was associated with induction of T-cell immunity against viral antigens and reduction of hepatic expression of Foxp3. Studies performed to elucidate the rational behind the lack of antiviral activity of IL-12 in animals with high viremia showed that the presence of high amounts of WHV-DNA in serum is associated with the absence of IL-12-responsiveness in vitro. In conclusion, IL-12-based gene therapy is an efficient approach to treat chronic hepadnavirus infection in all cases with viral load below $10^{10}$ vg/ml, which is the situation of most patients with chronic hepatitis B. The elucidation of the precise mechanisms responsible for the lack of response to IL-12 in animals with high viral load will be important for the development of more efficient therapies against chronic hepatitis infection.

**I-85 Increased regulatory T-cells impair adaptive immunity and favor disease progression in chronic HBV-infected patients**

F.S. Wang*. Research Center for Biological Therapy, Beijing Institute of Infectious Diseases, Beijing 302 Hospital, Beijing 100039, China

Persistent viral infection in liver is still a global threat to human health. It has been suggested that compromised immune responses play a critical role for chronic viral infection. It is, at least in part, shown that impaired innate and adaptive immunity as well as liver tolerance are responsible for the compromised immune responses, but the underlying cellular and molecular mechanisms remain largely undefined. Recent studies have suggested that CD4+CD25+ regulatory T-cells (Treg) are increased and linked to compromised immune responses in patients with hepatocellular carcinoma (HCC). This study attempts to further characterize CD4+CD25+FoxP3+ Treg in blood, tumor and non-tumor liver tissues of HCC patients, and understand how the Treg affect immune responses and contribute to disease progression. One-hundred and nineteen HCC patients with chronic hepatitis B virus (HBV) infection (designated as HBV-related HCC patients), 21 HBV-related liver cirrhosis (LC) patients, and 47 normal controls were enrolled. Flow cytometric, immunohistochemical, and immunosuppressive assays were employed for analyses of property of Treg. Multivariate analysis of prognostic factors for overall survival was made using Cox’s proportional hazards model. Circulating CD4+CD25+FoxP3+ Treg frequency was significantly increased and correlated with disease progression in HCC patients. An abundant accumulation of Treg concurrent with significantly reduced infiltration of CD8+ T-cells was found in tumor regions compared with non-tumor regions. Granzyme A, B and perforin expressions were dramatically decreased in tumor-infiltrating CD8+ T-cells. Furthermore, Treg of HCC patients inhibited proliferation, activation, degranulation, and production of Granzyme A, B and perforin of CD8+ T-cells induced by anti-CD3/CD28 antibodies. Importantly, increased numbers of circulating Treg were associated with high mortality and reduced survival time of HCC patients.

**Conclusion:** Increased CD4+CD25+FoxP3+ Treg may impair CD8+ T-cell function, promote disease progression and represent both a potential prognostic marker and a therapeutic target for HBV-related HCC individuals.