Retrovirology

Poster presentation

A HIV-1 Stimulating Host Factor Induced by HIV-1 Tat Protein

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The HIV-1 Tat gene is required for virus replication and disease. Tat was reported to be released from infected cells. Recombinant soluble Tat may be taken up by many cell types and transported to the nucleus as an active transcription factor leading to upregulation of viral replication in bystander cells. However, numerous attempts to use Tat protein or Tat expressing constructs for protective immunization in non human primate model produced controversial results, leading us to ask whether the effects of Tat might be indirect and result from increased expression of secondary mediators like cytokines or growth factors. Immunization with Tat protein produces antibodies to a limited number of linear epitopes in animals and human beings, mainly located in the N-terminus of the molecule. We generated a unique prototypic monoclonal antibody TR1 that recognizes an epitope in the N-terminus of HIV-1 Tat and inhibits Tat uptake by reporter cells. This antibody strongly neutralizes recombinant Tat protein in a cellular assay for the induction of a latent Tat deficient HIV-1 provirus. Expression of Tat protein in different cell types leads to the accumulation of a "transactivation activity" in culture medium. However, 1) this activity cannot be inhibited by Tat-neutralizing antibody TR1;

2) Tat protein is detected in the supernatants only in low nanomolar concentrations; 3) Similar amounts of exogenous recombinant Tat protein are not sufficient to induce detectable transactivation of in our assay system. This activity is also distinct from proinflammatory cytokines like TNF-a, IL-1b or IL-6. We hypothesize that positive effect of Tat on viral replication in bystander cells *in vitro* and possibly *in vivo* may be indirect and mediated by an unknown secondary cytokine(s) or growth factor(s) released from Tat expressing cells.