

THE FIFTH WUHAN INTERNATIONAL CONFERENCE ON LIVER AND CARDIOVASCULAR SCIENCE

A healthy model of health innovation

The growing prevalence of obesity, type-2 diabetes and high blood pressure has generated much media attention, as well as efforts to intervene. These conditions all raise the risk of non-alcoholic fatty liver disease (NAFLD), a common liver disorder often overlooked. "NAFLD is a looming public health threat," said Hongliang Li, dean of the School of Basic Medical Science, and director of the Institute of Model Animal (IMA) of Wuhan University, as he chaired a conference on liver and cardiovascular diseases. "We have considerably underestimated its threat."

Caused by the accumulation of extra fat in liver cells, fatty liver disease is traditionally considered a condition more prevalent among heavy drinkers. But it also affects light drinkers and non-drinkers as a metabolic syndrome. When it progresses, it can lead to inflammation, a condition known as non-alcoholic steatohepatitis (NASH), which can cause serious problems, including liver cancer and liver failure. However, key mechanisms leading to the condition are not yet understood.

The fifth Wuhan International Conference on Liver and Cardiovascular

Science (WICCS), hosted by IMA of Wuhan University, focuses on the pathogenesis of NAFLD, the pathology of metabolic disorder and chronic cardiovascular diseases, attempting to promote new diagnostic and treatment technologies targeting these conditions. It attracted to Wuhan more than 120 leading experts in the field and editors of influential journals, including 60 top experts from outside of China, to exchange the latest research discoveries, with a view to fostering collaboration to address this pressing public health challenge.

Exploration of NAFLD and related liver diseases

NAFLD is the most common chronic liver disease, with an estimated global prevalence rate of about 25%, said David E. Cohen from Weill Cornell Medical College, is the chief editor of *Hepatology*. In discussing NAFLD management strategies, Cohen disclosed the key roles of thioesterase superfamily member 1 in regulating the transportation of fatty acids and metabolism of glucose in liver cells.

In the field of liver sterol homeostasis, Peter Tontonoz from University of California, Los Angeles (UCLA), reported how LXRs affect cholesterol

movement within cells through regulating of the novel ER-resident transporter Aster-B. Both studies, together with reports from Jacob George, Samuel Klein, Richard Green, Gyongyi Szabo, Bernd Schnabl and others, shed light on new molecular targets that could potentially be leveraged in managing metabolic complications, including NAFLD, diabetes, and obesity.

In China, the prevalence rate of NAFLD is even higher, exceeding 29%. At this rate, the number of people with NAFLD is expected to reach 315 million in China by 2030, of which 48 million will be suffering from NASH, said Li.

Using clinical big data and multi-omics data, including proteomics and metabolomics techniques, Li explored the epidemiology of NAFLD and the mechanism of its progression to NASH. "We discovered a target that is promising in pre-clinical experiments," said Li. The target inhibitor worked

well in non-human primate models. "We hope our finding will improve understanding of NASH and provide a new route to finding its treatment," said Li.

Looking at the progression from NASH to liver cancer, Michael Karin from University of California, San Diego (UCSD), discussed metabolic and immune control of non-viral liver cancer. His work on the mediating function of Caspase-2 in de novo lipogenesis and cholesterol biosynthesis has helped establish molecular links between obesity, inflammation and cancer, revealing new targets for therapy, as well as treatment of NASH and other diseases. Also interested in the mechanism by which fibrosis precedes liver cancer, Robert Schwabe from Columbia University illustrated the origin and function of myofibroblasts in the development of liver cancer, which also provides a promising niche for liver cancer treatment.

Exploration of metabolic disorder and cardiovascular diseases

Focusing on the role of inflammation in the pathogenesis of heart failure, Joseph A. Hill from University of Texas (UT) Southwestern Medical Center, winner of the International Society for Heart Research's 2018 Research Achievement Award, discussed macrophages' role in inflammation responses and how cGAS responds to cytosolic DNA and mediates the protective inflammatory response of macrophages in heart muscles following myocardial ischemia. Hill's latest research also suggests that inflammation plays a key role in the pathogenesis of heart failure with preserved ejection fraction (HFpEF).

In battling HFpEF, Steven R. Houser, a world renowned expert in cardiovascular field from Temple University, reported that slow progressive pressure overload induces a

cardiopulmonary phenotype that resembles HFpEF patients and treating these animals with HAD inhibitors reserved pathological hypertrophy and reversed protein acetylation defects that were linked to diastolic filling abnormalities. This progress sheds light on the unmet clinical need to develop HFpEF therapies.

Another renowned expert in cardiovascular diseases, Kenneth Walsh, from University of Virginia, reported his team's latest work on clonal hematopoietic cell resulted from accumulation of somatic cell DNA mutations, and its role in cardiovascular diseases. Based on this, Walsh also proposed treatments to target potential mutations in epigenetic modifier genes.

Studying cardiovascular metabolism, Jane E. Freedman, from University of Massachusetts Medical School, suggested that circulating extracellular RNAs (ex-RNAs) can bridge obesity and the

metabolic syndrome. They interact with messenger RNAs and are distributed in the body via fatty tissue, playing a role in cardiovascular diseases and metabolic disorders.

World renowned experts in cardiovascular fields, such as Gerald W. Dorn II, David J. Lefer, Peter Liu, Qingbo Xu, Xinliang Ma, Yibin Wang, Walter J. Koch, Rong Tian and others also brought up their latest advance in deciphering the mechanism of cardiovascular diseases.

Furthermore, Philipp E. Scherer, from UT Southwestern Medical Center, introduced the central role of adipo-hepatic communication axis in the metabolic process. He pointed out that adipose tissue, while increasing the risks of diabetes and cardiovascular diseases, can protect liver and other tissue by preventing lipotoxicity. There were also talks about the role of nadph oxidases in liver fibrosis and liver cancer by UCSD's David Brenner; cellular recovery and functional

compensation after liver injury by Wolfram Goessling from Harvard University, and the use of genomic techniques for molecular typing, which enables personalized treatment for liver cancer, by Jessica Zucman-Rossi from University Paris Descartes.

Held every two years by IMA, WICCS is already in its 10th year, and has become a key event in the global community of liver metabolism and cardiovascular research. Though small-scale, the 'invitation-only' conference maintains its high quality and influence. As an effort of IMA to expand its international influence, WICCS has played a pivotal part in promoting China's research in the field and promoting international collaboration. ■



Hongliang Li

Dean of the School of Basic Medical Science, and director of the Institute of Model Animal (IMA) of Wuhan University