



## The 2nd EALA Meeting

### Moderator

Chun-Jen Liu .....	83
Yoon Jun Kim .....	84
Tetsuo Takehara .....	86
Tatsuya Kanto .....	87
Han-Chieh Lin .....	88
Jia-Horng Kao .....	96
Takumi Kawaguchi .....	103
Woo Jin Chung .....	104
Ming-Lung Yu .....	112

### Speaker

Current management and future perspectives of covert hepatic encephalopathy in East Asia	
Takao Miwa .....	89
Reversing cirrhosis: myth or reality? Advances in fibrosis regression	
Soon Sun Kim .....	91
Cracking the Code: Artificial intelligence-powered advances in liver cirrhosis and portal hypertension	
Hui-Chun Huang .....	94
Prophylactic corticosteroids to alleviate severe irAE of HCC – worthy of a second thought?	
Ann-Lii Cheng .....	97
Risk stratification, prognostication, and complication management in HCC: Insights from a hepatologist	
Yeonjung Ha .....	99
Prediction of hepatocellular carcinoma	
Taro Yamashita .....	101
GDF15 as a key driver and predictive biomarker in hepatocellular carcinoma: Evidence from basic and multicenter clinical studies	
Hayato Hikita.....	105
Future perspective of research for liver disease in the Asia-Pacific region	
Beom Kyung Kim .....	107
Microbial and metabolic signatures associated with graft status in pediatric liver transplantation	
Kai-Chi Chang .....	110

# The 2nd EALA Meeting

## Topic: The Advances and Innovations of Hepatology

### Agenda

**May 24 (Saturday)**

Venue: Room 1002, Chang Yung-Fa Foundation International Convention Center

Time	Topic	Speaker	Moderator
<b>13:10- Registration</b>			
13:30-13:40	Opening	Chun-Jen Liu Yoon Jun Kim Tetsuo Takehara	
<b>Session 1: Cirrhosis</b>			
13:40-14:00	Current management and future perspectives of covert hepatic encephalopathy in East Asia	Takao Miwa	Tatsuya Kanto Han-Chieh Lin
14:00-14:20	Reversing cirrhosis: myth or reality? Advances in fibrosis regression	Soon Sun Kim	
14:20-14:40	Cracking the Code: Artificial intelligence-powered advances in liver cirrhosis and portal hypertension	Hui-Chun Huang	
14:40-15:00	Break, Group photos		
<b>Session 2: HCC</b>			
15:00-15:20	Prophylactic corticosteroids to alleviate severe irAE of HCC – worthy of a second thought?	Ann-Lii Cheng	Jia-Horng Kao Yoon Jun Kim
15:20-15:40	Risk stratification, prognostication, and complication management in HCC: Insights from a hepatologist	Yeonjung Ha	
15:40-16:00	Prediction of hepatocellular carcinoma	Taro Yamashita	
<b>Session 3: Innovation in Hepatology</b>			
16:00-16:20	GDF15 as a key driver and predictive biomarker in hepatocellular carcinoma: Evidence from basic and multicenter clinical studies	Hayato Hikita	Takumi Kawaguchi Woo Jin Chung
16:20-16:40	Future perspective of research for liver disease in the Asia-Pacific region	Beom Kyung Kim	
16:40-17:00	Microbial and metabolic signatures associated with graft status in pediatric liver transplantation	Kai-Chi Chang	
17:00-17:10	Closing Remarks	Ming-Lung Yu / Yoon Jun Kim	
18:30-	2025 TASL STC & The 2nd EALA Meeting Gala Dinner (B2 Joyful Ballroom of Sheraton Grand Taipei Hotel)		

○ Each presentation: 13 min oral presentation + 7 min Q&A



## Moderator

**Chun-Jen Liu**

劉俊人 會長

Chun-Jen Liu is a Professor at the Department of Internal Medicine, National Taiwan University College of Medicine, and Director of the Hepatitis Research Center, Director of Gastroenterology & Hepatology, and Director of Clinical Trial Center, National Taiwan University Hospital. He achieved his MD and PhD at the National Taiwan University. Professor LIU's interests are in chronic hepatitis B and C, HCC, and nonalcoholic fatty liver disease, where his studies focus on the role of viral and host factors in the pathogenesis and treatment of chronic viral hepatitis, NAFLD and HCC. He has been actively involved in clinical trials for the treatment of chronic hepatitis C, chronic hepatitis B, HBV/HCV co-infection, NASH and hepatocellular carcinoma, and delivered the JGH Foundation Emerging Leader Lecture in APDW 2013. He is now the associate editor of the Journal of the Formosan Medical Association and Journal of Microbiology, Immunology and Infection. He has authored 380 papers in international, peer-reviewed journals including Gastroenterology, Hepatology, Gut, Journal of Hepatology, Clinical Infectious Diseases and Clinical Gastroenterology and Hepatology.

### **RESEARCH INTERESTS**

Hepatitis B, Hepatitis C, HCC, and Steatotic liver disease

### **REPRESENTATIVE PUBLICATIONS**

1. Liu CJ, Chen PJ, Lai MY, Kao JH, Chang CF, Wu HL, Shau WY, Chen DS. A prospective study characterizing full-length hepatitis B virus genomes during acute exacerbation. *Gastroenterology* 2003;124:80-90.
2. Liu CJ, Lo SC, Kao JH, Tseng PT, Lai MY, Ni YH, Yeh SH, Chen PJ, Chen DS. Transmission of occult hepatitis B virus by transfusion to adult and pediatric recipients in Taiwan. *J Hepatol* 2006;44:39-46.
3. Liu CJ, Lee PH, Lin DY, et al. Heparanase inhibitor PI-88 as adjuvant therapy for hepatocellular carcinoma after curative resection: A randomized phase II trial for safety and dose-finding. *J Hepatol* 2009;50:958-968.
4. Liu CJ, Chuang WL, Lee CM, et al. Peginterferon alfa-2a plus ribavirin for the treatment of dual chronic infection with hepatitis C and B viruses. *Gastroenterology* 2009;136:496-504.
5. Liu CJ, Chuang WL, Sheen IS, et al. Efficacy of ledipasvir and Sofosbuvir Treatment of HCV Infection in Patients Coinfected with HBV. *Gastroenterology* 2018;154:989-997



## **Moderator**

### **Yoon Jun Kim**

#### **AFFILIATION / INSTITUTION**

Seoul National University Hospital, Department of Internal Medicine and Liver Research Institute  
Seoul National University College of Medicine

#### **POSITION**

Professor of Medicine

#### **BRIEF INTRODUCTION**

Professor Yoon Jun Kim specializes in hepatology, particularly in the field of hepatocellular carcinoma. He operates a specialized clinic for hepatocellular carcinoma patients and provides expert care for conditions such as steatotic liver diseases, chronic hepatitis B, hepatocellular carcinoma, and liver transplantation. His research subjects are the treatment of hepatocellular carcinoma and the genetic factors of chronic hepatitis B. He actively conducts clinical studies on MASLD, viral hepatitis and hepatocellular carcinoma. Recently, he has been focusing on novel therapies for HBV, fatty liver and hepatocellular carcinoma, leading preclinical and large-scale multi-institutional clinical research for hepatocellular carcinoma and the development of new drugs for fatty liver and HBV infection. He utilizes radioembolization (Yttrium-90) actively and employs new targeted and immunotherapeutic agents for the treatment of hepatocellular carcinoma. He actively incorporates new treatment methods such as combination therapy, such as radioembolization + systemic treatments. He is particularly involved in numerous clinical trials for the use of new targeted and immunotherapeutic anticancer agents

Graduated from Seoul National University College of Medicine in 1992 and received Ph.D. from same college in 2001.

Professor of Medicine, Seoul National University College of Medicine  
Chief, Division of Gastroenterology, Seoul National University Hospital  
Director, Liver Cancer Center, Seoul National University Cancer Hospital

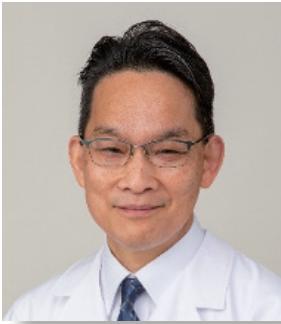
#### **MEMBERSHIP ACTIVITIES**

Chair of academic committee of The Korean Liver Cancer Study Group, 2013-2014  
Secretary General of The Korean Liver Cancer Study Group, 2014-2015  
Chair of academic committee of The Korean Radio-Embolization Association, 2013-2021  
Editor-in-Chief, Clinical and Molecular Hepatology, 2015-2019  
Editor-in-Chief Emeritus, Clinical and Molecular Hepatology, 2020-  
President of The Korean Radio-Embolization Association, 2021-  
President of The Korean Association for the Study of the Liver, 2024-

#### **RESEARCH INTERESTS**

HCC / HBV / Steatotic liver disease / radioembolization / clinical trial





## **Moderator**

### **Tetsuo Takehara**

#### **AFFILIATION / INSTITUTION**

Kansai Rosai Hospital

#### **POSITION**

Director General

#### **BRIEF INTRODUCTION**

Tetsuro Takehara graduated from Osaka University School of Medicine with his M.D. degree and received his Ph.D. degree from Osaka University in 1993. He studied at the Gastrointestinal Unit, Massachusetts General Hospital, USA, as a postdoctoral fellow for three years from 1998, became Associate Professor of Molecular Therapeutics at Osaka University Graduate School of Medicine in 2001, and then Associate Professor of Gastroenterology and Hepatology. In 2011, he became Professor of Gastroenterology and Hepatology, Osaka University Graduate School of Medicine; from 2021, he served as Director of Osaka University Hospital for two years. He is currently Director General, Kansai Rosai Hospital, Japan.

He has conducted outstanding basic and clinical research in the fields of hepatitis, cirrhosis and liver cancer, publishing more than 500 papers in high-impact international journals. In 2017, he received the Oda Award, the highest award of the Japan Society of Hepatology (JSH). He served as President of the Annual Meeting of JSH in 2020, of the Japanese Society of Gastroenterology (JSGE) in 2021 and of the Japanese Society of Internal Medicine in 2025, and will chair the 29th Congress of JSH in JDDW 2025.

From 2018, he is the current Director General, JSH.

#### **RESEARCH INTERESTS**

Hepatitis, Cirrhosis, Liver Cancer

#### **REPRESENTATIVE PUBLICATIONS**

1. Kudo S, Takehara T, et al. Collaborative orchestration of BH3-only proteins governs Bak/Bax-dependent hepatocyte apoptosis under antiapoptotic protein-deficiency in mice. *Cell Death Differ.* in press.
2. Shigeno S, Takehara T, et al. Intrahepatic exhausted antiviral immunity in an immunocompetent mouse model of chronic hepatitis B. *Cell Mol Gastroenterol Hepatol.* 2025;19(1):101412.
3. Furuse J, Takehara T, et al. A Phase II Placebo-Controlled Study of the Effect and Safety of Nanvuranlat in Patients with Advanced Biliary Tract Cancers Previously Treated by Systemic Chemotherapy. *Clin Cancer Res.* 2024 Sep 13;30(18):3990-3995.
4. Kumazaki S, Takehara T, et al. Serum growth differentiation factor 15 is a novel biomarker with high predictive capability for liver cancer occurrence in patients with MASLD regardless of liver fibrosis. *Aliment Pharmacol Ther.* 2024 Aug;60(3):327-339.



## **Moderator**

### **Tatsuya Kanto**

#### **AFFILIATION / INSTITUTION**

The Research Center for Hepatitis and Immunology, Japan Institute for Health Security (JIHS)

#### **POSITION**

Director General

#### **BRIEF INTRODUCTION**

Tatsuya Kanto is a researcher and hepatologist/physician with expertise in immunology in liver diseases. He got PhD degree at Osaka University and worked as a research associate for dendritic cell biology at the University of Pittsburgh, USA, from 1998 to 2001. He worked as an Associate Professor at Osaka University from 2003 to 2013 and moved to the National Center for Global Health and Medicine (NCGM). His current position is Director General at the Research Center for Hepatitis and Immunology, Japan Institute for Health Security (JIHS).

He has been working with the Ministry of Health, Labor, and Welfare to promote the Hepatitis Action Plan in Japan. His field of interest is the exploration of the pathogenesis of liver disease for the development of immune-based therapy against viral hepatitis, liver cirrhosis, and cancer. He has published more than 260 papers and invited review articles in peer-reviewed journals, such as *Hepatology*, *Journal of Hepatology*, *Immunity*, *Journal of Immunology* and *Gastroenterology*.

#### **RESEARCH INTERESTS**

Immunopathogenesis of viral hepatitis, MASLD/MASH, and liver cancer  
Development of immune modulators for the treatment of chronic HBV infection  
Establishment of therapeutic strategy for congestive liver disease, such as FALD  
Promotion of hepatitis countermeasures in Japan

#### **REPRESENTATIVE PUBLICATIONS**

1. Mino M, Kakazu E, Sano A, Tsuruoka M, Matsubara H, Kakisaka K, Kogure T, Sekine K, Aoki Y, Imamura M, Matsuda M, Yamazoe T, Mori T, Yoshio S, Inoue J, Masamune A, Kanto T. Comprehensive analysis of peripheral blood free amino acids in MASLD: the impact of glycine-serine-threonine metabolism. *Amino Acids*. 2024 Dec 24;57(1):3. doi: 10.1007/s00726-024-03433-2. PMID: 39718621
2. Kogiso T, Tokuhara D, Ohfuji S, Tanaka A, Kanto T. Evaluation of diagnostic criteria for mild-to-advanced stages of Fontan-associated liver disease: A nationwide epidemiological survey in Japan. *Hepatol Res* 2024 Nov 27. doi: 10.1111/hepr.14141. Online ahead of print.
3. Mori T, Yoshio S, Kakazu E, Kanto T. Active role of the immune system in metabolic dysfunction-associated steatotic liver disease. *Gastroenterol Rep (Oxf)*. 2024 Oct 15;12:goae089. doi: 10.1093/gastro/goae089. eCollection 2024. PMID: 39411101
4. Shigeno S, Kodama T, Murai K, Motooka D, Fukushima A, Nishio A, Hikita H, Tatsumi T, Okamoto T, Kanto T, Takehara T. Intrahepatic exhausted antiviral immunity in immunocompetent mouse model of chronic hepatitis B. *Cell Mol Gastroenterol Hepatol*. 2024 Sep 28:101412. doi: 10.1016/j.jcmgh.2024.101412. Online ahead of print. PMID: 39349249
5. Takeuchi Y, Nozawa A, Yukimoto A, Kitsuka M, Tateishi R, Kioke K, Okano K, Kanto T. Integrated policy of medical expense subsidies and clinical registry for patients with liver cancer and decompensated cirrhosis in Japan. *Hepatol Res*. 2024 Jun 15. doi: 10.1111/hepr.14085. Online ahead of print. PMID: 38877867



## Moderator

### Han-Chieh Lin

#### **AFFILIATION / INSTITUTION**

Division of Gastroenterology & Hepatology Taipei Veterans General Hospital

#### **POSITION**

Professor of Medicine

#### **BRIEF INTRODUCTION**

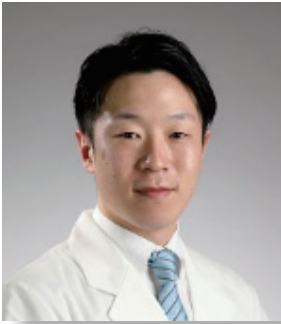
Dr. Han-Chieh Lin is a professor of Division of Hepatology & Gastroenterology at Taipei Veterans General Hospital and National Yang-Ming Chiao-Tung University. Dr. Lin was graduated from Taipei Medical University School of Medicine. He spent one year in Paris as a research fellow with Professor Didier Lebecq from 1989 to 1990. He had served as the Chief of the Division of Hepatology & Gastroenterology from 2006 to 2016. He was the president of TASL (2020-2022) and APASL (2023). He had been acting as an “Executive Committee Member” of the Asian Pacific Association for the Study of the Liver (APASL) from 2017 to 2020. He currently served as an “Steering Committee Member” of APASL since 2022. He was the awardee of the 3rd APASL Lesmana-Sollano Great Mentor Award (2023). Dr. Lin has deeply involved in the clinical and laboratory research of cirrhosis and portal hypertension. He has been invited to serve as an “Associate Editor” of “Liver International” from 2008 to 2014; “Journal of Hepatology” from 2015 to 2017; and “Hepatology International” from 2019 to present time. He was the Academic Editor of PLoS One from 2014 to 2020. He has published more than 350 peer-reviewed articles in SCI journals.

#### **RESEARCH INTERESTS**

Clinical and laboratory researches in “cirrhosis and portal hypertension” and “steatotic liver disease”

#### **REPRESENTATIVE PUBLICATIONS**

1. Lee KC, Wu PS, Lin HC\*. Pathogenesis and treatment of non-alcoholic steatohepatitis and its fibrosis. *Clin Mol Hepatol* 2023;29:77-98 .
2. Tsai YL, Liu CW, Hsu CF, Huang CC, Lin MW, Huang SF, Li TH, Lee KC, Hsieh YC, Yang YY, Lee TY, Liu HM, Huang YH, Hou MC, Lin HC\*. Obeticholic acid ameliorates hepatorenal syndrome in ascitic cirrhotic rats by down-regulating the renal 8-iso-PGF2 $\alpha$ -activated COX-TXA2 pathway. *Clin Sci* 2020;134:2055-73
3. Yang YY, Hsieh SL, Lee PC, Yeh YC, Lee KC, Hsieh YC, Wang YW, Lee TY, Huang YH, Chan CC, Lin HC\*. Long-term cannabinoid type 2 receptor agonist therapy decreases bacterial translocation in rats with cirrhosis and ascites. *J Hepatol* 2014;61:1004-13 .
4. Yang YY, Tsai TH, Huang YT, Lee TZ, Chan CC, Lee KC, Lin HC\*. Hepatic endothelin-1 and endocannabinoids-dependent effects of hyperleptinemia in nonalcoholic steatohepatitis-cirrhotic rats. *Hepatology* 2012;55:1540-50
5. Lin HC, Yang YY, Tsai TH, Huang CM, Huang YT, Lee FY, Liu TT, Lee SD. The relationship between endotoxemia and hepatic endocannabinoids in cirrhotic rats with portal hypertension. *J Hepatol* 2011;54:1145-53.



## Speaker

### Takao Miwa

#### **AFFILIATION / INSTITUTION**

Gifu University Hospital, Gifu, Japan

#### **POSITION**

Medical Doctor

#### **BRIEF INTRODUCTION**

Takao Miwa is a gastroenterologist and hepatologist whose academic and clinical career is centered at the Department of Gastroenterology/Internal Medicine at Gifu University Hospital. He earned his M.D. in 2015 and completed his Ph.D. in 2024, specializing in hepatology and nutrition. His professional career includes roles as both a physician and a researcher, with significant contributions in areas such as liver cirrhosis, nutrition, hepatic encephalopathy, sarcopenia, frailty, and steatotic liver disease. As a lead author, his publications have advanced research on zinc deficiency in patients with covert hepatic encephalopathy, the association between handgrip strength decline and hepatic encephalopathy, a simplified screening model for covert hepatic encephalopathy, the effectiveness of levocarnitine administration in patients with cirrhosis, and papers on new international standards for malnutrition, sarcopenia, and prognosis. These papers have been cited in guidelines by the European Association for the Study of the Liver and the Japan Society of Hepatology, contributing to the clinical management of liver cirrhosis. Additionally, his recent publications include a multicenter study on acute kidney injury and its association with amino acid imbalance in the Japanese population, and a nationwide survey on the current management and future perspectives of covert hepatic encephalopathy in Japan. The significance of his work is underscored by awards such as the JSGE-UEG Rising Stars award and multiple young investigator awards. Takao Miwa also serves on the editorial committee for the "Evidence-based Clinical Practice Guidelines for Liver Cirrhosis," highlighting his commitment to advancing medical standards and practices.

#### **RESEARCH INTERESTS**

Liver cirrhosis, Nutrition, Hepatic Encephalopathy, Sarcopenia, Frailty, Steatotic liver disease

1. Miwa T, Tsuruoka M, Ueda H, et al. Current management and future perspectives of covert hepatic encephalopathy in Japan: a nationwide survey. *J Gastroenterol.* 2025. doi: 10.1007/s00535-025-02232-0.
2. Miwa T, Suda G, Tateishi R, et al. Cachexia is an independent predictor of mortality in patients with cirrhosis. *Hepatol Res.* 2025. doi: 10.1111/hepr.14183.
3. Miwa T, Utakata Y, Hanai T, et al. Acute kidney injury development is associated with mortality in Japanese patients with cirrhosis: impact of amino acid imbalance. *J Gastroenterol.* 2024;59:849-857.
4. Miwa T, Hanai T, Nishimura K, et al. Usefulness of the Global Leadership Initiative on Malnutrition criteria to predict sarcopenia and mortality in patients with chronic liver disease. *Hepatol Res.* 2022;52:928-936.
5. Miwa T, Hanai T, Nishimura K, et al. Handgrip strength stratifies the risk of covert and overt hepatic encephalopathy in patients with cirrhosis. *JPEN J Parenter Enteral Nutr.* 2022;46:858-866.

## Current management and future perspectives of covert hepatic encephalopathy in East Asia

Dr. Takao Miwa

Covert hepatic encephalopathy (CHE) represents the mildest form of neurocognitive impairment in patients with cirrhosis, stemming from impaired liver functional reserve. Although asymptomatic, diagnosing CHE is crucial, as it affects approximately 20–40% of patients with cirrhosis and progresses to overt hepatic encephalopathy at an annual rate of 10%. Moreover, growing evidence highlights the significant impact of CHE on reduced quality of life, a higher incidence of falls and motor vehicle accidents, and increased mortality. Therefore, early detection and appropriate management of CHE are vital to prevent devastating outcomes in cirrhotic patients. Consequently, several global liver disease societies recommend screening for CHE in this patient group.

Despite these recommendations, a disconnect exists between the evidence on CHE and its management in real-world practice, limiting the generalization of management strategies. For instance, it remains unclear to what extent physicians treating patients with cirrhosis recognize CHE as a significant clinical concern. As a result, only a small proportion of these patients are likely to be screened for CHE in routine clinical practice. Moreover, the decision to test for CHE may be influenced by factors such as the clinical context, the time constraints, availability of diagnostic tools and standardized tests, and the expertise of healthcare providers. Additionally, the lack of direct evidence linking CHE to specific clinical outcomes or treatment efficacy may further impact clinical decision-making regarding cirrhosis management.

To address these issues, the first part will review the basic knowledge on the clinical implications and testing methods for CHE. In the second part, the presenter will present the findings of a nationwide survey in Japan that explores the current management and future perspectives of CHE, and will make a discussion with experts at the EALA Symposium.



## Speaker

**Soon Sun Kim**

### **AFFILIATION / INSTITUTION**

Ajou University School of Medicine

### **POSITION**

Professor

### **EDUCATIONAL**

1999-2005, Doctor of Medicine, Ajou University School of Medicine

2007-2010, Master in Medicine, Ajou University School of Medicine

2010-2013, Ph.D degree in Medicine, Ajou University School of Medicine

### **PROFESSIONAL EXPERIENCE**

2006-2010, Resident, Ajou University Hospital

2010-2012, Clinical fellow, Ajou University Hospital

2012-2016, Clinical Assistant professor, Ajou University Hospital

2016-2020, Assistant professor, Ajou University Hospital

2020-2025, Associate professor, Ajou University Hospital

2025-, Professor, Ajou University Hospital

### **RESEARCH INTERESTS**

Translational Research, Biomarker, HCC, Microbiome, Big-data, MASLD

### **REPRESENTATIVE PUBLICATIONS**

1. Son JA, Weon JH, Baek GO, et al. Circulating small extracellular vesicle-derived splicing factor 3b subunit 4 as a non-invasive diagnostic biomarker of early hepatocellular carcinoma. *J Exp Clin Cancer Res.* 2023;42(1):288. Published 2023 Oct 30. doi:10.1186/s13046-023-02867-y
2. Ahn HR, Baek GO, Yoon MG, et al. Hypomethylation-mediated upregulation of the WASF2 promoter region correlates with poor clinical outcomes in hepatocellular carcinoma. *J Exp Clin Cancer Res.* 2022;41(1):158. Published 2022 Apr 28. doi:10.1186/s13046-022-02365-7
3. Kim SS, Baek GO, Son JA, et al. Early detection of hepatocellular carcinoma via liquid biopsy: panel of small extracellular vesicle-derived long noncoding RNAs identified as markers. *Mol Oncol.* 2021;15(10):2715-2731. doi:10.1002/1878-0261.13049
4. Kim SS, Eun JW, Cho HJ, et al. Microbiome as a potential diagnostic and predictive biomarker in severe alcoholic hepatitis. *Aliment Pharmacol Ther.* 2021;53(4):540-551. doi:10.1111/apt.16200
5. Kim SS, Baek GO, Ahn HR, et al. Serum small extracellular vesicle-derived LINC00853 as a novel diagnostic marker for early hepatocellular carcinoma. *Mol Oncol.* 2020;14(10):2646-2659. doi:10.1002/1878-0261.12745

## Reversing cirrhosis: myth or reality? Advances in fibrosis regression

Prof. Soon Sun Kim

For many years, liver cirrhosis—considered the end-stage of chronic liver diseases—has been regarded as an irreversible condition. However, accumulating clinical and histopathologic data now suggest that liver fibrosis can, under certain circumstances, be at least partially reversible, and even cirrhosis itself may regress to some extent. Liver fibrosis, a common outcome of chronic hepatic injury regardless of etiology, is driven by hepatic stellate cell activation, transforming growth factor-beta signaling, and excessive extracellular matrix deposition. The possibility of modulating or reversing this process has prompted a shift from the conventional paradigm of halting fibrosis progression toward actively pursuing fibrosis regression.

The degree of reversibility varies by disease etiology. In viral hepatitis, particularly hepatitis C and hepatitis B, antiviral therapy has been shown to significantly improve histological outcomes, with well-documented cases of fibrosis and cirrhosis regression. In patients with metabolic dysfunction-associated steatohepatitis, weight loss exceeding 10% has been associated with histologic fibrosis improvement. Moreover, nuclear receptor-targeting agents have recently demonstrated fibrosis-stage improvement in selected patients. On the other hand, for alcohol-related liver disease, sustained abstinence remains the cornerstone of disease control and the strongest predictor of survival, although pharmacologic approaches to reversing fibrosis in this population have been largely unsuccessful to date.

These clinical observations have laid the foundation for antifibrotic drug development. Multiple therapeutic targets—transforming growth factor-beta, platelet-derived growth factor, lysyl oxidase-like 2, galectin-3, farnesoid X receptor, C-C chemokine receptor types 2 and 5, peroxisome proliferator-activated receptors, and thyroid hormone receptor beta—are currently under investigation, with a variety of drugs in different stages of development aimed at suppressing hepatic stellate cell activation or enhancing extracellular matrix degradation. Among these, the most notable progress has come from Resmetirom, a selective thyroid hormone receptor-beta agonist, which in 2024 became the first FDA-approved medication for the treatment of liver fibrosis in metabolic dysfunction-associated steatohepatitis. Similarly, Obeticholic acid, a farnesoid X receptor agonist, showed histologic improvement in a phase 3 trial but was withheld from approval due to safety concerns. Lanifibranor, a pan peroxisome proliferator-activated receptor agonist, demonstrated simultaneous disease resolution and fibrosis improvement in phase 2 and is now undergoing phase 3 evaluation. In contrast, drugs such as Belapectin (a galectin-3 inhibitor), Cenicriviroc (a dual C-C chemokine receptor inhibitor), Simtuzumab (a lysyl oxidase-like 2 antibody), and Selonsertib (an apoptosis signal-regulating kinase 1 inhibitor) failed to demonstrate sufficient efficacy in later-phase trials and have been discontinued or suspended.

These findings collectively suggest that while complete normalization of the liver is rare, meaningful structural and functional improvement is possible, particularly in earlier stages of fibrosis and in patients with preserved hepatic regenerative capacity. Pharmacologic reversal appears to be more successful when combined with effective treatment of the underlying etiology, metabolic correction, inflammation control, and hepatic regeneration.

In conclusion, the concept of reversing cirrhosis has moved beyond myth. With advances in antiviral therapy, metabolic intervention, and molecular targeting, fibrosis regression has become a clinically achievable goal





## Speaker

### Hui-Chun Huang

#### **AFFILIATION / INSTITUTION**

Taipei Veterans General Hospital and National Yang Ming Chiao Tung University School of Medicine, Taipei, Taiwan

#### **POSITION**

Chief, Division of Endoscopy Diagnosis and Treatment and Attending Physician, Division of Gastroenterology and Hepatology, Taipei Veterans General Hospital; Professor, National Yang Ming Chiao Tung University School of Medicine

#### **EDUCATIONAL**

M.D. National Yang-Ming University School of Medicine, Taiwan

Further Study: Research fellow, School of Medicine, Yale University, New Haven and Hepatic Hemodynamic Laboratory, VA Medical Center, West Haven, Connecticut, USA (2008)

#### **PROFESSIONAL EXPERIENCE**

- |                 |  |
|-----------------|--|
| 2015 to present | Professor, National Yang Ming Chiao Tung University School of Medicine, Taipei, Taiwan   |
| 2025 to present | Chief, Division of Endoscopy Diagnosis and Treatment, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan |
| 2016 to 2022    | Chief, Division of General Medicine, Department of Medicine, Taipei Veterans General Hospital                                  |
| 2003 to present | Attending physician, Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital     |
| 2025 to present | Director, The Digestive Endoscopy Society of Taiwan  |

#### **RESEARCH INTERESTS**

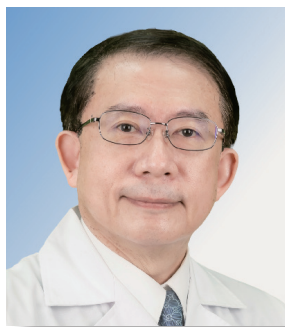
Pathogenesis and management of portal hypertension, liver cirrhosis and the related complications

1. Hsu SJ, Huang HC (corresponding author) et al., Caffeine ameliorates hemodynamic derangements and portosystemic collaterals in cirrhotic rats. *Hepatology* 2015;61:1672-84.
2. Huang HC, Lee FY et al., Cannabinoid receptor 2 agonist ameliorates mesenteric angiogenesis and portosystemic collaterals in cirrhotic rats. *Hepatology* 2012;56:248-58.
3. Zhang D, Huang HC et al., Reticulon 4B (Nogo-B) is a novel regulator of hepatic fibrosis. *Hepatology* 2011; 53:1306-15.
4. Huang HC, Lee FY et al., Chronic inhibition of nitric oxide increases the collateral vascular responsiveness to vasopressin in portal hypertensive rats. *J Hepatol* 2004;40:234-8.
5. Huang HC, Lee FY et al., Effects of somatostatin and octreotide on portal-systemic collaterals in portal hypertensive rats. *J Hepatol* 2002;36:163-8.

# Cracking the code: Artificial intelligence-powered advances in liver cirrhosis and portal hypertension

**Prof. Hui-Chun Huang**

Although the negative impacts of Liver cirrhosis and portal hypertension have been alleviated gradually via the advanced and timely treatment of various kinds of acute and chronic liver diseases, the early recognition of liver cirrhosis and clinically significant portal hypertension is still urgently required and the unmet needs are to be solved. Furthermore, this group of patients with critically limited liver reserve require personalized and sophisticated care that the incorporation of artificial intelligence into clinical practice is highly anticipated. Artificial intelligence has made great strides in various fields of medicine, and cumulating data show that artificial intelligence tools are promising in transforming the strategies of diagnosis and management by leveraging massive amounts of data. This talk will focus on the recent advances in artificial intelligence applied in liver cirrhosis and portal hypertension and hopefully, novel thinking and insights will be inspired.



## **Moderator**

### **Jia-Horng Kao**

#### **AFFILIATION / INSTITUTION**

Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine  
Department of Internal Medicine, National Taiwan University Hospital

#### **POSITION**

Chair Professor and Vice Superintendent

#### **BRIEF INTRODUCTION**

1. Graduated from the College of Medicine National Taiwan University in 1987 and received his Ph.D. from the Graduate Institute of Clinical Medicine at the same university in 1994
2. President of Taiwan Association for the Study of the Liver (TASL) from 2017 to 2019 and the Asian Pacific Association for the Study of the Liver in 2012, Director of the Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine from 2009 to 2015, Director of the Hepatitis Research Center at the National Taiwan University Hospital from 2003 to 2009, Secretary General of the Taiwan Association for the Study of the Liver between 2004 and 2005, and Vice Secretary General of the Gastroenterological Society of Taiwan from 2003 to 2006.
3. Steering Committee member of APASL, Council member of APAGE, the trustee of JGH foundation and the founding member of AASLD Asia Pacific Regional Advisory Council.

#### **RESEARCH INTERESTS**

Prevention, natural history, molecular virology, pathogenesis and treatment of chronic viral hepatitis and HCC.

#### **REPRESENTATIVE PUBLICATIONS**

1. Tseng TC, Liu CJ, Yang HC, Su TH, Wang CC, Chen CL, Kuo SFT, Liu CH, Chen PJ, Chen DS, Kao JH. High levels of hepatitis B surface antigen increase risk of hepatocellular carcinoma in patients with low HBV load. *Gastroenterology* 2012;142:1140-1149 (Correspondence author).
2. Tseng TC, Liu CJ, Hsu CY, Hong CM, Su TH, Yang WT, Chen CL, Yang HC, Huang YT, Fang-Tzu Kuo S, Liu CH, Chen PJ, Chen DS, Kao JH. High level of hepatitis B core-related antigen associated with increased risk of hepatocellular carcinoma in patients with chronic HBV infection of intermediate viral load. *Gastroenterology* 2019;157:1518-1529.e3 (Correspondence author).
3. Tseng TC, Chiang C, Liu CJ, Hong CM, Su TH, Yang HC, Yang WT, Liu CH, Chen PJ, Kao JH. Low Hepatitis B Core-Related Antigen Levels Correlate Higher Spontaneous Seroclearance of Hepatitis B Surface Antigen in Chronic Hepatitis B Patients with High Hepatitis B Surface Antigen Levels. *Gastroenterology* 2023;164:669-679.e6 (Correspondence author).
4. Liu CH, Cheng PN, Fang YJ, Chen CY, Kao WY, Lin CL, Yang SS, Shih YL, Peng CY, Chang YP, Huang SC, Su TH, Tseng TC, Liu CJ, Chen PJ, Kao JH. Risk of de novo HCC in patients with MASLD following direct-acting antiviral-induced cure of HCV infection. *J Hepatol.* 2025 Apr;82(4):582-593. (Corresponding author)
5. Tseng TC, Hosaka T, Pan MH, Liu CJ, Suzuki F, Chen CJ, Su TH, Kumada H, Yang WT, Yang HC, Liu CH, Chen PJ, Yang HI, Kao JH. Higher level of Hepatitis B Surface antigen associated with delayed development of hepatocellular carcinoma in immune-tolerant patients. *Hepatology.* 2025 Mar 20. doi: 10.1097/HEP.0000000000001313. (Corresponding author)



## Speaker

### **Ann-Lii Cheng**

#### **AFFILIATION / INSTITUTION**

National Taiwan University Cancer Center

#### **POSITION**

President Emeritus and Distinguished Attending Physician

#### **EDUCATIONAL**

- 1973 - 1980 M.D., National Taiwan University, College of Medicine, Taipei, Taiwan.  
 1989 - 1990 Visiting clinical fellow and research associate, Department of Human Oncology, Clinical Cancer Center, University of Wisconsin, Madison, Wisconsin, U.S.A.  
 1991-1994 Ph.D., Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine.

#### **PROFESSIONAL EXPERIENCE**

- 2025/02- Distinguished Attending Physician, Department of Medical Oncology, National Taiwan University Cancer Center  
 2020/08 Distinguished Chair Professor, National Taiwan University  
 2020/08- President Emeritus, NTU Cancer Center  
 2013/08-2020/07 Director, NTU Cancer Center  
 2015/08-2018/07 Vice Superintendent, National Taiwan University Hospital.  
 2009/08-2015/07 Director of Graduate Institute of Oncology, National Taiwan University College of Medicine  
 2009/08-2015/07 Chairman, Department of Oncology, National Taiwan University Hospital.  
 1987-2018/11 Attending Physician, Section of Medical Oncology, Department of Internal Medicine and Department of Oncology, National Taiwan University Hospital..

#### **RESEARCH INTERESTS**

Clinical and Translational research of hepatocellular carcinoma

#### **REPRESENTATIVE PUBLICATIONS**

- Cheng AL\* Hsu C, Chan SL, Choo SP, Kudo M. Challenges of combination therapy with immune checkpoint inhibitors for hepatocellular carcinoma. *J Hepatol.* 2020 Feb;72(2):307-319.
- Richard S. Finn, Shukui Qin, Masafumi Ikeda, Peter R. Galle, Michel Ducreux, Tae-You Kim, Masatoshi Kudo, Valeriy Breder, Philippe Merle, Ahmed O. Kaseb, Daneng Li, Wendy Verret, Derek-Zhen Xu, Sairy Hernandez, Juan Liu, Chen Huang, Sohail Mulla, Yulei Wang, Ho Yeong Lim, Andrew X. Zhu, Ann-Lii Cheng\*. Atezolizumab Plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med.* 2020 May 14;382(20):1894-1905.
- Cheng AL\*, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Lim HY, Kudo M, Breder V, Merle P, Kaseb AO, Li D, Verret W, Ma N, Nicholas A, Wang Y, Li L, Zhu AX, Finn RS. Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. *J Hepatol.* 2022 Apr;76(4):862-873.
- Shen YC, Liu TH, Nicholas A, Soyama A, Yuan CT, Chen TC, Eguchi S, Yoshizumi T, Itoh S, Nakamura N, Kosaka H, Kaibori M, Ishii T, Hatano E, Ogawa C, Naganuma A, Kakizaki S, Cheng CH, Lin PT, Su YY, Chuang CH, Lu LC, Wu CJ, Wang HW, Rau KM, Hsu CH, Lin SM, Huang YH, Hernandez S, Finn RS, Kudo M, Cheng AL\*. Clinical Outcomes and Histologic Findings of Patients With Hepatocellular Carcinoma With Durable Partial Response or Durable Stable Disease After Receiving Atezolizumab Plus Bevacizumab. *J Clin Oncol.* 2024 Dec;42(34):4060-4070.
- Shen YC, Chang NW, Yeh CP, Lin WY, Wei MF, Ou DL, Hsu CL, Cheng AL\*. Corticosteroid premedication on anti-tumor effect of immune checkpoint blockade in murine hepatocellular carcinoma models. *J Immunother Cancer.* 2025 Feb 20;13(2):e009704.

## Prophylactic corticosteroids to alleviate severe irAE of HCC – worthy of a second thought

Prof. Ann-Lii Cheng

Corticosteroid prophylaxis (CP) is a common practice in systemic chemotherapy. It is also a common practice in chemoimmunotherapy for lung cancer. However, because of an intuitive premise that CP might jeopardize anti-tumor effect of immune checkpoint inhibitors (ICI), it is not recommended in most other cancers receiving ICI.

Recently, novel systemic therapies for HCC, particularly those incorporating anti-PD1/L1 and anti-CTLA4, are often associated with alarming irAE, and thus rebooted our interest in seeking measures to change the status quo. As a step toward, we have recently reported interesting results of an HCC animal study, which suggests that neither low- nor high- doses of corticosteroids interfere with the anti-tumor effect of anti-CTLA4 plus anti-PD1 doublet. Review of the retrospective clinical studies provides very controversial conclusions. However, if the confounding factors of these retrospective studies can be well controlled, a potential benefit of CP to alleviate severe irAE while preserving anti-tumor efficacy appears possible. We propose that a prospective study to clarify this important question may be justified.



## Speaker

**Yeonjung Ha**

### **AFFILIATION / INSTITUTION**

CHA Bundang Medical Center, CHA University

### **POSITION**

Associate Professor

### **EDUCATIONAL**

2003-2009 Inje University College of Medicine, M.D. (summa cum laude)  
 2009 Internship, Asan Medical Center  
 2010-2013 Residency, Internal Medicine, Asan Medical Center  
 2012-2014 University of Ulsan College of Medicine, M.S.  
 2013 Short-term Training, Prince of Wales Hospital, Hong Kong S.A.R., China  
 2014-2015 Clinical Fellowship, Gastroenterology, Asan Medical Center  
 2014-2017 University of Ulsan College of Medicine, Ph.D.  
 2016-2023 Assistant Professor, Gastroenterology, CHA Bundang Medical Center  
 2017-2019 Visiting Scientist, Mayo Clinic, United States  
 2024- Associate Professor, Gastroenterology, CHA Bundang Medical Center

### **RESEARCH INTERESTS**

Hepatocellular carcinoma  
 Metabolic dysfunction-associated steatotic liver disease  
 Predictive modeling

### **REPRESENTATIVE PUBLICATIONS**

1. Ha Y, Lee S, Lim J, et al. A Machine Learning Model to Predict De Novo Hepatocellular Carcinoma Beyond Year 5 of Antiviral Therapy in Patients With Chronic Hepatitis B. *Liver Int* 2025;45(4):e16139. DOI: 10.1111/liv.16139.
2. Cheon J, Kim H, Kim HS, (...), Ha Y et al. Atezolizumab plus bevacizumab in patients with child-Pugh B advanced hepatocellular carcinoma. *Ther Adv Med Oncol* 2023;15:17588359221148541. DOI: 10.1177/17588359221148541.
3. Ha Y, Lim J, Chon YE, et al. Five-year on-treatment variables-based PPACS model predicts subsequent hepatocellular carcinoma in entecavir/tenofovir-treated patients. *Int J Cancer* 2023;153(12):2045-2054. DOI: 10.1002/ijc.34704.
4. Yang H, Kang B, Ha Y, et al. High serum IL-6 correlates with reduced clinical benefit of atezolizumab and bevacizumab in unresectable hepatocellular carcinoma. *JHEP Reports : innovation in hepatology* 2023;5(4):100672. DOI: 10.1016/j.jhepr.2023.100672.
5. Ha Y, Kim JH, Cheon J, Jeon GS, Kim C, Chon HJ. Risk of Variceal Bleeding in Patients With Advanced Hepatocellular Carcinoma Receiving Atezolizumab/Bevacizumab. *Clin Gastroenterol Hepatol* 2023;21(9):2421-2423.e2. DOI: 10.1016/j.cgh.2022.07.035.

## Risk stratification, prognostication, and complication management in hcc: insights from a hepatologist

Dr. Yeonjung Ha

The clinical complexity of hepatocellular carcinoma (HCC) arises from the interplay between tumor characteristics, liver function, and functional status, necessitating a multidimensional approach and emphasizing the critical role of hepatologists in risk stratification, prognostication, and management of cirrhosis-related complications that accompany treatment for HCC.

For risk stratification, the integration of artificial intelligence and machine learning algorithms into clinical practice is beginning to transform the landscape of clinical practice. These advanced computational models can synthesize high-dimensional data from clinical, imaging, and molecular sources to identify complex patterns that may elude conventional analytics.

For prognostication, growing evidence highlights the relevance of systemic inflammation and immune dysregulation in HCC. Circulating cytokines and inflammatory markers have emerged as potential biomarkers associated with tumor progression, therapeutic resistance, and overall survival. Incorporating these markers into prognostic models offers a biologically informed dimension that complements conventional risk factors.

For management of portal hypertension-related complications remains a cornerstone of optimizing patient outcomes. The natural history of cirrhosis frequently intersects with oncologic progression, giving rise to challenges such as ascites and variceal bleeding. Furthermore, treatment-related toxicities from systemic therapies require vigilant monitoring and early intervention. Locoregional therapies also carry procedural risks and must be judiciously balanced against tumor characteristics and liver function.

In summary, HCC requires a multidimensional management approach, wherein hepatologists play a central role in integrating evolving tools for risk stratification and prognostication, while navigating the complex interplay between tumor progression, liver dysfunction, and treatment-related complications.



## Speaker

### Taro Yamashita

#### **AFFILIATION / INSTITUTION**

Department of Gastroenterology/Kanazawa University Graduate School of Medical Sciences

#### **POSITION**

Professor, Department of Gastroenterology

Vice President, Kanazawa University Hospital Kanazawa University

#### **EDUCATIONAL**

1995 M.D. Kanazawa University School of Medicine

2000 Ph.D. Kanazawa University Graduate School of Medical Science

2005 Visiting Fellow, Laboratory of Human Carcinogenesis, National Cancer Institute, NIH

2008 Assistant Professor, Department of Gastroenterology, Kanazawa University

2016 Associate Professor, Department of General Medicine, Kanazawa University

2022 Professor, Department of Gastroenterology, Kanazawa University

#### **RESEARCH INTERESTS**

Liver Cancer, Cancer Stem Cell, Biomarker Molecularly Targeted Therapy

#### **REPRESENTATIVE PUBLICATIONS**

1. Machitani M, Nomura A, Yamashita T, et al. Maintenance of R-loop structures by phosphorylated hTERT preserves genome integrity. *Nat Cell Biol.* 2024 26(6) 932-945.
2. Matsuda Y, Ye J, Yamakawa K, Mukai Y, Azuma K, Wu L, Masutomi K, Yamashita T, et al. Association of longer telomere length in cancer cells and cancer-associated fibroblasts with worse prognosis. *J Natl Cancer Inst.* 2023 115(2):208-218.
3. Iida N, Mizukoshi E, Yamashita T, Yutani M, Seishima J, Wang Z, Arai K, et al. Chronic liver disease enables gut *Enterococcus faecalis* colonization to promote liver carcinogenesis. *Nat Cancer* 2021;2:1039-1054.
4. Yamashita T, Koshikawa N, et al. Serum laminin  $\gamma$ 2 monomer as a novel diagnostic and predictive biomarker for hepatocellular carcinoma. *Hepatology* 2021.
5. Yasukawa M, Ando Y, Yamashita T, et al. CDK1 dependent phosphorylation of hTERT contributes to cancer progression. *Nat Commun* 2020; 11 1557.

## Prediction of hepatocellular carcinoma

**Prof. Taro Yamashita**

Chronic liver diseases associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) infection are major causes of hepatocellular carcinoma (HCC), the most prevalent primary liver malignancy and the third leading cause of cancer-related death worldwide. Therefore, regular surveillance for HCC is recommended in patients with chronic liver disease associated with HBV and HCV infection even after viral eradication, especially those with cirrhosis, to detect the tumors at an early stage when curative treatments are available. In addition to imaging studies, the use of biomarkers is also recommended for HCC surveillance in those patients. Several serum biomarkers, including alpha-fetoprotein (AFP), AFP-L3, and des-gamma-carboxy prothrombin (DCP), have been proposed as potential tools for the early detection of HCC.

Here, we introduce the laminin  $\gamma 2$  monomer (LG2m) as a potential biomarker for HCC surveillance in chronic viral hepatitis patients. In our previous multicenter prospective cohort study, we demonstrated the utility of serum LG2m measurement for predicting HCC in chronic hepatitis C patients who achieved sustained virological responses after treatment with direct-acting antivirals. Recently, we also observed the clinical utility of LG2m as a biomarker for HCC surveillance in patients with chronic HBV infection in a retrospective study. We also summarize our recent multicenter prospective cohort study including about 5,800 patients with HBV/HCV infection and/or steatotic liver diseases.



## Moderator

### Takumi Kawaguchi

#### **AFFILIATION / INSTITUTION**

Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine

#### **POSITION**

Professor

#### **EDUCATIONAL**

1995, MD. Degree from Kurume University School of Medicine

1999, Ph.D. Degree in Kurume University Graduate School of Medicine

2000, Research Fellow, University of Texas, Southwestern Medical Center, Texas, USA.

2012, Assistant Prof. Div. of Gastroenterology, Dept. of Medicine, Kurume University School of Medicine

2022, Professor and Chairman, Div. of Gastroenterology, Dept. of Medicine, Kurume Univ. School of Med.

#### **COMMITTEE / MEMBER**

The Japan Society of Hepatology, International Committee Member

Evidence-Based Clinical Practice Guidelines for MASLD 2025, Committee Member

Clinical and Molecular Hepatology, Editorial Board Member

The Global MASH Council, Member

#### **RESEARCH INTERESTS**

Nutritional therapy for liver cirrhosis

Exercise and anti-diabetic therapy for MASLD

#### **REPRESENTATIVE PUBLICATIONS**

1. Suzuki H, Fujiwara N, Singal AG, Baumert TF, Chung RT, Kawaguchi T, Hoshida Y. Prevention of liver cancer in the era of next-generation antivirals and obesity epidemic. *Hepatology*. 2025 in press.
2. Hashida R, Nakano D, Kawaguchi M, Younossi ZM, Kawaguchi T. Changing from NAFLD to MASLD: The implications for health-related quality of life data. *J Hepatol*. 2024;80:e249-e251.
3. Nakano M, Kawaguchi M, Kawaguchi T. Almost identical values of various non-invasive indexes for hepatic fibrosis and steatosis between NAFLD and MASLD in Asia. *J Hepatol*. 2024;80:e155-e157.
4. Suzuki H, Tanaka T, Yamaguchi S, Miwa K, Kawaguchi T. Changing from NAFLD to MASLD: Similar prognosis of unresectable extrahepatic gastrointestinal cancer under chemotherapy between NAFLD and MASLD. *J Hepatol*. 2024;80:e150-e151.
5. Méndez-Sánchez N, Bugianesi E, Gish RG, Lammert F, Tilg H, Nguyen MH, Sarin SK, Fabrellas N, Zelber-Sagi S, Fan JG, Shiha G, Targher G, Zheng MH, Chan WK, Vinker S, Kawaguchi T, Castera L, Yilmaz Y, Korenjak M, Spearman CW, Ungan M, Palmer M, El-Shabrawi M, Gruss HJ, Dufour JF, Dhawan A, Wedemeyer H, George J, Valenti L, Fouad Y, Romero-Gomez M, Eslam M; Global multi-stakeholder consensus on the redefinition of fatty liver disease. *Global mul*



## **Moderator**

**Woo Jin Chung**

### **AFFILIATION / INSTITUTION**

Department of Internal Medicine ; Keimyung University Dongsan Hospital

### **POSITION**

Professor

### **EDUCATIONAL**

March 1988 - February 1994	Bachelor of Medicine Keimyung University, School of Medicine
March 1996 - February 1998	Degree of Master of Medical Science (Internal Medicine)Keimyung University, School of Medicine
March 1998 - February 2003	Degree of Ph.D. of Medical science (Physiology)Keimyung University, School of Medicine

### **POSTDOCTORAL TRAINING**

May 2002 - February 2003	Clinical fellow in Gastroenterology Keimyung University, Dongsan Medical Center
March 2003 - February 2004	Postdoctoral research fellow in Medicine (Dr. David A. Brenner) Columbia University, NY, USA.
March 2008 - August 2009	Postdoctoral research fellow in Medicine (Dr. Raymond Chung) Massachusetts General Hospital, Harvard Medical School.

### **RESEARCH INTERESTS**

Viral Hepatitis, Liver cirrhosis / HCC.

### **REPRESENTATIVE PUBLICATIONS**

1. Aetiology of chronic liver disease is a valuable factor for stratifying adverse outcomes of acute decompensation: prospective observational study. *Ann Med.* 2025 Epub 2025 Jan 24.
2. Diagnostic performance of procalcitonin for bacterial infection in severe alcoholic hepatitis compared with C-reactive protein. *BMC Gastroenterol.* 2024 Nov 25;24(1):428.
3. Next-generation sequencing analysis of hepatitis C virus resistance-associated substitutions in direct-acting antiviral failure in South Korea. *Clin Mol Hepatol.* 2023 Apr;29(2):496-509.
4. Platelet-to-White Blood Cell Ratio Is Associated with Adverse Outcomes in Cirrhotic Patients with Acute Deterioration. *J Clin Med.* 2022 Apr 27;11(9):2463.
5. Multicenter Analysis of Clinical Features and Prognosis of COVID-19 Patients with Hepatic Impairment. *Gut Liver.* 2021 Jul 15;15(4):606-615.



## Speaker

### Hayato Hikita

#### **AFFILIATION / INSTITUTION**

Graduate School of Medicine The University of Osaka

#### **POSITION**

Associate professor

#### **EDUCATIONAL**

2001: M.D., Osaka University School of Medicine

2001-2007: Residency, Osaka University Hospital & Osaka-Minami Medical Center

2007-2010: Graduate student, Dept. of Gastroenterology and Hepatology,

Osaka University, Graduate School of Medicine

2010: Ph.D. in Medical Science, Osaka University

2010-2012: Postdoctoral Fellow, Osaka University Hospital

2012-2022: Assistant Professor, Dept. of Gastroenterology and Hepatology,  
Osaka University, Graduate School of Medicine

2022-present: Associate Professor, Dept. of Gastroenterology and Hepatology,  
Osaka University, Graduate School of Medicine

Board-certified in Internal Medicine, Gastroenterology, Hepatology, and Endoscopy

Associate Editor: Hepatology Research, Journal of Gastroenterology

#### **RESEARCH INTERESTS**

- 1.Elucidation of the mechanisms of hepatocyte cell death and its role in the progression of liver diseases
- 2.Dissecting intercellular communication within the liver microenvironment during liver fibrosis, hepatocarcinogenesis, and tumor progression
- 3.Real-world data analysis of liver diseases using multicenter cohorts
- 4.Development of novel disease-related biomarkers in liver diseases

#### **REPRESENTATIVE PUBLICATIONS**

1. Kudo S, Hikita H, Takehara T, et al. Collaborative orchestration of BH3-only proteins governs Bak/Bax-dependent hepatocyte apoptosis under antiapoptotic protein-deficiency in mice. *Cell Death Differ.* 2025 in press
2. Kumazaki S, Hikita H, Takehara T, et al. Serum growth differentiation factor 15 is a novel biomarker with high predictive capability for liver cancer occurrence in patients with MASLD regardless of liver fibrosis. *Aliment Pharmacol Ther.* 2024 Aug;60(3):327-339.
3. Makino Y, Hikita H, Takehara T, et al. Constitutive Activation of the Tumor Suppressor p53 in Hepatocytes Paradoxically Promotes Non-Cell Autonomous Liver Carcinogenesis. *Cancer Res.* 2022 Aug 16;82(16):2860-2873.
4. Myojin Y, Hikita H, Takehara T, et al. Serum growth differentiation factor 15 predicts hepatocellular carcinoma occurrence after hepatitis C virus elimination. *Aliment Pharmacol Ther.* 2022 Feb;55(4):422-433.
5. Myojin Y, Hikita H, Takehara T, et al. Hepatic Stellate Cells in Hepatocellular Carcinoma Promote Tumor Growth Via Growth Differentiation Factor 15 Production. *Gastroenterology.* 2021 Apr;160(5):1741-1754. e16.

## **GDF15 as a key driver and predictive biomarker in hepatocellular carcinoma: Evidence from basic and multicenter clinical studies**

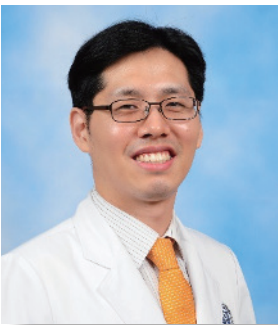
**Dr. Hayato Hikita**

Growth differentiation factor 15 (GDF15), a stress-induced cytokine, has been identified as a key regulator in the progression of hepatocellular carcinoma (HCC). Our basic research demonstrated that hepatic stellate cells (HSCs), under conditions of metabolic and inflammatory stress, promote tumor growth through autophagy-dependent GDF15 secretion (Gastroenterology, 2021). GDF15 expression was markedly elevated in HSCs within the tumor microenvironment, where it enhanced hepatoma cell proliferation via paracrine signaling. Loss-of-function experiments using GDF15-deficient HSCs revealed a significant reduction in tumor progression, highlighting GDF15's pivotal role in HSC-mediated carcinogenic crosstalk.

Subsequently, we validated the clinical significance of GDF15 as a biomarker for liver cancer development. In a large, multicenter cohort of hepatitis C patients achieving viral clearance, elevated baseline serum GDF15 levels were independently associated with future HCC development, even among patients with low fibrosis burden (Aliment Pharmacol Ther, 2021). A composite risk score combining GDF15, AFP, and the FIB-4 index enabled effective stratification of HCC risk across diverse fibrosis stages.

This finding was further extended to patients with metabolic dysfunction-associated steatotic liver disease (MASLD), where serum GDF15 levels were associated with histological activity and future HCC risk. Notably, GDF15 added incremental predictive value beyond conventional clinical indices, supporting its utility in risk assessment for MASLD-related hepatocarcinogenesis (Aliment Pharmacol Ther, 2024).

Most recently, we also demonstrated that high serum GDF15 is an independent risk factor for HCC development in patients with chronic hepatitis B treated with nucleos(t)ide analogs, despite effective viral suppression. (Hepatology Research, 2024). These findings underscore the dual significance of GDF15—as a pathogenic mediator and as a clinically applicable biomarker—for identifying high-risk individuals across diverse liver disease etiologies.



## Speaker

### **Beom Kyung Kim**

#### **AFFILIATION / INSTITUTION**

Department of Internal Medicine, Yonsei University College of Medicine

#### **POSITION**

Professor

#### **EDUCATIONAL**

1997-2003 Yonsei University College of Medicine, Seoul, Republic of Korea

2005-2007 Master Degree, Graduate School, Yonsei University College of Medicine, Seoul, Republic of Korea

2010-2013 Ph.D., Graduate School, Yonsei University College of Medicine, Seoul, Republic of Korea

#### **SUMMARY OF TRAINING AND EMPLOYMENT**

2003.Mar-2004.Feb Intern, Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea

2004.Mar-2008.Feb Resident, Department of Internal Medicine, Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea

2008.Apr-2011.Apr Military service as a doctor

2011.May-2013.Feb Fellow (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

2013.Mar-2018.Feb Contract employment doctor (Division of Gastroenterology), Severance Hospital, Yonsei University Health System / Assistant clinical professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

2018.Mar-2020.Feb Assistant professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

2020.Mar-2023.Feb Associate professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

2021.Aug-2022.Jul Visiting scholar at the NAFLD research lab, University of California San Diego, La Jolla, CA, USA

2023.Mar- Professor (Division of Gastroenterology), Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

#### **RESEARCH INTERESTS**

Major research interests:

Viral hepatitis, liver cirrhosis, and liver cancer

Epidemiology of liver disease

Pharmacoeconomics in liver disease

#### **REPRESENTATIVE PUBLICATIONS**

1. Kim BK, Bernstein N, Huang DQ, Tamaki N, Imajo K, Yoneda M, Sutter N, Jung J, Nguyen K, Nguyen L, Le T, Madamba E, Richards L, Valasek MA, Behling C, Sirlin CB, Nakajima A, Loomba R. Clinical and

histologic factors associated with discordance between steatosis grade derived from histology vs. MRI-PDFF in NAFLD. *Aliment Pharmacol Ther.* 2023 Jul;58(2):229-237. doi: 10.1111/apt.17564. Epub 2023 Jun 2.

2. Kim DS, Kim BK, Lee JS, Lee HW, Park JY, Kim DY, Ahn SH, Pyrsopoulos N, Kim SU. Noninvasive risk assessment of hepatic decompensation in patients with hepatitis B virus-related liver cirrhosis. *J Gastroenterol Hepatol.* 2023 Aug;38(8):1372-1380. doi: 10.1111/jgh.16210. Epub 2023 May 15.
3. Kim BK. How to deliver palliative care for patients with management in decompensated cirrhosis. *Hepatobiliary Surg Nutr.* 2023 Aug 1;12(4):576-579
4. Kim BK, Ahn SH. Prediction model of hepatitis B virus-related hepatocellular carcinoma in patients receiving antiviral therapy. *J Formos Med Assoc.* 2023 Jun 15:S0929-6646(23)00198-5. doi: 10.1016/j.jfma.2023.05.029. Online ahead of print.
5. Kim BK, Bergstrom J, Loomba R, Tamaki N, Izumi N, Nakajima A, Idilman R, Gumussoy M, Oz DK, Erden A, Truong E, Yang JD, Nouredin M, Allen AM, Loomba R, Ajmera V. Magnetic resonance Elastography-Based prediction model for hepatic decompensation in NAFLD; a Multi-Center cohort study. *Hepatology.* 2023 May 22. doi: 10.1097/HEP.0000000000000470. Online ahead of print.

## Future perspective of research for liver disease in the Asia-Pacific region

**Prof. Beom Kyung Kim**

The Asia-Pacific region covers over half of the world's population and has a high disease burden of liver diseases. This region had the highest number of liver-related mortality, with chronic hepatitis B virus (HBV) infection being the leading cause. However, the prevalence and management of liver diseases in this region are changing due to factors such as an aging population, urbanization, lifestyle changes, environmental pollution, and emerging infections. The researches in the field of hepatology in the Asia-Pacific region will face many challenges, including understanding and addressing the diversity of liver diseases among different populations. For example, there are significant variations in HBV genotypes, prevalence of co-infections (e.g. hepatitis D virus, hepatitis C virus, and human-immunodeficiency virus), other co-morbidities, pattern of disease progression, and treatment outcomes among different groups of patients. Additionally, new infection with outbreak, such as coronavirus, might pose a threat to public health in the field of hepatology. In addition to viral hepatitis, the most prominent pattern of the liver disease within the recent several decades in the Asia-Pacific region is the increased proportion of patients with metabolic-associated fatty liver disease (MAFLD). Since there has been no approved disease-specific medication against non-alcoholic fatty liver disease or MAFLD, the current strategies have focused only on the conventional approaches including life style modification and management of co-morbidities. In the near future, the novel medication and biomarkers will be available to treat such patients. To establish effective strategies for reduction of the burden of liver diseases is another major challenge. A multi-disciplinary approach involving prevention, early diagnosis and treatment, management of complications, public health interventions as well as development of newer treatment modality and biomarkers should be required to address this issue appropriately. However, there are barriers such as limited awareness, stigma, discrimination, poverty, lack of access to healthcare services, and insufficient funding.

In summary, the liver research in the Asia-Pacific region faces numerous challenges, but there are also opportunities to improve the health and well-being of millions of people who suffer from liver diseases. Collaborative and comprehensive efforts are needed to address the diversity of liver diseases among different populations, and innovative and sustainable solutions are necessary to overcome barriers to effective care.



## Speaker

### **Kai-Chi Chang**

#### **AFFILIATION / INSTITUTION**

Attending physician, Department of Pediatrics, National Taiwan University Hospital

#### **POSITION**

Assistant Professor

#### **EDUCATIONAL**

09/2001-06/2008	M.D.	College of Medicine, National Taiwan University
09/2013-01/2016	Master	Graduate Institute of Clinical Medicine, National Taiwan University
09/2017-01/2024	Ph.D.	Graduate Institute of Clinical Medicine, National Taiwan University
07/2008-06/2011	Resident	Department of Pediatrics, National Taiwan University Hospital
07/2011-06/2013	Fellow	Pediatric Gastroenterology, Hepatology, and Nutrition, National Taiwan University Hospital

#### **RESEARCH INTERESTS**

Viral hepatitis  
Pediatric liver transplantation  
Gut microbiota  
Obesity in children and metabolic dysfunction associated fatty liver disease

#### **REPRESENTATIVE PUBLICATIONS**

1. Chang KC, Chang MH, Chen HL, Cheng FW, Wu JF, Su WJ, Hsu HY, Ni YH. Survey of hepatitis B virus infection status after 35 years of universal vaccination implementation in Taiwan. *Liver Int.* 2024 Aug;44(8):2054-2062.
2. Chang KC, Chua HH, Chen YH, Tsuei DJ, Lee MH, Chiang CL, Jeng YM, Wu JF, Chen HL, Hsu HY, Ni YH, Chang MH. Hepatitis B virus X gene impacts on the innate immunity and immune-tolerant phase in chronic hepatitis B virus infection. *Liver Int.* 2022 Oct;42(10):2154-2166.
3. Liao FM, Chang KC, Wu JF, Chen HL, Ni YH, Chang MH. Direct Bilirubin and Risk of Biliary Atresia. *Pediatrics.* 2022 Jun 1;149(6):e2021053073.
4. Chang KC, Chang MH, Chen HL, Wu JF, Chang CH, Hsu HY, Ni YH. Universal Infant Hepatitis B Virus (HBV) Vaccination for 35 years: moving toward the Eradication of HBV. *J Infect Dis.* 2021 Aug 7;jiab401. Aug;50(3):306-316.
5. Chang KC, Chang MH, Lee CN, Chang CH, Wu JF, Ni YH, Wen WH, Shyu MK, Lai MW, Chen SM, Hu JJ, Lin HH, Hsu JJ, Mu SC, Lin YC, Liu CJ, Chen DS, Lin LH, Chen HL; Taiwan Study Group for the Prevention of Mother-to-Infant Transmission of HBV (PreMIT study). Decreased neonatal hepatitis B virus (HBV) viremia by maternal tenofovir treatment predicts reduced chronic HBV infection in children born to highly viremic mothers. *Aliment Pharmacol Ther.* 2019 Aug;50(3):306-316.

## Microbial and metabolic signatures associated with graft status in pediatric liver transplantation

Dr. Kai-Chi Chang

Liver transplantation is the only curative option for children with end-stage liver disease, yet long-term graft survival remains challenged by rejection episodes, even under standard immunosuppressive regimens. Recent evidence has highlighted the gut-liver immune axis as a potential modulator of transplant outcomes. In this context, our study investigates the roles of gut microbiota and circulating metabolites in shaping graft tolerance or rejection following pediatric liver transplantation.

We prospectively collected fecal and plasma samples from children with biliary atresia who underwent liver transplantation. Using 16S rRNA gene sequencing and untargeted plasma metabolomics, we profiled microbial and metabolic changes across pre-transplant, post-transplant tolerant, and rejection phases. A random forest classification model identified *Ruminococcus gnavus*, *Clostridium ramosum*, and *Bifidobacterium longum* as highly enriched during periods of clinical stability and graft tolerance. Their relative abundance inversely correlated with liver transaminases (AST and ALT) in select cases, suggesting a potential protective role against graft injury.

Metabolomic analysis further revealed that plasma L-isoleucine levels were significantly elevated during the tolerant state compared to both pre-transplant and rejection periods. This amino acid may serve as a functional mediator in the microbiota-immune interaction. Transplanting hepatocytes derived from green fluorescent protein (GFP) transgenic mice to wild recipient mice was performed. GFP localization in the liver indicating donor cell engraftment varied among recipient mice treated with *Ruminococcus gnavus* culture supernatant, *Bifidobacterium longum* culture supernatant, or L-isoleucine supplementation.

These preliminary findings underscore a potential gut microbial-metabolite signature linked to graft tolerance in pediatric liver transplant recipients. Further mechanistic studies are warranted, as they may offer new avenues for therapeutic modulation.