Antibodies to the HIV-1 Tat protein correlated with nonprogression to AIDS: a rationale for the use of Tat toxoid as an HIV-1 vaccine.


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OBJECTIVES: To investigate which immune parameters, such as antibodies against HIV-1 specificities, or viral parameters, such as p24 antigenemia, are predictive of disease progression. STUDY DESIGN: We performed studies on serum collected from individuals exhibiting two extremes of disease evolution--67 fast progressors (FP) and 182 nonprogressors (NP)--at their enrollment. After a 1- to 2-year clinical follow-up of 104 nonprogressors after their enrollment, we could determine the best serologic predictors for disease progression. METHODS: We investigated levels of antibodies to tetanus toxoid and to HIV antigens including Env, Gag, Nef, and Tat proteins, as well as p24 antigenemia, viremia, CD4 cell count, and interferon-alpha (IFN-alpha) titers in FPs and NPs, and we correlated these data with clinical and biologic signs of progression. RESULTS: p24 Antigenemia, a marker of viral replication, and anti-Tat antibodies were highly and inversely correlated in both groups (P < .001). Furthermore, anti-p24 antibodies and low serum IFN-alpha levels were correlated to the NP versus the FP cohort. Finally, among NPs, only antibodies to Tat and not to the other HIV specificities (Env, Nef, Gag) were significantly predictive of clinical stability during their follow-up. CONCLUSION: Antibodies toward HIV-1 Tat, which are inversely correlated to p24 antigenemia, appear as a critical marker for a lack of disease progression. This study strongly suggests that rising anti-Tat antibodies through active immunization may be beneficial in AIDS vaccine development to control viral replication.