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Editorial Board Member of *World Journal of Hepatology*, Nobuyuki Takemura, MD, PhD, FACS, Professor, Department of Hepato-Biliary-Pancreatic Surgery and Pediatric Surgery, Saitama Medical Center, Saitama Medical University, Saitama 350-8550, Japan. takemuranobu-tky@umin.ac.jp

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EDITORIAL

New markers of fibrosis in hepatitis C: A step towards the Holy Grail?

Konstantinos John Dabos

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Konstantinos John Dabos, Department of Hepatology, St Hohn's Hospital, Livingston EH54 6PP, West Lothian, United Kingdom

Corresponding author: Konstantinos John Dabos, MD, PhD, Doctor, Department of Hepatology, St Hohn's Hospital, Howden Road West, Livingston EH54 6PP, West lothian, United Kingdom. konstantinos.dabos@nhslothian.scot.nhs.uk

Abstract

In the present issue of the *World Journal of Hepatology*, Ferrassi *et al* examine the problem of liver fibrosis staging in chronic hepatitis C. They identify novel biomarkers in an effort to predict accurate fibrosis staging with the aid of the metabolome of Hepatitis C patients. Overall I think Ferrassi *et al* took a different approach in identifying fibrosis biomarkers, by looking at the patients' metabolome. Their biomarkers clearly separate patients from controls. They can also separate out, patients with minimal fibrosis (F0-F1 stage) and patients with cirrhosis (F4 stage). Obviously, if these biomarkers were to be widely used, tests for all the important metabolites would need to be readily available for use in hospitals or outpatient setting and that may prove difficult and above all, costly. Nevertheless, this step could eventually lead to a metabolomic approach for novel biomarkers of Fibrosis. Obviously, it would need to be validated, but could represent a step towards the Holy Grail of Hepatology.

Key Words: Hepatitis C metabolomics; Fibrosis; Non invasive markers; Metavir

Core Tip: A novel approach for identifying non-invasive biomarkers as a step towards an accurate serological tool for fibrosis staging in hepatitis C.

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INTRODUCTION

Hepatology is, relatively speaking, a newcomer amongst the medical specialities. Hepatologists have tirelessly worked towards better treatments for patients with liver disease and have achieved great goals resulting in transforming the lives of millions of people with liver disease. However, the ability to accurately estimate the amount of fibrosis in the liver without the need for a liver biopsy, which can be described as the Holy Grail of Hepatology remains unobtainable.

In contrast, one of the achievable goals in the near future is hopefully the elimination of hepatitis C[1]. Since the advent of Direct Acting Antivirals at the beginning of this century, we have been able to cure patients with hepatitis C with great efficacy. The goal of eliminating hepatitis C by 2030 is still a target the community strives towards.

Greatly reducing the numbers of patients with hepatitis C does not necessarily mean that patients with fibrosis and cirrhosis due to previous Hep C infection would not need any follow up[2]. There is still a risk of progression of their existing disease. Hepatologists would ideally like to be able to accurately predict at any point the possibility of progression of liver fibrosis in patient with hepatitis C.

There are already plenty of non invasive fibrosis assessment tests in Chronic Hepatitis C (CHC), which can be classified into physical and serological ones. The most common physical test used in the West is Transient Elastography (Fibroscan, Echosens)[3]. By measuring the liver elasticity it gives a pretty good approximation of the fibrosis stage in CHC. However, very expensive equipment is required and many resource strapped countries cannot rely on it for a comprehensive assessment of the affected population. Acoustic radiation force impulse elastography and magnetic resonance enterography (a 2D gradient recalled Echo) have also been used but are not widely available[4].

Many serological tests are available using direct and indirect biomarkers. Direct biomarkers such as Hyaluronic Acid, European Liver fibrosis panel, Procollagen II, (aspartate amino transferase) to platelets ratio and Non- alcoholic fatty liver diaseas fibrosis score can now be used routinely in clinical practice[5-8].

Indirect biomarkers, like red cell distribution width to platelets ratio, FIB-4 and the Forns index have been used with some success, as index tests, mainly to assess the probability of fibrosis in an individual[9-11]. Tests that combine direct and indirect biomarkers like the Fibro test and the Fibro meter index have also been used as well as combinations of serological and physical tests. The plethora of available tests indicates the lack of confidence in the Hepatology community that any one test alone can accurately predict a patient's liver fibrosis stage[4].

In the present issue of the *World Journal of Hepatology*, Ferrassi *et al*[12] examine the problem of liver fibrosis staging in CHC. They identify novel biomarkers in an effort to predict accurate fibrosis staging with the aid of the metabolome of hepatitis C patients

The authors collected plasma from 46 Patients with hepatitis C who had biopsy proven fibrosis staging, graded by the METAVIR score[12] to F1-F4 grades of fibrosis. They then used an untargeted metabolomic technique to analyse plasma metabolites, using mass spectrometry.

Their analysis found potential metabolites specific for each grade of fibrosis that showed a clustering tendency.those metabolites' clusters were more efficient in distinguishing stage F1 and stage F4 fibrosis on the METAVIR score as between F2 and F3 stages there was an overlap.

They also analysed the accuracy of the sets of metabolites specific for each grade and found that F2 markers were less specific but the sets for the other three grades showed good sensitivity and specificity scores.

The metabolites identified were sterols, fatty acids, lipids and coenzymes .In their discussion the authors point out that markers for F1 fibrosis are linked to the viral replication of the Hep C virus Furthermore, molecules identified as biomarkers in F2 fibrosis stage (*i.e.* ceramide) could be specifically produced in the context of CHC infection. These results make it impossible to generalise the observations to other chronic liver diseases.

CONCLUSION

Overall I think Ferrassi *et al*[11] took a different approach in identifying fibrosis biomarkers, by looking at the patients' metabolome. Their biomarkers clearly separate patients from controls. They can also separate out, patients with minimal fibrosis (F0-F1 stage) and patients with cirrhosis (F4 stage). Obviously, if these biomarkers were to be widely used, tests for all the important metabolites would need to be readily available for use in hospitals or outpatient setting and that may prove difficult and above all , costly. Nevertheless, this step could eventually lead to a metabolomic approach for novel biomarkers of Fibrosis. Obviously, it would need to be validated, but could represent a step towards the Holy Grail of Hepatology.

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FOOTNOTES

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Country/Territory of origin: United Kingdom

ORCID number: Konstantinos John Dabos 0000-0002-5082-0344.

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