



شبكة المعلومات الجامعية

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ





شبكة المعلومات الجامعية



شبكة المعلومات الجامعية

التوثيق الالكتروني والميكرو فيلم

جامعة عين شمس

التوثيق الالكتروني والميكرو فيلم

قسم

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بالرسالة صفحات
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**Defining the Role of Plasmacytoid Dendritic Cells
and Type I Interferon in Acute Hepatitis C
Patients**

By

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Approval Sheet

***"Defining the Role of Plasmacytoid Dendritic Cells and
Type I Interferon in Acute Hepatitis C Patients"***

By

Hala Mohamed Mohamed Mansour Gabr; M.Sc.

Approved By Committee in Charge

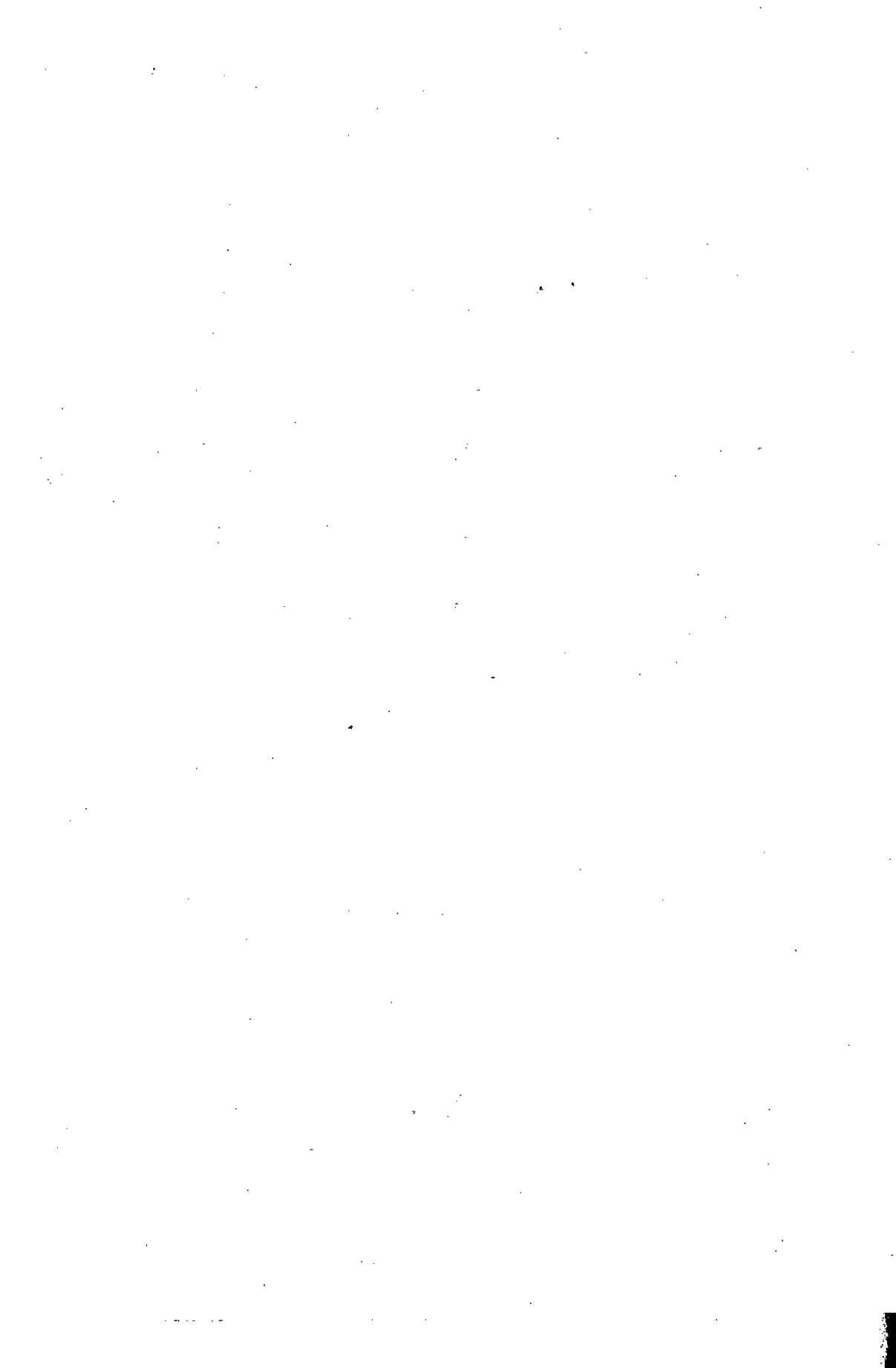
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Prof. Dr. Mona Mohamed Rafik

Prof. Dr. Aly Kholefy Ahmady

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Date: 07 February 2010



Abstract

The population of Egypt maintains one of the largest hepatitis C virus (HCV) epidemic in the world. It has been possible to recruit and follow a cohort of acutely infected individuals with the aim of characterizing the immune activation that occurs during the first six months of HCV infection. Specifically we hypothesized that plasmacytoid dendritic cells (pDCs) may play an integral role in orchestrating the host immune response as the main producers of type I interferon (IFN).

The percentage of pDCs (BDCA-2+/BDCA-4+) present in acute HCV patients was investigated; with no statistical difference in the median percentage of pDCs between healthy donors and acute HCV patients ($p=0.379$), or acute HCV patients that spontaneously cleared their virus and those that did not ($p=0.433$). Acute HCV pDCs showed a normal phenotype: CCR7^{lo}, CD86^{lo}, CXCR3^{lo}, HLA-DR^{hi}. In healthy individuals and acute HCV patients, the pDCs produced measurable amounts of IL1-Ra, IL12p40-70, IP-10, TNF- α , IFN- α and MIP-1 β , when stimulated by CpG, confirming that the pDC populations found in viremic patients are functional. Using real-time qPCR, a higher amount of CXCL10 mRNA was detected in acute HCV patient a difference that was borderline significant ($p=0.057$). Additionally, MxA induction was observed in some HCV acute patients but was not observed at all in healthy patients. These data demonstrate that pDCs circulating during acute HCV infection are consistent in number and surface phenotype as those present in healthy individuals, suggesting that an alternative cell type is responsible for IFN production.

Using clinically validated tests, the concentration of 85 plasma analytes were quantified. Interestingly, seven molecules were identified (sVCAM-1, β_2 M, TBG, Ferritin, sCD40, CXCL10, sICAM-1); those molecules discriminate cleared versus non-cleared HCV patients.

Overall, the present study demonstrates that the circulating pDCs in acute HCV patients are similar to those of healthy donors. Therefore, we recommend the use of pDCs stimulants as a viable drug target for the stimulation of endogenous type I IFN production, which may promote viral clearance in those patients who fail to achieve spontaneous clearance. We also recommend the association of pDCs agonist to the combined therapy by pegylated interferon and ribavirin for chronic HCV cases.



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