Extended Abstract

Journal of Molecular Microbiology

2020

Vol.4 No.2

Immune reconstitution inflammatory syndrome associated with HIV and cryptococcosis

Irina St.Louis
University of Minnesota, USA

Introduction & Aim

Paradoxical Cryptococcosis- associated immune reconstitution inflammatory syndrome (C-IRIS) occurs in 20% of HIV-infected patients with Cryptococcal Meningitis (CM) after they commence Antiretro Viral Therapy (ART). The pathogenesis of C-IRIS remains poorly understood, with few biomarkers to predict C-IRIS or to establish an early diagnosis. We investigated periferal blood transcriptomic profiles of ART-naive, advanced stage HIV-infected subjects with confirmed cryptococcal meningitis, in two recently completed clinical trials: Immune Restoration Disorders (IRD) and Cryptococcal Optimal ART Timing (COAT). The aims of presented research are to (1) Identify a dysregulation in gene expression underlying C-IRIS (2) Identify novel diagnostic or predictive transcriptomic biomarkers associated with the development of C-IRIS or death due to C-IRIS.

Method:

C-IRIS subjects were compared with controls, matched by age, gender, baseline HIV viral load and CD4+ T-cell counts. Subjects were were assigned into 4 groups (1) No C-IRIS or death (controls, appropriate immune restoration) (2) C-IRIS survivors (3) C-IRIS death and (4) Death but no C-IRIS (other causes). Gene expression was analized longitudinally, by whole genome microarrays or next generation sequencing, over 12 weeks on ART (at 0 (baseline), 2, 4, 8, 12 weeks after ART initiation).

Results:

The predictor screening algorithms identified the low expression of interferon-driven anti-viral defense pathway components such as interferon-inducible genes and higher expression of transcripts that encode for granulocyte-dependent pro-inflammatory response molecules as predictive biomarkers of subsequent C-IRIS at baseline. Subjects who developed early C-IRIS (occurred within 12 weeks of ART initiation) were characterized by upregulation of biomarker transcripts involved in innate immunity such as the inflammasome pathway while those with late C-IRIS events (occurs after 12 weeks of ART) were characterized by abnormal upregulation of transcripts expressed in T, B and NK cells, such as IFNG, C1QC, IL27 and others. The AIM2, HLA-DQA2 and BEX1 were identified as novel biomarkers for both early and late C-IRIS events. Majority of biomarker transcripts involved in innate immunity (inflammasome and toll-like receptor signaling), were upregulated to even higher levels in the C-IRIS death group. In addition, the upregulation of transcripts encoding components of IL6, B-cell signaling and Fc-gamma receptor-mediated phagocytosis were associated with death in those with C-IRIS. Patients from the death but no C-IRIS group showed significant activation of NFkB and death receptor pathways at baseline and strong signature of neutrophil activation/degranulation at 2 weeks on ART

Conclusion

Low levels of transcripts encoding components of interferon-driven antiviral immune responses prior to ART was predictive of the development of C-IRIS. Fatal C-IRIS events exhibited exaggerated inflammation, represented by upregulation of transcripts encoding components of both adaptive (B-cell) and innate immunity. Although each type of C-IRIS events have seemingly similar clinical manifestations, they have different molecular phenotypes and are driven by contrasting inflammatory signaling cascades. These results provides insight into the pathogenesis of C-IRIS that could be applied to developing diagnostic tests or targeted immunomodulatory treatments.

Biography:

Irina St. Louis has completed her MD and PhD degrees from Ural State Medical Academy, Russia. She has completed her Residency in Laboratory Pathology from Russian Medical Academy for Postgraduate Education, Moscow. She has joined the Department of Microbiology, at University of Minnesota, as a Postdoctoral trainee, followed by Fellowships at the University of Minnesota Super computing Institute and Lymphoma Research Foundation. She has worked as an Assistant Professor at the Department of Medicine. Her current clinical project focuses on the identification of molecular biomarkers for immune restoration diseases. She is engaged in many clinical studies, within the Global Health and International Medicine Program. These studies involve the stratification of AIDS patients, for optimal therapies and examining the immuno pathogenesis of immune restoration disorders, with an emphasis on defining the activation, maturation and regulation of the immune cell subsets involved.

This work is previously presented on 12th World Congress on Virology and Infectious Diseases
March 13-14, 2019 Singapore

The studies also include searches for biomarkers of Immune Reconstitution Inflammatory Syndrome (IRIS).

This work is previously presented on 12th World Congress on Virology and Infectious Diseases
March 13-14, 2019 Singapore