

Embracing basic and clinical innovation in hepatology

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The 5th issue of JHEP Reports highlights what our new journal and EASL stand for: Innovation; an open mind welcoming new ideas and underrepresented areas of hepatology; as well as a forum for all aspects of hepatology, ranging from cutting-edge basic research, through clinical practice and diagnostic tools, to public health policies. Providing such a forum and stimulating an active exchange between different areas of hepatology is what will propel our field forward. We therefore encourage all readers to look at the entire content of this issue, to see if there may be something interesting that could stimulate new ideas and cross-fertilization.

The review articles “Using CRISPR/CAS9 to model human liver disease”¹ and “Recent advances in liver transplantation for cancer: The future of transplant oncology”² are examples of innovation in the basic and clinical hepatology arena. The CRISPR/Cas9 technology, first discovered in bacteria as an immune defense mechanism, has revolutionized biomedicine as a powerful gene editing technology. While impacting on many areas of biomedical research and hopefully also treatment, CRISPR/Cas9 and hepatology are a perfect match because of the high transduction rates that can be achieved in hepatocytes, allowing researchers to genetically alter these cells and mimic many human diseases for basic or preclinical studies, as reviewed by Alves-Bezerra and colleagues.¹ As pointed out by the authors, CRISPR/Cas9 allows researchers to faithfully model acquired and inherited hepatic metabolic diseases as well as liver cancers in animals. The review authored by Sapisochin and colleagues² discusses the new clinical concept of liver transplantation for select patients with cholangiocarcinoma, colorectal and neuroendocrine liver metastases, as well as hepatic epithelioid hemangioendothelioma. Moreover, recent developments for liver transplantation in patients with hepatocellular carcinoma are also discussed, focusing on improved patient selection, options to increase the donor pool, and novel approaches to better predict risk of recurrence. The review article “Public health policies and alcohol-related liver disease”³ approaches the problem of alcohol-related liver disease (ALD) from a new angle. Ventura-Cots and colleagues remind us that about 1 in 13 men die from alcohol-related causes and that alcohol is the leading cause of death in men between 25–45 years of age, with negative consequences for patients, their families, and society as a whole. The authors highlight various public health policies including pricing/taxation, drinking age and youth-focused policies, restriction of alcohol sales by time

and location, and regulation of advertising that could be used to reduce the incidence of ALD. The authors propose that better understanding is needed and that this should lead to a package of regulation, specific for each country, that can decrease alcoholism and ALD.

JHEP Reports receives an increasing number of high-quality primary research articles, reflected by 4 papers published in this edition covering the factors that determine liver disease in the general population, the non-invasive diagnosis of non-alcoholic steatohepatitis (NASH) via a novel spectroscopic technique, the investigation of monocyte and macrophage populations in patients with primary sclerosing cholangitis (PSC), and the role of killer cell immunoglobulin receptor (KIR) alleles in the development of autoimmune hepatitis (AIH).

Männistö and colleagues⁴ investigate the importance of lipopolysaccharide (LPS) as a predictor of liver disease in the general population, using a cohort of 6,727 Finnish individuals. LPS is a cell wall component of gram-negative bacteria and a highly inflammatory mediator. As such, increased LPS levels may not only serve as a biomarker for a leaky gut but also actively contribute to the development of liver disease through the gut-liver axis.

Anty and colleagues employ fiber evanescent wave spectroscopy to non-invasively diagnose NASH.⁵ When performed in the mid-infrared spectral domain, this non-invasive absorption spectroscopic technique can define a patient's metabolic fingerprint. Using this approach, the authors identify NASH in a well-characterized cohort of severely obese patients, that underwent bariatric surgery, with good sensitivity and good negative predictive values. As suggested by the authors, this interesting new technique will require further validation, in particular in other patient groups with NASH outside of bariatric surgery.

Umemura and colleagues⁶ investigate the role of KIR alleles – which play an important role in the regulation of natural killer cells through their interactions with MHC class ligands – in AIH. The authors demonstrate the role of KIR alleles in combination with specific HLA alleles in the susceptibility and progression of AIH, with the KIR3DL1/HLA-B Bw4 KIR/HLA pair being associated with favorable clinical outcomes.

The study by Chen and colleagues⁷ investigated intrahepatic macrophage populations in patients with PSC. The authors found that there was a higher frequency of intrahepatic CD16+ monocytes and more CD68+CD206+macrophages, often expressing the bile acid receptor TGR5, in patients with PSC than in other liver diseases. However, further studies are needed to highlight the role of these populations and in particular the role of macrophage TGR5 in PSC.

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The editorial team at JHEP Reports is looking forward to receiving, reviewing and publishing papers from all areas of basic and clinical hepatology, in particular those that are innovative and/or uncover relevant aspects of basic and clinical hepatology that have not received sufficient attention in the field. Having stated this, we keep in mind that we strive to reveal novel fundamental insights – both in very basic and mechanistic, as well as in translational or clinical hepatology – with the ultimate goal of improving the understanding and treatment of liver disease and serving the interests of our patient community.

References

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