**Inflammomas and Th17 Activation in HIV+ Immunological Non-Responders**

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Abstract

**Background:** Inflammomas are multimeric protein platforms involved in the regulation of inflammatory responses. Inflammomas activity results in the production of proinflammatory cytokines and in Th17 activity (Mills K.H.G. et al., 2013; Peelen E. et al, Molecular Immunology 2015). Its role in immune reconstitution in HIV+ patients is nevertheless unclear. We analyzed possible associations between inflammasomes and Th17 activation and the degree of immune reconstitution in HIV+ patients.

**Methods:** Cross-sectional, single-study enrolling HIV-infected patients on antiretroviral therapy for ≥24 months and plasma HIV-RNA≤ 50,000 copies/ml, ≥12 months. Exclusion criteria: presence of actual opportunistic AIDS-related diseases, HIV or HCV coinfection, chronic inflammatory disorders, ongoing immunosuppressive therapy. Patients were classified as immunological responders (IR) or non-responders (INR) if CD4 count was ≥500 or <350 cells/µL, respectively. Immune markers (HLA-DR, CD3+, CD4+ T cells) in IR and INR individuals. Fold change mean values and SEM are shown. *p<0.05, **p<0.01. IFN-γ, IL-18, TNF-α and its receptor IL-1R1 are important for the early differentiation of Th17 responses, can amplify Th17 responses in presence of IL-23. (Choi et al. 2007; Kirk et al. 2007; Triant et al. 2007; Engels et al. 2008; Joshi et al. 2011)

**Results:**

- In INR compared to IR individuals:
  - CD4 and CD8 cells are more activated, the percentage of Th17 was significantly increased.
  - Immune recovery was independently associated with lower Th17 levels after adjustment for age and past AIDS.

**Materials and Methods**

- **Study Population and Inclusion Criteria:** 60 patients with HIV infection attending the HIV clinics of the San Gerardo Hospital (Monza, Italy). 22 were Immunological responders (IR) with lymphocyte T CD4+ count >500 cells/µL and 17 were immunological non responders (INR) patients with lymphocyte T CD4+ count <350. The inclusion criteria were: men and women ≥18 of age, HIV positivity tested with ELISA and confirmed by Western Blot, combined antiretroviral therapy, duration of ART ≥24 months, plasma HIV-RNA ≤50,000 copies/ml, for at least 12 months.

- **Analyses performed:**
  - T-cell activation markers: CD4, CD8, HLA-DR, CD38 (Flow Cytometry)
  - Evaluation of Th17 T cells CD4+/IL17+/RORγT+ cells upon stimulation with LPS (1 µg/mL) or HIV-1 HIV-1, Bal, adh/+/2 (AT2) treated virions (300 nM/mL) (Flow Cytometry)
  - Inflammomas pathway in LPS-stimulated PBMCs using a Real-Time PCR array including a set of 84 optimized primers on 96-wells plate (Real-Time PCR)
  - Real-Time PCR to evaluate the gene expression of proinflammatory cytokines

**Conclusions**

Higher levels of inflammasome activation, an increased percentage of Th17 and immune activation characterize the immune scenario of ART-treated INR patients; these alterations may contribute to the lack of CD4 recovery observed in INR.