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Immunological and molecular signatures of treatment response in HIV-1/HCV coinfected individuals undergoing Interferon/Ribavirin therapy

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HIV-1/HCV coinfection represents a significant burden on global economy and public health. Up to 30% of HIV-infected patients and 60-90% of HIV-infected injection drug users are infected with HCV. Although highly active anti-retroviral treatment (HAART) is fairly successful in controlling HIV-1 in HIV-1/HCV coinfected individuals, these individuals have increased HCV viremia and accelerated progression of HCV-related chronic liver disease compared to HCV monoinfected individuals. For many years PEGylated interferon -2a/2b (PEG-IFN -2a/2b) and an antiviral drug ribavirin (RBV) have been widely used for the treatment of HCV infection, however it has low treatment success (~50%) and considerable side effects. As a result, direct acting antivirals (DAAs) that can directly target viral replication are being developed. IFNs still form an important component of HCV treatment and therefore it is necessary to investigate the predictive factors of IFN-induced viral clearance. Since dendritic cells (DCs) play an important role in orchestrating innate and adaptive immune response against pathogens, we hereby investigate DC-based markers of successful treatment response in a cohort of HIV-1/HCV co-infected individuals undergoing IFN/RBV therapy. We investigated the quality of DCs with respect to various functional markers before and during the course of treatment in both responders (SVRs) and non-responders (NRs). Further, to understand the molecular basis of these responses, we analyzed the miRNA profile of patients' peripheral blood mononuclear cells. We also confirmed the expression of mRNA targets of miRNAs differentially expressed in SVRs and NRs. Collectively, results of this study led to identification of key immune and molecular signatures that correlate with the treatment response to IFN/RBV therapy in HIV-1/HCV co-infected patients.

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