Prof. Haitao Zhao—precision medicine and immunotherapy of hepatobiliary malignant tumor

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Expert's introduction

Prof. Haitao Zhao from the Department of Liver Surgery, Peking Union Medical College Hospital, was the leading scholar for the Ten Thousand Talent Program in 2017, and the founder of the 919 Tumor Precision Medicine Public Welfare Foundation. His primary areas of research include: precision medicine and hepatobiliary diseases. As a corresponding author, Prof. Zhao has published over 50 SCI articles, and the total amount of IF is more than 280. He is also the associate editor for *HBSN* (SCI IF 3.45) and the editor for WJG (IF: 3.3) (*Figure 1*).

Figure 1 Prof. Haitao Zhao.

Interview

HBSN: According to the epidemiological investigation, the liver cancer mortality rate has increased in many developed countries and regions, while it has been decreasing in some of the less developed areas like in China between the years of 1990 and 2015. What's the reason for this?

Prof. Zhao: From my point of view, the most important reason for this, is the influence of etiology. Currently, hepatitis C, non-alcoholic fatty liver disease and alcoholic liver disease are the main causes of liver cancer in the developed areas of the world like Europe and America. But historically, the overall incidences of liver cancer in these areas are not very high. With maturity, the discovery of these liver diseases from an early screening, as well as other liver disease caused by alcohol and obesity, the incidence of liver cancer as a whole has not really declined. Because the detection and prevention procedures of the other diseases in these areas are done well, the incidence of liver cancer has showed a relatively increasing trend. In other less developed areas like China, a large-scale hepatitis B vaccination program has led to a significant reduction in the prevalence of hepatitis B among people under 40. Meanwhile, the incidence rate of hepatocellular carcinoma (HCC) in China is on the decline due to the long period of usage of the hepatitis B vaccination. Compared with the same periods of time in history, although the incidence of HCC in our country (China) is generally declining, we're still facing a peaking amount of incidences for HCC diagnoses.

Overall, the main reason that liver cancer has seen a relative increase in frequency in those developed areas is mainly because of lifestyle and regular screening. Conversely, it has decreased in the less developed countries like China mainly resulted from the remittent burden of hepatitis infection, which was attributed to the widespread introduction of liver disease inoculations.

HBSN: As your study shows, TP53 mutation plays a leading role in biliary tract cancer. What is TP53, and what's the reason for its frequent mutation?

Prof. Zhao: Tumor protein p53 shortened as just p53, is any isoform of a protein encoded by homologous genes in various organisms; this is expressed as TP53 for humans, and Trp53 for mice. This homolog is crucial in multicellular

organisms, where it prevents cancer formation; thus, it functions as a tumor suppressor. P53 has been described as "the guardian of the genome" because of its role in conserving stability by monitoring genome mutation. The mutations of TP53 widely occur in various kinds of solid tumors, but the reason is still undefined. We only know that once TP53 mutates, it will lose its inhibitory effect on cancer cells, which leads to the development of a tumor. Although, some new research groups have worked on developing targeted drugs and therapies to prevent the TP53 protein from mutating; however, the progress made so far is not very ideal. This is because it has been proven to be difficult to develop drugs aimed at the gene itself. We can only seek to stop its mutation process by blocking its passageway, but such method still needs to be improved.

HBSN: We know that you are conducting some experimental studies for precision medicine and immunotherapy, could you tell us what kind of expectations you have?

Prof. Zhao: In fact, the usage of this precision medicine has just started, and we are still in the exploratory stage. Now, we can gradually treat some of the previously untreatable tumors, and develop newer targeted drugs for cancers. But there are plenty of drugs with unclear targets such as lenvatinib and regorafenib for a hepatobiliary cancer. It still takes a long time to develop this personalized precision medicine for each patient's each disease. We now are at a stage of collecting the different targets and gene mutations, in order to develop the corresponding drugs. Of course, I'm very optimistic about the prospects of the precision medicine, but at the same time I don't want it to be over-interpreted. The actual tests and results of these precision medicines need to be completed and confirmed by more experimental studies since it's still in the infancy stage, and we will look forward to its broad future. If precision medicine can be proved to be effective and it becomes popular, patients will be the ones who benefit the most from it.

HBSN: At the present, what do you think are the challenges or difficulties of developing precision medicine?

Prof. Zhao: Perhaps the biggest challenge now is the lack of spread and the popularization of the actual concept of precision medicine, as well as the lack of the wide range development of larger clinical trials. The study of precision medicine starts from every small experiment and then unfolds step by step. The process of developing precision medicine needs participation from the patients, an investment of the government, and an understanding of the public, as to carry out a deeper and further clinical practice and scientific research. There is a pressing need to form industry or national standards for this precision medicine, to better regulate the pace of its development. All the experts and scholars in the related fields should reach a consensus to make sure that this technology can get a standardized, and orderly promotion. Personally, I hope that this industry can develop faster, so that patients will benefit from it earlier. Currently in China, the government has paid great attention to the development of this precision medicine, and many of the newly developed drugs are now accessible to ordinary patients. In other words, the development of precision medicine will surely face adversity, with a complicated pathway, but eventually it will end in a bright future.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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