

## JHEP Reports: The fourth issue

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It is a real pleasure for me to introduce the fourth issue of *JHEP Reports*. This pleasure is associated with a significant challenge. I am often asked: "What is the place of *JHEP Reports* in the torrent of new publications?" Indeed, the number of scientific journals is greatly increasing. Based on the International Association of Scientific, Technical and Medical Publishers, there were about 33,100 active scholarly peer-reviewed (English-language) journals in 2018, publishing about 3 million articles per year.<sup>1</sup> In a parallel manner, the number of submissions of works to journals has never been so high. Recently, ScholarOne system and Editorial Manager each managed 2 million original submissions per year. Due to the worldwide increase in the number of researchers and submitted works, journals and publishers in collaboration with scientific societies must increase their offer. That is why the European Association for the study of the Liver (EASL) has decided to build a new journal, *JHEP Reports*. What are the specific features of *JHEP Reports* in the field of hepatology? I arbitrarily decided to present 3 of them:

- 1) **Open access:** The transmission of high-quality scientific information is a major challenge of our time. The ability to access the content of the articles (detailed materials and methods, supplementary data) is essential to progress by confirming or refuting published results and building new hypotheses. The open access format can increase the visibility and impact of scientific articles if high quality remains a requirement. Open access is a current trend in the scientific community. The Directory of Open Access Journals currently lists more than 13,000 journals (<https://doaj.org/>). In the world of Gastroenterology and Hepatology, high-quality open-access journals remain scarce. Open access also increases visibility beyond the scientific community. Indeed, the articles can be read by journalists, political decision-makers and patients, etc. The latter could open up various future possibilities regarding the types of publications (patient guidelines, epidemiology, cost-effective studies) that could be proposed to *JHEP Reports*.
- 2) **Quality:** The requirement for the quality of manuscripts required for publication is a prerequisite for the success of a scientific journal. At the beginning of a journal it is difficult to guarantee its quality. Our editorials and interventions could be seen as a charter of good conduct. *JHEP Reports* have several undeniable advantages. First, *JHEP Reports* is one of the official journals of EASL. The Editor-in-Chief has

been appointed and the team of Editors has been validated by the Governing Board of EASL. Thanks to this support, many key opinion leaders have written and will continue to write outstanding original up-to-date reviews on specific hepatology topics, avoiding overlap with other journals. In this issue, 3 remarkable reviews will discuss the biology of cholangiocarcinoma,<sup>2</sup> lean NASH<sup>3</sup> and the bidirectional relationship between NASH and diabetes.<sup>4</sup> For original submissions, we want to ensure a fast, demanding and fair peer-review process.

- 3) **Open-mindedness:** Some scientific concepts suffer from a lack of controversy and an overly narrow view of certainties. These narrow concepts potentially impede the progress of scientific knowledge. Manuscripts with results that do not confirm previous publications sometimes have difficulty being published in recognized journals. The absence of *a priori* judgment on the subject addressed and the reputation of the authors is a first step towards openness. This step requires the humility of Editors and Reviewers. In contrast, the requirements on the methods used to produce the results are the guarantees of scientific quality. In my opinion, the role of a scientific journal is to stimulate debate and highlight the relativity of the results with permanent scientific rigor. "If we value the pursuit of knowledge, we must be free to follow wherever that search may lead us." Adlai E. Stevenson Jr.

The success of *JHEP Reports* will depend mainly on the quality of the manuscripts submitted by the authors and the quality of the reviewing by the experts. To achieve our objectives, we need you. From now, thank you all.

For this fourth issue, we have 5 original papers on different topics.

### Autoimmune liver diseases

Oo *et al.* report preliminary results on the liver homing of infused autologous polyclonal regulatory T (Treg) cells in 4 patients with autoimmune hepatitis (AIH) (3 with compensated cirrhosis).<sup>5</sup> The primary objective of the present study is the tissue localization of indium-labelled Tregs for up to 3 days after infusion. By serial gamma camera and SPECT imaging, they observed that 22 to 44% of Tregs homed and remained in the patients' liver for at least 3 days, the other part going to bone marrow and spleen. They did not observe significant adverse events after infusions. This preliminary report is encouraging for the future of management of difficult-to-treat AIH. There is a clear medical need for better treatments in this liver disease.<sup>6</sup> Around 10% of patients do not tolerate standard treatment and another 10% do not respond adequately. Moreover, high-dose corticosteroids and

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azathioprine are associated with severe long-term side effects. Infusion of Tregs could be an attractive option but investigators must now translate their observations into clinical studies assessing outcomes.

### Viral hepatitis

Donkers, Appelman *et al.* explored the molecular interactions between the sodium taurocholate co-transporting polypeptide (NTCP), the entry receptor of hepatitis B and D virus (HBV/HDV) and Myrcludex B, a synthetic blocking peptide which has been evaluated in clinical studies.<sup>7</sup> As its name suggests, NTCP is also the principal uptake transporter of conjugated bile acids. Increased glycine and taurine-conjugated bile salts were observed in phase I and II studies assessing Myrcludex B in chronic HBV/HDV hepatitis, without clinical events.<sup>8</sup> The present study demonstrates with elegant experiments that the interaction between NTCP and Myrcludex B is strong, inducing prolonged increases in conjugated bile acids, with Myrcludex B able to transfer to newly synthesized NTCP. These observations could be the basis of optimization of NTCP inhibitors in HBV/HDV infections.

### NAFLD

Non-alcoholic fatty liver disease (NAFLD) has become the main cause of liver disease in Western countries. This is the case in adults but also in children. The prevalence of NAFLD among adolescents is estimated to be 11% in the United States.<sup>9</sup> This epidemic requires implementation of an efficient screening program. Ezaizi *et al.* observed, in a retrospective study, that ALT >45 UI/L and/or fatty liver on ultrasound were present in 58% of overweight/obese children (n = 344).<sup>10</sup> When they only applied the criteria of ALT >2x the gender specific cut-off to define NAFLD, they detected only 26% of children. The current study indicates that liver ultrasound in addition to ALT measurement is useful for the detection of NAFLD among overweight/obese children. Beyond the detection of fatty livers, it is essential to find reliable, non-invasive and non-expensive tools that can iden-

tify steatohepatitis and significant fibrosis, as this subgroup of children will require specific care.

### Cirrhosis

Diabetes is a well-known risk factor for bacterial infection. Patients with cirrhosis also have an increased susceptibility to infection. Some studies suggest that diabetes confers an additional risk of infection in a population of patients with compensated cirrhosis.<sup>11</sup> In contrast, it is currently unknown if it is the case for patients with decompensated cirrhosis. Bossen *et al.* took the advantage of 3 cohorts of patients (n = 1,198) with cirrhosis and ascites, included in 3 randomized controlled trials assessing sata-vaptan in the treatment of ascites, to explore this question.<sup>12</sup> They observed that patients with diabetes did not have an increased rate of infection or death after an infection compared to those without. This seems to be true for different severity stages of diabetes. These results suggest that, in decompensated cirrhosis, diabetes does not increase the susceptibility to infection.

Acute-on-chronic liver failure (ACLF) is a syndrome characterized by organ failures and high short-term mortality in patients with acute decompensation of cirrhosis.<sup>13</sup> Currently, no specific treatment has demonstrated a survival benefit in this medical condition. Prevention of the syndrome could be a more efficient strategy to improve patient outcomes. Identifying high-risk patients is essential. Zaccherini, Baldassare *et al.* assessed the accuracy of baseline (at admission) clinical characteristics to predict the occurrence of ACLF during hospitalization in a prospective observational study (n = 410).<sup>14</sup> They showed that lower hemoglobin level (<9.8 g/dl), higher leukocyte count (>5.59x10<sup>9</sup>/L) and higher MELD score (>13) were independent risk factors for ACLF. The presence of 1, 2 or 3 risk factors was associated with a cumulative incidence of ACLF of 6%, 21% and 59%, respectively. This simple tool can discriminate a subgroup of patients with a significant risk of developing ACLF. To generalize these data, the results should be validated in independent cohorts.

Enjoy the issue and do not hesitate to submit your works to *JHEP Reports*.

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### Conflicts of interest

TG advises Promethera Biosciences and Martin Pharmaceuticals.

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