Tissue Fibrosis

Samar Ibrahim, Mayo Clinic, USA

Short Talk: Lipid-Induced Endothelial Vascular Cell Adhesion Molecule 1 Promotes Nonalcoholic Steatohepatitis Pathogenesis

Wenke Jonas, German Institute of Human Nutrition, Germany

Short Talk: Immunity-Related GTPase IFGGA2 Induces Degradation of Hepatic Lipids by Lipophagy

WEDNESDAY, MARCH 24

Advances in Molecular and Immune Targeting of Hepatobiliary Cancers (8am Denver/Mountain Time Start) (EK29)

***Gregory J. Gores**, Mayo Clinic, USA

***Lopa Mishra**, George Washington University, USA

Tim F. Greten, NCI, National Institutes of Health, USA

Immunotherapies for Hepatobiliary Cancers: Current Status and Future Perspectives

R. Kate Kelley, University of California, San Francisco, USA

Developing Clinical Trials of Novel Therapeutic Agents and Treatment Combinations for Intrahepatic Cholangiocarcinoma

Bruno Sangro, Clinica Universidad de Navarra, Spain

Targeted Agent and Immune-Based Therapies for Hepatocellular Carcinoma

Miryam Müller, CRUK Beatson Institute, UK

Short Talk: Identifying Effective Subtype-Specific Treatment Responses in Hepatocellular Carcinoma in Genetically Engineered Mouse Models

Jonathan M. Hernandez, NCI, National Institutes of Health, USA

Short Talk: A Cytosolic Complex Between the Nuclear Export Protein XPO7 and Sterile 20-like Kinase (SLK) Drives Cholangiocarcinoma, and Reveals a Translatable Therapeutic Target

Massimiliano Cadamuro, University of Padua, Italy

Short Talk: Inhibition of YAP Activation Induces Cell Senescence and Autophagy while Blocking Cell Proliferation in Cholangiocarcinoma (CCA)

Man Hsin Cindy Hung, NCI, National Institutes of Health, USA

Short Talk: Tumor Methionine Metabolism Drives T-Cell Exhaustion in Hepatocellular Carcinoma

Andreas Prokesch, Medical University Graz, Austria

Short Talk: Overcoming HCC Drug Resistance by Targeting Metabolic Flexibility Conferred by p53

Emerging Therapies for NASH (8am Denver/Mountain Time Start) (EK28)

***Hannele Yki-Järvinen**, University of Helsinki, Finland

***Morris J. Birnbaum**, Pfizer Inc., USA

DGAT2 Inhibition for NASH

Chuhan Chung, Gilead Sciences, USA

Combination Therapies for NASH Cirrhosis

Greg Steinberg, McMaster University, Canada

Role of ATP Citrate Lyase (ACLY) in NASH and HCC

Kendra K. Bence, Pfizer Inc., USA

Inhibition of Fructose Metabolism for the Treatment of NAFLD

Lei Ling, NGM Biopharmaceuticals, USA

Therapeutic FGF19 in Non-Alcoholic Steatohepatitis

Aimee L. Edinger, University of California, Irvine, USA

Short Talk: A Drug-Like Sphingolipid Opposes Mitochondrial Fragmentation and Corrects the Metabolic Sequelae of Obesity

Brian Rady, Janssen R&D, USA

Short Talk: Inhibition of Hepatocyte Inflammasome Improves Features of NASH in foz/foz Mice

Haresh Sajiir, University of Queensland - Mater Research Institute, Australia

Short Talk: Development of Liver-Targeted Interleukin-22 for Fatty Liver Disease

Madhulika Tripathi, Duke-NUS Medical School Singapore, Singapore

Short Talk: HHcy is a Feature and Mediator of NASH that Permits B12 and Folate to be an Effective Therapy for NASH

Closing Remarks (Organizers) (10:55am Denver/Mountain Time Start) (EK29)

Closing Remarks (10:50am Denver/Mountain Time Start) (EK28)

Networking Lounge (Joint) (11am Denver/Mountain Time Start)