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Conceptual

Could HDFx Ameliorate the Infections and Potential Courses of Hepatocarcinomas and Cirrhosis Induced by Hepatitis B

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Globally, hepatitis B infection is a major public health problem, and infected patients can remain asymptomatic for decades. Approximately 90% of the world's population currently reside in regions of very high and intermediate hepatitis B infection [1]. These patients often, without knowing it, can transmit the virus to other family members, friends, and others carrying diverse diseases. Almost one million people /year die of complications due to infections caused by hepatitis B, including hepatocarcinomas and cirrhosis [2]. In the USA, today, there are as many as two million people living with chronic hepatitis B, who are totally unaware of their infection [3]. Interestingly, approximately 95% of the people with chronic hepatitis B infection come from intermediate/high prevalence countries, primarily due to a lack of screening [2-4]. About 260 million people worldwide are living with chronic hepatitis B infections [3-6].

Major concerns in the inflammatory events produced by hepatitis B viruses (HBV) in the liver center on the loss of immunocompetence of CD4 T-lymphocytes, CD8 T-lymphocytes, natural killer (NK) cells, Kupffer cells, and "pit cells" [4-11]. These cell types are normally "geared" to produce diverse antiviral molecules (i.e., interferons, tumor necrosis-alpha, and a number of interleukins) [7-11]. HBV not only severely hampers the production of these protective antiviral molecules, but results in reduction of these critical cell types in the liver [7,10,11]. So, in our opinion, any effective therapeutic measures against HBV infections, and the sequelae of events leading to cirrhosis and/or hepatocarcinomas, should focus on restoring these vital cell types and their immunocompetence, and thus prevent initiation of inflammatory events in the liver.

For the past several decades, our laboratories have been looking for and investigating peptides/proteins that have unique host-defense attributes [12-15]. These studies have led us to discover a conserved protein in mice, rats, guinea-pigs, rabbits, dogs, and sub-human primates that we have termed host-defense factor x

(HDFx) [14]. So far, through thousands of experiments, we have found and reported that "HDFx" is protective or ameliorative against lethal hemorrhage, lethal intestinal ischemic shock, a variety of endotoxins, trauma, multiple gram-negative and gram-positive bacteria, certain hemorrhagic fever viruses, NASH, several experimental forms of liver cancers, and "cytokine storms" [12-25]. In addition, HDFx stimulates production of immunocompetent T-lymphocytes in infections, immunocompetent NK, Kupffer, and pit cells [12-15,17-20,22]. Interestingly, HDFx causes regeneration of tissues damaged in a variety of pathobiology events in experimental animals [23, 25]. Due to HDFx's unique profile, we have suggested that it may prove very useful in more speedy recovery after orthopedic and other major surgeries, drug-resistant tuberculosis, carcinomas in the liver, and the aggressive changes observed in bacteria found in people/astronauts residing at the space-station [18-21, 23, 25].

A major problem in the progression of HBV infections in the liver is the severe inflammatory reaction causing clogging of capillary blood flow and its normal distribution/nutrition of liver parenchymal, Kupffer, and pit cells [8-11]. Close, histological examination of these tissues often reveals adhesion of leukocytes, macrophages, and platelets to the endothelial cell walls of the microscopic blood vessels with transudation of these blood-formed elements into the surrounding tissues and tissue spaces, leading to greater and greater inflammatory reactions [8-11]. Interestingly, HDFx possesses the unique ability of being able to maintain liver vasomotor tone, reduce adhesion and transudation of blood- formed elements under low-flow and inflammatory conditions, while accelerating the healing process, as observed in numerous experimental states of shock, endotoxemia, and trauma [14,15,25,27].

Conclusions

We have discovered a new host –defense biologic immunomodulator which may provide unique ways to ameliorate and prevent liver inflammatory reactions caused by hepatitis B viruses, and accelerate healing in damaged liver parenchymal, Kupffer, and pit cells induced by HBV. Use of HDFx in susceptible, high-risk patients could eventuate in markedly reduced hospitalizations, reduced- hospital costs, and reduction in development of liver cancers worldwide.

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