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Identification of genetic and proteomic biomarkers of immune reconstitution inflammatory syndrome in HIV+ patients who begin anti-retroviral therapy

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Immune reconstitution inflammatory syndrome (IRIS) refers to the paradoxical deterioration or unmasking of infections after antiretroviral therapy (ART). Although a high proportion of IRIS events are secondary to *M. tuberculosis* infection, a variety of other opportunistic infections have also been implicated. Our goal is to study highly specific molecules related to infection and systemic inflammation and to elucidate their potential predictive and diagnostic value as IRIS biomarkers. This is a prospective cohort study, currently, forty-eight HIV+ patients naïve to treatment have been enrolled. We evaluated markers of T cell activation (HLA DR, CD38 and Glut-1) and exhaustion (Tim-3 and PD-1) on CD4+ and CD8+ T cells, CD4 count and plasma viral load at baseline (pre-ART), 8 weeks after ART and around the IRIS events. Gene expression of Tim-3, Galectin-9, Glut-1, CXCL10 and Granulysin was analyzed by qPCR. Among the 48 HIV+ patients, 13 developed herpes associated-IRIS. At baseline HIV+ patients who lately developed IRIS showed an increased expression of Tim-3, PD-1 and Glut-1 receptors on T cells compared with those IRIS- (P=0.001). A highly activated phenotype (CD38, Glut-1, HLA-DR, Tim-3 and PD-1 expression) was also identified in HIV+IRIS+ patients. Early ART initiation resulted in a decline in CD38, PD-1, and Tim-3 expression on HIV+IRIS-patients at the 8 weeks (P=0.01). Tim-3 and Glut-1 mRNA relative expression levels were elevated after 8 weeks of ART and significantly more elevated during the IRIS events. Relative mRNA level of CXCL10, was reduced in HIV+IRIS- patients. Granulysin relative expression did not have significant changes among patients. Our data suggest that longitudinal measurements of T cell activation and exhaustion markers should be included alongside HIV-1 mRNA levels. This type of analysis is important for understanding the immune mechanisms underlying IRIS development, which must be explored in larger cohorts.

Biography

Ramon-Luing L A completed her PhD in the field of Engineering/Biochemistry with focus in Biotechnology (Research Center and Advanced Studies, CINVESTAV). She did a Postdoctoral training in the field of Trichomonosis (CINVESTAV) and Tuberculosis (Institute of Biomedical Research, UNAM). Since 2013, she has been a researcher in medical sciences at the National Institute of Respiratory Diseases and also a member of the National Research System of Mexico. To date, she has published 8 papers; currently she began to study HIV and respiratory diseases.

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