

Abstracts of papers presented
at the 2021 Cold Spring Harbor Asia Conference (*virtual*)

LIVER DEVELOPMENT, METABOLISM, DISEASE & CANCER

December 7–December 10, 2021

Arranged by

Gen-Sheng Feng, *University of California San Diego*

Lijian Hui, *Shanghai Institute of Biological Sciences*

Eli Pikarsky, *The Hebrew University of Jerusalem*

Jessica Zucman-Rossi, *Université de Paris*



Cold Spring Harbor Conferences Asia
Cold Spring Harbor Laboratory



LIVER DEVELOPMENT, METABOLISM, DISEASE & CANCER
Virtual Meeting

Tuesday, December 7 – Friday, December 10, 2021

Tuesday	9:00 am – 9:45 am	<i>Opening Remarks</i> Keynote Lecture: Ken Zaret
Tuesday	9:45 am – 12:00 pm	1 Liver Development
Tuesday	7:00 pm – 10:00 pm	2 iPS Cells and Liver Disorders
Wednesday	9:00 am – 9:40 am	Keynote Lecture: Gerald Shulman
Wednesday	9:45 am – 12:00 pm	3 Liver Metabolism and Metabolic Disease
Wednesday	7:00 pm – 10:00 pm	4 Liver Diseases and Cancer
Thursday	9:00 am – 12:00 pm	5 Liver Injuries and Cancer
Thursday	7:00 pm – 10:00 pm	6 Liver Diseases and Immunology
Friday	9:00 am – 11:00 am	7 HCC, Basic and Translational Research
Friday	11:00 am – 12:00 pm	<i>Happy Hour</i>

Times listed are **UTC/GMT+8** (*Beijing time*)

[Time Zone Converter](#)

PROGRAM

TUESDAY, December 7—9:00 AM ([UTC/GMT+8](#))

Opening Remarks by Organizers

KEYNOTE SPEAKER

Introduction by: Gen-Sheng Feng, University of California San Diego

Overcoming chromatin barriers in liver development and reprogramming

Ken Zaret, Megan Frederick, Edgar Luzete Monteiro, Ryan McCarthy, Kelsey Kaeding, Jingchao Zhang, Kenji Ito [30'+10']
Presenter affiliation: University of Pennsylvania, Philadelphia, Pennsylvania. 1

TUESDAY, December 7—9:45 AM ([UTC/GMT+8](#))

SESSION 1 LIVER DEVELOPMENT

Chairpersons: **Pamela Hoodless**, University of British Columbia, Vancouver, Canada
Stephen Duncan, Medical University of South Carolina, Charleston, South Carolina, USA

Cell diversity during hepatic specification

Pamela A. Hoodless [20'+5']
Presenter affiliation: BC Cancer, Vancouver, Canada; University of British Columbia, Vancouver, Canada. 2

Somatic mosaicism reveals adaptive pathways in chronic liver disease

Hao Zhu [20'+5']
Presenter affiliation: UT Southwestern, Dallas, Texas. 3

MiR-125b loss activated HIF1 α /pAKT loop, leading to trans-arterial chemoembolization resistance in hepatocellular carcinoma

Junfang Ji [8'+2']
Presenter affiliation: Zhejiang University, Hangzhou, China. 4

Break

A human iPSC-derived hepatocyte screen identifies a new class of molecules that inhibit production of apolipoprotein B

Stephen A. Duncan [20'+5']

Presenter affiliation: Medical University of South Carolina, Charleston, South Carolina.

5

Hepatocyte plasticity

Ashley E. Cast, Kari A. Huppert, Holger Willenbring, Stacey S. Huppert [20'+5']

Presenter affiliation: Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; University of Cincinnati College of Medicine, Cincinnati, Ohio.

6

Endothelial Wnt2 and Wnt9b regulate β -catenin signaling in murine liver zonation and regeneration

Shikai Hu, Minakshi Poddar, Sucha Singh, Aaron Bell, Satdarshan Monga [8'+2']

Presenter affiliation: Tsinghua University, Beijing, China; University of Pittsburgh, Pittsburgh, Pennsylvania.

7

TUESDAY, December 7—7:00 PM ([UTC/GMT+8](#))

SESSION 2 iPS CELLS AND LIVER DISORDERS

Chairpersons: **Jessica Zucman-Rossi**, Sorbonne Université, INSERM, Université de Paris, Paris, France
Atsushi Suzuki, Kyushu University, Fukuoka, Japan

Telomerase activation and telomere length in liver carcinogenesis

Jessica Zucman-Rossi [20'+5']

Presenter affiliation: Sorbonne Université, INSERM, Université de Paris, Paris, France.

8

CPA-seq reveals sRNome remodeling during hepatic reprogramming

Pengyu Huang [20'+5']

Presenter affiliation: Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China.

9

Dynamic cell contacts between periportal mesenchyme and ductal epithelium act as a rheostat for liver cell proliferation
Anna M. Dowbaj, Lucia Cordero-Espinoza, Timo N. Kohler, Clare Pacini, Ross Dobie, John R. Wilson-Kanamori, Palle Serup, Neil C. Henderson, Florian Hollfelder, Meritxell Huch [8'+2']
Presenter affiliation: Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany. 10

Two murine nonalcoholic steatohepatitis models with rapid progression of fulminant liver inflammation and tumorigenesis
Xinghui Li, Haiping Wang, Yandi Wu, Li Zou, Shijie Deng, Xinlu Fu, Tongsheng Huang, Conghui Shen, Teng Wu, Shijie Xiong, Ziqi Feng, Jiang Qian, Hui Li, Zhenyu Yang, Saifei Gao, Weibin Cai [8'+2']
Presenter affiliation: Sun Yat-sen University, Guangzhou, China. 11

Break

Direct reprogramming technology for basic research and clinical applications
Atsushi Suzuki [20'+5']
Presenter affiliation: Kyushu University, Fukuoka, Japan. 12

Miz1 suppresses liver tumorigenesis by restricting hepatocyte-driven macrophage activation and inflammation
Beicheng Sun [20'+5']
Presenter affiliation: The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China. 13

Hepatic sympathetic neuropathy in metabolic diseases
Jing Yang [20'+5']
Presenter affiliation: Peking University, Beijing, China. 14

Retinoids rescue ceruloplasmin secretion and alleviate oxidative stress in Wilson's disease-specific hepatocytes
Dan Song, Gou Takahashi, Yun-Wen Zheng, Mami Matsuo-Takasaki, Jingyue Li, Miho Takami, Yuri An, Yasuko Hemmi, Natsumi Miharada, Tsuyoshi Fujioka, Michiya Noguchi, Takashi Nakajima, Megumu K. Saito, Yukio Nakamura, Tatsuya Oda, Yuichiro Miyaoka, Yohei Hayashi [8'+2']
Presenter affiliation: RIKEN, Tsukuba, Japan; University of Tsukuba, Tsukuba, Japan. 15

Clonal structure and evolution in liver cancer based on single-cell somatic mutations

Xianbin Su, Ze-Guang Han [8'+2']

Presenter affiliation: Shanghai Jiao Tong University, Shanghai, China. 16

Exploring potential therapeutic strategies for liver cancer through functional genetic screens

Cun Wang [8'+2']

Presenter affiliation: Shanghai Cancer Institute, Shanghai, China. 17

WEDNESDAY, December 8—9:00 AM ([UTC/GMT+8](#))

KEYNOTE SPEAKER

Introduction by: Jiandie Lin, University of Michigan Medical Center, Ann Arbor, Michigan, USA

The evolutionary basis of insulin resistance—Implications for cardiometabolic disease, NAFLD/NASH and cancer

Gerald Shulman, George R. Cowgill [30'+10']

Presenter affiliation: Yale University School of Medicine, New Haven, Connecticut. 18

WEDNESDAY, December 8—9:45 AM ([UTC/GMT+8](#))

SESSION 3 LIVER METABOLISM AND METABOLIC DISEASE

Chairpersons: **Lianyou Rui**, University of Michigan Medical School, Ann Arbor, Michigan, USA
Brian Finck, Washington University in St. Louis, St. Louis, Missouri, USA

Reprogramming of liver microenvironment in NASH and NASH-associated liver cancer

Jiandie Lin [20'+5']

Presenter affiliation: University of Michigan Medical Center, Ann Arbor, Michigan. 19

Epigenetic impact on liver metabolism and regeneration

Liangyou Rui [20'+5']

Presenter affiliation: University of Michigan Medical School, Ann Arbor, Michigan. 20

Concurrent disruption of Ras/MAPK and NF-κB pathways induces circadian deregulation and hepatocarcinogenesis

Kaisa L. Hanley, Yan Liang, Xiaoxue Lin, Gaowei Wang, Gen-Sheng Feng [8'+2']

Presenter affiliation: University of California-San Diego, La Jolla, California.

21

Break

Targeting mitochondrial intermediary metabolism to treat NAFLD

Brian N. Finck [20'+5']

Presenter affiliation: Washington University in St. Louis, St. Louis, Missouri.

22

Scrambling in lipid transport and tissue homeostasis

Xiao-Wei Chen [20'+5']

Presenter affiliation: Peking University, Beijing, China.

23

TOX4, an insulin receptor-independent regulator of hepatic glucose production, is activated in diabetic liver

Liheng Wang, Junjie Yu, Qiuzhong Zhou, Xiaobo Wang, Maria Mukhanova, Wen Du, Lei Sun, Utpal B. Pajvani, Domenico Accili [8'+2']

Presenter affiliation: Vagelos College of Physicians and Surgeons of Columbia University, New York, New York.

24

Single-cell transcriptomic analysis reveals a hepatic stellate cell-activation roadmap and myofibroblast origin during liver fibrosis in mice

Wu Yang, Hao He, Tongtong Wang, Nan Su, Feng Zhang, Kai Jiang, Jing Zhu, Chonghe Zhang, Kongyan Niu, Luyue Wang, Xiaodong Yuan, Nan Liu, Lingjie Li, Wu Wei, Junhao Hu [8'+2']

Presenter affiliation: Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, China; University of Chinese Academy of Sciences, Beijing, China.

25

SESSION 4 LIVER DISEASES AND CANCER

Chairpersons: **Lijian Hui**, Shanghai Institute of Biological Sciences, Shanghai, China
Dawang Zhou, Xiamen University, Xiamen, China

Cell identity conversion and liver regeneration

Lijian Hui [20'+5']

Presenter affiliation: Center for Excellence in Molecular Cell Science, Chinese Academy of Sciences, Shanghai, China.

26

Divergent adaptive immune regulations in HBV-associated hepatocellular carcinoma

Pengyuan Yang [20'+5']

Presenter affiliation: Institute of Biophysics, CAS, Beijing, China.

27

Lecithin-cholesterol acyltransferase induced by PP2Ac α deficiency in liver regulates the homeostasis of liver/bone axis and ameliorates hepatic osteodystrophy disease

Ke Lu, Tianshu Shi, Hongliang Gao, Jing Wu, Chaojun Li, Bin Xue, Qing Jiang [8'+2']

Presenter affiliation: Sir Run Run Hospital, Nanjing Medical University, Nanjing, China.

28

Hepatic CDP-diacylglycerol synthase 2 deficiency causes mitochondrial dysfunction and promotes rapid progression of NASH and fibrosis

Jiesi Xu, Siyu Chen, Xun Huang [8'+2']

Presenter affiliation: Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, China.

29

Break

Glycogen accumulation and phase separation drives liver tumor initiation

Jiaxin Li, Weiji Zhang, Lanfen Chen, Dawang Zhou [20'+5']

Presenter affiliation: Xiamen University, Xiamen, China.

30

Stratification of hepatic immune cells in chronic hepatitis and liver cancer—Consequences for liver cancer therapy

Mathias Heikenwälder [20'+5']

Presenter affiliation: German Cancer Research Center (DKFZ), Heidelberg, Germany.

31

Pathway and regulation of hepatic lineage differentiation

Li Yang, Xin Wang, Wei-Lin Qiu, Zi-Ran Xu, Cheng-Ran Xu [20'+5']

Presenter affiliation: Peking University, Beijing, China.

32

Targeting nestin⁺ hepatic stellate cells ameliorates liver fibrosis by facilitating TβRI degradation

Yan Xu, Qi Zhang [8'+2']

Presenter affiliation: The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

33

A survey of optimal strategy for signature-based drug repositioning and an application to liver cancer

Chen Yang, Cun Wang, Hui Wang [8'+2']

Presenter affiliation: Shanghai Cancer Institute, Shanghai, China.

34

Integrated genomic and transcriptomic profiling to dissect the spatiotemporal evolution of metastatic hepatocellular carcinoma

Yunfan Sun, Pin Wu, Kaiqian Zhou, Zejian Wang, Zefan Zhang, Yuan Ji, Fenglin Zang, David H. Peng, Liye Zhang, Jia Fan [8'+2']

Presenter affiliation: ShanghaiTech University, Shanghai, China.

35

THURSDAY, December 9—9:00 AM ([UTC/GMT+8](#))

SESSION 5 LIVER INJURIES AND CANCER

Chairpersons: **David Brenner**, University of California-San Diego, La Jolla, California, USA

Xin Chen, University of California, San Francisco, San Francisco, California, USA

Nondegradable collagen increases liver fibrosis but not hepatocellular carcinoma in mice

David A. Brenner, Jacopo Baglieri, Tatiana Kisseleva, Xiao Liu, Michael Karin [20'+5']

Presenter affiliation: UC San Diego, La Jolla, California.

36

<p>Deciphering opposing roles of Shp2 in liver tumor cells and tumor microenvironment by single cell transcriptomics <u>Gen-Sheng Feng</u> [20'+5'] Presenter affiliation: University of California at San Diego, La Jolla, California.</p>	37
<p>Serotonin 1A receptor in portal vein as a novel therapeutic target for portal hypertension <u>Chang-Peng Zhu</u>, Shu-Qing Liu, Xin Zhang, Jordi Gracia-Sancho, Wei-Fen Xie [8'+2'] Presenter affiliation: Changzheng Hospital, Naval Medical University, Shanghai, China.</p>	38
<p>Molecular crosstalk in early mouse liver organogenesis <u>Sibyl Drissler</u>, Jeremy Lotto, Rebecca Cullum, Wei Wei, Pamela Hoodless [8'+2'] Presenter affiliation: Terry Fox Laboratory, Vancouver, Canada; University of British Columbia, Vancouver, Canada.</p>	39
<p>Break</p>	
<p>mTOR pathway in c-MYC driven hepatic carcinogenesis <u>Xin Chen</u> [20'+5'] Presenter affiliation: University of California, San Francisco, San Francisco, California.</p>	40
<p>Liver macrophage heterogeneity <u>Florent Ginhoux</u> [20'+5'] Presenter affiliation: Agency for Science, Technology and Research (ASTAR), Singapore.</p>	41
<p>Immunosuppression of metastasized and recurrent liver tumors by sustained activation of cytotoxic T lymphocytes Gen-sheng Feng, <u>Bing Xin</u>, Meixiang Yang, Panyisha Wu, Li Du, Enfu Hui [8'+2'] Presenter affiliation: University of California San Diego, La Jolla, California.</p>	42
<p>Identification of functional elements which the loss of H3K9me3-heterochromatin during liver and pancreatic beta cell development <u>Kenji Ito</u>, Greg Donahue, Kenneth S. Zaret [8'+2'] Presenter affiliation: University of Pennsylvania, Philadelphia, Pennsylvania.</p>	43

Investigating the therapeutic efficacy of a novel mTORC1 inhibitor, RMC-6272, on liver tumors with β -catenin activation
Yekaterina Y. Krutsenko, Junyan Tao, Mallika Singh, Satdarshan P. Monga [8'+2']
Presenter affiliation: University of Pittsburgh, Pittsburgh, Pennsylvania. 44

THURSDAY, December 9—7:00 PM ([UTC/GMT+8](#))

SESSION 6 LIVER DISEASES AND IMMUNOLOGY

Chairpersons: **Eli Pikarsky**, The Hebrew University of Jerusalem, Jerusalem, Israel
Jian-Gao Fan, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Opposing roles of lymphoid structures in liver cancer
Eli Pikarsky [20'+5']
Presenter affiliation: The Hebrew University of Jerusalem, Jerusalem, Israel. 45

Somatic mutagenesis in morphologically normal human tissues
Fan Bai [20'+5']
Presenter affiliation: School of Life Sciences, Peking University, Beijing, China. 46

Reprogramming the spleen into a functioning “liver” in vivo
Lei Dong [20'+5']
Presenter affiliation: Nanjing University, Nanjing, China. 47

Loss of RNF43/ZNRF3 predisposes to hepatocellular carcinoma by impairing liver regeneration and altering the liver lipid metabolic ground-state
German Belenguer, Gianmarco Mastrogianni, Clare Pacini, Zoe Hall, Michelle Vacca, Robert Arnes-Benito, Kourosh Saeb-Parsy, Bon-Kyoung Koo, Meritxell Huch [8'+2']
Presenter affiliation: The Max Planck Institute, Dresden, Germany. 48

Break

Updated prevalence of NAFLD and NASH in Asia
Jian-Gao Fan [20'+5']
Presenter affiliation: Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China. 49

Liver organoids as a tool to study biological principles of tissue regeneration and cancer across scales

Meritxell Huch [20'+5']

Presenter affiliation: Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany.

50

Dissecting metabolic zonation, liver homeostasis and regeneration using spatial transcriptomics

Jan S. Tchorz [20'+5']

Presenter affiliation: Novartis Institutes for BioMedical Research, Basel, Switzerland.

51

FRIDAY, December 10—9:00 AM ([UTC/GMT+8](#))

SESSION 7 HCC, BASIC AND TRANSLATIONAL RESEARCH

Chairpersons: **Xin Wei Wang**, National Cancer Institute, Bethesda, Maryland, USA
Paul Monga, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Targeting beta-catenin in HCC—Opportunities for precision treatments

Satdarshan (Paul) Singh Monga [20'+5']

Presenter affiliation: University of Pittsburgh and University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

52

Lineage tracing and single-cell analysis reveal proliferative Prom1+ tumor-propagating cells and their dynamic cellular transition during liver cancer progression

Stephanie Ma [20'+5']

Presenter affiliation: The University of Hong Kong, Hong Kong, China.

53

Break

Spatial single-cell dissection of tumor-immune landscape in liver cancer

Lichun Ma, Sophia Heinrich, Limin Wang, Friederike Mahn, Subreen Khatib, Marshonna Forgues, Michael Kelly, Stephen M. Hewitt, Jonathan M. Hernandez, Donna Mabry, Roman Klöckner, Tim F. Greten, Jens U. Marquardt, Xin Wei Wang [20'+5']

Presenter affiliation: National Cancer Institute, Bethesda, Maryland.

54

Gut-liver axis and autoimmune liver diseases

Xiong Ma [20'+5']

Presenter affiliation: Renji Hospital, Shanghai, China.

55

Chromatin dynamics and transcription factor networks driving hepatic fate in iPSC derived hepatocytes

Tabea L. Stephan, Rebecca Cullum, Sybil Drissler, Stephen A. Duncan, Pamela A. Hoodless [8'+2']

Presenter affiliation: BC Cancer Research Institute, Vancouver, Canada; University of British Columbia, Vancouver, Canada.

56