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Letters to the editor

Understanding the cellular and molecular mechanisms of hepatic fibrosis is essential for basic and clinical researchers

Dear Editors,

We have read with interest the recent Editorial by Dr. Panduro, who proposed a re-evaluation of medical training in hepatology programs at the pregraduate, graduate, and specialty levels, where basic knowledge integration is essential to reduce the gap between fundamental and applied sciences to improve patient therapeutics [1].

The extracellular matrix (ECM), formed by proteoglycans and fibrous proteins, is necessary not only as a supportive platform but also for the normal function of any tissue in the body. ECM homeostasis involves the synthesis and degradation of components in a finely regulated manner. Damage to the tissue alters ECM turnover, resulting in qualitative and quantitative alteration of the ECM components and triggering fibrosis [2, 3].

Several decades ago, Dr. Hans Popper [4] proposed that necrosis leads to fibrosis, and the molecular mechanisms involved have been further elucidated. The liver can be damaged by several factors, such as toxins, viruses, added fructose and alcohol. When injury occurs over a short period, some hepatocytes die, regeneration occurs, scar tissue is produced and degraded in a concerted manner, and the liver parenchyma is restored. However, if the insult persists for a long time, the synthesis of scar tissue continues, leading to fibrosis. Severe fibrosis may result in cirrhosis, which may progress to portal hypertension [5], ascites [6], hepatorenal syndrome [7], and hepatocellular carcinoma (HCC) [8]. Notably, early fibrosis is a reversible condition in most cases; unfortunately, edged fibrosis, consisting of thick bands of collagen surrounding hepatocytes, is considered irreversible. Therefore, fibrosis is the limiting step where reversion is feasible before complicated cirrhosis and HCC lead to patient death. In this context, a recent book [9] has been published that can be utilized by students in the areas of general medicine, hepatology, and gastroenterology and by basic and clinical researchers. The objective of this book is to provide the fundamental mechanisms of the molecular signaling pathways involved in fibrogenesis and fibrinolysis (the process of removing ECM proteins) and the different cell types that participate in these processes, underling the principal molecular targets to pave the way for the development of new liver antifibrotic drugs. This book consists of eleven chapters that describe the normal and diseased composition of the ECM; the pivotal role of inflammation in triggering the fibrotic process; the involved factors and cells in the synthesis and degradation of the ECM, including the role of reactive oxygen species and reactive nitric species in fibrogenesis [10]; the importance of dysregulation of gut microbiota, dysbiosis, to induce inflammation and thereby promote excessive ECM production; and the molecular signaling pathways involved in fibrogenesis in alcohol- [11], viral- [12], or cholestatic-related damage [13] or liver damage induced by metabolic diseases [14] that lead to fibrosis. In addition, the book includes a chapter that summarizes the most useful noninvasive markers of fibrosis to assess spot changes before it becomes severe and another chapter that critically describes the main experimental models of hepatic fibrosis to provide tools for research on the cellular and molecular mechanisms involved in fibrogenesis, aiming to identify suitable pharmacological targets. In summary, this book can be very useful for improving medical training at the pregraduate, graduate, doctoral, and specialty levels. Additionally, the content of this volume will be of use to researchers working in the basic and clinical investigation of hepatic pathologies.

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