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Tat is a naturally folded protein in blood

Erwann Loret

Equipe de Recherche Technologique 2011,
Faculté de Pharmacie, France

Tat is a regulatory viral protein known as transactivator of HIV-1 genes but Tat is also secreted in the blood from HIV-1 infected cells. Extra cellular Tat can cross cellular membranes to trigger apoptosis and might explain the incapacity of the cellular immunity to eliminate HIV-1 infected cells. There is a controversy regarding Tat structure with studies suggesting that Tat would be a naturally unfolded protein. Here, we show that synthetic Tat variants need to be folded to have a transactivation activity in a cellular assay but this folding is unstable regarding the buffers and/or pH used as solvent. We show also that the recognition of a Tat variant versus peptides, covering its sequence, was different. Using an indirect ELISA method with 40 HIV-1 infected patients sera in ELISA test, we show that Tat was recognized by 19 human sera either exclusively (n=8) or with Tat peptides (n=11). Dot Blot showed that unfolded Tat was no longer detectable by sera of the first group (n=8) compared to folded Tat. As a conclusion, this study suggests that Tat could be a naturally folded protein in the blood of HIV infected patients. Conformational epitopes might be the best targets for a vaccine against Tat.