To the Editor:

We read with interest the recent paper by Fouts et al. [1] showing that bacterial translocation occurs not only in rats with advanced CCl₄-induced cirrhosis but also in rats with early stages of liver injury. Furthermore, the authors suggest that bacterial translocation, mainly in these early stages, is due to increased intestinal permeability more than to changes in the intestinal microbiome. As probiotics can improve intestinal permeability and modulate gut flora [2], there is increasing interest in their possible efficacy to prevent bacterial translocation, and therefore, progression of liver damage and bacterial infections in liver diseases [2–5].

In a previous article published in the Journal of Hepatology [6], we found that a combination of the probiotic Lactobacillus johnsonii La1, vitamin C and glutamate decreased Gram-negative intestinal bacterial overgrowth, bacterial translocation, and intestinal oxidative damage in rats with cirrhosis induced by phenobarbital and CCl₄ administration. Similar results were obtained when rats received vitamin C and glutamate without L. johnsonii La1. However, as L. johnsonii La1 was not administered alone, the specific contribution of this probiotic could not be assessed in the previous study.

To determine the effect of L. johnsonii La1 on intestinal bacterial flora and bacterial translocation, we have recently studied 18 male Sprague-Dawley rats with cirrhosis induced by phenobarbital and CCl₄ through gastric intubation according to a previously described method [7]. When the rats developed ascites confirmed by paracentesis, they were randomized to receive L. johnsonii La1 alone, 10⁹ cfu/day by gastric intubation (n = 9) for 10 days, or water (n = 9). At laparotomy, we found no statistically significant differences between the two groups in the concentration of ileal water (n = 9). At laparotomy, we found no statistically significant liver damage and bacterial infections in liver diseases [2–5].

Furthermore, the authors suggest that bacterial translocation, mainly in these early stages, is due to increased intestinal permeability more than to changes in the intestinal microbiome. As probiotics can improve intestinal permeability and modulate gut flora [2], there is increasing interest in their possible efficacy to prevent bacterial translocation, and therefore, progression of liver damage and bacterial infections in liver diseases [2–5].

In a previous article published in the Journal of Hepatology [6], we found that a combination of the probiotic Lactobacillus johnsonii La1, vitamin C and glutamate decreased Gram-negative intestinal bacterial overgrowth, bacterial translocation, and intestinal oxidative damage in rats with cirrhosis induced by phenobarbital and CCl₄ administration. Similar results were obtained when rats received vitamin C and glutamate without L. johnsonii La1. However, as L. johnsonii La1 was not administered alone, the specific contribution of this probiotic could not be assessed in the previous study.

To determine the effect of L. johnsonii La1 on intestinal bacterial flora and bacterial translocation, we have recently studied 18 male Sprague-Dawley rats with cirrhosis induced by phenobarbital and CCl₄ through gastric intubation according to a previously described method [7]. When the rats developed ascites confirmed by paracentesis, they were randomized to receive L. johnsonii La1 alone, 10⁹ cfu/day by gastric intubation (n = 9) for 10 days, or water (n = 9). At laparotomy, we found no statistically significant differences between the two groups in the concentration of ileal enterobacteria (3.62 ± 0.29 vs. 4.43 ± 0.35 log₁₀ cfu/g feces, p = 0.07) or in the incidence of bacterial translocation assessed by microbiological cultures of mesenteric lymph nodes, ascites, or pleural fluid (4/9 vs. 4/9, p = 1). Neither were differences observed between the two groups regarding intestinal oxidative damage, evaluated by the ileal malondialdehyde concentration (0.82 ± 0.32 vs. 0.74 ± 0.21 nmol/mg protein, p = 0.90). The PCR reaction with specific primers for L. johnsonii La1 (oNCC2461-A and oNCC2461-B) failed to show intestinal colonization in the feces of rats treated with this bacterium.

These findings thus indicate that L. johnsonii La1 alone has no significant effect on intestinal flora and bacterial translocation in this experimental model of cirrhosis. Other studies evaluating Lactobacillus acidophilus and Lactobacillus casei GG in experimental prehepatic portal hypertension [3], and Lactobacillus rhamnosus GG in rats with CCl₄-induced cirrhosis [4] have reported similar results. The present data suggest that the beneficial effects observed in our previous study were mainly due to the antioxidant effect of vitamin C and glutamate. Oxidative damage in the intestinal wall seems to play a relevant role in the gut barrier failure leading to bacterial translocation in several experimental models of cirrhosis and portal hypertension [8,9]. The antioxidant effect of vitamin C and glutamate could have improved intestinal motility and gut permeability, and both these mechanisms would explain the decrease in intestinal bacterial overgrowth and bacterial translocation observed in our previous study [8–10].

Conflict of interest

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References

An unusual risk factor for intrahepatic cholangiocarcinoma

To the Editor:
In the July 2012 issue of the Journal of Hepatology, on the basis of the meta-analysis of 11 studies, Palmer and Patel [1] reported that hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) share common risk factors of tumour development, such as cirrhosis and chronic viral hepatitis. These findings may support the hypothesis that both HCC and ICC are derived from hepatic progenitor cells, and may explain the pathogenesis of combined hepatocellular and cholangiocellular carcinoma. In the report, extrahepatic cholangiocarcinoma (ECC) was excluded from the analysis because the clinicopathological features of ECC were different from ICC, and the specific risk factors for ICC, such as primary sclerosing cholangitis, hepatolithiasis, and biliary malformations were not within the scope of the analysis.

At the annual meeting of the Japan Society for Occupational Medicine held on May 31, 2012, Shinti Kumagai and colleagues reported five cases with cholangiocarcinoma among 40 workers at a printing company in Osaka, Japan [2]. Kumagai and colleagues estimated that the incidence of cholangiocarcinoma among employees of the printing company was about 600 times higher than the national average, which raised the discussion about health hazards caused by chemicals. Soon after the report by Kumagai and colleagues, seven additional employees who had worked at the printing firm between 1991 and 2003 were identified and presented with cholangiocarcinoma. Seven out of 12 employees with cholangiocarcinoma died at the average age of 37, being about half the national average age of death from cholangiocarcinoma [3–5]. On July 11, 2012, the Health, Labor and Welfare Ministry in Japan stated that a total of 17 cholangiocarcinoma patients with a mortality rate of 47% were identified from former and current workers of printing companies across Japan [6–7]. Of the first five cholangiocarinomas found at a printing company, four were ICCs [8], while details about the remaining cases have not been elucidated. Exposure to large amounts of volatile organic compounds, such as methylene chloride (dichloromethane), dichloropropane, and ethylene chloride, without adequate ventilation is assumed to be responsible for the development of cholangiocarcinoma in the printing firm [6–7]. These organic compounds are solved in cleansers to wash ink off of printing machines. More than 20 years ago, excess mortality from liver and biliary tract cancer among cellulose fiber production workers in the United States was reported [9]. Since during the cellulose triacetate production process, employees were mainly exposed to the solvent methylene chloride, the association between methylene chloride exposure and development of liver and biliary tract cancer was suggested. Further, women from bookprinting and offset printing industries in Denmark had an odds ratio of developing liver cancer (HCC, ICC, and combined carcinoma) in excess of 10.0 [10]. However, according to a 36.8-year follow-up of 1473 workers, exposed to methylene chloride on average for 9 years at a concentration of 19 ppm, at a plant producing cellulose triacetate film base, methylene chloride exposure was not associated with any cancer death [11]. The data collected at printing companies in Japan and genetic polymorphisms of the glutathione pathway involved in the metabolism of organic compounds suggest that inhalation of organic compounds may be a risk factor for ICC in a population, when exposure exceeds a threshold dose.

Conflict of interest
The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

References