World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v4.iSuppl2.29

World J Gastroenterol 1998 October 15; 4(Suppl2): 29
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

Immunological approaches to the breakdown of hepatitis B viral persistence

Geroge KK Lau

Geroge KK Lau, Division of Gastroenterology and Hepatology, University Department of Medicine, Queen Mary Hospital, Hong Kong, China

Author contributions: The author solely contributed to the work.

Correspondence to: Geroge KK Lau, Division of Gastroenterology and Hepatology, University Department of Medicine, Queen Mary Hospital, 102 Pokf ulum Road, Hong Kong, China

Received: June 20, 1998
Revised: July 22, 1998
Accepted: August 14, 1998
Published online: October 15, 1998

Key words: Hepatitis B/immunology; Hepatitis B virus; Hepatitis B/therapy; DNA, viral

Lau GKK. Immunological approaches to the breakdown of hepatitis B viral persistence. *World J Gastroenterol* 1998; 4(Suppl2): 29 Available from: URL: http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/29.htm DOI: http://dx.doi.org/10.3748/wjg.v4.iSuppl2.29

In order to resolve chronic HBV infection, it is pertinent to have a better understanding of the underlying mechanism of viral persistence. Though the exact mechanism that leads to HBV persistence is not yet clear, there is cumulating evidence suggesting that immune tolerance to HBV infection is important. It is generally believed that resolution of acute HBV infection requires adequate B and T cell responses which lead to the production of protective antibodies, as well as broad-based T-cell response against multiple HBV antigenic determinants located on the viral envelope, nucleocapsid and polymerase gene products[1]. Previously, it was demonstrated that serological clearance of HBsAg could occur after allogeneic bone marrow transplantation. Furthermore, it was shown that clearance of HBsAg in chronic HBV carriers was strongly associated with engraftment of anti-HBs positive marrows after allogeneic BMT[2]. This suggested that persistance of HBV infection is due to an immunological defect in the chronic HBV carriers, So far, the only form of immunomodulatory therapy approved for use in chronic HBV infection is IFN-α. In a meta-analysis that included 15 randomised controlled studies with a total of 837 adult chronic HBV carriers, IFN-α was found to be effective in terminating viral replication. The overall loss of HBsAg occurred 6% more often in IFN-α treated patients than the natural seroconversion seen in controls (7.8% compared with 1.8%, $P = 0.001$) and the loss of viral replication occurred approximately 20% more often in treated patients than in controls (33% *vs* 12% for the loss of HBeAg and 37% *vs* 17% for the loss of HBV DNA, $P = 0.0001$)[3]. In a recent 9-year follow-up study, it was found that IFN treatment resulted in higher and earlier r ates of cleared HBeAg and HBV DNA by hybridization in Chinese patients with chronic hepatitis B. Very few patients lost HBsAg despite sustained HBeAg clearance. There was no difference in incidence of hepatic complications between patient s and controls and between those who did and did not clear HBeAg[4]. Tα-1 is currently registered for treatment of chronic HBV infection in China. In a randomized placebo-controlled trial conducted in Taiwan, complete virological response (with clearance of HBeAg and serum HBV DNA by liquid hybridization) was significantly higher in those who receive Tα-1 ($n = 32$) for 6 mo t han the placebo group ($n = 32$, 40.6% *vs* 9.4%; $P = 0.004$), 18 mo after entry, although complete response was similar at the end of treatment[5]. In a recent study conducted in China, the safety and efficacy of Tα-1 for 6 mo was compared with combination of Tα-1 and IFN-α(3MU qd × 10 d then 3 × weekly for 6 mo) in the treatment of chronic HBV infection. Loss of HBeAg and HBV DNA was 27.8% in both groups at month 12. No significant side effect was observed in both groups[6]. Recently, several other forms of immunotherapy such as DNA vaccines, therapeutic vaccine, antigen-antibody complexes, infusion of lymphocytes from immuned donors, and *in vitro* priming of autologous lymphocytes are being developed. This together with the use of nucleoside analogues, such as lamivudine and famciclovir, may become part of the armamentarium in the treatment of chronic HBV infection in the near future.

REFERENCES

1 **Lau GK**, Wang B, Carman W. Immunological approaches to the breakdown of hepatitis B viral persistence. *Chin Med J* (Engl) 1998; **111**: 560-564 [PMID: 11245080]
2 **Lau GK**, Lok AS, Liang RH, Lai CL, Chiu EK, Lau YL, Lam SK. Clearance of hepatitis B surface antigen after bone marrow transplantation: role of adoptive immunity transfer. *Hepatology* 1997; **25**: 1497-1501 [PMID: 9185774 DOI: 10.1002/hep.510250631]
3 **Wong DK**, Cheung AM, O'Rourke K, Naylor CD, Detsky AS, Heathcote J. Effect of alpha-interferon treatment in patients with hepatitis B e antigen-positive chronic hepatitis B. A meta-analysis. *Ann Intern Med* 1993; **119**: 312-323 [PMID: 8328741 DOI: 10.7326/0003-4819-119-4-199308150-00011]
4 **Lau GKK**,Lim W,Lok ASF.Nine years follow-up after interferon (IFN) treatment for chronic hepatitis B (CHB) in Chinese patients. *Hepatology* 1997: **26**: 259A
5 **Chien RN**, Liaw YF, Chen TC, Yeh CT, Sheen IS. Efficacy of thymosin alpha1 in patients with chronic hepatitis B: a randomized, controlled trial. *Hepatology* 1998; **27**: 1383-1387 [PMID: 9581695 DOI: 10.1002/hep.510270527]
6 **Lu ZM**, Gao J, Yao GB, Ji YY, Wu XH, Zhang QB. Lau GKK and China Thymosin Study Group. A comparative trial of thymosin alone and thymosin plus interferon in the treatment of Chinese patients with chronic hepatitis B (CHB). *Hepatology* 1997; **26**: 426A

E- Editor: Li RF

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com