Programmed cell death ligand 1 (PD-L1) expression in HIV-associated Diffuse Large B-cellLymphoma – role and regulation

Zahra Latib

University of Cape Town

Introduction: The programmed death ligand 1 (PD-L1) is an essential protein involved in the modulation of immune responses [1]. In the tumour microenvironment (TME), the PD-1/PD-L1 axis is hijacked by cancer cells to escape immune surveillance, where cancer cells overexpress PD-L1 to evade cell death [2]. Diffuse Large B Cell Lymphoma (DLBCL), a highly aggressive cancer, is over-represented among HIV-infected individuals [3]. Studies have shown that PD-L1 is overexpressed in DLBCL, and even more so in HIV-associated DLBCL [4,5]. A recent study has reported that a population of regulatory B cells (Bregs), which suppress effector T cells, are elevated in HIV-positive patients prior to DLBCL diagnosis. These cells overexpress PD-L1, this suggests that PD-L1 plays a pertinent role inin the onset of DLBCL in HIV infected patients [4]. The role and regulation of PD-L1 in DLBCL, both within an HIV-negative and HIV-positive context, remain unclear, and forms the focus of this study.

Methodology: This study has three main objectives, the first being to measure and compare the population of Bregs, PD-L1-positivity, and soluble PD-L1 levels, in the blood of HIV-positive and -negative newly diagnosed DLBCL patients. The second objective will explore the tumour microenvironment (TME) of HIV-positive and HIV-negative formalin-fixed paraffin embedded (FFPE) DLBCL tissue samples to determine the effect of HIV-infection on PD-L1 and immune cells. The final objective involves exploring the relationship between HIV-1, the EBV nuclear antigen 2 (EBNA2), PD-L1 and c-MYC.

Results: Early results indicate the presence of the Breg population and PD-L1-positive Bregs in six newly diagnosed DLBCL patients recruited so far. Recruitment is ongoing. Additionally, an EBNA2- expressing DLBCL cell model was used to confirm the link between EBNA2 and c-MYC, where EBNA2 is shown to significantly enhance the expression of this oncogene. This model will be used to furtherexplore the regulation of PD-L1 by c-MYC, within the context of EBV, HIV and both.

Discussion and Conclusion: This study is still in its early phases, but the preliminary results have uncovered interesting data in the role and regulation of PD-L1 in DLBCL. The findings will assist in uncovering the unique pathobiology of HIV-associated lymphomas and lead to improved management of lymphoma in this population group.

Keywords: Programmed death ligand 1, immune surveillance, HIV-associated DLBCL, regulatory B cells, tumour microenvironment, EBNA2

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