

## Characterization of the antigenicity and immunogenicity of HIV Tat, a viral toxin

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HIV-1 Tat protein is released by infected cells and can affect bystander uninfected T cells and induce numerous biological responses which contribute to its pathogenesis. Our metabonomics study revealed that HIV-1 Tat causes significant and comprehensive metabolic changes, as represented by significant changes of 37 metabolites and 10 relevant enzymes in HIV-1 Tat treated cells, providing metabolic evidence of the complex pathogenic mechanism of HIV-1 Tat protein as a viral toxin. The anti-Tat antibody responses of Chinese individuals infected with HIV-1 demonstrated two types of anti-Tat responses: the major complete response and the alternative C-prone response, and revealed the low antigenicity of Tat protein and the antigenicity differences of between N region and C region of Tat protein. Our immunization results showed that the Tat N region inhibits the production of antibody against C region, and in contrast, Tat C region is necessary for the antibody production to N region. These immunization results revealed the interactions between Tat N region and C region could regulate the antigenicity and immunogenicity of HIV Tat, and contribute to the evasion of host's anti-Tat response. The data here could contribute to a better understanding of the significance of anti-Tat responses in preventing HIV pathogenesis, obligate Tat protein as "an important target" for therapeutic intervention and vaccine development, and could be useful for designing more effective vaccines in the future.

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