Published in final edited form as:

Hepatology. 2016 April ; 63(4): 1391–1392. doi:10.1002/hep.28419.

CD14⁺ regulatory Dendritic Cells in Hepatocellular Carcinoma and Cirrhotic patients

Shiroh Tanoue^{1,2} and David E. Kaplan^{1,2}

¹Medicine and Research Services, Philadelphia VA Medical Center, Philadelphia PA

²Division of Gastroenterology, Department of Medicine, University of Pennsylvania

Keywords

hepatitis C; cirrhosis

To the Editor

We read with great interest the article by Han et al.(1), who described a population of peripheral CD11b^{high}CD11c^{high} dendritic cells (DCs), termed CD14⁺ DCs, that appeared to be specifically found in HCC patients but not from healthy donors. CD11b⁺CD11c⁺ DCs have been shown to induce regulatory T-cells and secrete IL-10 and TGF- β in autoimmune disease models.(2, 3) BDCA1⁺ myeloid DC with a similar surface phenotype may have immunoregulatory functions in chronic viral hepatitis.(4)

Cirrhosis has an important impact on CD14⁺ monocyte frequency and phenotype (5) but non-HCC bearing cirrhotic patients were not included as a control group in this study. To confirm the study's findings and to determine any association of cirrhosis with the described phenotype, we recruited age-matched cirrhotic patients (CIR, n=20), hepatocellular carcinoma patients (HCC, n=10), and healthy donors (HD, n=7) and assessed the distribution of CD14⁺ DCs (CD11b^{high}CD11c^{high}HLA-DR⁺CD14⁺ cells) by flow cytometry.

Contrasting with Han et al., we could not reproduce the observed results regarding the increased frequency of this novel CD14⁺ DC subset in liver cancer patients, cirrhotic non-cancer patients or healthy donors (Figure 1A). Furthermore, we found no clear differences of phagocytic ability among monocytes, CD14⁺DCs, and MoDC derived from healthy donors and cirrhotic patients (Figure 1B). While we did identify that cirrhotic monocytes secreted higher levels of IL-10 than HD, CD14⁺ DCs and MoDC were no different in this respect between CIR and HD. (Figure 1C).

One possible cause for the discrepancy between our findings and those of Han et al. could be the effect of aging. While we recruited age-matched healthy donors, the healthy donors recruited by Han et al. were significantly younger than their HCC patients (median 27 versus

49 years old). Age-related increases in the prevalence of circulating CD11b⁺CD11c⁺ DCs was indeed identified in a mouse model of lupus.(6) On the other hand, Han et al. did include non-liver cancer controls that were age-matched and differed in frequency of CD14⁺ DC from their HCC patients. While we found no difference in CD14⁺ DC frequency between chronic hepatitis C-infected and non-HCV infected cirrhotic subjects (data not shown), it is possible that chronic hepatitis B infection could also explain differences in the frequency of CD14⁺ DC they observed.

In summary, we were unable to reproduce the findings of Han et al. with regard to the association of CD14⁺CD11b^{high}CD11c^{high} dendritic cells (DCs) with hepatocellular carcinoma. We recommend further validation of this putative HCC phenotype with the appropriate controls populations, specifically age-matched non-cancer-bearing cirrhotic, non-cirrhotic chronic viral hepatitis patients, and age-matched healthy donors.

Acknowledgments

Research Support:

This work was supported by R01 CA 166111 (DEK).

Abbreviations

CIR	liver cirrhotic patients
HCC	hepatocellular carcinoma patients, HCV, hepatitis C virus
HCV	hepatitis C virus
HD	healthy donor
DC	Dendritic cell
MoDC	Monocyte derived dendritic cell
FCM	Flow Cytometry

References

1. Han Y, Chen Z, Yang Y, Jiang Z, Gu Y, Liu Y, Lin C, et al. Hepatology. 2014; 59:567–579. [PubMed: 23960017]
2. Schmidt SV, Nino-Castro AC, Schultze JL. Front Immunol. 2012; 3:274. [PubMed: 22969767]
3. Li H, Zhang GX, Chen Y, Xu H, Fitzgerald DC, Zhao Z, Rostami A. J Immunol. 2008; 181:2483–2493. [PubMed: 18684939]
4. Dolganiuc A, Paek E, Kodys K, Thomas J, Szabo G. Gastroenterology. 2008; 135:2119–2127. [PubMed: 18835391]
5. Tanoue S, Chang LY, Li Y, Kaplan DE. Under Review. 2015
6. Ishikawa S, Nagai S, Sato T, Akadegawa K, Yoneyama H, Zhang YY, Onai N, et al. Eur J Immunol. 2002; 32:1881–1887. [PubMed: 12115607]

Figure 1.